

## CHEMICAL CONSTITUENTS OF THE FLOWERBUDS OF *Tussilago farfara*

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*Tussilago farfara* L. is a perennial herb blooming in winter, which grows widely in China and is widely cultivated in Gansu, Henan, Shanxi, Sichuan Qinghai, and Inner Mongolia Autonomous Provinces of China [1]. The flowerbuds 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], ten compounds were isolated from the ethanol extract of the flowerbuds of *T. farfara*, and purified by repeated chromatography on silica and Sephadex LH-20 gel columns. Compounds **1–3** and **6–8** 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 Assoc. 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 flowerbuds of *T. farfara* (4.8 kg) were repeatedly extracted by ethanol three times in an 80% water bath and kept for 6 h each time [6]. 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°C), EtOAc, and *n*-BuOH to yield the PE fraction (115.4 g), the EtOAc fraction (126.4 g), and the *n*-BuOH fraction (98.75 g) after concentrating and drying, respectively.

The PE fraction was chromatographed on a silica gel column (6.0 × 180 cm) and eluted with PE–acetone gradually (100:1, 80:1, 60:1, 40:1, 20:1, 10:1, 8:1, 6:1, 4:1, 2:1, 1:1, 0:1) to yield 18 fractions (Frs. 1–18) according to TLC analysis. Fraction Fr. 3 (60:1), Fr. 5 (40:1), Fr. 7 (20:1), Fr. 8 (10:1), and Fr. 11 (8:1) were chromatographed on a silica gel column repeatedly and eluted with PE–EtOAc, PE–acetone, and CHCl<sub>3</sub>–acetone gradually to yield compounds **1–10**.

**2-Aminoethyl Tetradecanoate (1).** Colorless powder, C<sub>16</sub>H<sub>33</sub>O<sub>2</sub>N. IR (KBr,  $\nu_{\max}$ , cm<sup>-1</sup>): 3465, 1741. HR-ESI-MS,  $m/z$  272.2582 [M + H]<sup>+</sup>, calcd 272.2584. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>,  $\delta$ , ppm, J/Hz): 0.87 (3H, t, J = 7.2), 1.25 (about 20H, br.s), 1.55 (2H, q, J = 7.6), 2.46 (2H, t, J = 7.6), 3.25 (2H, t, J = 5.6), 4.29 (2H, t, J = 5.6). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>,  $\delta$ , ppm): 13.8, 22.1, 24.5, 28.7, 29.0, 29.1, 29.5, 29.7, 29.9, 31.1, 31.5, 33.5, 39.2, 60.1, 174.4 [8].

**24-Methylenecycloartane-3 $\beta$ ,22-diol (2).** White amorphous powder, C<sub>31</sub>H<sub>52</sub>O<sub>2</sub>. IR (KBr,  $\nu_{\max}$ , cm<sup>-1</sup>): 3524, 2943, 2867, 1703, 1632, 1457, 1377, 1101, 1041, 895, 755, 554. EI-MS,  $m/z$ : 456 [M]<sup>+</sup>, 438 [M – H<sub>2</sub>O]<sup>+</sup>, 395, 339, 271, 232, 215, 203, 189, 175, 161, 43. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>,  $\delta$ , ppm): 31.51 (C-1), 30.56 (C-2), 78.2 (C-3), 40.5 (C-4), 48.2 (C-5), 21.8 (C-6), 27.6 (C-7), 48.0 (C-8), 20.2 (C-9), 26.0 (C-10), 26.0 (C-11), 36.5 (C-12), 45.4 (C-13), 47.9 (C-14), 33.0 (C-15), 26.1 (C-16), 50.1 (C-17), 17.8 (C-18), 29.8 (C-19), 41.0 (C-20), 12.4 (C-21), 69.2 (C-22), 36.6 (C-23), 154.6 (C-24), 33.4 (C-25), 23.0 (C-26), 21.7 (C-27), 19.0 (C-28), 14.5 (C-29), 25.4 (C-30), 108.9 (C-31) [9].

**$\beta$ -Amyrin-*n*-nonyl Ether (3).** White powder, C<sub>39</sub>H<sub>68</sub>O. HR-EI-MS,  $m/z$  552.5271 [M]<sup>+</sup>. IR (KBr,  $\nu_{\max}$ , cm<sup>-1</sup>): 1650, 1380, 1357, 1034. <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>,  $\delta$ , ppm): 37.8 (C-1), 27.4 (C-2), 79.0 (C-3), 39.0 (C-4), 54.4 (C-5), 19.0 (C-6), 32.8 (C-7), 37.5 (C-8), 47.0 (C-9), 36.0 (C-10), 23.1 (C-11), 121.8 (C-12), 145.3 (C-13), 41.2 (C-14), 26.0 (C-15), 27.3 (C-16), 32.8 (C-17), 47.0 (C-18), 46.8 (C-19), 31.7 (C-20), 35.0 (C-21), 37.2 (C-22), 28.3 (C-23), 15.8 (C-24), 16.1 (C-25), 16.1 (C-26), 26.0 (C-27), 28.4 (C-28), 33.1 (C-29), 23.6 (C-30), 62.6 (C-1'), 26.5 (C-2'), 25.2 (C-3'), 29.6 (C-4'), 29.5 (C-5'), 29.4 (C-6'), 31.8 (C-7'), 22.8 (C-8'), 14.3 (C-9') [10].

**Tussifarfin B (4).** Yellow oil, C<sub>28</sub>H<sub>44</sub>O<sub>6</sub>. HR-EI-MS,  $m/z$  499.3038 [M + Na]<sup>+</sup>. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>,  $\delta$ , ppm): 72.91 (C-1), 208.6 (C-2), 58.4 (C-3), 42.8 (C-4), 44.1 (C-5), 29.7 (C-6), 73.7 (C-7), 141.1 (C-8), 46.4 (C-9), 113.0

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(C-10), 27.8 (C-11), 21.5 (C-12), 15.4 (C-13), 74.9 (C-14), 16.9 (C-15), 165.8 (C-1'), 114.6 (C-2'), 161.6 (C-3'), 33.7 (C-4'), 11.8 (C-5'), 18.8 (C-6'), 175.2 (C-1''), 41.02 (C-2''), 26.4 (C-3''), 11.3 (C-4''), 16.21 (C-5''), 63.9 (C-1'''), 15.4 (C-2''') [2].

**Isobauerenol (5).** Colorless needles, C<sub>30</sub>H<sub>50</sub>O. EI-MS, *m/z*: 426 [M]<sup>+</sup>, 411, 408, 393, 273, 259, 247, 229, 205. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, δ, ppm): 35.0 (C-1), 24.1 (C-2), 79.0 (C-3), 37.8 (C-4), 50.5 (C-5), 19.2 (C-6), 27.4 (C-7), 134.4 (C-8), 134.2 (C-9), 37.5 (C-10), 20.6 (C-11), 29.1 (C-12), 38.2 (C-13), 41.1 (C-14), 25.2 (C-15), 38.0 (C-16), 31.9 (C-17), 52.4 (C-18), 32.0 (C-19), 36.0 (C-20), 29.6 (C-21), 33.1 (C-22), 28.0 (C-23), 15.7 (C-24), 20.0 (C-25), 22.2 (C-26), 15.5 (C-27), 38.2 (C-28), 25.2 (C-29), 22.4 (C-30) [11].

**2α,3β-Dihydroxylurs-12-en-28-oic Acid (6).** White powder, C<sub>30</sub>H<sub>48</sub>O<sub>4</sub>. EI-MS, *m/z*: 472 [M]<sup>+</sup>, 248, 233, 219, 203, 189, 133. <sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>, δ, ppm): 47.3 (C-1), 67.6 (C-2), 82.7 (C-3), 38.9 (C-4), 55.2 (C-5), 18.5 (C-6), 36.1 (C-7), 40.6 (C-8), 47.3 (C-9), 38.9 (C-10), 23.5 (C-11), 124.9 (C-12), 138.7 (C-13), 42.2 (C-14), 29.3 (C-15), 26.3 (C-16), 48.5 (C-17), 52.9 (C-18), 39.6 (C-19), 39.3 (C-20), 30.7 (C-21), 36.8 (C-22), 28.0 (C-23), 17.0 (C-24), 16.4 (C-25), 16.5 (C-26), 23.4 (C-27), 178.8 (C-28), 17.6 (C-29), 21.5 (C-30) [12].

**(4S)-Isosclerone (7).** Colorless oil, C<sub>10</sub>H<sub>10</sub>O<sub>3</sub>. HR-MS, *m/z* 178.0631, calcd 178.0630. IR (KBr, ν<sub>max</sub>, cm<sup>-1</sup>): 3386 br., 2957, 2933, 1735, 1636, 1455, 1243, 1219, 1199. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, δ, ppm): 204.3 (C-1), 34.6 (C-2), 31.2 (C-3), 67.7 (C-4), 117.8 (C-5, 7), 137.0 (C-6), 162.8 (C-8), 145.9 (C-4α), 122.8 (C-8α) [13].

**Methyl-2α-hydroxyursolate (8),** yellow powder, C<sub>31</sub>H<sub>50</sub>O<sub>4</sub>. EI-MS, *m/z* 486 [M]<sup>+</sup>. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, δ, ppm): 46.5 (C-1), 68.9 (C-2), 83.9 (C-3), 39.2 (C-4), 55.3 (C-5), 18.4 (C-6), 32.9 (C-7), 39.4 (C-8), 47.5 (C-9), 38.2 (C-10), 16.9 (C-11), 125.3 (C-12), 138.3 (C-13), 42.1 (C-14), 28.0 (C-15), 24.2 (C-16), 48.0 (C-17), 52.9 (C-18), 39.0 (C-19), 38.9 (C-20), 30.6 (C-21), 36.7 (C-22), 28.4 (C-23), 16.7 (C-24), 16.7 (C-25), 17.0 (C-26), 23.4 (C-27), 178.6 (C-28), 23.7 (C-29), 21.5 (C-30), 51.4 (28-CO<sub>2</sub>Me) [14].

**7β-[3'-Ethylcrotonyloxy]-1α-[2'-methylbutyryloxy]-3,14-dehydro-Z-notonipetranone (9).** Colorless gum, C<sub>26</sub>H<sub>38</sub>O<sub>5</sub>. EI-MS, *m/z*: 430 [M]<sup>+</sup>, 328, 316, 231, 214, 97. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, δ, ppm): 71.3 (C-1), 199.1 (C-2), 138.2 (C-3), 43.7 (C-4), 40.0 (C-5), 29.0 (C-6), 72.3 (C-7), 140.8 (C-8), 45.1 (C-9), 111.5 (C-10), 27.0 (C-11), 25.8 (C-12), 14.6 (C-13), 135.7 (C-14), 14.2 (C-15), 164.8 (C-1'), 113.6 (C-2'), 161.0 (C-3'), 32.8 (C-4'), 11.1 (C-5'), 17.9 (C-6'), 174.4 (C-1''), 39.5 (C-2''), 10.4 (C-3''), 15.5 (C-4''), 20.3 (C-5'') [11].

**Ursolic Acid (10).** Amorphous white powder, C<sub>30</sub>H<sub>48</sub>O<sub>3</sub>. ESI-MS, *m/z* 457 [M + H]<sup>+</sup>. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, δ, ppm): 38.3 (C-1), 27.0 (C-2), 76.8 (C-3), 38.1 (C-4), 54.6 (C-5), 18.0 (C-6), 32.6 (C-7), 38.2 (C-8), 46.9 (C-9), 36.6 (C-10), 22.7 (C-11), 124.5 (C-12), 138.1 (C-13), 41.6 (C-14), 27.4 (C-15), 23.8 (C-16), 46.7 (C-17), 52.3 (C-18), 38.4 (C-19), 38.3 (C-20), 30.1 (C-21), 36.2 (C-22), 28.1 (C-23), 15.2 (C-24), 15.9 (C-25), 16.8 (C-26), 23.1 (C-27), 178.1 (C-28), 16.7 (C-29), 21.4 (C-30) [15].

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