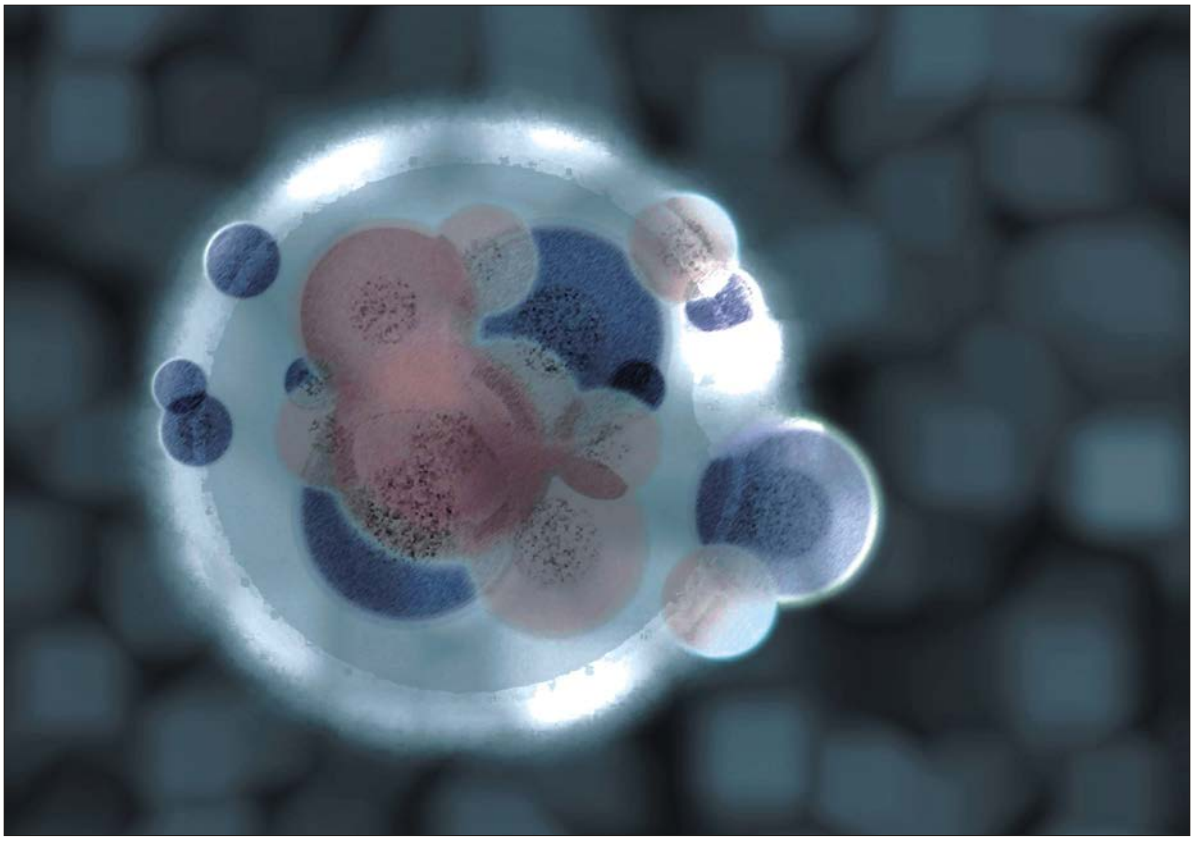

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Potency of Indonesian Medicinal Plants as Tyrosinase Inhibitor and Antioxidant Agent

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Abstract: The aim of this study is to screen whitening agent potency of 45 Indonesian plant materials from 35 species. All plant materials were extracted with methanol and 50% ethanol which resulted to 90 extracts. The methods for screening is based on tyrosinase inhibitor potency using mushroom tyrosinase and antioxidant activity using 1,1-diphenyl-2-picrylhydrazyl (DPPH). Scoring method was used to identify the best extract as whitening agent. Out of 90 extracts, merbau (*Intsia palembanica*) methanol and 50% ethanol extracts are the most potent extracts as tyrosinase inhibitor (for monophenolase and diphenolase). Their IC_{50} values are not significantly different with kojic acid as positive control. Based on antioxidant activity, merbau methanol extract (IC_{50}: 3.87 μg mL^{-1}) is the best antioxidant together with kayu putih (*Melaleuca cajuputi*) ethanol 50% extract (IC_{50}: 5.76 μg mL^{-1}) and *Rhizopora* sp. methanol extract (IC_{50}: 5.90 μg mL^{-1}). Their IC_{50} values are not significantly different with (+)-catechin (IC_{50}: 2.94 μg mL^{-1}) as positive control. In conclusion, merbau methanol extract is the most potent extract as whitening agent based on scoring data from its tyrosinase inhibitory and antioxidant activities.

Key words: Indonesian plants, tyrosinase inhibitor, antioxidant

INTRODUCTION

Finding skin whitening agent from natural sources is one of our research focus. To decrease hyperpigmentation or melanogenesis on skin, we need to reduce the formation of melanin. The formation of melanin in the human body is influenced or reduced by several mechanisms, including anti-oxidant, direct tyrosinase inhibition, melanin inhibition of migration from cell to cell and hormonal activities, etc (Prota and Thomson, 1976; Pawelek and Kormer, 1982).

On this research we focus on tyrosinase inhibitor and anti-oxidant. Tyrosinase (EC 1.14.18.1) is a multicopper monooxygenase enzyme with wide distribution either in plants, mushroom, insects, mammals, including in humans (Likhitwitayawuid, 2008). In plants and mushroom, tyrosinase will cause undesired enzymatic browning of farm products (Zheng *et al*., 2008). In insects, this enzyme is essential for the sclerotization of the exoskeleton, wound healing and parasite encapsulation (Likhitwitayawuid, 2008). In mammals including in humans, tyrosinase is responsible for melanogenesis or hyperpigmentation (Chang, 2009). Furthermore, it has been reported that tyrosinase might contribute to the dopamine neurotoxicity and neurdegeneration associated with Parkinson's disease (Zheng *et al*., 2008).

Tyrosinase inhibitor have been used frequently in cosmetics and depigmenting agents for hyperpigmentation. It catalyzes two different reactions using molecular oxygen; the ortho hydroxylation of tyrosine (mono-phenols) to 3,4-dihydroxyphenylalanine or DOPA (o-diphenols) named monophenolase activity and the oxidation of DOPA to dopaquinone (o-quinones) named diphenolase activity. The oxidation results in polymerized to brown, red, or black pigments by free radical coupling pathway (Sanchez-Ferrer *et al*., 1995).

Reactive Oxygen Species (ROS) is sometimes produced in melanin biosynthesis. These ROS enhance

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melamin biosynthesis, damage DNA and induce proliferation of melanosites (Yasui and Sakurai, 2003). Oxidative stress plays a role in pathogenesis of skin disorder (Yamakoshi *et al*., 2003). Besides, ROS scavengers such as antioxidants may reduce hyperpigmentation (Ma *et al*., 2001).

Many tyrosinase inhibitors and antioxidant agents have been tested as a way of preventing overproduction of melamin in epidermal layers (Cabanes *et al*., 1994) either from synthetic or natural resources. However, there is still a need to search for other potential compounds such as tyrosinase inhibitors from natural sources like plants.

Indonesia as a tropical country has many prospective natural resources. Some potent tyrosinase inhibitors from Indonesian plants have already been reported. For example, Arung *et al*. (2005) reported that about 44 Indonesian plants potency as tyrosinase inhibitors. Moreover, 14 other Indonesian medicinal plants from West Kalimantan potency as tyrosinase inhibitors were also reported (Arung *et al*., 2009). However, from these 58 Indonesian plants tested, there was no plant that showed an activity as potent as the positive control.

In this study, we focused on 35 different Indonesian plants species. We tried to find Indonesian plants with the most potent tyrosinase inhibitor and antioxidant activities. The method to select the plant species was based on searching for some Indonesian plants which are used traditionally for skin care and searching some prospective Indonesian woody plants. The results were interpreted using scoring system in selecting the best whitening agent based on the two tyrosinase inhibition and antioxidant activities. In this study, tyrosinase inhibitory in monophenolase and diphenolase activities and also antioxidant properties of 35 Indonesian plant species were investigated.

MATERIALS AND METHODS

Plant materials: Thirty five plant species used in this study were collected from Semarang, Tawangmangu, Bogor and Samarinda, Indonesia on 2008-2009. *Avicenia* sp., *Goniothalamus macrophyllus, Helminthostacys zeylanica*, *Intsia palembanica*, *Koompassia malaccensis*, *Lepisanthes amoena*, *Litsea firma* Hook f. Dehaasia, *Melaleuca cajuputi*, *Rhizopora* sp., *Vitex pubenscens* and *Xylocarpus granatvm* were collected from Samarinda, East Kalimantan Indonesia. Identification and voucher specimen were deposited in the Wood Anatomy Laboratory, Faculty of Forestry, Mulawarman University, East Kalimantan, Indonesia. *Swietenia* sp., *Terminalia catappa*, *Usnea misaminensis* and *Caesalpinia sappan* were collected from Semarang, Central Java, Indonesia. *Acorus calamus*, *Amomum cardamonum* and *Brucea javanica* were collected from Tawangmangu, Central Java, Indonesia. The others species were collected from Bogor, Indonesia. The identification and voucher specimen were deposited in Wanariset Samboja, Samarinda, Bogor Biopharmaca Research Center, Bogor Agricultural University, Bogor Indonesia and in Herbarium Bogoriense, Bogor, Indonesia.

Preparation of plant extracts: All samples were dried and grounded before being submitted to methanol and 50% (v/v) ethanol/water. The dried and powdered plant materials were extracted with solvents (1 g sample: 10 mL solvent) for 12 h for three times. The extracts were filtered using Whatman filter paper (No. 1) and concentrated *in vacuo* at 30°C using a rotary evaporator. The yields of extracts were then calculated.

Bioactivity tests: Inhibition of tyrosinase activity (monophenolase) and DOPA auto-oxidation (diphenolase).

This assay was performed using methods as described earlier (Curto *et al*., 1999; Nerya *et al*., 2003). Extracts were dissolved in DMSO (dimethyl sulphoxide) to a final concentration of 20 mg mL^{-1}. This extract stock solution was then diluted to 600 μg mL^{-1} in 50 mM potassium phosphate buffer (pH 6.5).

The extracts were tested at the concentrations ranging from 7.8125 to 2000 μg mL^{-1}. Kojic acid, which was used as positive control was also tested at concentrations 7.8125 to 500 μg mL^{-1}. In a 96-well plate, 70 μL of each extract dilution was combined with 30 μL of tyrosinase (Sigma, 333 Units mL^{-1} in phosphate buffer) in triplicate. After incubation at room temperature for 5 min, 110 μL of substrate (2 mM L-tyrosine or 12 mM L-DOPA) was added to each well. Incubation commenced for 30 min at room temperature. Optical densities of the wells were then determined at 510 nm with a multi-well plate reader. The concentration of plant extract at which half the original tyrosinase activity was inhibited (IC_{50}), was determined for each plant extract. Kojic acid (Sigma, Checz Republic) was used as positive control.

Antioxidant test: The antioxidant activity test was performed using 1,1-diphenyl-2-picrylhydrazyl (DPPH) as described in Batubara *et al*. (2009).

Statistical analysis: Data of tyrosinase inhibitory and antioxidant activities were expressed as Mean±SD The significant differences between groups were assessed by one-way ANOVA followed by comparisons of the groups with a control using Tukey's test, $p < 0.05$ was considered as significant.

RESULTS

Thirty five Indonesian plant species were collected to screen their tyrosinase inhibitory activity and antioxidant potency. The scientific, family, local name, part of plant used in this study, part of plant traditionally used, ethnic name and the traditional uses (Sangat *et al*., 2000) of samples are shown in Table 1. There were 35 species which consist of 17 species traditionally used for skin care and about 13 species are woody plants (Table 1) in Indonesia. We collected some woody plants to give added value on this species. From 35 Indonesian plant species, we collected 45 plant materials. All materials were extracted with methanol and 50% ethanol to get a total of 90 plant material extracts.

Ninety plant material extracts were screened for their potency as tyrosinase inhibitor in monophenolase and diphenolase activities and antioxidant activity. The results are shown in Table 2. The most potent material is *I. palembanica* wood methanol extract which has the best monophenolase (IC_{50}: 10.4 μg mL^{-1}) and diphenolase (IC_{50}: 40.4 μg mL^{-1}) activities and also antioxidant activity (IC_{50}: 3.87 μg mL^{-1}). The activities of *I. palembanica* are not significantly different with positive control.

Scoring system was used to select the best extract as whitening agent based on their activity to inhibit monophenolase reaction in tyrosinase, diphenolase reaction in tyrosinase and antioxidant. The IC_{50} which is not significantly different with the positive control got the highest score (8). The extract with no IC_{50} value got the lowest score (0). Selected potential extracts and their scores are shown in Table 3. Based on scoring system, *I. palembanica* methanol extract is the most potent extract as whitening agent. The next are *I.palembanica* ethanol 50% extract, *Rhizopora* sp. methanol extract and *X. granatus* methanol extract. There are about 22 plant extracts that have no activity as tyrosinase inhibitor antioxidant.

Table 1: Traditional uses of 35 plant species used in this study (Sangat *et al*., 2000)

			Part used			
Species	Family	Local name	In this study	Traditionally	Ethnic	Traditional use
Acorns calamns L.	Acoraceae	Jaringao	L	L	Sunda	Skin care after giving birth
Amomum cardamonum	Zingiberaceae	Kapulaga	S	S	Aceh	Face powder
Andrographis paniculata	Acanthaceae	Sambiloto	H	H	Jawa	Diabetes
Avicennia sp.	Verbenaceae	Api-api	W	W	Sunda	Birth control
Brucea javanica	Simaroubaceae	Buah makasar	L	L	Kutai	Acne
Caesalpinia sappan	Fabaceae	Secang	W	W	Maluk	Skin care
Codiaeum veriegatum	Euphorbiaceae	Puring	L	L	Kutai	Face powder
Curcuma domestica	Zingiberaceae	Kunyit	Rh	Rh	Sunda	Release itch
Curcuma xanthorrhiza	Zingiberaceae	Temulawak	Rh	Rh	Jawa	Skin care
Durio zibethinus	Bombacaceae	Durian	WB	WB	Kutai	Acne
Goniothalamus macrophyllus	Aunonaceae	Somputn	L, St, B	L	Dayak Ngaju	Skin care
Guazuma ulmifolia	Sterculiaceae	Jati Belanda	L	L	Jawa	Slimming agent
Gynura pseudochina	Compositae	Daun Dewa	L, Rh	L	Jawa	Acne
Helminthostachys zeylanica	Ophloglossaceae	Akar tunjuk langit	Fl, L, R, St	Fl	Kutai	Face powder
Intsia bijuga	Fabaceae	Keranji	W	SB	Aceh	Malaria
Intsia palembanica	Fabaceae	Merbau	W	R	Maluk	Impotency
Kaempferia galangal	Zingiberaceae	Kencur	Rh	Rh	Aceh	Face powder
Koompassia malaccensis	Fabaceae	Kempas	W	WB	Melayu tradisional	Anthelmintic
Lepisanthes amoena	Sapindaceae	Celekop	St, L	L	Dayak tunjung	Skin care
Litsea firma	Lauraceae	Medang	W	W	Sunda	Appetite
Melaleuca cajuputi	Myrtaceae	Gelam	W	W	Punan lisum	Itch
Morinda citrifolia	Rubitaceae	Mengkudu	F, L	F	Jawa	Hipertency
Murraya paniculata	Rutaceae	kemuning	L	L	Sunda	Skin care after giving birth
Phaleria papuana	Thymelacaceae	Mahkota dewa	F, L			
Piper vacumentosa	Piperaceae	Sirih merah	L	L	Sunda	Antidiabetes
Pogostemon cablin Benth.	Lamiaceae	Nilam	L	L	Sunda	Skin care after giving birth
Psidium guajava	Myrtaceae	Jambu Biji	L	L	Sunda,Jawa	Diarrhea
Rhizophora sp.	Rhyzoporaceae	Bakau	W	W	Sunda	Diarrhea
Swietenia sp.	Meliaceae	Mahoni	F, W	F	Sunda	Malaria
Talinum sp.	Portulaceae	Kolesom	L	L	Sunda	Tonicum
Terminalia catappa	Combretaceae	Ketapang	WB, W	WB	Sunda	Increasing breast milk
Tinospora tuberculata	Merispermaceae	Brotowali	St	St	Jawa, sunda	Anti-fungi
Usnea misaminensis	Usneaceae	Kayu angin	Li	Li	Ambon	Cough
Vitex pubenscens	Verbenaceae	Laban	WB, W	WB	Sunda	Backpain
Xylocarpus granatvm	Meliaceae	Boli	W			

L: leaves, S: Seeds, H: Herbs, W: Wood, B: Bark, WB: Wood bark, Li: Lichen, F: Fruits, St: Stem, Rh: Rhizome, R: Root; Fl: Flower; Ethnic Sunda stay in West Jawa, ethnic Jawa stays in East and Central Jawa and also in Yogyakarta (Jawa Island). Ethnic Aceh lives in Aceh province and Melayu Tradisional lives in Riau and Jambi province in Sumatera Island. Ethnic Kutai, Dayak Ngaju, Dayak Tunjung and Punan Lisum live in East Kalimantan (Kalimantan Island). Ethnic Maluk stays in Sumbawa Island and Ethnic Ambon lives in Seram Island (Ambon)

Table 2: Yield and IC_{50} values of monophenolase and diphenolase activities of tyrosinase and antioxidant activity from selected extracts

				IC_{50} (μg mL^{-1})		
Species	Part of plant	Solvent[a]	Yield[b] (%)	Monophenolase[c]	Difenolase[c]	Antioxidant[d]
Caesalpinia sappan	Wood	E	7.36	568.9±6.3^{c}	-	6.47±0.74^{bcd}
Curcuma longa	Rhizome	M	18.30	785.1±8.7^{e}	485.9±5.6^{c}	16.94±0.13^{h}
Curcuma longa	Rhizome	E	5.32	206.6±9.2^{b}	783.7±6.8^{d}	44.77±0.21^{lm}
Curcuma xanthorrhiza	Rhizome	M	26.1	267.3±6.1^{b}	903.7±8.6^{e}	80.72±0.21^{v}
Durio zibethinus	Wood bark	E	13.88	172.1±9.1^{b}	-	16.4±2.05^{h}
Goniothalamus macrophyllus	Root	M	7.62	405.7±15.6^{b}	1059.8±57.6^{f}	96.20±0.10^{AB}
Guazuma ulmifolia	Leaves	M	19.31	2503.0±215.4^{h}	-	112.31±0.13^{E}
Gynura pseudochina	Rhizome	M	5.80	1278.8±28.9^{gl}	-	131.37±0.20^{F}
Helminthostachys zeylanica	Flower	M	16.00	128.8±2.1^{b}	783.2±6.2^{d}	93.09±0.13^{xyz}
Helminthostachys zeylanica	Leaves	M	28.21	1400.4±19.0^{d}	-	-
Intsia bijuga	Wood	M	11.34	-	-	6.60±0.13^{bcd}
Intsia bijuga	Wood	E	12.23	-	-	12.1±0.56^{ef}
Intsia palembanica	Wood	M	4.66	10.4±3.7^{a}	40.4±3.8^{a}	3.87±0.52^{ab}
Intsia palembanica	Wood	E	16.72	14.8±1.2^{a}	67.5±6.3^{ab}	6.63±0.54^{bcd}
Koompassia malaccensis	Wood	M	4.55	315.4±13.9^{b}	-	9.51±0.91^{def}
Lepisanthes amoena	Stem	M	0.78	162.6±2.3^{b}	-	99.10±0.17^{BC}
Lepisanthes amoena	Leaves	M	11.86	243.6±4.9^{b}	-	17.25±0.16^{h}
Piper vnscumentosa	Leaves	M	7.53	1541.0±10.6^{de}	-	35.07±0.15^{k}
Psidium guajava	Leaves	E	22.90	2034.6±21.6^{f}	-	11.60±0.14^{f}
Rhizophora sp.	Wood	M	11.00	108.2±11.9^{b}	124.0±11.4^{b}	5.90±0.41^{abc}
Rhizophora sp.	Wood	E	19.67	171.1±7.7^{b}	1638.9±78.9^{g}	9.87±0.33^{ef}
Switenia sp.	Wood	M	7.47	1568.4±57.4^{e}	1719.7±61.3^{g}	8.34±0.92^{cde}
Talinum sp.	Leaves	M	4.11	2355.4±38.7^{g}	-	53.91±0.10^{pq}
Talinum sp.	Leaves	E	7.18	2833.2±70.3^{i}	-	53.72±0.17^{pq}
Terminalia catappa	Root	E	1.29	1941.8±62.5^{f}	-	42.42±0.53^{l}
Tinospora tuberculata	Stem	M	2.41	1334.7±39.8^{d}	-	-
Xylocarpus granatvm	Wood	M	3.48	215.1±6.4^{b}	199.7±12.2^{b}	23.75±0.69^{i}
Xylocarpus granatvm	Wood	E	2.81	213.3±9.0^{b}	-	23.8±1.28^{i}
Asam Kojat	Standard for tyrosinase			11.3±0.09^{a}	40.2±2.11^{a}	
(+)-catechin	Standard for antioxidant					2.94±0.03^{a}
Vitamin C	Standard for antioxidant					2.01±0.02^{a}

[a]: Solvents are M: Methanol and E: Ethanol 50%; [b]Based on dried sample; [c]: IC_{50}, concentration causing 50% inhibition, Data given as Mean±standard deviation of triplicate tests. Samples followed by the same letter are not significantly different according to Tukey's multiple comparison test at p = 0.05; [d]: Failed to achieve 50% inhibition at maximum concentration of 2500 μg mL^{-1}; [f]: Failed to achieve 50% inhibition at maximum concentration of 166.67 μg mL^{-1}

Table 3: Scoring activity data of some prospective extracts

		Score			
Species	Solvent	Tyrosinase (monophe-nolase)	Tyrosinase (dipheno- lase)	Antioxidant	Total
I. palembanica	MeOH	8	8	8.00	24.00
I. palembanica	EtOH 50%	8	8	7.75	23.75
Rhizopora sp.	MeOH	7	7	8.00	22.00
X. granatvm	MeOH	7	7	6.00	20.00
C. longa	MeOH	6	6	6.25	18.25
C. longa	EtOH 50%	7	5	5.00	17.00
Rhizopora	EtOH 50%	7	2	7.75	16.75
D. zibenthinns	MeOH	7	0	7.75	14.75
H. zeylanica (flower)	MeOH	7	5	2.00	14.00
K. melaceusis	MeOH	7	0	7.00	14.00
C. sappan	EtOH 50%	6	0	7.50	13.50
L. amoena (leaves)	MeOH	7	0	6.25	13.25
C. xanthorrhiza	MeOH	7	4	2.25	13.25
C. javanica	EtOH 50%	6	0	7.00	13.00
X. granatvm	EtOH 50%	7	0	6.00	13.00
G. macrophyllns (root)	MeOH	7	3	1.50	11.50

DISCUSSION

Based on the different constituents consisting in methanol and 50% ethanol extracts, we screened their activities. Different constituents will give different activities. Methanol extraction was performed to separate most of the semi-polar and polar constituents of the samples (Harborne, 1998) while 50% ethanol was chosen to separate most of polar constituents.

Based on tyrosinase (monophenolase) inhibitor activity, *I. palembanica* methanol (IC_{50}: 10.4 μg mL^{-1}) and 50% ethanol (IC_{50}: 14.8 μg mL^{-1}) extracts are the most

potent monophenolase inhibitor. These two extracts have IC_{50} value not significantly different with kojic acid (IC_{50}: 11.3 μg mL^{-1}) as positive control. There are 12 other prospective extracts as monophenolase inhibitor (with b mark after IC_{50} value shown in Table 2). If we compared these results with report from Arung *et al.* (2009) *I. palembanica* is more prospective. The most prospective sample reported by Arung *et al.* (2009) *Dendrophthoe petandra* aerial root, only had inhibition activity with inhibition level 74.3% at very high concentration (500μg mL^{-1}), while our best sample, *I. palembanica*, at concentration 125 μg mL^{-1} had inhibition level about 97.7%.

On diphenolase activity, there are two most potent extracts; *I. palembanica* methanol (IC_{50}: 40.4 μg mL^{-1}) and 50% ethanol (IC_{50}: 67.5 μg mL^{-1}) extracts. The IC_{50} values of these two extracts are not significantly different with kojic acid (IC_{50}: 40.2 μg mL^{-1}) as positive control. The other potential extracts are *Rhizopora* sp. methanol and *Xylocarpus granatvm* methanol extracts. These results also better compared to report of Arung *et al.* (2009). The most potent sample reported by Arung *et al.* (2009) *D. petandra* aerial root only had inhibition level about 55.9% at concentration 500 μg mL^{-1}, while our best sample, *I. palembanica*, had inhibition level about 73.5% at concentration 125 μg mL^{-1}.

Based on the combination activity in tyrosinase inhibition, methanol and 50% ethanol extract of *I. palembanica* are the most potent extracts. These two extracts have IC_{50} values in monophenolase and diphenolase activity that is not significantly different with kojic acid as positive control. Some literature reported some compounds isolated from *I. palembanica.* Hayashi *et al.* (1970), Imamura *et al.* (1974a, b) and Hilis and Yazaki (1973) reported that resveratrol 3,5,3',4'-tetrahydroxystilbene, robinetin main constituent (Fig. 1), myricetin, fisetin, quercetin, naringenin, ampelopsin and leucosianidin were isolated from *I. palembanica.* Among these isolated compounds, quercetin (Fig. 2) was reported by Kubo *et al.* (2007) had activity to inhibit tyrosinase activity. The activity of quercetin to inhibit tyrosinase activity is about 0.2 times of Kojic acid (Xie *et al.*, 2003) while methanol extract of *I.palembanica* has the activity with Kojic acid. Resveratrol and hydroxystilbene were also reported to inhibit tyrosinase activity (Chang, 2009).

Interestingly, *Intsia bijuga*, the species in the same genus with *I. palembanica*, has no activity to inhibit the monophenolase and diphenolase activities of tyrosinase. Hillis and Yazaki (1973) reported that robinetin is the main polyphenol of heartwood of *I. bijuga* together with 3,5,4'-tri-and 3,5,3',4'-tetra hydroxystilbenes, dihydromyricetin, myricetin and narigenin. This result shows that there is

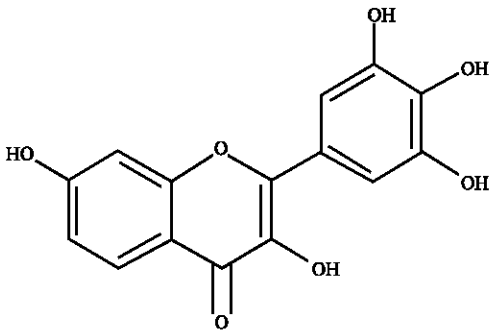

Fig. 1: Structure of robinetin, the main constituent in *I. palembanica*

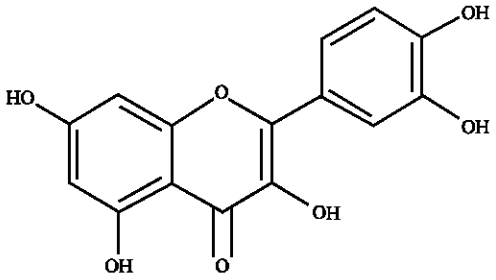

Fig. 2: Structure of quercetin

some active compounds present in *I. palembanica* that does not exist in *I. bijuga*. This indicates that even quercetin which has tyrosinase inhibitory activity were already isolated from *I. palembanica*, the search for more potent inhibitor tyrosinase compounds from *I. palembanica* is still needed.

As an antioxidant based on DPPH radical-scavenging activity, out of 90 plant extracts, there are 3 extracts which have IC_{50} value not significantly different with (+)-catechin (IC_{50}: 2.94 μg mL^{-1}) and vitamin C (IC_{50}: 2.04 μg mL^{-1}) as positive controls. These three extracts are *I. palembanica* methanol extract (IC_{50}: 3.87μg mL^{-1}), *Melaleuca cajuputi* ethanol 50% extract (IC_{50} : 5.76 μg mL^{-1}) and *Rhizopora* sp. methanol extract (IC_{50} : 5.90 μg mL^{-1}).

Methanol extract of *I. palembanica* is the most potent extract with maximum score of 24 followed by *I. palembanica* ethanol 50% extract (score 23.75). The other potential extracts are *Rhizopora* sp. methanol extract (score: 22) and *X. granatvm* methanol extract (score: 20).

The data on combined score activities showed that some of the Indonesian medicinal plants which are traditionally used as skin care have the ability as whitening agent, for example, *C. longa*, *D. zibenthinus*, *H. zeylanica* and *G. macrophyllus* (Table 1). Even the most potent extract as whitening agent (*I. palembanica*) has no traditional information about its use for skin care,

but Indonesian medicinal plants which are used for skin care also have activity as whitening agents.

These data prove the efficacies of the traditional knowledge. The efficacies of the traditional knowledge proven with scientific method can be employed to give a better understanding of the mechanisms of action of Indonesian medicinal plants. But to get more scientific data, searching and isolating the pure active compounds from the potential extract is still needed.

CONCLUSION

Out of 35 Indonesian plants species collected from Semarang, Tawangmangu, Samarinda and Bogor, Indonesia, the most potential species as whitening agent is *Intsia palembanica* based on scoring system of their activities as monophenolase inhibitor, diphenolase inhibitor in tyrosinase and antioxidant activity. *Intsia palembanica* has activities as monophenolase and diphenolase inhibitor of tyrosinase and antioxidant activity that is not significantly different with the positive control. Two other potential species based on the scoring system are *Rhizopora* sp. and *Xylocarpus granatvm.*

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