

# 目 錄

目 錄	I
表 目 錄	II
圖 目 錄	III
中文摘要	IV
英文摘要	V
第一章 緒 論	2-1
第二章 總 論	2-2
第一節 環 孢 靈 之 特	2-2
第三章 材 料 與 方 法	2-4
第一節 實 驗 材 料	2-4
一、 試 藥	2-4
二、 儀 器 設 備	2-4
三、 動 物	2-5
第二節 實 驗 方 法	2-6
一、 甘 草 水 煎 劑、 甘 草 酸 於 大 鼠 體	6
二、 甘 草 水 煎 劑 及 甘 草 酸 在 離 體 大 鼠 空 腸、 迴 腸 對 P-glycoprotein 功 能 之 影 響	2-8
第四章 結 果 與 討 論	2-10
第五章 結 論	2-19
參 考 文 獻	2-20

## 表 目 錄

<b>Table 2-1</b> Blood cyclosporine concentrations (ng/ml) after oral administration of cyclosporine (2.5 mg/kg) to rats	2-11
<b>Table 2-2</b> Blood cyclosporine concentrations (ng/ml) after oral administration of cyclosporine (2.5 mg/kg) with licorice decoction (75 mg/kg GZ) to rats	2-11
<b>Table 2-3</b> Blood cyclosporine concentrations (ng/ml) after oral administration of cyclosporine (2.5 mg/kg) with 100 mg/kg GZ to rats	2-12
<b>Table 2-4</b> Mean ( $\pm$ S.E.) pharmacokinetic parameters of cyclosporine in rats after giving cyclosporine (2.5 mg/kg) alone and coadministration with licorice (100 mg/kg GZ) or GZ 100 mg / kg	2 - 1 4

## 圖目錄

- Fig 2-1** Mean ( $\pm$ S.E.) blood concentration-time profiles of cyclosporine afteroral adiministration of cyclosporine alone (2.5 mg/kg) andcoadministration with licorice decoction (equivalent to 100 mg/kgGZ) or 100 mg/kg GZ to rats 2-13
- Fig. 2-2** Transport of rhodamine from serosal to mucosal surfaces across the everted jejunum in the absence or presence of licorice decoction or GZ at a concentration of 200  $\mu$ M or 400  $\mu$ M GZ. Each valueresresents the mean  $\pm$  S.E. (n = 3) 2-17
- Fig. 2-3** Transport of rhodamine from serosal to mucosal surfaces across the everted ileum in the absence or presence of licorice decoction or GZ at a concentration of 200  $\mu$ M or 400  $\mu$ M. Each value represents themean  $\pm$  S.E. (n = 3) 2-18

# 甘草之生物藥學研究 -

## (貳) 甘草、甘草酸與環孢靈之交互作用

研究生 經 總

中國醫藥學院 中國藥學研究所

### 摘 要

環孢靈為強效免疫抑制劑，治療指數狹小，口服後經由腸及肝臟之 CYP 3A4 代謝，甘草在臨床應用上極為普遍，具誘導 CYP 3A 之作用。本研究以大鼠單服環孢靈及併服甘草水煎劑或甘草酸，血中環孢靈濃度之定量，採臨床使用之螢光偏極免疫法，結果顯示併服甘草酸明顯降低環孢靈之吸收達 64 %，甘草水煎劑之影響則不明顯。體外翻腸試驗顯示甘草酸顯著增加 P-glycoprotein( P-gp ) 的外排功能，導致環孢靈的吸收顯著減少。

# Biopharmaceutical Studies of Licorice — Interactions between Licorice, Glycyrrhizin and Cyclosporine

Hui Ching

Graduate of Chinese Pharmaceutical Sciences  
China Medical College, Taichung, Taiwan, R. O. C.

## ABSTRACT

Licorice, one of the most commonly used herb in clinical Chinese medicine, was shown to be a CYP 3A inducer. Cyclosporine, a potent immunosuppressive agent with narrow therapeutic range, undergoes metabolism by hepatic and intestinal CYP3A4. To investigate the effect of licorice on the pharmacokinetics of cyclosporine, Sprague-Dawley rats were orally given cyclosporine alone and coadministered with licorice or glycyrrhizin. Fluorescence polarization immunoassay method was employed to determine the blood cyclosporine concentrations. The result showed that glycyrrhizin significantly decreased the absorption of cyclosporine by 64 %, but not affected by licorice. *In vitro* everted sac study showed that glycyrrhizin was a P-glycoprotein inducer.