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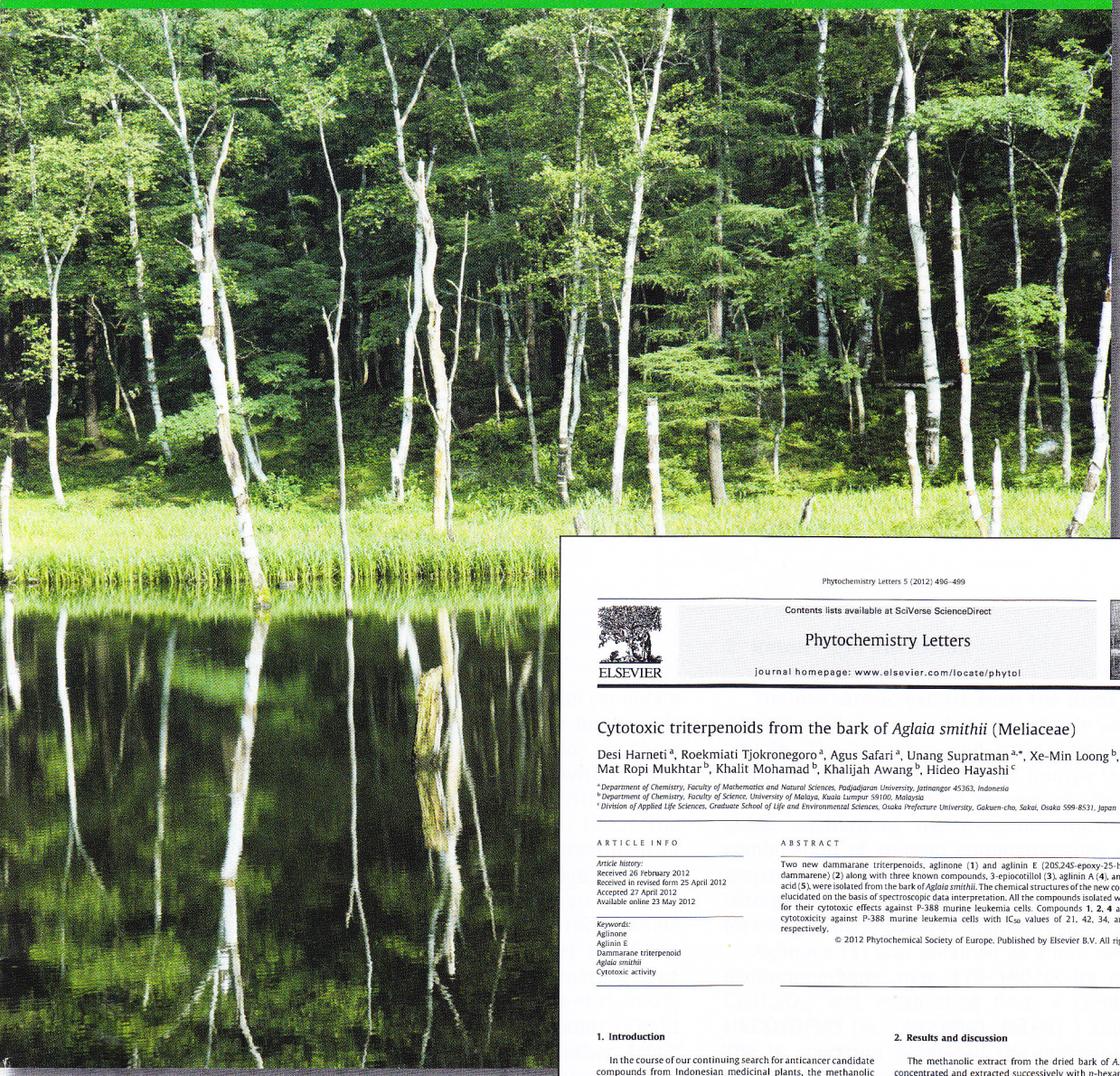

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Cytotoxic triterpenoids from the bark of *Aglaia smithii* (Meliaceae)

Desi Harneti [a], Roekmiati Tjokronegoro [a], Agus Safari [a], Unang Supratman [a,*], Xe-Min Loong [b], Mat Ropi Mukhtar [b], Khalit Mohamad [b], Khalijah Awang [b], Hideo Hayashi [c]

[a] Department of Chemistry, Faculty of Mathematics and Natural Sciences, Padjadjaran University, Jatinangor 45363, Indonesia
[b] Department of Chemistry, Faculty of Science, University of Malaya, Kuala Lumpur 59100, Malaysia
[c] Division of Applied Life Sciences, Graduate School of Life and Environmental Sciences, Osaka Prefecture University, Gakuen-cho, Sakai, Osaka 599-8531, Japan

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ABSTRACT

Two new dammarane triterpenoids, aglinone (**1**) and aglinin E (20*S*,24*S*-epoxy-25-hydroxy-1-en-dammarene) (**2**) along with three known compounds, 3-epiocotillol (**3**), aglinin A (**4**), and eichlerianic acid (**5**), were isolated from the bark of *Aglaia smithii*. The chemical structures of the new compound were elucidated on the basis of spectroscopic data interpretation. All the compounds isolated were evaluated for their cytotoxic effects against P-388 murine leukemia cells. Compounds **1**, **2**, **4** and **5** showed cytotoxicity against P-388 murine leukemia cells with IC_{50} values of 21, 42, 34, and 11 μg/mL, respectively.

1. Introduction

In the course of our continuing search for anticancer candidate compounds from Indonesian medicinal plants, the methanolic extract of *Aglaia smithii* (Meliaceae) was found to show cytotoxicity against P-388 murine leukemia cells with an IC_{50} of 20 μg/mL. *A. smithii* is a higher plant and widely distributed in South East Asia (Inada et al., 1997; Mabberley et al., 1995). The plant is used in Indonesian folk medicine for the treatment of fever, diarrhea, contused wound, coughs and skin diseases (Mabberley et al., 1995; Heyne, 1982). Previous phytochemical studies on *Aglaia* plants reported the presence of rocaglamide (Ishibashi et al., 1993; Wu et al., 1997; Nugroho et al., 1999), triterpenoid bisamides (Brader et al., 1998), dammarane-type triterpenoids (Roux et al., 1998; Khalit et al., 1999; Xie et al., 2007; Zhang et al., 2010) and cycloartane-type triterpenoids (Khalit et al., 1999). Although secondary metabolites of other *Aglaia* species have been investigated previously, the chemical composition of *A. smithii* is yet to be reported. The isolation, structure elucidation, and cytotoxic evaluation of these isolated compounds are described herein.

2. Results and discussion

The methanolic extract from the dried bark of *A. smithii* was concentrated and extracted successively with *n*-hexane, and ethyl acetate. The *n*-hexane and ethyl acetate extracts exhibited a cytotoxic activity against P-388 murine leukemia cells with IC_{50} values 28.1 and 32.8 μg/mL, respectively. By using cytotoxic assay to guide separations, the *n*-hexane fraction was separated by combination of column chromatography on silica gel G60 and preparative TLC on silica gel GF_{254} to afford four cytotoxic triterpenoids **2**–**5**. The ethyl acetate was worked up as described for compounds **2**–**5** and yielded one cytotoxic triterpenoid **1** (Fig. 1).

Aglinone (**1**) was obtained as white needle-like crystals from dichloromethane, m.p. 178–180 °C. Its molecular composition $C_{30}H_{48}O_5$, was established from a combined analysis of the HRESITOFMS (*m/z* 487.6941, $[M+H]^+$) and NMR data (Table 1). The IR spectrum suggested the presence of a hydroxyl group (3429 cm^{-1}), a carbonyl (1737 cm^{-1}) which correlated to a lactone, and olefinic group (1606 cm^{-1}). The ^{13}C NMR spectrum showed 30 carbon resonances, which were classified by their chemical shifts and the HMQC spectrum as seven methyls, ten methylenes, five methines (one olefinic), and eight quarternary carbons (one carbonyl and one olefinic carbon). These functionalities accounted for two out of the total seven degrees of unsaturation. The remaining five degrees of unsaturation were consistent with the molecule containing five rings. In addition, the presence of seven

* Corresponding author. Tel.: +62 22 7794391; fax: +62 22 7794391.
E-mail address: u_supratman@unpad.ac.id (U. Supratman).

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