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Der Pharmacia Lettre, 2015, 7 (3):153-156
(http://scholarsresearchlibrary.com/archive.html)

ISSN 0975-5071
USA CODEN: DPLEB4

Isoprenylated flavanone derivatives from *Macaranga hosei* King ex Hook.F.

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ABSTRACT

*Two isoprenylated flavanones, 4'-O-methyl-8-isoprenylnaringenin (**1**) and lonchocarpol A (**2**) have been isolated from the leaves of Macaranga hosei* King ex Hook.f. *The structure of both compounds have been elucidated based on its spectroscopic data, including UV, 1D and 2D NMR, and HREISMS spectra. Compounds **1–2** were evaluated for their radical scavenging against 2,2-diphenyl-1-picrylhydrazyl (DPPH), showing their IC_{50} were 1298.0 and 1115.7 μM, respectively.*

Keywords: *Macaranga hosei* King ex Hook.f., *isoprenylated flavanones*, *antioxidant*.

INTRODUCTION

The genus *Macaranga* is one of family Euphorbiaceae which contains about 300 species which are distributed besides in Indonesia, also found in Asia, Africa, Madagascar in the West to tropical Asia, North Australia, and the Pacific Islands in the East. From the literature research known that *Macaranga* produces phenolic compounds, particularly flavonoids and stilbenoids. The unique of flavonoids and stilbenoids compounds from this plant is terpenyl side chain, among isoprenyl (C_5), geranyl (C_{10}), farnesyl (C_{15}) and geranyl geranyl (C_{20}) [1,2,3]. Isoprenylated flavonoid compounds that found in *Macaranga* such as flavanone derivatives in *M. triloba* [4]. The flavonol derivatives were isolated in *M. gigantea*, *M. pruinosa*, and *M. rizhinoides* [5,6,7]. The dihidroflavonol derivatives were found in *M. conivera* [8]. From this research has been isolated two isoprenylated flavanones, 4'-*O*-methyl-8-isoprenylnaringenin (**1**) and lonchocarpol A (**2**) from the methanol extract of the leaves of *M. hosei*. The antioxidant properties of compounds **1-2** against DPPH is also briefly described.

MATERIALS AND METHODS

General

UV spectra was measured with a Shimadzu 1800 spectrometer, respectively. ^1H and ^{13}C NMR spectra were recorded with a JEOL ECS 400 spectrometer operating at 400 (^1H) and 100 (^{13}C) MHz in $CDCl_3$ using TMS as the internal standard. Mass spectra were obtained with a Waters LCT Premier XE. Vacuum liquid chromatography (VLC) and radial chromatography were carried out using Si gel 60 GF_{254} and Si gel 60 PF_{254}, for TLC analysis, pre-coated silica gel plates (Merck Kieselgel 60 GF_{254}, 0,25 mm thickness) were used.

Plant material

The leaves of *M. hosei* were collected from Samboja, East Kalimantan, Indonesia on Maret 2013. The species were identitified at the Herbarium Wanariset, Samboja, and a voucher specimen had been deposited at the Herbarium Wanariset, Samboja.

Extraction and isolation

The powdered and dried leaves of *M. hosei* (1.0 kg) were macerated in methanol at room temperature two times and, after evaporation of the methanol extract, gave a dark residue (120 g). The methanol extract was partitioned with *n*-hexane and ethyl acetate. The ethyl acetate extract (35 g) was further fractionated by VLC on silica gel (150 g) eluted with *n*-hexane- ethyl acetate of increasing polarity (9:1, 4:1; 7:3, 1:1, and 1:4) to give three major fractions A-C. Fraction B (2.75 g) was separated by coloumn chromatography eluted with *n*-hexane- ethyl acetate (9:1 to 7:3). On TLC analysis, fraction B showed two major spots on purification of this fraction using planar radial chromatography, and using *n* hexane-chloroform (7:3 to 3:7) to give compound **1** (21 mg) and **2** (27.8 mg).

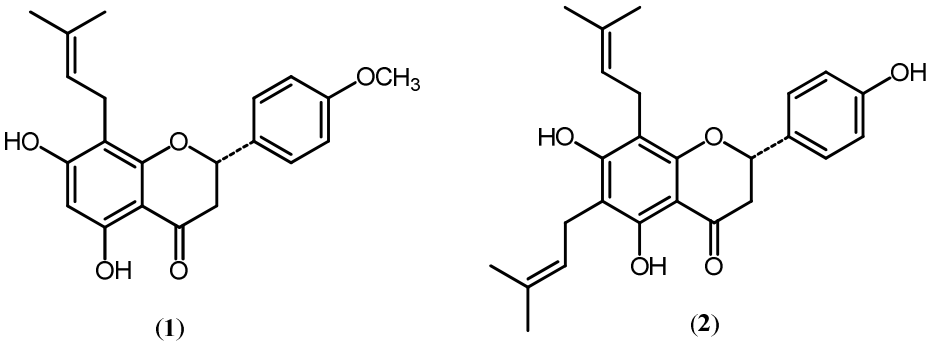

Figure 1. Flavanones isolated from *M. hosei*

4'-*O*-methyl-8-isoprenylnaringenin (**1**), pale white solid, UV-Vis (MeOH) : λ_{max} nm (log ε): 209 (4.53), 261 (4.56), 298 (4.67) and 337 sh (4.07), (MeOH+NaOH) 211 (4.59), 287 (4.64), and 334 (4.63) (MeOH+$AlCl_3$) 209 (4.62), 277 (4.70), and 312 (4.66), ($AlCl_3$+HCl) 210 (4.63), 282 (4.60) and 313 (4.62). HR-ESI-MS *m/z* $[M-H]^-$ 353.1380 (calcd for $C_{21}H_{22}O_5$: 353.1389). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H (ppm): 5.35 (1H, dd, *J* = 13.0, 3.0 Hz, H-2), 3.04 (1H, dd, *J* = 13.0, 17.0 Hz, H-3_{ax}), 2.79 (1H, dd, *J* = 17.0, 3.0 Hz, H-3_{eq}), 6.01 (1H, s, H-6), 7.36 (2H, d, *J* = 8.4 Hz, H-2'/6'), 6.93 (2H, d, *J* = 8.4 Hz, H-3'/5'), 3.28 (1H, d, *J* = 7.2 Hz, H-1''), 5.18 (1H, t like, *J* = 7.4 Hz, H-2''), 1.70 (3H, s, H-4''), 1.68 (3H, s, H-5''), 3.82 (3H, s, 4'-OCH_3), 11.99 (1H, s, 5-OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ_H (ppm): 78.8 (C-2), 43.2 (C-3), 196.6 (C-4), 103.2 (C-4a), 162.2 (C-5), 96.8 (C-6), 163.9 (C-7), 106.6 (C-8), 161.4 (C-8a), 130.8 (C-1'), 127.6 (C-2'/6'), 114.2 (C-3'/5'), 159.9 (C-4'), 21.9 (C-1''), 121.8 (C-2''), 134.6 (C-3''), 25.9 (C-4''), 17.9 (C-5''), 55.5 (4'-OCH_3).

Lonchocarpol A (**2**), yellow solid, UV/Vis (MeOH) : λ_{max} nm (log ε): 208 (4.75), 257 (4.81) and 306 sh (4.94), (MeOH+NaOH) 216 (4.63), 287 (4.66) and 318.0 sh (4.60). (MeOH+$AlCl_3$) 214 (4.49), 287 (4.28), and 331 sh (4.08), ($AlCl_3$+HCl) 211 (4.49), 286 (4.35), and 330 sh (4.17). HRESIMS: *m/z* $[M+H]^+$ 409.2015 (calcd for $C_{25}H_{29}O_5$: 409.2018). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H (ppm): 5.30 (1H, dd, *J* = 13.0, 3.0 Hz, H-2), 3.03 (1H, dd, *J* = 13.0, 17.0 Hz, H-3_{ax}), 2.79 (1H, dd, *J* = 17.0, 3.0 Hz, H-3_{eq}), 7.30 (2H, d, *J* = 8.4 Hz, H-2'/6'), 6.85 (2H, d, *J* = 8.4 Hz, H-3'/5'), 3.33 (1H, d, *J* = 7.2 Hz, H-1''), 5.22 (1H, t like, *J* = 7.2 Hz, H-2''), 1.80 (3H, s, H-4''), 1.70 (3H, s, H-5''), 3.28 (1H, d, *J* = 7.2 Hz, H-1'''), 5.20 (1H, t like, *J* = 7.2 Hz, H-2'''), 1.73 (3H, s, H-4'''), 1.68 (3H, s, H-5'''), 12.30 (1H, s, 5-OH), 6.40 (1H, s, 7-OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ_H (ppm): 78.6 (C-2), 43.3 (C-3), 196.8 (C-4), 102.9 (C-4a), 159.4 (C-5), 107.4 (C-6), 162.5 (C-7), 106.6 (C-8), 157.9 (C-8a), 130.9 (C-1'), 127.3 (C-2'/6'), 115.6 (C-3'/5'), 156.2 (C-4'), 22.0 (C-1''), 122.0 (C-2''), 134.8 (C-3''), 17.9 (C-4''), 25.9 (C-5''), 21.3 (C-1'''), 121.8 (C-2'''), 134.1 (C-3'''), 17.8 (C-4'''), 25.9 (C-5''').

DPPH scavenging activity test

Determination of the antioxidant activity of the isolated performed using reagent DPPH (2,2-diphenyl-1-picrylhydrazyl) was measured by UV spectrometer at λ 517 nm [9]. Determination of antioxidant activity done by the dissolving a compounds assay with methanol, then added solution of 0.1 M buffer acetate (pH 5.5) and added

DPPH radical solution of 5.10^{-4} M. Determination of the inhibition of isolated compounds against DPPH radical was observed using a spectrometer at λ 517 nm after incubation for 30 min at 20°C.

RESULTS AND DISCUSSION

Two isoprenylated flavanones, 4'-*O*-methyl-8-isoprenylnaringenin (**1**), and lonchocarpol A (**2**) have been isolated from the methanol extract of the leaves of *M. hosei*. The structures of these compounds were determined based on UV, HR-ESI-MS, 1D and 2D NMR data.

4'-*O*-methyl-8-isoprenylnaringenin (**1**) was isolated as a white solid, and the molecular formula $C_{21}H_{22}O_5$ was deduced from its HR-ESI-MS data. The UV spectra of **1** exhibited maxima typical for a flavanone structure (λ_{max} 209, 261, 298, and 337 sh), and showed bathochromic shifts on addition of $AlCl_3$ and NaOAc [10]. The ^{1}H NMR spectrum of **1** showed three doublet-doublet proton signals at δ_H 5.35 (1H, dd, *J* = 13.0, 3.0 Hz, H-2), 3.04 (1H, dd, *J* = 13.0, 17.0 Hz, H-3$_{ax}$), and 2.79 (1H, dd, *J* = 17.0, 3.0 Hz, H-3$_{eq}$) characteristic for the flavanone structure. The present of a pair of doublets at δ_H 7.36 and 6.93 (each 2H, *J* = 8.4 Hz) in aromatic region characteristic in the ring B. The ^{1}H NMR spectrum of **1** also showed signals for an isoprenyl (δ_H 5.18, 1H; 3.28, 2H; 1.70 and 1.69, each 3H) and a methoxyl (δ_H 3.82, 3H), and a proton singlet signal at δ_H 11.99 that are consistent with an OH-phenolic at C-5. Further analysis of the ^{1}H spectrum in the aromatic region in the ring A revealed the presence of a singlet of one-proton signal (δ_H 6.01), suggesting that the isoprenyl group is either at C-6 or C-8. By analysis of HMQC and HMBC spectra of **1**, the correlation of 5-OH phenolic signal (δ_H 11.99) with two aromatic quarternary (δ_C 162.2, C-5; 103.2, C-4a) and an aromatic methine (δ_C 96.8, C-6) carbon atoms, and consequently these correlations correspond to the isoprenyl group at C-8. Furthermore, the singlet signal of methoxyl (δ_H 3.82) has correlation with an oxyaryl carbon signal (δ_C 159.9), and correlation of δ_H 6.93 in the ring B correspond to the methoxyl group at C-4'. From the HR-ESI-MS, 1D and 2D NMR data, compound **1** was identified as 4'-*O*-methyl-8-isoprenylnaringenin [11].

Lonchocarpol A (**2**), was isolated as yellow solid, and and the UV spectra (λ_{max} 208, 257, and 306 sh), and the ^{1}H NMR spectra displayed an AMX spin system at δ_H 5.30 (1H, dd, *J* = 13.0, 3.0 Hz, H-2), 3.03 (1H, dd, *J* = 13.0, 17.0 Hz, H-3$_{ax}$), 2.79 (1H, dd, *J* = 17.0, 3.0 Hz, H-3$_{eq}$) characteristic for the flavanone structure. The HRESIMS spectrum showed a quasimolecular ion $[M+H]^+$ at *m/z* 409.2015 consistent to the molecular formula $C_{25}H_{29}O_5$, suggesting that **2** is a flavanone has two isoprenyl groups. The presence in the aromatic region of proton signals of a pair of doublets (*J* = 8.4 Hz) at δ_H 7.30 and 6.85 (each 2H), correspond to the signals of a *p*-hydroxyphenyl group at ring B. The ^{1}H NMR spectrum of **2** also showed two isoprenyl signals (δ_H 5.22 (1H, t like, *J* = 7.2 Hz, H-2''), 1.80 (3H, s, H-4''), 1.70 (3H, s, H-5''), 3.28 (1H, d, *J* = 7.2 Hz, H-1''), 3.28 (1H, d, *J* = 7.2 Hz, H-1'''), 5.20 (1H, t like, *J* = 7.2 Hz, H-2'''), 1.73 (3H, s, H-4'''), 1.68 (3H, s, H-5''') and a proton singlet signal at δ_H 12.30 that are consistent with an OH-phenolic at C-5. Based on 1D and 2D NMR data, the placement of two side chain isoprenyl groups at C-6 and C-8 of compound **2,** and identified as 6,8-diisoprenylnaringenin or known as lonchocarpol A. Further support for structure **2** were comparison with lonchocarpol A from *Erythrina fusca* [12].

CONCLUSION

Two isoprenyled dihydroflavanones, 4'-*O*-methyl-8-isoprenylnaringenin (**1**) and lonchocarpol A (**2**) have been isolated from the leaves of *M. hosei*. Their structures were elucidated on the basis of spectroscopic data. The antioxidant activity of 4'-*O*-methyl-8-isoprenylnaringenin (**1**) and lonchocarpol A (**2**) were evaluated against the DPPH radical scavenging showed radical scavenging activity with IC_{50} value 1298.0 and 1115.7 μM, respectively.

Acknowledgements
We would like to thank Herbarium Wanariset, Samboja, East Kalimantan, Samarinda, Indonesia for identifying the species.

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