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盆架树中单萜吲哚生物碱成分的分离与结构鉴定

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摘 要:本文对夹竹桃科盆架树属盆架树(*Winchia calophylla* A. DC.)小枝的化学成分进行了研究,从其甲醇提取物中分离得到4个单萜吲哚生物碱。采用波谱技术并结合文献分别鉴定为 echitamidine、17-*O*-acetyl-N_b-demethylechitamine、N_b-demethylechitamine、N_b-demethylechitamine *N*-oxide。

关键词:夹竹桃科;盆架树;化学成分;单萜吲哚生物碱

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The Isolation and Structural Identification of Monoterpenoid Indole Alkaloids from *Winchia calophylla*

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Abstract: *Winchia calophylla* A. DC. (Apocynaceae) as a traditional medicinal plant is mainly distributed in Yunnan and Hainan Province of China, India, Myanmar and Indonesia. The stem barks were used for the treatment of chronic tracheits in Dai Nationality in Xishuangbanna, Yunnan Province of China. In order to find the compounds with good biological activity, the chemical constituents research of the twigs of the titled plant was presented in this paper. Four monoterpenoid indole alkaloids were isolated from the methanol extracts. They were identified as echitamidine, 17-*O*-acetyl-N_b-demethylechitamine, N_b-demethylechitamine, and N_b-demethylechitamine *N*-oxide by using the spectroscopic technique and comparing with the literatures.

Key words: Apocynaceae; *Winchia calophylla*; chemical constituents; monoterpenoid indole alkaloid

盆架树(*Winchia calophylla* A. DC.)是夹竹桃科盆架树属植物,该属植物两种,分布于中国、印度、缅甸和印度尼西亚等地。我国产一种,分布于云南和海南[1]。据文献报道,盆架树中的生物碱以单萜吲哚生物碱为主,另见报道有三萜和单萜及其苷类等[2-4]。单萜吲哚生物碱具有良好的生理活性,例如有抗肿瘤活性的长春碱、具有脑保护作用的长春胺、降压良药利血平以及抗抑郁制剂依波加因等[5]。为了寻找结构新颖和活性较好的单萜吲哚生物碱,本研究对采自云南西双版纳的盆架树小枝的甲醇提取物的氯仿萃取部分的化学成分进行了初步的研究,通过核磁共振和质谱等波谱解析手段以及参考相关文献,报道从中分离鉴定的4个单萜吲哚生物碱。

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1 材料与仪器

1.1 材料

盆架树小枝于2012年8月采自云南省西双版纳,经中科院西双版纳植物园张顺成老师鉴定为夹竹桃科盆架树属植物盆架树(*Winchia calophylla*),样品标本(H20120802)存放于中国科学院昆明植物研究所植物化学与西部植物资源持续利用国家重点实验室。

1.2 仪器

Bruker AM-400、DRX-500 和 Avance III-600 核磁共振仪,以 TMS 作为内标;ESI 质谱由 Waters 2695HPLC-Thermofinnigan LCQ Advantage 离子阱质谱仪测定;高效液相为 Agilent 1100 和 1200,色谱柱为 Eclipse XDB-C18;Sephadex LH-20 为 Pharmacia 公司的产品;反相填充材料 Lichroprep RP-18 gel(20

~45 μm)为德国默克公司的产品;柱色谱和薄层色谱硅胶均为 GF_{254} 型青岛海洋化工厂的产品。显色剂为配制好的碘化铋钾溶液。

2 提取与分离

盆架树小枝(13 Kg)粉碎后,经甲醇回流提取 3 次,提取时间分别为 4,3,3 h,减压蒸馏回收甲醇得到浸膏,将浸膏加水稀释后用盐酸调 pH 值 2-3,石油醚和乙酸乙酯分别萃取 3 次,再用氢氧化钠调 pH 值 9-10,氯仿萃取 3 次,得总碱约 200 g。总碱部分(200 g)经硅胶柱层析、反相 RP-18 柱层析、Sephadex LH-20 以及 HPLC 等各种分离纯化手段得到化合物 **1**(29.6 mg),**2**(4.6 mg),**3**(23.4 mg)和 **4**(26.5 mg)。

3 结构鉴定

化合物 1 淡黄色油状液体,分子式为 $C_{20}H_{24}N_2O_3$;ESI^+-MS *m/z* 341 [M + H]$^+$;^{1}H NMR (400 MHz,$CDCl_3$) δ (ppm):8.61 (1H,br s,NH),7.16 (1H,d,*J* = 7.4 Hz,H-9),7.12 (1H,td,*J* = 7.4,1.0 Hz,H-11),6.90 (1H,t,*J* = 7.4 Hz,H-10),6.82 (1H,br d,*J* = 7.4 Hz,H-12),3.86 (1H,s,H-3),3.85 (3H,s,OMe),3.29 (1H,d,*J* = 2.0 Hz,H-15),3.24 (1H,dq,*J* = 9.2,6.2 Hz,H-19),3.05 (1H,m,H-5a),2.78~2.89 (3H,m,H-5b,6a,21a),2.00 (1H,dt,*J* = 13.0,2.6 Hz,H-14a),1.90 (1H,br t,*J* = 12.6 Hz,H-21b),1.81 (1H,m,H-6b),1.73 (1H,m,H-20),1.38 (1H,dt,*J* = 13.0,2.6 Hz,H-14b),1.13 (3H,d,*J* = 6.2 Hz,H-18)。^{13}C NMR (100 MHz,$CDCl_3$) δ (ppm):172.3 (C-17),168.9 (C-2),143.7 (C-13),135.6 (C-8),127.6 (C-11),121.4 (C-9),119.8 (C-10),109.6 (C-12),96.8 (C-16),68.4 (C-19),60.9 (C-3),57.1 (C-7),54.1 (C-5),51.9 (OMe-17),48.1 (C-21),45.8 (C-20),43.5 (C-6),31.0 (C-14),28.8 (C-15),19.8 (C-18),以上数据与文献[6-7]的波谱数据基本一致,可鉴定化合物 **1** 为 echitamidine。

化合物 2 淡黄色固体,分子式为 $C_{23}H_{28}N_2O_5$;ESI^+-MS *m/z* 413 [M + H]$^+$;^{1}H NMR (600 MHz,$CDCl_3$) δ (ppm):7.66 (1H,d,*J* = 7.6 Hz,H-9),7.02 (1H,t,*J* = 7.6 Hz,H-11),6.73 (1H,t,*J* = 7.6 Hz,H-10),6.53 (1H,d,*J* = 7.6 Hz,H-12),5.57 (1H,q,*J* = 6.9 Hz,H-19),4.77 (1H,d,*J* = 12.3 Hz,H-17a),4.58 (1H,d,*J* = 15.5 Hz,H-21a),4.38 (1H,dd,*J* = 10.1,4.9 Hz,H-3),3.83 (1H,d,*J* = 5.4 Hz,H-15),3.78 (3H,s,OMe),3.61 (1H,d,*J* = 12.3 Hz,H-17b),3.39 (1H,m,H-5a),3.27 (1H,d,*J* = 15.5 Hz,H-21b),3.00 (1H,dd,*J* = 11.5,8.3 Hz,H-5b),2.50 (1H,ddd,*J* = 15.6,10.1,5.4 Hz,H-14a),2.36 (1H,dt,*J* = 13.8,8.3 Hz,H-6a),2.13 (1H,dt,*J* = 13.8,8.3 Hz,H-6b),2.03 (3H,s,OAc-Me),1.79 (3H,dd,*J* = 6.9,1.5 Hz,H-18),1.69 (1H,dd,*J* = 15.6,4.9 Hz,H-14b)。^{13}C NMR (150 MHz,$CDCl_3$) δ (ppm):172.9 (C-22),170.3 (OAc-17),148.0 (C-13),134.3 (C-20),129.8 (C-8),129.5 (C-11),128.0 (C-9),126.9 (C-19),120.0 (C-10),111.2 (C-12),97.6 (C-2),67.7 (C-3),66.7 (C-17),60.1 (C-7),56.4 (C-21),54.0 (C-16),53.0 (C-5),52.5 (COOMe-22),44.7 (C-6),36.2 (C-15),31.6 (C-14),21.0 (OAc-17),15.2 (C-18),以上数据与文献[7-8]的波谱数据基本一致,可鉴定化合物 **2** 为 17-*O*-acetyl-N_b-demethylechitamine。

化合物 3 白色针状晶体,分子式为 $C_{21}H_{26}N_2O_4$;ESI^+-MS *m/z* 371 [M + H]$^+$;^{1}H NMR (400 MHz,CD_3OD) δ (ppm):7.69 (1H,d,*J* = 7.8 Hz,H-9),6.95 (1H,t,*J* = 7.8 Hz,H-11),6.61 (1H,t,*J* = 7.8 Hz,H-10),6.48 (1H,d,*J* = 7.8 Hz,H-12),5.41 (1H,q,*J* = 6.9 Hz,H-19),4.19~4.26 (2H,m,H-3,21a),4.10 (1H,d,*J* = 11.8 Hz,H-17a),3.85 (1H,d,*J* = 5.0 Hz,H-15),3.77 (3H,s,OCH_3),3.30 (1H,d,*J* = 11.8 Hz,H-17b),2.98 (1H,d,*J* = 16.0 Hz,H-21b),2.73 (1H,dd,*J* = 11.8,8.4 Hz,H-5a),2.58 (1H,ddd,*J* = 15.2,11.0,5.0 Hz,H-14a),2.09 (1H,m,H-6a),1.92 (1H,dd,*J* = 13.3,7.8 Hz,H-6b),1.78 (3H,dd,*J* = 6.9,1.8 Hz,H-18),1.51 (1H,dd,*J* = 15.2,5.0 Hz,H-14b)。^{13}C NMR (100 MHz,CD_3OD) δ (ppm):176.2 (C-22),150.6 (C-13),141.0 (C-20),132.4 (C-8),129.1 (C-9),128.5 (C-11),123.9 (C-19),119.0 (C-10),110.4 (C-12),96.3 (C-2),70.0 (C-3),67.1 (C-17),62.4 (C-16),58.2 (C-21),57.8 (C-7),55.0 (C-5),52.0 (OCH_3-22),47.6 (C-6),36.4 (C-15),33.6 (C-14),15.3 (C-18),以上数据与文献[9]的波谱数据基本一致,可鉴定化合物 **3** 为 N_b-demethylechitamine。

化合物 4 白色针状晶体,分子式为 $C_{21}H_{26}N_2O_5$;ESI$^+$-MS *m/z* 387 [M + H]$^+$;^{1}H NMR (400 MHz,CD_3OD) δ (ppm):7.72 (1H,d,*J* = 7.2 Hz,H-9),7.07 (1H,t,*J* = 7.2 Hz,H-11),6.71 (1H,t,*J* = 7.2 Hz,H-10),6.70 (1H,d,*J* = 7.2 Hz,H-12),5.79 (1H,q,*J* = 6.9 Hz,H-19),4.76 (1H,d,*J* = 15.0 Hz,H-21a),4.51 (1H,dd,*J* = 11.0,5.5 Hz,H-3),4.13 (1H,d,*J* = 15.0 Hz,H-21b),4.04 (1H,d,*J* = 4.6 Hz,H-15),3.95 (1H,d,*J* = 11.9 Hz,H-17a),3.82 (3H,s,OCH_3),3.40 (1H,dd,*J* = 12.4,8.0 Hz,H-5a),3.26 (3H,d,*J* = 11.9 Hz,H-17b),2.72 (1H,ddd,*J* = 15.2,11.0,5.5 Hz,H-14a),2.31 (1H,dt,*J* = 14.2,8.0Hz,H-6a),2.04 (1H,dd,*J* = 14.2,8.0 Hz,H-6b),1.85 (3H,dd,*J* = 6.9,2.0 Hz,H-18),1.71 (1H,dd,*J* = 15.2,4.6 Hz,H-14b)。^{13}C NMR (100 MHz,CD_3OD) δ (ppm):174.8 (C-22),149.3 (C-13),134.0 (C-8),131.4 (C-20),130.1 (C-11),129.4 (C-9),127.9 (C-19),120.1 (C-10),110.7 (C-12),99.7 (C-2),74.4 (C-21),71.5 (C-3),67.1 (C-5),66.6 (C-17),59.6 (C-16),56.9 (C-7),52.4 (OCH_3-22),41.3 (C-6),36.6 (C-15),33.1 (C-14),15.3 (C-18),以上数据与文献[9]的波谱数据基本一致,可鉴定化合物**4**为 N_b-demethylechitamine *N*-oxide。

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