National Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou, P.R. China

Two new components from *Serratula strangulata* Iljin

JING-QIU DAI, YAN-PING SHI, LI YANG and YU LI

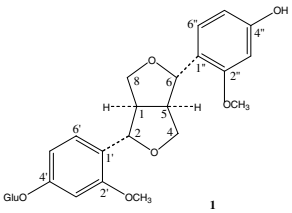
From the alcoholic extract of the whole plants of *Serratula strangulata*, two new compounds have been isolated and their structures established by spetroscopic methods as strangusin-A (**1**) and strangusin-B (**2**)

1. Introduction

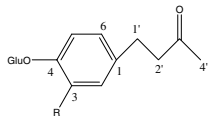
The genus *Serratula* (Compositae) consists of about 70 species distributed throughout the world. Among them, *S. chinensis* has been used as a folk medicine to treat chickenpox, toxicosis, high cholesterol [1]. A phytochemical study of the plant *S. strangulata* has not been reported so far. In this paper, we describe the isolation and structural elucidation of the chemical constituents from the whole plant of this species.

2. Investigations, results and discussion

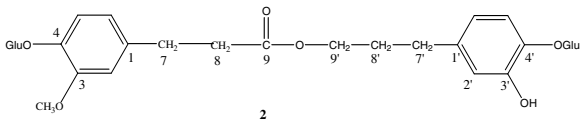
The alcoholic extract of the air-dried and powdered whole plants of *S. strangulata* was partitioned between water and ethyl acetate. The EtOAc-soluble part was concentrated and chromatographed over silica gel, to yield strangusin-A (**1**), strangusin-B (**2**), rheosimin-4-*O*-β-D-glucopyranside (**3**) [2], zingerone-4-*O*-β-D-glucopyranside (**4**) [2], 2-(*p*-hydroxyphenyl)-ethanol-1-*O*-β-D-glucopyranside (**5**) [3], *p*-methoxyphenyl-1-*O*-β-D-glucopyranoside (**6**) [4], 3,4-dihydroxyphenylformic acid (**7**) [5], Olmelin (**8**) [6], 5,6,7-trihydroxy-4′-methoxy-isoflavine (**9**) [7].



1



3. R=H
4. R=OCH$_3$



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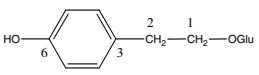

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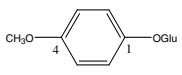

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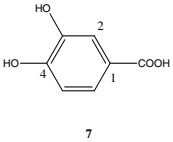

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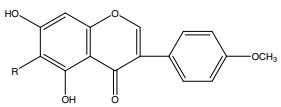

8 R = H
9 R = OH

Compound **1**, obtained as a colourless gum, was assigned the molecular formula $C_{26}H_{32}O_{11}$ by HR-FABMS (*m/z* 520.1957; Calc.: 520.1945). Its UV spectrum showed bands at 242 (log ε 4.23) and 280 nm (4.12), characteristic of a biphenyl chromophore. The IR spectrum (KBr) indicated the presence of hydroxyl (3383 cm^{-1}) and phenyl groups and double bonds (2929, 1602, 1514, 1462 cm^{-1}). The mass spectrum exhibited a base peak at *m/z* 325 [M-$C_6H_{11}O_5$−OMe−H]$^+$ and fragment ions at *m/z* 357 [M-$C_6H_{11}O_5$]$^+$ and 340[M-$C_6H_{11}O_5$−OH]$^+$. The ^{1}H NMR spectrum indicated the presence of two 1,2,4-trisubstituted benzene rings [δ 7.04 (1 H, d, J = 2.1 Hz), 6.91 (1 H, dd, J = 8.3, 2.1 Hz), 7.13 (1 H, d, J = 8.3 Hz); 6.98 (1 H, d, J = 1.8 Hz), 6.82 (1 H, dd, J = 8.2, 1.8 Hz), 6.78 (1 H, d, J = 8.2 Hz)], two methoxyl groups [3.83, 3.85 (each 3 H, s)] and an anomeric proton of glucopyranoside [δ 4.90 (d, J = 7.1 Hz)], acid hydrolysis of **1** gave glucose which was identified by TLC. Furthermore, the MS cleavage fragments of **1** at *m/z* 127 (CH_3−ArCHO), 118 (ArCH=C=O), 107 (ArCH=OH$^+$), 79 (ArH_2^+), and the ^{1}H NMR signals at δ 3.08 (m, H-1, 5), 4.66 (d, J = 4.3 Hz, H-2, 6), 4.20 (dd, J = 9.0, 6.6 Hz, H-4α, 8α), 3.85 (dd, J = 9.0, 2.4 Hz, H-4β, 8β), suggested **1** to be a lignan containing 3,7-dioxabicyclo [3.3.0] octane ring system [8–9].

In the ^{1}H-^{1}H COSY spectrum of **1**, there were significant cross-peaks between 3.08 (H-1, 5) and 3.85 (H-4 α, 8 β), and 4.20 (H-4 α, 8 α), H-1 and 4.66 (H-2); H-5 and 4.71 (H-6). This further testified the presence of furofuran ring in **1**. In the NOESY spectrum of **1**, there were significant cross-peaks between H-1 and H-8α, H-2 and H-8β, H-5 and H-4α, H-6 and H-4β, indicating H-1, 5 as α-orientated and H-2, 6 as β-orientated. Now, the only structural problem left was to ascertain the locations of glucose, hydroxy and two methoxyl groups. The HMBC spectrum exhibited related peaks at δ 156.65 (C-2′) and 3.85 (OCH_3) and 7.04 (H-3′); 156.73 (C-2″) and 3.83 (OCH_3) and 6.98 (H-3″); 124.60 (C-1′) and 7.13 (H-6′) and 4.66 (H-2); 122.96 (C-1″) and 6.78 (H-6″) and 4.71 (H-6); 155.97 (C-4″) and 6.82 (H-5″) and 6.98 (H-3″); 157.25 (C-4′) and 6.91 (H-5′) and 7.04 (H-3′) and 4.90 (the glucosyl C-1 proton signal). Consequently, the structure of **1** was established. This appears to be the first reported occurrence of a lignan in the family *Serratula*.

Compound **2** was obtained as a colourless gum. The IR spectrum showed the presence of hydroxyl (3389cm^{-1}), aromatic rings (3008, 1600, 1510 cm^{-1}) and carbonyl group (1708 cm^{-1}). FABMS exhibited the [M]$^+$ peak at *m/z* 670. The ^{13}C NMR and DEPT spectrum indicated that compound **2** possesses 16 × CH, 7 × CH_2, 1 × CH_3

and seven quarternary carbon atoms. Thus, the molecular formula of **2** was determined as $C_{31}H_{42}O_{16}$, which was confirmed by HR-FABMS (*m/z* 670.2469; Calc.: 670.2473). The ^{1}H NMR spectrum displayed resonances at δ 6.96 (1 H, d, J = 8.2 Hz), 6.62 (1 H, d, J = 1.4 Hz), 6.51 (1 H, dd, J = 8.2, 1.4 Hz), 6.74 (1 H, d, J = 1.1 Hz), 6.65 (1 H, d, J = 8.0 Hz), 6.56 (1 H, dd, J = 8.0, 1.1 Hz), indicating the presence of two 1,2,4-trisubstituted benzene rings. The ^{1}H NMR spectrum also showed the presence of two anomeric protons of glucopyranoside [δ 4.68 (d, J = 7.3 Hz), 4.26 (d, J = 7.6 Hz). These data together with ^{13}C NMR signals at δ 103.87 (CH), 74.19 (CH), 76.93 (CH), 70.70 (CH), 77.17 (CH), 62.03 (CH_2), andδ 104.30 (CH), 74.49 (CH), 77.47 (CH), 71.12 (CH), 77.68 (CH), 62.37 (CH_2), indicated compound **2** to have two β-glucosyl moiety [10].

In the ^{1}H-^{1}H COSY spectrum of **2**, there were significant cross-peaks between δ 2.67 (H-7) and 2.53 (H-8), 1.75 (H-8′) and 2.61 (H-7′) and 3.83 (H-9′), suggesting the presence of the partial structures $-CH_2-CH_2-$ and $-CH_2-CH_2-CH_2-$, respectively. the HMBC spectrum exhibited related peaks at δ 137.93 (C-1) and 2.67 (H-7) and 6.62 (H-2) and 6.51 (H-6); 144.56 (C-4) and 6.96 (H-5) and 4.68 (the glucosyl C-1 proton signal); 148.24 (C-3) and 3.83 (OCH3) and 6.62 (H-2); 175.26 (C-9) and 2.53 (H-8) and 3.83 (H-9′); 134.16 (C-1′) and 2.61 (H-7′) and 6.74 (H-2′) and 6.56 (H-6′); 148.30 (C-4′) and 6.65 (H-5′) and 4.26 (the glucosyl C-1′ proton signal). Furthermore, in its FABMS spectrum, the fragment ions at *m/z* 342 ($C_{16}H_{21}O_8^+$) and 358 ($C_{16}H_{21}O_9^+$) was due to the α-fragmentation around carbonyl group. Thus, the structure of **2** was deduced.

Table 1: ^{1}H and ^{13}C NMR data of compound 1 ($(CD_3)_2CO$, TMS, ppm)*

Carbon No.	δ_H	δ_C	DEPT
1	3.08 m	55.09	CH
2	4.66 d (4.3)	86.56	CH
4	4.20 dd (9.0, 6.6)	72.17	CH_2
	3.85 dd (9.0, 2.4)		
5	3.08 m	55.21	CH
6	4.71 d (4.2)	86.30	CH
8	4.20 dd (9.0, 6.6)	72.26	CH_2
	3.85 dd (9.0, 2.4)		
1′		124.60	C
2′		156.65	C
3′	7.04 d (2.1)	107.31	CH
4′		157.25	C
5′	6.91 dd (8.3, 2.1)	109.57	CH
6′	7.13 d (8.3)	130.13	CH
2′-OCH_3	3.85 s	56.39	CH_3
1″		122.96	C
2″		156.73	C
3″	6.98 d (1.8)	108.14	CH
4″		155.97	C
5″	6.82 dd (8.2, 1.8)	110.22	CH
6″	6.78 d (8.2)	130.50	CH
2″-OCH_3	3.83 s	56.20	CH_3
Glu			
1	4.90 d (7.1)	102.48	CH
2	3.44 dd (7.1, 8.0)	74.47	CH
3	3.83 dd (8.1)	77.70	CH
4	3.46 dd (8.0)	71.06	CH
5	3.50 ddd (8.0, 4.9, 1.1)	77.54	CH
6a	3.67 dd (11.8, 4.9)	62.42	CH_2
6b	3.80 dd (11.8, 1.1)		

* Assignment from ^{1}H-^{1}H COSY HMQC, HMBC and NOESY

3. Experimental

3.1. Equipment

^{1}H, ^{13}C NMR and 2D NMR spectra were scanned on a Bruker AM 400 FT-NMR spectrometer with TMS as internal reference. IR spectra were recorded on a Shimadzu UV-260 spectrophotometer. HR-FABMS, FABMS and EIMS data were obtained on a Bruker APEX II FT-MS and HP-5988 MS spectrometers respectively. Silica gel (200–300, 300–400 mesh) was used for CC and silica gel GF_{254} for TLC. Spots were detected on TLC under UV light or by heating after spraying with 5% H_2SO_4.

3.2. Plant material

The plant material was collected in August 1996 in Gansu Province of China and identified by Prof. Yong-Hong Zhang of Lanzhou University. A voucher specimen (No. 9602) has been deposited at the Lab. of Natural Products, Department of Chemistry, Lanzhou University, Lanzhou, P.R. China.

3.3. Extraction and isolation

The air-dried whole plants of *S. strangulata* (3 kg) were powdered and extracted three times (each 5 days) with alcohol at room temperature. The extract was concentrated under reduced pressure. The residue was suspended in H_2O, and extracted with pet. ether, EtOAC and BuOH, respectively. The EtOAC extract (40 g) was obtained and subjected to CC over silica gel (800 g, 200–300 mesh) with a pet. ether-Me_2CO gradient. It was separated into 6 crude fractions (fractions 1–6). From fraction 3 (pet. Ether-Me_2CO 7 : 1), a crude material was obtained and purified by rechromatography on a silica gel column (300–400 mesh with pet. Ether-Me_2CO 8 : 1) to give compounds **8** (70 mg) and **9** (50 mg). Fraction 5 (pet. Ether-Me_2CO 5 : 1) (15 g) was further separated by CC over silica gel using $CHCl_3$–MeOH (30 : 1) (2500 ml) and pet. ether-Me_2CO (5 : 1) (3000 ml) as eluants, and purified by preparative TLC with pet. ether-Me_2CO as irrigant finally giving 20 mg of **1,** 15 mg of **2**, 30 mg of **3**, 15 mg of **4**, 20 mg of **5**, 25 mg of **6**, 45 mg of **7**.

The known compounds were identified either by comparing their properties (m.p., IR, ^{1}H and ^{13}C NMR) with literature values or by comparing with authentic samples.

Table 2: ^{1}H and ^{13}C NMR data of compound 2 ($(CD_3)_2CO$, TMS, ppm)*

No.	δ_H (Hz)	δ_C	DEPT
1		137.93	C
2	6.62 d (1.4)	113.11	CH
3		148.24	C
4		144.56	C
5	6.96 d (8.2)	116.71	CH
6	6.51 dd (8.2, 1.4)	119.98	CH
7	2.67 dd (6.6)	32.37	CH_2
8	2.53 dd (6.6)	45.26	CH_2
9		175.26	C
1′		134.16	C
2′	6.74 d (1.1)	115.57	CH
3′		148.30	C
4′		145.56	C
5′	6.65 d (8.0)	119.00	CH
6′	6.56 dd (8.0, 1.1)	121.46	CH
7′	2.61 dd (7.5)	32.11	CH_2
8′	1.75 m	29.79	CH_2
9′	3.83 dd (6.0)	69.21	CH_2
glu			
1	4.68 d (7.3)	103.87	CH
2	3.20 dd (7.3, 8.0)	74.19	CH
3	3.41–3.77 m	76.93	CH
4	3.41–3.77 m	70.70	CH
5	3.41–3.77 m	77.17	CH
6	3.41–3.77 m	62.03	CH_2
1′	4.26 d (7.6)	104.30	CH
2′	3.34 dd (7.6, 8.1)	74.49	CH
3′	3.41–3.77 m	77.47	CH
4′	3.41–3.77 m	71.12	CH
5′	3.41–3.77 m	77.68	CH
6′	3.41–3.77 m	62.37	CH_2

* Assignment from ^{1}H-^{1}H COSY, HMQC and HMBC

3.4. Strangusin-A (**1**)

Colourless gum. $[\alpha]_D^{22}$ −59.8 (*c* 0.26, MeOH); UV ($CHCl_3$): 242 (log ε 4.23) and 280 nm (4.12); IR ν_{max}^{KBr} cm^{-1}: 3383, 2929, 2870, 1602, 1462, 1271, 1127, 1074, 1037, 815, 628; FABMS $[M]^+$ *m/z*: 520 (11), 481(5), 449 (7), 425 (10), 389 (22), 357 (62), 325 (100), 311 (49), 297 (45), 265 (40), 221 (10), 205 (20), 127 (24), 96 (2.5), 80 (10); ^1H and ^{13}C NMR: Table1.

3.5. Strangusin-B (**2**)

Colourless gum; $[\alpha]_D^{22}$ −81.7 (*c* 0.30, MeOH); IR ν_{max}^{KBr} cm^{-1}: 3389, 2922, 1708, 1601, 1514, 1430, 1370, 1276, 1074, 799, 582; FABMS $[M]^+$ *m/z*: 670 (5), 661 (7), 571 (8), 525 (9), 449 (10), 433 (21), 419 (10), 403 (8), 489 (15), 471 (7), 357 (33), 341 (100), 325 (45), 311 (24), 297 (27), 265 (20), 205 (7), 173 (8), 157 (6), 127 (25), 99 (15), 80 (7); ^1H and ^{13}C NMR: Table 2.

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Jing-Qui Dai
National Laboratory
of Applied Organic Chemistry
Lanzhou University
Lanzhou, Gansu 730000
China