川芎化学成分研究

常新亮[1,2], 马云保[1], 张雪梅[1], 江志勇[1], 陈纪军[1*]
(1. 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, 云南 昆明 650204;
2. 中国科学院 研究生院, 北京 100049)

[摘要] 目的:对伞形科藁本属植物川芎 *Ligusticum chuanxiong*干燥的根茎进行化学成分研究。方法:川芎的干燥根茎用水提取,依次用醋酸乙酯,正丁醇萃取,对醋酸乙酯部分采用各种柱色谱进行分离纯化,通过波谱数据分析进行结构鉴定。结果:从醋酸乙酯部分分离 11个化合物,分别鉴定为:(4*S*)-*p*-menth-1-ene-4, 7diol(**1**), aromadendrane-4α, 10β-diol(**2**), aromadendrane-4α, 10α-diol(**3**), aromadendrane-4β, 10β-diol(**4**), augustic acid(**5**),川芎三萜(xiongterpene, **6**),孕(甾)烯醇酮(pregnenolone, **7**),镰叶芹二醇[3(*R*), 8(*S*), 9(*Z*)-falcarindiol, **8**],洋川芎内酯 F(senkyunolide F, **9**),洋川芎内酯 I(senkyunolide I, **10**), 4羟基-3-丁基苯肽(4-hydroxyl-3-butylphthalide, **11**)。结论:化合物 **1**～**5**为首次从该种中分离得到。

[关键词] 川芎;伞形科;单萜;倍半萜;三萜
[中图分类号] R 284.1 [文献标识码] A [文章编号] 1001-5302(2007)15-1533-04

川芎系伞形科植物藁本属植物川芎 *Ligusticum chuanxiong* Hort的干燥根茎,为活血化瘀常用中药,有行气活血,祛风止痛之功效,用于月经不调,经闭痛经,跌打肿痛,头痛,风湿痹痛[1]。川芎的化学成分主要包括川芎嗪、阿魏酸和藁本内酯类化合物,文献[2]中已多有报道。作者从川芎水提物的醋酸乙酯部位中分离到 11个化合物,通过波谱数据分析并与文献对照,分别鉴定为:(4*S*)-*p*-menth-1-ene-4, 7-diol(**1**), aromadendrane-4α, 10β-diol(**2**), aromadendrane-4-α-, 10α-diol(**3**), aromadendrane-4β, 10β-diol(**4**), augustic acid(**5**),川芎三萜(xiongterpene, **6**),孕(甾)烯醇酮(pregnenolone, **7**),镰叶芹二醇[3(*R*), 8(*S*), 9(*Z*)-falcarindiol, **8**],洋川芎内酯 F(senkyunolide F, **9**),洋川芎内酯 I(senkyunolide I, **10**), 4羟基-3-丁基苯肽(4-hydroxyl-3-butylphthalide, **11**)。其中化合物 **1**为首次从该种中分离得到的单萜,化合物 **2**～**4**为首次从该种中分离得到的愈创木烷型倍半萜,化合物 **5**为首次从该种中分离得到的齐墩果烷型三萜。而在以前报道的川芎化学成分的文献中,萜类化合物的报道较少。

1 仪器与材料

Jasco DIP-370旋光仪。VG Auto Spec-3000型质谱仪(EIMS, FAB-MS)。Bruker AM 400, DRX-500型磁共振光谱仪,以 TMS为内标测定。柱色谱硅胶(200～300目)、硅胶 H和薄层色谱硅胶 GF254均为青岛海洋化工厂生产, Sephadex LH-20为 Pharmacia公司产品, C_8, C_{18}薄层板和柱色谱材料购自 Merck公司, Toyopearl HW-40和 MCI CHP-20P为三菱公司生产。

川芎于 2004年 5月购自昆明市菊花村药材市场,由中国科学院昆明植物研究所雷立功博士鉴定为 *L. chuanxiong*,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。

2 提取与分离

53 kg川芎的干燥根茎粉碎后,用 8倍量的水加热回流提取 3次,每次 1 h,浓缩至约 150 kg,依次用醋酸乙酯、正丁醇萃取 3次,回收溶剂后分别得到萃取物 306, 1.63 kg。醋酸乙酯部分(306 g)经硅胶柱色谱(200～300目),用氯仿-甲醇(100∶0～70∶30)进行梯度洗脱,经 TLC检查后合并得到 6个流分(Fr. 1-Fr. 6)。Fr. 3(105 g)经硅胶柱色谱(石油醚-醋酸乙酯, 95∶5～50∶50;石油醚-丙酮, 60∶40),再经 Sephadex LH-20(甲醇)柱色谱,纯化得到化合物 2(60 mg), 6(27 mg), 7(22 mg), 8(28 mg), 9(10 mg), 11(80 mg)。Fr. 4(37 g)经 MCI CHP-20P柱色谱(甲醇-水, 50∶50), Sephadex LH-20柱色谱(甲醇), Toyopearl HW-40柱色谱(甲醇)和硅

[收稿日期] 2007-03-01
[通讯作者] *陈纪军, Tel: (0871)5223265, Fax: (0871)5223265, E-mail: chenjj@mail.kib.ac.cn

胶 H柱色谱 (石油醚 醋酸乙酯, 90 :10),得到化合物 1(30 mg), 3(8 mg), 4(8 mg), 5(17 mg), 10(60 mg)。

3 结构鉴定

化合物 1 无定性粉末, $[\alpha]_D^{28}$ 14.9 (*c* 0.28, MeOH); EHMS *m/z*: 169 $[M-1]^+$ (2); ^{1}H-NMR (CD_3OD, 400 MHz) δ: 5.54 (1H, br s, H-2), 3.93 (1H, br s, H-7), 2.21 (2H, m, H-3), 0.95 (3H, d, *J* = 6.9 Hz, H-9), 0.92 (3H, d, *J* = 6.9 Hz, H-10); ^{13}C-NMR (CD_3OD, 100 MHz) δ: 138.1 (C-1), 121.0 (C-2), 34.7 (C-3), 73.1 (C-4), 31.9 (C-5), 23.7 (C-6), 67.1 (C-7), 38.1 (C-8), 17.4 (C-9), 17.2 (C-10)。以上数据与文献 [3,4]报道的 (4*S*)-*p*-menth-1-ene-4,7-diol 4-*O*-β-*D*-glucopyranoside的苷元部分相一致,故鉴定为 (4*S*)-*p*-menth-1-ene-4,7-diol。

化合物 2 无色针晶 (氯仿), $[\alpha]_D^{25}$ - 21.1 °(*c* 1.07, CH_3Cl); EHMS *m/z*: 238 $[M]^+$ (4); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.27 (3H, s), 1.20 (3H, s), 1.05 (6H, s); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ: 56.2 (C-1), 23.7 (C-2), 41.1 (C-3), 80.3 (C-4), 48.3 (C-5), 28.2 (C-6), 26.5 (C-7), 20.1 (C-8), 44.4 (C-9), 75.0 (C-10), 19.5 (C-11), 28.6 (C-12), 16.4 (C-13), 24.4 (C-14), 20.2 (C-15)。以上数据与文献 [5,6]报道的化合物 aromadendrane-4α,10β-diol一致。

化合物 3 无色针晶 (氯仿), $[\alpha]_D^{25}$ - 10.2 °(*c* 0.55, CH_3Cl); EHMS *m/z*: 238 $[M]^+$ (10); ^{1}H-NMR (CD_3OD, 400 MHz) δ: 1.28 (3H, s), 1.19 (3H, s), 1.09 (3H, s), 1.02 (3H, s); ^{13}C-NMR (CD_3OD, 100 MHz) δ: 56.8 (C-1), 24.7 (C-2), 42.0 (C-3), 81.1 (C-4), 47.6 (C-5), 30.4 (C-6), 27.7 (C-7), 20.2 (C-8), 43.8 (C-9), 73.0 (C-10), 21.2 (C-11), 29.2 (C-12), 16.3 (C-13), 24.3 (C-14), 30.7 (C-15)。以上数据与文献 [5,6]报道的化合物 aromadendrane-4α,10α-diol一致。

化合物 4 无色针晶 (氯仿), $[\alpha]_D^{20}$ - 39.3 °(*c* 0.60,氯仿); FAB-MS *m/z*: 238 $[M]^+$ (2); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.25 (3H, s), 1.21 (3H, s), 1.05 (3H, s), 1.00 (3H, s); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ: 54.5 (C-1), 23.8 (C-2), 40.3 (C-3), 80.3 (C-4), 47.5 (C-5), 24.9 (C-6), 26.1 (C-7), 20.3 (C-8), 44.1 (C-9), 75.5 (C-10), 19.0 (C-11), 28.8 (C-12), 16.4 (C-13), 25.6 (C-14), 19.7 (C-15)。以上数据文献 [5,6]报道的化合物 aromadendrane-4β,10-diol一致。

化合物 5 白色结晶 (丙酮); EHMS *m/z*: 472 $[M]^+$ (1); ^{1}H-NMR (CD_3OD, 400 MHz) δ: 5.25 (1H, br s, H-12), 3.62 (1H, m, H-3), 3.30 (1H, br s, H-2), 2.90 (1H, dd, *J* = 14.0, 4.0 Hz, H-18), 1.16 (3H, s, H-27), 1.01 (3H, s, H-25), 1.00 (3H, s, H-28), 0.96 (3H, s, H-23), 0.94 (3H, s, H-29), 0.83 (3H, s, H-30), 0.81 (3H, s, H-26); ^{13}C-NMR (CD_3OD, 100 MHz) δ: 48.1, (C-1), 69.5 (C-2), 84.4 (C-3), 40.6 (C-4), 56.7 (C-5), 19.6 (C-6), 33.9 (C-7), 39.2 (C-8), 49.0 (C-9), 40.5 (C-10), 24.0 (C-11), 123.5 (C-12), 145.2 (C-13), 42.9 (C-14), 28.8 (C-15), 24.6 (C-16), 47.6 (C-17), 42.7 (C-18), 47.2 (C-19), 31.6 (C-20), 34.9, (C-21), 33.8 (C-22), 29.3 (C-23), 17.5 (C-24), 17.1 (C-25), 17.7 (C-26), 26.4 (C-27), 181.8 (C-28), 33.6 (C-29), 24.0 (C-30)。以上数据与文献 [7]对照,鉴定为 augustic acid。

化合物 6 白色结晶 (甲醇); EHMS *m/z*: 602 $[M]^+$ (4); ^{1}H-NMR (C_5D_5N, 500 MHz) δ: 8.02 (1H, d, *J* = 15.9 Hz, H-3′), 7.65 (2H, d, *J* = 8.1 Hz, H-5′, 9′), 7.18 (2H, d, *J* = 8.1 Hz, H-6′, 8′), 6.70 (1H, d, *J* = 15.9 Hz, H-2′), 5.48 (1H, br s, H-12), 4.90 (1H, t, *J* = 9.1 Hz, H-3), 2.63 (1H, d, *J* = 11.2 Hz, H-18), 1.03 (3H, s, H-23), 1.01 (3H, d, *J* = 5.2 Hz, H-30), 0.94 (3H, s, H-24), 0.92 (3H, s, H-26), 0.89 (3H, s, H-27), 0.88 (3H, d, *J* = 7.0 Hz, H-29), 0.86 (3H, s, H 25); ^{13}C-NMR (C_5D_5N, 125 MHz) δ: 38.4 (C-1), 23.6 (C-2), 80.6 (C-3), 38.2 (C-4), 55.7 (C-5), 18.6 (C-6), 33.4 (C-7), 40.0 (C-8), 47.9 (C-9), 37.1 (C-10), 24.2 (C-11), 125.5 (C-12), 139.3 (C-13), 42.6 (C-14), 28.7 (C-15), 24.9 (C-16), 48.1 (C-17), 53.6 (C-18), 39.5 (C-19), 39.6 (C-20), 31.1 (C-21), 37.5 (C-22), 28.3 (C-23), 17.5 (C-24), 15.6 (C-25), 17.4 (C-26), 24.0 (C-27), 179.9 (C-28), 17.2 (C-29), 21.5 (C-30), 167.3 (C-1′), 115.9 (C-2′), 145.0 (C-3′), 126.3 (C-4′), 130.7 (C-5′), 116.9 (C-6′), 161.5 (C-7′), 116.9 (C-8′), 130.7 (C-9′)。以上数据与文献 [8]对照,鉴定为川芎三萜 (xiongterpene)。

化合物 7 无色针晶 (氯仿); EHMS *m/z*: 317

[M + 1]$^+$ (18); ^{1}H-NMR (CDCl$_3$, 400 MHz) δ: 5.34 (1H, br d, J = 5.2 Hz, H-6), 3.53 (1H, m, H-3), 2.52 (1H, t, J = 8.8 Hz, H-17), 2.12 (3H, s, H-21), 0.98 (3H, s, H-19), 0.62 (3H, s, H-18); ^{13}C-NMR (CDCl$_3$, 100 MHz) δ: 37.2 (C-1), 31.7 (C-2), 71.6 (C-3), 42.2 (C-4), 140.7 (C-5), 121.3 (C-6), 31.5 (C-7), 31.8 (C-8), 49.9 (C-9), 36.5 (C-10), 21.0 (C-11), 38.8 (C-12), 44.0 (C-13), 56.9 (C-14), 24.4 (C-15), 22.8 (C-16), 63.7 (C-17), 13.2 (C-18), 19.3 (C-19), 209.7 (C-20), 31.5 (C-21)。以上数据与文献 [9]对照,鉴定为孕 (甾)烯醇酮 (pregnenolone)。

化合物 8 浅黄色油状物; EI-MS m/z: 259 [M - 1]$^+$ (1); ^{1}H-NMR (CDCl$_3$, 400 MHz) δ: 5.93 (1H, m, H-2), 5.60 (1H, m, H-10), 5.52 (1H, br d, J = 8.2 Hz, H-9), 5.43 (1H, br d, J = 16.7 Hz, H-1a), 5.24 (1H, br d, J = 10.2 Hz, H-1b), 5.18 (1H, br d, J = 8.2 Hz, H-8), 4.91 (1H, d, J = 5.2 Hz, H-3), 2.08 (2H, q, J = 7.1 Hz, H-11), 0.90 (3H, t, J = 6.3 Hz, H-17); ^{13}C-NMR (CDCl$_3$, 100 MHz) δ: 117.2 (C-1), 135.8 (C-2), 63.4 (C-3), 79.8 (C-4), 70.2 (C-5), 68.7 (C-6), 78.3 (C-7), 58.5 (C-8), 127.6 (C-9), 134.5 (C-10), 27.6 (C-11), 29.2 (C-12), 29.2 (C-13), 29.1 (C-14), 31.7 (C-15), 22.6 (C-16), 14.0 (C-17)。以上数据与文献 [10]对照,鉴定为镰叶芹二醇 [3(R), 8(S), 9(Z)-falcarindiol]。

化合物 9 浅黄色油状物; EI-MS m/z: 206 [M]$^+$ (3); ^{1}H-NMR (CDCl$_3$, 400 MHz) δ: 6.20 (1H, dt, J = 8.7, 1.9 Hz, H-7), 6.10 (1H, dt, J = 8.7, 4.2 Hz, H-6), 5.30 (1H, d, J = 8.2 Hz, H-8), 4.59 (1H, m, H-9), 0.92 (3H, J = 7.4 Hz, H-11); ^{13}C-NMR (CDCl$_3$, 400 MHz) δ: 168.7 (C-1), 149.3 (C-3), 149.2 (C-3a), 19.2 (C-4), 23.4 (C-5), 132.7 (C-6), 117.3 (C-7), 125.9 (C-7a), 115.6 (C-8), 68.7 (C-9), 31.2 (C-10), 10.0 (C-10)。以上数据与文献 [11]对照,鉴定为洋川芎内酯 F (senkyunolide F)。

化合物 10 浅黄色油状物, EI-MS m/z: 224 [M]$^+$ (24); ^{1}H-NMR (CDCl$_3$, 400 MHz) δ: 5.28 (1H, t, J = 7.9 Hz, H-8), 4.48 (1H, d, J = 5.7 Hz, H-7), 0.95 (3H, t, J = 7.3 Hz, H-11); ^{13}C-NMR (CDCl$_3$, 100 MHz) δ: 168.9 (C-1), 152.6 (C-3), 147.9 (C-3a), 19.3 (C-4), 26.7 (C-5), 71.8 (C-6), 68.1 (C-7), 125.8 (C-7a), 114.5 (C-8), 28.1 (C-9), 22.3 (C-10), 13.5 (C-11)。以上数据与文献 [12, 13]对照,鉴定为洋川芎内酯 I (senkyunolide I)。

化合物 11 无色针晶 (丙酮); EI-MS m/z: 206 [M]$^+$ (5); ^{1}H-NMR (CD_3COCD_3, 400 MHz) δ: 9.31 (1H, s, -OH), 7.41 (1H, t, J = 7.7 Hz, H-6), 7.30 (1H, br d, J = 7.7 Hz, H-5), 7.17 (1H, br d, J = 7.7 Hz, H-7), 5.56 (1H, dd, J = 7.7, 2.8 Hz, H-3), 0.89 (3H, t, J = 6.9 Hz, H-11); ^{13}C-NMR (CD_3COCD_3, 100 MHz) δ: 170.7 (C-1), 80.9 (C-3), 136.9 (C-3a), 153.2 (C-4), 120.8 (C-5), 131.5 (C-6), 116.8 (C-7), 129.1 (C-7a), 33.1 (C-8), 27.6 (C-9), 23.1 (C-10), 14.1 (C-11)。以上数据与文献 [8]对照,鉴定为 4羟基-3-丁基苯肽 (4-hydroxyl-3-butylphthalide)。

[参考文献]

[1] 中国药典 [S]. 一部. 2005: 28.
[2] 郑虎占,董泽宏,佘 靖. 中药现代研究与应用 [M]. 第 1卷. 北京: 学苑出版社, 1998: 629.
[3] Ishikawa T, Takayanagi T, Kitajima J. Water-soluble constituents of cumin: monoterpenoid glucosides [J]. Chem Pharm Bull, 2002, 50 (11): 1471.
[4] Ishikawa T, Sega Y, Kitajima J. Water-soluble constituents of ajowan [J]. Chem Pharm Bull, 2001, 49 (7): 840.
[5] Goldsby G, Burke B A. Sesquiterpene iactones and a sesquiterpene diol from jamaican *Ambrosia peruviana* [J]. Phytochemistry, 1987, 26 (4): 1059.
[6] Beechan C M, Djerassi C. Terpenoids-Lxxiv The sesquiterpenes from the soft coral *Sinularia mayi* [J]. Tetrahedron, 1978, 34: 2503.
[7] Alam M S, Chopra N J, Ali M, et al. Oleanen and stigmasterol derivatives from *Ambroma augusta* [J]. Phytochemistry, 1996, 41: 1197.
[8] 肖永庆,李 丽,游小琳,等. 川芎化学成分研究 [J]. 中国中药杂志, 2002, 27 (7): 519.
[9] Szendi Z, Forg P, Sweet F. Complete ^{1}H and ^{13}C-NMR spectra of pregnenolone [J]. Steroids, 1995, 60: 442.
[10] Lechner D, Stavri M, Oluwatuyi M, et al. The anti-staphylococcal activity of *Angelica dahurica* (Bai Zhi) [J]. Phytochemistry, 2004, 65: 331.
[11] Tsuchida T, Kobayashi M, Kaneko K, et al. Studies on the constituents of Umbelliferae plants XVI. Isolation and structures of three new ligustilide derivatives from *Angelica acutiloba* [J]. Chem Pharm Bull, 1987, 35 (11): 4460.
[12] Wang P, Gao X, Wang Y, et al. Phthalides from the rhizome of *Ligusticum wallichii* [J]. Phytochemistry, 1984, 23 (9): 2033.
[13] Naito T, Katsuhara T, Niitsu K, Ikeya Y, et al. Two phthalides from *Ligusticum chuanxiong* [J]. Phytochemistry, 1992, 31 (2): 639.

第 32卷第 15期
2007年 8月

中国中药杂志
China Journal of Chinese Materia Medica

Vol 32, Issue 15
August, 2007

Studies on chemical constituents of rhizomes of Ligusticum chuanxiong

CHANG Xin-liang[1,2], MA Yun-bao[1], ZHANG Xue-mei[1], JIANG Zhi-yong[1], CHEN Ji-jun[1]

(1. *State Key Labortatory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming* 650204, *China;*
2. *Graduate School of Chinese Academy of Sciences, Beijing* 100049, *China)*

[Abstract] **Objective:** To study chemical constitutents of the rhizomes of *Ligusticum chuanxiong*. **Method:** The rhizomes of *L. chuanxiong* were extracted with water to afford a water extract which was participated between H_2O and EtOAc, *n*-BuOH, successively. The compounds were isolatedand purified by column chromatography from the EtOAc fraction, and identified based on spectral analyses. **Result:** Eleven compounds were isolated from the rhizomes of *L. chuanxiong*, and structures were characterized as (4*S*)-*p*-menth-1-ene-4, 7-diol (**1**), aromadendrane-4α, 10β-diol (**2**), aromadendrane-4β, 10α-diol (**3**), aromadendrane-4β, 10β-diol (**4**), augustic acid (**5**), xiongterpene (**6**), pregnenolone (**7**), 3(*R*), 8(*S*), 9(*Z*)-falcarindiol (**8**), senkyunolide F (**9**), senkyunolide I (**10**), 4-hydroxyl-3-butylphthalide (**11**). **Conclusion:** Compounds **1-5** were obtained from the rhizomes of *L. chuanxiong* for the first time.

[Key words] *Ligusticum chuanxiong*; Umbelliferae; monoterpenoids; sesquiterpenoids; triterpenoids

[责任编辑 戴 畅]

绿藻孔石莼脂类化学成分研究

徐娟华[1*], 卢启洪[1,2], 赵 昱[1]

(1. 浙江大学 药学院 中药与天然药物研究室, 浙江 杭州 310058;
2. 宁波中药制药厂, 浙江 宁波 315100)

[摘要] **目的**:研究石莼属植物孔石莼的脂类化学成分。**方法**:应用色谱技术进行分离和纯化,并根据理化性质和波谱数据进行结构鉴定。**结果**:从孔石莼的石油醚提取物中分离得到 7个脂类化合物,分别鉴定为顺式细辛醚 (*cis*-asarone, **1**)、反式 细辛醚 (*trans*-asarone, **2**)、欧细辛醚 (γ-asarone, **3**)、植物醇 (*trans*-phytol, **4**)、植物醇硬脂酸酯 (phytyl-stearate, **5**)、植物醇乙酸酯 (phytyl-acetate, **6**)、异植物醇 (isophytol, **7**)。**结论**:除化合物 **4**外,其余 6个化合物均为首次从该属植物中得到。

[关键词] 孔石莼;细辛醚;植物醇 (酯)

[中图分类号] R 284.1 [文献标识码] A [文章编号] 1001-5302(2007)15-1536-03

孔石莼 *Ulva pertusa* Kjellm为石莼科石莼属绿藻,广泛分布于西太平洋沿海,也已有试管培养的报道[1]。孔石莼历来作药用,唐代李珣《海药本草》和明朝李时珍《本草纲目》中均有记载,主为"下水、利小便"之功效;现代的《中国海洋药物辞典》和《中国药用海洋生物》等专著也记述其味咸性寒,有降低胆固醇和清热解毒、软坚散结、利水降压等作用[2,3]。为了探索其药用有效成分,作者对其化学成分进行了分离研究,并从石油醚部位分离鉴定了7个脂类化合物,分别为:顺式细辛醚 (*cis*-asarone, **1**)、反式 细辛醚 (trans-asarone, **2**)、欧细辛醚 (γ-asarone, **3**)、植物醇 (*trans*-phytol, **4**)、植物醇硬脂酸酯

[收稿日期] 2006-09-05

[基金项目] 浙江省教育厅科研项目 (20030358);浙江省经贸委中药现代化专项基金 (浙财建字[2003]137号)

[通讯作者] *徐娟华, Tel: (0571) 88208456, E-mail: phnosy@126.com