• 系統編號	RB8601-1215
• 計畫中文名稱	一些抽自蓼苓白朮湯的類黃鹼素之氣管鬆弛作 用(III)
• 計畫英文名稱	Relaxant Effects of Some Flavonoids Isolated from Sun-Liung-Pai-Tsu-Tang in Trachea. (III)
• 主管機關	行政院國家科學委員會
• 計畫編號	NSC84-2331-B038-027-M03
• 執行機構	私立台北醫學院
• 本期期間	8308 ~ 8407
• 報告頁數	0 頁
• 使用語言	中文；英文
• 研究人員	柯文昌 Ko, Wun-Chang
• 中文關鍵字	類黃素母酮；氣管鬆弛作用劑；鬆弛作用；蓼苓白朮湯
• 英文關鍵字	Flavonoid；Trachea relaxant；Relaxation effect；Sun-Liung-Pai-Tsu-Tang；Liquritin；Isorhamnetin
• 中文摘要	從參苓白朮散所分離出的五種類黃鹼素,分別爲 Isorhamnetin、Hesperetin、Hesperidin、Naringin 及 Liquiritin,其中以 Isorhamnetin 的氣管鬆弛作用最強,它對 Histamine(30.mu.M)、Carbachol(0.2.mu.M)及 Isotonic KCl(17.5mM)預先收縮的 IC/sub 50/分別爲 13.98.plmin.2.54 (n=7)、14.56.plmin.0.92(n=6)及 21.15.plmin.2.92 (n=9).mu.M,彼此間無意義差,顯示無特殊選擇性。 Isorhamnetin 的鬆弛作用無須仰賴上皮細胞,亦與.beta.-受容體活化或鉀通道開啓無關。它的鬆弛作用不被 2',5'-dideoxyadenosine (10.mu.M)、Methylene blue(25.mu.M)或 Oxyhemoglobin(10.mu.M)所影響,顯示它的鬆弛作用並非活化 Adenylate cyclase 或 Guanylate cyclase 而來。但它(30-100.mu.M)類似 Protein kinase C(PKC)抑制劑 Staurosporine (0.003-1.mu.M)能劑量依存性地抑制 PKC 活化劑 Phorbol 12-myristate 13-acetate(10.mu.M)引起的氣管收縮,因此它對 PKC 可能也有抑制作用,而使氣管平滑肌鬆弛。因 Isorhamnetin (15.mu.M)也會使 Staurosporine(1.mu.M);或 Nifedipine(10.mu.M)及 Staurosporine(1.mu.M)之共同存在下的最大鬆弛進一步鬆弛,因此不能排除它抑制 PKC 外,尚有其他鬆弛機轉。Isorhamnetin(7.5 及 15.mu.M)像 3-isobutyl-1-methyl-xanthine(3 及 6.mu.M)能使累積用量方式加入的 Forskolin 或 Nitroprusside 之對數劑量-反應曲線向左平行移動,而且呈劑量依存性,顯示它也有可能會抑制 Phosphodiesterase(PDE)。 參苓白朮散在臨床上對氣喘病人能減少支氣管擴張劑的使用,主要是因含 Isorhamnetin 之故,它使氣管鬆弛的可能機轉包括抑制外鈣流入和內鈣釋放、抑制 PKC 及抑制 PDE 而來。
• 英文摘要	The relaxant effect of isorhamnetin in trachealis was the most largest among these five flavonoids, isorhamnetin, hesperetin, hesperidin, naringin and liquiritin which have been isolated from a Chinese medicine "Sun-Liung-Pai-Tsu-San". Its IC/sub 50/ was 13.98.plmin.2.54 (n=7), 14.56.plmin.0.92 (n=6), and 21.15.plmin.2.92 (n=9).mu.M for the precontractions induced by histamine (30.mu.M), carbachol (0.2.mu.M) and

isotonic KCl (17.5mM), respectively. There was no significant difference among them. It shows that isorhamnetin has no special selectively to these three contractile agents. The relaxant effect of isorhamnetin was epithelium-independent, and was not correlated to .beta. adrenoreceptor activation or potassium channel opening. Its relaxant effect was not affected by 2',5'-dideoxyadenosine (10.mu.M), methylene blue (25.mu.M) or oxyhemoglobin (10.mu.M). It suggests that the relaxant effect of isorhamnetin may be not via activation of adenylate cyclase or guanylate cyclase. However, isorhamnetin, similar to protein kinase C (PKC) inhibitor staurosporine (0.003-1.mu.M), dose-dependently inhibited the precontraction induced by phorbol 12-myristate 13-acetate (10.mu.M), an activator of PKC in guinea pig trachealis. Therefore the relaxant effect of isorhamnetin may also be via inhibiting the PKC activity. However, isorhamnetin (15.mu.M) produced further relaxation after staurosporine (1.mu.M)---or both nifedipine (10.mu.M) and staurosporine (1.mu.M)-induced maximal relaxations. Therefore it may have other relaxing mechanism except inhibiting PKC. Isorhamnetin (7.5 and 15.mu.M), similar to 3-isobutyl-1-methyl-xanthine (3 and 6.mu.M), dose-dependently and parallelly leftward shifted the log dose-response curves of forskolin and nitroprusside. It shows that isorhamnetin may also inhibit activity of phosphodiesterase (PDE). Isorhamnetin, the most potent relaxant constituent, isolated from a Chinese medicine "Sun-Liung-Pai-Tsu-San", which has been clinically reported to lessen the using of bronchodilators in asthmatics, may relax tracheali via inhibiting calcium influx and calcium release from intracellular calcium stores, inhibiting PKC and inhibiting PDE.