OL 4 - Aggregation and Synthetic Studies on Chitosan and PEG-Grafted Chitosan

E. Fernandez-Megia, R. Novoa-Carballal, E. Quiñoa, R. Riguera

Departamento de Química Orgánica, Facultad de Química, and Unidad de RMN de Biomoléculas Asociada al CSIC, Universidad de Santiago de Compostela, Avda. de las Ciencias S.N. 15782 Santiago de Compostela, Spain.

In this presentation, we will show our most recent results on two areas of interest for the development of chitosan based drug delivery applications: (A) the intermolecular aggregation of chitosan in solution, and (B) a synthetic approach to targeted PEG-grafted chitosan incorporating ligands at the distal end of PEG.

A. In order to study the influence of the degrees of acetylation (DA) and polymerization (DPw) on the intermolecular aggregation of chitosan, chitosan samples with varying DA and DPw have been analyzed by pyrene fluorescence and NMR relaxation. As a result of these studies, two limiting aggregation behaviours are proposed as a function of DA and DPw. Looser and less hydrophobic aggregates, characterized by the presence of flexible chains, are produced at high DA. While, more hydrophobic and compact aggregates, constituted by stiffer chitosan chains, are obtained at low DA, and on increasing DPw in highly acetylated chitosans. We believe that the high compactness of this latter type of aggregation is most likely the reason for these aggregates have not been previously identified by viscometry and light scattering techniques.

B. With the aim of enhancing the stability and biocompatibility of chitosan in vivo, several synthetic approaches to PEG-grafted chitosan have been reported during the last decade by ours, and other research groups. In order to render these copolymers useful for active targeting, and antiadhesive therapy, we have recently embarked in a synthetic program oriented to the incorporation of ligands to the distal end of PEG. In this presentation we will show our results leading to PEG-grafted chitosans of various degrees of substitution, functionalized with biotin, cholesterol, D-mannose, and a coumarin fluorophore tag. The usefulness of these targeted chitosan-g-PEGs has been recently demonstrated by the application of one of the copolymers functionalized with biotin in the development of immunonanoparticles as promising drug carriers across the blood-brain-barrier.