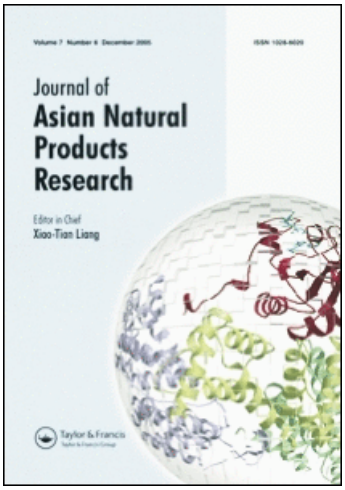

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A new indole alkaloid from *Arundo donax* L.

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A new indole alkaloid, named donasine, has been isolated from the rhizomes of *Arundo donax* L. Its structure was determined by X-ray crystallographic analysis and spectral methods. The primary pharmacological test showed that the compound has an action of reducing fever.

Keywords: Donasine; Indole alkaloid; *Arundo donax* L.; Action of reducing fever

1. Introduction

The plant of *Arundo donax* L. belongs to the family Gramineae, and is widely distributed in the southwest, south and east area of China. The rhizomes of *A. donax* can be used as a kind of antifebrile and diuretic medicine for the treatment of toothache, headache and high fever [1]. It was reported that several kinds of indole alkaloids have been isolated from *A. donax* [2–4]. A new alkaloid, donasine (**1**), has been isolated from the rhizomes of this plant. The structure of **1** was determined by X-ray crystallographic analysis and spectral methods, including 1D and 2D NMR techniques. Donasine(**1**) is a bistryptamine alkaloid having a novel framework. Primary pharmacological tests showed that **1** has an effect on reducing fever.

2. Results and discussion

Donasine (**1**) was obtained as a white amorphous powder. The HREIMS of **1** showed a quasi-molecular ion peak at *m/z* 409.2234 $[M + H]^+$, corresponding to the formula of $C_{23}H_{28}N_4O_3$. The X-ray crystal structure of **1** was determined. The result showed that donasine (**1**) is a bistryptamine alkaloid with a chiral carbon at C-17 (figure 1). The UV spectrum of **1** in methanol showed absorption bands at 215 and 265 $\sim$ 290 nm, which were the characteristics of indole ring. The IR spectrum of **1** showed characteristic absorptions of carbonyl (1713 cm^{-1}) and aromatic rings (1508, 1465, 1424, 1386 cm^{-1}). As seen in table 1, the ^1H NMR spectrum of donasine (**1**) suggested the existence of six aromatic protons at δ 6.23

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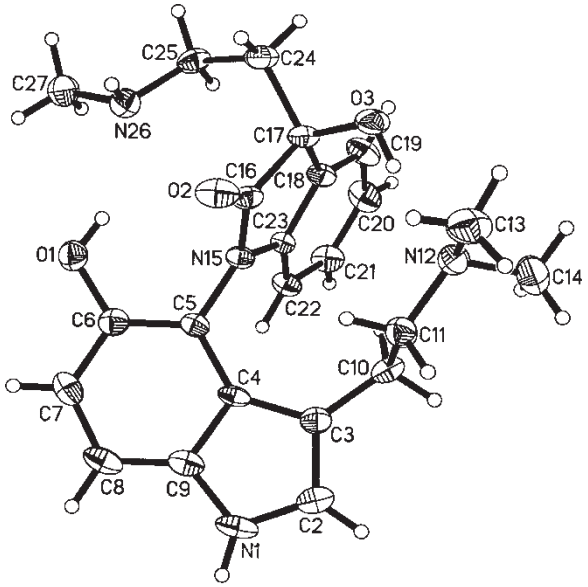

Figure 1. X-ray crystal structure of **1**.

Table 1. NMR spectral data of donasine (**1**) in DMSO-d_6.

No.	δ_H	*Mult* ($J = Hz$)[†]	^1H—^1H *COSY*	δ_C[‡]	*HMBC* ($H \rightarrow C$)
1	10.8	br, s	H-2		C-2, C-3, C-4
2	7.06	d (1.8)	H-1	125.3 d	C-3, C-4
3				111.1 s	
4				132.5 s	
5				124.8 s	
6				147.9 s	
7	7.30	d (8.4)	H-8	113.4 d	C-5, C-6
8	6.80	d (8.4)	H-7	112.2 d	C-4, C-6, C-9
9				110.4 s	
10	2.46	M	H-11	24.7 t	C-2, C-3, C-11
11	1.98	M	H-10	60.4 t	C-3, C-13, C-14
12					
13	1.71	S		44.3 q	C-11, C-14
14	1.71	S		44.3 q	C-11, C-13
15					
16				178.7 s	
17				74.7 s	
18				131.7 s	
19	7.41	d (7.2)	H-20	124.3 d	C-17, C-21, C-23
20	7.08	t (7.2)	H-19, H-21	123.0 d	C-18, C-22
21	7.18	t (7.2)	H-20, H-22	129.5 d	C-19, C-23
22	6.23	d (7.8)	H-21	109.8 d	C-18, C-20, C-23
23				144.2 s	
24	2.08, 2.28	M	H-25	36.3 t	C-16, C-17, C-25
25	2.23, 2.38	M	H-24	47.4 t	C-17, C-27
26					
27	2.11	S		36.5 q	C-25

[†] Multiples: s (single peak), d (double peaks), t (triple peaks);
[‡] Species of Carbon: s (quaternary carbon), d (CH), t (CH_2), q (CH_3).

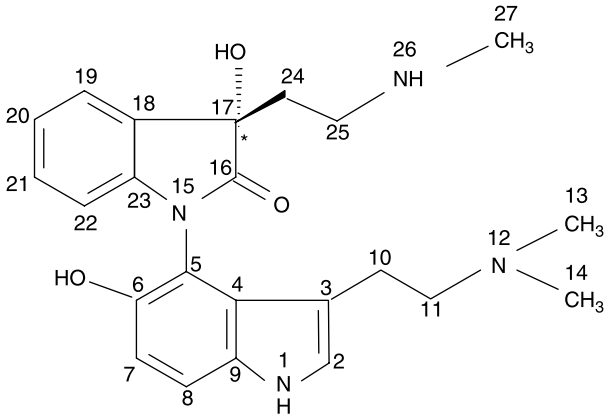

Figure 2. Structure of **1**.

(1H, d, 7.8), 6.80 (1H, d, 8.4), 7.08 (1H, t, 7.2), 7.18 (1H, t, 7.2), 7.30 (1H, d, 8.4) and 7.41 (1H, d, 7.2), in association with six methine carbons at δ 109.8, 112.2, 113.4, 123.0, 124.3, 129.5, and four quaternary carbons at δ 110.4, 131.7, 132.5, 144.2 in ^{13}C NMR spectrum. In the high-field of ^{1}H NMR spectrum, a singlet at δ 1.71 (6H, s) showed the presence of two methyls at N-12, while a singlet at δ 2.11 (3H, s) indicated one methyl group at N-26. The four multiplets at δ 2.46 $\sim$ 1.98 suggested the existence of methylene protons on the side chain of the indole ring. In the low-field of ^{1}H NMR spectrum, a N—H proton signal at δ 10.8 (1H, br, s) was observed. The ^{13}C NMR spectrum of **1** showed signals of a carbonyl carbon at δ 178.7 (C-16), an oxygenated aromatic carbon at δ 147.9 (C-6) and an oxygenated quaternary carbon at δ 74.7 (C-17). In addition, the relationships between H-7 and H-8, as well as H-19, H-20, H-21 and H-22, were established by ^{1}H—^{1}H COSY experiment. The structure of **1** was also supported by its HMBC spectra and it was shown in figure 2.

The pharmacological test demonstrated that the average increased temperature of the control team given **1** was evidently lower than that of the blank team at 0.5 $\sim$ 2 h ($\alpha = 0.10$) after injection. The results are showed in table 2.

3. Experimental

3.1 General experimental procedures

UV spectra were obtained on a GBC Cintra 10e dual-wavelength ultraviolet spectrometer. IR spectra were recorded on a Vector 22 infrared spectrometer. ^{1}H, ^{13}C and 2D NMR spectra

Table 2. Effect of donasine (**1**) on reducing fever ($n = 32$).

		Average increased temperature (°C)					
Effect time (hour)		0.5	1	2	3	4	5
Blank team		0.489	0.365	−0.093	−0.302	0.061	0.479
Control team		−0.313	−0.057	−0.393	−0.343	−0.104	0.514
t-Test ($t_{0.10,30} = 1.70$)	t value	4.75	2.66	1.83	0.18	0.67	0.17
	Conclusion	Evident	Evident	Evident	Not evident	Not evident	Not evident

were recorded on a Bruker Avance 600 MHz NMR instrument, TMS as the internal standard, and DMSO-d_6 as solvent. HREIMS spectra were measured on a BioTOFQ high differentiation MS instrument. Optical rotation was obtained on a PE-M341 polarimeter. X-ray crystal diffraction was obtained on a Siemens P4 quaternary diffractometer, the program used to data collection is *XSCANS* (Siemens, 1994), the program used to solve structure is *SHELXS* (Sheldrick, 1990), and the program used to refine structure is *SHELXL* (Sheldrick, 1997). The temperatures of the rats were measured by MC-3B Electronic Digital Thermometer. Silica gel H (Qingdao Haiyang Chemical Group Co. of China) was used for column chromatography. All other chemicals and solvents were analytical pure. TLC was performed on silica gel G plates (Qingdao Haiyang Chemical Group Co. of China). Spots were visualized by spraying with dilute bismuth potassium iodide solution. 2, 4-dinitrophenol was purchased from Shanghai Third Solvent Plant.

Wistar Rats used in the pharmacological test were purchased from experimental animal center of Sichuan University, which was verified by Sichuan experimental animal administration. The weight of each rat was about 200 g and the male and female were half and half.

3.2 Plant material

The rhizomes of *Arundo donax* L. were identified by Sichuan Province Drug and Food Control Institute. A voucher specimen (No. 03002) has been deposited at West China School of Pharmacy, Sichuan University.

3.3 Extraction and isolation

The powdered rhizomes of *A. donax* (10 kg) were decocted with water for 2 × 2 h. After concentration the decoction was precipitated in 80% of ethanol. The ethanolic filtrate was concentrated and adjusted to pH 10 ~ 11 with ammonia before being extracted by chloroform. The organic phase was separated and evaporated to dryness *in vacuo*. The residue was subjected to column chromatography over silica gel, eluting with a CH_2Cl_2—CH_3OH—$NH_3\,H_2O$ (8:2:0.2). Finally, donasine (**1**, 0.4 g) was obtained by repeated column chromatography and recrystallization.

Donasine (**1**), white amorphous powder, mp 201 ~ 202?; $[\alpha]_D^{20}$ 0 (*c* 0.6, DMSO), UV λ_{max} (CH_3OH) (nm): 215, 265 ~ 290; IR (KBr) ν_{max} (cm^{-1}): 3382, 2934, 2823, 1713, 1612, 1508, 1465, 1424, 1386, 1227, 1202, 1146, 1099, 857, 753; ^{1}H NMR (DMSO-d_6, 600 MHz), see table 1; ^{13}C NMR (DMSO-d_6, 150 MHz), see table 1; HREIMS: *m/z* 409.2234 $[M + H]^+$ (calcd for $C_{23}H_{28}N_4O_3$, 409.2226).

3.4 X-ray crystal structure

A colourless cuboid crystal from CH_2Cl_2—CH_3OH was mounted on a Siemens P_4 four-circle diffractometer and exposed to graphite-monochromated Mo $K\alpha$ radiation. The unit cell parameters are: $a = 16.381(2)$ Å, $b = 15.674(2)$ Å, $c = 16.549(3)$ Å in Orthorhombic, Pca2 (1) ($Z = 8$); $V = 4249.2(1)$ Å^3; $D_x = 1.277$ mg m^{-3}; Cell parameters from 31 reflections; $\theta = 3.57–12.77°$; $\mu = 0.086$ mm^{-1}; $T = 288(2)$ K; 0.50 × 0.34 × 0.30 mm. CCDC: 293677. ω scans; 5585 reflections collected; 5039 independent reflections; 2322 reflections

with $I > 2\sigma(I)$; $R_{int} = 0.0000$; $h = 0 \rightarrow 20$; $k = 0 \rightarrow 20$; $l = -21 \rightarrow 1$. Refinement on F^2; R_1 $[F^2 > 2\sigma(F^2)] = 0.0382$; $wR(F^2) = 0.0457$; $w = 1/[\sigma^2(F_o^2) + (0.0096P)^2]$, where $P = (F_o^2 + 2F_c^2)/3$; $\Delta\rho_{max} = 0.127\,e\text{Å}^{-3}$; $\Delta\rho_{min} = -0.152\,e\text{Å}^{-3}$; Extinction coefficient: 0.00137(7); 572 parameters. The positions of all H atoms on C were fixed geometrically, which C—H distances in the range 0.93–0.97 Å. The H atoms on O1, O3, O1′, O3′, N26, N26′ were located with synthesis of difference Fourier.

3.5 Pharmacological test

In the pharmacological test, all the rats were given 1.25% of 2, 4-dinitrophenol ethanol solution to cause fever. Then, the blank team was given the blank solvent by intramuscular injection and the control team was given the solution of donasine(**1**) with a dose of 0.8 mg/kg by the same means. The anal temperatures of the rats were measured respectively at 0.5,1,2,3,4,5 hours after injections. The distinction between the two teams' mean temperatures after fever was compared by t-Test (table 2).

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