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Cytotoxicity and Structure Activity Relationship of Dammarane-Type Triterpenoids from the Bark of *Aglaia elliptica* against P-388 Murine Leukemia Cells

Ace Tatang Hidayat[1,2], Kindi Farabi[1], Desi Harneti[1], Rani Maharani[1,2], Darwati[1], Nurlelasari[1], Tri Mayanti[1], Arlette Suzy Setiawan[3], Unang Supratman[1,2,*], and Yoshihito Shiono[4]

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Abstract – Six dammarane-type triterpenoids, dammar-24-en-3β-ol (**1**), 3β-epicabraleahydroxy lactone (**2**), (*E*)-25-hydroperoxydammar-23-en-3β,20-diol (**3**), dammar-24-en-3β,20-diol (**4**), 3β-acetyl-20*S*,24*S*-epoxy-25-hydroxy-dammarane (**5**), and 3β-epiocotillol (**6**) were isolated from the methanolic extract of the bark of *Aglaia elliptica*. The chemical structure were identified on the basis of spectroscopic evidence and by comparison with those spectra previously reported. Compounds **1** - **6** were isolated first time from this plant. Compounds **1** - **6**, along with a known synthetic analog, cabraleone (**7**) were evaluated their cytotoxic activity against P-388 murine leukimia cells *in vitro*. Among those compounds 3β-acetyl-20*S*,24*S*-epoxy-25-hydroxydammarane (**5**) showed strongest cytotoxic activity with IC_{50} value of 8.02 ± 0.06 μM.
Keywords – Dammarane-type Triterpenoids, *Aglaia elliptica*, Meliaceae, P-388 murine leukimia cell

Introduction

The genus *Aglaia* is the largest genus of the family of Meliaceae comprises more than 100 species distributed mainly in India, Indonesia, Malaysia and parts of the Western Pacific region.[1] In our continous search for cytotoxic constituents against P-388 murine leukemia cells from Indonesian *Aglaia* plants, we isolated and described two new cytotoxic dammarane-type triterpenoids, aglinone and aglinin E, from the bark of *A. Smithii*.[2] In the further screening for cytotoxic compounds from Indonesia *Aglaia* plants, we found that the *n*-hexane and ethyl acetate extract of *A. elliptica* exhibited a cytotoxic activity against P-388 murine leukemia cells with IC_{50} values of 67.70 and 32.69 μg/mL, respectively. *A. elliptica* is a higher plant and widely distributed in South East Asia.[3,4] The plant is used in Indonesian folk medicine for the treatment of fever, diarrhea, contused wound, coughs and skin diseases.[4] Previous phytochemical studies on *Aglaia* plants reported the presence of rocaglamide,[5,6,7] bisamides,[8,9] sesquiterpenoids,[10,11] diterpenoids,[12,13] dammarane-type triterpenoids,[14-16] cycloartane-type triterpenoids,[17,18] and apotirucallane triterpenoids.[19,20] Although secondary metabolites of other *Aglaia* species have been investigated previously, the chemical composition of *A. elliptica*is yet to be reported. The isolation and structure identification of dammarane-type triterpenoids from the bark of *A. elliptica* along with cytotoxic evaluation against P-388 murine leukemia cells are described herein.

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Experimental

General experimental procedures – The IR spectra were measured on a Perkin Elmer spectrum-100 FT-IR in KBr. Mass spectra were obtained with a Water Qtof HR-MS XEV^{otm} and Water TQD MS/MS mass spectrometers. NMR spectra were recorded with a JEOL ECZ A-600 spectrometer using tetra methyl silane (TMS) as an internal standard. Chromatographic separation were carried out on