Rational Design of Self-assembled Poly-L-Lactide Nanosystems for Drug Delivery

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Branched polymers have emerged as promising carriers for drug delivery since they have a higher surface area and more available functional groups compared to linear counterparts.1 These characteristics enable them to encapsulate or conjugate a larger amount of drug molecules. In addition, the branching architecture can be engineered to control the release kinetics of drugs by modifying the degree of branching or the composition and length of branches. Herein, the synthesis of branched poly-L-lactide (PLLA) is reported by using renewable polyols, glycerol (Gly) and diglycerol (DGly) as initiators. In order to evaluate the effect of branching chain length on polymer physico-chemical properties and drug availability, different L-lactide (L-LA)/OH molar ratios (8, 16 and 24) were investigated (Figure 1). Polymers with molecular weight (MW) ranging from 4100 to 20000 g mol−1 were obtained. An increase in polymer MW and gyration radius was observed with increasing L-LA/OH molar ratio. All branched polymers were amorphous, except for the polymer with the longest branches (DGly24-PLLA), and able to self-assemble in water giving 200 nm-in size polymer nanoaggregates. Usnic acid (UA), a hydrophobic, antimicrobial and anticancer natural compound, was encapsulated in the polymer nanoaggregates. Following encapsulation, a significant increase in UA apparent solubility in water together with a reduced toxicity in vitro was observed, highlighting the potentialities of the synthesized systems as carriers for drug delivery.