Pancreatic kallikrein: a mixture of proteolytic enzymes

Kallikrein is a pancreatic or urinary product which has been thought to be a circulatory hormone[1]. In attempting to purify active principles in pancreatic kallikrein*, we have not been able thus far to separate biological activity, as measured by the production of skin hemorrhages[2] from proteolytic activity.

This kallikrein preparation is a non-dialyzable fraction of an aqueous extract of a pancreatic autolysate which is precipitated between 0.35 and 1.00 saturated ammonium sulfate. Although it gives a single peak in the ultracentrifuge with a sedimentation constant of 3.2 S, equivalent to an average molecular weight of 45,000 (Fig. 1), glucose gradient electrophoresis reveals at least three peaks of proteolytic activity (Fig. 2). The ultracentrifugal analysis was done at a protein concentration of 1.6% in 0.1 *M* NaCl. The electrophoretic analysis was made with 20 mg of dried powder in a glucose gradient column made up in a 0.05 *M* Tris [Tris(hydroxymethyl) aminoethane] buffer of pH 8.6. The fractions were assayed for proteolytic activity by a modification of the fibrin plate method of Astrup, using both heated and unheated fibrin films.

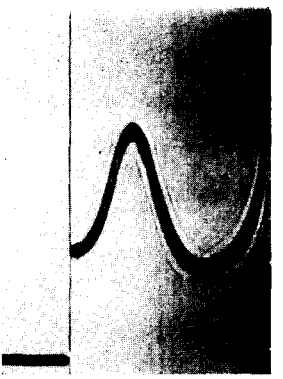

Fig. 1. Ultracentrifuge pattern of kallikrein. The direction of movement was from left to right.

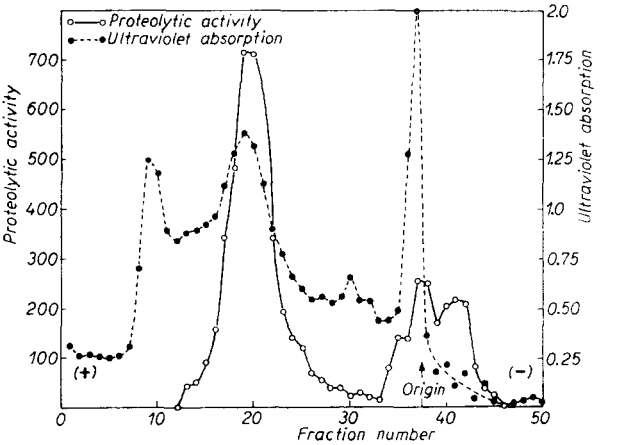

Fig. 2. Electrophoretic pattern of kallikrein. The analysis was performed in a glucose gradient column of about 30 cm length at 500 volts and 4 milliamperes.

Crystalline trypsin[2], chymotrypsin, and papain also produce skin hemorrhages. Both pancreatic kallikrein and trypsin produce contraction of the isolated guinea pig intestine, and arteriolar dilatation with resulting hypotension[3]. Urinary kallikrein has also been described[1] with similar biologic properties to pancreatic kallikrein. Normally urine contains pepsinogen but no proteolytic enzyme active at neutral pH; however, it does contain a potent activator of plasminogen[5].

Although the role of other biologic active factors cannot be ruled out, it is thus possible that both pancreatic and urinary kallikrein owe their biologic effects to proteolysis induced by pancreatic enzymes present in pancreatic kallikrein, and by the activator of plasminogen present in urinary kallikrein. The presence of more than one proteolytic enzyme in pancreatic kallikrein may account for the failure of its inhibition by certain trypsin and chymotrypsin inhibitors[6].

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