

A Morphinane Alkaloid from *Meconopsis quintuplinervia*

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Abstract: A new morphinane alkaloid named as mecoquitupline was isolated from *Meconopsis quintuplinervia* Regel. Its structure was elucidated to be 6-methoxy-17-methyl-2,3-[methylene bis(oxy)]-morphinan-5-en-7-one by spectroscopic techniques.

Keywords: *Meconopsis quintuplinervia* Regel, morphinane alkaloid, mecoquitupline.

Meconopsis quintuplinervia Regel is a traditional Tibetan medicine used for treatments of hepatitis and tuberculosis¹. Several chemical constituents have been reported from this plant^{2, 3}. Here we report the isolation and structural elucidation of a new morphinane alkaloid named as mecoquitupline **1** from the same plant collected in Qinghai province of China.

The ethanolic extract of the air-dried and ground whole plants of *Meconopsis quintuplinervia* Regel was subjected to column chromatography on macroporous adsorbent resin, normal phase and reverse phase silica gels and Sephadex LH-20 successively to yield a mixture. The mixture was further purified by preparative reverse phase HPLC to yield compound **1**, mp 192-194°C, $[\alpha]_D^{22} -52.8$ (c 0.11, CHCl₃). Its IR spectrum showed absorption bands for conjugated carbonyl group (1689 cm⁻¹) and aromatic ring (1506 and 1616 cm⁻¹). The positive FABMS spectrum of **1** exhibited a quasi-molecular ion peak at m/z 328 [M+H]⁺, and the molecular formula of **1** was established as C₁₉H₂₁NO₄ by the positive HRFABMS at m/z 328.1514 [M+H]⁺ (calcd. for C₁₉H₂₂NO₄ 328.1549). The ¹H NMR spectrum of **1** (see **Table 1**) showed three isolated singlets at δ 6.90, 6.61 and 6.27 (each 1H), and a characteristic signal at δ 5.94 (2H, br s) attributed to a dioxymethylene group. Methyl groups singlets at δ 3.68 and 2.44 (each 3H, s) indicated the presences of a methoxyl and a nitrogen methyl groups in the structure of **1**. The ¹³C NMR and DEPT spectra showed 19 carbon signals (see **Table 1**) including two methyl, five methylene, five methine, and seven quaternary carbons. The ¹H-¹H COSY spectrum of **1** revealed the presence of two spin systems CH₂-CH-CH-CH₂ and CH₂-CH₂ separated by quaternary carbons. All of the protonated carbons were assigned by HMQC experiment. The morphinane skeleton of **1** was established by the

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HMBC experiment (see **Figure 1**). Two and three bond correlations from the dioxymethylene protons to C-2 and C-3, methoxyl proton to C-6, nitrogen methyl proton to C-9 and C-16, H-5 to C-6, C-7, C-12, C-13, C-14 and C-15, and H₂-8 to C-6 and C-7 revealed that the structure of **1** is 6-methoxy-17-methyl-2,3-[methylenebis(oxy)]-morphinan-5-en-7-one. The relative stereochemistry at C-9, C-13 and C-14 were finally determined by NOE difference experiment. Irradiation of H-9 gave enhancements of H-14, and H-8 α , and irradiation of 8 β gave an enhancement of H-15 α .

Figure 1 The Structures and key HMBC correlations of **1**

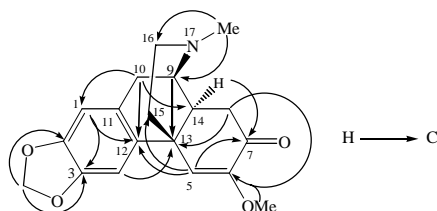


Table 1 NMR data for compound **1**^a

No.	¹ H	¹³ C (DEPT)	No.	¹ H	¹³ C (DEPT)
1	6.62, s 1.70, m	108.4 (CH)	11	-	129.8 (C)
2	-	146.8 (C)	12	-	133.5 (C)
3	-	146.5 (C)	13	-	36.6 (C)
4	6.90, s	104.2 (CH)	14	2.45, m	40.1 (CH)
5	6.27, s	120.9 (CH)	15 α	2.17, m	35.4 (CH ₂)
6	-	151.2 (C)	15 β	1.52, br d (10.8)	
7	-	194.2 (C)	16	2.14, dd (11.2, 3.0) 2.64, br d (11.3)	46.2 (CH ₂)
8 α	2.53, dd (18.0, 4.5)		17	2.44, s	42.5 (CH ₃)
8 β	3.41, dd (18.0, 15.2)	38.9 (CH ₂)	18	5.93, br s	101.3 (CH ₂)
9	3.10, m	56.7 (CH)	19	3.68, s	55.3 (CH ₃)
10	2.79, dd (18.3, 6.0) 3.08, br d (18.3)	28.3 (CH ₂)			

^a NMR data were measured in CDCl₃ at 300 MHz for proton and at 75 MHz for carbon. Proton coupling constants (*J*) in Hz are given in parentheses.

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