



ICPPS 2014

# Proceeding

## The 1<sup>st</sup> International Conference on Pharmaceutics & Pharmaceutical Sciences

Drug Delivery Systems:  
From Drug-Discovery, Pre-formulation, Formulation and Technological Approaches for  
Poorly Soluble Drugs and Protein

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# CERTIFICATE

This is to acknowledge that

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has successfully attended the

as **Poster Presenter**  
& **Participant**

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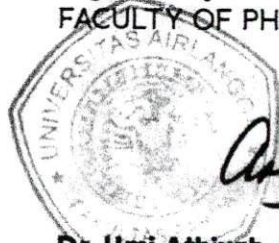
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From Drug-Discovery, Pre-formulation, Formulation and Technological Approaches for  
Poorly Soluble Drugs and Protein

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## IN VITRO ANTIMALARIAL ACTIVITY OF DICHLOROMETHANE SUB-FRACTION OF *Eucalyptus globulus* L. STEM AGAINST *Plasmodium falciparum*

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### INTRODUCTION

Malaria is a serious infectious disease caused by protozoan parasites in tropical and subtropical regions. In 2010, malaria was endemic in about 104 countries worldwide and approximately 219 million cases of malaria caused 660.000 deaths. Approximately 90 % of malaria deaths occur in Africa (WHO, 2012). Global spread of multiple drug-resistant malaria has become a major health problem and efforts to search for new antimalarial are needed.

*Eucalyptus globulus* is a plant of the Myrtaceae family that in Indonesia commonly known as kayu putih and empirically used as an antipyretic (Backer, 1968). In Brazil, *E. globulus* is used as an antimalarial plants (Nagpal et al., 2010). In Cameroon, *E. globulus*, *Carica papaya* and *Psidium guajava* leaves are mixed and boiled as a decoction that is drunk for the treatment of malaria (Titanji et al., 2008). In Venezuela, *E. globulus* leaves is boiled as decoction for the treatment of malaria (Carballo et al., 2004).

Our preliminary study showed that the 80% ethanol extract and dichloromethane fraction were very active as an antimalarial with IC<sub>50</sub> of 0.090 µg/mL and 0.022 µg/mL, respectively. This study aims to separate the dichloromethane fraction and to test antimalarial activity of its subfractions.

### MATERIAL AND METHODS

#### Plant Material

*Eucalyptus globulus* stem was obtained from

Cangar Forest at Malang, East Java on April 2010. Sample was authenticated by the authority of Purwodadi Botanical Garden, Bojonegara, East Java.

#### Separation Method

Vacuum liquid chromatography (VLC) of dichloromethane fraction of *E. globulus* stem was performed using hexane-CHCl<sub>3</sub> (25:75 gradient) to CHCl<sub>3</sub>-MeOH (98:2, 95:4, 90:10, 85:15 and 80:20).

#### Thin Layer Chromatography (TLC) Method

Sub-fractions obtained from Vacuum liquid chromatography (VLC) of dichloromethane fraction were monitored by TLC using silica gel F254 as stationary phase and chloroform-methanol (98:2) as mobile phase. The separated spots were visualized under ultra-violet light of two different wavelengths (UV254 nm and UV365 nm) and visible light before and after sprayed with 10% H<sub>2</sub>SO<sub>4</sub> and heated at 105°C for 5 minutes.

#### In Vitro Antimalarial Activity Test

Antimalarial activity of sub-fractions was assessed against *Plasmodium falciparum* strain 3D7 which is sensitive to chloroquine. This strain was maintained in continuous culture in flask according to the methodology described by Tragger and Jensen (1976).

Percentage inhibition was calculated using formula:

$$\left( \frac{\% \text{ parasitaemia in control wells} - \% \text{ parasitaemia of test wells}}{\% \text{ parasitaemia of the}}$$



IC<sub>50</sub> = 200 (Ngemenya et al., 2006).  
 IC<sub>50</sub> values refers to the concentration re-  
 quires to inhibit 50% of parasite's growth  
 (Mazzei et al., 2007).

**RESULTS AND DISCUSSION**

Column liquid chromatography of dichloro-  
 methane fraction produced 8 sub-fractions  
 (D.1-D.8 sub-fractions). TLC chromatogram of  
 dichloromethane sub-fractions was shown in  
 Figure 1.

Antimalarial activity test showed that IC<sub>50</sub> val-  
 ues of each dichloromethane sub-fractions was  
 16.284 µg/mL, 16.387 µg/mL, 0.053 µg/mL,  
 1.059 µg/mL, 0.318 µg/mL, 0.387 µg/mL, 0.150  
 µg/mL and 0.040 µg/mL. D.8 sub-fraction has  
 the lowest IC<sub>50</sub> value of 0.040 µg/L. This activ-  
 ity was analysed in accordance with the norm  
 of antimalarial activity of Rasoanaivo et  
 al. (2006). According to this norm, an extract is  
 very active if IC<sub>50</sub> < 5 µg/mL, active 5 µg/mL  
 < IC<sub>50</sub> < 50 µg/mL, weakly active 50 µg/mL <  
 IC<sub>50</sub> < 100 µg/mL and inactive IC<sub>50</sub> > 100 µg/  
 mL. Based on this classification, result from  
 this study of D.8 sub-fraction of *E. globulus*  
 stem with IC<sub>50</sub> of 0.040 µg/mL is said to have  
 very active antimalarial activity. The result of  
 antimalarial activity test of dichloromethane  
 sub-fractions (D.1 - D.8 sub-fractions) can be  
 seen in Table 1.

TLC test of sub-fractions indicated the pres-  
 ence of the most dominant spot (spot D) on  
 D.8 sub-fraction with R<sub>f</sub> values of 0.40 which  
 gave a red purple colour after sprayed with  
 10% H<sub>2</sub>SO<sub>4</sub> and heated at 105 oC for 5 min-  
 utes. Spot D began to appear on D.6 sub-frac-  
 tion which has the IC<sub>50</sub> value of 0.387 µg/L.  
 Colour intensity of spot D increased on D.7  
 and D.8 sub-fractions which have the IC<sub>50</sub> val-  
 ue lower than that of D.6 sub-fraction (0.387  
 µg/mL). From these data can be seen that the  
 higher concentration of spot D, the lower IC<sub>50</sub>  
 value of sub-fractions. Therefore, it can be  
 presumed that spot D on D.8 sub-fraction is a  
 substance that is responsible for activity of D.8  
 sub-fraction.

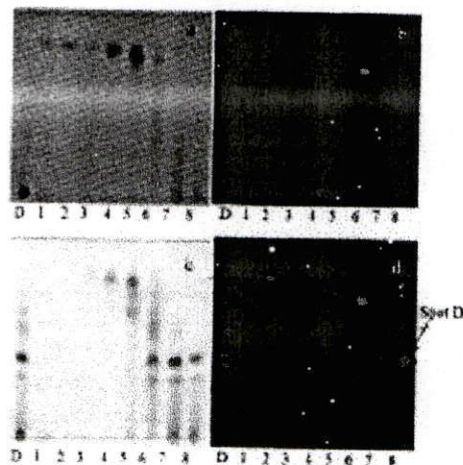


Figure 1. TLC chromatogram of dichloromethane sub-fraction using silica gel F254 as stationary phase and chloroform-methanol (98:2) as mobile phase, viewed under UV light : (a) 254 nm; (b) 366 nm; (c) after sprayed with 10% H<sub>2</sub>SO<sub>4</sub> and heated at 105oC for 5 minutes. (d) 366 nm after sprayed with 10% H<sub>2</sub>SO<sub>4</sub> and heated at 105oC for 5 minutes; D = dichloromethane fraction, D.1-D.8 = sub-fraction.

Table 1. IC<sub>50</sub> values of dichloromethane sub-fractions of *E. globulus* L. stem against *P. falciparum*

Sam- ple	Percent of average inhibitions at various doses (µg/ml.)					IC <sub>50</sub> (µg/mL.)
	100	10	1	0.1	0.01	
D.1	73.46	40.42	31.63	21.42	16.32	16.284
D.2	63.27	46.95	29.77	10.38	1.63	16.387
D.3	89.83	79.10	69.52	51.22	41.12	0.053
D.4	87.40	54.41	44.55	39.60	21.58	1.059
D.5	92.41	75.86	52.89	43.27	24.13	0.318
D.6	90.20	70.94	55.43	36.34	27.30	0.387
D.7	89.50	73.96	58.95	45.41	36.15	0.150
D.8	92.24	80.80	72.99	53.92	41.85	0.040

**CONCLUSION**

D.8 sub-fraction of *E. globulus* possesses a very active antimalarial activity and might be a good candidate for antimalarial. Further work



is suggested to isolate, identify and characterize the active principles from this substance.

#### ACKNOWLEDGEMENTS

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