• 計畫中文名稱	代謝症候群藥物之研發---降血糖化合物 nstpbp168 及其衍生物		
• 計畫英文名稱	Development of Drug for Metabolic Syndrome---Hypoglycemic Compound nstpbp168 and Its Derivatives		
• 系統編號	PD9808-0019	• 研究性質	應用研究
• 計畫編號	NSC98-2323-B038-001	• 研究方式	學術補助
• 主管機關	--	• 研究期間	9808 ~ 9907
• 執行機構	臺北醫學大學生藥學研究所		
• 年度	98 年	• 研究經費	3900 千元
• 研究領域	藥學		
• 研究人員	徐鳳麟		
• 中文關鍵字	代謝症候群；降血糖藥物；降血脂藥物；nstpbp168 化合物；TMU-STD 化合物；生技製藥國家型計畫		
• 英文關鍵字	Metabolic syndrome； Hypoglycemic drug； Anti-lipidemia drug； Nstpbp168；TMU-STD； NSTP		
• 中文摘要	依據前一年的研究結果及 97 年度成果發表會諸位諮議委員之意見，我們修正第三年計畫之部份內容。第三年之主要研究工作，擬進行 nstpbp168 相關衍生物之開拓、 nstpbp168 化學合成之最適當化以及 nstpbp168 衍生物之量產，提供進行毒理評估及臨床前研究所需要量。同時，更進一步確認 nstpbp168 相關衍生物對於第一及二型糖尿病治療效果、作用機制及毒理評估。本年度計畫以代謝症候群藥物，降血糖、降血脂新藥物之開發爲目標，進行候選化合物之實質探索，其工作重點如下： (1)標的化合物之製備及其衍生化合物之探索：擴大對 nstpbp168 及其衍生物降血糖、降血脂作用機轉之了解，並確認 nstpbp168 與其衍生物之化學結構及藥效之相互關係(SAR)，完成進行有效成分最適當化學結構之評估，以期找到最理想的化合物作爲降血糖新藥開發之先導化合物 (optimize lead compound)。另外，經由完成合成 nstpbp177、nstpbp169 的方法及合成 nstpbp168 化學修飾所得之化合物，除可增強其活性外，並可進一步用於動物體內代謝研究及活性代謝物研究之參考化合物。同時，持續探討具降血糖、降血脂作用之 Backup Compounds TMU-STDs，評估其於醫療上之應用價值，並建立有效成分之大量製備方法與步驟。 (2)標的化合物及其衍生化合物之化學全合成探討：提供探討 nstpbp168、169、 177 衍生物之藥理作用機制、藥物動力學、毒理學、安全性及最適當劑型等臨床前各項試驗之原料需求；發展具降血糖、降血脂作用 backup compound TMU-STDs 之大量合成方法與步驟。目前 nstpbp168 的初步合成已經完成，然而量產不易，原因爲中間體化合物 23 之後的官能基轉換產率太低，目前修訂合成途徑，由化合物 22 參考本計畫以完成之合成 nstpbp177 的方法合成 nstpbp168，未來將朝著量產的方向進行。 (3)進行標的化合物之動物實驗評估、藥理作用機制之探討，並檢討其之毒理性質：由臺大醫學院毒理研究所，劉興華教授另提計畫負責執行。 (4)臨床前試驗： 配合委外或合作方式，加快研發時程，執行先導性臨床試驗，評估先導化合物將來進入臨床試驗之可行性。此整合型計畫整體		

	之研發成果將有助於提高國內製藥領域之技術層次，同時，由於降血糖、降血脂新藥之研發，將可望提升國內製藥業之經濟效益。
• 英文摘要	According to the previous results and the comments of the committee, we revised the third year project. We will aim to develop nstpbp168 and its derivatives, optimization of synthesis and large-scale production for further needs in toxicology and preclinical evaluations such as the anti-diabetic effect of nstpbp168 and its derivatives in type I, II diabetic animal model, and their possible mechanisms of action and safety. In order to reach the goals in developing new drug candidates for metabolic syndrome, anti-hyperglycemic, and anti-lipidemia agents, the major tasks of candidates exploration are: (i) Preparation of chemical synthesized nstpbp168 and exploration its derivatives: completion of this task will result in further understanding the mechanisms of nstpbp168 and its derivatives towards anti-diabetic and anti-lipidemia effects. Their structure-activity relationships for structure optimization evaluation will be determined in order to optimize lead compound. Furthermore, synthesized compounds- nstpbp177, nstpbp169 and derivative of nstpbp168 may be used as reference compounds in the field of in vivo metabolism. At the same time, the establishments of large-scale preparation and schemes for those active compounds including Backup Compounds TMU-STDs with antihyperglycemic and anti-lipidemic activities will be continued. (ii) Development of total synthesis of target compound and its derivatives: completion of this part will result in continuous supplying target compounds (nstpbp168, 169, 177) for biological researches including pharmacological, pharmacokinetic, toxicological, safety and formulations. Currently, nstpbp168 has been successfully synthesized; however, we are facing difficulty in large-scale preparations due to the low functional group-converting rate of intermediate compound 23. Therefore, we will use compound 22 to synthesize nstpbp168 according to the schemes for nstpbp177 synthesis. (iii) Pharmacological and toxicological analysis of target compounds: these tasks will be proposed by professor Liu SH from department of toxicology of College of Medicine, Taiwan University. (iv) Preclinical studies will be completed by collaborations in order to fasten the research accomplishments in order to evaluate marketing values of lead compounds. This integrated project outcomes will facilitate the bio-technology promotion especially in pharmaceutics. Research and development on the anti-diabetic and anti-lipidemia new drugs will also improve the pharmaceutical economic benefits in Taiwan.