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Monoterpene glycosides from *Paeonia hybrida*

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ABSTRACT

Monoterpene glycosides (**1**–**5**, and **7**), together with 14 known compounds, were isolated from the methanol extract of the roots of *Paeonia hybrida*. These compounds included a paeoniflorin-related glycoside with a hybrid structure of paeoniflorin and paeonovicinoside (**1**), a monoterpene glucoside biogenetically related to lactiflorin (**2**), a paeoniflorin-related monoterpene (**3**), arbiflorin-related monoterpenes (**4** and **5**), and a tymol-related monoterpene glycoside (**7**). Their structures were elucidated by extensive spectroscopic examinations.

1. Introduction

Paeoniae Radix, one of the most important traditional medicines, has been used for remedies for gynecological problems cramps, pain, and dizziness in China and Japan (Jingsu New Medical College, 1977). The genus *Paeonia* was shown to contain a variety of paeoniflorin-related monoterpene glycosides (Kaneda et al., 1972; Shimizu et al., 1983; Lin et al., 1996; Murakami et al., 1996) and tannins (Nishizawa et al., 1983; Tanaka et al., 2000; Tanaka et al., 2003).

Paeonia hybrida Pall. (Paeoniaceae) is a folk medicine used in Uzbekistan, and a water decoction of its roots has been used to treat nerve disease (Konovalov et al., 1962). In our continuing study on medicinal plants of Uzbekistan, we have examined the roots of *P. hybrida*. This resulted in isolation of six new monoterpene glycosides, including five paeoniflorin-related compounds, together with 14 known compounds. We describe herein the isolation and structure elucidation of the six new compounds.

2. Result and discussion

The methanol extract of air-dried roots of *Paeonia hybrida* (2.2 kg) was partitioned between H_2O and EtOAc, and then H_2O and *n*-BuOH. The EtOAc and *n*-BuOH extracts were separated by repeated column chromatography using silica gel, Toyopearl HW-40, Sephadex LH-20, and Amberlite XAD-2, and by HPLC to give five new paeoniflorin-related compounds (**1**–**5**), one new monoterpene glycoside (**7**) and 14 known compounds. The known compounds were identified as paeoniflorin and benzoylpaeoniflorin (Kaneda et al., 1972), galloylpaeoniflorin (Kang et al., 1989), albiflorin (Kaneda et al., 1972), lactiflorin (Lang et al., 1990), paeoniflorigenone (Shimizu et al., 1981), paeonovicinoside (Zapesochnaya et al., 1992), 1,2,3,4,6-penta-*O*-galloyl-β-D-glucose (Nishizawa et al., 1983), vanillic acid, methylvanillate, benzoic acid, gallic acid and methyl gallate. Paeoniflorin was obtained as the main component in a yield of ca. 2% from dry weight of this material.

Compound **1** had the molecular formula of $C_{41}H_{50}O_{21}$ (HRESIMS spectral data and NMR spectroscopic data). The ^{1}H NMR spectrum of **1** displayed signals similar to those of paeoniflorin in showing the presence of three methylenes, two methines, one methyl, and a benzoyl, together with an anomeric resonance [δ_H 4.71 (1H, *d*, *J* = 7.6 Hz)] of a glucose moiety. It also showed signals ascribable to a 1,2-substituted aromatic group [δ_H 7.59 (1H, *dd*, *J* = 7.6, 1.6 Hz), 7.40 (1H, *dd*, *J* = 7.6, 1.6 Hz), 7.28 (1H, brd, *J* = 7.6 Hz), 7.09 (1H, brd, *J* = 7.6 Hz)], a characteristic methine [δ_H 6.03 (*s*)], and two sugar moieties. The ^{13}C NMR spectrum displayed, together with a signal pattern closely correlated with that of paeoniflorin, the presence of hexosyl and pentosyl moieties, an acetal carbon, as well as resonances arising from a 1,2-substituted aromatic ring. The ^{13}C NMR signals were closely correlated with the combined resonance patterns of paeoniflorin and paeonovicinoside; differences were found in the presence of the acetal carbon instead of the methyl carboxyl group, the chemical shifts for C-1 to C-6 in

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the paeonovicinoside moiety, and the resonances for C-3″ to C-6″ of the paeoniflorin moiety. These two moieties were shown to be connected through an acetal carbon by observation of the following HMBC correlations: δ_H 6.03 (paeonovicinoside derivative moiety H-7) with C-1 and C-2 in paeonovicinoside derivative moiety, with C-4″ and C-6″ in paeoniflorin moiety. The other observed HMBC correlations are also shown in Fig. 2. The linkages for three sugar moieties were concluded to be β in glucose and α in arabinose from the coupling constant values for the anomeric proton signals. The stereochemistry of H-7 in paeonovicinoside moiety was determined by the NOEDS experiment, in which enhancements were observed at δ_H 3.53 (H-4″ in paeoniflorin moiety) and 3.79 (H-6″ in paeoniflorin moiety) on irradiation of the H-7 signal in the paeonovicinoside moiety. On this basis, compound **1** was named paeonihybridin and elucidated as illustrated in Fig. 1.

The positive-ion HRESIMS of **2** gave a pseudo-molecular ion peak at *m*/*z* 487.1586 ([M + Na]$^+$, calcd for 487.1580), suggesting the molecular formula of $C_{23}H_{28}O_{10}$. The glycosidic nature of **2** was indicated by anomeric resonances [δ_H 4.61 (*d*, *J* = 7.7 Hz); δ_C 100.3]. The ^{1}H NMR spectroscopic data of **2** indicated the presence of one monosubstituted aromatic ring, three methines, two methylenes, one hydroxymethyl, one tertiary methyl, and one hexosyl moiety. In addition, the ^{13}C NMR spectrum exhibited the existence of two quaternary carbons including one oxygen-bearing carbon (δ_C 90.5) and an acetal carbon (δ_C 113.0). The ^{1}H–^{1}H COSY examination indicated occurrence of a CH–CH$_2$–CH–CH–CH$_2$ partial structure, which corresponded to the C-9–C-2–C-3–C-4–C-5 segment in the aglycone moiety. Furthermore, the analysis of the HMBC spectrum clearly indicated correlations of the segment with the quaternary carbons, the tertiary methyl group, and/or the hydroxymethyl group: H-2 with C-7; H-5 with C-1, C-6 and C-7; H-8 with C-4, C-6, C-7, and C-9; H-9 with C-1; Me-10 with C-1 and C-6. The locations of the sugar moiety and the benzoyl moiety were determined at C-6, and C-8, respectively, based on the HMBC correlations: H-8 with C-7′; H-2′ and H-6′ with C-7′; H-1″ with C-6. Taking the molecular formula into account, **2** should have an additional ether linkage in its molecule. Acetylation of **2** with Ac$_2$O/pyridine at room temperature gave a tetraacetate (**2a**) [HRESIMS *m*/*z*; 655.1976 (calcd. for $C_{31}H_{36}O_{14}Na$, 655.2003)]. The ^{1}H NMR spectrum of **2a** showed, together with four acetyl signals [δ_H 2.11, 2.08, 2.04, 2.01 (each 3H, *s*)], four down-field shifted resonances [δ_H 5.00 (1H, *dd*, *J* = 9.6, 8.0 Hz), 5.03 (1H, *t*, *J* = 9.6 Hz), 5.17 (1H, *t*, *J* = 9.6 Hz) and 4.16 (2H, *m*)]. These signals could be assigned to H-2, H-3, H-4, and H$_2$-6 of the sugar moiety, respectively, by the ^{1}H–^{1}H COSY analyses, and their coupling patterns indicated the sugar moiety to be glucose. The β-linkage of the glucosyl moiety was concluded from the coupling constant value. Production of the 2″,3″,4″,6″-tetraacetate indicated that the ether linkage was present at C-1–C-3. Based on these observations, the structure of **2**, designated paeobrin, was elucidated as in Fig. 1. Compound **2** was considered to be derived from paeoniflorin by the similar process for the production of lactiflorin (Lang et al., 1990) as shown in Scheme 1.

Compound **3** gave ^{1}H and ^{13}C NMR spectra similar to those of paeoniflorin, apart from the appearance of the signals in the aromatic region, which showed the presence of a 1,2-substituted aromatic ring; [δ_H 7.00 (brd, *J* = 8.0 Hz), 7.53 (*dt*, *J* = 8.0, 1.6 Hz), 6.97 (brt, *J* = 8.0 Hz), 7.94 (*dd*, *J* = 8.0, 1.6 Hz); δ_C 162.8, 137.0, 131.2, 120.4, 118.5, 113.6]. The molecular formula ($C_{23}H_{28}O_{12}$) of **3**, confirmed by HRESIMS [*m*/*z* 519.1459 (M + Na)$^+$] indicated one oxygen more than that of paeoniflorin, suggesting the presence of a salicyloyl group. The HMBC correlations observed in **3** were consistent with this structure. Therefore, structure **3** was identified as salicylpaeoniflorin (Fig. 1).

The ^{1}H and ^{13}C NMR spectra of **4** were closely correlated with those of 1-*O*-β-D-glucopyranosyl-paeonisuffrone (Murakami et al., 1996), except for the observation of signals due to a monosubstituted aromatic ring and an ester carbonyl group, suggesting the presence of a benzoyl group. The benzoyl group was concluded to be attached to C-8 of the aglycone moiety from the HMBC correlations: H$_2$-8 with C-7′; H-2′ and H-6′ with C-7′. Thus, **4** was elucidated as 6-*O*-β-D-glucopyranosyl-8-*O*-benzoyl-paeonisuffrone.

The same molecular formula of $C_{24}H_{30}O_{11}$ for **5** and **6** was established by the HRFABMS. The ^{1}H NMR spectra of **5** and **6** quite resembled each other, and also closely correlated with that of **4**, except for the appearance of a methine signal [δ_H 4.86 (*s*) for **5**; δ_H 5.14 (*s*) for **6**] and a methoxyl signal [δ_H 3.42 for **5**; δ_H 3.34 for **6**] in place of the H$_2$-9 resonances. The HMBC spectra of **5** and **6** displayed the same long-range correlations, and were also correlated with those of **4**; Me-10 with C-1, C-2, and C-6; H$_2$-2 with C-1 and C-3; H$_2$-5 with C-3, C-4, C-6, and C-7; H$_2$-8 with C-4, C-6, C-7, and C-7′; H-1″ with C-6. The presence of the methoxyl group at C-9 in each case was indicated by the HMBC correlations between the methine signal with C-1, C-4, C-6, C-7, and the methoxyl carbon. Therefore, compounds **5** and **6** are stereoisomers at C-9, each other. The NOEDS experiments were carried out with their tetraacetates (**5a** and **6a**, respectively) in order to elucidate the configuration at C-9. Thus, an NOE enhancement was obtained in

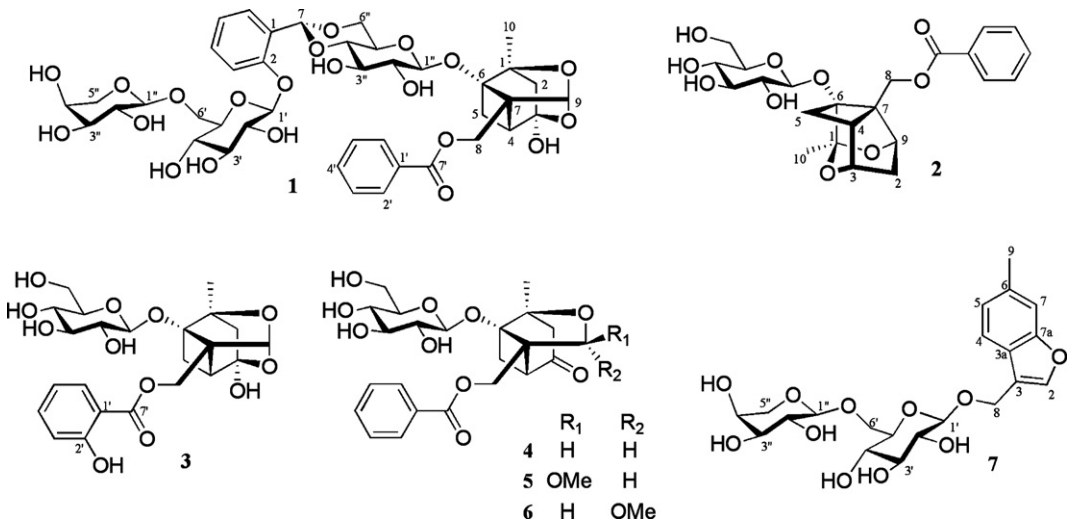


Fig. 1. Structures of **1**–**7** from *P. hybrida*.

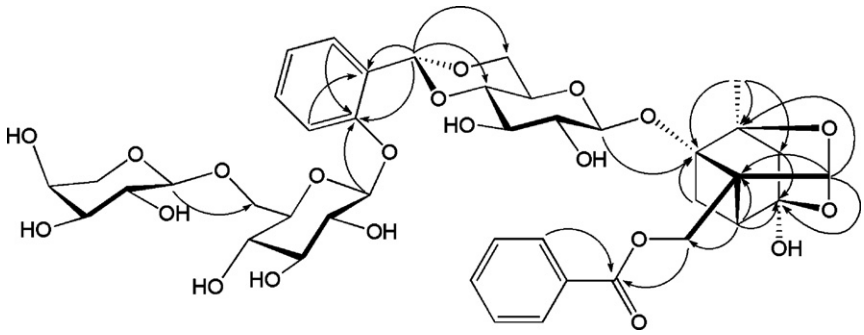
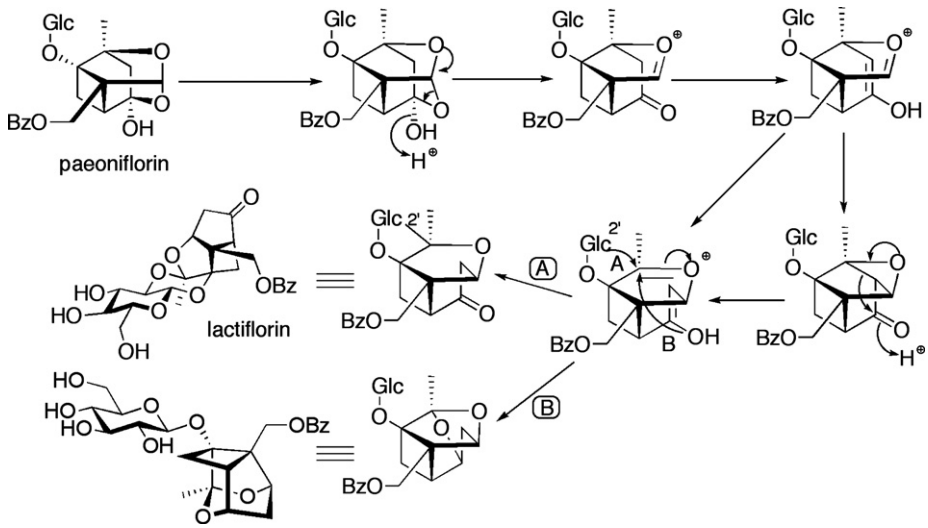


Fig. 2. HMBC correlations of compound **1**.



Scheme 1. Possible pathway from paeoniflorin to lactiflorin and **2**.

the acetoxyl signal (δ_H 2.12) attached to the glucosyl C-2″, together with H-9, on irradiation of the methoxyl signal in the case of **5a**. In contrast, irradiation of the methoxyl signal of **6a** showed NOE enhancements of H-2β, H-9, and H-2′ resonances (Fig. 3). These results indicated that the methoxyl group in **5a** was oriented in the *exo*-side, while that in **6a** was placed in the *endo*-side. From the observations described above, the structures of **5** and **6** were assigned as shown in Fig. 1. The elucidated structure **5** was the same as that of paeonidanin (Kostova et al., 1998). However, the ^{1}H and ^{13}C NMR spectroscopic data of tetraacetate of paeonidanin reported in the literature were inconsistent with those of **5a**, but they were the same as those of **6a**. Therefore, the structure for paeonidanin should be revised as for **6**.

The ^{1}H NMR spectroscopic data of compound **7** had four aromatic protons including a 1,3,4-trisubstituted benzene ring [δ_H 7.78 (*s*, H-2), 7.66 (*d*, *J* = 8.0 Hz, H-4), 7.31 (*d*, *J* = 1.6 Hz, H-7), and 7.13 (*dd*, *J* = 8.0, 1.6 Hz, H-5)], one methylene [δ_H 5.06, 4.87 (each *d*, *J* = 12.4 Hz, H-8)], and one methyl [δ_H 2.49 (*s*, Me-10)]. The existence of two sugar moieties was indicated by anomeric resonances [δ_H 4.43 (*d*, *J* = 7.6 Hz), 4.40 (*d*, *J* = 6.8 Hz)]. The carbon resonances

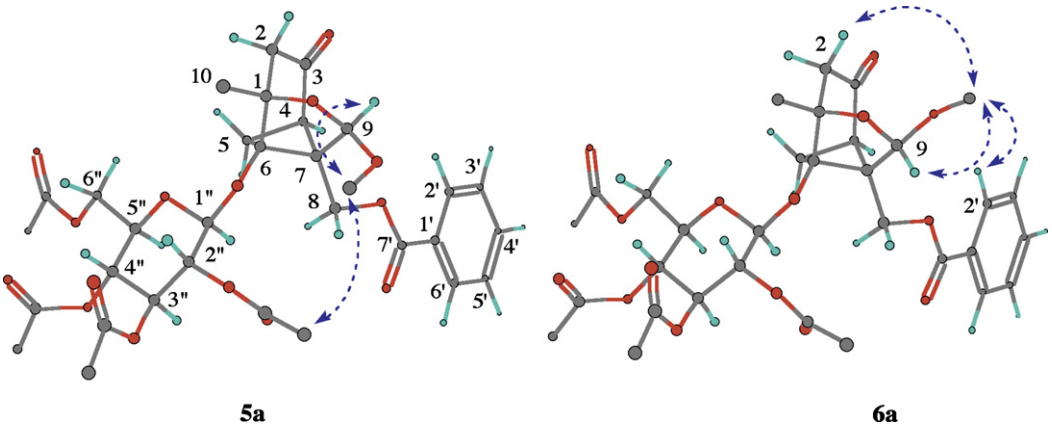


Fig. 3. Selected NOESY correlations and relative stereochemistry of **5a** and **6a** (hydrogen atoms of methyl groups were omitted).

arising from the sugar moieties coincided with those of paeonovicinoside, indicating the presence of an arabinopyranosyl-(1 → 6)-glucopyranosyl moiety. The aglycone part of **7** was elucidated as 6-methyl-benzofuran-3-methanol from analysis of its HMBC spectrum, and the following key long-range correlations were observed: H-2 with C-7a, and C-3a; H-4 with C-7a, and C-3; H-7 with C-3a; H_2-8 with C-3, and C-2; Me-9 with C-5, C-6, and C-7. The sugar linkages were concluded from the anomeric proton signals [δ_H 4.43 (*d*, *J* = 7.6 Hz, H-1′), 4.40 (*d*, *J* = 6.8 Hz, H-1″)]. From the spectroscopic evidence, **7** was assigned as 3-methyl-*O*-[α-arabinopyranosyl-(1 → 6)-β-glucopyranosyl]-6-methyl-benzofuran.

2.1. Concluding remarks

Compounds **1**–**6** are considered to be derived from paeniflorin, and therefore, most likely have the same absolute stereochemistry as paeoniflorin; however, their absolute stereochemistries still remain to be determined. The roots of *Paeonia hybrida* contained considerable amount of paeoniflorin (ca. 2%) and, therefore, this plant is similar to those medicinally Paeony roots used in Japan and China. In addition, it was shown to contain a variety of paeoniflorin-related monoterpenes, among which compounds **1** and **2** have unique structures. The isolation of compounds **1**–**6**, together with known paeoniflorin-related monoterpenes, suggested the presence of complicated metabolic pathway of peaoniflorin in *Paeonia hybrida*.

3. Experimental

3.1. General

Optical rotations were measured with a DIP-370 digital polarimeter (JASCO). IR spectra were recorded on a FT-IR 420 Fourier transform infrared spectrometer (JASCO). NMR (^{1}H NMR: 400 MHz, ^{13}C NMR: 100 MHz, using TMS as int. stand.) spectra were measured on an AVANCE 400 Fourier transform spectrometer (Bruker). MS were obtained on a JMS-SX102A (JEOL) and LCT PREMIER (Waters). Column chromatography: silica gel 60N (63–210 nm; Kanto Kagaku), Toyopearl HW-40 (Tosoh). Sephadex LH-20 (Pharmacia). HPLC columns: gel permeation (GS-310 2G; Asahipak), ODS (Mightysil RP-18 GP 250-20; Kanto Kagaku). TLC was conducted precoated Kieselgel 60 F254 plates (0.2 mm, Merck), and spots were located by ultraviolet illumination and by spraying cerium Sulfate–sulfuric acid reagent with heating.

3.2. Plant material

The roots of *Paeonia hybrida* Pall. were collected at Tashkent region, Uzbekistan, in August 2003. Herbarium specimens were deposited in the botanical garden of the University of Tokushima (Specimen Number: UTP040001).

3.3. Extraction and isolation

The dried roots of *P. hyrida* (2.2 kg) were extracted three times with MeOH at 60 °C. After concentration, the methanol extract was suspended in H_2O, and then successively partitioned with hexane, EtOAc, *n*-BuOH, and H_2O. The EtOAc layer (36.9 g) was subjected to a silica gel CC of increasing polarity ($CHCl_3$–MeOH, 100:0 → 1:1) to give fractions 1–9. Repeated CC of fraction 4 (2.0 g) with Toyopearl HW-40 ($CHCl_3$–MeOH, 1:1), silica gel ($CHCl_3$–MeOH, 9:1 → 1:1), and gel permeation chromatography (GPC) gave paeonifloigenone (37 mg) and methylvaillate (10 mg). Fraction 5 (1.1 g) was subjected to silica gel CC ($CHCl_3$–MeOH, 95:5 → 1:1) to give fractions 5.1–5.6. Fraction 5.5 was further passed through Toyopearl HW-40 CC ($CHCl_3$–MeOH, 1:1) and then ODS HPLC (MeOH–H_2O, 1:1) to give benzoic acid (37 mg). Fraction 5.6 was purified by Toyopearl HW-40 CC ($CHCl_3$–MeOH, 1:1) to give vanillic acid (21 mg). Fraction 6 (4.9 g) was applied of Toyopearl HW-40 ($CHCl_3$–MeOH, 1:1) CC to give further four fractions (6.1–6.4) and methylgallate (2.6 g). Fraction 6.3 was subjected to silica gel CC ($CHCl_3$–MeOH, 9:1 → 1:1) to give fractions 6.3.1–6.3.5. Fraction 6.3.4 was purified by GPC (MeOH) to give benzoylpaeoniflorin (43 mg) and lactiflorin (21 mg). Repeated GPC (MeOH) and ODS HPLC (MeOH–H_2O, 1:1) of fraction 6.3.5 gave **2** (5 mg). Fraction 7 (7.5 g) applied to a Sephadex LH-20 column (MeOH) to give fractions 7.1–7.5. Fraction 7.2 was subsequently separated by silica gel CC ($CHCl_3$–MeOH, 8:2 → 0:1) to give further seven fractions (7.2.1–7.2.7). Fraction 7.2.2 was separated by GPC (MeOH) to give fractions 7.2.2.1–7.2.2.6. ODS HPLC (MeOH–H_2O, 7:3) of fraction 7.2.2.6 gave **5** (11 mg). Fraction 7.2.3 was separated by GPC (MeOH) to give frac-

Table 1
NMR spectroscopic data for compound **1** and reference data in CD_3OD

Position	**1**		Reference
	^{1}H[a]	^{13}C[b]	^{13}C[a]
Paeoniflorin moiety			*Paeoniflorin*
1	–	87.0	87.2
2	1.87 (1H, *d*, 12.6)	44.5	44.5
	2.19 (1H, *d*, 12.6)		
3	–	106.3	106.4
4	2.65 (1H, *d*, 5.6)	43.9	43.9
5	1.93 (1H, *d*, 11.0)	23.3	23.4
	2.59 (1H, *dd*, 11.0, 5.6)		
6	–	89.6	89.3
7	–	72.3	72.1
8	4.89 (2H, AB*q*, 12.1)	61.7	61.7
9	5.48 (1H, *s*)	102.3	102.2
10	1.37 (3H, *s*)	19.6	19.6
1′	–	131.2	131.1
2′, 6′	8.18 (1H, *dd*, 8.0, 1.2)	130.7	130.6
3′, 5′	7.54 (1H, *t*, 8.0)	129.7	129.6
4′	7.67 (1H, *tt*, 8.0, 1.2)	134.5	134.4
7′	–	168.0	168.0
1″	4.71 (1H, *d*, 7.6)	100.7	100.1
2″	3.35 (1H, *m*)[c]	75.9	74.9
3″	3.59 (1H, *t*, 8.8)	74.6	77.8
4″	3.53 (1H, *t*, 8.8)	82.1	71.6
5″	3.47 (1H, *m*)	67.6	77.9
6″	3.79 (1H, *t*, 10.2)	69.9	62.8
	4.28 (1H, *dd*, 10.2, 4.8)		
Paeonovicinoside moiety			*Paeonovicinoside*
1	–	128.0	122.2
2	–	156.1	158.6
3	7.28 (1H, *brd*, 7.6)	117.9	119.2
4	7.40 (1H, *dt*, 7.6, 1.6)	131.5	135.4
5	7.09 (1H, *brt*, 7.6)	123.5	123.6
6	7.59 (1H, *dd*, 7.6, 1.6)	128.5	132.0
7	6.03 (1H, *s*)	98.5	168.5
1′	4.84 (1H, *d*, 6.8)	102.9	103.8
2′	3.53 (1H, *m*)	75.1	74.9
3′	3.51 (1H, *m*)	77.8	77.4
4′	3.47 (1H, *m*)	71.4	71.4
5′	3.66 (1H, *m*)	77.1	77.5
6′	3.81 (1H, *dd*, 9.6, 6.8)	69.4	69.6
	4.14 (1H, *dd*, 9.6, 1.6)		
1″	4.34 (1H, *d*, 6.7)	104.9	105.1
2″	3.62 (1H, *dd*, 8.8, 6.7)	72.4	72.5
3″	3.53 (1H, *m*)	74.1	74.2
4″	3.81 (1H, *m*)	69.3	69.6
5″	3.48 (1H, *dd*, 12.4, 1.6)	66.6	66.8
	3.86 (1H, *dd*, 12.4, 3.6)		
–OCH_3	–	–	52.8

[a] δ_H ppm (mult., *J* in Hz), 400 MHz.
[b] δ_C ppm, 100 MHz.
[c] Overlapped with solvent signals.

tions 7.2.3.1–7.2.3.11. Then, fraction 7.2.3.9 was purified by ODS HPLC (MeOH–H_2O, 7:3) to give paeonidanin (**6**; 22 mg). ODS HPLC (MeOH–H_2O, 1:1) of fraction 7.2.3.11 gave **4** (4 mg). A part (160 mg) of fraction 7.2.4 (5.2 g) was separated by GPC (MeOH) to give paeoniflorin (124 mg). Fraction 7.3 was further separated by silica gel CC ($CHCl_3$–MeOH, 8:2 → 0:1) and ODS HPLC (MeOH–H_2O, 3:2) to give fractions 7.3.1–7.3.5 and gallic acid (85 mg). Fraction 7.3.5 was purified by GPC (MeOH) and ODS HPLC (MeOH–H_2O, 1:1) to give fractions 7.3.5.1–7.3.5.3 and galloylpaeoniflorin (83 mg). Fraction 7.3.5.2 was further purified by GPC (MeOH) to give **3** (3 mg). Fraction 8 (13.6 g) was repeatedly separated by CC with Amberlite XAD-2 (MeOH–H_2O, 0:100 → MeOH–H_2O, 100:0), silica gel ($CHCl_3$–MeOH, 8:2 → 0:1) and Sephadex LH-20 (MeOH) to give 1,2,3,4,6-penta-*O*-galloyl-*β*-D-glucose (2.9 g).

The *n*-BuOH layer (74.2 g) was subjected to silica gel CC ($CHCl_3$–MeOH, 8:2 → 0:1) to give ten fractions (1–10). Fraction 6 (19.4 g) was mainly consisted of paeoniflorin, and pure sample (55 mg) was obtained from a part of fraction 6 (71 mg) by GPC (MeOH). Fraction 8 (2.5 g) was separated by Sephadex LH-20 (MeOH) and silica gel ($CHCl_3$–MeOH–H_2O, 8:2:0.2 → 7:3:0.5) to give fractions 8.1–8.10. Fraction 8.2 was purified by GPC (MeOH) to give paeonovicinoside (81 mg). Fraction 8.3 was separated by ODS HPLC (MeOH–H_2O, 1:1) to give fractions 8.3.1–8.3.8. Fraction 8.3.3 was purified by GPC (MeOH) to give albiflorin (71 mg). Fraction 8.3.8 was purified by GPC (MeOH) to give **1** (5 mg) and **7** (3 mg).

3.4. Paeonihybridin (*1*)

White amorphous powder; $[\alpha]_D$−22.8 (MeOH, *c* 0.5); HRESIMS *m/z* 901.2740 $[M + Na]^+$ (calcd. for $C_{41}H_{50}O_{21}Na$, 901.2742); IR (KBr) υ_{max} 3440, 2883, 1714, 1608, 1494, 1454, 1390, 1278 cm^{-1}; for ^1H NMR and; ^{13}C NMR spectroscopic data, see Table 1.

3.5. Paeobrin (*2*)

White amorphous powder; $[\alpha]_D$−23.5 (MeOH, *c* 0.2); HRESIMS *m/z* 487.1586 $[M + Na]^+$ (calcd. for $C_{23}H_{28}O_{10}Na$, 487.1580); IR (KBr) υ_{max} 3423, 2973, 1720, 1602, 1452, 1390, 1276 cm^{-1}; for ^1H NMR and; ^{13}C NMR spectroscopic data, see Table 2.

3.6. Salicylpaeoniflorin (*3*)

White amorphous powder; $[\alpha]_D$−2.3 (MeOH, *c* 0.3); HRESIMS *m/z* 519.1459 $[M + Na]^+$ (calcd. for $C_{23}H_{28}O_{12}Na$, 519.1478); IR (KBr) υ_{max} 3351, 1718, 1612, 1484, 1398, 1297 cm^{-1}; for ^1H NMR and ^{13}C NMR spectroscopic data, see Table 2.

Table 2
NMR spectroscopic data for compounds **2–6** in CD_3OD

Position	**2**		**3**		**4**		**5**		**6**	
	^1H[a]	^{13}C[b]	^1H[a]	^{13}C[b]	^1H[a]	^{13}C[b]	^1H[a]	^{13}C[b]	^1H[a]	^{13}C[b]
1	–	113.0	–	87.3	–	88.3	–	88.3	–	87.5
2	1.48 (1H, *ddd*, 12.4, 3.2, 2.2)	42.3	1.86 (1H, *d*, 12.6)	44.6	2.42 (1H, *d*, 17.2)	49.0[c]	2.46 (1H, *d*, 17.2)	51.3	2.54 (1H, *d*, 18.0)	49.7
	2.26 (1H, *brd*, 12.4)		2.24 (1H, *d*, 12.6)		3.09 (1H, *d*, 17.2)		3.14 (1H, *d*, 17.2)		2.94 (1H, *d*, 18.0)	
3	4.45 (1H, *m*)	78.6	–	106.4	–	211.9	–	211.3	–	209.5
4	2.79 (1H, *dd*, 7.3, 3.9)	41.4	2.64 (1H, *d*, 6.6)	44.0	3.03 (1H, *d*, 7.6)	50.3	3.08 (1H, *m*)	49.0	3.01 (1H, *m*)	48.4
5	2.04 (1H, *d*, 9.9)	22.7	2.00 (1H, *d*, 10.9)	23.2	2.46 (1H, *d*, 10.8)	29.3	2.46 (1H, *m*)	30.1	2.22 (1H, *dd*, 8.8, 1.6)	27.5
	2.54 (1H, *dd*, 9.9, 7.3)		2.54 (1H, *dd*, 10.9, 6.6)		3.08 (1H, *m*)		3.09 (1H, *m*)		3.00 (1H, *m*)	
6	–	90.5	–	89.4	–	87.2	–	85.3	–	88.5
7	–	68.3	–	72.1	–	62.3	–	64.9	–	65.1
8	4.90 (2H, *s*)	63.2	4.83 (1H, *d*, 13.1) 4.87 (1H, *d*, 13.1)	62.2	4.76 (1H, *d*, 11.7) 4.86 (1H, *d*, 11.7)	65.7	4.69 (1H, *d*, 11.6) 4.94 (1H, *d*, 11.6)	62.5	4.77 (1H, *d*, 12.0) 4.87 (1H, *d*, 12.0)	63.9
9	4.65 (1H, *m*)	82.9	5.46 (1H, *s*)	102.3	3.77 (1H, *d*, 10.2) 4.01 (1H, *d*, 10.2)	71.6	4.86 (1H, *s*)	106.0	5.14 (1H, *s*)	107.6
10	1.44 (3H, *s*)	18.5	1.41 (3H, *s*)	19.6	1.47 (3H, *s*)	20.4	1.52 (3H, *s*)	21.0	1.47 (3H, *s*)	20.7
1′	–	131.3	–	113.6	–	131.0	–	131.1	–	131.2
2′	8.06 (1H, *dd*, 7.8, 1.3)	130.5	–	162.8	8.04 (1H, *dd*, 8.0, 1.2)	130.6	8.04 (1H, *dd*, 7.8, 1.6)	130.5	8.06 (1H, *d*, 7.8)	130.6
3′	7.54 (1H, *t*, 7.8)	129.7	7.00 (1H, *brd*, 8.0)	118.5	7.54 (1H, *t*, 8.0)	129.7	7.54 (1H, *dd*, 7.8, 7.4)	129.7	7.53 (1H, *t*, 7.8)	129.6
4′	7.66 (1H, *dt*, 7.8, 1.3)	134.4	7.53 (1H, *dt*, 8.0, 1.6)	137.0	7.66 (1H, *dt*, 8.0, 1.2)	134.5	7.66 (1H, *dd*, 7.4, 1.6)	134.5	7.65 (1H, *t*, 7.8)	134.4
5′	7.54 (1H, *t*, 7.8)	129.7	6.97 (1H, *brt*, 8.0)	120.4	7.54 (1H, *t*, 8.0)	129.7	7.54 (1H, *dd*, 7.8, 7.4)	129.7	7.53 (1H, *t*, 7.8)	129.6
6′	8.06 (1H, *dd*, 7.8, 1.3)	130.5	7.94 (1H, *dd*, 8.0, 1.6)	131.2	8.04 (1H, *dd*, 8.0, 1.2)	130.6	8.04 (1H, *dd*, 7.8, 1.6)	130.5	8.06 (1H, *d*, 7.8)	130.6
7′	–	168.0	–	171.2	–	167.9	–	167.8	–	167.9
1″	4.61 (1H, *d*, 7.7)	100.3	4.56 (1H, *d*, 7.6)	100.2	4.67 (1H, *d*, 7.8)	100.3	4.60 (1H, *d*, 7.6)	100.2	4.60 (1H, *d*, 7.6)	100.0
2″	3.23 (1H, *d*, 8.8, 7.7)	75.1	3.23 (1H, *m*)	75.0	3.32 (1H, *m*)	75.1	3.29 (1H, *m*)	75.0	3.29 (1H, *m*)	75.0
3″	3.31 (1H, *m*)	78.1	3.35 (1H, *m*)[c]	78.1	3.38 (1H, *m*)[c]	78.1	3.30 (1H, *m*)	77.9	3.30 (1H, *m*)	78.1
4″	3.29 (1H, *m*)	71.7	3.28 (1H, *m*)	71.8	3.31 (1H, *m*)	71.8	3.40 (1H, *m*)	71.7	3.40 (1H, *d*, 8.4)	71.5
5″	3.27 (1H, *m*)	77.9	3.28 (1H, *m*)	78.0	3.32 (1H, *m*)	78.1	3.29 (1H, *m*)	78.1	3.29 (1H, *m*)	78.1
6″	3.69 (1H, *dd*, 11.8, 5.3)	62.8	3.64 (1H, *dd*, 11.6, 5.2)	62.9	3.66 (1H, *dd*, 12.0, 6.0)	62.9	3.67 (1H, *dd*, 11.6, 5.6)	62.9	3.65 (1H, *dd*, 11.6, 6.0)	62.9
	3.89 (1H, *dd*, 11.8, 1.8)		3.90 (1H, *d*, 11.6)		3.91 (1H, *dd*, 12.0, 2.0)		3.93 (1H, *dd*, 11.6, 2.0)	57.2	3.90 (1H, *dd*, 11.6, 1.4)	55.8
-OCH_3							3.42 (3H, *s*)		3.34 (3H, *s*)	

[a] δ_H ppm (mult., *J* in Hz), 400 MHz.
[b] δ_C ppm, 100 MHz.
[c] Overlapped with solvent signals.

3.7. 6-O-β-D-Glucopyranosyl-8-O-benzoyl-paeonisuffrone (**4**)

White amorphous powder; $[\alpha]_D$ −59.2 (MeOH, *c* 0.3); HRESIMS *m*/*z* 487.1550 $[M + Na]^+$ (calcd. for $C_{23}H_{28}O_{10}Na$, 487.1580); IR (KBr) υ_{max} 3480, 2875, 1716, 1600, 1513, 1450, 1278 cm^{-1}; for ^1H NMR and ^{13}C NMR spectroscopic data, see Table 2.

3.8. 9-Epi-paeonidanin (**5**)

White amorphous powder; $[\alpha]_D$ −98.0 (MeOH, *c* 0.8); HRFABMS *m*/*z* 517.1671 $[M + Na]^+$ (calcd. for $C_{24}H_{30}O_{11}Na$, 517.1686); IR (KBr) υ_{max} 3370, 2842, 1720, 1602, 1452, 1278 cm^{-1}; for ^1H NMR and ^{13}C NMR spectroscopic data, see Table 2.

3.9. Paeonidanin (**6**)

White amorphous powder; $[\alpha]_D$ −34.1 (MeOH, *c* 1.5); HRFABMS *m*/*z* 517.1664 $[M + Na]^+$ (calcd. for $C_{24}H_{30}O_{11}Na$, 517.1686); IR (KBr) υ_{max} 3459, 2908, 1714, 1602, 1452, 1276 cm^{-1}; for ^1H NMR and ^{13}C NMR spectral data, see Table 2.

3.10. 3-Methyl-O-[α-arabinopyranosyl-(1 → 6)-β- glucopyranosyl]-6-methyl-benzofuran (**7**)

White amorphous powder; $[\alpha]_D$ −25.7 (MeOH, *c* 0.1); HRESIMS *m*/*z* 479.1546 $[M + Na]^+$ (calcd. for $C_{21}H_{28}O_{11}Na$, 479.1529); ^1H NMR spectroscopic (400 MHz, CD_3OD): δ_H 7.78 (*s*, H-2), 7.66 (*d*, *J* = 8.0 Hz, H-4), 7.31 (*d*, *J* = 1.6 Hz H-7), 7.13 (*dd*, *J* = 8.0, 1.6 Hz, H-5), 5.06 (*d*, *J* = 12.4 Hz, H-8a), 4.87 (*d*, *J* = 12.4 Hz, H-8b), 4.43 (*d*, *J* = 7.6 Hz, H-1′), 4.40 (*d*, *J* = 6.8 Hz, H-1″), 4.18 (*dd*, *J* = 11.6, 2.4 Hz, H-6′a), 3.92 (*dd*, *J* = 12.4, 3.2 Hz, H-5′a), 3.84 (*m*, H-4″), 3.81 (*dd*, *J* = 11.6, 6.4 Hz, H-6′b), 3.66 (*dd*, *J* = 8.4, 6.8 Hz, H-2″), 3.57 (*dd*, *J* = 12.4, 2.0 Hz, H-5″b), 3.55 (*dd*, *J* = 8.4, 3.2 Hz, H-3″), 3.52 (*m*, H-5′), 3.35 (*m*, H-3′ and H-4′), 3.29 (*m*, H-2′), 2.49 (*s*, Me-10); ^{13}C NMR spectral data (100 MHz, CD_3OD): δ_C 157.4 (C-7a), 144.6 (C-2), 135.9 (C-6), 125.2 (C-5), 121.1 (C-4), 126.1 (C-3a), 118.4 (C-3), 112.3 (C-7), 105.3 (C-1″), 103.0 (C-1′), 77.8 (C-3′), 77.0 (C-5′), 75.0 (C-2′), 74.3 (C-3″), 72.4 (C-2″), 71.7 (C-4′), 69.6 (C-6′), 69.5 (C-4″), 66.8 (C-5″), 62.3 (C-8), 21.7 (C-9).

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