experimental research produces either inconsistent results (the rA residue conformation), or determination of which is beyond capabilities of contemporary experimental apparatuses (the mode of the hydrogen bond connection in the atypical terminal 1U-rG pair of residues in the tetraloop) Except it, we were interested in the influence of 2'hydroxyls groups on the stabilisation of the hairpin structure due to the creation of hydrogen bonds, either in the mentioned 1U-rG terminal pair of residues or elsewhere, because it seems to be the reason of the substantially higher thermodynamic stability of UNCG tetraloops in comparison with their deoxyoligonucleotide analogues

In our MDS the hairpin structure seemed to be stable in the temperature range up to 285 K with the rA residue in the C3endo/anti conformation In the case of higher temperatures the C3endo/anti conformation of the rA residue changed to the C2endo/syn conformation

One hydrogen bond between RU and 1G bases and the other between the RU 2'hydroxyl group and the rG base stable in both C3endo/anti and C2endo/syn conformations (proposed on the base of NMR results (Allain and Varani 1995) established in the course of our fully solvated MDS This kind of the hydrogen bond connection gives the explanation of higher stability of RNA loops in comparison with the same deoxy- sequences

We found also three other supplementary hydrogen bonds, which formed between 2'hydroxyl and site phosphate groups (in the stem in two cases and once in the loop sequence of the hairpin)

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X-Ray Crystal Structure of GpC phosphonate Analogue: A Promising Unit for the SNAIGE Strategy

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Key words: SNAIGE concept, crystal structure, GpC phosphonate analogue

Several new concepts called, as a whole, the SNAIGE concept (Synthetic Nucleic Acids Interfering with Gene Expression), have been introduced into chemotherapy in recent period of time, such as the idea of "antisense" oligonucleotides

The first X-ray crystal structure of novel-type diribonucleoside monophosphate analogues, the crystal structure of (guanosine-2'-O-phosphonomethyl)-5'-O-cytidine (G-p_cC 2') was determined Structural unit involves two asymmetric molecules of G-p_cC, Mg^{2+} and 13 H_2O, differing in conformation of phosphonate analog of phosphodiester linkage

($gg^{-}t$, tgt) and therefore even in intramolecular base-plane distances (3 602 Å, 3 298 Å) The extreme values, in comparison with these distances of similar compounds ($\approx$ 3 4 Å) indicate considerable conformational flexibility even in the crystal state Both guanosines exhibit *syn* and C2'-*endo* conformation, both cytidine are in *anti* and C3'-*endo* There are two quite unusual intermolecular H-bonds (N4*cyt* O1*phosph'*, O2*cyt* N4*cyt'*) in a crystal state

Because of a strong intramolecular stacking and an extreme stability against various nucleases, G-p_cC 2', analog with similar phosphonate analogues, will serve like a building unit of SNAIGE oligonucleotides

Computer-Aided Modelling of Polymeric Drugs

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Key words: computer modelling, polymeric drugs

Methods of computer-aided molecular modelling were used to elucidate the interaction of polymeric drugs with the lysosomotropic enzyme cathepsin B As a polymeric drug carrier, poly[N (2-hydroxypropyl)methacrylamide] was used Drugs (doxorubicin, methotrexate, and p-nitroaniline as a model) were linked to the polymer via a tertapeptide spacer The results of the molecular dynamics and energy minimisation procedures lead to a tetrahedral intermediate model and subsequent cleavage step model, which are in accord with the experimental data Drug docking shows an optimum interaction of the spacer GlyPheLeuGly- in the P1 P4 positions (Schechter and Berger 1968) of the cathepsin B active site Similarly, it was found that only little space in the S1' and S2 subsites is left free for bulkier drug molecules because an occluding loop formed mainly by His110 and His111 makes a barrier This explains why some drugs were situated in P1' position and other in P2 position

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