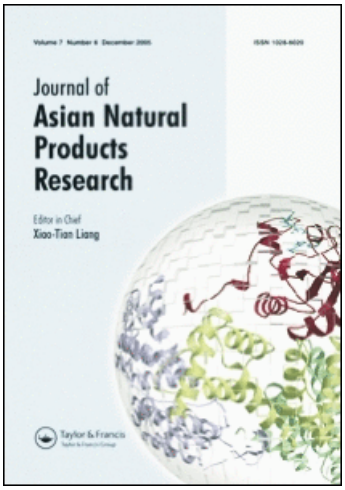

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Phenolic glycosides from leaves of *Hopiciopsis lobata*

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Note

Phenolic glycosides from leaves of *Hopiciopsis lobata*

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A new phenolic glycoside, 6′-[(*E*)-2″-hydroxymethyl, 2″-butenoyl] arbutin (**1**), and two known phenolic glycosides, 6′-[(*E*)-4″-hydroxycinnamoyl] arbutin (**2**) and 6′-[(*E*)-3″,4″-dihydroxycinnamoyl] arbutin (**3**), were isolated from the leaves of *Heliciopsis lobata* (Merr.) Sleum. Their structures were elucidated by various spectroscopic methods including 2D NMR spectroscopy.

Keywords: *Heliciopsis lobata* (Merr.) Sleum; Proteaceae; 6′-[(*E*)-2″-Hydroxymethyl, 2″-butenoyl] arbutin; 6′-[(*E*)-4″-Hydroxycinnamoyl] arbutin; 6′-[(*E*)-3″, 4″-Dihydroxycinnamoyl] arbutin

1. Introduction

Heliciopsis lobata (Merr.) Sleum. is a medicinal plant, family Proteaceae, that grows in Hainan province, China. The leaves of *H. lobata* are used to cure some diseases such as parotitis and cystitis. So far, no study on the chemical constituents of *Heliciopsis* plants has been reported. In our preliminary study, the H_2O extract of the leaves of *H. lobata* displayed appreciable inhibitory effects on HeLa, B16 and KB, and prompted us to further investigate the constituents of the plant. In this paper, we report the isolation and characterisation of three phenolic glycosides including one new compound and two known compounds from the genus for the first time. Structural elucidation (figure 1) of the three compounds was achieved mainly by 2D NMR and comparison with known compounds.

2. Results and discussion

Compound **1** was isolated as white powder. The quasi-molecular ion at *m/z* 371.1338 in the high-resolution ESI-MS showed the molecular formula of $C_{17}H_{22}O_9$. The absorptions at 3435, 1697, 1652, 1616 and 1508 cm^{-1} in the IR spectrum were assigned to phenolic

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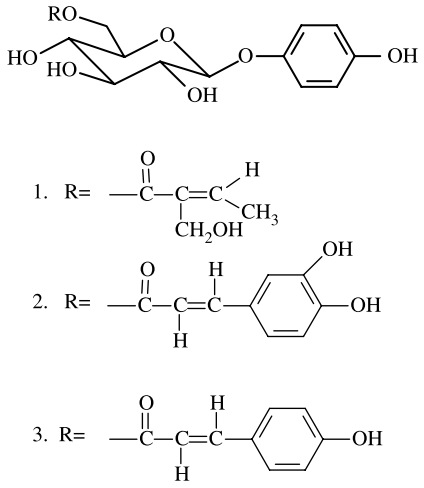

Figure 1. The structures of compounds **1**–**3**.

hydroxyl, carbonyl, double bond and benzene ring. The DEPT spectrum indicated the presence of one methyl carbon, two methylene carbons and ten methine carbons. The ^{1}H NMR spectrum of **1** in the aromatic region contained signals attributed to AA′BB′ system (δ 6.84 and 6.64, $J = 8.9$ Hz). In the HMBC spectrum, H-2, 6 (δ 6.84) were correlated with C-1 (δ 150.77), C-4 (δ 152.92) and C-3, 5 (δ 116.08), and H-3, 5 (δ 6.64) were correlated with C-1 (δ 150.77), C-4 (δ 152.92) and C-2, 6 (δ 118.19). A phenolic hydroxyl proton (δ 8.99) showed a correlation with C-3, 5 (δ 116.08) and C-4 (δ 152.92) in the HMBC spectrum (figure 2). Accordingly, **1** had a *p*-hydroxyphenyl group. The ^{1}H NMR spectrum of **1** showed the presence of a methyl connected with double bond (δ 1.89), which was correlated with C-2″ (δ 133.61) and C-3″ (δ 141.07) in the HMBC spectrum. The ^{13}C NMR spectrum of **1** showed an ester carbonyl (δ 167.00), which was correlated both with an oxygenated methylene (δ 4.17) and a vinyl proton (δ 6.85) in the HMBC spectrum. With the help of the HSQC spectrum, it was concluded that **1** has a 2-hydroxymethyl 2-butenoyl group. In the NOESY spectrum the proton signal at δ 4.17 (H-5″) was correlated with the methyl protons at δ 1.89 (H -4″), indicating that the 2-hydroxymethyl 2-butenoyl group had an *E*-configuration. Both ^{1}H NMR and ^{13}C NMR spectra of **1** showed the existence of a sugar moiety (anomeric proton at δ 4.68 and anomeric carbon at δ 102.02). The sugar moiety of **1** was identified as glucose by comparing ^{13}C NMR spectral data with the reported similar compounds [1–4] and further confirmed by comparison with authentic sample using PC and TLC after hydrolysis. In the HMBC spectrum, the cross-peak between the H-1′ signal at δ 4.68 and the C-1 signal at δ 150.77 suggested that **1** is a *p*-hydroxyphenyl glycoside

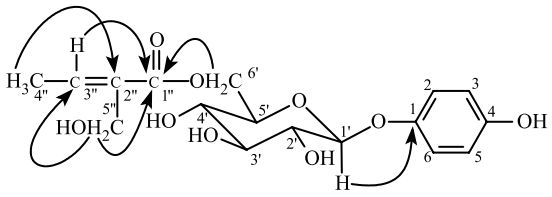

Figure 2. The key HMBC correlations of compound **1**.

derivative. The cross-peak between H-6′ (δ 4.44, 4.03) of the sugar moiety and the ester carbonyl signal (δ 167.00) of the 2-hydroxymethyl 2-butenoyl group suggested the esterification position of the 2-hydroxymethyl 2-butenoyl group at C-6′. Thus **1** was determined as 6′-[(*E*)-2″-hydroxymethyl, 2″-butenoyl] arbutin. The (*E*)-2-hydroxymethyl 2-butenoyl moiety seldom occurs in nature.

Compounds **2** and **3** were identified as 6′-[(*E*)-4″-hydroxycinnamoyl] arbutin and 6′-[(*E*)-3″, 4″-dihydroxycinnamoyl] arbutin by comparing their spectroscopic data with those of the known compounds [1].

3. Experimental

3.1 General experimental procedures

Melting points were determined on an X-4 micro melting-point apparatus and are uncorrected. IR spectra were obtained on a Nicolet Impact-410 spectrophotometer. 1D and 2D NMR spectra were recorded on a Brucker-DRX-600 spectrometer using TMS as an internal standard. HRESI-MS was measured on an Agilent 1100 MSD mass spectrometer. Silica gel H (10–40 μm, Qingdao Haiyang Chemical Co.) and macroporous resin (D-101) were used for column chromatography.

3.2 Plant material

Leaves of *Heliciopsis lobata* (Merr.) Sleum. were collected in Ledong county, Hainan Province, China, in April 2002 and identified by Professor Weiping Chen, Chinese Academy of Medical Sciences. A voucher specimen is deposited in the Herbarium of the Department of Pharmacy, Hainan Medical College.

3.3 Extraction and isolation

The leaves of *Heliciopsis lobata* (3.0 kg) were extracted with H_2O (3 × 5000 mL) for 2 h at 100°C, and the concentrated extract (559 g) was subjected to column chromatography on macroporous resin (2300 g) eluted with H_2O, 30% EtOH, 60% EtOH and 90% EtOH. The H_2O eluted fraction (336 g) was subjected to column chromatography on silica gel H (1500 g) eluted with a mixture of $CHCl_3$/MeOH gradually increasing polarity. The fraction (93 g) of $CHCl_3$/MeOH (100:4) was subjected to column chromatography on silica gel H (300 g) eluted with $CHCl_3$/EtOAc/MeOH gradually increasing polarity to yield compound **1** (230 mg) from the 7:2:3 ($CHCl_3$/EtOAc/MeOH) eluent. The fraction (163 g) of 30% EtOH was subjected to column chromatography on silica gel H (700 g) eluted with a mixture of $CHCl_3$/MeOH gradually increasing polarity. The fraction (25 g) eluted with $CHCl_3$/MeOH (100:8) was subjected to column chromatography on silica gel H (200 g) again eluted with petrol/EtOAc gradually increasing polarity to yield compound **2** (8 mg) from the 3:1 (petrol/EtOAc) eluent. The fraction (42 g) of 60% EtOH was subjected to column chromatography on silica gel H (200 g) eluted with a mixture of $CHCl_3$/MeOH gradually increasing polarity. The fraction (13 g) eluted with $CHCl_3$/MeOH (100:16) was subjected to column chromatography on silica gel H (60 g) again and eluted with $CHCl_3$/Me_2CO gradually increasing polarity to give compound **3** (21 mg) from the 1:2 ($CHCl_3$/Me_2CO) eluent.

3.3.1 6′-[(*E*)-2″-Hydroxymethyl, 2″-butenoyl] arbutin (1). White powder. IR $\nu_{max}\,cm^{-1}$: 3435, 2914, 2359, 1697, 1684, 1652, 1635, 1616, 1508, 1218, 1085, 1028, 778, 668. ^{1}H NMR (600 MHz, DMSO-d_6): table 1. ^{13}C NMR (150 MHz, DMSO-d_6): table 1. HRESI-MS *m/z*: 371.1338 $[M + H]^+$ (calcd for $C_{17}H_{23}O_9$, 371.1342).

3.3.2 Acid hydrolysis of 6′-[(*E*)-2″-hydroxymethyl, 2″-butenoyl] arbutin (1). A mixture containing compound **1** (2 mg), 1 ml MeOH and 0.5 ml 2 N HCl was refluxed at 100°C for 4 h. The solution was neutralised with 0.2 N NaOH. After filtering, the glucose was identified in the solution by comparison with authentic sample using PC and TLC.

3.3.3 6′-[(*E*)-3″,4″-Dihydroxycinnamoyl] arbutin (2). Yellow powder. IR $\nu_{max}\,cm^{-1}$: 3425, 1691, 1689, 1650, 1641, 1608, 1582, 1449, 1216, 1083, 1025, 775. ^{1}H NMR (600 MHz, DMSO-d_6): δ 6.90 (2H, d, $J = 8.9$ Hz, H-2, 6), 6.73 (2H, d, $J = 8.9$ Hz, H-3, 5), 9.01 (1H, br s, 4-OH), 4.78 (1H, d, $J = 7.5$ Hz, H-1′), 3.31–3.59 (4H, m, H-2′, 3′, 4′, 5′), 4.70 (2H, m, H-6′), 6.88 (1H, d, $J = 2.0$ Hz, H-2″), 6.69 (1H, d, $J = 8.8$ Hz, H-5″), 6.65 (1H, m, H-6″), 7.80 (1H, d, $J = 16.0$ Hz, H-7″), 6.46 (1H, d, $J = 16.0$ Hz, H-8″), 8.89 (1H, br s, 3″-OH), 9.53 (1H, br s, 4″-OH). ESI-MS *m/z*: 433 $[M - H]^{\square}$. The above data and ^{13}C NMR data were identical with those in the literature [1].

3.3.4 6′-[(*E*)-4″-Hydroxycinnamoyl] arbutin (3). White powder. IR $\nu_{max}\,cm^{-1}$: 3409, 1693, 1683, 1651, 1633, 1605, 1589, 1510, 1445, 1210, 1170, 1074, 829, 776. ^{1}H NMR (600 MHz, DMSO-d_6): δ 6.97 (2H, d, $J = 8.9$ Hz, H-2, 6), 6.72 (2H, d, $J = 8.9$ Hz, H-3, 5), 7.94 (1H, br s, 4-OH), 4.81 (1H, d, $J = 7.7$ Hz, H-1′), 3.47–3.74 (4H, m, H-2′, 3′, 4′, 5′), 4.45 (2H, m, H-6′), 7.58 (2H, d, $J = 8.6$ Hz, H-2″, 6″), 6.91 (2H, d, $J = 8.6$ Hz, H-3″, 5″), 7.65 (1H, d, $J = 16.0$ Hz, H-7″), 6.40 (1H, d, $J = 16.0$ Hz, H-8″), 8.89 (1H, br s, 4″-OH). ESI-MS *m/z*: 417 $[M - H]^{\square}$. The above data and ^{13}C NMR data were identical with those in the literature [1].

Table 1. NMR data of compound **1** (600 MHz for ^{1}H and 150 MHz for ^{13}C, DMSO-d_6).

No.	*^{1}H NMR*	*^{13}C NMR*	*HMBC (H → C)*
1		150.77	
2, 6	6.84 (2H, d, $J = 8.9$ Hz)	118.19	C-1, C-3, C-4, C-5
3, 5	6.64 (2H, d, $J = 8.9$ Hz)	116.08	C-1, C-2, C-4, C-6
4	8.99 (1H, s, OH)	152.92	C-3, C-4, C-5
1′	4.68 (1H, d, $J = 7.7$ Hz)	102.02	C-1, C-2′, C-5′
2′	3.23 (1H, m)	73.86	C-1′, C-3′
	5.29 (1H, d, $J = 5.1$ Hz, OH)		C-1′, C-2′, C-3′
3′	3.25 (1H, m)	77.11	C-2′, C-4′
	5.13 (1H, d, $J = 4.9$ Hz, OH)		C-2′, C-3′, C-4′
4′	3.19 (1H, m)	70.89	C-3′, C-5′, C-6′
	5.24 (1H, d, $J = 5.5$ Hz, OH)		C-3′, C-4′, C-5′
5′	3.57 (1H, m)	74.36	C-6′
6′	4.03 (1H, dd, $J = 7.6$ Hz, 11.7 Hz, H-α)	64.50	C-1″, C-5′
	4.44 (1H, dd, $J = 1.7$ Hz, 11.7 Hz, H-β)		C-1″
1″		167.00	
2″		133.61	
3″	6.85 (1H, m)	141.07	C-1″, C-2″
4″	1.89 (1H, d, $J = 7.2$ Hz)	14.80	C-2″, C-3″
5″	4.17 (1H, d, $J = 5.5$ Hz)	55.07	C-1″, C-2″, C-3″
	4.62 (1H, t, $J = 5.5$ Hz, OH)		C-2″, C-5″

Acknowledgements

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References

[1] A.S. Ahmed, N. Nakamura, M. Meselhy, H. El-Emary. *Phytochemistry*, **53**, 149 (2000).
[2] K. Machilda, M. Kikuchi. *Chem. Pharm. Bull.*, **41**, 248 (1993).
[3] N.B. Perry, N. Brennan. *J. Nat. Prod.*, **60**, 623 (1997).
[4] L. Verotta, F. Orsini, F. Pelizzoni, G. Torri, C.B. Rogers. *J. Nat. Prod.*, **62**, 1526 (1999).