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THE ANTIMALARIAL POTENTIAL OF MEDICINAL PLANTS USED FOR THE TREATMENT OF MALARIA IN CAMEROONIAN FOLK MEDICINE

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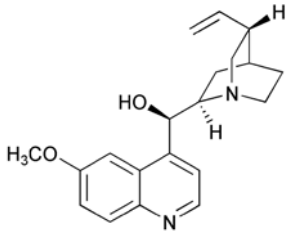
Abstract

Malaria remains one of the leading public health problems in Cameroon as in other parts of Sub-Saharan Africa. In the past decades, this situation has been aggravated by the increasing spread of drug-resistant *Plasmodium falciparum* strains. New antimalarial drug leads are therefore urgently needed. Traditional healers have long used plants to prevent or cure infections. This article reviews the current status of botanical screening efforts in Cameroon as well as experimental studies done on antimalarial plants. Data collected from 54 references from various research groups in the literature up to June 2007 shows that 217 different species have been cited for their use as antimalarials in folk medicine in Cameroon. About a hundred phytochemicals have been isolated from 26 species some among which are potential leads for development of new antiamalarials. Crude extracts and or essential oils prepared from 54 other species showed a wide range of activity on *Plasmodium spp.* Moreover, some 137 plants from 48 families that are employed by traditional healers remain uninvestigated for their presumed antimalarial properties. The present study shows that Cameroonian flora represents a high potential for new antimalarial compounds. Further ethnobotanical surveys and laboratory investigations are needed to fully exploit the potential of the identified species in the control of malaria.

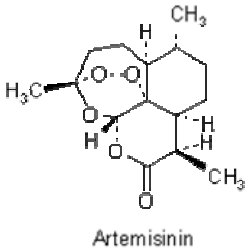
Introduction

Malaria is the world's most important parasitic disease especially when *Plasmodium falciparum* is the causative agent (Fisher and Bialek, 2002). Malaria is endemic in about 100 developing countries, accounting for about 40 to 45 million DALYs (Disability Adjusted Life Years) and kills an estimated 1.2 million people each year in Africa (WHO, 2001). In Cameroon and Sub-Saharan Africa, one in five children will die before they are five and 75 % of those deaths are attributed to malaria (Nwaka, 2005).

Pregnant women and children under five years of age are the most vulnerable. The socioeconomic consequences of this disease are particularly dramatic in rural areas where poverty and malnutrition are more



(1) Quinine



Artemisinin

(2) Artemisinin

pronounced. In the absence of an effective vaccine, the fight against malaria depends on chemotherapy and the reduction and prevention of human/*Anopheles* mosquito contacts through the use of insecticides treated bed nets, insecticides and environmental care.

Resistance of *P. falciparum* to commonly used antimalarial drugs is increasing in Cameroon as in other parts of Africa (Mbacham et al., 2004). This has resulted in resurgence in transmission and an increase in adverse outcomes due to therapy failure. Hence, new highly efficacious antimalarial agents are urgently needed. For thousands of years, plants have constituted the basis of traditional medicine systems and recently, natural products have been a good source of lead compounds for drug development. A good example against malaria is quinine **(1)**, isolated from *Cinchona* bark, which was used as a template for the synthesis of chloroquine and mefloquine. More recently, artemisinin **(2)** isolated from the Chinese plant *Artemisia annua*, has been used successfully against chloroquine-resistant *P. falciparum* strains (Schwikkard and Van Heerden, 2006).

In Cameroon, a large number of plant species have been identified as antimalarial medicinal plants. Pure products have been isolated from some of these plants amongst which are those whose antimalarial activities are comparable to or more active than chloroquine on sensitive and resistant stains of *P. falciparum* (Tane et al, 2005). It is therefore imperative that antimalarial drug development has to be pursued further, with these highly active products, to preclinical, clinical testing, manufacture and distribution and then finally to post marketing pharmacovigilance. In the present review, we report on the plants, which have been identified as antimalarial plants and the work done so far in evaluating their antimalarial potential. The review is structured according to plant families and the extent of investigations carried out in the specific plant families to date.

Methodology

The data on the medicinal plants were collected through a review of unpublished documents in the Library of the Faculty of Science, University of Yaoundé I, Cameroon, the Library of the Ministry of Scientific Research and Innovation, Yaoundé, Cameroon and through an internet search in www.google.com, www.scholar.google.com and www.pubmed.gov. We also collected information on antimalarial medicinal plants from members of research groups in the Laboratory of Phytobiochemistry and Medicinal Plants Studies, Laboratory of Organic Chemistry in the University of Yaoundé I, Laboratory of Phytochemistry at the Cameroonian Institute for Medical Research and Medicinal Plants Studies (IMPM), Yaoundé, the National Herbarium of Cameroon in Yaoundé and the Natural Products Chemistry Laboratory, University of Dschang, Cameroon.

Use of traditional remedies for the treatment of malaria and other fevers in Cameroon

The proportion of the populations using traditional remedies to treat malaria varies widely. Mostly in the rural areas, the use of plant medicines plays an important role in daily health care. Local medicines are even preferred to modern medicines in ethnic groups such as Baka Pygmies in South Eastern Cameroon. There exist two types of traditional pharmacopoeia: the specialized pharmacopoeia which is practiced by traditional healers for difficult health problems, and the popular or general pharmacopoeia which is common knowledge in a given community and is used by individuals mostly for treating ordinary ailments such as fever, malaria and diarrhoeas. Traditional medicines are commonly sold in markets and public places or administered by healers in traditional clinics. Whole plants or parts of them are prepared and administered as oral decoction, steam baths, infusion or enema. Most remedies are a concoction of two or more plant species and solvents used include water, palm wine or oils. Health problems are often self-treated first with the popular pharmacopoeia also called self-aid or auto-medication (Adjanouhoun et a.l., 1996; Betti, 2002, 2004).

Overview of Studies on Plant Species used as Antimalarial in Cameroonian Folk Medicine

A wide variety of plants found in the Cameroonian flora, belonging to several families have been identified through ethnobotanical and ethnopharmacological studies as antimalarial medicinal plants. Botanists have identified these plants and vouchers are found in the Limbe Botanic Garden and the National Herbaria in Yaoundé. Some of these plants have undergone various degrees of scientific investigation by various researchers mentioned in this paper. Following botanical identification the plant is collected, dried, macerated in various organic solvents, water and palm wine and the mixture filtered. The filtrate is concentrated by rotary evaporation to obtain the crude extract. The extract is then tested in various systems mainly *in vitro* incubation with *Plasmodium* parasite or *in vivo* in a malaria animal model. It is worth mentioning that several *Plasmodium falciparum* strains, which have been successfully adapted to *in vitro* culture, are employed in testing, while a number of animal and human models are also used for *in vivo* studies. Extracts with significant antiplasmodial

activity are fractionated using various techniques and the fractions are tested to identify their biological activity. Biologically active fractions then undergo purification to isolate the bioactive natural product(s). The pure product is further tested for antimalarial activity *in vitro* and *in vivo* as mentioned above. In the following sections we assess some families, which have been investigated so far in Cameroon.

Annonaceae

Enantia clorantha stem bark is widely used in Cameroon to treat malaria, other fevers and also jaundice (Adjanohoun et al., 1996). The aqueous extract of this plant suppressed *Plasmodium yoelii* infection in mice when given orally in drinking water decoction, 0.2-150 mg/mL, but not if given by oral cannulation or subcutaneously. Phytochemical analysis of the plant extract revealed alkaloids, saponins and simple sugars, but no bioactivity-guided fractionation was conducted (Agbaje and Onabanjo, 1991).

Annona muricata was investigated by Bidla et al (2004). A chloroform/methanol (1:1) leaf extract showed a 67% inhibition of *P. falciparum* F32 *in vitro* at 20 µg/mL The seeds of *Xylopia parviflora*, a shrub growing in the savanna region of Western Cameroon, are commonly used as a condiment and for the treatment of fevers. Six diterpenes isolated from the seeds of this plant have shown antimalarial activity (Akam et al, 2005).

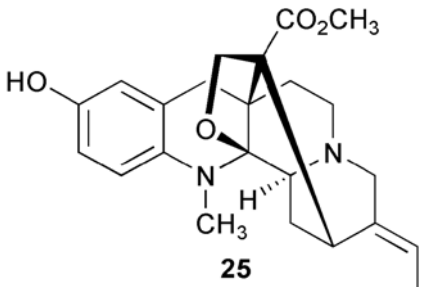
Four other species from this family (*Xylopia phloiodora*, *Xylopia aethiopica*, *Pachypodanthium confine*, and *Hexalobus crispiflorus)* were also investigated by Boyom et al (2003). Essential oils from these plants were active against the W-2 strain of *P. falciparum* in culture. The most effective was the oil of *Hexalobus crispiflorus*, with an IC_{50} of 2 µg/mL

Anacardiaceae

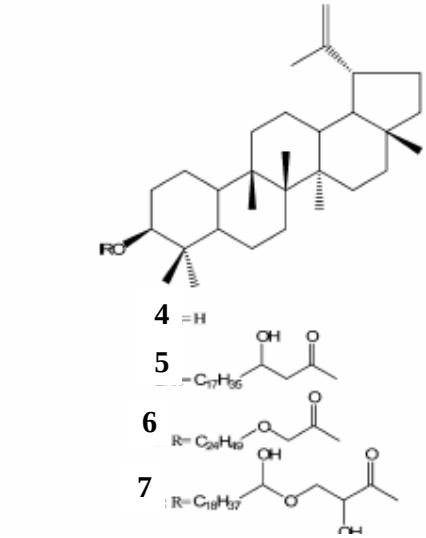
Bidla *et al* (2004) evaluated the *in vitro* antimalarial activity of *Mangifera indica*, which is grown widely in Cameroon for its fruits as food. The chloroform: methanol (1:1) extract showed a good activity on *P. falciparum in vitro* with a growth inhibition of 50.4% at 20 µg/mL

Apocynaceae

Alstonia boonei, *Picralima nitida* and *Rauvolfia vomitoria* have been identified by Adjanohoun et al (1996) for their use in the treatment of malaria by traditional healers in Cameroon. Tantchou *et al* (1986) investigated *Alstonia boonei* for its antimalarial activity using both the Giemsa slide method and hypoxanthine incorporation technique. When tested against the Viet Nam Smith strain of *P. falciparum*, the bark aqueous extract of *Alstonia boonei* showed a minimum inhibitory concentration of 3.2 µg/L for slide method versus 120 µg/Lfor radioactivity method. Many research groups investigated *Picralia nitida*. François *et al* (1996) tested the organic and aqueous extracts of its roots, stem bark, fruit rind, seeds and leaves. The dichloromethane extract of the roots was highly active (IC_{50} = 0.2 µg/mL) followed by stem bark dichloromethane extract (IC_{50} = 0.5 µg/mL) and fruit rind aqueous extract (IC_{50} = 1.5 µg/mL). Kapadia et al (1993) isolated the alkaloid akuamine **(3)** from the seeds of *Picralia. nitida* which was also reported to have shown activity against *Plasmodium*.



(3) Akuamine



Lupeol and derivatives

Rauvolfia vomitoria was investigated by Zirihi et al (2005). The stem bark alcoholic extract presented a significant inhibitory activity on *Plasmodium berghei* in mice.
Holarrhena floribunda has been used by Baka pygmies of Dja Division for many centuries to treat malaria. Extracts of the stem bark were investigated on *P. falciparum* strains by Fotie et al. (2005). The aqueous extract showed the highest activity on Indochina (W-2) strain with an IC_{50} of 1 µg/mL while the ethanol extract was most active against Sierra Leone *P. falciparum* (D-6) strain with an IC_{50} of 4.3 µg/mL. Lupeol **(4)** and its derivatives were isolated: -3-O-(3'hydroxyeicosanoyl)lupeol, **(5)** 3-O-(2'tetracosyloxy) acetyllupeol **(6)** and 3 – O[(1''-hydroxyoctadecyloxy) 2-hydroxypropanoyl] lupeol **(7)** were isolated from this plant and exhibited a significant antimalarial activity *in vitro*.

Asteraceae

Vernonia amygdalina, *Bidens pilosa*, *Microglossa pyrifolia*, *Conyza sumatrensis* were reported for their use as antimalarial remedies in Cameroon folk medicine (Adjanohoun et al., 1996). The petroleum ether/methanol (1:1) extract of the aerial part of *Microglossa pyrifolia* exhibited a high antiplasmodial activity (Köhler, 2002). The bioassay-guided fractionation of this extract by the same author led to the isolation of 18 natural compounds including furanoditerpenes and geranylgeraniol derivatives. Sinapyl diangelate, 1-acetyl-6E, 10E, 14E geranylgeraniol-19-oic acid and 19-oxo-6E, 10E, 14-geranylgeraniol were shown to have antimalarial activity , alongside a weak cytotoxic effect.

Andrade-Neto et al. (2004) tested the ethanol extract of *Bidens pilosa* leaves and found flavonoids as active compounds against *P. falciparum.*

Waako et al. (2005) evaluated the antimalarial activity of mature and very young leaves and the stem bark from *Aspilia africana* and both antibacterial and antiplasmodial activities were observed.

The soft aerial part of *Conyza sumatrensis* is mixed with other plants i.e. *Rauvolfia vomitoria* stem bark, lime fruit, *Carica papaya* mature leaves and *Cymbopogom citratus* leaves prepared as decoction for the treatment of malaria in western Cameroon (Adjanohoun et al., 1996).

Tithonia diversifolia, a multipotential medicinal plant widely known in Cameroon, has been reported for its antimalarial therapy. The macerated leaves are used for the treatment of fevers in children in western region of the country. Goffin et al (2002) investigated this plant *in vitro* against three strains of *P. falciparum*. The ether extract from aerial parts of the plant collected in Sao Tomé e Príncipe, demonstrated good antiplasmodial activity (IC_{50} on FCA strain: 0.75 µg/mL) and fractionation of this extract yielded the known sesquiterpene lactone tagitinin C as an active component against *Plasmodium* (IC_{50} on FCA strain: 0.33 µg/mL), but this compound was also cytotoxic (IC_{50} on HTC-116 cells: 0.7 µg/mL). However, the antiplasmodial activity of the Cameroonian varieties of this species has not been reported.

Bignoniaceae

The leaves and stem bark of *Spathodea campanulata* are widely used in Cameroon as antimalarial remedy. The aqueous, chloroform and hexane extracts of stem bark were investigated by Makinde et al (1988). When tested against *P. berghei* in mice with chloroquine as control, the hexane and chloroform extracts were the most effective. Amusan et al (1996) isolated ursolic acid and its two derivatives tomentosolic acid and 3β, 20 β-(dichloroxyurs 12 – 28) oic acid from stem bark, which suppressed malaria and prolonged the survival time of mice infected with *P. berghei*.

Capparidaceae

The plant *Buchholzia coriacea* has been reported for its use in the treatment of malaria and other fevers. The ground seeds is mixed with palm oil and taken orally as treatment for malaria (Adjanohoun et al, 1996).

Cleone rutidosperma was investigated for its antimalarial properties by Bidla *et al* (2004) and a 31.6% inhibition of *P. falciparum* growth was observed *in vitro* in the presence of 40 µg/mL of chloroform/methanol (1:1) extract of the plant.

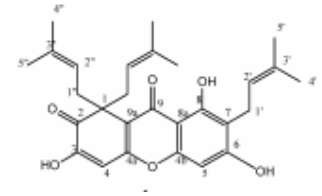
Caricaceae

Mature leaves of *Carica papaya* (paw paw) are widely used to treat malaria and splenomegaly while the fruit is used against anaemia, which can also be caused by malaria (Adjanohoun et al., 1996). The petroleum ether extract of the seed rind of this species showed a considerable antimalarial activity, with an IC_{50} of 15.19 µg/mL (Bhat and Surolia, 2001). This may be indicative of the presence of highly active compounds in this

plant. Ngemenya et al (2004) recorded very weak antiplasmodial activity in the leaves and seeds of *Carica papaya* with IC_{50} of about 60 µg/mL. However, there is no report on the phytochemistry of this plant with regards to its antiplasmodial activity.

Clusiaceae

Allanblackia monticola is a large forest tree found in West and South provinces of Cameroon where it is used as medicinal plant to treat several diseases including respiratory infections, toothache and diarrheoa. Azebaze et al (2006) isolated from the methanol extract of the stem bark, a new prenylated xanthenedione, allanxanthone C **(8)**, and five known xanthones, garciniafuran, tovophyllin A, rubraxanthone, norcowanin **(9)** and mangostin **(10)** and one saponin, stigmasterol-3-O-beta-D-glucopyranoside. The methanol extract and pure compounds showed IC_{50}s of 0.6 to 8.9 µg/mL on *P. falciparum*, F32 (chloroquine sensitive) and FcM29 (chloroquine resistant). Their cytotoxicity was estimated on human melanoma cells (A375) and the cytotoxicity/antiplasmodial ratio was found to be high i.e. between 15.45 and 30.46. This indicates that the safety margin of the extract is very large.



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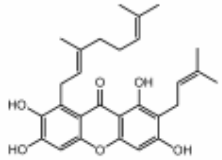

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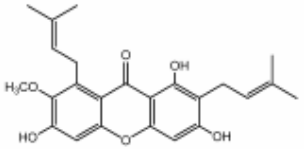

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Combretaceae

Terminalia superba leaves are used to treat malaria in parts of Southwest Cameroon. The methanol extract showed an IC_{50} of 19.5 µg/mL on *P. falciparum* F32 (Ngemenya et al., 2004).

Euphorbiaceae

The *Alchornea cordifolia* young shoots are used to treat malaria by Baka Pigmies of the East and South provinces. Banzouzi et al (2002) isolated ellagic acid from the leaves, which showed a good activity against *P. berghei* in mice with an IC_{50} in the range of 0.2-0.5µM.

*Alchroman*es *difformis* and *Mallotus oppositofolius* showed significant activities on *P. falciparum, in vitro*, with respectively 32.4% and 57% of inhibition at 40µg/mL chloroform/methanol (1:1) extract. (Bidla et al, 2004)

Essential oils from *Antidesma laciniatum* showed a considerable *in vitro* activity on W-2 *P. falciparum* strain (Boyom et al., 2003).

Ngamga et al. (2005) investigated *Millettia griffoniana*. They isolated two new prenylated isoflavonoids from the seeds, namely 7-methoxyebenosin and griffonianone E, which exhibited moderate trypanocidal and anti-plasmodial activities.

The ethyl acetate extract of *Euphorbia hirta* whole plant showed low inhibition of 13 % on *P. falciparum* F32 at 62.5 µg/mL (Ngemenya et al., 2004).

Fabaceae

A bioactivity-guided fractionation of extracts of roots and leaves of *Cajanus cajan* afforded two compounds, logistylin A and C and betulinic acid with a moderately high *in vitro* activity against the chloroquine-sensitive *P. falciparum* strain 3D7 (Duker-Eshun et al., 2004).

Leguminosae

Adjanohoun et al. (1996) reported the use of some plants of this family for the treatment of malaria symptoms in Cameroonian folk medicine. These include *Senna* sp. (*S.occidentalis* and *S. hirsute*) whose leaves are used as decoction and *Guibourtia tessmannii* (stem bark). Guibourtia tessmanii was tested by Tantchou et al

(1986) on Viet Nam Smith strain of *P. falciparum*. The bark aqueous extract exhibited remarkable activity with a minimum inhibitory concentration of 2.4 µg/L when using Giemsa slide method versus 3.8 µg/L for hypoxanthine technique.

Loganiaceae

Investigation of *Strychnos icaja* yielded vomicine, isostrychnine and three new sungucine derivatives, named isosungucine, 18-hydroxy-sungucine and 18-hydroxy-isosungucine. Some of these compounds were highly active against *P. falciparum in vitro*, particularly against the chloroquine-resistant strain (Frédérich et al., 2000).

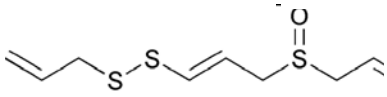
Lamiaceae

Tchoumbougnang et al. (2005) have investigated some species from this family. Essential oils from the leaves of *Ocimum. gratissimum* were tested against local isolates of *P. falciparum* and found to be highly active, with IC_{50}s from 6.9 to 14.9 µg/mL Ngemenya et al. (2004), recorded an IC_{50} of 29.5 µg/mL for *O. gratissimum* leaves on *P. falciparum* F32.

Achenbach et al. (1992) also investigated *Holshundia opposite.* The hexane extract of the root bark revealed a good *in vitro* activity against *P. falciparum* with IC_{50} of 5.6 µg/mL

Liliaceae

Allium sativum is widely used as a spice in Cameroon and has been investigated for its antimalarial activity. Perez et al. (1994) isolated ajoene (**11**) from this plant, which reduced considerably the severity of *P. berghei* infection in mice and was nontoxic. Ajoene was further tested for its antimalarial activity *in vivo* in a well-characterized murine model by Hilda et al. (1994). A single ajoene oral dose of 50 mg/kg, on the day of infection, suppressed the development of parasitemia with no obvious acute toxicity. A single dose combination of ajoene (50 mg/kg) and chloroquine (4.5 mg/kg), given on the day of the infection, completely prevented the subsequent development of parasitemia in infected mice.



(11) Ajoene

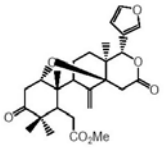
Malvaceae

Gossypol is abundant in cottonseed (*Gossypium spp.)* oil and exhibits a variety of biological activities, including antispermatogenic, anticancer, antiparasitic and antiviral activity. It also showed antimalarial activity against both chloroquine-sensitive and chloroquine-resistant strains of *P. falciparum*, with an IC_{50} of 10 µg/L But it is cytotoxic and its synthetic analogs retained the biological effects, including the antimalarial activity (Schwikkar and van Heerden 2006).

Meliaceae

The antimalarial properties of the crude water extract from *Khaya grandifoliola* stem bark in mice has been reported by Bickii et al. (2000) and Bumah et al. (2005). Bioassay-guided fractionation of stem bark and leaves extracts led to four main active compounds, namely Methylangolensate **(12)**, 7α- acetoxydihydronomilin **(13)**, 7α – obacunylacetate **(14)** and 22- hydroxyhopan-3-one **(15)**.

Ngemenya at al. (2006) investigated the antimalarial properties of *Turreanthus africanus* . A phytochemical analysis of the methylene chloride/methanol (1:1) extract of the seeds of the plant yielded seven compounds. Of four compounds tested, one (16-oxolabda-8 (17), 12(E)-dien-15-oic acid), showed the highest antiplasmodial activity (IC_{50} of 26 µg/mL) on chloroquine-sensitive *P. falciparum* F 32, *in vitro*; two others, namely (methyl-14,15-epoxylabda-8 (17), 12(E)-diene-16-oate, and turreanin A had moderate activity and one 17,20-Dihydroxypregn-4-ene-3,16-dione was inactive. These results appear to justify the use of *Turreanthus africanus* as antimalarial in Cameroonian folk medicine.



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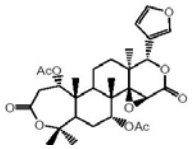

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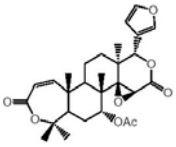

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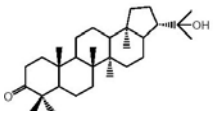

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Melianthaceae

Ngemenya et al (2005) investigated *Bersama engleriana*. The methanol extract of the leaves of this plant was highly active with IC_{50} of 2.7 µg/ml and was also highly active on schizonts. Tapondjou et al. (2006) isolated eight compounds including five 3 O-glucuronide triterpene saponins from the stem bark but there are no reports on the antiplasmodial activity of these compounds.

Menispermaceae

Peniantus longifolius was reported by Bidla et al. (2003) as an antimalarial plant in Cameroonian folk medicine. Two compounds, palmatine and jatrorrhizine, isolated from the stem bark methylene chloride/methanol (1:1) extract, showed promising *in vitro* activity on *P. falciparum* i.e. IC_{50} 350 ng/mL on the D-6 chloroquine-sensitive strain, from Sierra Leone and 284.3 ng/mL on the W-2 chloroquine-resistant strain from Indochina (Tane et al., 2005).

Monimiaceae

A phytochemical study of the methylene chloride/methanol (1/1) extract of the leaves of *Glossocalyx brevipes* Benth, led to five active compounds, namely three new derivatives of homogentisic acid, methyl-2 (1'β-geranyl-5' βhydroxy-2-oxocyclohex-3'enyl)acetate; 2-(1' β-5' β-hydroxy-2'-oxocyclohexyl)acetate and two known alkaloids, aristalolatam BII and liriodenine. These phytochemicals showed a modest *in vitro* activity against *P. falciparum* (Mbah et al., 2004).

Myrtaceae

Ethanol extract from *Eucalyptus robusta* leaves revealed a good antimalarial activity and Robustadial B was isolated from this plant (Xu et al., 1984).

Psidium guajava is a widespread plant in Cameroon. Its fruit is consumed and the leaves used to treat diarrhea in some parts of the country. Nundkumar and Ojewole (2002) investigated this plant using the parasite lactate dehydrogenase (pLDH) assay method, a recently developed *in vitro* enzymatic method for evaluating antiplasmodial activity. Of the aqueous leaf, stem-bark and fruit extracts tested on the chloroquine-sensitive *P. falciparum* D10 strain, the stem bark extract was the most active, with IC_{50} of 10-20 µg/mL. Phytochemical analysis revealed the presence of anthraquinones, flavonoids, seccoirridoids and terpenoids. But there is no report on the activity of the individual compounds.

Poaceae

Cymbopogon citratus is one of the most commonly used herbs in Cameroon to treat malaria and other fevers. The essential oils extracted from fresh leaves of this plant were active in the four-day suppressive *in vivo* test on *P. berghei* in mice giving IC_{50}s from 6 to 9.5 µg/mL (Tchoumbougnang et al., 2005).

Bidla et al. (2004) also investigated *Cimbopogon citratus* and they recorded an inhibition of 57.9% on *P. falciparum*, *in vitro*; with a 20 µg/mL chloroform/ethanol (1:1) extract.

Polygonaceae

Rumex abyssinia leaves are used for the treatment of malaria by some traditional practitioners of the Bassa tribe living in the equatorial rain forest area in the Littoral Province of Cameroon (Adjanohoun et al., 1996).

Piperaceae

Bidla et al. (2004) investigated *Piper unbellatum*. Chloroform/methanol (1:1) extract from leaves presented a moderate antimalarial activity when tested *in vitro* on *Plasmodium falciparum*.

Mbah (2003) and Ngemenya et al., (2004) investigated *Peperomia vulcanica* and observed a moderate *in vitro* activity on *P. falciparum* (70% inhibition by 40 μg/mL crude extract).

Rubiaceae

Coffea arabica, a source of caffeine, is an important cash crop in Cameroon, and a decoction of the leaves in water is used as an antimalarial remedy (Adjanohoun et al., 1996).

Morinda lucida is widely used in West and Central Africa; the leaves, stem bark or root bark are used to treat malaria and other tropical diseases. The petroleum ether extract and fractions of the leaf samples of *Morinda lucida* were evaluated for antimalarial effects against *P. falciparum* using the rabbit *in vivo* technique (Awe and Makinde, 1998). It was observed that the extract and some fractions inhibited the maturation of a drug sensitive strain of *P. falciparum*. Active anthraquinones were isolated from this plant, the most active being damnacanthal.

Rutaceae

Citrus sinensis is the most common antimalarial plant of this family. A decoction is prepared from roots (Adjanohoun et al., 1996).

Tane et al. (2005) investigated *Araliopsis tabuensis*. The stem bark of this plant showed a good *in vitro* activity against *P. falciparum,* with an IC_{50} of 895.6 and 1042.1 ng/mL for the D6 and W-2 strains, respectively. The bioassay guided fractionation yielded 13 alkaloids of which araliopdimerine-A was the most active with IC_{50} values of 34.1 ng/mL and 17.4 ng/mL for D6 and W-2 respectively.

Scrophulariaceae

The ethylacetate extract of *Scoparia dulcis* whole plant gave an IC_{50} of 19.5 μg/mL on *P. falciparum* (Ngemenya et al., 2004). Information from an online database shows that more than forty compounds from several chemical classes are present in this plant; the chemical classes include flavonoids, terpenoids, nitrogen heterocyclics, steroids, phenylpropanoids, benzenoids, alkaloids and saponins (www.rain-tree.com, 2004).

Simaroubaceae

Ngemenya et al. (2005) investigated *Odyendyea gabonensis*. The methanol extract of the leaves was highly active with IC_{50} 1.8 μg/mL on trophozoites and was also highly active on schizonts. Tane et al (2005) also investigated the stem bark and observed a remarkable activity on two *P. falciparum* clones, with IC_{50} of 111.9 ng/mL on the Sierra Leone D-6 strain and 101.5 ng/mL on the Indochina W-2 strain and then isolated three indole alkaloids with moderate activity and one quassinoid, ailanthinone. Ailanthinone isolated from stem bark displayed high activity against D-6 and W-2 strains with IC_{50} of 2.5 and 2.1 ng/mL respectively. Compared to the IC_{50} of the reference molecules, chloroquine (IC_{50} 4.6 ng/mL) and mefloquine (IC_{50} 2 ng/mL), this molecule is a potential lead for development of a new antimalarial agents.

Zingiberaceae

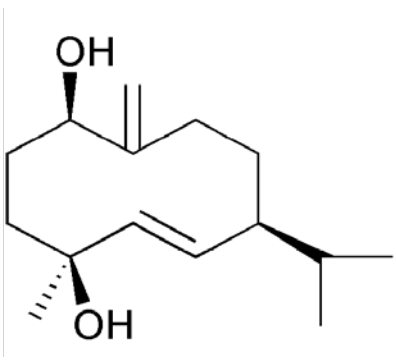
Some four *Aframomum spp* (*A. melegueta, A. zambesiacum, A. latifolium* and *A. sceptrum*) are used by traditional doctors in different regions of Cameroon for the treatment of malarial symptoms (Adjanohoun et al., 1996; Betti, 2004). Duker-Eshum *et al* (2002) investigated *A. latifolium* and *A. sceptrum*. Both presented a significant antiplasmodial activity. Some active compounds were isolated from their fruits: (+) S – nerolidol, 7 labdanes, coranarin B, galanal A & B, galanolactone, (E) – 8 β, 17 – epoxylabd -12 – ene – 15, 16 dial, (E) labda – 8 (17), 12 – diene-15, 16 dial. The labdanes showed a modest *in vitro* activity on chloroquine-sensitive *P. falciparum* strains.

Kenmogne et al. (2006) isolated five labdane diterpenoids from *A. zambesiacum*. Zambisiacolactone B was the most active with an IC_{50} of 4.97 μM in *vitro* against *P. falciparum*:

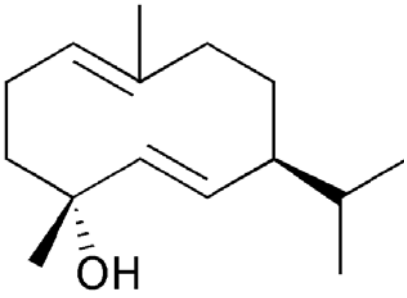
Powdered fruits of *Reneilmia cincinnata* are one of the major constituents of the ingredients of a steam bath used to treat fevers. A bioassay-guided fractionation of dichloromethane extract of the fruits led to the

isolation of six sesquiterpenoids of which two known ones were more active **(16** & **17)** (Tchuendem et al., 1999).

Ngemenya et al. (2004) demonstrated antiplasmodial activity in *Aframomum citratum.*



(16)



(17)

From the above review, it is clear that a wide variety of plant species and families employed in the treatment of malaria contain antiplasmodial products. However, few toxicity and *in vivo* studies have been conducted on these plant products. Clearly additional studies to determine the conditions for the safe use of these products in anti-malaria therapy are indicated.

Cameroonian Antimalarial Plants identified but not investigated

Following ethno botanical survey, some 137 species from 48 different families, which are used in traditional medicine to treat malaria, have been identified. These plants represent more than half of the antimalarial species and are listed on Table 1 (without an asterisk). Up to date, there is no evidence in the literature that any of these plants have been scientifically investigated to establish whether or not they have antimalarial activity.

Cameroonian medicinal plants tested for their antimalarial activity

These are plants from which crude extracts and essential oils have been prepared and tested. They comprise 54 species (21 families) some of which showed high antiplasmodial activities, IC_{50}s below 5 μg/mL down to less than 100 ng/mL on various species and strains of *Plasmodium*. These plants, some of which are shown on Table 2 need further investigation to identify the bioactive principles.

Antimalarial Phytochemicals isolated from Cameroonian medicinal plants

About a hundred active compounds have been isolated from some twenty-six Cameroonian medicinal plants (from 18 families), which showed a wide range of activity on *Plasmodium spp*. The isolated products correspond to diverse chemical classes namely various alkaloids, saponins, sugars, various terpenes, essential oils, flavonoids, xanthenes, xanthones, stilbenes, strychnines, sungucine derivatives, labdanes, amino acid derivatives, anthraquinones, and quassinoids.
Some plants, from which highly active and potential lead compounds have been isolated, are shown on Table 3 below.

Plant Antimalarials in Clinical Use in Cameroon

There are two well known antimalarials of plant origin, quinine and artemisinin, both of which are prescribed to malaria patients in Cameroon. The semi-synthetic analogues of artemisinin i.e. artesunate, artemether and arteether had been prescribed as single drugs for monotherapy but recently in combination with other antimalarials. A number of traditional preparations in the form of decoction, dried powder or ground material prepared from plants for consumption as teas, steam bath or enema are sold as herbal remedies; but most of these preparations have not been standardised as pharmaceutical products and are not on the official prescription list of antimalarial drugs. Some examples of the traditional preparations are given below.

(i) In the West Province, *Carica papaya, Eucalyptus globulus* and *Psidium guajava* leaves are mixed and boiled as a decoction that is drunk for the treatment of malaria. In the same area, stem backs from *Mangifera indicus* and *Citrus sinensis* are boiled and drunk or used as a steam bath against malaria.
(ii) In the Southwest of Cameroon, the Bakweris combine the trunk bark and seeds of *Turreanthus africanus* with *Carica papaya* leaves, the seeds of *Aframomum melegueta* and lime, which are boiled and used for treatment of malaria and other fevers, by drinking and or as a steam bath.
iii) In the South of Cameroon, an infusion of the stem bark of *Odyendyea gabonensis* is used to treat malaria.

Although traditional remedies are widely used to treat malaria, and are often more available and affordable than Western drugs, they are not without limitations. Some of the limitations include unpredictable efficacy, unestablished dosage and the short and long term safety are not known. Also studies carried out provide limited and imprecise information on the methods used to prepare the remedies, making it difficult to replicate them. Hence, further studies including controlled clinical trials are necessary before specific traditional remedies can be recommended on a large scale.

Conclusion and future directions

The present article brings out information on different medicinal plants used in various parts of Cameroon for the treatment of malaria according to the investigation each plant has gone through.

Over two hundred medicinal plants have been recorded herein for their use as antimalarials in Cameroonian folk medicine and about a hundred active phytochemicals isolated. Only one third of the

Table I: List of Cameroonian Medicinal Plants reported to have Antimalarial Activity

Family	Species	Local/Common Name ‡	Part(s) Used	Ref.
Acanthaceae	*Eremomastax speciosa*	Pèkidjum (Bandjoun)	Leaves	22
	Justicia insularis	Oyem ze (Ewondo)	Leaves	22
	Justicia flava	-	Leaves	22
	**Thomandersia hensii*	Ngoka (Baka)	Leaves, stem bark	16, 22
Annonaceae	**Annona muricata*	-	Leaves	14
	Cleistopholis patens	-	Stem bark	22
	**Enantia clorantha*	-	Stem bark	2
	**Hexalobus crispiflorus*	-	Leaf, seed	18
	Monodora myristica	Feb (Bulu)	Seed	22
	**Pachypodanthium confine*			
	Uvaria chamae	-	Leaf	18
	Uvariodendron spp.	-	Leaf	22
	Xylopia aethiopica	-	Leaf	45
	**Xylopia parviflora*,	-	Seed	18
	**Xylopia phloiodora*,	Poivre (French)	Seed	5
	**Xymolox monosperma*	-	Seed	18
		-	Leaf, stem bark	47
Anacardiaceae	*Amaranthus viridus Mangifera*	-	Leaf, stem bark	22
	caesia	-	Leaf, stem bark Leaf,	22
	**Mangifera indicus*	Mango	stem bark	14
	Spondias monbin slutea	-	Leaf	22
	Tricoscypha ferruginea	Amvut (Beti)	Leaf, stem bark	22
Apiaceae	*Centella asiatica*	-	Stem, leaves, roots	22
Apocynaceae	**Alstonia boonei*,	Ekuk (Ewondo)	Stem bark	2, 12, 46
	Alstonia congensis	Bokuka (Douala)	Leaf, stem bark	22
	Catharathus roseus	-	Roots,	21
	**Holarrhena floribunda*	-	Stem bark	24
	**Picralima nitida*	Ba'ab (Bakweri)	Root, stem bark, fruit	[2,7,
			rind, seed leaf.	16,
			Stem bark	25,27]
	Rauvolfia macrophylla	-	Stem bark	22
	Rauvolfia obscura	-	Stem bark	22
	**Rauvolfia vomitoria*	-		2, 54
	Tabernaemontanan crassa		Stem bark	

	Tabernaemontana penduliflora	Etoe (Ewondo)	Roots	22
	Voacanga africana	-	Stem bark	22
		Obeton (Bulu)		22
Asteraceae	*Acanthospermum hispidum*	-	Leaf	22
	**Ageratum conyzoides Aspilia africana*	King grass (SW)‡	Whole plant	2,38
	Bidens bipinata	-	Leaf, tops and stem bark	50
	**Bidens pilosa*	-	Stem bark,	22
	Conyza sumatrensis Emilia coccinea	Black jack (SW)‡	Leaf	2, 7
		-	Soft aerial parts	2
	Lagera alata Microglossa angolensis	Alo mvu (Ewondo)	Leaf	22
		-	Leaf	22
	Microglossa pyrifolia	-	Whole plant	38
	Spilanthes acmella	-	Aerial parts	2, 31
	Tithonia diversifolia	Ondondon si (Ewondo)	Leaf, flowers	22
	Triplotaxis stellulifera	Fleur jalousie (French)	Aerial parts	27
	Vernonia amygdalina	-	Leaf	22
	Vernonia conferta	Ndole (Batcham)	Leaf	2,12
		Abayak (Ewondo)	Fruit	22
Basellaceae	*Basella alba*	-	Leaf	2
Bignoniaceae	*Markhamia gellatiana*	-	Leaf	22
	Markhamia sessilis	-	Leaf	22
	**Spathodea campanulata*	-	Leaf, stem bark	6, 32
Bixaceae	*Bixa arellana*	-	Leaf	22
Bombacaceae	*Bombax flammeum*	-	Stem	22
Boraginaceae	*Chretia cymosa*	-	Leaf	22
Cannaceae	*Canna indica*	-	Stem, leaf	22
Capparidaceae	*Buchholzia coriacea Cadaba farinosa*	-	Leaf, seeds	2
		-	Leaf	21
	Cataeva adansonii	-	Stem,	22
	**Cleone rutidosperma*	-	Leaf	14
Caricaceae	**Carica papaya*	Paw paw or papaya (WC)‡	Leaf, pulp, rind, seed	2, 38
	Polycarpa glabrifolia	-	Leaf	22
Cleomaceae	*Cleome ciliata*	-	Stem bark	22
Clusiaceae	**Allanblackia monticola*	-	Stem bark	10
	Mammea africana	Abodzok (Ewondo)	Stem bark	22
Combretaceae	*Anogeius leiocarpus*	-	Leaf	22
	Combretum glutinosum	-	Leaf	22
	Combretum latialatum	-	Leaf	22
	Combretum micranthum	-	Leaf	22
	Combretum platysterum	-	Leaf	22
	Combretum spinesis	-	Leaf	22
	Guiera senegalensis	-	Leaf	22
	Terminalia ivorensis	-	Leaf	22
	Terminalia macroptera	-	Leaf	22
	**Terminalia superba*	Banga school (SW,NW)‡	Leaf	38
Commeliaceae	*Commelina benghalensis*	-	Leaf	22
	Palisota hirsuta	-	Leaf	22
	Pollia condensata	-	Leaf	22
Cucurbitaceae	**Momordica charantia*	-	Whole plant	38
	Momordica condensata	-	Leaf	22
Euphorbiaceae	**Alchornea cordifolia*	Aboué (Ewondo)	Young shoots, leaf	
			Leaf	11
	**Alchromaanes difformis,*			14
	**Antidesma laciniatum*	-	Leaf	
	Bridelia micrantha	-	Leaf	18

	**Euphorbia hirta*	-	Whole plant	22
	**Euphorbia poinsonni*	-	Leaf, stem bark	38
	**Mallotus oppositofolius*	-	Leaf	10
	Manihot esculenta	-	Leaf	14
	Manniophyton fulvum	-	Leaf	22
	**Neoboutonia velutina*	-	Leaf, stem bark	22
	**Phyllantus muellerianus*	-	Leaf, stem bark	44
	Ricinus cumunis	-	Leaf, seeds	10
		Ricin (French)		22
Fabaceae	**Cajanus cajan*	-	Roots, leaf	21
Hypericaceae	**Harungana madagascariensis*	-	Stem bark	22
	Psorosperuns febrifugum	-	Leaf	22
Labieae	*Lantana camara Mentha sylvestris*	-	Leaf	22
		-	Leaf	22
Loganiaceae (?)	**Strychnos icaja*	-	Root	26
Lamiaceae (Labiatae)	*Hoslundia opposita*,	-	Leaf, root bark	1
	**Ocimum gratissimum*	Masepu (SW)‡	Leaf	50
Lecythidaceae	*Napoleona vagelli*	-	Leaf	22
Leguminosae-Casesalpinoideae (Caesalpinaceae)	**Albisia zigia*	-	Leaf	2
	Cassia alata	Simgang (Bassa)	Stem bark, leaf and root	2,22
	Cassia hirsuta	-	Leaf	22
	Cassia occidentalis	-	Root	22
	Disthmonanthus benthamianus	Ngom (Ewondo)		
	Guibourtia tessmannii	-	Leaf	22
	Senna hirsuta	Lem (Bafang)	Stem bark, leaf	2, 22, 46
	Senna occidentalis	Bubinga (Ewondo)	Leaf	2
		-	Leaf	2
Leguminoceae-Papilionoideae	**Millettia griffoniana Milletia laurentii*	-	Leaf, stem bark	45
		-	Roots, leaf	22
	Melletia sanagana	-	Roots	2, 12
	Pennisetum purpureum	-	Leaf	22
	Pterocarpus soyauxii	-	Stem bark	22
Liliaceae	**Allium sativum*	-	Whole plant	28 43
Loganiaceae	*Anthocleista schweinfurthii*		Leaf	22
	Anthocleista vogellii	-		
		-	Stem bark	22
Malvaceae	*Gossypium spp.	Cotton	Cottonseed	22
	Hibiscus asper	-	Leaf	22
	Hibiscus tiliaceus	-	Leaf	22
	Sida acusa	-	Leaf	22
	Sida rhombifolia	-	Leaf	22
	Sida urens	-	Leaf	22
Meliaceae	*Azadirachta indica Cedrela odorata *Enthadrophragma angolense*	-	Leaves	22
		-	Leaves	22
	Hydrangea sp	-	Stem bark, leaf	15
	**Khaya grandifoliola*	-	Leaves	22
	**Khaya senegalensis Trichilia emetia*	-	Seed	17
		-	Leaf	38
	Trichilia gilletii	-	Leaves	22
	**Turreanthus africanus*	-	Leaves	22
		Mokwe (Bakweri)	seed	40
Meliantaceae	**Bersama engleriana*	-	Leaf	39
Menispermaceae	**Peniantus longifolius*	-	Stem bark	14 45
	Trichilisia gilletii	-	Leaf	22
Mimosaceae	**Cylicodiscus gabunensis*		Leaf, stem bark	22 38
	Tetrapleura tetraptera	-		

		-	Leaf	22
Monimiaceae	**Glossocalyx brevipes*	-	Leaf	35
Moraceae	**Ficus exasperata*	Keghawous (Oku)	Leaf	22
	**Ficus thonningii*	-	Leaf	44
	Milicia excelsa	Abang (Ewondo)	Leaf	22
	**Musa paradisiaca*	Plantain	Leaf	22
	Musa sapientum.	Odzoe (Ewondo)	Leaf	22
Myrtaceae	*Eucalyptus globulus*	Ntsedock (Bafang)	Leaf	22
	Eucalyptus grandis	Eucalyptus (French)	Leaf	22
	**Eucalyptus robusta*	-	Leaf, stem bark and fruit	53
	**Psidium guajava*	Guava tree (English) Afele (Ewondo)	Leaf, stem bark	41
	**Pycnanthus angolensis*	-	Leaf, stem bark	45
Nympheaceae	*Nymphea lotus*	-	Leaf	22
Ochnaceae	*Lophira alata*	-	Leaf	22
Arecaceae	*Cocos nucifera*	-	Leaf	22
Passifloraceae	*Passiflora foetida*	-	Leaf	22
Pentadiplandraceae	**Pentadiplandra brazzeana*	Liane blanche (French)	Leaf, stem bark	44
Piperaceae	**Piper nigrum*	-	Seed	14
	**Piper unbellatum.*	-	Leaf	14
	Peperomia pellucida	-	Leaf	34
	**Peperomia vulcanica*	-	Leaf	34
Poaceae (Gramineae)	**Cymbopogon citratus*	Fever grass (SW, NW)‡	Leaf	14 49
Polygonaceae	*Rumex abyssinia*	-	Leaf	2,
	Rumex abyssinicus	-	Leaf	22
Rubiaceae	*Cinchona calisaya*	-	Leaf	
	Cinchona ledgeriana	-	Leaf	22
	Cinchona succirubra	-	Leaf	22
	Coffea Arabica	-	Leaf	2, 22
	Crossopteryx febrifuga	-	Leaf	22
	Mitacarpus scaber Morinda	-	Leaf	22
	*confusa *Morinda lucida*	-	Leaf	22
	Mytragina ciliata Mytragina	-	Leaf, stem bark root bark	8
	stipulosa	-	Leaf	22
	**Schumanniophyton*	-	Leaf	22
	magnificum	-	Stem bark	16 22
Rutaceae	**Araliopsis tabuensis Citrus*	-	Stem bark	45
	limon	Citronier (French)	Roots, leaves Roots	22
	Citrus sinensis	-	Stem bark	2
	Fagara macrophylla	-	Fruit	22
	Zanthoxylum leprieurii,	-	Leaf, stem bark	2
	Zanthoxsylum lemarei	-		2
Sapindaceae	*Dedonaea viscosa*	-	Leaf	22
	Lecaniodiscus cupanoïdes	-	Root, Leaf	22
Scrophulariaceae	**Scoparia dulcis*	-	Whole plant	38
Simaroubaceae	*Brucea antidysanterica*	-	Roots, leaf	22
	Harrrisonia abyssinica	-	Roots, leaf	22
	**Odyendyea gabonensis*	Ozhèng (Ebolowa, S)‡	Leaf, stem bark	39 45
	Quassia africana	-	Roots, leaf	22
Ulmaceae	*Celtis cf. tessmannii Trama*	-	Leaf	22
	guineensis	-	Leaf	22
Verbenaceae	*Clerodendron scandens*	-	Leaf	22
	**Stachytapheta cayenensis*	-	Leaf	38

Vitaceae	*Cissus quadrangularis*	-	Leaf	22
Zingiberaceae	**Aframomum citratum*	Aligator pepper (SW, NW)‡	Fruit	38
	**Aframomum melegueta*	Ndong (Ewondo)	Fruit	2, 13
	**Aframomum latifolium*	-	Fruit	[2, 13 21
				[2, 13 2]
	**Aframomum sceptrum*	-	Fruit	
				[2, 13 30
	**Aframomum zambesiacum*			2, 13
		-	Fruit	14 48
	Costus dubius			34
	**Reneilmia cincinnata*	-	Fruit	
	Zingiber officinale	-	Fruit	
		-	Leaf	

* Plants species which have been scietifically investigated for antiplasomodial /antimalarial activity; the rest are still to be investigated

‡:- Region in Cameroon where name is used: SW – Southwest; WC –Whole of Cameroon; NW- Northwest; S- South

medicinal plants have been tested for their antimalarial activity, indicating that only a minority of the antimalarial plants has been validated. The development of new antimalarials from the highly active natural products, which have already been discovered, is crucial in order to overcome the increasing resistance of *Plasmodium* to available antimalarials. Therefore, there is a need to advance the work on plants which have already been shown to have antimalarial activity through further *in vitro* and *in vivo* testing in animal models of malaria followed by sub acute and chronic toxicity tests. This is likely to reveal suitable candidate molecules which may serve as leads which can be optimized followed by development into new antimalarials. This task will require capacity building in the various facets of such an approach, which capacity is inadequate at the moment

This strategy if pursued from drug discovery research on to preclinical followed by clinical studies will certainly yield the much desired highly efficacious and safe antimalarials.

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Table 2 Some medicinal plants tested for their antimalarial activity

Families	**Scientific name**	**Part(s) used**	**Mode of preparation**	**Extracts tested**	**Stage of validation**	**Ref.**
Annonaceae	*Annona muricana*	Leaves	Water decoction/oral	Methylene chloride/methanol (1:1)	ivt	(14
	Enantia clorantha	Leaves	Water decoction/ oral and infusion	Aqueous extract	ivv	(2) (3) (13
	Hexalobus crispiflorus	Leaves, seeds	Water decoction/ oral	Essential oils	ivt	(18
Anacardiaceae	*Mangifera indicus*	Leaves, roots	Water decoction/ oral and steam-bath	Methylene chloride/methanol	ivt	(14
Asteraceae	*Aspilia africana*	leaves, tops and stem bark	Water decoction/ steam bath	Methanol	ivt	(7)
	Tithonia diversifolia	Leaves	Water decoction/oral	Ether extract	ivt	(27
Caricaceae	*Carica papaya*	Rind, pulp	Water decoction/ oral	Petroleum ether		(10)
Combretaceae	*Terminalia superba*	Leaf	Water decoction/ oral	Methanol	ivt	(38)
Euphorbiaceae	*Alcronanes difformis*	Leaf	Water decoction/oral	Chloroform/methanol (1:1)	Ivt	(14)
Lamiaceae	*Hoslundia opposita*	Leaves, roots	Water decoction/ oral and steam-bath	Essential oil, hexane extract	(ivv)	(1)
Leguminoceae	*Millettia griffoniana*	Leaves and stem bark	Water decoction/ oral and steam-bath	Methylene chloride/methanol	ivt	(10)
Melianthaceae	*Bersama engleriana*	Leaves	Water decoction/ oral, infusion and steam-baths	Methylene chloride extract	ivt	(38), (47)
Rubiaceae	*Schumanniophyton magnificum*	Stem bark	Stem bark decoction	methanol and the water-ethanol extracts	ivt	(16)

Stage of validation: **ivt**: *in vitro inhibition assays using continuous P. falciparum culture;* **ivv**: *in vivo using animal models*; **ct**: clinical trials

Table 3: Some Phytochemicals isolated from Cameroon medicinal plants.

Families	Scientific name of the plant	Common names	Parts used	Mode of preparation	Extracts tested	Stage of validation	Phytochemicals isolated	Ref.
Annonaceae	*Xylopia parviflora*	Poivre de sedhion in French	Seeds	Water decoction/ oral and steam-baths	Essential oil	ivt	Diterpenes	(5)
Apocynaceae	*Holarrhena floribunda*		Stem bark	Water decoction/ oral and steam-baths	Aqueous and ethanol extracts	ivt	Lupeol, -3-(3'hydroxyeicosanoyl)lupeo, 3-O-(2'tetracosyloxy) acetyllupeol; 3 – O[(1''-hydroxyoctadecyloxy) 2-hydroxypropanoyl] lupeol.	(24)
	Picralima nitida	Ba'ab in Bakweri, Olape en Fang	Roots, stem bark, fruit rind, seeds and leaves.	Water decoction/ oral	Dichloromethane, aqueous, dichloromethane-methanol, methanol extracts	ivt	Akuammine	(2) (25) (29) (16)
Asteraceae	*Microglossa pyrifola*		Aerial parts	Oral water decoction, infusion	Petroleum ether/methanol 1:1	ivt	Sinapyl diangelate, 1-acetyl-6E, 10E, 14E geranylgeraniol-19-oic acid and 19-oxo-6E, 10E, 14-geranylgeraniol	(2) (31)
Clusiaceae	*Allanblackia monticola*		Stem bark	Water decoction /oral	Methanol extract	ivt	allanxanthone C, xanthones, garciniafuran, tovophyllin A, rubraxanthone, norcowanin and mangostin stigmasterol-3-O-beta-D-glucopyranoside	(9)
Euphorbiaceae	*Alchornea cordifolia*		Young shoots, leaves	Water decoction/ oral	methylene chloride / methanol (1:1)	ivt	Ellagic acid	(11)
Fabaceae	*Cajanus cajan*		Roots, leaves	Water decoction/ oral	methylene chloride / methanol (1:1)	ivt	Logistylin A and C and betulinic acid	(21)
Loganiaceae	*Strychnos icaja*		Roots	Water decoction/ oral and infusion	methylene chloride / methanol (1:1)	ivt	Vomicine, isostrychnine, isosungucine, 18-hydroxy-sungucine and 18-hydroxy-isosungucine	(26)

Liliaceae	*Allium sativum*		Whole plant	Water decoction/ oral, infusion	methylene chloride / methanol (1:1)	ct	Ajoene	(28) (41)
Malvaceae	*Gossypium spp.*	Cotton	seeds	Water decoction/ oral,	methylene chloride / methanol (1:1)	ivt	Gossypol	(44)
Menispermaceae	*Peniantus longifolius*		Stem bark	Water decoction/ oral	methylene chloride/methanol (1:1)	ivt	Palmatine and jatrorrhizine	(14) (45)
Rubiaceae	*Morinda lucida*		Leaves, stem bark and root bark	Water decoction/ oral, infusion and steam-baths	Petroleum ether	ivv	danacanthal	(8)
Rutaceae	*Araliopsis tabuensis*		Stem bark	Water decoction/ oral and steam-baths	methylene chloride / methanol (1:1)	ivt	araliopdimerine-A	(45)
Simaroubaceae	*Odyendyea gabonensis*		Leaves	Water decoction/ oral	aqueous, chloroform and hexane	ivt	Alanthinone, indole alkaloids, 11-hydroxycanthin-6-one, quassinoid ailanthinone	(38), (46)
Zingiberaceae	*Aframomum latifolium*		Fruit	Water decoction/ oral, infusion steam-baths	Hexane and Ethanol extract	ivt	(+) S – nerolidol, coranarin B, galanal A & B, galanolactone, (E) – 8 β, 17 – epoxylabd -12 – ene – 15, 16 dial, (E) labda – 8 (17), 12 – diene-15, 16 dial.	(2) (13) (20)
	Aframomum sceptrum		Fruit	Water decoction/ oral and steam-baths	Ethanol extract	ivt	(+) S – nerolidol, coranarin B, galanal A & B, galanolactone, (E) – 8 β, 17 – epoxylabd -12 – ene – 15, 16 dial, (E) labda – 8 (17), 12 – diene-15, 16 dial.	(2) (13) (20)
	Aframomum Zambesiacum		Fruits	Water decoction/ oral, infusion, enema and steam-baths	dichloromethane extract, methylene chloride extract	ivt	zambisiacolactone B	(2) (13) (30)
	Reneilmia cincinnata		Fruits	Water decoction/ oral and steam-baths	dichloromethane extract, methylene chloride extract	ivv	Sesquiterpenoids, Oplodiol, 1(10) E, 5E-germcradien-4α-ol and germacra-10 (14)-diene-1β-diol	(48)

Stage of validation: **ivt**: *in vitro inhibition assays using continuous P. falciparum culture;* **ivv**: *in vivo using animal models*; **ct**: clinical trial

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