Polymer Degradation and Stability 139 (2017) 1–19

Contents lists available at ScienceDirect

Polymer Degradation and Stability

journal homepage: www.elsevier.com/locate/polydegstab

Progress in biodegradable zwitterionic materials

Liuchun Zheng [a], Zhijuan Sun [b], Chuncheng Li [a, *], Zhiyong Wei [c], Priyesh Jain [d], Kan Wu [d]

[a] Beijing National Laboratory for Molecular Sciences, Key Laboratory of Engineering Plastics, Institute of Chemistry, Chinese Academy of Sciences (ICCAS), Beijing 100190, PR China
[b] Ocean College, Zhejiang University of Technology, Hangzhou, Zhejiang Province, 310014, PR China
[c] Department of Polymer Science and Materials, School of Chemical Engineering, Dalian University of Technology, Dalian 116024, PR China
[d] Department of Chemical Engineering, University of Washington, Seattle, WA 98195, USA

ARTICLE INFO

Article history:
Received 26 January 2017
Received in revised form
1 March 2017
Accepted 15 March 2017
Available online 18 March 2017

Keywords:
Zwitterions
Biodegradable
Non-fouling
Biocompatible

ABSTRACT

Zwitterionic polymers, consisting of polymer backbone of ester or amide (meth) acrylic acid or pyrrolidinium, exhibit excellent non-fouling property, and have received great attention since last decade. However, these polymers lack important biodegradability for their application in biomedicine or marine field. Developing degradable zwitterionic polymers will solve problem associated with traditional zwitterionic polymers and increase their potential to be used in biomedicine for achieving both non-fouling and degradability. Herein, we present a comprehensive review describing various strategies developed till now for achieving degradable zwitterionic materials. Synthesis and applications of zwitterionic polymers based on various biodegradable polyesters, polypeptides, and natural polysaccharides (chitosan, starch and cellulose) have been critically reviewed and summarized. The basic structural characteristics and properties of different types of zwitterionic materials and biodegradable zwitterionic materials have also been introduced briefly. To the best our knowledge, this is the first review focusing on biodegradable zwitterionic materials.

Contents

* Corresponding author.
E-mail address: lichch@iccas.ac.cn (C. Li).

http://dx.doi.org/10.1016/j.polymdegradstab.2017.03.015
0141-3910/

1. Introduction

The adsorption of biomolecules, cells, and microorganisms on surfaces of medical implants, drug carriers, biosensing, bioseperation and marine coating is a problematic phenomenon that often induces biological incompatibility, reduces sensitivity or increase production cost [1,2]. Poly(ethylene glycol) (PEG) is commonly used to address this problem because of its high hydrophilicity, non-toxicity, and anti-protein-fouling [3]. However, PEG has poor stability, induces PEG antibodies after repeated injection, and cannot be metabolized naturally [4,5], thereby restricting its applications. Hence, it is highly desirable to seek alternative non-fouling material other than PEG.

Poly(2-oxazoline)s, especially the water soluble poly(2-methyl-2-oxazoline) (PMOXA) and its deravatives, are investigated as highly promising alternatives of PEG. They have similar hydrophilicity, antifouling property, and biocompatibility properties [6,7] to PEG and better structural and chemical stability than PEG [8–10]. Furthermore, PMOXA can be readily synthesized by living cationic ring-opening polymerization (CROP) of 2-methyl-2-oxazoline, which is less labor demanding compared to the anionic polymerization of PEG. CROP allows the incorporation of a broad variety functional initiators, terminal groups, and particularly functional monomers in a controlled sequence and opens up new prospects to design and construct well-defined (co)polymers with sophisticated multifunctional architectures and the tuning of the polymer properties [11].

Zwitterionic material is another important class of materials used to construct non-fouling surfaces. They exhibit excellent non-fouling and biocompatibility due to their super hydrophilicity and strong interaction with water by ionic salvation [12]. It has been shown that zwitterions modified surfaces exhibit superior non-fouling properties than PEG and don't induce any antibody production as PEG [13]. Therefore, this review only focuses on zwitterionic materials. Generally, zwitterionic groups can be classified into betaine and mixed charged pairs. Betaines are characterized with identical numbers of positive and negative charges in series on the same side chain, i.e., the same repeating unit. Three most widely investigated betaines are sulfobetaine (SB), carboxybetaine (CB), and phosphorylcholine (PC). SB is most common, cheap and widely used zwitterion material that has great potential to be commercialized. Various SB based homopolymers and copolymers have been prepared and used to modify surfaces. The resulting surfaces demonstrate excellent anti-coagulant activity and non-fouling properties [14,15]. Recently, CB based materials have been studied extensively because of the ultra-low non-fouling property and easy for functionalization. The reactive −COOH group on CB can be used to conjugate bio-recognition compounds, such as RGD peptide [Arg-Gly-Asp-D-Tyr-Lys] and antibody, for targeted drug delivery or diagnostics, via conventional coupling chemistry, such as 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide and hydroxysuccinimide (EDC/NHS) [16,17]. PC group has a biomimetic structure similar to phospholipids head group in the cell membrane and possesses good biocompatibility. But the problem is that PC monomers are often difficult to synthesize [18]. Most commonly mixed charged zwitterions are amino groups and they often show pH-sensitivity. The synthesis of various types of zwitterionic polymers has been reviewed in detail by Laschewsky et al. [19,20], and the solution properties have been summarized by Lowe at al [21].

However, most of these current research and reviews focus on materials with non-degradable backbones composed of ester or amide (meth) acrylic acid or pyrrolidinium. These cannot be metabolized in vivo, which is a main concern when comes to application in biomedicine. These non-degrdable polymers may accumulate in the body as foreign entities, leading to formation of pathological tissue followed by induction of malignancy and thereby disrupting normal cell metabolism [22]. These non-degradable polymers are not environmentally friendly when used in marine coating. Therefore, it is imperative to study and develop biodegradable zwitterionic materials. But compared to non-degrdable zwitterionic materials, biodegradable zwitterionic materials have not been sufficiently studied.

Generally, biodegradable zwitterionic materials can be classified as polyester, polypeptide or natural occurring polysaccharide (such as cellulose, chitosan and starch) according to the backbones of these polymers. Zwitterionic moieties can be introduced into biodegradable materials in the form of polymers or small moieties. Zwitterionic polymers modified biodegradable materials tend to be partially biodegradable; while zwitterionic small moieties decorated biodegradable materials can be fully biodegradable. Various methods have been reported to introduce zwitterionic moieties into polymers, such as polycondensation, (controlled) radical polymerization, functional initiator, or post modification.

Ishihara et al. synthesized PC modified poly (lactic acid) by radical copolymerization of 2-methacryloyloxyethyl