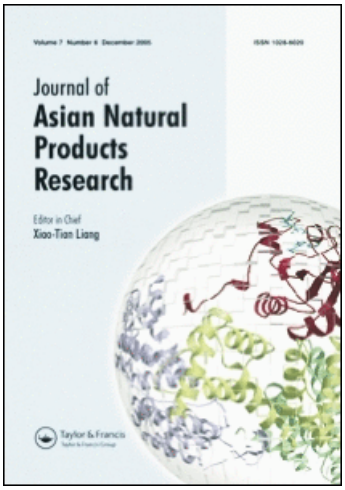

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Long-Ru Sun[a]; Xian Li[b]; Su-Xian Wang[b]
[a] School of Pharmacy, Shandong University, Jinan, China [b] Research Department of Natural Product Chemistry, Shenyang Pharmaceutical University, Shenyang, China

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Two new alkaloids from the rhizome of *Polygonatum sibiricum*

LONG-RU SUN†*, XIAN LI‡ and SU-XIAN WANG‡

†School of Pharmacy, Shandong University, 44 West Wenhua Road, Jinan 250012, China
‡Research Department of Natural Product Chemistry, Shenyang Pharmaceutical University, 103 Wenhua Road, Shenyang 110015, China

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Two new alkaloids named polygonatine A (**1**) and polygonatine B (**2**) have been isolated from the rhizome of *Polygonatum sibiricum* Redoute (Liliaceae). By spectral data (IR, UV, MS, 1D and 2D NMR) and chemical evidence, their structures were elucidated as 3-hydroxymethyl-5,6,7,8-tetrahydroindolizin-8-one (**1**) and 3-ethoxymethyl-5,6,7,8-tetrahydroindolizin-8-one (**2**).

Keywords: *Polygonatum sibiricum* Redoute; Alkaloids; Polygonatine A; Polygonatine B

1. Introduction

The rhizoma of *Polygonatum sibiricum* Redoute (Liliaceae), known as 'Huangjing' (a Solomon's seal) in traditional Chinese medicines, is used as a tonic and remedy to lung troubles and ringworm [1]. Various steroidal saponins [2], flavonoids [3] and only one alkaloid [4], polygonapholine, have been isolated from *Polygonatum* species. In our studies on the constituents of the rhizome of *Polygonatum sibiricum* we obtained two novel alkaloids, polygonatine A (**1**) and polygonatine B (**2**), and elucidated their structures on the basis of detailed analysis of their spectral data and chemical evidence. Their skeleton only has been reported as the volatile composition of Virginia tobacco analyzed with GC-MS [5].

2. Results and discussion

The alcoholic extract of the dried rhizomes of *Polygonatum sibiricum* was suspended in water and then extracted sequentially with light petroleum (60–90°C), chloroform, ethyl acetate and n-butanol. The chloroform fraction was then subjected to column chromatography, followed by preparative thin-layer chromatography or recrystallization and compounds **1** and **2** were obtained.

*Corresponding author. Tel.: +86-0531-8382012. Fax: +86-0531-8382019. E-mail: sunlr@sdu.edu.cn

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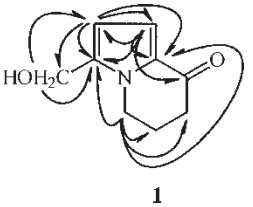
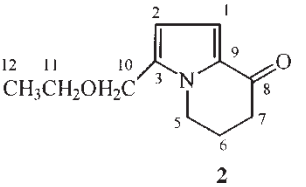
Table 1. NMR spectral data of **1** (in CD_3COCD_3) and **2** (in $CDCl_3$).

	1				*2*	
Carbon no.	^{13}C	^{1}H	^{1}H–^{1}H *COSY*	*HMBC*	^{13}C	^{1}H
1	112.9	6.77 *d* (4.0)	H-2	C-2, C-3, C-8, C-9	113.1	6.97 *d* (4.0)
2	110.3	6.15 *d* (4.0)	H-1	C-1, C-3, C-9, C-10	111.6	6.23 *d* (4.0)
3	138.7				134.3	
5	43.0	4.18 *m*	H_2-6	C-3, C-6, C-7, C-9	42.5	4.12 *t* (5.8)
6	24.0	2.25 *m*	H_2-5, H_2-7	C-5, C-8	23.4	2.29 *m*
7	36.5	2.49 *m*	H_2-6	C-5, C-6, C-8	36.0	2.60 *t* (6.4)
8	187.6				187.5	
9	132.0				131.8	
10	56.2	4.60 *s*		C-2, C-3	63.9	4.48 *s*
11					65.5	3.51 *q* (7.0)
12					15.1	1.22 *t* (7.0)

Compound **1** was obtained as colorless needles. It gave a positive reaction toward Dragendorff's reagent. The positive HRFAB MS showed its molecular formula to be $C_9H_{11}NO_2$. Absorption bands at 1535 and 1492 cm^{-1} in the IR spectrum indicated an aromatic ring. The fragment ions at *m/z* 120, 106 and 78 in its EI MS and only four carbon signals at δ 112.9, 110.3, 138.7 and 132.0 ppm in the lower field of its ^{13}C NMR spectrum suggested that the aromatic moiety is a pyrrole ring. Two doublets at δ 6.77 (1H, d, $J = 4.0$ Hz) and 6.15 (1H, d, $J = 4.0$ Hz) due to pyrrole protons were observed in lower field of the ^{1}H NMR spectrum, and correlate mutually in ^{1}H–^{1}H COSY (table 1). This indicates that the hydrogens at the two α positions of the pyrrole ring are substituted. Three additional multiplets at δ 4.18 (2H, m), 2.49 (2H, m) and 2.25 (2H, m), corresponding to three methylenes, were observed. The proton signal at δ 4.18 is associated with the signal at δ 2.25, the latter giving a correlation with the signal at δ 2.49 in the ^{1}H–^{1}H COSY. By a combination of these data in HMQC and HMBC spectra, the fragment moiety [—(5)CH_2—(6)CH_2—(7)CH_2—(8)CO—] was revealed. In the HMBC spectrum, H-5 of above moiety exhibited long-range correlations with C-3 and C-9, leading to the assignment of C-5 linked to the nitrogen of the pyrrole ring (figure 1). The IR absorption band at 1630 cm^{-1}, and the HMBC long-range correlation between H-1 and C-8, confirm that the carbonyl group of above fragment should be attached to one α position of the pyrrole ring. The other α position of the pyrrole ring is linked to another methylene group, as confirmed by the long-range correlations between the methylene protons (H-10) and C-2 and C-3 in the HMBC spectrum. The chemical shifts of H-10 (δ 4.60, s) and C-10 (δ 56.2) in the ^{1}H and ^{13}C NMR spectra, together with the absorption indicative of hydroxyl (3383 cm^{-1}) in the IR spectrum, suggest that the methylene group is also attached to a hydroxy group. Therefore, the structure of compound **1** was characterized as 3-hydroxymethyl-5,6,7,8-tetrahydroindolizin-8-one, named polygonatine A.



1



2

Figure 1. HMBC correlations of **1** and the structure of **2**.

Compound **2**, a pale yellow syrup, gave a positive reaction toward Dragendorff's reagent. Its EI MS exhibited many fragment ions that resembled those in the EI MS of **1** and gave the molecular ion peak at *m/z* 193; in combination with fifteen protons in its ^{1}H NMR spectrum and eleven carbon signals in its ^{13}C NMR spectrum its formula was deduced to be $C_{11}H_{15}NO_2$. The ^{1}H and ^{13}C NMR spectra of **2** were similar to those of **1**, except for the proton signals at δ 3.51 and 1.22 for H-11 and H-12 and the carbon signals at δ 65.5 and 15.1 for C-11 and C-12, respectively. This showed that **2** has the same skeleton as **1**. The two-proton quartet at δ 3.51 and the three-proton triplet at δ 1.22 composed of an A_2X_3 coupling system pattern indicate an ethoxy group. Thus, compound **2** should be designated as 3-ethoxymethyl-5,6,7,8-tetrahydroindolizin-8-one, named polygonatine B (figure 1).

3. Experimental

3.1 General experimental procedures

Melting points were measured on a Yanaco MP-S3 instrument and are uncorrected. UV and IR spectra were separately recorded with a Shimadzu UV-260 spectrophotometer and a Bruker IR S-55 spectrometer. NMR spectra were determined on Bruker AC (E)-300 (**1**, CD_3COCD_3) and Bruker AMX-250 (**2**, $CDCl_3$) spectrometers with TMS as an internal standard. EI MS and FAB MS were performed with a VG-7070E HF and a VG 70SE, respectively.

3.2 Plant material

The rhizomes of *Polygonatum sibiricum* Redoute were collected from Chengde County, Hebei Province, China, in September, 1996, and were identified by Professor Qi-Shi Sun, Department of Traditional Chinese Medicines, Shenyang Pharmaceutical University, China, where a voucher specimen has been deposited.

3.3 Extraction and isolation

Air-dried, powdered rhizomes of *Polygonatum sibiricum* (30 kg) were extracted under reflux with 90% EtOH (3 ×). The filtrates were then mixed and concentrated *in vacuo* to a syrup, which was suspended in water and extracted sequentially with light petroleum (60–90°C), $CHCl_3$, EtOAc and n-BuOH. The $CHCl_3$ fraction (93 g) was subjected to column chromatography on silica gel, eluted with light petroleum–acetone by a gradient method. The fraction eluted with light petroleum–acetone (100:6) was developed by silica gel preparative thin-layer chromatography (PTLC) with cyclohexane–acetone (7:1) to give **2** (23 mg). Another fraction eluting with light petroleum–acetone (100:35) was repeatedly chromatographed over a silica gel column with $CHCl_3$–MeOH and finally, after recrystallization from Me_2CO, yielded **1** (240 mg).

Polygonatine A (**1**) was obtained as colorless needles from acetone; mp 101–103°C; UV λ_{max} (nm) (lg ε): 298 (3.3), 206 (2.8). IR ν_{max} (cm^{-1}): 3383 (OH), 3125 (=CH), 2963, 2922, 2883 (CH_2, CH_3), 1630 ($\alpha\beta$ conjugated C=O), 1535, 1492 (aromatic ring), 798, 754, 618. ^{1}H, ^{13}C NMR, ^{1}H—^{1}H COSY, HMQC and HMBC (CD_3COCD_3): see table 1. HRFAB MS

m/z: $[M]^+$: 165.0824; calcd for $C_9H_{11}NO_2$, 165.0790. EI MS *m/z*: 165 (83.1) $[M]^+$, 148 (100), 136 (24.8), 120 (39.0), 109 (16.6), 108 (14.9), 80 (29.3), 78 (19.9).

Polygonatine B (**2**) was obtained as a pale yellow syrup; UV λ_{max} (nm) (lg ε): 323 (3.2), 214 (3.0). IR ν_{max} (cm^{-1}): 3120 (=CH), 2972, 2920, 2855 (CH_2, CH_3), 1661 (αβ conjugated C=O), 1600, 1538 (aromatic ring), 1090 (C—O—C). ^1H, ^{13}C NMR and ^1H—^{13}C COSY ($CDCl_3$): see table 1. EI MS *m/z*: 193 (100), 164 (14.71), 148 (99.96), 136 (15.59), 120 (42.73), 106 (21.84), 78 (19.19).

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