STRUCTURE OF THE POLYPEPTIDE ANTIBIOTICS A-128-OP AND A-128-P

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The antibiotics A-128-OP and A-128-P were obtained from the natural antibiotic neotelomycin [1] by separating it on a column of Sephadex G-25 [2]. The antibiotic A-128-OP contains one residue each of D-aspartic acid, D-serine, D-allothreonine, L-threonine, L-alanine, glycine, L-cis- and trans-3-hydroxyprolines, L-3-hydroxyleucine, L-β-methyltryptophan, and dehydrotryptophan (Δ-Trp); the antibiotic A-128-P has a similar composition, but in it the L-trans-3-hydroxyproline is replaced by L-proline. The configurations of the amino acids were determined by the highly active D-amine oxidase. The antibiotics studied have D-aspartic acid at the N end (Sanger's DNP method), four absorption maxima in the UV region (255, 277, 290, and 337 nm), and an absorption band at 1745 cm^{-1} in the IR spectrum which is characteristic for a lactone bond, and the latter disappears on mild alkaline hydrolysis. Under these conditions the inactive acid of the antibiotics is formed with C-terminal L-cis-3-hydroxyproline (by the hydrazinolysis method). Each component has one free NH_2 group and one free COOH group (by the partial substitution method) belonging to D-aspartic acid, which acylates the following amino acid by its β-COOH group. The molecular weight of the antibiotics is 1250-1300 (by potentiometric titration). The antibiotics are similar in biological activity and electrophoretic mobility, and proteolytic enzymes do not affect them.

In a study of the structures of the antibiotics under consideration, in order to determine the position of the tryptophan residues in the peptide chain we performed mild alkaline hydrolysis, after which we obtained two peptide fractions – water-soluble and water-insoluble peptides. In both cases we isolated from the water-insoluble fraction of peptides by the TLC method on silica gel C-terminal hexapeptides with β-Me-Trp and Δ-Trp. The structures of the hexapeptides were established by Edman's method (three steps), by hydrazinolysis, and by the action of carboxypeptidase C on the acids from the antibiotics. The hexapeptide from the antibiotic A-128-OP has the sequence H-Gly → t3HyP → e3HyLe → β-Me-Trp → Δ-Trp → c3HyP-OH, and that from A-128-P has the sequence H-Gly → Pro → e3HyLe → β-Me-Trp → e-Trp → c3HyP-OH. The N-terminal amino acid sequences of the antibiotics were determined after partial acid hydrolysis of their N-DNS derivatives with subsequent amino acid analysis of the di-, tri-, tetra-, and penta-DNS-peptides isolated by the TLE method on cellulose and on silica gel. It was found that in both antibiotics the following pentapeptide is present at the N- end: Asp-β → Ser → a-Thr → Thr → Ala.

By comparing the N- and C-terminal peptides we established the structures of the acids of the antibiotics A-128-OP and A-128-P. After determining the position of the lactone bond (oxidation of the antibiotics and their acids with CrO_3 followed by amino acid analysis) the following structural formula was proposed for the antibiotics A-128-OP (where X = OH) and A-128-P (X = H); these differ from the structures of the antibiotics telomycin [3] and LL-A-0341B [4] and are therefore new.

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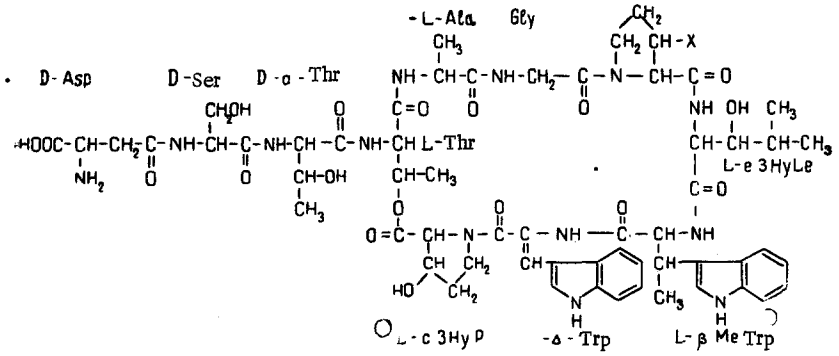

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