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• 計畫英文名稱	Enhancement of Anti-Diabetic Paeoniflorin in Low Bioavailability of Oral Absorption by Polymeric Micelles.		
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• 中文關鍵字	低生體可用率；芍藥甘；聚合載體；口服吸收		
• 英文關鍵字	bioavailability；paeoniflorin；polymeric micelles；absorption		
• 中文摘要	由於抗糖尿之芍藥甘在體內呈現低生物可用率，因此本計畫利用 PEO-OA 聚合載體，探討增加芍藥甘在胃腸道體外與體內之吸收與生物可用率；同時評估芍藥甘在家兔體內降血糖之能力與速度。首先利用 Pyrene- CMC 濃度測試、粒徑大小、Zeta 電位，評估聚合載體(PEO-OA)之物理化學特性。進而利用聚合載體(PEO-OA)，在不同五段腸胃道(胃、十二指腸、空腸、迴腸及結腸)之體外評估增加芍藥甘之吸收與穿透能力：分別以利用放射線親水性、疏水性之藥物(manntiol、estradiol)與組織電阻測試，同時進行體外穿透試驗，以了解不同聚合載體在體外對增加芍藥甘在胃腸道穿透機制。結果在濃度超過 0.01%(W/W) 以上，發現聚合載體可以形成並且粒徑可以大約分布在 20 nm 範圍。同時，在家兔胃腸道體外評估中，發現可以增加 mannitol 在五段腸胃道之穿透率(約 2.4 ~6.7 倍)；並且同時，降低五段腸胃道組織電阻測試。其次，進行體內口服投與與藥物動力學之觀察，發現芍藥甘之在體內血中濃度面積可以從 79.7 ± 32.8 增加至 312.8 ± 82.8 ng.hr/ml。同時，在 48 與 78 分鐘時，芍藥甘與聚合載體並用下，在正常家兔體內進行葡萄糖耐受性實驗時，具有降血糖表現。因此，此類聚合載體可以影響芍藥甘在細胞間之吸收並且可以有效產生降血糖之效果。		
• 英文摘要	The primary objective of this study was to evaluate the mechanisms of enhanced in vitro and in vivo paeoniflorin gastrointestinal (GI) permeation by PEO-OA polymeric micelles. In addition, the enhancement of the hypoglycemic pharmacodynamic effect of oral paeoniflorin was also evaluated in i.v. glucose-tolerance test. Characterization of physicochemical properties of an OA-PEO micellar solution was examined by the pyrene fluorescence probe method, critical micelle concentration, and dynamic light scattering.		

Modification of permeation ability and mechanisms of paeoniflorin absorption in the 5 segments of GI by OA-PEO polymeric micelles were evaluated by transcellular tracer, [14C]estradiol, and the paracellular tracer, [14C]mannitol in an in vitro transport study and transepithelial electrical resistance (TEER) measurements. The critical micellar concentration (CMC) results revealed that the fluorescence intensity increased to above 0.01% (w/w) of OA-PEO polymers with 20-nm-particle distribution ranges. Using 1% (w/w) of OA-PEO polymers, the tight junction permeabilities of 5 segments GI tract were significantly increased with the flux of [14C]mannitol and decreased the values of TEER. In 5 GI regions, the permeability coefficients of paeoniflorin were also enhanced by 2.4 to 6.7 times and the AUC increased from 79.7 $\pm$ HHH $\pm$ HHH 32.8 to 312.8 $\pm$ HHH $\pm$ HHH 82.8 ng.hr/ml. In addition, the hypoglycemia was marked at 48, and 78 min by oral paeoniflorin with OA-PEO polymeric micelles. Thus, absorption of paeoniflorin with OA-PEO polymeric micelles across rabbit GI regions is influence paracellular pathway. OA-PEO polymeric micelles could produce the enhancement of GI absorptions of paeoniflorin in vitro and in vivo.