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Novel Biodegradable Functional Amino Acid-based Poly(ester amide) Biomaterials: Design, Synthesis, Property and Biomedical Applications

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Abstract

A new family of biodegradable and functional amino acid-based poly(ester amide)s (AA-PEAs) have been designed and synthesized as a new generation of biodegradable biomaterials for biomedical applications. This paper provides an overview of this new generation of biodegradable biomaterials, their design strategy, synthesis, characterization, unique biological property and eventual biomedical applications. AA-PEAs are synthesized from 3 basic building blocks: amino acids, fatty diols and fatty diacids. Due to the enormous variety of these 3 building blocks, a wide range of AA-PEAs could be tailor-designed for meeting specific clinical needs. These AA-PEAs have been engineered into a variety of physical forms ranging from 3D microporous hydrogels, melt-spun fibers, electrospun fibrous membranes, films and microspheres. All these AA-PEAs have shown 2 unique biological properties: support natural wound healing, and muted inflammatory response.

Keywords: Amino Acids; Poly(ester amide); Biodegradable; Inflammation; Synthesis; Biomaterials; Biomedical Applications; Fibrous Membrane; Electrospinning; Hydrogels; Microspheres; Fibers

1 Introduction

Absorbable or biodegradable polymeric-based biomaterials have received a lot of attention since their successful commercial launch as absorbable suture materials in early 1970s [1, 2, 3]. Those absorbable biomaterials are from aliphatic polyesters like Polyglycolic Acid (PGA), Poly-L-lactide (PLA), Poly-ε-caprolactone (PCL), poly-*p*-dioxanone and their copolymers. Absorbable polyesters have very good mechanical property and can be fabricated by thermal means into variety physical forms like fibers and micro- or nanospheres. Due to the presence of ester linkage in the polymer backbone, absorbable polyesters are subject to hydrolytic degradation via bulk degradation mode. Consequently, absorbable polyesters are moisture sensitive and require either rigorous inert dry environment or vacuum seal for long-term storage and better shelf life. In addition, due to their bulk hydrolytic degradation mode, the release profiles of the impregnated

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drugs are difficult to achieve a liner fashion. Besides the original and commercially most successful use in wound closure devices, other biomedical applications of these absorbable polyesters have included drug carriers, components of orthopaedic, cardiovascular and dental devices, and scaffolds for tissue engineering.

One of the major drawbacks of these absorbable polyesters as biomaterials is the lack of functionality, i.e., no pendant functional groups for simple chemical modification or attachment of biologically active agents. Consequently, many functional absorbable aliphatic polyester derivatives have been developed and one unique approach is to introduce the natural amino acids into these absorbable polyester backbones [4-9]. The incorporation of natural amino acids will bring these aliphatic polyesters many new properties, such as functionality and charge property. One example of this approach is polyester-*b*-poly (amino acid) s, such as PLA-*b*-PLL and PCL-*b*-PLL [6, 7, 10]. This unique approach, however, has significantly altered the backbone structure of the original absorbable polyesters, and due to the tedious and complexity of the chemical reaction schemes, the yields of the final functional absorbable polyesters have been quite low and hence their acceptance for industrial use have been quite limited.

In late 1990s and early 2000s, a new family of functional amino acid-based poly (ester amide)s (AA-PEA) has been reported [11-13]. AA-PEAs differ from the traditional non-amino acid-based poly(ester amide)s that have been studied for many years [14-17]. Unlike the diamine-based non-amino acid PEAs, the amino acid-based PEAs derive their amide (or peptide) linkage from amino acids. As a result, the backbone chemical structure of AA-PEAs has both peptide and non-peptide bonds, and hence exhibit both proteins and non-protein properties, named as "pseudo-proteins". In this review, the basic design and synthesis strategies, the resulting chemical structure, property, fabrication/formulation and performance of the many generations of AA-PEAs will be given.

2 Basic Chemical Structure of Amino Acid-based Poly(ester amide)s and Their Design and Synthesis Strategies

The functional amino acid-based poly(ester amide)s are built from 3 basic non-toxic building blocks: amino acids, diols and diacids. Fig. 1 shows a generic chemical structure of the AA-PEA repeating unit:

As Fig. 1 shows, the 2 adjacent amino acid moieties per repeating unit are separated by both a diol (via 2 ester bonds) and diacid (via 2 peptide bonds) segments. Thus AA-PEAs are the same as polypeptides, except the sequence of peptide bonds are disrupted by ester bonds due to the

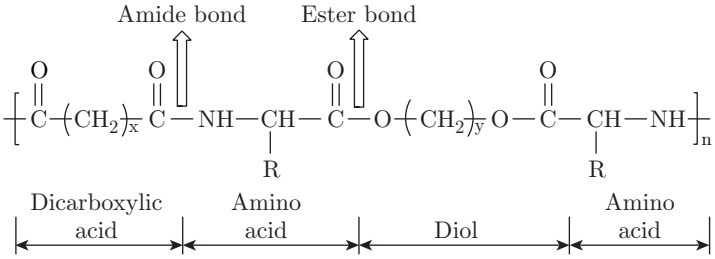

Fig. 1: General chemical repeating unit of a generic AA-PEA.