

Catechin Glycoside from *Ulmus davidiana*

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Abstract □ Catechin and catechin glycoside named uldavioside A were isolated from the Korean folk medicine *Ulmus davidiana*. Based on chemical and physicochemical evidences, their structure have been determined as (+)-catechin (**1**) and (+)-catechin-5-O-β-D-apiofuranoside (**2**).

Keywords □ *Ulmus davidiana*, catechin, catechin glycoside, uldavioside A.

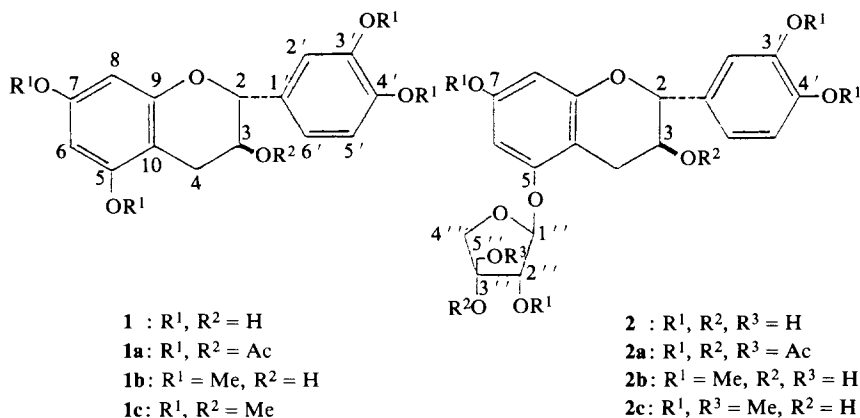
Ulmus davidiana Planch var. *Japonica* Nakai (Ulmaceae) is reputed in the Korean system of folk medicines to be effective for gastric cancer, gastroenteric disorder¹⁾, granulating, eruption, hemorrhoid and mastitis²⁾. As a part of our search for new biologically active substance from folk medicines, we investigated the chemical constituents of *Ulmus davidiana* and isolated a new catechin glycoside named uldavioside A (**2**). This paper deals with the structure elucidation of (+)-catechin (**1**) and catechin apioside (**2**). Up to now, a number of catechin type glycosides^{3,4)} and many glycosides having an apiosyl moiety have been reported⁵⁻⁸⁾.

Column chromatography of the methanol extract of the root bark of *Ulmus davidiana* gave **1** and **2**. **1**, $[\alpha]_D + 11.9^\circ$ (MeOH), was shown by its IR spectrum to have hydroxyl and aryl groups. The mass, ¹H and ¹³C NMR (Table I) spectra of **1** showed fragments and signals assignable to (+)-catechin.⁹⁻¹¹⁾ Acetylation of **1** liberated pentaacetate **1a**, whereas methylation of **1** afforded tetramethylate **1b** and pentamethylate **1c**. The isolated **1** and its derivatives (**1a**, **1b**) had mp, $[\alpha]_D$, ¹H and ¹³C NMR spectra identical to published data⁹⁻¹¹⁾. Based on the above evidence, **1** was determined as (+)-catechin.

The IR spectrum of **2**, $[\alpha]_D - 43.7^\circ$ (MeOH), shows the presence of hydroxyl and aryl groups. From the ¹H (experimental) and ¹³C NMR (Table I) spectra of **2**, **2** was suggested to catechin monoglycoside. Acid hydrolysis of **2** furnished (+)-cate-

chin (**1**)⁹⁻¹¹⁾ and methyl apiofuranoside⁸⁾ on the basis of the spectral evidence. An optical rotation ($[\alpha]_D^{22} + 8.9^\circ$ (H₂O, 10 hr); lit.⁸⁾: $[\alpha]_D^{22} + 9.1^\circ$) of apiose, which was obtained from acid hydrolysis of methyl apiofuranoside with 10% aq. H₂SO₄, indicated the presence of D-apiose in **2**. The anomeric configuration at the D-apiofuranoside linkage in **2** was assigned as β on the bases of the difference in molecular optical rotation ($\Delta[M]_D - 219^\circ$; lit.¹²⁾: methyl α-D-apiofuranoside, $\Delta[M]_D + 221^\circ$; methyl β-D-apiofuranoside, $\Delta[M]_D - 167^\circ$) between **1** and **2**, and by ¹³C NMR analysis of methyl D-apiofuranoside obtained by acid hydrolysis of **2**.⁸⁾ Acetylation of **2** gave heptaacetate **2a**, whereas methylation of **2** by prolonged CH₂N₂ treatment afforded tetramethylate **2b** and pentamethylate **2c**. The ¹H NMR spectra of **2a**, **2b** and **2c** suggested that sugar moiety is substituted in the phenolic hydroxyl, since there are three aromatic acetyl and methoxyl groups, and four aliphatic acetyl, and one and two methoxyl groups, respectively (experimental). The location of the sugar moiety in **2** was confirmed by mass fragment patterns of **2b** and **2c**; RDA fragments of B-ring were observed at *m/z* 180, respectively, by comparison of the ¹³C NMR spectra of **1** & **2** and **1b** & **2b**; the carbon resonance of C-10 was shifted downfield by 2.6 ppm and 3.3 ppm, respectively, while the carbon resonances of C-3' and C-4' nearly remained unchanged (Table I), and by application of a positive Gibbs' test (for phenol with no substituent in the *para* position)⁴⁾ on 7,3',4'-tri-O-methyl-(+)-catechin¹³⁾ which was obtained by acid

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Table I. ¹³C NMR data for compounds **1**, **1a**, **1b**, **1c**, **2**, **2a**, **2b**, and **2c**^a

carbon	1	1a ^b	1b	1c	2	2a ^c	2b	2c
2	82.9	77.6	81.4	79.8	82.9	77.4	81.7	81.8
3	68.1	68.2	67.5	76.8	67.8	68.3	68.0	68.2
4	29.3	23.9	27.4	24.8	29.2	23.4	27.6	27.8
5	157.1 ^d	149.4 ^d	159.3 ^d	159.7 ^d	157.9 ^d	155.5 ^d	158.7 ^d	158.8 ^d
6	96.5 ^e	108.7 ^e	92.8 ^e	93.0 ^e	97.1 ^e	104.0 ^e	96.8 ^e	97.1 ^e
7	158.1 ^d	154.3 ^d	158.3 ^d	158.7 ^d	156.8 ^d	154.5 ^d	156.3 ^d	156.7 ^d
8	95.4 ^e	107.6 ^e	91.4 ^e	91.8 ^e	96.1 ^e	103.8 ^e	93.1 ^e	93.1 ^e
9	158.5 ^d	149.8 ^d	155.0	155.3	157.8 ^d	149.8	155.2	155.3
10	100.8	110.1	101.5	101.4	103.4	106.7	104.8	103.4
1'	132.0	136.1	130.5	131.7	131.8	136.2	130.4	130.4
2'	115.8 ^f	123.6 ^f	109.9 ^f	110.1 ^f	115.7 ^f	123.5 ^f	110.1 ^f	110.0 ^f
3'	146.9	142.1 ^g	148.8	149.0 ^g	146.9	142.0 ^g	149.3	149.4
4'	146.9	142.0 ^g	148.8	148.9 ^g	146.9	141.9 ^g	149.3	149.4
5'	116.2 ^f	124.3 ^f	110.8 ^f	111.1 ^f	116.1 ^f	124.2 ^f	111.2 ^f	111.3 ^f
6''	119.5	121.7	119.6	119.5	119.4	121.5	119.9	119.9
1''					108.8	102.1	103.4	105.5
2''					77.8	76.1	86.1	86.5
3''					80.0	83.5	79.4	78.6
4''					75.4	73.0	75.0	75.0 ^g
5''					64.5	62.7	65.5	74.8 ^g
-OCH ₃			55.5	57.3			59.1	59.6
			55.5	55.9			55.9	59.2
			55.0	55.9			55.9	56.0
			54.9	55.5			55.6	56.0
				55.4				55.6

^a**1** was measured at 22.5 MHz and **2** was at 125 MHz in pyridine-*d*₅ with pyridine-*d*₅ (135.5 ppm) as the internal standard, and **1a**, **1b**, **1c**, **2a**, **2b**, and **2c** were at 125 MHz in CDCl₃ with CDCl₃ (77.1 ppm) as the int. standard.

^bAcetyl unit: 170.0, 168.8, 168.2, 167.9, 167.9, 21.0, 20.8, 20.6, 20.5, 20.5.

^cAcetyl unit: 170.3, 170.0, 169.5, 168.9, 168.4, 167.8, 167.8, 23.4, 20.6, 20.5, 20.5, 20.4, 20.3, 20.2.

^{d-g}Assignments may be interchangeable within the same vertical column.

hydrolysis of **2c**. Accordingly, from these observations, the structure of compound **2** was determined as (+)-catechin-5-O- β -D-apiofuranoside.

EXPERIMENTAL

Extraction and Isolation

The air-dried root bark of *Ulmus davidiana* (300 g) (collected at Mt. Wonhyo, Kyungnam Prefecture in April 1988) was finely cutted and refluxed with methanol for 5 hr(3 times). All the filtrates were concentrated under reduced pressure to afford the extract (22.6 g). The extract(5 g) was subjected to silica gel column chromatography(SiO₂, 70-230 mesh, Merck) developing with CHCl₃-MeOH (10:1 \rightarrow 3:1) to furnish (+)-catechin fraction(250 mg) and uldavioside A fraction(550 mg). The fraction containing (+)-catechin(250 mg) was purified with Sephadex LH-20(MeOH) to afford (+)-catechin(**1**) (180 mg). The uldavioside A fraction (550 mg) was successively purified by Si gel(CHCl₃-MeOH = 5:1), Sephadex LH-20(MeOH), and HPLC(Semi Prep Zorbax ODS, MeOH-H₂O = 5:1) to furnish uldavioside A(**2**) (285 mg).

1, yellowish amorphous solid, mp 175-176°, [α]_D + 11.9° (MeOH, c 1.0). UV λ λ_{max}^{MeOH} nm (log ϵ): 284(3.29). IR ν_{max}^{KBr} cm⁻¹: 3254, 1610. EIMS(probe), m/z (rel. int.): 290[M⁺] (48), 272[M⁺-H₂O](3), 152(46), 139(100). ¹H NMR(500 MHz, pyridine-d₃): δ 5.19(1H, d, J = 7.5 Hz, H-2), 4.59(1H, ddd, J = 8.5, 7.5, 5.5 Hz, H-3), 3.31(1H, dd, J = 16.0, 8.5 Hz, H-4), 3.67(1H, dd, J = 16.0, 5.5 Hz, H-4), 6.73, 6.64(both 1H, d, J = 2.0 Hz, H-6 and H-8), 7.64(1H, d, J = 1.8 Hz, H-2'), 7.24(1H, d, J = 8.0 Hz, H-5'), 7.20(1H, dd, J = 8.0, 1.8 Hz, H-6'). ¹³C NMR: as shown in Table I.

2, amorphous solid, [α]_D -43.7° (MeOH, c 0.52). IR ν_{max}^{KBr} cm⁻¹: 3380(*br*), 1615, 1600, 1040. ¹H NMR(500 MHz, pyridine-d₃): δ 5.17(1H, d, J = 7.5 Hz, H-2), 4.53(1H, ddd, J = 8.0, 7.5, 5.5 Hz, H-3), 3.57(1H, dd, J = 16.0, 5.5 Hz, H-4), 3.25(1H, dd, J = 16.0, 8.0 Hz, H-4), 6.80, 6.75(both 1H, s, H-6 and H-8), 7.25(1H, s, H-2'), 7.22(1H, d, J = 8.0 Hz, H-5'), 7.17(1H, d, J = 8.0 Hz, H-6'), 6.21(1H, d, J = 2.5 Hz, H-1'), 4.97(1H, d, J = 2.5 Hz, H-2'), 4.67, 4.39(ABq, J = 9.5 Hz, H₂-4'), 4.17, 4.15(both 1H, s, H₂-5'). ¹³C NMR: as shown in Table I.

Acid Hydrolysis of 2

A soln of **2** (80 mg) in 9% dry methanolic HCl (1.5 ml) was stirred at r.t. for 3 hr(N₂ atmosphere). The reaction mixture was neutralized with Ag₂CO₃

and filtrated. The residue, obtained by removal of the solvent, was purified by Si gel(CHCl₃-MeOH = 7:1) and then with Sephadex LH-20(MeOH) to furnish an aglycone (30 mg) and methyl apiofuranoside (15 mg). The aglycone was identical ([α]_D, ¹H NMR, ¹³C NMR) to (+)-catechin(**1**) and to published data.¹⁰ Methyl apiofuranoside, ¹H NMR (500 MHz, pyridine-d₃): δ 5.36(1H, d, J = 2.5 Hz, H-1), 4.63(1H, d, J = 2.5 Hz, H-2), 4.47, 4.30(ABq, J = 9.5 Hz, H₂-4), 4.10, 4.07(ABq, J = 11.0 Hz, H₂-5), 3.40(3H, s, H-methoxyl). ¹³C NMR (125 MHz, pyridine-d₃): δ 111.4(C-1), 77.6(C-2), 80.3(C-3), 74.9(C-4), 65.2(C-5), 55.2(C-methoxyl).

Heptaacetate(2a) of Compound 2

2a, [α]_D -40° (CHCl₃, c 1.2), IR $\nu_{max}^{CHCl_3}$ cm⁻¹: 1760(*sh*), 1745(*br*), 1217. EIMS(probe), m/z (rel. int.): 457[M⁺-apiose moiety](2), 398[458-AcOH](14), 356[398-COCH₂](10), 314[356-COCH₂](9), 272[314-COCH₂](8), 259(98), 139[259-2AcOH](100), 97(16), 43(44). ¹H NMR(500 MHz, CDCl₃): δ 5.15(1H, d, J = 6.0 Hz, H-2), 5.24(1H, ddd, J = 6.0, 6.0, 5.0 Hz, H-3), 2.78(1H, dd, J = 16.5, 5.0 Hz, H-4), 2.61(1H, dd, J = 16.5, 6.0 Hz, H-4), 6.58, 6.45(both 1H, d, J = 2.5 Hz, H-6 and H-8), 7.16(1H, s, H-2'), 7.18(1H, d, J = 8.5 Hz, H-5'), 7.23(1H, dd, J = 8.5, 1.8 Hz, H-6'), 5.61(1H, s, H-1'), 5.59(1H, s, H-2'), 4.82, 4.63(ABq, J = 12.5 Hz, H₂-4'), 4.38, 4.23(ABq, J = 10.5 Hz, H₂-5'), 2.27, 2.26, 2.25(each 3H, s, aromatic acetyls), 2.12, 2.11, 2.05, 1.98(each 3H, s, aliphatic acetyls). ¹³C NMR: as shown in Table I.

Tetramethylate (2b) and Pentamethylate (2c) of Compound 2

2b, [α]_D -77.8°(MeOH, c 1.0). IR $\nu_{max}^{CHCl_3}$ cm⁻¹: 3380(*br*), 1614, 1595, 1024. EIMS(probe), m/z (rel. int.): 478 [M⁺](15), 332 [M⁺-apiose moiety](94), 180(100), 165 (16), 153(90). ¹H NMR (500 MHz, CDCl₃): δ 4.64 (1H, d, J = 8.5 Hz, H-2), 4.03(1H, ddd, J = 9.0, 8.5, 5.5 Hz, H-3), 3.04 (1H, dd, J = 16.5, 5.5 Hz, H-4), 2.58(1H, dd, J = 16.5, 9.0 Hz, H-4), 6.30, 6.19(both 1H, d, J = 2.5 Hz, H-6 and H-8), 6.95 (1H, s, H-2'), 6.88, 6.97(both 1H, d, J = 8.0 Hz, H-5' and H-6'), 5.63(1H, d, J = 1.5 Hz, H-1'), 3.83(1H, d, J = 1.5 Hz, H-2'), 3.94, 3.89(ABq, J = 10.0 Hz, H₂-4'), 3.79, 3.51(ABq, J = 7.5 Hz, H₂-5'), 3.88, 3.88, 3.80(each 3H, s, aromatic methoxyls), 3.56(3H, s, aliphatic methoxyl). ¹³C NMR: as shown in Table I. **2c**, [α]_D -68.0° (CHCl₃, c 0.5). IR $\nu_{max}^{CHCl_3}$ cm⁻¹: 3580, 1618, 1597, 1060, 1027. EIMS(probe), m/z (rel. int.): 492 [M⁺] (32), 332[M⁺-apiose moiety](77), 313(16), 180

(100), 165 [180-CH₃](17), 153(76). ¹H NMR(500 MHz, CDCl₃): δ 4.64(1H, d, J = 8.5 Hz, H-2), 4.04(1H, ddd, J = 9.0, 8.5, 6.0 Hz, H-3), 3.05(1H, dd, J = 16.5, 6.0 Hz, H-4), 2.59(1H, dd, J = 16.5, 9.0 Hz, H-4), 6.32, 6.22(both 1H, d, J = 2.5 Hz, H-6 and H-8), 6.95(1H, d, J = 1.8 Hz, H-2'), 6.88(1H, d, J = 8.2 Hz, H-5') 6.97(1H, dd, J = 8.2, 1.8 Hz, H-6'), 5.63(1H, d, J = 2.5 Hz, H-1'), 3.91(1H, d, J = 2.5 Hz, H-2''), 4.04, 3.88(ABq, J = 10.0 Hz, H₂-4'), 3.44, 3.42(ABq, J = 11.0 Hz, H₂-5'), 3.89, 3.89, 3.81(each 3H, s, aromatic methoxyls), 3.55, 3.50 (both 3H, s, aliphatic methoxyls). ¹³C NMR: as shown in Table I.

Acid Hydrolysis of 2c

A soln of 2c(10 mg) in 9% dry methanolic HCl (1 ml) was stirred at r.t. for 3 hr(N₂ atmosphere). The reaction mixture was treated as described in the case of 2 and the residue thus obtained was purified by Si gel (*n*-hexane-AcOEt-MeOH = 3:3:0.1) to give 7,3',4'-tri-O-methyl-(+)-catechin(5 mg) identical to published data.¹³⁾

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