Antimalarial Herbal Plants in Kupang, Indonesia

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Abstract

Malaria is an infectious disease caused by Plasmodium parasite transmitted through female Anopheles mosquito bite. This disease is harmful because Plasmodium is known to be resistant to antimalarial drugs. The emergence of malaria resistance has raised concerns among researchers to look for any alternative antimalarial drugs. There are some plants potentially used as antimalarial drugs that should be well-documented through scientific research. This study aimed to get to know plant species that has antimalarial activity in Kupang region. Method: This research applied qualitative descriptive method while using exploration method specifically in the sampling process. Every sample is then taken for preservation as herbarium and identified based on its morphological features using determination key handbook. The result showed that there are 17 species of antimalarial plant in 10 observational sites. Those species of antimalarial plants i.e. Tithonia diversifolia, Momordica charantia, Cyperus rotundus, Strychnos lingustrina, Andrographis paniculata, Callicarpa longifolia, Tinospora crispa, Piper betle, Plectranthus scutellarioides, Alstonia scholaris, Carica papaya, Amaranthus spinosus, Arctocarpus champeden, Cassia siamea, Azadirachta indica, Helianthus annuus and Blumea balsamifera. Therefore, the availability of the plant species with antimalarial activity in Kupang needs to be explored and developed as an alternative approach for the society in treating Malarial diseases.

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INTRODUCTION

Malaria is an infectious disease caused by *Plasmodium falciparum*, *P. vivax*, *P. malariae*, *P. ovale* (Depkes RI, 2008a) and *P. knowlesi* (Singh et al., 2004) parasites, which reside and reproduce inside human blood cells and is transmitted through female *Anopheles* mosquito bite. The most abundant species found in Indonesia are *P. falciparum* and *P. vivax* (Depkes RI, 2008b). Up until now, malaria has still become a harmful disease which causes high morbidity and mortality (WHO, 2011). One reason is the resistance of *P. falciparum* towards chloroquine (Gunawan, 2010), sulfadoxine-pyrimethamine (SP) (Kemenkes RI, 2011), and even against artemisinin in areas between Cambodia and Thailand border (Noedl et al., 2008), Thailand, Myanmar, Cambodia and Vietnam (WHO, 2012). Therefore, new alternative of antimalarial drugs is needed to anticipate the resistance toward artemisinin.

Cases on Plasmodium resistance and no effective antimalarial drugs available has become the obstacles for researchers, and therefore through the use of natural substances will certainly become a solution for this case. Indonesia is rich with natural resources. There are around 30,000 plant species in Indonesia's tropical forest. Among 9,600 species of them is known to have medicinal properties, however, only 200 of them has been used as traditional medicine including the use as antimalaria drugs. Traditional medicinal plant is a plant used by traditional society, either its roots, stems, or leaves, to treat a disease because it is believed to cure the disease or that least o put out from its misery (Noorhidayah and Sidiyasa, 2006). Commonly, the medicinal plants used are taken from around their own neighborhood.

Previous studies showed that the plants used by the society as antimalarial drugs, have been scientifically proven to contain antimalarial compounds and have antimalarial activity. Some of those antimalarial herbal plants are brotowali (*Tinospora crispa*) (Adnan et al., 2001) & (Ihwan et al., 2014), Sambiloto (*Andrographis paniculata*) (Zein et al., 2013), Papaya (*Carica papaya*) (Falah et al., 2013) and Talikuning (*Anamirta cocculus*) (Muti’ah et al., 2010).

Efforts done by the society and researchers to develop medicine from natural materials has since grown rapidly and prospectively, that is supported by the availability of biological resources. Besides that, around 370 native ethnic groups with local wisdom (include in medicine) have also enriched the ethno-medicine treasure and nation’s culture. An understanding of sickness and health related with the use of local plants as traditional medicine is obtained from socialization which is trusted and believed to be true and also in herited from generation to generation (Rahayu et al., 2006). The same situation also occurs in Kupang city and Kupang regency of East of Nusa Tenggara province.

Society knowledge, especially in traditional medicine must be documented properly and scientifically. The delivery of information about the use of traditional medicine hereditarily until now is still by oral. Using plants to cure a disease by making a traditional herb is customary for Indonesian people. Various types of traditional herbal plants are formulated in Indonesia, either as a trademark for commercial or home made. Based on the description above, the necessity to conduct a research on antimalarial herbal plants is needed in Kupang City and Kupang Regency.

This study aimed to get to know the number and species of plants that has antimalarial activity in Kupang City and Kupang Regency. Therefore, the availability of natural resources (plant species with antimalarial potencies) in Kupang needs to be explored and developed, as a useful source of information for the society as an alternative approach in treating Malarial disease.

METHODS

This research was conducted from May to October 2015, in Kupang city (district of Alak, Maula, and Kelapa Lima) and Kupang regency (district of Amarasi, West Amarasi, West Kupang and East Kupang). Materials used in this research were a digital camera, a set of tools for herbarium (dry preservation) process (Murni et al., 2015), GPS (Global Positioning System), determination key handbook, and other relevant textbooks (Falah et al., 2013, Kinho et al., 2011).

The steps in this research were observation, determining the sampling locations, preparing apparatus and materials, and then sampling. Sampling was done through exploration method, i.e. by exploring every sampling area. Every plant species with antimalarial potencies or containing antimalarial compounds was documented by using digital camera. The obtained data on kinds of plants with antimalarial drug potentials or containing antimalarial compounds were then identified and described based on its morphological features and other related-literature studies.

Method for Herbarium Preparation

The process of making a dry herbarium is
done through these following steps (Murni et al, 2015):

1. Preparation of the Tools and Materials

2. Collection and Preservation during Sampling.
   a) Samples were taken with the size of 30 - 40 cm with also considering important organs or parts that should not be separated or cut-off as the specimen have to be in complete form. Terms for certain habitus: 1) Small-sized plants like grasses, herbs and bushes would be collected completely as one individual. 2) Trees, large bushes and lianas were collected limited to the size determined above starting from the bud; b) Samples were then pressed in newspaper folding, stacked, tied, stored inside plastic bags and sprayed with alcohol. It will then be enclosed firmly to make it air-tight.

3. Pressing and Drying. Before drying the samples, it would be preceded with alcohol spraying, then each was placed in newspaper foldings. It would then be pressed by using 32 x 42 cm sized cardboard or plywood on each side, with the maximum number of 50 specimens. The labeling card was made sure that it was clearly printed or written during this process. After pressing, specimens were tied and dried under sunlight for 46 - 48 hours.

4. Mounting. Dried specimens were mounted or sewed on a 28 - 30 cm x 39 - 42 cm herbarium sheet (manila paper). After mounting, each specimen was grouped according to its level of taxonomic classification.

5. Labelling
   Specimens mounted were each labelled permanently using a herbarium label listing important information on the specimen and was placed on the bottom-right side of the specimen.

RESULT AND DISCUSSION

Data on antimalarial herbal plants in Kupang in 10 observational sites is presented in Table 1. Ten of the observational sites on antimalarial herbal plants in Kupang is presented in Figure 1.

The result showed that there are 17 antimalarial herbs found in 10 observation sites. They were *T.diversifolia*, *M.charantia*, *C.rotundus*, *S.lingustrina*, *A.paniculata Nees*, *C.longifolia*, *T.crispa (L) Miers*, *P.betle L.*, *P.scutellarioides L.*, *A.scholaris (L.) R.Br*, *C.papaya L.* *A.champeden, C.siamea Lamk.*, *A.indica, H.annuus L.* and *B.balsamifera*. Some of these species were found in all of the observational sites while others were found in certain sites only. The data of this herbal distribution location is presented in Table 2.

Based on Table 2, certain species were found in all observational sites, but other types that were found in certain locations only. The 17 of antimalarial herbal plants are presented in the following figures (Figure 2).

The result showed that both of Kupang City and Kupang Regency have natural resources potentially capable to be developed and utilized for public welfare, notably in handling malarial diseases. These potencies are shown by the num-

<table>
<thead>
<tr>
<th>Location Site</th>
<th>District</th>
<th>Village</th>
<th>Coordinate Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kupang Regency</td>
<td>West Kupang</td>
<td>Tesabela</td>
<td>10°17′41.80″N 123°29′30.03″E</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tablolong</td>
<td>10°18′59.14″N 123°28′50.62″E</td>
</tr>
<tr>
<td></td>
<td>Amarasi</td>
<td>Tesbatan</td>
<td>10°05′42.06″N 123°56′09.92″E</td>
</tr>
<tr>
<td></td>
<td>West Amarasi</td>
<td>Teunbaun</td>
<td>10°18′16.71″N 123°42′33.50″E</td>
</tr>
<tr>
<td></td>
<td>East Kupang</td>
<td>Oesao</td>
<td>10°05′52.47″N 123°51′11.31″E</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nunhila</td>
<td>10°09′51.87″N 123°34′49.68″E</td>
</tr>
<tr>
<td>Kupang City</td>
<td>Alak</td>
<td>Alak</td>
<td>10°11′02.14″N 123°33′23.91″E</td>
</tr>
<tr>
<td></td>
<td>Maulafa</td>
<td>Maulafa</td>
<td>10°11′35.66″N 123°37′53.95″E</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sikumana</td>
<td>10°12′30.61″N 123°36′09.11″E</td>
</tr>
<tr>
<td></td>
<td>Kelapa Lima</td>
<td>Lasiana</td>
<td>10°08′15.19″N 123°40′02.13″E</td>
</tr>
</tbody>
</table>
mer of plants species as antimalarial drugs that are either grown in the wild or planted in the garden or in the home yard.

Literature studies gave information that these antimalarial herbal plants which are found in Kupang city and Kupang regency and that have been identified and tested in the laboratory, do have antimalarial activities. Moreover, the antimalarial active compounds with each of its parasite inhibition mechanism have also been identified (Table 3).

Table 2 shows 17 antimalarial activity of medicinal plants based on laboratory tests. Kem-bang bulan leaves (*T. diversifolia*) contain sesqi-
pene lactonetaginin compound (Syarif, 2012; Utami & Armiyanti, 2012), which have inhibition effect to P.berghei growth with its ED\textsubscript{50} value of 114 mg/kgbw (Budiati, 2011). Its inhibition mechanism is by inhibiting the polymerization of heme (Afiyah, 2007). Besides that, kembang bulan also has effective digestive toxic effect and contact toxic effect as biolarvicide to C. bezziana larvae, that can cause death, decrease pupa weight and inhibit the pupa formation and its hatch ability to become imago (Wahdana, 2014).

Pare fruit (M. charantia) contains many compounds, i.e. momordicin, momordine, quarine, hydroxytryamine, resin, saponin, alkaloid, flavonoid (Kurniawan & Ginanjar, 2005). However, its inhibition pathway is still unknown. Teki

**Figure 2.** Antimalarial herbal species in 10 observational sites
Table 3. The antimalarial potencies of medicinal plants

<table>
<thead>
<tr>
<th>Scientific Name</th>
<th>Local Name (Indonesian)</th>
<th>Plant Organ(s) used</th>
<th>Antimalarial compound</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Tithonia diversifolia</em></td>
<td>Kembang Bulan</td>
<td>Leaf</td>
<td>sesquiterpene lactone taginin C</td>
<td>(Syarif et al., n.d.), (Utami &amp; Armiyanti, 2012)</td>
</tr>
<tr>
<td><em>Momordica charantia</em></td>
<td>Pare / Paria</td>
<td>Fruit</td>
<td>momordicin, momordin, quarantine, hydroxtrytamine, resins, saponins, alkaloids, flavonoids</td>
<td>(Kurniawan dan Ginanjar, 2005)</td>
</tr>
<tr>
<td><em>Cyperus rotundus</em></td>
<td>Teki</td>
<td>Root, Stem, and Leaf</td>
<td>α-cyperon</td>
<td>(Nuri et al., 2010)</td>
</tr>
<tr>
<td><em>Strychnos linguistina</em></td>
<td>Bidara Laut</td>
<td>Sambiloto</td>
<td>strychnine, loganin, tannin andbrusin</td>
<td>(Setiawan et al., 2014), (Kemenkes RI, 2011)</td>
</tr>
<tr>
<td><em>Andrographis paniculata Nees</em></td>
<td>Sambiloto</td>
<td>Leaf</td>
<td>andrographolide</td>
<td>(Zein et al., 2013)</td>
</tr>
<tr>
<td><em>Callicarpa longifolia</em></td>
<td>Tabar Besi</td>
<td>Stem, Leaf</td>
<td>flavonoids and flavonols</td>
<td>(Pasaribu, 2014), (Falah et al., 2013), (Dewi et al., 2007)</td>
</tr>
<tr>
<td><em>Tinospora crispa (L.) Miers</em></td>
<td>Brotowali</td>
<td>Root, Stem and Leaf</td>
<td>tinokrisposid, berberine, palmitate</td>
<td>(Adnanet al., 2001), (Ihwanet al., 2014)</td>
</tr>
<tr>
<td><em>Piper betle L.</em></td>
<td>Sirih</td>
<td>Leaf</td>
<td>antymicin,piperaquine</td>
<td>(Nugroho, 2011)</td>
</tr>
<tr>
<td><em>Plectranthus scutellarioides L.</em></td>
<td>Miyana</td>
<td>Leaf</td>
<td>Essential oil, tannin, catechut tannin and flavonoids</td>
<td>(Nugroho, 2011)</td>
</tr>
<tr>
<td><em>Alstonia scholaris (L.) R.Br</em></td>
<td>Kayu Susu</td>
<td>Stem, Leaf</td>
<td>Echitamine, tubotaiwine, akuamicine, picrinine, echitamidine, strictamine</td>
<td>(Pankti et al., 2012)</td>
</tr>
<tr>
<td><em>Carica papaya L.</em></td>
<td>Pepaya</td>
<td>Root, Stem and Leaf</td>
<td>Alkaloids, karpain, caricaxantine, violaxantine, papain, saponins, flavonoids, polyphenol.</td>
<td>(Rehena, 2010)</td>
</tr>
<tr>
<td><em>Amaranthus spinosus L.</em></td>
<td>Bayam Duri</td>
<td>Root, Stem and Leaf</td>
<td>betalain, betaninandamarantin</td>
<td>(Susantiningsih, 2013)</td>
</tr>
<tr>
<td><em>Artocarpus champeden</em></td>
<td>Cempedak</td>
<td>Bark and Leaf</td>
<td>flavonoids artoindonesian E, heteroflavonon C, artoindonesian R, heterophyline, artoindonesian A-2, cycloheterophyline, artonin A, artokarpon A, artokarpon B</td>
<td>(Widyawaruyanti et al., 2011), (Hafid dkk., 2011)</td>
</tr>
<tr>
<td><em>Cassia siamea Lamk</em></td>
<td>Johar</td>
<td>Leaf</td>
<td>blumealaktone</td>
<td>Muis, 2015</td>
</tr>
<tr>
<td><em>Azadirachta indica</em></td>
<td>Nimba</td>
<td>Leaf</td>
<td>azadirachtin, nimbolide</td>
<td>(Aini et al., 2004), (Deshpande, et al., 2014)</td>
</tr>
<tr>
<td><em>Helianthus annuus L.</em></td>
<td>Bunga Matahari</td>
<td>Leaf</td>
<td>sesquiterpenelaktones</td>
<td>(Hayati, 2011)</td>
</tr>
<tr>
<td><em>Blumea balsamifera</em></td>
<td>Sembung</td>
<td>Leaf</td>
<td>flavanoids, terpenes, lactones, cineol, borneol, kamper, tannin, limonene, palmitine acid, myristine, alcohol, sesquiterpene, dimethyl ether chloracetophenone, pyrocatechin, glycosides and saponins,</td>
<td>(Falah et al., 2013), (Hani, 2008)</td>
</tr>
</tbody>
</table>
grass (*C. rotundus*) has compound with antimalarial activity, i.e. α-cyperon (Nuri et al., 2010), and it growth inhibition mechanism of parasite is through the reaction between unsaturated carbonyl group, β contained inside α-cyperon compound (Nuri et al., 2010).

Bidara Laut fruit (*S. lingustrina*) contains striknin, loganin, tannin, steroid and brucine (Setiawan et al., 2014; Suhada, 2013; Erlinda, 2013) Even though there are still no references explaining its inhibition pathway, Lubis (2008) noted that ethyl acetate fraction from *S. lingustrina* stem at the dose of 2.30 mh/kg bw has antimalarial activity towards *Plasmodium berghei*-infected mice. Moreover, Huda (2006) explained that water extract of *S. lingustrina* stem at effective dose of 50% (ED50) 0,45 mg/ kg bw have antimalarial potencies.

Sambiloto (*A. paniculata* Ness) contains andrographolide compound and have an *in vitro* antimalarial effect to *P. falciparum* (Zein et al., 2013) but still no reference describing its inhibition pathway towards parasite growth.

Tabar Besi (*C. longifolia*) contains flavonoids compound, and the flavonol isolated from ethyl acetate fraction, has high toxicity activity to shrimp larvae of *Artemiasalisina* Leach (Pasaribu, 2014). According to Dewi et al., (2007), Tabar besi is an antimalarial herbence used by the Kutai community.

Brotowali (*Tinosporacrispa* (L) Miers) contains compounds such as tinokrisposide, berberine, palmatine (Adnan et al., 2001; Ihwan et al., 2014). Berberine is a quaternary alkaloids compound containing quartenary nitrogen in its structure, which has been known to have inhibition activity towards *Plasmodium* growth by blocking the Colun intracellular transport (Ancelin & Vial, 1986). Colun is required for phospholipid biosynthesis in cellular membrane formation of parasite to cover up the parasitophorous vacuole, cytosol and other subcellular compartments that will consequently inhibit the formation of new parasites. Blocking of Colun transport has been used as one strategy in treating malaria (Rosenthal, 2003).

Berberine is an *in vitro* biosynthesis inhibitor of nucleic acid and protein of *P. falciparum* that shows strong interaction with DNA (Birdsall & Kelly, 1997). Compounds such as berberine and palmatineare also a quartenaryalkaloid and quinolin compound that only differ in its methoxyl and hydroxyl groups (Simanjuntak, 1995) also have the same type of activity, mechanism and inhibition target.

Adnan et al., (2001) explained that tinokrisposide compound is a compound with fu-
A. champeden Spreng also contains cyclohexetofillin which is able to inhibit the growth stadium of P. falciparum malarial parasite from the ring stadium to trofozoit stadium and causes abnormal morphology growth of the skizon stadium. Cyclohexetofillin also able to inhibit globin degradation in food vacuole of malarial parasites (Widyawaruyanti et al., 2011). Combination therapy of cempedak ethanol extract and artesunat is more effective as an in vivo antimalarial drug. This shows that cempedak is more effective if used as a part of a combination therapy (Hafid et al., 2011).

Johar (C.siamea Lamk) contains alkaloids, saponin, flavonoid, tannin, and triterpenoid which shows significant antiplasmodium activity with 31.44% of inhibition percentage (Fitrianingsih et al., 2010). Rahardjo et al., (2014) also concluded that water extract of johar leaves have inhibition ability to P. berghei growth in vitro in mice with ED_{50} value of 83.77412 mg/kg BW, but its inhibition mechanism is still unknown.

Nimba (A.indica) contains azadirachtin and nimboide. The inhibition mechanism of nimba seed extract or the antimalarial compound contained inside of it is supposedly related to the immune response of the parasite (Aini et al., 2004) and having antimalarial activity (Deshpande et al., 2014).

Sunflower (H.annuus L.) contains sesquiterpen, lactone, diterpene, monoterpenoids and phenol compounds. Sesquiterpene has been known to possess antimalarial activity (Hayati and Muti’ah, 2011) through the formation of free radicals that will deteriorate vital components of the parasite that will have fatal effect (Nurrachma & Putrianti, 2005).

Sembung (B.balsamifera) contains flavonoid, terpene, lactones, cineol, borneol, camper, tannin, limonene, palmitine acid, myristine, alcohol, sesquiterpene, dimethyl ether chloroacetophenon, pyrocatechin, glycoside and saponin (Hani, 2008; Falah et al., 2013), ethyl acetate fraction contains polyphenol, tannin, flavonoid, and monoterpene, sesquiterpene, and Quinone compound. Characterization result by uv spectrophotometry and infrared spectrophotometry for ethyl acetate active fraction have identified sesquiterpene lactone compound (blumenalactone) that possesses anti-plasmodium activity at dose of 118 mg/kg BW with inhibit percentage of 17,53% (Muis, 2015).

CONCLUSION


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