

However, activation of the kallikrein-kallidin system may be important in the etiology of three pathological conditions: (1) hereditary angioneurotic edema, which is associated with an inherited deficiency of a serum inhibitor to plasma kallikrein; (2) flushing in patients with carcinoid syndrome, which is associated with an elevation of blood kallidin; and (3) arthritides of various etiologies, in which kallidin levels are increased in synovial fluid.

50. The Role of Release of Acetylcholine in the Gut-Contracting Action of a Polypeptide from Brain.

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Crude substance P preparations from cattle brain were separated by aluminum oxide chromatography into three pharmacologically active fractions (F_a , F_b , F_c). The active principles of these fractions lose their biological activity during incubation with chymotrypsin and are therefore probably polypeptides. F_a and F_b are of basic nature; they cause relatively fast smooth-muscle contractions and lower the blood pressure of the atropinized rabbit. F_c , however, is acidic, and resistant to trypsin. It causes a slow kinin-like contraction of the guinea pig ileum and is inactive on the atropinized rabbit blood pressure. On the isolated guinea pig ileum, F_c can easily be differentiated from F_a , F_b , and bradykinin, for its action is antagonized by morphine (10^{-6} -g/ml), atropine (10^{-8} -g/ml), and cocaine (10^{-3} -g/ml), but enhanced by eserine (5×10^{-8} -g/ml). Higher concentrations of these drugs have only a very weak, if any, influence on the actions of F_a , F_b , and bradykinin. In the presence of F_c but not of F_b

the isolated gut releases an increased amount of an active material, which stimulates the dorsal muscle of the leech and is antagonized by *d*-tubocurarine (5×10^{-6} g/ml). It is concluded that the polypeptide of fraction F_c releases acetylcholine from the postganglionic neurons in the intestinal wall.

51. Microcirculatory Action of Polypeptides. B. W.

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A study was made of the vasoactive properties of polypeptides of biological origin together with some synthetic analogues. Vascular behavior was studied by direct microscopy of the mesentery in the rat and rabbit with the test substances added locally or intra-arterially into the mesenteric artery. The substances studied included bradykinin, substance P, angiotensin, vasopressin, eledoisin, PLV2, and a polypeptide from lysosomal granules. Constrictor and potentiating actions of the peptides directly were compared with their effects on the vascular response to catecholamines, serotonin, and histamine. The effects on vascular smooth muscle were not related to the permeability-increasing action of these principles. Some of the peptides such as bradykinin and vasopressin had a synergistic effect on small blood vessels in the presence of other vasoactive agents such as serotonin.

Although polypeptides have a direct effect on vascular endothelium, they also act indirectly through the release of other vasoactive agents. Their role in the genesis of tissue injury will be discussed on the basis of their locus of action in the terminal vascular bed.