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Research Article

Phenolic Constituents from *Fallopia multiflora* (Thunberg) Haraldson

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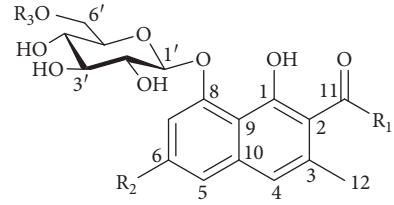
Four naphtolic glycosides (**1**–**4**), three anthraquinones (**5**–**7**), two stilbenes (**8**-**9**), one benzyl glycoside (**10**), and one flavonoid (**11**) were isolated from the roots of *Fallopia multiflora*. The new compounds were elucidated to be 6-hydroxymusizin 8-*O*-*α*-D-apiofuranosyl-(1→6)-*β*-D-glucopyranoside (**1**) and 6-methoxy-3-methyl-1,6,8-trihydroxy-2-naphthoic acid 8-*O*-*β*-D-glucopyranoside (**3**). Compound **3** could be an important marker for chemotaxonomy of *F. multiflora*. Benzyl gentiobioside (**10**) was isolated for the first time from the family Polygonaceae.

1. Introduction

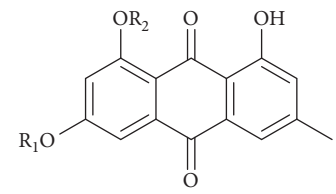
Fallopia multiflora (Thunberg) Haraldson (Polygonaceae), synonym *Polygonum multiflorum* Thunb., is an important medicinal plant in Oriental medicine. It is grown for various medicinal values ranging from bowel relaxation, antiaging, hair loss prevention, increasing sexual vigour, treatment of high cholesterol, high blood pressure, and inflammation [1]. Previous phytochemical investigations have revealed the presence of stilbenes and anthraquinones as major components in *F. multiflora* [2]. 2,3,5,4′-Tetrahydroxystilbene-2-*O*-*β*-D-glucopyranoside, emodin, and physcion are used as main markers for quality control of *F. multiflora* materials and related products [3]. Flavonoids and proanthocyanidins were also found in this plant [3, 4]. Several naphtolic compounds including torachrysone-8-O-*β*-D-glucopyranoside, torachrysone-8-O-(6′-O-acetyl)-*β*-D-glucopyranoside, and torachrysone-8-O-(6′-O-galloyl)-*β*-D-glucoside were also reported [3]. In the present study, a phytochemical investigation of the *Fallopia multiflora* roots led to the isolation of two new (**1** and **3**) and nine known compounds (Figure 1).

2. Experimental

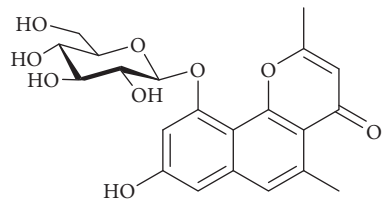
2.1. General. Thin layer chromatography was performed using precoated Kieselgel 60 F254 (Merck) and visualized by UV light 254 nm and 10% H_2SO_4 reagent under heating. Column chromatography was performed using silica gel 60 (Merck, 70–230 mesh). Optical rotations were read on a JASCO P-2000 digital polarimeter. NMR experiments were performed on a Bruker AM500 FT-NMR spectrometer. The HR-ESI-MS data were obtained from a LTQ Orbitrap XL Mass Spectrometer (Thermo Scientific). GC analysis was carried out on an Agilent 7890B GC System using a column SPB-1 (0.25 mm × 30 m), detector FID, column temp. 210°C, injector temperature 270°C, detector temperature 300°C, and He carrier gas.



1: $R_1 = CH_3$, $R_2 = OH$, R_3 = apiofuranoside
2: $R_1 = CH_3$, $R_2 = OMe$, $R_3 = H$
3: $R_1 = OH$, $R_2 = OMe$, $R_3 = H$



5: $R_1 = R_2 = H$
6: $R_1 = H$, R_2 = Glc
7: $R_1 = CH_3$, R_2 = glucopyranoside



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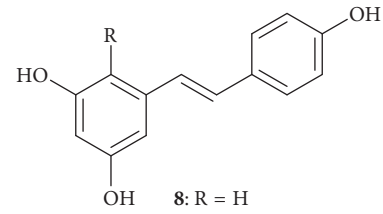
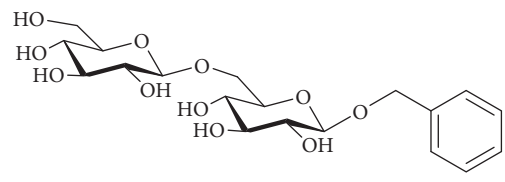


8: R = H
9: R = O-glucopyranoside



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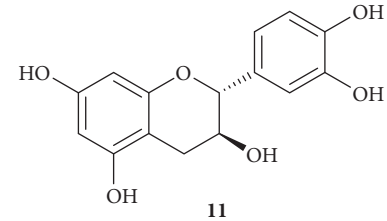

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Figure 1: The structure of compounds **1**–**11** isolated from *Fallopia multiflora*.

2.2. Plant Material. The roots of *F. multiflora* were collected in Dong Van commune, Ha Giang province, Vietnam, on October 2014 and identified by Dr. Nguyen The Cuong, Institute of Ecology and Biological Resources, VAST. Voucher specimens (HaGiang-03) have been deposited at the herbarium of the Institute of Ecology and Biological Resources.

2.3. Extraction and Isolation. The air-dried and powdered roots of *F. multiflora* (3.5 kg) were extracted with methanol (6 L × 3 times) in a sonic bath for 30 min at 40°C. The combined extracts were evaporated under reduced pressure to give crude extract (430.0 g), which was then resuspended in water (3 L) and successively partitioned by *n*-hexane and ethyl acetate (each 1 L × 3 times) to obtain *n*-hexane (51.7 g) and ethyl acetate (214.5 g) residues, respectively. The aqueous solution was passed through a Diaion HP-20 column and eluted by 0, 50, and 100% methanol in water to give three fractions W1-3. Fraction W3 was chromatographed on a silica gel column using mobile phase of a gradient of 0–100% methanol in dichloromethane to obtain seven fractions F1–7. Fraction F4 was purified by a silica gel column chromatography eluting with dichloromethane-methanol 6 : 1 (v/v) to yield **9** (457.0 mg). Fraction F5 was passed through a C-18 column using acetone-water 2 : 3 (v/v) as eluent to obtain **3** (8.0 mg). Compounds **1** (12.8 mg), **2** (5.4 mg), and **7** (4.5 mg) were purified from F6 by a silica gel column eluted by dichloromethane-methanol 6 : 1 (v/v). Repeated column chromatography using C18 and Sephadex LH-20 stationary phases were applied for fraction F7 to afford compounds **6** (6.8 mg) and **10** (6.0 mg). The ethyl acetate residue was fractionated by a silica gel column eluted by a gradient of 0–100% methanol in dichloromethane to obtain five fractions E1–5. Fraction E3 was subjected to a silica gel column eluted by *n*-hexane-ethyl acetate 5 : 1 (v/v) to obtain compounds **5** (90.4 mg). Compound **8** (3.4 mg) was purified from E4 by a Sephadex LH-20 column using methanol-water 1 : 1 (v/v). Similar Sephadex LH-20 column was applied for E5 to afford **4** (28.1 mg) and **11** (90.8 mg).

*2.3.1. 6-Hydroxymusizin 8-O-α-D-apiofuranosyl-(1→6)-β-D-glucopyranoside (**1**).* Yellow powder; $[\alpha]_D^{24} = +12.6^\circ$ ($c = 0.05$, CH_3OH); ^1H and ^{13}C NMR see Table 1; HR-ESI-MS: m/z 549.1578 $[M + Na]^+$ (calcd. 549.1584 for $C_{24}H_{30}NaO_{13}$).

*2.3.2. 6-Methoxy-3-methyl-1,6,8-trihydroxy-2-naphthoic acid 8-O-β-D-glucopyranoside (**2**).* Pale-yellow powder; $[\alpha]_D^{24} = +23.4^\circ$ ($c = 0.05$, CH_3OH); ^1H and ^{13}C NMR see Table 1; HR-ESI-MS: m/z 433.1110 $[M + Na]^+$ (calcd. 433.1111 for $C_{19}H_{22}NaO_{10}$).

2.3.3. Acid Hydrolysis and Sugar Identification. The compounds **1** and **3** (each 1 mg) were individually dissolved in 1 ml of dioxane/1 N HCl (1 : 1 v/v) and heated at 80°C for 3 h. The acidic solution was neutralized with silver carbonate and extracted with CH_2Cl_2. The aqueous layer was concentrated to dryness using nitrogen gas. The residue was then dissolved

Table 1: NMR data of compounds **1** and **3**.

Number	**1**		**3**	
	δ_H (mult., J in Hz)	δ_C	δ_H (mult., J in Hz)	δ_C
1	—	154.0	—	153.8
2	—	123.2	—	123.9
3	—	135.2	—	135.5
4	6.91 (1H, s)	119.6	7.05 (1H, s)	120.3
5	6.72 (1H, d, 2.0)	105.5	6.84 (1H, d, 2.0)	102.5
6	—	158.1	—	160.4
7	7.00 (2H, d, 2.0)	104.9	7.03 (1H, d, 2.0)	104.4
8	—	157.4	—	157.2
9	—	109.7	—	110.3
10	—	139.3	—	139.1
11	—	208.2	—	171.0
12	2.28 (3H, s)	20.2	2.30 (3H, s)	20.2
OCH_3	—	—	3.88 (3H, s)	55.9
$COCH_3$	2.60 (3H, s)	32.6	—	—
1′	5.07 (1H, d, 7.5)	104.3	5.12 (1H, d, 7.5)	104.1
2′	3.57 (1H, m)	74.9	3.58 (1H, m)	74.9
3′	3.51 (1H, t, 8.5)	78.1	3.54 (1H, m)	78.1
4′	3.45 (1H, m)	71.5	3.45 (1H, m)	71.3
5′	3.68 (1H, m)	77.6	3.56 (1H, m)	78.8
6′	3.70 (1H, m), 4.12 (1H, d, 9.5)	68.6	3.96 (1H, dd, 12.5, 2.5), 3.77 (1H, dd, 12.5, 5.5)	62.4
1″	5.05 (1H, d, 2.5)	111.0	—	—
2″	4.01 (1H, d, 2.5)	78.1	—	—
3″	—	80.5	—	—
4″	3.80 (1H, d, 9.5), 4.04 (1H, d, 9.5)	75.1	—	—
5″	3.36 (2H, m)	65.7	—	—

in 0.1 mL of pyridine, followed by addition of 0.1 mL of 0.06 M L-cysteine methyl ester hydrochloride in pyridine. After heating at 60°C for 2 h, 0.1 mL trimethylsilylimidazole was then added to the solution, followed by heating at 60°C for another 1.5 h. The dried product was partitioned with *n*-hexane and water (0.1 mL each), and the organic layer was analyzed by GC. D-glucose and D-apiose were detected at 14.15 and 4.61 min, respectively.

3. Results and Discussion

Compound **1** was obtained as a yellow powder with the molecular formula $C_{24}H_{30}O_{13}$, which was established from the HR-ESI-MS data with the ion peak at m/z 549.1578 $[M+Na]^+$. The ^1H NMR spectrum of **1** showed signals characteristic for an aromatic proton at δ_H 6.91 (1H, s, H-4), a pair of *meta*-coupled aromatic protons at δ_H 6.72 (1H, d, $J = 2.0$ Hz, H-5) and 7.00 (2H, d, $J = 2.0$ Hz, H-7), two downfielded methyl groups at δ_H 2.28 (3H, s, 3-CH_3), 2.60 (3H, s, CH_3CO), and two anomeric protons at δ_H 5.07 (1H, d, $J = 7.5$ Hz, H-1′) and 5.05 (1H, d, $J = 2.5$ Hz, H-1″). The coupling constants indicated the β ($J = 7.5$ Hz) and α ($J = 2.5$ Hz) conformations of the glycosyl units. Analysis of the ^{13}C NMR and HSQC spectra of **1** revealed the presence of an aromatic methyl at δ_C 20.2 (3-CH_3), an acetyl group (δ_C 208.2 and 32.6) and ten aromatic signals of a naphthalene skeleton (Table 1). In addition, an apiofuranosyl-(1→6)-glucopyranoside moiety was recognized [5]. Acid hydrolysis and GC analysis led to the identification of D-glucose and D-apiose. Comparison with reported data suggested the skeleton was 6-hydroxymusizin [6]. The HMBC correlations of **1** (Figure 2) confirmed that the glucose moiety attached to C-8 and the apiose unit attached to C-6′. From these findings, the structure of compound **1** was determined to be 6-hydroxymusizin 8-*O*-*α*-D-apiofuranosyl-(1→6)-*β*-D-glucopyranoside.

Compound **3** was obtained as a pale-yellow powder. Its molecular formula was determined as $C_{19}H_{22}O_{10}$ on the basis of the HR-ESI-MS that showed the ion peak at m/z 433.1110 $[M+Na]^+$. The ^1H NMR spectrum of **3** displayed resonances for an aromatic proton [δ_H 7.05 (1H, s, H-4)], two *meta*-coupled protons [δ_H 6.84 (1H, d, $J = 2.0$ Hz, H-5) and 7.03 (2H, d, $J = 2.0$ Hz, H-7)], an aromatic methyl [δ_H 2.28 (3H, s, 3-CH_3)], a methoxy group [δ_H 3.88 (3H, s, 6-OCH_3)], and a β-anomeric proton of a sugar moiety [δ_H 5.12 (1H, d, $J = 8.0$ Hz, H-1′). The ^{13}C NMR and HSQC spectra of **3** showed the signals characteristic for a methoxy, an aromatic methyl, a glucose moiety and a naphthalene skeleton. These data were almost identical to that of torachrysone 8-O-*β*-D-glucopyranoside (**2**) except for the replacement of the acetyl group by a carboxylic group (δ_C 171.0) at C-2 [7, 8]. The HMBC correlations confirmed the position of the methoxy and glucose groups at C-6 and C-8, respectively (Figure 2). Acid hydrolysis and GC analysis led to the identification of D-glucose. Therefore, compound **3** was deduced as 6-methoxy-3-methyl-1,6,8-trihydroxy-2-naphthoic acid 8-*O*-*β*-D-glucopyranoside.

By means of spectroscopic methods and in comparison with the reported data, the structure of the known compounds was identified as torachrysone 8-O-*β*-D-glucopyranoside (**2**),

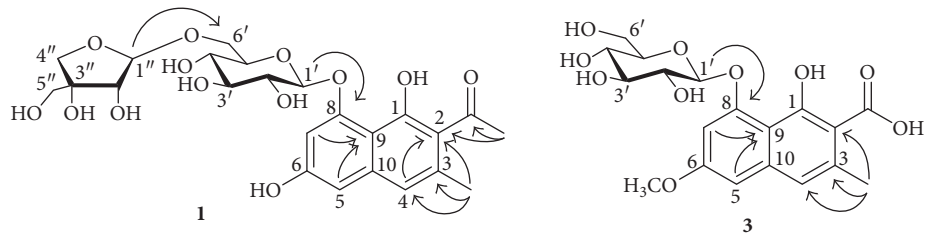

Figure 2: Key HMBC correlations of **1** and **3**.

pleuropyrone A (**4**), emodin (**5**), emodin 8-O-glucopyranoside (**6**), physcionin (**7**), resveratrol (**8**), 2,3,5,4′-tetrahydroxy stilbene-2-O-*β*-glucoside (**9**), benzyl gentiobioside (**10**), and catechin (**11**). Naphtolic derivatives including torachrysone 8-O-*β*-D-glucopyranoside (**2**) have been identified in the Polygonaceae [3,8–12] and other families such as Fabaceae, Rhamnaceae, Araliaceae, and Euphorbiaceae [13–16]. All those compounds possessed a hydroxyl group at C-1, an acetyl group at C-2, and a methyl at C-3 in the naphthalene skeleton. However, compound **3** bearing a carboxylic group instead of an acetyl group in the same skeleton has not been found previously from the natural source. Thus, compound **3** could be considered as a specific chemotaxonomic marker for *F. multiflora*. The anthraquinones and stilbenes including emodin (**5**), emodin 8-O-glucopyranoside (**6**) and 2,3,5,4′-tetrahydroxystilbene-2-O-*β*-glucoside (**9**) are main constituents of *F. multiflora* and have been listed as chemical markers for quality control of this plant material [2, 17]. The present study reports for the first time the occurrence of benzyl gentiobioside (**10**) in Polygonaceae, which can be used as a characteristic chemical constituent of *F. multiflora* in contrast to other species belonging to the genus *Fallopia* and family Polygonaceae.

4. Conclusion

Chemical investigation of the roots of *Fallopia multiflora* led to the isolation of eleven phenolic compounds including 8-*O*-*α*-D-apiofuranosyl-(1→6)-*β*-D-glucopyranoside (**1**), 8-O-*β*-D-glucopyranoside (**2**), 6-methoxy-3-methyl-1,6,8-trihydroxy-2-naphthoic acid 8-*O*-*β*-D-glucopyranoside (**3**), torachrysone pleuropyrone A (**4**), emodin (**5**), emodin 8-O-glucopyranoside (**6**), physcionin (**7**), resveratrol (**8**), 2,3,5,4′-tetrahydroxystilbene-2-O-*β*-glucoside (**9**), benzyl gentiobioside (**10**), and catechin (**11**). Compounds **1** and **3** were elucidated as new naphtolic glycosides. Of note, compound **3** bearing a carboxylic group instead of an acetyl group in the same skeleton has not been found previously from the natural source.

Data Availability

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Acknowledgments

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Supplementary Materials

HR-ESI-MS and NMR spectra of compounds **1** and **3**. (*Supplementary Materials*)

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