INHIBITORY EFFECT OF CHOLECYSTOKININ ON CHLORIDE SECRETION BY THE RECTAL GLAND OF SQUALUS ACANTHIAS

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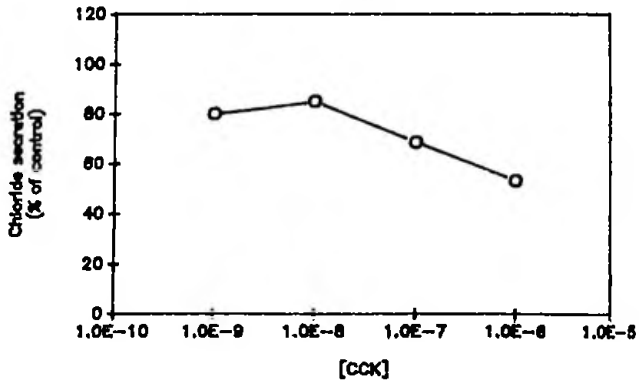
Among the many neurotransmitters present in nerves within the rectal gland is cholecystokinin. Cholecystokinin is a 33 amino-acid peptide found in the brain and in the gastrointestinal tract particularly in the duodenum and jejunum. In the brain it causes satiety and the release of oxytocin in rats and vasopressin in monkeys. In the gastrointestinal system it causes contraction of the gallbladder with the concomitant relaxation of the sphincter of Oddi and increases the hepatic secretion of bile. In the stomach it decreases motility. In the exocrine pancreas it is a weak stimulant of pancreatic secretion while it stimulates the release of insulin and glucagon from pancreatic islet cells. The effects of cholecystokinin on the rectal gland are not known. In these studies we examined the effect of cholecystokinin octapeptide (CCK) on chloride transport by the rectal gland.

Rectal glands were perfused in vitro by gravity, with shark Ringer's, at a pressure of 40 mm Hg and a temperature of 15°C. The secretion of chloride was stimulated with either vasoactive intestinal peptide or cyclic AMP from the beginning of the perfusion. Collections of rectal gland secretion were made every ten minutes and the volumes measured. Chloride in the secretion was measured by amperometric titration.

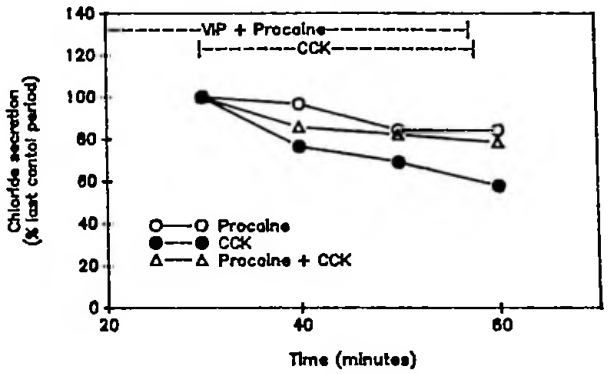
CCK had no effect on basal, unstimulated, chloride secretion. In glands stimulated with VIP it had a dose dependent inhibitory effect on the secretion of chloride. Figure 1 shows one representative experiment, out of six, depicting the dose related inhibition of chloride secretion by CCK in a gland stimulated with 10^{-9} M VIP. At a concentration of 10^{-6} M it caused a 50% decrease in the secretion of chloride, $p < 0.01$. Half maximal inhibition was seen at a concentration of 10^{-7} M. The effect was reversible.

Figure 1. Representative experiment, out of a total of six showing the dose dependent inhibitory effect of cholecystokinin (CCK) chloride secretion stimulated by VIP in isolated perfused rectal glands.



To determine whether the effect of CCK was mediated by the release of additional neurotransmitters from nerves within the gland, 10^{-2} M procaine was added to the perfusate to inhibit neurotransmitter release. As shown in a representative experiment in Figure 2, procaine prevented the inhibitory effect of CCK on VIP stimulated chloride secretion. This experiment suggested that the effect of CCK, like that previously demonstrated for bombesin, is mediated by the release of another neurotransmitter.

Figure 2. Representative experiment, out of a total of six, showing that procaine prevents the inhibitory effect of cholecystokinin on chloride secretion.



These experiments demonstrate that CCK, a peptide hormone, present in the nerves within the rectal gland reversibly inhibits stimulated chloride secretion by the rectal gland of the shark. The finding that the effect of CCK was blocked by procaine suggests that it does not exert its effect directly on the gland cells but requires the release of an additional neurotransmitter(s) from the nerves within the gland consistent with its effect to release oxytocin and vasopressin in the brain and insulin and glucagon in the endocrine pancreas. This observation is reminiscent of the inhibitory effect of bombesin on chloride secretion. Bombesin causes the release of somatostatin that mediates the inhibition. These experiments underline the complexity of the control of chloride secretion in the rectal gland of the shark where a variety of neurotransmitters are released in response to humoral and neural activity and serve as local regulators of secretion by the gland.

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