IONIC BASIS OF SECRETORY RESPONSE TO PHYSIOLOGICAL CONCENTRATION OF CHOLECYSTOKININ OCTAPEPTIDE IN ISOLATED PERFUSED RAT PANCREAS.

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1. The CCK-8-induced secretory responses were gradually inhibited (a) when NaCl in the perfusing solution was totally replaced with equimolar LiCl (26 mM Na^+ remained), (b) when KCl was totally replaced with equimolar NaCl, and (c) when 1 mM ouabain was added to the perfusing solution. The inhibitory influence on fluid secretion was greater than that on protein output, and the protein concentration of the pancreatic juice became higher during these treatments known to inhibit Na^+, K^+-ATPase.
2. The CCK-8-induced secretory responses were immediately inhibited when NaCl was totally (9 mM Cl^- remained) and partially (35 mM Cl^- remained) replaced with Na Isethionate. An almost identical inhibitory influence on fluid secretion and protein output were observed: the protein concentration of pancreatic juice remained unchanged during the stimulation in this low Cl^- environment.
3. The CCK-8-induced fluid secretion was slightly and insignificantly decreased and the protein output remained unchanged when 0.1 mM amiloride, a blocker of Na^+-H^+ antiporter, was added to the perfusing solution.
4. The CCK-8-induced fluid secretion was increased in the initial phase and decreased in the later phase whereas the protein output was gradually decreased when 0.1 mM SITS (4-acetamido-4'-isothiocyano-2, 2'-disulfonic acid stilbene), a blocker of Cl^--HCO_3^- antiporter, was added to the perfusing solution.
5. The CCK-8-induced fluid secretion was significantly inhibited, and the protein output was slightly and insignificantly decreased when 0.1 mM furosemide, a blocker of Na^+-K^+-$2Cl^-$ symporter, was added to the perfusing solution.
6. From these results, a model of cellular events in stimulus secretion coupling activated by stimulation with CCK-8 at a physiological concentration in pancreatic acinar cells is proposed as follows. (a) The activities of Na^+, K^+-ATPase as well as other secondary Na^+ transporting mechanisms may be responsible primarily for fluid secretion and secondarily be involved in protein output. (b) The transcellular Cl^- transport may play a cardinal role both in fluid secretion and protein output. (c) The Cl^--HCO_3^- antiporter and the Na^+-K^+-$2Cl^-$ symporter may be involved while the Na^+-H^+ antiporter may play a minor role.