

June 04-05, 2018
London, UKM José Carrero et al., Polym Sci 2018, Volume 4
DOI: 10.4172/2471-9935-C2-011

STUDY OF COUMARIN INCORPORATION IN THERAPEUTIC POLYMERS

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Poly(ethylene oxide)-poly(propylene oxide) (PEO-PPO) block copolymers stand out among amphiphilic molecules due to the possibility of modifying their hydrophilic/hydrophobic character easily, just varying the proportion between the PEO and PPO molecules respectively. This property together with their biocompatibility and biodegradability make them, and their derivatives, suitable for products formulation in industries ranging from agriculture to pharmaceuticals and controlled release of drugs. Thus, these copolymers are able to form thermodynamically stable micelles in aqueous solution above a certain copolymer concentration, CMC (critical micelle concentration) that can improve the poor solubility of the drugs. Moreover, the introduction of glycidyl propargyl ether (GPE), which contains triple bonds, in the copolymer chain allows to obtain functionalized terminal alkynyl-polyethers suitable for future click attachment, with the objective of enlarging the drug lifetime in the body. The ultimate purpose of this work is to obtain a tailor-made polymeric drug carrier able to incorporate the coumarin (anticancer agent) which will provide the two aforementioned benefits. First, PEO-PPO-GPE triblock copolymers were synthesized through nucleophilic ring-opening polymerization, maintaining the mass ratio between hydrophilic/hydrophobic segments (50/50) in all cases, but changing the ratio for the hydrophobic monomers (PPO and GPE) to increase the GPE mass percentages in the final copolymer from 0 to 15 percent. Subsequently, on the one hand, the coumarin was loaded in polymeric micelles with different percentages of GPE using direct dissolution method. Based on the DLS (Dynamic Light Scattering) results, the micelles size was in the suitable range (10-200 nm) to enable its absorbability by the target cells and this size increased when coumarin was added, confirming its incorporation. On the other hand, the click reaction based on the use of Cu (II) as catalyst, between the PEO-PPO-GPE copolymers and azide-coumarin was successfully carried out according to FTIR and NMR analysis.

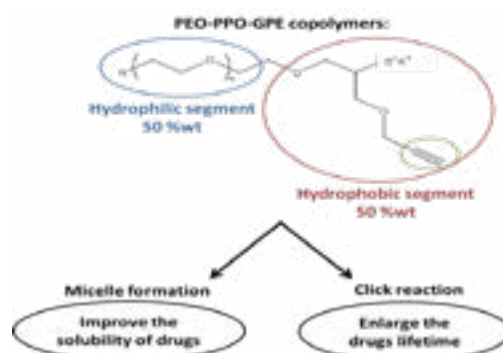


Figure 1: PEO-PPO-GPE copolymers structure and their possibilities of drugs incorporation

Recent Publications

1. Gracia E et al. (2017) Functionalization and optimization of PLA with coumarin via click chemistry in supercritical CO₂. *Journal of CO₂ Utilization*. 20:20-26.
2. De Haro J C, Rodríguez J F, Pérez Á and Carmona M (2016) Incorporation of azide groups into bio-polyols. *Journal of Cleaner Production*. 138(1): 77-82.
3. Borreguero A M et al. (2016) Zidovudine insertion in tailor-made propylene and ethylene oxide copolymers. *Reactive and Functional Polymers*. 101:1-8.
4. Cabezas L I et al. (2013) Production of biodegradable porous scaffolds impregnated with 5-fluorouracil in supercritical CO₂. *Journal of Supercritical Fluids*. 80:1-8.
5. Velencoso M M et al. (2013) Click-ligation of coumarin to polyether polyols for polyurethane foams. *Polymer International*. 62(5):783-790.

Biography

M José Carrero is PhD student at the University of Castilla-La Mancha (UCLM). Her research focuses on the synthesis of polymer-drug conjugates to controlled delivery of drugs, and currently she has participated in one congress obtaining the best presentation award in 2017.

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