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11-Methoxyviburtinal, A New Iridoid from *Valeriana jatamansi*

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Five compounds of iridoids, lignan and phenylpropanoid glycosides were isolated from the roots of *Valeriana jatamansi* by column chromatography. Their structures were elucidated as 11-methoxyviburtinal (**1**), baldrinal (**2**), prinsepiol-4-*O*-β-D-glucoside (**3**), coniferin (**4**), and hexacosanic acid (**5**) by spectroscopic analysis. 11-Methoxyviburtinal was a new compound, and others were isolated from the plant for the first time.

Key words: *Valeriana jatamansi*, Iridoids, Lignan, Phenylpropanoid, 11-Methoxyviburtinal, Prinsepiol-4-*O*-β-D-glucoside

INTRODUCTION

The roots of some species of *Valeriana* are extensively used as sedative and antispasmodic. *V. jatamansi* Jones is an annual herb widely distributed in south-western China, utilized as a Chinese folk medicine to possess hypnotic, tranquilizing and antiviral activities (Tang *et al.*, 2002; Ming *et al.*, 1997; *Zhang et al.*, 1986; Wang and Niu, 1980).

A considerable number of investigations on *Valeriana* species have yielded iridoids, sesquiterpenoids, lignans and alkaloids with pharmacological properties, including sedative, cytotoxic, antitumor, antioxidant, and vasorelaxant activities (Piccinelli *et al.*, 2004; Bach *et al.*, 1993; Thies *et al.*, 1981; Bounthanh *et al.*, 1981). Previous chemical studies on *V. jatamansi* revealed the presence of fifteen iridoids (Tang *et al.*, 2002; Zhang *et al.*, 1986), eleven flavones (Tang *et al.*, 2003), three sesquiterpenoids (Ming *et al.*, 1997), volatile constituents (Wang and Niu, 1980) and other compounds. Further investigation on the roots of this plant led now to the isolation of a new iridoid, 11-methoxyviburtinal (**1**), together with the known baldrinal (**2**), prinsepiol-4-*O*-β-D-glucoside (**3**), coniferin (**4**), and hexacosanic acid (**5**). We report here the isolation and structural elucidation of these compounds.

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MATERIALS AND METHODS

Instruments and regents

MS were determined on an API Qstar Pulsa LC/TOF mass spectrometer. FAB-MS were analyzed on a VG Autospec-3000 mass spectrometer. NMR spectra were measured on a Bruker DRX-500 spectrometer with TMS as int. standard. Silica gel (200-300 mesh) was used for column chromatography and silica gel GF_{254} for TLC (Qingdao Marine Chemical Co., China). Solvents were of the industrial purity and distilled before using.

Plant materials

The roots of *V. jatamansi* Jones were collected in July, 2003 from Gejiu of Yunnan province, China and identified by Dr. Xiao Lian, Department of Biology, Yunnan Normal University, where a voucher specimen (No. 0307013) was deposited.

Extraction and isolation

The air-dried and crushed roots of *V. jatamansi* Jones (4 kg) were extracted with 95% ethanol four times at room temperature. The extract was concentrated and the residue (350 g) was extracted with petroleum ether, chloroform and acetone successively. The acetone soluble extract (100 g) was subjected to column chromatography (silica gel 200-300 mesh) eluting with $CHCl_3$ and an increasing ratio of MeOH to afford 17 fractions. Fr. 5 (1.2 g) was further subjected to column chromatography (silica gel 200-300 mesh) eluting with $CHCl_3$-MeOH (9:1, v/v), and then isolated on a Sephadex LH-20 (20~80 um)

column eluting with MeOH-H_2O (9:1, v/v) to yield pure compounds **1** (3 mg), and **2** (7 mg). Fr. 9 (6.6 g) was further subjected to repeated column chromatography in the same way to obtain pure compounds **3** (28 mg), **4** (24 mg) and **5** (3 g).

Compound **1**

EI-MS *m/z* (rel. int., %): 190 $[M]^+$ (100), 189 (54), 160 (40), 159 (35), 132 (52), 131 (25), 103 (29), 102 (20), 77 (11); HR-ESI-MS $[M+H]^+$ *m/z* 191.0701, calcd for $C_{11}H_{11}O_3$, 191.0708; ^{1}H-NMR (500 MHz, Acetone-d_6) δ_H (ppm): 9.92 (1H, s, H-10), 9.20 (1H, s, H-1), 8.09 (1H, s, H-3), 7.94 (1H, d, *J* = 3.2 Hz, H-7), 6.65 (1H, d, *J* = 3.2 Hz, H-6), 4.66 (2H, s, H-11), 3.41 (3H, s, OMe); ^{13}C-NMR (125 MHz, Acetone-d_6) δ_C (ppm): 185.5 (C-10), 152.2 (C-1), 147.0 (C-7), 143.2 (C-3), 135.5 (C-5), 126.2 (C-8), 124.3 (C-9), 122.7 (C-4), 110.7 (C-6), 70.0 (C-11), 59.2 (C-OMe).

Compound **2**

FAB $[M+H]^+$ *m/z* 219; ^{1}H-NMR (500 MHz, Acetone-d_6) δ_H (ppm): 9.94 (1H, s, H-10), 9.21 (1H, s, H-1), 8.20 (1H, s, H-3), 7.96 (1H, d, *J* = 3.2 Hz, H-7), 6.69 (1H, d, *J* = 3.2 Hz, H-6), 5.30 (2H, s, H-11), 2.07 (3H, s, -$OCOCH_3$); ^{13}C-NMR (125 MHz, Acetone-d_6) δ_C (ppm): 185.6 (C-10), 171.5 (-O<u>C</u>OCH_3), 152.2 (C-1), 147.2 (C-7), 144.1 (C-3), 134.8 (C-5), 126.6 (C-8), 124.5 (C-9), 121.3 (C-4), 110.9 (C-6), 61.6 (C-11), 21.3 (-OCO<u>C</u>H_3).

Compound **3**

FAB $[M-Glc+H]^+$ *m/z* 373; ^{1}H-NMR (500 MHz, Acetone-d_6) δ_H (ppm): 7.15 (1H, d, *J* = 8.3 Hz, H-5), 7.11 (1H, d, *J* = 1.5 Hz, H-2), 7.04 (1H, d, *J* = 1.5 Hz, H-2), 6.95 (1H, dd, *J* = 8.3, 1.5 Hz, H-6'), 6.85 (1H, dd, *J* = 8.3, 1.5 Hz, H-6), 6.77 (1H, d, *J* = 8.3 Hz, H-5'), 5.01 (1H, s, H-7), 4.97 (1H, s, H-7'), 4.89 (1H, d, *J* = 7.4 Hz, Glc H-1"), 4.11 (2H, d, *J* = 9.6 Hz, H-9a and -9'a), 3.97 (2H, d, *J* = 9.6 Hz, H-9b and -9'b), 3.87 (3H, s, 3'-OMe), 3.86 (3H, s, 3-OMe), 3.85 (1H, dd, *J* = 12.0, 3.5 Hz, Glc H-6"a), 3.68 (1H, dd, *J* = 12.0, 4.5 Hz, Glc H-6"b), 3.50 (1H, m, Glc H-4"), 3.46 (1H, m, Glc H-5"), 3.40 (1H, m, Glc H-3"), 3.39 (1H, m, Glc H-2"); ^{13}C-NMR (125 MHz, Acetone-d_6) δ_C (ppm): 149.1 (C-3), 147.3 (C-3'), 146.3 (C-4), 146.1 (C-4'), 131.9 (C-1), 128.2 (C-1'), 120.3 (C-6'), 120.1 (C-6), 116.2 (C-5), 114.3 (C-5'), 111.5 (C-2'), 112.2 (C-2), 101.6 (Glc C-1"), 87.9 (C-8), 87.8 (C-8'), 87.7 (C-7'), 87.4 (C-7), 76.8 (Glc C-3"), 76.5 (Glc C-5"), 75.5 (C-9'), 75.4 (Glc C-2"), 75.3 (C-9), 73.6 (Glc C-4"), 61.2 (Glc C-6"), 55.4 (3-OMe), 55.1 (3'-OMe).

Compound **4**

FAB $[M+$ glycerol $+H]^+$ *m/z* 435; ^{1}H-NMR (500 MHz, CD_3OD) δ_H (ppm): 7.12 (1H, d, *J* = 8.3 Hz, H-5), 7.09 (1H, d, *J* = 1.6 Hz, H-2), 6.97 (1H, dd, *J* = 8.3, 1.6 Hz, H-6), 6.58 (1H, d, *J* = 16.0 Hz, H-7), 6.30 (1H, dt, *J* = 16.0, 5.4 Hz, H-8), 4.89 (1H, d, *J* = 7.4 Hz, Glc H-1'), 4.23 (2H, d, *J* = 5.4 Hz, H-9), 3.90 (3H, s, OMe), 3.89 (1H, dd, *J* = 11.7, 3.5 Hz, Glc H-6'a), 3.72 (1H, dd, *J* = 11.7, 3.5 Hz, Glc H-6'b), 3.50 (2H, m, Glc H-4', 5'), 3.41 (2H, m, Glc H-2', 3'); ^{13}C-NMR (125 MHz, CD_3OD) δ_C (ppm): 149.3 (C-3), 146.1 (C-4), 132.1 (C-1), 129.7 (C-7), 127.3 (C-8), 119.1 (C-6), 116.4 (C-5), 109.9 (C-2), 101.2 (Glc C-1'), 76.6 (Glc C-5'), 76.3 (Glc C-3'), 73.3 (Glc C-2'), 69.8 (Glc C-4'), 62.1 (C-9), 60.9 (Glc C-6'), 55.2 (OMe).

Compound **5**

EI-MS *m/z* (rel. int., %): 396 $[M]^+$ (8), 368 (65), 354 (53), 340 (100), 312 (23), 297 (39), 241 (37), 185 (36), 129 (66), 73 (97); ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H (ppm): 2.34 (2H, t, *J* = 7.4 Hz, H-2), 1.79 (2H, m, H-3), 1.29 (44H, br s, H-4~ H-25), 0.87 (3H, t, *J* = 6.4 Hz, H-26).

RESULTS AND DISCUSSION

The chromatographic separation of the acetone fraction from the roots of *V. jatamansi* led to the isolation of 11-methoxyviburtinal (**1**), baldrinal (**2**), prinsepiol-4-*O*-β-D-glucoside (**3**), coniferin (**4**), and hexacosanic acid (**5**).

Compounds **1** and **2** were both obtained as yellow amorphous powders. HR-ESI-MS exhibited $[M+H]^+$ of **1** at *m/z* 191.0701 (calcd for $C_{11}H_{10}O_3$, 191.0708) and FAB-MS showed $[M+H]^+$ of **2** at *m/z* 219. Their ^{1}H-NMR, ^{13}C-NMR, and DEPT spectra were very similar, exhibiting an aldehyde group [δ_H 9.92 (1H, s, H-10) and δ_C 185.5 (C-10) for **1**; δ_H 9.94 (1H, s, H-10) and δ_C 185.6 (C-10) for **2**], four olefinic protons [δ_H 9.20 (1H, s, H-1), 8.09 (1H, s, H-3), 6.65 (1H, d, *J* = 3.2 Hz, H-6), 7.94 (1H, d, *J* = 3.2 Hz, H-7) and δ_C 152.2 (C-1), 143.2 (C-3), 110.7 (C-6), 147.0 (C-7) for **1**; δ_H 9.21 (1H, s, H-1), 8.20 (1H, s, H-3), 6.69 (1H, d, *J* = 3.2 Hz, H-6), 7.96 (1H, d, *J* = 3.2 Hz, H-7) and δ_C 152.2 (C-1), 144.1 (C-3), 110.9 (C-6), 147.2 (C-7) for **2**] and an oxygenated methylene [δ_H 4.66 (2H, s, H-11) and δ_C 70.0 (C-11) for **1**; δ_H 5.30 (2H, s, H-11) and δ_C 61.6 (C-11) for **2**]. These features closely resembled those of diene iridoids isolated from Valerianaceae plants (Thies *et al*, 1981; Mikhova *et al*, 1987; Houghton, 1988), suggesting both were diene iridoids. The only difference between two compounds were observed on that there existed an methoxy group [(δ_H 3.41 (3H, s, OMe) and δ_C 59.2] in **1**, where **2** contained an acetyl group [δ_H 2.07 (3H, s, -$OCOCH_3$) and δ_C 171.5, 21.3]. The methoxy in **1** and acetyl group in **2** were deduced to be both at C-11 on the consideration of the saturated oxygenated carbon. Accordingly, the structures of **1** and **2** were elucidated as 11-methoxyviburtinal and baldrinal respectively on the basis of comparison of NMR data with that of baldrinal isolated from *V. wallichii* D C. (Thies, 1968; Houghton, 1988). As baldrinal was reported as a degradation product from valt-

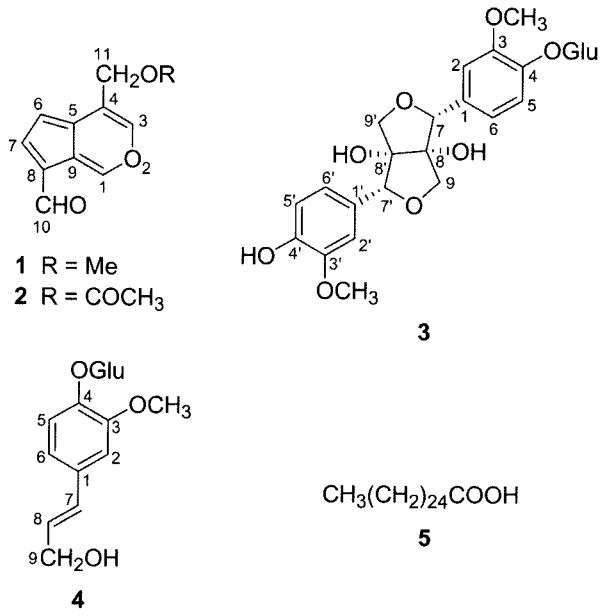

Fig. 1. Structures of compounds **1-5** isolated from *Valeriana jatamansi*

rate (Houghton, 1988; Bounthanh *et al.*, 1981; Thies, 1968), 11-methoxyviburtinal could be also a decomposed artifact.

Compound **3** was obtained as a white amorphous powder. FAB-MS exhibited $[M\text{-Glc+H}]^+$ of **3** at *m/z* 373. Its ^{13}C-NMR and DEPT spectra exhibited 26 signals including 12 carbons for two aromatic rings, two methylenes [δ_C 75.4 and 75.5 (C-9 and C-9′)], two methines [δ_C 87.4 and 87.7 (C-7 and C-7′)], two tertiary alcoholic carbons [δ_C 87.9 and 87.8 (C-8 and C-8′)], two methoxy carbons (δ_C 55.4 and 55.1) and six carbon resonances corresponding to a glucose moiety. The structure of **3** was unambiguously elucidated as prinsepiol-4-*O*-β-D-glucoside by extensive analysis of its ^{1}H-NMR, ^{13}C-NMR, DEPT, H-H Cosy, HMBC, and HMQC spectrum. It was just published on July, 2004 as a new compound isolated from *V. prionophylla* Standl (Piccinelli *et al.*, 2004).

Compound **4** was also obtained as a white amorphous powder. Its FAB-MS exhibited $[M + \text{glycerol} + H]^+$ at *m/z* 435. ^{13}C-NMR and DEPT spectra exhibited 16 signals including 6 carbons for an aromatic rings, two olefic methines [δ_C 129.7 (C-7) and 127.3 (C-8)], a methoxy carbon (δ_C 55.2), an oxygenated methylene carbon (δ_C 62.1) and six carbon resonances corresponding to a glucose moiety. The structure of **4** was elucidated as coniferin by 1D and 2D NMR studies and comparison with literature reports (Greca *et al.*, 1998; Matsumura *et al.*, 2002).

The structures of compounds **1-5** were shown in Fig. 1. Among the isolated compounds, 11-methoxyviburtinal (**1**) was a new compound, and others were isolated from *V. jatamansi* for the first time.

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