MANNOSYLATED AMPHIPHILIC AND DEGRADABLE PEO-B-PCL COPOLYMERS FOR DRUG DELIVERY SYSTEMS: PREPARATION AND SUGAR AVAILABILITY CHARACTERIZATIONS

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Over the last decade, polymer micelles and nanoparticles attracted an increasing interest in pharmaceutical research because they can be used as efficient drug delivery systems[1,2]. In this field, amphiphilic copolymers combining poly(ethylene oxide) and aliphatic polyester (such as poly(ε-caprolactone) (PCL) or polylactide (PLA)) are particularly of interest[3] because (i) PEO has unique protein- repellent properties and thus provides a stealth behaviour to the drug carriers and (ii) aliphatic polyesters are biocompatible and biodegradable hydrophobic matrices well-suited for the incorporation of an hydrophobic drug.

By end-capping the hydrophilic segment by a targeting moiety so that they may interact with membrane receptors, the biodistribution of polymeric micelles and nanoparticles stabilized with this copolymer can be modulated and can induce specific cellular uptake by receptor-mediated endocytosis. One class of interesting targeting agent is the saccharides, in particular the mannose, because of its specific interaction with mannose receptor, which are found on peripheral and bone marrow macrophages, dendritic cells and sinusoidal liver cells.

In this study, the reductive amination reaction is use to attach this targeting agent. After optimisation of the reaction with amino fluorescein, a model amine, mannosylated copolymer of PEO and PCL has been prepared. The surface availability of the saccharide upon the micelles in aqueous phosphate buffer was then assessed by DLS through binding with the protein Concanavalin A (ConA), a known mannose receptor. The interactions between the Bcla lectin and the mannosylated micelles have then been studied by Isothermal Titration Calorimetry (ITC) and the thermodynamic parameters have been obtained. This polymer is particularly useful for the stabilization of PLGA nanoparticles with the goal to target M cells for oral vaccination. [4]

References:

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