纤枝金丝桃中的一个新的多环多异戊烯基间苯三酚衍生物

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摘要: 采用硅胶柱色谱、反相C18色谱柱色谱、Sephadex LH-20凝胶柱色谱、高效液相色谱及中压半制备液相色谱等分离技术对纤枝金丝桃中的化学成分进行分离纯化, 通过MS、NMR等波谱数据结合理化性质鉴定化合物结构。从纤枝金丝桃80%乙醇提取物中分离得到11个化合物, 分别鉴定为hyperlagarone A (**1**)、hyperpatulone E (**2**)、hyperbeanol G (**3**)、uralione D (**4**)、tomoeone F (**5**)、pyramidatone A (**6**)、tomoeone A (**7**)、tomoeone B (**8**)、hyperbeanol C (**9**)、hyperbeanol A (**10**)、hypercohone G (**11**)。其中化合物**1**是未见报道的新化合物, 化合物**2**～**11**是首次从该植物中分离得到。对11个化合物进行基于L6骨骼细胞的促葡萄糖摄取实验, 结果显示化合物**7**、**8**均显示较强的促葡萄糖摄取活性。

关键词: 藤黄科; 纤枝金丝桃; 化学成分; 多环多异戊烯基间苯三酚; 葡萄糖摄取

中图分类号: R284 **文献标识码**: A **文章编号**: 0513-4870(2022)09-2767-07

A new polycyclic polyprenylated acylphloroglucinols from *Hypericum lagarocladum* N. Robson

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Abstract: Silica gel column chromatography, reversed phase C18 column chromatography, Sephadex LH-20 gel column chromatography, high performance liquid chromatography and medium performance semi preparative liquid chromatography were performed to separate and purify the chemical constituents of *Hypericum lagarocladum* N. Robson. Spectroscopic methods such as MS and NMR combined with physicochemical properties were applied in identifying the structures of the isolated compounds. A total of 11 compounds were isolated and identified as hyperlagarone A (**1**), hyperpatulone E (**2**), hyperbeanol G (**3**), uralione D (**4**), tomoeone F (**5**), pyramidatone A (**6**), tomoeone A (**7**), tomoeone B (**8**), hyperbeanol C (**9**), hyperbeanol A (**10**), and hypercohone G (**11**), respectively. Compound **1** is a new polycyclic polyprenylated acylphloroglucinol derivative, and compounds **2**−**11** are isolated from this plant for the first time. 11 compounds were tested for glucose uptake in L6 cells, and the results showed that compounds **7** and **8** had significant effect on glucose uptake.

Key words: Guttiferae; *Hypericum lagarocladum* N. Robson; chemical component; polycyclic polyprenylated acylphloroglucinol; glucose uptake

金丝桃属 (*Hypericum*) 归属于藤黄科植物, 世界约有400余种, 我国有55种8亚种, 分布较广泛, 各地均有, 特别是贵州、陕西、甘肃等地区。金丝桃属植物由于其化学结构新颖和药理活性丰富近年来备受关注[1]。目前关于金丝桃属植物的研究发现其有多种化

收稿日期: 2022-01-21; 修回日期: 2022-06-27.

基金项目: 国家自然科学基金项目 (81774000, 81573561); 湖北省卫健委中医药科研项目 (ZY2021M076).

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DOI: 10.16438/j.0513-4870.2022-0095

学成分, 已经发现的有黄酮类、甾体类、萜类, 尤其是近年来从金丝桃属植物中发现的独特的多环多异戊烯基间苯三酚衍生物类化合物 (polycyclic polyprenylated acylphloroglucinols, PPAPs) 引起了药学科研人员的广泛关注。在过去的15年间所报道的PPAPs已超过500余个[2]。由于独特的结构、特异性分布以及广泛的生物活性, PPAPs受到了植物化学、药理学和有机合成化学等相关学科研究人员的高度关注, 这些化合物的活性和合成研究也在近年来取得了巨大的研究成果[3]。

纤枝金丝桃 (*Hypericum lagarocladum* N. Robson) 为藤黄科金丝桃属植物, 分布于湖南西部、四川西部、贵州南部、云南中西部[4], 目前关于其化学成分方面的报道甚少。本课题组在对该植物进行初步成分分析时发现, 纤枝金丝桃含有较丰富的PPAPs成分, 综合利用各种分离提取技术对采自云南省昆明市的纤枝金丝桃的化学成分进行分离纯化, 从其石油醚和乙酸乙酯部位中分离得到了11个间苯三酚衍生物类化合物 (图1), 其中化合物**1**为未见报道的新化合物, 化合物**2**～**11**为首次从该植物中分离得到。

结果与讨论

1 结构鉴定

化合物**1**: 黄色油状; $[\alpha]_D^{20}$ −18 (*c* 0.5, CH_3OH); HR-ESI-MS显示 *m/z* 469.256 1 $[M+Na]^+$ ($C_{26}H_{38}O_6Na$, 计算值为469.257 0); UV(MeOH) λ_{max} (log ε) = 280 (3.52); IR (KBr) υ_{max}: 3 404、2 970、1 674、1 539、1 436 cm^{-1}; 结合核磁数据推断其分子式为$C_{26}H_{38}O_6$。其不饱和度为8。^{13}C NMR和DEPT (表1) 显示出26个碳信号: 包括10个季碳、4个次甲基、5个亚甲基、7个甲基。其中 δ_C 196.8、105.1、193.3、105.6、176.1、56.0和204.7这些典型的碳谱信号提示该化合物具有1个酰基间苯三酚类母核结构; δ_C 111.1、147.1与 δ_H 4.83 (1H, br s)、4.76 (1H, br s) 为典型的末端烯烃双键的信号[5-7]。^1H NMR谱显示出1个异丙基片段 [δ_H 3.81 (1H, sept, *J* = 6.7 Hz, H-24), 1.19 (3H, d, *J* = 6.7 Hz, H-25), 1.12 (3H, d, *J* = 6.7 Hz, H-26)], 基于以上数据推测化合物**1**是具有1个异丙基和1个末端双键的间苯三酚类衍生物。仔细对比hookerianone B[8]的1D-NMR数据和HMBC信号, 发现非常相似, 区别仅在于hookerianone B中1个异戊烯基片段被化合物**1**中甲基 (δ_C 26.6) 所取代, 据此推测两个化合物的结构差异在于化合物**1**的C-6存在1个甲基 (C-22) 取代了hookerianone A中的异戊烯基。结合HMBC图谱 (图2) 显示 δ_C 26.6 (C-22) 与 δ_H 1.48 (3H, s, H-22) 相关, HMBC图谱中H-22/C-1/C-5/C-6的相关进一步确定C-6与C-22相连, 由此可以确定该化合物的平面结构。

关于化合物**1**的相对构型, 在NOESY谱图中发现H-18/H-22存在相关信号, 据此推测H-18与H-22位于

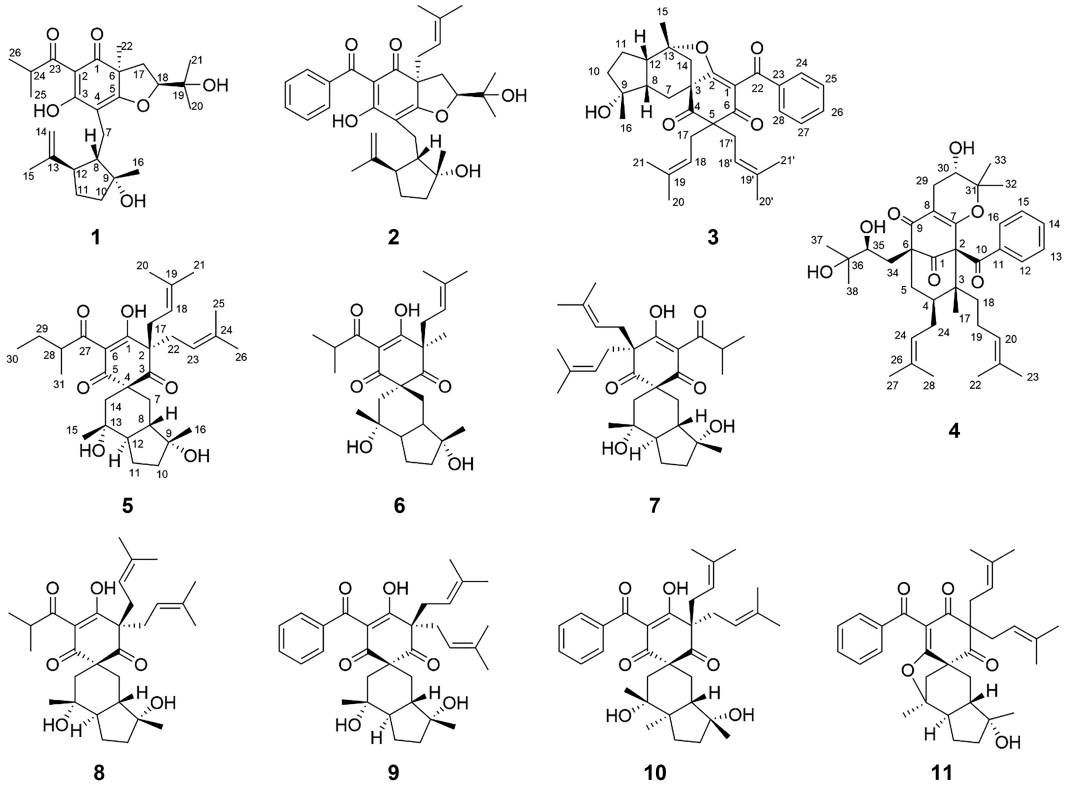

Figure 1 Structures of compounds **1**−**11**

Table 1 ^{1}H NMR (600 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) spectral data of compound **1**

Position	δ_H	δ_C	Position	δ_H	δ_C
1		196.8, C	14	4.83 (1H, br s), 4.76 (1H, br s)	111.1, CH_2
2		105.1, C	15	1.73 (3H, s)	18.9, CH_3
3		193.3, C	16	1.10 (3H, s)	28.4, CH_3
4		105.6, C	17	2.36 (1H, m)	32.2, CH_2
				2.06 (1H, dd, J = 12.4, 5.4 Hz)	
5		176.1 C	18	4.45 (1H, dd, J = 10.6, 5.4 Hz)	90.6, CH
6		56.0, C	19		70.4, C
7	2.39 (2H, m)	21.2, CH_2	20	1.39 (3H, s)	27.5, CH_3
8	1.86 (1H, m)	49.8, CH	21	1.15 (3H, s)	24.4, CH_3
9		80.3, C	22	1.48 (3H, s)	26.6, CH_3
10	1.75 (2H, m)	41.9, CH_2	23		204.7, C
11	1.84 (1H, m), 1.44 (1H, m)	27.8, CH_2	24	3.81 (1H, sept, J = 6.8 Hz)	34.3, CH
12	2.46 (1H, m)	53.2, CH	25	1.19 (3H, d, J = 6.8 Hz)	19.8, CH_3
13		147.1, C	26	1.12 (3H, d, J = 6.8 Hz)	18.8, CH_3

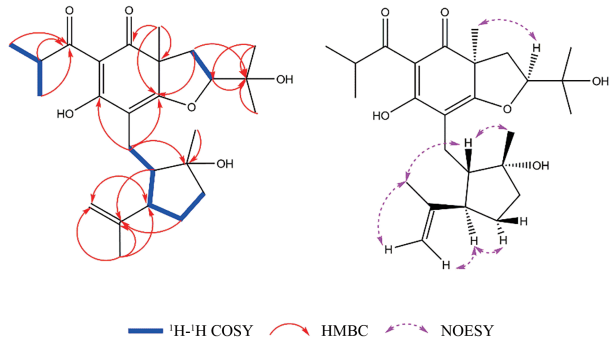

Figure 2 Key ^{1}H-^{1}H COSY, HMBC and NOESY correlations of compound **1**

同一侧。H-8/H-16/H-15存在相关信号, 同时H-15/H-14a存在相关信号, 而H-14b/H-11/H-10存在相关信号。据此推测7号位相连的五元环中H-8、Me-16与isoprorwnyl-12位于同一侧。

根据以上结论, 进一步推测化合物**1**的绝对构型存在4种情况。同时通过对比化合物**1**与hookerianone B的CD谱图发现两者的CD图谱非常相似, 而且有相同的Cotton效应 (在约234和348 nm有负Cotton效应, 在约273和302 nm有正Cotton效应), 据此推断化合物**1**的绝对构型与hookerianone B相同, 为6*S*,8*S*,9*R*,12*R*,18*S*。进一步通过ECD计算与CD实验值比较的方法确认化合物**1**的绝对构型。首先在Sybyl-X 1.1.0中使用MMFF94S力场的随机搜索对化合物**1**进行构象分析。随后用Gaussian 09软件在B3LYP/6-31G(d,p)水平对化合物**1**的所有构象进行了密度泛函理论 (DFT)的优化。选择Boltzmann-population超过1%的构象体进行ECD计算。然后在B3LYP/6-311G(d,p)水平上使用含时密度函数理论 (TD-DFT) 计算优化的构象。在相同DFT水平上使用SCRF/PCM方法评估MeOH溶液的溶剂效应。最后, 通过SpecDis 1软件生成玻尔兹曼平均ECD光谱。通过比较实验光谱和计算的ECD光谱 (图3), 证实化合物**1**的绝对构型为6*S*,8*S*,9*R*,12*R*,18*S*。由此, 化合物**1**的立体结构被确定, 并命名为hyperlagarone A。

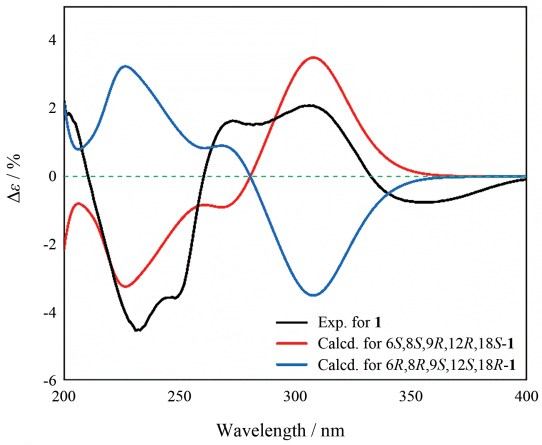

Figure 3 Experimental and calculated ECD spectra of compound **1**

2 葡萄糖摄取

利用基于L6细胞的促葡萄糖摄取实验研究分离的11个化合物对于L6骨骼肌细胞内葡萄糖摄取的影响情况, 以小檗碱作为阳性对照, 并设立空白对照组和实验组。结果表明, 在30 μg·mL^{-1}的浓度条件下, 以对照组为基准, 小檗碱促葡萄糖摄取倍数为3.54, 11个化合物中化合物**7**、**8**相对葡萄糖摄取水平为2.82和2.69, 显示较强的促葡萄糖摄取活性, 其他化合物均显示弱的促葡萄糖摄取活性。

实验部分

Bruker DRX-600 MHz核磁共振仪 (德国Bruker公司), Q-TOF Micro LC-MS-MS质谱仪, Waters 2535半制备型高效液相色谱仪、Waters 2998 DAD检测器、

Waters 2707自动进样器 (美国Waters公司), COSMOSIL C18 (250 mm × 10 mm, 5 μm) 半制备柱、COSMOSIL 5PFP (250 mm × 10 mm, 5 μm) 半制备柱 (日本COSMOSIL公司), HP-20大孔树脂 (日本三菱公司), GF_{254} 200～300、300～400目薄层硅胶板 (烟台江友硅胶开发有限公司), Sephadex LH-20葡聚糖凝胶 (美国Amersham公司), 色谱级甲醇及色谱级乙腈 (美国TEDIA试剂公司)。

纤枝金丝桃于2019年采集于云南省昆明市梁贡山, 经中南民族大学万定荣教授鉴定为藤黄科金丝桃属纤枝金丝桃 (*Hypericum lagarocladum* N. Robson)。植物标本 (SC0869) 现存放于湖北省武汉市中南民族大学药学院植物标本库。

1 提取与分离

取纤枝金丝桃干燥地上部分25.5 kg, 粉碎, 用80%的乙醇室温浸提 (4×20 L, 每次3天), 合并多次提取液, 减压浓缩至无醇味即得浸膏1.76 kg。将浸膏加5倍体积热水分散后, 依次用石油醚、乙酸乙酯、正丁醇萃取得到石油醚部位142 g、乙酸乙酯部位353 g、正丁醇部位693 g。将石油醚部位和乙酸乙酯部位合并, 用大孔树脂柱色谱进行粗分, 以水−乙醇梯度洗脱 (20%−30%−40%−50%−60%−70%−80%−90%−95%, *v*/*v*), 硅胶薄层色谱板检测合并得11个组分Fr. A～Fr. J。其中组分Fr. C (8.9 g) 用凝胶柱色谱粗分, 以甲醇 (加入0.1%甲酸) 洗脱, 合并得10个组分 (Fr. Ca～Fr. Ck)。Fr. Cb (2.1 g) 组分经半制备高效液相色谱分离得到化合物**5** (5.1 mg)、**6** (7.6 mg); Fr. Cc (125.6 mg) 经半制备高效液相色谱分离得到化合物**9** (10.5 mg)、**10** (8.2 mg); Fr. Cd (56.9 mg) 经半制备高效液相色谱分离得到化合物**11** (9.2 mg)。Fr. D (15.3 g) 用凝胶色谱粗分, 洗脱液TLC检测合并, 得到10个组分Fr. Da～Fr. Dj。Fr. Da (232.9 mg) 经半制备高效液相色谱分离得到化合物**7** (12.5 mg); Fr. Db (168.4 mg) 经高效液相色谱分离得到化合物**8** (3.2 mg); Fr. Df (98.4 mg) 经高效液相色谱分离得到化合物**4** (12.6 mg)。Fr. E (6.9 g) 用硅胶柱色谱经石油醚−乙酸乙酯梯度洗脱 (1∶0～0∶1), 经TLC检测合并分为Fr. Ea～Fr. Ef共6个组份。Fr. Eb (120.2 mg) 经凝胶柱色谱粗分, 得Fr. Eb1～Fr. Eb4共4个组分, Fr. Eb1 (51.2 mg) 经半制备高效液相色谱得到化合物**3** (6.8 mg), Fr. Eb3 (32.1 mg) 经半制备高效液相色谱得到化合物**1** (2.1 mg)、化合物**2** (9.6 mg)。

2 葡萄糖摄取

采用细胞葡萄糖检测试剂盒检测11个化合物对L6细胞葡萄糖摄取活性的影响。将L6细胞以每孔1×10^4～5×10^4细胞接种于96孔板, 每孔加入100 μL *α*-MEM培养基。孵育过夜后, 换用含2% FBS的*α*-MEM培养基, 每隔24 h换液一次, 连续培养7天, 待L6细胞分化后换用不含血清的*α*-MEM培养基饥饿细胞2 h。化合物**1**～**11**用含2-NBDG的无糖培养基配置成30 μg·mL^{-1}样品溶液 (含150 μg·mL^{-1} 2-NBDG)。每孔加入含待测样品的培养基100 μL, 于恒温细胞培养箱中孵育30 min。并设空白对照、胰岛素阳性对照组, 每组3个复孔。孵育结束后, 96孔板400 ×*g*离心5 min。吸去上清液, 每孔加入200 μL的试剂盒缓冲液, 混匀后, 室温下400 ×*g*离心5 min。弃上清液, 每孔加入100 μL缓冲液。酶标仪激发波长/发射波长 (485/535 nm) 下检测各孔吸收值。

3 结构鉴定

化合物**1**: 黄色油状; $[\alpha]_D^{20}$ −18 (*c* 0.5, CH_3OH); HR-ESI-MS显示*m/z* 469.256 1 $[M+Na]^+$ ($C_{26}H_{38}O_6Na$, 计算值为469.257 0); UV (MeOH) λ_{max} (log ε) = 280 (3.52) nm; IR (KBr) υ_{max}: 3 404、2 970、1 674、1 539、1 436 cm^{-1}; ^{1}H NMR、^{13}C NMR数据见表1

化合物**2**: 黄色油状; ESI-MS *m/z* 557 $[M+Na]^+$, 分子式为$C_{33}H_{42}O_6$。^{1}H NMR (600 MHz, $CDCl_3$) δ_H: 7.46 (2H, m, H-29, H-33), 7.45 (1H, m, H-31), 7.37 (2H, m, H-30, H-32), 5.14 (1H, t, *J* = 6.7 Hz, H-23), 4.80 (1H, m, H-14a), 4.74 (1H, m, H-14b), 4.54 (1H, m, H-18), 2.67 (1H, m, H-22a), 2.57 (1H, m, H-12), 2.48 (1H, m, H-7a), 2.46 (1H, m, H-22b), 2.13 (1H, m, H-17a), 1.95 (1H, m, H-7b), 1.92 (1H, m, H-11*α*), 1.83 (1H, m, H-8), 1.77 (1H, m, H-10*β*), 1.77 (3H, s, H-25), 1.72 (1H, m, H-10*α*), 1.72 (3H, s, H-15), 1.63 (3H, s, H-26), 1.45 (1H, m, H-11*β*), 1.31 (3H, s, H-20), 1.26 (1H, m, H-17b), 1.18 (3H, s, H-16), 1.16 (3H, s, H-21); ^{13}C NMR (150 MHz, $CDCl_3$) δ_C: 195.2 (C-1), 193.2 (C-3), 191.4 (C-27), 176.7 (C-5), 147.7 (C-13), 137.4 (C-24), 136.6 (C-28), 131.4 (C-31), 128.1 (C-29), 128.1 (C-33), 128.0 (C-30), 128.0 (C-32), 117.3 (C-23), 110.8 (C-14), 107.0 (C-2), 106.9 (C-4), 91.3 (C-18), 79.9 (C-9), 71.2 (C-19), 60.8 (C-6), 52.7 (C-12), 50.9 (C-8), 40.9 (C-10), 37.4 (C-22), 29.6 (C-17), 28.4 (C-16), 28.1 (C-11), 26.6 (C-20), 26.1 (C-21), 24.4 (C-25), 20.8 (C-7), 19.3 (C-15), 18.4 (C-26)。其波谱数据与文献[9]基本一致, 故确定为hyperpatulone E。

化合物**3**: 黄色油状; ESI-MS *m/z* 515 $[M-H]^-$, 分子式为$C_{33}H_{39}O_5$。^{1}H NMR (600 MHz, $CDCl_3$) δ_H: 7.85 (2H, d, *J* = 7.9 Hz, H-24, H-28), 7.52 (1H, t, *J* = 7.9 Hz, H-26), 7.40 (2H, t, *J* = 7.9 Hz, H-25, H-27), 5.04 (1H, t, *J* = 7.7 Hz, H-18′), 4.96 (1H, t, *J* = 7.8 Hz, H-18), 2.74 (1H, dd, *J* = 13.5, 7.8 Hz, H-17b), 2.62 (2H, m, H-17′),

2.50 (1H, d, *J* = 12.5 Hz, H-14*β*), 2.45 (1H, dd, *J* = 13.5, 7.8 Hz, H-17a), 2.17 (1H, m, H-12), 1.95 (2H, m, H-7), 1.94 (1H, m, H-10*β*), 1.79 (1H, m, H-11*α*), 1.74 (1H, m, H-10*α*), 1.68 (3H, s, H-20′), 1.66 (3H, s, H-20), 1.60 (3H, s, H-21′), 1.55 (1H, m, H-14*α*), 1.54 (3H, s, H-21), 1.41 (3H, s, H-15), 1.37 (1H, m, H-8), 1.28 (3H, s, H-16), 1.12 (1H, m, H-11*β*); ^{13}C NMR (150 MHz, $CDCl_3$) δ_C: 209.7 (C-4), 196.6 (C-6), 192.4 (C-22), 178.9 (C-2), 137.6 (C-23), 135.6 (C-19), 135.2 (C-19′), 133.3 (C-26), 129.6 (C-24, C-28), 128.5 (C-25, C-27), 119.3 (C-18′), 119.1 (C-18), 112.6 (C-1), 93.2 (C-13), 75.8 (C-9), 64.2 (C-5), 57.2 (C-3), 48.3 (C-8), 47.5 (C-12), 41.4 (C-10), 36.9 (C-17), 36.5 (C-14), 36.0 (C-17′), 33.0 (C-7), 27.0 (C-16), 26.2 (C-20, C-20′), 24.4 (C-11), 21.4 (C-15), 18.2 (C-21), 18.0 (C-21′)。其波谱数据与文献[10]基本一致, 故确定为hyperbeanol G。

化合物**4**: 黄色油状; ESI-MS *m/z* 621 $[M+Na]^+$, 分子式为$C_{38}H_{51}O_7$。^{1}H NMR (600 MHz, $CDCl_3$) δ_H: 7.66 (2H, d, *J* = 7.5 Hz, H-12, H-16), 7.42 (1H, t, *J* = 7.5 Hz, H-14), 7.30 (2H, t, *J* = 7.5 Hz, H-13, H-15), 5.02 (1H, t, *J* = 7.0 Hz, H-20), 4.94 (1H, t, *J* = 7.1 Hz, H-25), 3.59 (1H, t, *J* = 4.5 Hz, H-30), 3.55 (1H, dd, *J* = 9.9, 3.4 Hz, H-35), 2.59 (1H, m, H-29*β*), 2.25 (1H, m, H-19a), 2.24 (1H, m, H-29*α*), 2.19 (2H, m, H-24), 2.08 (2H, m, H-18), 2.07 (1H, m, H-34a), 2.00 (1H, m, H-19b), 1.99 (1H, dd, *J* = 13.4 Hz, 4.4 Hz, H-5*β*), 1.83 (1H, m, H-4), 1.74 (1H, m, H-24b), 1.67 (3H, s, H-27), 1.66 (3H, s, H-22), 1.66 (1H, m, H-34b), 1.63 (3H, s, H-23), 1.55 (3H, s, H-28), 1.45 (1H, m, H-5*α*), 1.24 (3H, s, H-37), 1.22 (3H, s, H-17), 1.21 (3H, s, H-38), 1.19 (3H, s, H-32), 0.52 (3H, s, H-33); ^{13}C NMR (150 MHz, $CDCl_3$) δ_C: 210.3 (C-1), 194.8 (C-9), 194.1 (C-10), 166.3 (C-7), 137.8 (C-11), 133.8 (C-26), 132.3 (C-14), 131.6 (C-21), 128.3 (C-12), 128.3 (C-16), 128.2 (C-13), 128.2 (C-15), 124.8 (C-20), 122.4 (C-25), 111.7 (C-8), 82.5 (C-31), 74.9 (C-35), 73.6 (C-2), 73.2 (C-36), 67.9 (C-30), 63.8 (C-6), 50.2 (C-3), 44.2 (C-4), 42.4 (C-5), 38.4 (C-18), 32.8 (C-34), 28.1 (C-24), 26.0 (C-19), 18.1 (C-22), 25.8 (C-27), 25.7 (C-29), 25.3 (C-32), 24.2 (C-33), 23.8 (C-37), 22.4 (C-38), 25.9 (C-23), 18.0 (C-28), 13.2 (C-17)。其波谱数据与文献[11]基本一致, 故确定为uralione D。

化合物**5**: 黄色油状; ESI-MS *m/z* 537 $[M+Na]^+$, 分子式为$C_{31}H_{46}O_6$。^{1}H NMR (600 MHz, $CDCl_3$) δ_H: 4.90 (1H, m, H-18), 4.72 (1H, m, H-23), 2.78 (1H, dd, *J* = 14.8, 6.4 Hz, H-28a), 2.74 (1H, m, H-17a), 2.72 (1H, m, H-28b), 2.68 (1H, m, H-22a), 2.52 (1H, dd, *J* = 13.6, 6.4 Hz, H-17b), 2.46 (1H, dd, *J* = 13.6, 7.6 Hz, H-22), 2.18 (1H, m, H-29), 2.01 (1H, d, *J* = 14.4 Hz, H-14*α*), 1.87 (1H, m, H-7*α*), 1.83 (1H, m, H-12), 1.80 (2H, m, H-11), 1.79 (2H, m, H-10), 1.77 (1H, m, H-8), 1.68 (1H, m, H-7*β*), 1.61 (3H, s, H-26), 1.55 (3H, s, H-21), 1.55 (1H, d, *J* = 14.4 Hz, H-14*β*), 1.52 (3H, s, H-25), 1.47 (3H, s, H-20), 1.25 (3H, s, H-16), 1.07 (3H, s, H-15), 0.98 (3H, d, *J* = 6.4 Hz, H-30), 0.96 (3H, d, *J* = 6.4, H-31); ^{13}C NMR (150 MHz, $CDCl_3$) δ_C: 209.0 (C-5), 207.5 (C-27), 196.9 (C-1), 196.5 (C-3), 137.4 (C-19), 137.1 (C-24), 118.2 (C-18), 118.1 (C-23), 113.2 (C-2), 79.0 (C-9), 72.8 (C-13), 63.0 (C-4), 61.3 (C-6), 51.3 (C-12), 47.8 (C-8), 44.6 (C-14), 41.7 (C-10), 40.7 (C-28), 38.2 (C-22), 37.1 (C-17), 27.3 (C-7), 27.1 (C-26), 26.6 (C-16), 26.1 (C-21), 26.1 (C-29), 23.2 (C-15), 21.6 (C-30), 18.1 (C-20), 18.0 (C-25), 16.78 (C-11), 11.9 (C-31)。其波谱数据与文献[12]基本一致, 故确定为tomoeone F。

化合物**6**: 黄色油状; ESI-MS *m/z* 469 $[M+Na]^+$, 分子式为$C_{26}H_{38}O_6$。^{1}H NMR (600 MHz, $CDCl_3$) δ_H: 4.59 (1H, t, *J* = 7.2 Hz, H-18), 3.59 (1H, sept, *J* = 6.4 Hz, H-24), 2.69 (1H, dd, *J* = 12.8, 7.2 Hz, H-17a), 2.40 (1H, dd, *J* = 12.8, 7.2 Hz, H-17b), 2.16 (1H, d, *J* = 13.6 Hz, H-14*β*), 1.99 (1H, m, H-7*α*), 1.82 (1H, m, H-8), 1.80 (1H, m, H-10), 1.78 (1H, m, H-12), 1.66 (1H, m, H-7*β*), 1.55 (3H, s, H-22), 1.52 (1H, m, H-14*α*), 1.51 (3H, s, H-21), 1.42 (1H, m, H-11), 1.39 (3H, s, H-20), 1.38 (3H, s, H-16), 1.21 (3H, d, *J* = 6.4 Hz, H-26), 1.12 (3H, d, *J* = 6.4 Hz, H-25), 0.99 (3H, s, H-15); ^{13}C NMR (150 MHz, $CDCl_3$) δ_C: 210.2 (C-5), 207.2 (C-23), 198.5 (C-1), 193.7 (C-3), 137.9 (C-19), 117.4 (C-18), 111.4 (C-2), 79.4 (C-9), 73.9 (C-13), 64.9 (C-4), 56.1 (C-6), 51.8 (C-12), 49.7 (C-14), 48.3 (C-8), 40.8 (C-17), 39.9 (C-10), 35.3 (C-24), 26.9 (C-16), 25.9 (C-21), 24.0 (C-7), 22.9 (C-22), 21.8 (C-11), 21.6 (C-15), 20.1 (C-26), 18.4 (C-25), 17.7 (C-20)。其波谱数据与文献[12]基本一致, 故确定为pyramidatone A。

化合物**7**: 黄色油状; ESI-MS *m/z* 499 $[M-H]^-$, 分子式为$C_{30}H_{43}O_6$。^{1}H NMR (600 MHz, $CDCl_3$) δ_H: 4.99 (1H, t, *J* = 7.6 Hz, H-18), 4.62 (1H, t, *J* = 7.9 Hz, H-23), 3.36 (1H, m, H-28), 2.77 (1H, dd, *J* = 13.6, 7.8 Hz, H-17a), 2.68 (1H, dd, *J* = 13.6, 7.8 Hz, H-17b), 2.59 (1H, dd, *J* = 13.2, 8.8 Hz, H-22a), 2.39 (1H, dd, *J* = 13.2, 8.8 Hz, H-22b), 2.16 (1H, dd, *J* = 13.5, 1.8 Hz, H-14*β*), 1.93 (1H, m, H-7*α*), 1.80 (2H, m, H-10), 1.78 (2H, m, H-11), 1.70

(1H, m, H-12), 1.69 (1H, m, H-7*β*), 1.68 (1H, m, H-8), 1.63 (3H, s, H-21), 1.57 (3H, s, H-20), 1.53 (3H, s, H-26), 1.38 (3H, s, H-16), 1.38 (3H, s, H-25), 1.27 (3H, d, *J* = 6.8 Hz, H-30), 1.16 (1H, d, *J* = 13.6, H-14*β*), 1.14 (3H, d, *J* = 6.8 Hz, H-29), 0.95 (3H, s, H-15); ^{13}C NMR (150 MHz, $CDCl_3$) δ_C: 207.4 (C-5), 205.3 (C-27), 198.4 (C-1), 197.6 (C-3), 138.2 (C-24), 135.8 (C-19), 119.4 (C-18), 117.0 (C-23), 113.3 (C-2), 79.4 (C-9), 73.4 (C-13), 65.4 (C-4), 62.0 (C-6), 52.1 (C-12), 50.4 (C-14), 48.1 (C-8), 41.2 (C-22), 39.8 (C-10), 34.6 (C-17), 34.3 (C-28), 26.9 (C-16), 26.1 (C-21), 26.0 (C-26), 24.1 (C-7), 21.7 (C-11), 21.3 (C-30), 20.5 (C-15), 18.0 (C-29), 17.9 (C-20), 17.8 (C-25)。其波谱数据与文献[12]基本一致, 故确定为tomoeone A。

化合物 **8**: 黄色油状; ESI-MS *m/z* 499 $[M-H]^-$, 分子式为 $C_{30}H_{43}O_6$。^{1}H NMR (600 MHz, $CDCl_3$) δ_H: 4.91 (1H, t, *J* = 7.6 Hz, H-18), 4.75 (1H, t, *J* = 7.4 Hz, H-23), 3.57 (1H, m, H-28), 2.74 (1H, dd, *J* = 14.0, 7.6 Hz, H-17a), 2.68 (1H, *J* = 13.6, 7.9 Hz, H-22b), 2.54 (1H, dd, *J* = 14.0, 7.6 Hz, H-17b), 2.49 (1H, dd, *J* = 13.6, 7.9 Hz, H-22a), 2.05 (1H, d, *J* = 14.5 Hz, H-14*β*), 1.89 (1H, m, H-7*β*), 1.87 (1H, m, H-12), 1.82 (2H, m, H-11), 1.81 (2H, m, H-10), 1.78 (1H, m, H-7*α*), 1.77 (1H, m, H-8), 1.75 (1H, m, H-14*α*), 1.62 (3H, s, H-21), 1.58 (3H, s, H-26), 1.52 (3H, s, H-20), 1.48 (3H, s, H-25), 1.27 (3H, s, H-16), 1.20 (3H, d, *J* = 6.7 Hz, H-29), 1.17 (3H, d, *J* = 6.7 Hz, H-30), 1.10 (3H, s, H-15); ^{13}C NMR (150 MHz, $CDCl_3$) δ_C: 208.9 (C-5), 207.9 (C-27), 196.7 (C-1), 196.5 (C-3), 137.5 (C-24), 137.1 (C-19), 118.2 (C-18), 118.0 (C-23), 112.6 (C-2), 79.0 (C-9), 72.9 (C-13), 62.9 (C-4), 61.3 (C-6), 51.2 (C-12), 47.8 (C-12), 44.5 (C-14), 40.7 (C-10), 38.3 (C-22), 37.2 (C-17), 35.4 (C-28), 27.1 (C-7), 26.6 (C-16), 26.1 (C-21), 26.1 (C-26), 23.2 (C-15), 21.6 (C-11), 19.7 (C-30), 19.2 (C-29), 18.1 (C-20), 18.0 (C-25)。其波谱数据与文献[12]基本一致, 故确定为tomoeone B。

化合物 **9**: 黄色油状; ESI-MS *m/z* 533 $[M-H]^-$, 分子式为 $C_{33}H_{41}O_6$。^{1}H NMR (600 MHz, $CDCl_3$) δ_H: 7.59 (2H, d, *J* = 7.8 Hz, H-29, H-33), 7.51 (1H, t, *J* = 7.8 Hz, H-31), 7.41 (2H, t, *J* = 7.8 Hz, H-30, H-32), 4.96 (1H, t, *J* = 7.8 Hz, H-18), 4.83 (1H, t, *J* = 7.9 Hz, H-23), 2.79 (1H, m, H-17a), 2.71 (1H, m, H-22a), 2.69 (1H, m, H-17b), 2.53 (1H, m, H-22b), 2.10 (1H, m, H-14*β*), 2.09 (1H, d, *J* = 13.8 Hz, H-7*α*), 1.81 (1H, m, H-7*β*), 1.80 (1H, m, H-14*α*), 1.78 (1H, m, H-10*β*), 1.75 (1H, m, H-12), 1.74 (1H, m, H-11*β*), 1.63 (1H, m, H-10*β*), 1.63 (3H, s, H-26), 1.62 (3H, s, H-21), 1.59 (3H, s, H-20), 1.51 (3H, s, H-25), 1.40 (1H, m, H-8), 1.35 (1H, m, H-11*α*), 1.29 (3H, s, H-16), 0.77 (3H, s, H-15); ^{13}C NMR (150 MHz, $CDCl_3$) δ_C: 208.4 (C-5), 197.2 (C-1), 195.8 (C-3), 195.4 (C-27), 137.8 (C-24), 136.7 (C-19), 136.6 (C-28), 131.8 (C-31), 128.5 (C-29, C-33), 127.7 (C-30, C-32), 118.6 (C-18), 117.5 (C-23), 114.1 (C-2), 79.3 (C-9), 73.4 (C-13), 64.9 (C-4), 62.0 (C-6), 52.2 (C-12), 47.9 (C-8), 47.6 (C-14), 40.2 (C-10), 39.6 (C-22), 36.1 (C-17), 27.1 (C-7), 26.8 (C-16), 26.2 (C-21), 26.1 (C-26), 21.8 (C-15), 21.7 (C-11), 18.0 (C-20), 18.0 (C-25)。其波谱数据与文献[13]基本一致, 故确定为hyperbeanol C。

化合物 **10**: 黄色油状; ESI-MS *m/z* 533 $[M-H]^-$, 分子式为 $C_{33}H_{41}O_6$。^{1}H NMR (600 MHz, $CDCl_3$) δ_H: 7.61 (2H, d, *J* = 7.0 Hz, H-29, H-33), 7.52 (1H, t, *J* = 7.0 Hz, H-30), 7.40 (2H, t, *J* = 7.0 Hz, H-30, H-32), 4.87 (2H, m, H-18, H-23), 2.82 (1H, m, H-17b), 2.76 (1H, m, H-22b), 2.63 (1H, m, H-17a), 2.61(1H, m, H-22b), 2.23 (1H, m, H-14*β*), 2.06 (1H, m, H-7*α*), 1.91 (1H, m, H-12), 1.87 (1H, m, H-10*β*), 1.82 (1H, m, H-10*α*), 1.79 (1H, m, H-11*β*), 1.65 (1H, m, H-11*α*), 1.63 (1H, m, H-14*α*), 1.62 (1H, m, H-8), 1.62 (3H, s, H-21), 1.61 (3H, s, H-26), 1.58 (3H, s, H-20), 1.53 (3H, s, H-25), 1.32 (1H, m, H-7*β*), 1.26 (3H, s, H-16), 1.15 (3H, s, H-16); ^{13}C NMR (150 MHz, $CDCl_3$) δ_C: 209.3 (C-5), 197.5 (C-3), 197.2 (C-27), 193.8 (C-1), 137.8 (C-24), 137.1 (C-19), 137.0 (C-28), 132.4 (C-31), 128.2 (C-30), 128.2 (C-32), 128.0 (C-29), 128.0 (C-33), 118.4 (C-18), 117.5 (C-23), 113.8 (C-2), 79.1 (C-9), 72.4 (C-13), 62.6 (C-4), 61.2 (C-6), 50.8 (C-12), 47.7 (C-8), 43.2 (C-14), 41.0 (C-10), 38.4 (C-22), 37.3 (C-17), 28.2 (C-7), 26.5 (C-16), 26.1 (C-21), 26.1 (C-26), 23.3 (C-15), 21.4 (C-11), 18.0 (C-20), 17.9 (C-25)。其波谱数据与文献[13]基本一致, 故确定为hyperbeanol A。

化合物 **11**: 黄色油状; ESI-MS *m/z* 517 $[M+H]^+$, 分子式为 $C_{33}H_{40}O_5$。^{1}H NMR (600 MHz, $CDCl_3$) δ_H: 7.81 (2H, d, *J* = 7.3 Hz, H-29, 33), 7.53 (1H, t, *J* = 7.3 Hz, H-31), 7.41 (2H, t, *J* = 7.3 Hz, H-30, 32), 5.03 (1H, m, H-23), 5.02 (1H, m, H-18), 2.70 (1H, m, H-17a), 2.63 (1H, m, H-22a), 2.60 (1H, m, H-22b), 2.41 (1H, dd, *J* = 14.5, 7.3 Hz, H-17b), 2.06 (1H, d, *J* = 11.8 Hz, H-14*β*), 2.03 (1H, m, H-7*β*), 1.98 (1H, m, H-12), 1.86 (1H, d, *J* = 11.8 Hz, H-14*α*), 1.78 (1H, m, H-10a), 1.69 (3H, s, H-20), 1.66 (3H, s, H-25), 1.63 (1H, m, H-10b), 1.62 (1H,

m, H-11a), 1.59 (1H, m, H-7α), 1.57 (3H, s, H-26), 1.51 (3H, s, H-21), 1.38 (3H, s, H-15), 1.29 (3H, s, H-16), 1.20 (1H, m, H-8), 1.14 (1H, m, H-11b); ^{13}C NMR (150 MHz, $CDCl_3$) δ_C: 208.9 (C-5), 197.0 (C-1), 192.2 (C-27), 177.5 (C-3), 137.9 (C-28), 135.9 (C-19), 135.3 (C-24), 133.3 (C-31), 129.3 (C-29, C-33), 128.4 (C-30, C-32), 120.2 (C-23), 118.9 (C-18), 113.5 (C-2), 91.7 (C-13), 76.9 (C-9), 64.3 (C-6), 58.8 (C-4), 49.2 (C-8), 47.8 (C-12), 44.2 (C-14), 40.1 (C-10), 39.8 (C-17), 35.5 (C-22), 32.7 (C-7), 26.8 (C-16), 26.2 (C-20), 26.1 (C-25), 22.5 (C-11), 21.9 (C-15), 18.1 (C-26), 17.9 (C-21)。其波谱数据与文献[14]基本一致, 故确定为hypercohone G。

作者贡献: 邓憬童负责实验实施及文章的撰写; 周童曦、程海涛、韩庆迪、刘阳参与数据分析; 王强、杨新洲负责实验设计、文章的审阅和提出论文写作的建议, 并最终定稿。

利益冲突: 作者声明无利益冲突。

References

[1] Song X, Zhu J, Lv HF. Advances in *Hypericum researches* [J]. Acta Bot Bor-Occid Sin (西北植物学报), 2005, 25: 844-849.

[2] Yang XW, Grossman RB, Xu G. Research progress of polycyclic polyprenylated acylphloroglucinols [J]. Chem Rev, 2018, 118: 3508-3558.

[3] Wang K, Wang Y, Wang ZM, et al. Three new polycyclic polyprenylated acylphloroglucinols from *Hypericum lagarocladum* [J]. Chin J Org Chem (有机化学), 2019, 39: 848-851.

[4] Editorial Committee of Flora of China. Flora of China (中国植物志) [M]. Beijing: Science Press, 1990, 50: 19.

[5] Hashida C, Tanaka N, Kashiwada Y, et al. Prenylated phloroglucinol derivatives from *Hypericum perforatum* var. *angustifolium* [J]. Chem Pharm Bull, 2008, 56: 1164-1167.

[6] Zhou ZB, Li ZR, Wang XB, et al. Polycyclic polyprenylated derivatives from *Hypericum uralum*: neuroprotective effects and antidepressant-like activity of uralodin A [J]. J Nat Prod, 2016, 79: 1231-1240.

[7] Zhou Z, Zhang Y, Pan K, et al. Cytotoxic polycyclic polyprenylated acylphloroglucinols from *Hypericum attenuatum*[J]. Fitoterapia, 2014, 95: 1-7.

[8] Wang QQ, Wang XD, Wu LZ, et al. Polyprenylated acylphloroglucinols as deubiquitinating protease USP7 inhibitors from *Hypericum hookerianum* [J]. Fitoterapia, 2020, 146: 104678.

[9] Wu ZN, Niu QW, Zhang YB, et al. Hyperpatulones A−F, polycyclic polyprenylated acylphloroglucinols from *Hypericum patulum* and their cytotoxic activities [J]. RSC Adv, 2019, 9: 7961-7966.

[10] Li YR, Xu WJ, Wei SS, et al. Hyperbeanols F−Q, diverse monoterpenoid polyprenylated acylphloroglucinols from the flowers of *Hypericum beanii* [J]. Phytochemistry, 2019, 159: 56-64.

[11] Zhou ZB, Li ZR, Wang XB, et al. Polycyclic polyprenylated derivatives from *Hypericum uralum*: neuroprotective effects and antidepressant-like activity of uralodin A [J]. J Nat Prod, 2016, 79: 1231-1240.

[12] Hashida W, Tanaka N, Kashiwada Y, et al. Tomoeones A−H, cytotoxic phloroglucinol derivatives from *Hypericum ascyron* [J]. Phytochemistry, 2008, 69: 2225-2230.

[13] Xuan QC, Yan L, Li KZ, et al. Spirocyclic acylphloroglucinol derivatives from *Hypericum beanii* [J]. Chem Pharm Bull, 2011, 59: 1250-1253.

[14] Yang DS, Li ZL, Yang YP, et al. Chemical constituents from *Hypericum beanii* [J]. Chin Herb Med, 2015, 7: 375-379.