



Review

Amphiphilic block co-polymers: Preparation and application in nanodrug and gene delivery

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ARTICLE INFO

Article history:

Received 16 December 2011

Received in revised form 28 February 2012

Accepted 2 March 2012

Available online 9 March 2012

Keywords:

Drug delivery

Nanotechnology

Polymeric micelles

Block co-polymers

Drug targeting

ABSTRACT

Self-assembly of amphiphilic block co-polymers composed of poly(ethylene oxide) (PEO) as the hydrophilic block and poly(ether)s, poly(amino acid)s, poly(ester)s and polypropyleneoxide (PPO) as the hydrophobic block can lead to the formation of nanoscopic structures of different morphologies. These structures have been the subject of extensive research in the past decade as artificial mimics of lipoproteins and viral vectors for drug and gene delivery. The aim of this review is to provide an overview of the synthesis of commonly used amphiphilic block co-polymers. It will also briefly go over some pharmaceutical applications of amphiphilic block co-polymers as “nanodelivery systems” for small molecules and gene therapeutics.

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1. Introduction

Amphiphilic block co-polymers (ABCs) have been in use as pharmaceutical excipients in different forms for a long time and their application is experiencing rapid growth in modern pharmaceutical sciences [1–4]. Traditionally ABCs have been used as stabilizing agents in the formulation of coarse and colloidal dispersions and as gels as depot or bioavailable formulations. More recently evidence has been provided for the potential use of ABCs as safer replacements for low molecular weight surfactants in the solubilization of poorly soluble drugs and core/shell association colloids for nanoscale delivery systems [5–7].

The rapid development of ABC applications in the pharmaceutical sciences is primarily due to the chemical flexibility of their structure, which provides an opportunity for the design of versatile drug carriers. For instance, the size of both the hydrophilic and the hydrophobic parts can be varied at will to achieve polymers of varied hydrophilic–lipophilic balance (HLB); the molecular weight of the polymer can be varied within a wide range while maintaining a constant HLB and, more importantly, both the hydrophilic and hydrophobic parts can be functionalized.

Among different structures, ABCs with poly(ethylene oxide) (PEO) as their hydrophilic block and poly(amino acid)s ((PLAA)s), poly(ester)s, poly(amine)s or poly(amine ester)s as their hydrophobic block represent the most extensively researched polymers for constructing nanoscale delivery systems. This is largely due to the expected low immunogenicity, the biodegradability and the biocompatibility which may make them suitable for human administration. Methods of chemical synthesis of these block co-polymers have advanced tremendously and been optimized in recent decades. Among these methods, ring-opening polymerization (ROP) has been intensively explored and extensively used to synthesize PEOs, PEO–polyester conjugates and PEO–PLAA conjugates. Therefore, ROP polymerization technique has also been continuously refined in recent years to achieve tailored properties and controlled architectures of ABCs [8–10]. For example, several possible combinations of initiators and catalysts have been evaluated to achieve the desired polymer architecture and properties [11–15]. Enzyme-catalyzed ROP has emerged as one of the most promising tools to synthesize polyesters, avoiding the use of organometallic catalysts and having the appeal of a “green-chemistry” [16]. Easy synthesis, the potential for scaled up production and the chemical flexibility of these ABCs produced by ROP will eventually facilitate the application of ABCs as drug carriers.

The aim of this review is to provide an overview of the general synthesis and engineering of ABCs for use as nanodelivery systems. Specific nanostructures formed from ABCs and used for drug and gene delivery applications, e.g. polymeric micelles, polymeric

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