

Synthetic macromolecules and nucleic acid: experimental and theoretical investigation of the structure of dendriplexes

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Dendrimers are monodisperse hyperbranched polymers with a well-defined structure. Their step-by-step synthesis allows a control of the molecular structure, going from a generation (G) to the following increasing the number of surface groups. One of the most studied dendrimers is poly(amidoamine) (PAMAM), especially in the context of drug/gene delivery. PAMAM dendrimers are biocompatible, water soluble and polycationic, which are interesting properties for non-viral vectors. The supramolecular complexes between polycationic dendrimer and polyanionic nucleic acid, called dendriplexes, are mainly formed by electrostatic interaction [1].

The dendriplexes were studied by ion mobility spectrometry to obtain their collision cross section (CCS) and, by comparison with the CCS obtained by molecular dynamics (MD) simulation, access information about their structure in the gas phase. A special attention was paid on the transition from the solution structure to the gas phase in MD, to reproduce the structures observed experimentally in mass spectrometry and ion mobility experiments. The direct simulation of the ion in the gas phase led to extended conformation, with an overestimation of the CCS up to 30% for the DNA duplexes. By simulating the desolvation process, compact conformations are obtained, giving a good agreement between experimental and theoretical CCS.

References

1. Dufès *et al.*, *Adv. Drug Deliv. Rev.*, **57**, 2177-2202 (2005)