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Medicinal Plants Constituting Antimalarial Herbal Preparations in the Ghanaian Market

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Authors' contributions

All authors collaborated in the conduct of the research. Authors SNOD and SOA designed the study and wrote the manuscript. Authors EAA and RN carried out the survey (i.e. collection of data for the study). Authors SNOD, DS and GOD took care of the literature searches and data analysis. The final manuscript was approved by all the authors.

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ABSTRACT

Aims: Malaria is hyper-endemic in many parts of Ghana, and a greater percentage of the population use herbal preparations to treat the disease. This study was conducted to find out the medicinal plants that constitute the components of antimalarial herbal mixtures sold in Ghana.
Place and Duration of Study: The study was conducted in Accra (the capital city of Ghana) and Kumasi (the second largest city in the country) by researchers from the Department of Pharmaceutical Sciences at Kumasi Polytechnic. It was carried out between May and July, 2012.
Methodology: The study was based on direct observation and recording of information on available antimalarial herbal products in some Pharmacies and Herbal Medicine Shops in the two cities.
Results: The study identified forty one different herbal mixtures used as antimalarials. Fifty seven plants belonging to 28 plant families, and one animal product (honey), were found to be the components of the herbal mixtures. *Cryptolepis sanguinolenta* and *Azadirachta indica*, respectively

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found in 29.3% and 22.0% of the preparations, were the commonest plant components.
Most of the plant components found are reported in traditional medicine or pharmacological studies to treat malaria. These antimalarial claims are indicative of indigenous knowledge in the management of malaria.
Conclusion: With the necessary product standardisation and safety investigations, some of the antimalarial herbal products may offer alternative treatment of malaria in Ghana.

Keywords: Antimalarial herbal mixture; Cryptolepis sanguinolenta; Azadirachta indica; medicinal plants.

1. INTRODUCTION

Malaria is a common infectious disease found mostly in the tropical climates. It is caused by a protozoan of the Plasmodium genus, and transmitted through the bite of the female Anopheles mosquito. Five species of the Plasmodium parasites (namely *P. falciparum, P. vivax, P. ovale, P. malariae and P. knowlesi*) are known to cause malaria worldwide [1]. *P. falciparum* is the most noxious and the species that preponderates in Ghana and Africa as a whole [2]. Clinical manifestations of the disease include fever, chills, prostration and anaemia, as well as delirium, metabolic acidosis and multi-organ system failure, which may be followed by coma and death [3,4].

It is estimated that in 2010, more than 200 million malaria cases were recorded in Africa, and approximately 781,000 deaths of which nearly 85% being children were documented [5]. In Ghana, malaria is hyper-endemic in all parts of the country, and the disease is a threat to the total population all year round. It is estimated that malaria tops the causes of morbidity in the country; responsible for 38% of all outpatients diseases, 36% of all hospital admissions, and 33% of deaths in children aged less than five years. In addition, it is estimated that annual reported cases of clinical malaria to health facilities range from 3.1 to 3.5 million, out of which 900,000 cases are recorded in children under five. In 2008 alone, it was estimated that about 14,000 deaths were recorded as being caused by malaria [6].

Many strategies are employed in malaria endemic zones in the treatment or management of the disease. These strategies vary from control of the mosquito vector through the use of insecticides and insecticide-treated bed-nets, to the use of drugs as preventive or treatment measures. In the prevention and/or treatment of malaria, either an orthodox drug or traditional (herbal) preparation is mostly used in many parts of Ghana. The orthodox medicines employed mostly in malaria treatment are the Artemisinin-based Combination Therapy (ACTs). The World Health Organisation (WHO) recommends five (5) types of ACTs namely artemether plus lumefantrine, artesunate plus amodiaquine, artesunate plus mefloquine, artesunate plus sulfadoxine- pyrimethamine, and dihydroartemisinin plus piperaquine for use in malaria treatment [7]. The herbal medicines are the various morphological parts of medicinal plants that are formulated to treat malaria. Some patients resort to the use of herbal preparations as their first choice of medication and others use it after the orthodox ones have failed; others still use them complementarily with the orthodox drugs.

The use of herbal antimalarials has gained prominence in the few past decades. The choice for herbals may be based on its availability and relative affordability [8] as well as its effectiveness. Furthermore, for decades most of the effective antimalarials have come from plants either directly or indirectly. For example quinine, an aminoquinoline alkaloid, has been in use for about 400 years since its discovery [9] from various species of Cinchona (Rubiaceae). Synthetic derivatives of quinine, such as mefloquine, primaquine and chloroquine have also been used at various stages to treat or prevent malaria [10]. The use of artemisinin and its derivatives from the Chinese medicinal plant *Artemisinin annua* [11] has also gained recognition as one of the most effective antimalarials, either alone or in a combination based therapy.

Traditional antimalarials are extensively employed among rural communities who readily look for remedies in plants in their local environments. The use of herbal remedies is, however, not restricted to only the rural folks, it is also important in urban areas of Ghana where conventional medicines are available [12].

Previous studies have documented over 1,200 plant species from 160 families used in the treatment of malaria or fever [8]. In Ghana, some ethnobotanical studies have been conducted on herbal therapies used for the treatment of malaria in different communities and localities [12-14]. These studies have always focused on plants purported to have antimalarial activities; none so far on the herbal constituents of the commercial antimalarial herbal mixtures.

Due to the upsurge in the use of herbal antimalarials some herbal practitioners and some local companies have formulated many herbal preparations and sell them to the public apparently for the treatment of malaria. Different plants are sometimes combined to produce these commercial herbal preparations. The aim of this study therefore was to identify the medicinal plants that constitute antimalarial herbal mixtures in Ghana in view of compiling the most commonly used plants.

2. METHODOLOGY

2.1 Ethical Considerations

In the study permission was sought from managers or attendants of facilities where herbal preparations are sold to carry out a research study on plant species found in the herbal antimalarials on sale to the general public. The aim of the study was explained to them.

2.2 Study Design

Outlets where medicinal products are sold in the study areas were visited, and available herbal medicinal products used in treatment of malaria were requested to be observed. The preparations were observed and the information needed (the plant species constituting the antimalarial herbal preparation per what is written on the labels) were recorded. In addition the manufacturing company and the Food and Drugs Authority (FDA) registration reference (if any) were also recorded. The FDA is a government agency that controls the manufacture, importation, exportation, distribution, use and advertisement of food, drugs, cosmetics, chemical substances and medical devices in Ghana.

2.3 Study Population

The study was conducted in Accra (the capital city of Ghana) and Kumasi (the second largest city in the country) from May to July 2012. These two cities are found in the most populous regions (the Greater Accra and Ashanti regions) in the country. According to the 2010 Population and Housing Census report, the Greater Accra and Ashanti regions have a respective population of 16.4% and 19.5% of the total national population.

Accra, the largest city and the administrative, communications and economic center of Ghana, is located at 5°30' North, 0°10' West. In Ghana there are ten (10) administrative regions, the Greater Accra Region (which has Accra as the Regional and National Capital) is the smallest region with regards to area as it occupies a meager 1.4% of total land surface area of Ghana. In terms of population, however, it is the second most populated region (after the Ashanti Region). Kumasi, which is about 270 km from the national capital Accra, is approximately 480 km north of the equator and 160 km north of the Gulf of Guinea. It is the capital city of the Ashanti region, an important and historical centre for Ghana. These two cities were chosen for the study because they are homes to many people from different ethnic backgrounds. Commercial activities are very high and almost every commercial product in the country could be found in these cities. In all, fifty one retail and wholesale Pharmacies and Licensed Chemical Shops, and nineteen Herbal Medicine Shops were visited for the data.

2.4 Eligibility Criteria

Every shop or store where herbal medicines are sold qualified to be part of the study. By this criteria, all Community Pharmacies (both retail and wholesale), Licensed Chemical Shops and Herbal Medicine Shops in the two cities in Ghana were eligible for the study. In Ghana, individuals who are not pharmacists but have been certified by the Pharmacy Council (a regulating body on medicines) can sell Class C (*over-the-counter*) drugs in what is commonly termed as Licensed Chemical Shops to the general public especially in rural areas.

2.5 Data Collection

The work is based on direct information gathered by personal contact with local outlets where herbal preparations used in treatment of malaria can be acquired by any individual. The required information designed for the study was observed and recorded with the assistance of the attendants.

2.6 Data Analysis

The data accumulated were analyzed using Microsoft Office (Excel) 2007. The number of herbal medicinal antimalarials encountered was recorded together with the local trade names of the products and their respective constituting plant species. The individual plant species were grouped into their particular plant families and their frequency of use recorded.

3. RESULTS AND DISCUSSION

The study identified forty one different antimalarial herbal mixtures in the study areas (Table 1). Fifty seven medicinal plant components belonging to 28 plant families (Table 2) were found in these herbal mixtures claimed to be useful in managing malaria. The preparations contained different number of plants ranging from one to seven (Table 1). Two preparations had only one plant each as constituent or component; and two had as many as seven plants constituting the mixture. On the average each preparation contained 3 to 4 plants. With the use of medicinal plants to treat disease, one plant preparation can contain literally hundreds of natural constituents, unlike western medicine where the active ingredient of a drug is mostly a single compound with discrete therapeutic role in the body. And for herbal preparations of multiple plants or herbs, several hundreds of natural compounds or constituents are to be expected. It has been claimed that the many different compounds from combination of plants play mutualistic and synergistic roles to augment the total effectiveness of the herbal mixtures, and this has been used as the greatest asset of phyto-therapy [15].

Most of the plant species found to be components of the antimalarial herbal mixtures sold on the market have been investigated for their antimalarial activities and phytochemical constituents. The plants that were found in more than 10% of the preparations encountered in the market included *Cryptolepis sanguinolenta, Azadirachta indica, Alstonia boonei, Morinda lucida, Nauclea latifolia, Khaya senegalensis, Vernonia amygdalina, Carica papaya, Rauwolfia vomitoria* and *Cassia siamea* as found in Fig. 1. *C. sanguinolenta* was found to be the most frequently used plant in Ghanaian antimalarial herbal mixtures.

Table 1. Antimalarial herbal products on the Ghanaian market and their constituent plants

Serial no	Herbal antimalarial product	Plant species of the product
1.	Adom malamix	*Cryptolepis sanguinolenta, Azadirachta indica*
2.	Adutwumwaa malamix	*Anthocleista nobilis, Vites grandifolia, Phyllanthus fraternus*
3.	Akos herbal mixture	*Alstonia boonei, Alchornea cordifolia, Musanga cecropioides*
4.	Alive fevicure mixture	*Phyllanthus niruri, Nauclea latifolia, Azadirachta indica*
5.	Angel herbal mixture	*Cola gigantean, Solanum torvum, Spathodea campanulata, Bombax buonopozense, Vernonia amygdalina*
6.	BRS mala mixture	*Tabernaemontana crassra, Acacia siamea, Morinda lucida*
7.	Crystal herbal mixture	*Azadirachta indica, Ocimum gratissimum, Carica papaya, Solanum torvum*
8.	Danaq herbal mixture	*Alstonia boonei, Vernonia amygdalina, Xanthoxyllum xantherozoides, Xylopia aethiopica*
9.	Duapa bitters	*Khaya senegalensis, Alchornea cordifolia, Trichilia heudoletii*
10.	Ebenezer favare mixture	*Alstonia boonei, Morinda lucida, Rauwolfia vomitoria, Tetrapleura tetraptera*
11.	Ebetoda bitters	*Khaya senegalensis, Anthocleista nobilis, Rauwolfia vomitoria, Urena lobata*
12.	Eff's malamix	*Nauclea latifolia, Cryptolepis sanguinolenta*
13.	Fosuaa herbal mixture	*Morinda lucida, Cassia alata, Theobroma cacao, Tectona grandis, Raphia hookeri, Carica papaya, Citrus aurantifolia*

Serial no	Herbal antimalarial product	Plant species of the product
14.	Fralena stop fever	*Cryptolepis sanguinolenta, Khaya senegalensis, Nauclea latifolia*
15.	Gidimal herbal	*Cryptolepis sanguinolenta, Morinda lucida, Nauclea latifolia*
16.	Golden herbal mixture	*Acacia nilotica, Azadirachta indica, Nauclea latifolia*
17.	Herbaquin	*Cryptolepsis sanguinolenta, Alstonia boonei, Azadirachta indica, Monodora myristica, Xylopia aethiopica*
18.	Krobo fever eduro	*Cryptolepis sanguinolenta, Vernonia amygdalina, Momordica charantia, Latifolia*
19.	Link malakill mixture	*Nauclea latifolia, Morinda lucida, Cryptolepis sanguinolenta*
20.	Malahela mixture	*Cassia siamea, Citrus aurantium, Ananas comosus, Saccharum officinarum*
21.	Malarigo mixture	*Citrus aurantifolia, Cassia siamea*
22.	Mama-mix mahoney malaria Mixture	*Alstonia boonei, Alstonia nooei, Cassia siamea, Chromolaena odorata*
23.	Masada mixture	*Cryptolepis sanguinolenta*
24.	Mensprin herbal mixture	*Carica papaya, Cleistopholis patens, Baphia nitida, Allium cepa*
25.	Misparone OA	*Pycnanthus angolensis, Mitragyna stipulosa, Ocimum gratissimum, Ricinodendron heudelotii*
26.	M-sons bitters	*Khaya senegalensis (stem bark), Rauwolfia vomitoria (stem bark), Ocimum gratissimum (leaves), Tetrapleura tetraptera (fruits, leaves)*
27.	New kingdom mixture	*Nauclea latifolia, Phyllanthus fraternus, Cryptolepis sanguinolenta*
28.	Nibima	*Cryptolepis sanguinolenta*
29.	Nkrumah herbal mixture	*Khaya senegalensis, Erythrina mildbraedii, Morinda lucida*
30.	Osei herbal malamix	*Citrus aurantifolia, Cassia siamea, Morinda lucida*
31.	Osompa tystrong syrup	*Dry Pawpaw leaves, Cassia alata*
32.	Roc mixture	*Allium sativum, Azadirachta indica, Cassia podocarpa, Citrus aurantifolia, Honey*
33.	Rooter mixture	*Aloe schweinfurthii, Khaya senegalensis, Pileostigma thonningii, Cassia siamea*
34.	Sak bitters	*Rauwolfia vomitoria, Vernonia amygdalina*
35.	Taabea herbal mixture	*Ocimum viride, Azadirachta indica, Paullinia pinnate, Tetrapleura tetraptera, Theobroma cacao, Moringa oleifera, Cymbopogon citratus*
36.	Time herbal mixture	*Cola gigantean, Solanum torvum, Spathodea campanulata, Bombax buonopozense, Vernonia amygdalina*
37.	Tinatett malakare	*Carapa procera, Cryptolepis sanguinolenta*
38.	Top fever syrup	*Azadirachta indica, Alstonia boonei*
39.	Typhofa – 202	*Ocimum viride 15%, Vernonia amygdalin 15% Morinda lucinda 25%, Alstonia boonei 25% Carica papaya 10%, Corn still 10%*
40.	Yaakson mixture	*Khaya ivorensis,Mangifera indica, Paullinia pinnata, Pycanthus angolensis, Rauwolfia vomitoria*
41.	Yafo fever mixture	*Cryptolepis sanguinolenta Azadirachta indica*

Table 2. The plants found in the mixtures, their families and frequency of mention

No.	Family	Plant components	Frequency of occurrence in preparations
1.	Anacardiaceae	*Magnifera indica*	1
2.	Annonaceae	*Cleistopholis patens*	1
		Monodora myristica	1
		Xylopia aethiopica	2
3.	Apocynaceae	*Alstonia boonei*	7
		Cryptolepis sanguinolenta	12
		Rauwolfia vomitoria	5
		Tabernaemontana crassa	1
4.	Arecaceae	*Raphia hookeri*	1
5.	Asteraceae	*Chromolaena odorata*	1
		Vernonia amygdalina	6
6.	Bignonaceae	*Spathodea campanulata*	2
7.	Bombacaceae	*Bombax buonopozense*	1
8.	Bromeliaceae	*Ananas comosus*	1
9.	Caricaceae	*Carica papaya*	5
10.	Cucurbitaceae	*Momordica charantia*	1
11.	Euphobiaceae	*Alchornea cordifolia*	2
		Phyllanthus fraternus	2
		Phyllanthus niruri	1
		Ricinodendron heudelotii	1
12.	Fabaceae	*Acacia nilotica*	1
		Baphia nitida	1
		Tetrapleura tetraptera	3
13.	Lamiaceae	*Ocimum gratissimum*	3
		Ocimum viride	2
		Vitex grandifolia	1
14.	Leguminosae	*Cassia podocarpa*	1
		Cassia siamea	5
		Cassia alata	2
		Erythrina mildbraedii	1
		Piliostigma thonningii	1
15.	Liliaceae	*Allium cepa*	1
		Allium sativum	1
		Aloe schweinfurthii	1
16.	Loganiaceae	*Anthocleista nobilis*	2
17.	Malvaceae	*Urena lobata*	1
18.	Meliacea	*Azadirachta indica*	9
		Carapa procera	1
		Khaya senegalensis	6
		Khaya ivorensis	1
		Trichilia heudoletii	1
19.	Moraceae	*Musanga cecropioides*	1
20.	Moringaceae	*Moringa oleifera*	1
21.	Myristacaceae	*Pycanthus angolensis*	1
22.	Poaceae	*Cymbopogon citratus*	1
		Saccharum officinarum	1
23.	Rubiaceae	*Mitragyna stipulosa*	1
		Morinda lucida	8
		Nauclea latifolia	7
24.	Rutaceae	*Citrus aurantifolia*	4
		Citrus aurantium	1
		Zanthoxylum zanthoxyloides	1
25.	Sapindaceae	*Paullinia pinnata*	2

No.	Family	Plant components	Frequency of occurrence in preparations
26.	Solanaceae	*Solanum torvum*	3
27.	Sterculiaceae	*Cola gigantea*	2
		Theobroma cacao	2
28.	Verbanaceae	*Tectona grandis*	1

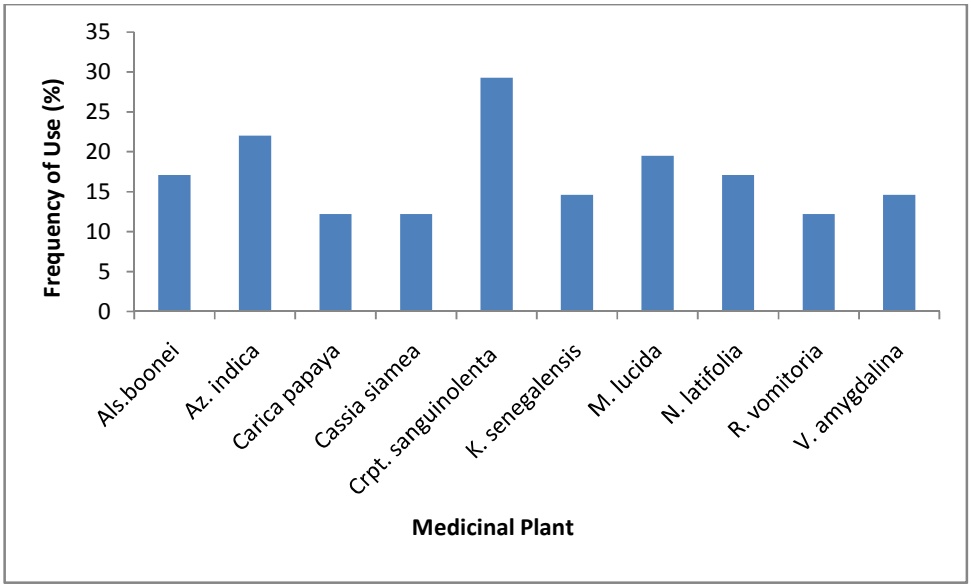

Fig. 1. Percentage of occurrence of commonly found plants in antimalarial herbal mixtures in Ghana

The medicinal plants that were categorized in the study were not identified. The information was based on what the manufacturers have indicated on the labels of the products. The important aspect of the work was to generate data on antimalarial medicinal plants that have been used locally to prepare mixtures for sale to the general public. Medicinal plants are normally identified by experts in order to be sure that the plant being used is the actual plant required.

For every four antimalarial herbal products on the Ghanaian market, at least one may contain *C. sanguinolenta*. This plant has been used in the management of malaria in Ghana and other African countries for a very long time; it is a well-known antimalarial ethnomedicinal plant in West Africa [16]. An alkaloidal compound, cryptolepine, isolated from the plant has been found to be responsible for the observed antimalarial activity. The compound has been investigated as a potential lead to new antimalarial [17]. In one study the compound had a potent in vitro antiplasmodial activity, but when given orally to mice, it could not cure the malaria; and it was found to be toxic when given intraperitoneally [18].

Azadirachta indica (family Meliceae) known commonly as neem tree, was also found to be frequently used in antimalarial herbal mixtures; it was found in 22.0% of the products. The plant is native to Asia [19] but has somehow naturalised in West Africa where it has various local names. It is sometimes used as an ornamental plant. Traditionally, it is used to treat various ailments including malaria [20]. The aqueous infusion, decoction and alcoholic extract of the stem bark and leaves of the plant are used to treat malaria in various West African countries [21] such as Ghana. A study conducted by Mehran [22] showed that neem tree has a potent and fast acting schizontocidal as well as gametocytocidal activity on *P. falciparum*. According to their study, the bark decoction of the plant when given thrice a day for four consecutive days had a cure rate of 100% and recrudescence rate of just about 1%.

Alstonia boonei De wild, belonging to the family Apocynaceae, is one of the medicinal plants mostly used in Africa folklore medicine to treat malaria [23,24]. A study conducted by Iyiola and others [25] showed that the ethanolic stem bark extract of the plant has a potent antimalarial

activity in an *in vivo* study in mice, producing a dose-dependent activity against the Plasmodium parasites in the suppressive, curative and prophylactic tests.

Other plants such as *Morinda lucida, Nauclea latifolia, Khaya senegalensis, Vernonia amygdalina, Carica papaya, Rauwolfia vomitoria* and *Cassia siamea* found to be present in most of the preparations encountered in the study, have also been reported to be useful in traditional medicine in managing malaria in various African communities [24,26,27]. The reported antimalarial activities of these plants are indicative of the scientific basis of indigenous knowledge of herbalists in treatment of malaria.

In the management of malaria using medicinal plants some practitioners incorporate plants that do not have antimalarial activity but may have properties such as analgesia, anti-pyrexia or anti-anaemia to give symptomatic relief. Others add plants or agents that may enhance the taste of the mixtures. For example, one of the products has honey (an animal product) as one of the ingredients. It was added perhaps to mask an unpleasant taste of the preparation as most antimalarial herbal mixtures have bitter taste. In another product, *Saccharum officinarum* commonly known as sugarcane was a component. Again this plant was possibly added as a sweetener, though it has been indicated that it has anti-pyretic activity [28], to improve taste but not necessarily as an antimalarial agent.

In the study, some of the plants indicated on the packaging or containers of the herbal mixtures could not be found in the literature. For instance one product contained *Alstonia nooei* as a component; this species 'nooei' was not found in the literature. Furthermore, some manufacturers had indicated only one of the two names for the binomial system of classification, and this makes it difficult to decipher in such situations if it is the genus or the species name being referred to. For example one product only indicated 'Latifolia'.

Good manufacturing practices (GMP) requires that labels on medications should among other things specify the ingredients (and the amount) used in the product. Almost all the antimalarial herbal products found did not indicate the morphological part of the plant used in the mixture; neither did they state the quantities of each plant used. Only one product each stated the morphological parts of the constituting plants and the amount (in percentage) of the plants used. In the Traditional System of treatment using herbal medicine, most practitioners shroud their activities (method of production and even the plant material) in secrecy. This, apparently, is to prevent others from making similar products or collecting the plant material from the wild for that purpose. Regulatory bodies in the country, such as the FDA and the Traditional Medicine Practice Council, should be proactive in their monitoring activities so that commercial products such as the antimalarial herbal mixtures could be properly standardized as these products are highly patronized.

4. CONCLUSION

The study has shown that there are many medicinal plants in Ghana that could be used in the management of malaria. Most of these plant species could be incorporated in the Ghana Herbal Pharmacopeia after scientific evaluation and safety profiles have been established. Additionally, if the regulating bodies could help establish better policies on practice and use of herbal medicines, especially with regards to good manufacturing practices (GMP) and standardization of the herbal antimalarials, some of these products may help minimize the incidence and cost of treatment of malaria in Ghana.

CONSENT

Not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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