Block copolymer of poly(ester amide) and polyesters: Synthesis, characterization, and in vitro cellular response

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Abstract

In order to expand the properties and applications of aliphatic absorbable polyesters, a new biodegradable block copolymer family, poly(ester amide)-b-poly(ε-caprolactone) (PEA-b-PCL), was synthesized and characterized. These copolymers were synthesized by first preparing L-phenylalanine-based poly(ester amide) macroinitiators (Phe-PEAs) with free amine end groups via a solution polycondensation. The amine-terminated Phe-PEA macroinitiators were then used to initiate the ring-opening polymerization of ε-caprolactone monomer to prepare the PEA-b-PCL copolymers. The molecular weight (MW) of PEA-b-PCLs can be well controlled by adjusting the Phe-PEA MW and weight ratio of ε-caprolactone to Phe-PEA, and ranged from 7 to 50 kg mol\(^{-1}\). The copolymers’ structure and properties were characterized by various physicochemical methods, such as nuclear magnetic resonance, gel permeation chromatography and solubility testing. The in vitro enzymatic biodegradation tests were performed to evaluate the biodegradation rate of the copolymers. The results showed that the introduction of Phe-PEA to PCL did not significantly change the degradation rate of PCL. Biological studies were conducted to assess the polymer’s biological properties, like supporting the cell attachment and proliferation, and inflammation response. The results showed that the bovine aortic endothelial cells had very good attachment and proliferation performance on PEA-b-PCL coating surface. TNF-α release profiles showed that PEA-b-PCL exhibited a muted J774 macrophage inflammatory response.

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1. Introduction

Although FDA-approved absorbable aliphatic polyesters have been widely used, the rapid development of biotechnology requires a new generation of absorbable polyesters or their derivatives with improved or expanded physicochemical, biological and mechanical properties [1–3]. Among many recently developed absorbable aliphatic polyester derivatives, one unique approach is to introduce the natural amino acids into these absorbable polyester backbones [2–7]. The incorporation of natural amino acids results in these aliphatic polyesters having many new properties, such as functionality and charge property. One example of this approach is polyester-b-poly(α-amino acid)s, such as PLA-b-PLL and PCL-b-PLL [4,5,8]. However, after such a significant polymer backbone modification, many of those absorbable polyester derivatives lost their very important mechanical and processing properties, which largely limited their applications. In addition, due to the complexity of such a significant polymer backbone modification, the yields were very low.

In this study, we reported the synthesis, characterization and in vitro biological evaluation of a new family of block copolymers of absorbable polyesters and amino acid-based poly(ester amide)s (AA-PEAs) using poly-ε-caprolactone (PCL) as the absorbable polyester and phenylalanine (Phe) as the amino acid in AA-PEA. The AA-PEAs (Fig. 1) are used here because of their well-known attractive biological properties like muted inflammation response [9–11], supporting endothelial cell attachment and proliferation [12–14] and controllable enzymatically catalyzed surface-erosion biodegradability [12–24]. The AA-PEA backbone consists of non-toxic building blocks like α-amino acids, fatty diols and dicarboxylic acids. The variety of combinations of three building blocks offered many different generations of AA-PEAs for different purposes [12–24]. The incorporation of AA-PEA into absorbable polyesters is expected to significantly improve the biological properties of absorbable polyesters due to the unique and attractive biological properties of AA-PEAs, such as muted inflammatory response and supporting cell growth [12–14].

In addition, AA-PEAs can bring useful pendant functional groups or charges like –COOH, –NH₂, –OH and >C=C< to absorbable polyesters, which are well known for their lack of functional groups [12–14,25,26]. Finally, the hybrid copolymers of AA-PEA and absorbable polyesters could provide two different modes of