A review of antimalarial plants used in traditional medicine in communities in Portuguese-Speaking countries: Brazil, Mozambique, Cape Verde, Guinea-Bissau, São Tomé and Príncipe and Angola

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The isolation of bioactive compounds from medicinal plants, based on traditional use or ethnomedical data, is a highly promising potential approach for identifying new and effective antimalarial drug candidates. The purpose of this review was to create a compilation of the phytochemical studies on medicinal plants used to treat malaria in traditional medicine from the Community of Portuguese-Speaking Countries (CPSC): Angola, Brazil, Cape Verde, Guinea-Bissau, Mozambique and São Tomé and Príncipe. In addition, this review aimed to show that there are several medicinal plants popularly used in these countries for which few scientific studies are available. The primary approach compared the antimalarial activity of native species used in each country with its extracts, fractions and isolated substances. In this context, data shown here could be a tool to help researchers from these regions establish a scientific and technical network on the subject for the CPSC where malaria is a public health problem.

Key words: antimalarial - medicinal plants - extracts - malaria - folk medicine

Malaria is a serious parasitic disease from tropical regions caused by a species of *Plasmodium* and transmitted by *Anopheles* mosquitoes. It is prevalent in approximately 100 countries in Africa, Southeast Asia and South America, where approximately 2.4 million people are at risk (Kager 2002). According to the World Malaria Report (WHO 2009a), there are approximately 250 million malaria cases and approximately one million people die from malaria each year.

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. Combination therapy has emerged as the best practical solution in overcoming the resistance of select strains. Therapeutics based on combinations with artemisinin and derivatives (ACTs), recommended by the World Health Organization (WHO), presently represent the most effective treatment of *P. falciparum* malaria infection (WHO 2008). Clinical resistance to these combinations has been recently reported in Cambodia (Noedl et al. 2008), suggesting that *P. falciparum* parasites have already developed the ability to grow in the presence of these antimalarials, which strongly suggests the need for further research into new antimalarials.

There is broad consensus on the urgent need for new, affordable and efficient compounds that could serve as primary molecules for antimalarial treatment. New highly-effective antimalarial drug candidates, based on new mechanisms of action or with new structures, are urgently needed to overcome the problem of rapid emergence of drug resistance and achieve long-term clinical efficacy.

Due to the crucial role that plant-derived compounds have played in drug discovery and development for the treatment of several diseases, the isolation of new bioactive compounds from medicinal plants based on traditional use or ethnomedical data appears to be a very promising approach (Newman 2008, Turschner & Efferth 2009).

There is a consensus among the scientific community that natural products have a dominant presence in discovering new leads for the development of drug treatment for human diseases. In fact, of the 877 novel medicines that were developed in the period between 1981-2002, 6% were natural products, 27% were derivatives of natural products and 16% were synthetics developed based on a natural product (Newman et al. 2003). At least 80% of the world population is estimated to be continuing use of such traditional medicines in primary health care, including 40,000-70,000 medicinal plants, approximately 20% of all higher-plant species (Verpoorte et al. 2006). In most cases, very little is known about the plants used in folk medicines.

Financial support: RIDES Malaria CPLP, CNPq, FAPEAM (to DFM) (PPP and PIPT projects), IFS (Sweden) (AF/18880), OPCW (Netherlands), CAPES-FCT (to JRAS and VER) (project 204/08)
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Received 25 March 2011
Accepted 26 July 2011

In malaria therapy, 11 drugs out of the antimalarials included in WHO therapeutic schemes for malaria treatment are natural products or their analogues or were design-based on the pharmacophores from natural products (Bourdy et al. 2008). The great significance of plant-derived drugs for the treatment of the disease is highlighted by quinine (derived from Cinchona tree), artemisinin (derived from Artemisia annua) and atovaquone (Malarone®), which is a synthetic compound (2-alkyl-3-hydroxynaphthoquinone) analogue of lapachol from the Tabebuia species (Bignoniaceae) (Oliveira et al. 2009).

This review was based on compilation of medicinal plants used in traditional medicine in the treatment of malaria infections in some countries of the Community of Portuguese-Speaking Countries (CPSC), which includes Angola, Brazil, Cape Verde, Guinea-Bissau, Mozambique and São Tomé and Príncipe (STP) and involved the comparison of popularly used native species and studies on the antimalarial activity of extracts, fractions and isolated substances.

The areas included in the CPSC are, to different degrees, developing nations where large fragments of the population have limited access to the National Health System. Consequently, these segments of the population use traditional medicine and their by products for therapy. This pattern is clearly observed in Africa. There is a large body of literature from studies in Africa, but they are from different time periods and, in some cases, references to malaria may be read as anti-fever. Due to the differences in methods, models or assays used, not all of the information is comparable. This review is intended to be useful for establishing networks aimed at training, data comparison, standardisation of techniques, incorporation of ethical issues into research and development activities and development of a website for the CPSC.

In this context, a selection of the botanical species used as antimalarials that are native to the CPSC is summarised, at the family level, in Fig. 1.

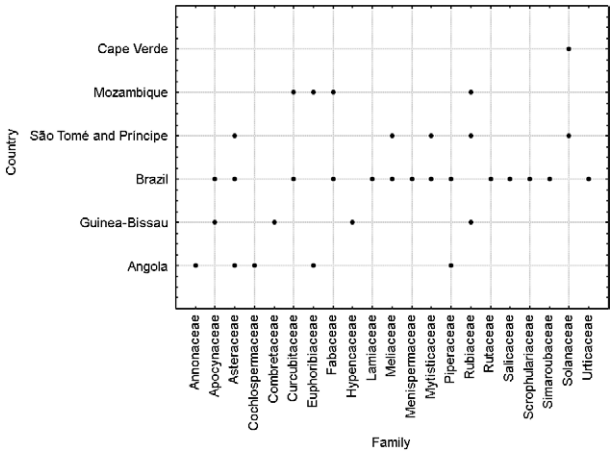

Fig. 1: distribution of plant families studied as antimalarial among Community of Portuguese-Speaking Countries.

Fig. 1 shows the correlation between 21 botanical families and the CPSC. Analysis of this figure indicates that seven families (Apocynaceae, Asteraceae, Cucurbitaceae, Fabaceae, Meliaceae, Myristicaceae and Piperaceae) have species commonly used by the CPSC to treat malaria. The Euphorbiaceae, Rubiaceae and Solanaceae families are represented by botanical species used primarily within African countries. Further, there are reports of other families of plants restricted to some countries: Angola (Annonaceae and Cochlospermaceae), Guinea-Bissau (Combretaceae and Hypencaceae) and Brazil have the most references to species belonging to the seven botanical families. Important correlations between each family, country, studied species, tested parts and scientific data from vitro and in vivo research are also provided in Table.

Brazil - In Brazil, malaria remains endemic in the Amazon, with a mortality of 58 patients out of 306,000 cases per year, largely due to late diagnosis, inadequate treatment or multidrug-resistant parasites. This acute disease presents with typical symptoms (e.g., headache and recurrent fever) and individuals affected by malaria in endemic areas often self-medicate with available antimalarial drugs or medicinal plants.

Three *Plasmodium* species occur in humans in Brazil: *P. falciparum*, the most deadly species; *Plasmodium vivax*, the most prevalent species, causing approximately 80% of the current cases, according to the Ministry of Health reports, and *Plasmodium malariae*, the least-prevalent species (Krettli et al. 2001).

There are several studies reporting exotic and native species used popularly in Brazil for the treatment of fever and malaria (Brandão et al. 1992, Milliken 1997, Oliveira et al. 2003, Botsaris 2007, Mariath et al. 2009). Other reviews have focused primarily on the in vitro antimalarial activity of alkaloids, discussing the different chemical classes and structure-activity relationship. Unfortunately, most of these compounds were not evaluated in vivo.

The application of ethnopharmacology in selecting plants with antimalarial uses represents a reasonable approach for identifying new drugs. In fact, in vivo pharmacological evaluation of 22 plants used by popular medicine in Brazil identified four plant species with activity against *Plasmodium berghei* in mice. The active plants were: *Esenbeckia febrifuga* (Rutaceae), *Lisianthus speciosus* (Gentianaceae), *Acanthospermum australe* (Compositae) and *Tachia guyanensis* (Gentianaceae) (Brandão et al. 1992). Among the 273 species tested based on random selection, only two, which represents 0.7%, exhibited activity: *Vernonia brasiliana* (Compositae) and *Eupatorium squalidum* (Compositae) (Brandão et al. 1992). In another study, 204 extracts were tested from Brazilian Cerrado plants, of which 32 (15.7%) showed significant parasite growth inhibition at 10 µg/mL. The most active families exhibited IC_{50} values ranging from 0.9 µg/mL (Flacourtiaceae and Sapindaceae) to 4.9 µg/mL (Apocynaceae and Annonaceae) (de Mesquita et al. 2007).

Extracts and active compounds from native species in Brazil that exhibited antimalarial activity are shown in Table. The most active species used in different Brazilian regions are described below.

Bidens pilosa (Asteraceae), popularly known as *picão* and *picão preto* in Brazil, is a species with extensive ethnopharmacological use (de Andrade-Neto et al. 2004). The popular use as an antimalarial was substantiated the crude ethanol extract of the whole plant, leaves and roots at concentrations of 25-50 µg/mL. Pharmacological activity was attributed to the presence of polyacetylene and flavonoids (Brandão et al. 1997), which was reinforced by data from Oliveira et al. (2004) correlating these substances with in vivo antimalarial activity.

A recent review on *Ampelozizyphus amazonicus* (Rhamnaceae), popularly called as *cervejeira*, *cerveja de índio*, *saracura*, *curupira-mirá* and *saracura-mirá*, summarised the importance of this native species as an antimalarial in endemic areas (Amaral et al. 2008). Although the prophylactic activity of the crude ethanol extract from the roots of this plant has been proven (Krettli et al. 2001, de Andrade-Neto et al. 2008), the mechanism of action and the active substances of *A. amazonicus* have not yet been identified.

Some botanical species used in folk phytotherapy in Brazil against malaria are known as *quinas*, for example, *Deianira erubescens*, *Strychnos pseudoquina* and *Remijia ferruginea* (de Andrade-Neto et al. 2003). In this context, ethanol extract from *R. ferruginea* (Rubiaceae) bark, popularly known as *quina-da-serra* or *quina-do-Brasil*, when evaluated against *P. berghei*, caused inhibition of up to 48% of parasite growth at a dose of 1,000 mg/kg but exhibited only minimal activity at the lower dose of 500 mg/kg (de Andrade-Neto et al. 2003).

Casearia sylvestris (Flacourtiaceae) is a plant popularly known as *guaçatonga* and antiplasmodial activity was found with extracts of different parts of this plant, with IC_{50} values ranging from 0.9 (stem wood) to 2.3 µg/mL (root wood) (de Mesquita et al. 2007).

The *Virola surinamensis* tree frequently grows on Amazonian riverbanks and is used in folk medicine for a variety of ailments. The *Waiãpi* Indians treat malaria with this species by inhalation of vapour prepared from leaves of the plant. The essential oil of the leaves (100 µg/mL) causes 100% inhibition in growth from the young trophozoite to schizont development stages and the sesquiterpenoid nerolidol (half of the oil dose) was identified as one of the active compounds (Lopes et al. 1999).

Mozambique - In Mozambique, malaria is the leading cause of morbidity and mortality, accounting for a third of all hospital deaths (USAID 2009). It is estimated that approximately 44,000-67,000 deaths are attributable to malaria each year (MH 2003). Approximately 9.8 million malaria cases were reported in 2006 (WHO 2009b).

Disease transmission is stable and the presence of the disease is endemic throughout the country due to unaffordable preventive means, favourable temperatures and rain patterns, abundant breeding sites and poverty-related improper housing (Mabunda 2006).

This high prevalence of CQ-resistant (CQR) *P. falciparum* strains has been reported throughout most of the territory (Mayor et al. 2001). Therapeutic regimens for the treatment of uncomplicated *P. falciparum* infections were changed in 2002 to the combination of S/P + amodiaquine and in 2004 were further altered to S/P + artesunate, in line with current WHO recommendations for the use of ACT's (WHO 2006).

In Mozambique, medicinal plants play a key role in basic healthcare (e.g., Verzar & Petri 1987, Jansen & Mendes 1991). Approximately 5,500 identified plant species are used in traditional medicine, representing more than 500 plant species (WCMC 1992).

The predominant plant species used in traditional medicine for the treatment of malaria infections as reported by Bandeira et al. (2001) were *Acacia karroo* Hayne, *Acacia nilotica*, *Senna abbreviata*, *Adansonia digitata*, *Alepidea amatymbica*, *Bridelia cathartica*, *Crossopteryx febrifuga*, *Euclea natalensis*, *Lippia javanica*, *Momordica balsamina*, *Rauwolfia caffra*, *Salacia kraussii*, *Senna occidentalis*, *Spirostachys africana*, *Tabenaemontana elegans*, *Trichilia emetic* and *Zanthoxylum capense*.

M. balsamina is used to cure vomiting with bile and fever, while *S. africana* is used as a therapeutic for headaches. *R. caffra*, which contains alkaloids, is used to treat malaria (van Wyk et al. 1997). *B. cathartica* is commonly used in southern Mozambique to heal malarial headaches. In Mozambique, a mixture of eucalyptus leaves, avocado and guava is traditionally used to treat bone articulation pain associated with malaria (Kolawole & Adesoye 2010).

In Central Africa, *C. febrifuga* root and bark have been used as febrifuge and an antipruritic lotion, respectively. In tropical Africa, the bark is used for fever, malaria, diarrhoea, colic, intestinal worms and application to wounds. This plant is also used for the treatment of syphilitic ulcers and the leaves are used for eye inflammation in neighbouring Tanzania (Maiga et al. 2006).

Although there is a long history of medicinal plant use in Mozambique, research related to the pharmacological evaluation and scientific validation of traditional practices is still very limited, generally covering only ethnobotanical aspects (e.g., Jansen & Mendes 1990, 1991).

Most studies on the pharmacological activity of plants used by traditional medicine in Mozambique have been conducted with specimens collected in other regions and the obtained results are only indicative because the activity of each plant depends on the region in which it grows or is cultivated (Table).

Results obtained by Ramalhete et al. (2008), with material collected in Mozambique, showed significant antiplasmodial activity for the ethyl acetate extract from aerial parts of *M. balsamina* (1.0 µg/mL) and for the hexane extract from leaves of *S. occidentalis* (19.3 µg/mL). Another group observed that ethanol extracts from the leaves of *S. occidentalis* had high in vitro antimalarial activity against a *P. falciparum* CQ-sensitive strain (< 3 µg/mL) (Tona et al. 2004). Interesting in vitro antimalarial activity was also found by Jurg et al. (1991) for crude root ethanol and aqueous extracts and stem ethanol extract of *B. cathartica* at a concentration of 0.05 µg/mL.

Previous studies on the in vitro antimalarial activity of aqueous extracts of leaves and roots from *S. abbreviata* demonstrated weak activity against *P. falciparum* (Connelly et al. 1996). However, extract from leaves of

TABLE

In vitro and in vivo antimalarial studies of extracts and substances from species used in Community of Portuguese-Speaking Countries

Plants species	Country	Parts tested	Sample	In vitro activity (IC_{50}) *Plasmodium falciparum*	In vivo in mice *Plasmodium berghei*	References
Annonaceae						
Hexalobus crispiflorus A. Rich	Angola	Stem bark	Essential oil (rich in sesquiterpenes)	2.0 µg/mL (W2)	-	Boyom et al. (2003)
Pachypodantium confine Engler and Diels	Angola	Stem bark	Essential oil (rich in sesquiterpenes)	16.6 µg/mL (W2)	-	Boyom et al. (2003)
Apocynaceae						
Aspidosperma vargasii A. DC.	Brazil	Barks	Ellipticine	73 nM	-	de Andrade-Neto et al. (2007)
Aspidosperma desmanthum Benth. Ex Müll. Arg.	Brazil	Barks	Aspidocarpine	19 nM	-	de Andrade-Neto et al. (2007)
Cryptolepis sanguinolenta (Lindl.) Schltr.	Guinea-Bissau	Leaves, roots	Cryptolepinoic acid	3.7 µM (K1)	-	Boye and Ampofo (1983)
			Cryptolepine	0.23 µM (K1)	-	Boye (1989)
				0.059 µM (T9/96)		Noamesi et al. (1991)
			Cryptoheptine	0.8 µM (K1)	-	Kirby and Paine (1995)
				1.2 µM (T9/96)		Wright et al. (1996, 2001),
			Ethanol and dichlorome-thane extracts	-	ED50 < 100 mg/kg per day	Paulo et al. (2000)
Geissospermum sericeum Benth. & Hook. f. ex Miers	Brazil	Bark	Hydroalcohol extract	1.78 µM	-	Steele et al. (2002)
			Flavopereirine	11.53 µM (K1)		
				1.83 µM (T9-96)		
			1,2-dehydrogeissoschizoline	27.26 µM (K1)		
				35.37 µM (T9-96)		
Peschiera fuchsiaefolia (A. DC.) Miers	Brazil	Stem bark, root bark	Alkaloid extract (stem bark)	495 ng/mL	-	Federici et al. (2000) Kaur et al. (2009)
			Alkaloid extract (root bark)	179 ng/mL		
			Voacamine	238 ng/mL		
Asteraceae						
Acanthospermum australe (Loefl.) Kuntze	Brazil	Whole plants	Aqueous extract	-	40% growth inhibition G1	Carvalho and Krettli (1991)

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Plants species	Country	Parts tested	Sample	In vitro activity (IC_{50}) *Plasmodium falciparum*	In vivo in mice *Plasmodium berghei*	References
Ageratum conyzoides L.	São Tomé and Príncipe	Aerial parts, leaves	Dichloromethane fraction	55 µg/mL (Dd2-CQ resistant)	-	Madureira et al. (2002b) Chenniappan and Kadarkarai (2010) Ukwe et al. (2010)
			Cyclohexane extract	12.08 µg/mL (MRC-Pf-43 P-CQ resistant)	-	
			Aqueous extract	-	400 mg/kg chemosuppression of 89.87%	
Artemisia gorgonum Webb	Cape Verde	Aerial parts	Essential oil	5.2 µg/mL	-	Ortet et al. (2010)
			Ridentin	3.8 µg/mL (FcB1)		
Bidens pilosa L.	Brazil	Whole plant	Ehanol extract	50 ug/mL	-	Brandão et al. (1997)
			Ethanol extract	-	250 mg/Kg - 36% GI	Oliveira et al. (2004)
Struchium sparganophorum (L.) Kuntze	São Tomé and Príncipe	Leaves	Petroleum ether fraction	< 10 µg/mL (Dd2)	-	Madureira et al. (2002b)
Tithonia diversifolia (Hemsl.) A. Gray	São Tomé and Príncipe	Aerial parts	Ethanol extract	15 µg/mL (Dd2)	-	Goffin et al. (2002)
			Petroleum ether fraction and dichloromethane fraction	< 10 µg/mL (Dd2)		Madureira et al. (2002b)
			Ether extract 0.75 µg/mL (FCA CQ-sensitive)	-		
			Tagitinin C 0.33 µg/mL (FCA)	-		
Vernonia amygdalina Delile	Angola, São Tomé and Príncipe	Leaves	Ethyl acetate fraction	< 10 µg/mL (Dd2)	-	Masaba (2000)
			Dichloromethane fraction	< 80 µg/mL (Dd2)	-	Madureira et al. (2002b)
			Acetone-water extract	25.5 µg/mL (CQ-sensitive)	-	Iwalokun (2008)
			Ethanol extract	19 µg/mL (Dd2)	-	
			Combination of CQ (5mg/) with 31.25, 62.5, 125mg/kg bw doses of leaves extract	-	72.7% GI	
Vernonia brasiliana (L.) Druce	Brazil	Leaves	Hexane extract	100 µg/mL	-	Alves et al. (1997)
			Lupeol	25 µg/mL	-	
			Hexane extract	-	1,000 mg/kg (45% growth inhibition)	

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Plants species	Country	Parts tested	Sample	In vitro activity (IC_{50}) *Plasmodium falciparum*	In vivo in mice *Plasmodium berghei*	References
Cochlospermaceae						
Cochlospermum tinctorium A. Rich.	Guinea-Bissau	Tubercles	Aqueous extract	1-2 µg/mL	-	Benoit et al. (1995)
Combretaceae						
Guiera senegalensis J.F. Gmel.	Guinea-Bissau	Roots	Harman and tetrahydroharman	< 4µg/mL	-	Ancolio et al. (2002) Azas et al. (2002)
Cucurbitaceae						
Cucurbita maxima Duch.	Brazil	Seeds	Ethanol extract	-	250 and 500 mg/kg - 50% GI	Amorim et al. (1991)
Momordica balsamina L.	Mozambique	Aerial parts	Balsaminoside A Karavilagenin E Balsaminoside A Karavilagenin E	4.6 µM (3D7) 7.4 µM (3D7) 4.0 µM (Dd2) 8.2 µM (Dd2)	-	Ramalhete et al. (2010)
Euphorbiaceae						
Bridelia cathartica Bertol. f.	Mozambique	Roots, stem	Ethanol and aqueous extracts	0.05 µg/mL	-	Jurg et al. (1991) Tona et al. (2004)
Bridelia ferruginea Benth.	Mozambique, Angola	Barks	Methanol extract	-	400 mg/Kg/body weight (bw) - 100% GI	Kolawole and Adesoye (2010)
Euphorbia hirta L.	Angola	Whole plant	Ethanol and dichloromethane extracts	60% inhibition	-	Tona et al. (1999)
			EtOH extract	-	~100 mg/kg per day	
			CH_2Cl_2 extract	-	> 100 mg/kg per day	
Fabaceae						
Andira inermis (W. Wright) Kunth	Brazil	Stem barks, leaves	Leaves lipophilic extract	56 µg/mL (poW) 58.6 µg/mL (Dd2)	-	Kraft et al. (2000)
			Stem bark lipophilic extract	52 µg/mL (poW) 108.7 µg/mL (Dd2)	-	
			Calycosin	4.2 µg/mL (poW) 2.0 µg/mL (Dd2)	-	
			Genistein	9.8 µg/mL (poW) 4.1 µg/mL (Dd2)	-	
Senna abbreviata Oliv.	Mozambique	Leaves	Aqueous ethanol (80%) extracts	-	111.0 mg/kg/wt	Connelly et al. (1996) Innocent et al. (2009)

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Plants species	Country	Parts tested	Sample	In vitro activity (IC_{50}) *Plasmodium falciparum*	In vivo in mice *Plasmodium berghei*	References
Senna occidentalis Linn.	Brazil, Mozambique	Leaves	Ethanol extract	(IC_{50} < 3 µg/mL) (CQ-sensitive)	-	Tona et al. (2004) Ramalhete et al. (2008)
			Hexane extract	19.3 µg/mL	-	
Hypencaceae						
Harungana madagascarien-sis Lam. Ex Poir.	Guinea-Bissau	Roots	MeOH-CH2Cl2 (1:1) root bark extract	25.12 µg/mL (W2)	-	Ancolio et al. (2002) Lenta et al. (2007)
			Bazouanthrone	1.80 µM (W2)	-	
			Ferruginin A	5.00 µM (W2)	-	
			Harunganin	2.70 µM (W2)	-	
			Harunganol A	3.70 µM (W2)	-	
			Harunganol B	3.70 µM (W2)	-	
			Friedelan-3-one	7.70 µM (W2)	-	
			Betulinic acid	5.10 µM (W2)	-	
Lamiaceae						
Ocimum gratissimum L.	Brazil	Leaves	Essential oil	-	200, 300 and 500 mg/kg 55-77.8% GI	Kaur et al. (2009)
Meliaceae						
Cedrela odorata L.	Brazil, São Tomé and Principe	Wood, leaves, stem barks	Ethanol extract	1.37 µg/mL (D6) 1.25µg /mL (W2)	-	Bray et al. (1990) MacKinnon et al. (1997)
			Dichloromethane fraction	50 µg/mL (Dd2 – CQ resistant)	-	Madureira et al. (2002b)
			Gedunin	0.72 µg/mL	-	
			Crude extracts	-	1,000 mg/kg/day - 73% GI	
Menispermaceae						
Abuta grandifolia (Mart.) Sandwith	Brazil	Leaves, barks	Alkaloid extract	< 1 µg/mL	-	Steele et al. (1999)
			Krukovine	0.44 µg/mL (K1-CQ resistant) 0.022 µg/mL (T9-96-CQ sensitive)	-	Garavito et al. (2006)
			Limacine	1.35 µg/mL (K1-CQ resistant)	-	
			Alkaloid extract	-	250 mg/kg/day - 66% GI	

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Plants species	Country	Parts tested	Sample	In vitro activity (IC_{50}) *Plasmodium falciparum*	In vivo in mice *Plasmodium berghei*	References
Myristicaceae						
Pycnanthus angolensis (Welw.) Warb.	São Tomé and Principe	Barks	Ethanol extract	< 5µg/mL (Dd2)	-	Madureira et al. (2002b)
			Dichloromethane extract	1.6 µg/mL (Dd2)	-	Abrantes et al. (2008)
Virola surinamensis (Rol. ex Rottb.) Warb	Brazil	Leaves	Essential oil (rich in nerolidol)	100 µg/mL = 100% GI	-	Lopes et al. (1999)
Piperaceae						
Piper umbellatum L.	Angola, Brazil and Mozambique	Leaves, stems	Ethanol extract	3.74 µg/mL (K1)	-	Roersch (2010)
			4-nerolidylcatechol	0.67 nM (K1)	-	
			Ethanol extract	-	250-1,250 mg/kg orally and 100-250 mg/kg subcutaneously - significant reduction of the parasitemia	
Pothomorphe peltata (L.) Miq.	Brazil	Leaves, roots	Hydroalcohol extract	3.74 µg/mL	-	Amorim et al. (1986, 1988)
			4-nerolidylcatechol	0.67 µM	-	de Andrade-Neto et al. (2007)
Rhamanaceae						
Ampelozizyphus amazonicus Ducke	Brazil	Roots	Ethanol extract	-	100 µg/mL 90% GI	Krettli et al. (2001)
					50 µg/mL 75% GI	de Andrade-Neto et al. (2008)
Rubiaceae						
Crossopteryx febrifuga (Afzel. ex G. Don) Benth.	Mozambique	Stem bark	Crude alkaloids	$4 < IC_{50} < 10$ (W2)	-	Elufioye and Agbedahunsi (2004)
			MeOH extract	IC_{50} >10 (W2)	-	
			Ethanol extract	-	31.94-70.97% suppression	
Morinda lucida Benth.	São Tomé and Principe	Barks, leaves, stem bark, roots	Ethanol extract	< 10 µg/mL (Dd2)	-	Koumaglo et al. (1992)
			Digitolutein	12.92 µg/mL	-	Madureira et al. (2002b)
			Rubiadin 1-methyl ether	8.10 µg/mL	-	
			Damnacanthal	9.20 µg/mL	-	
Remijia ferruginea (A. St.-Hil.) DC.	Brazil	Barks	Ethanol extract	-	1,000 mg/kg - 48% GI	de Andrade-Neto et al. (2003)
Sarcocephalus latifolius (Sm.) Bruce	Guinea-Bissau	Roots, stem bark, leaves, root	MeOH, MeOH/H_2O,	>50 µg/mL (W2)	-	Abreu and Pereira (2001)
			H_2O extracts	>125 µg/mL (K562S)		Gansané et al. (2010)
			CH_2Cl_2	>50 µg/mL (W2)	-	
				52.9 µg/mL (K562S)		
			Crude alkaloids	>50 µg/mL (W2) 90.2 µg/mL (K562S)	-	
			Strictosamide	moderate antimalarial activity	-	

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Plants species	Country	Parts tested	Sample	In vitro activity (IC_{50}) *Plasmodium falciparum*	In vivo in mice *Plasmodium berghei*	References
Rutaceae						
Esenbeckia febrifuga (A. St.-Hil.) A. Juss. ex Mart.	Brazil	Stem	Ethanol extract	15.5 µM (W2) 21.0 µM (3D7)	-	Dolabela et al. (2008)
			Skimmiamine	75.3 µM (W2)	-	
			γ-fagarine	109.8 µM (3D7)	-	
Salicaceae						
Casearia sylvestris var. *lingua* (Cambess.) Eichler	Brazil	Stem bark, roots	Hexane extract	0.9 µg/mL (stem wood) 2.3 µg/mL (root wood)	-	de Mesquita et al. (2007)
Scrophulariaceae						
Scoparia dulcis L.	Brazil	Aerial parts	(-)-Scopadulcic acid A	27.0 (D6) 19.0 µM (W2)	-	Riel et al. (2002)
Simaroubaceae						
Picrolemma sprucei Hook. f.	Brazil	Roots, stems	Aqueous extract	1.43 µg/mL	-	Bertani et al. (2005), de Andrade-Neto et al. (2007), Gansané et al. (2010)
			Neosergeolid	2.0 nM (K1)	-	
			Aqueous extract	-	95 mg/kg -78% GI	
Solanaceae						
Cestrum laevigatum var. puberuleum Sendtn.	São Tomé and Principe	Leaves	Dichloromethane fraction	50 µg/mL (Dd2 – CQ resistant)	-	Madureira et al. (2002b)
Urticaceae						
Cecropia pachystachya Trécul	Brazil	Leaves, wood, stem bark, roots	Tormentic acid	12.5 µg/mL (W2 – CQ-resistant)	-	Uchôa et al. (2010)
			Ethanol extract	-	250 mg kg^{-1} - 66% GI	
			Tormentic Acid	-	15 mg/kg -58% GI	
			β-sitosterol	-	51% GI	

CQ: chloroquine; Dd2: chloroquine-resistant *P. falciparum* strain; D6: chloroquine-resistant *P. falciparum* strain; ED50: median effective dose; FcB1: chloroquine-resistant *P. falciparum* strain; GI: growth inhibition; K1: chloroquine-resistant *P. falciparum* strain; K562S: human monocyte cell lines; MRC-Pf-43 P: chloroquine-resistant *P. falciparum* strain; poW: chloroquine-sensitive *P. falciparum* strain; T9/96: chloroquine-sensitive *P. falciparum* strain; W2: chloroquine-sensitive *P. falciparum* strain; 3D7: chloroquine-sensitive *P. falciparum* strain.

S. abbreviata was associated with in vivo antimalarial activity and these results support the traditional use of this species (Innocent et al. 2009). Of the other species of this genus, *S. occidentalis* is very common and widely distributed around the world. Ethanol extracts from leaves of this species showed a high in vitro antimalarial activity (< 3 µg/mL).

The in vitro antimalarial activity of methanol and alkaloid-rich extracts of *C. febrifuga* showed this plant's promise as the source of a malaria treatment (Sanon et al. 2003), which was confirmed in subsequent in vivo assays. The stem bark ethanol extract of *C. febrifuga* was investigated against malaria infections in vivo and the suppression of parasitaemia at the highest dose (400 mg/kg) was similar to CQ at 5 mg/kg and pyrimethamine at 1.2 mg/kg (Elufioye & Agbedahunsi 2004).

Cape Verde - In Cape Verde, malaria is primarily limited to the island of Santiago, with a very low prevalence of approximately 20-40 cases occurring annually. Generally, transmission occurs from September-November (WHO 2011). Malaria has been almost eradicated from the archipelago of Cape Verde (West Africa) following a sustained control programme between 1940-1970. In addition, malaria is considered to be in a pre-elimination phase in the islands and malaria prophylaxis is not recommended for tourists.

Climatic factors and topography are particularly reflected in the diversity of vegetation (Gomes et al. 2008). Medicinal plants are notably helpful in alleviating malaria symptoms such as fever, vomiting and diarrhoea.

Withania chevalieri is a shrub endemic to Cape Verde commonly used by local healers for malaria treatment (Gomes et al. 2008). *Artemisia annua* is one of the most important species used to treat malaria and several studies in search of other active compounds have been conducted with species of this genus. For example, *Artemisia gorgonum* volatile oil exhibited mild antiplasmodial activity in vitro (5.2 µg/mL) (Table) and this activity was due, at least in part, to a sesquiterpene lactone, arborescin (2% in the volatile oil), which was previously reported to inhibit the growth of *P. falciparum*. The leaves and flowers of *A. gorgonum* were investigated phytochemically and resulted in the isolation of approximately 14 compounds. Most of these compounds exhibited mild antimalarial activities and a sesquiterpene lactone, ridentin, was the most interesting with IC_{50} value of 3.8 µg/mL against *P. falciparum* (Ortet et al. 2008).

Guinea-Bissau - In Guinea-Bissau, 1,575 people were infected with malaria in 2008 (WHO 2008). The prevalence of malaria in the community is low. In 1990, a survey of children two-nine years old in rural Guinea-Bissau showed that *P. falciparum* was the most prevalent parasite (Jaenson et al. 1994).

CQR *P. falciparum* was first reported in Guinea-Bissau in 1990 (Hellgren et al. 1991). Since then, *Plasmodium* resistance has been monitored annually and results have indicated stability in the level of CQR parasites, despite the continued widespread use of CQ (Ursing et al. 2007).

In 2006, the malaria treatment policy in Guinea-Bissau was changed to artemether-lumefantrine as the first-line treatment of uncomplicated malaria. In practice, CQ is still used widely, with S/P as the second choice. In vivo studies have shown moderate but stable efficacy of CQ over the years (Kofoed et al. 2002, Rodrigues et al. 2008).

In 2006, a survey was conducted in Guinea-Bissau to contribute to the knowledge of medicinal plants of the country, and ethnopharmacological information on 150 plants used as medicine was assembled. Out of these 150 plants, Diniz et al. (2000) described 25 species with their vernacular names and uses in traditional medicine for the treatment of several diseases. In this list, only three medicinal plants are traditionally used in malaria treatment. Gomes et al. (2003) reported only six plants species used in ethnomedicine in Guinea-Bissau to treat malaria: *Sarcocephalus latifolius*, *Lippia chevalieri*, *Guiera senegalensis*, *Gardenia ternifolia*, *Piliostigma thonningi* and *Harungana madagascariensis*. Diniz et al. (2008) reported the use of *Zanthoxylum leprieuri*, *S. latifolius* and *Cryptolepis sanguinolenta* in malaria treatment. Out of the known plants used in traditional medicine in Guinea-Bissau, only *C. sanguinolenta* and *Cochlospermum tinctorium* were collected in the country and tested. There have been no studies with the other known medicinal plants used in Guinea-Bissau, as has been reported for other countries in Africa. Several studies were conducted with botanical species collected in different regions, thus preventing scientific validation of their use in traditional medicine in Guinea-Bissau.

Data presented below and in Table demonstrated the usefulness of some species as antimalarials in other endemic areas and the importance of testing to validate their traditional uses.

C. sanguinolenta is rich in indoloquinoline alkaloids. Crytoplepine, the predominant and the most studied alkaloid, has potent in vitro antimalarial activity (Noamesi et al. 1991, Kirby & Paine 1995, Wright et al. 1996, 2001, Cimanga et al. 1997) and action similar to CQ (Onyeibor et al. 2005).

The roots of *C. tinctorium*, traditionally called *Djánderé* in Guinea-Bissau (Bouquet 1968), are used in the treatment of liver diseases and malaria infection (Gomes et al. 2003). Benoit et al. (1995) performed in vitro assays with sensitive and resistant *P. falciparum* strains and established *C. tinctorium* antimalarial activity. Other studies of the extracts and essential oils prepared from leaves of this species of *C. tinctorium* also exhibited antiplasmodial activity (Benoit-Vical et al. 1999).

The indole alkaloid, strictosamide, was isolated from the root extract of *S. latifolius* and displayed moderate in vitro antimalarial activity against *P. falciparum* (Abreu & Pereira 2001). The evaluation of in vitro antimalarial activity of extracts from leaves showed that it was inactive against W2 strains with an IC_{50} value greater than 50 µg/mL (Gansané et al. 2010).

G. senegalensis has been used in the treatment of acute gastroenteritis and dysentery and as an antimalarial agent (Etkins & Ross 1982, Etkins 1988). Chloroform extract of *G. senegalensis* roots exhibited pronounced antimalarial activity, although fractions obtained from

this extract did not exhibit a significant increase in antimalarial activity compared with the crude extract. Two alkaloids isolated from the active extract of *G. senegalensis*, harman and tetrahydroharman, showed antimalarial activity (< 4 μg/mL) (Ancolio et al. 2002) and the latter did not present cytotoxicity and genotoxicity in the *Salmonella* Ames test (Azas et al. 2002).

An interesting in vitro synergistic antimalarial effect observed among compounds and extracts obtained from three plants commonly used as traditional remedies has been well demonstrated. *Mitragyna inermis* (total alkaloids + ursolic acid), *Nauclea latifolia* (total alkaloids) and *Feretia apodanthera* (methanol fraction) together with *G. senegalensis* (harman + tetrahydroharman) in different associations showed synergism. These combinations showed a strong and synergistic inhibitory effect in vitro (Azas et al. 2002). This work suggests that these associations can be considered good candidates for antimalarial combination therapy.

The leaves and stem bark of *H. madagascariensis* are used in ethnomedicine for the treatment of anaemia. The stem bark is also employed for nephrosis, malaria, gastrointestinal disorders and fever (Iwalewa et al. 2008). The stem bark ethanol extract showed significant antimalarial activity (0.517 μg/mL, CQ reference drug), thus indicating their positive role and justifying the use of this species in traditional medicine (Iwalewa et al. 2008).

The quinones bazouanthrone, harunganin, harunganol A, harunganol B and the terpenes feruginin A, friedelan-3-one and betulinic acid have been isolated from the root bark of this species of *H. madagascariensis* and they have shown in vitro antimalarial activity against the W2 strain of *P. falciparum*, of which bazouanthrone (IC_{50} of 1.80 mM) was the most active (Lenta et al. 2007).

STP - Malaria has long been a problem in STP, which stresses the health systems and hampers the economic development of the country (Teklehaimanot et al. 2009).

According to Martet et al. (1991), "Malaria has existed for a very long time on the archipelago. It is characterised by a permanent transmission with seasonal outbreaks that correspond with the end of the rainy season and the start of the dry one (April-May). Another slightly smaller peak occurs from November-December. Transmission decreases with altitude: above 300 m of altitude the bio-ecology of the main vector (*Anopheles gambiae*) and the drop in the density of the human population cause the transmission to decline.". Although all four species of *Plasmodium* have been detected, (Ceita 1986, Martet et al. 1991, Loureiro et al. 1996, Baptista et al. 1997, Lopes et al. 2002), *P. falciparum* predominates with prevalence rates exceeding 70% in some districts before the recent intensification (Pinto et al. 2000a). *An. gambiae* s.s. is the only malaria vector in the country (Pinto et al. 2000b).

In 2005, the National Centre of Endemic Diseases drafted a national malaria control strategy, which produced a rapid decline in malaria morbidity and mortality on the island of Príncipe. Confirmed malaria cases decreased from the annual average of 38,655 during 2000-2005 to 3,893 cases in 2009 (90% decline). In the same period, malaria admissions fell from an annual average of 12,367 to 1,514 in 2009 (88% decline) and malaria deaths also fell from 23 to 16. However, in 2009, the number of confirmed malaria cases increased from 1,647 to 3,893, a 140% increase since 2008 (WHO 2010). Malaria-related admissions rose from 850-950 (up 44%) and malaria-related deaths increased from 16 to 23 (up 44%). The reasons for this resurgence may be linked to the absence of indoor residual spraying (IRS), which was not implemented during 2008. Once the increase in cases was detected by the surveillance system, emergency IRS was implemented and malaria cases decreased during the second half of 2009 (WHO 2010).

On these islands, a large number of medicinal plants have been used for centuries by traditional medicine and there are many places where western medicine is practically nonexistent, if not nonexistent. There are few ethnobotanical records of the flora of STP, and those that exist are quite restricted (Madureira 2008).

Roseira (2004) compiled one of the few existing ethnobotanical records of the Santomean flora. Sequeira (1994) published an article about the uses of 53 medicinal plants.

Between 1993-2001, an extensive ethnopharmacology study was conducted, collecting information on 325 botanical species and recording more than 1,000 ways to prepare traditional remedies and their uses (Madureira et al. 2002b).

Among the catalogued species, six plants representing four families were found to be commonly used in the treatment of malaria/fever: *Morinda lucida* (Rubiaceae), *Cedrela odorata* (Meliaceae), *Tithonia diversifolia* (Asteraceae), *Vernonia amygdalina* (Asteraceae), *Ageratum conyzoides* (Asteraceae) and *Pycnanthus angolensis* (Myristicaceae).

Other plants, such as *Leonotis nepitifolia, Struchium sparganophorum and Cestrum laevigatum*, have also been reported as being commonly employed in the traditional medicine of STP. However, scientific data related to these species are largely nonexistent.

Madureira et al. (2002a) reported that extracts and fractions from *S. sparganophorum* have showed significant antimalarial activity in in vitro tests and in vivo assays (Table).

Traditionally, the roots, stem bark and leaves of *M. lucida* are widely used in tropical Africa due to their reputed therapeutic value in the treatment of antiparasitic diseases (Kambu 1990), such as malaria (Obih et al. 1985, Asuzu & Chineme 1990, Agomo et al. 1992, Koumaglo et al. 1992, Tona et al. 1999, Bello et al. 2009). Investigating the antimalarial activity of this medicinal plant, Obih et al. (1985) reported the effect of methanol extracts of the stem bark, leaves and root bark against *P. berghei* in mice, where the juice from fresh leaves at a 1:6 dilution showed a decrease in parasitaemia from the second day of treatment. A fraction obtained from the stem bark extract of this plant demonstrated antimalarial activity in vivo and the highest dose produced 96.4% suppression of parasitaemia (Obih et al. 1985).

Phytochemical analyses revealed that *M. lucida* contains various types of alkaloids-anthraquinones and anthraquinols (Adewunmi & Adesogan 1984). In fact, Koumaglo et al. (1992) associated the antiplasmodial

activity of *M. lucida* stem bark and root to the presence of the anthraquinones digitolutein, rubiadin-1-methyl-ether and damnacanthal.

C. odorata is considered one of the most valuable forest tree species in the tropics and is also one of the most widely distributed (Millán-Orozco et al. 2011). In the tropics, species of the Meliaceae family are extensively used as traditional medicine against malaria (Khalid et al. 1986, Phillipson & Wright 1991, Leaman et al. 1995) and fevers (Ayensu et al. 1981), a characteristic symptom of malaria. In Africa, the decoction of *C. odorata* barks is used against this disease (Madureira 2008) and antimalarial activity of some compounds in bark and leaves was reported (MacKinnon et al. 1997, Omer et al. 2003).

In work by MacKinnon et al. (1997), extracts of 22 species of Meliaceae, including *C. odorata*, were examined for their antimalarial activity using in vitro tests with two clones of *P. falciparum*, one sensitive to CQ (W2) and one CQR (D6). The ethanol extract of *C. odorata* wood exhibited the highest activity against both clones, with IC_{50} values of 1.25 µg/mL (D6) and 1.37 µg/mL (W2). This activity was associated with the presence of tetranortriterpenoids (limonoids), a class of compounds characteristic of the Meliaceae family (MacKinnon et al. 1997).

A member of the family Asteraceae, *T. diversifolia*, is widely used for the treatment of malaria in STP (Elufioye & Agbedahunsi 2004, Owoyele et al. 2004, Moronkola et al. 2007).

The importance of this species as an antimalarial has been documented by many authors who found activity for the nonpolar and medium polarity extracts (Goffin et al. 2002, Madureira et al. 2002a, Elufioye & Agbedahunsi 2004).

As expected for a member of Asteraceae family, this species contains sesquiterpene lactones tagitinin A-C and F. Tagitinin C was reported as an active antiplasmodial component (0.33 µg/mL), which also possessed cytotoxic properties (IC_{50} on HTC-116 cells: 0.706 µg/mL) (Goffin et al. 2002).

V. amygdalina, from the Asteraceae family, is commonly known as "bitter leaf" and often appears in traditional medicines in Africa. Acetone-water and ethanol extracts of the leaves showed crescent antiplasmodial activity (Masaba 2000, Madureira et al. 2002a, Iwalokun 2008). In addition, this species achieved special relevance, having been shown to possess potent antimalarial activity in human medicine (Abosi & Roseroka 2003).

Other pharmacological studies of *V. amygdalina* have demonstrated the inherent ability of aqueous leaf extract to assist the restoration of CQ efficacy as a prophylactic and chemotherapeutic agent against CQ-sensitive and resistant *P. berghei* infection in mice (Iwalokun 2008).

Also belonging to the Asteraceae family, preliminary evaluation of the antimalarial activity of *A. conyzoides* demonstrated that the aqueous extract of leaves exhibited dose-dependent activity in infected mice. At the dose of 400 mg/kg, this extract produced chemosuppression of 89.87%, which is higher than that of CQ (83.12%) at 5 mg/kg, indicating high antimalarial potential (Ukwe et al. 2010). It was also reported that non-polar extract of the leaves has moderate in vitro antiplasmodial activity (12.08 µg/mL) (Chenniappan & Kadarkarai 2010).

Dichloromethane, methanol and aqueous ethanol extracts of *P. angolensis* barks were evaluated for their in vitro antimalarial activity and dichloromethane extract was the most effective (IC_{50} of 1.6 µg/mL) (Abrantes et al. 2008).

Angola - Malaria is the leading cause of morbidity and mortality in Angola. According to the National Malaria Control Programme, four million clinical cases and 20,000 deaths were reported in 2005, accounting for 35% of the overall mortality in children under five and 25% of maternal deaths (WHO 2005). Malaria is endemic in most areas of the Angolan territory, with *P. falciparum* as the predominant infecting species (WHO 2005). The epidemiological characteristics of malaria in Angola vary from hyper-endemic (northern and north-eastern of the country) to mesoendemic stable and mesoendemic unstable (Menegon et al. 2009).

Angola is rich in many medicinal plants whose potential has yet to be explored. However, there is some information about medicinal plants in this country and their uses for the treatment of malaria. The primary species associated with disease treatment are *Artemisia afra, Gardenia jovis-tonantis, V. amygdalina, Conysa welwitschii, Lantana camara, Harungana madagascarensis, Psorosperum febrifugum, Paveta schumanniana, Crassocephalum rubens*, *Crassocephalum multicorymbosum and Cajanus cajan* (Van-Dúnem 1994, Bossard 1996).

Bridelia ferruginea is a shrub found in northern Angola that is popularly used to treat malaria. Kolawole & Adesoye (2010) conducted a study to evaluate the antimalarial activity of this species with a sensitive strain of *P. berghei* (Table). An extract of *Cochlospermum angolense* root, popularly used in Angola for the prophylaxis of malaria, exhibited in vitro activity against *P. falciparum* (50 µg/mL) (Presber et al. 1992).

Piper umbellatum is common species in Angola, Mozambique and Brazil, especially in the Amazon Region. This plant has been used to treat malaria and there has been a study describing the active compound of this species (de Andrade-Neto et al. 2008).

Another widespread species, *V. amygdalina*, is also used to treat malaria in Angola and recent in vivo studies carried out in Nigeria have shown the effectiveness of this species (Iwalokun 2008).

The stem bark essential oil of *Hexalobus crispiflorus*, characterised by high sesquiterpene content (99.5%), showed high activity against *P. falciparum* (2.0 µg/mL). Another species, *Pachypodanthium confine*, whose stem bark essential oil has lower amounts of sesquiterpenes (88%), was also assayed against the same strains. Results showed that the activity (16.5 µg/mL) was lower than that observed for *H. crispiflorus* essential oil. The authors suggested that the sequiterpene content could be responsible for the antimalarial properties (Boyom et al. 2003).

Correlation among genera from the CPSC*, extracts and antimalarial active chemical classes* - Fig. 2 shows thatterpenes and alkaloids are the dominant classes of substances with antimalarial activity found in the studied extracts. Active terpenes were found in hydrophilic and lipophilic extracts from twelve genera (*Cecropia*,

Cedrela, *Hexalobus*, *Pothomorphe*, *Artemisia*, *Scoparia*, *Pachypodantium*, *Tithonia*, *Piper*, *Virola*, *Picrolemma* and *Ocimum*). Active alkaloids were found in eight genera (*Abuta*, *Esenbeckia*, *Guiera*, *Aspidosperma*, *Harungana*, *Sarcocephalus*, *Geissospermum* and *Cryptolepsis*), the majority of which were obtained from alcohol or crude alkaloid extracts. Phenolics, from lipophilic extracts of *Andira* and *Harungana*, and steroids, from extracts of *Cecropia, Vernonia*, *Harungana* and *Momordica*, are additional active antimalarial classes that have been previously studied (Fig. 2).

Final considerations - Of the countries covered in this review, Brazil had the largest number of native species studied and active substances identified for the treatment of malaria parasites. The ethnopharmacological work in STP resulted in important surveys about medicinal plants popularly used in the region. It is important to emphasise that many of the studies using the African species were not performed at the place of their harvest, which can lead to changes in chemical composition with probable alterations to therapeutic action.

Regarding common use among the CPSC, Brazil and Mozambique share the common use of species from the botanical Fabaceae and Cucurbitaceae families. Among Fabaceae species, *S. occidentalis* is employed to treat malaria in both countries. Within the Cucurbitaceae family, there are reports on the common use of two taxa, *Cucurbita maxima* and *M. balsamina*.

In Brazil and STP, three botanical species distributed among the Myristicaceae and Meliaceae families have ethnopharmacological uses for malaria treatment and studies have corroborated their pharmacological activity against *P. falciparum*. In this context, two species of Myristicaceae, *V. surinamensis* and *P. angolensis*, occur in ecosystems in Brazil and Africa, respectively. The decoction of *C. odorata* bark of the Meliaceae family is popularly used in the same manner in both countries.

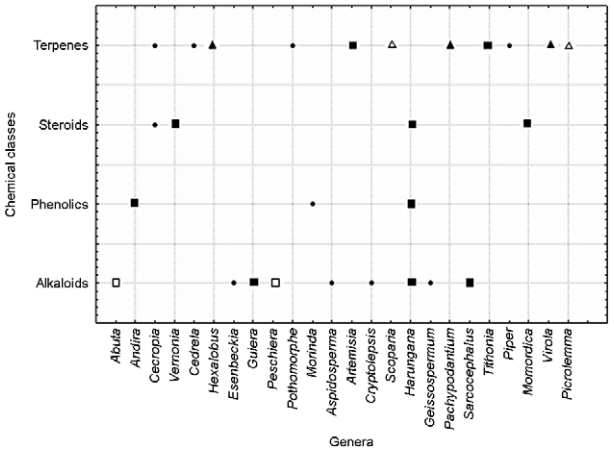

Fig. 2: comparison among genera from Community of Portuguese-Speaking Countries and antimalarial active chemical classes: •: alcohol extract; ▲: essential oil; ■: lipophilic extract; △: aqueous extract; □: alkaloid extract.

Eight botanical species of the Asteraceae family are distributed within four countries of the CPSC: three in Brazil (*A. australe*, *B. pilosa* and *V. brasiliana*), three in STP (*A. conyzoides*, *S. sparganophorum* and *T. diversifolia*) and one in Cape Verde (*A. gorgonum*). *V. amygdalina* is a commonly used botanical species in Angola and STP. The Piperaceae family is represented by two plant species, *Pothomorphe peltata* (Brazil) and *P. umbellatum* (Angola, Brazil and Mozambique), which are both employed to treat malaria.

There is a wide biodiversity in these countries that has not yet been thoroughly explored that represents a treasure of useful information in the search for antimalarials or treatments for other diseases.

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