



## A REVIEW ON WORLD'S POTENTIAL ANTI-MALARIAL PLANTS AND THEIR PHYTOCHEMICALS

<sup>1\*</sup>Shalini Rawat and <sup>2</sup>Seema Baniwal

<sup>1</sup>Department of Botany, Pt. L. M. S. Campus Rishikesh, SDSUV, Uttarakhand, India.

Corresponding author: 941157584, [rawatshalini18041975@gmail.com](mailto:rawatshalini18041975@gmail.com)

<sup>2</sup>Department of Chemistry, Pt. L. M. S. Campus Rishikesh, SDSUV, Uttarakhand

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### ABSTRACT

Malaria is one of the life-threatening parasitic diseases, endemic in tropical areas. The increased prevalence of malaria due to drug resistance leads to a high incidence of mortality. Drug discovery based on natural products and secondary metabolites is considered as alternative approaches for anti-malarial therapy. Herbal medicines have advantages over modern medicines, as less side effects, cost-effectiveness, and affordability encouraging the herbal-based drug discovery. This review covers thirteen important genera including *Artemisia*, *Cinchona*, etc., which are being used by the local inhabitants of the world as anti-malarial drug which is quite effective. It is advisable to make people aware of the significance and protection of such medicinal plants. Moreover, the active principle from these plant should be extracted and further investigated. to find new anti-malarial drug.

**Keywords:** Medicinal plants, Malaria, Anti-malarial drug, secondary metabolites-alkaloides.

### INTRODUCTION

Human malaria is caused by single celled microorganisms of the *Plasmodium* group. It is spread exclusively through bites of infected *Anopheles* mosquitoes. The mosquito bite introduces the parasites from the mosquito's saliva into a person's blood. The parasites travel to the liver where they mature and reproduce. Once the parasites are inside your body, they travel to the liver, where they mature. After several days, the mature parasites enter the bloodstream and begin to infect red blood cells. Within 48 to 72 hours, the parasites inside the red blood cells multiply, causing the infected cells to burst open. The parasites continue to infect red blood cells, resulting in symptoms that occur in cycles that last two to three days at a time. Five species of plasmodium can infect and be spread by humans. Most deaths are caused by *P. falciparum*, whereas *P. vivax*, *P. ovale*, and *P. malariae* generally cause a milder form of malaria.

Malaria mosquito borne disease that affects humans and other vertebrates. Human malaria causes symptoms that typically include fever, fatigue, vomiting, and headache. In severe cases, it can cause jaundice, seizures, coma, or death. The emergence and rapid spread of multidrug-resistant strains of *Plasmodium*, particularly *Plasmodium falciparum* represent a major problem for prophylaxis and treatment, which becomes more difficult and limits the choice of drugs used.

This has been identified as the current primary cause of control failure. The well-known use of chloroquine (CQ) and antifolates [sulfadoxine-pyrimethamine (S/P)] for malaria treatment are no longer effective in most endemic areas.

### Utility of medicinal plants against malarial treatment

Medicinal plants which constitute a segment of the flora provide raw material for use in all the indigenous systems of medicine in India namely Ayurveda, Unani, Siddha and Tibetan Medicine. According to the World Health Organization (WHO), 80% of the population in developing countries relies on traditional medicine, mostly in the form of plant drugs for their health care needs. Additionally, modern medicines contain plant derivatives to the extent of about 25%. There are estimated to be around 25000 effective plant based formulations available in Indian medicine (Shankar Rama 2013)

In the last decade, there has been a renewed interest in indigenous medicine worldwide, arising from the realization that orthodox medicine is not widespread. In poor countries, the healthcare is often sustained by other practices based on cultural alternatives. In many developing countries, one-fifth of patients use indigenous herbal remedies to treat malaria (Willcox and Bodeker 2004). Although modern medicine may be available in some communities, herbal medicines have often maintained popularity for historical and cultural reasons, in addition to their cheaper costs. The use of plant

remedies has steadily increased worldwide in recent years, as well as the search for new phytochemicals that potentially could be developed as useful drugs for the treatment of malaria and other infectious diseases (Willcox 1999). 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. 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 (Okello et al. 2019).

Quinine kills the malaria parasite by causing the food vacuole to swell thus increasing the granularity of the cell and lastly results in developed from natural products so as to overcome the barrier of drug resistance. The Chinese herbalists made use of artemisinin which was the active compound found in *Artemisia annua*, to cure fever. The decoction of leaves of this plant was found to be effective and was used as an antipyretic agent in 340 A.D. The hallmark of malaria is periodic chills which occur mainly during the synchronous asexual development and rupturing of erythrocytes by the parasite. (Noronha et al. 2020). The development of new anti-malarials from the highly active natural products, which have already been discovered, is crucial in order to overcome the increasing resistance of *Plasmodium* to available anti-malarial drugs. The study of medicinal plants for malaria not only advances our knowledge of world's flora but also provides new opportunities for the development of pharmaceutical and herbal remedies. These medicinal herbs have the potential to

advance medical research and development as the globe struggles to find sustainable and natural healthcare solutions.

The use of traditional medicine practices varies among countries, depending on the availability of "modern" medical facilities, cost of health care, and trust in the medical system for example, a shortage of medical facilities and allopathic practitioners in developing countries, such as Rwanda, India, and Ethiopia, results in traditional medicine practices being used by 60 to 70% of the population.

Following is the current status of the antimalarial drugs and their resistance.

Ensuring the safety, quality and effectiveness of medicinal plants and herbal drugs very recently became a key issue in industrialized and developing countries. By standardizing and evaluating the health of active plant-derived compounds, herbal drugs can help the emergence of a new era of the healthcare system to treat human diseases in the future. Awareness of traditional knowledge and medicinal plants can play a key role in the exploitation and discovery of natural plant resources. In order to maintain this knowledge, comprehensive approach and collaboration are needed to maintain historical records on medicinal plants and use these resources in favour of human beings, before they are destroyed forever.

## MATERIALS AND METHODS

Present review on Anti-malarial plants was to create as compilation of plant species that had been investigated as anti-malarial drug The information was compiled with the help of many official journals, publication, research papers written by various authors and obtained from Pubmed, Science direct, Research Gate, Google scholar Science Hub and other sources .

### Description of the plants

Thousands of plants have been reported from searched which are used against Malaria. But in this review the detailed description of only 13 plants is given. Table-2 comprises the Listed plants of the present study from them new hope of antimalarial drug which herbal medicine can be made for of malaria treatment.

#### 1. *Alstonia boone*

The plant parts have been traditionally used for its anti-malarial, aphrodisiac, anti-diabetic, antimicrobial, and antipyretic activities, which have also been proved scientifically. The plant parts are rich in various bioactive compounds such as echitamidine, N $\alpha$ -formylechitamidine, boonein, loganin, lupeol, ursolic acid, and  $\beta$ -amyryn among which the alkaloids and triterpenoids form a major portion.

#### 2. *Annona squamosa*

It is a small, well-branched tree or shrub from the family Annonaceae that bears edible fruits called sugar-apples or *sweetsops*. The use of a decoction of the leaves of *A. squamosa* to tackle malaria. The methanolic extract of leaves and a stem bark have been shown to possess antiplasmodial activity. leaves are antimicrobial, anti-inflammatory, antiulcer, antidiabetic, antidiarrheals, antiplatelet, antioxidant, and hepatoprotective, neuroprotective, and cytoprotective. Phytochemicals present in leaves include coumarins, tannins, cardiac glycosides, flavonoids, carbohydrates and saponins.

#### 3. *Artemisia annua*

Also known as sweet wormwood, sweet annie, sweet sagewort, annual mugwort or annual wormwood. It is native to



temperate Asia but naturalized in many countries including scattered parts of North America. Artemisinin is a sesquiterpene lactone with an endoperoxide bridge and has been produced as an anti-malarial drug. It is not soluble in water and the concentrations in these infusions are considered insufficient to treat malaria. Artemisinin-based remedies are the most effective drugs for the treatment of malaria. Several derivatives of the original compound have proved effective in the treatment of *Plasmodium falciparum* malaria.

#### 4. *Azadirachta indica*:

It is commonly known as margosa, Neem tree or Indian lilac is a tree in the mahogany family Meliaceae. It is native to the northeast of the Indian Subcontinent and to Indo-china, but is naturalized and grown around the world in tropical and subtropical area. It has been used in the traditional treatment of malaria for centuries. Components are effective against malaria parasites and toxic for resistant strains of malaria. These compounds are at least as effective against malaria as quinine and chloroquine. Drinking neem teas or chewing a couple of leaves every day reduces the possibility of contracting malaria. It is speculated that neem is even more effective against malaria in the body than in the laboratory because it is thought to stimulate the immune system. It also lowers the fever and increases the appetite, thus speeding recovery.

#### 5. *Cinchona officinalis*

*Cinchona* is a genus of flowering plants in the family Rubiaceae containing at least 23 species of trees and shrubs. All are native to the tropical Andean forest of western South America. A few species are reportedly naturalized in Central America, Jamaica, French Polynesia, Saint Helena in the South Atlantic. The bark of the *Cinchona* tree contains a number of medicinal compounds, including quinine and quinidine. Quinidine is used in pharmaceuticals as an anti-arrhythmic agent, suppressing abnormal rhythms of the heart and regulating the heartbeat. Though it is frequently found in anti-malarial drugs. *Cinchona* is used for increasing appetite, promoting the release of digestive juices; and treating bloating, fullness, and other stomach problems. It is also used for blood vessel disorders including hemorrhoids, varicose veins, and leg cramps. Some people use cinchona for mild attacks of influenza, swine flu, the common cold, malaria, and fever. Other uses are for cancer, mouth and throat diseases, enlarged spleen, and muscle cramps.

#### 6. *Coptis teeta*

*Coptis teeta*, a small perennial herb popularly known as coptis or mishmi Titab and Mamira belonging to family Ranunculaceae. It is a perennial stemless herb with horizontal

rootstocks and densely fibrous with yellowish brown externally and golden-yellow internally and very bitter in taste. It is a medicinal herb used for anti-inflammatory, mucolytic and anti-malarial actions. It is beneficial in malaria, in cough, cold and also in back ache, stomachache, cuts, wound, dysentery, cholera, diarrhoea, eye complaints, malarial fever, etc. It is also used as general bitter tonic. It regulates blood pressure and also helpful in anti-tumour and antibacterial activities. The rhizomes of *Coptis teeta* are pungent and bitter, cooling herb that contains several chemical compounds that are effective for inhibiting various microbes and also used to cure many ailments being safe and effective. The root contains 6–8.5% of berberine, which is the main active ingredient of the plant. It also contains various alkaloids like coptisine or coptina, Palmatine, Jateorrhizine, Epiberberine and Columbamine.

#### 7. *Curcuma longa* *Curcuma longa* is flowering plant of the ginger family Zingiberaceae.

It is perennial, rhizomatous, herbaceous plant native to the Indian subcontinent and southeast Asia that requires temperatures between 20 and 30 °C and high annual rainfall to thrive. Plants are gathered each year for their rhizome, some for propagation in the following season and some for consumption the treatment and management are instructed to soak the plant leave in hot water. They should then drink half a glass (about 0.25l). Curcumin or diferuloylmethane (from the roots) is a major curcuminoid and part of the Zingiberaceae family. It is an important phenol derivative that is known to have anti-inflammatory, anti-carcinogenic, antioxidant, antiapoptotic and angiogenesis modulation effects. Additionally, curcumin has antimalarial effects against various types of *Plasmodium* species through various mechanisms. Neem oil has been found to be an effective mosquito repellent. It has more than 100 bio-active ingredients and is rich in proteins. Its bio-active ingredients are anti-malarial, anti-inflammatory, anti-pyretic, anti-bacterial, insect-repellent.

#### 8. *Cymbopogon citratus*

*Cymbopogon citratus* belongs to family Poaceae commonly known as West Indian lemon grass or simply lemongrass. It is a tropical plant native to Maritime Southeast Asia and introduced to many tropical regions. They contain simple, bluish-green leaves with entire margins and are linear in shape. The leaf blades tend to be 18–36 inches long. Like other grasses, the leaves also have parallel venation. The essential oils of *Cymbopogon citratus* found to be 86.6% suppress in the growth of *plasmodium berghei* when compared with the popularly used drug chloroquine. It is a good source of vitamin A, C, folate, folic acid, magnesium, zinc, copper, iron, potassium. The antibacterial properties of lemongrass oil are useful in treating various infection of the upper respiratory tract, lungs and stomach. Its oil is active against fungal infection of the skin.



**Table 1. Anti-malarial drugs and their present Status of Resistance (Adapted from Noronha et al. 2020)**

| Drug                      | Introduced in the year | “First” year resistance reported | References                          |
|---------------------------|------------------------|----------------------------------|-------------------------------------|
| Quinine                   | 1632                   | 1910                             | Wongsrichanalai et al. (2002)       |
| Chloroquine               | 1945                   | 1957                             | Wongsrichanalai et al. (2002)       |
| Proguanil                 | 1948                   | 1949                             | Wongsrichanalai et al. (2002)       |
| Sulfadoxine-pyrimethamine | 1967                   | 1967                             | Wongsrichanalai et al. (2002)       |
| Mefloquine                | 1977                   | 1982                             | Wongsrichanalai et al. (2002)       |
| Atovaquone                | 1996                   | 1996                             | Carter et al. (2015)                |
| Artemisinin               | 1971                   | 1998                             | WHO (2014), Fairhurst et al. (2012) |

**Table 2: General details of the reviewed anti-malarial plants and its alkaloid composition**

| S.N. | Name of Plant               | Family        | Part Used       | Alkaloids Reported                               |
|------|-----------------------------|---------------|-----------------|--|
| 1    | <i>Alstania Boonei</i>      | Apocynaceae   | Bark and Leaves | Echitamidine, boonie, logania                    |
| 2    | <i>Annana Squamesa</i>      | Annoaceae     | Leaves          | Aporphine ,oxaperphine, proaperphine             |
| 3    | <i>Artemisia annua</i>      | Asteraceae    | Leaves          | Sesquiterpene,, endoperoxide, Lycoctonine        |
| 4    | <i>Azadirachta indica</i>   | Meliaceae     | Bark and Leaves | Azadirachtin, nimbin and nimbidine               |
| 5    | <i>Cinchona officinalis</i> | Rubiaceae     | Bark            | Quinine  |
| 6    | <i>Coptis teeta</i>         | Ranunculaceae | Bark and Root   | Berberine, palmatine, captisine                  |
| 7    | <i>Curcuma longa</i>        | Zingiberaceae | Root            | Curcumin, Gingerols, Curumineids                 |
| 8    | <i>Cymbopogon citratus</i>  | Poaceae       | Leaves          | Cymbopogenal, Cymbopogene                        |
| 9    | <i>Dacryodes edulis</i>     | Burseraceae   | Leaves and Bark | Ethyle gallate                                   |
| 10   | <i>Persea americana</i>     | Lauraceae     | Leaves and Bark | 4- acetoxy,1-2 dihydroxy heptodec-16ne, saponine |
| 11   | <i>Quassia amara</i>        | Simaroubaceae | Leaves and Bark | 2-methoxy- canthin-6, B-carbenite indele         |
| 12   | <i>Vernonia amygdalina</i>  | Asteraceae    | Leaves          | Lactucopicrin, mitraphylin, lactucin             |
| 13   | <i>Vitax penducularis</i>   | Laminaceae    | Bark and Leaves | Crisimaritin, Nitcetine, Lutealin                |

### 9.0 *Dacryodes edulis*

*Dacryodes edulis* is a fruit tree in the Burseraceae family native to Africa. It has various regional names safou, plum, African pear, bush pear, African plum, bush butter tree or butter fruit. Its fruit contain compounds which are responsible for the anti-

malarial activity. Their suitability leads for the treatment of drug resistant malaria. According to research, five compounds were isolated from ethyl acetate and hexane extracts of stem bark. The bark is pulped and then applied directly to the wound.

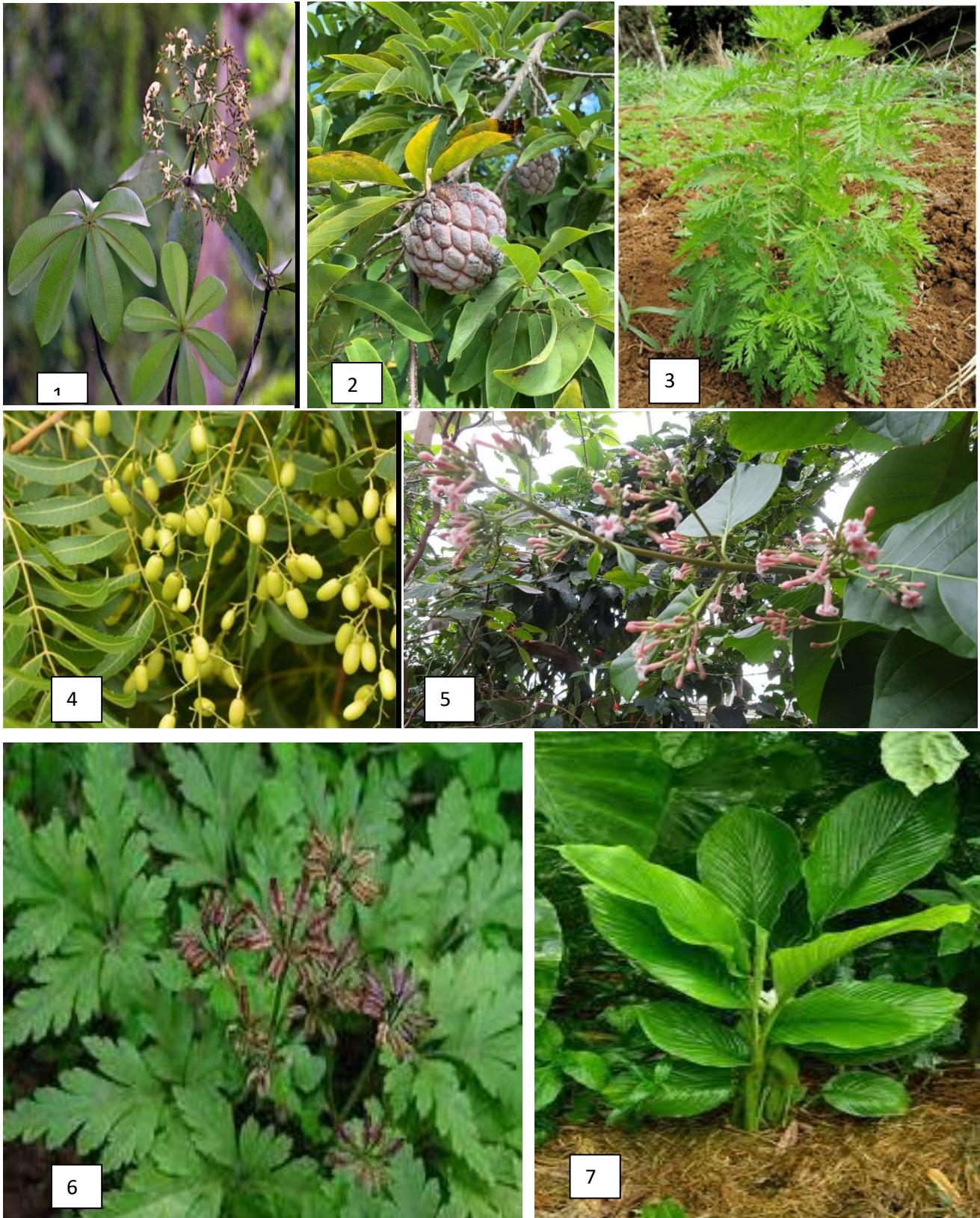


Plate-A 1. *Alstania boonei* 2. *Annana squamesa* 3. *Artemisia annua* 4. *Azadirachta indica*, 5. *Cinchona officinalis* 6. *Coptis teeta*, and 7. *Curcuma longa*

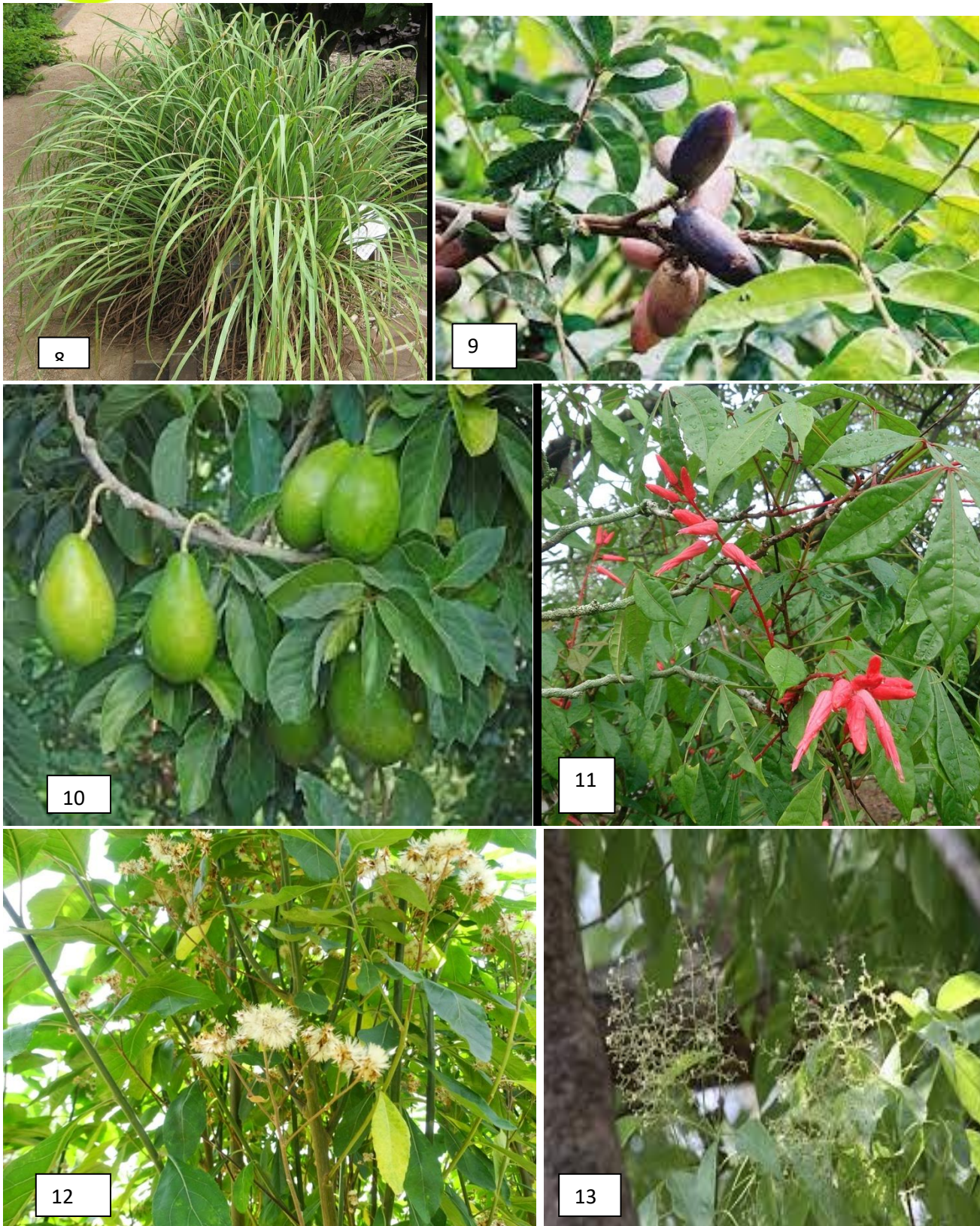


Plate B. 8. *Cymbopogon citrates* 9. *Dacryodes edalis*, 10. *Persea americana*, 11. *Quassia amara*, 12. *Vernonia amygdalina*, 13. *Vitax penducularis*.





It is also used in the treatment of leprosy, dysentery, anaemia, spitting blood, debility, stiffness, tonsillitis and skin diseases. The leaves are often crushed and the juice released to treat generalized skin diseases such as scabies, ringworm, rash and wound, while the stem or stem twigs are employed as chewing sticks for oral hygiene.

#### 10. *Vernonia amygdalina*

*Vernonia amygdalina* belong to family Asteraceae is a small shrub with dark green leaves and rough barks growing predominantly in tropical Africa. It is a bushy shrub or well-formed tree up to 7 m in height. Bark light grey or brown, rather rough and longitudinally flaking; branches brittle. It is consumed as vegetable and has high medicinal value. Smaller doses are prescribed for children according to their weight. This plant has ethno-medical use in treating venereal diseases, gastrointestinal problems and malaria. There are reports concerning the hypoglycaemic, antineoplastic antibacterial and antioxidant properties of the plant. In Africa infusion from the roots is given to children suffering from infection by a trematode (*Enterobius vermicularis*). A cold infusion of the root bark, together with other plants, is given in daily doses to treat bilharzia. The bark and root are taken as a tonic by people suffering from fevers; leaves are also pounded, the juice extracted and drunk for fever. The leaves are pounded and mixed with warm water for bathing to treat spots on the skin and nausea.

#### 11. *Persea americana*

*Persea Americana* is a medium-sized, evergreen tree in the laurel family Lauraceae, commonly known as Avocado It is native to the America and was first domesticated in Meso-america more than 5,000 years ago. Then as now it was prized for its large and unusually oily fruit. The seeds are used traditionally for the treatment of skin rashes, diarrhea, high blood pressure, dysentery, asthma and rheumatism. The plant is used in ethno-medicine for the treatment of malaria. It is rich in secondary metabolite compounds such as saponins, alkaloids, terpenoids, and flavonoids. It has antioxidant, anti-inflammatory, anti-lithiasis, anti-diabetic, antiprotozoal, antidiabetic and anticonvulsant properties. However, despite the reported use of the plant in ethno-medicines for malaria treatment. The leaves of the plant are traditionally used in the treatment of microbial infections, malaria, diabetes, high blood pressure, to stimulate uterine contractions and relief painful menstruations. The leaves and stem bark are also used to cure malaria and typhoid fever.

#### 12. *Quassia amara*

*Quassia amara*, also known as amargo, bitter-ash, bitter-wood. It is used as insecticide, in traditional medicine and as additive in the food industry. Tea made with the leaves of the *Q. amara*, is used against malaria the traditional medicine of French Guania. The leaves hexane from *Q. amara* was found to have high suppressive activity, at a concentration from 100 mg/kg body weight in mouse. In 2006, a study found that Simalikalactone D should be responsible for the antimalarial activity. In 2009, a new quassinoid was discovered, the simalikalactone E. This molecule inhibited the growth of falciperum *in vitro* by 50%. The effect was mostly found in the gametocyte, which is the stage that is fundamental for the transmission to mosquito. The tea from *Quassia amara* has also an effect on the red blood cells counts, the packed cell count, the packed cell volume and hemoglobin concentration. It has an anti-anemic property.

#### 13. *Vitex peduncularis*

*Vitex Peduncularis* is a moderate sized tree found belonging to family Lamiaceae. It is found in Southeast and South Asia, including in China, Cambodia, Bangladesh, India, Laos, Myanmar, Nepal, Thailand, and Vietnam. Traditionally, the boiled bark extract of *Vitex peduncularis* is used as a drink to treat the joint ache. It contains the compounds like peduncularaside, iridoid, anguside, vitexin, triterpenoids and flavonoids which act as anti-inflammatory properties. The plants are known to produce certain bioactive molecules which react with other organisms in the environment and in turn cause the inhibition of bacterial or fungal growth. It has been used over the past centuries as traditional medicine for treatment of malarial and black fevers. The bark is crushed and boiled. The steam vapor is inhaled by a patient suffering from malaria fever, infusion of leaves or of roots, bark or young stem bark is useful in malaria.

### RESULTS AND DISCUSSION

This review showed that the identified medicinal plants are potential source of new anti-malarial drugs. This provides a basis for investigating the anti-malarial efficiency and their phytochemistry. Studies have demonstrated that anti-malarial plants show promise for malaria treatment and prophylaxis It is crucial to protect these plant species. Threats that need urgent attention include habitat degradation, climate change, and overexploitation. To secure the survival of these important plant species, conservation measures must be priority. Further research is needed for the maximum utilization of their potential to serve mankind.

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