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Nine lignans from *Artemisia absinthium* L.

Abulajiang·Tulake, Yong Jiang, Peng-Fei Tu*

State Key Laboratory of Natural and Biomimetic Drugs, Peking University Health Science Center, Beijing 100191, China

Abstract: Nine lignans were isolated and purified by silica gel, ODS, Sephadex LH-20 column chromatographies, preparative HPLC and recrystallization from the aerial parts of *Artemisia absinthium* L., and identified as follows: diayangambin (**1**), sesartemin (**2**), epiyangambin (**3**), (+)arborone (**4**), (–)syringaresinol (**5**), epiashchantin (**6**), caruilignan C (**7**), 7β-caruilignan C (**8**), yangambin (**9**). Compounds **4**, **5**, **7**, **8** were isolated from this plant for the first time.

Keywords: *Artemisia absinthium* L.; *Compositae*; *Artemisia*; Lignan

CLC number: R284.2 **Document code:** A **Article ID:** 1003–1057(2012)4–360–05

1. Introduction

Artemisia absinthium L., commonly known as wormwood, is a yellow-flowering, perennial herbaceous plant belonging to *Compositae* family, has been commonly used in traditional Chinese medicines and Uighur Medicine named “Ku Ai”, for antiparasitic and to treat anorexia and indigestion, dizziness, headache, twinge of articular, general edema, irregular menses, skin itch and common cold[1,2]. According to previous studies, chemical constituents such as sesquiterpenes, dimeric guaianolides, flavones, lignans, volatile oil and tannins were isolated from this plant[2–8]. These constituents exhibited anti-inflammatory[9,10], antibiosis[11], anticancer[12] and anti-HIV activities[13]. And the plant materials of previous studies were from European countries, central Asian region. To study chemical constituents of *A. absinthium* grows in Xinjiang, we carry out a continuation study. In this paper, we report the isolation and structural elucidation of nine lignans from the aerial parts of *A. absinthium* L. and compounds **4**, **5**, **7**, **8** were isolated from this plant for the first time. Their structures were shown in Figure 1.

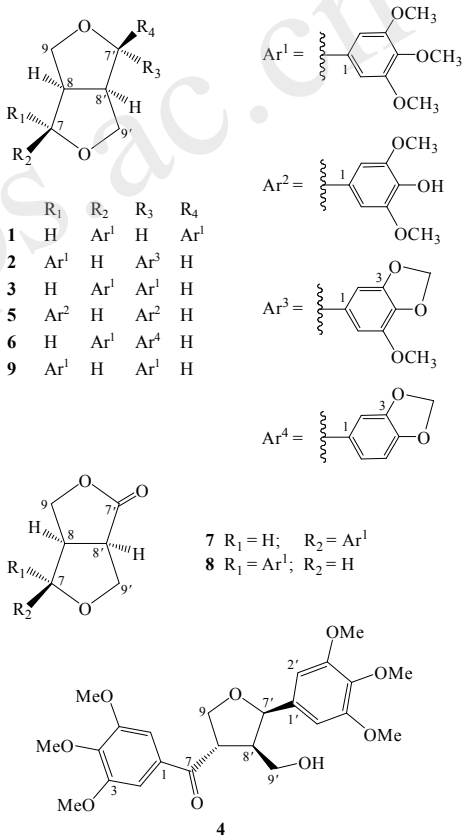

Figure 1. Chemical structures of compounds **1**–**9**.

2. Experimental

2.1. General procedures

NMR spectra were recorded on a Varian 500 spectrometer, operating at 500 MHz for ^{1}H NMR and 125 MHz for ^{13}C NMR. The chemical shifts

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*Corresponding author. Tel.: 86-10-82802750;
E-mail: pengfeitu@bjmu.edu.cn
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were given in δ (ppm) with deuterated solvents as standard. ESI-MS was measured on an Agilent 6320 ion trap MS spectrometer. Semi-preparative HPLC was carried on a Waters 600 instrument with ODS column (Grace Prevail C_{18} Column, 250 mm×10 mm, 5 μm and Beijing Chuangxin Tongheng Science and Technology Co., Ltd SP-120-10-C_{18}-AP, 250 mm× 10 mm, 10 μm) and C_{18} guard column with a 2996 photodiode array detector. Column chromatography was performed with silica gel (100–200 mesh, 200–300 mesh, Qingdao Haiyang Chemical Works), ODS (Merck) and Sephadex LH-20 (Pharmacia Co.). Analytical grade solvents were purchased from Beijing Chemical Factory.

2.2. Plant material

The aerial parts of *Artemisia absinthium* L. were collected in Urumqi Xinjiang, China in July, 2009. The plant material was authenticated by Prof. Peng-Fei Tu in School of Pharmaceutical Sciences, Peking University and Sulaiman·Halik in Xinjiang Institute for Drug Control. A voucher specimen was deposited at the Herbarium of the Peking University Modern Research Center for Traditional Chinese Medicine.

2.3. Extraction and isolation

Dried aerial parts (19 kg) of *A. absinthium* L. were cut and extracted three times with 95% EtOH. After evaporation of the solvent under reduced pressure, the residue was suspended in water and extracted with petroleum ether, chloroform, ethyl acetate, successively. The residue of the $CHCl_3$ layer (364 g) was fractionated by silica gel column chromatography using a step-wise gradient of petroleum ether and EtOAc to give six fractions. Fraction 4 was subjected to silica gel column chromatography (petroleum ether–EtOAc, 10:1–1:2, v/v) to afford sub-fractions 1–14. Sub-fraction 11 was recrystallized to obtain **1** (360 mg). Sub-fraction 8 was subjected to ODS open column chromatography (MeOH–H_2O, 40:60–90:10, v/v) and then was separated by semi-preparative HPLC (MeCN–H_2O, 50:50, v/v) to give **2** (86 mg). Sub-fraction 10 was subjected to ODS open column chromatography (MeOH–H_2O, 40:60–90:10, v/v) and Sephadex LH-20 column chromatography (MeOH) to give **3** (56 mg). Sub-fraction 13 was subjected to ODS open column chromatography (MeOH–H_2O, 40:60–90:10, v/v) and Sephadex LH-20 column chromatography (MeOH) to give **4** (133 mg). Fraction 6 was subjected to ODS open column chromatography (MeOH–H_2O, 40:60–80:10, v/v), Sephadex LH-20 column chromatography (MeOH) and then was separated by semi-preparative HPLC (MeCN–H_2O, 49:51, v/v) to give **5** (34 mg) and **6** (233 mg). The rest of fraction 4 and fraction 5 were combined together and subjected to ODS open column chromatography (MeOH–H_2O, 40:60–80:10, v/v), Sephadex LH-20 column chromatography (MeOH) and then were separated by semi-preparative HPLC (CH_3CN–H_2O, 43:57, v/v) to give **7** (10 mg), **8** (25 mg) and **9** (11 mg).

3. Identification

3.1. Diayangambin (1)

White needle (EtOAc); positive ESI-MS: *m/z* 469 $[M+Na]^+$; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.61 (s, 4H, H-2,6,2′,6′), 4.92 (d, 2H, *J* 4.5 Hz, H-7,7′), 3.89 (s, 12H, 3,5,3′,5′-OMe), 3.86 (s, 6H, 4,4′-OMe), 3.75 (dd, 2H, J_1 1.5 Hz, J_2 9.5 Hz, H_α-9,9′), 3.60 (dd, 2H, J_1 7 Hz, J_2 10 Hz, H_β-9,9′), 3.21 (m, 2H, H-8,8′); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 153.2 (C-3,5,3′,5′), 137.1 (C-1,1′), 134.6 (C-4,4′), 103.2 (C-2,6,2′,6′), 84.1 (C-7,7′), 68.9 (C-9,9′), 60.9 (4,4′-OMe), 56.1 (3,5,3′,5′-OMe), 49.4 (C-8,8′). These data were in good agreement with those of diayangambin[17].

3.2. Sesartemin (2)

Yellow oil (MeOH); positive ESI-MS: *m/z* 453 $[M+Na]^+$; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.57 (s, 2H, H-2,6), 6.55 (d, 1H, *J* 1.5 Hz, H-6′), 6.53 (d, 1H, *J* 1.5 Hz, H-2′), 5.95 (s, 2H, OCH_2O), 4.72 (d, 2H, *J* 4.5 Hz, H-7,7′), 4.29 (dd, 1H, J_1 6.7 Hz, J_2 9.2 Hz, H_α-9), 4.26 (dd, 1H, J_1 6.7 Hz, J_2 9.2 Hz, H_α-9′), 3.92 (dd, 1H, J_1 3.6 Hz, J_2 9.2 Hz, H_β-9), 3.91 (s, 3H, 5′-OMe), 3.90 (dd, 1H, J_1 3.6 Hz, J_2 9.2 Hz, H_β-9′), 3.87 (s, 6H, 3,5-OMe), 3.83 (s, 3H, 4-OMe),

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3.07 (m, 2H, H-8,8′); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 153.4 (C-3,5), 149.1 (C-3′), 143.4 (C-5′), 137.4 (C-4), 136.7 (C-1), 135.7 (C-1′), 134.6 (C-4′), 105.5 (C-6′), 102.8 (C-2,6), 101.4 (OCH_2O), 100.0 (C-2′), 85.9 (C-7′), 85.7 (C-7), 71.9 (C-9), 71.7 (C-9′), 60.8 (4-OMe), 56.6 (5′-OMe), 56.1 (3,5-OMe), 54.3 (C-8,8′). These data were in accordance with those of sesartemin[14,17].

3.3. Epiyangambin (3)

White needle (MeOH); positive ESI-MS: *m/z* 469 $[M+Na]^+$; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.60 (s, 2H, H-2,6), 6.59 (s, 2H, H-2′,6′), 4.87 (d, 1H, *J* 5.5 Hz, H-7), 4.45 (d, 1H, *J* 7.0 Hz, H-7′), 4.17 (d, 1H, *J* 9.5 Hz, H_β-9′), 3.91 (m, 2H, H_α-9,9′), 3.89–3.85 (m, 18H, 3,4,5,3′,4′,5′-OMe), 3.37 (m, 1H, H-8), 3.36 (m, 1H, H_β-9), 2.93 (m, 1H, H-8′); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 153.4 (C-3′,5′), 153.2 (C-3,5), 137.6 (C-4′), 137.0 (C-4), 136.8 (C-1′), 134.0 (C-1), 103.0 (C-2′,6′), 102.6 (C-2,6), 87.8 (C-7′), 82.2 (C-7), 71.1 (C-9′), 69.8 (C-9), 60.9 (4′-OMe), 60.8 (4-OMe), 56.2 (3,5,3′,5′-OMe), 54.5 (C-8′), 50.0 (C-8). These data were in agreement with those of epiyangambin[14,17].

3.4. (+)Arborone (4)

White powder (MeOH); positive ESI-MS: *m/z* 485 $[M+Na]^+$; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.43 (s, 2H, H-2,6), 6.55 (s, 2H, H-2′,6′), 5.03 (d, 1H, *J* 6.0 Hz, H-7′), 4.44 (t, 1H, *J* 8.0 Hz, H_β-9), 4.33 (ddd, 1H, J_1 2.8 Hz, J_2 5.6 Hz, J_3 8.0 Hz, H-8), 4.26 (dd, 1H, J_1 2.8 Hz, J_2 8.0 Hz, H_α-9), 3.94 (s, 3H, 4-OMe), 3.93 (s, 6H, 3,5-OMe), 3.87 (s, 6H, 3′,5′-OMe), 3.84 (s, 3H, 4′-OMe), 3.44 (d, 2H, *J* 6.8 Hz, H-9′), 2.91 (m, 1H, H-8′); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 198.5 (C-7), 153.4 (C-3,5), 153.2 (C-3′,5′), 143.0 (C-4), 137.1 (C-4′), 133.6 (C-1′), 131.3 (C-1), 106.4 (C-2,6), 102.5 (C-2′,6′), 81.6 (C-7′), 69.1 (C-9), 62.0 (C-9′), 61.0 (4-OMe), 60.9 (4′-OMe), 56.4 (3,5-OMe), 56.2 (3′,5′-OMe), 49.6 (C-8′), 48.8 (C-8). These data were in good agreement with those of (+)arborone[15].

3.5. (–)Syringaresinol (5)

White powder (MeOH); positive ESI-MS: *m/z* 457 $[M+K]^+$; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.59 (s, 4H, H-2,6,2′,6′), 5.52 (br s, 2H, 4,4′-OH), 4.74 (d, 2H, *J* 4.0 Hz, H-7,7′), 4.29 (dd, 2H, J_1 6.5 Hz, J_2 8.5 Hz, H_β-9,9′), 3.92 (dd, 2H, J_1 2.9 Hz, J_2 8.5 Hz, H_α-9,9′), 3.90 (s, 12H, 3,5,3′,5′-OMe), 3.10 (m, 2H, H-8,8′); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 147.1 (C-3,5,3′,5′), 134.3 (C-4,4′), 132.1 (C-1,1′), 102.7 (C-2,6,2′,6′), 86.0 (C-7,7′), 71.8 (C-9,9′), 56.4 (3,5,3′,5′-OMe), 54.3 (C-8,8′). These data were in good agreement with those of (–)syringaresinol[16,21].

3.6. Epiashchantin (6)

White needle (MeOH); positive ESI-MS: *m/z* 423 $[M+Na]^+$; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.78–6.88 (m, 3H, H-2′,5′,6′), 6.59 (s, 2H, H-2,6), 5.96 (s, 2H, OCH_2O), 4.86 (d, 1H, *J* 5.5 Hz, H-7), 4.44 (d, 1H, *J* 7.0 Hz, H-7′), 4.13 (dd, 1H, J_1 1.4 Hz, J_2 9.5 Hz, H_β-9′), 3.89 (s, 6H, 3,5-OMe), 3.86 (s, 3H, 4-OMe), 3.85 (m, 2H, H_α-9,9′), 3.36 (m, 1H, H-8), 3.34 (m, 1H, H_β-9), 2.89 (m, 1H, H-8′); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 153.2 (C-3,5), 148.0 (C-3′), 147.2 (C-4′), 136.9 (C-4), 135.1 (C-1′), 134.0 (C-1), 119.5 (C-6′), 108.2 (C-5′), 106.5 (C-2′), 102.6 (C-2,6), 101.0 (OCH_2O), 87.6 (C-7′), 82.2 (C-7), 71.0 (C-9′), 69.7 (C-9), 60.9 (4-OMe), 56.2 (3,5-OMe), 54.5 (C-8′), 50.1 (C-8). These data were in accordance with those of epiashchantin[14,17,18].

3.7. Caruiligan C (7)

White powder (MeOH); positive ESI-MS: *m/z* 317 $[M+Na]^+$; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.51 (s, 2H, H-2,6), 4.95 (d, 1H, *J* 6.0 Hz, H-7), 4.53 (d, 1H, *J* 9.5 Hz, H_β-9), 4.10 (dd, 1H, J_1 8.0 Hz, J_2 9.5 Hz, H_β-9′), 3.98 (dd, 1H, J_1 6.5 Hz, J_2 9.5 Hz, H_α-9), 3.88 (s, 6H, 3,5-OCH_3), 3.85 (s, 3H, 4-OCH_3), 3.83 (dd, 1H, overlapped, H_α-9′), 3.39 (m, 1H, H-8′); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 178.6 (C-7′), 153.5 (C-3,5), 137.4 (C-4), 132.1 (C-1), 102.7 (C-2,6), 84.2 (C-7), 70.9 (C-9), 68.4 (C-9′), 60.9 (4-OCH_3), 56.2 (3,5-OCH_3), 45.9 (C-8), 43.5 (C-8′). These data were in agreement with those of caruiligan C[19].

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3.8. 7β-Caruilignan C (8)

White powder (MeOH); positive ESI-MS: *m/z* 317 $[M+Na]^+$; ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 6.57 (s, 2H, H-2,6), 4.62 (d, 1H, *J* 7.0 Hz, H-7), 4.52 (dd, 1H, J_1 6.5 Hz, J_2 9.5 Hz, $H_β$-9), 4.40 (t, 1H, *J*9.0 Hz, $H_β$-9′), 4.37 (dd, 1H, J_1 2.0 Hz, J_2 9.8 Hz, $H_α$-9), 4.22 (dd, 1H, J_1 4.0 Hz, J_2 9.0 Hz, $H_α$-9′), 3.88 (s, 6H, 3′,5′-OCH_3), 3.85 (s, 3H, 4′-OCH_3), 3.46 (dt, 1H, J_1 4.0 Hz, J_2 9.0 Hz, J_3 9.0 Hz, H-8′), 3.14 (m, 1H, H-8). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 178.0 (C-7′), 153.6 (C-3,5), 138.0 (C-4), 134.5 (C-1), 102,8 (C-2,6), 86.2 (C-7), 70.2 (C-9′), 69.8 (C-9), 60.8 (4-OCH_3), 56.2 (3,5-OCH_3), 48.5 (C-8), 46.0 (C-8′). These data were in good agreement with caruilignan C called in an article[20]. But in another article[19] published in *Chem. Pharm. Bull.* in 2001, earlier than the former one, call compound **7** as caruilignan C, according to the structure, we called compound **8** as 7β-caruilignan C.

3.9. Yangambin (9)

White needle (MeOH); positive ESI-MS: *m/z* 469 $[M+Na]^+$; ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 6.58 (s, 4H, H-2,6,2′,6′), 4.76 (d, 2H, *J* 4.0 Hz, H-7,7′), 4.32 (dd, 2H, J_1 7.0 Hz, J_2 9.0 Hz, $H_α$-9,9′), 3.94 (dd, 2H, J_1 3.0 Hz, J_2 9.0 Hz, $H_β$-9,9′), 3.88 (s, 12H, 3,3′,5,5′-OCH_3), 3.85 (s, 6H, 4,4′-OCH_3), 3.11 (m, 2H, H-8,8′); ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 153.4 (C-3,5,3′,5′), 136.7 (C-1,1′), 137.5 (C-4,4′), 102.8 (C-2,6,2′,6′), 85.9 (C-7,7′), 72.0 (C-9,9′), 60.8 (4,4′-OCH_3), 56.2 (3,5,3′,5′-OCH_3), 54.3 (C-8,8′). These data were in accordance with those of yangambin[14,17].

Acknowledgements

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苦艾中的九个木脂素

阿不拉江·图拉克, 姜勇, 屠鹏飞*

北京大学医学部 天然药物及仿生药物国家重点实验室; 药学院 天然药物学系, 北京 100191

摘要: 从苦艾的地上部分通过硅胶、反相、凝胶柱层析, 制备高效液相色谱和重结晶手段分离纯化得到九个木脂素, 分别为 diayangambin (**1**), sesartemin (**2**), epiyangambin (**3**), (+)arborone (**4**), (–)syringaresinol (**5**), epiashchantin (**6**), caruiligan C (**7**), 7β-caruilignan C (**8**), yangambin (**9**)。其中化合物**4**, **5**, **7**, **8**为首次从苦艾中分离得到。

关键词: 苦艾; 菊科; 蒿属; 木脂素

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