Chemical study on *Pogostemon cablin*

By

Li Ping

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Institute of Chinese Medical Sciences

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Approved by _____

Supervisor

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硕士学位论文

广藿香化学成分研究

研究生姓名：李萍

导师：张庆文

专业：中药学

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澳门大学中华医药研究院

UNIVERSIDADE DE MACAU
仁義禮知信
澳門大學

摘要

中药广藿香为唇形科(Lamiaceae)刺蕊草属植物广藿香 *Pogostemoncablin* (Blanco)Benth．的干燥地上部分，原产于菲律宾和东南亚各地，后引人我国，目前在我国南方的广东省肇庆地区、湛江地区、广州郊区以及海南岛均有大量栽培，其中广州产的石牌藿香和肇庆产的肇香为广藿香的道地药材，是“十大南药”之一。不同产地的广藿香因其气候和生态环境差异较大，形态和性状差异显著。广藿香味辛，微温，归脾、胃、肺三经，具有芳香化浊，和中止呕，发表解暑的功效，用于湿浊中阻，脘痞呕吐，暑湿表证，湿温初起，发热倦怠，胸闷不舒，寒湿闭暑，腹痛吐泻，鼻渊头痛。前期的化学成分研究表明，广藿香富含挥发油类成分，非挥发性成分的研究相对较少。然而现代药理学相关研究表明，其非挥发性成分为其发挥促进消化，抗腹泻和镇痛作用的主要物质基础。

為進一步探索广藿香的藥效成分，為其開發利用及品質控制提供科學依據，本論文對广藿香進行了系統的化學成分研究。本论文運用矽膠柱層析色譜，葡聚糖凝膠柱色譜(Sephadex LH-20)，製備型高效液相色譜(Prep-HPLC)等分離純化手段，从广藿香乙醇提取物中分離得到 17 個化合物，並通過 NMR、MS 及计算化学等方法鑒定了它們的結構，分别為：广藿香聚酮苷 A(**PC-1**)、广藿香聚酮苷 B(**PC-2**)、5-羟基-3,4',7-三甲氧基黄酮(**PC-3**)、5-羟基-3,3',4',7-四甲氧基黄酮(**PC-4**)、4',5-二羟基-3,3',7-三甲氧基黄酮(**PC-5**)、芹菜素(**PC-6**)、3',5-二羟基-4',7-二甲氧基黄酮(**PC-7**)、3',5-二羟基-3,4',7-三甲氧基黄酮(**PC-8**)、白杨素(**PC-9**)、3,4',5-三羟基-7-甲氧基黄酮(**PC-10**)、3,5-二羟基-4',7-二甲氧基黄酮(**PC-11**)、鼠李素(**PC-12**)、商陆黄素(**PC-13**)、5-羟基-3',4',7-三甲氧基黄烷酮(**PC-14**)、广藿香酮(**PC-15**)、豆甾醇(**PC-16**)、β-谷甾醇(**PC-17**)。其中，化合物 **PC-1** 和 **PC-2** 为 2 个新的聚酮苷类化合物，**PC-7~PC-10** 为首次从该植物中分离得到。

此外，在上述化學成分研究基礎上，本論文建立了广藿香中广藿香酮以及 8 种黄酮类化合物 HPLC 含量测定方法，並采用该方法對 13 批市售广藿香藥材進行了定量分析。此方法簡單可靠，為首次採用 HPLC 法同時測定广藿香中挥发性成分和非挥发性成分的含量，為广藿香品質控制研究提供重要的參考。

關鍵詞：广藿香；黄酮类成分；广藿香酮；高速液相色谱；含量分析；品質控制

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Abstract

Pogostemon cablin [Family: Lamiaceae], a bushy herb known as patchouli, was widely used in traditional herbal medicine. It was also allowed to be used as the food additives for direct addition to food for human consumption as a natural flavoring substance in chinaand USA. The plant originates from tropical Asia, and it has been cultivated in South China and other tropical area worldwide because of its economic importance. The aerial part of *P. cablin* was called Guanghuoxiang in Chinese medicine to differentiate from another herb, Huoxiang, from the species *Agastacherugosa*.Guanghuoxiang is one of the top ten Cantonese medicines for the treatment of common cold, nausea, diarrhea, headaches and fever. It is widely used in the perfume industry and has a variety of pharmacological activities including anti-emetic, anti-inflammatory, anti-allergic, immunomodulatoryand antimicrobial actions.

As part of a program to asses the chemical and biological diversities of medicinal plants in south China, we had systematically carried out research on the chemical constituents of *P. cablin*.17 compounds were isolated and purified by various column chromatography on silica gel, Sephadex LH-20, Prep-HPLC, HSCCC and their structures were identified by spectroscopic methods (MS, UV, 1D and 2D NMR)as follows: cablinoneside A(**PC-1**),cablinoneside B(**PC-2**), 5-Hydroxy-3,4',7-trimethoxyflavone(**PC-3**), 5-Hydroxy-3, 3',4',7-tetramethoxyflavone(**PC-4**), 4',5-Dihydroxy-3,3',7-trimethoxyflavone(**PC-5**), apigenin(**PC-6**), 5,3'-Dihydroxy-7,4'-dimethoxyflavone(**PC-7**), 5,3'-Dihydroxy-3,7,4'-trimethoxyflavone(**PC-8**), 5,7-Dihydroxyflavone(**PC-9**), 3,5,4'-Trihydroxy-7-methoxyflavone(**PC-10**),3,5-Dihydroxy-7,4'-dimethoxyflavone(**PC-11**),rhamnetin(**PC-12**), ombuine(**PC-13**), 5-Hydroxy-7,3',4'-trimethoxyflavanone(**PC-14**), pogostone(**PC-15**), Stigmasterol(**PC-16**),Sitosterol(**PC-17**), repectively. Among them, **PC-7 ~PC-10**are isolated from this plant for the first time, **PC-1**and **PC-2** are two new compounds.

In this thesis, a high performance liquid chromatography (HPLC) method was developed and validated for simultaneous quantification of nine major components including volatile and non-volatile ingredientsin *Pogostemoncablin*(Blanco) Benth..The validated method was applied to quantitatively analyze 9 majorcompounds of 13 ‘Guanghuoxiang’ samples purchased from different place in China. It is helpful for

pharmacological evaluation and quality control of *P. cablin*.

Key words: *Pogostemoncablin*; Flavonoid; Pogostone; HPLC;Quantification; Quality control

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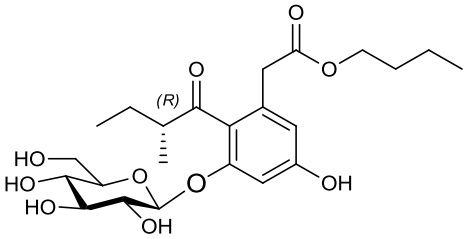
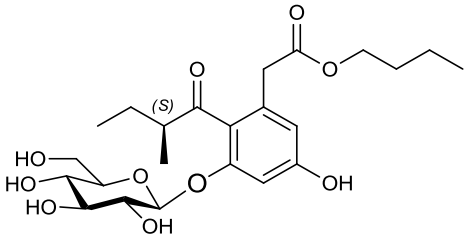
本論文鑒定的化合物結構式

帶*號者為新化合物



***PC-1**



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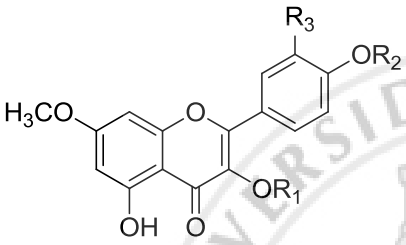
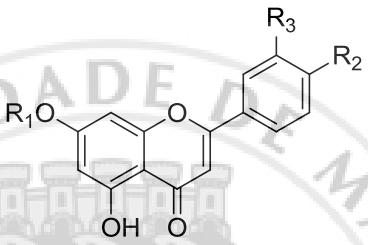
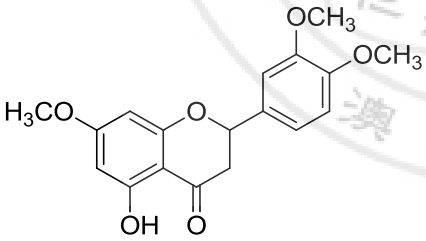




	R_1	R_2	R_3
PC-3	CH_3	CH_3	H
PC-4	CH_3	CH_3	OCH_3
PC-5	CH_3	H	OCH_3
PC-8	CH_3	CH_3	OH
PC-10	H	H	H
PC-11	H	CH_3	H
PC-12	H	H	OH
PC-13	H	CH_3	OH

	R_1	R_2	R_3
PC-6	H	OH	H
PC-7	CH_3	OCH_3	OH
PC-9	H	H	H



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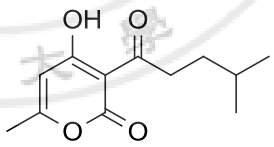

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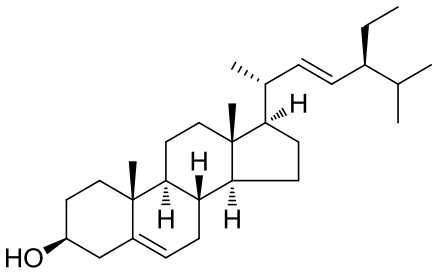

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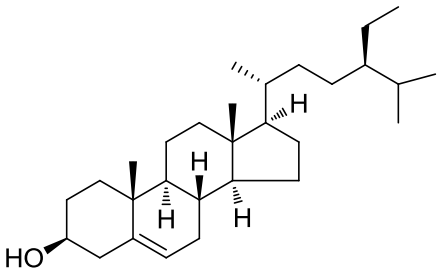

PC-17

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縮略詞表

缩写	英文	中文
mp	Melting point	熔点
UV	Ultra-Violet spectrum	紫外光谱
IR	Infra-Red spectrum	红外光谱
HR-ESI-MS	High Resolution Electrospray Ionization Mass Spectroscopy	高分辨电喷雾电离质谱
NMR	Nuclear Magnetic Resonance	核磁共振
DEPT	Distortionless Enhancement by Polarization Transfer	无畸变极化转移增益
HMBC	^{1}H-Detected Heteronuclear Multiple-Bond Correlation Spectroscopy	氢检测异核多键相关谱
HSQC	^{1}H-Detected Heteronuclear Single-Quantum Coherence Spectroscopy	氢检测异核单量子相关谱
^{1}H-^{1}H COSY	Two Dimensional ^{1}H Correlation Spectroscopy	^{1}H-^{1}H 同核相关谱
TOCSY	Total Correlation Spectroscopy	全相关谱
ROESY	Rotating Frame Overhauser Effect Spectroscopy	旋转坐标系中 NOE 效应
HPLC	High-performance liquid chromatography	高效液相色谱
HPLC-ESI-MS/MS	High-performance liquid chromatography-Electrospray Mass Spectroscopy	高效液相色谱-电喷雾离子阱质谱联用技术
ODS	Octadecylsiyl	十八烷基硅烷键合硅胶填料
TLC	Thin Layer Chromatography	薄层色谱

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