Two New Monoterpene Peroxide Glycosides from *Aster scaber*

Chil Mann Jung, Hak Cheol Kwon, Jung Ju Seo, Yasushi Ohizumi, Kimihiro Matsunaga, Shinya Saito, and Kang Ro Lee

Natural Products Laboratory, College of Pharmacy, Sung Kyun Kwan University, a Suwon 440–746, Korea, Korea Basic Science Institute, Seoul, 136–701, Korea, and Department of Pharmaceutical Molecular Biology, Graduate School of Pharmaceutical Sciences, Tohoku University, Aoba, Aremaki, Aoba-ku, Sendai 980–8578, Japan.

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The aerial part of *Aster scaber* THUNB. (Asteraceae) yielded two new monoterpene peroxide glycosides, (3S)-3-O-(3′,4′-diangeloyl-β-D-glucopyranosyloxy)-7-hydroperoxy-3,7-dimethylocta-1,5-diene (1) and (3S)-3-O-(3′,4′-diangeloyl-β-D-glucopyranosyloxy)-6-hydroperoxy-3,7-dimethylocta-1,7-diene (2), and five known compounds, α-spinasterol (3), germacra-4(15),5,10(14)-triene-1β-ol (4), 7-methoxy-4(15)-oppositen-1β-ol (5), 6α-methoxy-4(15)-eudesmane-1β-ol (6), and α-spinasterol 3-O-β-D-glucopyranoside (7). The structures were established by chemical and spectroscopic methods.

**Key words** *Aster scaber* THUNB; Asteraceae; monoterpene peroxide glycoside; (3S)-3-O-(3′,4′-diangeloyl-β-D-glucopyranosyloxy)-7-hydroperoxy-3,7-dimethylocta-1,5-diene; (3S)-3-O-(3′,4′-diangeloyl-β-D-glucopyranosyloxy)-6-hydroperoxy-3,7-dimethylocta-1,7-diene

*Aster scaber* THUNB. (Asteraceae) is widespread and cultivated as culinary vegetables in Korea.1 Aster species have been used in traditional Chinese medicine to treat bruises, snakebite, headache and dizziness.2,3 Recently, triterpene glycosides4–6 and volatile compounds7–9 have been reported from *Aster scaber*. In our previous study on this plant, we reported four quinic acid derivatives and their inhibitory activities against human immunodeficiency virus-1 (HIV-1) integrase.6 In our continuing study of this plant, we have isolated two new monoterpene peroxide glycosides (1, 2), together with three known sesquiterpenes (4–6) and two known sterols (3, 7). The present paper describes the isolation and structural characterization of these two new monoterpene peroxide glycosides (1, 2).

Five known compounds, α-spinasterol (3),10 germacra-4(15),5,10(14)-triene-1β-ol (4),8 7-methoxy-4(15)-oppositen-1β-ol (5),9 6α-methoxy-4(15)-eudesmane-1β-ol (6)9 and α-spinasterol 3-O-β-D-glucopyranoside (7)9 were characterized by comparing their physical and spectroscopic data with those reported in the literature.

Compound 1 was obtained as a colorless oil and positive periode test.10 Its molecular formula was determined as C26H40O10 by HR-ESI-MS spectrum. Its IR spectrum displayed absorption bands at 3450 and 1721 cm⁻¹, indicating the presence of hydroperoxy and ester groups. The 1H- and 13C-NMR spectra exhibited the presence of two angeloyl groups11 and a hexose sugar. 1H-NMR coupling constants and 13C-NMR chemical shifts data suggested that the sugar was glucose, and its J1,2 (8.0 Hz, diaxial) and J3,4 (9.6 Hz, diaxial) values in the 1H-NMR spectrum suggested that the sugar is β-D-glucopyranose.12,13 In addition, the 1H-NMR spectrum showed signals by three tertiary methyl groups at δ 1.30, 1.32 and 1.39, an aliphatic methylene at δ 2.35 (1H, dd, J1,2 = 14.6, 7.3 Hz) and 2.40 (1H, dd, J = 14.6, 7.3 Hz), five olefinic protons at δ 5.25 (1H, d, J = 17.0 Hz), 5.26 (1H, d, J = 10.8 Hz), 5.59 (1H, d, J = 15.8 Hz), 5.70 (1H, dt, J = 15.8, 7.3 Hz) and 5.88 (1H, dd, J = 17.0, 10.8 Hz), and hydroperoxy proton at δ 8.07 (1H, br s). The 13C-NMR spectrum showed ten carbon resonances in addition to the signals of two angeloyl and a glucosyl groups. These 1H- and 13C-NMR data led to the monoterpene structure 3-hydroxy-7-hydroperoxy-3,7-dimethylocta-1,5-diene. The relationship of the two angeloyl groups, the glucose, and the monoterpene moiety was established by the analysis of the 1H–1H COSY, HMQC and HMBE spectra. In the HMBE spectrum, long-range connectivities were observed between the H-3′ (δ 5.29) and the angeloyl ester carbons C-1′ (δ 168.5), the H-4′ protons (δ 5.09) and C-1″ (δ 167.6), and the anomic H-1′ proton (δ 4.56) and the C-3 carbon (δ 80.8), respectively. Thus, the gross structure of 1 was suggested to be 3-O-(3′,4′-diangeloyl-β-D-glucopyranosyloxy)-7-hydroperoxy-3,7-dimethylocta-1,5-diene.

The reductive cleavage of 1 with LiAlH4 afforded 3-O-β-D-glucopyranosyloxy-7-hydroxy-3,7-dimethylocta-1,5-diene (1a), which was identified by its 1H-NMR spectrum.14 Enzymatic hydrolysis of 1a afforded (3S)-3,7-dihydroxy-3,7-dimethylocta-1,5-diene (1b) and d-glucose, which were identified by its 1H-NMR spectrum13,15 for 1b and by co-TLC for glucose with authentic d-glucose, respectively. Based on the above evidence, the structure of 1 was determined as (3S)-3-O-(3′,4′-diangeloyl-β-D-glucopyranosyloxy)-7-hydroperoxy-3,7-dimethylocta-1,5-diene.

Compound 2 was obtained as a colorless oil and positive periode test.10 Its molecular formula was determined as C26H40O10 by HR-ESI-MS spectrum. The IR, 1H- and 13C-NMR spectra of 2 were very similar with those of 1. The only differences in the 1H-NMR spectra were observed in the signals of the monoterpene moiety. Comparing the 1H-NMR spectrum of 1 with that of 2, the absence of the signal at δ 5.73 (1H, dt, J = 15.9, 7.4 Hz) and 5.59 (1H, d, J = 15.9 Hz), and the appearance of new signals at δ 4.99 (1H, s) and 5.00 (1H, s) in the 1H-NMR spectrum of 2 indicated the shift of the hydroperoxide group from C-7 to C-6 in the monoterpene moiety. This was also supported by the appearance of a new proton signal at δ 4.32 (1H, br t, J = 5.4 Hz). These observations of the monoterpene moiety led to the structure of 3-hydroxy-6-hydroperoxy-3,7-dimethylocta-1,7-diene. The relationship of the two angeloyl groups, the glucose, and the monoterpene moiety was established by the analysis of the 1H–1H COSY, HMQC and HMBE spectra. The reductive
**Fig. 1. Structures of Compounds 1 and 2**

The text discusses the isolation and characterization of compounds 1 and 2 from Aster scaber plants. The isolation process involved extraction and isolation, followed by purification techniques such as chromatography and recrystallization. The compounds were subjected to various spectroscopic analyses, including NMR, to determine their chemical structures.

**Experimental**

**General** Mps: Gallenkamp melting point apparatus (uncorr.) NMR: Bruker AMX 500 and Varian UNITY INOVA 500. IR: Nicolet model 205 FT-IR spectrophotometer. MS: VG70-VSEQ mass spectrometer. HPLC: JAI LC-908 model with refractive index detector, UV detector and Ecomom CS 18 10u column (250 mm×22 mm). Column chromatography: silica gel (70—230 mesh and 230—400 mesh). TLC: Merck precoated Si gel F254 plates and RP-18 F254 plates. IRLC: Merck Lichroprep Lobar®-A Si 60 (240×10 mm).

**Plant Materials** Aster scaber plants were purchased in Chukryung Mt., Kyung-Do, Korea in September 1997. A voucher specimen (SKK-98-001) is deposited in the College of Pharmacy at Sung Kyun Kwan University.

**Extraction and Isolation** The dried and chopped aerial parts of Aster scaber (2 kg) were extracted with MeOH two times at room temp, and once at 50°C for 5 h. The resultant MeOH extract (200 g) was subjected to successive solvent partitioning to give CHCl3 (28 g), EtOAc (17 g) and n-ButOH (33 g) soluble fractions. The CHCl3 soluble fraction (28 g) was chromatographed on a silica gel column using a gradient solvent system of hexane-EtOAc (5:1—0:1) to give eight subfractions (F1—F8). The subfraction F5 was chromatographed over silica gel eluting with hexane-EtOAc (5:1) to give two subfractions (F51, F52). The first subfraction (F51) was subjected to Sep-Pak (RP-18, 40% acetonitrile) and purified by HPLC (40% acetonitrile, RP-18) to yield 1 (25 mg) and 2 (13 mg). The second subfraction (F52) was purified by recrystallization from the same solvent to afford 3 (240 mg). Supernat of F52 was chromatographed over silica gel Lobar®-A (35 g) and purified by recrystallization from the same solvent to afford 2 (30 mg). TLC: Merck precoated Si gel plates and RP-18 F254 plates. IRLC: Merck Lichroprep Lobar®-A Si 60 (240×10 mm).

**Reductive Cleavage** of 1 and 2 LiAlH₄ (10 mg) was added to a solution of 1 (5 mg) in 1 ml of THF. After 12 h reflux, 0.1 ml H₂O, 0.1 ml 25%NaOH and 0.3 ml H₂O were added to reaction mixture, successively. The mixture was filtered and the organic layer concentrated to afford 1a and 2a (2 mg).

**Enzymatic Hydrolysis** A solution of 1a (2 mg) and 10 mg cellulase (Merek) in 1 ml H₂O was stirred at 37°C for 24 h, followed by solvent partitioning with chloroform and water to afford 1b (0.8 mg) and d-glucose, respectively. Enzymatic hydrolysis of 2 was achieved in the same way to afford 2b (0.8 mg) and d-glucose.

The text concludes with a detailed description of the chemical structures of the isolated compounds, including their spectroscopic data and biological activities.
1.2 Hz, H-1a), 5.23 (1H, dd, $J=17.4$, 1.2 Hz, H-1b), 5.91 (1H, dd, $J=17.4$, 10.7 Hz, H-2).

References