

• 計畫中文名稱	Indirubin 及 Curcumin 在脊髓損傷之研究(I)		
• 計畫英文名稱	Preclinical Study of Indirubin and Curcumin in Spinal Cord Injury (I)		
• 系統編號	PC9706-0429	• 研究性質	基礎研究
• 計畫編號	NSC96-2314-B038-017-MY3	• 研究方式	學術補助
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• 執行機構	臺北醫學大學傷害防治學研究所		
• 年度	97 年	• 研究經費	1120 千元
• 研究領域	臨床醫學類		
• 研究人員	洪國盛,邱文達		
• 中文關鍵字	細胞凋亡；curcumin；indirubin；脊髓損傷；神經保護		
• 英文關鍵字	apoptosis；curcumin；indirubin；spinal cord injury；neuroprotection		
• 中文摘要	<p>Curcumin 可抑制細胞凋亡，文獻上也證實 curcumin 可保護細胞防止凋亡。在腦部外傷動物實驗證實 curcumin 提供神經保護及發炎抑制之功用。而目前對 curcumin 治療是否可促進外傷性脊髓受傷之功能恢復並無定論。為了評估 curcumin 是否可促進脊髓受傷之預後，我們將研究大白鼠脊髓半切之動物模式。在 curcumin 腹腔注射之後吾人將研究此脊髓受傷模式中發炎及細胞凋亡之情形。這些結果將作為脊髓損傷病人，另一治療選擇之理論根據，尤其在功能恢復，長期神經保護，抗發炎以及抑制細胞凋亡等功能上，這些療效之探討。Indirubin 乃從傳統中藥青黛所發現，並被證實對許多慢性疾病具有療效。Indirubin 之結構具有潛在 CDK 抑制之功能。類似其他的 CDK 抑制劑，Indirubin 也是 GSK3β 之有效抑制劑。此外，GSK3β 與 CDK5 可造成 tau 蛋白之不正常過磷酸化而堆積。Tau 過磷酸化也是脊髓損傷後及 Alzheimer 』s disease 之重要致病機轉及診斷依據。Indirubin 恰可同時抑制 GSK3β 和 CDK5 二路徑，進而防止 tau 病變。本研究將探討 Indirubin 在大鼠培養皮質神經元中之神經保護機轉。實驗結果將可成為 Indirubin 治療神經損傷之理論基礎，及前期臨床試驗之根據。第一年: Curcumin 動物實驗第二年: Indirubin 動物實驗第三年: 機轉實驗</p>		
• 英文摘要	<p>Curcumin (1,7-bis[4-hydroxy 3-methoxy phenyl]-1,6-heptadiene-3,5-dione) is a common dietary pigment and spice, and used as a traditional Indian medicine. Curcumin shows a variety of pharmacological effects, including anti-inflammatory, anticarcinogenic, anti-infectious, antioxidant, and hypocholesterolemic activities. Recent studies have shown that curcumin had anti-apoptotic effect, both dexamethane-induced apoptosis in rat thymocytes and chemotherapy-induced apoptosis in breast cancer cells were blocked by curcumin. Curcumin can also prevent ultraviolet irradiation-induced apoptotic changes, including loss of mitochondrial membrane potential (MMP), mitochondrial release of cytochrome C, and an increase of reactive oxygen species (ROS) formation, etc. However, whether curcumin could provide protection against apoptosis induced by spinal cord injury (SCI) is still unknown. Indirubin, a 3, 2 』 bisindole isomer of indigo, has originally been identified as the active principle of a traditional Chinese preparation and has been proven to exhibit effectiveness in various chronic diseases. Indirubin was detected to represent a novel lead structure with potent inhibitory potential towards cyclin-dependent kinases (CDKs). Like some other agents inhibiting cyclin-dependent kinases, these compounds were also found to be highly effective inhibitors of glycogen synthase kinase 3β (GSK3β). Furthermore, GSK3βtogether with CDK5 is responsible for most of the abnormal hyperphosphorylation of the microtubule-binding protein tau observed in paired helical filaments, which are diagnostic for spinal cord injury and Alzheimer 』s disease. Indirubin may inhibit both pathways of GSK3βand CDK5, and thus prevents tauopathy. To delineate the nature and mechanism of curcumin and indirubin in SCI, we will evaluate the effects of intraperitoneal curcumin or indirubin injection on rats after spinal cord hemisection. The specific aims were to answer the following questions: (1) Do alterations in motor function occur after curcumin or indirubin treatment? (2) How about the changes of neuron survival by curcumin or indirubin on cord hemisection? (3) Could curcumin or indirubin inhibit glial scar and</p>		

microglia activation after SCI? (4) Do cleavage of caspase-9, Bcl2 and apoptosis change in curcumin or indirubin treated group compared with vehicle controls? The overall objective of this study is to determine the neuroprotective, anti-inflammatory and anti-apoptotic effects of curcumin and indirubin in SCI.