Antimalarial plants of northeast India: An overview

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ABSTRACT

The need for an alternative drug for malaria initiated intensive efforts for developing new antimalarials from indigenous plants. The information from different tribal communities of northeast India along with research papers, including books, journals and documents of different universities and institutes of northeast India was collected for information on botanical therapies and plant species used for malaria. Sixty-eight plant species belonging to 33 families are used by the people of northeast India for the treatment of malaria. Six plant species, namely, *Alstonia scholaris, Coptis teeta, Crotolaria occulta, Ocimum sanctum, Polygala persicariaefolia, Vitex peduncularis*, have been reported by more than one worker from different parts of northeast India. The species reported to be used for the treatment of malaria were either found around the vicinity of their habitation or in the forest area of northeast India. The most frequently used plant parts were leaves (33%), roots (31%), and bark and whole plant (12%). The present study has compiled and enlisted the antimalarial plants of northeast India, which would help future workers to find out the suitable antimalarial plants by thorough study.

Key words: Alkaloids, malaria, medicinal plants, mosquito repellents, northeast India, traditional knowledge of medicine

INTRODUCTION

Malaria is caused by single-celled protozoan parasites called *Plasmodium* and transmitted to man through the *Anopheles* mosquito. It is one of the major fatal diseases in the world, especially in the tropics, and is endemic in some 102 countries, with more than half of the world population at risk with fatality rates being extremely high among young children below 5 years of age.[1] The World Health Organization estimates that there are between 300 and 500 million new cases of malaria worldwide, every year, mostly in Africa, Asia, South Pacific Islands and South America, which causes at least 1 million deaths annually. In spite of control programs in many countries, there has been very little improvement in the control of malaria, and infections can reduce the effectiveness of labor and can lead to both economic and human losses. Control of malaria is complex because of the appearance of drug-resistant strains of *Plasmodium* and with the discovery that man becomes infested with species of simian (monkey) malaria.[1] At the same time, the *Anopheles* mosquitoes have developed resistance to many insecticides.[2]

Spread of multidrug-resistant strains of *Plasmodium* and the adverse side effects of the existing antimalarial drugs have necessitated the search for novel, well-tolerated and more efficient antimalarial drugs that kill either the vector or the parasite. The use of plant-derived drugs for the treatment of malaria has a long and successful tradition. The first antimalarial drug was quinine, isolated from the bark of *Cinchona* species (Rubiaceae) in 1820. It is one of the oldest and most important antimalarial drugs, which is still used today. In 1940, another antimalarial drug, chloroquine, was synthesized and is being used for the treatment of malaria.[3] Unfortunately, after an early success, the malarial parasite, especially *Plasmodium falciparum*, also became resistant to chloroquine. Treatment of chloroquine-resistant malaria was done with alternative drugs or drug combinations, which were rather expensive and sometimes toxic.[4] The extract of the bark and leaves of *Azadirachta indica* has also been used in Thailand and Nigeria as an antimalarial for a long time. Charaka in 300 BC and Susruta in 200 BC reported the antimalarial and antipyretic activity of this

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species. Hence, it is clear that the main drugs developed for malaria and used until now (quina alkaloid derived drugs and artemisinin) were discovered based on traditional use and ethnomedical data.

In Ghana, several plant species including *Az. indica* A. Juss, (Meliaceae), *Cryptolepis sanguinolenta* (Lindl.) Schttr. (Asclepidaceae), *Nauclea latifolia* Sm. (Rubiaceae), *Ocimum viride* Willd. (Lamiaceae), *Alstonei boonei* De Willd (Apocynaceae), *Morinda lucida* Benth. (Rubiaceae), *Nyctanthes arbor-tristis* L. (Nyctaginaceae) and *Tinospora cordifolia* (Willd.) Miers ex Hook f. and Thomas[5,6] are used in the treatment of malaria. The list of antimalarial plants of India has not yet been completely searched out and it is an urgent need to compile this data. The aim of this study was to compile the antimalarial plants reported by different workers from northeast India. The present database of antimalarial plants would help the future phytochemist to evaluate the best antimalarial plants and it would be possible to formulate the most effective medicine from this region of the world. It might, therefore, be useful to test the antibacterial, antiviral and anti-inflammatory activities of these groups of plants. The present survey has provided information about the range of species of plants used in the treatment of malaria in northeast India. Accordingly, researchers should consider the ethnomedical information of all species before deciding which kind of screening should be used in the search for an antimalarial.

MATERIALS AND METHODS

All primary ethnobotanical studies from books and journals, research papers of different universities and institutes of northeast India were collected for information about botanical therapies and plant species used for malaria. Local traditional healers were interacted with for confirmation and validation as far as possible. Any data or references to plants used for malaria were carefully inserted into a template and botanical name and classification were re-examined and confirmed with the flora of northeast India and flora of India. For compliance of study, authors had interaction with traditional healers through interviews in the prominent communities of Adi (4), Apatani (2), Khampti (3), Mishmis (4), Nyishi (4), Monpa (6), Nocte (2), and Sherdukpens (2) in Arunachal Pradesh, Mizo (4) in Mizoram, Aos (3) in Nagaland, and Nepalis and Lepcha (2) in Sikkim. As per the available literature, various folklores treating malaria in different communities have been reported.[7-27]

RESULTS AND DISCUSSION

After thorough literature survey using the above method, it can be confirmed that 68 species of plants belonging to 33 families are used by the people of northeast India for the treatment of malaria [Table 1]. Of the 33 families studied, Verbenaceae (5), Acanthaceae (3), Asteraceae (5), Rubiaceae (3), Rutaceae (4), Lamiaceae (5), and Euphorbiaceae (3) are predominant in terms of the number of species used to treat malaria. Six plant species, namely, *Alstonia scholaris, Coptis teeta, Crotolaria occulta, Ocimum sanctum, Polygala persicariaefolia,* and *Vitex peduncularis*, have been reported by more than one worker from different parts of northeast India. The species reported to be used for the treatment of malaria were either found around the vicinity of their habitation and in the forest area of northeast India. More than 20 authors have reported antimalarial plants and the author himself has reported 10 antimalarial plants from different parts of Arunachal Pradesh.[7-9] Similarly 9,12, 4 and 2 species from Assam, Manipur, Mizoram and Sikkim respectively.[10- 12,15-23]

Most of the plants were reported from Assam, Arunachal Pradesh, Manipur and Mizoram, whereas Nagaland and Tripura have been less explored by any author. The plants recorded in this survey were used traditionally for the treatment of malaria and its symptoms. Majority of the plants were used as decoctions and some plants were used both internally and externally. Herbs and shrubs were found to be predominantly used as antimalarial drugs, and the most frequently used plant parts were leaves (33%), roots (31%), and bark and whole plant (12%). The enormous frequency of the usage of leaves in traditional preparations is related to their abundant availability and easy collection.

Information from traditional healers of Assam Ayurveda Regional Research Institute, Itanagar, revealed that they had used pills of *Kalmegh* (*Andrographis paniculata*), stem bark of *Latakaranja* (*Caesalpinia crista*) and *Guduchi* (*T. cordifolia*). Some species like *Holoptelea integrifolia* Planch, *T. cordifolia* (Willd.), *Calotropis procera* (Ait.) R. Br., *Nerium indicum* Mill., *Ajuga bracteosa* Wall., *Leucas cephalotes* Spreng., *Enicostemma hyssopifolium* (Willd.) Verdoorn, *Vernonia cinerea* Less., *Justicia adhatoda* Linn., *Orthospihon pallidus* Royle ex Benth., *Pongamia pinnata* (L.) Merr., *Nyctanthes arbortistis* L., *Calotropis gigantea* (L.) R. Br., *Capsicum annum* L., *Phyllanthus fraternus* L., *Plectranthus* sp., *Elephantopus scaber* Linn., *Combretum decandrum* Roxb., *Holarrhena antidysentrica* Wall., *Cleome viscosa* L., *Vernonia roxburghii* Less., *Achyranthes aspera* L. are also available in northeast India, but any report on their use in any part of northeast India has not yet been published.[28-30]

The knowledge of plants used in the treatment of malaria in northeast India, combined with the high level of correlation found with the uses of these plants (or related species) in diverse parts of India, indicates the inheritance of our ancestral knowledge throughout the country. It represents

Table 1: List of antimalarial plants reported from northeast India

Name of the plant	Family	Vern. name	Parts used	Methodology	References
Acacia farnesiana (L.) Willd	Mimosaceae	*Tarua kadam* (Ass)	Bark		[10]
Acorus calamus L.	Araceae	*Bach* (Beng), Sweet flag (Eng)	Rhizome	If taken with quinine, stops remittent fever	[15]
Adhatoda zeylanica Medicus	Acanthaceae	*Kawldai* (Mi)	Leaf	The leaves are boiled and the water is used for bathing and the leaf paste is applied on the whole body as an effective cure for chronic fever/malaria	[12]
Alstonia scholaris R.Br.	Apocynaceae	*Tun tong* (Khamti), *Chatiana* (Assamese), *Thamrita* (Mi)	Bark	Bark infusion is given once a day	[16], [17], [18], [7], [10], [19]
Andrographis paniculata Wall. Ex Nees	Acanthaceae	*Gokur* (Beng), *Kalmegh* (S), *Hnakapui* (Mi), *Vubati* (Man)	Leaf	Crushed raw leaves are taken orally for 2 days twice with half glass of milk	[20]
Artemisia nilagirica (C.B. Clarke) Pamp.	Asteraceae	*Koken* (Nyishi), *Sai* (Mi), *Laibakngou* (Man), *Nagdona*, *Tongloti* (Ass)	Leaf	Decoction of leaves is given	[21]
Asplenium adiantoides C. Chr.	Aspleniaceae	*Ruimangma* (Man)	Plant		[22]
Aster amellus L.	Asteraceae		Root		[22]
Berberis aristata DC.	Berberidaceae	*Daru Haridra* (S), *Drauhaldi* (Beng)	Root	The root bark is used as tonic	[15]
Betula alnoides Buch.-Ham	Betulaceae	*Hriang* (Mi), *Bhujpattra* (Hi)	Bark	Decoction is taken	[17]
Brucea javanica (Linn.) Merr.	Simaroubaceae	*Heining* (Man), *Tammu* (Rongmei	Fruit		[11]
Carica papaya L.	Caricaceae	*Papeya* (Beng)	Leaf		[10]
Cinchona officinalis Linn f.	Rubiaceae		Bark	The bark of the tree is grounded into powder and then it is boiled in water and fed to the patient	[23], [19]
Cinnamonum bejolghota (Buch.-Ham)	Lauraceae	*Tezpta* (Mi)	Bark and leaf	The bark and leaves are boiled with the leaves of Anacolosa crassipes. The water is used for bathing, the steam inhaled and the water taken internally	[12]
Cissampelos pareira L.	Menispermaceae	*Tubuki lot* (As), *Papurilota*	Root	Juice is used	[10]
Citrus medica L.	Rutaceae	*Baranimbu* (Beng)	Fruit	Juice is used	[10]
Citrus sinensis (L.) Osbeck	Rutaceae	*Musambi* (M, H and B) Sweet orange *Serthlum* (M), *Kamala-nimbu* (H)	Leaf	Decoction is taken	[24]
Clausena excavata Burm. f.	Rutaceae	*Bhant* (H)	Leaf	Juice rubbed to alleviate muscular pain	[25]
Clerodendron infortunatum Gaertn.	Verbenaceae	Assam	Root and leaf		[26]
Clerodendrum colebrookoianum Walp.	Verbenaceae	*Nephaphu* (Ass), Ar	Leaf	Decoction is given to cure	[25]
Clerodendrum serratum (L.) Moon	Verbenaceae	*Barangi* (H)	Root		[10]
Coptis teeta Wall	Rananculaceae	*Mishmi teeta*	Root, rhizome	It is administered orally at a dose of 150 g thrice a day	[27], [25], [7]
Crotolaria occulta Grab	Fabaceae		Plant	Plant juice taken with warm water	[7], [25]

Table 1 (contd...)

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Name of the plant	Family	Vern. name	Parts used	Methodology	References
Croton tiglium L.	Euphorbiaceae	*Jaiphal* (H)	Leaf, flower	Plant powder is consumed with a glass of water twice a day till cured	[20]
Croton caudatus Geisel	Euphorbiaceae		Root		[10]
Cynoglossum glochidion Wall.	Boraginaceae	*Nyumli Mento* (Monpa)	Root	Root pounded or powdered and mixed with water. 10 g is taken twice daily	[7]
Datura metel L.	Solanaceae	*Dhatura* (H)	Seed, leaf and root	In fever with catarrhal and cerebral complication	[21]
Dichroa febrifuga Lour.	Saxifragaceae	*Khawsik-damdawi* (Mi), *Basak* (H)	Root and leaf	Roots and leafy tops are used in malarial fever. Therapeutic activity is due to quinazoline derivatives	[21]
Elsholtzia blanda Benth	Lamiaceae	*Papit Namdung* (Adi) *Pheiri* (Tankhul), *Ban tulsi* (A)	Leaf	It is a mosquito repellent	[25]
Gomphostemma parviflora Wall.	Lamiaceae		Leaf		[10]
Halenia elliptica D. Don	Gentianaceae	*Qing ye dan* (Mon)	Plant	Taken orally in malarial fever	[7]
Hedyotis scandens Roxb.	Rubiaceae	*Bakrelara* (Nep) *Khangbai taak* (Rongmei)	Root and leaf	Infusion of the roots and leaves is taken as an effective remedy	[12]
Helianthus annus L.	Asteraceae	*Numitlei* (M), *Surajmukhi* (B and H)	Leaf and flower	Decoction of plant parts along with honey is prescribed	[11], [10]
Homonoia riparia Lour.	Euphorbiaceae	*Tuipui sulhla* (A)	Wood	Wood infusion is given	[11]
Hydrangea macrophylla (Thunb.) Ser.	Saxifragaceae		Leaf, root	Said to be more potent than quinine	[11]
Impatiens angustifolia Blume	Balsaminaceae		Leaf	Paste is given	[25]
Lantana camara L.	Verbenaceae	*Hlingpangpar* (Mi)	Plant	Plant decoction is given	[12]
Magnolia grandiflora L.	Magnoliaceae	*U-thambal* (M), *Andachampa* (H and B)	Bark		[11]
Melodinus monogynus Roxb.	Apocynaceae		Leaf, wood and root	Contains a narcotic poison. Used as antimalarial drug	[21]
Mesona wallichiana Benth.	Lamiaceae		Root	Boiled extract is given	[28]
Nasturtium officinale Br.	Brassicaceae	*Chhu-ra* (Nyishi)	Plant	Plant decoction (2–3 teaspoonful) taken twice daily	[7]
Ocimum sanctum L.	Lamiaceae	*Tulasi* (H and S)	Root	Decoction is given as diaphoretic	[17], [22]
Ocimum tenuiflorum L.	Lamiaceae		Root		[14]
Passiflora nepalensis Walp.	Pasifloraceae	*Nauawimu* (M)	Root	Decoction is taken	[24]
Picrasma javanica Bl.	Simaroubaceae	*Thingdamdawi*/*Khwsik-damdawi* thing	Bark	The inner bark is very bitter like cinchona. An infusion of the inner coat of bark is taken orally in lieu of quinine at a dose of tablespoonful (10 ml) twice daily	[12]
Piper mullesua Buch. Ham.	Piperaceae	*Pippali* (Adi)	Leaf, fruit	Dried plant is consumed during malaria and cough	[20]
Polygala persicariaefolia DC.	Polygalaceae		Plant	Boiled and decoction is given	[11], [25]

Table 1 (contd...)

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Name of the plant	Family	Vern. name	Parts used	Methodology	References
Randia fasciculata (Roxb.) DC.	Rosaceae	*Chhawntan* (M), *Horu-moyan*, *pulikaint* (As)	Leaf	Leaf mixed with Piper nigrum and their boiled juice extract is given	[26]
Rubus ellipticus Sm.	Rosaceae	*Hmutau*	Leaf	Root decoction used	[18]
Rubus				Leaf mixed with Piper nigrum and their boiled juice extract is given	[18]
Satyrium nepalanse D. Don	Orchidaceae		Tuber	Consumed as tonic	[25]
Sida rhombifolia L.	Malvaceae	*Boriala* (Ass)	Root	Boiled extract is given	[18]
Solanum vairum Cl.	Solanaceae	*Thitbyake* (Nyishis)	Root	Decoction of root is used	[7]
Solanum torvum Sw.	Solanaceae	*Gota begun*	Fruit	Burnt fruits are consumed	[20], [10]
Stephania japonica Miers.	Menispermaceae	*Rajpatha* (H)	Tuber	Sun-dried tuber powder is administered orally with boiled water twice a day for more than 4 days till malaria is cured	[20]
Strobilanthes auriculatus Nees	Acanthaceae	*Ramting* (M), *Rum* (Ass)	Leaf	Pounded leaves rubbed on the body during the cold stage of intermittent fever.	[21]
Swertia dilatata Wall.	Gentinaceae	*Sirota* (Ass)	Root	Powdered root is administered	[25]
Swertia nervosa Wall.	Gentinaceae	*Sirota* (Ass)	Plant	Decoction of plant is given	[25]
Taraxacum offcicinalis Wigg.	Asteraceae	*Pitachumki* (Beng), *Dudal* (Hindi)	Plant	Powder is used	[25]
Thalictrum foliolosum L.	Ranunculaceae	*Pilijari* (H), *Gurbiani* (Beng)	Rhizome and root	Extract is a bitter tonic	[7]
Vandellia sessiliflora Benth.	Scrophulariaceae		Plant	Decoction of whole plant is used	[7]
Vitex peduncularis Wall	Verbenaceae	*Thing-khawi-lu* (Mizo)	Bark, leaf, stem	The bark is crushed and boiled. The steam vapor is inhaled by a patient suffering from malarial fever; infusion of leaves or of root bark or young stem bark is useful in malaria and black water fever	[12], [17], [25]
Picrorhiza kurrooa Benth.	Scrophulariaceae		Root	Pounded in water and given	[15]
Xanthium strumarium L.	Asteraceae	*Agara* (Ass)	Leaf		[14]
Zanthoxylum hamiltonianum Wall.	Rutaceae		Root and bark		[27]

(Ass) - Assamese, (H)- Hindi, (Beng)- Bengali, (M) - Manipuri, (Mi) - Mizo, (S)- Sanskrit

sometimes the only available alternative malarial treatment in remote communities of the northeast India. Four species from Assam, Arunachal Pradesh, Meghalaya and Mizoram were also found to be used as mosquito repellents [Table 2]. Though species like *Homalomena aromatica*, *Ocimum gratissimum*, *Elsholtzia blanda*, *Eucalyptus globules* are written as repellents, whether these plants are repellents or insecticides or both has not yet been sufficiently proved. Local people of this region used these plants as a substitute for DDT and other insecticides, as it is well known that DDT and other insecticides have adverse effects on environment and human health. Several classes of the secondary plant metabolites are responsible for antimalarial activity, but the most important and diverse biopotency has been observed in alkaloids, quassinoids and sesquiterpene lactones. The active compounds isolated from antimalarial plants have been compiled from the review work of Saxena and others.[4] Plants which produce different antimalarial compounds, namely, alkaloids, quassinoids, sesquiterpenes, triterpenoids, flavonoids, etc. can be very important sources of antimalarial drugs. These compounds have low, moderate or high *in vitro* antiplasmodial activity, whereas some of them are inactive. They also gave a critical account of crude extracts, essential oils and active constituents with diverse chemical structure from higher plants possessing significant antimicrobial activity.

In the information obtained, also, there were many details

Table 2: Mosquito repellent reported from northeast India

Name of the plant	Family	Vern. name	Parts used	Methodology	References
Homalomena aromatica Schott.	Araceae	*Sugandhamantri* (Ass)	Rhizome	The burnt smoke of dried rhizome is used as mosquito repellent	[12]
Ocimum gratissimum L.	Lamiaceae	*Ramtulsi* (M., H and Beng.)	Plant	Used as mosquito repellent	[12]
Elsholtzia blanda Benth.	Lamiaceae	*Pheiri Bantulsi* (Ass)	Leaf	Leaf juice is used	[14], [25]
Eucalyptus globules Labill.	Myrtaceae	*Nasik* (M)	Leaf		[10]

(Ass) - Assamese, (H)- Hindi, (Beng)- Bengali, (M) - Manipuri, (Mi) - Mizo, (S)- Sanskrit

about the appropriate indication of each plant. For example, some plants are indicated to increase others' potency. There are also plants that are traditionally employed for specific symptoms or conditions that often accompany malaria, such as weakness, renal failure, body pain or cerebral malaria. Many plants that have been considered to lack activity against malaria due to absence of *in vitro* activity against *Plasmodium* can have other mechanisms of action. Some authors have underestimated the traditional plants used for malaria based exclusively on low activity against *Plasmodium in vitro* or in animal models. This can be a mistake of strategy or even methodology. There are many explanations for the absence of *in vitro* activity of an effective antimalarial drug. As an example, the active principle could be formed by hepatic metabolism, or as a result of transformation by gut bacteria. Other possible mechanisms of action include immunomodulation or interference with the invasion of new red blood cells by parasites, which can be species specific. Therefore, studies in human subjects, as well as the observance of ethnomedical detailed data, are required in order to exclude or confirm the activity of plants traditionally used to treat malaria.

Sixty-eight plants have been reported to act against malaria, either to kill *Plasmodium* sp. (e.g., *Al. scholaris*, *O. sanctum*) or to act as hepatic protector if used in combination with some other plant like *An. paniculata Co. teeta* or *Swertia chirayita*. This needs thorough screening by testing for active principles, toxicity of the extract and their pharmacological action to act against *Plasmodium* as well as hepatic protection. Therefore, it is required to carry out all possible studies on the selection basis of plants for strengthening and establishing them as a real drug before undertaking clinical trials. The plants which are commonly reported by different authors from different parts of northeast, such as *Al. scholaris, Co. teeta, Cr. occulta, O. sanctum, P. persicariaefolia, V. peduncularis*, should be given the priority for *in vitro* and *in vivo* studies.

There is a need to generate reliable scientific data to determine whether the plants currently used to treat malaria are actually effective. In the long term, this should help to prevent deaths due to ignorance and the misuse of plants for self-medication in the absence of advice from a qualified medical professional. Individual plants are rarely used alone. In most cases, they are used as mixtures like *Al. scholaris* with *An. paniculata* and *Artemisia nilagarica* with *Co. teeta* and *V. peduncularis* with *An. Paniculata*, etc. It will never be easy to determine which plants are likely to be the most useful and should be examined to isolate pure active compounds. Some antimalarial plants are used for preparing baths or for inhalations (aromatic plants). It might, therefore, be useful to test the antibacterial, antiviral and anti-inflammatory activities of these groups of plants.

CONCLUSION

The present survey has provided information about the range of species of plants used in the treatment of malaria in northeast India. (Accordingly, researchers should observe ethnomedical information of all species before deciding which kind of screening should be used in the search for antimalarial drugs.) It develops good scope for Pharmaceutics to develop new drug for malaria after combining drugs having action against *Plasmodium*, anti-inflammatory drugs as well as hepatic protector by using these traditional information and furnishing chemical analysis, pharmacological action, and *in vitro* studies. Traditional healers working in very remote parts of the region are paying much attention to treat various kinds of ailments. While using herbs for treatment, it has been observed that some are really devoted to the methodology of treatment, whereas some others concentrate on their use.

There is a need to generate reliable scientific data to determine whether the plants currently used to treat malaria are actually effective. In the long term, this should help to prevent deaths due to ignorance and the misuse of plants for self-medication in the absence of advice from a qualified medical professional. Individual plants are rarely used alone. In most cases, they are used as mixtures. It will never be easy to determine which plants are likely to be the most useful and should be examined to isolate pure active compounds. Some antimalarial plants are used for preparing baths or for inhalations (aromatic plants).

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