In some clinical and pharmacodynamic conditions, a decrease of kininogen level in plasma can be observed.

The general and circulatory picture during direct release of kinins by trypsin and kallikrein in man has been studied and compared with the clinical pharmacology of some hypotensive peptides such as synthetic bradykinin, kallidin, eledoisin, and physalaemin.[5, 6] The effects of some antifibrinolytic compounds such as Trasylol and ε-aminocaproic acid will be shown.

Some therapeutical trials with synthetic and natural peptides (plasma kinins) will be discussed.

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39. Contribution to the Sedative Action of Substance P. P. STERN (*Dept. of Pharmacology, Medical Faculty, Univ. of Sarajevo, Yugoslavia*).

We have already indicated that substance P (SP) acts as a sedative. In these experiments fighting male mice (fighting induced by keeping mice isolated from each other for 21 days) became tranquil 15 to 30 minutes after the application of SP. This effect has been examined with SP of purity 6 U, 75 U, and 300 U/mg. Groups of mice received from these fractions 5,000 U/kg injected in 0·2 cc/g, i.p. Substance P destroyed with chymotrypsin had no effect on the control group. Tranquil mice became belligerent again if given 25 mg demethylimpiramin i.p. We take this as additional evidence for the central sedative action of substance P. Since in this test impure (6 U) and relatively pure (300 U) SP had the same effect, we believe that the test could be applied for example during the purification of SP. Substance P is a polypeptide that not only contracts the ileum of the guinea pig but has a sedative action as well. We have already shown that the other central effects of pure SP do not parallel the effect on intestine; for example, purified SP (270 U/mg) no longer has antistrychnine-like action. On the other hand, Krivoy has showed that very pure SP (10,000 U/mg) still retains neurotropic action.

40. The Search for Peptides with Specific Antibradykinin Activity. JOHN MORROW STEWART and D. W. WOOLLEY (*The Rockefeller Institute, New York, N.Y., U.S.A.*).

Structure–activity relationships in the bradykinin molecule were studied with the aid of over forty new analogs of bradykinin. These analogs (octa-, nona-, and decapeptides) were synthesized and tested on smooth muscles for bradykinin potency and for their ability to act as antagonists of bradykinin. The compounds were made by slight modifications of the Merrifield method of solid-phase peptide synthesis, and were obtained analytically pure. Single replacements of one amino acid residue by some other were ineffective for formation of antimetabolites, as were changes in the optical configuration of the amino acids. Greatest antibradykinin activity was found among analogs in which both phenylalanines had been replaced by O-methyl tyrosine. These analogs showed antibradykinin activity on rat uterus at low concentrations, while at much higher concentrations bradykinin-like action was observed. The antibradykinin activity fluctuated widely from animal to animal. Various structural alterations, especially in the serine position and in the carboxyl end, were explored in an attempt to obliterate the bradykinin-like action with retention of the antibradykinin effect. No compound has yet been found which showed high potency as an antagonist but had no bradykinin-like activity.

41. An Apparatus to Simplify the Bioassay of Vasoactive Substances. E. STÜRMER and H. WOHLFART (*Biological and Medical Research Division, Sandoz Ltd., Basle, Switzerland*).

An automatic apparatus has been constructed for assaying vasoactive substances by comparing their effect on the blood pressure with that of standard substances. Standard or test solutions are automatically injected by the intravenous route with the aid of two infusion pumps, operated intermittently. Dosage and sequence of the injections follow a prearranged program. The blood pressure changes in response to the injections are recorded by means of a strain gauge and transformed to impulses. The reaction maxima are printed out and the results are evaluated by computer.

This procedure saves manpower and time and makes for greater accuracy.

42. Purification and Some Enzymatic Properties of Bradykinin-Releasing and -Destroying Enzymes in Snake Venoms. TOMOJI SUZUKI, SADAAKI IWANAGA and TADASHI SATO (*Institute for Protein Research, Osaka Univ., Osaka, Japan*).

During purification of the bradykinin-releasing enzyme of the venom of *Agkistrodon halys blom-*