系統編號	RN9311-0153
• 計畫中文名稱	Flavone 類植物成份之藥性開發---Alpha-naphthoflavone 之心血管疾病預防作用及抗癌潛力之研究
• 計畫英文名稱	Mechanism of Flavone Derivatives---Alpha-Naphthoflavone on Cardiovascular Protection and Cancer Prevention
• 主管機關	行政院國家科學委員會 • 計畫編號 NSC91-2320-B038-039
• 執行機構	臺北醫學大學藥學系
• 本期期間	9108 ~ 9207
• 報告頁數	18 頁 • 使用語言 中文
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• 中文關鍵字	心血管疾病; 一氧化氮; 血管放鬆; 抗血栓; 抗氧化; 抗基因毒性; 抗血管新生; 7,8-苯并黃酮
• 英文關鍵字	Cardiovascular diseases; Nitric Oxide; Vasorelaxation; Anti-thrombsis; Antioxidant; Anti-genotoxicity; Anti-angiogenesis; Naphthoflavone
• 中文摘要	Flavonoids 類化合物是廣泛存在於天然食物中的成份，目前在自然界存在的 flavonoids 約有四千多種已被分離出來，而真正被研究過的 flavonoids 卻只有少數的幾種。這些研究結果證實了此類化合物可能具有抗心血管疾病、抗氧化、抗病毒以及抗癌等作用的潛力，也讓多數學者認爲 flavonoids 具有相當大的醫療效益，值得投入更多的研究與開發。α-naphthoflavone 爲典型的 flavonoids 類化合物，曾有報導指出 α-naphthoflavone 可抑制一些致癌物因代謝活化後所產生的毒性作用，然而並沒有其它關於 α-naphthoflavone 是否與抗心血管疾病、抗氧化、抗病毒等相關聯的研究。在本計劃中我們首次發現了 α-naphthoflavone 可在血管內皮細胞刺激一氧化氮的生成，活化 guanylate cyclase 與 nitric oxide synthase 的活性。在分離出來的人類血小板實驗中亦可抑制血小板凝集因子(PAF)以及血栓素(Thrombin)所造成的凝集作用。顯示了 α-naphthoflavone 可能具有保護心血管疾病的功能，如抗血栓或降血壓等。除此之外，雖然有些報導指出 α-naphthoflavon 可能與抗癌作用有關，但並沒有完整的研究結果來証實它在癌症預防上的角色。因此在未來兩年，我們將以降低心血管疾病以及抗癌作用爲目的，進一步證實 α-naphthoflavone 在血管張力之調控與抗血栓作用，同時探討 α-naphthoflavone 與抗氧化、抗基因毒性、抗血管新生的關係。期望能開發出具多樣性效能之醫療用藥。
• 英文摘要	The effect of alpha-naphthoflavone (alpha-NF) on vascular function was studied in thoracic aorta isolated from rat and primary cultured human umbilical vein endothelial cells (HUVECs). alpha-NF dose-dependently induced relaxation of the phenylephrine

pre-contracted aorta in endothelium-dependent and independent manner at lower and higher concentrations, respectively. The cGMP, but not cAMP, content was increased significantly in alpha-NF treated aorta. Pretreatment with L-NAME or methylene blue significantly attenuated both alpha-NF induced vasorelaxation and the increase of cGMP content. The increase of cGMP content induced by alpha-NF was also inhibited when the extracellular Ca2+ was chelated with EGTA. These results suggested that the endothelium-dependent vasorelaxation induced by alpha-NF was most likely through the activation of nitric oxide synthase and guanylyl cyclase in Ca2+ dependent manner. In HUVECs, alpha-NF dose-dependently induced formation of NO and Ca2+ influx. The NO formation induced by alpha-NF was abolished when the extracellular Ca2+ was removed or when the HUVECs were pretreated with Ca2+ channel blockers, SKF 96365 and Ni2+, but not by L-type Ca2+ channel blocker verapamil. The Ca2+ influx, as measured by the 45Ca2+ uptake, induced by alpha-NF was also inhibited by SKF 96365 and Ni2+. Our data concluded that alpha-NF, at lower concentrations, induced endothelium-dependent vasorelaxation by promoting the extracellular Ca2+ influx in endothelium and the activation of the NO-cGMP pathway.