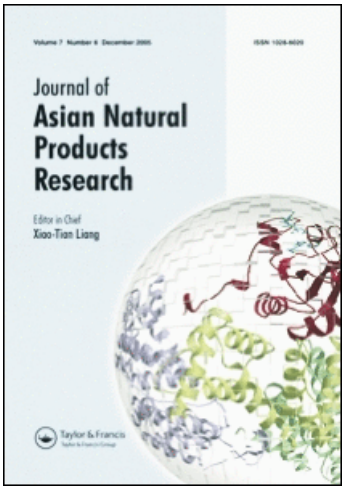

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Two new triterpenes from *Lysimachia foenum-graecum*

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ORIGINAL ARTICLE

Two new triterpenes from *Lysimachia foenum-graecum*

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Two new oleane-type triterpene saponins, lysimachiagenoside E (**1**) and lysimachiagenoside F (**2**), were isolated from the aerial parts of *Lysimachia foenum-graecum* Hance. The structures were elucidated on the basis of 1D and 2D NMR techniques, including $^{1}H-^{1}H$ COSY, HMQC, HMBC, TOCSY, ROESY experiments as well as chemical methods.

Keywords: *Lysimachia foenum-graecum* Hance; triterpene saponin; lysimachiagenoside E; lysimachiagenoside F

1. Introduction

Lysimachia foenum-graecum Hance (Primulaceae), distributed mainly in Guangxi and Yunnan Provinces of China, has been commonly used as a perfume plant and pest repellent. In Chinese folk medicine, the plant has also been used for the treatment of cold and headache [1]. We have reported the isolation of 21-*O*-angeloylbarringtogenol C, lysimachiagenosides A, C, and D from the aerial parts of *L. foenum-graecum* [2,3]. In our recent study, two new oleanane-type triterpenoid saponins, lysimachiagenosides E and F, were isolated and elucidated by NMR and MS techniques. In this paper, we describe the isolation and structural elucidation of lysimachiagenosides E and F.

2. Results and discussion

Compound **1** was obtained as a white powder. The ESI-MS of **1** showed a pseudomolecular ion at *m/z* 1319 $[M+Na]^+$, compatible with the molecular formula $C_{61}H_{100}O_{29}$, which was further verified by HR-FAB-MS at *m/z* 1319.6312 $[M+Na]^+$. Briefly, the analysis of NMR spectral data indicated that **1** was a saponin consisting of a triterpene aglycone and five monosaccharides. The ^{13}C NMR spectrum of **1** showed 61 carbon signals, from which 29 were assigned to five monosaccharide units, 30 to triterpene aglycone moiety, and the remaining 2 to acetoxy moiety. The analysis of NMR spectral data of **1** showed the elimination of an angeloyl moiety at C-28 in **1** when compared to (3β,16α,22α)-olean-12-ene-3,22-diol-16-*O*-acetyl-28-(2-methyl-2-butenoate)(16-*O*-acetyl-21-dehydroxy-28-*O*-angeloylbarringtogenol C) [2,3]. The hydroxyl substitution at C-28 was determined by HMBC correlations between the proton signal at δ_H 3.30 (1H, overlap, H-28a), 3.13 (1H, overlap, H-28b) and the carbon

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signals at δ_C 81.8 (C-22), 43.0 (C-17). This indicated that an angeloyl at C-28 is absent. Therefore, the aglycone of **1** was determined as 16-*O*-acetyl-21-dehydroxy barringtogenol C. Five monosaccharide units were determined from the TOCSY spectrum with the aid of COSY, HMQC, and HMBC spectra. Starting from the anomeric proton signal at δ_H 4.27 (1H, 7.5 Hz), six correlated carbon signals were observed in the TOCSY spectrum and determined in sequence to be at δ_C 103.9 (C-1), 73.5 (C-2), 75.9 (C-3), 69.6 (C-4), 75.7 (C-5), 61.0 (C-6), which suggested the presence of a glucosyl group. Similarly, the other three hexosyl sugar moieties were identified from the analysis of the TOCSY spectrum. The remaining five carbon signals suggested the presence of a pentosyl sugar moiety whose anomeric proton at δ_H 4.38 (1H, 8.0 Hz) was only correlated with four carbon signals at δ_C 103.1 (C-1), 76.9 (C-2), 70.5 (C-3), 76.2 (C-4) in the TOCSY spectrum, implying an arabinosyl group. The oxygen-bearing methylene at δ_C 61.0 was assigned to be at the C-5 position of the arabinosyl group based on the $^1H-^1H$ COSY and HMBC experiments. The above inferences for the monosaccharide unit were further confirmed by the TLC analysis of the acid hydrolysate of compound **1**. One of the glycosidic positions of the aglycone was determined to be at the C-3 position on the basis of the HMBC correlation between the anomeric proton of the arabinosyl group at δ_H 4.38 (1H, 8.0 Hz) and C-3. The connectivity among the monosaccharide units was established by the following HMBC correlations: H-1 (δ_H 4.21) of the inner glucosyl group with C-2 (δ_C 76.9) of the arabinosyl group; H-1 (δ_H 4.27) of the outer glucosyl group with C-4 (δ_C 76.2) of the arabinosyl group; H-1 (δ_H 4.23) of the outer glucosyl group with C-6 (δ_C 68.5) of the inner glucosyl group. Another glycosidic position of the aglycone was determined to be at the C-22 position on the basis of the HMBC correlation between the anomeric proton of the glucosyl group at δ_H 4.20 (1H, d, 7.8) and C-22 (δ_C 81.8) of the aglycone. The anomeric configurations of four glucosyl groups were determined to be of β-orientation from the coupling constants of the anomeric protons. Similarly, the anomeric proton of the arabinosyl group was found to be in the α-orientation (Table 2). Thus, the complete structure of **1** was elucidated as 3-*O*-β-glucopyranosyl(1 → 6)-β-glucopyranosyl (1 → 2)-[β-glucopyranosyl(1 → 4)]-α-arabinopyranosyl-16-*O*-acetyl-21-dehydroxy barringtogenol C 22-*O*-β-glucopyranoside, named lysimachiagenoside E (Figure 1).

Compound **2**, obtained as a white powder, displayed a quasimolecular ion peak at *m/z* 1361.6421 $[M+Na]^+$ in HR-FAB-MS, which is consistent with the molecular formula $C_{63}H_{102}O_{30}$. The comparison of NMR spectral data (Tables 1 and 2) of **2** with those of **1** revealed great similarity. The only difference was the presence of an acetoxy group in one glucose in **2**. With the aid of TOCSY, COSY, and HMQC spectra, an anomeric proton signal at δ_H 4.05 (1H, 7.5 Hz) was correlated with six carbon signals at δ_C 105.5 (C-1), 73.7 (C-2), 74.4 (C-3), 70.0 (C-4), 76.9 (C-5), 64.0 (C-6), indicating a glucose unit. The glucose was attached to C-22 of the aglycone based on the HMBC correlation between the anomeric protons at δ_H 4.05 and C-22. The downfield shift at δ_C 64.0 (C-6) indicated that the C-6 position of the glucosyl group was substituted by an acetoxy, which was confirmed by long-range correlations between the proton signal at δ_H 3.82 (H_2-6, br s) and the ester carbonyl signal at δ_C 170.0 and between the acetyl methyl proton signal at δ_H 2.02 (3H, s) and the carbon signals at δ_C 64.0 (C-6) and 170.0 (—CO—) in the HMBC spectrum. The configuration of the anomeric proton of glucose was established to be β based on the coupling constant of the anomeric

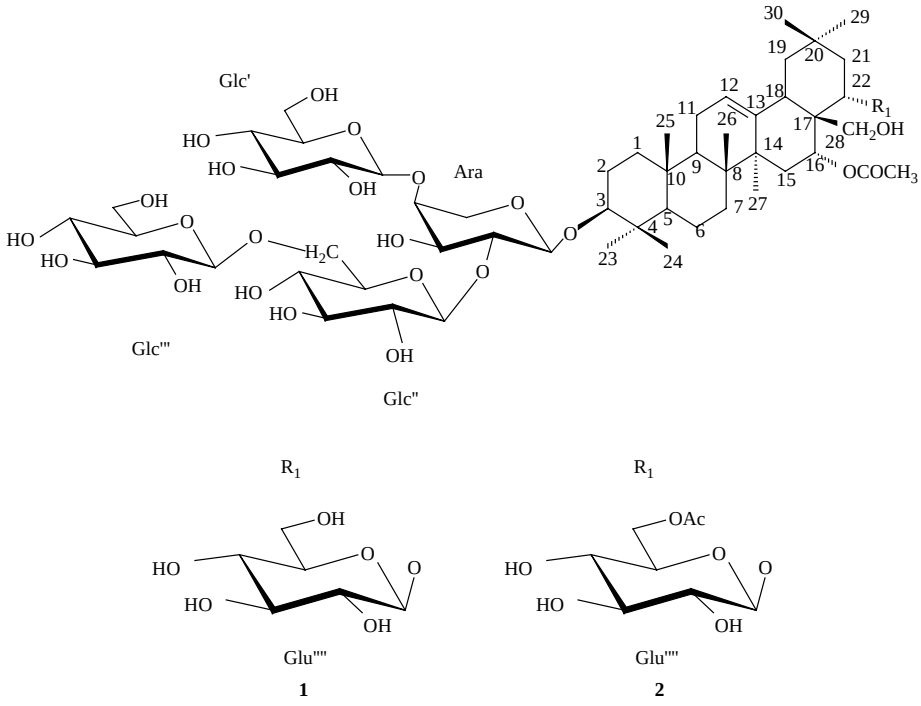

Figure 1. Structures of compounds **1** and **2**.

proton. Thus, the structure of **2** was established as 3-*O*-β-glucopyranosyl-(1 → 6)-β-glucopyranosyl(1 → 2)-[β-glucopyranosyl(1 → 4)]-α-arabinopyranosyl-16-*O*-acetyl-21-dehydroxy barringtogenol C 22-*O*-β-6-acetyl-glucopyranoside, named lysimachiagenoside F (Figure 1).

3. Experimental

3.1 General experimental procedures

Optical rotations were determined with a Perkin-Elmer model 241 polarimeter. UV spectra were taken on a Perkin-Elmer-554 spectrometer. IR spectra were run on a Nicolet Impact 400 grating infrared spectrophotometer. 1D and 2D NMR spectra were recorded on a Bruker Avance 500 spectrometer. Chemical shifts (δ) are given in ppm with TMS as an internal standard. MS and HR-MS were obtained using ESQUIRE-LC or APEX α FT-ICR-MS instruments. Silica gel precoated plates (Qingdao Ocean Chemical Co., Qingdao, China) were used in TLC. Detection was carried out by spraying with 10% H_2SO_4 solution followed by heating.

3.2 Plant material

The aerial parts of *L. foenum-graecum* were collected in Kunming City, Yunnan Province of China, in June 2001, and were identified by Prof. Ji Zhang. A voucher specimen (No. 0108127) is deposited in the Institute of Chinese Materia Medica, National Institute for the Control of Pharmaceutical and Biological Products.

3.3 Extraction and isolation

The aerial parts of *L. foenum-graecum* (3.0 kg) were extracted with 70% EtOH (2× 52 liters) under reflux. The combined filtrate was partitioned into petroleum ether, CH_2Cl_2, and the remaining ethanol fractions. The remaining ethanol fractions (160 g) were absorbed on a Diaion SP 825 column, and then sequentially eluted with

Table 1. ^{13}C NMR spectral data of compounds **1** and **2** (125 MHz, in DMSO-d_6).

C No.	**1**	**2**	C No.	**1**	**2**
1	38.1	38.2	Ara C-1	103.1	103.1
2	25.6	25.6	2	76.9	76.7
3	87.9	87.9	3	70.5	70.7
4	38.8	38.8	4	76.2	76.1
5	54.9	54.9	5	61.0	61.0
6	17.8	17.8	Glc C′-1	103.9	103.9
7	32.2	32.4	2	73.5	73.5
8	39.0	39.0	3	75.9	75.9
9	46.0	46.1	4	69.6	70.3
10	36.2	36.2	5	75.7	76.2
11	23.0	23.0	6	61.0	61.0
12	123.3	123.9	Glc C″-1	103.4	103.4
13	141.5	140.7	2	73.7	74.0
14	40.6	40.6	3	76.2	76.3
15	29.8	30.4	4	69.9	70.5
16	71.4	70.7	5	76.5	76.6
17	43.0	42.7	6	68.5	68.5
18	40.2	40.0	Glc C‴-1	103.6	103.7
19	46.4	46.2	2	73.5	73.8
20	30.9	29.6	3	76.2	76.4
21	43.6	43.5	4	70.5	70.6
22	81.8	77.4	5	76.6	76.8
23	27.5	27.6	6	61.5	61.1
24	16.3	16.3	Glc C⁗-1	105.2	105.5
25	15.4	15.4	2	72.8	73.7
26	16.8	16.4	3	73.8	74.4
27	26.5	26.6	4	69.6	70.0
28	65.7	67.3	5	76.5	76.9
29	33.4	33.3	6	60.6	64.0
30	24.9	24.7	1		170.0
1″	169.0	168.9	2		20.8
2″	21.9	21.9			

H_2O and EtOH. The fraction eluted with 50% EtOH (25 g) was subjected to silica gel column chromatography (7 × 100 cm) using the $CHCl_3$–MeOH gradient system to yield fractions I and II. Fraction II (1250 mg) was purified by repeated silica gel column chromatography using the $CHCl_3$–MeOH gradient system and a reversed-phase column (RP-18, 3.5 × 60 cm) using 65% MeOH as the eluent to give compounds **1** (6 mg) and **2** (5 mg).

3.3.1 *Lysimachiagenoside E (**1**)*

White powder, $[\alpha]_D^{24}$ −6.2 ($c = 0.14$, MeOH); UV (MeOH) λ_{max} (nm) (log ε): 210 (4.32); IR (KBr) ν_{max} (cm^{-1}): 3432 (OH), 1710 (C=O), 1241 (C=C); ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.21 (3H, s, Me-23), 0.83 (3H, s, Me-24), 0.94 (3H, s, Me-25), 0.74 (3H, s, Me-26), 1.21 (3H, s, Me-27), 0.89 (3H, s, Me-29), 0.87 (3H, s, Me-30), 3.00 (1H, dd-like, H-3), 0.70 (1H, d, $J = 10.5$ Hz, H-5), 1.54 (1H, m, H-9), 5.26 (1H, br s, H-12), 5.30 (1H, dd-like, H-16), 2.21 (1H, dd-like, H-18), 1.69 (1H, overlap, H-21a), 1.61 (1H, overlap, H-21b), 3.82 (1H, dd-like, H-22), 3.30 (1H, overlap, H-28a), 3.13 (1H, overlap, H-28b), 1.99 (3H, s, $COCH_3$); ^{1}H and ^{13}C NMR spectral data (Tables 1 and 2); ESI-MS: *m/z* 1319 $[M+Na]^+$; HR-FAB-MS: *m/z* 1319.6312 $[M+Na]^+$ (calcd for $C_{61}H_{100}O_{29}Na$, 1319.6248).

Table 2. ^{1}H NMR spectral data for the sugar moieties of compounds **1** and **2** (500 MHz, in DMSO-d_6).

H No.	**1**	**2**
Ara H-1	4.38 (1H, $J = 8.0$ Hz)	4.38 (1H, $J = 8.0$ Hz)
2	3.67	3.67
3	3.06	3.05
4	3.12	3.13
5	3.63, 3.42	3.63, 3.41
Glc H$'$-1	4.27 (1H, $J = 7.5$ Hz)	4.29 (1H, $J = 7.6$ Hz)
2	2.95	2.96
3	3.11	3.12
4	3.55	3.54
5	3.12	3.13
6	3.67, 3.40	3.66, 3.38
Glc H$''$-1	4.21 (1H, $J = 7.8$ Hz)	4.19 (1H, $J = 7.8$ Hz)
2	2.99	3.03
3	3.10	3.85
4	3.09	4.01
5	3.08	3.09
6	3.94, 3.55	3.94, 3.56
Glc H$'''$-1	4.23 (1H, $J = 7.8$ Hz)	4.21 (1H, $J = 7.8$ Hz)
2	2.94	2.95
3	3.06	3.06
4	3.08	3.07
5	3.09	3.09
6	3.64, 3.40	3.64, 3.42
Glc H$''''$-1	4.20 (1H, $J = 7.8$ Hz)	4.05 (1H, $J = 7.5$ Hz)
2	2.89	2.95
3	2.95	3.05
4	3.05	3.07
5	3.01	3.08
6	3.62, 3.41	3.82, 3.65
CO_2CH_3		2.02 (3H, s)

3.3.2 *Lysimachiagenoside F (**2**)*

White powder, $[\alpha]_D^{24}$ −8.6 ($c = 0.14$, MeOH); UV (MeOH) λ_{max} (nm) (log ε): 208 (4.16); IR (KBr) ν_{max} (cm^{-1}): 3430 (OH), 1715 (C═O), 1242 (C═C); ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.21 (3H, s, Me-23), 0.84 (3H, s, Me-24), 0.88 (3H, s, Me-25), 0.73 (3H, s, Me-26), 1.21 (3H, s, Me-27), 0.92 (3H, s, Me-29), 0.87 (3H, s, Me-30), 2.99 (1H, dd-like, H-3), 0.67 (1H, d, $J = 10.0$ Hz, H-5), 1.51 (1H, m, H-9), 5.21 (1H, br s, H-12), 5.24 (1H, dd-like, H-16), 2.49 (1H, dd-like, H-18), 1.74 (1H, overlap, H-21a), 1.62 (1H, overlap, H-21b), 3.67 (1H, overlap, H-22), 3.22 (1H, br s, H-28a), 3.11 (1H, d, $J = 9.0$ Hz, H-28b), 1.99 (3H, s, $COCH_3$); ^{1}H and ^{13}C NMR spectral data (Tables 1 and 2); ESI-MS: *m/z* 1361 $[M+Na]^+$; HR-FAB-MS: *m/z* 1361.6421 $[M+Na]^+$ (calcd for $C_{63}H_{102}O_{30}Na$, 1361.6354).

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