THE PARALLEL SYNTHESIS AND CYTOTOXIC EFFECT OF CARBOCYCLIC DISTAMYCIN ANALOGUES

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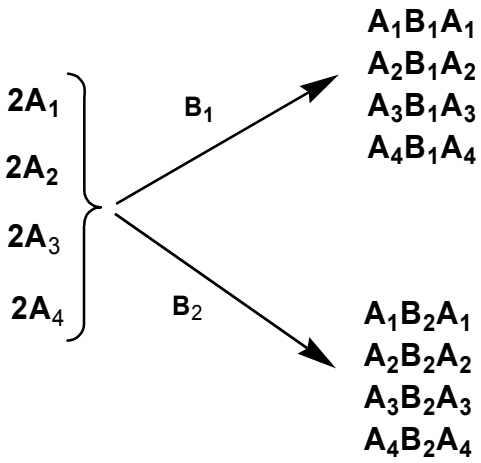
The natural antibiotics, netropsin and distamycin, be characterize by high selectivity of bond of regions DNA rich in the steam A - T, as well as the activity both antineoplastic, as and antiviral [1]. The model of binding netropsin and distamycin with B-DNA became the inspiration to searches of compounds with similar DNA-compound interaction.

In our investigations we concentrated on variously the put segments of benzene, uniting it inter the se and from some heterocyclic segments. We chose 4 different aromatic amines $\mathbf{A_1}$-$\mathbf{A_4}$ (2-aminothiazole, 2-amino-2-nitropyridine, 2-aminopyridine and 3-nitroaniline), which were acylated using terephtaloyl chloride ($\mathbf{B_1}$) and isophtaloyl chloride ($\mathbf{B_2}$). This procedure led to obtainment the trimmers **ABA**, analogues of distamycin. All of them were investigated and showed antiproliferative and cytotoxic effects in the standard cell line of mammalian tumour MCF-7.



Scheme 1. Parallel synthesis of analogues of distamycin.

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[1] Ch. Bailly, Sequence-specific recognition and modification of double-helical DNA by minor-groove binding conjugates structurally related to netropsin and distamycin, in: Advances in DNA Sequence-Specific Agents, 3 (1998) 97-156.