

治咳川贝枇杷滴丸提取物中化学成分分离

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【摘要】 目的:研究治咳川贝枇杷滴丸提取物中的化学成分。方法:通过正相硅胶、反相硅胶、聚酰胺、Sephadex LH-20等柱色谱方法以及制备型 HPLC 对治咳川贝枇杷滴丸提取物中的化学成分进行分离纯化,应用谱学技术鉴定化合物结构。结果:从治咳川贝枇杷滴丸提取物中分离得到 24 个化合物,分别鉴定为橙花叔醇-3-*O*-[α -L-吡喃鼠李糖基-(1 \rightarrow 4)- α -L-吡喃鼠李糖基-(1 \rightarrow 2)]- β -D-吡喃葡萄糖苷(1),橙花叔醇-3-*O*-[α -L-吡喃鼠李糖基-(1 \rightarrow 4)- α -L-吡喃鼠李糖基-(1 \rightarrow 6)]- β -D-吡喃葡萄糖苷(2),橙花叔醇-3-*O*-[α -L-吡喃鼠李糖基-(1 \rightarrow 4)- α -L-吡喃鼠李糖基-(1 \rightarrow 2)]-4-反-阿魏酰- α -L-吡喃鼠李糖基-(1 \rightarrow 6)]- β -D-吡喃葡萄糖苷(3), (6*S*, 7*E*, 9*R*)-6, 9-dihydroxy-4, 7-megastigmadien-3-one 9-*O*- β -D-apiofuranosyl-(1 \rightarrow 6)- β -D-glucopyranoside(4), 4-咖啡酰奎尼酸(5), 绿原酸(6), (6*S*, 7*E*, 9*R*)-9-hydroxy-4, 7-megastigmadien-3-one 9-*O*- β -D-glucopyranoside(7), 枇杷苷 II(8), 3, 4-二羟基苯甲酸(9), (6*R*, 7*E*, 9*R*)-9-hydroxy-4, 7-megastigmadien-3-one 9-*O*- β -D-glucopyranoside(10), (+)南烛木树脂酚 9'-*O*- β -D-吡喃木糖苷(11), (-)南烛木树脂酚 9'-*O*- β -D-吡喃木糖苷(12), 反丁烯二酸(13), 2, 6-dimethoxy-4-(2-propenyl) phenol 1-*O*- β -D-glucopyranoside(14), (+)南烛木树脂酚(15), 山奈酚(16), 对羟基苯酚(17), 对羟基苯甲酸(18), 对羟基肉桂酸(19), (6*S*, 7*E*, 9*R*)-6, 9-dihydroxy-4, 7-megastigmadien-3-one(20), 蔷薇酸(21), 乌苏酸(22), 3-呋喃甲酸(23), 香草酸(24)。结论:24 个化合物包括 8 个倍半萜类(1, 2, 3, 4, 7, 8, 10, 20), 4 个苯丙素类(11, 12, 14, 15), 9 个有机酸类(5, 6, 9, 13, 17, 18, 19, 23, 24), 2 个三萜类(21, 22), 1 个黄酮类(16)。这些化合物均首次从治咳川贝枇杷滴丸提取物中分离获得。

【关键词】 治咳川贝枇杷滴丸; 倍半萜类; 苯丙素类

【中图分类号】 R284.1 **【文献标识码】** A **【文章编号】** 1005-9903(2015)09-0074-06

【doi】 10.13422/j.cnki.syfjx.2015090074

Chemical Constituents from Extract of Zhike Chuanbei Pipa Dropping Pills LIU Rui, LIU Yong-bin, LI Mao, PAN Qin* (Tianjin Key Laboratory of Quality Control in Chinese Medicine, Tianjin Zhongxin Pharmaceuticals Research and Development Center, Tianjin 300457, China)

【Abstract】 **Objective:** To investigate the chemical constituents in the extract of Zhike Chuanbei Pipa dropping pills. **Method:** The compounds were isolated from the extract of Zhike Chuanbei Pipa dropping pills by a combination of various chromatographic techniques including column chromatography over silica gel, reversed-phase silica gel, sephadex LH-20 columns, and preparative HPLC. Their structures were identified by spectroscopic analysis including MS and NMR data. **Result:** Twenty-four compounds were isolated and identified as nerolidol-3-*O*-[α -L-rhamnopyranosyl-(1 \rightarrow 4)- α -L-rhamnopyranosyl-(1 \rightarrow 2)]- β -D-glucopyranoside(1), nerolidol-3-*O*- α -L-rhamnopyranosyl-(1 \rightarrow 4)- α -L-rhamnopyranosyl-(1 \rightarrow 6)- β -D-glucopyranoside(2), nerolidol-3-*O*-[α -L-rhamnopyranosyl-(1 \rightarrow 4)- α -L-rhamnopyranosyl-(1 \rightarrow 2)]-4-*trans*-feruloyl- α -L-rhamnopyranosyl-(1 \rightarrow 6)]- β -D-glucopyranoside(3), (6*S*, 7*E*, 9*R*)-6, 9-dihydroxy-4, 7-megastigmadien-3-one 9-*O*- β -D-apiofuranosyl-(1 \rightarrow 6)- β -D-glucopyranoside(4), 4-caffeoylquinic acid(5), chlorogenic acid(6), (6*S*, 7*E*, 9*R*)-9-hydroxy-4, 7-megastigmadien-3-one 9-*O*- β -D-glucopyranoside(7), eribotroside II(8), 3, 4-dihydroxy-benzoic acid(9), (6*R*, 7*E*, 9*R*)-9-hydroxy-4, 7-megastigmadien-3-one 9-*O*- β -D-glucopyranoside(10), (+)lyoniresinol 9'-*O*- β -D-xylopyranoside(11), (-)lyoniresinol 9'-*O*- β -D-xylopyranoside(12), fumaric acid(13), 2, 6-dimethoxy-4-(2-propenyl) phenol 1-*O*- β -D-glucopyranoside(14), (+)lyoniresinol(15), kaempferol(16), 4-hydroxy phenol(17), 4-hydroxy benzoic acid(18),

【收稿日期】 20140804(011)

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4-hydroxy cinnamic acid (**19**), (**6S**, **7E**, **9R**)-6, 9-dihydroxy-4, 7-megastigmadien-3-one (**20**), euscaphic acid (**21**), ursolic acid (**22**), 3-furancarboxylic acid (**23**), vanillic acid (**24**). **Conclusion:** Among the isolated twenty-four compounds, there are eight sesquiterpenoids (**1**, **2**, **3**, **4**, **7**, **8**, **10**, **20**), four phenylpropanoids (**11**, **12**, **14**, **15**), nine organic acids (**5**, **6**, **9**, **13**, **17**, **18**, **19**, **23**, **24**), two triterpenoids (**21**, **22**), one flavonoid (**16**). These compounds were obtained from the extract of Zhike Chuanbei Pipa dropping pills for the first time.

[**Key words**] Zhike Chuanbei Pipa dropping pills; sesquiterpenoids; phenylpropanoids

治咳川贝枇杷滴丸为天津中新药业集团股份有限公司第六中药厂生产的新药,系由枇杷叶、平贝母、桔梗、水半夏、薄荷脑精制而成,具宣肺降气、清热化痰之功,用于痰热郁肺所致咳嗽感冒。为阐明该滴丸的化学物质基础,董林毅^[1]用 UPLC-Q-TOF-MS 技术对其醇提取物中化学成分进行了快速表征,在没有对照品的情况下推测了 35 个化合物的结构。但文献没有报道治咳川贝枇杷滴丸中各成分的相对含量。基于此,本课题组采用 HPLC-ELSD 技术对该滴丸提取物进行表征,发现所得的色谱图与文献差异较大,提示其中含有较多无紫外吸收或质谱响应差的成分,因此有必要对治咳川贝枇杷滴丸提取物进行分离鉴定,并对其中主要色谱峰进行指认。本研究从该滴丸提取物中共分离得到 24 个单体成分,包括 8 个倍半萜类(化合物 **1, 2, 3, 4, 7, 8, 10, 20**), 4 个苯丙素类(**11, 12, 14, 15**), 9 个有机酸类(**5, 6, 9, 13, 17, 18, 19, 23, 24**), 2 个三萜类(**21, 22**), 1 个黄酮类(**16**)。这些化合物均首次从治咳川贝枇杷滴丸提取物中分离获得。

1 材料

1.1 仪器与试剂 Bruker AV-400 型核磁共振仪(瑞士 Bruker 公司), Quattro microTM API 型质谱仪(Waters 公司), SGW-2 型自动旋光仪(上海精密科学仪器有限公司);石油醚(60~90℃)、丙酮、三氯甲烷、二氯甲烷、甲醇、无水乙醇(分析纯,天津科密欧化学试剂有限公司), 色谱纯甲醇、乙腈(Honeywell 公司);反相 ODS 硅胶(日本 YMC 公司), 凝胶 SephadexTM LH-20 (GE Healthcare Bio-Sciences AB), 聚酰胺(60~100 目,浙江台州市路桥四甲生化塑料厂), 柱色谱用硅胶(60~100, 200~300 目,青岛海洋化工厂), 薄层色谱硅胶 GF₂₅₄(青岛海洋化工厂)。

1.2 样品来源 治咳川贝枇杷滴丸提取物由天津中新药业集团股份有限公司第六中药厂提供(批号 533003)。制备方法如下:(1)称取原料,4 种单味药材枇杷叶、桔梗、水半夏、平贝母按质量比 68:6:20:7 配比;(2)枇杷叶加水煎煮,滤过,浓缩至清膏,加入乙醇,充分搅拌,静置,取上清液,备用;(3)将平

贝母粉碎,与桔梗和水半夏用乙醇回流提取,滤过,滤液与步骤(2)获得的上清液合并,回收乙醇,浓缩至清膏,放冷至室温,加入丁酮萃取,回收丁酮并浓缩至稠膏。

2 提取分离

治咳川贝枇杷滴丸提取物约 1.98 kg 进行硅胶柱色谱分离,三氯甲烷-甲醇-水(100:0:0~70:30:2)梯度洗脱,洗脱液经薄层色谱检测合并,浓缩得到 12 个洗脱部分(Fr. 1~Fr. 12)。Fr. 12 约 170 g,取其中 70 g 经大孔树脂柱及凝胶柱色谱纯化富集,反相硅胶柱色谱分离,55% 乙醇水洗脱得化合物 **1**(800 mg)。Fr. 11(128 g)经正相硅胶柱色谱分离得 5 个组分,其中 Fr. 11-3(42.0 g)经反相硅胶柱色谱分离,以 40%~60% 乙醇水梯度洗脱,再经凝胶柱纯化脱色,得到化合物 **2**(71 mg)和化合物 **3**(25 mg)。Fr. 10 约 200 g,取其中一半经正相硅胶柱色谱分离得 4 个组分,其中 Fr. 10-3 约 50 g,取 25.0 g 样品经多次反相硅胶柱色谱分离,以 10%~20% 乙醇水梯度洗脱,凝胶柱反复纯化得到化合物 **4**(28 mg), **5**(28 mg), **6**(29 mg)。Fr. 9 约 218 g,取 88 g 经正相硅胶柱色谱分离得 5 个组分,其中 Fr. 9-3(20.0 g)经反相硅胶柱色谱分离,以 25%~35% 乙醇水梯度洗脱,再经凝胶柱纯化脱色,最后再次反相柱色谱,以 15% 乙腈水洗脱得到化合物 **7**(100 mg)和化合物 **8**(130 mg)。Fr. 8 约 335 g,取 115 g 经正相硅胶柱色谱分离得 5 个组分,其中 Fr. 8-2(28.6 g)用二氯甲烷溶解,过滤后滤液用凝胶柱色谱纯化,二氯甲烷-甲醇(1:1)洗脱,得流份 Fr. 8-2-4(230 mg),放置一段时间析出结晶得化合物 **9**(76 mg)。Fr. 8-3 和 Fr. 8-4 分别经凝胶柱色谱纯化得流份 Fr. 8-3-1(26.0 g)和 Fr. 8-3-2(4.4 g)和 Fr. 8-4-1(20.0 g)和 Fr. 8-4-2(1.5 g)。Fr. 8-3-1 经聚酰胺柱纯化,两次反相硅胶柱色谱层析,先后用 20%~35% 甲醇水,18%~20% 乙腈水洗脱,所得流份仍有杂质,最后用制备 HPLC 分离,以 17% 乙腈水(含 0.2% 甲酸)洗脱得到化合物 **10**(105 mg)。Fr. 8-4-1 经聚酰胺柱纯化,再经反相硅胶柱色谱,以 25%~40% 甲醇水梯度洗脱,最后用制备 HPLC 分离以 18% 乙腈水(含 0.2%

甲酸)洗脱得到化合物 **11** (130 mg) 和化合物 **12** (16 mg)。Fr. 7 (72 g) 分3次经凝胶柱色谱纯化分为4个组分。Fr. 7-3 (18.3 g) 放置一段时间有固体析出, 过滤, 固体经凝胶柱色谱纯化得化合物 **13** (160 mg); 母液经聚酰胺柱色谱得组分 Fr. 7-3-1, 经反相硅胶柱色谱, 以25%~35% 甲醇水洗脱, 所得流份再经凝胶柱纯化得化合物 **14** (120 mg)。Fr. 6 (105 g) 经正相硅胶柱色谱分为6个组分。Fr. 6-5 (10.5 g) 经凝胶柱色谱脱色, 所得流份 Fr. 6-5-1 (8.1 g) 经反相硅胶柱色谱, 20%~55% 乙醇水洗脱得化合物 **15** (400 mg)。Fr. 6-1 (5.4 g) 经凝胶柱色谱, 二氯甲烷-甲醇(1:1) 洗脱, 得流份 Fr. 6-1-1 (5.0 g) 及 Fr. 6-1-2 (75 mg)。Fr. 6-1-2 经乙醇-水结晶得化合物 **16** (60 mg); Fr. 6-1-1 经反相硅胶柱色谱, 12%~25% 甲醇水洗脱得化合物 **17** (32 mg), **18** (20 mg), **19** (300 mg)。Fr. 5 共219 g, 取其中83 g 经正相硅胶柱色谱分为7个组分。Fr. 5-5 (8.0 g) 经凝胶柱色谱, 二氯甲烷-甲醇(1:1) 洗脱得流份 Fr. 5-5-2 (2.7 g), 再经反相硅胶柱色谱, 32%~50% 乙腈水洗脱, 得化合物 **20** (30 mg) 和 **21** (250 mg), Fr. 3 (60 g) 经正相硅胶柱色谱分为13个组分。Fr. 3-6 (2.2 g) 经凝胶柱色谱纯化, 二氯甲烷-甲醇(1:1) 洗脱, 得流份 Fr. 3-6-1, 再经反相硅胶柱色谱, 70%~90% 乙醇水洗脱, 得到化合物 **22** (13 mg)。Fr. 3-7 (2.8 g) 经凝胶柱色谱纯化, 再经反相硅胶柱色谱, 5% 乙醇水洗脱, 得到化合物 **23** (323 mg)。Fr. 3-10 (2.1 g) 经凝胶柱色谱纯化, 再经反相硅胶柱色谱, 15% 乙醇水洗脱, 得到化合物 **24** (42 mg)。

3 结果与讨论

化合物 **1** 白色粉末(无水乙醇)。ESI-MS m/z 821 $[M - H]^-$ 。¹H-NMR (400 MHz, CD₃OD) δ : 5.92 (1H, dd, $J = 10.8, 17.6$ Hz, H-2), 5.31 (1H, d, $J = 1.2$ Hz, H-Rha-1'''), 5.22 (1H, d, $J = 17.6$ Hz, H-1 α), 5.21 (1H, d, $J = 10.8$ Hz, H-1 β), 5.15 (1H, d, $J = 1.2$ Hz, H-Rha-1''), 5.12 (1H, d, $J = 7.2$ Hz, H-6), 5.09 (1H, m, H-10), 4.71 (1H, d, $J = 1.2$ Hz, H-Rha-1'''), 4.41 (1H, d, $J = 7.2$ Hz, H-Glc-1'), 4.24~3.23 (20H, H-9 β , H-5 β 以及糖上氢质子信号), 2.06~2.00 (6H, m, H-4, H-8, H-9 α , H-5 α), 1.66 (3H, s, H-15), 1.60 (6H, s, H-12, H-14), 1.37 (3H, s, H-13), 1.25 (6H, d, $J = 6.4$ Hz, H-Rha-6''', H-Rha-6'''), 1.24 (3H, d, $J = 6.4$ Hz, H-Rha-6'')。¹³C-NMR (100 MHz, CD₃OD) δ : 115.8 (C-1), 144.5 (C-2), 81.9 (C-3), 42.6 (C-4), 25.9 (C-5), 125.6 (C-6),

136.1 (C-7), 40.8 (C-8), 27.9 (C-9), 125.7 (C-10), 132.0 (C-11), 16.2 (C-12), 22.8 (C-13), 18.8 (C-14), 23.6 (C-15), 98.2 (C-Glc-1'), 81.7 (C-Glc-2'), 77.7 (C-Glc-3'), 72.4 (C-Glc-4'), 76.4 (C-Glc-5'), 68.1 (C-Glc-6'), 103.5 (C-Rha-1''), 73.0 (C-Rha-2''), 72.4 (C-Rha-3''), 79.9 (C-Rha-4''), 68.0 (C-Rha-5''), 17.8 (C-Rha-6''), 102.1 (C-Rha-1'''), 72.2 (C-Rha-2'''), 72.0 (C-Rha-3'''), 74.1 (C-Rha-4'''), 69.8 (C-Rha-5'''), 18.1 (C-Rha-6'''), 101.3 (C-Rha-1''''), 72.5 (C-Rha-2''''), 72.5 (C-Rha-3''''), 73.8 (C-Rha-4''''), 70.5 (C-Rha-5''''), 17.9 (C-Rha-6'''')。以上数据与文献[2]报道一致, 故鉴定为 nerolidol-3-*O*- $\{\alpha$ -*L*-rhamnopyranosyl-(1 \rightarrow 4)- α -*L*-rhamnopyranosyl-(1 \rightarrow 2)-[α -*L*-rhamnopyranosyl-(1 \rightarrow 6)]- β -*D*-glucopyranoside}。

化合物 **2** 白色粉末(无水乙醇)。ESI-MS m/z 675 $[M - H]^-$ 。¹H-NMR (400 MHz, CD₃OD) δ : 5.93 (1H, dd, $J = 10.4, 18.0$ Hz, H-2), 5.27 (1H, d, $J = 18.0$ Hz, H-1 α), 5.27 (1H, d, $J = 1.2$ Hz, H-Rha-1'''), 5.21 (1H, H-1 β), 5.09 (2H, m, H-6, H-10), 4.71 (1H, d, $J = 1.2$ Hz, H-Rha-1'''), 4.40 (1H, d, $J = 7.2$ Hz, H-Glc-1'), 4.12~3.22 (16H, H-9 β , H-5 β 以及糖上氢质子信号), 2.05~1.96 (6H, m, H-4, H-8, H-9 α , H-5 α), 1.66 (3H, s, H-15), 1.59 (6H, s, H-12, H-14), 1.37 (3H, s, H-13), 1.26 (3H, d, $J = 6.4$ Hz, H-Rha-6'''), 1.23 (3H, d, $J = 6.4$ Hz, H-Rha-6'')。¹³C-NMR (100 MHz, CD₃OD) δ : 116.2 (C-1), 144.5 (C-2), 81.8 (C-3), 42.8 (C-4), 25.9 (C-5), 125.4 (C-6), 136.0 (C-7), 40.8 (C-8), 27.8 (C-9), 125.6 (C-10), 132.1 (C-11), 16.1 (C-12), 22.6 (C-13), 18.1 (C-14), 23.6 (C-15), 98.3 (C-Glc-1'), 74.1 (C-Glc-2'), 78.3 (C-Glc-3'), 72.2 (C-Glc-4'), 76.4 (C-Glc-5'), 68.0 (C-Glc-6'), 101.9 (C-Rha-1''), 72.3 (C-Rha-2''), 72.3 (C-Rha-3''), 79.8 (C-Rha-4''), 69.8 (C-Rha-5''), 17.8 (C-Rha-6''), 102.1 (C-Rha-1'''), 72.1 (C-Rha-2'''), 72.4 (C-Rha-3'''), 74.0 (C-Rha-4'''), 70.0 (C-Rha-5'''), 18.0 (C-Rha-6''')。以上数据与文献[2]报道一致, 故鉴定为 nerolidol-3-*O*- α -*L*-rhamnopyranosyl-(1 \rightarrow 4)- α -*L*-rhamnopyranosyl-(1 \rightarrow 6)- β -*D*-glucopyranoside。

化合物 **3** 白色粉末(无水乙醇)。ESI-MS m/z 997 $[M - H]^-$ 。¹H-NMR (400 MHz, CD₃OD) δ : 7.65 (1H, d, $J = 16.0$ Hz, H-2'''''), 6.38 (1H, d, $J = 16.0$ Hz, H-3'''''), 7.18 (1H, d, $J = 1.6$ Hz, H-

5^{'''}), 7.08 (1H, dd, $J = 1.6, 8.0$ Hz, H-9^{'''}), 6.81 (1H, d, $J = 8.0$ Hz, H-8^{'''}), 5.94 (1H, dd, $J = 10.4, 15.6$ Hz, H-2), 5.33 (1H, d, $J = 1.2$ Hz, H-Rha-1^{'''}), 5.24 (1H, d, $J = 15.6$ Hz, H-1 α), 5.20 (1H, d, $J = 10.4$ Hz, H-1 β), 5.15 (1H, d, $J = 1.2$ Hz, H-Rha-1^{''}), 5.11 (1H, H-6), 5.03 (1H, m, H-10), 4.77 (1H, d, $J = 1.2$ Hz, H-Rha-1^{''}), 4.43 (1H, d, $J = 7.2$ Hz, H-Glc-1[']), 3.61 (3H, s, 6^{'''}-OMe), 4.20 ~ 3.30 (20H, H-9 β , H-5 β 以及糖上氢质子信号), 2.08 ~ 1.88 (6H, m, H-4, H-8, H-9 α , H-5 α), 1.64 (3H, s, H-15), 1.56 (6H, s, H-12, H-14), 1.39 (3H, s, H-13), 1.26 (6H, d, $J = 6.4$ Hz, H-Rha-6^{'''}, H-Rha-6^{''}), 1.23 (3H, d, $J = 6.4$ Hz, H-Rha-6^{''})。 ¹³C-NMR (100 MHz, CD₃OD), δ : 115.7 (C-1), 144.7 (C-2), 82.0 (C-3), 42.7 (C-4), 25.9 (C-5), 125.5 (C-6), 136.2 (C-7), 40.8 (C-8), 27.8 (C-9), 125.6 (C-10), 132.0 (C-11), 16.3 (C-12), 22.8 (C-13), 18.1 (C-14), 23.6 (C-15), 98.2 (C-Glc-1[']), 81.6 (C-Glc-2[']), 77.7 (C-Glc-3[']), 72.3 (C-Glc-4[']), 76.2 (C-Glc-5[']), 68.1 (C-Glc-6[']), 103.6 (C-Rha-1^{''}), 73.0 (C-Rha-2^{''}), 72.5 (C-Rha-3^{''}), 79.9 (C-Rha-4^{''}), 67.8 (C-Rha-5^{''}), 17.8 (C-Rha-6^{''}), 101.9 (C-Rha-1^{'''}), 72.5 (C-Rha-2^{'''}), 71.8 (C-Rha-3^{'''}), 75.5 (C-Rha-4^{'''}), 67.7 (C-Rha-5^{'''}), 18.8 (C-Rha-6^{'''}), 101.4 (C-Rha-1^{''''}), 72.5 (C-Rha-2^{''''}), 72.6 (C-Rha-3^{''''}), 73.8 (C-Rha-4^{''''}), 70.5 (C-Rha-5^{''''}), 17.9 (C-Rha-6^{''''}), 168.9 (C-1^{''''}), 116.5 (C-2^{''''}), 147.1 (C-3^{''''}), 127.7 (C-4^{''''}), 111.8 (C-5^{''''}), 149.4 (C-6^{''''}), 150.7 (C-7^{''''}), 115.5 (C-8^{''''}), 124.1 (C-9^{''''}), 58.3 (6^{''''}-OMe)。以上数据与文献[2]报道一致,故鉴定为 nerolidol-3-*O*- α -L-rhamnopyranosyl-(1 \rightarrow 4)- α -L-rhamnopyranosyl-(1 \rightarrow 2)-[4-*trans*-feruloyl- α -L-rhamnopyranosyl-(1 \rightarrow 6)]- β -D-glucopyranoside}。

化合物4 白色粉末(无水乙醇)。ESI-MS m/z 517 [M - H]⁻, 553 [M + Cl]⁻。 ¹H-NMR (400 MHz, CD₃OD) δ : 5.89 (1H, s, H-4), 5.85 (2H, br s, H-7, H-8), 4.99 (1H, d, $J = 2.0$ Hz, H-Api-1^{''}), 4.41 (1H, m, H-9), 4.33 (1H, d, $J = 7.6$ Hz, H-Glc-1[']), 3.96 (1H, d, $J = 9.6$ Hz, H-Api-4^{''} α), 3.90 (1H, d, $J = 1.6$ Hz, H-Api-2^{''}), 3.76 (1H, d, $J = 9.6$ Hz, H-Api-4^{''} β), 3.60 (1H, s, H-Api-5^{''}), 3.16 ~ 3.98 (6H, 葡萄糖上氢质子信号), 2.52 (1H, d, $J = 16.8$ Hz, H-2 α), 2.14 (1H, d, $J = 16.8$ Hz, H-2 β), 1.92 (3H, s, H-13), 1.29 (3H,

d, $J = 6.0$ Hz, H-10), 1.04 (3H, s, H-11), 1.03 (3H, s, H-12)。 ¹³C-NMR (100 MHz, CD₃OD), δ : 42.5 (C-1), 50.7 (C-2), 201.3 (C-3), 127.2 (C-4), 167.3 (C-5), 80.1 (C-6), 131.6 (C-7), 134.9 (C-8), 77.0 (C-9), 21.1 (C-10), 23.5 (C-11), 24.7 (C-12), 19.7 (C-13), 102.6 (C-Glc-1[']), 75.2 (C-Glc-2[']), 77.9 (C-Glc-3[']), 71.6 (C-Glc-4[']), 78.0 (C-Glc-5[']), 68.6 (C-Glc-6[']), 111.0 (C-Api-1^{''}), 76.7 (C-Api-2^{''}), 80.5 (C-Api-3^{''}), 75.0 (C-Api-4^{''}), 65.6 (C-Api-5^{''})以上数据与文献[2,3]报道一致,故鉴定为 (6*S*, 7*E*, 9*R*)-6, 9-dihydroxy-4, 7-megastigmadien-3-one 9-*O*- β -D-apiofuranosyl-(1 \rightarrow 6)- β -D-glucopyranoside。

化合物7 白色粉末(无水乙醇)。ESI-MS m/z 385 [M - H]⁻, 409 [M + Na]⁺。 ¹H-NMR (400 MHz, CD₃OD) δ : 5.87 (1H, s, H-4), 5.86 (2H, br s, H-7, H-8), 4.42 (1H, m, H-9), 4.34 (1H, d, $J = 7.6$ Hz, H-Glc-1[']), 3.15 ~ 3.86 (6H, 葡萄糖上氢质子信号), 2.52 (1H, d, $J = 16.8$ Hz, H-2 α), 2.15 (1H, d, $J = 16.8$ Hz, H-2 β), 1.92 (3H, s, H-13), 1.29 (3H, d, $J = 6.4$ Hz, H-10), 1.04 (3H, s, H-11), 1.03 (3H, s, H-12)。 ¹³C-NMR (100 MHz, CD₃OD), δ : 42.4 (C-1), 50.7 (C-2), 201.2 (C-3), 127.2 (C-4), 167.2 (C-5), 80.0 (C-6), 131.5 (C-7), 135.3 (C-8), 77.3 (C-9), 21.2 (C-10), 23.4 (C-11), 24.7 (C-12), 19.5 (C-13), 102.7 (C-Glc-1[']), 75.2 (C-Glc-2[']), 78.1 (C-Glc-3[']), 71.6 (C-Glc-4[']), 78.0 (C-Glc-5[']), 62.8 (C-Glc-6['])。以上数据与文献[4]报道一致,故鉴定为 (6*S*, 7*E*, 9*R*)-9-hydroxy-4, 7-megastigmadien-3-one 9-*O*- β -D-glucopyranoside。

化合物8 白色粉末(无水乙醇)。ESI-MS m/z 525 [M + Na]⁺, 537 [M + Cl]⁻。 ¹H-NMR (400 MHz, CD₃OD) δ : 5.88 (1H, s, H-4), 5.76 (1H, dd, $J = 15.2, 6.4$ Hz, H-8), 5.65 (1H, d, $J = 15.2, 9.2$ Hz, H-7), 5.00 (1H, d, $J = 2.4$ Hz, H-Api-1^{''}), 4.35 (1H, m, H-9), 4.33 (1H, d, $J = 7.6$ Hz, H-Glc-1[']), 3.96 (1H, d, $J = 9.6$ Hz, H-Api-4^{''} α), 3.90 (1H, d, $J = 2.4$ Hz, H-Api-2^{''}), 3.76 (1H, d, $J = 9.6$ Hz, H-Api-4^{''} β), 3.57 (1H, s, H-Api-5^{''}), 3.15 ~ 3.93 (6H, 葡萄糖上氢质子信号), 2.70 (1H, d, $J = 8.8$ Hz, H-6), 2.45 (1H, d, $J = 16.8$ Hz, H-2 α), 2.05 (1H, d, $J = 16.8$ Hz, H-2 β), 1.94 (3H, brs, H-13), 1.29 (3H, d, $J = 6.4$ Hz, H-10), 1.04 (3H, s, H-11), 1.03 (3H, s, H-

12)。¹³C-NMR (100 MHz, CD₃OD), δ: 37.1 (C-1), 48.3 (C-2), 202.1 (C-3), 126.1 (C-4), 165.9 (C-5), 56.7 (C-6), 129.0 (C-7), 138.1 (C-8), 77.2 (C-9), 21.1 (C-10), 27.6 (C-11), 28.1 (C-12), 23.8 (C-13), 102.6 (C-Glc-1'), 75.2 (C-Glc-2'), 78.0 (C-Glc-3'), 71.6 (C-Glc-4'), 78.0 (C-Glc-5'), 68.5 (C-Glc-6'), 111.0 (C-Api-1''), 77.0 (C-Api-2''), 80.5 (C-Api-3''), 75.0 (C-Api-4''), 65.6 (C-Api-5'')。以上数据与文献[3-4]报道一致,故鉴定为枇杷苷II。

化合物10 白色粉末(无水乙醇)。ESI-MS *m/z* 393 [M + Na]⁺, 405 [M + Cl]⁻。¹H-NMR (400 MHz, CD₃OD) δ: 5.88 (1H, s, H-4), 5.78 (1H, dd, *J* = 15.6, 6.4 Hz, H-8), 5.64 (1H, d, *J* = 15.6, 9.2 Hz, H-7), 4.40 (1H, m, H-9), 4.35 (1H, d, *J* = 8.0 Hz, H-Glc-1'), 3.15 ~ 3.98 (6H, 葡萄糖上氢质子信号), 2.67 (1H, d, *J* = 9.2 Hz, H-6), 2.43 (1H, d, *J* = 16.8 Hz, H-2α), 2.04 (1H, d, *J* = 16.8 Hz, H-2β), 1.94 (3H, brs, H-13), 1.29 (3H, d, *J* = 6.4 Hz, H-10), 1.04 (3H, s, H-11), 1.03 (3H, s, H-12)。¹³C-NMR (100 MHz, CD₃OD), δ: 37.1 (C-1), 48.3 (C-2), 202.0 (C-3), 126.1 (C-4), 165.8 (C-5), 56.7 (C-6), 128.8 (C-7), 138.2 (C-8), 77.0 (C-9), 21.0 (C-10), 27.6 (C-11), 28.0 (C-12), 23.7 (C-13), 102.4 (C-Glc-1'), 75.2 (C-Glc-2'), 77.9 (C-Glc-3'), 71.5 (C-Glc-4'), 78.0 (C-Glc-5'), 62.7 (C-Glc-6')。以上数据与文献[4]报道一致,故鉴定为(6*R*,7*E*,9*R*)-9-hydroxy-4,7-megastigmadien-3-one 9-*O*-β-*D*-glucopyranoside。

化合物11 白色粉末(甲醇)。ESI-MS *m/z* 551 [M - H]⁻。[α]_D²⁰ + 16.5° (*c* 0.25, MeOH)。¹H-NMR (400 MHz, CD₃OD) δ: 6.55 (1H, s, H-2), 6.41 (2H, s, H-2', 6'), 4.36 (1H, d, *J* = 6.8 Hz, H-7'), 4.19 (1H, d, *J* = 6.8 Hz, H-Xyl-1''), 3.83 (3H, s, 3-OMe), 3.77 ~ 3.84 (2H, m, H-9'α, H-Xyl-5''α), 3.73 (6H, s, 3', 5'-OMe), 3.63 (1H, dd, *J* = 10.8, 4.4 Hz, H-9α), 3.48 (1H, dd, *J* = 10.8, 6.4 Hz, H-9β), 3.45 (1H, m, H-9'β), 3.40 (1H, m, H-Xyl-4''), 3.31 (3H, s, 5-OMe), 3.30 (1H, m, H-Xyl-3''), 3.19 (1H, m, H-Xyl-5''β), 3.15 (1H, t, *J* = 9.6 Hz, H-Xyl-2''), 2.70 (1H, dd, *J* = 15.2, 4.8 Hz, H-7α), 2.61 (1H, dd, *J* = 15.2, 11.2 Hz, H-7β), 2.04 (1H, m, H-8'), 1.68 (1H, m, H-8); ¹³C-NMR (100 MHz, CD₃OD) δ:

148.9 (C-3', 5'), 148.6 (C-3), 147.6 (C-5), 139.4 (C-1'), 138.9 (C-4), 134.5 (C-4'), 130.1 (C-1), 126.4 (C-6), 107.8 (C-2), 106.9 (C-2', 6'), 105.5 (C-Xyl-1''), 78.0 (C-Xyl-3''), 74.9 (C-Xyl-2''), 71.2 (C-Xyl-4''), 71.0 (C-9'), 67.0 (C-Xyl-5''), 66.0 (C-9), 60.0 (5-OMe), 56.8 (3', 5'-OMe), 56.6 (3-OMe), 46.7 (C-8'), 43.0 (C-7'), 40.5 (C-8), 33.9 (C-7)。以上数据与文献[5]报道一致,故鉴定为(+) lyoni-resinol 9'-*O*-β-*D*-xylopyranoside。

化合物12 白色粉末(甲醇)。ESI-MS *m/z* 551 [M - H]⁻。[α]_D²⁰ - 15.2° (*c* 0.23, MeOH)。¹H-NMR (400 MHz, CD₃OD) δ: 6.56 (1H, s, H-2), 6.41 (2H, s, H-2', 6'), 4.22 (1H, d, *J* = 6.8 Hz, H-7'), 4.09 (1H, d, *J* = 7.2 Hz, H-Xyl-1''), 3.85 (3H, s, 3-OMe), 3.79 ~ 3.88 (2H, m, H-9'α, H-Xyl-5''α), 3.74 (6H, s, 3', 5'-OMe), 3.63 ~ 3.57 (3H, m, H-9α, 9β, 9'β), 3.49 (1H, m, H-Xyl-4''), 3.29 (3H, s, 5-OMe), 3.27 (1H, m, H-Xyl-3''), 3.18 (1H, m, H-Xyl-5''β), 3.12 (1H, t, *J* = 9.6 Hz, H-Xyl-2''), 2.68 (2H, m, H-7), 2.02 (1H, m, H-8'), 1.72 (1H, m, H-8); ¹³C-NMR (100 MHz, CD₃OD) δ: 148.9 (C-3', 5'), 148.6 (C-3), 147.5 (C-5), 139.6 (C-1'), 138.9 (C-4), 134.5 (C-4'), 130.1 (C-1), 126.3 (C-6), 107.7 (C-2), 106.9 (C-2', 6'), 105.0 (C-Xyl-1''), 78.0 (C-Xyl-3''), 74.9 (C-Xyl-2''), 71.3 (C-Xyl-4''), 71.1 (C-9'), 67.1 (C-Xyl-5''), 66.0 (C-9), 59.9 (5-OMe), 56.8 (3', 5'-OMe), 56.6 (3-OMe), 46.9 (C-8'), 43.3 (C-7'), 40.7 (C-8), 34.0 (C-7)。以上数据与化合物11基本一致,旋光值相反,与文献[6]报道一致,故鉴定为(-) lyoni-resinol 9'-*O*-β-*D*-xylopyranoside。

化合物14 白色粉末(甲醇)。ESI-MS *m/z* 379 [M + Na]⁺。¹H-NMR (400 MHz, DMSO) δ: 6.49 (2H, s, H-3, 5), 5.95 (1H, m, H-2'), 5.10 (1H, dd, *J* = 16.8, 1.6 Hz, H-3'α), 5.05 (1H, dt, H-3'β), 4.83 (1H, d, *J* = 7.2 Hz, H-Glc-1''), 3.74 (6H, s, 2, 6-OMe), 3.60 (1H, d, *J* = 10.8 Hz, H-Glc-6''α), 3.41 (1H, d, *J* = 10.8, 5.2 Hz, H-Glc-6''β), 3.29 (1H, d, *J* = 6.8 Hz, H-1'), 3.01 ~ 3.30 (4H, 葡萄糖2,3,4,5位氢质子信号); ¹³C-NMR (100 MHz, DMSO) δ: 152.6 (2, 6-OMe), 137.4 (C-2'), 135.4 (C-4), 132.9 (C-1), 115.9 (C-3'), 106.6 (C-3, 5), 102.8 (C-Glc-1''), 77.1 (C-Glc-5''), 76.5 (C-Glc-3''), 74.2 (C-Glc-2''), 70.0 (C-

Glc-4"), 60.9 (C-Glc-6"), 56.3 (2, 6-OMe), 39.6 (C-1')。以上数据与文献[4]报道一致,故鉴定为 2, 6-dimethoxy-4-(2-propenyl) phenol 1-*O*- β -D-glucopyranoside。

化合物 **15** 白色粉末(无水乙醇)。ESI-MS m/z 419 [M - H]⁻。[α]_D²⁰ + 2.6° (c 0.30, MeOH)。¹H-NMR(400 MHz, DMSO) δ : 8.14 (1H, s, 4-OH), 7.96 (1H, s, 4'-OH), 6.55 (1H, s, H-2), 6.29 (2H, s, H-2', 6'), 4.63 (1H, t, J = 6.4 Hz, 9-OH), 4.48 (1H, t, J = 6.4 Hz, 9'-OH), 4.23 (1H, d, J = 6.4 Hz, H-7'), 3.77 (3H, s, 3-OMe), 3.63 (6H, s, 3', 5'-OMe), 3.45 (1H, m, H-9 α), 3.23 ~ 3.31 (3H, m, H-9 β , H-9'), 3.31 (3H, s, 5-OMe), 2.61 (1H, dd, J = 14.4, 11.6 Hz, H-7 α), 2.43 (1H, dd, J = 14.4, 4.4 Hz, H-7 β), 1.92 (1H, m, H-8'), 1.43 (1H, m, H-8); ¹³C-NMR(100 MHz, DMSO) δ : 147.5 (C-3', 5'), 146.8 (C-3), 146.4 (C-5), 137.7 (C-1'), 137.2 (C-4), 133.4 (C-4'), 128.6 (C-1), 125.0 (C-6), 106.7 (C-2), 106.0 (C-2', 6'), 64.6 (C-9), 62.3 (C-9'), 58.9 (5-OMe), 56.1 (3', 5'-OMe), 55.7 (3-OMe), 46.6 (C-8'), 40.4 (C-7'), 38.9 (C-8), 32.2 (C-7)。以上数据与文献[5]报道一致,故鉴定为 (+)-lyoniresinol。

化合物 **20** 无色油状物(甲醇-水)。ESI-MS m/z 223 [M - H]⁻。¹H-NMR(400 MHz, CD₃OD) δ : 5.87 (1H, s, H-4), 5.79 (2H, br s, H-7, H-8), 4.32 (1H, m, H-9), 2.48 (1H, d, J = 16.8 Hz, H-2 α), 2.14 (1H, d, J = 16.8 Hz, H-2 β), 1.91 (3H, br s, H-13), 1.24 (3H, d, J = 6.4 Hz, H-10), 1.04 (3H, s, H-11), 1.02 (3H, s, H-12)。¹³C-NMR(100 MHz, CD₃OD) δ : 42.4 (C-1), 50.7 (C-2), 201.2 (C-3), 127.1 (C-4), 167.4 (C-5), 79.9 (C-6), 129.9 (C-7), 136.9 (C-8), 68.6 (C-9), 23.8 (C-10), 23.4 (C-11), 24.5 (C-12), 19.5 (C-13)。以上数据与文献[4]报道一致,故鉴定为 (6*S*, 7*E*, 9*R*)-6,9-dihydroxy-4,7-megastigmadien-3-one。

化合物 **5, 6, 9, 13, 16 ~ 19, 21 ~ 24** 的结构由 ESI-MS, ¹H-NMR, ¹³C-NMR 等波谱方法鉴定,与文献报道的数据一致,分别鉴定为 4-咖啡酰奎尼酸^[7], 绿原酸^[7], 3,4-二羟基苯甲酸^[8], 反丁烯二

酸^[9], 山柰酚^[9], 对羟基苯酚^[10], 对羟基苯甲酸^[8], 对羟基肉桂酸^[10], 蔷薇酸^[11], 乌苏酸^[11], 3-咪喃甲酸^[12], 香草酸^[12]。

依据分离所得的化合物及一些对照品对治咳川贝枇杷滴丸提取物的色谱峰进行指认,明确了其中 80% 以上的成分。这一研究结果与董林毅等所得结论互为补充。HPLC-ELSD 技术能体现各成分的相对含量,而 UPLC-Q-TOF-MS 技术利于微量成分的检测与鉴别,两种技术结合应用才能全面反映治咳川贝枇杷滴丸中的化学物质基础。

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[责任编辑 顾雪竹]