• 系統編號	RC8901-0506		
• 計畫中文名稱	應用多二元醇飽和甘油酯做爲藥物滲透之載體與增強劑的研究		
• 計畫英文名稱	Polyglycolized Saturated Glycerides as a Carrier and Enhancer for Drug Penetration		
• 主管機關	行政院國家科學委員會	• 計畫編號	NSC88-2314-B038-101
• 執行機構	台北醫學院藥學系		
• 本期期間	8708 ~ 8807		
• 報告頁數	0 頁	• 使用語言	英文
• 研究人員	何秀娥 Ho, Hsiu-O		
• 中文關鍵字	聚二元醇飽和甘油酯；藥物載體；穿透增強劑；前列腺素		
• 英文關鍵字	Polyglycolized saturated fatty acid ester；Drug carrier；Penetration enhancer；Prostaglandin；Gelucire system		
• 中文摘要	本研究利用實驗設計法定量地檢視 Gelucire 基劑其融點和 HLB 值對前列腺素 E/sub 1/和其 Alkyl ester 通過皮膚障礙層的滲透影響性。七個處方包含有 0.1mg/mg 模式藥物和不同比例的 Gelucire 44/14,50/02 和 37/02 並以 4:1 的比例添加 Lauroglycol。對於 PGE/sub 1/而言,其最大的流通率在 35.9493 和 33.3300nmole/cm/sup 2/per h 之間,此時處方的 HLB 值爲 6.6,融點爲 41-54.degree.C。對於 Methyl PGE/sub 1/而言,其最大的流通率爲 76.6214nmole/cm/sup 2/per h,此時處方的 HLB 值爲 5.3,融點爲 46-50.degree.C。對於 Ethyl PGE/sub 1/而言,其最大的流通率爲 33.4468nmole/cm/sup 2/per h 之間,此時處方的 HLB 值爲 5.3,融點爲 46-50.degree.C。對於 Isopropyl PGE/sub 1/而言,其最大的流通率爲 15.4577,此時處方的 HLB 值爲 5.3,融點爲 46-50.degree.C。對於 Butyl PGE/sub 1/而言,其最大的流通率爲 13.6691nmole/cm/sup 2/per h 之間,此時處方的 HLB 值爲 6.6,融點爲 41-48.degree.C。對於 PGE/sub 1/和 alkyl ester 而言,在不同的 Gelucire system 其加強滲透的作用不同。對於模式選擇的結果顯示三個 Gelucire grade 對 PGE/sub 1/的流通率其作用以三個因子沒有相互作用的 Quadratic model 最適當。而 PGE/sub 1/alkyl ester 最適當的是 Linear model。對於 PGE/sub 1/而言,Gelucire 44/14 和 Gelucire 50/02 相互作用有一個最大的正值,緊接著是 Gelucire 44/14 和 Gelucire 37/02。結果顯示 PGE/sub 1/經由老鼠皮膚的滲透速率藉由 Gelucire 44/14 和 Gleucire 50/02 的組合能大幅被加強。然而 Gelucire 50/02 和 37/02 的相互作用顯示負值。此可能是由於這二個 Gelucire grade 的 HLB 值均太低,以致於無法加速 Gelucire 處方的自身乳化作用,而阻礙了 PGE/sub 1/的滲透。此與加強 PGE/sub 1/和其 alkyl ester 的滲透速率必須有適當 HLB 值的 Gelucire 系統結果一致。此結果亦顯示具高融點和低 HLB 值的 Gelucire 50/02 會減少 PGE/sub 1/ alkyl ester 的滲透速率。但是,Gelucire 50/02 和 37/02 提昇 PGE/sub 1/ alkyl ester 的滲透速率相似,會隨著增加 Alkyl chain 的長度而		

減少。此可由 Gelucire 50/02 和 37/02 的 HLB 值相同來解釋。在本實驗中 Gelucire system 的 HLB 值影響比融點大。

- 英文摘要

In this study, the influence of the melting point and HLB value of Gelucire-based formulations on the permeation of model drugs, including PGE/sub 1/ and its alkyl esters, through the skin barrier was examined quantitatively with an experimental design. Seven formulations consisting of three grades of Gelucire (44/14, 50/02, and 37/02) at different ratio with the addition of lauroglycol at a fixed ratio of 4:1 to a total Gelucire amount were prepared with model drugs in a concentration of 0.1mg/mg. For PGE/sub 1/, the maximal flux at this concentration was between 35.9493 and 30.3300nmole/cm/sup 2/ per h and occurred at the HLB value of 6.6 and melting point ranged from 41-54.degree.C. For methyl ester of PGE/sub 1/, the maximal flux appeared to be 76.6214nmole/cm/sup 2/ per h and occurred at the HLB value of 5.3 and melting point ranged from 46-50.degree.C. As to ethyl ester of PGE/sub 1/, the maximal flux was around 33.4468nmole/cm/sup 2/ per h and occurred at the HLB value of 5.3 and melting point ranged from 46-50.degree.C. The maximal flux was 15.4577nmol/cm/sup 2/ per h for isopropyl ester of PGE/sub 1/ and appeared at the HLB of 5.3 and melting point ranged from 46-50.degree.C. Butyl ester of PGE/sub 1/ showed its maximal flux to be around 13.6691nmol/cm/sup 2/ per h and occurred at the HLB value of 6.6 and melting point ranged from 41-48.degree.C. The promotion of penetration for PGE/sub 1/ and its alkyl esters seem to be maximized at different Gelucire system. The results of model selection demonstrate that the quadratic model, which has no interaction term of three factors, was the most statistically appropriate model for describing the overall effect of three Gelucire grades on the flux of PGE/sub 1/. On the other hand, linear model was the most suitable for four PGE/sub 1/ alkyl esters. For PGE/sub 1/, the interactive effect of Gelucire 44/14 and Gelucire 50/02 on the flux of PGE/sub 1/ was the greatest with a positive sign, followed by Gelucire 44/14 and 37/02 with a positive sign. As a result, the penetration rate of PGE/sub 1/ through mouse skin was greatly enhanced with using a combination of Gelucire 44/14 and 50/02. However, the interactive effect of Gelucire 50/02 and 37/02 showed a negative sign. It may be that HLB value of these two Gelucire grades are too lower to accelerate the self-emulsification of Gelucire formulation hindering the penetration of PGE/sub 1/. This was consistent with the result that an optimal HLB value of Gelucire system is necessary to improve the permeation rate of PGE/sub 1/ and its alkyl esters. Results also demonstrate that a higher melting point and a lower HLB value of Gelucire 50/02 resulted in decreasing permeation rate of PGE/sub 1/alkyl esters. But the tendency for Gelucire 50/02 and 37/02 to promote the penetration of PGE/sub 1/ alkyl esters was similar and the extent of the influence decreased with increased alkyl chain length. It is possibly explained by the fact that the HLB value of Gelucire 50/02 and 37/02 is equal. Similarly, the influence of HLB value of Gelucire system was more profound than that of the melting point examined in this study.