HETEROCYCLES, Vol. 65, No. 5, 2005, pp. 1189 - 1196
Received, 13th January, 2005, Accepted, 22nd March, 2005, Published online, 24th March, 2005

FOUR NEW COUMARIN GLUCOSIDES FROM THE ROOTS OF *HERACLEUM RAPULA*

Weilie Xiao, [a,b] Shenghong Li, [a,*] Yunheng Shen, [a,b] Xiaoli Li, [a,b] and Handong Sun [a,*]

a) State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, The Chinese Academy of Sciences, Kunming 650204, Yunnan, P. R. China; Tel: 86- 871-5223251. Fax: 86- 871-5216343, E-mail: shli@mail.kib.ac.cn and hdsun@mail.kib.ac.cn

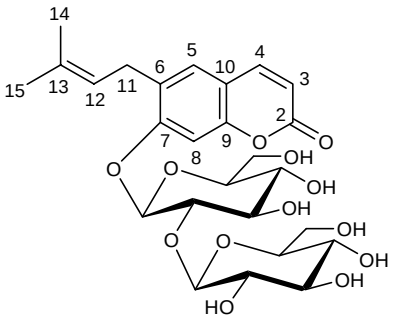
b) The Graduate School of the Chinese Academy of Sciences, Beijing 100039, P. R. China

Abstract – Four new coumarin glucosides, 7-*O*-[β-D-glucopyranosyl-(1→2)-β-D-glucopyranosyl]demethylsuberosin (**1**), 8-*O*-[β-D-apiofuranosyl-(1→6)-β-D-glucopyranosyl]-8-hydroxybergapten (**2**), 8-*O*-[β-D-apiofuranosyl-(1→6)-β-D-glucopyranosyl]xanthotoxol (**3**), and 5-*O*-[β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl]-8-hydroxybergaptol (**4**), were isolated from the roots of *Heracleum rapula*. The structures of these compounds were determined on the basis of their 1D NMR, 2D NMR and HRMS spectral data. Their inhibitory effects on rabbit platelet aggregation respectively induced by PAF, AA and APD were tested. Weak to moderate inhibitory activities for each compound were observed.

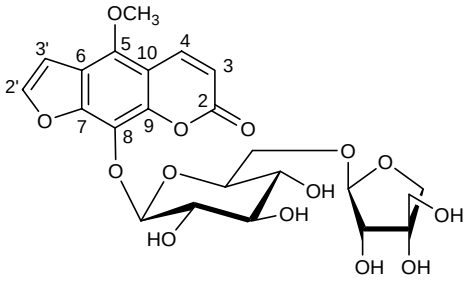
INTRODUCTION

Heracleum rapula (Umbelliferae), widely distributed in Yunnan province of China, has been used in Chinese traditional folk medicine for rheumatic disease, lumbago, gastralgia, and injuries from falls, contusions and strains. It can also used for dispelling wind, removing dampness, expelling cold and relieving pain. [1] It has been reported that the water extract showed antibiotic and antiasthmatic effects, according to the results of pharmcological experiments.[2] Our previous studies have shown the presence of a series of coumarins in this plant.[1, 3-4] Reinvestigation of the more polar part of the acetone extract of this

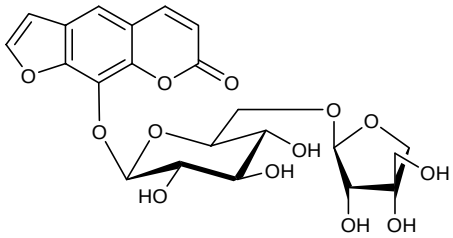
plant led to the isolation of four new coumarin glucosides, 7-*O*-[β-D-glucopyranosyl-(1→2)-β-D-glucopyranosyl]demethylsuberosin (**1**), 8-*O*-[β-D-apiofuranosyl-(1→6)-β-D-glucopyranosyl]-8-hydroxybergapten (**2**), 8-*O*-[β-D-apiofuranosyl-(1→6)-β-D-glucopyranosyl]xanthotoxol (**3**), and 5-*O*-[β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl]-8-hydroxybergaptol (**4**). This paper deals with the isolation and structure elucidation of the four new compounds and their antiplatelet aggregation activity tested.



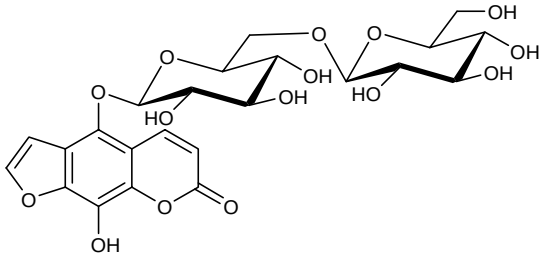
1



2



3



4

RESULTS AND DISCUSSION

Compound (**1**), showed a molecular ion peak at *m/z* = 554 in its negative ESIMS, consistent with a molecular formula of $C_{26}H_{34}O_{13}$, which was confirmed by its HRESIMS. The ^1H and ^{13}C NMR spectra (Tables 1 and 2) coupled with the UV absorptions at 207, 292, 323, 389 nm and the IR absorptions at 1623 and 1720 cm^{-1} suggested that **1** possesses a coumarin skeleton. In the ^1H NMR spectrum of **1**, the presence of two typical aromatic proton singlets at δ_H 7.25 (1H, s) and 7.27 (1H, s) indicated a 6, 7-disubstituted coumarin. In addition, the NMR spectra also showed proton signals at δ_H 1.67 (3H, s), 1.76 (3H, s), 3.70 (1H, dd, *J* = 9.4, 19.8 Hz), 3.88 (1H, dd, *J* = 9.4, 19.8 Hz), 5.60 (1 H, t, *J* = 9.4 Hz) and carbon signals at δ_C 18.0 q, 25.8 q, 28.2 t, 122.7 d, 133.4 s, suggesting the existence of a 3,3-dimethyl-allyl chain, which was attached to C-6 by the HMBC cross-peaks from proton at δ_H 5.60 (H-12) to C-6 and from proton at δ_H 3.70 and 3.88 (H-11) to C-5 and C-7. Comparison of the NMR spectral data of **1** with those of a known isoprenylated coumarin, demethylsuberosin[5] revealed that the two compounds were very alike except for the appearance of two additional glucoses [δ_H 5.69 (1H, d, *J* = 7.1 Hz) and 5.50

(1H, d, J = 7.8 Hz), anomeric protons; δ_C 99.9 d, 83.4 d, 78.9 d , 70.8 d , 78.2 d, 62.7 t, 106.5 d , 76.7 d, 78.7 d, 71.6 d, 78.2 d, and 62.2 t] in **1**. The largely downfield-shifted C-2 signal of glc-1 from *ca.* δ_C 74 d to 83.4 d, along with the ^3J correlations between H-1 of glc-2 and C-2 of glc-1, and between H-2 of glc-1 and C-1 of glc-2 in the HMBC spectrum (Table 3), indicated a glc-2(1→2)glc-1 linkage. Furthermore, the sugar chain was unambiguously assigned to be at C-7 based on the obvious HMBC correlation from the anomeric proton of glc-1 to C-7. Both glucoses were deduced to have β-configuration from the coupling constants (J = 7.1 and 7.8 Hz respectively) of their anomeric protons. Thus, **1** was elucidated as 7-*O*-[β-D-glucopyranosyl-(1→2)-β-D-glucopyranosyl]demethylsuberosin.

Compound (**2)**, obtained as pale yellow amorphous solid, had a molecular formula of $C_{23}H_{26}O_{14}$ as determined by its HREIMS (found: 526.1249; calcd: 526.1244). In the ^{1}H and ^{13}C NMR spectra (Tables 1 and 2), signals in the aromatic region were typical of linear furanocoumarins.[6] The shapes and the absorption of UV spectrum (204, 221, 249, 255, 261, 310 nm) indicated the existence of a 5, 8-dioxygenated psoralen skeleton.[7] A methoxyl singlet at δ_H 3.98 (3H, s) showed ^{1}H-^{13}C long-range correlation with the carbon signal at δ_C 144.7 (s, C-5) in the HMBC spectrum suggesting that it was assignable to C-5 of the coumarin nucleus. By further analysis of the NMR spectra, there were still signals arising form two sugars observed obviously. One was recognized as a β-apiose [δ_H 5.55 (1H, br s, api-H-1), other signals overlapped between δ_H 4.05-4.55; δ_C 110.8 d, 77.8 d, 80.6 s, 74.9 t, 65.7 t], and the other as a β-glucose [δ_H 6.23 (1H, d, J = 6.9 Hz, glc-H-1), other signals overlapped between δ_H 4.08-4.53; δ_C 104.1 d, 75.4 d, 78.5 d, 71.4 d, 77.8 d, 68.2 t]. In the HMBC spectrum (Table 3), the anomeric proton of glucose demonstrated ^{1}H-^{13}C long-range correlation with C-8 at δ_C 125.4 s, meanwhile, H-1 of the apiose showed cross peak with C-6 of the glucose at δ_C 68.2 t and *vice versa*, which unambiguously established an api(1→6)glc sugar chain at C-8. The sugar chain with an api(1→6)glc linkage is the same as occurred in 13-O-[β-D-apiofuranosyl-(1→6)-β-D-glucopyranosyl]-(12*R*)-heraclenol previously isolated from *H. rapula*.[4] Therefore, **2** was identified as 8-O-[β-D-apiofuranosyl-(1→6)-β-D-glucopyranosyl]-8-hydroxybergapten.

Compound (**3)** was also obtained as pale yellow amorphous solid with a quasi-molecular ion peak at m/z = 495 $[M-H]^-$ in its negative-ion ESI-MS, corresponding to a molecular formula of $C_{22}H_{24}O_{13}$, which was verified by HRESIMS (found: 496.1145; calcd: 496.1138). It has been found that compound (**3)** shared most structural features (both sugar chain and linear furanocoumarin skeleton) with **2** by detailed comparison of their ^{1}H and ^{13}C NMR spectral data (Tables 1 and 2) and further analysis of the HMBC spectrum (Table 3) of **3**. The only difference between the compounds (**2)** and (**3)** could be rationalized to a methoxy group, which occurred at C-5 of **2** while disappeared in **3**. This was supported by the consideration that **3** was 30 molecular mass units less than **2**, and by the observation of an one-proton

singlet, rather than a three-proton singlet (OCH_3), at δ_H 7.56 in **3**, which was assignable to H-5 on the basis of its HMBC interactions with C-4, C-6 and C-7. In addition, the similarities of ^1H NMR spectral data of **3** with those of xanthotoxol [8] supported xanthotoxol as the aglycone of **3.** Accordingly, **3** was determined as 8-O-[β-D-apiofuranosyl (1→6)-β-D-glucopyranosyl]xanthotoxol.

Table 1 ^1H NMR (500 MHz) spectrum of Compounds (**1-4)** in Pyridine-d_5.[a]

No.	**1**	**2**	**3**	**4**
3	6.31 (d, 9.4)	6.29 (d, 9.7)	6.35 (d, 9.5)	6.41 (d, 9.8)
4	7.65 (d, 9.4)	7.93 (d, 9.7)	8.13 (d, 9.5)	8.89 (d, 9.8)
5	7.25 (s)	—	7.56 (s)	—
8	7.27 (s)	—	—	—
11	3.70 (dd, 9.4, 19.8)	—	—	—
	3.88 (dd, 9.4, 19.8)	—	—	—
12	5.60 (t, 9.4)	—	—	—
14	1.67 (s, 3H)	—	—	—
15	1.76 (s, 3H)	—	—	—
2′	—	7.94 (br s)	7.87 (br s)	7.89 (d, 2.2)
3′	—	7.08 (br s)	7.03 (br s)	7.84 (d, 2.2)
OH	—	—	—	5.20 (s)
OCH_3	—	3.98 (s, 3H)	—	—
Sugar-1	Glc-1	Glc	Glc	Glc-1
1	5.69 (d, 7.1)	5.73 (d, 6.9)	5.74 (d, 7.1)	5.38 (d, 7.5)
2	4.51 (m)	4.40 (overlap)	4.38 (overlap)	4.35 (overlap)
3	3.96 (m)	4.39 (overlap)	4.34 (overlap)	4.31 (overlap)
4	4.33 (overlap)	4.08 (m)	4.09 (m)	4.26 (m)
5	4.45 (m)	4.17 (m)	4.26 (overlap)	4.17 (m)
6	4.48 (overlap)	4.53 (d, 10.0)	4.52 (d, 10.0)	4.93 (d, 10.2)
—	4.43 (m)	4.14 (d, 10.0)	4.11 (d, 10.0)	4.35 (overlap)
Sugar-2	Glc-2	Api	Api	Glc-2
1	5.50 (d, 7.8)	5.55 (br s)	5.52 (d, 1.6)	5.01 (d, 7.7)
2	4.14 (m)	4.55 (br s)	4.59 (d, 1.6)	4.04 (m)
3	4.07 (m)	—	—	4.23 (overlap)
4	4.33 (overlap)	4.30 (d, 9.3)	4.32 (d, 9.2)	4.23 (overlap)
—	—	4.20 (d, 9.3)	4.26 (d, 9.2)	—
5	4.40 (m)	4.05 (2H, s)	4.17 (2H, s)	3.88 (m)
6	4.48 (overlap)	—	—	4.36 (overlap)
—	4.34 (overlap)	—	—	4.51 (d, 10.0)

a Coupling constants were presented in Hertz, δ in ppm. Unless otherwise indicated, all proton signals integrated to 1H.

Compound (**4)** exhibited a molecular ion peak at *m/z* = 541 $[M-H]^-$ in its negative-ion ESI-MS, which in combination with the ^1H and ^{13}C NMR spectra (Tables 1 and 2) and HRESIMS, established a molecular formula of $C_{23}H_{26}O_{15}$. Like compounds (**2**)and (**3)**, the ^1H and ^{13}C signals in aromatic region of the NMR spectra of **4** were also diagnostic of a linear furanocoumarin.[6] The similarities of the shape and absorption

of UV spectrum (205, 220, 249, 269, 312 nm) of **4** to those of **2** suggested that **4** was another 5, 8-dioxygenated psoralen derivative close to **2**. Additionally, the existence of two β-glucoses was readily identified from the ^{1}H and ^{13}C NMR spectra. The connectivity among the two sugar units was elucidated as glc-2(1→6)glc-1 from the obviously downfield-shifted C-6 from the normal *ca.* δ_C 62 to 70.3, as well as the HMBC correlations (Table 3) between H-1/C-1 of glc-2 and C-6/H-6 of glc-2. The sugar chain was deduced to be attached to C-5 based on the HMBC correlation between H-1 of glc-1 at δ_H 5.38 (1H, d, J = 7.5 Hz) to C-5 at δ_C 139.3 s. Therefore, substituent located at C-8 (s, 129.2) should be a hydroxyl group, which was supported by the HMBC correlations from δ_H 5.20 (8-OH) to C-7 and C-9. Accordingly, **4** was characterized as 5-O-[β-D-glucopyranosyl (1→6)-β-D-glucopyranosyl]-8-hydroxybergaptol.

Table 2 ^{13}C NMR (125 MHz) spectrum of Compounds (**1-4)** in (D_5) Pyridine, δ in ppm.

	1	**2**	**3**	**4**
2	161.0 (s)	160.6 (s)	160.7 (s)	161.0 (s)
3	113.6 (d)	115.5 (d)	114.6 (d)	113.2 (d)
4	143.9 (d)	139.6 (d)	145.5 (d)	141.3 (d)
5	128.1 (d)	144.7 (s)	109.7 (d)	139.3 (s)
6	128.3 (s)	115.5 (s)	118.7 (s)	122.9 (s)
7	158.7 (s)	149.5 (s)	147.6 (s)	147.5 (s)
8	102.5 (d)	125.4 (s)	141.2 (s)	129.2 (s)
9	154.4 (s)	143.7 (s)	144.0 (s)	140.3 (s)
10	113.5 (s)	107.9 (s)	114.4 (s)	110.6 (s)
11	28.2 (t)	—	—	—
12	122.7 (d)	—	—	—
13	133.4 (s)	—	—	—
14	18.0 (q)	—	—	—
15	25.8 (q)	—	—	—
2′	—	146.1 (d)	146.7 (d)	146.3 (d)
3′	—	105.4 (d)	104.5 (d)	107.1 (d)
OCH_3	—	60.8 (q)	—	—
Sugar-1	Glc-1	Glc	Glc	Glc-1
1	99.9 (d)	104.1 (d)	103.1 (d)	106.9 (d)
2	83.4 (d)	75.4 (d)	75.1 (d)	75.4 (d)
3	78.9 (d)[a]	78.5 (d)	78.6 (d)	78.5 (d)
4	70.8 (d)	71.4 (d)	71.7 (d)	71.8 (d)
5	78.2 (d)	77.8 (d)	78.0 (d)	77.5 (d)
6	62.7 (t)	68.2 (t)	69.0 (t)	70.3 (t)
Sugar-2	Glc-2	Api	Api	Glc-2
1	106.5 (d)	110.8 (d)	111.1 (d)	105.4 (d)
2	76.7 (d)	77.8 (d)	78.0 (d)	75.2 (d)
3	78.7 (d)[a]	80.6 (s)	81.0 (s)	78.5 (d)
4	71.6 (d)	74.9 (t)	75.1 (t)	71.4 (d)
5	78.2 (d)	65.7 (t)	65.4 (t)	78.5 (d)
6	62.2 (t)	—	—	62.5 (t)

[a] Signals in the same position may be exchanged between the two glucoses.

Table 3 Selected HMBC Correlations of Compounds (**1-4)**

No.	**1**	**2**	**3**	**4**
3	2	2, 10	2	2, 10
4	2, 5, 9	2, 5, 10	2, 5, 9	5, 9, 10
5	4, 11, 10	—	4, 6, 7	—
8	6, 7, 9	—	—	—
11	5, 7, 12, 13	—	—	—
12	14, 15	—	—	—
14	12, 13	—	—	—
15	12, 13	—	—	—
2′	—	3′, 7	3′, 6, 7	3′, 6, 7
3′	—	6, 7	2′, 5, 6	2′, 6, 7
OH	—	—	—	7, 9
OCH_3	—	5	—	—
Sugar-1	Glc-1	Glc	Glc	Glc-1
1	7	8	8	5
6	—	Api-1	Api-1	Glc-2-1
Sugar-2	Glc-2	Api	Api	Glc-2
1	Glc-1- 2	Glc-6	Glc-6	Glc-1-6

Compounds (**1-4)** belong to the rare type natural coumarins in which glycosylation occurred directly at their nucleus. All the four compounds were evaluated for their *in vitro* inhibitory activity against rabbit platelet aggregation induced by PAF (platelet activating factor), AA (arachidonic acid), and ADP (adenosine diphosphate), respectively, using the same bioassay methods as previously described.[9] Ginkgolide B (BN52021) and aspirin were used as positive controls, and 0.3% DMSO was used as contrast. Only weak to moderate inhibitory activities were observed for each compound (Table 4).

Table 4 Percentage Inhibition of Compounds (**1-4)** on the Aggregation of Rabbit Platelets Induced by PAF, AA, and ADP

Compound (10 mg/L)	Aggregation %		
	PAF (7.2 nmol / L)	AA (0.35μmol / L)	ADP (3 μmol / L)
DMSO	60.3±2.9	72.6±3.3	69.5±3.2
1	59.6±2.8	76.6±2.9	65.3±2.4
2	61.2±0.8	67.5±2.2	68.5±4.1
3	56.3±2.8	76.9±5.2	64.6±5.2
4	50.1±2.2 [a]	70.1±2.5	71.3±3.8
BN52021	0.6±0.1 [b]		
Aspirin		4.7±0.8 [b]	65.9±5.3

[a]$P < 0.05$ and [b]$P < 0.05$, as compared with control (*t*-test). The data were expressed as means ± S.D. of 4 rabbits.

EXPERIMENTAL

General Experimental Procedures. Melting Point was obtained on a XRC-1 micro melting point

apparatus and uncorrected. Optical rotations were measured with a Horiba SEPA-300 polarimeter. UV spectra were obtained using a Shimadzu UV-2401A spectrophotometer. A Tenor27 spectrophotometer was used for scanning IR spectroscopy with KBr pellets. MS spectra were performed on a VG Autospec-3000 spectrometer under 70 eV. 1D and 2D NMR spectra were recorded on Brucker AM-400 and DRX-500 spectrameters. Unless otherwise specified, chemical shift (δ) were expressed in ppm with reference to the solvent signals. HPLC separations were performed on a HP 1100 apparatus equipped with a UV detector and Zorbax SB-C-18 (Agilent, 9.4 mm × 25 cm) column. Column chromatography was performed with silica gel (200-300 mesh, Qing-dao Marine Chemical Inc., Qing-dao, P. R. China), silica gel H (60μm, Qing-dao Marine Chemical Inc.) and Diaion HP-20. Fractions were monitored by TLC and spots were visualized either under UV light (256 nm) or by heating Si gel plates sprayed with 10% H_2SO_4 in EtOH.

Plant material. The roots of *H. rapula* were collected in Dali Prefecture of Yunnan Province in 2003. The identity of the plant material was verified by Prof. Zhongwen Lin and a voucher specimen (KIB 2003-7-15-012) is kept at the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences.

Extraction and Isolation. The air-dried roots (4.0 kg) were milled and extracted with acetone (3×15 L) at rt for 24 h. The solvent was evaporated to give a deep-brown residue, which was suspended in water and partitioned with EtOAc to afford 100 g of EtOAc-soluble residue. This part was not used for further investigation because a more thorough work on it was carried out previously.[3] The water layer was directly subjected to column chromatography over Diaion 101 macroporous resin (800 g) eluting with H_2O, aqueous MeOH (30%, 40%, 60%) and MeOH to give five parts. The 40% MeOH part (20.0 g) was rechromatographied over a silica gel column eluting with a gradient system of $CHCl_3$/MeOH (8:1, 4:1, 2:1, 1:1) and Me_2CO to give five fractions I-V. Fraction II (2 g) was again chromatographied over silica gel column eluting with $CHCl_3$/Me_2CO (3:1 to 1:2 and 0:1) to give six sub-fractions A1-A6. Sub-fraction A3 afforded **1** (20 mg) and sub-fraction A4 afforded **2** (5 mg) by semi-preparative HPLC with 33% and 35% MeOH in H_2O as the mobile phases respectively. Fraction III (2.7 g) was further subjected to colomn chromatography over silica gel (200-300 mesh) developing with EtOAc/MeOH (5:1, 3:1, 1:1, 0:1) and monitored with TLC to give four sub-fractions B1-B4. Sub-fraction B1 yielded **3** (6 mg) by semi-preparative HPLC with 35% MeOH in H_2O as the mobile phase. In the same way with 30% MeOH in H_2O as eluents, sub-fraction B2 provided **4** (8 mg).

7-*O*-[β-D-Glucopyranosyl-(1→2)-β-D-glucopyranosyl]demethylsuberosin (1): pale yellow amorphous solid; $[\alpha]_D^{26.6}$ +3.41° (*c* = 0.11, MeOH); UV (MeOH) λ_{max}: 207, 292, 323, 389 nm; IR (KBr) ν_{max}: 3359, 2922, 2853, 1720, 1623, 1383, 1268, 1166, 1078, 1037, 997, 822, 596 cm^{-1}; negative ESIMS: m/z 553 $[M-H]^-$; HRESIMS: m/z 553.1956 $[M-H]^-$ (calcd for $C_{26}H_{34}O_{13}$553.1921); ^1H and ^{13}C NMR spectral data

see Tables 1-2.

8-*O*-[β-D-Apiofuranosyl-(1→6)-β-D-glucopyranosyl]-8-hydroxybergapten (2): pale yellow amorphous solid; $[\alpha]_D^{26.7}$ -66.48° (*c* = 0.16, MeOH); UV (MeOH) λ_{max}: 204, 221, 249, 255, 261, 310 nm; IR (KBr) ν_{max}: 3417, 2928, 1720, 1630, 1480, 1402, 1153, 1065, 1006, 574, 529 cm^{-1}; negative ESIMS: m/z 525 $[M-H]^-$; HRESIMS: m/z 525.1249 $[M-H]^-$ (calcd for $C_{23}H_{26}O_{14}$ 526.1244); ^1H and ^{13}C NMR spectral data see Tables 1-2.

8-*O*-[β-D-Apiofuranosyl-(1→6)-β-D-glucopyranosyl]xanthotoxol (3): pale yellow amorphous solid; $[\alpha]_D^{21.8}$ -77.38° (*c* = 0.56, MeOH); UV (MeOH) λ_{max}: 206, 249, 294, 301 nm; IR (KBr) ν_{max}: 3430, 2925, 2883, 1712, 1627, 1581, 1396, 1346, 1307, 1178, 1074, 1043, 749, 593, 569 cm^{-1}; negative ESIMS: m/z 495 $[M-H]^-$; HRESIMS: m/z 495.1145 $[M-H]^-$ (calcd for $C_{22}H_{24}O_{13}$ 496.1138); ^1H and ^{13}C NMR spectral data see Tables 1-2.

5-*O*-[β-D-Glucopyranosyl-(1→6)-β-D-glucopyranosyl]-8-hydroxybergaptol (4): pale yellow amorphous solid; $[\alpha]_D^{26.7}$-16.08° (*c* = 0.11, MeOH); UV (MeOH) λ_{max}: 205, 220, 249, 269, 312 nm; IR (KBr) ν_{max}: 3422, 2921, 1716, 1597, 1475, 1346, 1207, 1130, 1063, 828, 568, 535 cm^{-1}; negative ESIMS: m/z 541 $[M-H]^-$; HRESIMS: m/z 541.1200 $[M-H]^-$ (calcd for $C_{23}H_{26}O_{15}$ 542.1993); ^1H and ^{13}C NMR spectral data see Tables 1-2.

ACKNOWLEDGEMENTS

Financial support was provided by grants from the National Natural Science Foundation of China (No. 30200349), the Natural Science Foundation of Yunnan Province (No. 2002C0017Q), and the Young Academic and Technical Leader Raising Foundation of Yunnan Province (No. 2003RC07, awarded to Dr. Shenghong Li).

REFERENCES

1. H. D. Sun, Z. W. Lin, and F. D. Niu, *Acta Bot. Sin.,* 1978, **20**, 244.
2. S. X. Deng and Y. Q. Mo, *Zhongcaoyao,* 1989, **20**, 419.
3. X. M. Niu, S. H. Li, B. jiang, Q. S. Zhao, and H. D. Sun, *J. Asian Nat. Prod. Res.,* 2002, **4,** 33.
4. X. M. Niu, S. H. Li, L. X. Wu, L, Li, L. H. Gao, and H. D. Sun, *Planta Medica,* 2004, **70**, 578.
5. H. Fujiwara, T. Yokoi, S. Tani, Y. Saiki, and A. Kato, *Yakugaku Zassi,* 1980, **100**, 1258.
6. V. K. Ahluwalia, D. R. Boyd, A. K. Jain, C. H. Khanduri, and D. Sharma, *Phytochemistry*, 1988, **27**, 1181.
7. S. K. Garg, S. R. Gupta, and N. D. Sharma, *Phytochemistry*, 1979, **18**, 352.
8. M. Gellert, K. Szendrei, I Novak, K. Csedo, and J. Reisch, *Phytochemistry,* 1972, **11**, 2894.
9. Z. Q. Shen, L. Li, L. O. Wu, W. P. Liu, and Z. H. Chen, *Platelets,* 1999, **10**, 345.