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**Wafaa M Hikal**

<sup>a)</sup> Department of Biology,  
Faculty of Science, University of  
Tabuk, P.O. Box 741, Tabuk,  
Saudi Arabia

<sup>b)</sup> Water Pollution Research  
Department, Environmental  
Research Division, National  
Research Centre, 33 El-Bohouth  
St., Dokki, Giza, Egypt

**Latifah SE Alhawiti**

Department of Biology, Faculty  
of Science, University of Tabuk,  
P.O. Box 741, Tabuk, Saudi  
Arabia

**Abeer A Mahmoud**

Botany Department (Plant  
Physiology Section), Faculty of  
Agriculture, Cairo University,  
Gammaa St, Giza, Egypt

**Kirill G Tkachenko**

V.L. Komarov Botanical  
Institute of the Russian  
Academy of Sciences, 2 Prof.  
Popova St., Saint Petersburg,  
Russia

**Hussein AH Said-Al Ahl**

Medicinal and Aromatic Plants  
Research Department, National  
Research Centre, 33 El-Bohouth  
St., Dokki, Giza, Egypt

**Corresponding Author:****Hussein AH Said-Al Ahl**

Medicinal and Aromatic Plants  
Research Department, National  
Research Centre, 33 El-Bohouth  
St., Dokki, Giza, Egypt

# *Cissampelos pareira*: A potential source of medicine to treat malaria

**Wafaa M Hikal, Latifah SE Alhawiti, Abeer A Mahmoud, Kirill G Tkachenko and Hussein AH Said-Al Ahl**

**Abstract**

*Cissampelos pareira*, velvetleaf of the Menispermaceae family is important in folk medicine of tropical and sub-tropical regions since ancient times. This makes it a promising multi-purpose plant for use as therapy for the treatment of various diseases including malaria. Treatment with medicinal plants and the use of their biologically active products, especially as anti-malaria, has become a very important and urgent matter due to the need for new anti-parasite drugs, as a result of the emergence of some strains of parasites resistant to chemotherapy. The present review highlights the importance of *Cissampelos pareira* as an antimalaria agent and the possibility of using *Cissampelos pareira* as the most valuable and promising plant in the pharmaceutical industry to treat malaria.

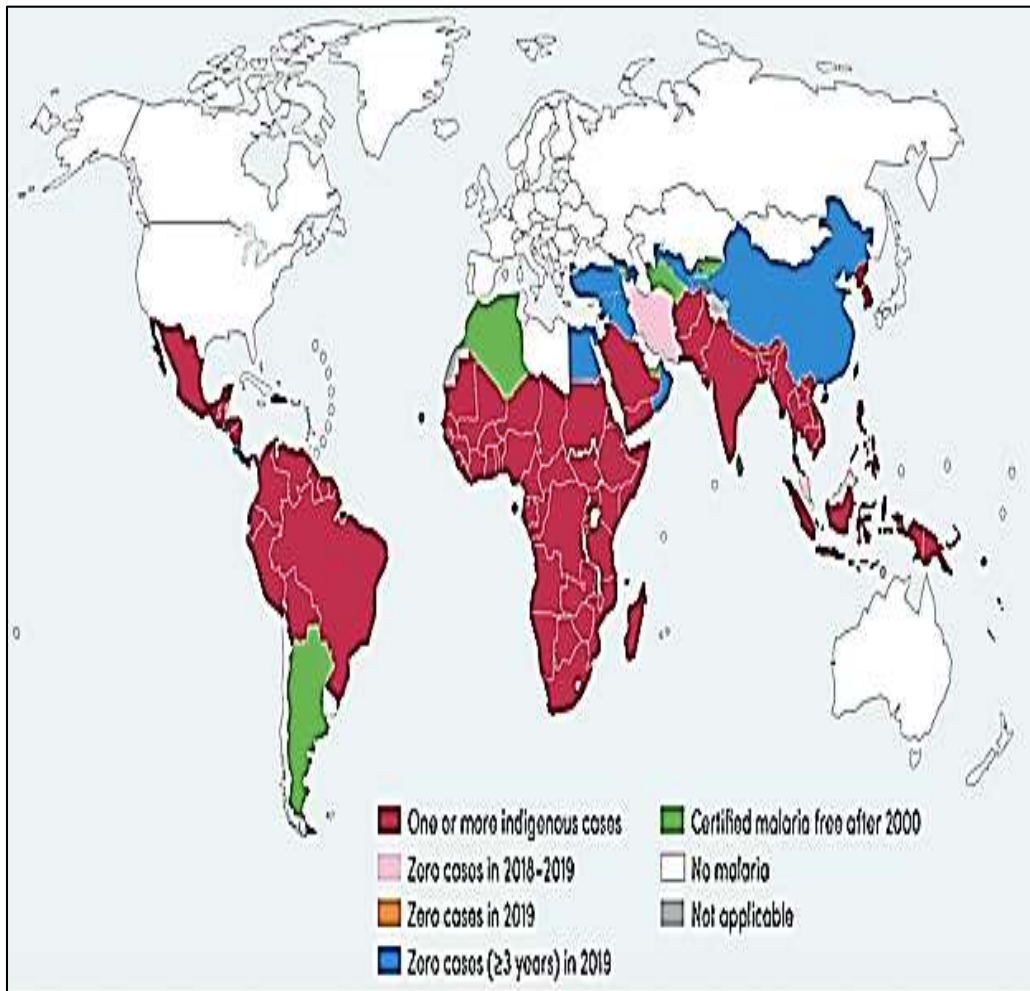
**Keywords:** *Cissampelos pareira*, Antiplasmodial compounds, mosquitoes, Phytotherapy

**Introduction**

Medicinal plants have ingredients that can treat a disease or can be used to manufacture useful drugs. Herbal medicines are an important part of culture and traditions all over the world. For centuries people have used their knowledge about the environment to treat various ailments. For example, the Chinese herbalists have used extracts of the Qinghao plant; *Artemisia annua* also known as sweet wormwood for malaria treatment for over 1,500 years. Most communities heavily rely on medicinal plants to prevent and treat diseases. About 80% of people in Africa depend on traditional medicine. Traditional healers prescribe medicinal plants to treat various illnesses. These plants are an accessible and affordable form of treatment for communities across the continent [1-5].

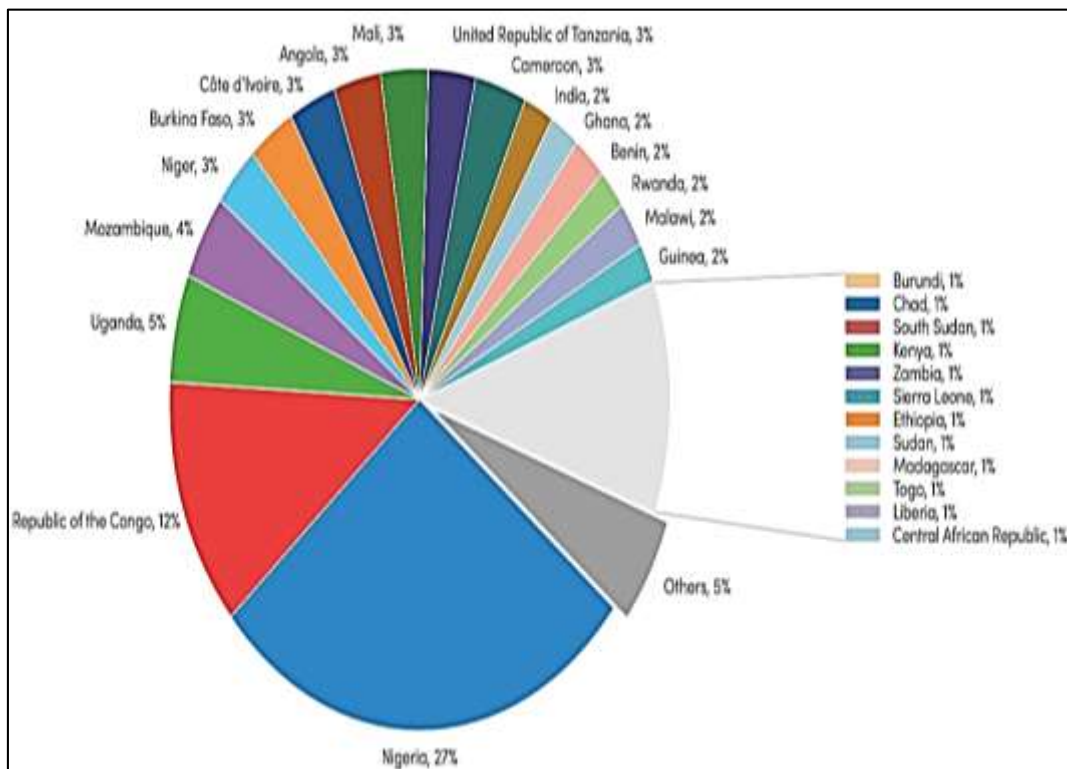
Malaria is a life-threatening disease and still considered as a major global health problem, but it is preventable and treatable. Malaria is a major public health problem in some countries especially in Africa, according to the latest World malaria report, released on 30 November 2020, there were 229 million cases of malaria in 2019 compared to 228 million cases in 2018. The estimated number of malaria deaths stood at 409 000 in 2019, compared with 411 000 deaths in 2018. The WHO African Region continues to carry a disproportionately high share of the global malaria burden. In 2019, the region was home to 94% of all malaria cases and deaths. In 2019, 6 countries accounted for approximately half of all malaria deaths worldwide: Nigeria (23%), the Democratic Republic of the Congo (11%), United Republic of Tanzania (5%), Burkina Faso (4%), Mozambique (4%) and Niger (4% each). Children under 5 years of age are the most vulnerable group affected by malaria; in 2019 they accounted for 67% (274 000) of all malaria deaths worldwide [1]. As shown in Figures 1 and 2 [1].

Malaria is caused by *Plasmodium* parasites. The parasites are spread to people through the bites of infected female Anopheles mosquitoes, called "malaria vectors." There are 5 parasite species that cause malaria in humans, and 2 of these species – *P. falciparum* and *P. vivax* – pose the greatest threat. In 2018, *P. falciparum* accounted for 99.7% of estimated malaria cases in the WHO African Region 50% of cases in the WHO South-East Asia Region, 71% of cases in the Eastern Mediterranean and 65% in the Western Pacific. *P. vivax* is the predominant parasite in the WHO Region of the Americas, representing 75% of malaria cases. 49 However, figure 3 shows epidemiological trends of Malaria in India (2000-2019) Pv; *Plasmodium Vivax* & pf; *Plasmodium falciparum* [1, 2, 6].



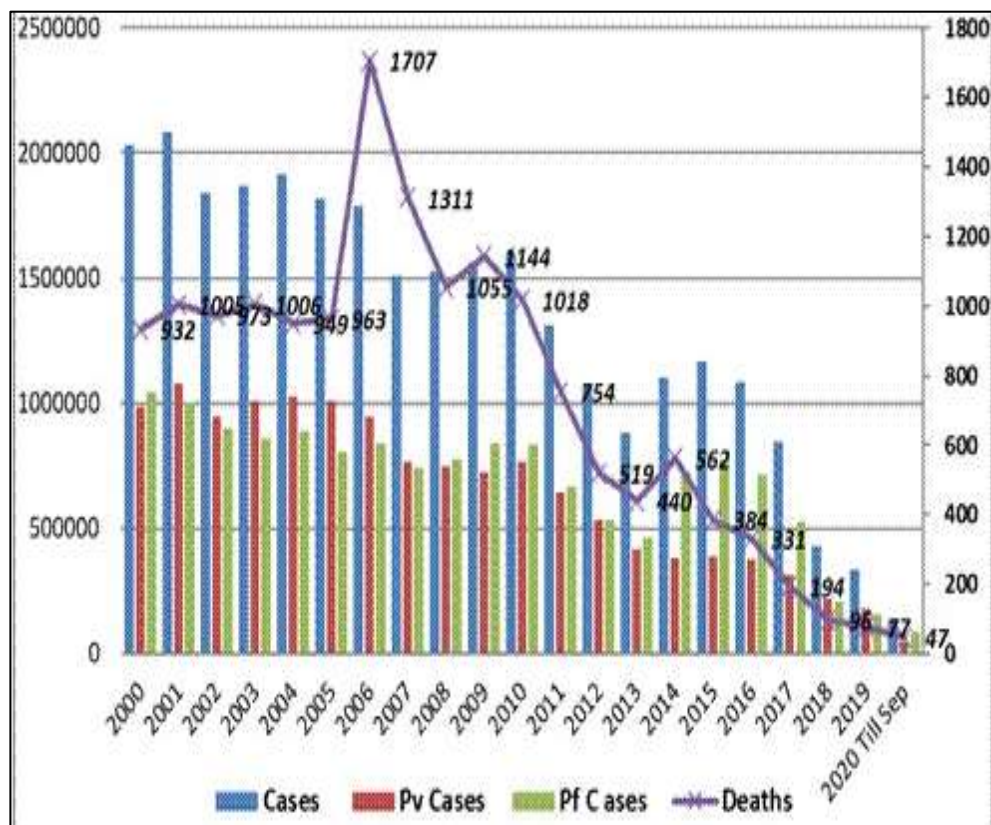
Source: WHO database

Fig 1: Countries with indigenous cases in 2000 and their status by 2019



Source: WHO database

Fig 2: Distribution of malaria cases



Source: WHO database

**Fig 3:** Epidemiological trends of Malaria in India (2000-2019) Pv; *Plasmodium Vivax* & pf; *Plasmodium Falciparum*

Drug resistance has led to most of the malaria drugs in the market becoming ineffective in treating the disease. There is therefore an urgent and continuous call to search for new antimalarial agents. Most of the drugs used to treat malaria are either derived from plants or are products of natural sources. For example, quinine, an antimalarial, comes from the medicinal plant *Cinchona succirubra*. Artemisinin is derived from *Artemisia annua*, another medicinal plant. These previous successes underscore the importance of medicinal plants in the fight against malaria and as a rich reservoir from which new antimalarial drugs can be developed. Scientific evaluation for safety, efficacy and quality of medicinal plant preparations is important in safeguarding users. From our research, we found out that those medicinal plants are a potential source of new antimalarial drugs or preparations [1-3, 7].

From the previous reports, we noticed that, the effect of combining some plant extracts against a multi-drug resistant malaria parasite, *Plasmodium falciparum* and observed that in some cases the plants depicted higher efficacy when in combination as opposed to the single extracts, besides, the tested plant extracts to be safe and effectively kill malaria parasites [1, 2]. As is done in traditional medicine, adopting medicinal plants as sources of antimalarial treatment will be beneficial because the drugs would be cheaper to produce, more cost effective for patients and easily accessible, and after that work to establish appropriate dosages and mode of administration for effective treatment in humans after conducted clinical trial [2].

The aim of the study was to identify and evaluate the safety of sampled medicinal plants in treating malaria. We selected some plants have historically been used by traditional health practitioners to treat malaria and were subjected to laboratory

tests in search of their anti-parasitic properties. and also investigated whether the plants were used singly or in combination with others. some plants have high potential antimalarial efficacy. These medicinal plants have the highest ability to kill the malaria parasite. Therefore, it is our duty to protect these high value medicinal plants are found so as to encourage their preservation as sources of raw materials for the preparation of antimalarial medicines, and also cultivating these plants as a future source of the raw material and as an income generating activity for the engaged communities. One of the important plants in this regard is *Cissampelos pareira*.

## 2. *Cissampelos pareira*

*Cissampelos pareira* (velvetleaf) is a species of flowering plant belongs to the family Menispermaceae has worldwide distribution, occurring in tropical and subtropical regions of the Americas, Africa and Asia. It is the most popular species of *Cissampelos*, known for its medicinal uses of leaves and roots [8]. It is a climbing shrub with green leaves, orange to red drupe berries, horseshoe shaped seeds and brown to yellowish roots. Its aerial parts contain number of secondary plant metabolites like flavonoids, alkaloids, tannins, volatile oils, glycosides [9]. Some attention has been paid to it for its purported antimalarial properties in particular [10], as well as in India for its antiviral properties, especially against Dengue virus. [11].

*Cissampelos pareira* is used traditionally in India as a remedy for the treatment of various diseases including malaria [12] and have multipurpose activities; namely, analgesic, antiabortive, antiarthritic, anticancer, antidiarrheal, antihistaminic, antiinflammatory, antileukemic, antilithic, antimalarial, antioxidant, antiplasmodial, antipyretic, antiradicular, antiseptic, antispasmodic, antitypanosomic, antiulcer,

aphrodisiac, astringent, bactericide, cardiotoxic, CNS-depressant, diuretic, emmenagogue, expectorant, febrifuge,

hepatoprotective, hypertensive, hypotensive, piscicide, purgative, respirodepressant, sedative and stimulant<sup>[9, 13-15]</sup>.

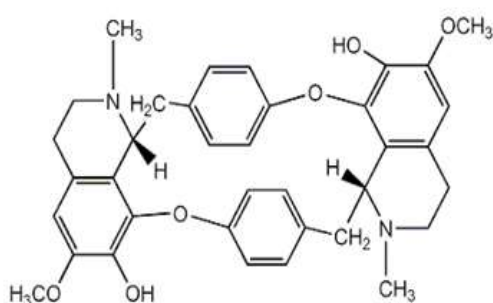


Fig 4: *Cissampelos pareira*, (Leaves, Flowers and fruits)<sup>[16]</sup>.

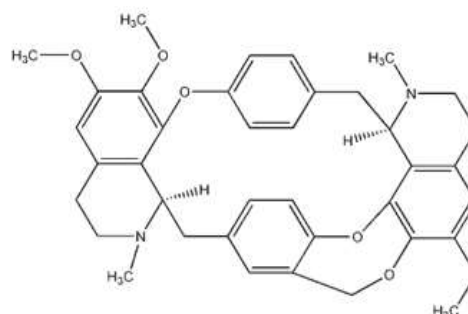
### 3. Chemical Compositions

Reza *et al.*<sup>[15]</sup> found that, the extract of *Cissampelos pareira* whole plant exhibited the presence of several phytochemical compounds including saponins, gums and carbohydrates, reducing sugars. To date, Kumari *et al.*<sup>[17]</sup> demonstrated that,

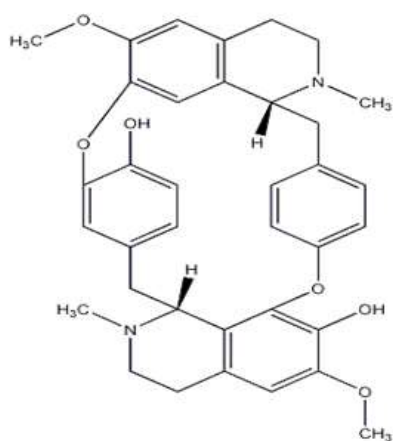
approximately 54 phyto-molecules have been isolated from *Cissampelos pareira* including mainly isoquinoline alkaloids along with few flavonoids, flavonoid glycosides, terpenoids and fatty acids. Figure 5 shows some chemical structures isolated from *Cissampelos pareira*.



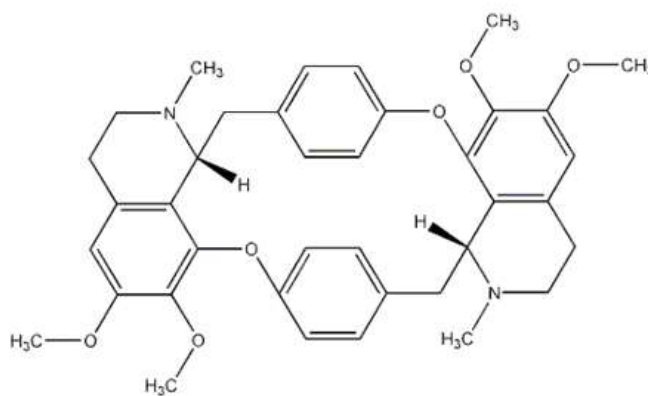
Isobebeerin



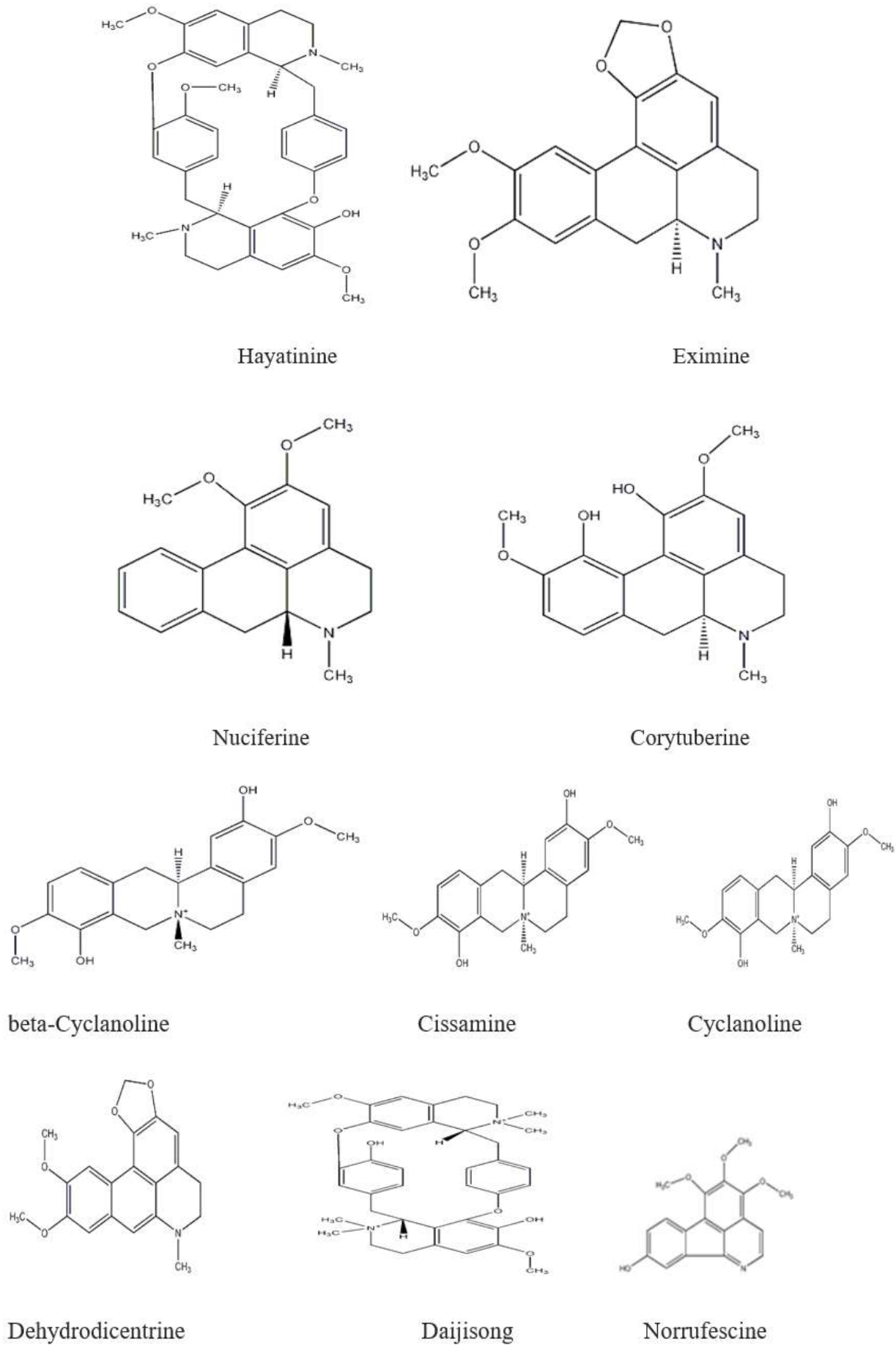
Insularine



l-Curine



Cycleanine



**Fig 5:** Some chemical structures isolated from *Cissampelos pareira*

#### 4. Anti-malaria activity of *Cissampelos pareira*

Kumari *et al.* [17] found that, *Cissampelos pareira* has been extensively used in the traditional medicinal system since the ancient time for the treatment of numerous diseases such as ulcer, wound, rheumatism, fever, asthma, cholera, diarrhoea, inflammation, snakebite, malaria, rabies, and also recommended for blood purification. However, studies demonstrated that, crude extracts of *C. pareira* have shown various pharmacological activities such as antipyretic, anti-inflammatory, antiarthritic, antiulcer, antidiabetic, anticancer, antifertility, antimicrobial, antioxidant, antivenom, antimalarial, and immunomodulatory.

Singh and Banyal [18] showed that, *Cissampelos pareira* inhibited the propagation of rodent parasite *Plasmodium berghei* *in vivo*. In a typical fourday experiment, the BALB/c mice were administered with ethanol extracts of *Cissampelos pareira*. The root extract of *Cissampelos pareira* resulted in inhibition of *Plasmodium berghei* significantly.

*Cissampelos pareira* is a potential plant is a potential source of new anti-malarial drugs. Rukunga *et al.* [19] identify the anti-plasmodial potential of some plants used in preparing herbal remedies for malaria in Kenya. The extracts were tested against chloroquine sensitive (NF54) and resistant (ENT30) *P. falciparum* strains *in vitro*. The most active extracts were from *Zanthoxylum chalybeum* (Rutaceae) with an IC<sub>50</sub> value of 3.65µg/ml, *Cyperus articulatus* (Cyperaceae) with 4.84µg/ml, and *Cissampelos pareira* (Menispermaceae) with 5.85µg/ml.

Further, Bhatt *et al.* [12] isolated a new isoquinoline alkaloid, namely pareirarine from root along with five known compounds magnoflorine, magnocurarine, salutaridine, cissamine and hayatinine. Also, they concluded that, the hydro ethanolic extract of *Cissampelos pareira* root was active with IC<sub>50</sub> values (µg/ml) of 1.42 and 1.15 as well as root ethyl acetate fraction (IC<sub>50</sub> 4.0 µg/ml), stem water fraction (IC<sub>50</sub> 4.4 µg/ml), and root water fraction (IC<sub>50</sub> 8.5 µg/ml) against malaria, respectively. The antimalarial potential of *Cissampelos pareira* may be attributed to isoquinoline type alkaloids present in this plant and also provides the scientific evidence for the traditional use of this plant in treatment of malaria. The most potent fractions were root ethyl acetate fraction (IC<sub>50</sub> 4.0 µg/ml), stem water fraction (IC<sub>50</sub> 4.4 µg/ml), and root water fraction (IC<sub>50</sub> 8.5 µg/ml). Hayatinine, a bisbenzylisoquinoline alkaloid, isolated from root ethyl acetate fraction was most promising compound with IC<sub>50</sub> of 0.41 µM (chloroquine resistance) and 0.509 µM (chloroquine sensitive). Magnocurarine and cissamine were also found active with IC<sub>50</sub> values of 12.51 and 47.34 µM against chloroquine resistance and 12.54 and 8.76 µM against chloroquine sensitive, respectively.

#### 5. Reports some of the purported benefits

There are many studies confirmed the medicinal importance of *Cissampelos pareira* different parts (whole vine, seed, bark and leaf) used for medicinal effect are [13]. Leaves contain alkaloids like tetrandrine, which has analgesic effect and has recently been shown to have antitumor and antileukemic properties. Also, roots and stem contain the bisbenzylisoquinoline alkaloids that have been demonstrated as anti-inflammatory agent [13]. Which explains the traditional use of *C. pareira* in the treatment of pain, fever, diarrhea and infection. *C. pareira* is thought to be responsible for many of its properties like antioxidant and anti-inflammatory [13, 15]. In

addition to Wimpy *et al.* [20], who explained that *C. pareira* is a plant whose various parts which traditionally in India for treatment of many diseases like inflammation, pain, haemorrhage, gastrotoxicity, cancer, diarrhoea, diabetes, cardiotoxicity, sores and used in hepatoprotective. The biological activity *C. pareira* includes anti-cancerous, anti-fertility, anti-asthmatic, anti-diabetic, analgesic, hepatoprotective and anti-inflammatory type of activities. The leaf of *C. pareira* contains various phytoconstituents including alkaloids, terpenoids and flavonoids [20].

Indian and Thai people used *Cissampelos pareira* as a medicinal herb for treating fever and analgesic [21]. They noticed that *C. pareira* pectin from leaves have antioxidant and anti-inflammatory property. So, *Cissampelos pareira* pectin is used in functional dietary products and herb-based pharmaceuticals. Bala *et al.* [22] showed that, isolated isoquinoline alkaloid of *Cissampelos pareira* along with six known isoquinoline alkaloids, namely, magnoflorine, magnocurarine, cissamine, curine, hayatinine and cycleanine. Magnoflorine and magnocurarine were isolated for the first time from *C. pareira*. The chloroform (CPCF) and n-butanol (CPBF) fractions showed cytotoxic efficacy against KB cells. Among pure compounds, hayatinine was found to be most active against KB and A549, while, cycleanine against KB cells.

#### 7. Conclusion

African Traditional Medicine is used for the healthcare of about 80% of the rural populations of the continent of Africa. The practices of African Traditional Medicinemade use of plant-products, which are known to contain plant-based secondary metabolites or natural products, likely to play key roles in drug discovery. For various reasons, including resistance of strains of *Plasmodium* to known anti-malarial drugs, local African populations often resort to plant-based treatments and/or a combination of this and standard anti-malarial regimens. The current review, along with the previous studies that covers data for antiplasmodial compounds from African flora, could serve as the baseline data for the discovery of new anti-malarial compounds from Africa. It will take effective prevention, accurate and timely diagnosis and treatment to successfully eliminate malaria. But none of this will help if the causative agents become resistant to the drugs used for treatment.

#### 8. Conflict of interest

The authors have no conflict of interest.

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