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Arginine Vasotocin

IN connexion with the programme being carried out in this Department on the relationship of the structures of the posterior pituitary hormones to their biological properties, an analogue was synthesized[1] containing the ring of oxytocin attached to the side-chain of arginine vasopressin; for convenience, this substance was called arginine vasotocin. This highly purified compound was tested for its uterus-contracting activity with the isolated rat uterus and for its pressor activity in the rat. Our best information at the present time is that the arginine vasotocin has approximately twice the rat-uterus contracting activity and about one-fourth the rat-pressor activity of arginine vasopressin.

Although the arginine vasotocin is not as active with regard to pressor activity as arginine vasopressin, the high pressor activity of the vasotocin is noteworthy in indicating the contribution to pressor activity of the basic amino-acid in the side-chain, since oxytocin, which differs from arginine vasotocin in having leucine in place of arginine in the side-chain, has approximately one-tenth the pressor activity of the arginine vasotocin. The results also indicate that the phenylalanine in the ring of arginine vasopressin is of significance to pressor activity, since the vasopressin is more active than vasotocin, which has *iso*leucine in place of the phenylalanine. Furthermore, the fact that arginine vasotocin has twice the oxytocic activity of arginine vasopressin indicates that *iso*leucine in place of phenylalanine raises the oxytocic activity. In other words, replacement of phenylalanine by *iso*leucine has decreased the pressor activity and raised the oxytocic activity.

Because of the interesting pharmacological properties of arginine vasotocin, a sample of the synthetic product was made available to Prof. H. B. van Dyke for more extensive pharmacological investigation.

In view of the strong evidence of the possible occurrence of arginine vasotocin in non-mammalian sources adduced by Sawyer, Munsick and van Dyke (preceding communication) and the possible correlation of their work with the results of Pickering and Heller (preceding communication) on the occurrence of an active peptide in certain non-mammalian vertebrate neurohypophyses, it was felt that this brief communication on arginine vasotocin would be appropriate.

If subsequent chemical results substantiate the evidence for the occurrence in Nature of arginine vasotocin, the synthesis of the arginine vasotocin would represent a remarkable example of the synthesis of a polypeptide hormone before its identification as a natural product.

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COUNTER-CURRENT DISTRIBUTION OF PROTEINS IN AQUEOUS POLYMER PHASE SYSTEMS

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THE method of counter-current distribution has been shown to be one of the most efficient tools for analysing mixtures of substances of biochemical interest such as polypeptides. So far, it has mainly been applied to low molecular substances but recently a number of proteins such as insulin[1], adrenocorticotropine[2], growth hormone[2], lactogenic hormone[2], lysozyme[3,4], ribonuclease[4], casein[5-7], serum albumin[8], and hæmoglobin[9] have also been successfully distributed. One of the advantageous features of counter-current distribution is that it is based upon several steps each involving a state of equilibrium between two liquid phases. Generally a state of equilibrium is supposed to be more easily obtained between two liquid phases than between, for example, a solid phase and a liquid phase. For macromolecules this difference in equilibrium behaviour may be expected to be more pronounced than for low molecular weight substances. It would therefore be of the greatest interest if counter-current distribution can be applied also for large molecular weight substances such as proteins and nucleic acids. Many difficulties present themselves, however, when carrying out liquid–liquid extractions of proteins. Thus they show a general tendency, due to their large molecular size, to be distributed unilaterally and there is always a risk of denaturation which may be caused by the interfaces and the organic solvents of the phase system. In some cases, for example, with serum albumin[8], these difficulties have been successfully avoided by introducing complexing agents such as trichloracetic acid. The effect of these is to stabilize the protein against denaturation and to make it more soluble in the organic phase.

The present communication describes another approach to overcome these difficulties, namely, the

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