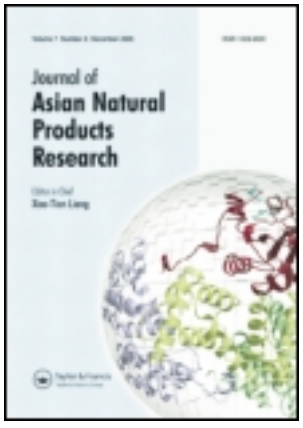

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Chemical constituents from *Astilbe chinensis*

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A new compound, 11-*O*-(3′-*O*-methylgalloyl)-bergenin (**1**), along with 11 known compounds (**2**–**12**), has been isolated from the rhizome of *Astilbe chinensis*. The chemical structure of compound **1** was determined by IR, MS, and NMR spectral data. All compounds were evaluated for the cytotoxic activity *in vitro*, and compound **4** showed a moderate cytotoxic activity against HepG2 cells.

Keywords: *Astilbe chinensis*; 11-*O*-(3′-*O*-methylgalloyl)-bergenin; cytotoxic activity

1. Introduction

Astilbe chinensis (Maxim.) Franch. et Sav. (*A. chinensis*) is a perennial herbaceous plant growing at altitudes of 390–3600 m in China, Russia, Japan, and Korea. Its rhizome is used for the treatment of headache, arthralgia, chronic bronchitis, and stomachalgia as a traditional Chinese medicine [1–3]. Modern pharmacological research indicated antineoplastic and immunomodulating activities of the whole methanol extracts of *A. chinensis* [4]. But up to date, little is known about the detailed chemical information relating to its antineoplastic activity. In this study, the chemical constituents of the extracts from the title plant were investigated, and one new compound, 11-*O*-(3′-methylgalloyl)-bergenin (**1**) (Figure 1), together with 11 known ones, daucosterol (**2**), 3β,6β-dihydroxyolean-12-en-27-oic acid (**3**) [5], 3-hydroxyolean-12-en-27-oic acid (**4**) [6], 2-hydroxyphenylacetic acid (**5**), 11-*O*-galloylbergenin (**6**) [7], bergenin (**7**), isoastilbin (**8**) [8], 11-*O*-(4-hydroxybenzoyl) bergenin (**9**) [9], 3β-acetoxyolean-12-en-27-oic acid (**10**) [5], 3,5,7-trihydroxychromone 3-*O*-α-L-rhamnopyranoside (**11**) [10], and β-sitosterol (**12**), was isolated. All these compounds were screened with *in vitro* cytotoxic model, among which compound **4** showed a moderate inhibition effect on the growth of HepG2 cells.

2. Results and discussion

Compound **1** was obtained as white amorphous powder. The molecular formula $C_{22}H_{22}O_{13}$ was determined by HR-ESI-MS at *m/z* 495.1117 $[M + H]^+$. Four phenolic hydroxyl groups were indicated in the ^1H NMR spectrum by four proton signals at δ_H 8.31 (s), 9.16 (s), 9.33 (s), and 9.75 (s), and two aromatic methoxyls were revealed by the signals at δ_H 3.73 (3H, s) and δ_C 60.2 and the signals at δ_H 3.83 (3H, s) and δ_C 56.4. The AB system of two aromatic protons at δ_H 7.14 and 7.08 (each 1H, d, $J = 1.8$ Hz) indicated the presence

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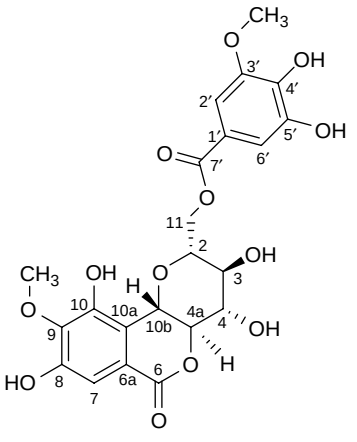

Figure 1. Structure of compound **1**.

of a *meta*-tetrasubstituted benzene ring, and the proton singlet at δ_H 6.98 (1H, s) suggested the presence of a *penta*-substituted benzene ring. Apart from 12 aromatic carbons, there exist two carbonyl groups, one oxygenated methylene, five oxygenated methines, and two methoxyl carbons. The ^{1}H and ^{13}C NMR spectral data of compound **1** were similar to those of 11-*O*-galloylbergenin (**6**) [7], except for the presence of one additional methoxyl group in compound **1**. In the HMBC spectrum, long-range correlations were observed for H-2′ to C-7′, H-6′ to C-7′, and 3′-OCH$_3$ to C-3′, indicating that the additional methoxyl group was attached to C-3′ (δ_C 148.5) (Figure 2). In the NOESY experiment, the cross peak between H-2′ and 3′-OCH$_3$ was in accordance with the above finding, while the correlations of H-10b with H-2 and H-4 and of H-3 with H-4a were in agreement with the configurations of C-2, C-3, C-4, C-4a, and C-10b as shown in Figure 2. Therefore, the structure of compound **1** was elucidated as 11-*O*-(3′-*O*-methylgalloyl)-bergenin.

Compounds **1**–**12** were evaluated for their antineoplastic activities. Compound **4** showed a moderate cytotoxic activity against HepG2 cells (GI_{50} 6.69 μg/ml).

3. Experimental

3.1 General experimental procedures

Optical rotations were measured on a Perkin-Elmer 341 polarimeter. UV spectrum was recorded on a Perkin-Elmer Lambda 35 spectrometer. IR spectrum was recorded on a Perkin-Elmer Spectrum-one FT-IR spectrometer. The ^{1}H, ^{13}C, NOESY, HMQC, and HMBC NMR spectra were performed using a Bruker Avance 600 spectrometer (600 MHz). Chemical shifts (δ) are reported in ppm relative to an internal TMS standard, and the coupling constant (J) in Hz. ESI-MS was recorded on a Finnigan LCQ^{DECA} mass spectrometer. HR-ESI-MS was recorded on a Bruker Bio TOF Q mass

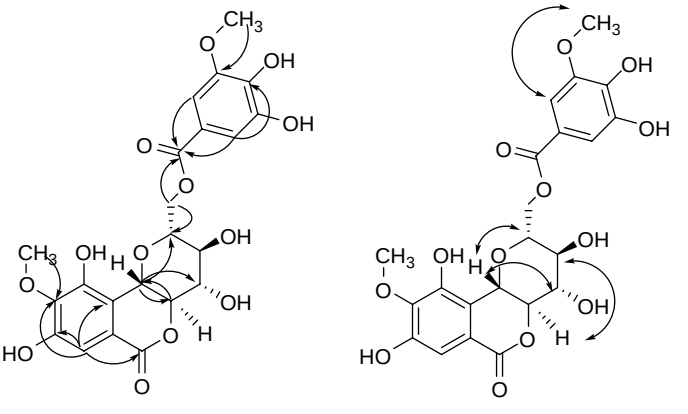

Figure 2. Key HMBC (→) and NOESY (↔) correlations of compound **1**.

spectrometer. Column chromatography was performed on silica gel (160–200 and 200–300 mesh, Qingdao Marine Chemical Co., Ltd, Qingdao, China) and ODS (Nacalai, Tokyo, Japan).

3.2 Plant material

The roots of *A. chinensis* were purchased from local herbal market, which were collected in October 2009, and identified by Prof. Xin-Fen Gao of Chengdu Institute of Biology. A voucher specimen (No. 20090089) is deposited in Herbarium of Chengdu Institute of Biology.

3.3 Extraction and isolation

Dried roots of *A. chinensis* (7 kg) were powdered and extracted with 95% ethanol (101 × 4) to give a crude ethanol extract (884 g). The residue was suspended in water and extracted successively with petroleum ether (31 × 4), ethyl acetate (31 × 4), and *n*-butanol (31 × 4). The solvents were removed under reduced pressure to yield 48 g of petroleum ether extract, 72 g of ethyl acetate extract, and 88 g of *n*-butanol extract. The ethyl acetate extracts were subjected to column chromatography over silica gel (160–200 mesh, 800 g), and eluted with a gradient solvent system of chloroform/methanol (9:1 to 1:1) to yield seven fractions (Fraction 1 − Fraction 7). Compound **3** (210 mg) was precipitated from Fraction 4, and the remaining residue of Fraction 4 (11 g) was subjected to column chromatography over silica gel and eluted with petroleum ether/ethyl acetate (5:1 to 1:1) to give six fractions (Fraction 4-1 − Fraction 4-6). Compound **5** (38 mg) was crystallized from Fraction 4-2. Compound **2** (160 mg) was precipitated from Fraction 5, and the remaining residue of Fraction 5 (6 g) was chromatographed on a silica gel column, and eluted in a gradient manner with petroleum ether/ethyl acetate (3:1 to 1:3) to give six fractions (Fraction 5-1 − Fraction 5-6). Compounds **1** (90 mg) and **9** (13 mg) were precipitated from Fraction 5-5 and Fraction 5-4, respectively. Compound **7** (2.78 g) was crystallized from Fraction 6. The remaining residue of Fraction 6 (5 g) was subjected to column chromatography over ODS with methanol/water (30–50%) as eluting system, to give compounds **6** (40 mg) and **8** (12 mg). The aliquot of petroleum ether extract (45 g) was subjected to column chromatography over

Table 1. ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) spectral data of **1** in DMSO-d_6 (δ in ppm, J in Hz).

No.	δ_C	δ_H	No.	δ_C	δ_H
2	79.1	3.88, ddd, J = 9.2, 7.3, 2.2	10b	72.7	5.04, d, J = 10.6
3	71.0	3.37, dt, J = 9.2, 5.1	11	64.2	4.19, dd, J = 12.1, 7.3 4.77, dd, J = 12.1, 2.2
4	73.9	3.69, dt, J = 9.2, 5.1	1′	119.5	
4a	80.0	4.02, dd, J = 10.6, 9.2	2′	105.3	7.08, d, J = 1.8
6	163.8		3′	148.5	
6a	118.6		4′	140.1	
7	110.1	6.98, s	5′	145.9	
8	151.5		6′	111.3	7.14, d, J = 1.8
9	141.1		7′	166.0	
10	148.4		3′—OCH_3	56.4	3.83, s
10a	116.2		9—OCH_3	60.2	3.73, s
3—OH		5.67, d, J = 5.1	10—OH		8.31, s
4—OH		5.72, d, J = 5.1	4′—OH		9.33, s
8—OH		9.75, s	5′—OH		9.16, s

silica gel (160–200 mesh, 680 g) and eluted with a gradient solvent system of petroleum ether/ethyl acetate (50:1 to 1:1) to give 8 fractions (Fraction 1 − Fraction 8). Compound **10** (412 mg) was crystallized from Fraction 5, and compound **12** (540 mg) was precipitated afterward from the remaining solution of Fraction 5. Compound **4** (80 mg) was precipitated from Fraction 7. The *n*-butanol extract was subjected to column chromatography over silica gel (80–100 mesh, 1000 g), and eluted with a gradient solvent system of chloroform/methanol (15:1 to 1:1) to give six fractions (Fraction 1 − Fraction 6). The Fraction 4 (0.8 g) was chromatographed on an ODS column eluted with methanol/-water (10–40%) to give compound **11** (2.4 mg).

*3.3.1 11-O-(3′-O-methylgalloyl)-bergenin (**1**)*

White amorphous power, $[\alpha]_D^{20}$ + 72.0 (*c* 0.5, MeOH); UV λ_{max} (MeOH): 258 nm; IR ν_{max} (KBr): 3352, 1708, 1615, 1518, 1462, 1353, 1227, 1091 cm^{-1}; ^1H NMR and ^{13}C NMR (DMSO-d_6) spectral data see Table 1; HR-ESI-MS: *m/z* 495.1117 $[M + H]^+$ (calcd. for $C_{22}H_{23}O_{13}$ 495.1139).

3.4 Cytotoxic assay

The cytotoxicity of the isolated compounds was tested in the HepG2 cell line with taxol as positive control. HepG2 cells were seeded into 96-well plates and cultured overnight. After incubation with the respective compounds for 48 h, the cell number was measured with sulforhodamine B (SRB) method [11], and compound **4** exhibited moderate cytotoxicity against the Hep G2 cell line with GI_{50} 6.69 μg/ml.

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