

( $gg^-t$ ,  $tgt$ ) 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<sub>c</sub>C 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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