三角叶凤毛菊中的三萜化合物

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[摘要] **目的**:研究三角叶凤毛菊 *Saussurea deltoidea* (DC.) Schulz-Bip. 中具有抗肿瘤活性的三萜类化学成分。**方法**:利用正/反相硅胶柱色谱色谱、凝胶分子筛色谱、HPLC 等色谱学方法分离、纯化化合物,运用波谱学方法鉴定化合物结构。**结果**:从三角叶凤毛菊乙酸乙酯萃取部位分离鉴定出 7 个三萜类化合物,其结构分别为:taraxast-20-ene-3β, 3-*O*-diol (1), 3β-hydroxy-11-oxo-ursan-12-ene(2),3β-hydroxy-taraxast-20-ene-30-aldehyde(3), 21α-hydroxy-taraxasterol (4), ursan-9 (11),12-diene-3β-ol (5), ursan-9 (11),12-diene-3β-*O*-acetate (6), 3β-hydroxy-9 (11),12-diene-oleanol (7)。**结论**:7 个三萜类化合物都是首次从该植物中分离得到。

[关键词] 三角叶凤毛菊;三萜;抗肿瘤植物
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Triperpenoids from *Saussurea deltoidea*

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[**Abstract**] **Objective**: Investigate the triperpenoids of *Saussurea deltoidea* with antitumor activities. **Method**: Use various chromatography methods such as silica gel, RP-18 silica gel, Sephadex LH-20 column chromatography, HPLC, et al. **Result**: Seven compounds were isolated from the title plant. Their structures were elucidated by spectral analysis. 7 triperpenoids were isolated and elucidated as taraxast-20-ene-3β, 30-diol (1), 3β-hydroxy -11-oxo-ursan-12-ene (2), 3β-hydroxy-taraxast-20-ene-30-aldehyde (3), 21α-hydroxy-taraxasterol (4), ursan-9 (11),12-diene-3β-ol (5), ursan-9 (11),12-diene-3β-*O*-acetate (6), 3β-hydroxy-9 (11), 12-diene-oleanol (7). **Conclusion**: All the compounds were isolated from *S. deltoidea* for the first time.

[**Key words**] *Saussurea deltoidea*; triperpenoids; antineoplastic herb

三角叶凤毛菊 *Saussurea deltoidea* (DC.) Schulz-Bip. 是菊科凤毛菊属植物,分布在全国各地[1]。据《中华本草》记载,三角叶凤毛菊以根入药,用于治疗风湿痹痛、腹泻、虚热盗汗、头晕耳鸣等症。对于三角叶凤毛菊化学成分研究的报道较少,肖海涛等[2]从该植物地上部分分离鉴定出 15 个化合物,并测定了其细胞毒活性,孟阿兰等[3]对其营养成分氨基酸、维生素和矿物质的含量进行了相关报道。但对该属其他种的化学成分研究较多,主要有倍半萜、三萜、木脂素、甾体及其他类型化合物。ZHANG Bei-bei 等[4]从矮丛凤毛菊 *S. eopygmaea* 中分离鉴定出 17 个化合物,SUN Chang-ming 等[5]从云木香 *S. lappa* 中分离得到多个倍半萜及其二聚体,如 lappadilactone, dehydrocostuslactone, costunolide 等;WANG Hong-bing 等[6]从绵头雪莲花 *S. laniceps* 中分离得到愈创木烷型和桉叶烷型倍半萜;CHENG Qi-fan 等[7]分别从凤毛菊属不同植物中分离得到木脂素类化合物。该属植物中分离得到的化合物具有

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广泛的药理活性,如从云木香中分离得到的倍半萜 cynaropicrin 具有抑制多种肿瘤细胞生长[8]、激活黏附因子[9]等活性。为寻找三角叶凤毛菊中具有抗肿瘤作用的活性成分,本实验对该植物乙酸乙酯部位进行了化学成分研究,从其全草甲醇提取物的乙酸乙酯萃取部位中分离鉴定出 7 个三萜类化合物,均是首次从该植物中分离得到。

1 材料与方法

样品于 2006 年 8 月采自昆明,由中国科学院昆明植物研究所李西文研究员鉴定为三角叶凤毛菊 *S. deltoidea*,标本存放于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。

旋光经 SEPA-300 仪测定,质谱(EI-MS, FAB-MS)用 VG Autospec-3000 型质谱仪测定(其中 EI-MS 在 70 eV 下测定),核磁共振谱用 Bruker AM-400 和 DRX-500 超导核磁共振仪测定(TMS 为内标),薄层色谱板和柱色谱硅胶由青岛海洋化工厂生产,Sephadex LH-20 为 Pharmacia 公司生产,RP-18 反相硅胶为 Merck 公司生产,HPLC 半制备柱为 YMC-Pack,ODS。

2 提取分离

采集三角叶凤毛菊全草晾干,碾成粉末(20 kg)后用工业甲醇热提 3 次,每次加热浸泡 3 h,将提取液合并浓缩得到浸膏2 000 g。浸膏溶于水,分别用石油醚、乙酸乙酯和正丁醇进行萃取,每种溶剂萃取至有机层几近无色,浓缩各萃取液成浸膏。

乙酸乙酯浸膏 400 g,将此浸膏经过 100 ~ 200 目硅胶,用三氯甲烷-甲醇(100∶1 ~ 2∶1)进行洗脱,经薄层色谱合并得 8 组分 A ~ H,组分 B 经过 200 ~ 300 目硅胶,石油醚-丙酮(10∶1 ~ 3∶1)洗脱,经 TLC 合并得 B_1 ~ B_3 3 部分,B_1 部分经过 Sephadex LH-20 凝胶色谱分离,再经 H 级硅胶以石油醚-三氯甲烷 3∶1洗脱分离得到化合物 3(14 mg)和 5(5 mg),B_2 部分使用 HPLC 经 100% 甲醇洗脱得到化合物 6(11 mg)和 7(8 mg),B_3 部分经过 Sephadex LH-20 凝胶色谱划段分离,再经 400 ~ 600 目硅胶以石油醚-三氯甲烷 2∶1洗脱得到化合物 1(50 mg),2(26 mg)和 4(19 mg)。

3 结构鉴定

化合物 1　无色结晶,熔点 199 ~ 200 ℃。EI-MS:442 $[M]^+$(53),^{1}H-NMR ($CDCl_3$, 500 MHz):δ3.21 (1H, dd, J = 11.5, 4.8 Hz, H-3), 5.59 (1H, d, J = 6.7 Hz, H-21), 0.77 (3H, s, H-23), 0.98 (3H, s, H-24), 0.86 (3H, s, H-25), 1.05 (3H, s, H-26), 0.97 (3H, s, H-27), 0.77 (3H, s, H-28), 1.01 (3H, d, J = 6.3 Hz, H-29), 4.02 (1H, d, J = 12.6 Hz, H-30a), 4.13 (1H, d, J = 12.5 Hz, H-30b)。^{13}C-NMR ($CDCl_3$, 125 MHz)-DEPT, δ38.7 (t, C-1), 27.6 (t, C-2), 79.0 (d, C-3), 38.8 (s, C-4), 55.3 (d, C-5), 18.3 (t, C-6), 34.2 (t, C-7), 41.1 (s, C-8), 50.4 (d, C-9), 37.1 (s, C-10), 21.5 (t, C-11), 27.0 (t, C-12), 39.1 (d, C-13), 42.3 (s, C-14), 27.4 (t, C-15), 36.7 (t, C-16), 34.4 (s, C-17), 48.4 (d, C-18), 32.0 (d, C-19), 143.7 (s, C-20), 120.7 (d, C-21), 41.6 (t, C-22), 15.4 (q, C-23), 28.0 (q, C-24), 16.3 (q, C-25), 16.0 (q, C-26), 14.7 (q, C-27), 17.7 (q, C-28), 22.5 (q, C-29), 65.5 (t, C-30)。以上数据与文献[10]报道的化合物 taraxast-20-ene-3β,30-diol 的波谱数据一致,故化合物 1 确定为 taraxast-20-ene-3β,30-diol。

化合物 2　白色粉末,熔点 168 ~ 169 ℃。EI-MS:440 $[M]^+$(30), 273 (100), 232 (56), ^{1}H-NMR ($CDCl_3$, 400 MHz):δ3.25 (1H, dd, J = 9.4, 5.3 Hz, H-3), 2.35 (1H, s, H-9), 5.56 (1H, s, H-12), 0.83, 0.96, 1.02, 1.19, 1.19, 1.32 (each 3H, s, H-23, 24, 25, 26, 27, 28), 0.81, 0.84 (each 3H, d, J = 5.6 Hz, H-29, 30)。^{13}C-NMR ($CDCl_3$, 100 MHz)-DEPT:δ39.1 (t, C-1), 27.2 (t, C-2), 78.7 (d, C-3), 39.0 (s, C-4), 54.8 (d, C-5), 17.5 (t, C-6), 32.8 (t, C-7), 43.6 (s, C-8), 61.5 (d, C-9), 36.9 (s, C-10), 199.8 (s, C-11), 130.4 (d, C-12), 164.9 (s, C-13), 45.0 (s, C-14), 27.2 (t, C-15), 27.4 (t, C-16), 33.9 (s, C-17), 58.9 (d, C-18), 39.1 (d, C-19), 39.2 (d, C-20), 30.8 (t, C-21), 40.8 (t, C-22), 28.0 (q, C-23), 15.5 (q, C-24), 16.5 (q, C-25), 18.4 (q, C-26), 20.5 (q, C-27), 28.8 (q, C-28), 17.4 (q, C-29), 21.1 (q, C-30)。信号 δ 199.8(s),164.9(s)和 130.4(d)提示可能存在 α, β 不饱和酮结构单元存在,以上数据与文献[10-11]比较,确定化合物 2 为 3β-hydroxy-11-oxo -ursan-12-ene。

化合物 3　白色针状结晶,熔点 187 ~ 188 ℃。EI-MS:m/z 440 $[M]^+$(5),^{1}H-NMR ($CDCl_3$, 500

MHz): δ3.20 (1H, dd, J = 11.5, 4.8 Hz, H-3), 6.71 (1H, dd, J = 6.4, 2.6 Hz, H-21), 0.97 (3H, s, H-23), 0.77 (3H, s, H-24), 0.85 (3H, s, H-25), 1.01 (3H, s, H-26), 0.97 (3H, s, H-27), 0.67 (3H, s, H-38), 1.02 (3H, d, J = 2.5 Hz, H-29), 9.36 (1H, s, H-30)。^{13}C-NMR ($CDCl_3$, 125 MHz)-DEPT: δ38.7 (t, C-1), 27.4 (t, C-2), 79.0 (d, C-3), 38.8 (s, C-4), 55.2 (d, C-5), 18.2 (t, C-6), 34.1 (t, C-7), 41.0 (s, C-8), 50.3 (d, C-9), 37.1 (s, C-10), 21.4 (t, C-11), 27.2 (t, C-12), 39.0 (d, C-13), 42.2 (s, C-14), 26.8 (t, C-15), 43.0 (t, C-16), 34.8 (s, C-17), 48.1 (d, C-18), 29.3 (d, C-19), 148.4 (s, C-20), 149.3 (d, C-21), 36.4 (t, C-22), 28.0 (q, C-23), 15.4 (q, C-24), 16.3 (q, C-25), 15.9 (q, C-26), 14.7 (q, C-27), 23.1 (q, C-28), 17.5 (q, C-29), 194.1 (d, C-30)。以上数据与与化合物 1 的碳氢谱比较发现化合物 3 为化合物 1 的 30 位羟基氧化成醛基而得,参照文献[10,12]确定化合物 3 为 3β-hydroxy-taraxaster-20-ene-30-aldehyde。

化合物 4　白色粉末,熔点 170 ~ 172 ℃。EI-MS: 442 $[M]^+$ (8), ^{1}H-NMR ($CDCl_3$, 500 MHz): δ3.20 (1H, dd, J = 11.4, 4.7 Hz, H-3), 0.69 (1H, br. d, J = 8.7 Hz, H-5), 2.16 (1H, m, H-19), 4.41 (1H, dd, J = 8.9, 5.3 Hz, H-21), 1.33 (1H, m, H-22a), 1.95 (1H, dd, J = 13.8, 9.1 Hz, H-22b). 0.96 (3H, s, H-23), 0.76 (3H, s, H-24), 0.84 (3H, s, H-25), 1.01 (3H, s, H-26), 0.95 (3H, s, H-27), 0.76 (3H, s, H-28), 1.20 (3H, d, 7.0 Hz, H-29), 4.89 (1H, s, H-30a), 4.98 (1H, s, H-30b)。^{13}C- NMR ($CDCl_3$, 100 MHz)-DEPT: δ38.7 (t, C-1), 27.3 (t, C-2), 79.0 (d, C-3), 38.8 (s, C-4), 55.3 (d, C-5), 18.2 (t, C-6), 34.0 (t, C-7), 40.9 (s, C-8), 50.3 (d, C-9), 37.1 (s, C-10), 21.3 (t, C-11), 26.1 (t, C-12), 38.9 (d, C-13), 42.2 (s, C-14), 26.3 (t, C-15), 37.6 (t, C-16), 33.9 (s, C-17), 48.4 (d, C-18), 38.0 (d, C-19), 156.5 (s, C-20), 71.2 (d, C-21), 48.7 (t, C-22), 27.9 (q, C-23), 15.4 (q, C-24), 16.2 (q, C-25), 15.9 (q, C-26), 14.7 (q, C-27), 18.2 (q, C-28), 28.4 (q, C-29), 113.6 (t, C-30)。以上数据与文献[13]报道的化合物 21α-hydroxy-taraxasterol 波谱数据,确定化合物 4 为 21α-hydroxy-taraxasterol。

化合物 5　白色固体粉末,熔点 155 ~ 156 ℃。EI-MS: m/z 424 $[M]^+$ (100)。^{1}H-NMR ($CDCl_3$, 400 MHz): δ3.27 (1H, dd, J = 11.5, 4.8 Hz, H-3), 5.48 (1H, d, J = 5.8 Hz, H-11), 5,62 (1H, d, J = 5.8 Hz, H-12), 0.83 (3H, d, J = 6.8 Hz, H-29), 0.96 (3H, br s, H-30)。^{13}C-NMR ($CDCl_3$, 100 MHz)-DEPT: δ37.2 (d, C-1), 27.8 (d, C-2), 78.7 (d, C-3), 38.6 (s, C-4), 51.0 (d, C-5), 18.3 (t, C-6), 31.9 (t, C-7), 40.6 (s, C-8), 154.4 (s, C-9), 38.8 (s, C-10), 115.3 (d, C-11), 122.9 (d, C-12), 141.2 (s, C-13), 43.0 (s, C-14), 28.1 (t, C-15), 26.0 (t, C-16), 33.6 (s, C-17), 57.2 (d, C-18), 38.9 (d, C-19), 39.4 (d, C-20), 31.1 (t, C-21), 41.3 (t, C-22), 28.2 (q, C-23), 17.3 (q, C-24), 17.5 (q, C-25), 22.0 (q, C-26), 25.4 (q, C-27), 28.8 (q, C-28), 15.6 (q, C-29), 21.5 (q, C-30)。以上数据与文献[14]报道的化合物 ursa-9 (11), 12-dien-3β-ol 波谱数据一致,确定化合物 5 为 ursa-9 (11), 12-dien-3β-ol。

化合物 6　白色无定形粉末,熔点 164 ~ 166 ℃。EI-MS: m/z 466 $[M]^+$ (90), ^{1}H-NMR ($CDCl_3$, 500 MHz): δ4.52 (1H, dd, J = 11.5 and 4.6 Hz, H-3), 5.44 (1H, d, J = 5.7 Hz, H-11), 5.59 (1H, d, J = 5.7 Hz, H-12), 2.06 (3H, s, CH_3CO)。^{13}C-NMR ($CDCl_3$, 125 MHz)-DEPT: δ37.0 (t, C-1), 24.3 (t, C-2), 80.6 (d, C-3), 38.5 (s, C-4), 51.2 (d, C-5), 18.2 (t, C-6), 32.0 (t, C-7), 40.7 (s, C-8), 154.2 (s, C-9), 37.9 (s, C-10), 115.5 (d, C-11), 123.0 (d, C-12), 141.4 (s, C-13), 43.1 (s, C-14), 28.2 (t, C-15), 26.1 (t, C-16), 33.7 (s, C-17), 57.3 (d, C-18), 39.0 (d, C-19), 39.4 (d, C-20), 31.2 (t, C-21), 41.4 (t, C-22), 28.1 (q, C-23), 17.4 (q, C-24), 17.5 (q, C-25), 22.1 (q, C-26), 25.4 (q, C-27), 28.7 (q, C-28), 16.7 (q, C-29), 21.5 (q, C-30), 171.0 (s, MeCO), 21.5 (q, CH_3CO)。化合物 6 与化合物 5 的碳氢谱比较发现,化合物 6 多了一个乙酰基信号,参照文献[14]确定化合物 6 为 ursa-9 (11), 12-dien-3β-*O*-acetate。

化合物 7　白色固体粉末,熔点 163 ~ 164 ℃。

EI-MS: *m/z* 424 [M]$^+$ (100)。^{1}H-NMR ($CDCl_3$, 400 MHz): δ3.27 (1H, dd, J = 10.4 and 4.7 Hz, H-3), 5.60 (1H, d, J = 5.8 Hz, H-11), 5.53 (1H, d, J = 5.8 Hz, H-12)。^{13}C NMR ($CDCl_3$, 100 MHz)-DEPT: δ37.0 (d, C-1), 27.8 (d, C-2), 78.7 (d, C-3), 38.9 (s, C-4), 51.1 (d, C-5), 18.3 (t, C-6), 32.1 (t, C-7), 38.7 (s, C-8), 154.3 (s, C-9), 40.6 (s, C-10), 115.7 (d, C-11), 120.6 (d, C-12), 147.1 (s, C-13), 42.7 (s, C-14), 25.6 (t, C-15), 25.6 (t, C-16), 32.1 (s, C-17), 45.5 (d, C-18), 46.8 (t, C-19), 31.1 (s, C-20), 34.6 (t, C-21), 37.1 (t, C-22), 28.7 (q, C-23), 15.7 (q, C-24), 20.0 (q, C-25), 20.9 (q, C-26), 25.3 (q, C-27), 28.2 (q, C-28), 23.7 (q, C-29), 33.2 (q, C-30)。以上数据与文献[15]报道的化合物 3β-hydroxy-9(11), 12-diene-oleanol 波谱数据一致,故确定化合物 7 为 3β-hydroxy-9 (11), 12-diene-oleanol。

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