• 系統編號	RC9008-0433		
• 計畫中文名稱	斑蝥胺素衍生物以及相關酸酐胺素的合成及其活性評估		
• 計畫英文名稱	Synthesis of Cantharidinimide Derivatives and Related Acid Anhydrided Imides and Their Bioactivity		
• 主管機關	行政院國家科學委員會	• 計畫編號	NSC89-2314-B038-018
• 執行機構	台北醫學院藥學研究所		
• 本期期間	8808 ~ 8907		
• 報告頁數	12 頁	• 使用語言	中文
• 研究人員	林本元 Lin, Pen-Yuan		
• 中文關鍵字	斑蝥素胺；抗腫瘤活性；細胞毒性		
• 英文關鍵字	Cantharidinimide；Antitumor activity；Cytotoxicity		

• 中文摘要

斑蝥素（Cantharidin）爲昆蟲斑蝥（Spanish fly, Lytta caragarae p.）或豆斑蝥（Epicauta gorhami）的主要成分，其毒性高，且爲強烈皮夫刺激劑，因毒性太強而無法應用於實際臨床治療，但有些報導其胺素的衍生物，如斑蝥胺素及 N-甲基斑蝥素胺等，其毒性低，且具抗肝癌作用，即在組織培養中對小白鼠的蛋白酵素（Protein phosphatase）有抑制作用以及具抗 KB 細胞作用。本計畫合成數種斑蝥胺素類化合物以及相關的胺素，例如 Phthalic, Himic, Citraconic imides。我們發現部分斑蝥胺素以及其它胺素，尤其具 NO/sub 2/基團之 Imide 具抗 Hep-3B 及 SK-Hep-1 之肝癌細胞及抗凝血作用並對 Xanthine oxidase 有明顯作用。本實驗以 in vitro 方式進行斑蝥胺素的抗腫瘤篩選，以 MTT 呈色分析法檢測藥物對癌細胞的毒殺作用，以 FACS 分析 imides 對癌細胞的細胞週期影響，以 Anti-CD11b monoclonal antibody 測定藥物對 HL-60 細胞分化的影響，並以 Soft agar clonogenic assay 分析藥物殺死癌細胞的作用。在 in vivo 中用小鼠進行活體的抗腫瘤試驗。

• 英文摘要

Cantharidin is the active principle of Lytte caragarae, Mylabris phalerata and Epicauta gorhami and various other insect species. According to the previous reports that cantharidin and their analogue showed to exhibit a wide spectrum of biological activities including antitumor properities. Its vesicant and toxic properties make it clinical activity useless. Several of cantharidinimides without the two methyl groups show avticonvulsant activity, N-methylcantharidinimide show less toxic and inhitory action on tumor S-180 in animal and H-22 tumor cell in rat and parts of cantharidinimides derivatives showed antihepatoma action on Hep-3B and SK-Hep-1 liver cancer cells. Here we used cantharidin, phthalic anhydride, himi anhydride, citraconic anhydride etc. as

starting material and diaminobenzene or ortho, meta and para aminobenzylamines and diaminoanilines derivatives as amines sources to synthesis various other cantharidinmides and imides by heated at ca. 200℃ in base condition. We found that some imides are less toxic and more effect to cancer cells, Hep-3B and Sk-Hep-1 when functional NO/sub 2/ existed and some imides showed effects on xanthine oxidase. The aim of this study is to synthesize and screen some less toxic and more effect new cantharidinimides superior to those currently available for the treatment of cancer. We study in this project in vitro to screen antitumor activity, cytotoxic activity assay by MTT assay, analysis of DNA profile by FACS (Fluorenscence-activated cell sorting), Detenction of the differentiation f HL-60 cell by anti-CD 11b monoclonal antibody and formation of colony in soft agar. In vivo we use rats for evalution of antitumor activity.