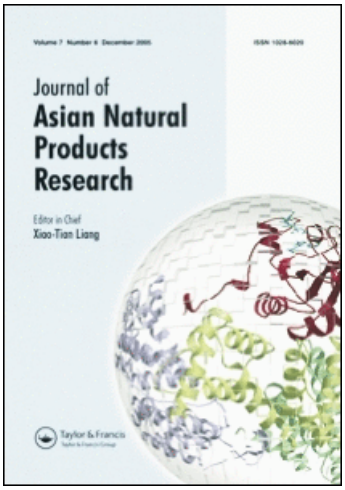

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TWO NEW QUINOLINE GLYCOALKALOIDS FROM *ECHINOPS GMELINII*

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Two new glycosidic quinoline alkaloids, 1-methyl-4-methoxy-8-(β-D-glucopyranosyloxy)-2(1*H*)-quinolinone (**1**) and 4-methoxy-8-(β-D-glucopyranosyloxy)-2(1*H*)-quinolinone (**2**), have been isolated from the 1-butanol extract of the aerial parts of *Echinops gmelinii* (Compositae). Structural elucidation of the two new glycoalkaloids was based on their ^{1}H, ^{13}C, DEPT, HSQC, COSY, HMBC NMR spectra and high-resolution FAB-MS data. These two compounds are rare examples of quinoline alkaloidal glycosides from natural sources.

Keywords: *Echinops gmelinii*; Compositae; Quinoline; Glycoalkaloids

INTRODUCTION

Echinops gmelinii Turcz. (Compositae) is widespread in north China. The roots of the plant are used in folk medicine as antipyretic and antidote to treat mastitis, lymph node tuberculosis, and anal fistula [1]. Previous phytochemical studies on the species of *Echinops* have resulted in the isolation of alkaloids, flavonoids, thiophenes, and triterpenoids [2]. The five alkaloids identified from *Echinops* plants are echinorine, echinopsine, echinopsidine, echinozolinone and 7-hydroxyechinozolinone, which have quinoline or 4-quinozolinone skeletons [3–5], but none of them are glycosidic alkaloids. We report here the isolation and structural elucidation of two new quinoline glycoalkaloids from BuOH extract of the aerial parts of *E. gmelinii*, 1-methyl-4-methoxy-8-(β-D-glucopyranosyloxy)-2(1*H*)-quinolinone (**1**) and 4-methoxy-8-(β-D-glucopyranosyloxy)-2(1*H*)-quinolinone (**2**) (Fig. 1). To the best of our knowledge, these two new glycoalkaloids are rare examples of quinoline alkaloidal glycosides from natural sources.

RESULTS AND DISCUSSION

Compound **1** was obtained as white needles. The FAB-MS spectrum of **1** (under positive mode) gave a quasi-molecular ion at *m*/*z* 368 and a fragment ion at *m*/*z* 206 corresponding to $[M + H]^+$ and $[M + H - 162]^+$, respectively, indicating that the molecule contains an odd

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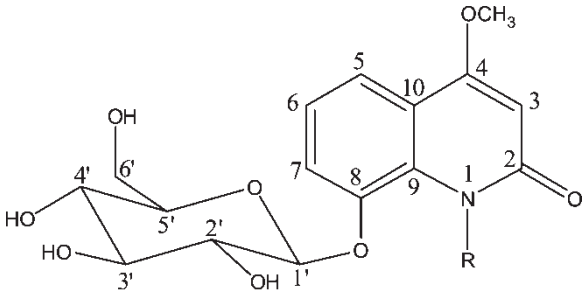

1 R=CH_3

2 R=H

FIGURE 1 Structure of compounds **1** and **2**.

number of nitrogen atom(s) and a hexose sugar moiety. The molecular formula of $C_{17}H_{21}NO_8$ of **1** was determined by a strong $[M + H]^+$ ion peak at *m/z* 368.1355 in the high-resolution FABMS spectrum. The ^{1}H NMR spectrum of **1** shows two methyl proton signals at δ 4.30 (s) and 3.71 (s). As indicated by the shifts of the corresponding ^{13}C signals (δ 35.3 and 55.9) obtained from the HSQC spectrum, the two signals belonged to an *N*-methyl group and an *O*-methyl group. The six carbon signals at δ 104.0, 79.1, 78.9, 74.9, 71.2, and 62.5 (Table I) and the anomeric proton signal at δ 5.62 (d, $J = 6.9$ Hz) suggest the existence of a glucopyranosyl group in β-form. Acid hydrolysis of **1** and subsequent co-TLC analysis with authentic sugar confirmed the sugar moiety was glucose. Besides the above-mentioned methyl and glucopyranosyl signals, the DEPT-135 spectrum of **1** displays four methine signals, while the ^{13}C spectrum showed the presence of five quaternary carbons. Also, the ^{1}H NMR spectrum of **1** has a set of signals typical of an AMX spin system of aromatic proton signals (δ 7.85, d, $J = 8.0$ Hz; 7.11, dd, $J = 8.0$, 8.0 Hz; 7.65, d, $J = 8.0$ Hz) and

TABLE I ^{1}H and ^{13}C NMR spectral data of compounds **1** and **2** in C_5D_5N

	1		***2***	
No.	^{13}C	^1H	^{13}C	^1H
2	164.6	–	165.9	–
3	97.3	6.22 (1H, s)	96.7	6.20 (1H, s)
4	162.3	–	165.1	–
5	117.3	7.65 (1H, d, $J = 8.0$ Hz)	116.6	7.55 (1H, d, $J = 8.0$ Hz)
6	122.5	7.11 (1H, dd, $J = 8.0$, 8.0 Hz)	122.4	7.08 (1H, dd, $J = 8.0$, 8.0 Hz)
7	119.0	7.85 (1H, d, $J = 8.0$ Hz)	117.4	7.76 (1H, d, $J = 8.0$ Hz)
8	147.2	–	145.2	–
9	132.4	–	130.2	–
10	119.0	–	116.8	–
$N-CH_3$	35.3	4.30 (3H, s)	–	–
OCH_3	55.9	3.71 (3H, s)	55.9	3.56 (3H, s)
1′	104.0	5.62 (1H, d, $J = 6.9$ Hz)	104.0	5.54 (1H, d, $J = 7.2$ Hz)
2′	74.9	ca. 4.34 (overlapped)	75.1	ca. 4.44 (overlapped)
3′	78.9	ca. 4.34 (overlapped)	77.7	ca. 4.43 (overlapped)
4′	71.2	ca. 4.34 (overlapped)	71.3	ca. 4.40 (overlapped)
5′	79.1	4.12 (1H, m)	79.3	4.18 (1H, m)
6′	62.5	4.56 (1H, br d, $J = 12.0$ Hz) 4.40 (1H, dd, $J = 12.0$, 5.6 Hz)	62.5	4.61 (1H, br d, $J = 11.2$ Hz) ca. 4.43 (overlapped)

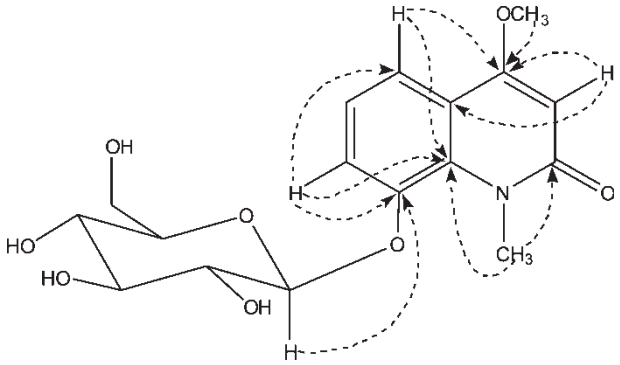

FIGURE 2 Key HMBC correlations of **1**.

one aromatic proton singlet at δ 6.22. Detailed analysis of the 1D and 2D NMR spectra of **1** (Fig. 2) and comparison with literature data [4,6] establish a trisubstituted 2(1*H*)-quinolinone. HMBC correlations between methyl protons at δ 4.30 and both carbon signals at δ 164.6 (C-2) and δ 132.4 (C-9) confirm that the aglycone fragment possesses a quinoline instead of an isoquinoline skeleton and that the methyl group is attached to the nitrogen. Similarly, the methoxy group at C-4 is proved by the HMBC correlation between the methyl proton signal at δ 3.71 and the carbon signal at δ 162.3 (C-4). Moreover, HMBC correlation signals between the C-4 signal at δ 162.3 and both the aromatic proton signals at δ 6.22 (H-3) and δ 7.65 (H-5) further confirm the 2-quinolinone structure. Likewise, the HMBC correlation between the anomeric proton at δ 5.62 (H-1′) and the C-8 signal at δ 147.2 indicates the glycosidic position is at C-8. Therefore, the structure of **1** is unambiguously identified as 1-methyl-4-methoxy-8-(β-D-glucopyranosyloxy)-2(1*H*)-quinolinone (Fig. 1).

Compound **2** was also obtained as white needles. Its positive FAB-MS spectrum gave a quasi-molecular ion at *m/z* 354 (14 mass units less than **1**) and a fragment ion at *m/z* 192, corresponding to $[M + H]^+$ and $[M + H - 162]^+$, respectively. Its molecular formula was determined as $C_{16}H_{19}NO_8$ by the $[M + H]^+$ ion peak at *m/z* 354.1174 in the HR-FABMS spectrum. NMR spectra of **2** suggest one methoxy group, one glucopyranosyl group, and a 2-quinolinone skeleton, with a close resemblance to the spectra of **1**. The NMR spectra of **1** and **2** differ in that the spectrum of **2** lacks the signals of a methyl group attached to the nitrogen. Thus, we assign the structure of **2** as 4-methoxy-8-(β-D-glucopyranosyloxy)-2(1*H*)-quinolinone (Fig. 1).

EXPERIMENTAL

General Experimental Procedures

Melting points were determined on a XT4A micro-melting point apparatus and are uncorrected. Optical rotation was measured on a Perkin-Elmer Model 341 polarimeter. IR spectra were recorded with a Hitachi 270-30 infrared spectrometer. NMR spectra were recorded in C_5D_5N on a Bruker AV400 NMR spectrometer. FAB mass spectra were obtained on a VG ZAB-HZ mass spectrometer, and high resolution FAB-MS on an Autospec-UltimaETOF mass spectrometer. Silica gel (100–200 mesh, 200–300 mesh and GF_{254} Type 60, Qingdao Marine Chemical Co.) was used for open-column chromatography and TLC. Spots were visualized on TLC by I_2 vapor.

Plant Material

The aerial parts of *Echinops gmelinii* (Compositae) were collected in Shapotou, Ningxia Province, China, in September 2001 and identified by Dr Ji Ma of Lanzhou Desert Research Institute, Chinese Academy of Sciences, where a voucher specimen has been deposited.

Extraction and Isolation

The 95% ethanol extract of the aerial parts (3 kg) of *Echinops gmelinii* was concentrated and then diluted with H_2O to 2 L. The water suspension was re-extracted with light petroleum (60–90°C), ethyl acetate and 1-butanol in turn and yielded 87 g of butanol extract. The butanol extract was exposed to D101 macroporous resin column, eluting with a gradient of ethanol in water (H_2O, 30% EtOH, 50% EtOH, 70% EtOH, and EtOH). The 30% aqueous ethanol eluate (29.4 g) was subjected to silica gel column chromatography and eluted with EtOAc–EtOH–H_2O [EtOAc–EtOH–H_2O 19:1:0.5 (7 L), 9:1:0.5 (7 L), 8.5:1.5:1 (5 L), 8:2:1.5 (5 L), 6.5:3.5:2.5 (5 L)] to afford 58 fractions. Fractions 29–30 were treated with MeOH and compound **1** (200 mg) was crystallized as white needles. The filtrate of fractions 29–30 and fractions 27, 28, 31, and 32 were combined and applied to open silica-gel column and eluted with $CHCl_3$–MeOH–H_2O (8.5:1.5:1), to furnish **1** and **2** (12 mg).

1-Methyl-4-methoxy-8-(β-D-glucopyranosyloxy)-2(1H)-quinolinone (1)

Compound **1** was obtained as white needles from MeOH, mp $>$ 300°C, $[\alpha]_D^{20}$ $-20.4°$ (*c* 0.54, pyridine); IR (KBr) ν_{max} (cm^{-1}) 3494 (O–H), 2918, 1641 (C=O), 1570, 1404 (C–N), 1261, 1247, 1084, 1055, 1022, 837, 744; ^1H (400 MHz, C_5D_5N) and ^{13}C NMR (100 MHz, C_5D_5N) spectral data, see Table I; FAB-MS *m/z* 368 $[M + H]^+$, 206 $[M + H - 162]^+$, HR FAB-MS *m/z* 368.1355 $[M + H]^+$ (calcd for $C_{17}H_{22}NO_8$, 368.1345).

4-Methoxy-8-(β-D-glucopyranosyloxy)-2(1H)-quinolinone (2)

Compound **2** was obtained as white needles from MeOH, mp 242°C (dec.), $[\alpha]_D^{20}$ $-4.3°$ (*c* 0.23, pyridine); IR (KBr) ν_{max} (cm^{-1}) 3448 (O–H), 2924, 1642 (C=O), 1562, 1402 (C–N), 1272, 1236, 1096, 1038, 828, 740; ^1H NMR (400 MHz, C_5D_5N) and ^{13}C NMR (100 MHz, C_5D_5N) spectral data, see Table 1; FAB-MS *m/z* 354 $[M + H]^+$, 192 $[M + H - 162]^+$, HR FAB-MS *m/z* 354.1174 $[M + H]^+$ (calcd for $C_{16}H_{20}NO_8$, 354.1189).

Acid Hydrolysis of Compounds 1 and 2

Compound **1** (20 mg) was heated in 1 ml of 1 M HCl (dioxane–H_2O, 1:1) at 90°C for 2 h in a water bath. After dioxane was removed under reduced pressure, the hydrolysate and authentic glucose were applied to the same silica-gel TLC plate. The TLC plate was developed by $CHCl_3$–MeOH–H_2O–acetic acid (glacial) 99.5%, AR (16:9:2:3), sprayed with 10% H_2SO_4 in EtOH, and heated [7]. The R_f of glucose is 0.54. By the same method, the sugar moiety of compound **2** (2 mg) was also identified as glucose.

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