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Triterpenoids from *Orostachys japonicus*

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Abstract – Triterpenoids were isolated from the whole plant of *Orostachys japonicus* (Crassulaceae) by repeated column chromatography. Their structures were identified as friedelin (**1**), glutinol (**2**), β-sitosterol (**3**), friedelinol (**4**), 5α,8α-peroxyergosterol (**5**), β-sitostenone (**6**) and glutinone (**7**) by spectral analysis. Among them, compounds **5** and **6** were isolated for the first time from this plant.
Keywords – *Orostachys japonicus*, Crassulaceae, Triterpenoid, 5α,8α-Peroxyergosterol, β-Sitostenone

Introduction

Orostachys japonicus is genus of the family Crassulaceae. It has been used as traditional medicine that is an anti-inflammatory and a haemostatic agent (Kim, 1984).

Investigations on the compounds from *O. japonicus* have revealed the presence of glutinone, friedelin, β-amyrin, glutinol, *epi*-friedelanol and 1-hexatriacontanol (Park *et al.*, 1991b), kaempferol, quercetin, astragalin, quercitrin, *iso*-quercitrin, cynaroside, afzelin, 3-*O*-α-L-rhamnosyl-7-*O*-β-D-glucosyl kaempferol and 3,7-di-*O*-β-D-glucosyl kaempferol (Park *et al.*, 1991c), taraxerone, stigmast-4-ene-3-one and ergost-4-ene-3-one (Park *et al.*, 1994), 4-hydroxybenzoic acid, 3,4-dihydroxybenzoic acid, gallic acid and methyl gallate (Park *et al.*, 2000), and gossypetin 8-*O*-α-D-lyxopyranoside (Sung *et al.*, 2002). The MeOH extract of *O. japonicus* was shown to have a protective effect on H_2O_2-induced apoptosis in GT1-1 mouse hypothalamic neuronal cell line, which was detected by flow cytometry after propidium iodide staining (Yoon *et al.*, 2000). The *n*-BuOH fraction of this plant showed the most effective anti-mutagenic activity against aflatoxin (Park *et al.*, 1991a). Another various researches on this plant were conducted (Choi *et al.*, 1994; Kim *et al.*, 2003; Kim *et al.*, 2004; Park and Song, 2001; Shin *et al.*, 1994; Yang and Choi, 1992).

In a series of investigations to evaluate bioactive principles from Korean plants, several compounds were isolated from *O. japonicus*. This paper describes the isolation and structural elucidation of compounds from *O. japonicus*.

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Experimental

Instruments and reagents – Silica gel 60 (MERCK Co., 0.063-0.200 mm) was used for open column chro matography. Silica gel plates (Merck Co., Kieselgel 60 F_{254}) were used for TLC. Spots were detected by spraying with 20% H_2SO_4 in MeOH and heating. ^{1}H- and ^{13}C-NMR spectra were recorded with a Varian Gemini 2000 (300 MHz) NMR spectrometer. EI-MS spectra were measured with a Hewlett Packard 5989B mass spectrometer. Other reagents were commercial grade without purification.

Plant materials – The whole plant of *Orostachys japonicus* A. Berger was provided by Prof. Sun Ha Paek, Seoul National University College of Medicine, Korea in 2001, and verified by Prof. Emeritus H. J. Chi, Natural Products Research Institute, Seoul National University, Korea.

Extraction and isolation – The air-dried powdered whole plant of *O. japonicus* was extracted three times with MeOH under reflux. The resultant extracts were combined and concentrated under reduced pressure to afford the residue. The MeOH extract was suspended in water and then fractionated successively with equal volumes of *n*-hexane, CH_2Cl_2, EtOAc and *n*-BuOH, leaving residual water-soluble fraction. Each fraction was evaporated *in vacuo* to yield the residues of *n*-hexane, CH_2Cl_2, EtOAc and *n*-BuOH fractions.

A portion of the *n*-hexane fraction was chromatographed on silica gel column eluting with a gradient of *n*-hexane-EtOAc to afford compounds **1** (23 mg), **2** (18 mg), **3** (20

mg), **4** (14 mg), **5** (16 mg), and **6** (12 mg). A portion of the CH_2Cl_2 fraction was chromatographed on silica gel column eluting with a gradient of *n*-hexane-EtOAc to afford compound **7** (15 mg).

Compound 1 – EI-MS (70 eV, rel. int., %): *m/z* 426 $[M]^+$ (100), 411 (22.4), 341 (13.3), 302 (44.2), 273 (64.2), 246 (39.5), 205 (58.9); ^{1}H-NMR (300 MHz, $CDCl_3$-*d*): (1.17 (3H, s, 30-Me), 1.04 (3H, s, 27-Me), 1.00 (3H, s, 28-Me), 0.99 (3H, s, 26-Me), 0.95 (3H, s, 29-Me), 0.88 (3H, s, 23-Me), 0.86 (3H, s, 25-Me), 0.72 (3H, s, 24-Me); ^{13}C-NMR (75 MHz, $CDCl_3$-*d*): δ 213.1 (C-3), 59.4 (C-10), 58.2 (C-4), 53.1 (C-8), 42.8 (C-18), 42.1 (C-5), 41.5 (C-2), 41.3 (C-6), 39.7 (C-14), 39.2 (C-22), 38.3 (C-13), 37.4 (C-9), 36.0 (C-16), 35.6 (C-19), 35.3 (C-11), 35.0 (C-29), 32.7 (C-21), 32.4 (C-15), 32.1 (C-30), 31.8 (C-28), 30.5 (C-12), 29.7 (C-17), 28.1 (C-20), 22.2 (C-1), 20.2 (C-26), 18.6 (C-27), 18.2 (C-7), 17.9 (C-25), 14.6 (C-24), 6.8 (C-23).

Compound 2 – EI-MS (70 eV, rel. int., %): *m/z* 426 $[M]^+$ (4.1), 408 (3.3), 274 (78.2), 259 (72.8), 254 (86.5), 245 (15.1), 218 (84.7), 205 (42.2); ^{1}H-NMR (300 MHz, $CDCl_3$-*d*): δ 5.35 (1H, m, H-6), 3.63 (1H, t, *J* = 3 Hz, H-3), 1.17, 1.14, 1.09, 1.04, 1.00, 0.99, 0.96, 0.85 (each 3H, s, 8×tert Me); ^{13}C-NMR (75 MHz, $CDCl_3$-*d*): δ 141.7 (C-5), 122.1 (C-6), 72.7 (C-3), 49.1 (C-8), 47.4 (C-10), 44.5 (C-18), 39.3 (C-4), 38.9 (C-1), 37.4 (C-9), 36.1 (C-19), 35.3 (C-11), 35.0 (C-14), 34.8 (C-23), 34.3 (C-22), 34.0 (C-7), 32.8 (C-15), 32.1 (C-30), 31.9 (C-13), 29.7 (C-16), 29.4 (C-17), 29.3 (C-20), 29.1 (C-21), 28.3 (C-28), 27.9 (C-2), 25.7 (C-29), 24.8 (C-12), 19.6 (C-25), 18.2 (C-27), 17.7 (C-24), 16.9 (C-26).

Compound 3 – EI-MS (70 eV, rel. int., %): *m/z* 414 $[M]^+$ (100), 396 (42.7), 329 (28.1), 303 (34.4), 273 (24.9), 255 (24.8), 213 (23.7), 199 (10.7), 159 (19.0), 145 (22.6); ^{1}H-NMR (300 MHz, $CDCl_3$-*d*): δ 5.34 (1H, br d, *J* = 5.1 Hz, H-6), 3.52 (2H, m, H-3), 1.00 (3H, s, 19-Me), 0.93 (3 H, d, *J* = 6.6 Hz, 21-Me), 0.84 (3H, t, *J* = 7.6 Hz, 29-Me), 0.82 (3H, d, *J* = 7.3 Hz, 26-Me), 0.79 (3H, d, *J* = 6.8 Hz, 27-Me) 0.68 (3H, s, 18-Me); ^{13}C-NMR (75 MHz, $CDCl_3$-*d*): δ 140.7 (C-5), 121.7 (C-6), 71.8 (C-3), 56.8 (C-14), 56.1 (C-17), 50.1 (C-9), 45.8 (C-24), 42.3 (C-13), 40.4 (C-12), 39.8 (C-4), 37.3 (C-1), 36.5 (C-10), 36.1 (C-20), 34.0 (C-22), 31.9 (C-7), 31.6 (C-8), 29.7 (C-2), 29.4 (C-25), 28.2 (C-16), 26.1 (C-23), 24.3 (C-15), 23.1 (C-28), 21.1 (C-11), 19.8 (C-26), 19.4 (C-27), 19.0 (C-19), 18.8 (C-21), 12.0 (C-29), 11.9 (C-18).

Compound 4 – EI-MS (70 eV, rel. int., %): *m/z* 428 $[M]^+$ (100), 414 (49.1), 399 (12.8), 368 (5.0), 287 (8.8), 269 (9.7), 227 (32.7), 152 (77.9); ^{1}H-NMR (300 MHz, $CDCl_3$-*d*): δ 4.35 (1H, t, *J* = 3 Hz, H-3), 1.37 (3H, s, 30-Me), 1.25 (3H, s, 27-Me), 1.15 (3H, s, 28-Me), 0.93 (3H, s, 26-Me), 0.91 (3H, s, 29-Me), 0.85 (3H, s, 23-Me), 0.82 (3H, s, 25-Me), 0.74 (3H, s, 24-Me); ^{13}C-NMR (75 MHz, $CDCl_3$-*d*): δ 73.3 (C-3), 56.1 (C-10), 55.8 (C-4), 53.6 (C-8), 45.8 (C-18), 44.5 (C-5), 42.5 (C-2), 42.3 (C-6), 39.6 (C-14), 39.1 (C-22), 38.5 (C-13), 37.9 (C-9), 37.0 (C-16), 36.1 (C-19), 34.3 (C-11), 33.9 (C-29), 31.9 (C-21), 29.9 (C-15), 29.4 (C-30), 29.2 (C-28), 28.2 (C-12), 26.1 (C-17), 24.2 (C-20), 21.0 (C-1), 19.8 (C-26), 19.5 (C-27), 19.0 (C-7), 18.7 (C-25), 14.1 (C-24), 6.7 (C-23).

Compound 5 – EI-MS (70 eV, rel. int., %): *m/z* 428 $[M]^+$ (20.1), 410 (25.9), 396 (100), 337 (14.6), 285 (13.8), 251 (26.1), 211 (11.1), 157 (11.4), 119 (11.8), 81 (31.9), 69 (69.7); ^{1}H-NMR (300 MHz, $CDCl_3$-*d*): δ 6.50 (1H, d, *J* = 8.4 Hz, H-7), 6.24 (1H, d, *J* = 8.4 Hz, H-6), 5.22 (1H, dd, *J* = 6.9, 15.3 Hz, H-22), 5.13 (1H, dd, *J* = 6.9, 15.3 Hz, H-23), 3.98 (1H, m, H-3), 1.00 (3H, d, *J* = 6.6 Hz, 21-Me), 0.99 (3H, s, 19-Me), 0.98 (3H, d, *J* = 6.6 Hz, 28-Me), 0.90 (3H, d, *J* = 6.6 Hz, 26-Me), 0.87 (3H, d, *J* = 6.6 Hz, 27-Me), 0.68 (3H, s, 18-Me); ^{13}C-NMR (75 MHz, $CDCl_3$-*d*): δ 135.4 (C-6), 135.2 (C-22), 132.3 (C-23), 130.7 (C-7), 82.1 (C-5), 79.4 (C-8), 66.5 (C-3), 56.2 (C-17), 51.7 (C-14), 51.1 (C-9), 44.6 (C-13), 42.8 (C-24), 39.7 (C-20), 39.3 (C-12), 36.9 (C-4,10), 34.7 (C-1), 33.1 (C-25), 30.1 (C-2), 28.6 (C-16), 23.4 (C-11), 20.9 (C-21), 20.6 (C-15), 19.9 (C-27), 19.6 (C-26), 18.2 (C-19), 17.5 (C-28), 12.9 (C-18).

Compound 6 – EI-MS (70 eV, rel. int., %): *m/z* 412 $[M]^+$ (100), 398 (23.4), 368 (8.8), 296 (6.5), 271 (6.7), 210 (8.4), 196 (20.4); ^{1}H-NMR (300 MHz, $CDCl_3$-*d*): (5.61 (1H, br d, *J* = 5.1 Hz, H-6), 0.99 (3H, s, 19-Me), 0.94 (3H, d, *J* = 6.6 Hz, 21-Me), 0.84 (3H, t, *J* = 7.6 Hz, 29-Me), 0.82 (3H, d, *J* = 7.3 Hz, 26-Me), 0.79 (3H, d, *J* = 6.8 Hz, 27-Me) 0.68 (3H, s, 18-Me); ^{13}C-NMR (75 MHz, $CDCl_3$-*d*): δ 199.3 (C-3), 146.3 (C-5), 123.7 (C-6), 56.1 (C-14), 55.7 (C-17), 49.4 (C-9), 45.8 (C-24), 42.2 (C-13), 39.3 (C-12), 39.1 (C-4), 37.5 (C-1), 36.9 (C-10), 36.1 (C-20), 33.9 (C-22), 31.9 (C-7), 31.2 (C-8), 29.7 (C-2), 29.4 (C-25), 28.2 (C-16), 25.9 (C-23), 23.0 (C-15), 22.6 (C-28), 21.4 (C-11), 19.7 (C-26), 19.0 (C-27), 18.7 (C-19), 18.2 (C-21), 11.9 (C-29), 11.6 (C-18).

Compound 7 – EI-MS (70 eV, rel. int., %): *m/z* 424 $[M]^+$ (57.2), 409 (25.1), 300 (55.5), 274 (100), 259 (52.7), 245 (25.3), 218 (47.5), 205 (86.6); ^{1}H-NMR (300 MHz, $CDCl_3$-*d*): δ 5.55 (1H, m, H-6), 1.28, 1.24, 1.22, 1.08, 1.02, 0.99, 0.96, 0.72 (each 3H, s, 8×tert Me); ^{13}C-NMR (75 MHz, $CDCl_3$-*d*): δ 202.9 (C-3), 141.6 (C-5), 122.5 (C-6), 50.0 (C-8), 47.1 (C-10), 43.9 (C-18), 39.3 (C-4), 38.9 (C-1), 37.6 (C-9), 35.9 (C-19), 35.1 (C-11), 34.9 (C-14), 34.5 (C-23), 34.1 (C-22), 34.0 (C-7), 32.3 (C-15),

32.0 (C-30), 31.9 (C-13), 29.9 (C-16), 29.6 (C-17), 29.4 (C-20), 29.3 (C-21), 28.5 (C-28), 27.4 (C-2), 26.0 (C-29), 24.9 (C-12), 19.9 (C-25), 18.4 (C-27), 17.4 (C-24), 15.6 (C-26).

Results and Discussion

A chromatographic separation of the *n*-hexane and CH_2Cl_2 fractions from *O. japonicus* led to the isolation of compounds **1-7**. Among them, the isolation of friedelin (**1**), glutinol (**2**), β-sitosterol (**3**), friedelinol (**4**), and glutinone (**7**) from this plant was already reported by Park *et al.* (1991b). The isolation of compounds **5** and **6** from this plant are described here for the first time.

Compound **5** was obtained as amorphous powder. Each spectrum of **5** was similar to that of ergosterol. In the EIMS, molecular ion peak showed at *m/z* 428 and characteristic fragment ion peak of ergosterol peroxide showed at *m/z* 396 $[M-O_2]^+$. In the ^{1}H-NMR spectrum, the presence of two double bonds at δ 6.50 (H-7), 6.24 (H-6) and δ 5.22 (H-22), 5.13 (H-23) was observed together with six Me signals. 28 carbon signals containing carbon signals adjacent to peroxy group at δ 82.1 (C-5) and 79.4 (C-8) were observed in the ^{13}C-NMR spectrum. Accordingly, the structure of **5** was elucidated as 5α,8α-peroxyergosterol (ergosterol peroxide) by comparing its spectral data in the literature. It has previously been isolated from *Ajuga remota* (Kuria *et al.*, 2002), *Chlorella vulgaris* (Yasukawa *et al.*, 1996), *Citrus aurantium* (Huang *et al.*, 2001), *Cordyceps sinensis* (Bok *et al.*, 1999), *Ganoderma lucidum* (Mizushina *et al.*, 1998), *Lepiota americana* (Kim *et al.*, 2000), *Paecilomyces tenuipes* (Nam *et al.*, 2001) and *Paecilomyces* sp. J300 (Kwon *et al.*, 2002).

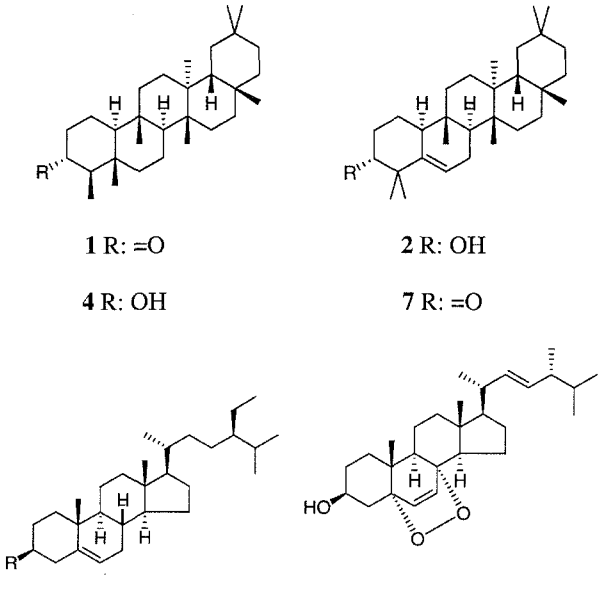

Fig. 1. Structures of compounds 1-7.

Compound **6** was obtained as white crystals. Each spectrum of **6** was similar to that of β-sitosterol (Compound **3**). In the EIMS, molecular ion peak showed at *m/z* 412. In the ^{1}H-NMR spectrum, the angular methyl singlet signals of 18-Me and 19-Me at 0.68 and 0.99, and the doublet of 21-Me, 26-Me and 27-Me at 0.94, 0.82 and 0.79 were observed, respectively. The broad doublet at δ 5.61 showed H-6 of olefinic proton. 29 carbon signals containing a ketone signal at δ 199.3 (C-3) were observed in the ^{13}C-NMR spectrum. Accordingly, the structure of **6** was elucidated as β-sitostenone (stigmast-5-en-3-one) by comparing its spectral data in the literature. It has previously been isolated from *Aleurites moluccana* (Satyanarayana *et al.*, 2001), *Casearia membranacea* (Ch ang *et al.*, 2003), *Dipladenia martiana* (De Carvalho *et al.*, 2001), and *Harrisonia abyssinica* (Balde *et al.*, 2000).

To the best of our knowledge, this is the first report on the isolation of 5α,8α-peroxyergosterol (**5**) and β-sitostenone (**6**) from *O. japonicus*.

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