

Potency of the Indonesian Medicinal Plants as Antimalarial Drugs

By:
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SUMMARY

The Indonesian traditional herbal medicine has been practiced for many centuries in Indonesia to treat malaria diseases. Although modern medicine is becoming increasingly important, herbal medicine is still very popular. In order to select raw material for preparation of safety herbal medicines, forty five medicinal plants have been tested for acute toxicity in mouse at a dose 715 mg/kg body weight. The extracts of *Asclepias curassavica* leave, *Alstonia scholaris* leave, *Decospermum fruticosum* leave, *Elaocarpus petiolatus* bark, *Elaocarpus parvifolius* bark, *Eurycoma longifolia* root, *Garcinia rigida* bark, *Nephelium lappaceum* bark, *Pentaspodan motleyi* leave, *Picrasma javanica* leave, *Phyllanthus niruri* whole, *Quassia indica* leave, *Syzygium pycnanthum* bark, *Tetrasera scandens* leave, *Cratoxylum glaucum* bark, *Sandoricum emarginatum* bark, *Mallotus paniculatus* leave, *Microcos ovatalanceolata* bark, *Poikilospermum suaveolens* leave, *Fibraurea chloroleuea* leave, *Tetrasera scandens* root, and *Timonius billitonensis* bark showed toxicity with mortality level of 20-100%. The remaining 32 plant extracts were not toxic at dose tested. The toxic plant species should be considered in the preparation of herbal medicines. Of the safety extracts were tested for their antimalarial activity against *Plasmodium berghei* in vivo at a dose 715 mg/kg body weight. Extract of *Carica papaya* leave was most active than other plant extracts with parasitemia 1.13%, while control showed 17.21%. More research is needed to scientifically prove efficacy and to identify antimalarial constituents in the plant extracts.

Key words: Indonesian medicinal plant, jamu, toxicity, antimalarial activity, *Plasmodium berghei*.

INTRODUCTION

Malaria is one of the most serious infections disease causes of morbidity and mortality each year in Indonesia. Antimalarial drugs are not generally available in the isolated villages, thus the diseases are almost treated traditionally with local medicinal plants. The gradual shift from nomadic to sedentary communities, increasing populations, and deforestation have shown to contribute to an increase in the incidence of malaria in Indonesia (Leaman et al., 1995).

Until comparatively recent years chloroquine was highly effective against malaria, but in the 1970s has turned bad. The malaria parasite developed resistance to chloroquine and its effectiveness declined. This is a result of the incorrect use of chloroquine in the countries where malaria is endemic. After World War II, scientists had attempted to eradicate malaria globally by destroying its vector mosquito using the insecticide DDT (1,1,1-trichloro-2,2-bis-*p*-chlorophenyl ethane). This was discontinued when scientists realized that this toxic material had entered into food chain. The search for novel compounds effective against *Plasmodium* strains resistant has led to increased interest in new malaria remedies from natural sources (Phillipson and Wright, 1991).

In many tropical countries, plants have traditionally been used to treat fever and other symptoms associated with malaria (Phillipson and O'Neill, 1986; Noster and Kraus, 1990). Two plants have yielded antimalarial drugs that are highly effective against resistant *P. falciparum* parasites, quinine and quinidine were isolated from *Cinchona* tree bark and artemisinin was isolated from *Artemisia annua*. With the development a continuous *in vitro* cultivation of

P. falciparum in human erythrocytes (Trager and Jenssen, 1979) and subsequently an *in vitro* microdilution assay for *P. falciparum* (Desjardins et al., 1989), many crude extracts from various medicinal plants mainly used as antipyretics and analgesics (Mukherjee, 1991) or claimed to be effective against malaria daily traditional healers practices, have been screened for their antimalarial activity against malaria parasite (Gessler et al., 1994). Some of these extracts showing strong antimalarial activity were selected and extensively studied leading to the isolation and characterization of the active constituents.

The Indonesian communities have used forests as source of food, energy, and economy since the beginning of prehistory. Later, as their culture developed, the use of forests became more important as source of medicinal plants for their primary health care and medicines. The art and knowledge of the use of those medicinal plants were mainly kept by few people known locally as "pawang or dukun". By having this knowledge, the "dukun or pawang" had an important role in the society normally as informal leader. Due to this, the art and knowledge of the use of medicinal plants were normally kept in the family and not everybody could learn. Nowadays, seems that the young generations are not interested in these arts and knowledges, besides the old traditional healers do not teach all of what they know. It is difficult to find real and qualified traditional healers now (Sukrasno et al., 1994).

Many medicinal plants are used in Indonesia to treat malaria without any scientific evidence. Some of these plants could be potentially toxic effects when ingested. This article reviews a basis for the use of Indonesian medicinal plants and preliminary screening for their antimalarial activity.

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Indonesian medicinal plants

Indonesia is one of the richest countries in the world in natural resources. The area of Indonesian tropical forests covers about 143 million hectares and is inhabited by about 80% of the world's medicinal plants. It is estimated that the Indonesian tropical forests inhabit 28,000 plant species. PT Eisei (1995) published the Dictionary of Indonesian Medicinal Herbs containing more than 2,500 plant species which potentially. These numbers are potentially to be updated due to the continuing inventory and investigation of yet unidentified species. According to the National Agency of Drug and Food Control (BPOM), 283 plant species have been officially registered for their medicinal use.

Phytochemical and biological studies including extraction, isolation, and identification of active compounds have been developed to date. To conduct research directed to the development of medicinal plants, many institutions such as the Ministry of Health, Ministry of Forestry, Ministry of Environment, Ministry of Agriculture, the National Development Planning Agency (BAPPENAS), the National Agency of Drug and Food Control (BPOM), the Universities, the Indonesian Institute of Science (LIPI), the Herbarium Bogoriense, and also non-governmental institutions are engaged.

There are about 810 companies active in Indonesian traditional medicine of which 87 are classified as traditional medicine industry and 723 as small industry of traditional medicine. In 2005, an amount of 872 companies in this field have been registered at BPOM. In addition, 462 companies from foreign countries also play a role in the production of Indonesian traditional medicine. About 20 local companies are the major players. In the period between January to June 2005, the export of medicinal plants reached an amount of 126.8 million USD (Ministry of Industry, Republic of Indonesia).

Intellectual property right, indigenous knowledge, benefit sharing, efficacy, and safety are issues that must be considered in the further development of Indonesian medicinal plants. When new plant-derived therapeutics based on indigenous knowledge are being explored, it is important that the companies return benefits to the native population and the local governments from which the research material was obtained. Harvesting too much and cultivating too little may render medicinal plants into endangered species. It is important to take into account that the individuals or institutions exploring the medicinal plant material also have responsibilities for the conservation.

Based on Medicinal Herb Index in Indonesia (1995) and Prosea (1999), 45 plant species belonging to 27 families were used by people to treat malaria and related ailments in Indonesia (Table 1). Most of the plants used against a variety of infections such as skin itch, scabies, wound, malaria, and intestinal disease, are typical diseases of a tropical country. Thus, the searches for new antimicrobial and antimalarial agents from plant materials are desirable. Interest in plant antimicrobial agent has been reawakened because of the current resistance problems associated with the use of penicillin and other antibiotics (Recio et al., 1989). The spread of

chloroquine-resistant *P. falciparum* and the alarming emergence of multidrug-resistant strains have raised an urgent need to search new antimalarial drugs from natural sources (Bickii et al., 2000).

Table 1. List of medicinal plants and their traditional medicinal uses.

No	FAMILY, Species	Uses in Traditional Medicine
1	ANACARDIACEAE <i>Pentaspadon motleyi</i>	Dermatosis, malaria, and scabies.
2	ANNONACEAE <i>Annona reticulata</i> <i>Cananga odorata</i>	Diarrhea, fever, anthelmintic, and malaria. Scabies, edema, malaria, and fever.
3	APOCYNACEAE <i>Alstonia scholaris</i> <i>Cerbera manghas</i>	Chancre, fever, dermatosis, nephritis, diabetes, malaria, hypertension, anthelmintic, depurative, and beri-beri. Constipation, purgative, emetic, itch, rheumatism, dermatosis, and malaria.
4	ASELEPIACEAE <i>Asclepias curassavica</i>	Malaria.
5	ASTERACEAE <i>Elephantopus scaber</i>	Malaria, fever, anemia, dysentery, cough, galactagogue, aphtha, diarrhea, metritis, leukorrhea, and smallpox.
6	CAESALPINIACEAE <i>Cassia alata</i>	Anthelmintic, laxative, herpes, scabies, ringworm, and malaria.
7	CARICACEAE <i>Carica papaya</i>	Renal calculus, anthelmintic, liniment, head-ache, laxative, gastrosplasm, fever, asthma, beri-beri, anorexia, depurative, combustion, and malaria.
8	CULIACEAE <i>Cratogeomys glaucum</i> <i>Garcinia rigida</i> <i>Garcinia benthamiana</i>	Malaria. Malaria. Malaria.
9	DILLENIACEAE <i>Tetracera scandens</i>	Antidote, malaria, and cold.
10	ELAEOCARPACEAE <i>Elaeocarpus petiolatus</i> <i>Elaeocarpus parvifolius</i>	Fever and malaria. Malaria.
11	EUPHORBIACEAE <i>Mallotus paniculatus</i> <i>Phyllanthus niruri</i>	Malaria. Epilepsy, malaria, constipation, hypertension, aphtha, menstrual disorder, abdominalgia, tooth-ache, dysuria, gonorrhea, syphilis, diarrhea, fever, tetanus, depurative, anticonvulsant, urinary calculus, and albuminuria.
12	FABACEAE <i>Pongamia pinnata</i>	Antidote, scabies, beri-beri, rheumatism, malaria, diabetes, and dermatosis.
13	FLACOURTIACEAE <i>Pongium edule</i>	Malaria.
14	LEGUMINOSAE <i>Cassia seanae</i> <i>Cassia fistula</i>	Malaria. Laxative, fever, ringworm, and malaria.
15	MAGNOLIACEAE <i>Aromadendron nutans</i> <i>Michellia campaka</i>	Malaria. Malaria.
16	MELASTOMATACEAE <i>Melastoma malabathricum</i>	After childbirth, tooth-ache, tonic, diarrhea, dysentery, leukorrhea, smallpox, and malaria.

17	MELIACEAE	
	<i>Lansium domesticum</i>	Dysentery, malaria, antidote, eye disease, fever, and anthelmintic.
	<i>Sandoricum emarginatum</i>	Malaria.
18	MENISPERMACEAE	
	<i>Arcangelisia flava</i>	Joundice, stomachic, anthelmintic, smallpox, malaria, and aphtha.
	<i>Fibraurea chloroleuca</i>	Eye disease, dysentery, diabetes, chancre, head-ache, and malaria.
	<i>Tinospora tuberculata</i>	Abdominalgia, fever, diabetes, scabies, and malaria.
19	MORACEAE	
	<i>Artocarpus heterophylla</i>	Fever, malaria, boil, and diarrhea.
	<i>Morus alba</i>	Fever, malaria, diabetes, gonorrhea, dysuria, rheumatism, and hypertension.
	<i>Poikilospermum suaveolens</i>	Eye disease, fever, malaria, and itch.
20	MYRTACEAE	
	<i>Decaspermum fruticosum</i>	Dysentery and malaria.
	<i>Syzygium pycnanthum</i>	Malaria.
21	POACEAE	
	<i>Imperata cylindrica</i>	Venereal disease, malaria, hematuria, renal disease, wound, fever, hypertension, neuropathy, and ringworm.
22	RUBIACEAE	
	<i>Nauclea subdita</i>	Malaria.
	<i>Pleiocarpidia enneandra</i>	Malaria.
	<i>Timonius billitonensis</i>	Malaria.
23	SAPINDACEAE	
	<i>Nephelium lappaceum</i>	Fever, malaria, dysentery, astrigent, and after childbirth.
24	SIMAROUBACEAE	
	<i>Eurycoma longifolia</i>	Fever, depurative, dysentery, aphtha, tonic, anorexia, afterchildbirth, head-ache, wound, chancre, venereal disease, smallpox, and malaria.
	<i>Picrasma javanica</i>	Fever, malaria, and chancre.
	<i>Quassia indica</i>	Fever, tonic, stomachic, emmenagogue, itch, purgative, malaria, cholecystopathy, rheumatism, and contusion.
25	TILIACEAE	
	<i>Microcos ovato lanceolata</i>	Malaria.
26	VERBENACEAE	
	<i>Peronema canescens</i>	Tooth-ache, malaria, fever, and dermatosis.
27	ZINGIBERACEAE	
	<i>Curcuma zedoaria</i>	Malaria.

Preparation of the Indonesian traditional herbal medicine (*jamu*)

The *jamu* arising from experiences of the past and embedded in the culture of society constantly changes and develops. Along with allopathic medicine it shares issues in appropriate and rational use. These include qualification and licensing of the provider, proper use of good quality products, good communication between traditional medicine providers and patients, and provision of scientific information and guidance to the public. Although pharmacological effects of herbal constituents have been recorded, there is an apparent lack of record data reporting their effectiveness.

To assure the proper use of such products, the Indonesian government has divided the medicinal plants in three categories such as *jamu*, standardized herbal medicines, and phytomedicine. The therapeutic effects of *jamu* have to be supported by empirical data. The efficacy of standardized herbal medicine has to be proved in pre-clinical trials and standardization on active compound. For phytomedicine clinical trials have to be available. The Indonesian government has launched the Centre for Development and Application of Traditional Treatment in 1995. The Centre's activities include research, testing, education, training and service of traditional treatment. Other activities include selecting, testing, certifying, registration and licensing, inventory, screening, clinical testing, utilization and evaluation of traditional medicine, and compilation of laws applicable to traditional treatment.

Jamu is produced by household scale industries in a simple and traditional way. Traditional *jamu* makers also care about hygiene, sanitation, and chemical contaminations from biological or non-biological sources. The way of preparation is often different from producer to producer. Production steps like selection of raw materials, sorting, grating, scraping, crushing, mixing and cooking, followed by boiling of the plant material in a hygienic way can differ significantly. From this background, professional training was necessary to introduce certain standards like standardization of the raw materials and hygienic production methods. The most important aspect of the training is the introduction of scientific aspects of *jamu*. From household scale industries, *jamu* has been developed and is now produced by the traditional medicine industry. To prepare *jamu*, the industries use the modern technologies and their activities are based on a scientific approach. They have to follow the directions for good manufacturing production (GMP). *Jamu* made by the industry is not anymore only in the form of a decoction but also in the form of a tablet, pill, powder, pastille, capsule, extract, cream, and ointment.

The Indonesian government through the Ministry of Health and BPOM has regulated *jamu* and phytomedicines. The regulations are aimed to develop herbal medicinal products, to protect the people from adverse effects, and to watch over the quality, efficacy, and efficiency. Three categories of Indonesian medicinal plants have been regulated by BPOM through a regulation HK.00.05.4.2411, 2004. For the production of *jamu*, standardized herbal medicines, and phytomedicine, the industries have to refer to GMP guidelines with regulation 659/MENKES/SK/X/1991. This regulation has been renewed by BPOM in 2005 with regulation HK.00.05.4.1380. GMP includes all aspects of production such as raw material, production process, quality control, factory building, workers, management, instrument, and sanitation.

The traditional medicine industries as well as the products have to be registered in the BPOM. Using this regulation, the production and distribution of traditional medicine could be controlled to fulfill the requirements according GMP. There are several forms of traditional medicine such as powders, pills, capsules,

crude extracts, tablets, and liquids. These products have to be produced according to the description published in regulation 661/MENKES/SK/VII/1994. To develop the traditional medicines, the Indonesian government has established the Centre for Development of Traditional Medicine. The Centre is supported by regulation number 0584/MENKES/SK/VI/1995.

Toxicity of medicinal plant

In preliminary screening to evaluate their toxicity, 45 extracts of medicinal plants have been tested for acute toxicity in mouse at a dose 715 mg/kg body weight. Toxicity of the extracts was determined by observation which mouse dead or alive for 7 days after intraperitoneal injection. Toxicity of the medicinal plant extract is summarized in Table 2.

Table 2. The yield of extraction and toxicity of the medicinal plant extract in mouse

No	Medicinal Plant	Part	Yield (%)	Toxicity*
1	<i>Asclepias curassavica</i>	leave	15.7	+++++
2	<i>Artocarpus heterophyllus</i>	leave	24.3	-
3	<i>Alstonia scholaris</i>	leave	34.8	+++++
4	<i>Annona reticulata</i>	leave	25.5	-
5	<i>Arcangelisia flava</i>	leave	19.6	-
		stem	5.0	-
		root	3.8	-
6	<i>Aromadendron nutans</i>	bark	8.0	-
7	<i>Cananga odorata</i>	leave	28.9	-
8	<i>Cassia seana</i>	leave	31.0	-
9	<i>Cassia fistula</i>	leave	22.9	-
10	<i>Cassia alata</i>	leave	26.3	-
11	<i>Carica papaya</i>	leave	25.5	-
12	<i>Cerbera manghas</i>	leave	33.4	-
13	<i>Cratogeomys glaucum</i>	bark	9.5	++++
14	<i>Decospermum fruticosum</i>	leave	30.9	+++++
15	<i>Elaeocarpus petiolatus</i>	bark	11.3	+++++
16	<i>Elaeocarpus parvifolius</i>	bark	9.2	+++++
17	<i>Elephantopus scaber</i>	whole	15.7	-
18	<i>Eurycoma longifolia</i>	root	2.1	+++++
19	<i>Fibraurea chloroleuea</i>	leave	19.4	++
20	<i>Garcinia rigida</i>	bark	16.0	+++++
21	<i>Garcinia benthamiana</i>	bark	6.6	-
22	<i>Imprata cylindrica</i>	rhizome	9.6	-
23	<i>Lansium domesticum</i>	leave	7.5	-
		bark	18.7	-
24	<i>Mallotus paniculatus</i>	leave	22.2	+++
25	<i>Melastoma malabathricum</i>	leave	15.6	-
26	<i>Morus alba</i>	leave	20.0	-
27	<i>Michellia campaka</i>	leave	14.3	-
		bark	22.4	-
28	<i>Microcos ovato lanceolata</i>	bark	6.0	+++
29	<i>Nauclea subdita</i>	bark	6.0	-
		root	9.8	-
30	<i>Nephelium lappaceum</i>	bark	17.4	+++++
31	<i>Pentaspodan motleyi</i>	leave	31.3	+++++
32	<i>Peronema canescens</i>	leave	17.0	-
33	<i>Pierasma javanica</i>	leave	39.2	+++++
34	<i>Pleiocarpidia enneandra</i>	stem	7.0	-
		root	7.0	-
35	<i>Pongamia pinnata</i>	leave	20.4	-
36	<i>Pongium edule</i>	leave	33.2	-
37	<i>Poikilospermum suaveolens</i>	leave	24.7	+++
38	<i>Phyllanthus niruri</i>	whole	18.7	+++++
39	<i>Quassia indica</i>	leave	22.5	+++++
40	<i>Sandoricum emarginatum</i>	bark	11.6	++++
41	<i>Syzygium pycnanthum</i>	bark	10.8	+++++
42	<i>Tetraseria scandens</i>	leave	18.5	+++++
		root	4.9	+
43	<i>Tinospora tuberculata</i>	Stem-a	3.0	-
44	<i>Timonius billitonensis</i>	bark	11.8	+
45	<i>Curcuma zedoaria</i>	rhizome	10.1	-

*Toxicity scale: +++++ (mortality 100%), ++++ (mortality 80%), +++ (mortality 60%), ++ (mortality 40%), + (mortality 20%), and - (no mortality).

Table 2 showed the extracts of *Asclepias curassavica* leave, *Alstonia scholaris* leave, *Decospermum fruticosum* leaves, *Elaocarpus petiolatus* bark, *Elaocarpus parvifolius* bark, *Eurycoma longifolia* root, *Garcinia rigida* bark, *Nephelium lappaceum* bark, *Pentaspodan motleyi* leave, *Pierasma javanica* leave, *Phyllanthus niruri* whole, *Quassia indica* leave, *Syzygium pycnanthum* bark, and *Tetrasera scandens* leaves were strong toxic to mice (mortality 100%), while *Cratoxylum glaucum* bark and *Sandoricum emanginatum* bark showed mortality 80%. *Mallotus paniculatus* leave, *Microcos ovatolanceolata* bark, and *Poikilospermum suaveolens* leave showed mortality 60%, while *Fibraurea chloroleuca* leave showed mortality 40%. Plant extracts showed mortality 20% were *Tetrasera scandens* root and *Timonius billitonensis* bark. The remaining 32 extracts of medicinal plant were not acute toxic to mouse at the dose tested for 7 days (Subeki, 2001). The plant extracts containing toxic constituents should be considered in the preparation of *jamu*.

Antimalarial activity of medicinal plant

The safety medicinal plant extracts were assessed for *in vivo* antimalarial activity in a 4-day suppressive test against malarial parasite of *Plasmodium*

berghei (Peter, 1980). Mice were inoculated with *P. berghei*, each mouse received 1×10^7 infected erythrocytes by an intraperitoneal injection on the first day of the experiment. Each mouse was administered with an intraperitoneal injection of 200 μ l of 0.2% CMC solution containing 715 mg extracts per kg body weight of mouse for 4 consecutive days. Control was given 0.2% CMC solution without plant extract. The test a blood smear was taken on day 5 and the mice were killed. Percentage of parasitaemia was determined microscopically by comparison of the parasitaemia of treated mice with parasitaemia of control group. Screenings of *in vivo* antimalarial activity of safety medicinal plant are summarized in Fig 1.

Fig. 1 indicated the effects of medicinal plant extracts on *P. berghei* growth *in vivo*. Extract of *carica papaya* leave showed parasitaemia 1.13% most active than other extracts at a dose 715 mg/kg body weight, while control showed 17.21%. Extracts of *Lansium domesticum* bark, *Tinospora tuberculata* stem, *Melastoma malabathricum* leave, *Arcangelisia flava* root-stem, *Michelia campaka* bark, and *Imprata cylindrica* rhizome showed parasitaemia less than 5.0%. Remaining 9 plant extracts showed less active with parasitaemia more than 5.0% (Subeki, 2001).

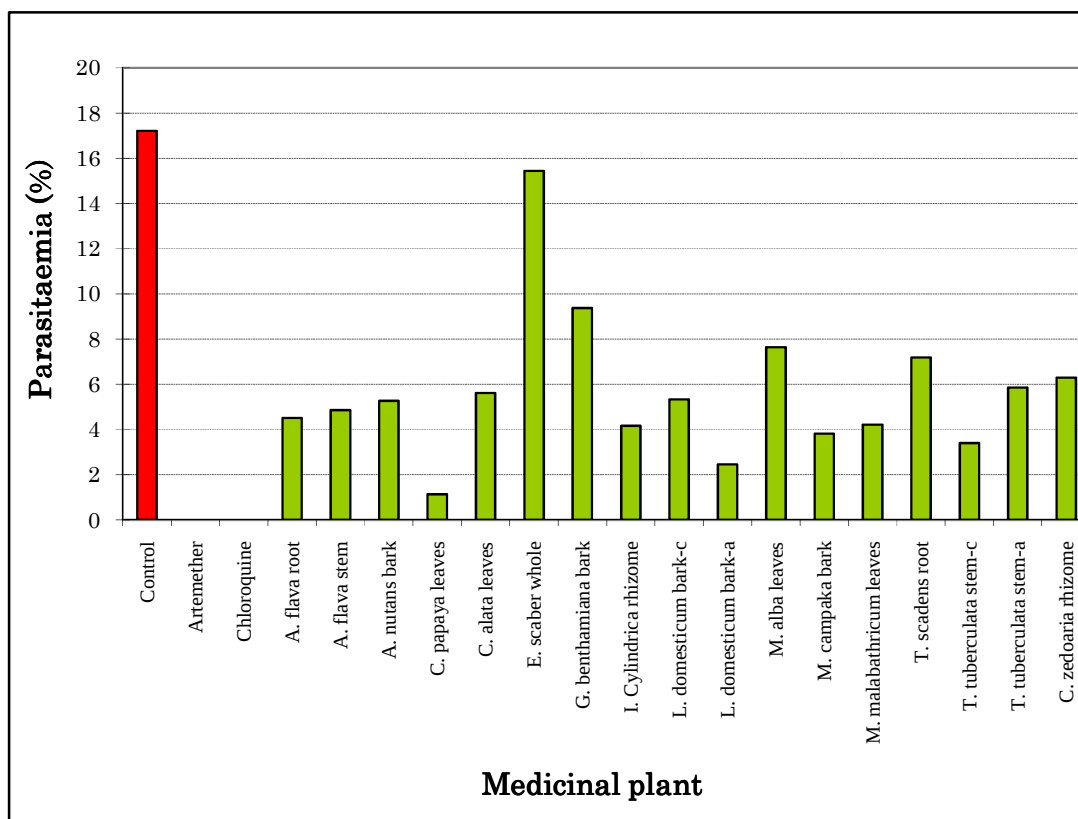


Fig. 1. antimalarial activity of the medicinal plant extracts against *Plasmodium berghei* *In vivo*

CONCLUSIONS

Indonesia is one of the richest countries in the world in natural resources. In particular the variety of plant species is enormous, so that Indonesian medicinal plants are very important from the viewpoint of finding new naturally occurring drug materials. Based on Medicinal Herb Index in Indonesia and according to bitter taste of aerial parts of plants, 45 plant species belonging to 27 families used in the Indonesian traditional herbal medicine for treatment malaria were collected. Plant extracts were tested in a preliminary biological screening for acute toxicity in mouse at a dose 715 mg/kg body weight. The extracts of *Asclepias curassavica* leave, *Alstonia scholaris* leave, *Decospermum fruticosum* leave, *Elaocarpus petiolatus* bark, *Elaocarpus parvifolius* bark, *Eurycoma longifolia* root, *Garcinia rigida* bark, *Nephelium lappaceum* bark, *Pentaspodan motleyi* leave, *Pierasma javanica* leave, *Phyllanthus niruri* whole, *Quassia indica* leave, *Syzygium pycnanthum* bark, *Tetraseria scandens* leave, *Cratoxylum glaucum* bark, *Sandoricum emarginatum* bark, *Mallotus paniculatus* leave, *Microcos ovatolanceolata* bark, *Poikilospermum suaveolens* leave, *Fibraurea chloroleuea* leave, *Tetraseria scandens* root, and *Timonius billitonensis* bark showed acute toxic in mouse with mortality level of 20-100%.

The remaining 32 extracts of medicinal plant were not toxic at dose tested. Of the safety plant extracts were then tested for their antimalarial activity against *Plasmodium berghei* *in vivo* at a dose 715 mg/kg body weight for 4 days. Extract of *Carica papaya* leave was most active than other plant extracts with parasitemia 1.13%, while control showed 17.21%. *Lansium domesticum* bark, *Tinospora tuberculata* stem, *Melastoma malabathricum* leaves, *Arcangelisia flava* stem, *Michelia campaka* bark, and *Imprata cylindrica* rhizome showed parasitaemia less than 5.0%. The remaining plant extracts showed less active with parasitaemia more than 5.0%.

REFERENCES

- Bickii, J., Njifutie, N., Foyere, J.A., Basco, L.K., and Ringwald, P. 2000. In vitro antimalarial activity of limonoids from *Khaya grandifoliola* C.D.C (Meliaceae). *J. Ethnopharmacol.* 69: 27-33.
- Desjardins, R.E., Canfield, C.J., Haynes, J.D., and Chulay, J.D. 1979. Quantitative assessment of antimalarial activity *in vitro* by a semiautomated microdilution technique. *Antimicrob. Agents Chemother.* 16: 710-718.
- Gessler, M.C., Nkunya, M.H.H., Mwasumbi, L.B., Heinrich, M., and Tanner, M. 1993. Screening Tanzanian medicinal plants for antimalarial activity. *Acta Tropica* 56: 65-77.
- Leaman, D.J., Arnason, J.T., Yusuf, R., Sangat Roemantyo, H., Soedjito, H., Angerhofer, C.K., and Pezzuto, J.M. 1995. Malaria remedies of the Kenyah of the Apo Kayan, East Kalimantan, Indonesian Borneo: a quantitative assessment of local consensus as an indicator of biological efficacy. *J. Ethnopharmacol.* 49: 116.
- Medicinal Herb Index in Indonesia. 1995. Indeks tumbuh-tumbuhan obat di Indonesia. PT. Eisai Indonesia.
- Mukherjee, T. 1991. Antimalarial herbal drugs. A review. *Fitoterapia* 42: 197-204.
- Noster, S. and Kraus, L.J. 1990. In vitro activity of *Coulera latiflora* and *Exosteme caribaeum* extracts on *Plasmodium falciparum*. *Planta Med.* 56: 63-65.
- Peters, W. 1980. Chemotherapy and drug resistance in malaria, vol. 1, 2nd edition. Academic Press. London. p. 113.
- Phillipson, J.D. and O'Neill, M.J. 1986. Novel antimalarial drugs from plants? *Parasitol. Today* 2: 355-358.
- Phillipson, J.D. and Wright, C.W. 1991. Antiprotozoal agents from plant sources. *Planta Med.* 57 (Supplement Issue I): S53-S59.
- PROSEA: Plant Resources of South East Asia 12. 1999. Medicinal and poisonous plants I. In: De Padua LS, Bunyapraphatsara N and Lemmens RHMJ (Eds.) Prosea Bogor Indonesia.
- Recio, M.C., Rios, J.L. and Villar, A. 1989. A review of some antimicrobial compounds isolated from medicinal plants reported in the literature 1978-1988. *Phytotherapy Res.* 3: 117-125.
- Subeki. 2001. Chemical studies on medicinal plants in Kalimantan. Thesis. Graduate School of Agriculture, Hokkaido University, Japan. p. 110.
- Sukrasno, Kusmardiyani, S., and Suganda, A.G. 1994. Proceeding: Plants in medicine, validation and development. Bandung Institute of Technology and the British Council Jakarta. Bandung.
- Trager, W. and Jenssen, J.B. 1979. Human malaria parasites in continuous cultures. *Sciences* 196: 673-675.