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CHEMICAL CONSTITUENTS FROM THE STEM BARK OF *Trewia nudiflora*

Shao-Hua Wu,[1*] Yue-Mao Shen,[2] You-Wei Chen,[1] Zhi-Ying Li,[1] Li-Yuan Yang,[1] and Shao-Lan Li[1]

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Trewia nudiflora L. is the only member of the genus *Trewia* (Euphorbiaceae), which is mainly distributed in India, Malaysia, and southwest of China. Previous studies have shown that the seed of *T. nudiflora* is a rich source of maytansinoid tumor inhibitors [1, 2]. Phytochemical studies are mainly focused on the seed and pericarp of the plant; however, there are only few reports on its stem bark [3, 4].

The air-dried powdered stem bark of *T. nudiflora* (8.8 kg) was extracted with 95% EtOH three times at room temperature. The EtOH extract was concentrated in vacuum to give a residue. The residue was suspended in water and successively treated with EtOAc. The EtOAc extract (32 g) was subjected to chromatography on silica gel eluting with $CHCl_3$–MeOH gradient (1:0–0:1) to give nine fractions (I–IX). Fraction III was repeatedly subjected to column chromatography on RP-18 silica gel with MeOH-H_2O (2:3) and Sephadex LH-20 with MeOH to give compound **1** (9 mg). Repeated chromatography of fraction IV on silica gel with petroleum ether–Me_2CO gradient (4:1, 7:3, 6:4) and RP-18 silica gel with MeOH–H_2O gradient (2:3, 1:1) afforded compounds **2** (6 mg) and **3** (10 mg). Fraction V was submitted to repeated column chromatography on silica gel with $CHCl_3$–MeOH gradient (15:1, 10:1) and RP-18 silica gel with MeOH–H_2O gradient (3:7, 2:3) to afford compounds **4** (13 mg), **5** (18 mg), and **6** (10 mg). Fraction VI was chromatographed on silica gel column with $CHCl_3$–MeOH (8:1) to yield compounds **7** (16 mg) and **8** (13 mg).

Trewiasine was isolated from the stem bark of *T. nudiflora* for the first time. Compounds **2**–**8** were isolated from this plant for the first time. The structures of these compounds were confirmed using a combination of spectral analyses, including NMR and mass spectrometry, and by comparison with reported spectroscopic data in the literature.

Trewiasine (1). $C_{37}H_{52}ClN_3O_{11}$, colorless crystals, mp 180–182°C. ESI-MS *m/z*: 772 $[M+Na]^+$. ^1H NMR (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 2.19 (1H, dd, J = 14.5, 3.1, H-2a), 2.56 (1H, dd, J = 14.5, 12.0, H-2b), 4.77 (1H, dd, J = 12.0, 3.1, H-3), 0.78 (3H, s, 4-CH_3), 3.02 (1H, d, J = 9.7, H-5), 1.28 (3H, d, J = 6.3, 6-CH_3), 4.29 (1H, m, H-7), 3.53 (1H, d, J = 9.0, H-10), 5.74 (1H, dd, J = 15.1, 9.0, H-11), 6.46 (1H, dd, J = 15.1, 11.2, H-12), 6.99 (1H, d, J = 11.2, H-13), 1.54 (3H, s, 14-CH_3), 4.87 (1H, s, H-15), 6.55 (1H, d, J = 1.5, H-17), 7.24 (1H, d, J = 1.4, H-21), 3.35 (3H, s, 10-OCH_3), 3.37 (3H, s, 15-OCH_3), 4.01 (3H, s, 20-OCH_3), 3.18 (3H, s, 18-NCH_3), 5.39 (1H, m, H-2′), 1.29 (3H, d, J = 6.8, 2′-CH_3), 2.89 (3H, s, 2′-NCH_3), 2.79 (1H, m, H-4′), 1.13 (3H, d, J = 6.8, 4′-CH_3), 1.08 (3H, d, J = 6.5, 4′-CH_3), 6.28 (1H, s, 9-NH). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 32.3 (C-2), 78.1 (C-3), 59.9 (C-4), 67.4 (C-5), 38.8 (C-6), 74.1 (C-7), 36.0 (C-8), 80.7 (C-9), 85.3 (C-10), 129.6 (C-11), 132.5 (C-12), 127.8 (C-13), 142.0 (C-14), 86.6 (C-15), 141.3 (C-16), 120.2 (C-17), 139.2 (C-18), 119.2 (C-19), 156.2 (C-20), 108.7 (C-21), 176.7, 170.8, 168.7, 152.2 (4 × C=O), 56.3, 56.5, 56.7 (3 × OCH_3), 14.5, 13.0, 11.9, 9.9 (4 × CH_3), 35.2 (18-NCH_3), 30.6 (2′-NCH_3), 52.4 (C-2′), 30.4 (C-4′), 19.4, 18.8 (2 × 4′-CH_3) [1, 2].

Balanophonin (2). $C_{20}H_{20}O_6$, pale yellow oil. EI-MS (70 eV) *m/z* (%): 356 $[M]^+$ (82), 338 (100), 326 (55), 306 (18), 295 (7), 152 (24), 137 (22), 115 (12), 77 (14). ^1H NMR (500 MHz, CD_3COCD_3, δ, ppm, J/Hz): 7.04 (1H, d, J = 1.9, H-2), 6.81 (1H, d, J = 8.1, H-5), 6.88 (1H, dd, J = 8.1, 1.9, H-6), 5.65 (1H, d, J = 6.7, H-7), 3.64 (1H, m, H-8), 3.85 (2H, d, J = 4.9, H-9), 7.29 (1H, d, J = 1.7, H-2′), 7.31 (1H, d, J = 1.7, H-6′), 7.58 (1H, d, J = 15.8, H-7′), 6.66 (1H, dd, J = 15.8, 7.8, H-8′), 9.63 (1H, d, J = 7.8, H-9′), 3.82 (3H, s, 3-OMe), 3.89 (3H, s, 5′-OMe). ^{13}C NMR (125 MHz, CD_3COCD_3, δ, ppm): 133.7 (C-1), 110.5 (C-2), 148.4 (C-3), 147.5 (C-4), 115.7 (C-5), 119.7 (C-6), 89.4 (C-7), 54.2 (C-8), 64.1 (C-9), 128.9 (C-1′), 119.6 (C-2′), 131.2 (C-3′), 152.4 (C-4′), 145.6 (C-5′), 113.5 (C-6′), 154.1 (C-7′), 127.1 (C-8′), 193.8 (C-9′), 56.2 (3-OMe), 56.4 (5′-OMe) [5].

1) Yunnan Institute of Microbiology, Yunnan University, Kunming 650091, P. R. China, e-mail: shwu123@126.com; 2) State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650204, P. R. China. Published in Khimiya Prirodnykh Soedinenii, No. 4, pp. 456–457, July–August, 2009. Original article submitted November 26, 2007.

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Ficusal (3). $C_{18}H_{18}O_6$, pale yellow oil. EI-MS (70 eV) *m/z* (%): 330 $[M]^+$ (75), 312 (100), 300 (44), 297 (52), 267 (35). ^{1}H NMR (500 MHz, CD_3COCD_3, δ, ppm, J/Hz): 6.93 (1H, d, J = 1.7, H-2), 6.69 (1H, d, J = 8.1, H-5), 6.77 (1H, dd, J = 8.1, 1.7, H-6), 5.57 (1H, d, J = 6.8, H-7), 3.54 (1H, m, H-8), 3.73 (2H, d, J = 4.2, H-9), 7.40 (1H, s, H-2′), 7.29 (1H, s, H-6′), 9.70 (1H, s, H-7′), 3.69 (3H, s, 3-OMe), 3.79 (3H, s, 5′-OMe). ^{13}C NMR (125 MHz, CD_3COCD_3, δ, ppm): 133.4 (C-1), 110.6 (C-2), 147.6 (C-3), 148.4 (C-4), 115.8 (C-5), 119.8 (C-6), 89.8 (C-7), 53.8 (C-8), 64.2 (C-9), 132.3 (C-1′), 121.4 (C-2′), 131.1 (C-3′), 154.8 (C-4′), 145.8 (C-5′), 113.3 (C-6′), 190.9 (C-7′), 56.2 (3-OMe), 56.3 (5′-OMe) [6].

***erythro*-Guaiacylglycerol-β-coniferyl Aldehyde Ether (4)**. $C_{20}H_{22}O_7$, pale yellow oil. EI-MS (70 eV) *m/z* (%): 374 $[M]^+$ (4), 356 (10), 342 (3), 326 (58), 297 (10), 204 (100), 178 (85), 161 (28), 152 (9), 137 (68), 124 (25). ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 7.12 (1H, s, H-2), 6.74 (1H, d, J = 8.2, H-5), 6.87 (1H, dd, J = 8.2, 1.9, H-6), 5.66 (1H, d, J = 5.5, H-7), 4.95 (1H, m, H-8), 3.63 (1H, dd, J = 12.0, 3.8, H-9a), 3.34 (1H, dd, J = 12.0, 5.5, H-9b), 7.23 (1H, s, H-2′), 6.94 (1H, d, J = 8.1, H-5′), 7.09 (1H, dd, J = 8.1, 1.7, H-6′), 7.39 (1H, d, J = 15.9, H-7′), 6.62 (1H, dd, J = 15.9, 7.8, H-8′), 9.65 (1H, d, J = 7.8, H-9′), 3.85 (3H, s, 3-OMe), 3.93 (3H, s, 3′-OMe). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 131.3 (C-1), 108.8 (C-2), 146.7 (C-3), 145.7 (C-4), 114.4 (C-5), 119.0 (C-6), 73.3 (C-7), 88.5 (C-8), 61.2 (C-9), 129.6 (C-1′), 111.1 (C-2′), 151.2 (C-3′), 150.7 (C-4′), 123.2 (C-5′), 120.1 (C-6′), 152.1 (C-7′), 127.7 (C-8′), 193.4 (C-9′), 55.9 (3-OMe), 56.0 (3′-OMe) [7, 8].

***threo*-Guaiacylglycerol-β-coniferyl Aldehyde Ether (5)**. $C_{20}H_{22}O_7$, pale yellow oil. EI-MS (70 eV) *m/z* (%): 374 $[M]^+$ (3), 356 (12), 326 (45), 297 (6), 204 (100), 178 (55), 161 (24), 153 (34), 137 (89), 124 (18). ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 7.12 (1H, s, H-2), 6.72 (1H, d, J = 7.9, H-5), 6.84 (1H, dd, J = 7.9, 1.7, H-6), 5.63 (1H, d, J = 5.8, H-7), 4.92 (1H, m, H-8), 3.60 (1H, dd, J = 12.0, 3.9, H-9a), 3.29 (1H, dd, J = 12.0, 5.2, H-9b), 7.23 (1H, s, H-2′), 6.92 (1H, d, J = 8.0, H-5′), 7.06 (1H, dd, J = 8.0, 1.8, H-6′), 7.36 (1H, d, J = 15.9, H-7′), 6.60 (1H, dd, J = 15.9, 7.6, H-8′), 9.63 (1H, d, J = 7.6, H-9′), 3.82 (3H, s, 3-OMe), 3.87 (3H, s, 3′-OMe). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 131.8 (C-1), 109.3 (C-2), 146.6 (C-3), 145.3 (C-4), 114.3 (C-5), 119.2 (C-6), 74.0 (C-7), 86.2 (C-8), 61.4 (C-9), 129.4 (C-1′), 111.0 (C-2′), 151.4 (C-3′), 150.0 (C-4′), 123.1 (C-5′), 119.6 (C-6′), 152.1 (C-7′), 127.6 (C-8′), 193.4 (C-9′), 55.9 (3-OMe), 56.0 (3′-OMe) [7–8].

3,3′-Di-*O*-methylellagic Acid (6). $C_{16}H_{10}O_8$, yellow powder, mp >300°C. EI-MS (70 eV) *m/z* (%): 330 $[M]^+$ (100), 315 (50), 300 (8), 287 (14), 231 (35), 203 (10), 160 (17). ^{1}H NMR (500 MHz, DMSO-d_6, δ, ppm, J/Hz): 7.50 (2H, s, H-5 and 5′), 4.03 (6H, s, 2 × OMe), 10.75 (2H, br.s, 4- and 4′-OH). ^{13}C NMR (125 MHz, DMSO-d_6, δ, ppm): 111.6 (C-1 and 1′), 141.1 (C-2 and 2′), 140.3 (C-3 and 3′), 152.1 (C-4 and 4′), 111.6 (C-5 and 5′), 112.1 (C-6 and 6′), 158.3 (C-7 and 7′), 60.8 (2 × OMe) [9].

3-*O*-Methylellagic Acid-4′-*O*-α-L-rhamnopyranoside (7). $C_{21}H_{18}O_{12}$, yellow powder, mp >300°C. FAB-MS (negative) *m/z*: 461 $[M–H]^–$. ^{1}H NMR (500 MHz, DMSO-d_6, δ, ppm, J/Hz): 7.50 (1H, s, H-5), 7.72 (1H, s, H-5′), 4.02 (3H, s, 3-OMe), 5.46 (1H, br.s, H-1″), 4.92 (1H, m, H-2″), 4.70 (1H, m, H-3″), 3.52 (1H, dd, J = 6.2, 9.2, H-4″), 3.84 (1H, m, H-5″), 1.12 (3H, d, J = 6.1, H-6″), 10.78 (1H, s, OH). ^{13}C NMR (125 MHz, DMSO-d_6, δ, ppm): 111.4 (C-1), 136.1 (C-2), 140.1 (C-3), 152.6 (C-4), 111.3 (C-5), 107.1 (C-6), 158.6 (C-7), 114.3 (C-1′), 141.3 (C-2′), 141.8 (C-3′), 146.4 (C-4′), 111.6 (C-5′), 113.0 (C-6′), 158.7 (C-7′), 60.9 (3-OMe), 100.1 (C-1″), 69.8 (C-2″), 69.9 (C-3″), 71.7 (C-4″), 70.1 (C-5″), 17.8 (C-6″) [10].

3,3′-Di-*O*-methylellagic Acid-4′-*O*-α-L-rhamnopyranoside (8). $C_{22}H_{20}O_{12}$, yellow powder, mp 185–187°C. FAB-MS (negative) *m/z*: 475 $[M–H]^–$. ^{1}H NMR (500 MHz, DMSO-d_6, δ, ppm, J/Hz): 7.49 (1H, s, H-5), 7.77 (1H, s, H-5′), 4.05 (3H, s, 3-OMe), 4.06 (3H, s, 3′-OMe), 5.54 (1H, br.s, H-1″), 4.89 (1H, m, H-2″), 4.67 (1H, m, H-3″), 3.48 (1H, dd, J = 8.9, J = 6.1, H-4″), 3.84 (1H, m, H-5″), 1.12 (3H, d, J = 6.1, H-6″). ^{13}C NMR (125 MHz, DMSO-d_6, δ, ppm): 111.1 (C-1), 140.7 (C-2), 140.1 (C-3), 149.9 (C-4), 111.5 (C-5), 111.7 (C-6), 158.1 (C-7), 113.8 (C-1′), 141.4 (C-2′), 141.7 (C-3′), 152.6 (C-4′), 111.5 (C-5′), 112.3 (C-6′), 158.1 (C-7′), 60.8 (3-OMe), 61.3 (3′-OMe), 100.1 (C-1″), 70.2 (C-2″), 70.0 (C-3″), 71.4 (C-4″), 69.8 (C-5″), 17.7 (C-6″) [11].

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