# NEW IRIDOID TRIMERS AND TETRAMERS FROM SEEDS OF EUCOMMIA ULMOIDES

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Four new iridoid glycosides, ulmoidosides A, B, C and D (**1-4**), were isolated from the seeds of Eucomia ulmoides. These compounds on alkaline hydrolysis provided a sole product, geniposidic acid (**5**). Their structures have been determined as an ester trimer (**1**) and a tetramer (**3**) bonding each other between C-11 and C-10 of geniposidic acid and as their respective 10-O-monoacetates (**2** and **4**) by spectral and chemical methods.

**KEYWORDS** Eucommia ulmoides; Eucommiaceae; iridoid trimer; iridoid tetramer; geniposidic acid oligomer; aucubin

Eucommiae Cortex, the barks of Eucommia ulmoides Oliv. (Eucommiaceae) is a Chinese crude drug used as a tonic and an antihypertensive medicine.[1] Isolation and structure elucidation of several lignan glycosides and iridoids from the barks and leaves of this plant were reported previously by other groups.[2] As a part of our continuing chemical studies on the various glycosides, we have investigated the glycosides of the seeds of this plant. From the dil.MeOH extract, four new iridoid glycosides named ulmoidoside A (**1**, 0.30%), B (**2**, 0.10%), C (**3**, 0.03%) and D (**4**, 0.17%) were isolated along with a known compound, aucubin (1.7%). The structures of the new compounds were determined by spectral and chemical anlaysis.

Ulmoidoside A (**1**), $[\alpha]_D$ +7.5°(water), a white powder, showed IR absorptions due to the hydroxyl functions (3432 $cm^{-1}$) and α,β-unsaturated ester carbonyl groups (1698 and 1636 $cm^{-1}$), and UV absorptions with a maximum at 239 nm (log ε 4.39) due to the α,β-unsaturated carbonyl group. The negative FAB-MS of **1** exhibited a molecular peak at 1085 $[M-H]^-$, together with weak peaks at m/z 922 $[M-glc-H]^-$, 729 $[M-m/z\ 356-H]^-$ and 373 $[M-m/z\ 356x2-H]^-$. The $^1$H-NMR spectrum (Table I) of **1** showed characteristic peaks for iridoid glycoside; signals due to the olefinic protons at δ 7.61 (2H, s), 7.36 (1H, s), 5.89 (1H, s), 5.86 (1H, s) and 5.85 (1H, s), hydroxymethyl protons at δ 4.90 (4H, m), 4.33 (1H, d, J=14 Hz) and 4.22 (1H, d, J=14 Hz) and anomeric protons at δ 4.78 (3H, br d, J=8 Hz). Moreover, the $^{13}$C-NMR spectrum (Table II) of **1** displayed signals due to two α,β-unsaturated ester groups at δ 170.0, 170.1, 154.6x2, 113.0 and 113.2, an α,β-unsaturated carboxylic acid system at δ 174.8, 151.4 and 116.7 and three β-glucopyranosyl anomeric carbons at δ 100.9x2, 101.1, suggesting that **1** should be the ester oligomer of iridoid glucoside. On alkaline treatment with 0.5 N NaOH, **1** afforded an iridoid glucoside (**5**), which was identified as geniposidic acid by comparison of $[\alpha]_D$ and $^1$H- and $^{13}$C-NMR spectra with the reported data.[3] A comparative study of the $^{13}$C-NMR spectrum of **1** with that of **5** (salt) revealed that the chemical shifts assignable to the C-3, C-4 and C-11 in the b and c moieties, and C-10 in the a and b moieties in **1** were shifted to δ 154.6x2; 113.0 and 113.2; 170.0 and 170.1; 64.2 and 64.3, respectively. On the other hand, there was one unit of non-shifted carbon signals at δ 151.4, 116.7, 61.9, 174.8. Therefore, the structure of **1** could be represented as an ester trimer of geniposidic acid as shown in the formula.

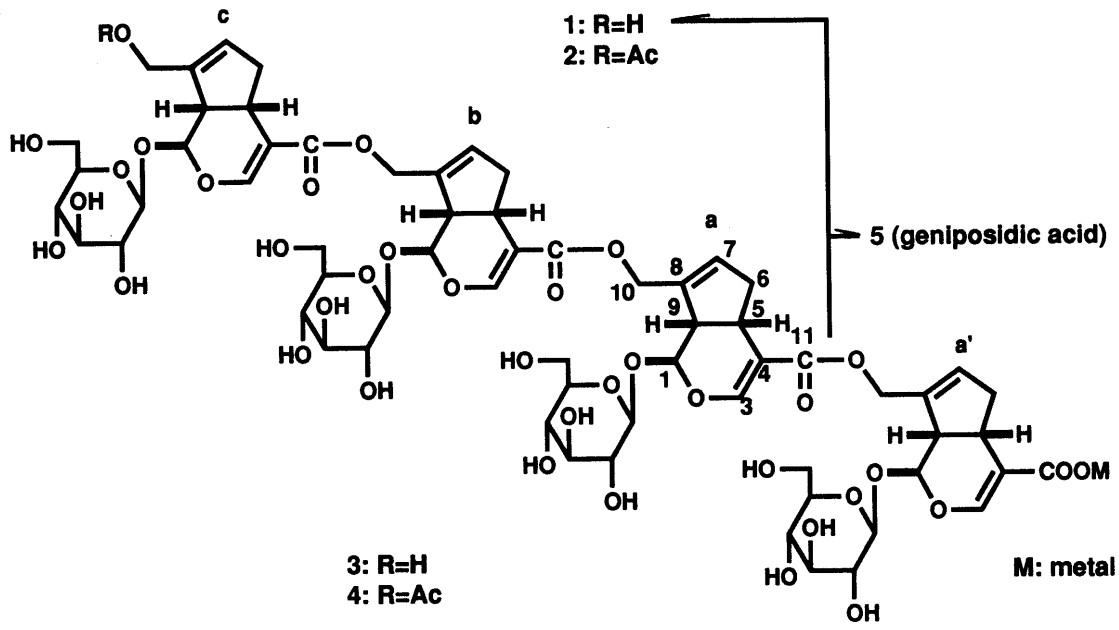
Ulmoidoside B (**2**), $[\alpha]_D$ +8.3°, showed absorption bands at 3448 (OH), 1702 and 1636 $cm^{-1}$

Table I. $^1$H-NMR Data for 1-5 ($CD_3OD+D_2O$)

| | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| Ac | | 2.13(3H,s) | | 2.11(3H,s) | |
| H-6 | 2.15(3H,m) | 2.17(3H,m) | 2.14(4H,m) | 2.12(4H,m) | 2.11(1H,dd,J=7,17) |
| H'-6,H-9 | 2.84(2H,m) | 2.83(6H,m) | 2.84(8H,m) | 2.80(8H,m) | 2.83(2H,m) |
| H-5 | 3.20-3.55 | 3.20-3.55 | 3.19-3.55 | 3.17-3.55 | 3.17(1H,dd,J=7,7) |
| glc | (15H,m) | (15H,m) | (20H,m) | (20H,m) | |
| H-2,3,4 | | | | | 3.40(3H,m) |
| glc H-5 | | | | | 3.52(1H,m) |
| glc $H_2$-6 | 3.69(1H,d, J=12) | 3.71(3H,d, J=12) | 3.71(4H,d, J=12) | 3.68(4H,d, J=12) | 3.69(1H,dd,J=5,12) |
| | 3.88(3H,d, J=12) | 3.88(3H,d, J=12) | 3.88(4H,d, J=12) | 3.85(4H,d, J=12) | 3.88(1H,d,J=12) |
| $H_2$-10 | 4.22(1H,d, J=14)c | 4.90(6H,m) | 4.22(1H,d, J=14)c | 4.75-4.95 (12H,m) | 4.22(1H,d,J=14) |
| | 4.33(1H,d, J=14)c | | 4.33(1H,d, J=14)c | | 4.32(1H,d,J=14) |
| | 4.90(4H,m) | | 4.90(6H,m) | | |
| glc H-1 | 4.78(3H,d,J=8) | 4.77(3H,d,J=8) | 4.80(4H,d,J=8) | | 4.78(1H,d,J=8) |
| H-1 | 5.18(1H,d,J=7) | 5.20(1H,d,J=7) | 5.19(4H,d,J=7) | 5.12(1H,d, J=7) | 5.17(1H,d,J=7) |
| | 5.19(1H,d,J=7) | 5.22(1H,d,J=7) | 5.24(2H,d,J=7) | 5.19(3H,d, J=7) | |
| | 5.23(1H,d,J=7) | 5.24(1H,d,J=7) | | | |
| H-7 | 5.85(1H,s) | 5.87(1H,s) | 5.85(2H,s) | 5.84(3H,s) | 5.84(1H, s) |
| | 5.86(1H,s) | 5.90(1H,s) | 5.89(2H,s) | 5.87(1H,s) | |
| | 5.89(1H,s) | 5.92(1H,s) | | | |
| H-3 | 7.36(1H,s)a | 7.40(1H,s)a | 7.24(1H,s)a' | 7.33(1H,s)a' | 7.37(1H,s) |
| | 7.61(2H,s) | 7.61(1H,s) | 7.61(3H,s) | 7.57(3H,s) | |
| | | 7.62(1H,s) | | | |

Table II. $^{13}$C-NMR Data for 2-5 ($CD_3OD+D_2O$)

| | 1 | 2 | 3 | 4 | 5(C-11 COONa) |
|---|---|---|---|---|---|
| C-1 | 98.4a | 98.4a | 98.1a' | 98.3a' | 98.6 |
| | 99.0 | 99.1x2 | 99.0x2 | 99.0x2 | |
| | 99.2 | | 99.3 | 99.2 | |
| C-3 | 151.4a | 152.0a | 149.6a' | 151.5a' | 151.9 |
| | 154.6x2 | 154.7x2 | 154.7x3 | 154.7x3 | |
| C-4 | 113.0 | 112.9x2 | 112.9 | 112.8x3 | 116.2 |
| | 113.2 | 115.9a | 113.0 | 116.3a' | |
| | 116.7a | | 113.2 | | |
| | | | 118.9a' | | |
| C-5 | 36.6 | 36.5 | 36.5x2 | 36.4x2 | 37.0 |
| | 36.9 | 36.7 | 36.8 | 36.5x2 | |
| | 37.1 | 36.8 | 37.2 | | |
| C-6 | 40.4 | 40.5x3 | 40.4 | 40.4x4 | 40.2 |
| | 40.6x2 | | 40.5x2 | | |
| | | | 40.6 | | |
| C-7 | 129.7c | 132.5x2 | 129.8c | 132.3x3 | 130.1 |
| | 132.3 | 132.8 | 132.5x3 | 132.9 | |
| | 132.5 | | | | |
| C-8 | 139.7 | 139.4 | 139.5 | 139.1x2 | 144.0 |
| | 139.8 | 139.5 | 139.6x2 | 139.4x2 | |
| | 144.7c | | 144.5c | | |
| C-9 | 47.6 | 47.8 | 47.5 | 47.6 | 47.7 |
| | 48.2 | 48.1 | 48.1x2 | 47.9x2 | |
| | 48.5 | 48.3 | 48.7 | 48.4 | |
| C-10 | 61.9c | 64.2 | 61.9c | 64.3x2 | 61.8 |
| | 64.2 | 64.6x2 | 64.3x2 | 64.6x2 | |
| | 64.3 | | 64.4 | | |
| C-11 | 170.0 | 170.2x2 | 170.1 | 170.0x3 | 174.5 |
| | 170.1 | 174.5a | 170.2x2 | 174.7a' | |
| | 174.8a | | 177.2a' | | |
| glc C-1 | 100.9x2 | 101.0x3 | 100.9x2 | 100.9x2 | 100.7 |
| | 101.1 | | 101.0x2 | 101.0x2 | |
| glc C-2 | 75.2x3 | 75.1x3 | 75.1x4 | 74.8x4 | 74.9 |
| glc C-3 | 78.5x3 | 78.5x3 | 78.5x4 | 78.2x4 | 78.2 |
| glc C-4 | 71.8x3 | 71.7x3 | 71.7x4 | 71.4x4 | 71.6 |
| glc C-5 | 78.0 | 78.0x3 | 78.0x4 | 77.7x4 | 77.8 |
| | 78.1x2 | | | | |
| glc C-6 | 62.9 | 63.0x3 | 63.0x4 | 62.8x4 | 62.6 |
| | 63.1x2 | | | | |
| Ac | | 21.9 | | 22.1 | |
| | | 174.8 | | 175.1 | |




(α,β-unsaturated ester) in the IR spectrum. In the negative FAB-MS, there was a molecular ion peak at m/z 1127 $[M-H]^-$ along with other fragment ions at m/z 771 [M-H-m/z 356]$^-$, 729 [m/z 771-$CH_2CO$]$^-$, 415 [M-H-m/z 356x2]$^-$ and 373 [m/z 415-$CH_2CO$]$^-$ and its spectrum had a pattern similar to that of **1**. The $^1$H-NMR spectrum of **2** showed the presence of an acetyl group at δ 2.13 and other signals were analogous to those of **1**. Comparison of the $^1$H- and $^{13}$C-NMR spectra of **2** with those of **1** disclosed that the chemical shifts due to the terminal C-10 position (hydroxymethyl) in **2** was shifted to $\delta_H$ 4.90 (m) and $\delta_C$ 64.2 (t), thus the acetyl group was attached to the terminal hydroxymethyl moiety (C-10) in **1**. Therefore, the structure of **2** was concluded to be 10-O-acetylulmoidoside A.

Ulmoidoside C (**3**), $[\alpha]_D$ +9.5°, showed absorption bands similar to those of **1** in the IR (3432, 1702, 1636 $cm^{-1}$) and the UV 236 nm (log ε 4.51) spectra. The negative FAB-MS exhibited a molecular ion peak at m/z 1441 $[M-H]^-$ along with fragment ions at m/z 1085 [M-H-m/z 356]$^-$, 729 [M-H-m/z 356x2]$^-$, 373 [M-H-m/z 356x3]$^-$, suggesting that **3** was an ester tetramer of iridoid glycoside. On alkaline hydrolysis, **3** afforded **5**. The $^1$H- and $^{13}$C-NMR spectra of **3** showed peaks very similar to those of **1**, except peaks in the ester part. Therefore, the structure of **3** was characterized as an ester tetramer of geniposidic acid as shown in the formula.

Ulmoidoside D (**4**), $[\alpha]_D$ +15.4°, showed the IR, UV and $^1$H- and $^{13}$C-NMR spectra similar to those of **2**. In the negative FAB-MS, a molecular ion peak at m/z 1483 $[M-H]^-$, together with other fragment ions at m/z 1127 [M-m/z 356-H]$^-$, 1085 [m/z 1127-$CH_2CO$]$^-$, 771 [M-m/z 356x2-H]$^-$, 729 [m/z 771-$CH_2CO$]$^-$, 415 [M-m/z 356x3-H]$^-$ and 373 [m/z 415-$CH_2CO$]$^-$ was observed, therefore the structure of **4** was determined to be the monoacetate of **3** as shown in the formula. This is the first report of the isolation of the ester trimer and tetramer of the iridoid glucoside from the plant.

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