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INFLUENCES OF pH VALUE OF PERFUSING SOLUTION ON OXIDATIVE PHOSPHORYLATION PROCESS AND SECRETORY PROCESS IN THE ISOLATED PERFUSED RAT PANCREAS.

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Influences of extracellular pH value (pHe) on the oxidative phosphorylation process and the secretory process in the pancreatic acinar cell were examined by recording secretory responses, redox state of cytochromes, oxygen consumption, and ATP content in the isolated perfused rat pancreas.

1) Lowering the pHe value in a perfusing solution from 7.3 to 6.8 induced simultaneous oxidation of cytochrome a(a_3), b, and c+c_1, and further lowering to 6.0 induced larger oxidation of the cytochromes. Lowering the pHe value reduced oxygen consumption of the pancreas. On the contrary, raising the pHe value from 7.3 to 8.0 induced reduction of the cytochromes, and caused a slight increase in oxygen consumption.

2) Lowering the pHe value to 6.8 or to 6.0 significantly increased the ATP content.

3) Lowering the pHe value to 6.0 significantly inhibited pancreatic juice flow, protein output, and amylase output induced by continuous stimulation with 10^{-10} M cholecystokinin-octapeptide (CCK–8). On the contrary, raising the pHe value to 8.0 always inhibited pancreatic juice flow, protein output, and amylase output induced by CCK–8 (10^{-10} M).

4) Lowering the pHe value to 6.0 also reduced protein output to 20% of the control output induced by 2×10^{-11} M CCK–8 in the standard solution. Restoration of the pHe value from 6.0 to 7.3 after cessation of continuous CCK–8 stimulation caused a marked increase in protein output, which depended on $[Ca^{2+}]_0$. Lowering pHe value to 6.0 and $[Ca^{2+}]_0$ to 0 nullified the CCK–8 induced secretory response.

5) Based on these results, it was concluded that (1) lowering the pH level of perfusing solution may result in decrease of the intracellular pH level, which in turn acts on the respiratory chain in the acinar cell, and that (2) lowering the pH level of perfusing solution may potentiate ATP synthesis by amplifying the proton gradient between the cytosol and intramitochondrial space. However, ATP thus synthesized cannot potentiate the stimulus-secretion coupling in acinar cells.

6) Stimulus-secretion coupling consisted of the following two steps : (1) secretagogues induced an increase in $[Ca^{2+}]_i$, and (2) the increased $[Ca^{2+}]_i$ extrusion of the secretory granules. Lowering pHe level seemed to inhibit the first step of the coupling.