CADMIUM AUGMENTS THE STIMULATION OF CHLORIDE SECRETION BY FORSKOLIN IN THE PERFUSED RECTAL GLAND OF SQUALUS ACANTHIAS

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We previously reported that cadmium reversibly blocks the effects of multiple agonists that inhibit forskolin-stimulated secretion in the rectal gland, including adenosine (Forrest et al., Center for Membrane Toxicology Studies Annual Report 1986), peptide YY (Grasso et al. Bull MDIBL 29:57, 1990) and somatostatin (Forrest et al. Bull MDIBL 30: 117, 1991). Blocking of the inhibitory effects of somatostatin was present even at low concentrations (5-25μM) of cadmium. We noted that the effects of cadmium to block the inhibitory effects of these agonists (adenosine, peptide YY, and somatostatin) in each instance occurred after a delay of 8-10 min following the addition of forskolin and the agonist (see Forrest et al. Bull MDIBL, 57, 1991) One interpretation of these studies is that cadmium blocks inhibition, at least in part, by augmenting forskolin-mediated secretion.

In the present studies, we examined whether low concentrations of cadmium could augment basal or forskolin-stimulated chloride secretion in the isolated perfused rectal gland.

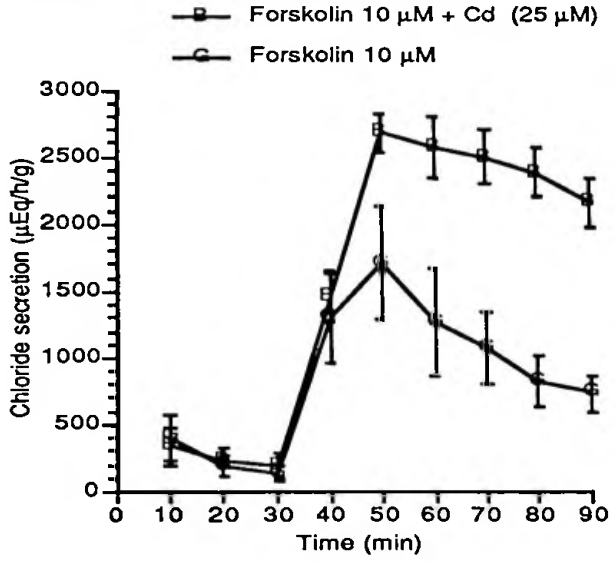

Figure 1. Effects of cadmium on basal and forskolin-stimulated chloride secretion ($p>0.05$ at 40 min and $p<0.01$ at 60-90 min).

In all experiments cadmium was added to the perfusion medium at the onset of the experiment. As shown in Figure 1 (left) cadmium (25μM) had no detectable effect on basal chloride secretion in the perfused gland. When forskolin (10 μM) was added after 30 min of basal secretion, the presence of cadmium (25μM) resulted in a definite and sustained augmentation of forskolin-stimulated chloride secretion (see Figure 1) This augmentation of secretion was not present during the first 10 min of perfusion with forskolin but was evident at all subsequent time points examined (50-90 min).

These findings suggest that at least a component of the effects of cadmium to block multiple inhibitory agonists (adenosine, peptide YY, somatostatin) may be explained by an effect of cadmium to augment forskolin-stimulated secretion. The diterpene forskolin stimulates adenylate cyclase by directly activating the

catalytic unit of cyclase and by interacting with the coupling of the Gs alpha subunit with the catalytic subunit. Both GTP binding proteins and the catalytic subunit of cyclase are known to have sites that are sensitive to divalent cations. Thus, the observed response could be due to an effect of cadmium on G protein or catalytic unit function or an effect of cadmium to block either the release or action of local inhibitory autacoids.

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