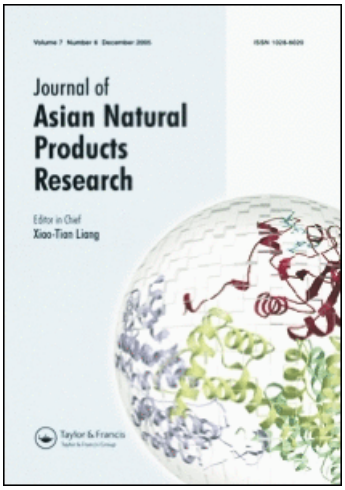

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Cimifoetisides VI and VII Two new cyclolanostanol triterpene glycosides from the aerial parts of *Cimicifuga foetida*

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Cimifoetisides VI and VII Two new cyclolanostanol triterpene glycosides from the aerial parts of *Cimicifuga foetida*

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Two new cyclolanostanol triterpene glycosides, cimifoetiside VI (**1**) and cimifoetiside VII (**2**), and one known compound were isolated from the aerial parts of *Cimicifuga foetida* L. On the basis of spectral and chemical evidences, the structures of **1** and **2** were elucidated to be (23*R*,24*S*)-24-*O*-acetylisodahurinol-3-*O*-β-D-galactopyranoside and (23*R*,24*R*)-24-*O*-acetylshengmanol-3-*O*-β-D-glucopyranosyl-(1″ → 2′)-β-D-xylopyranoside. The known compound was identified as (23*R*,24*R*)-24-*O*-acetylshengmanol-3-*O*-β-D-galactopyranoside (**3**).

Keywords: *Cimicifuga foetida*; Ranunculaceae; Cyclolanostanol triterpene glycosides; Cimifoetiside VI; Cimifoetiside VII

1. Introduction

The rhizome of *Cimicifuga foetida* L. (Ranunculaceae) has been used as traditional medicine recorded in the Chinese pharmacopoeia (2000 edition). It is used as a cooling and detoxifying agent and for alleviation of fever, pain, and inflammation [1]. The chemical constituents of the rhizome have been investigated thoroughly [2–4]. The total saponin of the aerial parts from this plant showed significant antiosteoporosis action to the model of rat Ostroblastoma cell line (UMR 106) and osteoprogenitor cell-line (HOSTE 85) *in vitro*. The chemical constituents of the aerial parts of the plant have been studied by our group. We now report the isolation and structure elucidation of two new cyclolanostanol triterpene glycosides, cimifoetiside VI (**1**) and cimifoetiside VII (**2**).

2. Results and discussion

CimifoetisideVI (**1**) was isolated as amorphous powder, mp 200–202°C ($CHCl_3$), $[\alpha]_D^{20}$ −65.4 (*c* 0.22, $CHCl_3$). The negative ESI-MS showed a peak at *m/z* 715 $[M + Na]^+$.

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The HRFAB-MS exhibited the molecular ion peak at *m/z* 715.4025, corresponding to the molecular formula of $C_{38}H_{60}O_{11}$, which also was confirmed by ^{13}C NMR and ^{1}H NMR spectral data. The IR spectrum showed strong hydroxyl bands at 3700–3040 cm^{-1} and an ester carbonyl band at 1730 cm^{-1}. The ^{1}H NMR spectrum showed signals due to cyclopropane protons at δ 0.20, 0.45 (each **1**H, d, $J = 4.0$ Hz), six methyl singlets at δ 0.98, 1.02, 1.16, 1.32, 1.50, 1.69 and one anomeric proton at δ 0.88 (1H, d, $J = 7.5$ Hz). The signals for a galactose moiety assigned as 4.88 (H-1′), 4.48 (H-2′), 4.18 (H-3′), 4.60 (H-4′), 4.10 (H-5′), 4.48 (H-6′) were also observed in the ^{1}H NMR spectrum. The corresponding carbon signals were assigned to a galactose moiety at δ 107.5, 73.2, 75.5, 70.3, 76.8, 62.4 in the ^{13}C NMR spectrum. All the above evidence suggested that **1** was a 9,19-cycloartane triterpene monoglycoside. On acid hydrolysis of **1**, galactose was detected from the aqueous fraction by comparison of TLC (n-BuOH/AcOH/H_2O, 4:1:1) with authentic sample.

Through analysis of the of ^{1}H–^{1}H COSY, HMQC, HMBC spectral data, ^{1}H and ^{13}C signals for compound **1** were fully assigned (table 1). In the HMBC spectrum, significant correlations were observed between H-1′ (δ 4.88) and C-3 (δ 88.7), H-16 (δ 3.77) and C-15 (δ 213.9); CH_3-28 (δ 0.98) and C-15 (δ 213.9); H-24 (δ 5.30) and the acetyl carbonyl group (δ 171.1), suggesting the sugar moiety was located at C-3, the ketone group at C-15 and the acetyl at C-24. The relative stereochemistry of C-16 was determined on the NOE experiment. Irradiation at CH_3-28 increased the signal intensity of H-16.By comparing the coupling constants of the H-23 and H-24 of **1** with those of 24-*O*-acetyldahurinol or 24-*O*-acetylisodahurinol [5], the configurations of C-23 and C-24 were assigned as *R* and *S*, respectively.

According to the coupling constants of H-1′ ($J = 7.0$ Hz), the galactose moiety should be the β-anomer. Thus, compound **1** was elucidated as (23*R*,24*S*)-24-*O*-acetylisodahurinol-3-O-β-D-galactopyranoside, and named as cimifoetiside VI (figure 1).

Cimifoetiside VII (**2**) was obtained as amorphous powder, mp 173 ~ 175°C (MeOH), $[\alpha]_D^{20}$ −7.2 (*c* 0.56, MeOH). The negative ESI-MS showed a peak at *m/z* 865 $[M + Na]^+$. The HRFAB-MS exhibited the molecular ion peak at *m/z* 865.4599, corresponding to the molecular formula of $C_{43}H_{70}O_{16}$, which also was confirmed by ^{13}C NMR and ^{1}H NMR spectral data. The IR spectrum showed broad hydroxyl bands at 3700–3040 cm^{-1} and an ester carbonyl band at 1730 cm^{-1}. The ^{1}H NMR spectrum showed the presence of a cyclopropane methylene at δ0.26, 0.53 (each 1H, d, $J = 3.5$ Hz), six *tert*-methyl groups at δ 1.13, 1.22, 1.25, 1.26, 1.46, 1.48, and two anomeric protons at δ 5.38 (1H, d, $J = 8.0$ Hz), 4.84 (1H, d, $J = 6.5$ Hz). The ^{13}C NMR spectrum exhibited signals for a xylose moiety at δ 105.5, 83.5, 78.0, 71.0, 66.7 and a glucose moiety at δ 106.2, 77.0, 78.1, 71.3, 78.2, 62.8. All the above evidence suggested that **2** was a 9,19-cycloartane triterpene diglycoside. Comparison of ^{13}C NMR data of **2** with those of the known compound, 24-epi-24-*O*-acetylshengmanol-3-O-β-D-galactopyranoside (**3**) [6], showed very similar signals except for the signals of sugar moieties. On acid hydrolysis of **2**, xylose and glucose were detected from the aqueous fraction by TLC analysis (n-BuOH/AcOH/H_2O, 4:1:1) comparing with authentic samples.

The ^{1}H NMR and ^{13}C NMR data were assigned with the aid of ^{1}H–^{1}HCOSY, HMQC and HMBC experiments (table 1). In the HMBC spectrum, significant correlations were observed between H-1′ (δ 4.84) and C-3 (δ 88.5); H-1″ (δ5.38) and C-2′ (δ 83.5), suggesting the sugar moiety was located at C-3 position, the glucosyl was connected with C-2′ of the xylosyl.

According to the coupling constants of H-1′ ($J = 6.5$ Hz) and H-1″ ($J = 8.0$ Hz), the sugar moieties were assigned as β-anomers. The relative stereochemistry of C-15 and C-16 was

Table 1. NMR spectral data of compounds **1** and **2** (500 Hz for ^{1}H and 125 Hz for ^{13}C in C_5D_5N, δ ppm, J in Hz).

Position	***1***		***2***	
	^{13}C	^{1}H	^{13}C	^{1}H
1	32.4	0.97m, 1.45m	32.4	1.21m, 1.55m
2	30.0	1.85m, 2.41m	30.1	1.95m, 2.32m
3	88.5	3.51 (dd, 4.0, 11.5)	88.6	3.41 (dd, 4.0, 1.0)
4	41.2		41.3	
5	47.3	1.23m	47.6	1.28m
6	20.9	0.69 (br q), 1.45m	21.5	0.72 (br q), 1.51
7	25.9	1.01m, 1.92m	26.5	1.07m, 2. 05m
8	43.6	1.68	49.0	1.76
9	20.2		20.0	
10	27.0		27.1	
11	26.0	1.03m, 2.24m	26.8	1.07m, 2.05m
12	31.2	1.08m, 1.58m	34.0	1.53m, 1.70m
13	39.9		42.3	
14	55.0		46.8	
15	213.9		82.2	4.13s
16	84.2	3.77 (d, 11.5)	103.0	
17	52.2	1.57	60.9	1.80 (d, 10)
18	19.8	1.16 s	20.3	1.25s
19	31.1	0.20 (d, 4.0)	30.7	0.26 (d, 3.5)
		0.45 (d, 4.0)		0.53 (d, 3.5)
20	33.2	1.78 m	27.4	1.46m
21	20.0	0.90 (d, 6.0)	21.1	0.96 (d, 5.5)
22	38.6	1.45m, 1.72m	33.0	2.10m, 2.22m
23	78.9	4.23 (d, 11.5)	74.2	4.35m
24	79.8	5.30 (d, 2.5)	81.2	5.62 (d, 8.5)
25	72.0		72.3	
26	26.8	1.50 s	26.6	1.48s
27	27.0	1.69 s	27.1	1.46s
28	17.6	0.98 s	11.8	1.22s
29	25.7	1.32 s	25.8	1.26s
30	15.4	1.02 s	15.5	1.13s
*C*OCH$_3$	171.1		171.3	
CO*C*H$_3$	20.7	2.14s	21.1	2.00s
1′	107.5	4.88 (d, 7.5)	105.5	4.84 (d, 6.5)
2′	73.2	4.48 m	83.5	4.18
3′	75.5	4.18 (dd, 3.5, 9.0)	78.0	4.10
4′	70.3	4.60 (d, 3.0)	71.0	4.14
5′	76.8	4.10 (dd, 6.0, 6.0)	66.7	3.63, 4.28
6′	62.4	4.48, m		
1″			106.2	5.38 (d, 8.0)
2″			77.0	4.25
3″			78.1	4.23
4″			71.3	4.35
5″			78.2	4.22
6″			62.8	4.45, 4.44

Signals were assigned by ^{1}H—^{1}H COSY, HMQC, HMBC spectra.

determined on the NOE experiment. Irradiation at H-24 and CH_3-18 enhanced the signal intensities of the H-16 and H-15, respectively. By comparing the coupling constants of the H-23 and H-24 signals of **2** with those of the known compound (**3**), the configurations of C-23 and C-24 were assigned as *R* and *R*, respectively. Thus, compound **2** was elucidated as (23*R*,24*R*) 24-*O*-acetylshengmanol-3-*O*-β-D-glucopyranosyl-(1″ → 2″)-β-D-xylopyranoside, and named as cimifoetiside VII.

The known compound was identified by comparison of their physical and spectral data with those published in the literature [6].

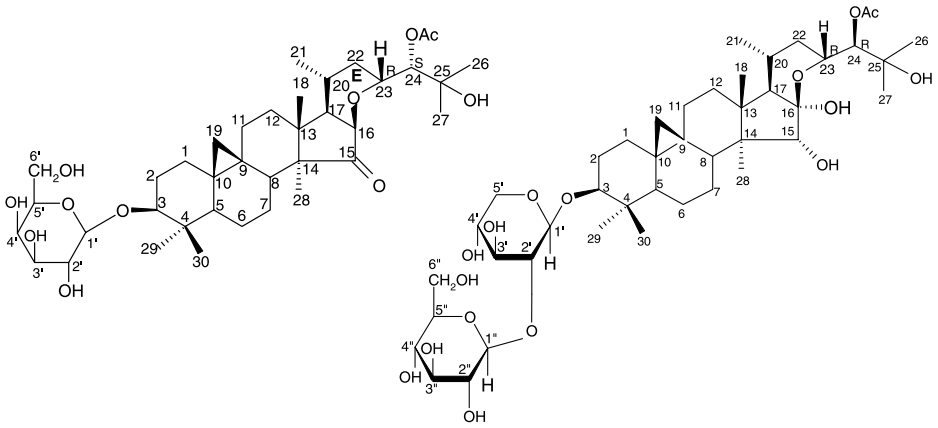

Figure 1. Structures of compounds **1** and **2**.

3. Experimental

3.1 General experimental procedures

Melting points were determined on a Fisher–Johns melting point apparatus and are uncorrected. Optical rotations were obtained on a Perkin–Elmer 341 polarimeter. IR spectra were recorded on a Perkin–Elmer 983G spectrometer. NMR spectra were measured on a Bruker Am-500 (500 MHz) instrument, and chemical shifts were referenced to TMS. FAB-MS data were recorded on a Zabspec instrument.

3.2 Plant material

The aerial parts of *Cimicifuga foetida* were collected in Ankang, Shanxi Province, China, in August 1998 and identified by one of the authors, Ruile Pan, Associate Professor. A voucher specimen has been deposited in the Herbarium of the institute.

3.3 Extraction and isolation

The powdered air-dried aerial parts of *Cimicifuga foetida* (9.5 kg) were extracted exhaustively with boiling 80% EtOH. The alcoholic solution was concentrated *in vacuo* to yield a syrup-like extract (1.1 kg), which was mixed with siliceous earth (80–100 mesh) and eluted with hexane, EtOAc, and 80% EtOH to give three fractions, I (35 g), II (260 g), and III (220 g).

Fraction II was subjected to column chromatography over silica gel (100–200 mesh, 2000 g) and eluted with an eluent of $CHCl_3$/MeOH (100:0/20:80), yielding 1–10 fractions. Fraction 7 (20 g) was rechromatographed on silica gel (100–200 mesh, 400 g), eluted with $CHCl_3$/MeOH (9:1) as solvent, to afford three subfractions 7a–7c. Subfraction 7a (1.2 g) was chromatographed on an ODS column with MeOH/H_2O (3:2) as eluent, to afford compound **1** (15 mg). Fraction 9 (16 g) was rechromatographed on silica gel (100–200 mesh, 300 g), eluted with $CHCl_3$/MeOH (9:1) as solvent, to afford five subfractions 10a–10e. Compound **2** (20 mg) and compound **3** were purified from the subfraction 10c and 10a respectively by ODS columns with MeOH/H_2O (3:2) as fluent phase.

3.3.1 Cimifoetiside VI (1). White amorphous powder, mp 200–202°C, $[\alpha]_D^{20}$ −65.4 (*c* 0.34, $CHCl_3$). IR (KBr) ν_{max}: 3040–3700, 2940, 2880, 1740, 1730, 1378, 1260, 1060, 1010 cm^{-1}. ^1H NMR and ^{13}C NMR: see table 1. Positive ESI-MS *m/z*: 715 $[M + Na]^+$. HRFAB-MS *m/z* 715.4025 $[M + Na]^+$ (calcd. for $C_{38}H_{60}O_{11}$ Na, 715.4033).

3.3.2 Cimifoetiside VII (2). White amorphous powder, mp 173–175°C, $[\alpha]_D^{20}$ −7.2 (*c* 0.56, MeOH). IR (KBr) ν_{max}: 3040–3700, 2940, 2880, 1730, 1394, 1260, 1180, 1080, 1040 cm^{-1}. ^{13}C NMR and ^1H NMR: see table 1. Positive ESI-MS *m/z*: 865 $[M + Na]^+$. HRFAB-MS *m/z* 865.4599 $[M + Na]^+$ (calcd. for $C_{43}H_{70}O_{16}$ Na, 865.4562).

3.3.3 24-Epi-acetylshengmanol-3-*O*-β-D-galactopyranoside (3). White amorphous powder, mp 229–230°C; ^1H NMR and ^{13}C NMR data consistent with literature values [6].

3.3.4 Acid hydrolysis of compounds 1 and 2. Compounds **1** and **2** (each 5 mg) were refluxed with 5% HCl in MeOH (5 ml) for 6 h. Each mixture was diluted with H_2O and neutralized with $NaHCO_3$. The neutral hydrolysate revealed the presence of xylose, glucose and galactose by TLC (n-BuOH/AcOH/H_2O, 4:1:1) when compared with authentic samples. The authentic samples were purchased from the Pfanstiehl Chemical Corp., Waukegan, IL (Lot no. 1279)

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References

[1] The Pharmacopoeia Commission of P. R. China, *The Chinese Pharmacopoeia*, 2000 Edn., **I**, p. 55, Chemical Industry Publishing House, Beijing (2000).
[2] S. Kadota, J.X. Li, K. Tanaka, T. Namba. *Tetrahedron*, **51**, 1143 (1995).
[3] J.X. Li, S. Kadota, X.F. Pu, N. Tsuneo. *Tetrahedron Lett.*, **35**, 4575 (1994).
[4] N.Q. Zhu, Y. Jiang, M.F. Wang, C. Ho. *J. Nat. Prod.*, **64**, 627 (2001).
[5] A. Kusano, M. Shibano, G. Kusano. *Yakugaku. Zasshi.*, **96**, 82 (1976).
[6] A. Kusano, M. Shibano, G. Kusano. *Chem. Pharm. Bull.*, **44**, 2078 (1996).