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, Crotalaria 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...
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 A. indica A. Juss, (Meliaceae), Cryptolepis sanguinolenta (Lindl.) Schrtr. (Asclepiadaceae), Nancea latifolia Sm. (Rubiaceae), Ocimum viride Willd. (Lamiaceae), Astilne boonei De Willd (Apocynaceae), Morinda lucida Bent. (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 Sherdukpen (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.[10-27]

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, Captis teeta, Crotonia 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.[10-12] 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 (Cassalpinia crista) and Guduchi (T. cordifolia). Some species like Holoptela integrofolia Planch, T. cordifolia (Willd.), Calotropis procera (Ait.) R. Br., Nerium indicum Mill., Ajuga bracteosa Wall., Lucas cepalates Spreng., Enicostemma hyssopifolium (Willd.) Verdoorn, Vernonio cinera Less., Justicia adhatoda Linn., Orthosiphon pellidus Royle ex Benth., Pongomia pinnata (L.) Merr., Nyctanthes arbortistis L., Calotropis gigantea (L.) R. Br., Capsicum annuum L., Phyllanthus fraternus L., Plecuranthus sp., Elephantsopus acuber Linn., Combretum decandrum Roxb., Holarrhena antidysenterica Wall., Cleome viscosa L., Vernonio 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.) Wild.   | Mimosaceae          | Tarua kadam (Ass.)                | Bark       | If taken with quinine, stops remittent fever                                | [10]       |
| *Acorus calamus* L.              | Araceae             | Bach (Beng), Sweet flag (Eng)     | Rhizome    |                                                                              | [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), Hnkapul (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), Laiakong (Man), Nagdana, 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 Harida (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] |
| *Cinnamomum 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 pareia* 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), Kamalanimbu (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 colebrookiianum* Walp. | Verbenaceae         | Nepaphu (Ass), Ar                 | Leaf       | Decoction is given to cure                                                  | [25]       |
| *Clerodendrum serratum* (L.) Moon | Verbenaceae         | Barangi (H)                       | Root       |                                                                              | [10]       |
| *Coptis teeta* Wall              | Ranunculaceae       | 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           | Nyumli Mentu (Monpa)| Root       | Root pounded or powdered and mixed with water. 10 g is taken twice daily    | [10]       |
| Cynoglossum hochidion Wall.     | Boraginaceae            | Nyumli Mento        | 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           | Khowsik-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               | Papat Namdung (Adi) Pheiri (Tanhkhu), 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) Bakrelara (Nep) Khangbai taak (Rongmei) | Plant | Taken orally in malarial fever                                              | [7]        |
| Hedyotis scandens Roxb.         | Rubiaceae               |                     | Root and leaf | Infusion of the roots and leaves is taken as an effective remedy            | [12]       |
| Helianthus annus L.             | Asteraceae              | Numitei (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) | Plant |                                                                 | [11]       |
| Melodinus monogynus Roxb.       | Apocynaceae             |                     | Leaf and wood, 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       | Decoction is taken                                                          | [14]       |
| Passiflora nepalensis Walp.     | Passifloraceae          | Nauawimu (M)        | Root       |                                                                                | [24]       |
| Picrasma javanica Bl.           | Simaroubaceae           | Thingdamdawi/Khwsik-damdawi thing | Bark |                                                                                | [12]       |
| Piper mellesua 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             | Chhawtang (M), Horumoyan (As), 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*                               | Family               |                   |            |                                                                             |            |
| *Satyrium nepalense* 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       | Rapatha (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), Run (Ass) | Leaf       | Pounded leaves rubbed on the body during the cold stage of intermittent fever. | [21]       |
| *Swertia dilatata* Wall.              | Gentianaceae         | Sirota (Ass)      | Root       | Powdered root is administered                                                | [25]       |
| *Swertia nervosa* Wall.               | Gentianaceae         | Sirota (Ass)      | Plant      | Decoction of plant is given                                                  | [25]       |
| *Taraxacum officin released* Wigg.    | Asteraceae           | Pitchumki (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]       |
| *Zanthoxyllum hamitonianum* Wall.     | Rutaceae             |                   | Root and bark |                                                                             | [27]       |

(As) - 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
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*, *Ca. teeta* or *S. 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*, *Ca. teeta*, *Cr. oculta*, *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 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).

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