Isoquinoline Alkaloids from *Corydalis taliensis*

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Corydalis taliensis Franch is a perennial herb used for treatment of rheumatic arthritis, toothache, and hepatitis. The chemical investigation of this plant resulted in the isolation of a new compound, named taliensineside (**1**). Its structure was identified on the basis of spectral evidence. In addition, thirteen known isoquinoline alkaloids (**2** – **14**) were isolated and identified by spectroscopic analysis and comparison of their spectral data with those reported previously.

Key words: Corydalis taliensis Franch, Isoquinoline Alkaloid, Talensineside

Introduction

Corydalis taliensis Franch is a perennial herb that grows at an altitude of 1500 – 1800 m in Yunnan Province, China [1]. The whole plant is used for treatment of rheumatic arthritis, toothache and hepatitis by the natives [2]. Previous chemical investigation of this plant reported seven alkaloids [3]. During our search for bioactive entities from indigenous Yunnan herbs, we undertook a chemical study of the whole plant of *C. taliensis*, which led to the isolation of fourteen isoquinoline alkaloids, one of which is new.

Result and Disscusion

The ethanol extract of the whole plant of *C. taliensis* was partitioned between H_2O/$CHCl_3$ and then between *n*-BuOH/H_2O. The two extracts were subjected to repeated column chromatography on silica gel and Sephadex LH–20, leading to the isolation of a new isoquinoline alkaloid (**1**), together with thirteen known ones. The thirteen known isoquinoline alkaloids were identified as 6-acetonylacetylcorynoline (**2**) [4], sibiricine (**3**) [5], (+)-adlumidine (**4**) [6], tetrahydrothalifendine (**5**) [7], (+)-corynoline (**6**) [8], isocorynoline (**7**) [8], acetylcorynoline (**8**) [9], (*S*)-bulocapnine (**9**) [10], *N*-methylcalycinine (**10**) [11], 9,10-dihydroxy-2,3-dimethoxytetrahydroprotoberberine (**11**) [12], (*S*)-reticuline (**12**) [13], (–)-oblongine (**13**) [14], and magnoflorine (**14**) [15] by their spectral data and comparison of those reported (Fig. 1).

Compound **1** tested positive to Dragendorff's reagent. The molecular formula was determined to be $C_{25}H_{33}NO_{10}$ based on the ESIMS, exhibiting the molecular ion peak at *m/z* = 508 $[M+H]^+$, which was further confirmed by HRESIMS at *m/z* = 508.2182 (calcd. 508.2171). Its IR spectrum indicated the presence of hydroxy groups (3340 cm^{-1}) and aromatic rings (1628, 1510 and 1447 cm^{-1}). Compound **1** showed four singlet signals (δ = 7.00, 6.73, 6.38, 6.12) in the ^1H NMR spectrum, suggesting the presence of two 1,2,4,5-tetrasubstituted aromatic rings, in addition to one *N*-methyl group (δ = 2.75, s) and two methoxyl groups (δ = 3.85, s; 3.82, s). The ^{13}C NMR spectrum of compound **1** revealed 25 carbon atoms, among which 17 carbons including two aromatic rings, three methylenes, one methine, and one *N*-methylene possessed the characteristic of *N*-methylbenzenylisoquinoline, which was further confirmed by COSY and HMQC spectra. The ^{13}C NMR data of compound **1** were similar to those of fumarizine [16] except for further six carbons accounting for a D-glucopyranosyl moiety. Acid hydrolysis of compound **1** afforded D-glucose, which was detected by TLC and identified by comparison with an authentic sample. The ^1H NMR signal of **1** at δ = 4.86 (1H, d, J = 7.3 Hz, 1′-H) suggested the presence of a β-D-glucopyranoside moiety. In the HMBC spectrum, a significant correlation was observed between

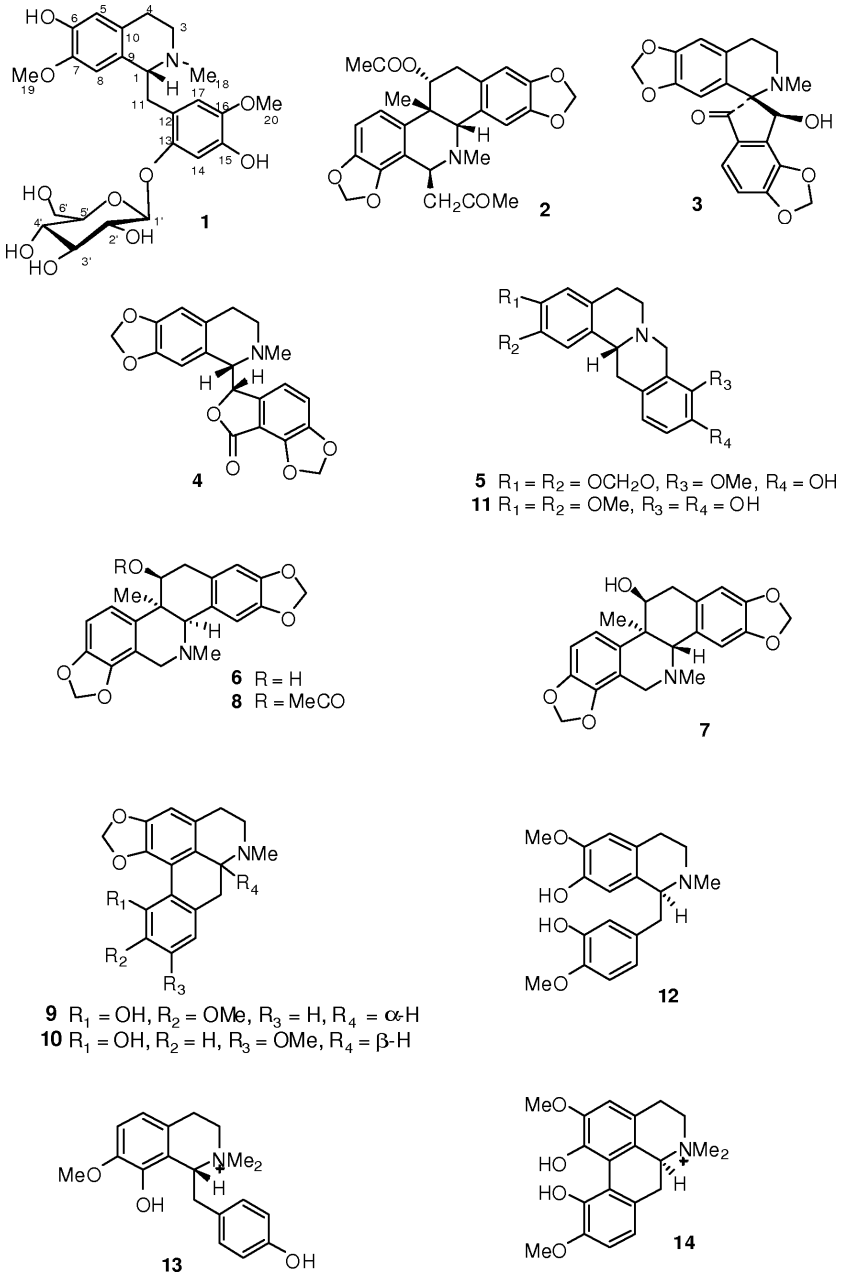

Fig. 1. Structures of compounds **1** – **14** isolated from *C. taliensis*.

the signals at δ = 4.86 (1H, d, J = 7.3 Hz, 1′-H) and 150.6 (s, C-13), suggesting that the glucose moiety was linked to the C-13 position as shown in Fig. 2. Two methoxyl groups at C-7 and C-16 were also confirmed by the correlation of δ = 3.85 (3H, s, 19-H) with 148.7 (s, C-7) and of δ = 3.82 (3H, s, 20-H) with 148.9 (s, C-16). The optical rotation value of compound **1** ($[\alpha]_D^{17} = -2.3$) numerically corresponds to the sum of an aglycone and β-D-glucopyranose ($[\alpha]_D^{17}$ = 70.5 [17]), suggesting that the aglycone is laevorotatory. The skeleton of the *N*-methyl benzenylisoquinoline alkaloid in the *R*-form (fumarizine, $[\alpha]_D$ = −63.2 [16]) is laevorotatory, while the *S*-form (dehassiline, $[\alpha]_D$ = 63.9 [18]) is dextrorotary. Therefore,

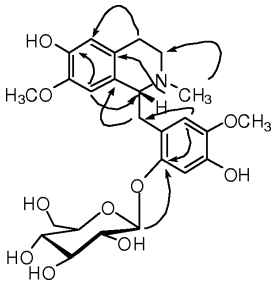

Fig. 2. Key HMBC correlations of compound **1**.

the stereochemistry of compound **1** at C-1 is proposed to be *R*. Based on the above evidence, the structure of compound **1**, named taliensineside, was elucidated to be (1*R*)-13-*O*-β-D-glucopyranosyl-6,13,15-trihydroxy-7,16-dimethoxy-*N*-methyltetrahydroisoquinoline.

Experimental Section

General

Melting points were obtained on an XRC-1 micro-melting point apparatus and are uncorrected. Optical rotations were measured on a Horiba SEPA-300 polarimeter. UV spectra were obtained in a UV-210A spectrometer. IR spectra were obtained with a Bio-Rad FTS-135 spectrometer with KBr pellets. MS were recorded on a VG Auto spec-3000 spectrometer or on a Finnigan MAT 90 instrument. The 1D and 2D NMR spectra were recorded on a Bruker AM-400 or a Bruker DRX-500 instrument with TMS as an internal standard. Column chromatography was performed on silica gel G (200 – 300 mesh, Qingdao Marine Chemical Inc., China), silica gel H (10 – 40 μm, Qingdao Marine Chemical Inc., China), reversed phase C-8 silica gel (40 – 63 μm, Merck, Darmstadt, German), and Sephadex LH-20 (25 – 100 μm, Amersham Bioscience). Fractions were monitored by TLC, and spots were visualized by spraying the silica gel plates with Dragendorff's reagent.

Plant material

The whole plant of *C. taliensis* Franch was collected in Aziying of Kunming, Yunnan province, China, in May 2006. The plant was identified by Prof. Yu Chen, Kunming Institute of Botany, Kunming, Chinese Academy of Sciences, P. R. China, where the voucher specimen [KUN No. 0745244] was deposited.

Extraction and isolation

The whole plant of air-dried *C. taliensis* (3.5 kg) was ground, and then refluxed in 95 % EtOH (4.0 L) for 3×3 h. After removal of the solvent by evaporation, the concentrated extract was suspended in water and extracted successively with chloroform and then *n*-butanol. The chloroform extract (16.2 g) was divided into five fractions (fr. B1 – B5) by column chromatography (CC) on silica gel eluted with CH_3Cl/Me_2CO (3 : 2). Fr. B1 (2.60 g) was submitted to H silica gel eluting with $CHCl_3/Me_2CO$ (20 : 1 – 10 : 1) to obtain **2** (4 mg) and **3** (18 mg). Fr. B2 (1.58 g) was subjected repeatedly to CC with $CHCl_3/Me_2CO$ (9 : 1) to yield **4** (614 mg), **5** (15 mg) and **6** (448 mg). Fr. B3 (2.26 g) was further separated into three fractions. (fr. B3-1 – B3-3). Compound **8** (305 mg) was isolated from fr. B3-2 by CC eluted with petroleum ether/EtOAc (6 : 1). Fr. B3-3 was submitted to H silica gel by using petroleum ether/Me_2CO (5 : 1) to give **7** (25 mg). Fr. B4 (1.54 g) was chromatographied repeatedly over H silica gel with $CHCl_3/Me_2CO$ (3 : 1) and Sephadex LH-20 with $CHCl_3$/MeOH (3 : 2) to give **9** (3 mg), **10** (10 mg) and **11** (21 mg). Pure **12** (12 mg) was obtained from fr. B5 (0.52 g) by CC with $CHCl_3/Me_2CO$ (1 : 1). The *n*-butanol extract (9.68 g) was partitioned into seven fractions (fr. C1 – C7) by CC with $CHCl_3$/MeOH/EtOAc/H_2O (4 : 5 : 2 : 1). Fr. C3 (2.07 g) was subjected to H silica gel eluted with $CHCl_3$/MeOH/H_2O (from 7 : 3 : 0.5 to 6 : 4 : 0.4) to yield four fractions (fr. C3-1 – C3-4). Compound **13** (11 mg) was isolated from fr. C3-3 by CC with $CHCl_3$/MeOH/H_2O (7 : 12 : 8). Fr. C3-4 was chromatographied by CC using $CHCl_3$/MeOH/H_2O (7 : 12 : 8) to yield **14** (30 mg) and two fractions (fr. C3-4-1 and C3-4-2). Fr. C3-4-2 was subjected to reversed phase C-8 silica gel with MeOH/H_2O (95 : 5) and purified by Sephadex LH-20 eluted with H_2O to yield **1** (5 mg).

Taliensineside (**1**): Yellow amorphous powder. – UV (MeOH): $\lambda_{max}(\lg \varepsilon_{max})$ = 205.4 nm (4.43), 288.0 nm (2.57). – $[\alpha]_D^{17} = -2.3$ (c = 0.20, MeOH). – IR (KBr): ν = 3340, 2955 – 2855, 1628, 1510, 1447, 1073 cm^{-1}. – ^1H NMR (400 MHz, CD_3OD): δ = 2.75 (s, 3H, 18-H), 2.88 (dd, J = 9.4, 8.1 Hz, 11b-H), 2.97 (m, 1H, 4b-H), 3.08 (m, 1H, 4a-H), 3.15 (m, 1H, 3b-H), 3.30 (m, 1H, 11a-H), 3.33 (m, H, 4′-H), 3.45 (m, 1H, 2′-H), 3.46 (m, 1H, 5′-H), 3.49 (m, 1H, 3′-H), 3.65 (m, 1H, 3a-H), 3.68 (dd, J = 11.9, 2.0 Hz, 1H, 6′b-H), 3.82 (s, 3H, 20-H), 3.85 (s, 3H, 19-H), 3.92 (dd, J = 11.9, 2.0 Hz, 1H, 6′a-H), 4.46 (d, J = 9.4, 5.7 Hz, 1H, 1-H), 4.86 (d, J = 7.3 Hz, 1H, 1′-H), 6.12 (s, 1H, 8-H), 6.38 (s, 1H, 17-H), 6.73 (s, 1H, 5-H), 7.00 (s, 1H, 14-H). – ^{13}C NMR (100 MHz, CD_3OD): δ = 64.2 (C-1), 46.8 (C-3), 24.0 (C-4), 112.6 (C-5), 145.5 (C-6), 148.7 (C-7), 115.9 (C-8), 130.0 (C-9), 123.0 (C-10), 36.5 (C-11), 120.0 (C-12), 150.6 (C-13), 103.6 (C-14), 142.9 (C-15), 148.9 (C-16), 118.8 (C-17), 36.5 (C-18), 55.6 (C-19), 56.4 (C-20), 104.3 (C-1′), 78.5 (C-2′), 75.2 (C-3′), 71.8 (C-4′), 78.5 (C-5′), 62.8 (C-6′). – MS ((+)-ESI): m/z (%) = 508 (100) $[M+H]^+$. – HRMS ((+)-ESI): m/z = 508.2182 (calcd. 508.2171 for $C_{25}H_{34}NO_{10}$, $[M+H]^+$).

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