Two New Iridoids from the Root and Rhizome of *Valeriana jatamansi* JONES

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Two new iridoids, jatamanvaltrates P and Q (**1** and **2**, resp.), together with three known iridoids, rupesin B (**3**), chlorovaltrate (**4**), and valtrate (**5**), were isolated from the root and rhizome of *Valeriana jatamansi* JONES. The structures of the new compounds were elucidated by spectroscopic analyses, including 2D-NMR techniques.

Introduction. – *Valeriana jatamansi* JONES belongs to the genus *Valeriana* of the Valerianaceae family, and it is a native of mainland China and India, and known as a versatile medicinal plant, traditionally used as sedative, nervine, detoxicant, antispasmodic, and carminative agent [1–3]. In our continuing search for new bioactive natural products from this plant, two new iridoids, jatamanvaltrates P and Q (**1** and **2**, resp), along with three known iridoids, rupesin B (**3**), chlorovaltrate (**4**), and valtrate (**5**), were isolated from the root and rhizome part of *V. jatamansi*. Herein, we report the isolation and structure elucidation of the new compounds.

Results and Discussion. – Repeated column chromatography of the petroleum ether (PE) extract from the root and rhizome part of *V. jatamansi* afforded compounds **1**–**5**.

Jatamanvaltrate P (**1**) was obtained as amorphous white powder, its molecular formula, $C_{27}H_{40}O_{10}$, was deduced from HR-ESI-MS (*m*/*z* 547.2530 ($[M+Na]^+$)). The IR spectrum showed the absorption bands for OH (3452 cm^{-1}) and ester CO (1736 cm^{-1}) groups. The ^1H- and ^{13}C-NMR spectra (*Tables 1* and *2*) exhibited signals corresponding to two trisubstituted olefinic groups (δ(H) 6.69 (*s*, H–C(3)); δ(C) 148.0 (C(3)) and 108.7 (C(4)); δ(H) 5.78 (*dd*, $J = 2.4$, 2.4, H–C(6)); δ(C) 117.5 (C(6)) and 139.0 (C(5))), and a hemiketal CH group (δ(H) 6.26 (*d*, $J = 10.2$, H–C(1)); δ(C) 92.5 (C(1))). These data, together with the resonances of four ester CO groups at δ(C) 173.0, 171.8, 170.8, and 170.7, led to the assumption that compound **1** is a valtrate

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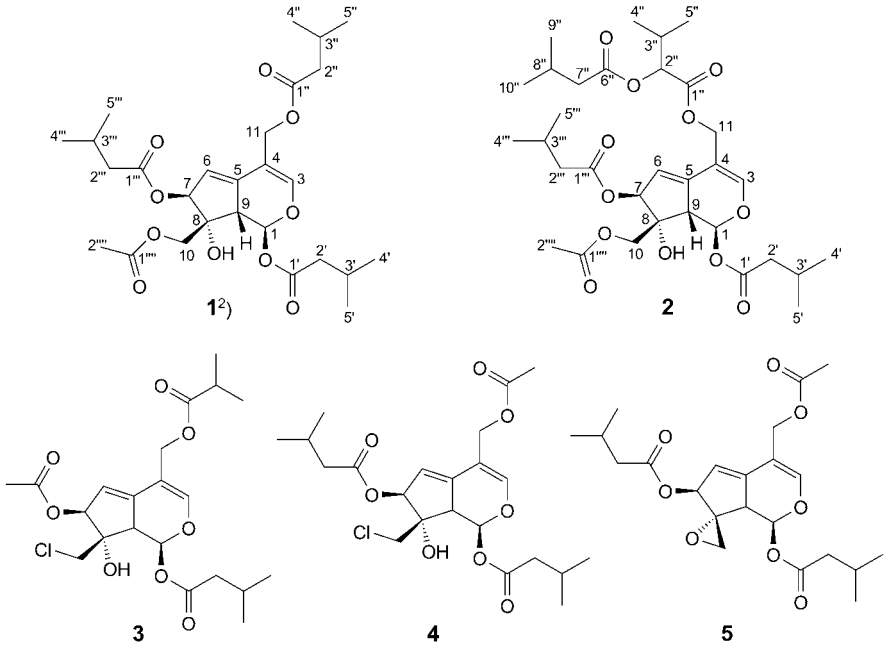

Table 1. *^{1}H-NMR Data of* **1**, **2**, *and Jatamanvaltrate K* (at 600 MHz, in $CDCl_3$ at 27°; δ in ppm, J in Hz)

Position	**1**	**2**	Jatamanvaltrate K
1	6.26 (*d*, *J* = 10.2, 1 H)	6.23 (*d*, *J* = 10.2, 1 H)	6.20 (*d*, *J* = 10.2, 1 H)
3	6.69 (*s*, 1 H)	6.69 (*s*, 1 H)	6.70 (*s*, 1 H)
6	5.78 (*dd*, *J* = 2.4, 2.4, 1 H)	5.78 (*d*, *J* = 2.4, 2.4, 1 H)	5.50 (*dd*, *J* = 1.8, 1.8, 1 H)
7	5.49 (*d*, *J* = 3.0, 1 H)	5.40 (*d*, *J* = 2.4, 1 H)	5.75 (*d*, *J* = 0.6, 1 H)
9	2.95 (*dd*, *J* = 10.2, 3.0, 1 H)	2.93 (*dd*, *J* = 10.2, 3.0, 1 H)	2.67 (*dd*, *J* = 10.2, 1.8, 1 H)
10	4.40 (*d*, *J* = 11.4, 1 H), 4.33 (*d*, *J* = 11.4, 1 H)	4.30 (*d*, *J* = 12.0, 1 H), 4.70 (*d*, *J* = 12.0, 1 H)	3.78 (*s*, 1 H)
11	4.72 (*d*, *J* = 12.6, 1 H), 4.66 (*d*, *J* = 12.6, 1 H)	4.72 (*d*, *J* = 12.6, 1 H), 4.65 (*d*, *J* = 12.6, 1 H)	4.75 (*d*, *J* = 12.0, 1 H), 4.63 (*d*, *J* = 12.0, 1 H)
2′	2.22 (*dd*, *J* = 3.6, 7.8, 2 H)	2.23–2.27 (*m*, 2 H)	2.29 (*m*, 2 H)
3′	2.16–2.19 (*m*, 1 H)	2.11–2.14 (*m*, 1 H)	2.15 (*m*, 2 H)
4′, 5′	0.97 (*d*, *J* = 6.6, 6 H)	0.95 (*dd*, *J* = 6.6, 6 H)	1.01 (*d*, *J* = 6.6, 6 H)
2″	2.33 (*d*, *J* = 7.2, 2 H)	4.75 (*d*, *J* = 4.2, 1 H)	2.09 (*s*, 3 H)
3″	2.08–2.11(*m*, 1 H)	2.20–2.21 (*m*, 1 H)	
4″, 5″	1.01 (*d*, *J* = 6.6, 6 H)	1.01 (*d*, *J* = 7.2, 6 H)	
7″		2.29–2.33 (*m*, 2 H)	
8″		2.18–2.19 (*m*, 1 H)	
9″, 10″		1.00 (*d*, *J* = 6.6, 6 H)	
2‴	2.15 (*dd*, *J* = 3.0, 7.8, 2 H)	2.34–2.36 (*m*, 2 H)	2.29 (*m*, 2 H)
3‴	2.06–2.07 (*m*, 1 H)	2.06 –2.10 (*m*, 1 H)	2.15 (*m*, 1 H)
4‴, 5‴	0.94 (*d*, *J* = 6.6, 6 H)	1.02 (*d*, *J* = 6.6, 6 H)	1.01 (*d*, *J* = 6.6, 6 H)
2⁗	2.05 (*s*, 3 H)	2.05 (*s*, 3 H)	

[2]) Iridoid atom numbering. For systematic names, see the *Exper. Part.*

Table 2. *^{13}C-NMR Data of* **1**, **2**, *and Jatamanvaltrate K* (at 150 MHz, in $CDCl_3$ at 27°; δ in ppm)

C-Atom	**1**	**2**	Jatamanvaltrate K
1	92.5	92.6	91.8
3	148.0	148.0	147.8
4	108.7	108.7	108.1
5	139.0	138.9	135.4
6	117.5	117.6	117.4
7	83.1	83.0	80.2
8	80.1	80.0	82.1
9	48.4	48.3	47.3
10	65.4	65.7	67.0
11	60.9	60.9	60.8
1′	170.8	170.8	170.9
2′	43.0	43.0	43.2
3′	25.7	25.7	25.6
4′	22.3	22.3	22.2
5′	22.3	22.3	22.3
1″	170.7	169.6	171.0
2″	43.1	76.9	21.0
3″	25.7	30.0	
4″	22.2	18.8	
5″	22.2	17.1	
6″		173.7	
7″		43.2	
8″		25.6	
9″		22.3	
10″		22.3	
1‴	171.8	171.8	173.8
2‴	43.4	43.1	43.4
3‴	25.6	25.5	25.8
4‴	22.3	22.2	22.4
5‴	22.3	22.2	22.3
1⁗	173.0	170.9	
2⁗	20.9	20.9	

hydrin-type iridoid, with four acyloxy substituents, which could be readily identified as three isovaleroxy and one AcO group by comparison with the reported ^{1}H- and ^{13}C-NMR data of the known valepotriates [2][3]. The connectivities of the acyloxy substituents to the iridoid nucleus were fully assigned by HMBC experiments. The linkage of three isovaleroxy groups to C(1), C(7), and C(11) were established by the HMBCs (*Fig.*) from H–C(1), H–C(7), and H–C(11) to the CO C-atoms δ(C) 170.8, 173.0, and 170.7, resp., while the connection of the AcO group to C(10) was determined on the basis of the HMBC from H–C(10) to the CO C-atom with the signal at δ(C) 171.8.

The NMR data of **1** were closely similar to those of jatamanvaltrate K (*Tables 1* and *2*), an acylated iridoid also isolated from *V. jatamansi* [2], except for the presence of an isovaleroxy group instead of an AcO group at C(11), and an AcO group instead of a OH group at C(10) in **1**. The relative configuration of **1** was elucidated by NOESY

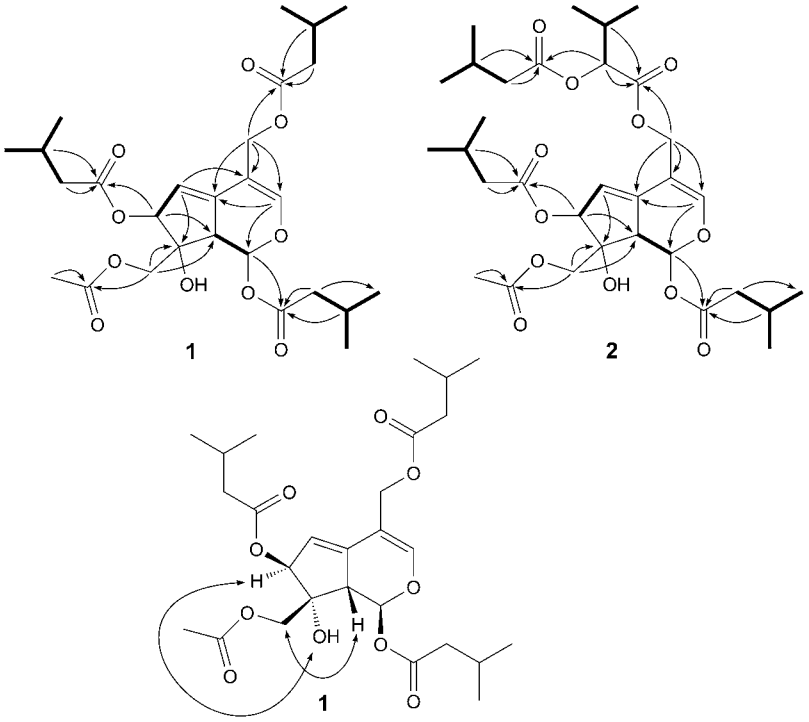

Figure. *Key HMBCs* (arrows), *and COSY* (bold lines) *and NOESY* (double-headed arrows) *correlations of* **1** *and* **2**

experiments. Since all the naturally occurring valepotriates exhibit an α-orientation for H–C(1) and β-orientation for H–C(9) [2][4], NOESY correlations H–C(9)/CH_2(10), and HO–C(8)/H–C(7) indicated that CH_2(10) has a β-orientation, and that H–C(7) and HO–C(8) were α-oriented. Based on biogenetic considerations, **1** was assumed to possess the same absolute configuration as jatamanvaltrate K [2]. Therefore, the structure of jatamanvaltrate P (**1**) was identified as (1*S*,7*S*,8*R*,9*S*)-10-acetoxy-1,7,11-triisovaleroxyvaltrate hydrin.

Jatamanvaltrate Q (**2**) was obtained as colorless oil and its molecular formula, $C_{32}H_{48}O_{12}$, was deduced from HR-ESI-MS (*m*/*z* 647.3048 ($[M+Na]^+$). The IR spectrum also indicated the presence of OH (3462 cm^{-1}) and ester CO groups (1739 cm^{-1}). According to the molecular formula and NMR data, **2** was determined to possess almost the same pattern as **1**, differing only in the signals due to the presence of an α-(isovaleroxy)isovaleroxy residue at C(11) instead of an isovaleroxy group, which was readily confirmed by the observed HMBC from CH_2(11) to the CO C-atom with the signal at δ(C) 169.6. Furthermore, all of the key NOESY correlations supporting the structure of **1** were also observed in the 2D-NMR spectrum of **2**, suggesting that the configuration of **2** was the same as **1**. Accordingly, **2** was identified as (1*S*,7*S*,8*R*,9*S*)-10-acetoxy-11-[α-(isovaleroxy)isovaleroxy]-1,7-diisovaleroxyvaltrate hydrin.

The known iridoid compounds were identified as rupesin B (**3**) [5], chlorovaltrate (**4**) [5], and valtrate (**5**) [6][7] by comparing their ^{1}H- and ^{13}C-NMR data with those reported in the literature. All these three known compounds have been previously reported from *V. jatamansi*.

Experimental Part

General. Anal. TLC: silica-gel plates (SiO_2; *Yantai Institute of Chemical Technology*), with petroleum ether (PE)/AcOEt 10:1; visualization under UV light, and by spraying with 7% aq. H_2SO_4, followed by heating. Column chromatography (CC): silica gel (SiO_2; 200–300, or 300–400 mesh; *Qingdao Marine Chemical Factory*). Optical rotations (ORD): *JASCO P-1020* spectropolarimeter. UV Spectra: *Shimadzu UV-260* spectrophotometer, in anh. MeOH; λ_{max} (log ε) in nm. IR Spectra: *Avatar 360-ESP* spectrophotometer (*Thermo Nicolet*), as KBr pellets; in cm^{-1}. ^{1}H- and ^{13}C-NMR Spectra: *Bruker Avance* 600 MHz spectrometer, in $CDCl_3$; δ in ppm, J in Hz. HR-ESI-MS: *Bruker APEX 7.0 TESLA FT-MS* apparatus.

Plant Material. The root and rhizome of *V. jatamansi* were collected in Guiyang, Guizhou Province, P. R. China, in September of 2011. A herbarium specimen (#201209) was deposited with the School of Pharmacy, Second Military Medical University, P. R. China.

Extraction and Isolation. The air-dried root and rhizome (1.6 kg) of *V. jatamansi* were extracted exhaustively with 95% aq. EtOH at r.t. 3 × 24 h. The EtOH extract was concentrated *in vacuo* to yield a semisolid (138 g), which was subjected to *D101* macroporous resin, first eluted with 70% aq. EtOH and then with 85% aq. EtOH. The 85% aq. EtOH eluate was collected and concentrated *in vacuo* to yield a residue (46 g), which was suspended in H_2O (500 ml), and subsequently extracted with PE (3 × 500 ml). The combined org. phase was concentrated to yield a residue (12.6 g), which was fractioned by CC (*Sephadex LH-20*; CH_2Cl_2/MeOH 1:1) to give two subfractions. The first subfraction (9.6 g) was further purified by CC (SiO_2 (153 g); PE/AcOEt gradient) to afford five fractions, *Frs. 1–5*. *Fr. 4* (1.0 g) was purified by reversed-phase prep. HPLC (*RP18*, 5 μm, 300 × 10 mm, 208 nm, MeOH/H_2O 85:15) to give **1** (43.6 mg), **2** (23.9 mg), **3** (50.1 mg), **4** (23.4 mg), and **5** (74.4 mg).

Jatamanvaltrate P (=*(1S,6S,7R,7aS)-7-[(Acetyloxy)methyl]-1,6,7,7a-tetrahydro-7-hydroxy-4-{[(3-methylbutanoyl)oxy]methyl}cyclopenta[c]pyran-1,6-diyl Bis(3-methylbutanoate)*; **1**). Amorphous powder. $[\alpha]_D^{25} = +189.8$ ($c = 0.22$, MeOH). UV (MeOH): 256 (2.37). IR (KBr): 3451, 2962, 1735, 1641, 1371, 1103, 983. ^{1}H- and ^{13}C-NMR: see *Tables 1* and *2*, resp. HR-ESI-MS: 547.2530 ($[M+Na]^+$, $C_{27}H_{40}NaO_{10}^+$; calc. 547.2519).

Jatamanvaltrate Q (=*{(1S,6S,7R,7aS)-7-[(Acetyloxy)methyl]-1,6,7,7a-tetrahydro-7-hydroxy-1,6-bis[(3-methylbutanoyl)oxy]cyclopenta[c]pyran-4-yl}methyl 3-Methyl-2-[(3-methylbutanoyl)oxy]butanoate*; **2**). Colorless oil. $[\alpha]_D^{25} = +76.1$ ($c = 0.16$, MeOH). UV (MeOH): 256 (2.02). IR (KBr): 3462, 2960, 2925, 1739, 1641, 1610, 1468, 1371, 1097, 1026. ^{1}H- and ^{13}C-NMR: see *Tables 1* and *2*, resp. HR-ESI-MS: 647.3048 ($[M+Na]^+$, $C_{32}H_{48}NaO_{12}^+$; calc. 647.3043).

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