Polytrimethylene Carbonate Nanoparticles formulation for drug delivery A preliminary study

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Over the past decade, the use of aliphatic polycarbonates has attracted increased attention in the field of drug delivery owing to their ability to form biocompatible nanocarriers that are safer and less toxic than viral ones and some synthetic gold standard polymers (e.g. poly(ethylenimine, PEI)[1]. Moreover, their fast biodegradability and resorbability occurring without the formation of acidic compounds make them more attractive than some aliphatic polyesters currently in use (e.g. PLA, PCL)[2]. Particularly, polytrimethylene carbonate (PTMC) is widely studied for soft tissue regeneration and functionalized micelles and hydrogels formation regarding its low glass transition temperature (~ - 20°C) and its hydrophobicity[3]. Its controlled and easy synthesis by ring-opening polymerization (ROP) of the commercially available trimethylene carbonate (TMC), using a metal-free and non-toxic catalyst[4], allows fast production of well-defined samples (dispersity, Đ ~1,1)[5].

This communication presents a preliminary study on nanoformulation of solid PTMC nanoparticles using the double emulsion – evaporation technique[6]. Its relevance for drug delivery was assessed by repeatability of the size and their ability to encapsulate a model ionisable drug, disodium cromoglycate, classically used for asthma treatment.

Controlled PTMC-OH sample was produced according to a well-reported protocol[5] using DBU (1 Eq.) as catalyst, resulting in polymer chains characterized by an average molecular weight and a dispersity of Mn = 4.400 g/mol and Đ ~ 1,3, respectively. Nanoparticles were then produced by a double-emulsion evaporation technique involving 3 phases (w/o/w): i. an aqueous phase containing the drug dissolved in deionized (DI) water ; ii. an organic phase composed of PTMC dissolved in dichloromethane (DCM) ; iii. a second aqueous phase with polyvinyl alcohol (PVA) surfactant at 2,5 % (w/v) in DI water. Each sonication is achieved during 2 minutes (Pulse mode, Intensity 4, Cycle 20) in an ice bath. Nanoparticles size (Z_{size} ~ 180 nm) and zeta potential (ζ_{pot} ~ 0 mV) were measured by dynamic light scattering (DLS) and showed a good repeatability. Images were obtained with TEM. The entrapment efficiency (EE) of the drug was found to be around 15 % and was calculated by an indirect method using HPLC-UV (detector was set at 326 nm, separation was performed on a Luna C18 Column in isocratic mode with a monobasic potassium phosphate (0,025 M, pH 3.0) / Methanol (55/45 v/v) mixtures as mobile phase at 20 °C; flow rate = 1 mL/min).

Through our approach, we have validated that this family of bioresorbable polymers offers great potential in the field of controlled drug release.

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