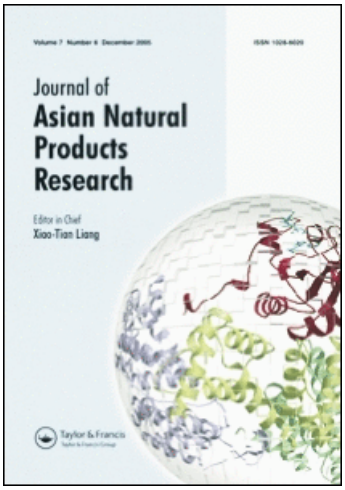

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A NEW FLAVONE 2′-GLUCOSIDE FROM *ANDROGRAPHIS ALATA*

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A new flavone glucoside, 5,2′,6′-trihydroxy-7-methoxyflavone 2′-*O*-β-D-glucopyranoside has been isolated from the whole plant of *Andrographis alata*. The structure was elucidated on the basis of spectral and chemical evidence.

Keywords: *Andrographis alata*; Acanthaceae; Flavone glucoside; 5,2′,6′-Trihydroxy-7-methoxyflavone 2′-*O*-β-D-glucopyranoside

Andrographis alata Nees (Acanthaceae) is an erect herb found widely in South India [1]. *Andrographis* species are noted for profuse production of 2′-oxygenated flavones [2–11]. *A. alata* has not been investigated earlier, and the phytochemical investigation of the whole plant of this species has resulted in the isolation and characterization of a new flavone glucoside, 5,2′,6′-trihydroxy-7-methoxyflavone 2′-*O*-β-D-glucopyranoside **(1)**.

RESULTS AND DISCUSSION

Compound **1** was obtained as pale yellow needles, m.p. 138–139°C. The positive ion FABMS showed $[M+H]^+$ peak at *m/z* 463 corresponding to molecular formula $C_{22}H_{22}O_{11}$ (corroborated by ^{13}CNMR spectrum), and a significant fragment at *m/z* 301 $[M+H-162]^+$ indicating the presence of a

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hexosyl moiety in **1**. The UV absorption maxima of **1** in MeOH (258, 300 nm) and with shift reagents suggested that it is a 5-hydroxyflavone with protected 7-hydroxyl group.

The ^{1}HNMR spectrum of **1** showed the presence of a methoxyl (δ 3.89), a hydroxyl (δ 10.17), a chelated hydroxyl (δ 12.93) and a singlet at δ 6.34 assigned to H-3. It also showed three consecutive aromatic protons with signals at δ 6.66 (d, $J = 8.3$ Hz), 6.75 (d, $J = 8.3$ Hz) and 7.29 (t, $J = 8.3$ Hz), and two *meta* coupled doublets ($J = 1.9$ Hz) at δ 6.40 and 6.62, respectively. This signal pattern resembled those of 5,7,2′,6′-tetraoxygenated flavones [12–14]. It also showed an anomeric proton signal at δ 4.92 indicating the presence of a sugar moiety. The presence of two phenolic hydroxyls and a hexose sugar residue in **1** was further evidenced by the formation of a hexaacetate (M^+, 714).

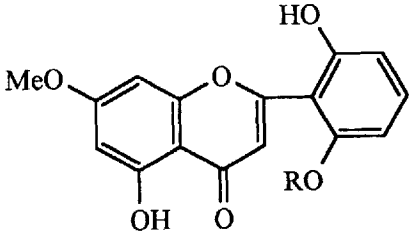
Acid hydrolysis of **1** with 2 N HCl afforded glucose and an aglycone **(2)**. The UV absorption maxima of **2** (258 and 303 nm) was very similar to **1** and the fact that both the glycoside **(1)** and the aglycone **(2)** did not show any bathochromic shift of band II absorption maximum with NaOAc indicated the presence of a methoxyl at C-7. This suggested that the sugar residue in **1** should be present in ring B. The EIMS of **2** exhibited a molecular ion at *m/z* 300 and the diagnostic peaks of retro-Diels–Alder cleavage of ring C at *m/z* 167 and 134 indicating the presence of a hydroxyl and a methoxyl in ring A, and two hydroxyls in ring B.

The ^{1}HNMR spectrum of **2** showed the AB_2 type aromatic proton signals of ring B at δ 7.12 (1H, t, $J = 8.2$ Hz) and 6.42 (2H, d, $J = 8.2$ Hz)

TABLE I HMBC correlations of compounds **1** and **2**

Carbon	*Correlated protons*	
	1	**2**
2	3	3
3		
4	3	3
5	6, OH-5	6, OH-5
6	8, OH-5	8, OH-5
7	6, 8, OMe-7	6, 8, OMe-7
8	6	6
9	8	8
10	3, 6, 8, OH-5	3, 6, 8, OH-5
1′	3, 3′, 5′	3, 3′, 5′
2′	3′, 4′, 1″	3′, 4′, OH-2′
3′	5′	5′
4′	3′, 5′	3′, 5′
5′	3′	3′
6′	4′, 5′, OH-6′	4′, 5′, OH-6′

characteristic of 4′ and 3′,5′ protons of 2′,6′-dihydroxy (or methoxy) flavones [15–17]. The chemical shift values of the carbons on the B-ring of **2** were similar to those observed for the B-ring carbons of 2′,6′-dihydroxy-flavones [12, 17]. The presence of 2′,6′-dihydroxy substitution in **2** was further supported by HMBC spectrum (Table I) as both these hydroxyl bearing carbons (δ 156.5) showed cross peaks with *ortho* (δ 6.42) and *meta* (δ 7.12) protons. Thus the structure of **2** was elucidated as 5,2′,6′-tri-hydroxy-7-methoxyflavone, which has not been reported earlier from any plant source or synthesized.



1 R = Glc
2 R = H

The position of glucose in **1** was determined by analysis of its HMBC spectrum (Table I) in which the anomeric proton signal at δ 4.92 (H-1″) showed long range correlation with the carbon at δ 156.3 (C-2′), indicating that the glucose moiety is linked to C-2′ hydroxyl group of **2**. The coupling constant ($J = 7.8$ Hz) of the anomeric proton signal indicated the β-configuration of the glucopyranoside moiety. Thus **1** was characterized as 5,2′,6′-trihydroxy-7-methoxyflavone 2′-*O*-β-D-glucopyranoside.

EXPERIMENTAL SECTION

General Experimental Procedures

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. Optical rotation was measured in MeOH at 25°C on a Perkin-Elmer 241 polarimeter. IR spectra were recorded in KBr disks on a Bio-Rad Win FT-IR spectrophotometer and UV spectra on a Shimadzu UV-240 spectrophotometer. FABMS was obtained in positive ion mode using a glycerol matrix on VG Micro Mass ZAB-HF mass spectrometer.

EIMS was recorded on a VG Micro mass 7070 H mass spectrometer at 70 eV. ^{1}H and ^{13}CNMR spectra were determined on a Bruker AM-300.13 spectrometer at 300.13 and 75.43 MHz, respectively using DMSO-d_6 or $CDCl_3$ with TMS as internal standard.

Plant Material

The whole plant of *A. alata* was collected in January 1995 at Talakona, near Tirupati, Andhra Pradesh, India. A voucher specimen (KMC-951) is deposited in the Herbarium of the Department of Botany, Sri Venkateswara University, Tirupati.

Extraction and Isolation

The air-dried and powdered whole plant (2.5 kg) of *A. alata* was successively extracted with hexane, Me_2CO and MeOH. Concentration of Me_2CO extract afforded a brown viscous residue (120 g). It was fractionated with hexane and C_6H_6, and the residue (52 g) left behind on column chromatography over silica gel (200 g) using $CHCl_3$/EtOAc step gradient gave **1** (90 mg).

5,2′,6′-Trihydroxy-7-methoxyflavone 2′-O-β-D-glucopyranoside **(1)** Compound **1** was obtained as pale yellow needles from MeOH, 80 mg, m.p. 138–139°C, $[\alpha]_D^{25}$ − 10.4 (*C* 0.1, MeOH); UV (MeOH) λ_{max} (log ϵ) 258 (4.61), 300 (4.46); +NaOMe 270, 290, 364; +NaOAc 259, 299; +NaOAc/H_3BO_3 259, 299; +$AlCl_3$ 269, 315, 368; +$AlCl_3$/HCl 269, 315, 368 nm; IR (KBr) ν_{max} 3400 (OH), 2907, 1661 (C=O), 1604 (C=C) cm^{-1}: ^{1}HNMR (300 MHz, DMSO-d_6) δ 12.93 (1H, s, OH-5), 10.17 (1H, s, OH-6′), 7.29 (1H, t, J = 8.3 Hz, H-4′), 6.75 (1H, d, J = 8.3 Hz, H-3′), 6.66 (1H, d, J = 8.3 Hz, H-5′), 6.62 (1H, d, J = 1.9 Hz, H-8), 6.40 (1H, d, J = 1.9 Hz, H-6), 6.34 (1H, s, H-3), 4.92 (1H, d, J = 7.8 Hz, H-1″), 3.89 (3H, s, OMe-7); 3.70 (1H, br d, J = 12 Hz, H-6″a), 3.40 (1H, br d, J = 12 Hz, H-6″b), 3.27 (1H, ddd, J = 9, 9, 9 Hz, H-5″), 3.19 (1H, dd, J = 9, 9 Hz, H-3″), 3.08 (1H, dd, J = 9, 9 Hz, H-4″), 3.06 (1H, dd, J = 7.8, 9 Hz, H-2″); ^{13}CNMR (75 MHz, DMSO-d_6) δ 181.9 (C-4), 165.0 (C-7), 161.6 (C-2), 161.1 (C-5), 158.2 (C-9), 156.3 (C-2′) 156.1 (C-6′), 132.1 (C-4′), 112.4 (C-3), 110.0 (C-1′), 109.4 (C-5′), 105.4 (C-3′), 104.9 (C-10), 100.5 (C-1″), 97.7 (C-6), 92.5 (C-8), 76.9 (C-5″), 76.6(C-3″), 73.1(C-2″), 69.5(C-4″), 60.6(C-6″), 55.9 (OMe-7); FABMS *m/z* $[M+H]^+$ 463 (29), $[M+H-162]^+$ 301 (14).

Hexaacetate of **1** Acetylation of **1** (10 mg) with Ac_2O (1.5 ml) and C_5H_5N (0.3 ml) at room temp for 48 h resulted in a white amorphous solid which on crystallization from Me_2CO afforded colourless needles (9 mg),

m.p. 184–185°C; IR (KBr) ν_{max} 2950, 1759, 1654, 1620 cm^{-1}; ^{1}HNMR (300 MHz, $CDCl_3$) δ 7.47 (1H, t, J = 8.3 Hz, H-4′), 7.11 (1H, d, J = 8.3 Hz, H-5′), 6.95 (1H, d, J = 8.3 Hz, H-3′), 6.78 (1H, d, J = 2.5 Hz, H-8), 6.63 (1H, d, J = 2.5 Hz, H-6), 6.14 (1H, s, H-3), 5.22–5.11 (4H, m, H-2″, 3″, 4″, 5″), 5.08 (1H, d, J = 7.8 Hz, H-1″), 4.30 (1H, br d, J = 12 Hz, H-6″a), 4.20 (1H, br d, J = 12 Hz, H-6″b), 3.89 (3H, s, OMe-7), 2.42 (3H, s, OAc-5), 2.17 (3H, s, OAc-2′), 2.08–1.79 (12H, 4 × OAc); EIMS m/z $[M]^+$ 714 (1), 672 (23), 384 (12), 342 (7), 300 (4).

Acid hydrolysis of **1** Compound **1** (20 mg) was refluxed at 100°C for 2 h with 2 N HCl in MeOH (10 ml). The acid hydrolysate was extracted with EtOAc and evaporated to dryness to yield a yellow amorphous solid which on crystallization from MeOH afforded 12 mg of compound **2**, while the sugar in the aqueous layer was identified as glucose by paper chromatography.

5,2′,6′-Trihydroxy-7-methoxyflavone **(2)** Compound **2** was obtained as yellow needles (MeOH), 12 mg, m.p. 210–211°C; UV (MeOH) λ_{max} (log ϵ) 258 (4.55), 303 (4.20); +NaOMe 257 sh, 290 sh, 357; +NaOAc 258, 305; +NaOAc/H_3BO_3 258, 305; +$AlCl_3$ 267, 286 sh, 318, 365; +$AlCl_3$/HCl 267, 286 sh, 318, 365 nm; IR (KBr) ν_{max} 3372 (OH), 1647 (C=O), 1618, 1562, 1456 cm^{-1}; ^{1}HNMR (300 MHz, DMSO-d_6) δ 12.89 (1H, s, OH-5), 9.89 (2H, s, OH-2′,6′), 7.12 (1H, t, J = 8.2 Hz, H-4′), 6.62 (1H, d, J = 2.2 Hz, H-8), 6.42 (2H, d, J = 8.2 Hz, H-3′, 5′), 6.40 (1H, d, J = 2.2 Hz, H-6), 6.27 (1H, s, H-3) 3.84 (3H, s, OMe-7); ^{13}CNMR (75 MHz, DMSO-d_6) δ 181.9 (C-4), 165.1 (C-7), 162.7 (C-2), 161.2 (C-5), 158.2 (C-9), 156.5 (C-2′, 6′), 131.9 (C-4′), 112.0 (C-3), 108.1 (C-1′), 106.4 (C-3′, 5′), 104.7 (C-10), 97.8 (C-6), 92.4 (C-8), 55.9 (OMe-7); EIMS m/z $[M]^+$ 300 (100), 283 (5), 272 (11), 167 (60), 166 (12), 137 (16), 134 (7).

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