THE REGULATION OF KALLIKREIN SECRETION FROM ISOLATED SUBMANDIBULAR GLAND SLICES BY NEUROTRANSMITTERS, CYCLIC NUCLEOTIDES AND CALCIUM

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Enzyme secretion by exocrine glands is considered to be controlled by adenosine 3'5' cyclic monophosphate (cyclic AMP). This second messenger concept was critically examined using isolated guinea-pig submandibular gland slices, incubated in modified Krebs-Ringer solution, and the secretion of kallikrein together with the morphological changes which accompany the secretory process was determined in response to noradrenaline, acetylcholine, dibutyryl cyclic AMP and dibutyryl cyclic GMP.

Noradrenaline activates adenylate cyclase and raises the intracellular levels of cyclic AMP in the submandibular gland of the guinea-pig. The relative role of α and β-adrenoceptors in mediating kallikrein secretion was investigated. Phenylnephrine was marginally more effective than isoprenaline but neither was as potent as noradrenaline. Both phentolamine and propranolol were required to fully inhibit the noradrenaline response. The kallikrein release by noradrenaline was accompanied by vacuolation and depletion of secretory granules in the acinar cells with no apparent changes in the striated duct cells. Although dibutyryl cyclic AMP showed qualitatively similar morphological events, they were of lesser magnitude and in time-course studies were observed at much longer incubations.

Significant kallikrein secretory response was obtained with acetylcholine which was completely blocked by atropine. Kallikrein secretion was associated with vacuolation and depletion of granules in acinar cells which were not as marked as those observed with noradrenaline. Since acetylcholine does not activate adenylate cyclase nor does it raise cyclic AMP levels in the submandibular gland, it is considered that the secretory effects of acetylcholine are probably mediated by cyclic GMP. Neither the secretion of kallikrein nor acinar and junctional cell granule numbers were significantly affected by dibutyryl cyclic GMP.

Incubation of the gland slices in calcium-free medium containing 1mM EGTA considerably reduced the secretory response to acetylcholine and noradrenaline but to a lesser extent that of dibutyryl cyclic AMP. Incubation medium with 5 and 10 mM calcium significantly increased the secretion of kallikrein by only acetylcholine; these results followed corresponding morphological changes in acinar cells.

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