BOMBESIN INHIBITS STIMULATED CHLORIDE SECRETION BY THE RECTAL GLAND OF Squalus acanthias.

Patricio Silva, Patricio Silva, Jr, Judd Landsberg, Marcela Silva
Stephanie Lear and Franklin H. Epstein
Department of Medicine Beth Israel Hospital and Harvard Medical School, Boston, MA 02215

Bombesin is a tetradecapeptide present in nerve fibers in the rectal gland of the shark together with vasoactive intestinal peptide (VIP) (Holmgren et al., Cell Tissue Res 234:595, 1983). Initially found in the skin of anurans, it is a neurotransmitter present in vertebrate brain and gut. It is a potent stimulant of gastric and pancreatic secretions, that produces hypothermia, hypertension, antidiuresis and hyperglycemia and reduces net sodium and chloride reabsorption in dog jejunum (Barbezat et al., Dig Dis Sci 28:273, 1983).

Isolated rectal glands were perfused as previously described (Silva et al., Am J Physiol 233:F298, 1977). Bombesin administered as boluses (final concentration 10^{-4}M) or a constant infusion (final concentration 10^{-6}M) did not alter basal chloride secretion.

To test the effect of bombesin on stimulated secretion of chloride, rectal glands were perfused with VIP at a constant concentration of 2×10^{-9}M. To achieve relatively constant stimulation of chloride secretion in these conditions, albumin was added to the perfusate at a final concentration of 0.1 mg/ml in order to prevent the binding of VIP to the perfusion system. After thirty minutes of perfusion, a constant infusion of bombesin 8×10^{-7}M was added to the perfusate and continued for another thirty minutes after which perfusion was continued with VIP alone. Representative control and bombesin experiments are shown in Figure 1. Bombesin reduced the secretion of chloride by 53.8±4.4%, n=8, $p<0.01$. The effect of bombesin was rapidly reversible, with chloride secretion returning to the levels of control perfusions immediately after discontinuation of the bombesin infusion.

Because the effect of bombesin to inhibit the effect of VIP can take place before or after the generation of cyclic AMP we tested the effect of bombesin on cyclic AMP stimulated chloride secretion. Rectal glands were perfused with 5×10^{-5}M dibutyryl cyclic AMP and 2.5×10^{-4}M theophylline throughout the experiment. Bombesin 8×10^{-7}M was administered as a continuous infusion for thirty minutes, thirty minutes after beginning the experiment. At the end of the bombesin infusion the perfusion was continued with dibutyryl cyclic AMP and theophylline alone. Representative control and bombesin experiments are shown in Figure 2. Bombesin reduced the effect of dibutyryl cyclic AMP by 44.7±5.4%, n=6, $p<0.01$. As was the case with VIP the effect was reversible, but not as rapidly as with VIP.

Bombesin has no effect on basal chloride secretion but inhibits chloride secretion after stimulation with VIP and also after stimulation with cyclic AMP. These results suggest that bombesin exerts its effect at a site distal to that of the generation of cyclic AMP, an effect similar to that previously reported by us for somatostatin. Additional effects prior to the generation of cyclic AMP cannot be ruled out. Bombesin is present together with VIP, somatostatin and cholecystokinin in the nerve fibers within the rectal gland. Bombesin may be released together with VIP from the nerve endings in response to nerve stimulation or to increases in circulating ANP. We do not know yet whether bombesin's effect to inhibit chloride is direct or indirect. The similarity of its effect to that of somatostatin suggests that bombesin might inhibit chloride secretion by causing the release of somatostatin from the nerve fibers.

Figure 1

Effect of bombesin on the secretion of chloride by a rectal gland stimulated with VIP 4×10^{-8}M

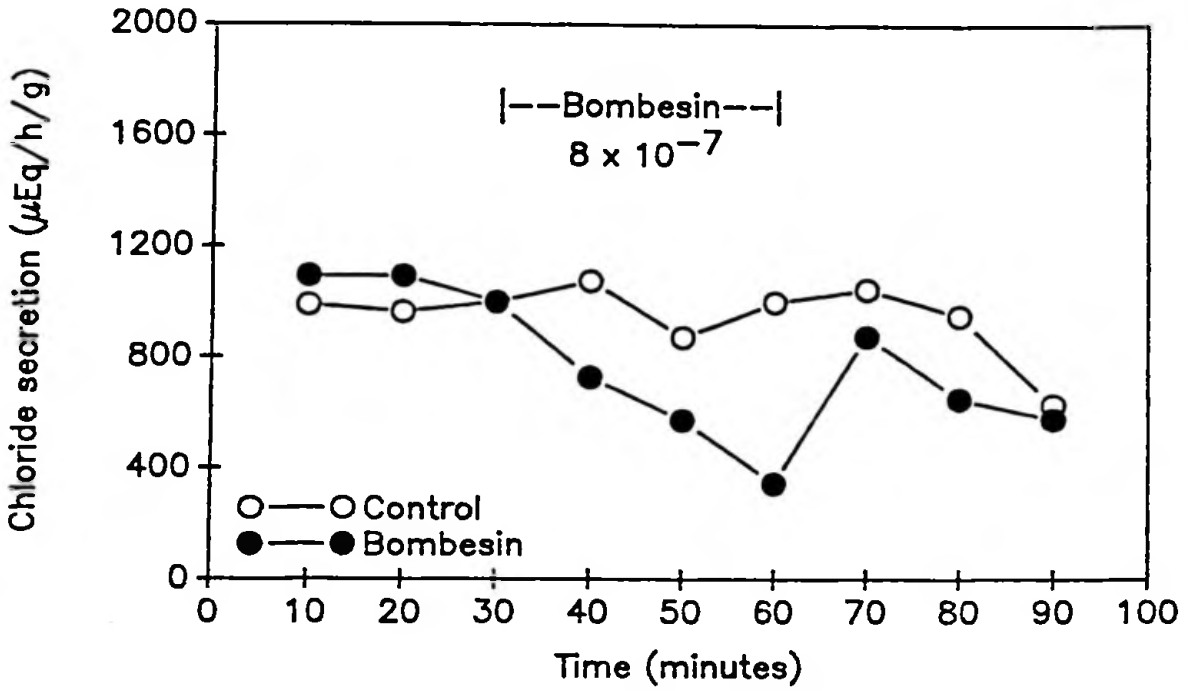
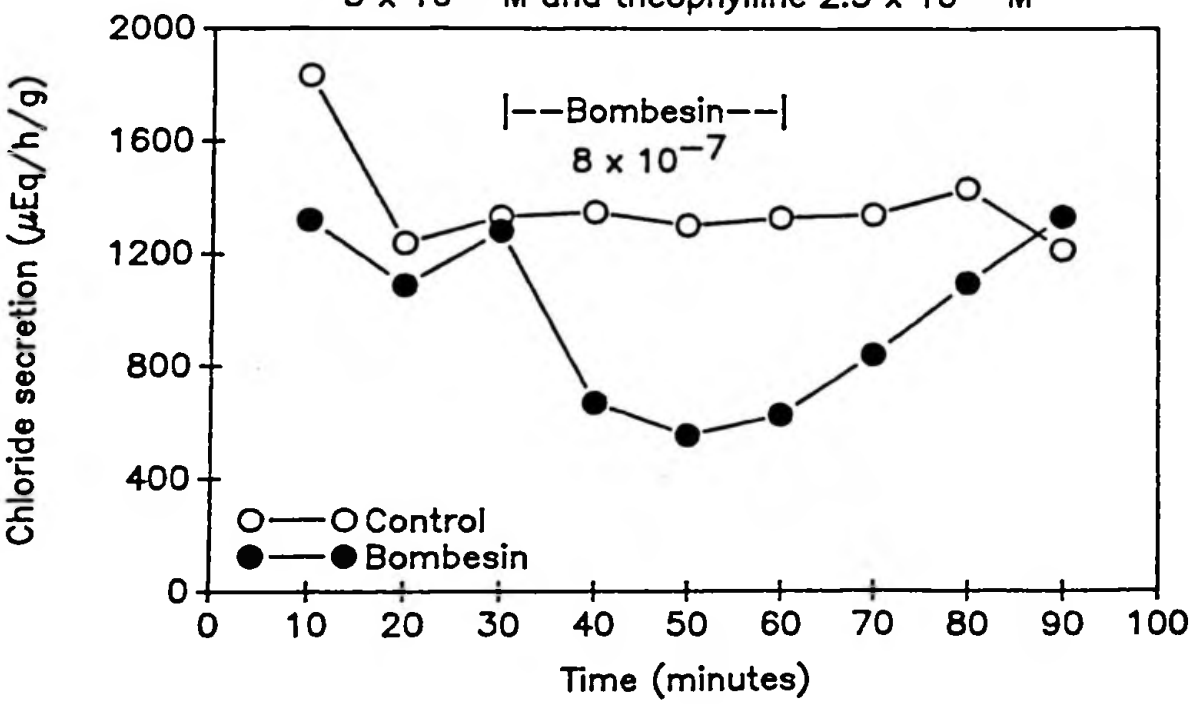


Figure 2

Effect of bombesin on the secretion of chloride by a rectal gland stimulated with dibutyryl cyclic AMP 5×10^{-5}M and theophylline 2.5×10^{-4}M



The observation that bombesin, present in the nerve fibers within the rectal gland together with VIP, has the capacity to inhibit the effect of VIP, suggests the potential for peptide mediated local modulation of transport.

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