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Dihydroflavonol and Flavonol Derivatives from *Macaranga recurvata*

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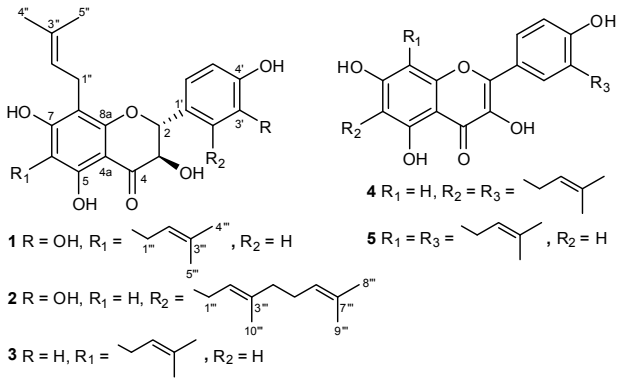
Two new dihydroflavonol derivatives, macarecurvatins A and B, have been isolated from the leaves of *Macaranga recurvata* (Euphorbiaceaae), along with the known compounds diisoprenylaromadendrin, glyasperin A and broussoflavonol F. The structures of the new compounds were determined on the basis of spectroscopic evidence. Upon cytotoxic evaluation against P-388 cells, macarecurvatin B showed strong activity with an IC_{50} of 0.83 μM.

Keywords: Macarecurvatins A and B, Flavanol, Dihydroflavonol, *Macaranga recurvata*, Euphorbiaceae, P-388 cells.

In our previous reports, we disclosed the presence of isoprenylated and geranylated flavonoids [1-4], and phenolic derivatives containing an irregular sesquiterpenyl side chain, from Indonesian *Macaranga* [3,5]. In continuation of these chemical investigations, we have examined *M. recurvata* Gage and succeeded in isolating two new dihydroflavonols, trivially named as macarecurvatins A (**1**) and B (**2**), together with the known compounds 6,8-diisoprenyl-aromadendrin (**3**) [6], glyasperin A (**4**) [7], and broussoflavonol F (**5**) [8]. This paper discusses the structure elucidation of the new compounds. Also, cytotoxic properties of compounds **1**-**5** against murine leukemia P-388 cells are briefly described.



Macarecurvatin A (**1**), obtained as a yellowish solid, $[\alpha]_D^{20}$ +40.4 (*c* 0.32, MeOH), showed a quasimolecular ion $[M+H]^+$ at *m*/*z* 441.1902 corresponding to the molecular formula $C_{25}H_{28}O_7$. The UV spectrum of **1** exhibited absorption maxima at λ_{max} 204 and 291 nm, and showed bathochromic shifts on addition of NaOH, $AlCl_3$, and NaOAc solution. In the ^{1}H NMR spectrum, the presence of a pair of doublets at δ_H 4.97 and 4.56, as well as a singlet of a chelated –OH group at δ_H 11.97, are reminicent of a 2,3-dihydroflavonol structure. This was substantiated by the presence of a conjugated carbonyl group (δ_C 198.8) and two methines of oxycarbons (δ_C 84.3 and 73.3). The presence of five signals of oxyaryl carbons (δ_C 162.7, 159.7, 158.7, 146.4, and 145.7) suggested that **1** has the basic structure of taxifolin (= 5,7,3',4'-tetrahydroxy-2,3-dihydroflavonol). Furthermore, by the observation of four methyl singlets in the ^{1}H NMR spectrum (δ_H 1.75, 1.64, 1.60, and 1.55), together with two vinyl (δ_H 5.17 and 5.13) and two methylene (δ_H 3.32 and 3.24) signals, this compound should contain two isoprenyl groups. In the aromatic region of ^{1}H NMR spectrum, three signals at δ_H 7.07, 6.91, and 6.85 were observed with multiplicities consistent with the structural unit of the ring B of taxifolin, and, consequently, the isoprenyl groups must be located at C-6 and C-8. Key ^{1}H-^{13}C long range correlations found in the HMBC spectrum, particularly from the chelated –OH (δ_H 11.97) and the methylene (δ_H 3.32 and 3.24) signals confirmed the assignment of structure **1** for macarecurvatin A. From the coupling constant of H-2/H-3 (11.5 Hz, *trans*) and the sign and value of its specific optical rotation, the stereochemistry at C-2 and C-3 was determined to be 2*R*,3*R* [9].

Macarecurvatin B (**2**), obtained also as a yellowish solid, has the molecular formula $C_{30}H_{36}O_7$, deduced from the $[M+H]^+$ ion at *m*/*z* 509.2534. The UV absorptions of **2** had very similar characteristics to those of **1**, and the NMR parameters in **2** (Table 1) also showed characteristics of the taxifolin structure. The presence of geranyl and isoprenyl groups in **2** was indicated by the ^{1}H NMR signals of five methyl singlets (δ_H 1.58, 1.54, 1.54, 1.51, and 1.51), together with three methine vinyl (δ_H 5.20, 5.12, and 5.02), and four methylene (δ_H 3.58, 3.16, 1.98 and 1.95) signals. Furthermore, a singlet (δ_H 6.07) of aromatic signals was found, suggesting that one of the side chain groups must be located either at C-6 or C-8. In the HMBC spectrum, the chelated-OH signal (δ_H 11.65) was correlated with an oxyaril (δ_C 162.6), a quarternary (δ_C 101.4), and a methine (δ_C 96.6) carbon signals, showing that C-6 is unsubstituted. The methylene signal that showed long-range correlations with the oxyaril carbon signals (δ_C 165.4 and 161.1) in the A-ring was a doublet at δ_H 3.16, which, from its COSY spectrum, is part of the isoprenyl group (δ_H 5.12, 3.16, 1.58, 1.51). Consequently, the geranyl group must be the side chain of ring B. From the presence of a pair of *ortho*-coupled doublets (J = 8.4 Hz) at δ_H 7.05 and 6.82, this group should be located at C-2'. Analysis of HMQC and HMBC spectra confirmed the assignment of structure **2**. By the same argument used for **1** ($J_{H\text{-}2/H\text{-}3}$ = 11.7 Hz; $[\alpha]_D^{20}$ +35.3 (*c* 0.24, MeOH), the stereo-chemistry at C-2 and C-3 was also determined to be 2*R*,3*R* [9].