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ANTIMALARIAL, ANTI-TERMITE, AND ANTIFUNGAL ACTIVITIES FROM EXTRACT OF THE ROOT OF *Lansium domesticum* CORR.

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ABSTRACT

Phytochemical screening of the crude extract and their fractions from the root of *L. domesticum* exhibited various groups of secondary metabolites. The root powder was macerated by methanol, then the crude extract was stepwise partitioned with *n*-hexane and chloroform. The crude extract and all fractions were phytochemically tested for alkaloids, terpenoids, flavonoids, and phenolics, and it was evaluated for antimalarial, anti-termite, and antifungal activities. The results revealed that at 5% ($^{w}/_{v}$) chloroform fraction which contained flavonoids and triterpenoids showed high antimalarial activity against *Plasmodium falciparum* with IC_{50} value 1.4 µg/mL and methanol fraction at a concentration of 5% ($^{w}/_{v}$) which contained phenolics showed anti-termite and antifungal activities by 100% mortality against *Coptotermes curvignathus* and 100% inhibition to fungal mycelia growth of *Tyromyces palustris* (TYP), respectively.

Keywords: Meliaceae, *Lansium domesticum*, Antimalaria, Anti-termite, and Anti-fungi.
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INTRODUCTION

Lansium domesticum is a fruit plant of the Meliaceae which is widely distributed in Southeast Asian countries.[1-2] The burnt dried peels are applied as mosquito repellent.[3] The seeds are believed to be toxic to the malaria parasite.[4] In North Kalimantan including Malaysia, the leaves, peels, bark, and seeds have been used to treat malaria and fever.[5-7] Predominantly chemical constituents obtained from the leaves, peels, seeds, and bark of *L. domesticum* were triterpenoids. Two tetranortriterpenoids, Domesticulides B and C, were isolated from the seeds of *L. domesticum* and gave strong antimalarial activity against *Plasmodium falciparum*.[8] Kokosanolides A and B that were characterized from the seeds and bark of *L. domesticum* cv Kokossan, respectively, showed antifeedant activity against the insect larvae of *Epilachna vigintioctopunctata*.[9] Additionally, methanol extract and wood vinegar from *Toona sinensis* (Meliaceae) revealed anti-termite activity against *Coptotermes curvignathus*.[10,11] The presence of flavonoids, terpenoids, tannins, phenols, and saponins has also been identified from the stem bark of *L. domesticum* together with its antioxidant activity[12] and recently, an onoceranoid exhibited weak cytotoxic activity obtained from peels of *L. domesticum*.[13] Despite the importance of such use and its chemical components, in this paper we report the identification of secondary metabolites and investigate their biological activities such as for antimalarial, anti-termite, and antifungal from the root of *L. domesticum*.

EXPERIMENTAL

Sample Preparation, Extraction, and Partition

The root of *L. domesticum* (5 Kg) was collected from Pontianak, West Kalimantan, Indonesia on March 2021. The dried root was powdered and macerated by MeOH (10 L) for 3x24 hours and dried under reduced

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pressure with the rotary evaporator. Subsequently, the crude extract was partitioned stepwise with *n*-hexane and chloroform.

Phytochemical Screening[14]
The crude extract and 3 fractions (*n*-hexane, chloroform, and methanol) were screened for alkaloids (Dragendorff reagent), flavonoids (Shinoda test), phenolics (5% $FeCl_3$), and triterpenoids (Liebermann-Burchard test).

Bioactivity Assays
Antimalarial (*in vitro*) activity against *Plasmodium falciparum* strain 3D7 was conducted by using Giemsa stain.[15] In brief, 10 mg of each of the crude extract and fraction was dissolved in 1 mL DMSO (10,000 µg/mL). Each solution was diluted to 100, 10, 1, 0.1, and 0.01 µg/mL. Synchronized parasite (ring stadium) with ± 1% parasitemia was cultured with the samples. A 2 µL sample of each concentration was taken and put in 96-well culture plates then 198 µL of the parasite was added. The culture plates were incubated inside a chamber for 48 hours at 37 °C. Finally, parasite-infected erythrocytes were harvested, made a thin smear on glass objects, and stained with 20% Giemsa.

Anti-termite activity against *Coptotermes curvignathus* was directed by the No-Choice Test referring to Ohmura *et al*. 2000 with some modification.[16] Briefly, filter papers (Whatman No. 1, 30 mm diameter) were permeated with 5% ($^{w}/_{v}$) each of crude extract and fraction for an hour, air-dried for a day, and weighed before the test. The control papers were treated with distilled water, organic solvents, and the regent 50sc (BASF). The test was run with plastic cups (bottom diameter 5 cm, height 6 cm). Each cup was filled with sterilized sea sand (50 mesh, 10 g) on the bottom and moistened with 2 mL of distilled water. A 40 mm diameter plastic saucer holding a paper was placed on top of sea sand, then 55 termites (50 workers and 5 soldiers) were introduced. All treatment units were maintained at 26.9 °C – 28.3 °C and 70% – 82% humidity in the dark room for 3 weeks. Each treatment was carried out for five replications.

Antifungal activity against 3 species of wood decay, *Coriolus versicolor* (COV), *Shizophyllum commune* (SC), and *Tyromyces palustris* (TYP) was performed by inhibition of the mycelial growth method.[17] In brief, each 2.5 mL of crude extract and fraction was added to potato dextrose agar (PDA) solution until 10 mL in A Petri dish. The 5 mm mycelium of each fungal from the 7-day old culture was placed in the center of each PDA plate and incubated for 7-days at room temperature. The fungal mycelia growth was measured by measuring the diameter of the growing fungal colonies using a digital caliper. The inhibition of the growth of fungal mycelia were evaluated at the end of the incubation period by the formula:

$$\text{Inhibition (\%)} = \frac{\text{Growth in control (mm)} - \text{growth in treatment (mm)}}{\text{Growth in control (mm)} - \text{mycelia in early incubation (mm)}} \times 100\%$$

RESULTS AND DISCUSSION

Table-1 showed the crude extract of the root of *L. domesticum* contained alkaloids, flavonoids, phenolics, and triterpenoids. The major and the second components of the crude extract of the root were a semipolar fraction of 38.6 % and a polar fraction of 32.9%. Semi-polar and polar fractions are composed of flavonoids, phenolics, and triterpenoids. According to literature, flavonoids, and phenolics, including terpenoids have been identified from the extract of stem bark of *L. domesticum*.[12]
Antimalarial activity was evaluated for all samples (crude extract and 3 fractions) against *P. falciparum* strain 3D7. Generally, all samples showed antimalarial activity (Table-2). Two fractions (chloroform and methanol) showed the highest antiplasmodial activity with IC_{50} values <5 µg/mL and the others (crude extract and *n*-hexane fraction) gave lower IC_{50} values than the former, with 5.85 and 29.45 µg/mL, respectively. Jonville *et al*. 2008 said that antiplasmodial activity with IC_{50} < 5 µg/mL is categorized as high.[18] The main chemical constituents in chloroform and methanol fractions were flavonoids, triterpenoids, and phenolics which suggested that they are responsible for antimalarial agent. According to some literature, flavonoids such as luteolin, diprenylated flavanone, and (+)-catechin 3-gallate have shown high antiplasmodial activities with IC_{50} values 11, 3.9, and 1.0 µM, respectively, and phenolic constituents such

as chrobisiamone A, scutianthraquinones A, and scutianthraquinone D revealed antiplasmodial activities with IC_{50} values 5.6, 1.7, and 5.0 μM, respectively.[19]

Table-1: Secondary Metabolite Components of the Root of *L. domesticum*

Secondary metabolites	Fractions (gram)			crude extract (141.2 g)
	n-hexane (12.1 g)	chloroform (54.6 g)	methanol (46.5 g)	
Alkaloids	+	-	-	+
Flavonoids	-	+	-	+
Phenolics	-	-	+	+
Triterpenoids	-	+	-	+

(+): detected; (-): undetected

Table-2: Inhibition Values of Crude Extract and Fractions of the *L. domesticum* Root

No	Sample	Concentration (μg/mL)					IC_{50} (μg/mL)
		100	10	1	0.1	0.01	
1	HF	59.1	40.4	25.3	12.8	2.5	29.4
2	CF	100.0	70.9	45.2	25.4	6.6	1.4
3	MF	100.0	62.4	31.7	18.5	3.2	3.6
4	CE	100.0	55.9	30.8	13.5	3.7	5.8

HF: n-hexane fraction, CF: chloroform fraction, MF: methanol fraction, CE: crude extract

Moreover, plants of Meliaceae are also known for their antifeedant as *Azadirachta indica* produces azadirachtin which has many biological activities including insecticides.[20] Further, anti-termite and antifungal activities were performed for the crude extract and fractions in order to introduce other biological activities of *L. domesticum*. The anti-termite activity was conducted by No-Choice Test against *Coptotermes curvignathus*. Figure-1 displays the effects of crude extract and fractions on the feeding activity of subterranean termites. All impregnated filter papers showed a weight loss from 69.7 until 88.3 % after 21 days. These values were higher in comparison with that of the control filter paper with 8.04 % and similar to a filter paper treated with 5% regent 50sc.

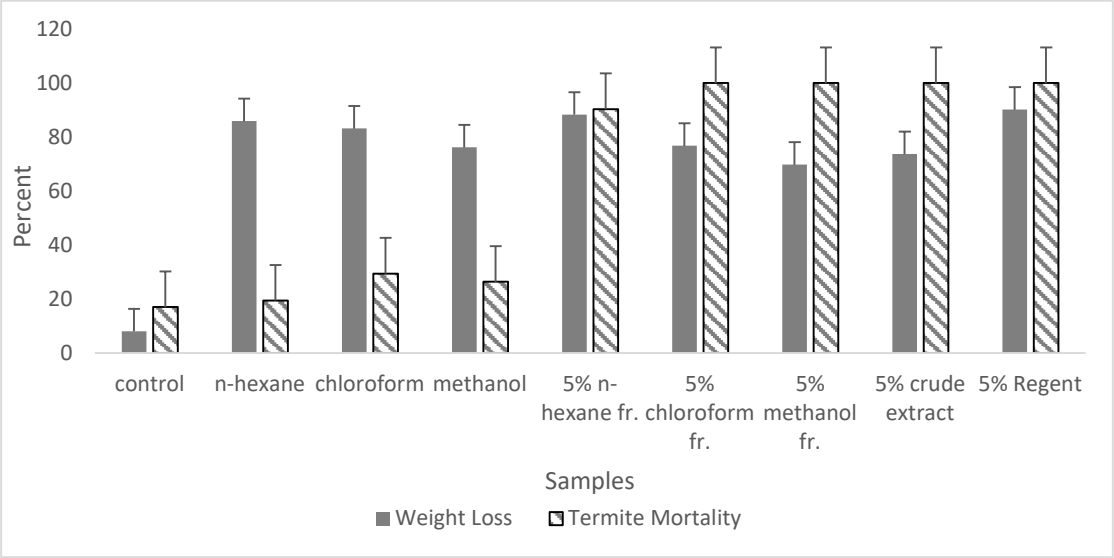

Fig.-1: Weight Loss of Filter Papers Treated with Controls, Crude Extract, and Fractions and Termite Mortality after 21 days bioassays

Additionally, the highest termite mortality (100%) was observed when termites exposed to all treated paper discs at the dose of 5% ($^{w}/_{v}$), except for 5% *n*-hexane fraction. It was also revealed that the crude extract and 3 fractions showed weak antifeedant activity by its weight loss between 69.7 – 88.3%. The 5% regent played as antifeedant as well as toxic to termites. This evidence suggested that the samples contain some toxic constituents to termite. In other words, it proved that the crude extract of the root of *L. domesticum*

contained insecticidal constituents, especially against *C. curvignathus.* Furthermore, antifungal activity against 3 species of wood decay, COV, SC, and TYP were investigated. The inhibitory effects of crude extract and 3 fractions of *L. domesticum* on mycelial growth of COV, SC, and TYP are given in Fig.-2. All fractions and crude extract with 5% ($^{w}/_{v}$) concentration showed inhibitory effect on mycelial growth in comparison to a control (PDA). 5% ($^{w}/_{v}$) chloroform fraction showed complete inhibition against three fungi. 5% ($^{w}/_{v}$) *n*-hexane fraction also inhibited two fungi, SC and TYP by 100%, and 5% ($^{w}/_{v}$) methanol fraction and the crude extract could inhibit the grow of mycelia of TYP by 100%. The last two samples might be applied specifically to inhibit TYP mycelia growth.

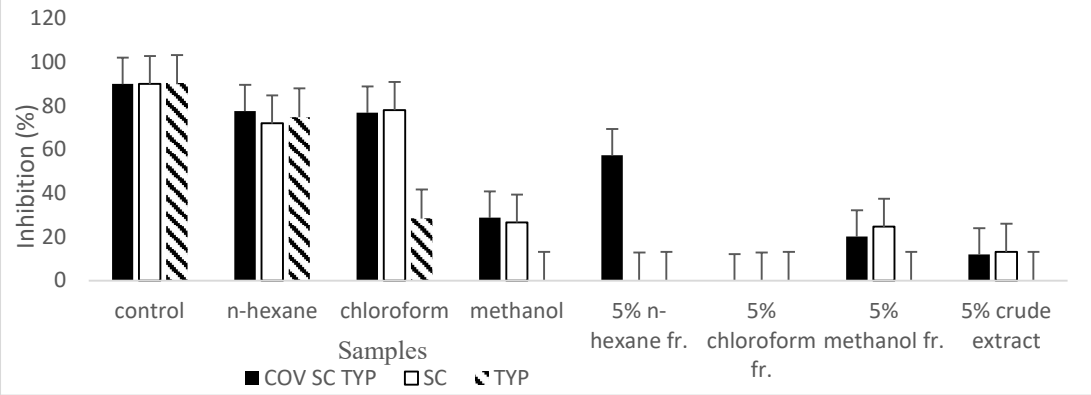

Fig.-2: Inhibition of Fungal Mycelia Growth of *Coriolus versicolor* (COV), *Shyzophylum commune* (SC), and *Tyromyces palustris* (TYP)

CONCLUSION

Crude extract of the root of *L. domesticum* contained alkaloids, flavonoids, triterpenoids, and phenolics, and it showed various biological activities including, antiplasmodial, anti-termite, and antifungal. 5% ($^{w}/_{v}$) chloroform fraction performed high activity against P. *falciparum* strain 3D7 with IC_{50} value 1.4 µg/mL, it also showed 100% mortality effect to subterranean termite *C. curvignathus*, and inhibited mycelia growth of three fungi COV, SC, and TYP. Further purification toward the fractions by several chromatographic techniques including HPLC equipped with a C_{18} column is under going to obtain pure compounds and determine their structures which are responsible for those activities.

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