

• 計畫中文名稱	Flurbiprofen 水性凝膠之生體外及生體內經皮吸收研究		
• 計畫英文名稱	In vitro and in vivo Transdermal Delivery of Flurbiprofen from Hydrogels		
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• 研究人員	方嘉佑		
• 中文關鍵字	Flurbiprofen；經皮輸藥系統；經皮吸收；水性凝膠；；；		
• 英文關鍵字	Flurbiprofen；Transdermal delivery；Transdermal absorption；Hydrogel；；；		
• 中文摘要	Flurbiprofen (2-(2-fluoro-4-biphenyl)-propionic acid) 為一種非固醇類抗發炎劑 (Non-steroidal Anti-inflammatory drugs, NSAIDs)，其具有止痛、抗發炎、抑制血小板凝集及退熱等藥理療效。在藥物動力學方面 flurbiprofen 之體內半衰期謹約 3 至 4 小時，且一般投藥頻率一天須 3 甚至 4 次，較其他 NSAIDs 藥物為高，因此基本上 flurbipofen 合適以經皮輸藥系統方式投與以避免肝臟首渡效應 (first-pass effect) 的發生並達到控制釋出 (controlled release) 的目的以減少投藥頻率。藥物以經皮輸藥方式給予時其載體 (carriers; vehicles) 之不同會明顯影響其經皮吸收能力，若藥物將來擬應用於臨床上則固體或半固體劑型較溶液製劑更為適當，一般而言現今臨床上使用之劑型以貼片型式及軟膏製劑較常被應用，今擬以 flurbiprofen 為模式藥物，設計其水性凝膠半固體劑型從事生體外及生體內經皮吸收研究。由於水性凝膠其處方除了少部份高分子聚合物 (polymers) 以外，其餘幾乎皆為水或緩衝液，因此其製造成本基本上相當低廉，而且外觀透明質感極佳，消費者接受度頗高。本計畫中擬使用製備水性凝膠之高分子聚合物皆為較新型之原料，以有別於之前本研究室常用之傳統材料包括：Carbopol 934、polyvinylpyrrolidone、Eudragit 及 methylcelluloce 等。本計畫將分為生體外評估及生體內評估兩部份進行，在體外評估方面最主要是以人工 cellulose 膜、離體人類上皮組織及裸鼠全皮為主要滲透障壁，經由選擇生體外試驗較適宜之處方進行生體內經皮吸收之評估，配合藥物動力學研究檢視 flurbiprofen 於生體內之經皮吸收能力，並與體內實驗數據結果進行比較以評定是否具有相關性，除此之外亦與其他 NSAINSAIDs 藥物做比較並藉以修正處方設計。		
• 英文摘要	Flurbipofen can both cure burn, UV-irradiated and traumatic skins. The aim of this study is to investigate the effect of flurbipofen on the in vitro topical and transdermal permeation. The study also quantifies the skin irritation and damage produced by application of these drugs on traumatic skin. The developed method presented in this study is able to distinguish between epidermal and dermal changes in histological structure, thereby allowing differentiation between mild and moderate irritants. Different methods of transdermal enhancement have been found to increase drug delivery via different mechanisms. This study also examines the skin permeation of these drugs in the hydrogel bases. Since hydrogels can each individually increase transdermal drug delivery, it is hypothesized		

that the hydrogels may result in a greater enhancement than that resulting from each method alone. The diffusion cell used in this in vitro study was Franz vertical diffusion assembly. The skin was mounted on the receptor compartment with the SC side facing upwards into the donor compartment. The receptor compartment (10 ml) was filled with a ethanol/pH 7.4 citrate-phosphate buffer (1:1) mixture. Both donor fluids showed the solution type. The available area of the Franz cell was 1.77 cm². The receptor compartment was maintained at 37°C and stirred by a magnetic bar at 600 rpm. At appropriate intervals, 200 µl aliquots of receptor medium were withdrawn and immediately replaced by an equal volume of fresh receptor solution. The samples were analyzed by HPLC methods reported previously.