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略字表

| | |
|---------------------|---|
| APAP | acetaminophen |
| CC | column chromatography |
| CMC | carboxyl methyl cellulose |
| ^{13}C NMR | carbon nuclear magnetic resonance, CMR |
| COSY | correlated spectroscopy |
| DEPT | distortionless enhancement by polarization transfer |
| DMSO | dimethyl sulfoxide |
| DPPH | 1,1-Diphenyl-2-picrylhydrazyl |
| fMLP | <i>N</i> -formyl-Met-Leu-Phe |
| HMBC | heteronuclear multiple-bond connectively |
| HMQC | ^1H -detected heteronuclear multiple-quantum coherence |
| HPL | <i>Hypoestes purpurea</i> leaf |
| ^1H NMR | proton nuclear magnetic resonance, PMR |
| IL1- β | interleukin 1 β |
| IR | infrared spectrophotometry |
| MS | mass spectrophotometry |
| MTS | 5-(3-carboxymethoxyphenyl)-2-(4,5-dimethylthiazolyl)- 3-(4-sulfophenyl) tetrazolium salt |
| NOSY | nuclear overhauser and exchange spectroscopy |
| PGE ₂ | prostaglandin E ₂ |
| SF | <i>Strobilanthes formosanus</i> MOORE |
| SFL | <i>Strobilanthes formosanus</i> leaf |
| SFR | <i>Strobilanthes formosanus</i> root |
| SFS | <i>Strobilanthes formosanus</i> stem |
| TLC | thin layer chromatography |
| TMS | tetramethylsilane |
| UV | ultraviolet spectrophotometry |

爵床科植物台灣馬藍(*Strobilanthes formosanus* MOORE)及六角英(*Hypoestes purpurea* R. BROWN)之化學成分與藥理活性評估

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摘 要

爵床科馬藍屬植物台灣馬藍(*Strobilanthes formosanus* MOORE)及槍刀菜屬植物六角英(*Hypoestes purpurea* R. BROWN)皆為台灣之民間藥，均具有清熱解毒、行血散瘀之功效，常應用於感冒發熱、咽喉腫痛、腮腺癌、肝炎、刀槍創傷出血等之治療，且皆尚未有任何相關之藥理、化學成分研究報導。本研究經由對爵床科馬藍屬及槍刀菜屬植物之藥用植物學、成分與藥理學等各項文獻考察與整理，並進行台灣馬藍(*S. formosanus*)及六角英(*H. purpurea*)之化學成分與藥理學活性評估研究，以供作本屬植物後續研究之參考。

在成分研究方面，從台灣馬藍分離得到七個化合物，經光譜分析鑑定其結構為 4'-hydroxy-5,7-dimethoxyflavone (1), 3'-hydroxy-5,7-dimethoxy-flavone 4'-O-β-D-apiofuranoside (2), 5,7-dimethoxyflavone 4'-O-[β-D-apiofuranosyl (1→5)-β-D-glucopyranoside] (3), lupeol (4), betulin (5), 2,6-dimethoxy-1,4-benzoquinone (6), stearic acid (7)。其中 3'-hydroxy-5,7-dimethoxyflavone 4'-O-β-D- apiofuranoside (2)及 5,7-dimethoxyflavone 4'-O-[β-D-apiofuranosyl (1→5)-β-D-glucopyranoside] (3)二個化合物為自然界中首次分離得到之新化合物。從六角英葉部之甲醇萃取物，共分離出六個化合物，經光譜分析及與文獻比對後，鑑定其結構為 hypopurpurin A (1), hypopurpurin B (2), hypopurpurin C (3), uracil (4), vanillic acid (5)及 1-triacontanol (6) 其中 hypopurpurin A (1), hypopurpurin B (2)及 hypopurpurin C (3)為自然界中首次分離出之新化合物。

在急性毒性結果顯示，台灣馬藍之甲醇萃取物口服之急性毒性較小(> 10 g/kg)，而腹腔注射則具有較強之急性毒性(LD₅₀ = 3.99 g/kg)。鎮靜作用方面，台灣馬藍對於 pentobarbital 引起之睡眠時間(sleeping time)有延長作用，且具有劑量

依存性(dose dependent)，對於正向反射(righting reflex)消失之時間(即 onset)則有縮短之效。

鎮痛實驗顯示，對於福馬林誘發舔足的前後期反應時間及醋酸誘發小鼠扭體反應均呈現劑量依存性的抑制作用；在室溫下對正常大鼠肛溫變化之影響方面，台灣馬藍甲醇萃取物可對大鼠產生降溫作用，且在 30 分鐘時降至最低，其後則慢慢回復，且具有劑量依存性之關係。對 IL-1 β 誘發高溫大鼠肛溫變化之影響方面，台灣馬藍甲醇萃取物可顯著降低 IL-1 β 所誘發之發燒現象，且具有劑量依存性之關係。對 PGE₂ 誘發高溫大鼠肛溫變化之影響，台灣馬藍甲醇萃取物無法降低 PGE₂ 所誘發之發燒現象。

在抗發炎試驗方面，台灣馬藍根部、莖部及葉部之甲醇萃取物，對 fMLP 引發嗜中性白血球釋放 β -glucuronidase 和 lysozyme 的體外試驗，均有顯著抑制作用 ($p \leq 0.05$)；抗過敏試驗方面，台灣馬藍根部、莖部及葉部之甲醇萃取物對於 compound 48/80 引發肥滿細胞釋放 β -glucuronidase 和 histamine 的體外試驗有明顯抑制作用($p \leq 0.05$)，故可確認台灣馬藍確實具有抗發炎活性及抗過敏活性。

在細胞毒殺活性試驗方面，結果顯示台灣馬藍根、莖、葉之甲醇萃取物、正己烷層及乙酸乙酯層對於胃癌細胞(NUGC)及鼻咽癌細胞(HONE)皆不具抑制效果。同時，由本植物分離出兩個新化合物 2 及 3 對於胃癌細胞(NUGC)及鼻咽癌細胞(HONE)也不具抑制效果。

在自由基清除能力試驗方面，台灣馬藍根及莖部之乙酸乙酯層、正丁醇層在 200 $\mu\text{g/mL}$ 及 400 $\mu\text{g/mL}$ 時對 DPPH 自由基清除能力較為顯著，葉部各層在不同濃度下則未見特別顯著之效果。而六角英葉部氯仿層、正丁醇層及水層對於清除 DPPH 自由基的能力均介於 50~60 %，效果並未特別顯著，其有效成分尚待進一步評估與探討。

Evaluation of Chemical Constituents and Pharmacological Activities
of Acanthaceae Plants — *Strobilanthes formosanus* MOORE and
Hypoestes purpurea R. BROWN

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Abstract

Strobilanthes formosanus MOORE and *Hypoestes purpurea* R. BROWN are native Acanthaceae plant of Taiwan. In folk medicine, they are used to clear away heat and toxic material and are used to promote blood circulation and remove stasis. The plants are used in Chinese folk medicine for the treatment of cough, fever, sore-throats, mumps, hepatitis, and incised wounds with hemorrhage. There are no chemical and pharmacological investigations that support these traditional claims. This study was first based on the investigations and literature survey of ethnobotany, phytochemistry and pharmacology of *Strobilanthes* and *Hypoestes* genus, and evaluation of chemical constituents and pharmacological activities of *Strobilanthes formosanus* MOORE and *Hypoestes purpurea* R. BROWN. We hope to provide some information for subsequent research.

In the phytochemical study, seven compounds were isolated from *S. formosanus* and were elucidated as 4'-hydroxy-5,7-dimethoxyflavone (1), 3'-hydroxy-5,7-dimethoxyflavone 4'-*O*- β -D-apiofuranoside (2), 5,7-dimethoxyflavone 4'-*O*-[β -D-apiofuranosyl (1 \rightarrow 5)- β -D-glucopyranoside] (3), lupeol (4), betulin (5), 2,6-dimethoxy-1,4-benzoquinone (6), stearic acid (7). Among them, 3'-hydroxy-5,7-dimethoxy-flavone 4'-*O*- β -D-apiofuranoside (2) and 5,7-dimethoxy-flavone 4'-*O*-[β -D-apiofuranosyl (1 \rightarrow 5)- β -D-glucopyranoside] (3) were new compounds. From the leaf of methanolic extracts of *H. purpurea*, six compounds were isolated and were elucidated as hypopurpurin A (1), hypopurpurin B (2), hypopurpurin C (3),

uracil (4), vanillic acid (5) and 1-triacontanol (6). Among them, hypopurpurin A (1), hypopurpurin B (2) and hypopurpurin C (3) were new compounds.

The intraperitoneal LD₅₀ of the methanol extract of *S. formosanus* on mice was 3.99 g/kg and oral acute toxicity was more than 10 g/kg. The methanol extract also shortened the onset and prolonged the sleeping duration induced by pentobarbital in mice.

This study also evaluated the analgesic and antipyretic effects of the methanolic extract of *S. formosanus* in animal models. The extract significantly and dose-dependently inhibited the writhing response of mice and decreased the licking time in both the early and late phases in the formalin test. In unanesthetized rats, the extract went down to the fall at 30 min and caused a dose-related fall in colonic temperature at room temperature. The fever induced by interleukin-1 β (lateral cerebral ventricle injection) was attenuated by treatment with the extract. However, the extract did not attenuate pyrexia induced by PGE₂.

In this study, the root, stem and leaf of *S. formosanus* were also investigated for their cytotoxicity, antiinflammatory and 1,1-Diphenyl-2-picrylhydrazyl free radical scavenging activities. The crude methanol extract and two new compounds did not showed cytotoxicity against NUGC and HONE. A significant ($p \leq 0.05$) inhibition of neutrophil degranulation induced by fMLP and mast cell degranulation induced by compound 48/80 were also exhibited by the extract.

The EtOAc and *n*-BuOH layers of the root and stem of *S. formosanus* showed significant scavenging effect against 1,1-Diphenyl-2-picrylhydrazyl at 200 μ g/mL and 400 μ g/mL. For the CHCl₃, *n*-BuOH and water layer of *H. purpurea*, the scavenging activity effect were between 50~60 %.