九华黄精的化学成分及其抗炎活性研究

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摘　要:研究"十大皖药"品种——九华黄精(*Polygonatum cyrtonema* Hua in Jiuhua Mountain)块状根茎的化学成分及其抗炎活性。综合采用硅胶柱色谱、MCI 柱色谱、Sephadex LH-20 凝胶柱色谱及半制备高效液相色谱等方法从九华黄精生药材的 85% 乙醇提取物中共分离得到 16 个化合物,并通过^{1}H NMR、^{13}C NMR、HR-ESI-MS 技术鉴定了化合物结构,分别为 polygodoside H(**1**)、polygonatumoside G(**2**)、25(*S*)-funkioside B(**3**)、typaspidoside A(**4**)、芦丁(**5**)、木犀草素-7-*O*-芸香糖苷(**6**)、山柰酚-7-*O*-*β*-*D*-吡喃葡萄糖苷(**7**)、槲皮素-3-*O*-*β*-*D*-吡喃葡萄糖苷(**8**)、芹菜素-7-*O*-*β*-*D*-葡萄糖苷(**9**)、落叶松脂醇-4-*O*-*β*-*D*-葡萄糖苷(**10**)、5-*O*-咖啡酰奎宁酸甲酯(**11**)、4-*O*-咖啡酰奎宁酸甲酯(**12**)、3,5-*O*-二咖啡酰奎宁酸甲酯(**13**)、3,4-*O*-二咖啡酰基奎宁酸甲酯(**14**)、4,5-*O*-二咖啡酰基奎宁酸甲酯(**15**)、对羟基肉桂酸甲酯(**16**),所有化合物均是首次从九华黄精中分离得到。活性筛选结果显示化合物 **1**~**3**、**5**~**8** 均能够有效抑制 LPS 诱导的 RAW 264.7 细胞释放 NO,且无细胞毒作用,IC_{50} 值范围为 8.28~41.85 μmol/L,表现出一定程度的抗炎活性。

关键词:九华黄精;化学成分;结构鉴定;抗炎活性

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Chemical constituents from *Polygonatum cyrtonema* Hua in Jiuhua Mountain and their anti-inflammatory activity

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Abstract: This study aims to investigate the chemical constituents from the massive rhizomes of *Polygonatum cyrtonema* Hua in Jiuhua Mountain, together with their inflammatory activities. Sixteen compounds were isolated and purified from the 85% ethanol extract of the title plant by using systematic separation methods, including silica gel column chromatography, MCI column chromatography, Sephadex LH-20 gel column chromatography and semi-preparative liquid chromatography. Their structures were identified as polygodoside H (**1**), polygonatumoside G (**2**), 25(*S*)-funkioside B (**3**), typaspidoside A (**4**), rutin (**5**), luteolin-7-*O*-rutinoside (**6**), kaempferol-7-*O*-*β*-*D*-glucoside (**7**), quercetin-3-*O*-*β*-*D*-glucopyranoside (**8**), apigenin-7-*O*-*β*-*D*-glucoside (**9**), lariciresinol glycoside (**10**), 5-*O*-caffeoylquinic acid methyl ester (**11**), 4-*O*-caffeoylquinic acid methyl ester (**12**), 3,5-*O*-dicaffeoylquinic acid methyl ester (**13**), 3,4-*O*-dicaffeoylquinic acid methyl ester (**14**), 4,5-*O*-dicaffeoylquinic acid methyl ester (**15**), *trans*-*p*-coumaric acid methyl ester (**16**) by ^{1}H NMR, ^{13}C NMR and HR-ESI-MS. All the compounds are isolated from this plant for the first time. Biologically, all compounds were subjected to evaluate their anti-inflammatory activities *via* inhibiting NO production in LPS-stimulated RAW 264.7 cells *in vitro*. The results indicated that compounds **1**-**3**, **5**-**8** showed a moderate inhibitory effect against NO production with IC_{50} values of 8.28-41.85 μmol/L and

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without cytotoxicity against the cells, showing a certain degree of anti-inflammatory activity.

Key words: *Polygonatum cyrtonema* Hua in Jiuhua Mountain; chemical constituents; structure identification; anti-inflammatory activity

多花黄精(*Polygonatum cyrtonema* Hua)为百合科(Liliaceae)黄精属(*Polygonatum* Mill.)植物,始载于晋代《名医别录》,具有补中益气、除风湿、安五脏之功效,是2020版《中华人民共和国药典》中收载的3种中药黄精基原品种之一,主产于浙江、湖南、安徽、湖北、江西等地[1-3]。其中,安徽省青阳县九华山地区道产的九华黄精(*Polygonatum cyrtonema* Hua in Jiuhua Mountain)隶属多花黄精,药食两用,素有"地藏黄精"和"黄精之王"之称,为国家地理标志产品,亦是安徽省重点开发的"十大皖药"品种之一[3]。现代药理学研究表明,九华黄精具有抗炎、抗氧化、降血糖、抗菌、抗病毒等生物活性,临床可用于治疗脾胃虚弱、精血亏损、高血压、内热消渴、腰膝酸软、须发早白、体倦乏力、口干食少、肺燥咳嗽等病症[4,5]。作为一种久负盛名的传统中药,九华黄精药用历史悠久、疗效显著,但长久以来国内外对黄精的化学成分研究主要集中于多糖类成分,对小分子化学成分的研究报道较为欠缺[6-9]。基于此,本研究以九华黄精生药材的85%乙醇提取物为研究对象,综合各类现代色谱分离技术系统挖掘九华黄精中小分子化学成分,并对所得单体化合物进行体外抗炎活性筛选,以期进一步丰富九华黄精的药效物质基础,也为九华黄精药材资源的合理开发及利用奠定理论依据。

1 材料与方法

1.1 仪器与试剂

Bruker Avance III 500 核磁共振仪(德国 Bruker,TMS 作为内标);Waters Synapt G2 TOF-ESI-MS 高分辨质谱仪(美国 Waters);Waters LC-2535 制备/半制备型高效液相色谱仪,配 UV-2489 型紫外检测器(美国 Waters);RP-C_{18}半制备色谱柱(250 mm × 10 mm,250 mm × 20 mm,5 μm,日本 YMC);MCO-18AIC 二氧化碳培养箱(日本 SANYO);MK3 酶标仪(美国 Thermo)。

Sephadex LH-20 羟丙基葡聚糖凝胶柱色谱填料(美国 GE);MCI 柱色谱填料:GHP 20P(75 ~ 150 μm)(日本 Mitsubishi);薄层层析硅胶板(HSGF$_{254}$,青岛海洋化工有限公司);各种柱色谱用硅胶均为青岛海洋化工有限公司出品;色谱甲醇(美国 Fisher);氘代试剂(德国 Merck);甲醇、二氯甲烷(分析纯,苏州强盛化学试剂有限公司);*N*-硝基-*L*-精氨酸甲酯(NG-nitro-*L*-arginine methyl ester,*L*-NAME)(批号:0001418328,纯度≥99%,美国 Sigma);DMSO:(批号:67-68-5,纯度≥99%,法国 MP Bio);RAW 264.7 细胞(中国医学科学院基础医学研究所国家实验细胞资源共享平台);DMEM 培养基(批号:SH30284.01,美国 Hyclone);胎牛血清(批号:ST190318,德国 PAN-BiotechGmbh);Griess 试剂盒(批号:011020200325,碧云天生物科技有限公司);革兰氏阴性菌脂多糖(LPS)(批号:057M4013V,美国 Sigma)。

1.2 植物材料

九华黄精生药材于2020年6月购自安徽省青阳县九华中药材科技有限公司,经安徽省芜湖市皖南医学院药学院柳春燕副研究员鉴定为百合科黄精属植物九华黄精(*Polygonatum cyrtonema* Hua in Jiuhua Mountain)的干燥块茎,样品标本(编号:2020JHHJ)现保存于皖南医学院逸夫科技楼109实验室生物标本柜。

1.3 提取分离

干燥的九华黄精生药材20 kg,切碎,按照1∶10料液比,添加85%乙醇加热冷凝回流提取3次,每次2 h。合并三次所得提取液,减压浓缩至原体积1/10后干燥得到浸膏物。浸膏物重新溶解于适量的蒸馏水中,依次经乙酸乙酯、正丁醇反复多次萃取,合并多次萃取液,减压浓缩干燥后得到乙酸乙酯萃取物170 g,正丁醇萃取物220 g。选取正丁醇萃取物进一步分析,经装填10倍体积的100 ~ 200目硅胶柱色谱,依次用二氯甲烷-甲醇(20∶1→0∶1)梯度洗脱,通过TLC监测后合并各组分并将其依次命名为Fr. C-1 ~ Fr. C-5。

通过MCI柱色谱对组分Fr. C-1(20.0 g)进行下一步分离纯化,采用不同比例的甲醇-水溶液梯度洗脱,得到Fr. C-1-1(30%甲醇部位)、Fr. C-1-2(60%甲醇部位)、Fr. C-1-3(90%甲醇部位)三个组分。Fr. C-1-1样品用甲醇溶解、过滤,经Sephadex LH-20羟丙基葡聚糖凝胶柱色谱(纯甲醇)等度洗脱除色素,然后采用高压制备液相色谱分离(RP-C_{18}色

谱柱,20 mm × 250 mm,5 μm;甲醇-水 60∶40,8 mL/min 等度洗脱),得三个组分(Fr. C-1-1-1 ~ Fr. C-1-1-3)。Fr. C-1-1-1(120.0 mg)再经半制备液相色谱分离、纯化(RP-C_{18}色谱柱,10 mm × 250 mm,5 μm;甲醇-水 40∶60,2 mL/min 等度洗脱)得化合物 **1**(7.8 mg,t_R = 26.8 min)与 **4**(10.2 mg,t_R = 17.6 min)。Fr. C-1-1-2(108.5 mg)经半制备液相色谱分离、纯化(RP-C_{18}色谱柱,10 mm × 250 mm,5 μm;甲醇-水 42∶58,2 mL/min 等度洗脱)得化合物 **2**(9.6 mg,t_R = 24.3 min)与 **3**(13.1 mg,t_R = 27.8 min)。Fr. C-1-1-3(202.0 mg)经半制备液相色谱分离、纯化(RP-C_{18}色谱柱,10 mm × 250 mm,5 μm;甲醇-水 50∶50,2 mL/min 等度洗脱)得化合物 **5**(4.6 mg,t_R = 16.3 min)、**6**(7.6 mg,t_R = 20.8 min)与 **9**(4.2 mg,t_R = 23.2 min)。

采用减压硅胶柱色谱(100 ~200 目)、经二氯甲烷-甲醇(20∶1→1∶1)梯度洗脱体系对组分 Fr. C-2(35.2 g)进行分离,并采用 TLC 检测合并得到 4 个组分(Fr. C-2-1 ~ Fr. C-2-4)。Fr. C-2-1 通过减压 MCI 柱色谱分离,采用甲醇-水体系(30%、60%、90%)梯度洗脱,得三个组分即:Fr. C-2-1-1 ~ Fr. C-2-1-3。组分 Fr. C-2-1-1(2.5 g)用甲醇溶解、过滤,采用 Sephadex LH-20 羟丙基葡聚糖凝胶柱色谱(纯甲醇)等度洗脱除色素,然后采用高压制备液相色谱分离(RP-C_{18}色谱柱,20 mm × 250 mm,5 μm;甲醇-水 60∶40,8 mL/min 等度洗脱),得四个组分(Fr. C-2-1-1-1 ~ Fr. C-2-1-1-4)。Fr. C-2-1-1-1(78.0 mg)经半制备液相色谱分离、纯化(RP-C_{18}色谱柱,10 mm × 250 mm,5 μm;甲醇-水 45∶55,2 mL/min 等度洗脱)得化合物 **7**(13.2 mg,t_R = 17.6 min)、**8**(17.6 mg,t_R = 19.8 min)与 **10**(3.6 mg,t_R = 24.3 min)。Fr. C-2-1-1-2(138.5 mg)经半制备液相色谱分离、纯化(RP-C_{18}色谱柱,10 mm × 250 mm,5 μm;甲醇-水 42∶58,2 mL/min 等度洗脱)得化合物 **13**(9.6 mg,t_R = 32.3 min)与 **14**(13.1 mg,t_R = 34.8 min)。Fr. C-2-1-1-3(202.0 mg)经半制备液相色谱分离、纯化(RP-C_{18}色谱柱,10 mm × 250 mm,5 μm;甲醇-水 50∶50,2 mL/min 等度洗脱)得化合物 **11**(4.6 mg,t_R = 18.8 min)、**12**(7.6 mg,t_R = 20.2 min)。Fr. C-2-1-1-4(58.0 mg)经半制备液相色谱分离、纯化(RP-C_{18}色谱柱,10 mm × 250 mm,5 μm;甲醇-水 50∶50,2 mL/min 等度洗脱)得化合物 **15**(5.9 mg,t_R = 16.8 min)与 **16**(9.8 mg,t_R = 18.5 min)。

1.4　化合物抑制 NO 生成活性测定与细胞活力检测

采用格里斯试剂法(Griess)评价各化合物对 RAW 264.7 细胞释放 NO 的影响,并采用 CCK-8 法检测其对细胞活力的影响,在排除细胞毒活性的前提下检测各化合物的抗炎活性[10,11]。取对数生长期的 RAW 264.7 细胞种于 96 孔板中、培养过夜,次日采用 100 ng/mL 的 LPS 造模并给药,实验设空白组(加 100 μL 培养基)、模型组(加 50 μL 的 100 ng/mL LPS、50 μL 培养基)、阳性药组(加 50 μL 的 100 ng/mL LPS、50 μL 不同浓度的 L-NAME)、给药组(加 50 μL 的 100 ng/mL LPS、50 μL 不同浓度的药物)。继续培养 24 h 后,取各组上清 50 μL,分别加入 50 μL Griess Reagent Ⅰ与 Griess Reagent Ⅱ试剂后用酶标仪于 540 nm 测定吸光度值,计算半数抑制浓度(IC_{50})值;随后,往 96 孔板中各组剩余的培养液中加入 CCK-8 试液 20 μL,置于恒温培养箱中培养 2 h,随后于 450 nm 测其吸光度值、计算细胞存活率。

1.5　统计学处理

采用 GraphPad Prism 7.0 软件对各组数据进行统计学分析,每组数据均以三次独立的重复实验的平均值 ± 标准差($\bar{x} \pm s$)表示。

2　结果

2.1　结构鉴定

化合物 1　白色无定形粉末;HR-ESI-MS:*m/z* 751.425 2[M + Na]$^+$(计算值 $C_{38}H_{64}O_{13}Na$,751.424 5),分子式为 $C_{38}H_{64}O_{13}$;^{1}H NMR(500 MHz,C_5D_5N)δ:5.52(1H,d,J = 5.6 Hz,H-6),4.84(1H,d,J = 7.8 Hz,H-1″),4.82(1H,d,J = 7.8 Hz,H-1′),4.45(1H,d,J = 10.2 Hz,H-1),4.27(1H,m,H-22),3.88(1H,dd,J = 11.6,3.8 Hz,H-3),3.85(1H,m,H-16),2.93(1H,m,H-14),2.79(1H,m,H-11α),2.78(1H,m,H-15α),2.66(1H,m,H-4α),2.58(1H,m,H-4β),2.54(1H,m,H-20),2.32(1H,m,H-24α),2.11(1H,m,H-15β),2.02(1H,m,H-12α),1.94(1H,m,H-2α),1.93(1H,br s,H-17),1.82(1H,m,H-23α),1.78(1H,m,H-24β),1.77(1H,m,H-7α),1.76(1H,m,H-23β),1.64(1H,m,H-2β),1.63(1H,m,H-25),1.58(1H,m,H-11β),1.45(1H,m,H-9),1.43(1H,m,H-7β),1.39(1H,m,H-12β),1.33(1H,m,H-8),1.24(1H,s,H-19),

1.14(1H,d,J = 7.0 Hz,H-21),1.04(1H,s,H-18),0.92(1H,d,J = 6.2 Hz,H-26),0.91(1H,d,J = 6.2 Hz,H-27);^{13}C NMR(125 MHz,C_5D_5N)δ:82.3(C-1),36.9(C-2),68.2(C-3),42.8(C-4),139.6(C-5),124.8(C-6),32.0(C-7),33.3(C-8),50.4(C-9),42.9(C-10),24.0(C-11),41.0(C-12),42.3(C-13),55.2(C-14),37.7(C-15),83.5(C-16),58.2(C-17),14.0(C-18),14.8(C-19),36.2(C-20),12.8(C-21),73.2(C-22),33.8(C-23),37.2(C-24),28.9(C-25),23.0(C-26),23.2(C-27),107.2(C-1′),75.3(C-2′),78.9(C-3′),71.3(C-4′),67.6(C-5′),102.3(C-1″),75.7(C-2″),78.3(C-3″),71.8(C-4″),78.8(C-5″),63.0(C-6″)。以上数据与文献报道[12]基本一致,故鉴定化合物为 polygodoside H。

化合物 2 白色无定形粉末;HR-ESI-MS:m/z 633.3631[M+Na]$^+$(计算值 $C_{33}H_{54}O_{10}Na$,633.3615),分子式为 $C_{33}H_{54}O_{10}$;^{1}H NMR(500 MHz,C_5D_5N)δ:5.85(1H,dd,J = 12.6,7.2 Hz,H-16),5.52(1H,d,J = 9.6 Hz,H-6),4.92(1H,dd,J = 7.2,3.6 Hz,H-26α),4.72(1H,d,J = 7.8 Hz,H-1′),3.52(1H,dd,J = 7.2,3.0 Hz,H-26β),2.93(1H,br s,H-17),2.68(2H,br d,J = 7.2 Hz,H-4),2.57(1H,m,H-7α),2.38(1H,m,H-15α),2.34(1H,dd,J = 12.6,7.6 Hz,H-2α),2.32(1H,t,J = 7.2 Hz,H-20),2.14(1H,dd,J = 9.6,6.6 Hz,H-8),2.02(1H,dd,J = 9.6,3.6 Hz,H-12α),2.12(1H,m,H-24α),2.01(1H,m,H-23α),1.97(1H,m,H-23β),1.94(1H,m,H-25),1.93(1H,m,H-7β),1.84(1H,m,H-1α),1.83(1H,m,H-9),1.81(1H,m,H-15β),1.79(2H,m,H-11),1.78(1H,m,H-24β),1.78(1H,br d,J = 9.6 Hz,H-12β),1.54(1H,dt,J = 12.6,3.6 Hz,H-2β),1.34(1H,t,J = 7.2 Hz,H-21),1.14(1H,dd,J = 13.6,3.6 Hz,H-1β),1.14(1H,s,H-18),1.12(1H,s,H-19),1.05(1H,d,J = 7.2 Hz,H-27);^{13}C NMR(125 MHz,C_5D_5N)δ:38.2(C-1),32.0(C-2),71.4(C-3),43.6(C-4),141.2(C-5),121.8(C-6),26.6(C-7),35.8(C-8),43.8(C-9),37.0(C-10),20.6(C-11),32.6(C-12),45.6(C-13),86.4(C-14),40.2(C-15),81.9(C-16),60.7(C-17),20.3(C-18),19.5(C-19),40.9(C-20),16.8(C-21),111.1(C-22),37.3(C-23),28.5(C-24),34.1(C-25),75.6(C-26),17.5(C-27),105.2(C-1′),75.4(C-2′),78.6(C-3′),71.2(C-4′),78.5(C-5′),61.2(C-6′)。以上数据与文献报道[13]基本一致,故鉴定化合物为 polygonatumoside G。

化合物 3 白色无定形粉末;HR-ESI-MS:m/z 617.3658[M+Na]$^+$(计算值 $C_{33}H_{54}O_9Na$,617.3666),分子式为 $C_{33}H_{54}O_9$;^{1}H NMR(500 MHz,C_5D_5N)δ:5.86(1H,dd,J = 12.6,7.2 Hz,H-16),5.52(1H,d,J = 9.6 Hz,H-6),4.91(1H,dd,J = 7.2,3.6 Hz,H-26α),4.70(1H,d,J = 7.8 Hz,H-1′),3.51(1H,dd,J = 7.2,3.0 Hz,H-26β),2.94(1H,br s,H-17),2.93(1H,m,H-14),2.78(1H,m,H-11α),2.65(2H,br d,J = 7.2 Hz,H-4),2.48(1H,m,H-15α),2.47(1H,m,H-7α),2.35(1H,t,J = 7.2 Hz,H-20),2.24(1H,dd,J = 12.6,7.6 Hz,H-2α),2.12(1H,m,H-24α),2.01(1H,m,H-12α),2.00(1H,m,H-23α),1.98(1H,m,H-23β),1.95(1H,m,H-25),1.92(1H,m,H-7β),1.83(1H,m,H-15β),1.76(1H,m,H-24β),1.74(1H,m,H-1α),1.58(1H,m,H-11β),1.54(1H,dt,J = 12.6,3.6 Hz,H-2β),1.42(1H,m,H-9),1.40(1H,m,H-12β),1.35(1H,m,H-8),1.32(1H,t,J = 7.2 Hz,H-21),1.15(1H,dd,J = 13.6,3.6 Hz,H-1β),1.13(1H,s,H-18),1.12(1H,s,H-19),1.04(1H,d,J = 7.2 Hz,H-27);^{13}C NMR(125 MHz,C_5D_5N)δ:37.9(C-1),32.5(C-2),71.2(C-3),43.5(C-4),142.2(C-5),121.2(C-6),32.6(C-7),32.0(C-8),50.5(C-9),37.2(C-10),21.3(C-11),40.2(C-12),41.0(C-13),56.8(C-14),32.7(C-15),81.3(C-16),64.0(C-17),16.6(C-18),19.8(C-19),40.8(C-20),16.7(C-21),110.8(C-22),37.3(C-23),28.4(C-24),34.6(C-25),75.5(C-26),17.6(C-27),105.3(C-1′),75.4(C-2′),78.7(C-3′),71.4(C-4′),78.6(C-5′),60.0(C-6′)。以上数据与文献报道[13]基本一致,故鉴定化合物为(25S)-funkioside B。

化合物 4 白色无定形粉末;HR-ESI-MS:m/z 1249.5480[M+Na]$^+$(计算值 $C_{56}H_{90}O_{29}Na$,1249.5465),分子式为 $C_{56}H_{90}O_{29}$;^{1}H NMR(500 MHz,C_5D_5N)δ:5.53(1H,d,J = 7.2 Hz,H-1‴),5.25(1H,br s,H-6),5.20(1H,d,J = 7.2 Hz,H-1⁗),5.13(1H,d,J = 9.6 Hz,H-1″),4.86(1H,m,H-16),4.82(1H,d,J = 7.8 Hz,H-1′),4.79(1H,d,J = 7.2 Hz,H-1⁗′),3.95(1H,dd,J = 7.2,3.6 Hz,H-26α),3.54(1H,dd,J = 7.2,3.0

Hz,H-26β),2.94(1H,m,H-17),2.78(1H,dd,*J* = 12.6,6.0 Hz,H-11α),2.65(2H,br d,*J* = 7.2 Hz,H-4),2.15(1H,m,H-20),2.04(1H,m,H-2β),2.03(1H,m,H-15β),2.00(2H,m,H-23),1.98(1H,m,H-24α),1.91(1H,m,H-25),1.85(1H,m,H-8),1.82(1H,m,H-7β),1.67(1H,m,H-24β),1.63(1H,m,H-2α),1.62(1H,m,H-15α),1.58(1H,dd,*J* = 12.6,9.6 Hz,H-11β),1.52(1H,m,H-21),1.44(1H,m,H-7α),1.40(1H,m,H-14),1.35(1H,m,H-1β),1.28(1H,m,H-9),1.14(1H,s,H-18),1.00(1H,d,*J* = 7.2 Hz,H-27),0.82(1H,s,H-19),0.74(1H,m,H-1α);^{13}C NMR(125 MHz,C_5D_5N)δ:37.3(C-1),30.0(C-2),78.2(C-3),39.5(C-4),140.8(C-5),121.5(C-6),32.0(C-7),31.0(C-8),52.5(C-9),37.8(C-10),37.3(C-11),212.2(C-12),55.4(C-13),56.0(C-14),31.7(C-15),79.8(C-16),54.8(C-17),16.2(C-18),18.8(C-19),41.2(C-20),15.7(C-21),110.8(C-22),37.2(C-23),28.4(C-24),34.5(C-25),75.4(C-26),17.6(C-27),102.9(C-1′),73.3(C-2′),75.7(C-3′),79.4(C-4′),75.6(C-5′),60.7(C-6′),105.3(C-1″),81.5(C-2″),86.8(C-3″),70.4(C-4″),77.8(C-5″),63.1(C-6″),104.9(C-1‴),76.4(C-2‴),77.8(C-3‴),71.2(C-4‴),78.9(C-5‴),62.6(C-6‴),105.1(C-1⁗),75.2(C-2⁗),78.8(C-3⁗),70.8(C-4⁗),67.5(C-5⁗),105.2(C-1′′′′′),75.4(C-2′′′′′),78.8(C-3′′′′′),71.8(C-4′′′′′),78.6(C-5′′′′′),62.9(C-6′′′′′)。以上数据与文献报道[14]基本一致,故鉴定化合物为 typaspidoside A。

化合物 5　黄色无定型粉末;HR-ESI-MS:*m/z* 609.148 0[M - H]$^-$(计算值 $C_{27}H_{29}O_{16}$,609.145 6),分子式为 $C_{27}H_{30}O_{16}$;^{1}H NMR(500 MHz,DMSO-d_6)δ:12.49(1H,s,5-OH),7.56(1H,s,H-2′),7.54(1H,d,*J* = 8.2 Hz,H-6′),6.85(1H,d,*J* = 8.2 Hz,H-5′),6.35(1H,s,H-8),6.20(1H,s,H-6),5.35(1H,d *J* = 6.6 Hz,H-1″),4.42(1H,s,H-1‴),0.97(3H,d,*J* = 6.4 Hz,H-6‴);^{13}C NMR(125 MHz,DMSO-d_6)δ:156.5(C-2),133.3(C-3),177.4(C-4),161.2(C-5),98.8(C-6),164.3(C-7),93.7(C-8),156.6(C-9),103.9(C-10),121.2(C-1′),115.3(C-2′),144.8(C-3′),148.5(C-4′),116.3(C-5′),121.6(C-6′),101.2(C-1″),74.1(C-2″),76.5(C-3″),70.6(C-4″),75.9(C-5″),67.0(C-6″),100.8(C-1‴),70.4(C-2‴),70.0(C-3‴),71.9(C-4‴),68.3(C-5‴),17.8(C-6‴)。以上数据与文献报道[15]基本一致,故鉴定化合物为芦丁。

化合物 6　黄色无定型粉末;HR-ESI-MS:*m/z* 593.150 1[M - H]$^-$(计算值 $C_{27}H_{29}O_{15}$,593.150 6),分子式为 $C_{27}H_{30}O_{15}$;^{1}H NMR(500 MHz,C_5D_5N)δ:7.60(1H,dd,*J* = 8.8 Hz,2.2 Hz,H-6′),7.55(1H,d,*J* = 2.2 Hz,H-2′),6.92(1H,d,*J* = 8.8 Hz,H-5′),6.75(1H,s,H-3),6.40(1H,d,*J* = 3.0 Hz,H-8),6.18(1H,d,*J* = 3.0 Hz,H-6);^{13}C NMR(125 MHz,C_5D_5N)δ:164.9(C-2),103.8(C-3),182.5(C-4),161.8(C-5),99.8(C-6),162.8(C-7),94.5(C-8),157.5(C-9),105.6(C-10),121.7(C-1′),116.8(C-2′),144.4(C-3′),148.5(C-4′),115.3(C-5′),121.7(C-6′),102.3(C-1"),74.5(C-2"),76.4(C-3"),70.1(C-4"),75.5(C-5"),67.8(C-6"),100.8(C-1‴),70.8(C-2‴),70.6(C-3‴),72.3(C-4‴),68.9(C-5‴),16.6(C-6‴)。以上数据与文献报道[16]基本一致,故鉴定化合物为木犀草素-7-*O*-芸香糖苷。

化合物 7　黄色无定型粉末;HR-ESI-MS:*m/z* 447.094 0[M - H]$^-$(计算值 $C_{21}H_{19}O_{11}$,447.092 7),分子式为 $C_{21}H_{20}O_{11}$;^{1}H NMR(500 MHz,C_5D_5N)δ:7.85(2H,dd,*J* = 8.2,2.4 Hz,H-2′,6′),6.90(2H,dd,*J* = 8.2,2.4 Hz,H-3′,5′),6.75(1H,d,*J* = 2.4 Hz,H-8),6.45(1H,d,*J* = 2.4 Hz,H-6),5.05(1H,d,*J* = 7.2 Hz,H-1″),3.92(1H,dd,*J* = 12.0,2.4 Hz,H-6″α),3.72(1H,dd,*J* = 12.0,2.4 Hz,H-6″β);^{13}C NMR(125 MHz,C_5D_5N)δ:148.6(C-2),138.7(C-3),177.8(C-4),162.5(C-5),100.2(C-6),164.3(C-7),95.5(C-8),157.3(C-9),106.8(C-10),123.8(C-1′),131.2(C-2′,6′),116.9(C-3′,5′),161.4(C-4′),102.4(C-1″),75.5(C-2″),79.6(C-3″),71.6(C-4″),79.2(C-5″),62.7(C-6″)。以上数据与文献报道[17]基本一致,故鉴定化合物为山柰酚-7-*O*-β-*D*-葡萄糖苷。

化合物 8　黄色无定型粉末;HR-ESI-MS:*m/z* 463.088 2[M - H]$^-$(计算值 $C_{21}H_{19}O_{12}$,463.087 7),分子式为 $C_{21}H_{20}O_{12}$;^{1}H NMR(500 MHz,C_5D_5N)δ:7.73(1H,d,*J* = 2.4 Hz,H-2′),7.58(1H,dd,*J* = 8.2,2.4 Hz,H-6′),6.88(1H,d,*J* = 8.2 Hz,H-5′),

6.20(1H,d,J =2.4 Hz,H-6),6.38(1H,d,J = 2.4 Hz,H-8),5.24(1H,d,J = 7.2 Hz,H-1″);^{13}C NMR(125 MHz,C_5D_5N)δ:158.6(C-2),135.6(C-3),179.8(C-4),163.2(C-5),99.6(C-6),166.2(C-7),94.5(C-8),159.2(C-9),105.6(C-10),123.2(C-1′),116.2(C-2′),145.8(C-3′),149.8(C-4′),117.7(C-5′),123.6(C-6′),104.3(C-1″),75.7(C-2″),78.5(C-3″),71.3(C-4″),78.2(C-5″),62.5(C-6″)。以上数据与文献报道[18,19]基本一致,故鉴定化合物为槲皮素-3-*O*-β-*D*-吡喃葡萄糖苷。

化合物 9 黄色无定形粉末;HR-ESI-MS:m/z 431.097 5[M - H]$^-$(计算值 $C_{21}H_{19}O_{10}$,431.097 8),分子式为 $C_{21}H_{20}O_{10}$;^{1}H NMR(500 MHz,CD_3OD)δ:7.92(2H,dd,J =8.2,2.4 Hz,H-2′,6′),6.92(2H,dd,J =8.2,2.4 Hz,H-3′,5′),6.83(1H,d,J = 2.4 Hz,H-8),6.67(1H,s,H-3),6.50(1H,d,J =2.4 Hz,H-6),5.08(1H,d,J =6.8 Hz,H-1″);^{13}C NMR(125 MHz,CD_3OD)δ:166.9(C-2),104.2(C-3),184.2(C-4),163.1(C-5),101.3(C-6),164.6(C-7),96.1(C-8),159.2(C-9),107.2(C-10),123.3(C-1′),129.8(C-2′,6),117.3(C-3′,5′),162.8(C-4′),101.5(C-1″),74.7(C-2″),77.8(C-3″),71.2(C-4″),78.5(C-5″),62.5(C-6″)。以上数据与文献报道[20]基本一致,故鉴定化合物为芹菜素-7-*O*-β-*D*-葡萄糖苷。

化合物 10 白色无定形粉末;HR-ESI-MS:m/z 523.219 0[M + H]$^+$(计算值 $C_{26}H_{35}O_{11}$,523.217 9),分子式为 $C_{26}H_{34}O_{11}$;^{1}H NMR(500 MHz,CD_3OD)δ:7.08(1H,d,J = 8.4 Hz,H-5),6.90(1H,dd,J = 2.4 Hz,H-2′),6.76(1H,dd,J = 8.4,2.4 Hz,H-6′),6.74(1H,dd,J = 8.4,2.4 Hz,H-6),6.72(1H,d,J = 8.4 Hz,H-5′),6.89(1H,d,J = 2.4 Hz,H-2),4.62(1H,d,J = 6.0 Hz,H-1″),3.78(1H,m,H-3″),3.94(1H,m,H-5″),3.66(1H,m,H-4″),3.60(1H,dd,J = 12.0,6.0 Hz,H-6″α),3.56(1H,m,H-2″),3.20(1H,dd,J = 12.0,6.0 Hz,H-6″β);^{13}C NMR(125 MHz,CD_3OD)δ:138.1(C-1),110.0(C-2),149.4(C-3),145.8(C-4),116.5(C-5),118.2(C-6),82.4(C-7),52.7(C-8),59.1(C-9),132.1(C-1′),112.0(C-2′),147.6(C-3′),144.4(C-4′),114.8(C-5′),120.7(C-6′),32.2(C-7′),42.4(C-8′),72.2(C-9′),101.5(C-1″),73.5(C-2″),76.4(C-3″),69.9(C-4″),76.8(C-5″),61.1(C-6″)。以上数据与文献报道[21]基本一致,故鉴定化合物为落叶松脂醇-4-*O*-β-*D*-葡萄糖苷。

化合物 11 白色粉末;HR-ESI-MS:m/z 369.118 0[M + H]$^+$(计算值 $C_{17}H_{21}O_9$,369.118 6),分子式为 $C_{17}H_{20}O_9$。^{1}H NMR(500 MHz,CD_3OD)δ:7.59(1H,d,J = 15.0 Hz,H-7′),7.06(1H,d,J = 2.4 Hz,H-2′),6.94(1H,dd,J = 8.4,2.4 Hz,H-6′),6.75(1H,d,J = 8.4 Hz,H-5′),6.36(1H,d,J = 15.0 Hz,H-8′),4.30 ~ 4.27(3H,m,H-3,4,5),3.75(3H,s,7-OMe),2.33 ~ 1.99(4H,m,H-2,6);^{13}C NMR(125 MHz,CD_3OD)δ:74.5(C-1),36.6(C-2),69.1(C-3),71.3(C-4),70.7(C-5),36.6(C-6),174.1(C-7),126.3(C-1′),113.7(C-2′),148.2(C-3′),145.8(C-4′),115.2(C-5′),121.7(C-6′),145.4(C-7′),113.8(C-8′),167.0(C-9′),51.7(7-OMe)。以上数据与文献报道[22]基本一致,故鉴定化合物为 5-*O*-咖啡酰奎宁酸甲酯。

化合物 12 白色粉末;HR-ESI-MS:m/z 369.117 8[M + H]$^+$(计算值 $C_{17}H_{21}O_9$,369.118 6),分子式为 $C_{17}H_{20}O_9$;^{1}H NMR(500 MHz,CD_3OD)δ:7.56(1H,d,J = 15.0 Hz,H-7′),7.04(1H,d,J = 2.4 Hz,H-2′),6.92(1H,dd,J = 8.4,2.4 Hz,H-6′),6.73(1H,d,J = 8.4 Hz,H-5′),6.36(1H,d,J = 15.0 Hz,H-8′),4.30 ~ 4.27(3H,m,H-3,4,5),3.75(3H,s,7-OMe),2.33 ~ 1.99(4H,m,H-2,6);^{13}C NMR(125 MHz,CD_3OD)δ:75.0(C-1),40.8(C-2),64.3(C-3),77.2(C-4),67.6(C-5),37.0(C-6),174.3(C-7),121.6(C-1′),113.6(C-2′),145.4(C-3′),148.2(C-4′),115.(C-5′),126.2(C-6′),145.6(C-7′),113.7(C-8′),167.5(C-9′),52.9(7-OMe)。以上数据与文献报道[23]基本一致,故鉴定化合物为 4-*O*-咖啡酰奎宁酸甲酯。

化合物 13 白色粉末;HR-ESI-MS:m/z 529.134 0[M - H]$^-$(计算值 $C_{26}H_{25}O_{12}$,529.134 6),分子式为 $C_{26}H_{26}O_{12}$;^{1}H NMR(500 MHz,CD_3OD)δ:7.65(1H,d,J = 15.0 Hz,H-7″),7.6(1H,d,J = 15.0 Hz,H-7′),7.12(2H,d,J = 2.4 Hz,H-2′,H-2″),7.00(2H,d,J = 8.4 Hz,H-5′,H-5″),6.82(2H,dd,J = 8.4,2.4 Hz,H-6′,H-6″),6.36(1H,d,J = 15.0 Hz,H-8′),6.28(1H,d,J = 15.0 Hz,H-8″),4.32 ~ 4.28(3H,m,H-3,4,5),3.74(3H,s,7-OMe),2.32 ~ 1.98(4H,m,H-2,6);^{13}C NMR(125 MHz,CD_3OD)δ:74.8(C-1),35.6(C-2),72.1(C-

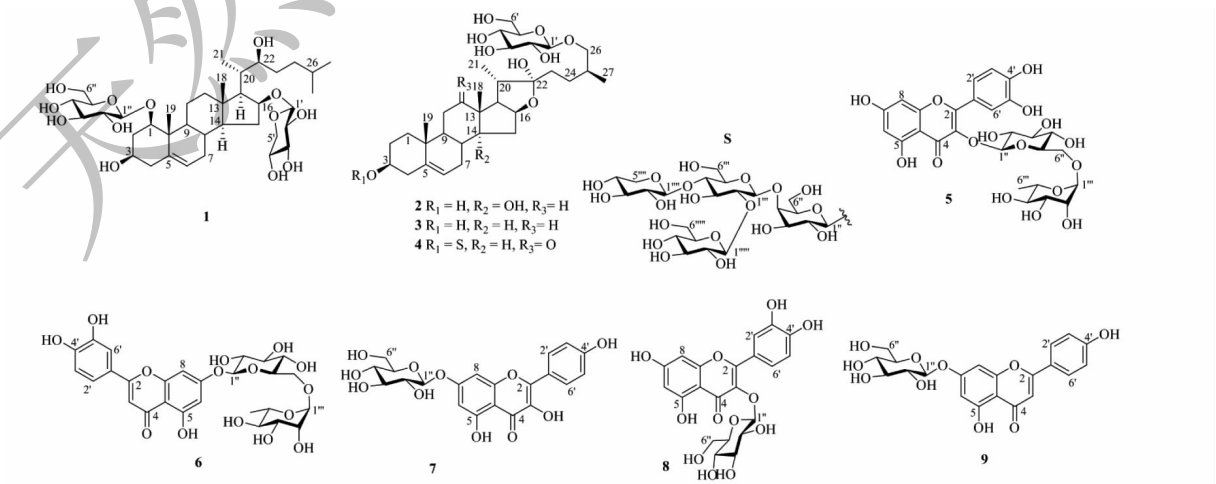
3),69.8(C-4),72.3(C-5),36.8(C-6),175.6(C-7),127.5(C-1′),127.8(C-1″),115.3(C-2′,2″),146.8(C-3′),146.9(C-3″),149.6(C-4′),149.8(C-4″),116.5(C-5′),116.6(C-5″),123.0(C-6′),123.1(C-6″),147.1(C-7′),147.4(C-7″),114.9(C-8′),115.5(C-8″),168.0(C-9′),168.7(C-9″),53.0(7-OMe)。以上数据与文献报道[24]基本一致,故确定该化合物为3,5-*O*-二咖啡酰奎宁酸甲酯。

化合物 14　白色粉末;HR-ESI-MS:*m/z* 529.134 1[M-H]⁻(计算值 $C_{26}H_{25}O_{12}$,529.134 6),分子式 $C_{26}H_{26}O_{12}$;^{1}H NMR(500 MHz,CD_3OD)δ:7.62(1H,d,*J* = 15.0 Hz,H-7′),7.56(1H,d,*J* = 15.0 Hz,H-7″),7.14(1H,d,*J* = 2.4 Hz,H-2′),7.06(1H,d,*J* = 2.4 Hz,H-2″),6.64(1H,dd,*J* = 8.4,2.4 Hz,H-6′),6.62(1H,dd,*J* = 8.4,2.4 Hz,H-6″),6.58(2H,d,*J* = 8.4 Hz,H-5′,H-5″),6.13(1H,d,*J* = 15.0 Hz,H-8′),6.05(1H,d,*J* = 15.0 Hz,H-8″),4.10 ~ 4.27(3H,m,H-3,4,5),3.73(3H,s,7-OMe),2.14 ~ 2.23(4H,m,H-2,6);^{13}C NMR(125 MHz,C_5D_5N)δ:75.6(C-1),38.8(C-2),68.8(C-3),74.6(C-4),68.3(C-5),38.7(C-6),175.0(C-7),126.6(C-1′,1″),116.0、116.1(C-2′,2″),146.9(C-3′,3″),150.8、150.9(C-4′,4″),116.9、117.0(C-5′,5″),122.5(C-6′,6″),147.8、147.9(C-7′,7″),114.7、114.9(C-8′,8″),167.0、167.5(C-9′,9″),52.7(7-OMe)。以上数据与文献报道[25]基本一致,故确定该化合物为3,4-*O*-二咖啡酰基奎宁酸甲酯。

化合物 15　白色粉末,HR-ESI-MS:*m/z* 529.134 0[M-H]⁻(计算值 $C_{26}H_{25}O_{12}$,529.134 6),分子式 $C_{26}H_{26}O_{12}$;^{1}H NMR(500 MHz,CD_3OD)δ:7.56(1H,d,*J* = 15.0 Hz,H-7′),7.54(1H,d,*J* = 15.0 Hz,H-7″),7.12(1H,d,*J* = 2.4 Hz,H-2′),7.02(1H,d,*J* = 2.4 Hz,H-2″),6.9(1H,dd,*J* = 8.4,2.4 Hz,H-6′),6.87(1H,dd,*J* = 8.4,2.4 Hz,H-6″),6.74(1H,d,*J* = 8.4 Hz,H-5′),6.72(1H,d,*J* = 8.4 Hz,H-5″),6.28(1H,d,*J* = 15.0 Hz,H-8′),6.23(1H,d,*J* = 15.0 Hz,H-8″),4.25(3H,m,H-3,4,5),3.72(3H,s,7-OMe),2.32 ~ 1.98(4H,m,H-2,6);^{13}C NMR(125 MHz,CD_3OD)δ:75.3(C-1),41.2(C-2),69.7(C-3),75.3(C-4),66.1(C-5),36.6(C-6),176.2(C-7),127.8(C-1′,1″),115.2(C-2′,2″),146.7(C-3′,3″),149.5(C-4′,4″),116.6(C-5′,5″),123.2、123.4(C-6′,6″),147.4(C-7′,7″),114.6、115.1(C-8′,8″),168.5、168.6(C-9′,9″),53.0(7-OMe)。以上数据与文献[26]报道基本一致,故确定该化合物为4,5-*O*-二咖啡酰基奎宁酸甲酯。

化合物 16　白色粉末;HR-ESI-MS:*m/z* 179.070 5[M+H]⁺(计算值 $C_{10}H_{11}O_3$,179.070 8),分子式为 $C_{10}H_{10}O_3$;^{1}H NMR(500 MHz,C_5D_5N)δ:7.45(1H,dd,*J* = 8.4,2.4 Hz,H-2、H-6),7.48(1H,d,*J* = 15.0 Hz,H-7),6.59(H,dd,*J* = 8.4,2.4 Hz,H-3、H-5),6.31(H,d,*J* = 15.0 Hz,H-8),3.80(3H,s,9-OMe)。^{13}C NMR(125 MHz,C_5D_5N)δ:125.8(C-1),130.5(C-2、C-6),116.6(C-3、C-5),161.3(C-4),145.1(C-7),114.5(C-8),167.5(C-9),51.1(9-OMe)。以上波谱数据与文献报道[27]对比基本一致,故鉴定化合物为对羟基肉桂酸甲酯。

化合物 **1 ~ 16** 的结构式见图1。



续图1(Continued Fig.1)

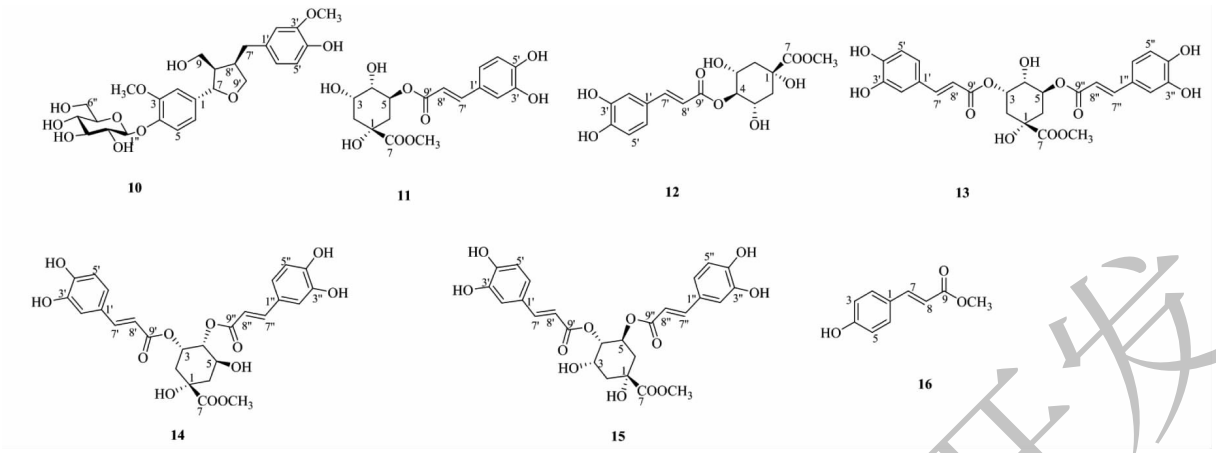


图 1 化合物 1 ~ 16 的结构

Fig. 1 Structures of compounds **1-16**

2.2 抑制 NO 生成活性研究结果

所述单体化合物的抗炎活性筛选结果见表 1 所示,化合物 **1 ~ 3**、**5 ~ 8** 均能够有效抑制 LPS 诱导的 RAW 264.7 细胞释放 NO,且无细胞毒作用,IC_{50} 值范围为 8.28 ~ 41.85 μmol/L,表现出一定程度的抗炎活性。其中,化合物 **2** 与 **3** 的抗炎活性显著优于阳性对照药 *L*-NAME。化合物 **4** 在最大安全剂量下对 NO 生成的抑制率小于 50%,化合物 **9 ~ 16** 无明显活性。

表 1 不同单体化合物对 LPS 诱导 RAW 264.7 细胞产生 NO 的影响($\bar{x} \pm s$, $n = 3$)

Table 1 Effects of different compounds on NO production in LPS-induced RAW 264.7 cells($\bar{x} \pm s$, $n = 3$)

化合物 Compound	IC_{50}(μmol/L)
1	12.93 ± 0.27
2	9.80 ± 0.32
3	8.28 ± 0.75
5	41.85 ± 1.31
6	40.62 ± 2.43
7	12.85 ± 0.31
8	15.62 ± 0.43
L-NAME	35.96 ± 2.90

注:*L*-NAME 为阳性对照。

Note: *L*-NAME was used as the positive control.

3 结论

本研究从安徽道产大宗药材——九华黄精生药材的 85% 乙醇提取物中分离并鉴定出 16 个化合物,包括甾体皂苷类化合物、黄酮类化合物、酚酸类化合物。所有化合物均是首次从九华黄精中分离得到。抗炎活性实验结果表明,部分化合物具有良好的抗炎活性,其中两个甾体皂苷类化合物(**2** 和 **3**)的抗炎活性尤为显著、优于阳性对照药 *L*-NAME。以上提示,九华黄精中甾体皂苷类成分可能是其发挥抗炎活性的主要功效物质、具有潜在的开发价值,值得后续进一步的深入研究。通过对九华黄精中小分子化学成分及抗炎活性研究,为丰富九华黄精的化学成分及阐明其药效物质基础奠定了坚实的理论基础,也为九华黄精药材的深入开发利用提供了参考依据。

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