

from the membrane electrical resistance. Because the P_K+ value without enniatin *B* is very low, a small alteration in the membrane structure induced by the presence of enniatin *B* may be sufficient to increase P_K+ many times. The thiourea permeability coefficient, which is high compared with P_K+ , may at the same time undergo a relatively small change. It is interesting that Cass and Finkelstein⁸ have detected no effect on the diffusion of tagged water by using a protein molecule which considerably lowers the electrical resistance in lipid membranes.

We conclude that, as well as having a selective influence on cation permeability as demonstrated by Mueller and Rudin⁴, enniatin *B* affects the permeability of an un-ionized molecule as thiourea. The mechanism of enniatin *B* action on thiourea permeability has not been clarified, however. It seems possible that the interaction between the peptide and the lipids makes the membrane more polar, so as to increase thiourea permeability.

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Occurrence of the Neurotoxic α -Amino- β -oxalylaminopropionic Acid in Two Species of *Crotalaria*

THE toxicity of various species of *Crotalaria* to animals, and on occasion to man, has been widely reported and several different pyrrolizidine alkaloids have been isolated from or identified in plants of this genus. Among species which have been reported as toxic are *Crotalaria incana* L. and *C. mucronata* Desv.¹ and both are known to synthesize alkaloids^{2,3}.

The possibility that toxic compounds other than alkaloids are present in these two species was suggested when extracts of their seeds (alone of twenty-seven species analysed) were found to contain a ninhydrin-reacting compound which occupied the same position on 2D chromatograms as α -amino- β -oxalylaminopropionic acid (the neurotoxic amino-acid common to those species of *Lathyrus* responsible for classical lathyrism in man and domestic animals⁴⁻⁶). The identity of this compound as the β -oxalylamino-acid was established by co-chromatography with authentic material in six solvent systems and ionophoresis at four pH values. Confirmation was obtained by eluting the compound from ionophoresis papers, hydrolysing it in acid solution and identifying the products as $\alpha\beta$ -diaminopropionic acid (by co-chromatography, ionophoresis and colour reactions^{7,8}) and oxalic acid (by reaction with alkaline potassium permanganate and with potassium ferrocyanide-ferrous ammonium sulphate reagent⁹).

By subjecting the original extracts to high-voltage ionophoresis on paper at pH 3.0 it was possible to resolve the oxalylamino-acid "stripe" into a major faster-moving

component corresponding to α -amino- β -oxalylaminopropionic acid and a minor component (judged by colour yield with ninhydrin) which showed identical ionic mobility with the isomeric α -oxalylamino- β -aminopropionic acid previously identified in *Lathyrus sativus*, *L. cicera* and *L. clymenum*¹⁰. Like the α -oxalyl compound in the *Lathyrus* species, the slower moving component in the *Crotalaria* extracts failed to chelate with cupric ions¹¹ and reacted less rapidly with ninhydrin.

The occurrence of α -amino- β -oxalylaminopropionic acid in a second genus of the Leguminosae belonging to the Genisteae rather than to the Viciae suggests that this neurotoxic compound may be more widely distributed than studies of the Viciae (in which it has only been found in certain species of *Lathyrus*) have suggested.

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Synthetic I-N-Carbamylhemicystine-2-O-methyltyrosine-oxytocin (N-Carbamyl-O-methyl-oxytocin): a Specific Antagonist to the Actions of Oxytocin and Vasopressin on the Uterus and Mammary Gland

CYANATE reacts with the terminal amino groups of proteins and peptides to form *N*-carbamyl derivatives¹. Bisset, Poisner and Smyth² tested the biological activity of oxytocin which had been carbamylated by reaction with cyanate. The products of the reaction specifically inhibited the response of the isolated rat uterus, rat blood pressure and chicken blood pressure to oxytocin but had a weak stimulant action, like that of oxytocin itself, on the rat uterus *in situ* and on the guinea-pig mammary gland, both isolated and *in situ*. At the time, these effects were attributed to the formation of I-*N*-carbamyl-oxytocin³. In later work, however, Smyth⁴ showed that the inhibitory properties were caused by the presence in the reaction mixture of a trace of a dicarbamyl derivative of oxytocin, *N*-carbamyl-*O*-carbamyl-oxytocin, in which not only the terminal amino (NH₂) group of the hemicystine residue but also the phenolic hydroxyl (OH) group of the tyrosine residue had undergone carbamylation, and he went on to describe the preparation of a series of stable, doubly modified analogues which were specific antagonists of oxytocin without intrinsic activity on the isolated uterus^{4,5}. I-*N*-Carbamyl-oxytocin, in contrast, was shown to be a weak agonist with no inhibitory action⁴.

The *O*-carbamyl substituent is unstable at physiological pH (ref. 4). A synthetic analogue, *O*-methyl-oxytocin, which has a stable substituent in the tyrosine hydroxyl group, was prepared independently by Law and du Vigneaud⁶ and by Jošt, Rudinger and Šorm^{7,8}. This