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Two new phenylpropanoids from *Penthorum chinense* Pursh

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ABSTRACT

The chemical investigation of *Penthorum chinense* resulted in the isolation of two new phenylpropanoids (**1** and **2**) along with three known compounds (**3–5**). The structures of the compounds **1** and **2** were determined by interpretation of the spectroscopic data, including IR, HR-ESI-MS, ^{1}H NMR, ^{13}C NMR, DEPT, COSY, HMBC and HMQC. Moreover, all the compounds were evaluated for their hepatoprotective activity in H_2O_2-induced cytotoxicity in HL-7702 cells, and compounds **2–4** (2.5 μg/mL) showed a moderate hepatoprotective activity against H_2O_2-induced cell damage.

1. Introduction

Penthorum chinense Pursh (*P. chinense* Pursh), belonging to the Saxifragaceae family, is a traditional Chinese medicine, distributed in eastern Asia. The aerial parts of this plant have been widely used as a diuretic, to improve blood circulation, and for the treatment of liver disease (Wang et al., 2015a,b). Previous phytochemical studies on *P. chinense* have revealed the presence of flavonoids, polyphenols and steroids (Feng et al., 2001; Deng and Yang, 2007; Huang et al., 2014; Wang et al., 2014). Our research group has long been focused our attention on the investigation of the active constituents of *P. chinense* and consequently revealed several new isolates (Huang et al., 2014, 2015).

In our continuing work on the evaluation of the hepatoprotective activities of compounds from *P. chinense*, here, we report the further chemical investigation, which led to the isolation of two new phenylpropanoids (**1** and **2**) and three known compounds, 2′,4′,6′-trihydroxydihydrochalcone-4′- *O*-β-$_D$-glucopyranoside (**3**) (Wilianms, 1979), alpinetin-7-*O*-β-$_D$-glucopyranoside (**4**) (Wang et al., 2014) and quercitrin (**5**) (Hur et al., 2001). In addition, we evaluated the hepatoprotective activities of these compounds against H_2O_2-induced cytotoxicity in HL-7702 cells.

2. Results and discussion

Initially, the 80% EtOH extract of *P. chinense* was partitioned with petroleum ether, ethyl acetate (EtOAc), and *n*-butyl alcohol (*n*-BuOH). The EtOAc fraction was repeatedly subjected to column chromatography on silica gel, Sephadex LH-20, octadecyl silane (ODS), and semi-preparative HPLC to yield five compounds, including two new compounds, **1** and **2**, and three known ones (**3–5**) (Fig. 1).

Compound **1** was isolated as a brownish-yellow amorphous powder, and its molecular formula was established as $C_{25}H_{28}O_{11}$ through HRESIMS (*m/z* 527.1594 $[M + Na]^+$) and NMR spectroscopic data (Table 1). Its IR spectrum indicated the presence of a hydroxyl group (3411.0 cm^{-1}), a carbonyl group (1652.7 cm^{-1}), and an aromatic ring (1569.7 cm^{-1}, 1498.2 cm^{-1}). On the other hand, the ^{1}H NMR showed signals for one methanone group (δ_H 2.53, 3H, s), one methoxy group (δ_H 3.76, 3H, s), a single 1,2,3,4-tetrasubstituted phenyl group (δ_H 6.62, 1H, d, J = 9.0 Hz, H-5; δ_H 6.83, 1H, d, J = 9.0 Hz, H-6), and a single 1,2,4,5- tetrasubstituted phenyl group (δ_H 7.12, s, H-2′; δ_H 8.13, s, H-5′). Additionally, analysis of its NMR data indicated the presence of one *trans*-arylpropenoxy unit (δ_H 6.82, 1H, d, J = 15.6 Hz; δ_H 6.59, 1H, dd, J = 15.6, 6.6 Hz; δ_H 1.93, 3H, d, J = 6.6 Hz), two carbonyl carbons (δ_C 204.3 and 198.9) and one β-$_D$-glucopyranose ($J_{H\text{-}1''}$ = 7.6 Hz) unit, confirmed further through acid hydrolysis and comparison of specific rotation. The correlations between H-6, H-2′ and C-7 in the HMBC spectrum indicated that two benzene rings were connected by a carbonyl bridge (Fig. 2). The HMBC correlations between H-7′ and C-3′, C-9′, and C-5′ suggested that the *trans*-arylpropenoxy substituent was attached at C-4′. Moreover, the HMBC correlations from H-6 (δ_H 6.83, 1H, d, J = 9.0 Hz) and H-2′ (δ_H 7.12, 1H, s) to C-7 (δ_C 204.3) validated the assumption that the benzene rings were connected through a carbonyl linker. The HMBC correlations from H-9 to C-8 and C-6′ indicated that the acetyl group (C8-C9) was located at C-6′, whereas the correlations between H-$_{OMe}$ and C-3 confirmed that the C-3 was substituted by a methoxyl group. The C-4 was substituted by the β-glucopyranose group, as inferred by the correlations from H-1″ to C-4. Finally, both C-

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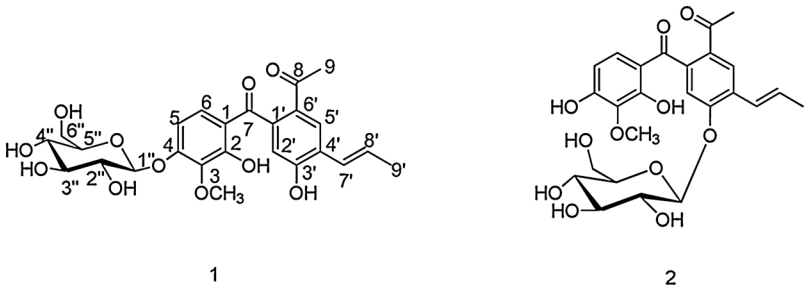

1 2

Fig. 1. Compounds **1–2** isolated from *Penthorum chinense*.

Table 1
NMR data for compounds.1–2.

Position	1[a]		2[b]	
	δ_H (*J* in Hz)	δ_C	δ_H (*J* in Hz)	δ_C
1	–	117.8 C	–	113.5 C
2	–	157.9 C	12.37	156.9 C
3	–	138.2 C	–	134.6 C
4	–	157.3 C	–	157.3 C
5	6.62(1H, d, 9.0)	107.9 CH	6.31(1H, d, 9.0)	108.2 CH
6	6.83(1H, d, 9.0)	128.9 CH	6.70(1H, d, 9.0)	128.4 CH
7	–	204.3 C	–	200.8 C
8	–	198.9 C	–	197.1 C
9	2.53(3H, s)	26.7 CH_3	2.53(3H, s)	27.2 CH_3
1'	–	140.7 C	–	138.3 C
2'	7.12(1H, s)	115.9 CH	7.12(1H, s)	114.0 CH
3'	–	159.8 C	–	155.9 C
4'	–	127.5 C	–	127.3 C
5'	8.13(1H, s)	125.4 CH	8.13(1H, s)	128.2 CH
6'	–	130.8 C	–	129.9 C
7'	6.82(1H, d, 15.6)	126.0 CH	6.82(1H, d, 16.2)	124.0 CH
8'	6.59(1H, dd, 15.6, 6.6)	129.5 CH	6.59(1H, dd, 16.2, 6.6)	128.9 CH
9'	1.93(3H, d, 6.6)	19.2 CH_3	1.93(3H, d, 6.6,)	18.7 CH_3
OMe	3.76(3H, s)	61.4 CH_3	3.91(3H, s)	59.6 CH_3
1''	4.99(1H, d, 7.8)	101.7 CH	5.08(1H, d, 7.2)	99.6 CH
2''	3.52(1H, t, 8.4)	74.8 CH	3.31(1H, t, 8.4)	73.2 CH
3''	3.45(1H, t, 8.4)	78.0 CH	3.27(1H, t, 8.4)	76.2 CH
4''	3.39(1H, d, 8.4)	71.2 CH	3.20(1H, d, 7.2)	69.3 CH
5''	3.42(1H, d, 8.4)	78.3 CH	3.31(1H, t, 8.4)	76.6 CH
6''	3.84(1H, dd, 1.8, 12.0)	62.4 CH_2	3.55(1H, d, 10.8)	60.3 CH_2

[a] NMR data recorded in DMSO-*d6*.
[b] NMR data recorded in CD_3OD.

2 and C-3′ were established to be attached to the hydroxyl group according to the molecular formula $C_{25}H_{28}O_{11}$ and their carbon positions (δ_C 159.7, C-2; δ_C 159.8, C-3′). Thus, the overall structure of compound **1** was deduced to be (*4′E*)-2, 3′-dihydroxy-3-methoxy-6′-methanone-benzophenone-4-*O*-β-$_D$-glucopyranoside.

Compound **2** was assigned the molecular formula $C_{25}H_{28}O_{11}$ based on the HRESIMS data (*m/z* 527.1525 $[M + Na]^+$). The IR spectrum was similar to that of **1,** suggesting that **2** also possessed hydroxyl, olefinic and carbonyl groups, as well as aromatic ring substituents. The ^1H and ^{13}C NMR data for **2** were analogous to those of **1**, which suggested that the compounds were closely related structurally. The C-3′ attachment of the β-glucopyranose was verified by HMBC correlations between H-1″ and C-3′. Finally, both C-2 and C-4 were assigned hydroxyl substituents based on the molecular formula $C_{25}H_{28}O_{11}$ and their carbon chemical shifts (δ_C 156.9, C-2; δ_C 157.3, C-4). Therefore, the structure of **2** was deduced to be (*4′E*)-2, 4-dihydroxy-3-methoxy -6′-methanone-benzophenone-3′-*O*-β-$_D$-glucopyranoside.

The structures of the known compounds, 2′,4′,6′-trihydroydihydrochalcone-4′- *O*-β-$_D$-glucopyranoside (**3**) (Wilianms, 1979), alpinetin-7-*O*-β-$_D$-glucopyranoside (**4**) (Wang et al., 2014) and quercitrin (**5**) (Hur et al., 2001), were identified based on the comparison of their MS and NMR data with literature values. Furthermore, the compounds **1–5** were evaluated for their hepatoprotective activities against H_2O_2-induced toxicity in HL-7702 cells. As shown in Table 2, compounds **2–4** exhibited moderate hepatoprotective activities.

3. Materials and methods

3.1. General experimental procedures

Optical rotations were measured on a Perkin-Elmer 341 digital polarimeter at 589 nm. IR spectra were recorded from KBr disks on an Intelligent Fourier Nicolet FTIR 6700 Infrared Spectrometer. The NMR spectra, including ^1H, ^{13}C, DEPT and 2D-NMR, were recorded on the Bruker AC-600 spectrometer with chemical shifts reported as δ values, using TMS as the internal standard. HRESIMS data were obtained on an Agilent Technologies 6538 UHD Accurate-Mass Q-TOF LC/MS spectrometer (Agilent Technologies, MA, USA). Thin-layer chromatography (TLC) was performed on TLC plates (Silica gel HSGF254, Jiangyou company of Yantai; RP-18 F254, Merck) and the spots were visualized by heating after dipping into 10% H_2SO_4. Silica gel (100–200 and 200–300 mesh, Jiangyou company of Yantai), Sephadex LH-20 (Pharmacia), ODS (43 ~ 60 μm, Merck), and MCI gel (Mitsubishi chemical corporation) were used for column chromatography.

3.2. Plant material

The dry aerial parts of *P. chinense* were provided by Gulin GANSU Pharmaceutical Co., Ltd (Sichuan, China) in September 2009 and the plant was identified by Prof. Wansheng Chen. A voucher specimen (No. IT100629) was deposited in the Department of Pharmacognosy of the Second Military Medical University, Shanghai, P.R. China.

3.3. Extraction and isolation

The dry aerial parts of *P. chinense* (10 kg) were chopped and extracted thrice with 80% EtOH (3 × 80 L, 2 h each) under reflux. The obtained extracts were concentrated under reduced pressure below 60 °C to give a residue (1167 g), and the residue was successively partitioned with petroleum ether (3 × 1.0 L), EtOAc (3 × 2.0 L), and *n*-BuOH (2 × 1.5 L). Next, the EtOAc-soluble residue (100 g) was subjected to silica gel chromatography (1 kg, 8 × 100 cm) and was eluted with CH_2Cl_2/CH_3OH (50:1, 30:1, 20:1, 10:1, 5:1, and 0:1, v/v) to afford 100 fractions (1 L each), which were then combined based on TLC profiles to afford four fractions **A** (8.1 g), **B** (27 g), **C** (23 g) and **D** (32 g). Fraction **A** (8.1 g) was applied to an ODS column with MeOH/H_2O (2:8, 4:6, 5:5, and 1:0, v/v) to obtain four fractions (Fr. A-1 to Fr. A-4). Fr. A-2 (1830 mg) was further subjected to a Sephadex LH-20 column (80 g, 1.5 × 150 cm), eluted with MeOH/H_2O (2:8, 5:5, 8:2, and 1:0, v/v) and divided into four main subfractions (Fr. A-2-1 to Fr. A-2–4). Then, Fr. A-2-1 (230 mg) was purified through a Sephadex LH-20 column (80 g, 1.5 × 150 cm) by eluting with MeOH/H_2O (4:6, v/v) to yield the compound **1**