Mechanism of relaxant action of leuteolin in isolated guinea pig trachea

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摘要.

Abstract

We have investigated the mechanisms of action of luteolin, a flavone found in Perilla frutescens, a Chinese herbal medicine for treating asthma. In fact, luteolin occurs mostly as a glycoside in many plant species. The tension changes of tracheal segments were isometrically recorded on a polygraph. Luteolin concentration-dependently relaxed histamine (30 pM)-, carbachol (0.2 pM)- and KCl (30 mM)-induced precontractions, and inhibited cumulative histamine- and carbachol-induced contractions in a non-competitive manner. Luteolin also concentration-dependently and non-competitively inhibited cumulative Ca2+-induced contractions in depolarized (K+, 60 mM) guinea-pig trachealis. The nifedipine (10 pM)-remaining tension of histamine (30 μM)-induced precontractions was further relaxed by luteolin, suggesting that no matter whether VDCCs were blocked or not, luteolin may have other mechanisms of relaxant action. The relaxant effect of luteolin was unaffected by the removal of epithelium or by the presence of propranolol (1 pM), 2',5'-dideoxy-adenosine (10 μM), methylene blue (25 pM), glibenclamide (10 pM), Nω-nitro-1-arginine (20 μM), or α-chymotrypsin (1 U/mL). However, luteolin (10-20 pM) produced parallel and leftward shifts of the concentration-response curve of forskolin or nitroprusside. Luteolin or IBMX at various concentrations (10-300 μM) concentration-dependently and significantly inhibited cAMP- and cGMP-PDE activities of the trachealis. The IC50 values of luteolin were estimated to be 32.4 and 34.6 pM, respectively. IBMX at various concentrations (10-300 μM) selectively inhibited neither cAMP-, nor cGMP-PDE activity. In contrast to IBMX, luteolin at 100 and 300 μM more potently ($P < 0.05$) inhibited cGMP-, than cAMP-PDE activity. The above results indicate that the mechanisms of relaxant action of luteolin may be due to its inhibitory effects on both PDE activities and its reduction on [Ca2+]i of the trachealis.