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A NEW IRIDOID GLUCOSIDE FROM *Lamiophlomis rotata*

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A new iridoid glucoside and seven known compounds were isolated from the herb of Lamiophlomis rotata *(Benth.) Kudo, which is a Tibetan folk medicine. The structure of the new iridoid glucoside was elucidated by spectroscopic methods. The others were lamiophlomiol A, shanzhigenin methyl ester, loganin, 8-*O*-acetyl-shanzhiside methyl ester, schismoside, phlomiol, and 7,8-dehydropenstemoside.*

Key words: *Lamiophlomis rotata* (Benth.) Kudo, iridoid glucoside.

Lamiophlomis rotata (Benth.) Kudo is a Tibetan folk medicine used to alleviate pain, promote blood circulation, remove blood stasis, and subdue swelling [1]. Iridoid glucosides, phenylethanoid glycosides, and flavonoids are the main components in *L. rotata*, which is widely used in Tibet and Mongolia for its good pharmacological activities [2]. Herein we report the isolation and characterization of one new iridoid glucoside (**1**), in addition to seven known iridoids from the herb of *L. rotata*.

The known compounds were identified by comparing their ^{1}H NMR and ^{13}C NMR spectra with those published in the literature for lamiophlomiol A [3], shanzhigenin methyl ester [4], loganin [5], 8-*O*-acetylshanzhiside methyl ester [6], schismoside [7], phlomiol [8], and 7,8-dehydropenstemoside [9]. Shanzhigenin methy lester, loganin, schismoside, and phlomiol were isolated for the first time from *L. rotata*.

Compound **1** in the IR spectrum (KBr) showed absorptions for OH (3450 cm^{-1}) and α,β-unsaturated ester (1698 and 1637 cm^{-1}). The UV absorption at 236 nm also confirmed the existence of these unsaturated functional groups. ESI-MS showed quasimolecular ion peaks at *m/z* 575 $[M+Na]^+$, 591 $[M+K]^+$, and 1127 $[2M+Na]^+$, suggesting its molecular formula to be $C_{23}H_{36}O_{15}$, which was supported by ^{13}C NMR-DEPT spectra.

From its ^{1}H NMR spectrum, the signals of two β-D-glucoses at δ 4.50 (d, J = 8 Hz, H-1′), 4.23 (d, J = 8 Hz, H-1″), an alkene proton at δ 7.37 (d, J = 5 Hz, H-3), a methoxyl at δ 3.64 (s, H-12), and a methyl at δ 0.97 (d, H-10) were observed. Except the carbons of glucoses, ^{13}C NMR-DEPT experiments differentiated the skeleton carbons of **1** as a carbonyl (167.59, C-11), a double bond (152.52, 109.67, C-3 and C-4), a methoxyl (51.55, C-12), CH_2 (41.34, C-7), 5 × CH [including one hemiacetal (95.14, C-1), one oxygenated methine (75.63, C-6), C-5 (40.96), C-8 (32.17), and C-9 (41.80)], and CH_3 (16.81, C-10). The above spectral information was similar to the known compound 6α-dihydrocornic acid, indicating that **1** was an iridoid glucoside [10].

In the HMBC spectrum (Fig. 1), the correlations of δ_H 4.50 (H-1′) to δ_C 95.14 (C-1) and δ_H 4.23 (H-1″) to δ_C 68.88 (C-6′) suggested that glucose was substituted at the C-1 position and two glucoses were joined at 1→6, while δ_H 7.37 (H-3) to δ_C 40.96 (C-5) and δ_C 95.14 (C-1) indicated that the α,β-unsaturated ester was substituted at the C-5 and C-1 position. C-1 (δ 95.14) in **1** was in the α-orientation [11]. The relative stereochemistry of **1** was further determined by the NOESY experiment (Fig. 1). The correlations of δ 5.40 (H-1), δ 2.49 (H-5), δ 4.08 (H-6), δ 2.71 (H-9), and δ 0.97 (H-10) suggested that the H-1, H-5, H-6 and H-9 were in the β-orientation. Hence, the structure of the new iridoid glucoside was assigned to be 6α-dihydrocornic methyl ester-6′-*O*-β-D-glucopyranoside.

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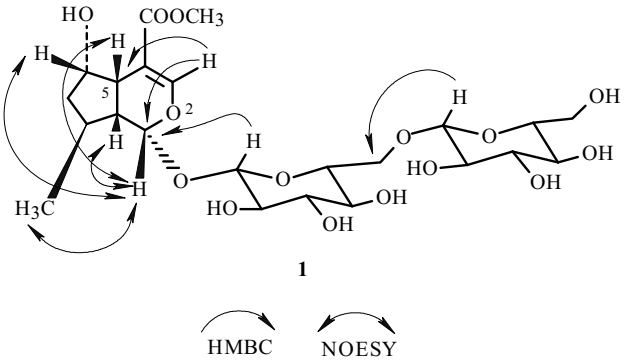

Fig. 1. The key correlations in HMBC and NOESY spectra of **1**.

EXPERIMENTAL

The solvent systems chloroform and methanol in different ratios and *n*-butanol–acetic acid–water (4:1:5) were used. TLC used HSGF-254 plates (10–40 μm, Yantai, P. R. China). Column chromatography was performed on silica gel H (200–300 mesh, Yantai, P. R. China), macroporous adsorptive resin AB-8 (0.8–1.2 mm, Tianjin, P. R. China), and Sephadex LH-20 (Pharmacia).

Spots of compounds on TLC could be stained with iodine or developed using 10% H_2SO_4–C_2H_5OH solution.

NMR spectra were recorded on a Bruker DRX-500 spectrometer at 500 MHz for ^1H NMR and 125 MHz for ^{13}C NMR. Chemical shifts are expressed in δ values with reference to DMSO-d_6 as internal standard, and coupling constants (J) are given in Hz; ESI-MS was recorded on a Varian MAT-212 mass spectrometer; melting point was measured on a ZMD83-1 electrothermal melting point apparatus and uncorrected; IR was recorded on a Brucker Vector 22 spectrometer with KBr pellet.

Extraction and Isolation of Iridoids. The dried and powdered herb of *L. rotata* (1.5 kg) was extracted under reflux with 70% alcohol (v/v) three times. The combined alcohol extract was concentrated in vacuo to 0.4 L and diluted with water to 0.8 L.Then the extract was shaken with petroleum ether, ethyl acetate, and *n*-butanol successively.

The *n*-butanol fraction (67.3 g) was dissolved with water (0.27 L) and chromatographed over the macroporous adsorptive resin AB-8, eluting with a gradient mixture of water and alcohol. The compositions of fractions (0.5 L) were analyzed by TLC. Similar fractions were combined to afford fraction 1, 16.0 g (water); fraction 2, 27.5 g (30% alcohol), and fraction 3, 11.5 g (90% alcohol). Fraction 2 was subject to chromatography on Si-gel columns eluting with a gradient mixtures of chloroform–methanol and Sephadex LH-20 with a gradient mixture of methanol–water to yield eight iridoids: lamiophlomiol A (60 mg), shanzhigenin methyl ester (40 mg), loganin (25 mg), 8-*O*-acetyl shanzhiside methyl ester (40 mg), schismoside (15 mg), phlomiol (40 mg), 7,8-dehydropenstemoside (35 mg), and 6α-dihydrocornic methyl ester-6′-*O*-β-D-glucopyranoside (**1**) (15 mg).

Compound 1: white amorphous powder, mp 147–150°C; UV (λ_{max}, CH_3OH, nm): 236; ESI-MS *m/z*: 575 $(M+Na)^+$, 591 $(M+K)^+$, 1127 $(2M+Na)^+$.

^1H NMR (DMSO-d_6, δ, ppm, J/Hz): 5.40 (1H, s, 1-H), 7.37 (1H, d, J = 5, 3-H), 2.49 (1H, br.s, 5-H), 4.08 (1H, br.s, 6-H), 1.68 (1H, m, 7-H), 1.30 (1H, m, 7-H), 2.49 (1H, br.s, 8-H), 2.71 (1H, d, J = 7, 9-H), 0.97 (3H, d, J = 5, 10-H), 4.50 (1H, d, J = 8, Glc1′-H), 3.00 (1H, br.s, Glc2′-H), 3.19 (1H, br.s, Glc3′-H), 3.10 (1H, br.s, Glc4′-H), 3.10 (1H, br.s, Glc5′-H), 4.02 (1H, d, J = 11, Glc6′-H), 3.70 (1H, m, Glc6′-H), 4.23 (1H, d, J = 8, Glc1″-H), 3.00 (1H, br.s, Glc2″-H), 3.19 (1H, br.s, Glc3″-H), 3.10 (1H, br.s, Glc4″-H), 4.08 (1H, br.s, Glc5″-H), 3.77 (1H, br.s, Glc6″-H), 3.49 (1H, br.s, Glc6″-H), 3.64 (3H, s, OCH_3).

^{13}C NMR (DMSO-d_6, δ, ppm): 95.1 (1-C), 152.5 (3-C), 109.7 (4-C), 40.9 (5-C), 75.6 (6-C), 41.3 (7-C), 32.2 (8-C), 41.8 (9-C), 16.8 (10-C), 167.6 (11-C), 51.6 (-OCH_3), 98.9 (Glc1′-C), 73.9 (Glc2′-C), 77.0 (Glc3′-C), 70.5 (Glc4′-C), 76.9 (Glc5′-C), 68.9 (Glc6′-C), 103.7 (Glc1″-C), 73.3 (Glc2″-C), 77.0 (Glc3″-C), 70.4 (Glc4″-C), 76.3 (Glc5″-C), 61.5 (Glc6″-C).

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