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A STUDY OF THE MECHANISM OF THE INTERACTION OF NUCLEOPEPTIDES WITH DNA BY THE METHOD OF CIRCULAR DICHROISM

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We have previously established that the nucleopeptides L-lysyl-L-β-(thymin-1-yl)-α-alanyl-L-lysine (I) and L-lysyl-L-β-(adenyl-9-yl)-α-alanyl-L-lysine (II) are capable of binding to polynucleotides and causing the stabilization of the double helices of such natural polynucleotides as the DNA of bacteriophage C_D and the double-stranded RNA of bacteriophage f2 [1].

H-L-Lys-X-L-Lys-OH

I. X=L-Tal; II. X=L-Aal; III. X=Gly; IV. X=L-Tyr.

In order to take into account the contribution of electrostatic interactions due to the lysine residues, in parallel experiments we studied the laws of the heat denaturation of complexes of polynucleotides with the nucleopeptides (I) and (II), and also of complexes of the polynucleotides with the reference glycine-containing peptide (III), serving as a standard of comparison.

The experimental results obtained have permitted us to formulate a hypothesis according to which the observed effect of the stabilization polynucleotide helices under the action of nucleopeptides may be due to the formation of hydrogen bonds between the nitrogen bases of the nucleopeptides and the corresponding heterocycles of the polynucleotides. The experimental results available at the present time did not permit definite conclusions to be drawn relative to whether, in this process, the intercalation of the ring systems of the thymine and adenine of the trinucleotides between the nucleic bases of the polynucleotides took place. To solve this problem, we have investigated the circular dichroism (CD) spectra of complexes of DNA with the nucleopeptides (I) and (II) and also with the reference glycine-containing peptide (III) (Fig. 1). It was established that the CD spectra of the polynucleotides scarcely differed in the presence of the nucleopeptides mentioned when recorded in the differential regime relative to the nucleopeptides.

In the light of information obtained previously concerning the laws of change of the CD spectra of complexes of polynucleotides with the tyrosine-containing tripeptide (IV), and also results on the complex-formation of polynucleotides with the peptide antibiotic bacitracin and other ligands [2-4], the new experimental information that has now been obtained on the CD spectra of complexes of DNA with nucleopeptides permits the definite conclusion to be drawn that the ring systems of thymine and adenine present in the structure of nucleopeptides do not intercalate on interaction with DNA but form hydrogen bonds with the hydrogen bases of the DNA, which leads to the stabilization of the DNA double helix.

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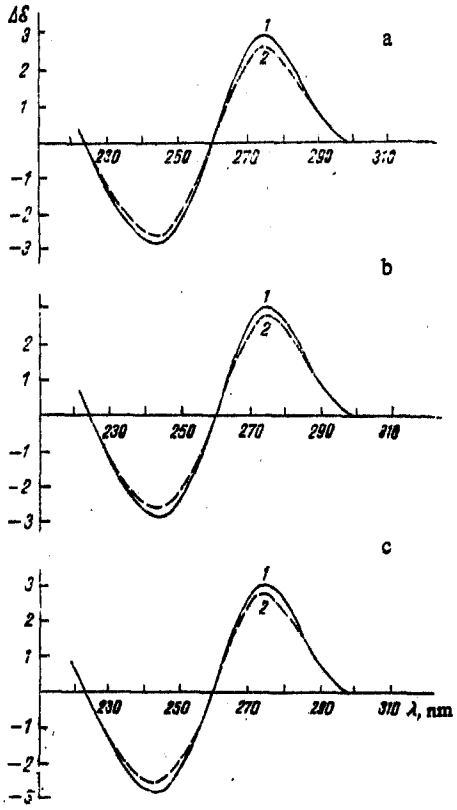

Fig. 1. Circular dichroism spectra of DNA (1) and its complexes (2) with H-L-Lys-Gly-L-Lys-OH (a), I-L-Lys-L-Tal-L-Lys-OH (b) and H-L-Lys-L-Ala-L-Lys-OH (c) in 10^{-3} M Tris-HCl buffer, pH 7.1, containing 10^{-3} M NaCl and $5 \cdot 10^{-5}$ M EDTA: DNA-peptide ratio 1 : 3.

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