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The synthesis, some physicochemical properties, and biochemical studies of fluorescent symmetrical dimeric bisbenzimidazolesDBP(n)

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A new series of fluorescent symmetrical dimeric bisbenzimidazoles DBP(n) was prepared (Fig. 1). Synthesized molecules consisted of two AT-specific bisbenzimidasole blocks connected by the linker. The DBP(n) differ from the previous series DB(n)[1] by 1,4-piperazine fragment in the center of the oligomethylene linker which addedtwo morepositive charges into the molecule.

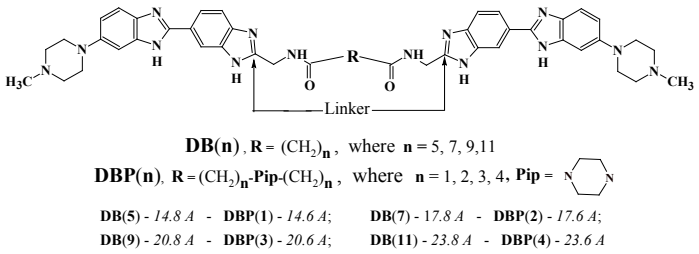
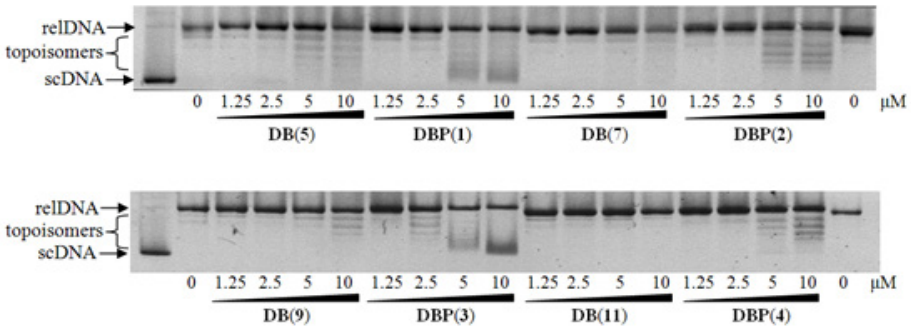


Fig.1.Dimeric bisbenzimidazolesDB(n)&DBP(n)and the pairwise comparison of DB(5,7,9,11) and DBP(1,2,3,4) linker lengths.

The formation of DBP(n)-DNA complexes localized in the minor DNA groove was shown using physicochemical methods. The DBP(n)at micromolar concentrations demonstrated the in vitroinhibitory activity toward eukaryotic DNA topoisomerase I (topo-I) [2]and DNA methyltransferaseDnmt3a [3].The comparison of the DBP(n) synthesized with the DB(n) counterparts synthesized previouslydemonstrated in vitro



The DBP(n)were notmutagenic: they did not cause point mutagenesis in the Ames testand did not display mutagenic or recombinogenic activities in the SMART test.Unlike the DB(n) series, the DBP(n) were soluble well in aqueous solutions (at concentrations 10 M or higher). Also, they penetrated cell and nuclear membranes and stained DNA in live cells.The DBP(n) showed higher cytotoxic properties toward human breast adenocarcinoma MCF-7 cell line than toward human normal kidney epithelial NKE-hTERT cells. Also, they displayed a moderate effect on the reactivation of gene expression [4].

[1]Ivanov A.A., Salyanov V.I., Streltsov S.A., Cherepanova N.A., Gromova E.S., Zhuze A.L. (2011) DNA sequence-specific ligands: XIV. Synthesis of fluorescent biologicaly activedimeric bisbenzimidazoles – DB(3, 4, 5, 7, 11).Bioorg. Chem. (Moscow), 37(4) 472-482.[2] Susova O.Yu., Ivanov A.A., Ruiz S.S.Morales, Lesovaya E.A., Gromyko A.V., Streltsov S.A., Zhuze A.L. (2010)