Two New Acylated Iridoid Glucosides from the Aerial Parts of *Paederia scandens*

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Received May 6, 2004; accepted July 12, 2004

Two new acylated iridoid glucosides were isolated from the aerial parts of *Paederia scandens* along with six known iridoid glucosides. The structures of two new compounds were elucidated as 6′-*O*-*E*-feruloylmonotropein (1) and 10-*O*-*E*-feruloylmonotropein (2) by spectroscopic methods.

Key words *Paederia scandens*; iridoid glucoside; 6′-*O*-*E*-feruloylmonotropein; 10-*O*-*E*-feruloylmonotropein

Paederia scandens (LOUR.) MERRILL (Rubiaceae) is a climbing plant, distributed in the southern region of the Korean peninsula, Vietnam, India, China, Japan, the Philippines and the U.S.A. Previous phytochemical investigations afforded paederoside, asperuloside, paederosidic acid, deacetylasperuloside, scandoside, and asperulosidic acid from the leaves and stems of this plant.[1] Recently, 6β-*O*-sinapoyl scandoside methyl ester, paederosidic acid methyl ester and three dimeric iridoid glucosides were newly isolated from the roots of this plant.[1,2] The roots, leaves, bark and fruit of this plant have been used as treatments for jaundice, dysentery, and dyspepsia in Korea. Also, it was reported that paederoside and asperuloside from this plant exerted an inhibitory effect on Epstein-Barr virus activation.[3] In this paper, we report the isolation and structural elucidation of two new acylated iridoid glucosides, along with the six known iridoid glucosides from the aerial parts of this plant.

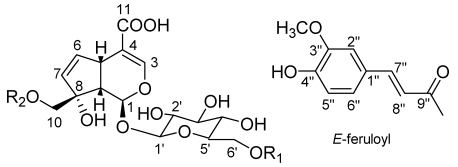
The MeOH extract of the aerial parts of *P. scandens* was suspended with water and then partitioned with *n*-hexane, CH_2Cl_2, EtOAc, and *n*-BuOH, successively. The *n*-BuOH soluble fraction was separated by a series of SiO_2, reversed-phase C_{18} MPLC, Sephadex LH-20, and reversed-phase C_{18} HPLC to give two new acylated iridoid glucosides (**1**, **2**) and six known iridoid glucosides, which were identified as daphylloside (**3**),[4] paederoside (**4**),[5] paederosidic acid methyl ester (**5**),[1] deacetylasperuloside (**6**),[5] 6α-hydroxygeniposide (**7**)[6] and paederosidic acid (**8**).[5]

Compound **1** was obtained as a crystalline solid, and its molecular formula of $C_{26}H_{30}O_{14}$ was confirmed by a qausimolecular ion $[M+Na]^+$ at *m*/*z* 589.1526 in HR-FAB-MS. The ^{1}H-NMR spectrum showed three olefinic proton signals at δ 5.60 (1H, d, J=5.1 Hz, H-7), 6.20 (1H, dd, J=5.1, 2.2 Hz, H-6) and 7.36 (1H, s, H-3), a multiplet signal at δ 3.58 (3H, H-5, H_2-10), and an anomeric proton at δ 4.69 (1H, d, J=7.7 Hz, H-1′), the data of which suggested that either a monotropein or gardenoside skeleton was present in **1**.[6] By comparing the chemical shifts of C-6 (δ 138.9), C-7 (δ 134.5), and C-9 (δ 46.3) with those of the literature in the ^{13}C-NMR spectrum,[7] it was possible to conclude that **1** possessed a monotropein skeleton in its structure. Morever, a feruloyl unit was observed in the ^{1}H-NMR spectrum. The olefinic proton signals at δ 6.41 (1H, d, J=15.9 Hz) and 7.64 (1H, d, J=15.9 Hz) were assigned to H-8″ and 7″, respectively, with a *trans* orientation. The signals belonging to the 1,3,4-trisubstituted benzene ring appeared at δ 6.80 (1H, d, J=8.3 Hz, H-5″), 7.08 (1H, dd, J=8.3, 1.7 Hz, H-6″), and 7.20 (1H, d, J=1.7 Hz, H-2″). A methoxy group was found on the C-3″ by HMBC correlations from the signal at δ 3.88 (OCH_3) to the signal at δ 150.2 (C-3″), which was supported by the NOESY peaks between the signal at δ 3.88 (OCH_3) and the signal at δ 7.20 (H-2″). The position of a feruloyl group in **1** was predicted to be at the hydroxy group of C-6′, which was inferred from the downfield shift of C-6′ (δ 65.4) in comparison with the literature.[7] This statement was confirmed by the aid of the HMBC technique, which displayed three bond correlations between H-6′ (δ 4.33) and C-9″ (δ 169.9). Thus, **1** was elucidated to be 6′-*O*-*E*-feruloylmonotropein.

The HR-FAB-MS of **2** exhibited a quasimolecular ion $[M+Na]^+$ at *m*/*z* 589.1522 corresponding to the molecular formula of $C_{26}H_{30}O_{14}$, which was the same value as **1**. The ^{1}H- and ^{13}C-NMR spectra of **2** were similar to those of **1**, except that the chemical shifts of H-6′ and C-6′ appeared in the upfield region, whereas the signals of H-10 were shifted to the downfield region, when compared to **1**. These phenomena gave a hint that a feruloyl group was substituted at the hydroxy group of C-10 in **2**. Furthermore, this assumption proved to be true by the cross peaks between H_2-10 (δ 4.20, 4.34) and C-9″ (δ 169.8) in the HMBC spectrum. Based on the above data, the structure of **2** turned out to be 10-*O*-*E*-feruloylmonotropein, as shown in Fig. 1.

Experimental

General Experimental Procedures Optical rotation was measured with a JASCO DIP-1000 digital polarimeter (Tokyo, Japan). FAB-MS spectra were obtained on a JEOL JMS-AX505WA. UV and IR spectra were recorded on a Shimadzu UV-2101 and JASCO FT/IR-300E, respectively. ^{1}H-



	R_1	R_2
1	*E*-feruloyl	H
2	H	*E*-feruloyl

Fig. 1. The Chemical Structures of **1** and **2**

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and ^{13}C-NMR spectra were recorded on a Bruker spectrometer at 400 MHz and at 100 MHz, respectively, with tetramethylsilane as an internal standard. Column chromatography was performed using a Sephadex LH-20 (Pharmacia) and Kiesegel 60 (Art. 7734; Merck, Darmstadt, Germany). HPLC was performed on a column of YMC (J'sphere ODS-H80, S-4 μm, 250×10 mm i.d., Japan). TLC was conducted on pre-coated Kiesegel 60 F_{254} plates (Art. 5715; Merck, Darmstadt, Germany). Spots on TLC were detected under UV light.

Plant Materials The aerial parts of *P. scandens* were collected from the Chusan Experimental Station of the Southern University Forest, College of Agricultural & Life Sciences, Seoul National University in 2002, and identified by one of us (J.H.P). A voucher specimen (SNUPC-012) has been deposited at the College of Pharmacy, Seoul National University.

Extraction and Isolation The aerial parts of *P. scandens* (3.0 kg) were dried at room temperature and then extracted with MeOH. The MeOH extract (340 g) was concentrated *in vacuo* into a residue, which was suspended with water and then subsequently partitioned with *n*-hexane (2 l), CH_2Cl_2 (2 l), EtOAc (2 l), and *n*-BuOH (2 l), successively. The *n*-BuOH soluble fraction (46.0 g) was fractionated using silica gel column chromatography ($CHCl_3$–MeOH=10 : 1→1 : 1) into twelve fractions (PB 1—12). PB 3 fraction (2.0 g) was subjected to reversed-phase C_{18} column chromatography and produced five sub-fractions (PB 31—35). PB 32 was purified using HPLC (MeCN–H_2O=18 : 82, 2 ml/min) to yield **3** (8.7 mg, t_R: 16.2 min). PB 33 was applied to Sephadex LH-20 (MeOH) and then separated using HPLC (MeCN–H_2O=18 : 82, 2 ml/min) to yield **4** (10.0 mg, t_R: 26.5 min) and **5** (9.0 mg, t_R: 31.5 min). PB 5 (3.7 g) was subjected to reversed-phase C_{18} column chromatography (MeOH–H_2O=3 : 7→5 : 5) and produced six sub-fractions (PB 51—PB 56). PB 53 and PB 54 were fractionated by Sephadex LH-20 into four fractions (PB 531—534, PB 541—544), respectively. From PB 533, compound **1** (18.0 mg, t_R: 24.8 min) was purified using HPLC (MeCN–H_2O=17 : 83, 2 ml/min) and from PB 544, compound **2** (12.0 mg, t_R: 22.7 min) was isolated using HPLC (MeCN–H_2O=20 : 80, 2 ml/min). PB 6 (6.0 g) was subjected to reversed-phase C_{18} column chromatography (MeOH–H_2O=1 : 9→5 : 5) and produced five sub-fractions (PB 61—65). PB 61 was subjected to Sephadex LH-20 (MeOH) and yielded four sub-fractions (PB 611—614). PB 611 was applied to HPLC (MeCN–H_2O=10 : 90, 2 ml/min) and afforded **6** (11.7 mg, t_R: 11.7 min) and **7** (10.0 mg, t_R: 14.2 min). PB 614 also was purified by HPLC (MeCN–H_2O=15 : 85, 2 ml/min) and then gave **8** (15.0 mg, t_R: 14.8 min).

6′-*O*-*E*-Feruloylmonotropein (**1**): A crystalline solid; mp 143—144 °C (MeOH); HR-FAB-MS *m*/*z*: 589.1526 (Calcd for $C_{26}H_{30}O_{14}Na$: 589.1533); $[\alpha]_D^{20}$: −30.2° (*c*=0.24, MeOH); UV λ_{max} (MeOH) nm (log ε): 218 (4.03), 235 (4.06), 327 (3.97); IR ν_{max} (KBr, cm^{-1}): 3426, 2930, 1693, 1633, 1515, 1163, 1075; ^{1}H-NMR (CD_3OD) δ: 2.69 (1H, d, *J*=6.6 Hz, H-9), 3.23 (1H, t, *J*=8.0 Hz, H-2′), 3.38—3.44 (2H, m, H-3′, H-4′), 3.53—3.58 (4H, m, H-5, H_2-10, H-5′), 3.88 (3H, s, OCH_3), 4.33 (1H, dd, *J*=11.7, 5.6 Hz, H-6′a), 4.50 (1H, d, *J*=11.7 Hz, H-6′b), 4.69 (1H, d, *J*=7.7 Hz, H-1′), 5.57 (1H, d, *J*=2.2 Hz, H-1), 5.60 (1H, d, *J*=5.1 Hz, H-7), 6.20 (1H, dd, *J*=5.1, 2.2 Hz, H-6), 6.41 (1H, d, *J*=15.9 Hz, H-8″), 6.80 (1H, d, *J*=8.3 Hz, H-5″), 7.08 (1H, dd, *J*=8.3, 1.7 Hz, H-6″), 7.20 (1H, d, *J*=1.7 Hz, H-2″), 7.36 (1H, s, H-3), 7.64 (1H, d, *J*=15.9 Hz, H-7″).^{13}C-NMR (CD_3OD) see Table 1.

10-*O*-*E*-Feruloylmonotropein (**2**): A crystalline solid; mp 147—148 °C (MeOH); HR-FAB-MS *m*/*z*: 589.1522 (Calcd for $C_{26}H_{30}O_{14}Na$: 589.1533); $[\alpha]_D^{20}$: −26.0° (*c*=0.23, MeOH); UV λ_{max} (MeOH) nm (log ε): 219 (4.12), 234 (4.17), 327 (4.14); IR ν_{max} (KBr, cm^{-1}): 3423, 2936, 1694, 1633, 1515, 1159, 1073; ^{1}H-NMR (CD_3OD) δ: 2.71 (1H, dd, *J*=8.6, 2.2 Hz, H-9), 3.21 (1H, t, *J*=8.3 Hz, H-2′), 3.31—3.37 (3H, m, H-3′, H-4′, H-5′), 3.58—3.65 (2H, m, H-5, H-6′a), 3.84 (1H, d, *J*=12.4 Hz, H-6′b), 3.89 (3H, s, OCH_3), 4.20 (1H, d, *J*=11.1 Hz, H-10a), 4.34 (1H, d, *J*=11.1 Hz, H-10b), 4.68 (1H, d, *J*=7. 9 Hz, H-1′), 5.69 (2H, m, H-1, H-7), 6.28 (1H, dd, *J*=5.5 2.4 Hz, H-6), 6.40 (1H, d, *J*=15.8 Hz, H-8″), 6.81 (1H, d, *J*=8.2 Hz, H-5″), 7.09 (1H, dd, *J*=8.2, 1.8 Hz, H-6″), 7.21 (1H, d, *J*=1.8 Hz, H-2″), 7.39 (1H, s, H-3), 7.64 (1H, d, *J*=15.8 Hz, H-7″). ^{13}C-NMR (CD_3OD) see Table 1.

Table 1. The ^{13}C-NMR Chemical Shifts of **1** and **2**

Carbon	**1**	**2**
1	95.9	95.6
3	152.5	152.9
4	112.5	112.6
5	40.0	40.1
6	138.9	139.4
7	134.5	133.8
8	86.8	85.2
9	46.3	47.3
10	69.1	70.0
11	169.9	169.8
1′	100.9	100.7
2′	75.4	75.4
3′	78.6	78.8
4′	72.2	72.2
5′	76.6	79.1
6′	65.4	63.3
1″	128.5	128.5
2″	112.5	112.6
3″	150.2	150.2
4″	151.4	151.5
5″	117.3	117.3
6″	125.1	125.1
7″	148.0	148.1
8″	116.0	115.9
9″	169.9	169.8
OMe	57.3	57.3

Acknowledgments We thank Jong-Young Park at the Chusan Experimental Station of Southern University Forest, Seoul National University, for collecting plant materials. This work was supported by Korea Research Foundation Grant (KRF-2003-015-E00217).

References

1) Quang D. N., Hashimoto T., Tanaka M., Dung N. X., Asakawa Y., *Phytochemistry*, **60**, 505—514 (2002).
2) Otsuka H., *Natural Medicines*, **56**, 59—62 (2002).
3) Kapadia G. J., Sharma S. C., Tokuda H., Nishino H., Ueda S., *Cancer Lett.*, **102**, 223—226 (1996).
4) Inouye H., Ueda S., Hirabayashi M., Shimokawa N., *Yakugaku Zasshi*, **86**, 943—947 (1966).
5) Inouye H., Okigawa M., Shimokawa N., *Chem. Pharm. Bull.*, **17**, 1949—1954 (1969).
6) Boros C. A., Stermitz F. R., *J. Nat. Prod.*, **53**, 1055—1147 (1990).
7) Chaudhuri R. K., Afifi-Yazar F. Ü., Sticher O., *Tetrahedron*, **36**, 2317—2326 (1980).