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Flavestin K, An Isoprenylated Stilbene from the Leaves of *Macaranga recurvata* Gage

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Abstract – A new isoprenylated stilbene, flavestinK (**1**) together with two known isoprenylated stilbenes, flavestin B (**2**), flavestin G (**3**), and two isoprenilated flavanones, 4-*O*-methyl-8-isoprenylnaringenin (**4**) and 8-isoprenyl-5,7-dihydroxyflavanone (**5**) were isolated from the leaves of *Macaranga recurvata* Gage. All of the structures have been determined based on HRESIMS, 1D and 2D NMR spectral data. All of the isolated compounds were evaluated for their cytotoxicity against three human cancer cells (HeLa, T47D and WiDr). Compound **1** showed higher activity than doxorubicin against HeLa cells with IC_{50} value of 13.1 μg/mL.
Keywords – Flavestin K, Stilbene, *Macaranga recurvata*, Cytotoxicity

Introduction

Macaranga recurvata Gage (Euphorbiaceae), locally known as 'Mahang merah' is one pioneer plant and found endemic in Kalimantan Island, Indonesia. The genus *Macaranga* have been showed a number of phenolic compounds, predominantly flavonoids and stilbenes with terpenylated side chain (isoprenyl, geranyl and farnesyl) in aromatic ring.[1-4] Based on previously report, two isoprenylated dihydroflavonols, macarecurvatins A and B from the leaves of *M. recurvata* showed cytotoxicities against murine leukemia.[5] Isoprenylation of flavonoids and stilbenes seems to be a key factor to enhance their cytotoxicity.

In this research paper, we desiderate to report the isolation of a new isoprenylated stilbene, flavestin K (**1**) along with four known compounds, flavestin B (**2**), flavestin G (**3**), 4′-*O*-methyl-8-isoprenylnaringenin (**4**) and 8-isoprenyl-5,7-dihydroxyflavanone (**5**) from the leaves of *M. recurvata* (Fig. 1). The cytotoxic activities of compounds **1-5** against three human cancer cells (HeLa, T47D and WiDr) are also reported.

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Experimental

General experimental procedures – 1D NMR (^{1}H and ^{13}C), 2D NMR (HMQC and HMBC) spectra were recorded with a JEOL JNM-ECA 400 FT NMR spectrometer operating at 400 MHz usingdeuterated solvent (peaks: δ_H 2.04 and δ_C 29.8 for acetone-d_6 as reference standard). High resolution mass spectra were measured on an ESI-TOF Waters LCT Premier X Emass spectrometer. All of compounds were dissolved in methanol and were measured by UV spectrophotometer Shimadzu 1900. The functional group of compounds in KBr were measured by IR Tracer-100 Shimadzu FT IR spectrophotometer. Column chromatography (CC) was performed using Si gel 60 G and centrifugal planar chromatography (CPC) was performed using Si gel 60 PF_{254}. TLC analysis was performed using on pre-coated Si gel 60 GF_{254} 0.25 mm thickness plates.

Plant materials – The leaves of *M. recurvata* were collected from Muara Teweh, North Barito Districts, East Kalimantan, Indonesia on Feb. 2018, and identified by senior botanist Mr. Ismail Rachman from the Herbarium Bogoriense, Center of Biological Research and Development, National Institute of Science, Bogor, Indonesia.

Extraction and isolation – The air-dried and powdered leaves of *M. recurvata* (3.5 kg) were extracted with MeOH (2 × 15 L) at room temperature for two days, and