The Japanese Society of Pharmacognosy

—Note— Natural Medicines 51(3), 275-277 (1997)

Studies on the Constituents of *Eucommia ulmoides* Iridoids from the Leaves

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(Received July 15, 1996)

From the leaves of *Eucommia ulmoides* OLIVER., seven iridoids were isolated, which were identified as eucommiol, 1-deoxyeucommiol, epieucommiol, asperuloside, asperulosidic acid, deacetylasperulosidic acid, and 10-acetyl scandoside by direct comparison with authentic samples or by spectral data.

Keywords——*Eucommia ulmoides*; iridoid; eucommiol; epieucommiol; asperuloside; asperulosidic acid; 10-acetyl scandoside

Eucommia ulmoides OLIVER. (Eucommiaceae) is distributed in the midstream region of the Yangzi river and in southern China. The bark of this plant has long been used as an antihypertensive, diuretic, sedative, tonic and nourishing medicine in China. A number of papers on the pharmacological and chemical studies of this bark were reported.[1-7]

Further, Namba *et al.* reported the chemical and pharmacological studies[8-10] on the leaves of this plant, the decoction of which is taken as beverage, and we reported that the leaves contained geniposidic acid and syringaresinol diglucoside,[11] and that a water extract of the leaves possessed an antihypertensive action.[12] In the present paper we report isolation and identification of seven iridoids from the commertially obtained leaves sold as tea.

A methanolic extract of the leaves (6.3 kg) was partitioned between water and $CHCl_3$, and the aq. layer (97.5 g) was subjected to MCI gel CHP20P column chromatography eluting with water gradiently mixed with MeOH to give six fractions (Frs. 1-6). Fr. 2 (14.0 g) was further purified first by chromatorex ODS column chromatography (25% MeOH→MeOH) and subsequently by silica gel column chromatography to give compounds **1** (168 mg), **4** (108 mg), **5** (61 mg), **6** (35 mg) and **7** (7 mg), which were identified as eucommiol,[13] asperuloside,[14] asperulosidic acid,[14] deacetyl asperulosidic acid,[14] and 10-acetyl scandoside,[14] respectively, by ^{1}H-NMR and ^{13}C-NMR (TABLE I) spectra and by direct comparison with respective authenetic specimens.

When, the leaves (927 g) were extracted with water and the water extract was subjected to MCI gel CHP-20P chromatography (H_2O→MeOH), three fractions Fr. I, II, and III were obtained. Fr. I (29.7 g) was chromatographed on chromatorex ODS (H_2O) and MCI gel CHP-20P (H_2O) to give **1** (64 mg). Fr. II was also purified by Sephadex LH-20 (H_2O→MeOH) and chromatorex ODS (25% MeOH→35% MeOH) column chromatographies to give compounds **2** (12 mg) and **3** (8 mg).

2 was identical as 1-deoxyeucommiol.[10]

The ^{1}H- and ^{13}C-NMR (TABLE I) spectra of **3** obtained as amorphous powder were similar to those of **1**. The ^{1}H-NMR signals of H_2-2′ at δ 1.38; 1.74, H_2-2″ at δ 3.58, and H_2-3′ at δ 4.02; 4.19 in **1** were shifted to δ 1.34; 2.00, δ 3.46; 3.91, and δ 3.87; 4.51, respectively, in **3**. This fact suggested that the hydroxy group at C-1 in **3** was α (*quasi axial*) to H_2-2′, H_2-2″ and H-3′, which caused lower-field shifts of their signals. Therefore, the structure of **3** was determined to be an epimer of **1**, and was named epieucommiol. **3**, **5**, **6** and **7** were identified in the leaves of this plant for the first time (Chart 1).

EXPERIMENTAL

The optical rotations were measured on a JASCO DIP-360 automatic digital polarimeter. ^{1}H- and ^{13}C-NMR spectra were measured in D_2O or CD_3OD on JEOL EX 270 MHz, JNM-GX 400 MHz, α-500 MHz spectrometers and chemical shifts were given on a δ (ppm) scale with tetramethylsilane as an internal (CD_3OD) or external (D_2O) standard. FAB-MS and EI-MS were measured on a JEOL DX-303HF spectrometer. Column chromatography was carried out on Kieselgel 60 (230-400 mesh, Merck), Sephadex LH-20 (Pharmacia), MCI gel CHP-20P (Mitsubishi Chemical Ind.), and Chromatrex ODS (Fuji-Davidson Chemical Ltd.). TLC was performed on pre-coated Kieselgel 60 F254 plates (Merck).

Eucommiol (1) Oil, Pos. FAB-MS *m/z*: 211 $[M+Na]^+$, $[\alpha]_D^{26}$ −21.2° (c=1.00, H_2O), ^{1}H-NMR (in D_2O) δ: 1.38

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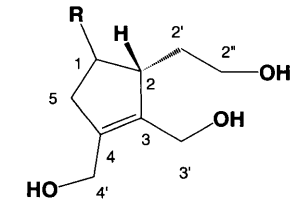
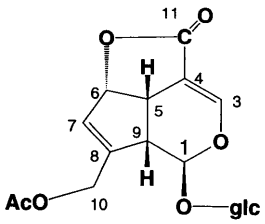
TABLE I. ^{13}C-NMR Spectral Data for Compounds **1**–**7** in D_2O

C	1	2	3	4*	5	6	7
1	75.3	27.1	78.1	94.1	101.2	101.1	97.8
2	52.9	42.1	51.1				
3	137.1	139.0	132.6	151.1	155.9	152.4	149.2
4	139.8	139.8	134.0	106.9	108.0	112.3	115.6
5	42.3	34.4	41.4	38.2	41.8	42.3	45.6
6				87.1	75.0	75.3	81.7
7				129.7	132.1	129.6	132.0
8				145.0	144.9	150.2	141.7
9				46.0	45.7	45.5	46.9
10				62.7	63.8	61.0	63.5
11				173.4	172.3	175.6	176.5
2′	33.1	32.0	33.1				
2″	60.9	59.9	67.8				
3′	56.2	54.7	57.7				
4′	57.9	56.9	65.5				
Glc-1				100.8	100.0	99.8	99.5
Glc-2				75.7	73.5	75.3	73.6
Glc-3				79.1	76.8	76.6	76.5
Glc-4				72.4	70.2	70.4	70.4
Glc-5				79.3	77.0	77.0	77.0
Glc-6				63.6	62.0	61.5	61.5
Ac				173.1	175.0		174.9
				21.5	21.4		21.2

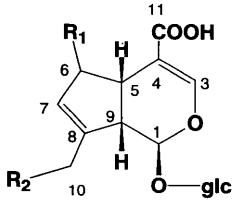
*Measurement made in CD_3OD.



1: R = —OH eucommiol
2: R = H 1-deoxyeucommiol
3: R = ···OH epieucommiol



4: asperuloside



5: R_1 = ···OH ; R_2 = OAc asperulosidic acid
6: R_1 = ···OH ; R_2 = OH deacetyl asperulosidic acid
7: R_1 = —OH ; R_2 = OAc scandoside 10-*O*-acetate

Chart 1.

(1H, m, H*a*-2′), 1.74 (1H, m, H*b*-2′), 2.22 (1H, br d, J=17.1 Hz, H*a*-5), 2.62 (1H, br d, J=9.2 Hz, H-2), 2.76 (1H, dd, J=5.5, 17.1 Hz, H*b*-5), 3.58 (2H, m, H_2-2″), 4.02 (1H, d, J=12.8 Hz, H*a*-3′), 4.09 (1H, br s, H-1), 4.10 (2H, s, H_2-4′), 4.19 (1H, d, J=12.8 Hz, H*b*-3′).

1-Deoxyeucommiol (2) Oil, $[\alpha]_D^{28}$ −3.2° (c=0.76, H_2O), ^{1}H-NMR (in D_2O) δ : 1.34 (1H, m, H*a*-2′), 1.46 (1H, m, H*a*-1), 1.82 (1H, m, H*b*-2′), 1.95 (1H, m, H*b*-1), 2.29 (1H, m, H*a*-5), 2.31 (1H, m, H*b*-5), 2.77 (1H, m, H-2), 3.56 (2H, m, H_2-2″), 4.03 (1H, d, J=12.8 Hz, H*a*-3′), 4.11 (1H, d, J=12.8 Hz, H*a*-4′), 4.13 (1H, d, J=12.8 Hz, H*b*-4′), 4.19 (1H, d, J=12.8 Hz, H*b*-3′).

Epieucommiol (3) Oil, EI-MS m/z; 152 $[M-2H_2O]^+$, $[\alpha]_D^{25}$ −6.4° (c=0.77, H_2O), ^{1}H-NMR (in D_2O) δ : 1.34 (1H, ddd, J=4.3, 12.2, 12.8 Hz, H*a*-2′), 2.00 (1H, br dd, J=5.8, 12.2 Hz, H*b*-2′), 2.25 (1H, br d, J=15.9 Hz, H*a*-5), 2.56 (1H, br d, J=7.3 Hz, H-2), 2.67 (1H, dd, J=7.9, 15.9 Hz, H*b*-5), 3.46 (1H, t, J=12.2 Hz, H*a*-2″), 3.87 (1H, br d, J=13.4 Hz, H*a*-3′), 3.91 (1H, dd, J=3.3, 12.2 Hz, H*b*-2″), 4.02 (1H, d, J=12.2 Hz, H*a*-4′), 4.05 (1H, br s, H-1), 4.06 (1H, br d, J=12.2 Hz, H*b*-4′), 4.51 (1H, br d, J=13.4 Hz, H*b*-3′).

Asperuloside (4) Amorphous powder, Neg. FAB-MS m/z; 413 $[M-H]^-$, $[\alpha]_D^{26}$ −79.0° (c=1.02, H_2O), ^{1}H-NMR (in CD_3OD) δ : 2.08 (3H, s, Ac), 3.20 (1H, br t, J=7.9 Hz, glc H-2), 3.27 (1H, m, glc H-4), 3.30 (1H, br s, H-9), 3.38 (2H, m, glc H-3, 5), 3.69 (2H, m, H-5, glc H*a*-6), 3.92 (1H, dd, J=2.0, 11.7 Hz, glc H*b*-6), 4.66 (1H, d, J=14.3 Hz, H*a*-10), 4.69 (1H, d, J=7.7 Hz, glc H-1), 4.78 (1H, d, J=14.3 Hz, H*b*-10), 5.57 (1H, d, J=6.6 Hz, H-6), 5.73 (1H, s, H-7), 5.95 (1H, s, H-1), 7.31 (1H, s, H-3).

Asperulosidic acid (5) Amorphous powder, Pos.

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FAB-MS m/z; 455 $[M+Na]^+$, $[\alpha]_D^{28}$ +20.2° (c=0.85, MeOH), ^{1}H-NMR (in D_2O) δ : 2.10 (3H, s, Ac), 2.70 (1H, br t, J=8.1 Hz, H-9), 3.06 (1H, br t, J=6.7 Hz, H-5), 3.30 (1H, dd, J=7.9, 8.9 Hz, glc H-2), 3.34 (1H, m, glc H-4), 3.40 (1H, m, glc H-5), 3.45 (1H, t, J=8.9 Hz, glc H-3), 3.64 (1H, dd, J=5.5, 12.2 Hz, glc Ha-6), 3.83 (1H, br d, J=12.2 Hz, glc H*b*-6), 4.75 (1H, d, J=7.9 Hz, glc H-1), 4.80 (1H, d, J=15.0 Hz, H*a*-10), 4.85 (1H, m, H-6), 4.87 (1H, d, J=15.0 Hz, H*b*-10), 4.96 (1H, d, J=9.2 Hz, H-1), 6.05 (1H, s, H-7), 7.63 (1H, s, H-3).

Deacetyl asperulosidic acid (6) Amorphous powder, Neg. FAB-MS m/z; 389 $[M-H]^-$, $[\alpha]_D^{26}$ +6.4° (c=1.03, H_2O), ^{1}H-NMR (in D_2O) δ : 2.54 (1H, br t, J=8.2 Hz, H-5), 3.00 (1H, br t, J=6.7 Hz, H-9), 3.29 (1H, br t, J=8.8 Hz, glc H-2), 3.32 (1H, m, glc H-4), 3.35 (1H, m, glc H-5), 3.43 (1H, t, J=9.2 Hz, glc H-3), 3.61 (1H, dd, J=5.2, 12.8 Hz, glc H*a*-6), 3.78 (1H, br d, J=12.8 Hz, glc H*b*-6), 4.19 (1H, br d, J=15.3 Hz, H*a*-10), 4.37 (1H, br d, J=15.3 Hz, H*b*-10), 4.75 (1H, br d, J=8.5 Hz, glc H-1), 4.77 (1H, m, H-6), 4.85 (1H, d, J=9.2 Hz, H-1), 5.94 (1H, br s, H-7), 7.35 (1H, s, H-3).

10-Acetyl scandoside (7) Amorphous powder, Pos. FAB-MS m/z; 455 $[M+Na]^+$, $[\alpha]_D^{28}$ −4.5° (c=0.52, H_2O), ^{1}H-NMR (in D_2O) δ : 2.07 (3H, s, Ac), 2.93 (1H, br t, J=7.0 Hz, H-5), 3.02 (1H, br t, J=7.0 Hz, H-9), 3.24 (1H, dd, J=8.0, 9.2 Hz, glc H-2), 3.34 (1H, t, J=9.2 Hz, glc H-4), 3.36 (1H, m, glc H-5), 3.42 (1H, t, J=9.2 Hz, glc H-3), 3.63 (1H, dd, J=5.5, 12.2 Hz, glc H*a*-6), 3.81 (1H, br d, J=12.2 Hz, glc H*b*-6), 4.51 (1H, br s, H-6), 4.72 (1H, d, J=8.0 Hz, glc H-1), 4.76 (2H, br s, H_2-10), 5.08 (1H, d, J=6.7 Hz, H-1), 5.86 (1H, s, H-7), 7.14 (1H, s, H-3).

REFERENCES

1) K. Imai, T. Kishi, H. Inoue, N. Nishiyama, Y. Saito, *Yakugaku Zasshi*, **108**, 57 (1988).
2) T. Deyama, S. Nishibe, S. Kitagawa, Y. Nomura, Y. Ogihara, T. Takeda, T. Ohmoto, T. Nikaido, U. Sankawa, *Chem. Pharm. Bull.*, **36**, 435 (1988).
3) T. Deyama, T. Ikawa, S. Kitai, S. Nishibe, *Chem. Pharm. Bull.*, **34**, 523 (1986).
4) T. Deyama, *Chem. Pharm. Bull.*, **34**, 4933 (1986).
5) T. Deyama, T. Ikawa, S. Kitai, S. Nishibe, *Chem. Pharm. Bull.*, **35**, 1785 (1987).
6) T. Deyama, T. Ikawa, S. Kitai, S. Nishibe, *Chem. Pharm. Bull.*, **35**, 1803 (1987).
7) T. Deyama, S. Kitai, S. Nishibe, Y. Ogihara, T. Takeda, T. Ohmoto, T. Nikaido, U. Sankawa, *Chem. Pharm. Bull.*, **36**, 435 (1988).
8) T. Namba, M. Hattori, J. N. Yie, Y. H. Ma, Y. Nomura, S. Kaneko, Y. Kitamura, T. Koizumi, K. Katayama, W. Lu, *J. Med. Pharm. Soc. WAKAN-YAKU*, **3**, 89 (1986).
9) Y. H. Ma, J. N. Yie, M. Hattori, S. Kaneko, Y. Nomura, K. Wakaki, Y. Kurashige, T. Namba, *J. Med. Pharm. Soc. WAKAN-YAKU*, **4**, 26 (1987).
10) M. Hattori, Q. M. Che, M. B. Gewali, Y. Nomura, Y. Tezuka, T. Kikuchi, T. Namba, *Shoyakugaku Zasshi*, **42**, 76 (1988).
11) A. Simoyama, M. Yamadaki, Y. Nakazawa, S. Yahara, T. Nohara, *Shoyakugaku Zasshi*, **47**, 56 (1993).
12) C. Tanaka, S. Yahara, T. Nohara, T. Nakamura, Y. Nakazawa, S. Onizuka, M. Ono, Abstract Papers of the 43rd Annual Meeting of the Japanese Society of Pharmacognosy, Tokyo, p. 106 (1996).
13) A. Bianco, C. Iavarone, C. Trogolo, *Tetrahedron*, **30**, 4117 (1974).
14) H. Inoue, M. Okigawa, N. Shimokawa, *Chem. Pharm. Bull.*, **17**, 1949 (1969).

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