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CHEMICAL CONSTITUENTS OF THE FLOWER BUDS OF *Tussilago farfara*. II

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Tussilago farfara L. is a perennial herb blooming in winter, which grows widely in China and is also widely cultivated in Gansu, Henan, Shanxi, Sichuan Qinghai, and Inner Mongolia Autonomous Provinces of China [1]. The flower buds of *T. farfara* are used as an important traditional Chinese medicine (Kuandong flower) for the treatment of cough, bronchitis, and asthmatic disorders [2]. As part of the continuous phytochemical research on Chinese and Tibetan traditional herbal medicine [3–7], seven compounds were isolated from the ethanol extract of the flower buds of *T. farfara*, and purified by repeated chromatography on silica and Sephadex LH-20 gel columns. Compounds **1–3**, **5**, and **6** were isolated from this plant for the first time.

The fresh air-dried plants of *T. farfara* were collected from Dingxi City, Gansu Province of China on October, 2014, and identified by Asst. Prof. Lin Yang of Lanzhou University of Technology. A voucher specimen (No. 20141022) has been deposited at the Laboratory of Natural Drugs of the School of Life Science and Engineering, Lanzhou University of Technology, Lanzhou, China.

The air-dried, powdered flower buds of *T. farfara* (4.8 kg) were extracted by ethanol in a 80°C water bath, kept for 6 h each time [6], and repeated 3 times. The ethanol extract was filtered and concentrated to dryness under reduced pressure. The crude extract (1007.33 g) was successively extracted with petroleum ether (90–100°), EtOAc, and *n*-BuOH, to yield the PE fraction (115.4 g), EtOAc fraction (126.4 g), and *n*-BuOH fraction (98.75 g) after concentrating and drying.

The EtOAc fraction (60 g) was chromatographed on a silica gel column (4.0 × 120 cm), eluted with $CHCl_3$–MeOH (100:1–0:1) gradually to yield 21 fractions (Frs.1–21) according to TLC analysis. Fraction 4 (0.46 g) was re-treated on a silica gel (300–400 mesh, 15 g) column eluted with $CHCl_3$–acetone (4:1) to obtain **1** (10 mg), and further eluted with $CHCl_3$–acetone (2:1) to obtain **2** (12 mg).

Fractions 8, 12, 13, 16, and 19 were re-treated on polyamide and silica gel (300–400 mesh) columns repeatedly and eluted with MeOH–H_2O or $CHCl_3$–MeOH at different ratios to obtain compounds **3** (5.7 mg), **4** (3.8 mg), **5** (4.6 mg), **6** (3.5 mg), and **7** (13.5 mg).

Ixocarpalactone B (1). White powder, mp 145–148°C, $C_{28}H_{38}O_8$. HR-FAB-MS *m/z* 525.2456 $[M + Na]^+$. ^1H NMR (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.08 (3H, s, H-18), 1.17 (3H, d, J = 7.2, H-27), 1.20 (3H, d, J = 7.2, H-28), 1.46 (3H, s, H-19), 1.51 (3H, s, H-21), 3.20 (1H, br.s, H-6), 3.76 (1H, d, J = 6.0, H-4), 4.20 (1H, s, H-22), 4.50 (1H, m, H-16), 6.30 (1H, d, J = 9.8, H-2), 6.98 (1H, dd, J = 9.8, 6.0, H-3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 12.2 (C-28), 14.4 (C-27), 15.0 (C-18), 17.0 (C-19), 21.0 (C-11), 27.6 (C-21), 29.6 (C-8), 31.3 (C-7), 34.1 (C-15), 40.1 (C-12), 42.5 (C-13), 43.2 (C-25), 45.5 (C-9), 48.1 (C-10), 50.1 (C-24), 55.0 (C-14), 59.6 (C-6), 64.0 (C-17), 64.1 (C-5), 70.6 (C-4), 72.3 (C-22), 74.2 (C-20), 75.1 (C-16), 108.9 (C-23), 133.0 (C-2), 145.2 (C-3), 177.6 (C-26), 202.7 (C-1) [8].

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3,4-Di-*O*-caffeoylquinic Acid Methyl Ester (2). White powder, mp 112–115°C, $C_{26}H_{25}O_{12}$. ESI-MS *m/z* 553 $[M + Na]^+$. ^1H NMR (400 MHz, CD_3OD, δ, ppm, J/Hz): 1.91, 1.98 (each 1H, m, H-6), 2.0, 2.24 (each 1H, m, H-2), 3.71 (3H, s, OCH_3), 4.33(1H, m, H-5), 5.09 (1H, dd, J = 2.8, 8.0, H-4), 5.74 (1H, m, H-3), 6.19, 6.10 (each 1H, d, J = 16.8, H-8′, 8″), 6.74 (2H, d, J = 8.0, H-5′, 5″), 6.97 (2H, dd, J = 8.0, 2.0, H-6′, 6″), 7.06, 7.05 (each 1H, d, J = 2.0, H-2′, 2″), 7.59, 7.48 (each 1H, d, J = 16.8, H-7′, 7″). ^{13}C NMR (100 MHz, CD_3OD, δ, ppm): 39.5 (C-6), 46.0 (C-2), 51.6 (7-OCH_3), 64.0 (C-5), 70.6 (C-3), 72.8 (C-4), 74.2 (C-1), 113.5 (C-8″), 113.8 (C-8′), 114.1 (C-2′, 2″), 115.1 (C-5″), 115.2 (C-5′), 126.2 (C-1′, 1″), 121.6 (C-6′, 6″), 145.4 (C-3″), 145.7 (C-3′), 146.0 (C-7″), 146.3 (C-7′), 148.0 (C-4″), 148.3 (C-4′), 166.5 (C-9″), 167.5 (C-9′), 174.2 (C-7) [9].

4,5-Di-*O*-caffeoylquinic Acid Butyl Ester (3). Pale yellow gum, $C_{29}H_{32}O_{12}$. ESI-MS *m/z* 595 $[M + Na]^+$. ^1H NMR (400 MHz, CD_3OD, δ, ppm, J/Hz): 0.90 (3H, t, J = 7.2, H-11), 1.25 (2H, q, J = 7.2, H-10), 1.63 (2H, m, H-9), 2.09 (1H, m, H-6*β*), 2.20 (1H, m, H-2*β*), 2.26 (1H, br.d, J = 11.2, H-2*α*), 2.33 (1H, dd, J = 13.6, 2.8, H-6*α*), 4.09 (2H, m, H-8), 4.35 (1H, m, H-5), 5.08 (1H, dd, J = 8.8, 2.8, H-4), 5.54 (1H, m, H-3), 6.11 (1H, d, J = 1.8, H-8″), 6.27 (1H, d, J = 15.6, H-8′), 6.73 (2H, d, J = 8.4, H-6′, 6″), 6.98 (2H, dd, J = 8.4, 1.6, H-5′, 5″), 7.00 (1H, d, J = 1.6, H-2″), 7.02 (1H, d, J = 1.6, H-2′), 7.52 (1H, d, J = 15.6, H-7″), 7.59 (1H, d, J = 15.6, H-7′). ^{13}C NMR (100 MHz, CD_3OD, δ, ppm): 12.7 (C-11), 19.4 (C-10), 29.3 (C-9), 37.0 (C-2), 37.3 (C-6), 65.0 (C-8), 67.3(C-3), 67.7 (C-5), 73.3 (C-4), 74.5 (C-1), 113.2 (C-8″), 113.4 (C-8′), 113.8 (C-2′, 2″), 115.1 (C-5′, 5″), 121.8 (C-6′, 6″), 126.3 (C-1″), 126.5 (C-1′), 145.4 (C-3″), 146.0 (C-7″), 146.2 (C-3′), 146.3 (C-7′), 148.1 (C-4″), 148.3 (C-4′), 167.4 (C-9′), 166.7 (C-9″), 173.8 (C-7) [10].

Chlorogenic Acid (4). White needles, mp 244–246°C, $C_{16}H_{18}O_9$. IR (KBr, ν_{max}, cm^{-1}): 3400, 1697, 1600, 1591, 1520. FAB-MS *m/z* 355 $[M + H]^+$. ^1H NMR (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.74 (1H, br.d, J = 15.2, H-2*β*), 1.78 (1H, t, J = 9.6, H-6*β*), 1.91 (1H, t, J = 9.6, H-6*α*), 1.96 (1H, br.d, J = 15.2, H-2*α*), 3.53 (1H, d, J = 9.6, H-5), 4.15 (1H, m, H-4), 5.2 (1H, dt, J = 9.6, 7.2, H-3), 6.20 (1H, d, J = 16.0, H-8′), 6.72 (1H, d, J = 8.0, H-5′), 7.0 (1H, br.d, J = 8.0, H-6′), 7.02 (1H, br.s, H-2′), 7.40 (1H, d, J = 16.0, H-7′). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 38.5 (C-2), 38.8 (C-6), 70.3 (C-3), 71.0 (C-5), 72.8 (C-4), 76.0 (C-1), 115.1 (C-8′), 115.8 (C-2′), 117.1 (C-6′), 122.6 (C-5′), 126.6 (C-1′), 146.4 (C-3′), 146.6 (C-7′), 146.9 (C-4′), 167.6 (C-9′), 180.0 (C-7) [11].

Moluccanic Acid Methyl Ester (5). Colorless gum, $C_{18}H_{24}O_3$. IR (KBr, ν_{max}, cm^{-1}): 3412, 3020, 2931, 1738, 1713, 1612, 1583, 1498, 1294, 1203, 1019, 895, 870. EI-MS *m/z* 288 $[M]^+$; positive HR-ESI-MS *m/z* 311.1626 $[M + Na]^+$ (calcd for $C_{18}H_{24}O_3Na$, 311.1623). ^1H NMR (400 MHz, CD_3OD, δ, ppm, J/Hz): 1.21 (3H, s, H-20), 1.79 (3H, s, H-19), 1.90, 1.81 (each 1H, s, H-6), 2.13, 1.99 (each 1H, m, H-1), 2.26, 1.96 (each 1H, m, H-2), 2.40 (1H, dd, J = 2.8, 11.8), 2.40 6.76 (1H, d, J = 2.4, H-11), 2.73, 2.71 (each 1H, s, H-7), 3.59 (3H, s, OCH_3), 4.70, 4.96 (each 1H, br.s, H-18), 6.72 (1H, dd, J = 2.4, 8.0, H-13), 6.95 (1H, d, J = 8.0, H-14). ^{13}C NMR (100 MHz, CD_3OD, δ, ppm): 22.5 (C-19), 25.3 (C-6), 27.7 (C-20), 29.3 (C-7), 29.7 (C-2), 35.6 (C-1), 41.0 (C-10), 47.0 (C-5), 51.6 (C-OCH_3), 112.7 (C-11), 113.3 (C-13), 114.3 (C-18), 128.8 (C-8), 129.9 (C-14), 145.5 (C-9), 146.3 (C-4), 153.7 (C-12), 174.6(C-3) [12].

2-(3′-*O*-*β*-D-Glucopyranosyl-4′-hydroxyphenyl)-ethanol (6). Colorless gum, $C_{14}H_{20}O_9$. FAB-MS *m/z* 339 $[M + Na]^+$. ^1H NMR (400 MHz, CD_3OD, δ, ppm, J/Hz): 2.73 (2H, t, J = 7.2, H-2), 3.40 (1H, m, H-4″), 3.41 (1H, m, H-2″), 3.49 (1H, td, J = 10.4, 7.2, H-5″), 3.71 (2H, t, J = 7.2, H-1), 3.73 (1H, dd, J = 11.8, 5.6, H-3″), 3.90 (2H, dd, J = 14.0, 1.2, H-6″), 4.80 (1H, d, J = 7.6, H-1″), 6.77 (1H, d, J = 8.4, 2.0, H-6′), 6.79 (1H, dd, J = 8.4, 2.0, H-5′), 7.09 (1H, d, J = 2.0, H-2′). ^{13}C NMR (100 MHz, CD_3OD, δ, ppm): 39.0 (C-2), 61.2 (C-6″), 63.0 (C-2), 70.0 (C-4″), 74.0 (C-2″), 76.6 (C-5″), 77.0 (C-3″), 102.7 (C-1″), 114.7 (C-6′), 117.6 (C-5′), 124.0 (C-2′), 130.9 (C-1′), 145.0 (C-3′), 145.2 (C-4′) [13].

2-{[(2*S*)-2-Hydroxypropanoyl]amino}benzamide (7). Pale yellow powder, $C_{10}H_{12}N_2O_3$. IR (KBr, ν_{max}, cm^{-1}): 3355, 1664, 1590, 1524, 1450, 1393, 1304, 1122, 758, 630. ESI-MS *m/z* 231 $[M + Na]^+$. ^1H NMR (400 MHz, CD_3OD, δ, ppm, J/Hz): 1.33 (3H, d, J = 6.8, H-3′), 4.12 (1H, q, J = 6.8, H-2′), 7.13 (1H, d, J = 8.4, H-5), 7.46 (1H, t, J = 8.4, H-4), 7.71 (1H, t, J = 8.4, H-3), 8.19, 7.62 (each 1H, s, $CONH_2$), 8.50 (1H, d, J = 8.4, H-6). ^{13}C NMR (100 MHz, CD_3OD, δ, ppm): 21.0 (C-3′), 68.4 (C-2′), 120.4 (C-5), 121.4 (C-1), 123.1 (C-3), 128.0 (C-6), 132.0 (C-4), 139.2 (C-2), 171.8 ($CONH_2$), 175.2 (C-1′) [14].

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