



Research Article

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A new flavone from *Andrographis beddomei*

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ABSTRACT

A new flavone, 7,8,2',3'-tetramethoxyflavone (**1**) together with three known flavones, 5,7,2',3'-tetramethoxyflavone (**2**), skullcapflavone I 2'-methyl ether (**3**) and echiodin (**4**), and two known labdane type diterpenoids 14-deoxy-11,12- didehydroandrographolide (**5**) and neoandrographolide (**6**) were isolated from the whole plant of *Andrographis beddomei*. The structural elucidation of the new compound (**1**) and the known compounds (**2-6**) have been established by extensive 1D and 2D NMR spectral studies.

Keywords: *Andrographis beddomei*, Acanthaceae, whole plant, flavonoids, labdane diterpenoids

INTRODUCTION

Andrographis beddomei C.B. Clarke (Acanthaceae) is a straggling undershurb found widely in Lankamalai Hills of Cuddapah, Andhra Pradesh, South India [1]. *Andrographis* species find extensive application in traditional medicine in the treatment of dyspepsia, influenza, malaria and respiratory infections [2,3]. In our systematic search for chemical constituents from *Andrographis* species [4], we have investigated the whole plant of *A. beddomei*, a plant hitherto not examined for its chemical constituents and report herein the isolation and structural elucidation of a new flavone, 7,8,2',3'-tetramethoxyflavone (**1**) besides three known flavones, 5,7,2',3'-tetramethoxyflavone (**2**), skullcapflavone I 2'-methyl ether (**3**) and echiodin (**4**), and two known labdane type diterpenoids, 14-deoxy-11,12-didehydroandrographolide (**5**) and neoandrographolide (**6**).

EXPERIMENTAL SECTION

General Experimental Procedures

Melting points were determined using a Kofler hot stage apparatus and are uncorrected. UV spectra were measured in MeOH on a Shimadzu UV-1800 spectrophotometer. IR spectra were recorded on a Bruker Alpha Eco ATR-FTIR spectrophotometer. ¹H and ¹³C NMR spectra were recorded on a Bruker Avance 600 and 400 spectrometers operating at 600.19 and 400.13, and 150.93, 100.62 MHz, respectively using CDCl₃ with TMS as internal standard. ¹H-¹H COSY, HSQC, HMBC and NOESY spectra were obtained using standard pulse sequences. ESI-TOFMS was recorded in positive mode on an API Q-STAR PULSA of Applied Biosystem. Column chromatography (CC) was performed on silica gel (Acme) finer than 200 mesh (0.08 mm). TLC was performed on silica gel 60 F₂₅₄ precoated plates (Merck).

Plant material

The whole plant of *A. beddomei* C.B. Clarke was collected in February 2010 at Lankamalai Hills of Cuddapah, Andhra Pradesh, South India and identified by Dr. K. Madhava Chetty, Assistant Professor, Department of Botany, Sri Venkateswara University, Tirupati, India, where a voucher specimen (DG-105) has been deposited.

Extraction and isolation

Shade dried and powdered whole plant of *A. beddomei* (2.5 kg) was successively extracted with *n*-hexane (3 x 9L), Me₂CO (3 x 9L) and MeOH (3 x 9L) at room temperature. The concentrated *n*-hexane extract on purification over a silica gel column using *n*-hexane-EtOAc step gradient (7:3 and 1:1) yielded **1** (11 mg) and **2** (15 mg), respectively. The Me₂CO extract was defatted with *n*-hexane and the residue obtained was purified over a silica gel column using *n*-hexane-EtOAc step gradient (1:1 and 3:7) to yield **3** (20 mg) and **4** (24 mg). The MeOH extract was soxhleted with *n*-butanol and the *n*-butanol soluble portion was column chromatographed over silica gel using *n*-hexane-EtOAc step gradient (6:4 and 3:7) to yield **5** (40 mg) and **6** (14 mg).

RESULTS AND DISCUSSION

Compound **1**, isolated as pale yellow amorphous solid, showed a [M+H]⁺ peak at *m/z* 343.1187 in its positive ESI-TOFMS spectrum, consistent with the molecular formula C₁₉H₁₈O₆. This was corroborated by the ¹³C NMR spectrum, which showed signals for all the 19 carbons present in the molecule. Positive Shinoda test and the UV absorption maxima of **1** in MeOH at 254 and 306 nm suggested that **1** was a flavone derivative [5]. The IR spectrum of **1** showed a strong absorption band at 1637 cm⁻¹ due to conjugated carbonyl function.

The ¹H NMR spectrum of **1** showed a sharp singlet at δ 6.86 assigned to H-3 of a flavone moiety as it correlated with the carbon at δ 111.7 in its HSQC spectrum. It also showed a typical ABC spectrum for three adjacent aromatic protons at δ 7.01 (1H, dd, *J* = 8.1, 1.4 Hz), 7.13 (1H, dd, *J* = 8.1, 7.9 Hz) and 7.33 (1H, dd, *J* = 7.9, 1.4 Hz) characteristic of H-4', H-5' and H-6' protons of a 2', 3'-dioxxygenated flavone [6]. A pair of *ortho*-coupled doublets at δ 7.90 and 6.98, corresponding to one proton each, were assigned to H-5 and H-6, respectively as they showed HMBC correlations with C-6, C-7, C-4, C-8a; and C-4a, C-5, C-7 and C-8, respectively in its HMBC spectrum (Figure 1). It also displayed signals for four methoxyl groups at δ 3.93, 3.92, 3.86 and 3.84. The methoxyl groups at δ 3.93 and δ 3.86 were placed at C-7 and C-3' as they showed NOE correlations with H-6 (δ 6.98) and H-4' (δ 7.01), respectively in the NOESY spectrum (Figure 1). The methoxyl group at δ 3.92 was placed at C-8 as the methoxyl carbon resonated at δ 61.6, which is characteristic of di-*ortho* substituted methoxyl group [6], further supported by NOE correlation with C-7 methoxyl protons (δ 3.93) in the NOESY spectrum. The methoxyl group at δ 3.84 was placed at C-2' as it showed cross correlations with H-6' (δ 7.33) and H-4' (δ 7.01) in the HMBC spectrum, further evidenced by NOE correlation with H-3 in its NOESY spectrum. From the foregoing spectral studies, the structure of compound **1** was established as 7,8,2',3'-tetramethoxyflavone.

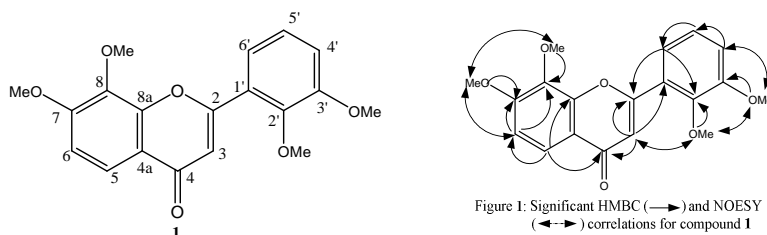


Figure 1: Significant HMBC (—→) and NOESY (---→) correlations for compound **1**

7, 8, 2', 3'-Tetramethoxyflavone (1)

Pale yellow amorphous solid (MeOH); mp: 110-112°C; FT-IR ν_{max} : 2928, 2836, 1637 (>C=O), 1628, 1599, 1567, 1511, 1469, 1423, 1395, 1365, 1290, 1259, 1172, 1143, 1087, 1035, 984, 954, 851, 785 cm⁻¹; UV (MeOH) λ_{max} (log ϵ): 254 (4.58), 306 (4.52) nm; ¹H NMR (600.19 MHz, CDCl₃): δ 7.90 (1H, d, *J* = 9.0 Hz, H-5), 7.33 (1H, dd, *J* = 7.9, 1.4 Hz, H-6'), 7.13 (1H, dd, *J* = 8.1, 7.9 Hz, H-5'), 7.01 (1H, dd, *J* = 8.1, 1.4 Hz, H-4'), 6.98 (1H, d, *J* = 9.0 Hz, H-6), 6.86 (1H, s, H-3), 3.93 (3H, s, OMe-7), 3.92 (3H, s, OMe-8), 3.86 (3H, s, OMe-3'), 3.84 (3H, s, OMe-2'); ¹³C NMR: (150.93 MHz, CDCl₃): 178.3 (>C=O), 161.4 (C-2), 156.5 (C-7), 153.4 (C-3'), 150.8 (C-8a), 148.1 (C-2'), 136.8 (C-8), 125.9 (C-1'), 124.3 (C-5'), 121.0 (C-5), 120.8 (C-6'), 117.9 (C-4a), 114.9 (C-4'), 111.7 (C-3), 109.8 (C-

6), 61.6 (OMe-8), 61.0 (OMe-2'), 56.3 (OMe-7), 55.6 (OMe-3'); ESI-TOFMS (positive ion mode) m/z (rel.int.): 343.1187 $[M+H]^+$ (100) (calcd. for $C_{19}H_{18}O_6+H$, 343.1176).

By comparison of the spectral data with literature values, the known compounds were identified as 5,7,2',3'-tetramethoxyflavone (**2**) [7], skullcapflavone I 2'-methyl ether (**3**) [8], echiodin (**4**) [9], 14-deoxy-11,12-didehydroandrographolide (**5**) [10] and neoandrographolide (**6**) [11].

CONCLUSION

The isolation of compound **1** constitutes the first report of the occurrence of a new and rare flavone with 7,8-dioxygenation in ring-A and 2',3'-dioxygenation in ring-B.

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