• 系統編號	RB8404-1362
• 計畫中文名稱	2,6- 二氨基已酸/鈉共同運輸系統作爲眼角膜穿透增強劑
• 計畫英文名稱	Lysine/Na Cotransport System as a Corneal Penetration.
• 主管機關	行政院國家科學委員會
• 計畫編號	NSC82-0412-B038-029-T
• 執行機構	台北醫學院藥學系
• 本期期間	8203 ~ 8302
• 報告頁數	0 頁
• 使用語言	英文
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• 中文關鍵字	2,6-二氨基已酸/鈉運輸系統；穿透增強劑； 眼角膜；穿透率；離胺酸
• 英文關鍵字	Lysine/Na transport system；Penetration enhancer；Cornea；Permeability； Lysine
• 中文摘要	此項研究計畫主要方向是利用 2,6-二氨基已酸/鈉共同運輸系統,一般藥品或大分子對眼角膜穿透能力。基於生物科技新潮流走向,對於胺基酸,蛋白質給藥途徑將會有重大影響。但是一般胺基酸與蛋白質由於含有大量正負電荷及大分子量因素,在正常途徑給藥方式下,會出現吸收不易現象,而其主要阻力出於細胞與細胞間組織-Tight junction。爲增加藥品吸收程度,目前有二個主要方向:(1)利用 2,6-二氨基已酸/鈉系統。(2)對細胞內骨骼(Cytoskeleton)控制。在 Robinson lab,證明在兔子的眼角膜內含有 2,6-二氨基已酸/鈉運輸系統,且需要能量支持。這項研究計畫主要利用這個系統,對放射性甘油,Glutamic acid,---經細胞間傳送,二氫基女性素(Estradiol)---經細胞內傳遞三類藥品,進行影響穿透能力控制。結果利用 L-lsyin/Na system 發現其 Glyerol and glutamic acid 的 Permeability coefficient 有增加效果。而爲進一步證明影響穿透力,不是基滲透壓因素,分別用三個方法來決定。首先同時放置同等滲透壓力 Lysine 於二測,其次利用已六醇作同等滲透壓方式,以及抑制 2,6-二氨基已酸/鈉機制-烏亦盆(Ouabain),作同樣三種不同藥品穿透能力實驗步驟,來分別影響因素。結果並不受滲透壓的影響,而只對 Lysine 的濃度有變化。再從 Ouabain 來阻止這個系統,結果亦可以阻斷穿透力。同時運用 Resistance 的結果也有同樣的趨向。
• 英文摘要	The purpose of the present study is to assess the ability of a proposed sodium/lysine cotransport system to enhance penetration of certain solutes. Permeability studies utilizing C14-glycerol and glutamic acid as probe molecules were conducted to determine the effect of lysine on drug molecules transported via the paracellular pathway. Quantitative assessment of the promoting effect was obtained, using measurement of transepithelial membrane resistance, since electrical resistance measurements indicate changes in the

dimension of the aqueous transport pathway. The results showed that the transport of L-lysine, which is sodium-dependent and energy driven, increased the permeability of glycerol and glutamic acid in the rabbit cornea. This effect was dependent on the concentration of L-lysine and not noted with mannitol at an equivalent osmotic pressure. Ouabain eliminated this enhancing effect by shutting down the Na/sup +//K/sup +/ ATPase enzyme. The enhancement mechanism of L-lysine required electrolytes present in glutathione bicarbonate ringers solution that are not supplied by sodium chloride. The permeability of estradiol was not affected by L-lysine, indicating that the mechanism of enhancement does not involve the transcellular pathway. The resistance results showed that L-lysine greatly reduced corneal resistance, translating to an increase in permeability of the paracellular space. Ouabain eliminated this effect on the resistance. The reduction in resistance by L-lysine was reversible and not reproduction by an equivalent osmotic load provided by mannitol.