海南狗牙花的生物碱化学成分研究

张东博[1]，杨 勇[1]，宋忠兴[1]，孙 萌[2]，李啟恩[3]，唐志书[1*]

1. 陕西中医药大学/陕西省中药资源产业化协同创新中心/陕西省中药基础与新药研究重点实验室/陕西省风湿与肿瘤类中药制剂工程技术研究中心，陕西 咸阳 712083
2. 兰州大学 功能有机分子化学国家重点实验室，甘肃 兰州 730000
3. 青海大学藏医学院，青海 西宁 810001

摘 要：目的 对海南狗牙花 *Ervatamia hainanensis* 的生物碱化学成分进行研究。**方法** 采用硅胶、Sephadex LH-20、MCI 以及半制备 HPLC 等色谱方法进行分离纯化，根据理化性质和现代波谱学技术鉴定化合物的结构。**结果** 从海南狗牙花甲醇提取物中分离得到 12 个生物碱，分别鉴定为冠狗牙花碱（**1**）、19-表海尼山辣椒碱（**2**）、9,10-二甲氧基冠狗牙花碱（**3**）、老刺木碱（**4**）、老刺木碱-4-氮氧化物（**5**）、3-oxo-19-*epi*-heyneanine（**6**）、劲直胺（**7**）、deacetylakuammiline（**8**）、pandine（**9**）、rhazicine（**10**）、rhazicine *N*(4)-oxide（**11**）、rhazimine（**12**）。**结论** 化合物 **8**、**10**～**12** 为首次从该属植物中分离得到，化合物 **3**、**5**～**7** 为首次从该植物中分离得到。

关键词：夹竹桃科；狗牙花属；海南狗牙花；单萜吲哚生物碱；喹啉生物碱；9,10-二甲氧基冠狗牙花碱

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Study on alkaloids from *Ervatamia hainanensis*

ZHANG Dong-bo[1], YANG Yong[1], SONG Zhong-xing[1], SUN Meng[2], LI Qi-en[3], TANG Zhi-shu[1]

1. Shaanxi University of Chinese Medicine/Shaanxi Collaborative Innovation Center of Chinese Medicinal Resource Industrialization/Shaanxi Province Key Laboratory of New Drugs and Chinese Medicine Foundation Research/Shaanxi Rheumatism and Tumor Center of TCM Engineering Technology Research, Xianyang 712083, China
2. State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, China
3. College of Tibetan Medicine, Qinghai University, Xining 810001, China

Abstract: Objective To study the alkaloids from *Ervatamia hainanensis*. **Methods** The alkaloids were isolated and purified by silica gel, MCI, Sephadex LH-20 column chromatography, and semi-preparative HPLC, and their structures were elucidated by physical and spectroscopic analysis. **Results** Twelve alkaloids were obtained and identified as coronaridine (**1**), 19-*epi*-heyneanine (**2**), 9,10-dimethoxycoronaridine (**3**), vobasine (**4**), vobasine *N*(4)-oxide (**5**), 3-oxo-19-*epi*-heyneanine (**6**), strictamine (**7**), deacetylakuammiline (**8**), pandine (**9**), rhazicine (**10**), rhazicine *N*(4)-oxide (**11**), and rhazimine (**12**). **Conclusion** Compounds **8** and **10**—**12** are isolated from the genus *Ervatamia* Stapf for the first time, while compounds **3** and **5**—**7** are firstly obtained from *E. hainanensis*.

Key words: Apocynaceae; *Ervatamia* Stapf; *Ervatamia hainanensis* Tsiang; monoterpenoid indole alkaloids; quinoline alkaloids; 9,10-dimethoxycoronaridine

海南狗牙花 *Ervatamia hainanensis* Tsiang 为夹竹桃科（Apocynaceae）狗牙花属 *Ervatamia* Stapf 植物，又名单根木、山辣椒树、独根木、鸡爪花，产于海南、广东、广西和云南等省区，生于海拔 100～530 m 的山地疏密林中。其根药用，降压疗效比萝芙木还要好，海南民间用于治疗毒蛇咬伤、风湿骨痛、跌打瘀肿、乳痈、疖肿等疾病[1]。植物化学和药理学研究表明海南狗牙花富含骨架结构多变的吲哚类生物碱，其具有降压、抗肿瘤、抗乙酰胆碱酯酶、戒毒等多种活性，一直以来是研究的热点[2-7]。

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作者简介：张东博（1982—），男，陕西咸阳人，讲师，博士，主要从事中药及天然产物化学研究。Tel: 18391829787 E-mail: symensu@163.com

*通信作者 唐志书（1972—），男，博士，教授，硕士生导师，主要从事中药高新制备技术应用研究，中药资源开发与综合利用研究。E-mail: tzs6565@163.com

本课题组在对海南狗牙花抗炎活性实验中发现，该植物的生物碱提取物具有显著的抗炎活性。为进一步阐明其药效物质基础，本实验对海南狗牙花的总生物碱提取物进行了系统化学成分的研究，从中分离得到 12 个生物碱单体，根据理化性质和波谱学分析进行了结构鉴定，包括 5 个依波格类单萜吲哚生物碱：冠狗牙花碱（coronaridine，**1**）、19-表海尼山辣椒碱（19-*epi*-heyneanine，**2**）、9,10-二甲氧基冠狗牙花碱（9,10-dimethoxycoronaridine，**3**）、3-oxo-19-*epi*-heyneanine（**6**）、pandine（**9**）；4 个柯南因-士的宁类单萜吲哚生物碱：老刺木碱（vobasine，**4**）、老刺木碱-4-氮氧化物 [vobasine *N*(4)-oxide，**5**]、劲直胺（strictamine，**7**）、deacetylakuammiline（**8**）；3 个喹啉类生物碱：rhazicine（**10**）、rhazicine *N*(4)-oxide（**11**）、rhazimine（**12**）。化合物 **8**、**10**～**12** 为首次从该属植物中分离得到，化合物 **3**、**5**～**7** 为首次从该植物中分离得到。尤其值得注意是，本研究首次报道喹啉生物碱（**10**～**12**）和单萜吲哚生物碱（**1**～**9**）同时存在于海南狗牙花中，这从化学成分的角度进一步支持了喹啉生物碱可源于单萜吲哚生物碱的生源途径[8-9]。

1 材料与仪器

Varian Mercury plus-400 和 Varian Mercury-600 型核磁共振仪（德国 Bruker 公司）；Waters 高效液相色谱仪 1525EF（美国 Waters 公司）；HPLC 半制备柱（250 mm×10 mm，5 μm，美国 Waters 公司）；HP5988A GCMS spectrometer 型质谱仪（安捷伦公司）；薄层色谱硅胶 GF_{254} 和柱色谱硅胶（200～300 目，中国青岛海洋化工）；MCI 树脂（日本 Mitsubishi 公司）；Sephadex LH-20 凝胶（美国 Amersham Biosciences 公司）；ODS 柱色谱材料（C_{18}，日本 YMC 公司）；其他试剂均为分析或色谱纯。

海南狗牙花于 2009 年 7 月采自于海南省屯昌县，植物样品由海南师范大学高级工程师钟琼芯教授鉴定为海南狗牙花 *Ervatamia hainanensis* Tsiang 的枝叶，植物标本（2009021）现保存于兰州大学天然有机研究室。

2 提取与分离

干燥海南狗牙花的枝叶 5.9 kg，粉碎后用工业甲醇于室温下冷浸提取 4 次，每次冷浸 7 d。提取液减压浓缩得浸膏 580 g。将提取浸膏分散于蒸馏水中，用 2%的 HC1 水溶液调 pH 2～3，用等体积的醋酸乙酯萃取 3 次后，水相用 10%的氨水溶液调至 pH 9～10，用等体积的氯仿萃取 3 次，回收氯仿后得到生物碱总浸膏 6.3 g。将生物碱总浸膏（6.3 g）通过 MCI 凝胶柱，用水-甲醇（1∶0→0∶1）梯度洗脱，得到共 8 个流分（Fr. 1～8）。Fr. 7（1.2 g）经反复 Sephadex LH-20 柱色谱分离纯化得到化合物 **1**（30.8 mg）、**11**（4.8 mg）、**12**（6.2 mg）和流分 Fr. 7A；流分 Fr. 7A（0.4 g）经硅胶柱色谱分离，石油醚-丙酮（4∶1）等度洗脱得到化合物 **7**（1.9 mg）。流分 Fr. 6（1.8 g）经硅胶柱色谱分离，石油醚-氯仿-醋酸乙酯-二乙胺（4∶1∶1∶0.006）等度洗脱得到化合物 **2**（9.8 mg）、**9**（10.2 mg）和流分 Fr. 6A（0.35 g）；流分 Fr. 6A（0.35 g）经 Sephadex LH-20（氯仿-甲醇）柱色谱反复分离纯化得到化合物 **3**（1.2 mg）、**4**（7.2 mg）和流分 Fr. 6A1；流分 Fr. 6A1（0.15 g）经半制备高效液相色谱，以乙腈-水（70∶30）为流动相，得到化合物 **5**（1.9 mg）。Fr. 5（0.1 g）经过 ODS 柱色谱，以水-甲醇（7∶3→2∶8）梯度洗脱，得化合物 **8**（2.6 mg）。Fr. 4（0.7 g）经过 ODS 柱色谱，以水-甲醇（7∶3→2∶8）梯度洗脱，得化合物 **6**（2.8 mg）和 **10**（6.3 mg）。

3 结构鉴定

化合物 **1**：白色粉末，易溶于氯仿、甲醇，碘化铋钾反应阳性；$C_{21}H_{26}N_2O_2$，EI-MS *m/z*: 338 $[M]^+$；^{1}H-NMR (400 MHz, $CDCl_3$) δ: 2.95 (1H, d, J = 8.4 Hz, H-3a), 2.84 (1H, d, J = 8.4 Hz, H-3b), 3.44 (1H, m, H-5a), 3.25 (1H, m, H-5b), 3.24 (1H, m, H-6a), 3.08 (1H, m, H-6b), 7.53 (1H, d, J = 7.6 Hz, H-9), 7.14 (1H, dd, J = 8.0, 7.6 Hz, H-10), 7.17 (1H, dd, J = 8.0, 7.6 Hz, H-11), 7.28 (1H, d, J = 7.6 Hz, H-12), 1.93 (1H, m, H-14), 1.80 (1H, m, H-15a), 1.19 (1H, m, H-15b), 2.64 (1H, d, J = 12.6 Hz, H-17a), 1.95 (1H, dd, J = 12.6, 2.0 Hz, H-17b), 0.97 (3H, t, J = 6.8 Hz, H-18), 1.61 (1H, m, H-19a), 1.51 (1H, m, H-19b), 1.38 (1H, m, H-20), 3.61 (1H, brs, H-21), 3.75 (3H, s, COOMe)；^{13}C-NMR (100 MHz, $CDCl_3$) δ: 136.7 (C-2), 51.6 (C-3), 53.2 (C-5), 22.2 (C-6), 110.3 (C-7), 128.9 (C-8), 118.5 (C-9), 119.3 (C-10), 122.0 (C-11), 110.4 (C-12), 135.5 (C-13), 27.4 (C-14), 32.1 (C-15), 55.2 (C-16), 36.5 (C-17), 11.7 (C-18), 26.8 (C-19), 39.2 (C-20), 57.5 (C-21), 52.7 (COOMe), 175.7 (COOMe)。以上数据与文献报道一致[10]，故将化合物 **1** 鉴定为冠狗牙花碱。

化合物 **2**：白色粉末，易溶于氯仿、甲醇，碘

化铋钾反应阳性；$C_{21}H_{26}N_2O_3$，EI-MS *m/z*: 354 $[M]^+$；^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.02 (1H, m, H-3a), 2.78 (1H, d, *J* = 9.0 Hz, H-3b), 3.50 (1H, m, H-5a), 3.19 (1H, m, H-5b), 3.13 (2H, m, H-6), 7.51 (1H, d, *J* = 8.0 Hz, H-9), 7.13 (1H, t, *J* = 8.0 Hz, H-10), 7.20 (1H, t, *J* = 8.0 Hz, H-11), 7.29 (1H, d, *J* = 8.0 Hz, H-12), 2.01 (1H, m, H-14), 1.94 (1H, m, H-15a), 1.60 (1H, m, H-15b), 2.67 (1H, d, *J* = 12.0 Hz, H-17a), 2.04 (1H, m, H-17b), 1.16 (3H, d, *J* = 6.0 Hz, H-18), 4.22 (1H, dq, *J* = 6.0, 3.0 Hz, H-19), 1.52 (1H, m, H-20), 3.91 (1H, brs, H-21), 3.77 (3H, s, COOMe)；^{13}C-NMR (100 MHz, $CDCl_3$) δ: 135.8 (C-2), 51.2 (C-3), 52.1 (C-5), 21.4 (C-6), 109.6 (C-7), 128.3 (C-8), 118.3 (C-9), 119.3 (C-10), 122.1 (C-11), 110.8 (C-12), 135.5 (C-13), 26.7 (C-14), 22.8 (C-15), 54.0 (C-16), 36.8 (C-17), 20.3 (C-18), 71.3 (C-19), 39.4 (C-20), 59.7 (C-21), 52.8 (COOMe), 174.8 (COOMe)。以上数据与文献报道一致[11]，故将化合物 **2** 鉴定为 19-表海尼山辣椒碱。

化合物 **3**：白色粉末，易溶于氯仿，碘化铋钾反应阳性；$C_{23}H_{30}N_2O_4$，EI-MS *m/z*: 398 $[M]^+$；^{1}H-NMR (400 MHz, $CDCl_3$) δ: 2.91 (1H, brd, *J* = 8.4 Hz, H-3a), 2.83 (1H, brd, *J* = 8.4 Hz, H-3b), 3.38 (1H, m, H-5a), 2.97 (1H, m, H-5b), 3.21 (1H, m, H-6a), 3.13 (1H, m, H-6b), 6.91 (1H, s, H-9), 6.79 (1H, s, H-12), 1.88 (1H, m, H-14), 1.73 (1H, m, H-15a), 1.13 (1H, m, H-15b), 2.56 (1H, brd, *J* = 12.0 Hz, H-17a), 1.90 (1H, dd, *J* = 12.0, 2.0 Hz, H-17b), 0.90 (3H, t, *J* = 7.4 Hz, H-18), 1.44 (1H, m, H-19a), 1.33 (1H, m, H-19b), 1.28 (1H, m, H-20), 3.54 (1H, brs, H-21), 3.90 (3H, s, 10-OCH_3), 3.92 (3H, s, 11-OCH_3), 3.72 (3H, s, COOMe)；^{13}C-NMR (150 MHz, $CDCl_3$) δ: 135.0 (C-2), 51.1 (C-3), 53.0 (C-5), 22.1 (C-6), 110.3 (C-7), 121.1 (C-8), 100.6 (C-9), 144.5 (C-10), 146.7 (C-11), 94.4 (C-12), 129.8 (C-13), 27.3 (C-14), 32.1 (C-15), 55.1 (C-16), 36.8 (C-17), 11.6 (C-18), 26.6 (C-19), 39.3 (C-20), 57.7 (C-21), 56.5 (10-OMe), 56.3 (11-OMe), 52.7 (COOMe), 175.8 (COOMe)。以上数据与文献报道一致[12-13]，故将化合物 **3** 鉴定为 9,10-二甲氧基冠狗牙花碱。

化合物 **4**：淡黄色油状固体，易溶于氯仿，碘化铋钾反应阳性；$C_{21}H_{24}N_2O_3$，EI-MS *m/z*: 352 $[M]^+$；^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.97 (1H, m, H-5), 3.42 (1H, dd, *J* = 14.6, 8.0 Hz, H-6a), 3.50 (H, dd, *J* = 14.6, 10.0 Hz, H-6b), 7.72 (1H, d, *J* = 8.0 Hz, H-9), 7.15 (1H, m, H-10), 7.30～7.37 (2H, m, H-11, 12), 2.72 (1H, dd, *J* = 13.6, 7.2 Hz, H-14a), 3.31 (1H, dd, *J* = 13.6, 11.6 Hz, H-14b), 3.77 (1H, m, H-15), 2.82 (1H, t, *J* = 3.3 Hz, H-16), 1.71 (3H, d, *J* = 7.8 Hz, H-18), 5.46 (1H, q, *J* = 7.8 Hz, H-19), 2.98 (1H, d, *J* = 14.4 Hz, H-21a), 2.66 (3H, s, COOMe), 2.61 (3H, s, NMe)；^{13}C-NMR (100 MHz, $CDCl_3$) δ: 134.1 (C-2), 190.2 (C-3), 57.2 (C-5), 20.4 (C-6), 120.3 (C-7), 128.6 (C-8), 120.9 (C-9), 120.4 (C-10), 126.7 (C-11), 111.8 (C-12), 136.4 (C-13), 43.1 (C-14), 30.5 (C-15), 46.6 (C-16), 12.3 (C-18), 120.4 (C-19), 135.9 (C-20), 51.9 (C-21), 171.3 (COOMe), 50.4 (COOMe), 42.3 (NMe)。以上数据与文献报道一致[14]，故将化合物 **4** 鉴定为老刺木碱。

化合物 **5**：白色粉末，易溶于氯仿、甲醇，碘化铋钾反应阳性；$C_{21}H_{24}N_2O_4$，EI-MS *m/z*: 368 $[M]^+$；^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.16 (1H, m, H-5), 3.74 (1H, dd, *J* = 14.8, 8.2 Hz, H-6a), 3.26 (1H, dd, *J* = 14.8, 10.0 Hz, H-6b), 7.62 (1H, d, *J* = 8.0 Hz, H-9), 7.09 (1H, ddd, *J* = 8.0, 6.8, 1.0 Hz, H-10), 7.25 (1H, ddd, *J* = 8.0, 6.8, 1.0 Hz, H-11), 7.31 (1H, d, *J* = 8.0 Hz, H-12), 2.63 (1H, dd, *J* = 13.6, 7.2 Hz, H-14a), 2.91 (1H, dd, *J* = 13.6, 11.2 Hz, H-14b), 3.62 (1H, m, H-15), 4.16 (1H, m, H-16), 1.68 (3H, dd, *J* = 7.6, 1.8 Hz, H-18), 5.57 (1H, q, *J* = 7.6 Hz, H-19), 4.37 (1H, d, *J* = 14.4 Hz, H-21a), 3.52 (1H, d, *J* = 14.4 Hz, H-21b), 2.54 (3H, s, COOMe), 3.36 (3H, s, NMe)；^{13}C-NMR (100 MHz, $CDCl_3$) δ: 133.8 (C-2), 189.1 (C-3), 73.2 (C-5), 25.1 (C-6), 116.4 (C-7), 127.4 (C-8), 120.0 (C-9), 120.7 (C-10), 126.6 (C-11), 112.1 (C-12), 136.4 (C-13), 42.2 (C-14), 28.7 (C-15), 40.5 (C-16), 12.7 (C-18), 127.9 (C-19), 129.3 (C-20), 64.2 (C-21), 171.1 (COOMe), 50.3 (COOMe), 56.1 (NMe)。以上数据与文献报道一致[15]，故将化合物 **5** 鉴定为老刺木碱-4-氮氧化物。

化合物 **6**：白色粉末，易溶于氯仿、甲醇，碘化铋钾反应阳性；$C_{21}H_{24}N_2O_4$，EI-MS *m/z*: 368 $[M]^+$；^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.46 (1H, m, H-5a), 3.18 (1H, m, H-5b), 3.24 (2H, m, H-6), 7.48 (1H, d, *J* = 7.6 Hz, H-9), 7.08 (1H, t, *J* = 7.6 Hz, H-10), 7.16 (1H, t, *J* = 7.6 Hz, H-11), 7.25 (1H, d, *J* = 7.6 Hz,

H-12), 2.62 (1H, brs, H-14), 2.00 (1H, m, H-15a), 1.38 (1H, m, H-15b), 2.65 (1H, dd, *J* = 14.8, 1.6 Hz, H-17a), 2.36 (1H, m, H-17b), 1.33 (3H, d, *J* = 6.4 Hz, H-18), 3.80 (1H, m, H-19), 1.83 (1H, m, H-20), 5.10 (1H, s, H-21), 3.75 (3H, s, COOMe); ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 135.7 (C-2), 172.7 (C-3), 42.2 (C-5), 21.0 (C-6), 109.4 (C-7), 127.8 (C-8), 118.4 (C-9), 119.7 (C-10), 122.5 (C-11), 110.6 (C-12), 133.2 (C-13), 38.0 (C-14), 27.4 (C-15), 55.7 (C-16), 35.9 (C-17), 21.4 (C-18), 70.1 (C-19), 41.3 (C-20), 53.1 (C-21), 175.8 (COOMe), 53.0 (COOMe)。以上数据与文献报道一致[15]，故将化合物 **6** 鉴定为 3-oxo-19-*epi*-heyneanine。

化合物 **7**：白色粉末，易溶于氯仿、甲醇，碘化铋钾反应阳性；$C_{20}H_{22}N_2O_2$，EI-MS *m*/*z*: 322 $[M]^+$；^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 4.68 (1H, d, *J* = 5.2 Hz, H-3), 2.63～2.75 (2H, m, H-5), 2.97 (1H, m, H-6a), 1.74 (1H, dd, *J* = 13.7, 2.7 Hz, H-6b), 7.62 (1H, d, *J* = 7.2 Hz, H-9), 7.16 (1H, t, *J* = 7.2 Hz, H-10), 7.34 (1H, t, *J* = 7.2 Hz, H-11), 7.43 (1H, d, *J* = 7.2 Hz, H-12), 2.58 (1H, m, H-14a), 1.99 (1H, dd, *J* = 14.0, 3.6 Hz, H-14b), 3.69 (1H, m, H-15), 2.08 (1H, d, *J* = 3.6 Hz, H-16), 1.55 (3H, dd, *J* = 7.2, 3.6 Hz, H-18), 5.49 (1H, q, *J* = 7.2 Hz, H-19), 4.05 (1H, d, *J* = 16.4 Hz, H-21a), 3.12 (1H, d, *J* = 16.2 Hz, H-21b), 3.71 (3H, s, COOMe); ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 191.3 (C-2), 55.1 (C-3), 52.0 (C-5), 36.1 (C-6), 56.2 (C-7), 138.2 (C-8), 123.5 (C-9), 125.6 (C-10), 128.1 (C-11), 119.8 (C-12), 155.5 (C-13), 33.7 (C-14), 32.5 (C-15), 55.4 (C-16), 12.9 (C-18), 120.9 (C-19), 146.3 (C-20), 53.7 (C-21), 171.7 (COOMe), 51.6 (COOMe)。以上数据与文献报道一致[16]，故将化合物 **7** 鉴定为劲直胺。

化合物 **8**：无色针状晶体（氯仿），碘化铋钾反应阳性；$C_{21}H_{24}N_2O_3$，EI-MS *m*/*z*: 352 $[M]^+$；^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 4.60 (1H, d, *J* = 4.8 Hz, H-3), 3.68 (1H, m, H-5α), 2.05 (1H, dd, *J* = 15.6, 4.0 Hz, H-5β), 2.64 (2H, m, H-6), 7.64 (1H, d, *J* = 7.6 Hz, H-9), 7.18 (1H, td, *J* = 7.6, 1.2 Hz, H-10), 7.35 (1H, td, *J* = 7.6, 1.2 Hz, H-11), 7.53 (1H, d, *J* = 7.6 Hz, H-12), 2.44 (1H, ddd, *J* = 16.0, 4.2, 3.6 Hz, H-14a), 1.90 (1H, d, *J* = 14.4 Hz, H-14b), 3.64 (1H, m, H-15), 2.97, 2.88 (2H, ABq, *J* = 12.2 Hz, H-17), 1.62 (3H, dd, *J* = 7.2, 3.6 Hz, H-18), 5.46 (1H, q, *J* = 7.2 Hz, H-19), 4.10 (1H, brd, *J* = 17.2 Hz, H-21a), 3.14 (1H, d, *J* = 17.2 Hz, H-21b), 3.84 (3H, s, COOMe)；^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 190.6 (C-2), 54.6 (C-3), 53.9 (C-5), 38.0 (C-6), 58.7 (C-7), 139.7 (C-8), 125.9 (C-9), 128.5 (C-10), 124.6 (C-11), 121.5 (C-12), 155.8 (C-13), 30.6 (C-14), 34.7 (C-15), 60.5 (C-16), 64.2 (C-17), 13.4 (C-18), 119.5 (C-19), 144.3 (C-20), 52.1 (C-21), 173.6 (COOMe), 52.0 (COOMe)。以上数据与文献报道一致[17]，故将化合物 **8** 鉴定为 deacetylakuammiline。

化合物 **9**：白色粉末，易溶于氯仿、甲醇，碘化铋钾反应阳性；$C_{21}H_{24}N_2O_3$，EI-MS *m*/*z*: 352 $[M]^+$；^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 3.57 (1H, s, H-3), 3.17 (1H, brt, *J* = 10.0 Hz, H-5α), 2.68 (1H, m, H-5β), 2.18 (1H, ddd, *J* = 12.4, 10.0, 8.0 Hz, H-6a), 1.96 (1H, dd, *J* = 12.4, 10.0 Hz, H-6b), 7.21 (1H, d, *J* = 8.0 Hz, H-9), 6.94 (1H, t, *J* = 8.0 Hz, H-10), 7.16 (1H, t, *J* = 8.0 Hz, H-11), 6.83 (1H, d, *J* = 8.0 Hz, H-12), 1.56 (1H, d, *J* = 5.2 Hz, H-14), 1.63 (1H, dd, *J* = 12.8, 7.2 Hz, H-15a), 1.36 (1H, d, *J* = 12.8 Hz, H-15b), 2.89 (1H, s, H-17), 0.99 (3H, t, *J* = 7.6 Hz, H-18), 1.93 (1H, m, H-19a), 1.79 (1H, m, H-19b), 3.60 (1H, s, H-21), 3.79 (3H, s, COOMe); ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 164.9 (C-2), 68.9 (C-3), 50.6 (C-5), 41.4 (C-6), 60.2 (C-7), 130.5 (C-8), 121.4 (C-9), 120.9 (C-10), 127.7 (C-11), 109.6 (C-12), 144.3 (C-13), 43.1 (C-14), 44.1 (C-15), 96.4 (C-16), 40.8 (C-17), 8.2 (C-18), 30.2 (C-19), 82.1 (C-20), 77.0 (C-21), 168.0 (COOMe), 51.1 (COOMe)。以上数据与文献报道一致[18]，故将化合物 **9** 鉴定为 pandine。

化合物 **10**：无色块状晶体（甲醇），碘化铋钾反应阳性；$C_{21}H_{24}N_2O_4$，EI-MS *m*/*z*: 368 $[M]^+$；^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 3.56 (1H, m, H-3), 3.56 (1H, m, H-5α), 2.76 (1H, dd, *J* = 10.2, 4.8 Hz, H-5β), 2.23 (1H, dd, *J* = 16.0, 3.6 Hz, H-6a), 2.91 (1H, d, *J* = 16.0 Hz, H-6b), 7.29 (1H, d, *J* = 8.0 Hz, H-9), 6.86 (1H, t, *J* = 8.0 Hz, H-10), 7.10 (1H, t, *J* = 8.0 Hz, H-11), 6.56 (1H, d, *J* = 8.0 Hz, H-12), 2.02 (1H, dd, *J* = 14.0, 0.9 Hz, H-14a), 2.31 (1H, d, *J* = 14.0 Hz, H-14b), 3.58 (1H, s, H-15), 4.90 (1H, brs, H-17), 1.49 (3H, dd, *J* = 6.8, 1.6 Hz, H-18), 5.38 (1H, q, *J* = 7.2 Hz, H-19), 2.96 (1H, d, *J* = 8.0 Hz, H-21a),

3.95 (1H, d, *J* = 16.2 Hz, H-21b), 3.56 (3H, s, COOMe)；^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 111.1 (C-2), 57.5 (C-3), 48.4 (C-5), 23.1 (C-6), 49.8 (C-7), 126.1 (C-8), 127.3 (C-9), 119.6 (C-10), 128.6 (C-11), 116.0 (C-12), 142.6 (C-13), 27.7 (C-14), 37.0 (C-15), 57.4 (C-16), 84.6 (C-17), 12.7 (C-18), 118.3 (C-19), 141.1 (C-20), 54.3 (C-21), 170.9 (COOMe), 51.7 (COOMe)。以上数据与文献报道一致[19]，故将化合物 **10** 鉴定为 rhazicine。

化合物 **11**：白色块状固体，易溶于甲醇，碘化铋钾反应阳性；$C_{21}H_{24}N_2O_5$，EI-MS *m*/*z*: 384 $[M]^+$；^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 4.57 (1H, brs, H-3), 4.44 (1H, brt, *J* = 12.8 Hz, H-5α), 3.35 (1H, dd, *J* = 12.0, 3.6 Hz, H-5β), 2.91 (1H, ddd, *J* = 17.6, 17.6, 5.4 Hz, H-6a), 2.56 (1H, m, H-6b), 7.24 (1H, d, *J* = 8.0 Hz, H-9), 6.84 (1H, t, *J* = 8.0 Hz, H-10), 7.05 (1H, t, *J* = 8.0 Hz, H-11), 6.52 (1H, d, *J* = 8.0 Hz, H-12), 2.27 (1H, brd, *J* = 14.4 Hz, H-14a), 2.54 (1H, m, H-14b), 3.60 (1H, brs, H-15), 4.87 (1H, brs, H-17), 1.50 (3H, dd, *J* = 7.2, 2.0 Hz, H-18), 5.48 (1H, brq, *J* = 7.2 Hz, H-19), 4.25 (1H, brd, *J* = 14.4 Hz, H-21a), 3.71 (1H, d, *J* = 16.0 Hz, H-21b), 3.54 (3H, s, COOMe)；^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 110.7 (C-2), 79.9 (C-3), 63.9 (C-5), 20.9 (C-6), 47.4 (C-7), 126.7 (C-8), 127.2 (C-9), 122.8 (C-10), 127.9 (C-11), 116.0 (C-12), 141.6 (C-13), 25.2 (C-14), 34.8 (C-15), 56.7 (C-16), 85.2 (C-17), 12.9 (C-18), 119.2 (C-19), 131.0 (C-20), 72.6 (C-21), 171.8 (COOMe), 51.9 (COOMe)。以上数据与文献报道一致[20]，故将化合物 **11** 鉴定为 rhazicine *N*(4)-oxide。

化合物 **12**：白色块状固体，易溶于氯仿、甲醇，碘化铋钾反应阳性；$C_{21}H_{22}N_2O_3$，EI-MS *m*/*z*: 350 $[M]^+$；^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 3.91 (1H, d, *J* = 5.2 Hz, H-3), 2.95～3.11 (2H, m, H-6), 3.78 (1H, m, H-5a), 2.80 (1H, dd, *J* = 15.6, 3.2 Hz, H-5b), 7.29～7.44 (4H, m, H-9～12), 2.49 (1H, dq, *J* = 14.8, 2.8 Hz, H-14a), 2.11 (1H, dd, *J* = 14.8, 2.4 Hz, H-14b), 3.77 (1H, m, H-15), 7.70 (1H, s, H-17), 1.59 (3H, dd, *J* = 7.2, 2.4 Hz, H-18), 5.57 (1H, q, *J* = 7.2 Hz, H-19), 4.12 (1H, dt, *J* = 17.2, 2.0 Hz, H-21a), 3.25 (1H, d, *J* = 17.2 Hz, H-21b), 3.53 (3H, s, COOMe)；^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 214.5 (C-2), 61.2 (C-3), 51.7 (C-5), 32.2 (C-6), 53.2 (C-7), 128.3 (C-8), 128.4 (C-9), 128.1 (C-10), 128.9 (C-11), 120.8 (C-12), 142.1 (C-13), 30.4 (C-14), 37.4 (C-15), 58.1 (C-16), 160.6 (C-17), 13.0 (C-18), 125.1 (C-19), 137.5 (C-20), 53.1 (C-21), 168.5 (COOMe), 52.2 (COOMe)。以上数据与文献报道一致[19]，故将化合物 **12** 鉴定为 rhazimine。

参考文献

[1] 中国科学院中国植物志编辑委员会. 中国植物志 [M]. 北京: 科学出版社, 1977.

[2] Zhang H, Wang X N, Lin L P, *et al*. Indole alkaloids from three species of the *Ervatamia* genus: *E. officinalis*, *E. divaricata*, and *E. divaricata* Gouyahua [J]. *J Nat Prod*, 2007, 70(1): 54-59.

[3] Zhang D B, Yu D G, Sun M, *et al*. Ervatamines A-I, anti-inflammatory monoterpenoid indole alkaloids with diverse skeletons from *Ervatamia hainanensis* [J]. *J Nat Prod*, 2015, 78(6): 1253-1261.

[4] Kai T, Zhang L, Wang X, *et al*. Tabersonine inhibits amyloid fibril formation and cytotoxicity of Aβ (1-42) [J]. *ACS Chem Neurosci*, 2015, 6(6): 879-888.

[5] Ingkaninan K, Changwijit K, Suwanborirux K. Vobasinyl-iboga bisindole alkaloids, potent acetylcholinesterase inhibitors from *Tabernaemontana divaricata* root [J]. *J Pharm Pharmacol*, 2006, 58(6): 847-852.

[6] He D Y, McGough N N H, Ravindranathan A, *et al*. Glial cell line-derived neurotrophic factor mediates the desirable actions of the anti-addiction drug ibogaine against alcohol consumption [J]. *J Neurosci*, 2005, 25(3): 619-628.

[7] Ma K, Wang J S, Luo J, *et al*. Tabercarpamines A-J, apoptosis-inducing indole alkaloids from the leaves of *Tabernaemontana corymbosa* [J]. *J Nat Prod*, 2014, 77(5): 1156-1163.

[8] Cai X H, Bao M F, Zhang Y, *et al*. A new type of monoterpenoid indole alkaloid precursor from *Alstonia rostrata* [J]. *Org Lett*, 2011, 13(14): 3568-3571.

[9] Cai X H, Li Y, Su J, *et al*. Novel indole and quinoline alkaloids from *Melodinus yunnanensis* [J]. *Nat Prod. Bioprospect*, 2011, 1(1): 25-28.

[10] Okuyama E, Gao L H, Yamazaki M. Analgesic components from bornean medicinal plants, *Tabernaemontana pauciflora* Blume and *Tabernaemontana pandacaqui* Poir [J]. *Chem Pharm Bull*, 1992, 40(8): 2075-2079.

[11] 杨婷婷, 唐本钦, 范春林, 等. 海南狗牙花枝叶化学成分的研究 [J]. 中草药, 2013, 44(9): 1082-1085.

[12] Zocoler M A, de Oliveira A J B, Sarragiotto M H, *et al*. Qualitative determination of indole alkaloids of *Tabernaemontana fuchsiaefolia* (Apocynaceae) [J]. *J Braz Chem Soc*, 2005, 16(6B): 1372-1377.

[13] Van Beek T A, Verpoorte R, Svendsen A B, *et al*. Antimicrobially active alkaloids from *Tabernaemontana chippii* [J]. *J Nat Prod*, 1985, 48(3): 400-423.

[14] Ahond A, Bui A M, Potier P, *et al*. Carbon-13 nuclear magnetic resonance analysis of vobasine-like indole alkaloids [J]. *J Org Chem*, 1976, 41(10): 1878-1879.

[15] Clivio P, Richard B, Hadi H A, *et al*. Alkaloids from leaves and stems bark of *Ervatamia polyneura* [J]. *Phytochemistry*, 1990, 29(9): 3007-3011.

[16] Rahman A, Rehman H. Isolation and NMR studies on rhazimal and strictamine [J]. *Planta Med*, 1986, 52(3): 230-231.

[17] Kan C, Deverre J R, Sevenet T, *et al*. Indole alkaloids from *Kopsia deverrei* [J]. *Nat Prod Lett*, 1995, 7(4): 275-281.

[18] Le Men J, Hoizey M J, Lukacs G, *et al*. Structure de la pandine alcaloïde hexacyclique du type ψ-vincadifformine [J]. *Tetrahedron Lett*, 1974, 15(36): 3119-3122.

[19] Hu W L, Zhu J P, Umberto P, *et al*. Revision of the structures of rhazicine and rhazimine, two alkaloids from *Melodinus acutiflorus* [J]. *Phytochemistry*, 1987, 26(9): 2625-2630.

[20] Hu W, Hesse M. The alkaloids of *Melodinus acutiflorus*. Rhyzicine *N*-oxide [J]. *Planta Med*, 1988, 54(3): 235-236.