3-Methylquercetin 對離體天竺鼠氣管的鬆弛作用

Relaxant Effect of 3-Methylquercetin in Isolated guinea Pig Trachea

中文摘要

3-Methylquercetin (3-MQ)可使離體天竺鼠氣管產生鬆弛作用，它對 histamine (30 μM、carbachol(0.2 μM)及 isotonic KCI(17.5mM)預先收縮的 IC50 分別爲 13.98±2.54 (n=7)、14.56±0.92 (n=6)及 21.15±2.92 (n=9) μM，彼此間無意義差，顯示無特殊選擇性。

3-MQ (30 μM)預處理 20 分鐘，對累加 histamine 引起的收縮呈非競爭性的抑制，求得的 pD2'值爲 5.29±0.15 (n=8)，有意義的大於鬆弛 histamine (30 μM)預縮的-logIC50，顯示對內鈣釋放的抑制較有選擇性。

3-MQ (30 μM)對高鉀(60mM)無鈣溶液，因外鈣增加而引起的收縮，能有意義的抑制，顯示它會抑制外鈣經由 voltage dependent calcium cliannel(VDC)的流入。然而對 histamine (30 μM)的預縮，它能夠使 nifedipine (10 μM)的最大鬆弛進一步鬆弛，顯示它除了可能抑制 VDC 外尚有其他鬆弛機轉。

3-MQ 的鬆弛作用無須仰賴上皮細胞，亦與β-受體活化或鉀通道開啓無關。它的鬆弛作用不被 2',5'-dideoxyadenosine (10 μM)、methylene blue (25 μM)或 oxyhemoglobin (10 μM)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 μM)類似 protein kinase C (PKC)抑制劑 staurosporine (0.003-1 μM)能劑量依存性地抑制PKC活化劑phorbol12-myristate 13-acetate (10 μM)引起的氣管收縮，因此它對 PKG 可能也有抑制作用，而使氣管平滑肌鬆弛。因 3-MQ (15 μM)也會使 staurosporine (1 μM);或 nifedipine (10 μM)及 staurosporine (1 μM)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。3-MQ (7.5 及 15 μM)像 3-isobutyl-1-methyl-xanthine (3 及 6 μM)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)。

3-MQ 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

3-Methylquercetm (3-MQ) had relaxant effects in guinea pig trachealis. Its IC50 was 13.98±2.54 (n=7), 14.56±0.92 (n=6) and 21.15 ± 2.92 (n=9) μM for the precontractions induced by histamine (30 μM), carbachol (0.2 μM) and isotonic KC1 (17.5 mM), respectively. There was no significant difference among them. It shows that 3-MQ has no special selectivity to these three contractile agents.

Pretreatment of tracheahs with 3-MQ (30 µM) for 20 min non- competitively inhibited the contractions induced by cumulative histamine. Its calculated pD2' value was 5.29 ±0.15 (n=8). It is significantly greater than the -logIC50 for the precontraction induced by histamine (30 µM). It shows that 3-MQ selectively inhibits more on the calcium release from intracellular calcium stores. 3-MQ (30 µM) significantly inhibited the cumulative calcium-induced contractions in guinea pig trachealis, incubated in high potassium (60 mM) calcium-free medium. This suggests that 3-MQ may inhibit calcium influx through voltage dependent calcium channels (VDC). However, it produced further relaxation after nifedipine (10 µM)-induced maximal relaxation. This suggests that 3-MQ may have other relaxing mechanism in addition to its inhibiting VDC.
The relaxant effect of 3-MQ was epithelium-independent, and was not correlated to β adrenoreceptor activation or potassium channel opening. Its relaxant effect was not affected by 2',5'- dideoxyadenosme (10µM), methylene blue (25 µM) or oxyhemoglobin (10 µM). The data suggest that the relaxant effect of 3-MQ may be not via activation of adenylate cyclase or guanylate cyclase. However, 3-MQ, similar to protein kinase C (pKC) inhibitor staurosporme (0.003-1 µM), dose-dependently inhibited the precontraction induced by phorbol 12-myristate 13- acetate (10 µM), an activator of PKC in guinea pig trachealis. Therefore the relaxant effect of 3-MQ may also be via inhibiting the PKC activity. However, 3-MQ (15 µM) produced further relaxation after the relaxant effect produced by either staurosporme (1 µM)- or nifedipine (10 µM) and staurosporine (1 µM). Therefore it may have additional relaxing mechanism. 3- MQ (7.5 and 15 µM), similar to 3-isobutyl-1-methyl-xanthine (3 and 6 µM), parallelly shifted leftward the log dose-response curves of forskolin and nitroprusside in a dose-dependent phasion. This shows that 3-MQ may also inhibit activity of phosphodiesterase (PDE).
3-MQ may relax tracheali via inhibition of calcium influx, calcium release from intracellular calcium stores, PKC, and PDE