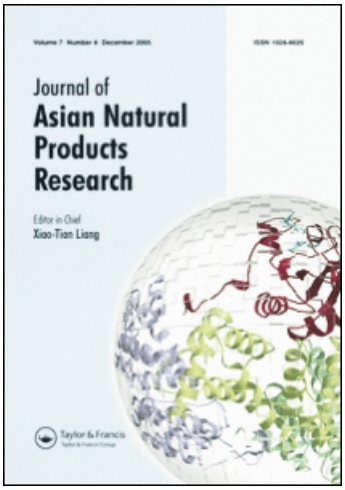

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CHESTNUTAMIDE: A NOVEL ALKALOID FROM FLOWERS OF *CASTANEA MOLLISSIMA* BLUME

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A novel alkaloid, chestnutamide, was isolated from the flowers of *Castanea mollissima* Blume. The structure was determined on the basis of spectral analysis.

Keywords: *Castanea mollissima* Blume; Chestnutamide

INTRODUCTION

Castanea mollissima Blume (Fagaceae) is a chestnut tree, widely distributed in China and whose fruits are edible. The flowers of this species have been well documented as herbal medicine for the treatment of diarrhea [1]. In addition, it has been cultivated artificially as a kind of economical plant in abundant resource. Previous chemical investigation on this species demonstrated the presence of tannins [2]. In the present paper, we report the isolation and structure elucidation of a new alkaloid named chestnutamide.

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RESULTS AND DISCUSSION

Compound **1** was obtained as white crystals. The molecular formula $C_{14}H_{12}N_2O_2$ was determined on the basis of its HREIMS (*m/z* 240.0903 calcd. for $C_{14}H_{12}N_2O_2$, 240.0898). According to this formula, 10 degrees of unsaturation were calculated and accounted for the presence of a benzene ring, two carbonyl groups, a double bond and three additional unsaturated degrees coming from a polycyclic system based on analysis of the spectral data.

The IR spectrum of **1** exhibited absorption bands for aromatic ring (1590, 1569 and 1531 cm^{-1}) and carbonyl group (1700 cm^{-1}). Its UV spectrum showed characteristic absorption bands at λ_{max} (log ε): 220 (4.12), 253 (4.72), 340 (3.32) and 355 (3.29) nm, which was similar to those of balfourodine, a kind of 4-quinolinone-related compound [3], revealing the presence of a 4-quinolinone skeleton in the molecule. This was further confirmed by the chemical shift of 4-carbonyl group at δ 173.5 in the ^{13}C NMR spectrum [4]. The signals for aromatic protons at δ 8.15 (J = 7.6, 1.4 Hz), 7.76, 7.64 (J = 7.5, 1.4 Hz) and 7.37 in the ^1H NMR spectrum revealed a 2,3-disubstituted pattern for 4-quinolinone by comparison with the data of a 4-quinolinone-related compound [4]. Analysis of the ^1H–^{13}C COSY spectrum of **1** suggested that the protons at δ 1.13 and 2.31 were linked to the carbon at δ 28.9, δ 4.63 to δ 61.9, δ 2.26 (2H) to δ 29.1, δ 3.46 and 3.27 to δ 41.6. The ^1H–^1H COSY spectra further indicated the presence of the fragment, —CH_2—CH—CH_2—CH_2—, starting from the correlations of H-6 (δ 2.31 and 1.13) with H-5 (δ 4.63), H-5 (δ 4.63) with H-4 (δ 2.26) and H-4 (δ 2.26) with H-3 (δ 3.27 and 3.47). The connectivities of C-7-C-6a-C-6 -C-5-C-4-C-3-C-2 were also established by the HMBC correlations of H-6/C-7 and H-4, H-5/C-2. There was only one nitrogen atom left which should be connected with C-12a, C-5 and C-2. H-6α (δ 2.31) was located at the deshielding zone of C-7 carbonyl group and shifted the down field in the ^1H NMR spectrum, otherwise, the chemical shifts of H-6α and H-6β should display smaller difference [5, 6]. A significant cross peak between H-5 and H-6α was observed in the NOESY spectrum, indicating that the two protons were located at the same side of the ring, this was consistent with the stereochemistry of pyrrolizidine alkaloids, namely the *cis*-(N-1 electrons and H-5 syn) fused rings [7]. From the structure of **1**, the formation of intramolecular hydrogen bond between the carbonyl group of C-2 amide and the proton bearing N-12 was evident from the ^1H NMR signal for the H-12 at δ 12.61. Based on the above data, the structure of **1** was determined as 12-hydro-2-oxo-pyrrolizidino[2,3-b]quinolin-7 (2H)-one, named chestnutamide.

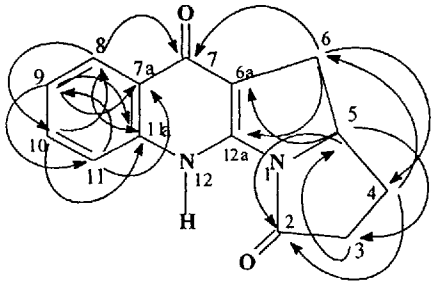

FIGURE 1a The key HMBC correlations for **1**.

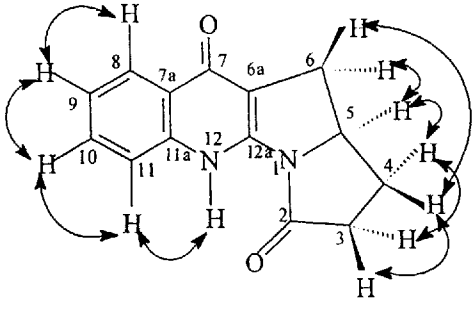

FIGURE 1b The key NOESY correlations for **1**.

EXPERIMENTAL SECTION

General Experimental Procedures

Melting points were determined on a WL-1 capillary melting point apparatus and are uncorrected. UV spectra were obtained on a Shimadzu UV-2201 instrument. IR spectra were recorded on a Perkin-Elmer 983 FT infrared spectrometer. Optical rotation was measured on Perkin Elmer 241 polarimeter. NMR spectra were run on a Bruker AM 500 with TMS as internal standard, EIMS and HREIMS were obtained on a ZAB-2F mass spectrometer, FABMS were performed on Zabspec E mass spectrometer.

Plant Material

The flowers of *Castanea mollissima* Blume were collected in Fei county, Shandong Province, China, in June, 1996 and identified by Dr. Jun-Bo Xin.

A voucher specimen is deposited in the herbarium of Department of Botany, China Pharmaceutical University.

Extraction and Isolation

Dry flowers (6.0 kg) were ground into crude powder and extracted with C_2H_5OH to afford 620 g of a residue on removal of solvent. The ethanolic extract was suspended in water and then partitioned with petroleum ether, chloroform, ethyl acetate and *n*-butanol successively. The $CHCl_3$ residue (157.0 g) was repeatedly subjected to Si gel column chromatography and eluted with a gradient of $CHCl_3$–MeOH (95 : 5 to give **1** (50 mg).

Chestnutamide (1)

m p 178°C; $[\alpha]_D^{25} = -0.016$ (*c* 0.250, $CHCl_3$); UV (MeOH) λ_{max} (log ε): 220 (4.12), 253 (4.72), 340 (3.32), 355 (3.29) nm; IR(KBr) ν_{max}: 3070, 3016, 2933, 2886, 1700, 1627, 1590, 1569, 1531, 1470, 1389, 1224, 1200, 1182, 1155, 909, 790, 768, 694; ^{1}H and ^{13}C NMR data see Table I. HREIMS *m/z*: 240.0903 $[M]^+$ (calcd for $C_{14}H_{12}N_2O_2$, 240.0898); EIMS *m/z*: 240, 211, 184, 170, 156, 142, 115, 92, 77, 63, 51, 41.

TABLE I NMR spectral data for compound **1** in $CDCl_3$

Position	^{13}C *NMR(ppm)*	^{1}H *NMR(ppm J in Hz)*	^{1}H–^{1}H *COSY*	*HMBC*
2	166.3			
3	41.6	3.27 dd (17.6, 8.5)	H-3, H-4	C-2, C-4, C-5
		3.46 dd (17.6, 8.5)	H-3, H-4	C-2, C-4, C-5
4	29.1	2.26 m	H-3, H-5	C-2, C-3, C-5, C-6
5	61.9	4.63 m	H-6, H-4	C-3, C-4, C-6, C-12a, C-6a
6	28.9	2.31 dd (15.3, 8.6)	H-6, H-5	C-6a, C-7, C-12a, C-5, C-4
		1.13 dd (15.3, 3.5)	H-6, H-5	C-6a, C-7, C-12a, C-5, C-4
6a	141.3			
7	173.5			
7a	125.0			
8	125.5	8.15 dd (7.6, 1.4)	H-9, H-10	C-7, C-7a, C-9, C-10, C-11a
9	123.7	7.37 m	H-8, H-10, H-11	C-7a, C-8, C-10, C-11
10	119.5	7.76 m	H-8, H-9, H-11	C-8, C-9, C-11, C-11a
11	132.2	7.64 dd (7.5, 1.4)	H-9, H-10	C-7a, C-9, C-10, C-11a
11a	126.5			
12		12.61		
12a	140.4			

Acknowledgments

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