

药用狗牙花枝叶的生物碱类成分研究

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摘要: 目的 研究药用狗牙花 *Ervatamia officinalis* 枝叶的化学成分。方法 采用硅胶、ODS、Sephadex LH-20、HPLC 等色谱方法进行分离纯化, 并根据化合物的理化性质及波谱学数据鉴定其化学结构。结果 从药用狗牙花枝叶的总生物碱部位中分离得到 14 个生物碱类化合物, 分别鉴定为 7S-coronaridine hydroxyindolenine (1)、7S-voacangine hydroxyindolenine (2)、coronaridine (3)、19S-heyneanine (4)、voacangine (5)、tabernaemontanine (6)、dregamine (7)、3-(2-oxopropyl) coronaridine (8)、3-oxovoacangine (9)、voastrictine (10)、16R,19E-isositsirikine (11)、16R,19Z-isositsirikine (12)、16R,19E-isositsirikine *N*₄-oxide (13)、geissoschizol (14)。结论 化合物 8~14 为首次从该植物中分离得到。

关键词: 夹竹桃科; 药用狗牙花; 生物碱; 3-oxovoacangine; voastrictine; geissoschizol

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Studies on alkaloids from twigs and leaves of *Ervatamia officinalis*

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Abstract: Objective To study the chemical constituents in the twigs and leaves of *Ervatamia officinalis*. **Methods** The chemical constituents were isolated from the total alkaloids of the twigs and leaves of *Ervatamia officinalis* by using silica gel, ODS, Sephadex LH-20, and HPLC. The chemical structures of the compounds were identified based on their physical and chemical properties and spectroscopic methods. **Results** Fourteen alkaloids were isolated and identified as 7S-coronaridine hydroxyindolenine (1), 7S-voacangine hydroxyindolenine (2), coronaridine (3), 19S-heyneanine (4), voacangine (5), tabernaemontanine (6), dregamine (7), 3-(2-oxopropyl) coronaridine (8), 3-oxovoacangine (9), voastrictine (10), 16R,19E-isositsirikine (11), 16R,19Z-isositsirikine (12), 16R,19E-isositsirikine *N*₄-oxide (13), and geissoschizol (14). **Conclusion** Compounds 8—14 are obtained from this plant for the first time.

Key words: Apocynaceae; *Ervatamia officinalis* Tsiang; alkaloids; 3-oxovoacangine; voastrictine; geissoschizol

药用狗牙花 *Ervatamia officinalis* Tsiang 为夹竹桃科狗牙花属植物, 灌木, 高 2~4 m, 具乳汁, 除花被毛外, 其他部分无毛, 在我国主要分布于广东、海南和云南等省。其根可药用, 海南民间有用作治肚痛^[1]。课题组前期从药用狗牙花中分离鉴定了多种骨架新颖的单萜吲哚类生物碱化合物^[2-3], 本实验又从药用狗牙花分离得到 14 个单萜吲哚生物碱, 分别鉴定为 7S-coronaridine hydroxyindolenine (1)、7S-voacangine hydroxyindolenine (2)、coronaridine

(3)、19S-heyneanine (4)、voacangine (5)、tabernaemontanine (6)、dregamine (7)、3-(2-oxopropyl) coronaridine (8)、3-oxovoacangine (9)、voastrictine (10)、16R,19E-isositsirikine (11)、16R,19Z-isositsirikine (12)、16R,19E-isositsirikine *N*₄-oxide (13)、geissoschizol (14)。化合物 8~14 为首次从该植物中分离得到。

1 仪器与材料

JASCO P-2000 旋光仪 (日本 Jasco 公司); X-5

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型显微熔点测定仪(北京泰克仪器公司); Jasco FT/IR-480 Plus Fourier Transform 型红外光谱仪(日本 Jasco 公司); Jasco V-550 型紫外-可见光谱仪(日本 Jasco 公司); Agilent 6210 LC/MSD TOF 质谱仪(美国安捷伦公司); Bruker AV-600/AV-400 型超导核磁共振仪(美国 Bruker 公司); Agilent 1200 分析及制备型高效液相色谱仪(美国安捷伦公司)。

柱色谱用硅胶(100~200、200~300 目, 青岛海洋化工厂); 硅胶 GF₂₅₄ 薄层预制板(烟台化学工业研究所); 碳十八烷基反相键合硅胶(ODS)柱色谱材料(Merck 公司); Sephadex LH-20(美国 Amersham Biosciences Swede 公司); 所用试剂均为市售分析纯和色谱纯。

药用狗牙花药材为 2014 年 9 月采自海南省, 经海南大学黄世满教授鉴定为狗牙花属药用狗牙花 *Ervatamia officinalis* Tsiang 的干燥枝叶。标本(2014092010)保存于暨南大学中药及天然药物研究所。

2 提取与分离

药用狗牙花干燥枝叶 18.0 kg, 粉碎成粗粉, 用 95%乙醇在室温下渗漉提取, 减压浓缩得总浸膏(0.8 kg), 加水混悬后, 用 10%盐酸调 pH 值至 2~3, 氯仿萃取, 酸水层用氨水调 pH 值至 9~10, 氯仿萃取, 减压浓缩得到粗总生物碱部位(65.3 g)。粗总生物碱部位经硅胶柱色谱, 氯仿-甲醇(100:0→0:100)系统梯度洗脱, 经薄层色谱(TLC)分析, 合并得到 12 个馏份(Fr. 1~12)。结合 LC-MS-UV 分析, 取碘化铋钾阳性显色馏份 3 经凝胶 Sephadex LH-20 柱色谱(氯仿-甲醇 1:1)、ODS 以及 HPLC 制备得到化合物 **1**(20.0 mg, 乙腈-水 41:59, $t_R=36.0$ min), **2**(5.3 mg 乙腈-水 41:59, $t_R=60.5$ min), **3**(25.0 mg, 乙腈-水 70:30, $t_R=41.5$ min), **4**(36.5 mg, 乙腈-水 47:53, $t_R=29.0$ min), **5**(15.0 mg, 乙腈-水 70:30, $t_R=21.5$ min); 馏份 4 经凝胶 Sephadex LH-20 柱色谱(氯仿-甲醇 1:1)、ODS 以及 HPLC 制备得到化合物 **8**(17.0 mg, 乙腈-水 58:42, $t_R=57.5$ min), **9**(4.2 mg, 乙腈-水 37:63, $t_R=41.1$ min); 馏份 5 经凝胶 Sephadex LH-20(氯仿-甲醇, 1:1)柱色谱、ODS 以及 HPLC 制备得到化合物 **6**(5.0 mg, 乙腈-水 40:60, $t_R=37.5$ min), **7**(17.5 mg, 甲醇-水 40:60, $t_R=27.4$ min), **10**(32.5 mg, 乙腈-水 29:71, $t_R=13.2$ min), **11**(20.0 mg, 乙腈-水 29:71, $t_R=36.0$ min), **12**(31.1

mg, 乙腈-水 29:71, $t_R=39.0$ min), **13**(1.8 mg, 乙腈-水 10:90, $t_R=13.1$ min), **14**(3.6 mg, 甲醇-水 48:52, $t_R=57.5$ min)。

3 结构鉴定

化合物 **1**: 黄色粉末, 改良碘化铋钾反应为阳性。 $[\alpha]_D^{25} -38.3^\circ$ (c 0.81, CH₃OH); UV $\lambda_{\max}^{\text{MeOH}}$ (nm): 210, 222, 289; IR $\nu_{\max}^{\text{KBr}}$ (cm⁻¹): 1 735, 1 557, 1 459; HR-ESI-MS m/z : 355.200 8 [M+H]⁺; ¹H-NMR (400 MHz, DMSO-*d*₆) δ : 7.37 (1H, d, $J=7.5$ Hz, H-9), 7.33 (1H, d, $J=7.5$ Hz, H-12), 7.29 (1H, t, $J=7.5$ Hz, H-11), 7.21 (1H, t, $J=7.5$ Hz, H-10), 5.78 (1H, s, OH), 3.92 (1H, brs, H-21), 3.54 (3H, s, 22-OCH₃), 3.39 (1H, m, H-5 α), 2.85 (1H, m, H-5 β), 2.66 (1H, m, H-3), 2.64 (1H, m, H-17 α), 2.14 (1H, m, H-17 β), 1.84 (1H, m, H-6 α), 1.82 (1H, m, H-14), 1.75 (1H, m, H-6 β), 1.64 (1H, m, H-15 α), 1.43 (1H, m, H-19a), 1.32 (1H, m, H-19b), 1.24 (1H, m, H-20), 0.95 (1H, m, H-15 β), 0.82 (3H, t, $J=7.4$ Hz, H-18); ¹³C-NMR (100 MHz, DMSO-*d*₆) δ : 190.5 (C-2), 172.4 (C-22), 151.4 (C-13), 143.1 (C-8), 128.7 (C-11), 126.1 (C-12), 121.7 (C-10), 120.1 (C-9), 87.2 (C-7), 57.6 (C-16), 55.3 (C-21), 52.4 (22-OCH₃), 49.0 (C-5), 48.7 (C-3), 37.4 (C-20), 36.7 (C-17), 33.4 (C-6), 31.7 (C-15), 26.7 (C-14), 26.5 (C-19), 11.6 (C-18)。以上化合物数据与文献报道一致^[4], 故鉴定化合物 **1** 为 7S-coronaridine hydroxyindolenine。

化合物 **2**: 黄色粉末, 改良碘化铋钾反应为阳性。 $[\alpha]_D^{25} -75.5^\circ$ (c 0.80, CH₃OH); UV $\lambda_{\max}^{\text{MeOH}}$ (nm): 207, 299; HR-ESI-MS m/z : 385.212 3 [M+H]⁺; ¹H-NMR (400 MHz, DMSO-*d*₆) δ : 7.27 (1H, d, $J=8.3$ Hz, H-9), 6.93 (1H, d, $J=2.5$ Hz, H-12), 6.82 (1H, dd, $J=8.3, 2.5$ Hz, H-11), 5.78 (1H, s, OH), 3.88 (1H, brs, H-21), 3.76 (3H, s, 10-OCH₃), 3.54 (3H, s, 22-OCH₃), 3.38 (1H, m, H-5 α), 2.84 (1H, m, H-5 β), 2.64 (1H, m, H-3), 2.61 (1H, d, $J=13.9$ Hz, H-17), 2.13 (1H, m, H-17), 1.82 (1H, m, H-6 α), 1.81 (1H, m, H-14), 1.74 (1H, m, H-6 β), 1.63 (1H, m, H-15 α), 1.42 (1H, m, H-19a), 1.33 (1H, m, 19b), 1.22 (1H, m, H-20), 0.95 (1H, m, H-15 β), 0.82 (3H, t, $J=7.4$ Hz, H-18); ¹³C-NMR (100 MHz, DMSO-*d*₆) δ : 188.0 (C-2), 172.5 (C-22), 158.3 (C-10), 144.8 (C-8), 144.8 (C-13), 121.7 (C-9), 120.5 (C-12), 113.2 (C-11), 87.2 (C-7), 57.4 (C-16), 55.6 (10-OCH₃), 55.4 (C-21), 52.3

(22-OCH₃), 48.9 (C-3), 48.6 (C-5), 37.4 (C-20), 36.5 (C-17), 33.7 (C-6), 31.7 (C-15), 26.6 (C-14), 26.5 (C-15), 11.5 (C-18)。以上化合物数据与文献报道一致^[5], 故鉴定化合物 **2** 为 7*S*-voacangine hydroxyindolenine。

化合物 **3**: 白色粉末, 改良碘化铋钾反应为阳性。 $[\alpha]_D^{25} -89.4^\circ$ (c 0.74, CH₃OH); UV $\lambda_{\max}^{\text{MeOH}}$ (nm): 209, 222, 284; IR $\nu_{\max}^{\text{KBr}}$ (cm⁻¹): 3 375, 1 723, 1 653, 1 459; HR-ESI-MS m/z : 389.207 0 [M+H]⁺; ¹H-NMR (400 MHz, CDCl₃) δ : 7.87 (1H, s, NH), 7.27 (1H, d, J = 7.6 Hz, H-9), 7.17 (1H, t, J = 7.6 Hz, H-11), 7.15 (1H, d, J = 7.6 Hz, H-12), 7.11 (1H, t, J = 7.6 Hz, H-10), 3.74 (3H, s, 22-OCH₃), 3.60 (1H, brs, H-21), 3.34 (1H, m, H-6 α), 3.25 (1H, m, H-6 β), 3.20 (1H, m, H-5 α), 3.04 (1H, m, H-5 β), 2.94 (1H, m, H-3 α), 2.84 (1H, m, H-3 β), 2.62 (1H, m, H-17 α), 1.95 (1H, m, H-17 β), 1.91 (1H, m, H-14), 1.77 (1H, m, H-15 α), 1.61 (1H, m, H-19 α), 1.48 (1H, m, H-19 β), 1.38 (1H, m, H-20), 1.16 (1H, m, H-15 β), 0.94 (3H, t, J = 7.4 Hz, H-18); ¹³C-NMR (100 MHz, CDCl₃) δ : 175.7 (C-22), 136.6 (C-2), 135.5 (C-13), 128.8 (C-8), 121.9 (C-11), 119.2 (C-10), 118.4 (C-9), 110.3 (C-12), 110.3 (C-7), 57.4 (C-21), 55.1 (C-16), 53.1 (C-5), 52.5 (22-OCH₃), 51.6 (C-3), 39.1 (C-20), 36.5 (C-17), 32.0 (C-15), 27.4 (C-14), 26.7 (C-19), 22.1 (C-6), 11.6 (C-18)。综上所述, 以上化合物数据与文献报道一致^[4], 故鉴定化合物 **3** 为 coronaridine。

化合物 **4**: 白色粉末, 改良碘化铋钾反应为阳性。 $[\alpha]_D^{25} -15.5^\circ$ (c 0.81, CH₃OH); UV $\lambda_{\max}^{\text{MeOH}}$ (nm): 210, 224, 284; IR $\nu_{\max}^{\text{KBr}}$ (cm⁻¹): 3 382, 1 726, 1 459; HR-ESI-MS m/z : 355.201 5 [M+H]⁺; ¹H-NMR (400 MHz, CD₃OD) δ : 7.39 (1H, d, J = 7.8 Hz, H-9), 7.25 (1H, d, J = 7.8 Hz, H-12), 7.04 (1H, t, J = 7.8 Hz, H-11), 6.97 (1H, t, J = 7.8 Hz, H-10), 4.07 (1H, m, H-19), 3.91 (1H, brs, H-21), 3.69 (3H, s, 22-OCH₃), 3.39 (1H, m, H-5 α), 3.12 (1H, m, H-5 β), 3.07 (1H, m, H-6 α), 3.05 (1H, m, H-6 β), 2.80 (1H, m, H-3 α), 2.78 (1H, m, H-3 β), 2.74 (1H, m, H-17 α), 1.97 (1H, m, H-17 β), 1.94 (1H, m, H-14), 1.65 (1H, m, H-15 α), 1.51 (1H, m, H-15 β), 1.22 (1H, m, H-20), 1.11 (3H, d, J = 6.3 Hz, H-18); ¹³C-NMR (100 MHz, CD₃OD) δ : 175.2 (C-22), 137.7 (C-2), 137.6 (C-13), 129.3 (C-8), 122.6 (C-11), 119.8 (C-10), 118.8 (C-9), 111.7 (C-12),

110.1 (C-7), 72.5 (C-19), 59.8 (C-21), 55.1 (C-16), 53.9 (22-OCH₃), 53.8 (C-5), 53.2 (C-3), 40.9 (C-20), 37.2 (C-17), 28.0 (C-14), 25.0 (C-15), 22.0 (C-6), 20.6 (C-18)。以上化合物数据与文献报道一致^[5], 故鉴定化合物 **4** 为 19*S*-heyneanine。

化合物 **5**: 黄色粉末, 改良碘化铋钾反应为阳性。 $[\alpha]_D^{25} -16.4^\circ$ (c 0.76, CH₃OH); UV $\lambda_{\max}^{\text{MeOH}}$ (nm): 207, 282; HR-ESI-MS m/z : 369.217 3 [M+H]⁺; ¹H-NMR (400 MHz, CD₃OD) δ : 7.14 (1H, d, J = 8.7 Hz, H-12), 6.93 (1H, d, J = 2.4 Hz, H-9), 6.81 (1H, td, J = 8.7, 2.4 Hz, H-11), 3.85 (3H, s, 10-OCH₃), 3.71 (3H, s, 22-OCH₃), 3.55 (1H, brs, H-21), 3.39 (1H, m, H-5 α), 3.21 (1H, m, H-5 β), 3.15 (1H, m, H-6 α), 2.97 (1H, m, H-6 β), 2.91 (1H, m, H-3 α), 2.81 (1H, m, H-3 β), 2.58 (1H, m, H-17 α), 2.28 (1H, m, H-17 β), 1.88 (1H, m, H-14), 1.73 (1H, m, H-15 α), 1.57 (1H, m, H-19 α), 1.44 (1H, m, H-19 β), 1.33 (1H, m, H-20), 1.13 (1H, m, H-15 β), 0.90 (3H, t, J = 7.4 Hz, H-18); ¹³C-NMR (100 MHz, CD₃OD) δ : 175.7 (C-22), 154.0 (C-10), 137.5 (C-2), 130.5 (C-13), 129.3 (C-8), 111.8 (C-11), 111.1 (C-12), 110.1 (C-7), 100.8 (C-9), 57.5 (C-21), 56.0 (10-OCH₃), 55.1 (C-16), 53.1 (C-5), 52.5 (22-OCH₃), 51.5 (C-3), 39.1 (C-20), 36.5 (C-17), 32.0 (C-15), 27.3 (C-14), 26.7 (C-19), 22.2 (C-6), 11.6 (C-18)。以上化合物数据与文献报道一致^[5], 故鉴定化合物 **5** 为 voacangine。

化合物 **6**: 黄色粉末, 改良碘化铋钾反应为阳性。 $[\alpha]_D^{25} -36.9^\circ$ (c 0.86, CH₃OH); UV $\lambda_{\max}^{\text{MeOH}}$ (nm): 211, 239, 315; IR $\nu_{\max}^{\text{KBr}}$ (cm⁻¹): 3 321, 1 725, 1 573, 1 454; HR-ESI-MS m/z : 355.201 8 [M+H]⁺; ¹H-NMR (400 MHz, CDCl₃) δ : 8.94 (1H, s, NH), 7.70 (1H, d, J = 8.1 Hz, H-9), 7.33 (1H, m, H-11), 7.32 (1H, m, H-12), 7.14 (1H, d, J = 8.1 Hz, H-10), 3.93 (1H, m, H-5), 3.45 (1H, m, H-6 α), 3.41 (1H, m, H-14 α), 3.29 (1H, dd, J = 14.6, 8.1 Hz, H-6 β), 3.18 (1H, dd, J = 13.0, 3.6 Hz, H-21 α), 3.01 (1H, t, J = 3.0 Hz, H-16), 2.75 (1H, m, H-14 β), 2.71 (1H, m, H-15), 2.61 (3H, s, 22-OCH₃), 2.56 (3H, s, N₄-CH₃), 2.48 (1H, d, J = 13.0 Hz, H-21 β), 1.73 (1H, m, H-19 α), 1.52 (1H, m, H-20), 1.49 (1H, m, H-19 β), 0.97 (3H, t, J = 7.2 Hz, H-18); ¹³C-NMR (100 MHz, CDCl₃) δ : 190.9 (C-3), 172.2 (C-22), 136.5 (C-13), 134.1 (C-2), 128.7 (C-8), 126.8 (C-11), 121.0 (C-9), 120.8 (C-7), 120.4 (C-10), 111.9

(C-12), 57.0 (C-5), 50.4 (22-OCH₃), 46.7 (C-21), 45.8 (C-14), 43.6 (C-16), 43.2 (N₄-CH₃), 42.7 (C-20), 31.9 (C-15), 25.5 (C-19), 18.7 (C-6), 12.9 (C-18)。以上化合物数据与文献报道一致^[6], 故鉴定化合物 **6** 为 tabernaemontanine。

化合物 **7**: 黄色粉末, 改良碘化铯钾反应为阳性。[α]_D²⁵ -59.3° (*c* 0.86, CH₃OH); UV $\lambda_{\max}^{\text{MeOH}}$ (nm): 211, 239, 315; IR $\nu_{\max}^{\text{KBr}}$ (cm⁻¹): 3 321, 1 725, 1 573, 1 454; HR-ESI-MS *m/z*: 355.201 8 [M+H]⁺; ¹H-NMR (400 MHz, CDCl₃) δ : 8.91 (1H, s, NH), 7.70 (1H, d, *J* = 8.0 Hz, H-9), 7.33 (1H, m, H-11), 7.32 (1H, m, H-12), 7.15 (1H, d, *J* = 8.0 Hz, H-10), 3.98 (1H, m, H-5), 3.89 (1H, t, *J* = 3.0 Hz, H-16), 3.37 (1H, m, H-6 α), 3.32 (1H, m, H-14 α), 3.11 (1H, t, *J* = 12.2 Hz, H-14 β), 2.89 (1H, m, H-15), 2.78 (1H, m, H-6 β), 2.67 (1H, m, H-21 α), 2.64 (3H, s, 22-OCH₃), 2.62 (3H, s, N₄-CH₃), 2.60 (1H, m, H-21 β), 1.89 (1H, m, H-20), 1.40 (1H, m, H-19 α), 1.37 (1H, m, H-19 β), 1.01 (3H, t, *J* = 7.4 Hz, H-18); ¹³C-NMR (100 MHz, CDCl₃) δ : 191.6 (C-3), 171.5 (C-22), 136.5 (C-13), 134.2 (C-2), 128.6 (C-8), 126.9 (C-11), 121.0 (C-9), 120.5 (C-7), 120.5 (C-10), 111.9 (C-12), 56.9 (C-5), 50.5 (C₂₂-OCH₃), 49.2 (C-16), 48.9 (C-21), 43.6 (N₄-CH₃), 42.6 (C-20), 39.4 (C-14), 30.8 (C-15), 23.6 (C-19), 20.3 (C-6), 11.6 (C-18)。化合物 **7** 的 NMR (CDCl₃) 谱与化合物 **6** 非常相似, 差别在于化合物 **7** 的 H-21 向高场位移, H-20 和 H-16 向低场位移。综上所述, 以上化合物数据与文献报道一致^[6], 故鉴定化合物 **7** 为 dregamine。

化合物 **8**: 黄色粉末, 改良碘化铯钾反应为阳性。[α]_D²⁵ -15.7° (*c* 0.82, CH₃OH); UV $\lambda_{\max}^{\text{MeOH}}$ (nm): 207, 223, 285; IR $\nu_{\max}^{\text{KBr}}$ (cm⁻¹): 3 351, 1 725, 1 629, 1 460; HR-ESI-MS *m/z*: 395.232 9 [M+H]⁺; ¹H-NMR (600 MHz, CDCl₃) δ : 7.79 (1H, s, NH), 7.46 (1H, d, *J* = 7.6 Hz, H-9), 7.24 (1H, d, *J* = 7.6 Hz, H-12), 7.15 (1H, t, *J* = 7.6 Hz, H-11), 7.08 (1H, t, *J* = 7.6 Hz, H-10), 3.70 (3H, s, 22-OCH₃), 3.58 (1H, brs, H-21), 3.33 (1H, m, H-3), 3.28 (1H, m, H-5 α), 3.19 (1H, m, H-6 α), 3.17 (1H, m, H-5 β), 3.00 (1H, m, H-6 β), 2.69 (1H, dd, *J* = 16.2, 4.2 Hz, H-17 α), 2.65 (1H, d, *J* = 13.7 Hz, H-24 α), 2.52 (1H, dd, *J* = 16.2, 8.7 Hz, H-17 β), 2.11 (3H, s, H-26), 1.99 (1H, d, *J* = 13.7 Hz, H-24 β), 1.70 (1H, s, H-14), 1.59 (1H, m, H-19 α), 1.58

(1H, m, H-15 α), 1.43 (1H, m, H-19 β), 1.27 (1H, m, H-20), 1.25 (1H, m, H-15 β), 0.89 (3H, t, *J* = 7.4 Hz, H-18); ¹³C-NMR (150 MHz, CDCl₃) δ : 208.8 (C-25), 175.8 (C-22), 136.7 (C-2), 135.6 (C-13), 128.9 (C-8), 122.1 (C-11), 119.4 (C-10), 118.6 (C-9), 110.5 (C-12), 110.2 (C-7), 58.4 (C-21), 55.4 (C-3), 54.9 (C-16), 52.8 (22-OCH₃), 51.6 (C-5), 46.9 (C-24), 38.7 (C-20), 37.9 (C-17), 31.1 (C-26), 31.0 (C-14), 27.2 (C-15), 27.0 (C-19), 22.2 (C-6), 11.8 (C-18)。以上化合物数据与文献报道一致^[7], 故鉴定化合物 **8** 为 3-(2-oxopropyl) coronaridine。

化合物 **9**: 黄色粉末, 改良碘化铯钾反应为阳性。[α]_D²⁵ -15.7° (*c* 0.82, CH₃OH); UV $\lambda_{\max}^{\text{MeOH}}$ (nm): 207, 299; IR $\nu_{\max}^{\text{KBr}}$ (cm⁻¹): 3 351, 1 725, 1 629, 1 460; HR-ESI-MS *m/z*: 383.197 2 [M+H]⁺; ¹H-NMR (400 MHz, CDCl₃) δ : 7.99 (1H, s, NH), 7.14 (1H, d, *J* = 8.7 Hz, H-9), 6.94 (1H, d, *J* = 2.3 Hz, H-12), 6.82 (1H, dd, *J* = 8.7, 2.3 Hz, H-11), 4.53 (2H, brs, H-21), 4.51 (1H, m, H-5 α), 3.86 (3H, s, 10-OCH₃), 3.74 (3H, s, 22-OCH₃), 3.25 (1H, m, H-6 α), 3.20 (1H, m, H-6 β), 3.18 (1H, m, H-5 β), 2.66 (1H, m, H-17 α), 2.64 (1H, m, H-14), 2.01 (1H, m, H-17 β), 1.74 (1H, m, H-15 α), 1.74 (1H, m, H-20), 1.54 (1H, m, H-19 α), 1.43 (1H, m, H-19 β), 1.40 (1H, m, H-15 β), 1.00 (3H, t, *J* = 7.4 Hz, H-18); ¹³C-NMR (100 MHz, CDCl₃) δ : 175.9 (C-22), 173.2 (C-3), 154.3 (C-10), 134.8 (C-2), 131.0 (C-13), 128.3 (C-8), 112.7 (C-11), 111.5 (C-12), 109.3 (C-7), 100.6 (C-9), 56.3 (C-21), 56.1 (10-OCH₃), 55.7 (C-16), 53.1 (22-OCH₃), 42.8 (C-5), 38.3 (C-20), 36.1 (C-17), 35.6 (C-14), 31.2 (C-15), 27.8 (C-19), 21.3 (C-6), 11.5 (C-18)。以上化合物数据与文献报道一致^[5], 故鉴定化合物 **9** 为 3-oxovoacangine。

化合物 **10**: 无色方晶 (甲醇), 改良碘化铯钾反应为阳性。mp 164~166 °C; [α]_D²⁵ +336.1° (*c* 0.86, CH₃OH); UV $\lambda_{\max}^{\text{MeOH}}$ (nm): 211, 230, 283, 307, 321; IR $\nu_{\max}^{\text{KBr}}$ (cm⁻¹): 3 200, 1 510, 1 444; HR-ESI-MS *m/z*: 293.167 1 [M+H]⁺; ¹H-NMR (400 MHz, CDCl₃) δ : 8.46 (1H, d, *J* = 8.3 Hz, H-9), 8.42 (1H, s, H-2), 7.98 (1H, d, *J* = 8.3 Hz, H-12), 7.61 (1H, t, *J* = 8.3 Hz, H-11), 7.54 (1H, t, *J* = 8.3 Hz, H-10), 5.26 (1H, q, *J* = 6.7 Hz, H-19), 3.99 (1H, s, H-3), 3.32 (1H, brs, H-15), 3.10 (1H, m, H-5 α), 2.85 (1H, d, *J* = 12.9 Hz, H-21 β), 2.75 (1H, m, H-5 β), 2.62 (1H, m, H-6 α), 2.54 (1H, m,

H-6 β), 2.54 (1H, m, H-21 α), 2.10 (1H, m, H-14 α), 2.03 (1H, m, H-14 β), 1.83 (3H, d, J = 6.7 Hz, H-18); ^{13}C -NMR (100 MHz, CDCl_3) δ : 151.2 (C-2), 148.4 (C-13), 146.8 (C-17), 134.8 (C-20), 130.8 (C-16), 130.2 (C-12), 128.5 (C-11), 127.1 (C-9), 126.6 (C-10), 125.4 (C-8), 118.9 (C-19), 77.4 (C-7), 67.4 (C-3), 53.2 (C-5), 52.8 (C-21), 41.0 (C-6), 32.9 (C-15), 25.7 (C-14), 13.0 (C-18)。以上化合物数据与文献报道一致^[8], 故鉴定化合物 **10** 为 voastrictine。

化合物 **11**: 黄色粉末, 改良碘化铯钾反应为阳性。 $[\alpha]_{\text{D}}^{25} +21.1^\circ$ (c 0.70, CH_3OH); UV $\lambda_{\text{max}}^{\text{MeOH}}$ (nm): 223, 281; IR $\nu_{\text{max}}^{\text{KBr}}$ (cm^{-1}): 3 363, 1 721, 1 649, 1 450; HR-ESI-MS m/z : 355.201 2 $[\text{M}+\text{H}]^+$; ^1H -NMR (400 MHz, CD_3OD) δ : 7.39 (1H, d, J = 7.8 Hz, H-9), 7.31 (1H, d, J = 7.8 Hz, H-12), 7.06 (1H, t, J = 7.8 Hz, H-11), 6.98 (1H, t, J = 7.8 Hz, H-10), 5.64 (1H, q, J = 6.7 Hz, H-19), 4.18 (1H, brs, H-3), 3.75 (3H, s, 22-OCH₃), 3.52 (1H, d, J = 12.2 Hz, H-21 α), 3.46 (1H, d, J = 6.6 Hz, H-17), 3.17 (1H, m, H-5 α), 3.13 (1H, m, H-15), 3.00 (1H, m, H-21 β), 2.98 (2H, m, H-5 β , 6 α), 2.62 (1H, m, H-6 β), 2.46 (1H, m, H-16), 2.25 (1H, m, H-14 α), 2.13 (1H, m, H-14 β), 1.68 (3H, dd, J = 6.7, 1.4 Hz, H-18); ^{13}C -NMR (100 MHz, CD_3CD) δ : 176.6 (C-22), 137.9 (C-13), 135.5 (C-2), 134.5 (C-20), 128.5 (C-8), 124.7 (C-19), 122.1 (C-11), 119.8 (C-10), 118.7 (C-9), 112.1 (C-12), 107.3 (C-7), 63.2 (C-17), 54.0 (C-21), 53.7 (C-3), 52.3 (22-OCH₃), 51.8 (C-5), 51.0 (C-16), 34.1 (C-15), 31.5 (C-14), 18.9, (C-6), 13.5 (C-18)。以上化合物数据与文献报道一致^[9], 故鉴定化合物 **11** 为 16*R*,19*E*-isositsirikine。

化合物 **12**: 黄色粉末, 改良碘化铯钾反应为阳性。 $[\alpha]_{\text{D}}^{25} -69.9^\circ$ (c 0.85, CH_3OH); UV $\lambda_{\text{max}}^{\text{MeOH}}$ (nm): 223, 281; IR $\nu_{\text{max}}^{\text{KBr}}$ (cm^{-1}): 3 363, 1 721, 1 649, 1 450; HR-ESI-MS m/z : 355.201 2 $[\text{M}+\text{H}]^+$; ^1H -NMR (400 MHz, CD_3OD) δ : 7.41 (1H, d, J = 7.9 Hz, H-9), 7.32 (1H, d, J = 7.9 Hz, H-12), 7.06 (1H, t, J = 7.9 Hz, H-11), 6.99 (1H, t, J = 7.9 Hz, H-10), 5.54 (1H, q, J = 6.8 Hz, H-19), 4.18 (1H, brs, H-3), 3.96 (1H, dd, J = 10.6, 4.1 Hz, H-17 α), 3.82 (1H, m, H-17 β), 3.74 (1H, d, J = 12.0 Hz, H-21 α), 3.51 (3H, s, 22-OCH₃), 3.18 (1H, m, H-5 α), 3.03 (1H, m, H-5 β), 3.02 (1H, m, H-6 α), 3.01 (1H, m, H-15), 2.99 (1H, m, H-21 β), 2.65

(1H, m, H-6 β), 2.59 (1H, m, H-16), 2.31 (1H, m, H-14 α), 2.15 (1H, m, H-14 β), 1.62 (3H, d, J = 6.8 Hz, H-18); ^{13}C -NMR (100 MHz, CD_3CD) δ : 175.9 (C-22), 138.0 (C-13), 136.3 (C-20), 134.7 (C-2), 128.6 (C-8), 123.8 (C-19), 122.2 (C-11), 119.9 (C-10), 118.7 (C-9), 112.1 (C-12), 107.7 (C-7), 63.2 (C-17), 54.8 (C-21), 53.8 (C-3), 52.0 (C-5), 51.8 (C-16), 51.7 (22-OCH₃), 34.8 (C-15), 30.8 (C-14), 19.1, (C-6), 13.7 (C-18)。化合物 **12** 的 NMR (CD_3OD) 谱与化合物 **11** 非常相似, 差别在于化合物 **12** 的 C-16 和 C-17 位 ^1H -NMR 的化学位移均向低场位移, 并且在 NOESY 谱中, H-18 与 H-21 α 有 NOE 相关, 说明化合物 **12** 中的双键构型为 *Z* 式。其与文献报道的数据一致^[10], 故鉴定化合物 **12** 为 16*R*,19*Z*-isositsirikine。

化合物 **13**: 黄色粉末, 改良碘化铯钾反应为阳性。 $[\alpha]_{\text{D}}^{25} -18.5^\circ$ (c 0.72, CH_3OH); UV $\lambda_{\text{max}}^{\text{MeOH}}$ (nm): 220, 280; IR $\nu_{\text{max}}^{\text{KBr}}$ (cm^{-1}): 3 390, 1 724, 1 652, 1 454; HR-ESI-MS m/z : 371.196 5 $[\text{M}+\text{H}]^+$; ^1H -NMR (600 MHz, CD_3OD) δ : 7.47 (1H, d, J = 7.9 Hz, H-9), 7.34 (1H, d, J = 7.9 Hz, H-12), 7.14 (1H, t, J = 7.9 Hz, H-11), 7.05 (1H, t, J = 7.9 Hz, H-10), 5.88 (1H, q, J = 7.1 Hz, H-19), 4.52 (1H, brs, H-3), 4.34 (1H, d, J = 12.6 Hz, H-21 α), 3.77 (3H, s, 22-OCH₃), 3.74 (1H, m, H-5 α), 3.70 (1H, m, H-5 β), 3.48 (1H, d, J = 5.9 Hz, H-17), 3.43 (1H, d, J = 12.6 Hz, H-21 β), 3.33 (1H, m, H-6 α), 3.14 (1H, m, H-6 β), 3.14 (1H, m, H-15), 2.74 (1H, m, H-16), 2.31 (1H, m, H-14 α), 2.22 (1H, m, H-14 β), 1.79 (3H, dd, J = 7.1, 1.4 Hz, H-18); ^{13}C -NMR (150 MHz, CD_3CD) δ : 175.6 (C-22), 138.7 (C-13), 132.2 (C-20), 131.1 (C-2), 128.7 (C-8), 127.6 (C-19), 123.3 (C-11), 120.5 (C-10), 119.1 (C-9), 112.5 (C-12), 106.0 (C-7), 71.1 (C-3), 67.5 (C-5), 62.8 (C-21), 62.7 (C-17), 52.4 (C-16), 52.4 (22-OCH₃), 49.6 (C-14), 33.2 (C-15), 20.0 (C-6)。化合物 **13** 的 NMR 图谱与化合物 **11** 比较相似, 差别在于化合物 **13** 的 C-3、C-5 和 C-21 的 ^1H -和 ^{13}C -NMR 化学位移值均向低场位移, 结合分子式, 提示化合物为 **11** 的氮氧化衍生物。综上所述, 以上化合物数据与文献报道一致^[10], 故鉴定化合物 **13** 为 16*R*,19*E*-isositsirikine *N*₄-oxide。

化合物 **14**: 黄色粉末, 改良碘化铯钾反应为阳性。 $[\alpha]_{\text{D}}^{25} -50.9^\circ$ (c 0.80, CH_3OH); UV $\lambda_{\text{max}}^{\text{MeOH}}$ (nm): 240, 280; IR $\nu_{\text{max}}^{\text{KBr}}$ (cm^{-1}): 3 223, 1 634, 1 450;

HR-ESI-MS m/z : 297.195 7 $[M+H]^+$; 1H -NMR (600 MHz, CD_3OD) δ : 7.38 (1H, d, $J = 7.8$ Hz, H-9), 7.30 (1H, d, $J = 7.8$ Hz, H-12), 7.04 (1H, t, $J = 7.8$ Hz, H-11), 6.97 (1H, t, $J = 7.8$ Hz, H-10), 5.53 (1H, q, $J = 6.7$ Hz, H-19), 4.21 (1H, brs, H-3), 3.61 (1H, d, $J = 12.0$ Hz, H-21 α), 3.40 (1H, m, H-17), 3.18 (1H, m, H-5 α), 3.05 (1H, m, H-5 β), 3.03 (1H, m, H-15), 2.96 (1H, m, H-21 β), 2.93 (1H, m, H-6 α), 2.62 (1H, m, H-6 β), 2.23 (1H, m, H-14), 1.67 (3H, dd, $J = 6.7, 1.4$ Hz, H-18), 1.56 (1H, m, H-16a), 1.41 (1H, m, H-16b), 1.33 (1H, m, H-15); ^{13}C -NMR (150 MHz, CD_3CD) δ : 138.0 (C-13), 137.8 (C-20), 134.9 (C-2), 128.6 (C-8), 122.2 (C-11), 120.0 (C-10), 119.8 (C-9), 118.6 (C-19), 111.9 (C-12), 107.1 (C-7), 61.1 (C-17), 54.6 (C-3), 54.0 (C-21), 51.9 (C-5), 36.9 (C-16), 33.4 (C-14), 32.3 (C-15), 18.2 (C-6), 13.2 (C-18)。综上所述, 以上化合物数据与文献报道一致^[11], 故鉴定化合物 **14** 为 geissoschizol。

4 讨论

据文献报道, 化合物 **3** 具有一定的抗肿瘤活性, 其在体外对淋巴细胞性白血病 P-388 细胞的半数有效剂量 (ED_{50}) 为 $0.43 \mu g/mL$ ^[12]。

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