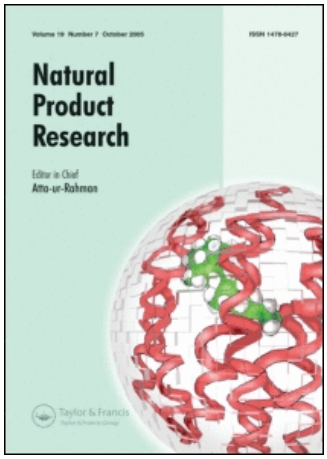

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The glycosides from **Lomatogonium rotatum**

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The glycosides from *Lomatogonium rotatum*

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A new phenyl glycoside, 2-(3′-*O*-β-D-glucopyranosyl)benzoyloxygentisic acid (**1**), along with seven known glycosides **2**–**8** was isolated from Tibetan herbal medicine *Lomatogonium rotatum*. The structures of the compounds were elucidated by spectroscopic methods including 1D and 2D NMR techniques and MS data.

Keywords: Gentianaceae; *Lomatogonium rotatum*; Phenyl glycoside

1. Introduction

Lomatogonium rotatum, belonging to the family of *Lomatogonium* in Gentianaceae, is a traditional Tibetan herbal medicine growing in Qinghai-Tibet Plateau. There are about 18 species of this genus recorded in the world and about 17 species are found in China. The aerial parts of *L. rotatum* are used in Tibetan medicine to treat liver, gall bladder and speen diseases. Precious chemical works of the plant showed that the major constituents of *L. rotatum* were xanthones, flavonoids and iridoids [1–3]. Pharmacological studies indicated that xanthones have various biological effects such as anti-inflammatory, anti-virus, hepatoprotective activity, and exciting the central nervous system [4]. The continuation of our research work for bioactive compounds have led to the isolation of a new phenyl glycoside 2-(3′*O*-β-D-glucopyranosyl) benzoyloxygentisic acid (**1**) and other seven known glycoside compounds isoorientin (**2**), mangiferin (**3**), swertipunicoside (**4**), swertianolin (**5**), isovitexin (**6**), swertisin (**7**) and 7-*O*-[α-L-rhamnopyranosyl-(1→2)-β-D-xylopyranosyl]-1,8-dihydroxy-3-methoxyxanthone (**8**). The structures of the compounds were elucidated by spectroscopic methods, especially 2D NMR experiments. Except compound **2**, others were all firstly isolated from the plant. In this article, we describe the isolation and structural elucidation of these compounds.

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2. Results and discussion

Compound **1**, white power, m.p. 159–160°C. The IR spectrum showed the absorption bands of hydroxy (3396 cm^{-1}), carbonyl (1730 cm^{-1}), carboxyl (1670 cm^{-1}), aromatic (1617, 1485 cm^{-1}) groups. The molecular formula $C_{20}H_{20}O_{11}$ of **1** was determined by the negative HRESI-MS at m/z 435.0934 $[M-H]^-$ (Calcd 435.0932) and its ^{13}C NMR (DEPT) data. In comparison with NMR spectra of 5-(3′-glucosyl)benzoyloxygentisic acid [5], **1** was agreement in the sugar moiety and the aglycone. The ^1H NMR spectrum of **1** showed an anomeric proton [δ_H 4.95 (d, $J=7.1$ Hz)], ABX-type aromatic [δ_H 7.04 (d, $J=8.9$ Hz), 7.46 (d, $J=8.9$ Hz), 7.66 (d, $J=2.9$ Hz)] and ABCD-type aromatic [δ_H 7.42 (br dd, $J=8.2$, 1.6 Hz), 7.54 (t, $J=8.1$ Hz), 7.77 (br d, $J=7.7$ Hz), 7.74 (br s)] proton signals. The ^{13}C NMR spectrum (table 1) showed signals due to one glucose moiety (δ_C 61.6, 70.7, 74.2, 77.4, 78.1, 101.8), two aromatic rings (12 carbons), one carbonyl (δ_C 165.4) and one carboxyl (δ_C 171.9) carbons. The assignment of protons and carbons was achieved on the basis of ^1H–^1H COSY and HMQC. According to the results of HMBC correlation, the glucose C-1″ proton was linked to the C-3′ position through its C-1″ position. The correction among δ_C 165.4 and δ_H 7.74, 7.77 revealed the linkage of the carbonyl carbon to the C-1′. The correction among δ_H 7.66 and δ_C 171.9, 143.1 determined the position of the carboxyl to be at C-1. Thus the structure of **1** was identified as 2-(3′-glucosyl) benzoyloxygentisic acid as shown in figure 1.

Table 1. ^1H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra data of **1** in DMSO-d_6.

C	δ_C	δ_H (J, Hz)	C	δ_C	δ_H (J, Hz)
1	114.3s		4′	122.9d	7.42 (br dd, 8.2, 1.6)
2	143.1s		5′	131.0d	7.54 (t, 8.1)
3	118.9d	7.04 (d, 8.9)	6′	124.2d	7.77 (br d, 7.7)
4	130.3d	7.46 (dd, 8.9, 2.9)	7′	165.4s	
5	159.7s		1″	101.8d	4.95 (d, 7.1)
6	123.5d	7.66 (d, 2.9)	2″	74.2d	3.28 (m)
7	171.9s		3″	77.4d	3.28 (m)
1′	131.1s		4″	70.7d	3.18 (m)
2′	118.6s		5″	78.1d	3.36 (m)
3′	158.6s		6″	61.6t	3.48 (m), 3.69 (m)

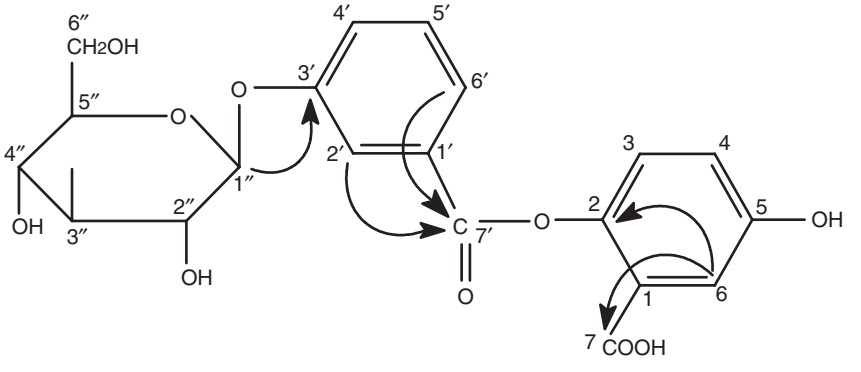

Figure 1. The structure and the key corrections in HMBC of compound **1**.

3. Experimental

3.1. *General experimental procedures*

Melting points were measured on an XRC-1 micromelting apparatus and uncorrected. IR spectra were recorded on a Nicolet MX-1 spectrometer with KBr pellets. UV spectrum was taken on a Varian CARY 300 Bio UV-Visible spectrophotometer. HRESIMS was recorded with a Bruker Daltonics Apex II. 1D and 2D NMR experiments were measured on either a Bruker-AM-400 or a Advance-DMX-500 spectrometer with the solvents DMSO-d_6 used as internal standard. Silca gel (Qingdao Haiyang Chemical Plant) was used for column chromatography. Lobar Li Chroprep RP-18 (Merck) and Sephadex LH-20 (Pharmacia) were used for CC. All solvents used were of analytical grade.

3.2. *Plant materials*

The whole plant *L. rotatum* was collected from Qinghai province, P.R. China, in 2000, and identified by Prof. Jian-Quan Liu, Northwest Plateau Institute of Biology, The Chinese Academy of Sciences. A voucher specimen was deposited in the herbarium of Tibetan Medicine research center, Northwest Plateau Institute of Biology, The Chinese Academy of Sciences.

3.3. *Extraction and isolation*

The air-dried whole plant (9.0 kg) of *L. rotatum* were extracted with 90% EtOH three times at room temperature, and the solvent was evaporated *in vacuo*. The residue (1500 g) was suspended in H_2O (2.0 L) and extracted with petroleum ether, ethyl acetate and *n*-butanol to obtain ethyl acetate fraction (170 g) and *n*-butanol fraction (370 g).

The *n*-butanol fraction (150 g) was chromatographed over silica gel column chromatography eluting with chloroform followed by increasing concentration of methanol to give fractions I–IX. Fraction VIII (19 g) was applied to silica gel CC eluting with $CHCl_3$–MeOH to give subfractions 1–9. Subfraction 4 was separated by RP-18 CC eluting with 50%, 70% MeOH and purified by sephadex LH-20 CC eluted with MeOH to give 2-(3′-*O*-*β*-D-glucopyranosyl)benzoyloxygentisic acid (**1**) (38 mg) and isoorientin (**2**) (68 mg). Subfraction 5 was separated by RP-18 eluting with 50%, 70% MeOH and purified by sephadex LH-20 eluting with MeOH to yield mangiferin (**3**) (35 mg) and swertipunicoside (**4**) (26 mg). Subfraction 6 was separated by sephadex LH-20 CC eluted with MeOH to give two segments: 6A and 6B; Segment 6A was chromatographed on silica gel CC eluting with $CHCl_3$–MeOH and purified by sephadex LH-20 CC eluting with MeOH to yield swertianolin (**5**) (120 mg) and isovitexin (**6**) (12 mg); Segment 6B was firstly chromatographed on silica gel CC eluting with $CHCl_3$–MeOH, then separated by RP-18 eluting 30%, 50% MeOH and purified by sephadex LH-20 eluting with MeOH to obtain swertisin (**7**) (54 mg) and 7-*O*-[*α*-L-rhamnopyranosyl-(1→2)-*β*-D-xylopyranosyl]-1,8-dihydroxy-3-methoxy xanthone (**8**) (68 mg).

3.4. *Identification*

2-(3′-*O*-*β*-D-glucopyranosyl)benzoyloxygentisic acid (**1**), $C_{20}H_{20}O_{11}$, white powder, m.p. 159–160°C. UV (MeOH) λ_{max} nm (log ε): 214; IR ν_{max}^{KBr} cm^{-1}: 3396, 1730, 1670, 1617, 1485; HRESI-MS (*m*/*z*): 435.0934 $[M-H]^-$ (Calcd for $C_{20}H_{19}O_{11}$, 435.0927). ^1H and ^{13}C NMR spectral data see table 1.

Isoorientin (**2**), yellow needle, m.p. 242–244°C. ^1H NMR (400 MHz, DMSO-d_6) δ_H: 7.43 (1H, d, $J=8.3$ Hz, H-6′), 7.41 (1H, s, H-2′), 6.90 (1H, d, $J=8.1$ Hz, H-5′), 6.67 (1H, s, H-3), 6.48 (1H, s, H-8), 4.61 (1H, d, $J=9.9$ Hz, glu-1H). ^{13}C NMR spectral data see table 2 [6].

Mangiferin (**3**) $C_{19}H_{18}O_{11}$, yellow needle, m.p. 250–252°C. ^1H NMR (400 MHz, DMSO-d_6) δ_H: 7.37 (1H, s, H-8), 6.86 (1H, s, H-5), 6.37 (1H, s, H-4), 4.60 (1H, d, $J=9.8$ Hz). ^{13}C NMR spectral data see table 2 [7].

Swertipunicoside (**4**), $C_{33}H_{26}O_{17}$, yellow needle, m.p. > 300°C. ^1H NMR (400 MHz, DMSO-d_6) δ_H: 7.38(1H, s, H-8′), 7.22 (1H, d, $J=6.4$ Hz, H-6), 6.71 (1H, s, H-4), 6.57 (1H, d, $J=4.6$ Hz, H-5′), 6.46 (1H, s, H-2), 4.81 (1H, d, $J=9.6$ Hz, glu-1H), 3.93 (3H, s, –OCH_3). ^{13}C NMR spectral data see table 2 [8].

Table 2. ^{13}C NMR spectra data of **2**, **3**, **4**, **5**, **6**, **7** and **8** (δ_C, 100 MHz, DMSO-d_6).

C	**3**	**5**	C	**4**	C	**2**	**6**	**7**	C	**8**
1	161.67	162.65	1	161.91					1	161.73
2	107.48	97.07	2	97.54	2	163.12	163.50	164.65	2	97.28
3	163.71	166.21	3	167.09	3	102.71	102.77	104.02	3	167.06
4	93.18	92.17	4	92.96	4	181.76	181.93	181.636	4	92.79
4a	156.09	156.36	4a	157.43	5	156.09	156.24	156.73	4a	157.43
4b	150.65	145.00	4b	143.76	6	108.74	108.69	109.62	4b	150.20
5	102.48	140.97	5	136.70	7	163.72	163.44	163.79	5	105.72
6	153.92	120.91	6	127.06	8	93.40	93.66	95.33	6	126.15
7	143.61	112.33	7	113.01	9	160.58	160.66	160.23	7	138.99
8	107.93	149.39	8	150.30	10	103.31	103.35	104.52	8	150.13
8a	111.58	112.00	8a	107.43	1′	118.86	121.09	120.90	8a	107.32
8b	101.17	103.47	8b	102.13	2′	113.2	128.46	128.42	8b	101.63
9	178.96	181.00	9	184.17	3′	145.63	115.99	115.88	9	184.01
OCH_3		56.03	OCH_3	56.22	4′	149.57	161.19	161.20	OCH_3	56.14
glu-1	72.95	103.08	1′	160.51	5′	115.94	115.99	115.88	rha-1	99.80
glu-2	70.51	73.31	2′	106.63	6′	121.33	128.46	128.42	rha-2	69.45
glu-3	78.87	75.63	3′	160.54	OCH_3			56.37	rha-3	70.41
glu-4	70.10	69.52	4′	103.48	glu-1	72.94	73.08	72.71	rha-4	71.65
glu-5	81.46	77.34	4a′	153.63	glu-2	70.51	70.60	70.81	rha-5	68.34
glu-6	61.37	60.63	4b′	150.62	glu-3	78.84	78.94	78.98	rha-6	17.78
			5′	102.43	glu-4	70.10	70.22	70.17	xyl-1	100.36
			6′	154.08	glu-5	81.45	81.55	81.74	xyl-2	77.09
			7′	145.48	glu-6	61.38	61.47	61.66	xyl-3	76.28
			8′	107.36					xyl-4	70.41
			8a′	111.48					xyl-5	65.53
			8b′	101.37						
			9′	179.40						
			glu-1′	74.05						
			glu-2′	71.76						
			glu-3′	77.78						
			glu-4′	69.21						
			glu-5′	81.06						
			glu-6′	60.15						

Swertianolin (**5**), $C_{20}H_{20}O_{11}$, pale-yellow needles, m.p. 195–197°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.27 (1H, d, $J = 9.0$ Hz, H-6), 7.13 (1H, d, $J = 9.0$ Hz, H-7), 6.58 (1H, d, $J = 1.9$ Hz, H-4), 6.38 (1H, d, $J = 1.9$ Hz, H-2), 4.80 (1H, d, $J = 7.5$ Hz, glu-1H), 3.69 (3H, s, –OCH_3). ^{13}C NMR spectral data see table 2 [9].

Isovitexin (**6**), $C_{21}H_{20}O_{10}$, yellow needle, m.p. 216–218°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.93 (2H, d, $J = 8.8$ Hz, H-2′, 6′), 6.92 (2H, d, $J = 8.8$ Hz, H-3′, 5′), 6.77 (1H, s, H-3), 6.50 (1H, s, H-8), 4.59 (1H, d, $J = 10.0$ Hz, glu-1H). ^{13}C NMR spectral data see table 2 [10].

Swertisin (**7**), $C_{22}H_{22}O_{11}$, pale-yellow needles, m.p. 234–236°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.96 (2H, d, $J = 8.7$ Hz, H-2′, 6′), 6.93 (2H, d, $J = 8.7$ Hz, H-3′, 5′), 6.64 (1H, d, $J = 6.0$ Hz, H-3), 6.62 (1H, d, $J = 3.0$ Hz, H-8), 4.61 (1H, d, $J = 7.5$ Hz, glu-1H), 3.88 (3H, d, $J = 8.7$Hz, -OCH_3). ^{13}C NMR spectral data see table 2 [11].

7-*O*-[α-L-rhamnopyranosyl-(1→2)-β-D-xylopyranosyl]-1,8-dihydroxy-3-methoxyxanthone (**8**), $C_{25}H_{28}O_{24}$, yellow needle, m.p. 236–238°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.51(1H, d, $J = 9.0$ Hz, H-6), 6.95 (1H, d, $J = 9.0$ Hz, H-5), 6.56 (1H, d, $J = 2.0$ Hz, H-4), 6.35 (1H, d, $J = 2.0$ Hz, H-2), 5.14 (1H, d, $J = 7.2$ Hz, xyl-1H), 5.08 (1H, d, $J = 3.0$ Hz, rha-1H), 3.89 (3H, s, –OCH_3), 1.10 (3H, d, $J = 3.9$ Hz, rha-6H). ^{13}C NMR spectral data see table 2 [12].

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