• 計畫中文名稱	疏水性與親水性咖啡酸酯對於黃嘌呤氧化脢之抑制作用		
• 計畫英文名稱	Xanthine Oxidase Inhibition of Hydrophobic and Hydrophilic Ester of Caffeic Acid		
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• 研究人員	林俊茂		
• 中文關鍵字	抗氧化;咖啡酸;綠原酸;高通量;活性氧自由基;表面電漿共振;黃嘌呤氧化?		
• 英文關鍵字	antioxidant; caffeic acid; chlorogenic acid; high throughput; reactive oxygen species; SPR; xanthine oxydase		
• 中文摘要	咖啡酸(caffeic acid)、caffeic acid phenethyl ester(CAPE)、綠原酸(chlorogenic acid)等是已被明確分離並鑑定的天然物有效成分。其基本結構都是屬於 C6-C3 phenylpropanoid,CAPE是以 phenethyl 酯化咖啡酸,具有增加的疏水性特徵;而綠原酸是以 quinic acid 酯化咖啡酸,具有增加的親水性特徵。在本實驗室先前的研究報告中,建立了一套解釋 C6-C3 phenylpropanoid在抑制黃嘌呤氧化酶的立體化學理論。其中,帶有疏水性基團的扁平結構對於結合至活性中心是有幫助的,因此能達到較佳的抑制活性,對於大部分的 C6-C3 phenylpropanoid是適用的結論。據此,綠原酸帶有親水性的非扁平結構取代基,原來推測應有很差的黃嘌呤氧化酶抑制活性,然而很有趣的,綠原酸卻有較咖啡酸更強的黃嘌呤氧化酶抑制活性。顯然的,雖然是類似的結構,但是綠原酸卻是透過不同於咖啡酸、CAPE的抑制機制達到黃嘌呤氧化酶抑制活性。由於黃嘌呤氧化酶的產物包含活性氧自由基及尿酸,而綠原酸本身又是不錯的自由基清除者,如今意外的又發現其具有很強的黃嘌呤氧化酶的抑制活性。因此探討其不同於其他 C6-C3 phenylpropanoids的機制後,對於涉及黃嘌呤氧化酶相關疾病的新藥開發將有所幫助。表面電漿共振技術是一無需標幟值測結合動力學的高敏度篩選策略。黃嘌呤氧化酶抑制劑已經常用於各種醫療應用,黃嘌呤氧化酶抑制劑的高通量篩選將有益於新藥開發。我們將開發製作以表面電漿共振技術爲值測基準的黃嘌呤氧化酶晶片,該晶片將可提供基礎研究上進行酵素動力學的平台,及藥物開發上高通量篩選藥物的平台。		
• 英文摘要	Caffeic acid \(\) caffeic acid \(\) caffeic acid phenethyl ester(CAPE) \(\) chlorogenic acid represent identified natural polyphenols. The chemical structures		

of caffeic acid, CAPE, and chlorogenic acid are categorized in C6-C3 phenylpropanoids and bear two hydroxyls on the benzene rings. CAPE is phenethyl ester of caffeic acid that results in increased hydrophobicity. In contrast, chlorogenic acid is quinilic ester of caffeic acid that results in increased hydrophilicity. In our previous report, structure-activity relationships of caffeic acid analogues on binding to the active site of xanthine oxidase (XO) and the stereochemistry of various substitution groups interactions with residues of XO has been concluded. Additional hydrophobic stabilization occurred due to the hydrophobic pocket of XO and the phenethyl group of CAPE. Because caffeic acid lacks this extra stabilization, it exhibited lower inhibition potency toward XO than CAPE. Basis on the conclusion it is expected that chlorogenic acid bearing a bulky non-planner quinilic ester would display very weak inhibition of XO. Interestingly, our preliminary results show that chlorogenic acid exhibits stronger XO inhibition activity than caffeic acid. It implicates that chlorogenic acid inhibits XO via binding to the sites different to those of caffeic acid and CAPE. XO is an important source of free radicals and uric acid that has been reported in various physiological and pathological models. Chlorogenic acid has been shown to be effective in scavenging ROS. Now further disclosing the detailed binding mechanisms toward XO will be beneficial for new drug development for XO-associated diseases. Surface plasmon resonance (SPR) technology is expanding strategies for a sensitive screening method based on label-free detection of binding kinetics. Xanthine oxidase inhibitors have been used on various therapeutically applications. High throughput screening of Xanthine oxidase inhibitors will be beneficial on new drug development. We will generate xanthine oxidase chips besis on SPR technology that will provide platform for enzyme kinetic study in basic research and for high throughput drug screening in medicinal development.