INDOLE ALKALOIDS FROM *Ervatamia flabellformia*

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Ervatamia flabellformia Tsiang (Apocynaceae) [1] is a common plant cultivated in Yunnan and Guanxi provinces of China, and its chemical constituents have not been reported yet. As a part of our continuous research on anti-addictive constituents from the genus Ervatamia [2, 3], thirteen indole alkaloids were isolated from the stems of *Ervatamia flabellformia*.

The stems of *E. flabellformia* were collected in October 2002 in Xishuangbanna, Yunnan province and identified by senior engineer Wang Hong, Xishuangbanna Tropical Botanic Garden of the Chinese Academy of Science. A voucher specimen (No. 200210-1) has been deposited in the Herbarium of the School of Pharmacy, Second Military Medical University, Shanghai.

The air-dried and powdered stems (12 kg) were extracted with 95% EtOH (50 L) under reflux. After removal of EtOH by evaporation under reduced pressure, the residues were extracted with 2% HCl. The aqueous layer was basified with NH_4OH and partitioned with $CHCl_3$. The $CHCl_3$ layer was dried over Na_2SO_4 and evaporated under reduced pressure to give 45 g of crude alkaloid fraction, which was submitted to repeated column chromatography over silica gel and Sephadex LH20 (MeOH) to yield 13 indole alkaloids.

All compounds were identified by spectroscopic methods, including NMR and mass spectrometry (NMR spectra were acquired on a Bruker DRX-500 spectrometer with TMS as internal standard, operating at 500 MHz for ^1H and ^{13}C; ESIMS data were obtained on a Q-Tof micro mass spectrometer; silica gel H (10–40 μm) for column chromatography and HPTLC plates precoated with silica gel HF_{254} (5–7 μm) were supplied by Zhifu Huangwu Silica Gel D & R Plant, Yantai, China; Sephadex LH-20 and ODS were purchased from Pharmacia and Merck, respectively. The spectroscopic data of all compounds were in good agreement with the literature data [4–14]. All these structures are isolated from *E. flabellformia* for the first time.

Dihydroperivine (1), colorless cubic crystal (methyl acetate), $C_{20}H_{24}N_2O_3$. ^1H and ^{13}C NMR data are shown in Tables 1 and 3 [4].

3-(*R*)-Hydroxyvoacangine (2), white powder, $C_{22}H_{28}N_2O_4$. EI-MS *m/z* (%): 368 (M^+, 16), 366 (18), 339 (7), 353 (24), 370 (11), 244 (38), 225 (31), 185 (33), 124 (22). ^1H and ^{13}C NMR data are shown in Tables 1 and 3 [5].

19-Heyneanine (3), white powder, $C_{21}H_{26}N_2O_3$. EI-MS *m/z* (%): 354 (M^+, 100), 339 (67), 309 (18), 253 (10), 214 (42), 195 (15), 168 (18), 140 (31), 130 (20), 94 (38). ^1H and ^{13}C NMR data are shown in Tables 1 and 3 [6, 7].

Ibogaine (4), yellow powder, $C_{20}H_{26}N_2O$. EI-MS *m/z* (%): 310 (M^+, 68), 295 (9), 280 (12), 225 (41), 186 (10), 149 (40), 136 (100), 135 (80), 122 (51). ^1H and ^{13}C NMR data are shown in Tables 1 and 3 [8].

Coronaridine hydroxyindolenine (5), white powder, $C_{21}H_{26}N_2O_3$. EI-MS *m/z* (%): 354 (M^+, 82), 337 (100), 325 (9), 295 (12), 230 (10), 244 (47), 188 (16), 161 (22), 136 (12), 122 (15), 108 (10). ^1H and ^{13}C NMR data are shown in Tables 1 and 3 [6, 9].

Voacangine hydroxyindolenine (6), white powder, $C_{22}H_{28}N_2O_4$. EI-MS *m/z* (%): 384 (M^+, 93), 367 (100), 190 (43), 122 (49), 55 (45), 44 (53), 42 (55), 41 (77). ^1H and ^{13}C NMR data are shown in Tables 2 and 3 [10].

19,20-Dehydroervatamine (7), white powder, $C_{21}H_{24}N_2O_3$. ESI *m/z*: 352 (M^+). ^1H and ^{13}C NMR data are shown in Tables 2 and 3 [11].

(–)-Hecubine (8), white powder, $C_{20}H_{26}N_2O$. ESI m/z: 310 (M^+). ^1H and ^{13}C NMR data are shown in Tables 2 and 3 [12].

(–)-Mehranine (9), white powder, $C_{20}H_{26}N_2O$. EI-MS *m/z* (%): 310 (M^+, 89), 166 (31), 158 (67), 144 (100), 108 (62), 42 (35), 41 (36). ^1H and ^{13}C NMR data are shown in Tables 2 and 3 [12].

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TABLE 1. ^{1}H NMR Data for Compounds **1-5** (δ, ppm, J/Hz)

C atom	**1**[b]	**2**[a]	**3**[b]	**4**[c]	**5**[b]
3		4.01 d (J = 8)	3.00 m	2.95 m	2.48 m
			2.80 d (J = 9.0)		2.97 dd (J = 15, 4)
5	3.92 m	3.21 m	3.17 m	3.23 m	3.52 m
		3.39 m	3.42 m	3.02 m	
6	3.34 m	3.00 dd (J = 16, 1)	3.12 m	3.23 m	2.75 m
	3.25 m	3.15 m		2.51 m	
9	7.70 d (J = 8)	6.93 d (J = 2)	7.47 d (J = 8)	6.86 d (J = 1.5)	7.46 d (J = 8)
10	7.09 t (J = 8)		7.07 t (J = 8)		7.23 t (J = 8)
11	7.29 t (J = 8)	6.82 dd (J = 8, 2)	7.17 t (J = 8)	6.62 dd (J = 9.5, 1.5)	7.31 t (J = 8)
12	7.38 d (J = 8)	7.15 d (J = 8)	7.26 d (J = 8)	7.10 d (J = 9.5)	7.34 d (J = 8)
14	2.86 m	1.88 m	1.96 m	1.77 m	1.84 m
15	2.68 m	1.12 dd (J = 10, 7)	1.78 m	1.09 d (J = 12)	1.10 m
		1.73 t (J = 10)	1.83 m	1.77 m	1.78 m
16	2.84 m			2.87 m	
17		1.90 m	2.04 dd (J = 12, 2)	2.02 m	1.91 m
		2.68 dd (J = 12, 2)	2.60 d (J = 12)	1.37-1.50 m	2.01 d (J = 12)
18	0.96 t (J = 7.5)	0.91 s	1.26 d (J = 6)	0.86 t (J = 7)	0.87 t (J = 7)
19	1.22 m	1.45 m	3.90 dq (J = 6, 3)	1.37-1.50 m	1.48 m
	1.66 m	1.58 m			
20	1.22 m	1.32 m	1.42 m	1.37-1.50 m	1.41 m
21	2.36 d (J = 13, 6)	3.87 s	4.10 s	2.72 br	3.81 s
	2.66 m				
$COOCH_3$		3.71 s			3.68 s
OCH_3	2.61 s	3.83 s	3.73 s	3.74 s	
N-H		7.69 s		10.35 s	

[a]Solution in $CDCl_3$; [b]solution in CD_3OD; [c]solution in DMSO-d_6.

Ervadivaricatine A (10), yellow powder, $C_{43}H_{54}N_4O_{45}$. ESI *m/z*: 706 (M^+); ^{1}H NMR ($CDCl_3$, δ, ppm, J/Hz): 0.82 (3H, t, J = 7.5), 0.96 (3H, t, J = 7), 2.43 (3H, s), 2.63 (3H, s), 3.64 (3H, s), 3.98 (3H, s), 5.08 (1H, s), 6.69 (1H, s), 6.92 (1H, s), 7.04 (3H, m), 7.48 (2H, m), 7.69 (1H, s). ^{13}C NMR data are shown in Table 4 [13].

Ervadivaricatine B (11), yellow powder, $C_{43}H_{54}N_4O_5$. ESI *m/z*: 706 (M^+); ^{1}H NMR ($CDCl_3$, δ, ppm, J/Hz): 0.86 (3H, t, J = 7.5), 0.94 (3H, t, J = 7), 2.42 (3H, s), 2.69 (3H, s), 3.63 (3H, s), 3.96 (3H, s), 5.07 (1H, s), 6.70 (1H, s), 6.90 (1H, s), 7.03 (3H, m), 7.44–7.56 (3H, m). ^{13}C NMR data are shown in Table 4 [13].

Ervahanine A (12), yellow powder, $C_{42}H_{50}N_4O_4$. ESI *m/z*: 704 (M^+); ^{1}H NMR ($CDCl_3$, δ, ppm, J/Hz): 0.82 (3H, t, J = 7.5), 1.67 (3H, d, J = 7), 2.53 (3H, s), 2.63 (3H, s), 3.64 (3H, s), 5.32 (2H, q, J = 7.5), 6.96 (1H, dd, J = 8, 1), 6.99 (1H, s), 7.04 (3H, m), 7.35 (1H, d, J = 8), 7.56 (1H, dd, J = 8, 1). ^{13}C NMR data are shown in Table 4 [14].

Conodurine (13), yellow powder, $C_{43}H_{52}N_4O_5$. ESI *m/z*: 674 (M^+); ^{1}H NMR ($CDCl_3$, δ, ppm, J/Hz): 0.81 (3H, d, J = 7.5), 2.47 (3H, s), 2.63 (3H, s), 3.64 (3H, s), 3.97 (3H, s), 5.32 (2H, m), 6.82 (1H, d, J = 8.5), 7.01–7.16 (3H, m), 7.24 (1H, d, J = 8.5), 7.70 (1H, d, J = 8.5). ^{13}C NMR data are shown in Table 4 [14].

TABLE 2. ^{1}H NMR Data for Compounds **6-9** (δ, ppm, J/Hz)

C atom	**6** (CD_3OD)	**7** ($CDCl_3$)	**8** ($CDCl_3$)	**9** (DMSO-d_6)
2				3.28 m
3	2.72 s		A: 2.67 d (J = 12)	A: 2.31 d (J = 13)
			B: 3.28 (J = 12)	B: 3.35 d (J = 13)
5	A: 2.95 m	A: 2.28 d (J = 12)	A: 2.37 dt (J = 13, 5)	A: 2.15 m
	B: 3.48 m	B: 3.46 br.d (J = 12)	B: 2.60 dt (J = 13, 3.5)	B: 3.01 m
6	A: 1.86 m	A: 2.90 d (J = 16)	2.87 m	A: 1.44 m
	B: 1.94 m	B: 3.64 d (J = 16)		B: 2.15 m
9	6.90 d (J = 2.5)	7.61 d (J = 8)	7.45 d (J = 7)	6.57 t (J = 7)
10		7.17 ddd (J = 8, 7, 1)	7.07 t (J = 7)	6.38 d (J = 7)
11	6.80 dd (J = 2.5, 8)	7.35 ddd (J = 8, 7, 1)	7.15 t (J = 7)	7.00 m
12	7.34 d (J = 8)	7.44 d (J = 8)	7.26 d (J = 7)	7.00 m
14	1.90 br	A: 2.48 dd (J = 16, 11)	3.13 m	3.22 m
		B: 3.11 d (J = 16)		
15	A: 1.08 m	3.56 dd (J = 11,4)	2.92 dd (J = 4, 1)	2.85 d (J = 4)
	B: 1.71 m			
16			A: 2.78 m	A: 0.98 m
			B: 4.20 t (J = 14.5)	B: 1.72 m
17	A: 2.47 d (J = 12)		A: 1.73 d (J = 14)	A: 1.25 m
	B: 2.70 m		B: 2.22 m	B: 1.64 m
18	0.86 t (J = 7)	1.62 dd (J = 7, 2)	0.75 t (J = 7.5)	0.75 t (J = 7)
19	1.41 m	5.47 q (J = 7)	1.15 m	1.15 m
20	1.41 m			
21	3.76 s	A: 2.65 d (J = 12)	A: 1.75 d (J = 12)	2.27 s
		B: 3.12 D (J = 12)	B: 2.52 d (J = 12)	
$COOOCH_3$	3.70 s	3.61 s		
OCH_3	3.81 s			
NCH_3		2.33 s	3.71 s	2.68 s
N-H		9.12 s		

TABLE 3. ^{13}C NMR Data for Compounds **1-9** (δ, ppm)

C atom	**1**[b]	**2**[a]	**3**[b]	4[c]	**5**[b]	**6**[b]	**7**[a]	**8**[a]	**9**[c]
2	135.2	137.6	136.1	143.4	189.6	186.9	132.8	140.8	72.01
3	193.6	95.8	51.0	49.7	49.1	48.7	193.6	53.8	52.42
5	51.4	51.2	52.3	54.1	49.5	49.1	61.0	53.6	52.12
6	24.4	21.8	22.0	20.2	34.3	34.2	31.9	26.3	40.61
7	121.8	109.8	110.1	107.4	88.8	88.3	119.5	109.3	50.95
8	129.4	128.7	128.9	129.5	143.1	144.4	127.3	127.8	136.33
9	121.8	100.6	118.8	99.8	121.7	108.0	120.2	117.6	121.32
10	121.1	154.0	119.8	152.9	121.2	159.2	120.6	118.5	116.80
11	127.4	112.0	128.9	109.5	129.5	113.7	126.5	120.3	127.38
12	113.3	111.2	110.8	110.7	127.1	121.3	112.3	108.5	106.30
13	138.6	130.6	135.9	129.5	151.8	144.8	136.8	136.9	149.99
14	40.2	29.9	27.4	26.0	27.4	27.0	43.9	52.4	52.12
15	32.4	24.9	29.0	31.8	32.4	32.1	34.2	59.4	56.00
16	50.2	54.1	54.3	40.2	59.12	58.6	49.3	21.0	19.68
17		35.5	37.1	34.1	35.2	34.6	12.6	35.3	23.10
18	11.4	11.6	22.6	11.7	11.9	11.5	121.7	7.5	7.16
19	26.9	26.6	71.2	27.5	27.0	26.5	136.0	32.5	27.04
20	45.7	37.7	40.1	41.4	38.0	37.6	61.5	33.8	34.14
21	40.8	55.5	53.1	56.8	53.4	58.5	175.3	58.1	66.33
22	172.8	174.8	175.3		174.0	173.9			
$COOCH_3$		52.7	54.6		58.7	53.2	52.5		
OCH_3	50.8	56.2		55.3		55.7			
NCH_3								30.0	31.11

[a]Solution in $CDCl_3$; [b]solution in CD_3OD; [c]solution in DMSO-d_6.

TABLE 4. ^{13}C NMR Data for Compounds **10-13** ($CDCl_3$, δ, ppm,)

C atom	**10**	**11**	**12**	**13**	C atom	**10**	**11**	**12**	**13**
2	135.8	136.0	137.4	136.1	2′	130.3	130.7	136.6	136.1
3	38.9	38.1	45.4	35.3	3′	36.4	33.3	51.9	51.4
5	59.6	59.5	60.0	59.8	5′	53.1	53.2	53.2	52.5
6	18.0	19.4	19.3	19.4	6′	22.2	22.3	22.3	22.1
7	110.4	110.8	110.4	109.1	7′	109.9	110.0	110.1	110.0
8	129.6	130.0	129.8	129.5	8′	130.0	130.7	127.6	124.5
9	117.3	117.4	117.4	118.1	9′	99.2	99.8	118.8	117.2
10	119.0	118.8	119.2	119.5	10′	150.8	151.3	119.6	105.2
11	121.6	121.4	121.7	122.2	11′	127.4	127.4	140.1	152.2
12	109.7	109.7	109.9	109.8	12′	110.0	110.4	109.4	114.5
13	137.2	137.4	136.1	136.7	13′	138.0	137.8	135.7	135.2
14	39.0	39.0	39.4	33.7	14′	27.3	27.5	27.3	27.2
15	34.3	32.1	33.8	33.5	15′	31.9	31.5	32.2	31.8
16	43.1	49.6	47.2	47.3	16′	54.9	55.0	55.2	54.8
17					17′	51.9	52.2	36.5	34.8
18	12.8	11.5	12.5	12.3	18′	11.6	11.3	11.6	11.8
19	25.5	23.6	118.7	118.7	19′	26.7	26.8	26.6	26.6
20	42.8	43.9	137.7	137.7	20′	38.9	36.5	39.2	39.1
21	47.2	49.9	52.6	52.7	21′	57.1	57.0	57.1	57.7
22	171.5	171.7	171.9	171.9	22′	175.2	175.1	175.5	175.1
$N\text{-}CH_3$	49.9	49.9	42.3	42.3	$COOCH_3$	52.4	52.2	52.6	52.4
$COOCH_3$	42.6	42.5	49.9	49.9	OCH_3	56.1	56.2		57.0

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