Journal of Ethnopharmacology 172 (2015) 333–346

Contents lists available at ScienceDirect

Journal of Ethnopharmacology

journal homepage: www.elsevier.com/locate/jep

Medicinal plants and finished marketed herbal products used in the treatment of malaria in the Ashanti region, Ghana

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ARTICLE INFO

Article history:
Received 19 February 2015
Received in revised form
20 June 2015
Accepted 23 June 2015
Available online 4 July 2015

Keywords:
Malaria
Antimalarial
Treatment
Medicinal plants
Finished marketed herbal products

ABSTRACT

Ethnopharmacological relevance: Ethnobotanical survey was performed to document medicinal plants employed in the management of malaria in the Bosomtwe and Sekyere East Districts of the Ashanti Region (Ghana), in comparison with the plant ingredients in herbal antimalarial remedies registered by the Ghana Food and Drug Administration.
Materials and methods: Two hundred and three (203) herbalists from 33 communities within the two districts were interviewed on medicinal plants they use to manage malaria. A literature search was made to determine already documented plants. In addition, 23 finished marketed herbal products indicated for the management of malaria were identified and their labels examined to find out which of the plants mentioned in our survey were listed as ingredients and whether these products are in anyway regulated.
Results: Ninety-eight (98) species of plants were cited for the management of malaria. In comparison with literature citations, 12 (12.2%) species were reported for the management of malaria for the first time and 20 (20.4%) others for the first time in Ghana. Twenty-three (23) finished marketed herbal antimalarial products examined contained aerial or underground parts of 29 of the plants cited in our survey as ingredients. Twenty-two (22) of these products have been registered by the Ghana Food and Drugs Authority, four (4) of which were included in the recommended herbal medicine list for treating malaria in Ghana.
Conclusion: This study provides new additions to the inventory of medicinal plants used for the management of malaria and reports the commercial availability and regulation of finished marketed labelled herbal products intended for the treatment of malaria in Ghana.

1. Introduction

Malaria is a life-threatening disease caused by protozoan parasites of the genus Plasmodium, whose transmission through the Anopheles mosquito is affected by climate and geography (Snow et al., 2005). Approximately half of the world's population is at risk. The greatest impact of the disease is felt in Sub-Saharan Africa, where most malaria cases and deaths occur (WHO, 2014). However, Asia, Latin America, and to a lesser extent the Middle East and parts of Europe are also affected. In 2013, 97 countries and territories had ongoing malaria transmission (WHO, 2014). In Ghana, there were about 8.4 million suspected cases and 2500 attributed deaths in 2013 (Ghana population: 25.9 million) (WHO, 2014), the main parasite responsible being *Plasmodium falciparum* (WHO, 2013b). The disease places significant financial hardships on both households and the national economy. It was estimated

Abbreviations: ACT, artemisinin-based combination therapy; BD, Bosomtwe District; FDA, Food and Drug Authority; GDP, Gross Domestic Products; KNUST, Kwame Nkrumah University of Science and Technology; PRK, the percentage of respondent with knowledge about a particular plant species; SED, Sekyere East District; WHO, World Health Organization

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http://dx.doi.org/10.1016/j.jep.2015.06.041
0378-8741/

that 1% increase in the malaria morbidity rate will slow down the rate of real gross domestic products (GDP) growth by 0.41% (Asante and Asenso-Okyere, 2003).

WHO's approaches to malaria control are multi-faceted, involving prevention and case management (WHO, 2011). Among the prevention methods are control of the malaria vector using long-lasting insecticidal nets and indoor residual spraying: These interventions work by reducing both the human–vector contact and the lifespan of female mosquitoes (White et al., 2014). The other is the intermittent preventive treatment which is the administration of a full course of an effective antimalarial treatment at specified time points to a defined population at risk of malaria, regardless of whether the recipients are parasitaemic, with the objective of reducing the malaria burden in the target population (WHO, 2011). Case management, on the other hand, involves the treatment of confirmed malaria cases using WHO recommended chemotherapy for malaria (WHO, 2011). Currently, treatment with artemisinin-based combination therapies (ACTs) are the major drugs for the treatment of malaria (WHO, 2010b). However, ACTs are faced with some challenges, among which are their high cost (Mutabingwa, 2005) and the emerging parasite resistance to artemisinin-based drugs (WHO, 2010b).

In Ghana, where malaria is a major developmental challenge, many people use medicinal plants for treatment, especially in rural communities. Plants used in malaria and fever account for 6% of the medicinal plants of the Ghanaian domestic market (Van Andel et al., 2012). Many of these plants have been used in the management of the disease for centuries and numerous studies have documented this indigenous knowledge in some localities (Abbiw, 1990; Asase et al., 2005, 2010; Asase and Asafo-Agyei, 2011; Asase and Oppong-Mensah, 2009; Dokosi, 1998; Mshana et al., 2001). However, some sites are yet to be studied, leaving a knowledge-gap in the documentation of these medicinal plants. Besides, the face of herbal medicine practice has changed over the years; some practitioners have moved from the hitherto extemporaneous preparations of home-made remedies to commercial production of finished/mixture marketed herbal products, made of a single or combination of medicinal plants.

We surveyed the medicinal plants used by the indigenes of the Bosomtwe and Sekyere East Districts of the Ashanti region of Ghana to manage or treat malaria. The data obtained were compared with similar studies from other parts of Ghana, Africa and the world. We also examined marketed herbal antimalarial products distributed in some health facilities in Kumasi, the Ashanti Regional capital of Ghana, to ascertain which plants mentioned in our survey are ingredients and to assess the regulatory status of these products.

2. Materials and method

2.1. Study areas

The study areas encompass 2 districts of the Ashanti Region, Ghana: Bosomtwe and Sekyere East Districts (Fig. 1). Bosomtwe District lies within latitudes 6° 43′ North and longitudes 1° 46′ West and it spreads over a land area of 68,179 km^2. It has an estimated population of about 94,000 (Ghana Statistical Service, 2010). The Sekyere East district, on the other hand, lies between latitudes 6° 45′ and 7° 32′ North and longitude 0° 22′ West. It has a land area of about 4231.4 km^2 and an estimated population of about 62,000 (Ghana Statistical Service, 2010). These areas share common climatic conditions; the equatorial zone with a rainfall regime typical of the moist semi-deciduous forest zone of Ghana. The communities are mostly rural. The residents are typically farmers and majority of the towns lack public healthcare facilities. The population is mainly of the Akan-speaking ethnic group of Ghana.

2.2. Data collection

Prior to data collection, informants' consent was sought by administering informed consent forms after explaining the purpose of the study to participants. The forms were filled and

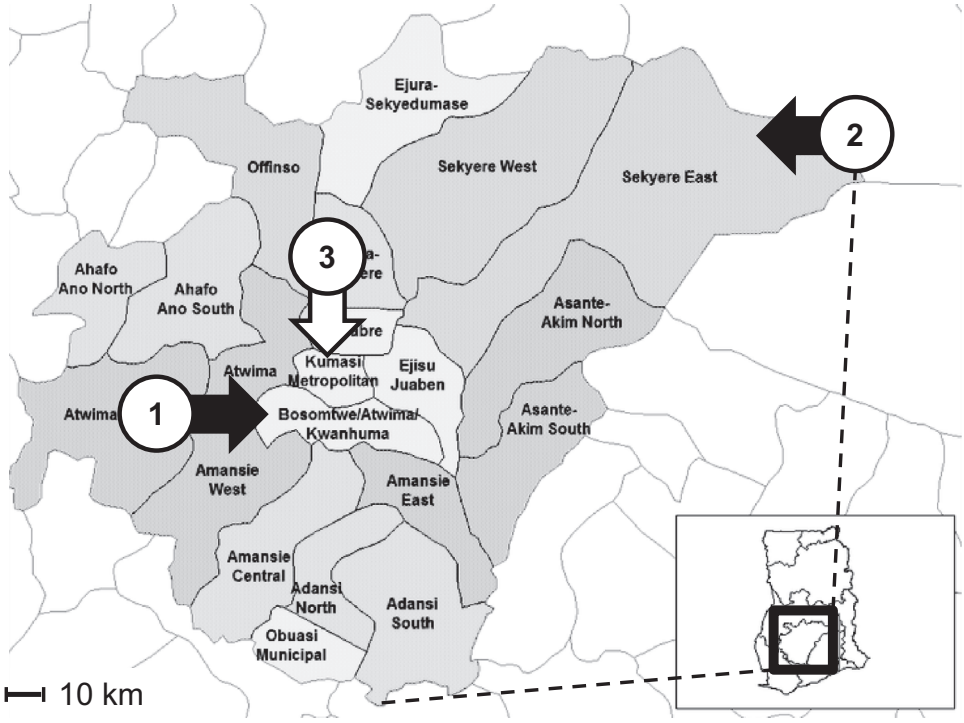

Fig. 1. District map of Ashanti region, Ghana, showing the study areas: (1) Bosomtwe and (2) Sekyere East Districts; (3) Kumasi Metropolitan Area. Source: Adapted from Wikimedia Creative commons.

Table 1
Medicinal plants used by herbalists in Bosomtwe and Sekyere East Districts (Ghana) to treat malaria.

Family/Botanical name	Local name	Part used	State	Preparation[a] /association	SED [c]	BD [c]	PRK (%)	Previous reports
Acanthaceae								
Justicia carnea Lindl.	Ntumunum	L	f	With *T. procumbens* and *C. odorata* leaves.	+		0.99	
Amaranthaceae								
Amaranthus spinosus L.[b]	Yaa asantewaa	L	d	With *Z. officinale*, *V. amydalina* leaves and *X. aethiopica* seeds.		+	0.49	[5]
Cyathula prostrata (L.) Blume	Mpupua	R	d	Sole component, boiled or infused in water.		+	0.49	[25]
Gomphrena celosioides Mart.[b]	Nkasɛnkasɛ	L, SB	d, f	1. Stem bark steeped in water with crushed *Z. officinale* rhizome, used as enema. 2. With S. siamea root.	+	+	0.99	[20]
Amaryllidaceae								
Allium cepa L.	Gyene	B	f, d	Steeped with *A. comosus* leaves and peel, and *V. amygdalina* leaves and drink as required.		+	0.49	[16;32;34]
Allium sativum L.	Gyenekankan	B	f	1. With *A. indica*: drunk, used as a bath or as enema. 2. With *P. fraternus*, *A. comosus* peels and *V. amygdalina* leaves.	+	+	1.97	[3;34]
Anacardiaceae								
Mangifera indica L.[b]	Mango	L	f	With *S. alata* and *T. tetraptera* leaves.	+	+	11.82	[9;40;13]
Spondias mombin L.[b]	Atoa	L, SB	f, d	Leaves and stem bark together with *L. camara* and *M. lucida* leaves.		+	2.96	[2;38;39]
Annonaceae								
Cleistopholis patens (Benth.) Engl. and Diels [b]	Ngonenkye-ne	L	d, f	With *C. papaya* and *M. indica* leaves and *S. torvum* fruits.	+	+	3.94	[2;38]
Polyalthia longifolia (Sonn.) Thwaites[b]	Weeping willow	L	f, d	With *A. indica* leaves.	+	+	4.43	[15]
Xylopia aethiopica Dunal[b]	Hwentia	S	d	1. With dried *C. papaya* leaves. 2. With *M. indica* stem bark.		+	1.48	[9;11;39]
Apocynaceae								
Alstonia boonei De Wild [b]	Emee/Nyamedua	L	f	Sole component.	+	+	10.34	[9;26]
Periploca nigrescens Afzel.	Abakamo	L	f	With *N. laevis* leaves.	+		1.97	
Rauvolfia vomitoria Afzel.[b]	Kakapenpen	L	f	With *A. zygia* and *L. camara* leaves.	+	+	4.43	[2;40]
Secamone afzelii (Roem.and Schult.) K. Schum.	Kwatemaa	A	f, d	1. With *S. campanulata* stem bark. 2. With *M. indica* and *S. occidentalis* leaves. 3. With Ficus spp. and saltpetre.		+	1.48	
Arecaceae								
Cocos nucifera L.[b]	Kube	SB, L	f	Stem bark with leaves.	+		1.97	[9;22;39]
Elaeis guineensis Jacq.[b]	Abɛ	L	d	With *T. orientalis* leaves.	+		1.48	[8;3;39]
Asteraceae								
Ageratum conyzoides L.[b]	Guakro	L	f	With *V. amygdalina* leaves.	+		2.46	[2;3;11]
Bidens pilosa L.[b]	Gyinantwi	L	d	With dried *T. cacao* leaves.	+	+	3.94	[5]
Chromolaena odorata L.[b]	Acheampong	L	f	1. Boiled with *C. × limon* fruit then added with sugar. 2. With *C. citratus* leaves.	+	+	7.39	[3;5;16]
Emilia sonchifolia (L.) DC.[b]	Guakoro	L	f, d	With *M. pudica* and *E. hirta* leaves.		+	0.49	[2]
Launaea taraxacifolia (Willd.) Amin ex C. Jeffrey	Mmrobo	L	f	With *C. odorata* and *T. procumbens* leaves.	+	+	2.96	
Tridax procumbens L.b	Nantwi bini	L	f	Sole component.	+	+	7.39	[28]
Vernonia amygdalina Delile (accepted name: *Gymnanthemum amygdalinum* (Delile) Sch. Bip. ex Walp.)[b]	Awonwono	L, ST	f	1. Stem chewed, swallowing the liquid. 2. Leaves steeped in water with *A. sativum* bulb.	+	+	10.84	[7;11;39]
Bignoniaceae								
Newbouldia laevis (P.Beauv.) Seem.[b]	Sesemɛsa	L, SB	f, d	Leaves or stem bark with *M. indica* dried leaves.	+	+	8.37	[2;3;39]
Spathodea campanulata P. Beauv.[b]	Akuakuoninsuo	L, SB	f	1. Stem bark with *S. alata* leaves and of *C. × aurantifolia* fruits. 2. Leaves with *P. guajava* and *C.*	+	+	3.94	[3;6]

Table 1 (*continued*)

Family/Botanical name	Local name	Part used	State	Preparation[a] /association	SED [c]	BD [c]	PRK (%)	Previous reports
				smeatmannii leaves.				
Boraginaceae								
Heliotropium indicum L.[b]	Kɔmfemtikorɔ	L	f	With *M. indica* and *C. odorata* leaves, drunk for 7 days.		+	0.49	[2;32;39]
Bromeliaceae								
Ananas comosus L. Merr.[b]	Aborobɛ	FP, L	f	1. Leaves or fruit peels with *P. fraternus* and *T. cacao* leaves. 2. Fruit peels with *A. boonei*, *L. camara* and *C. smeatmanii* leaves.	+	+	5.42	[9;39]
Cannabaceae								
Trema orientalis (L.) Blume	Sesea	L	f	With *F. exasperata* leaves.		+	0.99	[11]
Caricaceae								
Carica papaya L.[b]	Bofire	L	f	With *T. grandis*, *T. cacao*, *A. indica* leaves and *C.* × *aurantifolia* fruit.	+	+	9.36	[9;11;39]
Chrysobalanaceae								
Parinari excelsa Sabine	Kwaed/Afamua	L, SB	f	Leaves or stem bark. [a]	+		0.49	[10]
Combretaceae								
Combretum ghasalense Engl. and Diels[b]	Kwahinkwagya	S	d, f	Ground small piece of seeds, added to moistened *M. puberula* leaves, instilled into nose.		+	0.49	[7]
Combretum mucronatum Schumach. and Thonn.[b]	Hwerɛmo	L	d	With *F. sycomorus* stem bark and *C.* × *aurantifolia* fruitthen added with honey.		+	1.48	[2]
Terminalia catappa L.[b]	Abrofo nkateɛ	L	f	With *A. boonei* leaves.	+	+	7.39	[5;16]
Terminalia ivorensis A. Chev.[b]	Emire	L, SB	f, d	Leaves and stem bark together with *E. mildbraedii* leaves.	+	+	4.43	[6]
Cucurbitaceae								
Momordica charantia L.[b]	Nyanyaa	L	f	Sole component, ground, added with palm wine.	+	+	3.45	[2;5;26]
Dioscoreaceae								
Dioscorea dumetorum (Kunth) Pax	Nkamfoɔ	L	f	1. Leaves boiled in strained corn (Zea mays L., Poaceae) dough liquid. 2. With *P. longifolia* leaves. 3. With *T. catapa* and *S. alata* leaves. 4. Added with sugar.		+	0.49	[13]
Euphorbiaceae								
Alchornea cordifolia (Schumach. and Thonn.) Müll.Arg.[b]	Ogyama	L	f	With *R. vomitoria* and *L. camara* leaves.	+	+	7.39	[9;29]
Euphorbia hirta L.[b]	Kakaweadwe	L	f	With *T. ivorensis* leaves and stem bark.		+	0.49	[14;40]
Grossera vignei Hoyle	Dubrafoo	L	f	Sole component, boiled with the filtrate from strained corn (Z. mays L.) dough.	+		0.49	
Jatropha curcas L.[b]	Nkrandedua	L	f, d	With *P. fraternus*, *O. gratissimum* leaves and *C.* × *limon* fruit.	+	+	4.43	[7;29;27]
Manihot esculenta Crantz[b]	Bankye	L	f, d	1. With *P. americana* and *T. cacao* leaves. 2. With *P. americana* and *A. boonei* leaves.		+	0.49	[2;11;39]
Mareya micrantha (Benth.) Müll. Arg.b	Dubrafo	L	f	With *O. gratissimum* and *A. boonei* leaves.	+	+	1.48	[9;40]
Fabaceae								
Albizia ferruginea (Guill. and Perr.) Benth.	Awiemfo-samina	L	f	With *P. fraternus* and *C. citratus* leaves.		+	0.99	[40]
Albizia zygia (DC.) J.F.Macbr.[b]	Okoro	L	f	Crushed, strained and used as enema.		+	0.99	[2;37;38]
Amphimas pterocarpoides Harms	Yaya	L	f	With *P. fraternus* leaves, drunk or used as enema.	+		1.97	
Erythrina mildbraedii Harms	Eya	L	d, f	With *C. sanguinolenta* root.		+	0.49	
Mimosa pudica L.	Nana aberewa	L	f	Ground with *Z. officinale* rhizome and *P. guineense* seeds, strained and used as enema.		+	0.49	[1]
Senna alata (L.) Roxb.[b]	Simpe	L	f, d	1. Boiled, allowed to cool and used as	+	+	6.4	[9;40]

Table 1 (*continued*)

Family/Botanical name	Local name	Part used	State	Preparation[a] /association	SED [c]	BD [c]	PRK (%)	Previous reports
				enema. 2. Dried leaves with *X. aethiopica*.				
Senna occidentalis (L.) Link[b] (syn. *Cassia occidentalis* L.)	Nkwadaa borɔdeɛ	L	f	1. With *B. pilosa* and *M. lucida* leaves. 2. With *T. daniellii*, *T. tetraptera* and *C. prostrata* leaves.	+	+	4.93	[9;3;31]
Senna siamea (Lam.) H.S. Irwin and Barneby[b]	Acacia	R	f	Sole component.		+	2.96	[4;8;32]
Tetrapleura tetraptera (Schumach. and Thonn.) Taub.[b]	Prekesɛ	L, F, SB	f, d	1. Leaves with *C. anisata* leaves. 2. Fruits with *A. indica* leaves. 3. Chopped stem bark.	+	+	8.37	[2;3]
Gentianaceae								
Anthocleista nobilis G.Don [b]	Wudini kɛtɛ (Bontodie)	L, SB	f	1. Leaves with *T. grandis* and *A. indica* leaves. 2. Stem bark with *A. indica* leaves.		+	0.99	[6]
Huaceae								
Afrostyrax lepidophyllus Mildbr.	Duagyanne	S	d	Seven crushed seeds with *U. guineensis* stem bark, steeped in hot water, drunk.	+		5.91	[29]
Lamiaceae								
Ocimum canum L.	Akokobesa	L	f	With *M. oleifera* and *A. vera* leaves.	+		0.49	[22]
Ocimum gratissimum L.[b]	Nunum	L	f	1. With *M. oleifera* leaves. 2. With *P. americana* leaves.	+	+	8.87	[9;3;29]
Tectona grandis L. f. [b]	Teak	L	f, d	With *P. capitata* leaves.	+	+	7.88	[8;22]
Lauraceae								
Persea americana Mill.[b]	Paya	L	f, d	With *M. indica*, *S. occidentalis* and *M. oleifera* leaves.	+	+	6.4	[5;11]
Loranthaceae								
Phragmanthera capitata (Spreng.) Balle	Nkranpan	L	f, d	1. With *T. grandis* leaves. 2. With *C. sanguinolenta* roots.	+	+	2.96	[17]
Malvaceae								
Bombax buonopozense P.Beauv.[b]	Akata	SB	f, d	With *P. fraternus* leaves.	+	+	5.91	[6]
Cola nitida (Vent.) Schott and Endl.	Bese	L	f	With *P. longifolia* leaves and *P. fraternus*, drunk for three days.		+	0.49	
Cola gigantea A. Chev.[a]	Watapuo	L	f	With *T. grandis* leaves.	+		1.48	[2]
Pterygota macrocarpa K. Schum.	Kyerere	L	f	With *T. grandis* and *L. camara* leaves.	+		0.99	
Sida cordata (Burm.f.) Borss. Waalk.	Tentene	L	f	With *O. canum* and *C. citratus* leaves.		+	0.49	
Sida cordifolia L.	Akyerekyere	A	f, d	Sole component.	+		0.99	[21]
Theobroma cacao L.[b]	koko	L	d	With *B. vulgaris* leaves.	+	+	7.88	[6;16]
Marantaceae								
Thaumatococcus daniellii (Benn.) Benth. and Hook. f.[b]	Aworomo	L	f, d	With *S. alata*, *T. tetraptera* and *C. prostrata* leaves.		+	0.49	[9]
Meliaceae								
Azadirachta indica A. Juss.[b]	Neem	L	f	Sole component.	+	+	20.2	[4;9;39]
Khaya senegalensis (Desr.) A.Juss.[b]	Kuntunkuri	SB	f	With *B. buonoponzense* stem bark and leaves and *B. vulgaris* leaves.		+	0.99	[7;39]
Moraceae								
Ficus exasperata Vahl.	Nyankyerɛne	L	f	With *M. pudica* leaves.	+	+	3.45	[22]
Ficus sycomorus L.	Odoma	L	f	With *T. orientalis* leaves.		+	0.99	[33]
Moringaceae								
Moringa oleifera Lam.[b]	Moringa	L, S	f, d	1. Leaves boiled in strained corn (Z. mays L.) dough liquid. 2. Seed chewed, swallowing of the liquid.	+	+	6.4	[8;37;39]
Musaceae								
Musa paradisiaca L.[b]	Borɔdeɛ	R, L	f, d	1. Petiole with *P. fraternus* and *G. amygdalinum* leaves. 2. Leaves steeped in water. 3. Roots steeped in water with *Z.*		+	1.48	[5;36;19]

Table 1 (*continued*)

Family/Botanical name	Local name	Part used	State	Preparation[a] /association	SED [c]	BD [c]	PRK (%)	Previous reports
				officinale rhizome, used as enema.				
Musa sapientum L.[b]	Kodu	L	f	Petiole with *P. fraternus* and *G. amygdalinum* leaves.	+	+	3.45	[8]
Myristicaceae								
Pycnanthus angolensis (Welw.) Warb[b]	Otie	L	f	With *R. vomitoria* and *M. indica* leaves.	+		2.96	[6;40;24]
Myrtaceae								
Psidium guajava L.[b]	Guava	L	f	Boiled with *N. laevis* leaves and added with fruits juice of *C.* × *aurantifolia*.	+	+	5.91	[6;13]
Pandaceae								
Microdesmis puberula Hook.f. ex Planch.	Ofemma	L	f	Note: induces vomiting which is stopped once a meal is taken.	+	+	2.46	[11]
Papaveraceae								
Argemone mexicana L.	Akusiribie	A	f, d	1. Sole component. 2. With *M. charantia* and *M. oleifera* leaves.	+		0.49	[16;18;39]
Periplocaceae								
Cryptolepis sanguinolenta (Lindl.) Schltr.[b]	Nibima	R	d	1. With *A. boonei* and *L. camara* leaves and of *A. comosus* peels. 2. Powdered root infused in hot water.	+		4.43	[3;28]
Phyllanthaceae								
Phyllanthus fraternus G.L. Websterb	Bɔ womma gu wakyi	WP	f, d	1. Boiled with *C. citratus* leaves in strained corn dough liquid. 2. With *C. papaya*, *P. americana*, *O. gratissimum* and *G. amygdalinum* leaves.	+	+	14.78	[35]
Uapaca guineensis Müll. Arg.	Kontan	SB	d	Dried stem bark crushed, added with seven *A. melegueta* seeds, steeped in hot water.		+	0.49	[23]
Piperaceae								
Piper guineense Schumach. and Thonn.[b]	Soro wisa	S	d	Seeds crushed with *M. puberula* leaves and *Z. officinale* rhizome, strained and used as enema.	+	+	1.97	[9;29]
Poaceae								
Bambusa vulgaris Schrad.[b]	Pamporo	L	d, f	1. With *C.* × *aurantifolia* leaves. 2. With *P. longifolia* leaves.	+	+	5.42	[5]
Cymbopogon citratus (DC) Stapf.[b]	Esrɛ (lemon grass)	L	f	With *T. catapa*, *N. laevis* and *B. buonopozense* leaves.	+	+	10.84	[9;36;39]
Saccharum officinarum L.[b]	Ahwedeɛ	ST, L	f	Stem and leaves with *N. laevis* leaves.	+	+	3.45	[8;11;39]
Rubiaceae								
Morinda lucida Benth.[b]	Konkroma	L, SB	f	Leaves and stem bark.	+	+	6.9	[9;16]
Rutaceae								
Citrus × *aurantiifolia* (Christm.) Swingle[b]	Ankagyua	L, F	f	1. Leaves with *O. gratissimum* and *T. catapa* leaves. 2. Leaves with *J. curcas* and *T. procumbens* leaves, added with juice of the fruit.	+	+	7.88	[9;38]
Citrus × *limon* (L.) Osbeck	Ankagyua	F, L	f	Fruit with *G. amygdalinum*, *S. occidentalis* and *T. grandis* leaves.	+	+	5.91	[11;34;39]
Clausena anisata (Willd.) Hook.f. ex Benth.[b]	Saman nobi	F, L	f	1. Fruits with *S. mombin* and *S. campanulata* leaves. 2. Fruits or leaves with *P. longifolia*, *T. catapa* and *C. odorata* leaves.		+	0.99	[28;39]
Zanthoxylum leprieurii Guill. and Perr.	Oyaa	L, SB	f, d	Leaves or stem bark with Khaya spp. stem bark.		+	0.49	
Sapindaceae								

Table 1 (*continued*)

Family/Botanical name	Local name	Part used	State	Preparation[a] /association	SED [c]	BD [c]	PRK (%)	Previous reports
Paullinia pinnata L.[b]	Tuantini	L	f	1. Leaves boiled: steam-bath with the hot decoction. 2. Poultice applied on the body.		+	0.99	[7;38;39]
Solanaceae								
Solanum torvum Sw.[b]	Nsususwa	F, L	f	1. Leaves with sugar added after decoction. 2. Fruits with of *M. indica* stem bark and *S. officinarum* stem.		+	2.46	[8]
Solanum tuberosum L.	Potato	L	f	With *T. procumbens* and *P. guajava* leaves.	+		0.99	[12]
Thelypteridaceae								
Cyclosorus afer Ching	Mmɛyaa (abɛya)	L	d	With *S. alata*, *T. tetraptera* and *T. daniellii* leaves.	+	+	2.96	
Verbenaceae								
Lantana camara L.[b]	Ananse dokono	L	d	With *Z. leprieurii* leaves.		+	1.97	[5;18;37;38]
Xanthorrheaceae								
Aloe vera (L.) Burm. f	Aloe vera	L	f	1. Sole component. 2. With *A. indica* leaves.	+		1.48	[31;34]
Zingiberaceae								
Aframomum melegueta (Roscoe) K. Schum.[b]	Fom wisa	L	f, d	With *E. hirta* leaves.		+	0.49	[9;11;38]
Zingiber officinale Roscoe[b]	Akakaduro	Rh	f, d	With *C. papaya* leaves and *M. indica* stem bark.	+	+	3.45	[9;16;30]

Plant parts: A: aerial part; F: fruit; L: leaves; R: root; RB: root bark; RH: rhizome; S: seed; SB: stem bark; ST: stem; WP: whole plant.
State: f: fresh; d: dried. PRK: Percentage of the respondents with knowledge about the use of the plant for the management of malaria.
[d] Previous reports of traditional use: [1] (Aarthi and Murugan, 2011); [2] (Abbiw, 1990); [3] (Adebayo and Krettli, 2011); [4] (Al-Adhroey et al., 2010); [5] (Asase and Asafo-Agyei, 2011); [6] (Asase and Oppong-Mensah, 2009); [7] (Asase et al., 2005); [8] (Asase et al., 2010); [9] (Asase et al., 2012); [10] (Attioua et al., 2012); [11] (Betti et al., 2013); [12] (Chen et al., 2010); [13] (Dike et al., 2012); [14] (Dokosi, 1998); [15] (Gbedema, 2014); [16] (Idowu et al., 2010); [17] (Jiofack et al., 2009); [18] (Kamaraj et al., 2012); [19] (Kaou et al., 2008); [20] (Köhler et al., 2002); [21] (Konaté et al., 2012); [22] (Koudouvo et al., 2011); [23] (Macfoy, 2013); [24] (Madureira et al., 2002); [25] (Mbatchi et al., 2006); [26] (Ménan et al., 2006); [27] (Mesfin et al., 2012); [28] (Mshana et al., 2001); [29] (Muganza et al., 2012); [30] (Nagendrappa et al., 2013); [31] (Nguta et al., 2010); [32] (Olorunnisola et al., 2013); [33] (Sanon et al., 2003); [34] (Saotoing et al., 2011); [35] (Sittie et al., 1998); [36] (Stangeland et al., 2011); [37] (Tabuti, 2008); [38] (Traore et al., 2013); [39] (Yetein et al., 2013); [40] (Zirihi et al., 2005).
[a] Otherwise indicated: Oral route; decoction alone or in combination, drunk as required.
[b] Plants already documented in Ghana.
[c] +: mentioned in studied District (Sekyere East District: SED; Bosomtwe District: BD).

willingly signed or thumb printed (by respondents who were illiterate) prior to the administration of questionnaires. The protocol for the study was approved by the Faculty of Pharmacy and Pharmaceutical Sciences Research Ethic Review Committee, and the research was performed in consultation with the chiefs and opinion leaders of the various communities who facilitated the identification of recognized herbalists.

Two hundred and three (203) herbalists in the Bosomtwe (100) and Sekyere East (103) districts respectively were interviewed using a semi-structured validated questionnaire (see Supplementary material S1). Purposive sampling technique was employed in selecting the respondents, members of the communities helped to identify the respondents who were known herbalists. Data collection involved both home and field interviews. Questions on practitioners' demography covered name/ID, gender, age, level of formal education, profession or career, duration of practice and how traditional healing skill or knowledge was acquired. Questions related to malaria included respondent's knowledge in malaria, ability to diagnose it, symptoms of the disease, experience with malaria cases and treatment, and if their assistance was sought by people suffering from malaria. Questions on medicinal plants used to treat malaria included local name(s) and if known, scientific name(s) of plant(s) employed, part/organ of the plant, the form in which it is used, the method of preparation and administration, known side effects and contraindications. Oral and informal interviews were also carried out with both closed and open ended questions.

During the field interview, the respondents took the interviewer to the field where they normally collected their medicinal plants. Samples of the plant species were collected to prepare herbarium specimens. The identities of plant species were authenticated by Dr. G.H. Sam of Department of Herbal Medicine, Faculty of Pharmacy and Pharmaceutical Sciences, Kwame Nkrumah University of Science and Technology (KNUST), Kumasi, Ghana in comparison with reference materials of the herbarium of the same Department and with database sources at the Forest Research Institute of Ghana (FORIG), Fumesua, Ghana. Specimens with voucher numbers (see Supplementary material S2) were deposited at the Herbarium of KNUST. The taxonomic validity of the plant names were checked using the plant database; www.thePlantList.org (accessed January, 2015).

2.3. Survey of finished marketed herbal products for the management of malaria

A survey was also conducted in 3 herbal medicine wholesale

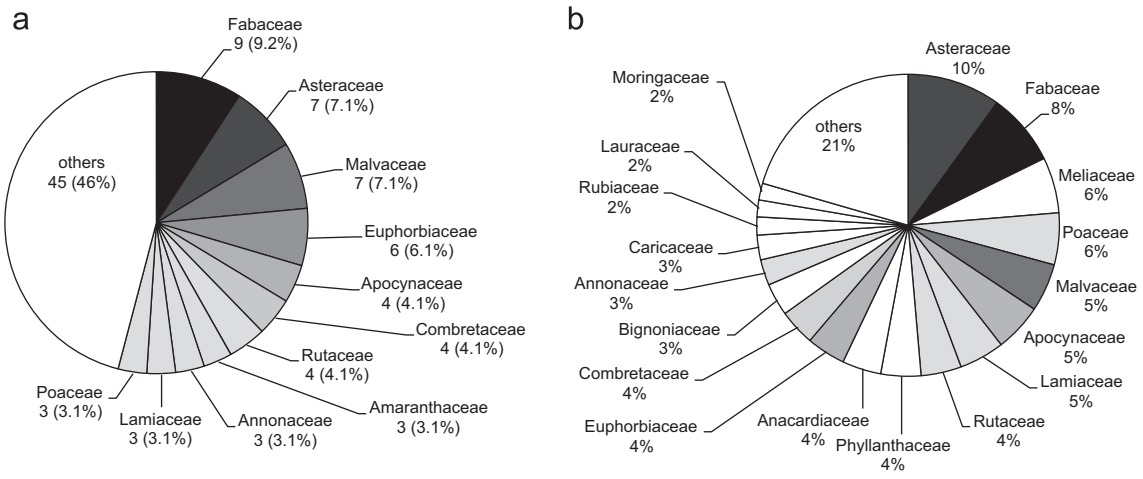

Fig. 2. (a) Number/percentage of plant species cited for major family and (b) percentage representation of plant families cited in the survey.

shops, 3 herbal medicine retail shops, 3 community pharmacies and 2 herbal clinics within the Kumasi Metropolitan area of the Ashanti Region of Ghana to identify finished marketed herbal antimalarial products on sale, examine their active plant component (see Supplementary material S3) and also assess their regulatory status within the national and international framework.

2.4. Statistical analysis

The knowledge on medicinal plants used in the treatment of malaria among the herbalists in the study areas was analysed using the percentage of respondent with knowledge about a particular plant species (PRK) (Asase et al., 2005). PRK was calculated as the percentage of respondents who mentioned the plant in comparison with the total number of respondents in both districts.

3. Results

3.1. Respondents' demographics

The study was done in 33 towns and villages in the 2 districts, the Bosomtwe and the Sekyere East Districts of the Ashanti Region of Ghana, over a period of six months, from June to November 2012. The respondents were traditional healers above 20 years of age, living in the study areas. They were known in the communities as people who have knowledge of medicinal plants, sought by users of medicinal plants for assistance and have experience in treating malaria. The respondents included herbalists from herbal clinic settings, practitioners with shrines and other people who practice herbal medicine as pastime. The former two offer their services for fees and the later often receive payment in the form of cash or kind for their services. The latter constitute 162 (79.8%) of the respondents. Of the 203 respondents, 134 (66.0%) had practiced for more than 10 years. While 51 (25.1%) of the respondents had no western-type education, the majority (152; 74.8%) had education, ranging from basic to tertiary level. Ninety-four (94; 46.3%) were females. All the 203 herbalists interviewed in the 2 districts said they employed various medicinal plants species for the treatment of malaria. According to the herbalists, anyone with malaria may demonstrate one or more of the following symptoms: elevated body temperature, bitterness in the mouth, nausea and vomiting, chills, headache, joint pains, restlessness, body weakness, loss of appetite, insomnia, intense amber urine colour, yellowish eye colour and stomach upset. The most commonly reported of these symptoms are headache, nausea and vomiting, bitterness in the mouth, loss of appetite, high temperature and chills. The herbalists considered malaria treatment as a remedy which relieves these clinical signs and symptoms and they use this to judge the effectiveness of their remedies since there is no laboratory facility within these communities to facilitate the confirmation or absence of parasitaemia.

3.2. Plant species employed in the management of malaria

Ninety-eight (98) plants species belonging to 85 genera in 48 families were cited for the treatment or management of malaria in the survey (Table 1). Eighty (80) species were recorded in Bosomtwe and sixty-five (65) in Sekyere East District. Forty-seven (47; 47.9%) of the 98 were cited in both districts. Eighteen (18; 18.4%) of the species mentioned in Sekyere East District were not encountered during the survey in Bosomtwe District, while 33 (33.7%) of species were cited only in Bosomtwe. Thirty-five (35) of the

65 Species cited in only a district have PRK less than 1 (PRK < 1). The plants were mostly flowering-species (1 fern was cited). The predominant family was the Fabaceae with 9 species (3 of which belong to the genus, *Senna*) followed by Asteraceae and Malvaceae, and then Euphorbiaceae, Combretaceae and Rutaceae among others (Fig. 2). Eleven genera including *Allium*, *Albizia*, *Citrus*, *Cola*, *Combretum*, *Ficus*, *Musa*, *Ocimum*, *Sida*, *Solanum* and *Terminalia* had 2 members each. *Azadirachta indica* was the most frequently cited (PRK = 20.20%), followed by *Phyllanthus fraternus* (PRK = 14.78%), *Mangifera indica* (PRK = 11.82%), *Cymbopogon citratus*, *Vernonia amygdalina* (PRK = 10.84%) and *Alstonia boonei* (PRK = 10.34%). The PRK for the rest of the species ranged from 0.49% to

9.36% (Table 1).

In terms of growth habit, trees predominate (45%) while herbs formed 34%, shrubs, 15% and climbers, 6%. The main part employed was the leaf followed by the stem bark, root, fruit and seed, whole plant and bulb (Fig. 3). Recipes were mostly decoctions and plant species were employed either as sole or multi-components in different combinations. Often, the choice of combination of plants for a recipe depended on the individual herbalist. The literature review revealed that 12 of the identified plant species including *Amphimas pterocarpoides*, *Cola nitida*, *Secamone afzelii*, *Cyclosorus afer*, *Erythrina mildbraedii*, *Grossera vignei*, *Justicia carnea*, *Launaea taraxacifolia*, *Periploca nigrescens*, *Pterygota macrocarpa*, *Sida cordata* and Zanthoxylum leprieurii are being reported for the first time for the traditional management of malaria and another 20 for the first time in Ghana (see Supplementary material S4).

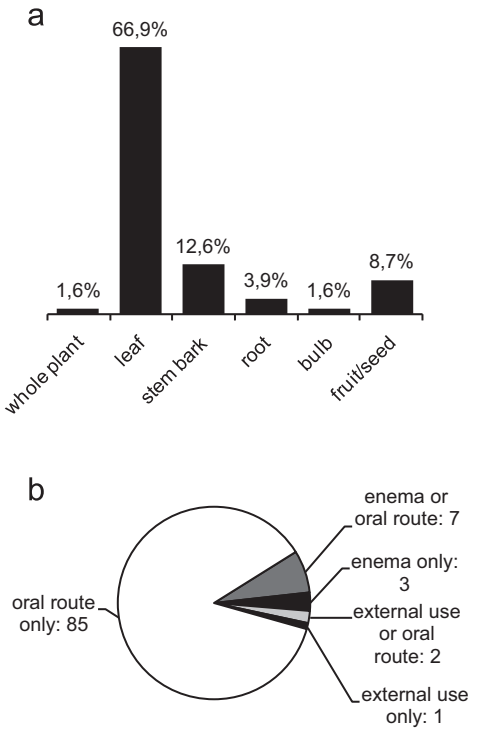

Fig. 3. (a) Plant parts employed in the treatment of malaria, as percentage of all parts use. (b) Route of administration of the various preparations.

3.3. Finished/mixture marketed labelled herbal antimalarial products

Twenty-three (23) finished/mixture marketed labelled herbal products, formulated as decoctions and intended for the treatment of malaria, were identified in a survey carried out in community pharmacies, herbal wholesale and retail shops, and herbal clinics in Kumasi, the Ashanti Regional capital of Ghana (Table 2). Twenty-two (22, 95.7%) of the products surveyed were registered by Ghana's food and drug regulatory authority (FDA) and therefore bear registration numbers. These products contained 29 (29.6%) of the medicinal plants cited in the ethnobotanical survey (Table 1) as plant constituents, the majority of which have PRK higher than 4. Five (5) of the identified finished marketed products were prepared from a single plant, while the others contained a combination of two (2) to seven (7) medicinal plants. These products are indicated for malaria and sometimes related conditions such as jaundice, typhoid fever, fatigue and loss of appetite. Four (4, 13.8%) of the finished marketed remedies surveyed formed part of the recommended herbal medicine list for treating malaria in Ghana (Ministry of Health, 2008). These products were dispensed in both public and private herbal clinics, sold in herbal shops, community pharmacies and licensed chemical stores as over the counter products for the treatment of malaria in Ghana. However, only those on the recommended herbal medicine list for treating malaria are dispensed in public herbal clinics. The dosage regimen usually covers 7 days or more. The herbal clinics are often operated by traditional herbalists (private herbal clinics) as well as medical herbalists (both public and private herbal clinics). The medical herbalists hold the BSc degree in Herbal medicine from the Kwame Nkrumah University of Science and Technology (KNUST), Kumasi, Ghana. The herbal shops are often supervised by traditional herbalists or by lay persons while the community pharmacies are supervised by pharmacists.

The most employed of the cited plants in the finished/mixture herbal products for managing malaria was *Cryptolepis sanguinolenta*. It occurred in 11 (47.8%) of the remedies, followed by *Morinda lucida*, *Vernonia amygdalina* and *Azadirachta indica* which were used in 5 products each; *Alstonia boonei*, *Senna siamea* and *Xylopia aethiopica* in 3 products each. Nine (9) plants including *Alchornea cordifolia*, *Carica papaya*, *Cola gigantea*, *Khaya senegalensis*, *Paullinia pinnata*, *Solanum torvum*, *Spathodea campanulata*, *Tetrapleura tetraptera* and *Theobroma cacao* were active components of 2 products each. Ten (10) plants comprising *Ageratum conyzoides*, *Anthocleista nobilis*, *Bombax buonopozense*, *Citrus* × *aurantifolia*, *Cymbopogon citratus*, *Mangifera indica*, *Moringa oleifera*, *Phyllanthus fraternus*, *Pycnanthus angolensis*, *Rauvolfia vomitoria* and *Momordica charantia* were each used in a single (1) product.

Twenty-two (22) of the active plants components in the registered products have been investigated for antimalarial activity (Table 3). Most have shown moderate to strong activity, including aqueous extracts which can be considered as relevant in regard to

Table 2
Plants species used in the marketed herbal antimalarial products examined in Kumasi, Ghana.

Ghana FDA registration number of product	Medicinal plant components
FDB/HD 02-1007	*Khaya senegalensis*, *Cryptolepis sanguinolenta*
FDB/HD 02-7046	*Cryptolepis sanguinolenta*, *Alstonia boonei*, *Azadirachta indica*, *Morinda lucida*, *Xylopia aethiopica*
FDB/HD 05-10083	*Cryptolepis sanguinolenta*
FDB/HD 05-8060	*Cryptolepis sanguinolenta*
FDB/HD 05-9075	*Cola gigantea*, Solanum torvum, *Spathodea campanulata*, *Vernonia amygdalina*
FDB/HD 06-7058	*Alstonia boonei*, *Vernonia amygdalina*, *Xylopia aethiopica*
FDB/HD 07-5054	*Alstonia boonei*, *Azadirachta indica*
FDB/HD 07-7096	*Cryptolepis sanguinolenta*
FDB/HD 09-4071	*Cryptolepis sanguinolenta*, *Momordica charantia*, *Vernonia amygdalina*
FDB/HD 10-5095	*Anthocleista nobilis*, *Phyllanthus fraternus*
FDB/HD 11-9128	*Cryptolepis sanguinolenta*, *Morinda lucida*
FDB/HD 12-10154	*Cryptolepis sanguinolenta*
FDB/HD 12-10169	*Cola gigantea*, *Solanum torvum*, *Spathodea campanulata*, *Bombax buonopozense*, *Vernonia amygdalina*
FDB/HD 12-12213	*Azadirachta indica*, *Paullinia pinnata*, *Theobroma cacao*, *Tetrapleura tetraptera*, *Cymbopogon citratus*, *Moringa oleifera*
FDB/HD 12-2011	*Mangifera indica*, *Paullinia pinnata*, *Pycnanthus angolensis*, *Rauvolfia vomitoria*
FDB/HD 12-2018	*Morinda lucida*
FDB/HD 12-8101	*Carica papaya*, *Xylopia aethiopica*, *Alchonea cordifolia*
FDB/HD 12-9121	*Tetrapleura tetraptera*, *Theobroma cacao*, *Carica papaya*, *Ageratum conyzoides*, *Alchonea cordifolia*, *Senna siamea*
FDB/HD 12-9141	*Cryptolepis sanguinolenta*, *Morinda lucida*
FDB/HD 13-1020	*Azadirachta indica*, *Cryptolepis sanguinolenta*, *Vernonia amygdalina*
FDB/HD: 10-5092	*Cryptolepis sanguinolenta*, *Azadirachta indica*
FDB/HD: 11-6035	*Citrus aurantifolia*, *Senna siamea*, *Morinda lucida*
Unregistered	*Senna siamea*, *Khaya senegalensis*

Table 3
Plants species contained in the marketed herbal antimalarial products whose extract(s) reportedly showed antimalarial activity.

Cited medicinal plant contained in registered products and investigated	Extracts studied
Ageratum conyzoides[a,b,c]	Dichloromethane extracts of the whole plant (Owuor et al., 2012), aqueous extracts of the whole plant (Ukwe et al., 2010)
Alchornea cordifolia[a]	Ethanol, chloroform and ether extracts of leaves. (Banzouzi et al., 2002); Aqueous extracts of leaves (Valentin et al., 2000)
Alstonia boonei[a,b]	Aqueous and ethanol extracts of leaves and stem bark (Adepiti et al., 2014; Ménan et al., 2006)
Anthocleista nobilis[a]	Aqueous, methanol and dichloromethane extracts of leaves (Sanon et al., 2003)
Azadirachta indica[a,b,d]	Aqueous extract of leaves (Adepiti et al., 2014)
Bombax buonopozense[b]	Methanol/water extract of leaves (Akuodor et al., 2012)
Carica papaya[a]	Aqueous extract of leaves (Bhat and Surolia, 2001)
Cryptolepis sanguinolenta[a,c]	Ethanol and dichloromethane extracts of root (Ansah and Gooderham, 2002; Tona et al., 1999)
Cymbopogon citratus[a,b]	Essential oil from aerial parts (Bidla et al., 2004; Tchoumbougnang et al., 2005)
Mangifera indica[a]	Ethanol extract of stem bark (Zirihi et al., 2005); aqueous extract of leaves (Adepiti et al., 2014)
Morinda lucida[a,b]	Aqueous, ethanol and dichloromethane extracts of leaves (Makinde and Obih, 1985; Tona et al., 1999)
Moringa oleifera[a]	Acetone extract of leaves (Patel et al., 2010)
Momordica charantia[a,b]	Aqueous extract of leaves (Gbeassor et al., 1990; Ueno et al., 1996)
Paullinia pinnata[a]	Methanol extracts of leaves, stem and root (Okpekon et al., 2004)
Phyllanthus fraternus[a]	Isolated alkamides and aqueous extract of whole plant (Sittie et al., 1998)
Pycnanthus angolensis[a]	Aqueous, methanol and ethanol extracts of stem bark (Abrantes et al., 2008; Ancolio et al., 2002; Zirihi et al., 2005)
Rauvolfia vomitoria[a]	Ethanol extract of root bark (Zirihi et al., 2005)
Senna siamea[a]	Aqueous, methanol and chloroform extracts of leaves (Sanon et al., 2003)
Spathodea campanulata[b]	Hexane and chloroform extracts of stem bark (Makinde et al., 1988)
Tetrapleura tetraptera[b]	Ethanol extract of fruit (Okokon et al., 2007)
Vernonia amygdalina[a,b,c]	Aqueous, ethanol and dichloromethane extracts of leaves (Abosi and Raseroka, 2003; Tona et al., 2004)
Xylopia aethiopica[a]	Ethanol extract of leaves and stem bark (Boyom et al., 2011)

[a] Plants tested by in vitro method.
[b] Plants tested by in vivo method.
[c] Plant tested in clinical trials (Willcox, 2011).
[d] Plant with established antiplasmodial activity recorded in WHO monograph on selected medicinal plants (WHO, 2007).

traditional use.

4. Discussion

Altogether, ninety-eight (98) plant species were recorded for the treatment or management of malaria in the two study areas (Table 1). The two districts are culturally and ethnically homogenous communities in the Ashanti Region of Ghana, with the population being mainly of the Asante-Twi ethnic group. Since these two survey areas share common vegetation and climate, it was expected that they would employ common medicinal species for the management of various diseases including malaria. However, only 46.5% of plants were cited in both districts for the management malaria, thirteen (13) having a PRK > 10%. Species mentioned in one district only generally have a poorly significant use (35 have a PRK < 1%), as expected. Exceptions to this are *Afrostyrax lepidophyllus* and *Cryptolepis sanguinolenta*, which though mentioned in only one district, have PRKs as high as 5.91 and 4.43 respectively. The latter species is a well-known and studied plant for its anti-malarial property in Ghana (Abbiw, 1990; Ansah and Gooderham, 2002; Asase et al., 2005). Its PRK therefore appears relatively low in regard to its assessed clinical efficacy (Bugyei et al., 2010) and presence in nearly half of surveyed Ghana FDA-registered herbal antimalarial products. Nevertheless, the availability of this species in the study areas might account for this observation. Other plants that were cited in only one district but having relatively high PRK, comparable to those mentioned in both districts, include *Pycnanthus angolensis*, *Senna siamea*, *Solanum torvum* and *Spondias mombin*. Their widespread use within one locality only also illustrates a local discrepancy in their perceived efficacy.

According to the respondents, the herbal antimalarial preparations from these plants were safe for use by all classes of people and have long history of use without any demonstrable harm. However, a few contraindications and side effects were mentioned: *Carica papaya* and *Senna siamea* were said to be contraindicated in pregnancy. Side effects stated included frequent urination from the use of *Tridax procumbens*, diarrhoea from *Senna alata* and vomiting from the use of *Mareya micrantha*, especially when taken without food. However, for some plants with established toxicities, no specific warnings were recorded during the survey. Typical examples being the hepatotoxicity reported with *Lantana camara* in several animal species, which could yield concern regarding its chronic use (Sharma et al., 2007), and *Momordica charantia*, which is also used as an abortifacient in Ghana (van Andel et al., 2012) and which yielded fatal hypoglycaemia in children (Raman and Lau, 1996).

Based on literature search, only 66 (67.3%) of the 98 plants we recorded have already been documented in Ghana. Altogether 86 (87.8%) were documented worldwide (Table 1). *Azadirachta indica* which was the most frequently cited species (PRK = 20.2%) in our study was also the most common species encountered in all other such surveys examined. The frequent encounter of the use of these plants for the management of malaria across geographical boundaries strongly suggests their perceived efficacy. Indeed, many have been reported to possess antiplasmodial property (see Table 3).

Twelve (12; 12.2%) of the plants recorded in our study are reported for the first time for the traditional treatment of malaria (Table 1). However, antiplasmodial activity was reported for some related species. For example, *Sida acuta* was successfully tested by Karou et al. (2003) against fresh clinical isolates of *Plasmodium falciparum*, in vitro. The presence of cryptolepine, a powerful antimalarial alkaloid justifying the use of *Cryptolepis sanguinolenta*, has been mentioned in the *Sida genus*. However, the use of Sida

spp. might also be related to the presence of ephedrine, a powerful stimulant (Chatterjee et al., 2013). Similarly, an aqueous extract of *Cola caricaefolia* was reported to exhibit significant antiplasmodial activity against both chloroquine sensitive and chloroquine-resistant strains of *P. falciparum*, in vitro (Ménan et al., 2006). On the other hand, the genus is a well-known source of the stimulant compound, caffeine, which might alleviate some symptoms of the disease. Whereas the leaf of *C. nitida* is used to manage malaria in Ghana as we report here, interestingly, high intake of the seeds mimicked malaria symptoms among healthy volunteers in Nigeria (Alaribe et al., 2003). The leaf, however, may not demonstrate the same malaria-like effect since the two organs may differ in their secondary metabolic contents which are responsible for any biological activity. It would, nevertheless, worth it to investigate the leaf for such effect. The Erythrina species, *E. fusca*, *E. variegata* and *E. abyssinica* exerted significant antimalarial activity against chloroquine-sensitive (D1) and various chloroquine/multi-drug-resistant strains of *P. falciparum* (Herlina et al., 2009; Khaomek et al., 2008; Yenesew et al., 2004). Other species belonging to genera reported here, such as *Justicia betonica* (Bbosa et al., 2013) and *Secamone Africana*, often confused with *Secamone afzelii*, (Schmelzer and Gurib-Fakim, 2013) showed in vitro antiplasmodial properties. Hence the traditional use of *Sida cordifolia*, *Erythrina mildbraedii*, *Cola nitida*, *Justicia carnea* and *Secamone afzelii* for the treatment of malaria may be justified by an actual antiplasmodial potential. Also, acridone alkaloids from the fruit of *Zanthoxylum leprieurii*, a species inventoried during this survey have been found to possess antiplasmodial activity against 3D7 strain of *P. falciparum* (Tchinda et al., 2009). Other species of this genus are used as such in other areas, due to their alkaloidic contents (Jullian et al., 2006; Randrianarivelojosia et al., 2003). Convergence of use for traditional treatment of malaria at the generic level can also be noticed for *Cyclosorus afer*, in regard to *C. interruptus* from Papua New Guinea (Oyen, 2010).

Of the 98 plant species mentioned in the survey, 29 (29.6%) served as active plant components in 23 finished marketed herbal products intended for the treatment of malaria (Table 2). The 29 are widely used species for the treatment of malaria in Ghana and have been used since time immemorial (Abbiw, 1990; Asase et al., 2010, 2012, 2005; Asase and Asafo-Agyei, 2011; Asase and Oppong-Mensah, 2009; Dokosi, 1998; Mshana et al., 2001).

Most of the registered herbal remedies were multi-plant combinations containing between 2 and 7 different medicinal plant materials. The use of such combinations in the management of malaria is common and widespread in Ghana and is also observed in neighbouring countries (Asase et al., 2012, 2005; Dike et al., 2012). However, only few antimalarial evaluation of combinations were conducted in vitro or in vivo (Ankrah et al., 2003; Bertania et al., 2005; Martey et al., 2013; Tepongning et al., 2011; Willcox, 2011) but some have proved synergistic as in the case of a mixture of *Azadirachta indica*, *Alstonia boonei*, *Mangifera indica* and *Morinda lucida* in *P. berghei* infested mice (Adepiti et al., 2014).

Cryptolepis sanguinolenta was the most employed, occurring in 11 products, 4 in which it was used alone. It was one of the few species of the 98 to have reportedly undergone clinical trials for efficacy and safety evaluation (Willcox, 2011, Table 3). Bugyei et al. (2010) indeed demonstrated that the tea bag formulation of the root powder was non-toxicand highly effective in the treatment of acute uncomplicated malaria on relatively short treatment regimens, with parasite clearance similar to that induced by usual doses of *Artemisia annua* leaves and *Cinchona* sp. bark herbal teas in similar conditions (for a comparison of these trials, see Willcox (2011)). The genotoxic potential of the active principle of *C. sanguinolenta*, cryptolepine, is reported not to be associated with severe side effects (Appiah, 2009) but warrants surveillance.

Azadirachta indica, though the most frequently cited species for managing malaria in our and other Ghanaian field studies, was employed in as few as 5 finished marketed herbal antimalarial products. It is noteworthy that the in vitro antimalarial property of *Azadirachta indica* has been reported in WHO monographs on selected medicinal plants (WHO, 2007). The leaves of *Vernonia amygdalina*, which are included in 5 of the registered combinations, also proved clinically effective (Willcox et al., 2011). It was however observed that plants such as *Argemone mexicana*, which was inventoried in our and other field surveys and has clinical data on its antimalarial activity (Willcox, 2011; Willcox et al., 2011) and preclinical evidence of safety (Njan, 2012), was not included in any of the marketed products identified.

The manufacture and the sale of these products are regulated under an Act of the Ghanaian Parliament, Act 851 (Public Health Act, 2012). Additionally, the herbal products are registered by Ghana's FDA in accordance with national guidelines (Ghana, 2013b), which largely conform to WHO African region's guidelines for registration of herbal medicinal products (WHO, 2010a). However, there is no clinical data in support of these products and their use therefore is fundamentally based on anecdotal evidence of efficacy. Such products, therefore, fall under "Category 2" herbal products as defined by WHO (2010a). While many of the plants used in these product are reported safe and did not show significant treatment-related toxicity in treated animals (Grover and Yadav, 2004; Moura et al., 2005; Oduola et al., 2010) and on cells (Sanon et al., 2013), others have been reported for some levels of toxicity. For example, *Alstonia boonei* stem bark extract is reported to show reversible antifertility toxicity in treated rats (Raji et al., 2005) and *Paullinia pinnata* root exhibited moderate cytotoxicity against some cell lines (Ayim et al., 2008). The root of *Rauvolfia serpentina* is known for its cardiac and central nervous system side effects, linked to its content in reserpine and other indolomonoterpenes (Klyushnichenko et al., 1995). Such issues are of prime concern regarding clinical use and registration (Willcox et al., 2011).

The labels on the finished marketed herbal antimalarial products generally conformed to the Ghana FDA's labelling requirements (Ghana, 2013a), indicating product names, names of active plant constituents (but without mentioning the parts used nor proportions), therapeutic indications, mode of administration, dosage regimen and sometimes dosages for children, duration of use, contraindications, warnings and precautions, manufacturing and expiry dates, batch numbers and name of manufacturer or company with full address. However, the packages do not contain information leaflets. Due to lack of data, information on drug interactions and dosage for the elderly were absent, though they might be appropriate. It is therefore important that scientists work in tandem with the herbalists in the development of these remedies, in order to address these challenges, in respect of national and WHO standards. Such cooperation shall ideally be supportive of pharmacovigilance.

Many medicinal plants used as home-remedies to manage malaria are currently used for large scale production of finished marketed herbal products in Ghana, providing accessibility and quality-products to many patients, especially in urban areas. This, thus contributes to WHO's goal of promoting universal health coverage through accessibility to medication (WHO, 2013a). However, large scale commercial production of finished herbal products coupled with the extensive harvest and informal sales of medicinal plants in the Ghanaian markets (Asase and Oppong-Mensah, 2009) is prone to lead to unsustainable exploitation. This is a potential threat to survivability of medicinal plants used for these preparations and might particularly be the case for several of the species identified with high PRK in our survey, when compared to sales volumes estimated by Van Andel et al. (2012) for the country. Indeed, *Afrostyrax lepidophyllus*, *Morinda lucida* or

Rauvolfia vomitoria are wild plants accounting among the most frequently encountered species at the Ghanaian markets, with high sales volumes. Efforts towards the conservation of such plants are crucial (Cordell, 2014). Fortunately, in Ghana, cultivation of some medicinal plants by farmers and herbalists (e.g. *Moringa oleifera*, *Khaya senegalensis*, *Xylopia aethiopica*) has started on a large scale, for direct use and retail.

Also, with the increasing availability of finished remedies in commercial quantities and the fact that some of these products have not been authorized by the drug regulatory authority of Ghana's FDA (Table 2), it is important to ensure strict regulation in order not to compromise the health and safety of the people who patronize them. It is also important that scientists work with herbalists to conduct clinical trials on these products as recommended by the WHO (2010a). Case-control and retrospective studies could be conducted (Graz, 2013) to ascertain the claims of registered herbal products whose access to the market did not rely on specific clinical studies.

5. Conclusion

Despite the various documentations on the medicinal plants used to manage malaria in Ghana, many such plants remain undocumented. Also, many medicinal plants are currently used for commercial production of finished marketed herbal antimalarial products in the country.

This study thus adds to the existing literature on plants used to treat malaria and has thrown light on the development of herbal antimalarial products in Ghana.

Competing interest

The authors declare no conflict of interest.

Acknowledgements

We are most grateful to the herbalists in the Bosomtwe and Sekyere East Districts of the Ashanti region, Ghana, for freely sharing their knowledge and time with us during the study. We also feel indebted to the chiefs and the opinion leaders of the various communities and many citizens of the two Districts who helped us in identifying the herbalists. We recognize the contributions of Misses Amanda Akomah-Donkor and Bertha Ewune Ekosse in conducting the survey. We are grateful to Dr. G.H. Sam of Department of Herbal Medicine, Faculty of Pharmacy and Pharmaceutical Sciences, Kwame Nkrumah University of Science and Technology (KNUST), Kumasi, Ghana, for the authentication of the plants. We acknowledge the staff of Forestry Research Institute of Ghana (FORIG) especially Mr. M.F. Mensah for their technical assistance in the identification of some of the plants. Map (Fig. 1) was adapted from Wikimedia Creative commons. We acknowledged the referees for their meticulous evaluation of the manuscript.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.jep.2015.06.041.

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