

extracts on isolated organs (guinea pig ileum, rat uterus, hen rectal caecum, rabbit jejunum) and on rabbit blood pressure was the same in each case. The activity of both preparations was destroyed by trypsin. After separation on  $\text{Al}_2\text{O}_3$  columns, both preparations consisted of Zetler's fraction  $F_a$ . The Euler-Gaddum extract contained in addition a small amount of  $F_b$ . Some differences between the extracts could be found after separation in paper chromatography and electrophoresis.

Four regions of the brain containing different amounts of substance P were extracted with both methods; the activity ratios between the regions were the same with each method. After the extraction with chloroform-methanol, no substance P activity remained in the tissue.

Separation of the chloroform-methanol extract by lipid extraction methods shows that the activity goes with the phosphatide fraction. From these experiments it is concluded that substance P in the brain tissue is bound to phosphatides.

- 25. Plasma Kinins and the Sympathetic Nervous System.** GRAHAM P. LEWIS (*CIBA Laboratories, Horsham, Sussex, England*).  
No abstract received.

- 26. The Influence of Substitution or Omission of an Amino Group on the Hypotensive Activity of the C-Terminal Sequences of Eledoisin.** K. LÜBKE and E. SCHRÖDER (*Schering AG, Hauptlaboratorium, West Berlin, Germany*).

Most of the analogues of eledoisin described in the literature were obtained by substituting amino acids in the peptide chain or by shortening it. Only little is known about the influence of non-peptidic substituents on the activity. Therefore we investigated the hypotensive activity of several acyl derivatives of the C-terminal eledoisin sequences. The C-terminal heptapeptide H-Asp-Ala-Phe-Ileu-Gly-Leu-Met-NH<sub>2</sub> is approximately four times more active than the C-terminal hexapeptide H-Ala-Phe-Ileu-Gly-Leu-Met-NH<sub>2</sub>. But this increase in activity does not depend on original aspartic acid residue in position 5. A number of other  $\alpha$ -amino acid residues also cause an increase (two- to fourfold). To clarify the question whether an extension of the peptide chain enhances the activity, we synthesized acyl hexapeptides with the formyl-, caprinoyl-, palmitinoyl-, chloroacetyl-, succinoyl-, hydroxyisovaleryl-, *p*-amino benzoyl-, nicotinoyl-, and *n*-butylcarbonyl group as acyl residues. The importance of the free amino groups is examined with the Lys<sup>6</sup>-heptapeptide H-Lys-Ala-Phe-Ileu-Gly-Leu-Met-NH<sub>2</sub>. The possible acetyl derivatives ( $\alpha$ -acetyl-,  $\epsilon$ -acetyl-, and  $\alpha, \epsilon$ -diacetyl-) and the possible des-amino derivatives (des- $\alpha$ -amino =  $\epsilon$ -amino caprinoyl-,

des- $\epsilon$ -amino = norleucyl, and des- $\alpha, \epsilon$ -diamino = caprinoyl-) were synthesized.

The hypotensive activity of all the described derivatives will be discussed with regard to the influence of the structure on the biological activity.

- 27. The Measurement of Kinin-Releasing Enzymes in Plasma.** J. MARGOLIS (*Children's Medical Research Foundation, Royal Alexandra Hospital for Children, Sydney, Australia*).

The rapid phase in the release of kinin by plasma kallikrein(s) is a specific reaction which utilizes a susceptible part (approximately 25%) of kininogen complex (component B) and involves two distinct components of the releasing enzyme system: component A and Hageman factor (HF). These were measured in terms of  $\mu\text{g}/\text{min}$  of bradykinin-equivalent (BK-*eq*) produced from a suitable substrate. Removal of inhibitors by various methods resulted in marked slowing of the reaction and apparent loss of specificity but, with the addition of EDTA and corrections for dilution, temperature, and kininogen content, reproducible results were obtained on intact plasma. In this substrate, activated HF is a potent releasing agent. By fractional elution from kaolin, at pH 11.6, stable preparations were obtained, capable of producing more than 80  $\mu\text{g}/\text{min}$  BK-*eq*/mg enzyme protein at 22° in undiluted systems. This is equivalent to 200 units of kallikrein ('Glumorin' F.B.A.) per mg. Activated HF is inactive in 'B-depleted' plasma which is still a satisfactory substrate for glandular kallikreins. Component A is necessary for the formation of soluble kallikrein in plasma or fractions activated by contact. It was assayed in samples treated with glass or kaolin and an excess of activated HF. The results were expressed either as per cent activity relative to a standard or in absolute units ( $\mu\text{g}/\text{min}/\text{ml}$ ). Unexpected discrepancies in the latter led to a re-examination of the kinin-releasing mechanisms in plasma.

- 28. Automated Peptide Synthesis.** R. B. MERRIFIELD (*The Rockefeller Institute, New York, N.Y., U.S.A.*).

In an effort to simplify and accelerate the synthesis of peptides, a new approach to the problem was devised. It was called solid-phase peptide synthesis, and was based on the idea that peptides could be assembled in a stepwise manner while attached at one end to an insoluble solid particle. With the peptide securely bound in the solid phase it was possible to purify each of the intermediates simply and quickly by thorough washing, rather than by recrystallization or other tedious procedures. The method was applied to the synthesis of bradykinin, methionyl-lysyl-bradykinin, and angiotensin. The products were obtained in good