文章编号:1001-6880(2014)Suppl-0211-04

# 王不留行的化学成分研究

张艳玲[1,3],肖同书[2],蒋骊龙[1],李友宾[3,4]*

[1]南京中医药大学附属中西医结合医院中药质量研究室,南京 210046;[2] 中国药科大学天然药化教研室,南京 211199;[3]中国中医科学院江苏分院和江苏省中医药研究院中药代谢组研究室,南京 210028;[4] 海南医学院药学院,海口 571199

**摘　要**:利用柱色谱技术从王不留行(*Vaccaria segetalis*)85% 醇提物的乙酸乙酯萃取部分中分离得到 10 个化合物,经 MS、NMR 等波谱技术分别鉴定为:α-波甾醇(**1**)、豆甾-7,22-二烯-3-酮(**2**)、豆甾-1,5-二烯-3-醇(**3**)、丝石竹酸(**4**)、16-羟基丝石竹酸(**5**)、原儿茶酸(**6**)、王不留行环肽 A(**7**)、王不留行环肽 B(**8**)、腺苷(**9**)、牡蛎素(**10**),其中化合物 **2** ~ **6** 为首次从该植物中分离。

**关键词**:王不留行;化学成分

**中图分类号**:R284.2　　**文献标识码**:A

# Chemical Constituents of *Vaccaria segetalis*

ZHANG Yan-ling[1,3], XIAO Tong-shu[2], JIANG Li-long[1], LI You-bin[3,4]*

[1]*Department of Pharmaceutical Analysis Hospital of Integrated Traditional Chiese and Western Medicine Affiliated to Nanjing University of Chinese Medicine, Nanjing 210046, China*; [2]*Department of Phytochemistry, China Pharmaceutical University, Nanjing 211199, China*; [3]*Department of Metabolomics, Jiangsu Province Academy of Traditional Chinese Medicine and Jiangsu Branch of China Academy of Chinese Medical Sciences, Nanjing 210028, China*; [4]*School of Pharmacy, Hainan Medical University, Haikou, 571199, China.*

**Abstract**: Ten known compounds were isolated from the ethanol extract of the seeds of *Vaccaria segetalis*. On the basis of MS and NMR analysis, these compounds were determined as α-spinasterol (**1**), stigmast-7,22-dien-3-one (**2**), stigmast-1,5-dien-3-ol (**3**), gypsogenic acid (**4**), 16-hydroxygypsogenic acid (**5**), protocatechuic acid (**6**), segetalins A (**7**), segetalins B (**8**), adenosine (**9**) and vitexin (**10**). Among them, compounds **2-6** were obtained from this plant for the first time.

**Key words**: *Vaccaria segetalis*; chemical constituents

王不留行为石竹科植物麦蓝菜 *Vaccaria segetalis* (Neck.) Garcke 的干燥成熟种子,始载于《神农本草经》,列为上品,是传统常用中药之一。有活血通经、下乳消肿、利尿通淋等功效,常用于治疗经闭、痛经、乳汁不下等症[1]。其植物资源丰富,除华南外,全国各地均有分布,尤以河北产量最大[2]。据文献报道王不留行含有三萜皂苷、环肽、黄酮和类脂等多种化学成分[3,4],具有重要的药用价值及广泛的药理活性。本课题组前期对常用活血化瘀草药提取物抑制凝血因子 Xa 筛选结果表明王不留行具有较好的活性[5],进一步发现抑制凝血因子 Xa 的部位为乙酸乙酯部位。为发现其抑制凝血因子 Xa 的活性成分,本研究对王不留行 85% 乙醇提取物的乙酸乙酯萃取部位进行了化学成分研究,从中分离纯化得到 10 个化合物,分别鉴定为 α-波甾醇(**1**)、豆甾-7,22-二烯-3-酮(**2**)、豆甾-1,5-二烯-3-醇(**3**)、丝石竹酸(**4**)、16-羟基丝石竹酸(**5**)、原儿茶酸(**6**)、王不留行环肽 A(**7**)、王不留行环肽 B(**8**)、腺苷(**9**)、牡蛎素(**10**)。其中化合物 **2** ~ **6** 为首次从王不留行中分离得到。

## 1　仪器和材料

Brucker AV-300 型核磁共振仪(TMS 内标);Agilent1100 系列 LC-MSD Trap 质谱仪;Buchi 型旋转蒸发仪(瑞士 Buchi 公司);Sephadex LH-20 和 RP-C18 反相制备色谱填料(12Å,50 μm,Merck 公司);MDS-5-300 反相制备色谱填料(200 ~ 300 目,北京麦迪生新技术开发中心);MCI 反相柱色谱填料(CHP20P,

收稿日期:2013-11-01　　接受日期:2014-02-25

基金项目:江苏省六大人才高峰项目(2012-YY-011);国家自然科学基金(81460591)

* 通讯作者 Tel:86-013372018792; E-mail:liyoubinli@sohu.com

70 ~ 150 μm,日本 Mitsubishi Chemical Corporation 产品);$RP18F_{254}$反相板(Merck 公司);薄层色谱及柱色谱硅胶(青岛海洋化工厂);本实验所用试剂均为分析纯。

王不留行饮片于 2011 年 3 月购自安徽泸濡中药科技有限公司,批号 20101212,产地河北。经江苏省中医药研究院李友宾教授鉴定为麦蓝菜 *Vaccaria segetalis* (Neck.) Garcke 的干燥成熟种子,凭证样本(编号:S-13-00002)存于江苏省中医药研究院中药化学研究室。

## 2 提取和分离

王不留行饮片 5 kg,8 倍量 85% 乙醇回流提取 3 次,每次 2 h,合并提取液,减压浓缩至无醇味,分散在 2 L 水中,依次用石油醚、乙酸乙酯和正丁醇分别萃取三次,浓缩得到乙酸乙酯部位浸膏 19.1 g,硅胶拌样后干法上硅胶柱层析(200 ~ 300 目,500 g),依次用氯仿-甲醇(100∶0→3∶1)梯度洗脱,收集流份,点薄层板合并相同点,共得到 8 个组分(Fr. 1 ~ Fr. 8)。其中 Fr. 1、Fr. 4、Fr. 6 和 Fr. 7 经过反复硅胶、Sephadex LH-20、MCI、ODS 反相等柱色谱和重结晶方法,从 Fr. 1 中分离得到化合物 **1**(44.2 mg)、**2**(20.2 mg)和 **3**(17.7 mg);Fr. 4 中分离得到化合物 **4**(54.4 mg)、**5**(38.6 mg)和 **6**(16.1 mg);Fr. 6 中分离得到化合物 **7**(84.5 mg)和 **8**(34.4 mg);Fr. 7 中分离得到化合物 **9**(75.7 mg)和 **10**(121.3 mg)。

## 3 结构鉴定

**化合物 1** 无色片晶(石油醚-乙酸乙酯)。ESI-MS:*m/z* 413 [M + H]$^+$;$^1$H NMR ($CH_3Cl$-$d_3$, 300 MHz) δ:3.58 (1H, m, H-3), 5.03 (1H, dd, *J* = 15.0, 8.1 Hz, H-7), 0.56 (3H, s, $CH_3$-18), 0.80-0.84 (9H, m, $CH_3$-19, 26, 27), 1.00 (3H, d, *J* = 6.6, $CH_3$-21), 5.14-5.22 (2H, m, H-22, 23), 0.85 (3H, d, *J* = 6.3, $CH_3$-29);$^{13}$C NMR ($CH_3Cl$-$d_3$, 75 MHz) δ:37.1 (C-1), 31.4 (C-2), 71.0 (C-3), 38.0 (C-4), 40.3 (C-5), 29.6 (C-6), 117.4 (C-7), 139.5 (C-8), 49.4 (C-9), 34.2 (C-10), 21.5 (C-11), 39.5 (C-12), 43.3 (C-13), 55.1 (C-14), 23.0 (C-15), 28.5 (C-16), 55.9 (C-17), 12.0 (C-18), 13.0 (C-19), 40.8 (C-20), 21.0 (C-21), 138.1 (C-22), 129.4 (C-23), 51.2 (C-24), 31.8 (C-25), 21.4 (C-26), 19.0 (C-27), 25.4 (C-28), 12.2 (C-29)。以上光谱数据与文献[6]报道一致,故化合物 **1** 鉴定为 α-波甾醇。

**化合物 2** 白色针晶(石油醚-乙酸乙酯)。ESI-MS:*m/z* 411 [M + H]$^+$。$^1$H NMR ($CH_3Cl$-$d_3$, 300 MHz) δ:5.06 (1H, dd, *J* = 15.0, 8.1 Hz, H-7), 0.58 (3H, s, $CH_3$-18), 0.79-0.84 (9H, m, $CH_3$-19, 27, 29), 1.04 (3H, d, *J* = 6.6 Hz, $CH_3$-21), 5.13-5.21 (2H, m, H-22, 23), 0.83 (3H, d, *J* = 6.3, $CH_3$-26);$^{13}$C NMR ($CH_3Cl$-$d_3$, 75 MHz) δ:38.1 (C-1), 44.2 (C-2), 212.0 (C-3), 38.8 (C-4), 42.9 (C-5), 30.1 (C-6), 117.0 (C-7), 139.5 (C-8), 48.9 (C-9), 34.4 (C-10), 21.7 (C-11), 39.3 (C-12), 43.2 (C-13), 55.0 (C-14), 23.0 (C-15), 28.5 (C-16), 55.9 (C-17), 12.1 (C-18), 12.4 (C-19), 40.8 (C-20), 21.4 (C-21), 138.0 (C-22), 129.6 (C-23), 51.2 (C-24), 31.9 (C-25), 21.1 (C-26), 19.0 (C-27), 25.4 (C-28), 12.2 (C-29)。以上数据和文献[7]报道数据基本一致,故化合物 **2** 鉴定为豆甾-7,22-二烯-3-酮。

**化合物 3** 无色片晶(石油醚-乙酸乙酯)。ESI-MS:*m/z* 413 [M + H]$^+$。$^1$H NMR ($CH_3Cl$-$d_3$, 300 MHz) δ:5.16 (1H, m, H-1), 5.03 (1H, dd, *J* = 15.0, 8.1 Hz, H-2), 3.52 (1H, m, H-3), 5.35 (1H, d, *J* = 4.8 Hz, H-6), 0.68 (3H, s, $CH_3$, H-18), 0.93 (3H, d, *J* = 6.3 Hz, $CH_3$, H-19), 0.97 (3H, d, *J* = 6.3 Hz, $CH_3$, H-21), 0.79-0.85 (9H, m, 3$CH_3$, H-26, 27, 29);$^{13}$C NMR ($CH_3Cl$-$d_3$, 75 MHz) δ:138.4 (C-1), 129.3 (C-2), 71.8 (C-3), 42.3 (C-4), 140.8 (C-5), 121.7 (C-6), 29.7 (C-7), 31.7 (C-8), 50.2 (C-9), 36.2 (C-10), 21.1 (C-11), 37.3 (C-12), 39.8 (C-13), 56.8 (C-14), 24.3 (C-15), 28.2 (C-16), 56.1 (C-17), 11.9 (C-18), 19.4 (C-19), 34.0 (C-20), 18.8 (C-21), 31.9 (C-22), 26.1 (C-23), 45.9 (C-24), 29.2 (C-25), 19.0 (C-26), 19.8 (C-27), 23.1 (C-28), 12.0 (C-29)。以上数据和文献[8]报道数据基本一致,故化合物 **3** 鉴定为豆甾-1,5-二烯-3-醇。

**化合物 4** 无色细针晶(氯仿-甲醇);Libermann-Burchard 反应呈阳性。ESI-MS *m/z*:487[M + H]$^+$。$^1$H NMR ($C_5H_5N$-$d_5$, 300 MHz) δ:5.66 (1H, t, *J* = 7.8 Hz, H-3), 5.48 (1H, br. s, H-12), 3.27 (1H, d, *J* = 13.5 Hz, H-18), 1.62 (3H, s, H-24), 0.99 (3H, s, H-25), 1.00 (3H, s, H-26), 1.23 (3H,

s,H-27),0.92 (3H,s,H-29),0.96 (3H,s,H-30);$^{13}$C NMR ($C_5H_5N$-$d_5$,75 MHz) δ:39.0 (C-1),27.8 (C-2),75.4 (C-3),54.4 (C-4),51.9 (C-5),21.6 (C-6),33.1 (C-7),40.1 (C-8),48.3 (C-9),36.8 (C-10),23.8 (C-11),122.4 (C-12),144.8 (C-13),42.1 (C-14),28.3 (C-15),23.7 (C-16),46.4 (C-17),42.0 (C-18),46.6 (C-19),30.9 (C-20),34.2 (C-21),33.2 (C-22),180.6 (C-23),12.2 (C-24),15.9 (C-25),17.3 (C-26),26.1 (C-27),180.1 (C-28),33.0 (C-29),23.6 (C-30)。以上数据和文献[9]报道的丝石竹酸基本一致,故化合物**4**鉴定为丝石竹酸。

**化合物5** 无色细针晶(氯仿-甲醇)。ESI-MS *m/z*:503 [M+H]$^+$。$^1$H NMR ($C_5H_5N$-$d_5$,300 MHz) δ:4.69 (1H,t,*J* = 7.8 Hz,H-3),5.65 (1H,br.s,H-12),5.20 (1H,br.s,H-16),3.61 (1H,m,H-18),,1.64 (3H,s,H-24),1.03 (3H,s,H-25),1.05 (3H,s,H-26),1.17 (3H,s,H-27),1.79 (3H,s,H-29),1.00 (3H,s,H-30);$^{13}$C NMR ($C_5H_5N$-$d_5$,75 MHz) δ:39.1 (C-1),27.8 (C-2),75.5 (C-3),54.4 (C-4),52.0 (C-5),21.7 (C-6),33.3 (C-7),40.2 (C-8),42.1 (C-9),36.9 (C-10),23.8 (C-11),122.2 (C-12),145.1 (C-13),42.1 (C-14),36.2 (C-15),74.6 (C-16),48.8 (C-17),41.4 (C-18),47.5 (C-19),31.0 (C-20),36.2 (C-21),32.8 (C-22),180.7 (C-23),12.2 (C-24),16.1 (C-25),17.4 (C-26),27.1 (C-27),180.7 (C-28),33.3 (C-29),24.7 (C-30)。以上数据和文献[10]报道的基本一致,故化合物**5**鉴定为16-羟基丝石竹酸。

**化合物6** 黄色粉末(甲醇)。ESI-MS *m/z*:155 [M+H]$^+$。$^1$H NMR ($CH_3OH$-$d_4$,300 MHz) δ:7.46 (1H,d,*J* = 2.1 Hz,H-2),6.81 (1H,d,*J* = 8.1 Hz,H-5),7.44 (1H,dd,*J* = 2.1,8.1 Hz,H-6);$^{13}$C NMR ($CH_3OH$-$d_4$,75 MHz) δ:123.4 (C-1),116.3 (C-2),146.3 (C-3),151.9 (C-4),118.2 (C-5),124.5 (C-6),170.8 (C-7)。以上数据和文献[11]报道的基本一致,故化合物**6**鉴定为原儿茶酸。

**化合物7** 无色针状结晶(甲醇)。ESI-MS *m/z*:610 [M+H]$^+$。$^1$H NMR ($C_5H_5N$-$d_5$,300 MHz) δ:11.86 (1H,s,N-H,Trp),9.42 (1H,d,*J* = 5.4 Hz,N-H,Trp),7.07 ~ 7.65 (5H,Trp),4.98 (1H,dd,*J* = 5.7,16.2 Hz,Trp),4.83 ~ 4.96 (2H,m,α-H,Trp,Val$^2$),10.50 (1H,d,*J* = 6.6 Hz,N-H,Ala),3.96 (1H,m,Ala),1.70 (3H,d,*J* = 6.9 Hz,Ala),8.08 (1H,d,*J* = 12.9 Hz,N-H,Val$^1$),5.16 (1H,m,α-H,Val$^1$),1.56 (3H,d,*J* = 6.9 Hz,Val$^1$),1.26 (3H,d,*J* = 6.9 Hz,Val$^1$),7.64 (1H,d,*J* = 9.9 Hz,N-H,Val$^2$),0.98 (3H,d,*J* = 6.3 Hz,Val$^2$),0.92 (3H,d,*J* = 6.6 Hz,Val$^2$),5.01 (1H,d,*J* = 8.7 Hz,α-H,Pro),8.37 (1H,t,*J* = 5.1 Hz,N-H,Gly),4.43 (1H,dd,*J* = 5.4,16.5 Hz,Gly);$^{13}$C NMR ($C_5H_5N$-$d_5$,75 MHz) δ:Trp:175.1,137.5,127.9,124.4,121.9,119.3,118.9,112.0,110.0,57.0,26.4;Ala:171.9,50.9,16.0;Val$^1$:172.4,56.3,30.9,20.1,17.9;Val$^2$:174.4,61.4,31.4,19.5,19.0;Pro:173.0,61.3,47.6,32.3,22.2;Gly:171.0,44.3。以上数据与文献[12]报道的基本一致,故化合物**7**鉴定为王不留行环肽A。

**化合物8** 无色针状晶体(甲醇)。ESI-MS *m/z*:485 [M+H]$^+$。$^1$H NMR ($C_5H_5N$-$d_5$,300 MHz) δ:10.82 (1H,s,N-H,Trp),7.72 (1H,d,*J* = 8.1 Hz,Trp),7.52 (1H,d,*J* = 10.8 Hz,Trp),7.10 (1H,s,Trp),7.04 (1H,t,*J* = 7.2 Hz,Trp),6.96 (1H,t,*J* = 7.2 Hz,Trp),3.18 (1H,m,β-H,Trp),7.93 ~ 7.98 (3H,m,N-H,Trp,Ala$^1$,Ala$^2$),4.20 (2H,m,α-H,Trp,Ala$^2$),1.96 (1H,m,β-H,Val),1.71-1.22 (6H,m,2$CH_3$,Ala$^1$,Ala$^2$),0.84-0.86 (6H,m,2$CH_3$,Val),4.06 (2H,m,α-H,Ala$^1$,Gly),8.41 (1H,d,*J* = 5.4 Hz,N-H,Gly);$^{13}$C NMR ($C_5H_5N$-$d_5$,75 MHz) δ:Trp:171.0,136.0,127.2,123.5,120.9,118.3,118.3,111.4,109.9,56.1,26.4;Ala$^1$:171.3,49.7,17.0;Ala$^2$:172.1,48.4,17.1;Val:170.3,59.5,29.6,19.1,18.1;Gly:43.4,169.6,43.4。以上光谱数据与文献[13]报道的基本一致,故化合物**8**鉴定为王不留行环肽B。

**化合物9** 无色针状晶体(甲醇)。ESI-MS *m/z*:268[M+HI$^+$。$^1$H NMR (DMSO-$d_6$) δ:8.14 (1H,s,H-2),8.34 (1H,s,H-8);$^{13}$C NMR (DMSO-$d_6$) δ:156.2 (c-6),152.5 (C-2),49.1 (c-4),140.0 (C-8),119.4 (C-5),88.0 (C-1′),86.0 (C-4′),73.5 (C-2′),70.7 (C-3),61.7 (C-5′)。以上光谱数据与文献[14]报道的基本一致,故化合物**9**鉴定为腺苷。

**化合物10** 黄色粉末(甲醇),Mg-HCl反应呈阳性。EI-MS *m/z*:432 [M$^+$]。$^1$H NMR (DMSO-$d_6$) δ:3.26 ~ 3.87 (m,6H,H-2,6′′),4.69 (d,1H,*J* = 9.9 Hz,H-1′′),6.27 (s,1H,H-6),6.78 (s,1H,H-

3),6.89 (d,2H,$J$ = 8.7 Hz,H-3′,5′),8.02 (d,2H,$J$ = 8.7Hz,H-2′,6′),10.36 (s,1H,4′-OH),10.84 (s,1H,7-OH),13.16 (s,1H,5-OH);$^{13}$C NMR (DMSO-$d_6$) δ:164.0 (C-2),102.4 (C-3),182.1 (C-4),156.0 (C-5),98.1 (C-6),162.6 (C-7),104.0 (C-8),160.4 (C-9),104.6 (C-10),121.6 (C-1′),129.0 (C-2′),116.0 (C-3′),161.1 (C-4′),115.8 (C-5′),128.5 (C-6′),78.7 (C-1″),73.3 (C-2″),70.8 (C-3″),70.5 (C-4″),81.8 (C-5″),61.3 (C-6″)。以上光谱数据与文献[15]报道的基本一致,故化合物 **10** 鉴定为牡蛎素。

**参考文献**


1 Chinese Pharmacopoeia Commission(国家药典委员会). Pharmacopoeia of the People′s Republic of China(中华人民共和国药典). Beijing:China Medical Science Press,2010. Vol Ⅰ,49.

2 Jiangsu New Medical College(江苏新医学院). Materia medica(中药大辞典), Shanghai, Shanghai Science and Technology Publisher,1986,311.

3 Sang SM(桑圣民),Mao SL(毛士龙),Lao AN(劳爱娜),*et al*. Studies on the chemical constituents of the seeds of *Vaccaria segetalis*(NECK) GARCKE. Ⅲ. *Nat Prod Res Dev*(天然产物研究与开发),1999,12(3):12-15.

4 Sang SM(桑圣民),Xia ZH(夏增华),Mao SL(毛士龙),*et al*. Studies on the flavonol glycosides from the seeds of *Vaccaria segetalis*. *Chin J Chin Mater Med*(中国中药杂志). 2000,25:221-222.

5 Shen S(沈舒),Wang Q(王琼),Li YB(李友宾),*et al*. Effect of factor Xa inhibition about 18 kinds of Chinese traditional medicines of promoting blood circulation for removing blood stasis. *Inf Tradit Chin Med*(中医药信息),2012,29:20-22.

6 Xiong J(熊江),Zhou J(周俊),Dai HF(戴好富),*et al*. Chemical constituents from *Phytolacca polyandra*. *Acta Bot. Yunnanica*(云南植物研究),2002,24:401-405.

7 Gu XJ(顾晓洁),Li YB(李友宾). Studies on chemical constituents of *Prunella vulgaris*. *Chin J Chin Mater Med*(中国中药杂志),2007,32:923-926.

8 Dumlu MU,Gurkan E. A new active compound from *Centaurea species*. *Z Naturforsch. C*,2006,61(1-2):44-46.

9 Park SY,Yook CS,Nohara T. New oleanene glycosides from the leaves of *Acanthopanax japonicus*. *Chem Pharmaceut Bull*,2005,53:1147-1151.

10 Sang SM,Zou M,Lao AN,*et al*. A new triterpenoid saponin from the seeds of *Vaccaria segetalis*. *Chinese Chem. Lett*,2000,11:49-52.

11 Wu ZJ,Ouyang MA,Yang CR. Polyphenolic constituents of *Salvia sonchifolia*. *Acta Bot. Yunnanica*,1999,21:393-398.

12 Morita H,Yun YS,Takeya K,*et al*. Segetalin A,a new cyclic hexapeptide from *Vaccaria segetalis*. *Tetrahedron Lett*,1994,35:9593-9596.

13 Morita H,Yun YS. Takeya K,*et al*. Segetalins B,C and D,three new cyclic peptides from *Vaccaria segetalis*. *Tetrahedron Lett*,1995,51:6003-6014.

14 Liu J(刘净),Yu ZB(于志斌),Zhou YW(周亚伟),*et al*. Chemical constituents from *Portuluca oleracea* L. *Nat Prod Res Dev*(天然产物研究与开发),2003,1:196.

15 Wen ZM(文志明),Xu L(徐礼). Isolation and elucidation of chemical constituents of Shandanshaoyao decoction (Ⅱ). *Chin J Chin Mater Med*(中国中药杂志),2001,26:474-476.


(上接第 207 页)


9 Tian HZ(田宏哲),Xu J(徐静),Hu R(胡睿),*et al*. Composition analysis of lignans from *Schisandra Chinensis* (Turcz.) Baill by LC-MS/MS. *Nat Prod Res Dev*(天然产物研究与开发),2012,24:32-35.

10 Zhang CX(张崇禧),Wang X(王雪),Na W(那微),*et al*. Chemical constituents of *Isodon. excia* (Maxin.) Hara in Changbai Mountain. *J Chin Tradit Pat Med*(中成药),2008,30:102-104.