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Supramolecular complex formed by DNA oligonucleotide and thiacalix[4]arene. NMR-spectroscopy and molecular docking

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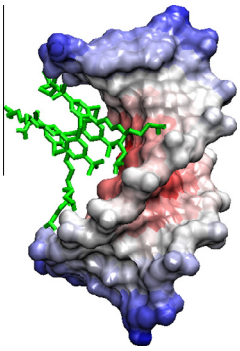
HIGHLIGHTS

- Complexation of calixarene with DNA was studied using NMR and molecular docking.
- From docking simulations we select the complexes compatible with NMR constraints.
- Oligonucleotide in solution exists in double- and single-stranded helixes.

GRAPHICAL ABSTRACT



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ABSTRACT

The combination of NMR-spectroscopy and molecular docking was applied to investigate the complexation of thiacalix[4]arene with DNA. We have studied the structure of supramolecular complex formed by palindromic decamer DNA d(GCGTTAACGC)2 and tetrasubstituted at lower rim of *p-tert*-butyl thiacalix[4]arene in *1,3-alternate* conformation. With the help of NMR it is shown that oligonucleotide in solution exists in two states: double-stranded helix (dominant structure in solution) and single-stranded form (minor structure) rolled up in a "hairpin" with equilibrium between them. Both complementary methods, NMR and molecular docking, revealed the formation of molecular complex by thiacalix[4]arene and palindromic decamer DNA. Different possible conformations of the complexes were analyzed by means of molecular docking. We used the experimental constraints in molecular docking to identify the complexes, which were in agreement with the NMR data.

Introduction

Over the past decades, the combined use of both molecular docking and high-resolution NMR data in the study of receptor (DNA or protein) – ligand interactions has become a productive trend [1–18]. Both methods provide valuable information for determining the structure and dynamics of the biomacromolecular/ligand complexes. Moreover, they have proved to be perfectly complementary techniques. In particular, their combination is widely used in drug discovery research [15]. The experimental restraints provided by NMR are able to significantly improve the accuracy of docking experiments [14]. The NMR structures have the following advantages over the X-ray ones: the former can be resolved in solution and they incorporate dynamical information [2]. Thus, they are supposed to be of superior biological relevance.

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