Mechanisms of relaxant action of 3-O-methylquercetin in isolated guinea pig trachea

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摘要

Abstract

We investigated the mechanisms of action of 3-O-methylquercetin (3-MQ), isolated from Rhamnus nakaharai (Hayata) Hayata (Rhamnaceae) which is used as a folk medicine for treating constipation, inflammation, tumors and asthma in Taiwan. The tension changes of tracheal segments were isometrically recorded on a polygraph. 3-MQ concentration-dependently relaxed histamine (30 μM)-, carbachol (0.2 pM)- and KCI (30 mM)-induced precontractions, and inhibited cumulative histamine-, and carbachol-induced contractions in a non-competitive manner. 3-MQ also concentration-dependently and non-competitively inhibited cumulative Ca2+-induced contractions in depolarized (K+, 60 mM) guinea-pig trachealis. The nifedipine (10 μM)-remaining tension of histamine (30 μM)-induced precontraction was further relaxed by 3-MQ, suggesting that no matter whether VDCCs were blocked or not, 3-MQ may have other mechanisms of relaxant action. The relaxant effect of 3-MQ was unaffected by the removal of epithelium or by the presence of propranolol (1 pM), 2',5'-dideoxyadenosine (10 μM), methylene blue (25 μM), glibenclamide (10 μM), Nω-nitro-L-arginine (20 μM), or α-chymotrypsin (1 U/ml). However, 3-MQ (7.5-15 pM) and IBMX (3-6 μM). a positive control, produced parallel and leftward shifts of the concentration-response curve of forskoline (0.01-3 μM) or nitroprusside (0.01-30 μM). 3-MQ or IBMX at various concentrations (10-300 pM) concentration-dependently and significantly inhibited cAMP- and cGMP-PDE activities of the trachealis. The IC50 values of 3-MQ were estimated to be 13.8 and 14.3 μM, respectively. The inhibitory effects of 3-MQ on both enzyme activities were not significantly different from those of IBMX, a non-selective PDE inhibitor. The above results reveal that the mechanisms of relaxant action of 3-MQ maybe due to its inhibitory effects on both PDE activities and its subsequent reducing effect on [Ca2+] of the

trachealis.