

• 系統編號	RB8404-1361		
• 計畫中文名稱	丙酮酸對藥物乙醯反應之影響		
• 計畫英文名稱	Effects of Pyruvic Acid on Acetylation of Drugs.		
• 主管機關	行政院國家科學委員會	• 計畫編號	NSC82-0412-B038-017
• 執行機構	台北醫學院藥學系		
• 本期期間	8202 ~ 8301		
• 報告頁數	0 頁	• 使用語言	中文
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• 中文關鍵字	乙醯化；多形性；表現型；丙酮酸		
• 英文關鍵字	Acetylation；Polymorphism；Phenotype；Pyruvic acid		
• 中文摘要	<p>遺傳多型(Polymorphism)影響藥物代謝已經證實。其中乙醯化遺傳多型(Acetylation polymorphism)之研究又多與乙醯轉化有關。然而,先前研究曾指出,不同表現型家兔之內生丙酮酸濃度有明顯不同,並且藥物乙醯化亦與丙酮酸抱合代謝之間具有消長關係,因此懷疑丙酮酸之代謝與乙醯藥物之間有否關聯。故本研究之目的在於瞭解家兔體內丙酮酸(PA)之變化,並探討丙酮酸對 Sulfadiazine(SDZ)藥物動力學之影響。以 SDZ 為標的藥物,檢測家兔之乙醯化表現型,共計 23 隻雄性紐西蘭家兔,其中慢速乙醯化型 9 隻,快速乙醯化型 14 隻,經靜脈投予不同劑量之 PA,在 100mg/kg-200mg/kg 的範圍中,家兔體內 PA 的代謝情形為一 Dose-independent 的現象,其 AUC 與劑量之間呈線性關係(0 至無限時間,$Y=21.570X-535.508, r^2=0.9396$; 0 至 40 分鐘,$Y=12.275X-518.391, r^2=0.9997$)。不同乙醯表現型家兔所得之各項動力學參數,統計學上並無差異($p>0.05$)。顯示 PA 在兩種乙醯表現型之體內變化並無不同。又以靜脈連續輸注的方式投予 PA,將 PA 維持在一定恆定之高濃度 100.µg/ml 下,再投與 SDZ,探討此時 PA 對於 SDZ 之影響。其結果以 ANOVA 分別檢定慢速及快速乙醯化型家兔之 SDZ 藥物動力學之各項參數間的變異。結果顯示快速乙醯化型兔子不受高濃度 PA 之影響($p>0.05$)。但在慢速乙醯化型家兔,在 β-half life 顯示有意義差異($p<0.01$),由 115.74.plmin.37.41min 降為 62.96.plmin.13.09min,明顯的加速排泄。由此在相同之高濃度下,PA 對於乙醯多型有不同之作用。其可能之原因為藥物乙醯化之加速及產生丙酮酸抱合代謝。</p>		
• 英文摘要	<p>Polymorphism is an important factor that affect the metabolism of drugs. Mechanism of acetylation polymorphism is more certain in recent decade. Most of the related researches focus on the N-acetyltransferase. However, in our previous report, we indicated that</p>		

there were different level of endogenous pyruvic acid concentration between slow and rapid acetylation rabbits. There also existed a reverse relationship between acetylation and pyruvate-conjugation of INH. The purpose of this study was to assess the influence of pyruvic acid on the pharmacokinetics of sulfadiazine in rabbits. Acetylation phenotype of rabbits were determined by using sulfadiazine as an indicating drug, and there were twelve slow acetylation rabbits and fourteen rapid acetylation rabbits used in this experiments. After different dose administration of pyruvic acid (100mg/kg-200mg/kg), elimination of pyruvic acid represent a dose independence in rabbits. AUC (area under curve) is proportional to various doses (time: from 0 to infinite, $Y=21.570X-535.508$, $r^2=0.9396$; time: from 0 to 40 min, $Y=12.275X-518.391$, $r^2=0.9997$). There were no significant differences between acetylation phenotype and the elimination of pyruvic acid. ($p>0.05$)< Maintaining 100mg/ml plasma concentration of pyruvic acid by I.V. infusion to rabbits, the influences of pyruvic acid to the elimination of sulfadiazine were evaluated. ANOVA was used to analysis the differences of pharmacokinetic parameters of sulfadiazine between control and PA infused rabbits. On rapid acetylators, there were no significant differences in all pharmacokinetic parameters ($p>0.05$). On the other way, difference of .beta.-half life in slow acetylators were obtained ($p<0.01$). .beta.-half life were 115.74.plmin.37.41 min in control and 62.96.plmin.13.09 min in PA infused. The reason of influence of PA on slow acetylation rabbits may be pyruvic acid enhance the acetylation of sulfadiazine or the conjugation of pyruvic acid and sulfadiazine.