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QUANTITATIVE ESTIMATION OF THE CONTRIBUTION OF AMIDE GROUPS OF THE OLIGOPEPTIDE ANTIBIOTIC DISTAMYCIN A INTO SPECIFICITY OF ITS BINDING TO BASES OF DOUBLE-HELIX DNA

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According, to the model suggested by us earlier[1,2], the specificity of distamsycin A binding to AT pairs involve a hydrogen bonding of the amide groups of the antibiotic molecule to the O2 oxygens of thymines and the N3 nitrogens, of adenines facing into the minor groove of the DNA double helix. In present work the energy of interaction of distamycin amide groups with pyrimidine O_2 and purine N_3 atoms of DNA have been investigated by the use of distamycin A analogs having different numbers of pyrrol carboxamide groups and labeled with fluorescent dansyl-chromophore. The binding isotherms of the analogs to synthetic polydeoxyribonucleotides were obtained. Analysis of the experimental data leads to the following conclusions: (1) the free energy of binding of the analogs to poly(dA)*poly(dT) depends linearly on the number of amide groups in the molecule of the analog; (2) attachment of each pyrrolcarboxamide group to poly(dA)*poly(dT) produces changes of 2 kcal/mole in the free energy; (3) attachment of a pyrrolcarboxamide unit to poly(dG)*poly(dC) results in the free energy change of 0.95 kcal/mole; the binding of analogs to poly(dA)* poly(dT) is a cooperative process, presumbly, dependent on conformational changes induced by the binding of analogs to DNA. The most significant result of this worn is that the free energy of binding of pyrrolcarbcxamide group to each of the four bases in DNA double helix is determined. Stereochemical aspects of these binding interactions and possible implications for protein-DNA recognition will be discussed.