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Two New Phenylpropanoid Glycosides from the Aerial Parts of *Paederia scandens*

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Paederia scandens (Lour.) Merrill (Rubiaceae) is a climbing plant, distributed in southern region of the Korea Peninsula, Vietnam, India, China, Japan, the Philippines, and the USA.[1] The roots, leaves, bark, and fruits of this plant have been used to treat jaundice, dysentery, and dyspepsia, in Korea.[2] Previous investigations on this plant have reported the occurrence of iridoid glycosides[1,2,3] and the pharmacological activities including the inhibitory effects against Epstein-Barr virus activation[4] and xanthine oxidase,[5] antinociceptive activity,[6,7] and uricosuric effect.[5] The present study described the isolation of two new phenylpropanoid glycosides **1** and **2**, along with two known flavonoid glycosides **3** and **4** from the aerial parts of *P. scandens*. The structures of the known compounds **3** and **4** were confirmed by interpreting the measured 1D and 2D NMR spectroscopic data and comparing these data with the published values, rutin, and kaempferol-3-*O*-rutinoside, respectively.[8] It is the first time that these isolates have been isolated from this plant.

Compound **1** was obtained as an amorphous powder, and its molecular formula of $C_{22}H_{32}O_{13}$ was confirmed by the presence of a sodiated molecular ion $[M+Na]^+$ at *m/z* 527.1745 in the HR FAB-MS. The ^{1}H-NMR spectrum (Table 1) displayed a singlet peak at δ_H 7.19, two doublet peaks at δ_H 6.80 (1H, *J* = 8.1 Hz, H-5) and 7.06 (1H, *J* = 8.1 Hz, H-6), two doublet peaks at δ_H 7.63 (1H, *J* = 15.8 Hz, H-7) and 6.39 (1H, *J* = 15.8 Hz, H-8) due to *trans* oriented olefinic protons, and a methoxy peak at δ_H 3.89, which was assigned as a feruloyl group on the basis of further investigation using HMQC and HMBC spectra (Fig. 2). The proton signals at δ_H 1.10-4.60 seemed to comprise two sugar units. The assignments of these sugar signals were facilitated by the COSY and TOCSY techniques. An anomeric pro-

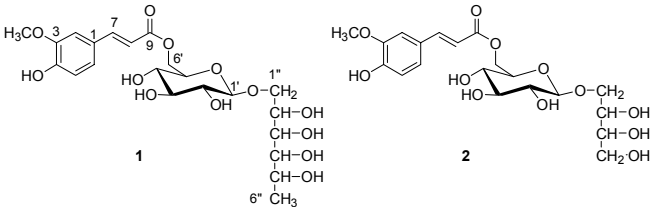


Figure 1. The chemical structures of **1** and **2**.

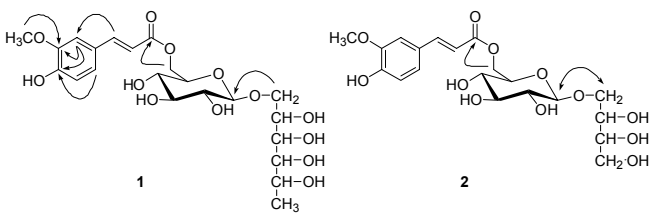


Figure 2. Key HMBC correlations of **1** and **2**.

Table 1. ^{1}H and ^{13}C-NMR chemical shifts of **1** and **2**

Position	**1**		**2**	
	δ_H	δ_C (mult.)[a]	δ_H	δ_C (mult.)[a]
1	-	128.3 (s)	-	128.5 (s)
2	7.19 s	112.5 (d)	7.20 d 1.6	112.5 (d)
3	-	150.2 (s)	-	150.2 (s)
4	-	151.6 (s)	-	151.5 (s)
5	6.80 d 8.1	117.3 (d)	6.80 d 8.0	117.3 (d)
6	7.06 d 8.1	125.1 (d)	7.07 dd 8.0, 1.6	125.0 (d)
7	7.63 d 15.8	148.0 (d)	7.63 d 15.9	147.9 (d)
8	6.39 d 15.8	116.0 (d)	6.39 d 15.9	116.0 (d)
9	-	169.9 (s)	-	169.9 (s)
1′	4.35 d 7.6	105.8 (d)	4.34 d 7.6	105.8 (d)
2′	3.26 m	76.0 (d)	3.25 m	76.0 (d)
3′	3.38 m	78.5 (d)	3.38 m	78.5 (d)
4′	3.38 m	72.4 (d)	3.38 m	72.4 (d)
5′	3.54 m	76.4 (d)	3.56 m	76.3 (d)
6′	4.30 dd 11.7, 5.7 4.51 dd 11.7, 2.1	65.4 (t)	4.30 dd 12.0, 5.0 4.51 dd 12.0, 1.8	65.4 (t)
1″	4.11 dd 10.2, 2.2 3.69 dd 10.2, 6.0	74.1 (t)	4.08 dd 9.1, 2.1 3.66 m	73.8 (t)
2″	3.82 m	72.6 (d)	3.71 m[b]	73.3 (d)[b]
3″	3.58 m	73.7 (d)	3.61 m[b]	74.3 (d)[b]
4″	3.57 m	75.6 (d)	3.61 m 3.71 m	65.4 (t)
5″	3.84 m	71.2 (d)	-	-
6″	1.17 d 6.5	20.4 (q)	-	-
OCH_3	3.89 s	57.3 (q)	3.87 s	57.3 (q)

[a]Multiplicity was deduced from the DEPT and HMQC spectroscopic data. [b]Assignments are interchangeable.

ton at δ_H 4.35 (1H, d, J = 7.6 Hz, H-1′) was coupled with a proton signal at δ_H 3.26 (1H, m, H-2′) in the ^{1}H-^{1}H COSY and showed correlations with four proton signals (H-2′, H-3′, H-4′, and H-5′) in the TOCSY spectrum. In addition, the couplings between H-5′ (δ_H 3.54) and H-6′ (δ_H 4.30 and 4.51) were observed in the ^{1}H-^{1}H COSY and TOCSY. These data enabled the assignment of the signals belonging to a glucopyranoside together with DEPT and HMQC data. The remaining part was assigned as acyclic sugar moiety, a hexane-1,2,3,4,5-pentanol, by using the sequentially observed correlations from H-1″ to H-6″ in the ^{1}H-^{1}H COSY and the partially observed correlations of H-1″ to H-2″, H-3″, and H-4″ in the TOCSY spectra, as well as examination of DEPT, HMQC, and HMBC data.[9,10] The connection between feruloyl and glucose was confirmed by the HMBC correlations (Fig. 2) from H-6′ (δ_H 4.30, 4.51) to C-9 (δ_C 169.9). The chemical shift of C-1″ (δ_C 74.1) and three-bond correlations between H-1″ (δ_H 4.11 and 3.69) and C-1′ (δ_C 105.8) made it possible to locate the hexane-1,2,3,4,5-pentanol on C-1′. However, the absolute configurations of the sugars in **1** were not determined. Therefore, the structure of this compound (**1**) was established as hexane-1,2,3,4,5-pentanol 1-*O*-β-(6-*O*-(*E*)-feruloyl) glucopyranoside, and it has been named paederol A.

The molecular formula of compound **2**, $C_{20}H_{28}O_{12}$, was deduced from the quasimolecular ion peak at *m/z* 483.1464 $[M+Na]^+$ in the HRFABMS. The comparison of ^{1}H and ^{13}C NMR spectral data of **2** with those of **1** revealed the presence of an identical feruloyl glucose unit in **1** as well as a different sugar moiety from **1**. Two oxymethylene signals of H-1″ (δ_H 4.08 and 3.66), and H-4″ (δ_H 3.61 and 3.71), and two oxymethine signals of H-3″ (δ_H 3.61) and H-2″ (δ_H 3.71) were observed in the ^{1}H, DEPT, and HMQC data, indicating a butane 1,2,3,4-tetraol moiety.[9] This assumption was supported by comparing ^{1}H and ^{13}C chemical shifts of **2** with published values. The downfield-shifted chemical shift of C-1″ (δ_C 73.8) and the HMBC correlations between H-1″ and C-1′ (δ_C 105.8) as well as H-1′ and C-1″ confirmed the location of butane tetraol on C-1′ through ether linkage. Accordingly, this compound (paederol B) was determined to be a butane-1,2,3,4-tetraol 1-*O*-β-(6-*O*-(*E*)-feruloyl) glucopyranoside. The absolute configurations of the sugars remained unresolved in the present study. To our knowledge, thus far, there has been no report of phenylpropanoid glycosides with acyclic sugars.

Among the isolates, the two new compounds **1** and **2** were tested for cytotoxicity against three human cancer cell lines, Lu1 (lung cancer), LNCaP (prostate cancer), and MCF-7 (breast cancer) but were found to be inactive (ED_{50} > 10 μg/mL).

Experimental Section

General 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-NMR and ^{13}C-NMR spectra were recorded on a Bruker spectrometer at 400 MHz and at 100 MHz, respectively. 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 the TLC were detected under UV light.

Plant materials. The aerial parts of *P. scandens* were collected from Chusan Experimental Station of Southern University Forest, College of Agricultural & Life Sciences, Seoul National University in 2002. A voucher specimen (SNUPC-012) was deposited at the College of Pharmacy at 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). The PB 8 fraction (3.3 g) was subjected to reversed-phase C_{18} column chromatography (MeOH-H_2O = 2:8→5:5) and produced four sub-fractions (PB 81~84). The PB 83 was applied to Sephadex LH-20 (MeOH) and then separated using HPLC (MeCN-H_2O = 17:83, 2 mL/min) to yield compound **2** (5.0 mg, t_R 32.9 min). The PB 9 (2.7 g) was subjected to reversed-phase C_{18} column chromatography (MeOH-H_2O = 2:8→5:5) and produced five sub-fractions (PB 91~PB 95). The combined PB 92 and PB 93 was fractionated by Sephadex LH-20 into four fractions (PB 931~934). From the PB 934, compound **1** (3.4 mg, t_R 36.47 min) was purified using HPLC (MeCN-H_2O = 17:83, 2 mL/min). The PB 94 was subjected to Sephadex LH-20 (MeOH) and yielded four sub-fractions (PB 941~944). The PB 943 was applied to HPLC (MeCN-H_2O = 10:90, 2 mL/min) and afforded compounds **3** (34 mg, t_R 13.41 min) and **4** (10.0 mg, t_R 17.86 min).

Compound 1 (paederol A)**:** amorphous solid; HR FAB-MS *m/z* 527.1745 $[M+Na]^+$ (Calcd for $C_{22}H_{32}O_{13}Na$, 527.1741); $[\alpha]_D^{20}$ −11.0° (*c* 0.16, MeOH); UV λ_{max} (MeOH) nm (log ε): 233 (3.94), 324 (4.10); IR ν_{max} (KBr, cm^{-1}) 3367, 2929, 1696, 1631, 1596, 1515, 1275, 1169, 1077; ^{1}H-NMR (CD_3OD) and ^{13}C-NMR (CD_3OD) see Table 1.

Compound 2 (paederol B)**:** amorphous solid; HR FAB-MS *m/z* 483.1464 $[M+Na]^+$ (Calcd for $C_{20}H_{28}O_{12}Na$, 483.1478); $[\alpha]_D^{20}$ −16.2° (*c* 0.14, MeOH); UV λ_{max} (MeOH) nm (log ε): 233 (3.97), 323 (4.14); IR ν_{max} (KBr, cm^{-1}) 3393, 2932, 1696, 1631, 1596, 1515, 1274, 1172, 1078; ^{1}H-NMR (CD_3OD) and ^{13}C-NMR (CD_3OD) see Table 1.

Cytotoxicity evaluation. All the isolates were assessed with the Lu1 (human lung carcinoma), LNCaP (hormone-dependent human prostate carcinoma), and MCF-7 cancer cell lines, using established protocols.[11]

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