DESIGN OF NEW MULTIFUNCTIONAL NANOCARRIERS FOR PROTEIN DELIVERY

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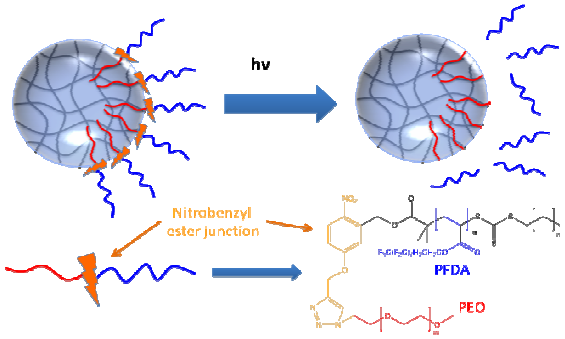
Polymeric nanoparticles have been widely investigated for their applications in drug delivery systems. There have been numerous studies on multifunctional polymeric nanoparticles for the controlled release and targeted delivery of hydrophobic drugs. There remain however obstacles to overcome in the design of efficient multi-purpose nanocarriers for protein delivery. The aim of this project is to develop a novel strategy for the design of nanocarriers able to encapsulate therapeutic proteins in their core, as well as bearing targeting and imaging agents on their surface. Tailoring of surface functionalities will enable nanocarriers to deliver proteins in a targeted manner and facilitating their theranostic applications. In addition to this objective, polymerizations will be carried out in supercritical carbon dioxide ($scCO_2$), which confers environmentally benign features to the process[1].

Multifunctional nanocarriers are obtained *via* heterogeneous free-radical polymerization in $scCO_2$. In order to ensure the successful dispersion in $scCO_2$, a novel photocleavable diblock CO_2-philic stabilizer is employed. This diblock stabilizer is constituted of 2 different segments, a CO_2-phobic block of poly(ethylene oxide) (PEO) and a CO_2-philic block of poly(1,1,2,2-tetrahydroperfluorodecyl acrylate) (PFDA) linked with an o-nitrobenzyl based photocleavable junction[2]. The general strategy involves synthesis of reversible chain transfer agent based on PEO (PEO-CTA)[3] functionalized with o-nitrobenzyl photocleavable group. Thereafter PEO-hv-CTA is utilized for CO_2-philic segment (PFDA) synthesis *via* reversible addition fragmentation chain transfer (RAFT) polymerization. Dispersion polymerizations of hydrophilic monomer, 2-hydroxyethyl methacrylate (HEMA), in $scCO_2$ were performed in the presence of a cross-linking agent (EGDMA) and the photoclevable stabilizer, leading to sub-micronic hydrogels. Once exposed to UV light, the o-nitrobenzyl junctions present at the surface of the particle are cleaved, thus providing water dispersible hydrogels.



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