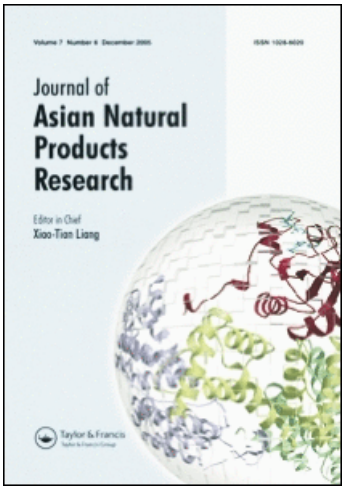

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A new diterpenoid alkaloid from *Aconitum jaluense*

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A new diterpenoid alkaloid, jaluenine (**1**), has been isolated from the roots of *Aconitum jaluense*. The structure of jaluenine was determined by spectroscopic methods including two dimensional NMR (^{1}H-^{1}H COSY, HMQC, HMBC, NOESY).

Keywords: *Aconitum jaluense*; Ranunculaceae; Diterpenoid alkaloid; Hetisine; Jaluenine

1. Introduction

Twenty-three species of *Aconitum* plants are found in Korea [1], but little is known about the chemical composition of these plants [2–10]. We reported the isolation and identification of nine norditerpenoid alkaloids from the Aconiti Tuber [11]. Further investigation on norditerpenoid and diterpenoid alkaloids from *Aconitum* plants led to the isolation of seven known norditerpenoid alkaloids and a napelline-type diterpenoid alkaloid from the roots of *A. jaluense* Komar. (Ranunculaceae) [12]. *Aconitum jaluense* is widespread in remote mountainous regions of the Korean peninsula. The root part of this plant has been used as a substitute for aconite in Korean folk medicine [1,13]. Further investigation on this plant resulted in the isolation of a new diterpenoid alkaloid, jaluenine (**1**). In this paper we describe the isolation and structural elucidation of **1**.

2. Results and discussion

The root parts of *A. jaluense* were extracted, as described in the experimental section, to give an alkaloid fraction. This fraction was separated with a silica gel column ($CHCl_3$/MeOH, gradient), in which fraction 6 was further purified by a silica gel column (cyclohexane/EtOAc/Et_2NH = 10:1:0.2) to afford a new alkaloid, jaluenine (**1**).

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The molecular formula of jaluenine (**1**), amorphous solid, $[\alpha]_D^{23} = +19.3$, was established to be $C_{29}H_{33}NO_6$ by its HREIMS *m/z* 491.2307 $[M]^+$. The IR spectrum showed absorption bands for hydroxyls (3432 cm^{-1}), esters (1721, 1273, 1246 cm^{-1}), exocyclic double bond (1655, 885 cm^{-1}) and aromatic CH (714 cm^{-1}). The ^1H and ^{13}C NMR spectra confirmed the presence of an angular methyl group [δ_H 1.15, 3H, s; δ_C 25.1 (q)], an exocyclic double bond [δ_H 4.74, 2H, br s; δ_C 108.3 (t), 145.4 (s)], an acetyl group [δ_H 1.99, 3H, s; δ_C 21.0 (q), 170.5 (s)], two oxygenated methines [δ_H 3.76, 1H, br d, $J = 1.8$ Hz, 3.62, 1H, d, $J = 3.0$ Hz; δ_C 70.3 (d), 71.3 (d)], and a benzoate group [δ_H 7.95, 2H, dt, $J = 1.5$, 7.2 Hz, 7.45, 2H, tt, $J = 1.2$, 7.2 Hz and 7.57, 1H, dt, $J = 1.2$, 7.2 Hz; δ_C 129.7 (s), 129.5 (d), 128.7 (d), 133.4 (d), 165.7 (s)], but indicated the absence of methoxyl, *N*-methyl or *N*-ethyl groups. Since seven out of 14 degrees of unsaturation were thus accounted for, it was concluded that **1** contained heptacyclic skeleton as in hetisine-type diterpenoid alkaloids [14]. The ^1H-^1H COSY and HMQC spectra disclosed connectivities (figure 1) of C-1 to C-3, C-5 to C-7, C-9, C-11 to C-14, and C-15 to C-17. HMBC correlations (figure 1) of H-1 to C-5 and C-20, H-5 to C-3 and C-20, H-7 to C-9, H-13 to C-16, and H-17 to C-12 allowed us to deduce the hetisine-type skeleton, in which two secondary hydroxyl groups were attached to C-3 and C-7, respectively. The remaining benzoate and acetate groups in **1** must occupy the C-2 and C-13 positions. Three-bond correlations obtained from the HMBC experiment showed the correlations of H-2 to a benzoyl carbonyl signal and H-13 to an acetyl carbonyl signal. Thus, the structure of jaluenine was elucidated to be **1**. The relative stereochemistry for the two hydroxyl groups at C-3 and C-7, a benzoyloxy group at C-2 and an acetoxyl group at C-13 were determined from NOESY spectrum. The observed small coupling constant ($J = 1.8$ Hz) of the H-3 excluded axial–axial relationship of the vicinal H-2 and H-3 protons, but either the axial–equatorial or the equatorial–equatorial orientation remained. The equatorial configuration of the H-3 coupled with the small coupling constant ($J = 1.8$ Hz) with the H-2 ($W_{\frac{1}{2}} = 10.2$ Hz) and the observed NOESY correlations between H-20 and H-2′, 6′ are consistent with a H-2β and H-3α relative configurations at carbons C-2 and C-3 in **1**. This assignment was further supported by the identical chemical shifts for the C-2 and C-3 of **1**, compared to those of sadosine (**2**) [15]. Observed NOESY correlation between the H-7 and the H-14 establishes the relative configuration of the proton at C-7 as α. A comparison of the ^{13}C chemical shifts of **1** with those of venudelphine (**3**) [16] supported the above observation. Stronger upfield shifts observed in C-15 ($\Delta\delta = -5.0$) than in C-14 ($\Delta\delta = -3.6$) were noteworthy when compared with those of venudelphine due to the γ-gauche effect exerted by the hydroxyl group at C-7 in the β-configuration [17]. By analogy with other diterpenoid alkaloids possessing an oxygen function at C-13 (venudelphine [16], fissumine [18], cardiopine [19], cossonine [20]), the α-configuration was assigned to the C-13 ester group [21]. The spatial correlations were also shown between the H-13β signal at δ_H 5.08 and the H-12, H-14 and H-15β, supporting the presence of an acetoxy group at the C-13 in an α configuration in **1**. Therefore, the structure of jaluenine was determined as **1**.

3. Experimental

3.1 General experimental procedures

Melting points were measured on a Mitamura-Riken apparatus, and are uncorrected. The optical rotations were determined on a JASCO P-1020 polarimeter. The IR spectra were obtained on a JASCO FT/IR-5300 spectrometer. EI mass spectra were obtained on a

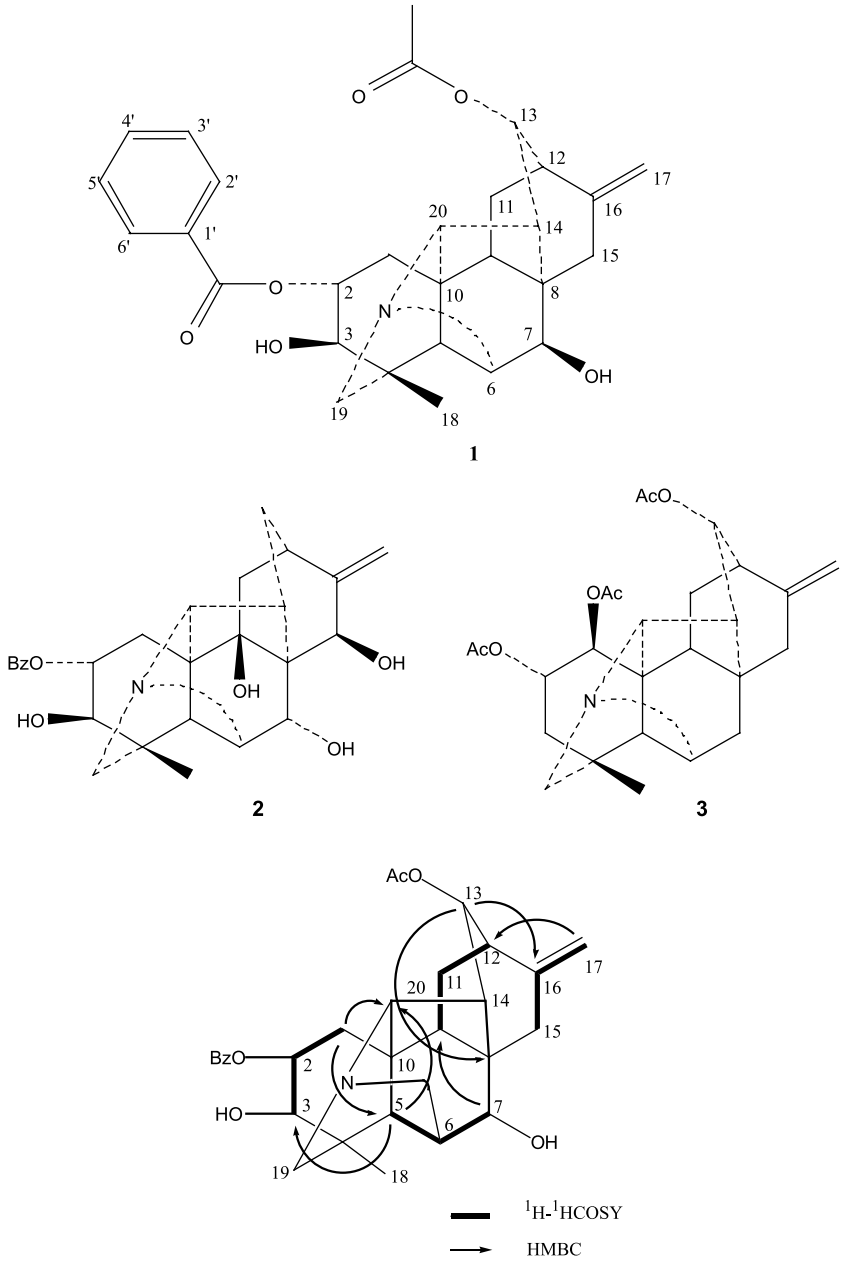

Figure 1. Selected ^{1}H-^{1}H COSY and HMBC correlations for **1**.

Hewlett-Packard 5989B spectrometer. The NMR spectra were measured on a Varian Gemini 2000 instrument (300 MHz) or a Bruker AM-500 (500 MHz), and the chemical shifts were referenced to TMS. TLC was performed on silica gel $60F_{254}$ (Merck).

3.2 Plant material

The root parts of *Aconitum jaluense* were collected in August 2000 at Mt. Changbaek, Kangwon province, Korea, and authenticated by one of authors (KHB). The voucher

specimen (No. KSS 010811) has been deposited in the herbarium of Natural Products Research Institute, Seoul National University.

3.3 Extraction and isolation

Powdered roots of *Aconitum jaluense* (330 g) were extracted four times with MeOH at room temperature. The MeOH extracts were combined and evaporated under reduced pressure to dryness. This was partitioned with 3% aqueous NH_4OH and $CHCl_3$. The $CHCl_3$ extract (5.5 g) was separated into seven fractions by chromatography on a silica gel column with a gradient eluent of $CHCl_3$–MeOH (96:4 → 0:100). Fraction 6 was further purified by chromatography on a silica gel column using cyclohexane–EtOAc–Et_2NH (10:1:0.2) as the eluent to yield jaluenine (**1**, 12 mg).

Jaluenine (**1**) was obtained as an amorphous solid from MeOH, mp 114–116°C, $[\alpha]_D^{23} = +19.3$ (c 0.27, $CHCl_3$); IR (KBr) ν_{max} 3432 (OH), 1721 (ester CO), 1655 (C═C), 1273, 1246 (ester CO), 1069, 1026, 885 (C═CH_2), 714 (aromatic C—H) cm^{-1}; ^{1}H- and ^{13}C-NMR data (see table 1); EIMS *m/z* 491 $[M]^+$(5), 474 $[M - HO]^+$(6), 369 $[M - C_6H_5COOH]^+$(71), 341 $[M - (C_6H_5COOH + CO)]^+$(29), 310 $[M - (CH_3COO + C_6H_5COOH)]^+$(5), 309 $[M - (CH_3COOH + C_6H_5COOH)]^+$(4), 105 $[C_6H_5C{\equiv}O^+]$ (100), 77 (49); HREIMS *m/z* 491.2307 (calcd for $C_{29}H_{33}NO_6$ $[M]^+$, 491.2308), ^{1}H-^{1}H NOESY signal (correlated signal), H-2β (H-1, H-3α), H-3α (H-18), H-5 (H-18), H-6 (H-18), H-7α (H-14), H-12 (H-11, H-13β,

Table 1. NMR data for jaluenine (**1**) in $CDCl_3$.

Position	δ_H *(J)*	δ_C *(DEPT)*	*HMBC*
1	2.18*	26.8 (CH_2)	C-2, 3, 5, 10, 20
	2.44 (dd, 4.8, 15.3)		
2	5.41 (m, $W_{\frac{1}{2}} = 10.2$ Hz)	73.6 (CH)	C-10, COC_6H_5
3	3.76 (br d, 1.8)	70.3 (CH)	C-1, 2, 4, 5
4	–	41.7 (C)	
5	2.04 (br s)	54.1 (CH)	C-3, 7, 10, 18, 19, 20
6	3.35 (br s)	70.5 (CH)	C-7, 10
7	3.62 (d, 3.0)	71.3 (CH)	C-8, 9
8	–	45.5 (C)	
9	2.20*	39.0 (CH)	
10	–	46.2 (C)	
11	1.03 (dt, 3.0, 14.4)	29.4 (CH_2)	C-16
	1.90 (ddd, 3.0, 11.1, 14.4)		
12	2.51*	38.2 (CH)	
13	5.08 (d, 4.8)	70.9 (CH)	C-8, 12, 14, 16, $COCH_3$
14	1.50 (br d, 1.8)	55.2 (CH)	C-7, 8, 9, 10, 13, 20
15	2.20*	29.1 (CH_2)	C-8, 14, 16
	2.77 (dt, 1.5, 17.7)		
16	–	145.4 (C)	
17	4.74 (br s)	108.3 (CH)	C-12, 15
18	1.15 (s)	25.1 (CH_3)	C-3, 4, 5, 19
19	2.52 (d, 12.6)	61.2 (CH_2)	C-3, 4, 18, 20
	3.05 (d, 12.6)		
20	2.95 (br s)	75.4 (CH)	C-1, 6, 8, 14, 19
$COCH_3$	1.99 (s)	21.0 (CH_3)	$COCH_3$
$COCH_3$	–	170.5 (C)	
1′	–	129.7 (C)	
2′,6′	7.95 (dt, 1.5, 7.2)	129.5 (CH)	C-2′, 4′, 6′, COC_6H_5
3′,5′	7.45 (tt, 1.2, 7.2)	128.7 (CH)	C-2′, 6′
4′	7.57 (dt, 1.2, 7.2)	133.4 (CH)	C-2′, 6′
COC_6H_5	–	165.7 (C)	

* Overlapped signals.

H-17), H-13β (H-12, H-14, H-15β), H-14 (H-7α, H-13β, H-15β), H-15β (H-14), H-17 (H-12), H-18 (H-3α, H-5, H-6, H-19β), H-19α (H-20), H-19β (H-18), H-20 (H-1α, H-11α, H-19α), H-2′/6′ (H-20).

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