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Chemical constituents from leaves of *Cinnamomum subavenium*

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ABSTRACT

A new eudesmane sesquiterpene glycoside, 1α,6β-dihydroxy-5,10-bis-epi-eudesm-15-carboxaldehyde-6-*O*-β-D-Glucopyranoside (**1**), together with eleven known compounds (**2**–**12**) were isolated from the leaves of *Cinnamomum subavenium* Miq. Their structures were elucidated by a combination of spectroscopic data analysis and comparison with literature data. All compounds were isolated from *C. subavenium* for the first time. The chemotaxonomic significance of the isolated compounds was summarized.

1. Subject and source

Cinnamomum subavenium. Miq (Lauraceae) is a medium-sized evergreen tree which has been used in folk medicine to treat carcinomatous swelling, stomachache, chest pain, abdominal pain, hernia, diarrhea, rheumatism, nausea and vomiting in China (Liu et al., 2011). The leaves of *C. subavenium* was collected at Enshi, Hubei Province, China, in July 2012. The voucher specimen (No. 2012-0710) was deposited in the herbarium.

2. Previous work

Previous phytochemical investigations on *C. subavenium* resulted in the isolation of butanolide, ionone, sesquiterpenoid, monoterpenoid, benzenoid, polyprenol, chlorophyll, steroid and aliphatic compound (Lin et al., 2009; Chen et al., 2006; Chen and Wang, 2011). To today, about 38 compounds have been isolated from *C. subavenium* growing in Taiwan (Lee et al., 2012).

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3. Present work

3.1. Extraction and isolation

The dried leaves of *C. subavenium* (15 Kg) were extracted with 90% aqueous EtOH (25 L × 3 times) at the room temperature. The combined filtrates were concentrated under vacuum to afford 750 g of crude extract, which was suspended in H_2O (4.0 L) and partitioned successively with petroleum ether (60–90 °C), $CHCl_3$, and EtOAc. The EtOAc portion (250 g) was subjected to polyamide column eluted with H_2O to get aqueous phase. On evaporation, the aqueous phase was chromatographed over silica gel and eluted with a MeOH–$CHCl_3$ gradient to obtain five fractions, A-E. Fraction B was subjected to column chromatography (CC) on silica eluted with $CHCl_3$/MeOH (60:1) to yield compound **2**. Fraction C was divided into two sub-fractions, C_1 and C_2, by CC eluting with $CHCl_3$/MeOH (15:1). Sub-fraction C_1 was subjected to a Sephadex LH-20 column eluted with MeOH, and then purified by semi-preparative HPLC (30% MeOH in H_2O, flow rate 1.5 mL/min, wavelength 210 nm) to yield compound **1** (7.0 mg, retention time 28 min) and **3** (6.5 mg, retention time 33 min). Subfraction C_2 was subjected to a Sephadex LH-20 column eluted with MeOH, and then purified by semi-preparative HPLC (20% MeOH in H_2O, flow rate 1.5 mL/min, wavelength 210 nm) to yield compound **4** (5.0 mg, t_R 26 min) and **5** (7.5 mg, t_R 32 min). Fraction D was applied to RP-C_{18} gel column eluted with MeOH/H_2O (3:17), providing three sub-fractions, D_1, D_2, and D_3. Sub-fraction D_2 was subjected to a Sephadex LH-20 column eluted with MeOH to give three fractions, D_2A, D_2B, and D_2C. D_2B was purified by semi-preparative HPLC (40% MeOH in H_2O, flow rate 1.5 mL/min, wavelength 210 nm) to obtain compounds **6** (9.0 mg, t_R 31 min) and **7** (3.2 mg, t_R 36 min). D_2C was purified by semi-preparative HPLC (32% MeOH in H_2O, flow rate 1.5 mL/min, wavelength 210 nm) to obtain compound **8** (6.0 mg, t_R 23 min). Fraction E was subjected to a Sephadex LH-20 column eluted with MeOH to give three subfractions, E_1, E_2, and E_3. Subfraction E_1 was subjected to CC on silica eluted with petroleum/acetone (1:1) to yield compound **9** (7.0 mg). Compounds **10** (10.0 mg) and **11** (7.0 mg) were isolated from sub-fraction E_2 by CC on silica eluted with petroleum/acetone (1.5:1). Sub-fraction E_3 was subjected to a Sephadex LH-20 column eluted with MeOH to obtain **12** (6.0 mg). The chemical structures of **1**–**12** were shown in Fig. 1.

Compound **1** was isolated as an amorphous powder, [α]20 D+ 12.3 (*c* 0.06, MeOH). Its molecular formula was determined to be $C_{39}H_{54}O_6$ by the (+)-HRESIMS sodiated molecular ion peak at *m/z* 455.2238 $[M + Na]^+$ (calcd. for $C_{21}H_{36}O_9$ Na^+, *m/z* 455.2257). The IR spectrum showed the presence of hydroxy group (3379 cm^{-1}), and aldehyde group (2928, 2876, and 1762 cm^{-1}) absorption. The ^1H NMR spectrum of **1** (Table 1) exhibited three methyl singlets at δ_H 1.71 (3H, s), δ_H 1.47 (3H, s), and δ_H 1.11 (3H, s), two protons attached to oxygenated carbons at δ_H 3.54 (1H, dd, $J = 4.0$, 11.2 Hz) and δ_H 4.61 (1H, dd, $J = 6.0$, 11.2 Hz), one anomeric proton at δ_H 5.11 (1H, d, $J = 7.0$ Hz), and one aldehyde proton at δ_H 9.75 (1H, d, $J = 3.2$). The ^{13}C NMR, DEPT, and HSQC spectra for **1** showed 21 carbon signals differentiated as three methyls, four methylenes, five methines (including two oxygenated), two quaternary carbons (including an oxygenated carbonyl), one aldehyde group. Moreover, one set of proton signals at δ_H 3.58–4.44, 5.11, and their corresponding carbons resonating at δ_C 62.9, 71.1, 74.6, 78.1, 78.6, and 101.4, suggested the presence of a hexose residue.

The correlations of HMBC (Fig. 2) from H-12, H-13 to a quaternary carbon (bearing hydroxyl) at δ_C 73.7 (C-11) and from H-13 to C-12 showed that C-12 and C-13 were respectively attached to the C-11. The HMBC correlations from H-14 to the quaternary carbon C-10 indicated that C-14 was connected with C-10.^1H–^1H COSY correlation from H-15 (δ_H 9.75, d, $J = 3.2$ Hz, 1H) to H-4 indicated that C-15 was attached to C-4, which was confirmed by HMBC correlations from H-15 to C-3 and C-5. It also indicated that C-6 was attached between C-5 and C-7 by the correlations of ^1H–^1H COSY from H-5 to H-6 then to H-7 and the HMBC correlations from H-6 and H-7 to C-11. C-1 was attached to C-2 based on the ^1H–^1H COSY correlations from H-1 to H-2 then to H-3 and the correlation of HMBC from H-14 to C-1. And the correlation of HMBC from H-1' (δ_H 5.22, d, $J = 7.7$ Hz, 1H) to C-6 indicated that the glycosidic site was attached to C-6. All the information mentioned above indicated that **1** had the same scaffold as dictamnosides I (Chang et al., 2001). The absence of the methyl signal at δ_H 1.28, together with the presence of an additional aldehyde (δ_H 9.98) indicated the structure of **1** as shown in Fig. 1.

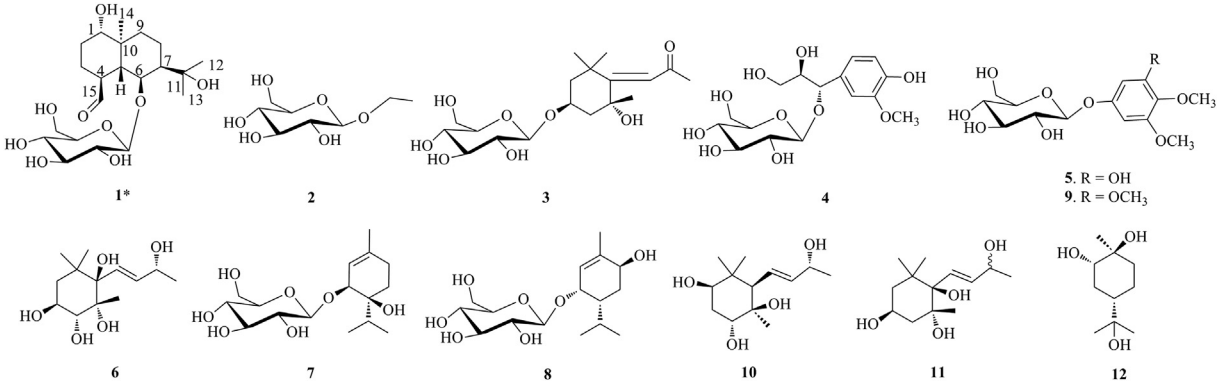

Fig. 1. Structures of compounds **1**–**12**.