# REVIEW





# Systematic review on traditional medicinal plants used for the treatment of malaria in Ethiopia: trends and perspectives

Getachew Alebie<sup>1\*</sup>, Befikadu Urga<sup>2</sup> and Amha Worku<sup>1</sup>

# Abstract

**Background:** Ethiopia is endowed with abundant medicinal plant resources and traditional medicinal practices. However, available research evidence on indigenous anti-malarial plants is highly fragmented in the country. The present systematic review attempted to explore, synthesize and compile ethno-medicinal research evidence on antimalarial medicinal plants in Ethiopia.

**Methods:** A systematic web search analysis and review was conducted on research literature pertaining to medicinal plants used for traditional malaria treatment in Ethiopia. Data were collected from a total of 82 Ethiopian studies meeting specific inclusion criteria including published research articles and unpublished thesis reports. SPSS Version 16 was used to summarize relevant ethno-botanical/medicinal information using descriptive statistics, frequency, percentage, tables, and bar graphs.

**Results:** A total of 200 different plant species (from 71 families) used for traditional malaria treatment were identified in different parts of Ethiopia. Distribution and usage pattern of anti-malarial plants showed substantial variability across different geographic settings. A higher diversity of anti-malarial plants was reported from western and southwestern parts of the country. Analysis of ethno-medicinal recipes indicated that mainly fresh leaves were used for preparation of remedies. Decoction, concoction and eating/chewing were found to be the most frequently employed herbal remedy preparation methods. Notably, anti-malarial herbal remedies were administered by oral route. Information on potential side effects of anti-malarial herbal preparations was patchy. However, some anti-malarial plants were reported to have potentially serious side effects using different local antidotes and some specific contra-indications.

**Conclusion:** The study highlighted a rich diversity of indigenous anti-malarial medicinal plants with equally divergent herbal remedy preparation and use pattern in Ethiopia. Baseline information gaps were observed in key geographic settings. Likewise, herbal remedy toxicity risks and countermeasures generally entailed more exhaustive investigation. Experimental research and advanced chemical analysis are also required to validate the therapeutic potential of anti-malarial compounds from promising plant species.

Keywords: Medicinal plants, Malaria, Ethiopia

# Background

Malaria remains one of the world's leading health problems, causing about 429,000 deaths in 2015, the vast majority of deaths (99%) were due to *Plasmodium falciparum* malaria [1]. In that year, most (92%) of the deaths

\*Correspondence: gechalebie@gmail.com

<sup>1</sup> Department of Biology, Jigjiga University, P.O. Box-1020, Jijiga, Ethiopia Full list of author information is available at the end of the article

were estimated to have occurred in the sub-Saharan Africa region. Children were particularly affected by the disease with 70% of malaria-caused deaths occurring among the under five-year age group [1, 2]. In Ethiopia, the majority (around 68%) of populations live in areas deemed malarious or potentially malarious [3]. Despite recent improvements in malaria control strategies, the disease remains a major public health problem and a



© The Author(s) 2017. This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/ publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.

leading cause of outpatient consultations, admissions and death in the country [4, 5].

In recent years, emergence of drug-resistant *Plasmodium* species has exacerbated the health and economic impact of malaria. In particular, *P. falciparum* (the most pathogenic human parasite) has developed resistance to virtually all currently available anti-malarial drugs [6]. Consequently, research for alternative antimalarial drugs has accelerated over the last two decades [7]. Historically, medicinal plants have been the focus of many researches aimed at discovering alternative anti-malarial drugs in different parts of the world [8]. This has led to the discovery of numerous antimalarial compounds with significant structural varieties, including quinines, triterpenes, sesquiterpenoids, quassinoids, limnoids, alkaloids, lignans, and coumarins [9].

Around 80% of Ethiopian populations (particularly rural societies) still rely on traditional medicinal plants to fight a number of diseases. This was attributed to high cost of modern drugs, paucity and inaccessibility of modern health services, and cultural acceptability of traditional medicine [10, 11]. Communities inhabiting different localities in the country have developed their own medical plant arsenals and knowledge on their utilization, management and conservation [12]. A large variety of medicinal plants are used as traditional malaria remedy in different parts of Ethiopia [13–17].

Proper documentation of traditional medicine and plants used in the prophylaxis and treatment of malaria constitutes an important task not only in preserving precious indigenous knowledge and biodiversity but also in enhancing community access to and stakes in improvement of malaria control interventions. It is also crucial for stimulating future research on safety and efficacy of medicinal plants and identification of chemical entities that could be developed into new standardized phytomedicines. In contrast, ethno-botanical and ethno-pharmacological research on indigenous antimalarial plants is still at a rudimentary stage in Ethiopia [18]. Moreover, available research evidence on indigenous anti-malarial plants is highly fragmented, which underscores serious need for systematic compilation and synthesis.

The present systematic review attempted to explore, synthesize and compile ethno-medicinal research findings on anti-malarial plants in Ethiopia.

## Methods

A systematic analysis and review of research literature related to medicinal plants used for traditional malaria treatment in Ethiopia was conducted between April and October 2016.

## Search strategy

A web-based systematic research literature search strategy was employed. Ethno-botanical/ethno-medicinal studies reporting on medicinal plants used for traditional malaria treatment in Ethiopia were gathered by two different search approaches, including:

- Search for unpublished MSc/PhD thesis research reports using Google search engine and local university websites;
- Search for published journal articles using international scientific databases including PubMed, Science direct, Web of Science, Google scholar, AJOL, etc.

Literature search was performed using the following key terms: Ethiopia/Ethiopian plants/Ethiopian medicinal plants/Ethiopian anti-malarial plants, Malaria/Antimalarial/Anti-malarial plants, Traditional/Traditional knowledge/Traditional Medicine/Traditional medicinal plants, Medicinal Plants/Medicinal herbs, Indigenous/ Indigenous knowledge, Plants/Herbal/Medicine/Remedies, Folk Medicine/Folk remedies/Home remedies/ Herbal remedies, Ethnobotany/Ethnobotanical, Ethnopharmacology/Ethnopharmacological, Ethnomedicine/ Ethnomedicinal, Ethnopharmaceutical, Medico-cultural.

#### Screening and criteria

Screening of search outputs was performed in two stages. First, the title and abstract of identified journal articles/ theses was overviewed. Thereafter, suitable articles/theses were downloaded and critically inspected for inclusion in the review. Literature screening was based on the following inclusion and exclusion criteria.

## Inclusion criteria

Published and unpublished ethno-botanical and ethnomedicinal surveys reporting on anti-malarial plant/s, conducted at any time period in Ethiopia

#### **Exclusion criteria**

The following types of research data were excluded from analysis:

- Data from review articles, historical documents or experimental studies;
- Data from published and unpublished ethno-botanical and ethno-medicinal surveys lacking information on anyone of the following: study areas/localities, informant's involvement, scientific plant names, and not reporting information about anti-malarial medicinal plants;
- Data from non-open access journal articles or partially accessed (abstract only) articles.

# Data retrieval

Relevant information pertaining to Ethiopian anti-malarial medicinal plants was retrieved using a structured Excel format by directly quoting reported values. In order to provide uniform information on preparation methods of the remedy, the following terms were established, and they signified the respective preparation processes described herein: Concoction: mixing/combining different ingredients to make a dish; Decoction: boiling the materials and extracting essences or active ingredients; Infusion: macerating/soaking the materials in a liquid or water; Homogenization: homogenizing ingredients; Pounding: grinding, pulverizing, chopping or crushing of ingredients; *Cooking:* preparing food (remedy) for eating by adding ingredients; Smoking: burning dry materials and inhaling the smoke; Bathing/evaporating: boiling the materials and taking the vapour or steam through intranasal and whole body.

In addition, missed information in some studies, particularly local name and habit of the plants, and misspelled scientific names were retrieved from Natural Database for Africa (NDA), Version 2.0. In case of some research papers lacked geographic locations of the study localities/districts, information was retrieved through direct web (Google) searching.

#### Data analysis

All data were entered into Statistical Software Packages for Social Science (SPSS, software version 16.0). A descriptive statistical methods, percentage and frequency were used to analyse ethno-botanical data on reported medicinal plants and associated indigenous knowledge. The results were presented using charts and tables.

## Results

# Overview of ethno-medicinal studies on medicinal plants

Ethno-medicinal studies on plants demand standard procedures for botanical identification and reliable documentation of indigenous knowledge pertaining to plant distribution, management and traditional medicinal use. A total of 82 original ethno-medicinal studies representing ten different regions in Ethiopia were included in this review. Both published and unpublished (M.Sc. and Ph.D. theses) research reports were reviewed. Overall, the reviewed research reports exhibited comparable qualities compared to slightly modified versions of the criteria set by Willcox et al. [19]. Study quality inconsistencies were noted with regard to sampling and number of knowledgeable informants, as well as completeness of herbal remedy recipe, prescription and dosage, side effects, and antidote information reported (Table 1). Current findings reflect potentially important information gaps and need for standardization of ethno-medicinal studies on indigenous medicinal plants in Ethiopia.

#### Anti-malarial medicinal plants in Ethiopia

In aggregate, 82 studies identified a total 200 different plant species used in traditional malaria treatments throughout Ethiopia. Additional file 1 summarizes the distribution of the reported plants according to administrative regions and floristic areas of collection. Additional file 2 summarizes the detail of traditional herbal medicine used for the treatment of malaria in Ethiopia.

# Geographic distribution of anti-malarial plants

The geographic distribution of anti-malarial plants is likely to be predicated on local trend with regard to disease risk, floral diversity and cultural diversity, including traditional medicinal practices. The western lowlands of Oromia, Amhara, Tigray, Southern Nation and Nationality People (SNNP), and almost the entire areas of Benishangul Gumuz and Gambella regions represent the major malarial hotspots in Ethiopia [20]. As shown in Fig. 1, a higher diversity of plants used to treat malaria (94 plant species) was reported from the SNNP region [21-40] followed by Oromia (60) [41-64], Amhara (47) [65-84], Somali (29) [85, 86], and Tigray (24) [87-95] regions. In agreement, others have indicated that medicinal plants were concentrated in southern and southwestern parts of Ethiopia, which possess high biological and cultural diversity [96, 97]. The majority of the plants reported in Amhara (60%) and Oromia (53%) regions were shared by other regions. The Amhara and Oromia regions share boundaries with many other regions in Ethiopia and are likely to share common flora and cultural practices, including in ethno-medicine. Moreover, the limited number of plants reported from highland areas, including Addis Ababa [98] and Harari [99] regions is attributed to zero prevalence of malaria or minimal transmission. Insufficiencies of plants were also reported from the lowland arid regions, including Afar [53, 100, 101] and Dier Dewa [102]. Both regions are characterized by moderate malaria transmission. Despite having rich floral diversity and intense malaria transmission risk, reporting of antimalarial plants was very low in Benishangul Gumuz [69, 103, 104] and nil in Gambella region (Fig. 1). This may reflect a lack of pertinent ethno-medicinal cultural practices, however, the prevailing gap is probably attributed to serious lapses in ethno-botanical research and documentation of medicinal knowledge and resource in the two regions.

#### **Diversity of anti-malarial plants**

The anti-malarial plant species identified in different region of Ethiopia belonged to 71 different plant families (Additional file 2). Cited plant families included: Fabaceae (18), Lamiaceae (17), Euphorbiaceae (11), Asteraceae (10), Cucurbitaceae and Solanaceae (8 each), Rubiaceae and

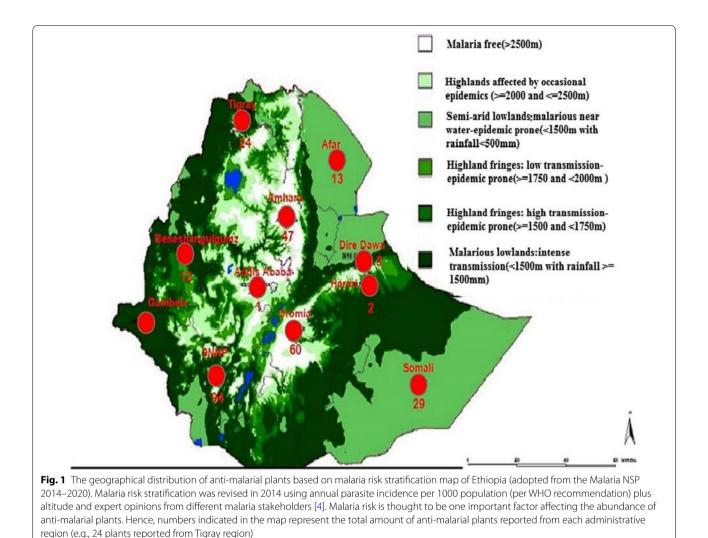
Evaluation parameters	Total number of studies ( $n = 82$ )		
	Criterion	Frequency (%)	
Paper types	Published article	64 (78.0)	
	Unpublished thesis	18 (22.0)	
Botanical identification	Plant collected and verified with informant	3 (3.6)	
	Voucher specimen in herbarium	18 (22.0)	
	Formal identification by botanist	13 (15.9)	
	All	44 (53.6)	
	None	4 (4.9)	
Informants reliability	$\geq$ 10 informants interviewed		
	Yes	74 (90.2)	
	No	8 (9.8)	
	$\geq 2$ informants mention use of plant for malaria treatment		
	Yes	66 (80.5)	
	No	16 (19.5)	
	Informant(s) experience of treating malaria		
	Yes	61 (74.4)	
	No	21 (25.6)	
	Reliable (fulfill all above criteria)		
	Yes	53 (64.6)	
	No	29 (35.4)	
Researcher reliability	Used same language as informants		
	Yes	78 (95.1)	
	No	4 (4.9)	
	Recorded Ethno-medicinal information		
	At least PU, PM and AR	15 (18.3)	
	Detailed	58 (70.7)	
	Poor	9 (11.0)	

Table 1 Characteristics of studies on medicinal plants used for the treatment of malaria in Ethiopia

PU part used, PM preparation method, RA administration routes

Aloaceae (6 each), Acanthaceae (5), Moraceae, Brassicaceae and Capparidaceae (4 each), Asclepiadaceae, Anacardiaceae, Apocynaceae, Apiaceae, Malvaceae, Meliaceae, Rutaceae, Ranunculaceae, Rosaceae, Menispermaceae, and Verbnaceae (3 each). The more frequently cited species were: Allium sativum (31), Carica papaya (20), Vernonia amygdalina (18), Croton macrostachyus (16), Lepidium sativum (15), Justicia schimperiana (9), Phytolacca dodecandra (8), Dodonaea angustifolia, and Melia azedarach (7 each), Clerodendrum myricoides (6), Aloe sp., Azadirachta indica, Brucea antidysenteric, Calpurnia aurea and Eucalyptus globulus (5 each), Ajuga integrifolia, Carissa spinarum, Artemisia afra, Moringa stenopetala, Ruta chalepensis, Salvadora persica, and Tamarindus indica (4 each). Frequent citation of particular plant species or families could indicate potentially higher bioactive antimalarial content. Such evidence is pertinent for prioritizing future pharmacological research agendas.

The majority of the anti-malarial plants reported in Ethiopia were shrubs and herbs, 37 and 33.5%, respectively, while tree and climbers was least reported, 23 and 6.5%, respectively. Similar observation was reported in other countries [105, 106]. This trend may be attributed to the abundance and easy access of these growth forms in the country. Others have suggested that shrubs may hold higher content of potential anti-malarial phytochemicals, such as alkaloids and flavonoids [107]. One possible mechanism for the link between shrubs and content of potential anti-malarial phytochemicals could be the diversity and abundance of these plants in different habitats. Secondary metabolites are thought to be required in the adaptation of plants with their environment. In light of this, abundance of shrubs in various habitats could offer a great chance to interact with diverse of biotic and abiotic factors, such as temperature, light intensity, soil nutrients, water supply, herbivore and microbial attack, which might trigger many complex biochemical processes pertaining to synthesize structurally and chemically diverse metabolites with significant antimalarial activities, including alkaloids and flavonoids.



#### **Recipe reports**

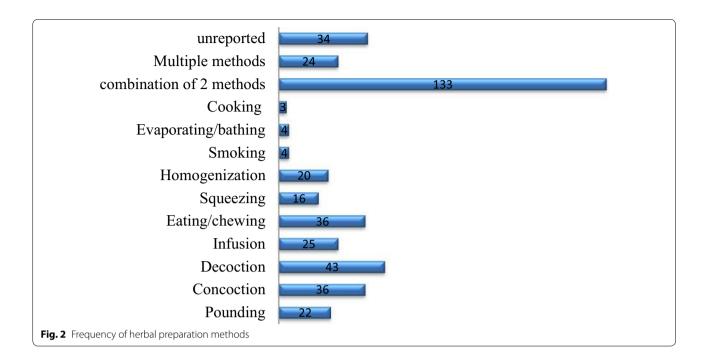
#### Preparation of herbal recipes for malaria treatment

Practitioners used either a single method (209) or combinations of two (133) and more (24) methods for preparing anti-malarial herbal remedies. Decoction, concoction, eating/chewing, infusion, and pounding represented the most common independent herbal remedy preparation. Of the herbal remedies prepared by two or more methods, 71.3% were started by pounding or crushing (Fig. 2). Studies from other parts of Africa have also reported that decoction was the most frequently used method of herbal remedy preparation, commonly using water as a solvent [105, 108–111]. Water is a cheaply available solvent that can dissolve a high number of metabolites, and high temperature would permit a rapid extraction of active ingredients. Concoction was also noted as a common method of herbal remedy preparation in Africa [112-114]. This method is believed to enhance synergic effect of medicinal plants and increase the efficacy of herbal remedies. Preference for eating/chewing and pounding/crushing might be related to ease of preparation, and easily available local tools, including stones.

Some of the anti-malarial herbal preparations were prepared from mixtures of two or more different plant species. Notable examples reported in Ethiopia include:

 Allium sativum individually combined with one of the following plants; Girardinia diversifolia [41], Lepidium sativum [50, 88], Ruta chalepensis [87], Datura stramonium [50], Otostegia integrifolia [72], Ocimum basilicum [45], Ginger officinale [45, 50], Cicer arietinum [75], Carica papaya [29, 50], Capsicum annuum [42, 43], Artemisia afra [42], Croton macrostachyus [56], Brucea antidysenterica [65] or with groups of plants such as: Artemisia afra, Ruta chalepensis and Lepidium sativum [31]; Solanum dasyphyllum, Lepidium sativum, Withania Somnifera, Schinus molle, and Sida schimperi [65];



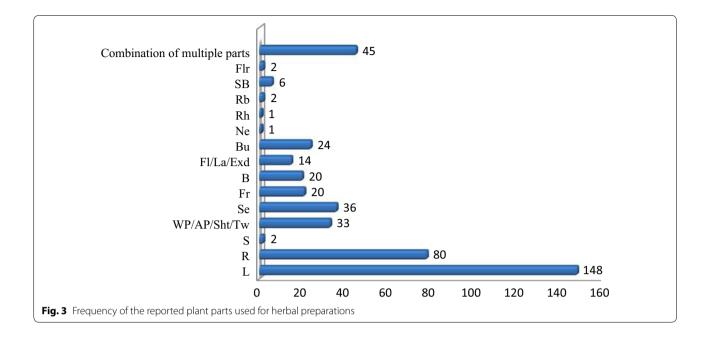


- Leucas stachydiformis with Ocimum lamiifolium [49];
- *Maerua oblongifolia* with *Withania Somnifera* [86];
- Asparagus africanus with Aloe sp. [86];
- Droguetia iners with Premna oligotricha [39];
- Rumex abysinicus with Zehneria scabra [69];
- Silene macrosolen with Echinops kebericho [65];
- *Vernonia amygdalina* with *Ruta chalepensis* [45, 50, 87] or *Carica papaya* [32];
- Justicia schimperiana with Rumex nervosus and Vernonia amygdalina [42];
- *Senna italica* with *Indigofera* sp. or *Zaleya pentandra* [100];
- Lepidium sativum with Echinops kebericho and Croton macrostachyus [31, 49];
- Salvadora persica with Lycium shawii and Acalypha sp. [100];
- Aloe sp. with Asparagus africanus and Senna italica [86];
- Croton macrostachyus with Gardenia lutea or Azadirachta indica and Carica papaya [69];
- *Capsicum annuum* with *Otostegia integrifolia*, *Ocimum gratissimum*, *Prunus persica* and *Schinus molle* [69];
- Hagenia abyssinica with Silene macrosolen, Phytolacca dodecandra, Cucumis ficifolius and Clerodendrum myricoides [83];
- Securidaca longipedunculata with Carissa spinarum, Capparis tomentosa, Withania somnifera and Cucurbita sp. [73].

Aside from anti-malarial plants, various other additives were also used in some herbal preparations. Commonly reported additives include: animal products (egg, meat and milk), honey, sugar, tea, salt, soup, Eragrostis tef dough, coffee, lemon, injera, local alcoholic drinks (areke, tella). Additives were mostly used to moderate the power and/or improve the taste and enhance the efficacy and healing conditions of the remedy [35, 39, 43, 48, 49, 83, 88]. This could possibly be attributed to synergistic effects of the mixtures that might contain a range of pharmacologically active compounds potentially augmenting the chance of the drug interacting with numerous, varied biological targets. Their interaction might influence selectivity, availability, absorption and displacement (distribution) of the remedy, and bioactivity, including enzyme activities. Thus, such traditional practices could provide the opportunity to understand drug interaction and mechanisms of actions, and pave the way to discovering lead structures for the development of novel anti-malarial drugs.

# Plant parts used and condition of preparations

The majority of anti-malarial herbal remedies were prepared from a single plant part while some were prepared from a combination of two or more plant parts. Leaf and root were the most frequently used plant parts (Fig. 3). Leaves were indicated to be the plant parts most commonly used by traditional medicine practitioners in many African countries [115–117]. Leaves are responsible for synthesizing the majority of plant secondary metabolites.



This makes them an abundant source of active chemical entities, which can be extracted with relative ease. Regular harvest of leaves poses no/low threat to individual plants survival. This encourages the frequent and safe utilization of leaves in herbal preparations. Plant root structures, such as tuber and rhizome, can be rich sources of potent bio-active chemical compounds. However, frequent usage of roots for herbal preparations can be risky to the survival of a plant species. Therefore, application of proper harvesting strategies and conservation measures is necessary to ensure sustainable utilization of medicinal plant resources.

The majority (62%) of anti-malarial herbal remedies were prepared from fresh plant materials followed by dry (20.9%) and both fresh and dry materials (5%). On the other hand, plant conditions used for this matter are not indicated in 12.1% of the study reports. The predominant use of fresh materials for herbal preparation probably reflects an attempt to capture potent, volatile substances that determine therapeutic efficacy of herbal preparations [118]. Dry materials could be preferred when the plant is poorly accessible. As reported in some of the reviewed studies, some practitioners travel a long distance to collect medicinal plants and practice long-term preservation.

## Routes of administration and dosage of herbal remedies

Anti-malarial herbal remedies were primarily administered through oral route (82.7%), while rarely administered through nasal (5.5%) and whole body (2.8%). Yet, few (9%) reports failed to indicate administration routes of herbal remedies. Liquid herbal preparations made from both fresh and dry materials were taken orally. Fresh solid materials were also eaten and chewed directly upon collection or after initial pounding/crushing. Meanwhile, dry solid materials were smoked and administered through intranasal. These findings were compatible to the observations reported from other countries [112-114]. Malaria is a disease caused by protozoan intracellular haemo-parasites and its treatment entails delivering adequate circulating concentration of appropriate anti-protozoal chemicals. The oral route is a convenient and non-invasive method of systemic treatment. The route permits relatively rapid absorption and distribution of active chemical compounds from herbal remedies, enabling the delivery of adequate curative power [88].Potential risk of enzymatic breakdown and microbial fermentation of active chemical entities may necessitate alternative routes of herbal remedy administration.

Herbal remedy dosage was basically determined by edibility of the plant parts used. In case of remedies prepared from non-edible plants/parts, dose was prescribed based on age, physical strength and health status of patients. However, full dosage determination varied from healer to healer. Variations were noted in the measurement units used for dose estimation, and in the frequency and duration of herbal treatment prescribed. Dose of herbal preparations was usually estimated using different locally available materials/means, including plastic/ glass/steel cups (could be coffee-cup, teacup, water-cup) or gourd utensils, number of drops for liquid materials; teaspoons for powders; counting the number of units for seeds, leaves and fruits; index finger estimation of root size. Generally, recommendation was made to administer the herbal remedies twice or three times per day for one, two or three consecutive days to many months or until recovery. Lack of precision and standardization is widely acknowledged to be an important drawback of traditional healthcare systems [119–122].

#### Adverse effects, antidotes and contra-indications

In settings where traditional medicine is keen, the pharmacological effect of medicinal plants is generally ascribed to their active and 'safe' content that will only exert quick effect when taken in large quantities. However, the majority of the reviewed reports made no mention of possible side effects to different herbal preparations. Nevertheless, herbal preparations made from some anti-malarial plants were reported to have side effects, such as vomiting, nausea, diarrhoea, headache, urination, heartburn, and nightmare [22, 31, 43, 54, 67, 68, 71, 75, 86, 87, 100]. This may be attributed to different underlying factors, including improper dosing, toxic plant chemicals, toxic metabolic byproducts, etc. Teff injera and porridge, Shiro wot (pulse grain sauce), coffee, milk and milk products, honey, Shoforo (infusion made from coffee peel), Tela, barley soup and juice of Sansevieria ehrenbergii were reported as antidotes for potential herbal remedy side effects [22, 31, 43, 54, 67,

68, 71, 75, 87]. Some anti-malarial plants were reported as contra-indicated to the elderly, pregnant women, children, physically weak persons, and patients with hepatitis [31, 42, 43, 54, 66–68, 71, 75, 86–88, 100] (Table 2). Current observations indicate existence of critical researchevidence gaps with regard to the potential toxicities and corresponding counteracting mechanisms of anti-malarial plants in Ethiopia. This gap represents an important roadblock to effective development and exploitation of indigenous medicinal plant resources.

## Trends in anti-malarial plant research and development

In different African countries, many of the anti-malarial plants identified in this paper have demonstrated promising therapeutic potential on pre-clinical and clinical investigations. Notable examples were *Artemisia annua* [123, 124], *Ajuga remota* [125], *Azadirachta indica* [126–128], *Argemone mexicana* [129, 130], *Vernonia amygdalina* [131–135], *Asparagus africanus* [136], *Uvaria leptocladon* [137], and *Gossypium* spp. [138]. In parallel, multiple promising candidate anti-malarial compounds have been identified from these plant resources [139–145]. Consequently, international market demand (Switzerland, France, China, etc.) for African medicinal plants has exhibited sustained growth. Export of promising indigenous medicinal plant resources offers substantial contribution to the economy and growth of

Species	Side effects	Antidotes	Contra-indication
Croton macrostachyus	Diarrhoea, vomiting, headache, urination	Teff injera and porridge	Pregnant women
Hagenia abyssinica	Vomiting and diarrhoea	Shiro Wot	
Aloe sp.	Nausea, vomiting, diarrhoea	_	Pregnant women
Euphorbia abyssinica	Headache, diarrhoea, vomiting	Coffee and milk, red <i>teff</i> porridge, a lot of <i>aguat</i>	Pregnant women
Anethum graveolens	Vomiting, nausea, diarrhoea	-	_
Asparagus africanus	Vomiting, nausea, diarrhoea	_	_
Aloe otallensis	Vomiting and diarrhoea	Honey	_
Cadaba farinose	Headache	Shoforo	_
Canthium pseudosetiflorum	Vomiting	Shoforo	_
Cyperus distans	Nausea and vomiting	Shoforo	_
Hypoestes forskaoli	Headache, heartburn, nausea/ vomiting and nightmare	Juice of Sansevieria ehrenbergii	-
Phytolacca dodecandra	Vomiting and diarrhoea	Milk, red teff porridge, coffee, Tela	Children, pregnant women, patient with hepatitis
Justice schimperiana	Vomiting and diarrhoea	Milk, red teff porridge	Children, pregnant women
Andrachne aspera	_	_	Pregnant women
Gnidia involucrata	-	-	Patient with hepatitis, babies/old peo- ple, pregnant women
Ajuga integrifolia	Vomiting and diarrhoea	Boiled coffee, milk or barley soup	Pregnant women, physically weak person

Table 2 Side effects, antidotes and contra-indications of some plants used for traditional malaria treatment in Ethiopia

African countries. For instance, export of traditional medicines contributed an estimated R2.9 billion to South Africa's economy [146]. Likewise, Egypt's 2008 exports of selected medicinal plants amounted to 77,850,312 kg with a reported value of US \$174,227,384 [147].

Despite the remarkable historic success of traditional medicinal practices and abundance of indigenous medicinal plant resources (Additional file 1), anti-malarial ethno-pharmacological research in Ethiopia remains at primitive stage, with scope limited to evaluating crude extracts from various anti-malarial plants against Plasmodium berghei. A prominent gap is evident with regard to research geared towards identifying plant bioactive entities, and establishing the efficacy and safety of medical plants through in vitro assays using human Plasmodium parasites, in vivo assay involving higher animal models and randomized clinical trials. Absence of favourable medicinal plant research and development impedes optimum exploitation of potential economic benefits. Thus, despite holding one of the richest (diversity and quantity) resources in the continent, large-scale production and export of medicinal plants has remained limited in Ethiopia. Prevailing scenarios underscore a pressing need for enhancing pre-clinical and clinical research aimed at developing safe, effective and affordable alternative anti-malarial agents from indigenous plant resources. This requires collaborative engagement involving government bodies, researchers, traditional healers, and prospective business investors.

# Conclusion

The study highlighted that a rich diversity of indigenous medicinal plants were commonly used for traditional treatment of malaria in Ethiopia. Ethno-medicinal research on distribution and usage pattern of anti-malarial plants shows substantial variability across a spectrum of geographic and social strata in the country. Baseline information gaps are evident in key geographic settings, such as the Beshangul Gumuz and Gambella regions. Divergent preparation and use patterns of antimalarial herbal remedies, as well as associated toxicity risks and countermeasures, generally demand deeper, exhaustive investigations. Experimental research and advanced chemical analysis are required to identify and validate the therapeutic potential of anti-malarial chemical compounds from promising plant species, with due consideration to efficacy and safety issues. Sustainable development and exploitation of indigenous medicinal plant resources entails coordinated multidisciplinary research programmes that give due credit to traditional practitioners and engage with commercial investors.

# **Additional files**

Additional file 1. Distribution of the reported medicinal plants used for the treatment of malarial based on administrative regions, and floristic areas of collection confined.

Additional file 2. Medicinal plant families, species, local name, habit, parts used, preparation methods and other medicinal values of plants used for the treatment of malaria in Ethiopia.

#### Authors' contributions

GA, BU and AW separately attained materials from different sources and jointly prepared the initial draft paper. All authors systematically reviewed the final version of the manuscript. All authors read and approved the final manuscript.

#### Author details

<sup>1</sup> Department of Biology, Jigjiga University, P.O. Box-1020, Jijiga, Ethiopia. <sup>2</sup> College of Veterinary Medicine, Jigjiga University, P.O.Box-1020, Jijiga, Ethiopia.

#### Acknowledgements

Not applicable.

#### **Competing interests**

The authors declare that they have no competing interests.

#### Availability of data and materials

All data pertaining to this study are within the manuscript and the supporting files.

#### **Consent for publication**

Not applicable.

#### Ethics approval and consent to participate

Not applicable.

# Funding

Not applicable.

#### **Publisher's Note**

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Received: 21 November 2016 Accepted: 22 July 2017 Published online: 01 August 2017

#### References

- 1. WHO. World malaria report. Geneva: World Health Organization; 2015.
- 2. WHO. World Malaria Report. Geneva: World Health Organization; 2014.
- Woime AW. Changes in the spread of malaria in Ethiopia: case study from Awassa and Hossana area 2006–2007. MSc Thesis; 2008. https:// brage.bibsys.no/xmlui/handle/11250/2438939. Accessed 25 Jul 2016.
- FMOH. National strategic plan for malaria prevention, control and elimination in Ethiopia: 2014–2020. Addis Ababa: Federal Ministry of Health of Ethiopia; 2014.
- Tiruneh A. GIS and remote sensing based assessment of malaria risk mapping for Boricha Woreda, Ethiopia. MSc Thesis; 2010. http://etd.aau. edu.et/handle/123456789/779. Accessed 25 Jul 2016.
- Ashley EA, Dhorda M, Fairhurst RM, Amaratunga C, Lim P, Suon S, et al. Spread of artemisin in resistance in *Plasmodium falciparum* malaria. N Engl J Med. 2014;371:411–23.
- Petros Z. The need of standardized herbal remedies as alternate sources of antimalarial products in Ethiopia—updated review. Pharmacol Online. 2011;3:1440–7.

- 8. Ntie-Kang F, Amoa OP, Lifongo LL, Ndom JC, Sippl W, Mbaze LM. The potential of anti-malarial compounds derived from African medicinal plants, part II: a pharmacological evaluation of non-alkaloids and non-terpenoids. Malar J. 2014;13:81.
- Phillipson D, Wright W. Can ethnopharmacology contribute to the development of anti- malarial agents? J Ethnopharmacol. 1991;32:155–65.
- 10. Fullas F. The role of indigenous medicinal plants in Ethiopian healthcare. London: African Renaissance; 2007.
- 11. Desissa D, Binggeli P. Uses and conservation status of medicinal plants used by the Shinasha people; 2000. http://www.mikepalmer.co.uk/ woodyplantecology/ethiopia/shinasha.html.
- 12. Pankhurst R. A historical reflection on the traditional Ethiopian pharmacopeias. J Ethiop Pharm Assoc. 1965;2:29–33.
- 13. Debella A, Taye A, Abebe D, Mudi K, Melaku D, Taye G. Screening of some Ethiopian medicinal plants for mosquito larvicidal effects and phytochemical constituents. Pharmacol Online. 2007;33:231–43.
- 14. Misganaw N, Moges S, Tadele M, Tesera M, Temesgen T, Raja N. Evaluation of multi potential bioactive endod, *Phytolacca dodecandra* (L'Herit) berries extracts against immature filarial vector *Culex quinquefasciatus* Say (Diptera: Culicidae). Res J Environ Earth Sci. 2012;4:697–703.
- Mengiste B, Makonnen E, Urga K. *In-vivo* antimalarial activity of *Dodonaea Angustifolia* seed extracts against *Plasmodium berghei* in mice model. Momona Ethiop J Sci. 2012;4:47–63.
- Eyasu M, Shibeshi W, Giday M. *In vivo* antimalarial activity of hydromethanolic leaf extract of *Calpurnia aurea* (Fabaceae) in mice infected with chloroquine sensitive *Plasmodium berghei*. Int J Pharmacol. 2013;2:131–42.
- 17. Bantie L, Assefa S, Teklehaimanot T, Engidawork E. *In vivo* antimalarial activity of the 51 crude leaf extract and solvent fractions of *Croton macrostachyus* Hocsht (Euphorbiaceae) against *Plasmodium berghei* in mice. BMC Complement Alternat Med. 2014;14:79.
- Hunde D, Asfaw Z, Kelbessa E. Use of traditional medicinal plants by people of 'Boosat' sub district, Central Eastern Ethiopia. Ethiop J Health Sci. 2006;16:141–55.
- Willcox M, Benoit-Vical F, Fowler D, Bourdy G, Burford G, Giani S, et al. Do ethnobotanical and laboratory data predict clinical safety and efficacy of anti-malarial plants? Malar J. 2011;10(Suppl 1):S7.
- Ketema T, Bacha K, Birhanu T, Petros B. Chloroquine-resistant *Plasmodium vivax* malaria in Serbo town, Jimma zone, south-west Ethiopia. Malar J. 2009;8:177.
- Asnake S, Teklehaymanot T, Hymete A, Erko B, Giday M. Survey of medicinal plants used to treat malaria by Sidama People of Boricha District, Sidama Zone, South Region of Ethiopia. Evid Based Complement Alternat Med. 2016; ID 9690164.
- 22. Paulos B. Ethnopharmacological survey of medicinal plants among the Hamer Ethnic Group, Hamer Woreda, South Omo Zone, SNNPR, Ethiopia and evaluation of a selected plant for its antimalarial Activity. MScThesis; 2012. http://etd.aau.edu.et/handle/123456789/6221. Accessed 1 Aug 2016.
- Dori UG, Deressa W, Esposito F, Habluetzel A. Perceptions and practices of the Konso community (South-west Ethiopia) relating to malaria: implications for control. Malar World J. 2012;3:9.
- Maryo M, Nemomissa S, Bekele T. An ethnobotanical study of medicinal plants of the Kembatta ethnic group in Enset-based agricultural landscape of Kembatta Tembaro (KT) Zone, Southern Ethiopia. Asian J Plant Sci Res. 2015;5:42–61.
- Agisho H, Osie M, Lambore T. Traditional medicinal plants utilization, management and threats in Hadiya Zone, Ethiopia. J Med Plants Stud. 2014;2:94–108.
- 26. Tamrat S. Study of useful plants in and around Gate Uduma (Traditional Gedeo Homegardens Gardens) in Kochere Wereda of Gedeo zone, SNNPR, Ethiopia: An ethnobotanical approach. MSc Thesis; 2011. http:// etd.aau.edu.et/bitstream/123456789/245/3. Accessed on 1 Aug 2016.
- Tamrat S. An ethnobotanical study of medicinal plants in Wondo genet natural forest and adjacent kebeles, Sidama Zone, SNNP Region, Ethiopia. MScThesis; 2011. http://etd.aau.edu.et/bitstream/123456789/244/3. Accessed 17 Aug 2016.
- 28. Mesfn F, Seta T, Assefa A. An ethnobotanical study of medicinal plants in Amaro Woreda, Ethiopia. Ethnobot Res Appl. 2014;12:341–54.

- Regassa R. Assessment of indigenous knowledge of medicinal plant practice and mode of service delivery in Hawassa city, southern Ethiopia. J Med Plants Res. 2013;7:517–35.
- 30. Temam T, Dillo A. Ethnobotanical study of medicinal plants of Mirab-Badwacho district, Ethiopia. J BioSci Biotechnol. 2016;5:151–8.
- Mesfin F, Demissew D, Teklehaymanot T. An ethnobotanical study of medicinal plants in Wonago Woreda, SNNPR, Ethiopia. J Ethnobiol Ethnomed. 2009;5:28.
- Andarge E, Shonga A, Agize M, Tora A. Utilization and conservation of medicinal plants and their associated indigenous knowledge (IK) in Dawuro Zone: An ethnobotanical approach. Int J Medicinal Plant Res. 2015;4:330–7.
- Teklehaymanot T, Giday M. Quantitative ethnobotany of medicinal plants used by Kara and Kwego semi-pastoralist people in lower Omo River Valley, Debub Omo Zone, Southern Nations, Nationalities and Peoples Regional State, Ethiopia. J Ethnopharmacol. 2010;130:76–84.
- Assefa A, Abebe T. Ethnobotanical study of wild medicinal trees and shrubs in Benna Tsemay District, Southern Ethiopia. J Sci Dev. 2014;2:1.
- Seid MA, Aydagnehum SG. Medicinal plants biodiversity and local healthcare management system in Chencha District, Gamo Gofa, Ethiopia. J Pharmacogn Phytochem. 2013;2:284–93.
- Giday M, Asfaw Z, Woldu Z. Ethnomedicinal study of plants used by Sheko ethnic group of Ethiopia. J Ethnopharmacol. 2010;132:75–85.
- Giday M, Asfaw Z, Woldu Z, Teklehaymanot T. Medicinal plant knowledge of the Bench ethnic group of Ethiopia: an ethnobotanical investigation. J Ethnobiol Ethnomed. 2009;5:24–34.
- Giday M, Asfaw Z, Woldu Z. Medicinal plants of the Meinit ethnic group of Ethiopia: an ethnobotanical study. J Ethnopharm. 2009;124:513–21.
- Tolossa K, Debela E, Athanasiadou S, Tolera A, Ganga G, Jos G. Ethnomedicinal study of plants used for treatment of human and livestock ailments by traditional healers in South Omo, Southern Ethiopia. J Ethnobiol Ethnomed. 2013;9:32.
- Abbink J. Plant use among the Suri people of southern Ethiopia: a system of knowledge in danger? Afrikanistische Arbeitspapiere. 2002;70:199–206.
- Zerabruk S, Yirga G. Traditional knowledge of medicinal plants in Gindeberet district, Western Ethiopia. S Afr J Bot. 2012;78:165–9.
- 42. Eneyew A, Asfaw Z, Kelbessa E, Nagappan R. Ethnobotanical study of traditional medicinal plants in and around Fiche District, Central Ethiopia. Curr Res J Biol Sci. 2014;6:154–67.
- Megersa M, Asfaw Z, Kelbessa E, Beyene A, Woldeab B. An ethnobotanical study of medicinal plants in Wayu Tuka District, East Welega Zone of Oromia Regional State, West Ethiopia. J Ethnobiol Ethnomed. 2013;9:68.
- Tadesse M, Hunde D, Getachew Y. Survey of medicinal plants used to treat human diseases in Seka Cherkosa, Jimma Zone, Ethiopia. Ethiop J Health. 2005;15:89–106.
- Alito MK. Use and managment of medicinal plants by indigenous people of Jima Rare District in Oromia Region, Ethiopia. MScThesis; 2011. http://213.55.85.90/bitstream/handle/123456789/3258. Accessed 1 Sept 2016.
- Birhanu T, Abera D, Ejeta E. Ethnobotanical study of medicinal plants in selected Horro Gudurru Woredas, Western Ethiopia. J Biol Agric Healthc. 2015;5:83–93.
- Kenea O, Tekie H. Ethnobotanical survey of plants traditionally used for malaria prevention and treatment in selected resettlement and indigenous villages in Sasiga District, Western Ethiopia. J Biol Agric Healthc. 2015;5:1–9.
- Abera B. Medicinal plants used in traditional medicine by Oromo people, Ghimbi District, Southwest Ethiopia. J Ethnobiol Ethnomed. 2014;10:40.
- Etana B. Ethnobotanical study of traditional medicinal plants of Goma Wereda, Jima Zone of Oromia region, Ethiopia. MScThesis; 2010. http:// etd.aau.edu.et/handle/123456789/317. Accessed 11 Sept 2016.
- Amenu E. Use and management of medicinal plants by indigenous people of Ejaji Area (Chelya Woreda) West Shoa, Ethiopia:an ethnobotanical approach. MScThesis; 2007. http://www.ethnopharmacologia. org/prelude2016/pdf/biblio-ha-53-amenu.pdf. Accessed 11 Sept 2016.
- Belayneh A, Asfaw Z, Demissew S, Bussa NF. Medicinal plants potential and use by pastoral and agro-pastoral communities in Erer Valley of Babile Wereda, Eastern Ethiopia. J Ethnobiol Ethnomed. 2012;8:42.

- Lulekal E, Kelbessa E, Bekele T, Yineger H. An ethnobotanical study of medicinal plants in Mana Angetu District, southeastern Ethiopia. J Ethnobiol Ethnomed. 2008;4:10.
- Beche D, Gebeyehu G, Feyisa K. Indigenous utilization and management of useful plants in and around Awash National Park, Ethiopia. J Plant Biol Soil Health. 2016;3:12.
- Hunde D, Asfaw Z, Kelbessa E. Use of traditional medicinal plants by people of 'Boosat' Sub District, Central Eastern Ethiopia. Ethiop J Health Sci. 2006;16:141–55.
- Eshete AM, Kelbessa E, Dalle G. Ethnobotanical study of medicinal plants in Guji Agro-pastoralists, Blue Hora District of Borana Zone, Oromia Region, Ethiopia. J Med Plants Stud. 2016;4:170–84.
- Bekele G, Reddy PR. Ethnobotanical study of medicinal plants used to treat human ailments by Guji Oromo Tribes in Abaya District, Borana, Oromia, Ethiopia. Univers J Plant Sci. 2015;3:1–8.
- Tolosa E. Use and conservation of traditional medicinal plants by indigenous people in Gimbi Woreda, Western Wellega, Ethiopia. MSc Thesis; 2007. http://hdl.handle.net/123456789/132. Accessed 11 Sept 2016.
- Parvez N, Yadav S. Ethnopharmacology of single herbal preparations of medicinal plants in Asendabo district, Jimma, Ethiopia. Indian J Tradit Knowl. 2010;9:724–9.
- Asefa A, Urga K, Guta M, Mekonene W, Melaku D, Mudie K, et al. In vivo antimalarial activities of plants used in Ethiopian traditional medicine, Delomenna, Southeast Ethiopia. Ethiop J Health Sci. 2007;17:1–12.
- Balemie K, Kelbessa E, Asfaw Z. Indigenous medicinal plant utilization, management and threats in Fentalle Area, Eastern Shewa, Ethiopia. Ethiop J Biol Sci. 2004;3:37–58.
- Eneyew A, Asfaw Z, Kelbessa E, Nagappan R. Status of medico-cultural commercial plants at fiche town market Ethiopia. Int J Pharm Healthcare Res. 2013;1:227–36.
- 62. Abera B. Medicinal plants used in traditional medicine in Jimma Zone, Oromia, Southwest Ethiopia. Ethiop J Health Sci. 2003;13:85–94.
- Feyssa DH, Njoka JT, Asfaw Z, Nyangito MM. Uses and management of *Ximenia americana*, Olacaceae in semi-arid East Shewa, Ethiopia. Pakistan J Bot. 2012;44:1177–84.
- Wondimu T, Asfaw Z, Kelbessa E. Ethnobotanical study of medicinal plants around 'Dheeraa' town, Arsi Zone, Ethiopia. J Ethnopharmacol. 2007;112:152–61.
- Abebe E, Nemomissa S, Asfaw Z. Ethnobotanical study on medicinal plants used by local communities in Debark Wereda, North Gondar Zone Regional State, Ethiopia. MSc Thesis; 2012. http://hdl.handle. net/123456789/373.Accessed 11 Sept 2016.
- Berhan A, Asfaw Z, Kelbessa E. Ethnobotany of plants used as insecticides, repellents and anti-malarial agents in Jabitehnan District, West Gojjam. SINET Ethiop J Sci. 2006;29:87–92.
- Limenih Y, Umer S, Wolde-Mariam M. Ethnobotanical study on traditional medicinal plants in Dega Damot Woreda, Amhara Region, North Ethiopia. Int J Res Pharm Chem. 2015;5:258–73.
- Gebeyehu G. An ethnobotanical study of traditional use of medicinal plants and their conservation status in Mecha Wereda, West Gojam Zone of Amhara Region, Ethiopia. MScThesis; 2011. http://hdl.handle. net/123456789/381.Accessed 11 Sept 2016.
- Giday M, Teklehaymanot T, Animut A, Mekonnen Y. Medicinal plants of the Shinasha, Agew-awi and Amharapeoples in northwest Ethiopia. J Ethnopharmacol. 2007;110:516–25.
- Getaneh S, Girma Z. An ethnobotanical study of medicinal plants in Debre Libanos Wereda, Central Ethiopia. Afr J Plant Sci. 2014;8:366–79.
- Amsalu N. An ethnobotanical study of medicinal plants in Farta Wereda, South Gondar, Amhara Region, Ethiopia. MSc Thesis; 2010. http://etd. aau.edu.et/bitstream/123456789/1432/3/109242 287664342941072536296319568051762. Accessed 14 Sept 2016.
- 72. Getnet Z, Chandrodyam S, Masresha G. Studies on traditional medicinal plants in Ambagiorgis area of Wogera District, Amhara Regional State, Ethiopia. Int J Pure Appl Biosci. 2016;4:38–45.
- 73. Teklehaymanot T, Giday M, Medihin G, Mekonnen Y. Knowledge and use of medicinal plants by people around Debrelibanos Monastery in Ethiopia. J Ethnopharmacol Ethnomed. 2007;111:271–83.
- Alemayehu G, Asfaw Z, Kelbessa E. Ethnobotanical study on medicinal plants used by indigenous local communities in Minjar-Shenkora Wereda, North Shewa Zone of Amhara Region, Ethiopia. J Med Plants Stud. 2015;3:1–11.

- 75. Chekole G, Asfaw Z, Kelbessa E. An ethnobotanical study of plants used in traditional medicine and as wild foods in and around Tara Gedam and Amba remnant forests in Libo Kemkem Wereda, South Gonder zone, Amhara region, Ethiopia. J Ethnobiol Ethnomed. 2015;11:4.
- Lulekal E, Asfaw Z, Kelbessa E, Van Damme P. Ethnomedicinal study of plants used for human ailmentsin Ankober district, North Shewa zone, Amhara region, Ethiopia. J Ethnobiol Ethnomed. 2013;9:63.
- 77. Mohammed A. Traditional use, management and conservation of useful plants in dry land parts of north Shoa zone of the Amhara national region: an ethnobotanical approach. MSc Thesis. Addis Ababa: Addis Ababa University; 2004.
- Alemayehu G, Asfaw Z, Kelbessa E. Plant diversity and ethnobotany in Berehet District, North Shewa Zone of Amhara Region (Ethiopia) with emphasis on wild edible plants. J Med Plants Stud. 2015;3:93–105.
- Mekuanent T, Zebene A, Solomon Z. Ethnobotanical study of medicinal plants in Chilga district, Northwestern Ethiopia. J Nat Remedies. 2015;15:2320–3358.
- Ragunathan M, Abay SM. Ethnomedicinal survey of folk drugs used in Bahirdar Zuria district, Northwestern Ethiopia. Indian J Trad Knowl. 2009;8:281–4.
- Reta H. An ethnobotanical study of useful plants of the farming site in Gozamen Wereda, East Gojjam Zone of Amhara Region, Ethiopia. MSc Thesis; 2010. http://etd.aau.edu.et/handle/123456789/316. Accessed 14 Sept 2016.
- 82. Teklehaymanot T, Giday M. Ethnobotanical study of medicinal plants used by people in Zegie peninsula, Northwestern Ethiopia. J Ethnobiol Ethnomed. 2007;3:12.
- Meragiaw M, Asfaw Z, ArgawM. The Status of Ethnobotanical Knowledge of Medicinal Plants and the Impacts of Resettlement in Delanta, Northwestern Wello, Northern Ethiopia. Evid Based Complement Alternat Med. 2016; ID 5060247.
- Birhanu Z, Endale A, Shewamene Z. An ethnomedicinal investigation of plants used by traditional healers of Gondar town, NorthWestern Ethiopia. J Med Plants Stud. 2015;3:36–43.
- Issa A. Ethno medicinal study of plants in Jigjiga Woreda, Eastern Ethiopia. MSc Thesis; 2015. http://etd.aau.edu.et/bitstream/123456789/8252/1/Arebu%20Issa. Accessed 28 Sept 2016.
- Mesfin A, Giday M, Animut A, Teklehaymanot T. Ethnobotanical study of antimalarial plants in Shinile District, Somali Region, Ethiopia, and in vivo evaluation of selected onesagainst *P. berghei*. J Ethnopharmacol. 2012;139:221–7.
- 87. Araya S, Abera B, Giday M. Study of plants traditionally used in public and animal health management in Seharti Samre District, Southern Tigray, Ethiopia. J Ethnobiol Ethnomed. 2015;11:22.
- Teklay A, Abera B, Giday M. An ethnobotanical study of medicinal plants used in Kilte Awulaelo district, Tigray Region of Ethiopia. J Ethnobiol Ethnomed. 2013;9:65.
- Mesfin K, Tekle G, Tesfay T. Ethnobotanical study of traditional medicinal plants used by indigenous people of Gemad District, Northern Ethiopia. J Med Plants Stud. 2013;1:4.
- Yirga G. Assessment of traditional medicinal plants in Endrta District, South-eastern Tigray, Northern Ethiopia. Afr J Plant Sci. 2010;4:255–60.
- 91. Birhane E, Aynekulu E, Mekuria W, Endale D. Management, use and ecology of medicinal plants in the degraded dry lands of Tigray, northern Ethiopia. J Med Plants Res. 2011;5:309–18.
- Gidey M, Beyene T, Signorini MA, Bruschi P, Yirga G. Traditional medicinal plants used by Kunama ethnic group in Northern Ethiopia. J Med Plants Res. 2015;9:494–509.
- Zenebe G, Zerihun M, Solomon Z. An ethnobotanical study of medicinal plants in Asgede Tsimbila District, Northwestern Tigray, Northern Ethiopia. Ethnobot Res Appl. 2012;10:305–20.
- Abdurhman N. Ethnobotanical study of medicinal plants used by local people in Ofla Wereda, Southern Zone of Tigray Region Ethiopia. MScThesis; 2010. http://etd.aau.edu.et/bitstream/123456789/1581/3/1090569 45437087248632365896849715752740. Accessed 17 Sept 2016.

 Yirga G. Assessment of indigenous knowledge of medicinal plants in Central Zone of Tigray, Northern Ethiopia. Afr J Plant Sci. 2010;4:6–11.

- 96. Edwards S. The ecology and conservation status of medicinal plants on Ethiopia - What do we know? In: Medhin Z, Abebe D, editors. Conservation and Sustainable use of medicinal plants in Ethiopia, Proceedings of National Workshop on Biodiversity Conservation and Sustainable use of medicinal plants in Ethiopia. Addis Ababa: Institute of Biodiversity Conservation and Research; 2001. p. 46–55.
- 97. Yineger H, Yewhalaw D. Traditional medicinal plant knowledge and use by local healers in Sekoru District, Jimma Zone, Southwestern Ethiopia. J Ethnobiol Ethnomed. 2007;3:24.
- Bekele B, Asfaw Z, Petros B, Tekie H. Ethnobotanical study of plants used for protection against insect bite and for the treatment of livestock health problems in rural areas of Akaki District, Eastern Shewa, Ethiopia. Topclass J Herbal Med. 2012;1:12–24.
- Berhane T, Vijaibasker G. Assessment of traditional home remedy usage among people in Harar, Ethiopia. Int J Pharm Sci Res. 2015;6:2451–61.
- Seifu T, Asres K, Gebre-Mariam T. Ethnobotanical and ethnopharmaceutical studies on medicinal plants of Chifra District, Afar Region, North Eastern Ethiopia. Ethiop Pharm J. 2006;24:41–58.
- Meragiaw M. Wild useful plants with emphasis on traditional use of medicinal and edible plants by the people of Aba'ala, North-eastern Ethiopia. J Med Plant Herb Ther Res. 2016;4:1–16.
- 102. Belayneh A, Bussa NF. Ethnomedicinal plants used to treat human ailments in the prehistoric place of Harla andDengego valleys, eastern Ethiopia. J Ethnobiol Ethnomed. 2014;10:18.
- Mengesha GG. Ethnobotanical survey of medicinal plants used in treating human and livestock health problems in Mandura Woreda of Benishangul Gumuz, Ethiopia. Adv Med Plant Res. 2016;4:11–26.
- Flatie T, Gedif T, Asres K, Gebre-Mariam T. Ethnomedical survey of Berta ethnic group Assosa Zone, BenishangulGumuz regional state, mid-west Ethiopia. J Ethnobiol Ethnomed. 2009;5:14.
- 105. Nguta JM, Mbaria JM, Gakuya DW, Gathumbi PK, Kiama SG. Antimalarial herbal remedies of Msambweni, Kenya. J Ethnopharmacol. 2010;128:424–32.
- 106. Tabuti JRS, Lye KA, Dhillion SS. Traditional herbal drugs of Bulamogi, Uganda: plants, use and administration. J Ethnopharmacol. 2003;88:19–44.
- 107. Asase A, Akwetey GA, Achel DG. Ethnopharmacological use of herbal remedies for the treatment of malaria in the Dangme West District of Ghana. J Ethnopharmacol. 2010;3:367–76.
- Muthaura CN, Rukunga GM, Chhabra SC, Mungai GM, Njagi ENM. Traditional phytotherapy of some remedies used in treatment of malaria in Meru district of Kenya. S Afr J Bot. 2007;73:402–11.
- 109. Mpiana PT, Ngbolua KN, Mudogo V, Tshibangu DST, Atibu EK, Mbala BM, et al. The potential effectiveness of medicinal plants used for the treatment of sickle cell disease in the Democratic Republic of Congo folk medicine: a review. In: Gupta VK, Singh GD, editors. Traditional and folk herbal medicine. New Delhi: Daya Publishing House; 2012.
- 110. Sofowora A. Medicinal plants and traditional medicine in Africa. 2nd ed. Spectrum Books; 1993. ISBN 9782462195, 9789782462190.
- Dibong SD, Mbondo ME, Ngoye A, Kwin MF, Betti JC. Ethnobotanique et phytomédecine des plantes médicinales de Douala, Cameroun. J Appl Biosci. 2011;37:2496–507.
- Adekunle MF. Indigenous uses of plant leaves to treat malaria fever at Omo Forest reserve (OFR) Ogun state, Nigeria. Ethiop J Environ Stud Manag. 2008;1:31–5.
- Musa SM, Abdelrasool FE, Elsheikh AE, Ahmed LAMN, Mahmoud ALE, Yagil SM. Ethnobotanical study of medicinal plants in the Blue Nile State, South-eastern Sudan. J Med Plants Res. 2011;5:4287–97.
- 114. Maroyi A. Traditional use of medicinal plants in south-central Zimbabwe: review and perspectives. J Ethnobiol Ethnomed. 2013;9:31.
- Katemo M, Mpiana PT, Mbala BM, Mihigo SO, Ngbolua KN, Tshibangu DST, et al. Ethnopharmacological survey of plants used against diabetes in Kisangani City (D.R. Congo). J Ethnopharmacol. 2012;144:39–43.
- Idowu OA, Soniran OT, Ajana O, Aworinde DO. Ethnobotanical survey of antimalarial plants used in Ogun State, Southwest Nigeria. Afr J Pharm Pharmacol. 2010;4:55–60.
- 117. Pousset JL. Plantes médicinales africaines. Utilisation pratique, vol. 2. Paris: ACCT; 1989.
- 118. Addis G, Baskaran R, Raju M, Ushadevi A, Asfaw Z, Woldu Z, Baskaran V. Effect of blanching and drying process on carotenoids composition of underutilized Ethiopian (*Coccinia grandis* L. Voigt) and Indian (*Trigonella foenum-graecum* L.) green leafy vegetables. J Food Process Preserv. 2009;33:744–62.

- 119. Getahun A. Some common medicinal and poisonous plants used in Ethiopian folk medicine. Addis Abeba: Addis Abeba University; 1976. p. 3–63.
- 120. Sofowora EA. Medicinal plants and traditional medicine in Africa. New York: Wiley; 1982.
- Abebe D. Traditional medicine in Ethiopia: the attempts being made to promote it for effective and better utilization. SINET Ethiop J Sci. 1986;96:1–69.
- Giday M, Asfaw Z, Elmquist T, Woldu Z. An ethnobotanical study of medicinal plants used by Zay people in Ethiopia. J Ethnopharmacol. 2003;85:43–52.
- Mueller MS, Runyambo N, Wagner I, Borrmann S, Dietz K, Heide L. Randomized controlled trial of a traditional preparation of *Artemisia annua* L (Annual Wormwood) in the treatment of malaria. Trans R Soc Trop Med Hyg. 2004;98:318–21.
- 124. Yao-De W, Qi-Zhong Z, Jie-Sheng W. Studies on the antimalarial action of gelatin capsule of *Artemisia annua*. Clin J Parasitol. 1992;10:290–4.
- Kuria KAM, Chepkwony H, Govaerts C, Roets E, Busson R, de Witte P, et al. The antiplasmodial activity of isolates from *Ajuga remota*. J Nat Prod. 2002;65:789–93.
- Bidla G, Titanji VPK, Jako B, Ghazali GE, Bolad A, Berzins K. Anti-plasmodial activity of seven plants used in African folk medicine. Indian J Pharm. 2004;36:245–6.
- 127. Kirira PG, Rukunga GM, Wanyonyi AW, Muregi FM, Gathirwa JW, Muthaura CN, et al. Anti-plasmodial activity and toxicity of extracts of plants used in traditional malaria therapy in Meruand Kilifi Districts of Kenya. J Ethnopharm. 2006;106:403–7.
- MacKinnon S, Durst T, Arnason JT, Angerhofer C, Pezutto J, Sanchez-Vindas PE, et al. Antimalarial activity of tropical Meliaceae extracts and gedunin derivatives. J Nat Prod. 1997;60:336–41.
- 129. Simoes-Pires CA. Investigation of antiplasmodial compounds from various plant extracts: *Argemone mexicana* L. (Papaveraceae), *Licania octandra* (Hoffmanns. ex. Roem & Schult) Kuntze (Chrysobalanaceae) and *Syzygium cumini* (L.) Skeels (Myrtaceae). Geneva: Université de Geneve, Section des Sciences Pharmaceutiques, Laboratoire de Pharmacognosie et Phytochimie; 2009.
- Willcox ML, Graz B, Falquet J, Sidibe O, Forster M, Diallo D. Argemone Mexicana decoction for the treatment of uncomplicated falciparum malaria. Trans R Soc Trop Med Hyg. 2007;101:1190–8.
- 131. Ohigashi H, Hoffman MA, Izutsu D, Koshimizu K, Kawanaka M, Sugiyama H, et al. Toward the chemical ecology of medicinal plant use in chimpanzees: the case of *Vernonia amygdalina*, a plant used by wild chimpanzees possibly for parasite-related diseases. J Chem Ecol. 1994;20:541–53.
- Cubukcu B, Bray DH, Warhurst DC, Mericli AH, Ozhatay N, Sariyar G. In vitro antimalarial activity of crude extracts and compounds from Artemisia abrotanum L. Phytother Res. 1990;4:203–4.
- Pillay P, Vleggaar R, Maharaj VJ, Smith PJ, Lategan CA, Chouteau F, et al. Antiplasmodial hirsutinolides from *Vernonia staehelinoides* and their utilization towards a simplified pharmacophore. Phytochem. 2007;68:1200–5.
- 134. Tona L, Cimanga RK, Mesia K, Musuamba CT, De Bruyne T, Apers S, et al. *In vitro* antiplasmodial activity of extracts and fractions from seven medicinal plants used in the Democratic Republic of Congo. J Ethnopharmacol. 2004;93:27–32.
- Challand S, Willcox M. A clinical trial of the traditional medicine Vernonia amygdalina in the treatment of uncomplicated malaria. J Altern Complement Med. 2009;15:1231–7.
- Oketch-Rabah HA, Dossaji SF, Christensen SB, Frydenvang K, Lemmich E. Antiprotozoal compounds from *Asparagus africanus*. J Nat Prod. 1997;60:1017–22.
- Nkunya MH, Weenen H, Bray DH, Mgani QA, Mwasumbi LB. Antimalarial activity of Tanzanian plants and their active constituents: the genus Uvaria1. Planta Med. 1991;57:341–3.
- Deck LM, Royer RE, Chamblee BB, Hernandez VM, Malone RR, Torres JE, et al. Selective inhibitors of human lactate dehydrogenases and lactate dehydrogenase from the malarial parasite *Plasmodium falciparum*. J Med Chem. 1998;41:3879–87.
- 139. Musuyu Muganza D, Fruth BI, Nzunzu Lami J, Mesia GK, Kambu OK, Tona GL, et al. *In vitro* antiprotozoal and cytotoxic activity of 33 ethonopharmacologically selected medicinal plants from Democratic Republic of Congo. J Ethnopharmacol. 2012;141:301–8.

- 140. Koch A, Tamez P, Pezzuto J, Soejarto D. Evaluation of plants used for antimalarial treatment by the Masai of Kenya. J Ethnopharm. 2005;101:95–9.
- Gakunju DMN, Mberu EK, Dossaji SF, Gray AI, Waigh RD, Waterman PG, et al. Potent antimalarial activity of the alkaloid nitidine, isolated from a Kenyan herbal remedy. Antimicrob Agents Chemother. 1995;39:2606–9.
- 142. Bah S, Jager AK, Adsersen A, Diallo D, Paulsen BS. Antiplasmodial and GABA(A)- benzodiazepine receptor binding activities of five plants used in traditional medicine in Mali, West Africa. J Ethnopharmacol. 2007;110:451–7.
- Okpako LC, Ajaiyeoba EO. In vitro and in vivo antimalarial studies of Striga hermothica and Tapinanthus sessilifolius extracts. Afr J Med Sci. 2004;33:73–5.
- 144. Vonthron-Senecheau C, Weniger B, Ouattara M, Bi FT, Kamenan A, Lobstein A, et al. *In vitro* antiplasmodial activity and cytotoxicity of ethnobotanically selected Ivorian plants. J Ethnopharmacol. 2003;87:221–5.
- Julianti T, De Mieri M, Zimmermann S, Ebrahimi SN, Kaiser M, Neuburger M, et al. HPLC based activity profiling for antiplasmodial compounds in the traditional Indonesian medicinal plant *Carica papaya* L. J Ethnopharmacol. 2014;155:426–34.
- 146. Dold AL, Cocks ML. The trade in medicinal plants in the Eastern Cape Province, South Africa. S Afr J Sci. 2002;98:589.
- Abdel-Azim NS, Shams KA, Shahat AA, EL-Missiry MM, Ismail SI, Hammouda FM. Egyptian herbal drug industry: challenges and future prospects. Res J Med Plants. 2011;5:136–44.

# Submit your next manuscript to BioMed Central and we will help you at every step:

- We accept pre-submission inquiries
- Our selector tool helps you to find the most relevant journal
- We provide round the clock customer support
- Convenient online submission
- Thorough peer review
- Inclusion in PubMed and all major indexing services
- Maximum visibility for your research

Submit your manuscript at www.biomedcentral.com/submit

