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草麻黄茎化学成分的分离和结构鉴定

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摘 要:深入研究草麻黄(*Ephedra sinica* Stapf)茎的化学成分。草麻黄茎经溶剂提取和萃取粗分离后,用硅胶柱色谱分离技术分离纯化化学成分,用^{1}H NMR,^{13}C NMR,MS 等方法结合文献确定化学结构。从草麻黄茎的乙醇提取物中分离并鉴定了 9 个化合物:苯甲酸(**1**),反式肉桂酸(**2**),对羟基苯乙酸(**3**),绿原酸(**4**),原儿茶酸(**5**),鸟嘌呤(**6**),牧荆素(**7**),大黄酸(**8**),对氨基苯酚(**10**)。化合物 **3**,**6**~**9** 为首次从草麻黄中分离得到。

关键词:草麻黄;化学成分;黄酮;有机酸

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Separation and Identification of the Chemical Constituents from the Stems of *Ephedra sinica*

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Abstract:This study was to investigate the chemical constituents of the stems of *Ephedra sinica*. After the plant materials were extracted and fractionated with solvents,column chromatography over silica gel was used to isolate and purified the compounds. The structures were elucidated on the basis of ^{1}H NMR,^{13}C NMR,and MS analyses and comparison with the data of literatures. Nine compounds were isolated from this plant and their structures were identified as benzoic acid(**1**),*trans*-cinnamic acid(**2**),*p*-hydroxyphenylacetin acid(**3**),chlorogenic acid(**4**),protocatechuic acid(**5**),adenine(腺嘌呤)(**6**),vitexin(**7**),rhein(**8**),and *p*-aminophenol(**9**),respectively. Compounds **3**,**6-9** were identified from the title plant for the first time.

Key words:*Ephedra sinica*;chemical constituents;flavanoids;organic acids

草麻黄是中药麻黄的基源植物之一,为麻黄科 Ephedraceae 麻黄属植物草麻黄 *Ephedra sinica* Stapf 的干燥草质茎入药,主要分布于辽宁、吉林、内蒙古、河北、山西、河南西北部及陕西等省区。具有发汗、散寒、平喘、利水的功效,用于治疗风寒感冒、咳喘、支气管哮喘、水肿等症[1]。文献报道已从包括草麻黄在内的麻黄属植物中分离鉴定了苯丙胺类生物碱、黄酮、有机酸等多类化学成分。鉴于麻黄在中药中具有重要的地位,并具有多种药理作用,同时作为深入研究常用中草药化学成分的工作内容,作者对草麻黄草质茎的化学成分进行了研究。前文曾报道了一个新的麻黄碱类似物和一个新的萘衍生物的结构[2]。本文进一步从草麻黄中分离鉴定了 9 个化合物,其中 5 个化合物为首次从草麻黄中分离得到。

1 仪器、材料与试剂

Boetius 显微熔点测定仪(温度未校正),Q-STAR 型质谱仪,美国 Varian 公司 MERCURY-300,400 型核磁共振仪。柱色谱硅胶(200~300 目)和薄层色谱用硅胶 GF_{254} 均为青岛海洋化工厂产品。实验所用试剂均为分析纯。

实验药材购于安徽亳州药材市场,由药物研究所马林副研究员鉴定为麻黄科麻黄属植物草麻黄 *Ephedra sinica* Stapf 的干燥草质茎。

2 提取与分离

取草麻黄的干燥草质茎 30 Kg,用 80% 乙醇回流提取 3 次,每次加热回流时间分别为 2,1,1 h;合并提取液,减压浓缩后得到提取粗浸膏(4.2 kg)。

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此粗浸膏用 800 mL 蒸馏水和 1300 mL80% 乙醇混悬后依次用石油醚、乙酸乙酯、正丁醇萃取,减压回收溶剂后得到相应 3 种不同极性提取部分:石油醚部分(100 g),乙酸乙酯部分(86 g)和正丁醇部分(67 g)。正丁醇部分(67 g)用 200 ~ 300 目硅胶柱色谱分离,用氯仿-甲醇混合溶剂(100∶0 ~ 100∶1 ~ 50∶1 ~ 25∶1 ~ 15∶1 ~ 10∶1 ~ 5∶1 ~ 3∶1 ~ 1∶1 ~ 0∶100)进行梯度洗脱,洗脱部分经薄层检测后合并为 6 个部分(分别记为 Fr. 1-6)。取 Fr. 2(氯仿-甲醇 100∶1 洗脱部分),经反复硅胶柱色谱,氯仿 – 甲醇系统梯度洗脱,得到化合物 **1**(30 mg)、**2**(18 mg)、**3**(6 mg)。取 Fr. 3(氯仿-甲醇 50∶1-25∶1 洗脱部分),再经硅胶柱色谱,氯仿-甲醇梯度洗脱,得到化合物 **4**(7 mg)、**5**(7 mg)、**6**(8 mg)。取 Fr. 5(氯仿-甲醇 10∶1 洗脱部分),再经硅胶柱色谱,氯仿-甲醇梯度洗脱,得到化合物 **7**(10 mg)、**8**(8 mg)。取 Fr. 6(氯仿-甲醇 5∶1 ~ 3∶1 洗脱部分),经反复硅胶柱层析,氯仿 – 甲醇系统梯度洗脱,得到化合物 **9**(7 mg)。

3 结构鉴定

化合物 1 无色针状结晶(氯仿);mp. 121 ~ 123 ℃;^{1}H NMR($CDCl_3$,300 MHz)δ: 7.49(2H,brt, J = 7.2Hz,H-3,5),7.63(1H,tt,J = 7.5,2.1 Hz,H-4),8.13(2H,dm,J = 7.2 Hz,H-2,6)。^{13}C NMR($CDCl_3$,100 MHz)δ:128.5(C-3,5),129.3(C-1),130.2(C-2,6),133.8(C-4),172.3(C = O)。根据文献[3]鉴定为苯甲酸。

化合物 2 无色针状结晶(氯仿);mp. 133 ~ 135 ℃;^{1}H NMR($CDCl_3$,300 MHz)δ: 6.47(1H,d,J = 15.9 Hz,H-8),7.41(3H,m,H-3,4,5),7.54(2H,m,H-2,6),7.81(1H,d,J = 15.9 Hz,H-7)。^{13}C NMR($CDCl_3$,100 MHz)δ: 117.3(C-8),128.4(C-2,6),129.0(C-3,5),130.8(C-4),134.0(C-1),147.1(C-7),172.6(C-9)。根据文献[4]鉴定为反式肉桂酸。

化合物 3 白色粉末; ESIMS m/z:151 [M-H]$^-$;^{1}H NMR(CD_3COCD_3,300 MHz) δ:10.58(1H,brs,COOH),8.19(1H,s,9-OH),7.12(2H,dm,J = 8.4 Hz,H-2,6),6.77(2H,dm,J = 8.4 Hz,H-3,5),3.49(2H,s,H-7)。^{13}C NMR(CD_3COCD_3,100 MHz) δ:173.1(C-8),157.1(C-4),131.2(C-2,6),126.6(C-1),115.9(C-3,5),40.4(C-7)。根据文献[5]鉴定为对羟基苯乙酸。

化合物 4 白色粉末;ESIMS m/z:353 [M-H]$^-$;^{1}H NMR(DMSO-d_6,300 MHz)δ: 12.40(1H,br s,COOH),9.58(1H,s,OH),9.14(1H,s,OH),7.41(1H,d,J = 15.9 Hz,H-7′),7.02(1H,br s,H-2′),6.98(1H,br d,J = 8.1 Hz,H-6′),6.76(1H,d,J = 8.1 Hz,H-5′),6.14(1H,d,J = 15.9 Hz,H-8′),5.54(1H,br s,OH),5.05(1H,m,H-3),4.92(1H,d,J = 5.1 Hz,OH),4.76(1H,d,J = 5.7 Hz,OH),3.91(1H,br s,H-5),3.55(1H,br s,H-4),2.02(2H,m,H_2-6),1.93(1H,dd,J = 13.5,3.6 Hz,H-2a),1.77(1H,dd,J = 13.2,7.5 Hz,H-2b)。根据文献[6]鉴定为绿原酸。

化合物 5 白色粉末;负离子 ESIMS m/z:153 [M-H]$^-$;^{1}H NMR(DMSO-d_6,300 MHz) δ:9.61(1H,br,OH),9.32(1H,br,OH),7.32(1H,d,J = 2.1 Hz,H-2),7.27(1H,dd,J = 8.1,2.1 Hz,H-6),6.76(1H,d,J = 8.1 Hz,H-5)。根据文献[7]鉴定为原儿茶酸。

化合物 6 白色无定形粉末;ESIMS m/z:136 [M + H]$^+$;^{1}H NMR(DMSO-d_6,300 MHz) δ:12.82(1H,br s,N(9)H),8.08(1H,br s,N(1)H or 8-H),8.06(1H,s,H-8 or N(1)H),7.08(2H,s,2-NH_2)。根据文献[8]鉴定为鸟嘌呤。

化合物 7 黄色粉末;ESIMS m/z:431 [M-H]$^-$;^{1}H NMR(DMSO-d_6,400 MHz)δ:13.16(1H,s,5-OH),10.81(1H,s,7-OH),10.32(1H,s,4′-OH),8.02(2H,d,J = 8.8 Hz,H-2′,6′),6.88 (2H,d,J = 8.4 Hz,H-3′,5′),6.77(1H,s,H-3),6.26(1H,s,H-6),4.97(2H,m,OH),4.69(1H,ov,OH),4.67(1H,d,J = 7.8 Hz,H-1″),4.58(1H,t,J = 5.6Hz,OH-6″),3.20-3.80(6H,m,H-2″,3″,4″,5″,H_2-6″)。^{13}C NMR(DMSO-d_6,100 MHz) δ:182.1(C-4),163.9(C-2),162.5(C-7),161.1(C-4′),160.4(C-5),156.0(C-9),129.0(C-2′,6′),121.6(C-1′),115.8(C-3′,5′),104.6(C-8),104.0(C-10),102.4(C-3),98.1(C-6),81.8(C-5″),78.6(C-3″),73.4(C-1″),70.8(C-2″),70.5(C-4″),61.3(C-6″)。根据文献[9]鉴定为牧荆素。

化合物 8 黄色粉末;负离子 ESIMS m/z:283.3 [M-H]$^-$; ^{1}H NMR(DMSO-d_6,300 MHz) δ:11.90(2H,s,2 × OH),8.13(1H,d,J = 1.5 Hz,H-2),7.83(1H,t,J = 7.8 Hz,H-6),7.76(1H,d,J = 1.5 Hz,H-

4),7.74(1H,br d, J = 7.8 Hz,H-7),7.41(1H,br d,J = 7.8 Hz,H-5);^{13}C NMR(DMSO-d_6,100 MHz) δ:191.4(C-9),181.1(C-10),165.5(COOH),161.4(C-8),161.1(C-1),138.0(C-3),137.6(C-6),133.9(C-11),133.3(C-14), 124.6(C-7),124.1(C-4),119.4(C-5),118.8(C-2,13),116.3(C-12)。根据文献[10]鉴定为大黄酸。

化合物 9 白色粉末;ESIMS m/z:110 [M + H]$^+$; ^{1}H NMR(DMSO-d_6,300 MHz)δ:8.32(1H,s,OH),6.46(2H,d,J = 8.7 Hz,H-2,6),6.40(2H,d,J = 8.7 Hz, H-3,5),4.36(2H,s,NH_2)。^{13}C NMR(DMSO-d_6,100 MHz)δ:148.2(C-1),140.6(C-4),115.5(C-2,6),115.2(C-3,5)。根据文献[11]鉴定为对氨基苯酚。

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