Complexes formed between DNA and poly(amido amine) dendrimers of different generations

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Abstract

Gene therapy holds a promise in healing cancer and other genetic diseases by directly delivering therapeutic DNA into living cells. Although viruses have been demonstrated to be efficient delivery vectors, their toxicity and immunogenicity have limited their general use. Poly (amidoamine) (PAMAM) dendrimers, being protonated under physiological conditions, have great potential as nonviral vectors for gene transfection. Many experimental and simulation studies have been performed to study the effect of dendrimer size, charge, and salt concentration on the structure and transfection efficiency of condensed DNA aggregates. In our study we investigated the complexation of dendrimers with DNA molecule using theoretical model and Coarse-Grained molecular dynamics simulations.

Throughout the study, first we emphasized on the effect of the medium's environments on the complexation of LPE chain with one dendrimer, namely the concentration of 1:1 salt solution, dielectric permittivity of the solvent, and pH conditions. Other factors have been investigated such as size and charge of the dendrimers, degree of polymerization of the LPE chain, and it's rigidity. Then we investigated the effect of the salt concentration on the interaction between linearized DNA plasmids (4331 bp) and positively charged dendrimers of generations 1, 2, 4, 6 and 8, previously studied experimentally. It is found that in the first case of complexation of LPE chain with one dendrimer, the wrapping degree of the chain around the dendrimer increases by increasing dendrimer's charge, Bjerum length, length of the LPE chain, and salt concentration. Also, charge inversion of dendrimer is obtained, and the value of the inverted charge increases by increasing the above mentioned parameters. While the complex shows more wrapping degrees, and less inverted charge as the pH of the solution decreases.

In the case of complexation of DNA plasmids with dendrimer of different generations, the wrapping length of the LPE chain depends on dendrimer generation. With small generations, the optimal wrapping length of LPE chain around dendrimer increases by increasing the salt concentration, while, the complexation is insensitive to ionic strength with large generations.