

延胡索中生物碱成分的研究

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摘 要 目的 提取分离延胡索中的生物碱供延胡索种质评价使用。方法 运用色谱学和波谱学方法分离鉴定延胡索中的生物碱。结果 从延胡索总碱中分离得到了 13种生物碱, 鉴定了其中 12种生物碱的结构, 分别为: *d*-紫堇碱、四氢巴马亭、脱氢紫堇碱、四氢黄连碱、四氢小檗碱、异紫堇球碱、原托品碱、四氢非洲防己胺、氯仿巴马亭、saulatine 海罂粟碱、脱氢海罂粟碱。结论 生物碱 saulatine 为首次从罂粟科植物中分得, 异紫堇球碱为首次从延胡索中分得。

关键词 延胡索; 异喹啉生物碱; 异喹啉苄咪唑啉型生物碱; 分离; 鉴定

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延胡索为罂粟科紫堇属植物延胡索 (*Corydalis yanhusuo* W. T. Wang) 的干燥块茎, 具有活血、利气、止痛的功效, 其主要活性成分为异喹啉生物碱^[1]。延胡索生物碱的化学研究始于二十世纪二十年代, 到目前为止已从延胡索中分得生物碱近二十个, 其类型分属原小檗碱型、原托品碱型、阿朴菲型、苯并菲啶型等四种异喹啉型生物碱, 其中多数属原小檗碱型, 少数为阿朴菲型与原托品碱型, 只有一个为苯并菲啶型。最近, 我们在对延胡索种质资源进行研究的过程中, 对延胡索中的生物碱进行了分离制备, 从其总碱中分得 13个生物碱单体, 鉴定了其中的 12个, 其中异紫堇球碱 (isocorybulbine) 为首次从延胡索中分得; saulatine 为首次从罂粟科植物中分得, 这也是首次从罂粟科植物中获得异喹啉苄咪唑啉型 (isoquinobenzazepine type) 生物碱, 以前此类生物碱仅在防己科和小檗科植物中发现。

1 仪器与材料

紫外光谱用岛津 Shimadzu UV-2501 PC紫外可见分光光度计测定; 红外光谱用 Nicolet Impact 410 型红外光谱仪 (KBr压片) 测定; 质谱用 HP5973N MSD质谱仪 (EI) 及 Hewlett Packard 1100 MSD质谱检测器 (ESI) 测定; 核磁共振谱用 Bruker DPX-300型核磁共振仪 (TMS内标) 测定。

柱层析及薄层层析硅胶均为青岛海洋化工厂产

品 所用试剂均为分析纯

延胡索购自浙江东阳, 经作者鉴定为延胡索 *Corydalis yanhusuo* 的块茎。

2 提取分离

延胡索干燥块茎 8.0 kg, 粉碎, 用 95% 工业乙醇回流提取 3次, 减压回收乙醇, 浸膏用 2% 盐酸捏溶提取至残渣生物碱反应不明显, 用石油醚预萃取三次, 盐酸液用 10% NaOH调 pH 12以上, 用氯仿反复萃取, 合并氯仿液并回收氯仿得总碱。总碱经硅胶柱层析分离, 石油醚-氯仿-乙酸乙酯梯度洗脱, 反复分离纯化, 先后得碱I (1200 mg)、碱II (800 mg)、碱III (90 mg)、碱IV (80 mg)、碱V (140 mg)、碱VI (30 mg)、碱VII (170 mg)、碱VIII (420 mg)、碱IX (130 mg)、碱X (20 mg)、碱XII (390 mg) 和碱XIII (20 mg)。

3 结构鉴定

碱I 无色棱状柱晶 (甲醇) $UV_{\lambda_{max}}^{MeOH}$ nm: 285
ESI-MS m/z : 370 [M+H]⁺。IR (KBr) cm^{-1} : 2963, 2903, 1609, 1493, 1227, 854, 797 ¹HNM R (CDCl₃) δ
6.90 (1H, d, J = 8.4 Hz, 12-H), 6.82 (1H, d, J = 8.4 Hz, 11-H), 6.69 (1H, s, 1-H), 6.61 (1H, s, 4-H), 4.20 (1H, d, J = 15.8 Hz, 8-He), 3.88 (12H, m, 4

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OCH₃), 3.69(1H, d, J = 2.3 Hz, 14-H), 3.50(1H, d, J = 15.8 Hz, 8-Ha), 3.23(1H, m, 13-H), 3.11(2H, m, 6-H), 2.60(2H, m, 5-H), 0.95(3H, d, J = 6.9 Hz, CH₃) ¹³C-NMR(CDCl₃) δ 149.9(C-9), 147.6(C-3), 147.1(C-2), 146.0(C-10), 134.8(C-12a), 128.4, 128.3(C-4a, -14a, -8a), 123.9(C-12), 111.1(C-11), 110.9(C-4), 108.6(C-1), 62.9(C-14), 60.0(-OCH₃), 56.0(-OCH₃), 55.8(-OCH₃), 55.7(-OCH₃), 54.4(C-8), 51.3(C-6), 38.2(C-13), 29.2(C-5), 18.2(-CH₃) 碱I的IR光谱与Sadtler标准红外光谱Corydaline相同, ¹H和¹³C-NMR数据与紫堇碱(*d*-Corydaline)数据一致^[2, 51], 推定碱I为*d*紫堇碱

碱II 无色片状结晶(甲醇) UV_{max}^{MeOH} nm 285 ESI-MS m/z : 356[M+H]⁺. IR(KBr) cm⁻¹: 2940, 2927, 1610, 1522, 1493, 1455, 1256, 1229, 1080, 858, 784 ¹H-NMR(CDCl₃) δ 6.89(1H, d, J = 8.4 Hz), 6.80(1H, d, J = 8.4 Hz), 6.73(1H, s), 6.62(1H, s), 4.26(1H, d, J = 15.8 Hz), 3.89(3H, s), 3.88(3H, s), 3.86(3H, s), 3.85(3H, s), 3.59(2H, m), 3.23(3H, m), 2.85(1H, m), 2.66(2H, m) ¹³C-NMR(CDCl₃) δ 150.3(C-9), 147.6, 147.5(C-2, C-3), 145.2(C-10), 129.7(C-14a), 128.6(C-12a), 127.7(C-8a), 126.8(C-4a), 123.8(C-12), 111.5(C-4), 111.1(C-11), 108.7(C-1), 60.2, 59.3(C-14, OCH₃), 56.1(OCH₃), 55.9(OCH₃), 55.8(OCH₃), 53.9(C-8), 51.5, 36.3(C-13), 29.1(C-5) 碱II的IR光谱与Sadtler标准红外光谱Tetrahydropalmatine相同, ¹³C-NMR数据与四氢巴马亭(Tetrahydropalmatine)数据一致^[2], 推定碱II为四氢巴马亭。

碱III 黄色晶状粉末 UV_{max}^{MeOH} nm 284, 336 ESI-MS m/z : 366 IR(KBr) cm⁻¹: 3386, 1604, 1522, 1276, 807 ¹H-NMR(CDCl₃) δ 10.67(1H, s), 7.91(1H, d, J = 9.3 Hz), 7.86(1H, d, J = 9.3 Hz), 7.16(1H, s), 6.93(1H, s), 5.30(2H, br. s), 4.36(3H, s), 4.08(3H, s), 4.00(3H, s), 3.94(3H, s), 3.26(2H, br. s), 2.97(3H, s) ¹³C-NMR(CDCl₃) δ 151.4, 150.6, 147.8, 146.5, 146.2, 133.8, 132.3, 128.7, 125.5, 121.8, 119.8, 119.3, 114.0, 110.8, 63.2, 57.3, 57.1, 56.6, 56.3, 28.2, 18.0 以上数据与去氢紫堇碱(Dehydrocorydaline)数据对比^[4, 1], 推定碱III为去氢紫堇碱。

碱IV 白色针状粉末(甲醇) UV_{max}^{MeOH} nm 291 ESI-MS m/z : 324[M+H]⁺. ¹H-NMR(CDCl₃) δ 6.72(1H, s, 1-H), 6.68(1H, d, J = 7.8 Hz, 11-H), 6.63(1H, d, J = 7.8 Hz, 12-H), 6.59(1H, s, 4-H), 5.95(2H, s, O-CH₂-O), 5.92(2H, s, O-CH₂-O), 4.09(1H, d, J = 15.2, 8-He), 3.59(1H, d, J = 3.2 Hz, 14-H), 3.54(1H, d, J = 15.2, 8-Ha), 3.23(1H, dd, J = 16.0和3.6 Hz, 13-He), 3.12(2H, m, 6-H), 2.79(1H, m, 13-Ha), 2.64(2H, m, 5-H) ¹³C-NMR(CDCl₃) δ 146.2, 146.0, 145.0, 143.3(C-10), 130.7(C-14a), 128.5(C-12a), 127.7(C-4a), 121.0(C-12), 108.4(C-4), 106.7(C-11), 105.5(C-1), 101.0(O-CH₂-O), 100.8(O-CH₂-O), 59.7(C-14), 52.9(C-8), 51.2(C-6), 36.4(C-13), 29.5(C-5) 以上数据与四氢黄连碱(Tetrahydrocoptisine)数据一致^[2], 推定碱IV为四氢黄连碱。

碱V 白色毛状针晶(甲醇) UV_{max}^{MeOH} nm 285 ESI-MS m/z : 340[M+H]⁺. ¹H-NMR(CDCl₃) δ 6.87(1H, d, J = 8.3 Hz), 6.79(1H, d, J = 8.3 Hz), 6.73(1H, s), 6.59(1H, s), 5.92(2H, s, O-CH₂-O), 4.24(1H, d, J = 15.7 Hz), 3.85(6H, s, 2×OCH₃), 3.54(2H, m), 3.19(3H, m), 2.82(1H, m), 2.64(2H, m) ¹³C-NMR(CDCl₃) δ 150.3(C-9), 146.2(C-2和C-3), 145.1(C-10), 130.8(C-14a), 128.3(C-12a), 127.8(C-4a和C-8a), 123.9(C-12), 111.0(C-11), 108.4(C-4), 105.5(C-1), 100.8(O-CH₂-O), 60.2(C-14), 59.2(-OCH₃), 55.9(-OCH₃), 53.9(C-8), 51.4(C-6), 36.4(C-13), 29.5(C-5) 以上数据与四氢小檗碱(Tetrahydroberberine)数据一致^[2, 51], 推定碱IV为四氢小檗碱。

碱VI 无色方晶(甲醇) UV_{max}^{MeOH} nm 284 EI-MS m/z (%): 355[M]⁺ (44), 340[M-CH₃]⁺ (14), 324[M-OCH₃]⁺ (7), 178 (100), 163 (27). ¹H-NMR(CDCl₃) δ 6.90(1H, d, J = 8.4 Hz, 12-H), 6.84(1H, d, J = 8.4 Hz, 11-H), 6.69(2H, s, 1-H, 4-H), 5.47(1H, OH), 4.21(1H, d, J = 15.9 Hz, 8-He), 3.90(3H, s, OCH₃), 3.89(3H, s, OCH₃), 3.88(3H, s, OCH₃), 3.70(1H, br. s, 14-H), 3.51(1H, d, J = 16.0 Hz, 8-Ha), 3.19(3H, m, 6-H, 13-H), 2.58(2H, m, 5-H), 0.98(3H, d, J = 6.8 Hz, CH₃) ¹³C-NMR(CDCl₃) δ 150.1, 145.4, 145.1, 143.8, 135.2, 129.3, 128.6, 128.1, 123.8, 114.1, 111.3, 108.1, 63.1, 60.0, 56.2, 56.0, 54.4, 51.3, 38.6, 29.2, 18.1

以上数据与紫堇球碱 (Corybulbine) Apocavidine Isoapocavidine以及紫堇碱数据进行对比^[5, 9, 10], 推定碱VI为异紫堇球碱 (Isocorybulbine).

碱VII 白色粉末 $UV_{\max}^{MeOH}$ nm 292 ESI-MS m/z : 354 $[M+H]^+$. IR (KBr) cm^{-1} : 2831, 1672, 1612, 1488, 1259, 972, 795 1H NMR (DMSO- d_6) δ 6.96(1H, s), 6.81(1H, s), 6.73(1H, d, $J=7.9$ Hz), 6.68(1H, d, $J=7.9$ Hz), 6.00(2H, s), 5.94(2H, s), 3.81(1H, br. s), 3.51(2H, br. s), 3.33(1H, s), 2.81(1H, br. s), 2.50(1H, s), 2.41(2H, br. s), 1.82(3H, s). ^{13}C NMR (DMSO- d_6) δ 194.7 (C-14), 147.4 (C-3), 145.9 (C-2), 145.5 (C-9), 145.4 (C-10), 136.1 (C-4a), 132.8 (C-14a), 129.7 (C-12a), 125.1 (C-12), 118.4 (C-8a), 110.5 (C-4), 107.5 (C-1), 106.4 (C-11), 101.2 (O-CH₂-O), 100.8 (O-CH₂-O), 57.5 (C-6), 50.8 (C-8), 46.1 (C-13), 41.2 (N-CH₃), 30.6 (C-5). 以上数据与原托品碱 (protopine)数据一致^[2], 推定碱VII为原托品碱.

碱VIII 白色粉末 $UV_{\max}^{MeOH}$ nm 286 ESI-MS m/z : 342 $[M+H]^+$. 1H NMR (DMSO- d_6) δ 8.68(1H, s), 6.89(2H, d, $J=8.0$ Hz), 6.70(1H, s), 6.64(1H, s), 4.06(1H, d, $J=15.8$ Hz), 3.77(3H, s), 3.73(3H, s), 3.72(3H, s), 3.36(2H, m), 3.14(2H, m), 2.88(1H, m), 2.51(3H, m). ^{13}C NMR (DMSO- d_6) δ 150.0 (C-9), 146.2 (C-10), 144.8 144.6 (C-2和 C-3), 130.1 (C-14a), 128.5 (C-12a), 127.8 (C-8a), 124.9 (C-4a), 123.9 (C-12), 112.6 (C-4), 112.0 (C-11), 111.4 (C-1), 59.7 58.8 (C-14, 9-OCH₃), 55.9 55.7 (2-OCH₃), 53.6 (C-8), 51.3 (C-6), 36.0 (C-13), 28.7 (C-5). 以上数据与文献四氢非洲防己胺 (tetrahydrocolumbamine)数据基本一致^[2], 推定碱VIII为四氢非洲防己胺.

碱IX 淡黄色粉末 $UV_{\max}^{MeOH}$ nm 283, 354 ESI-MS m/z : 470 $[M+H]^+$. IR (KBr) cm^{-1} : 2927, 1605, 1511, 1241, 1091, 806 1H NMR (CDCl₃) δ 7.21(1H, s), 6.99(1H, d, $J=8.5$ Hz), 6.92(1H, d, $J=8.5$ Hz), 6.65(1H, s), 6.15(1H, br. s), 5.65(1H, s), 3.91(12H, m), 3.73(1H, m), 3.45(1H, m), 2.76(1H, m), 1.59(1H, m). ^{13}C NMR (CDCl₃) δ 149.7, 149.2, 147.8, 146.4, 137.6, 129.3, 127.5, 123.4, 118.6, 114.9, 114.6, 110.9, 107.1, 105.5, 96.9, 73.6, 61.0, 56.3, 56.1, 55.9, 51.8, 29.9 1H NMR与文献氯仿巴马亭 (palmatine chloroform)一致, 对比

氯仿小檗碱¹³C NMR数据^[3, 6], 并结合 ESI-MS数据推定碱IX为氯仿巴马亭. 由于我们在延胡索生物碱提取及分离的过程中均使用了氯仿, 因此氯仿巴马亭极有可能是人工产物, 它在药材中应以巴马亭的形式存在.

碱X 白色粉末 $UV_{\max}^{MeOH}$ nm 282, 312 EI-MS m/z (%): 397 $[M]^+$ (68), 368(100), 354(28), 338(92), 191(32). IR (KBr) cm^{-1} : 2946, 1671, 1633, 1598, 1445, 1270, 883 1H NMR (CDCl₃) δ 7.33(1H, s, 1-H), 7.06(1H, d, $J=8.3$ Hz, 13-H), 6.91(1H, d, $J=8.3$ Hz, 12-H), 6.74(1H, s, 4-H), 5.20(1H, s, 14-H), 4.61(1H, m, 9-He), 3.96(3H, s, OCH₃), 3.90(3H, s, OCH₃), 3.86(3H, s, OCH₃), 3.82(3H, s, OCH₃), 3.88(1H, m, $J=18.9$ Hz, 9-Ha), 3.35(2H, m, 6-H), 3.04(2H, m, 5-H). ^{13}C NMR (CDCl₃) δ 198.4 (C-15), 169.1 (C-8), 153.4 (C-10), 152.5 (C-3), 148.4 (C-2), 145.6 (C-11), 132.9 128.9 (C-4a和 C-15a), 126.1 124.3 (C-9a和 C-13a), 123.5 (C-13), 112.5 (C-4), 111.6 (C-1), 110.6 (C-12), 66.7 (C-14), 60.7 (OCH₃), 56.2 (OCH₃), 56.0 (OCH₃), 55.9 (OCH₃), 42.7 (C-6), 33.0 (C-9), 32.2 (C-5). 以上数据与 saulatine数据一致^[7], 推定碱X为 saulatine.

碱XII 棕色固体 $UV_{\max}^{MeOH}$ nm 301 EI-MS m/z (%): 355 $[M]^+$ (86), 354 $[M-H]^+$ (100), 340 $[M-CH_3]^+$ (58), 324 $[M-OCH_3]^+$ (32). 1H NMR (CDCl₃) δ 8.10(1H, s, 11-H), 6.79(1H, s, 8-H), 6.59(1H, s, 3-H), 3.93(3H, s, OCH₃), 3.91(3H, s, OCH₃), 3.88(3H, s, OCH₃), 3.66(3H, s, OCH₃), 3.03(4H, m, 4-He, 5-He, 6-He, 7-He), 2.61(3H, m, 4-Ha, 5-Ha, 6-H), 2.55(3H, s, NCH₃). ^{13}C NMR (CDCl₃) δ 151.9 (C-2), 148.0 (C-9), 147.5 (C-10), 144.3 (C-1), 129.3 (C-7a), 128.8 (C-13a), 127.1 (C-3b), 126.9 (C-11b), 124.5 (C-11a), 111.7 (C-11), 110.9 (C-8), 110.4 (C-3), 62.5 (C-6a), 60.3 (OCH₃), 60.1 (OCH₃), 55.9 (OCH₃), 55.8 (OCH₃), 53.2 (C-5), 43.9 (NCH₃), 34.5 (C-7), 29.2 (C-4). 以上数据与海罂粟碱 (glaucine)数据一致^[2, 5, 8, 11], 推定碱XII为海罂粟碱.

碱XIII 绿棕色晶状粉末 $UV_{\max}^{MeOH}$ nm 284, 333 EI-MS m/z (%): 353 $[M]^+$ (100), 338 $[M-CH_3]^+$ (70), 322 $[M-OCH_3]^+$ (5), 307 $[M-CH_3-OCH_3]^+$ (11). 1H NMR (CDCl₃) δ 9.10(1H, s, 11-H), 7.06(1H, s, 8-H), 6.98(1H, s, 3-H), 6.59(1H, br. s,

7-H), 4.02 (3H, s, OCH₃), 4.02 (3H, s, OCH₃), 4.01 (3H, s, OCH₃), 3.89 (3H, s, OCH₃), 3.35 (2H, t, *J* = 5.6 Hz, 5-H), 3.27 (2H, t, *J* = 5.6 Hz, 4-H), 3.06 (3H, s, NCH₃) ¹³C NMR (CDCl₃) δ 150.7, 149.2, 146.3, 146.0, 144.6, 130.3, 129.6, 125.3, 118.5, 118.2, 110.5, 109.1, 106.6, 102.0, 60.0, 56.4, 55.8, 55.6, 50.6, 40.5, 29.7 以上数据与脱氢海罂粟碱 (dehydroglaucone) 数据一致^[5, 11], 推定碱X III为脱氢海罂粟碱

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Alkaloids from *Rhizoma corydalis*

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ABSTRACT **AIM** To isolate alkaloids from the tuber of *Corydalis yanhusuo* for evaluating the quality of *Corydalis* germ plasm. **METHODS** Chromatographic and spectroscopic methods were used to isolate and identify the alkaloids. **RESULTS** Thirteen alkaloids were obtained, among which, twelve compounds were identified as *d*-corydaline, tetrahydropalmatine, dehydrocorydaline, tetrahydrocoptisine, tetrahydroberberine, isocorybulbine, protopine, tetrahydrocolumbamine, palmatine chloroform, saulatine, glaucine and dehydroglaucine respectively. **CONCLUSION** Saulatine, an isoquinobenzazepine type alkaloids, was obtained from *Papaveraceae* for the first time and isocorybulbine was firstly obtained from *Corydalis yanhusuo*.

KEY WORDS *Corydalis yanhusuo*; Isoquinoline alkaloids; Isoquinobenzazepine alkaloids; Isolation; Identification