Effect of deoxypurine and deoxypyrimidine compounds on the vascular responsiveness of bovine coronary and lingual arteries

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As little is known about the vascular effects of 2′-deoxy derivatives of purine and pyrimidine compounds, some derivatives have been examined on bovine coronary and lingual artery (1–1·5 mm o.d.) strips prepared and mounted as described by Scholar and Dalske 1979).

Controls were incubated with an equal volume of the appropriate solvent (50% ethanol).

Compounds used included deoxyadenosine, deoxyguanosine, deoxyguanosine 5′-phosphate (dGMP), deoxyinosine, deoxyinosine 5′-phosphate (dIMP), deoxythymidine, deoxycytidine and deoxyuridine (P-L Biochemicals). Histamine dihydrochloride was obtained from Nutritional Biochemicals Co. Dipyridamole (Persantin) a gift from Boehringer-Ingelheim Ltd, when used, was at 10^{-4} M and was added 30 min before a contraction was induced. All solutions were made fresh daily; working concentrations of the compounds were made by dilution of concentrated stock solutions stored frozen at − 20 °C.

Data were expressed as percent relaxation (mean ± s.e.) induced relative to the initial contraction by histamine or KCl in each individual strip and were analysed by Student's *t*-test.

Deoxyadenosine, deoxyguanosine, and deoxyinosine produced significant ($P < 0.05$) and approximately equal relaxation of the bovine lingual artery at concentrations greater than 10^{-6} M (10–15% relaxation increasing to 40% at 10^{-4} M Fig. 1). dGMP and dIMP produced similar effects. Deoxythymidine, deoxycytidine and deoxyuridine produced about the same degree of relaxation, although the maximum responses (about 30%) were less than those of the deoxypurine compounds. Dipyridamole had no effect on the relaxation produced by any of the deoxy compounds used. Neither the deoxypurine nor the deoxypyrimidine compounds produced significant relaxation of the coronary artery.

These results are the first indication that deoxypurine and deoxypyrimidine compounds are active on vascular smooth muscle. Although the concentrations at which the deoxy compounds produced their effects are relatively high, there are circumstances which could result in elevated concentrations of these compounds in vivo. Certain immunodeficiency diseases produce deoxynucleosides in amounts several hundredfold above normal (Mitchell et al 1978). Several cytotoxic drugs used as antineoplastic or immunosuppressive agents are deoxynucleoside analogues and these affect vascular smooth muscle. For example, cyclocytidine, a depot form of arabinofuranosylcytosine (ara-C) has been shown to affect noradrenaline release from adrenergic neurons (Burks et al 1978).

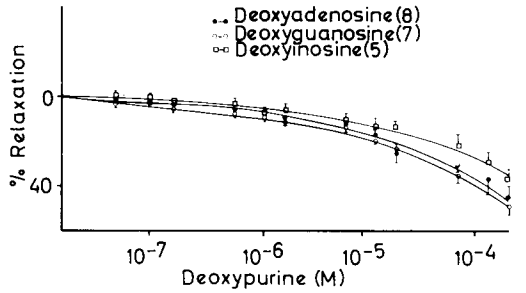

FIG. 1. Effect of deoxyadenosine, deoxyguanosine and deoxyinosine on the preconstricted bovine lingual artery. Number of experiments in parentheses.

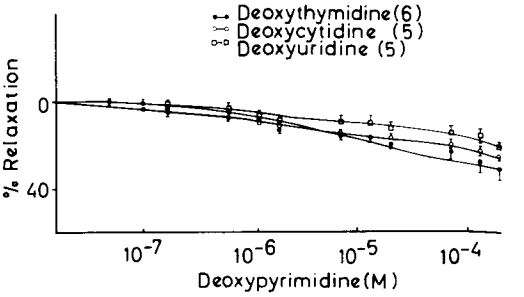

FIG. 2. Effect of deoxythymidine, deoxycytidine and deoxyuridine on the preconstructed bovine lingual artery. Number of experiments in parentheses.

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