POLYMERIC NANOSTRUCTURES FOR BIOMEDICAL APPLICATIONS: CLICKABLE DENDRITIC POLYMERS AND PEG-GRAFTED CHITOSAN

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The necessity of selectively delivering structurally complex drugs, proteins and nucleic acids to specific target cells, requires from stabilized nanostructures with demonstrated stability in vivo, as well as low toxicity and immunogenicity. The possibility of incorporating ligands, antibodies, fluorescent markers and other tags on the surface of the drug carrier requires a careful design and synthesis of these structures. Similarly, since most of the ligand-receptor interactions in Nature are inherently multivalent, the use of nanometric multivalent ligands has opened up the possibility of inhibiting or promoting many natural processes. With the aim of obtaining more efficient drug delivery systems and multivalent ligands, our group has recently started a program directed to the preparation of biocompatible polymeric nanostructures based on biopolymers and dendrimers.

More specifically, we have described the synthesis of azido terminated dendrimers[1] and PEG-dendritic block copolymers,[2] that can be efficiently functionalized under aqueous media by means of Click chemistry. Under these conditions, unprotected alkyne derived carbohydrate residues could be incorporated on the surface of these dendrimers in reproducible high yields, and requiring only catalytic amounts of Cu. Preliminary results of the interaction of the resulting glycodendrimers with lectins show an increasing aggregation ability with dendrimer generation, in accordance with the cluster glycoside effect.

Also, we have recently described on the preparation of graft copolymers of chitosan (a natural polysaccharide with high biocompatibility and biodegradability)[3] and PEG, incorporating biologically active molecules and tags at the distal end of PEG.[4] Experimental conditions allowing the preparation of multifunctional graft copolymers incorporating simultaneously several active molecules and tags in controlled ratios will be also presented, as well as the application of these copolymers to the development of active drug delivery systems.[5]

References:

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