Progress in Polymer Science 53 (2016) 207–248

Contents lists available at ScienceDirect

Progress in Polymer Science

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

Self-assembling polymer systems for advanced treatment of cancer and inflammation

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ARTICLE INFO

Article history:
Received 28 October 2014
Received in revised form 25 May 2015
Accepted 9 July 2015
Available online 26 July 2015

Keywords:
Self-assembling polymers
Nanoparticles
Micelles
Amphiphilic polymers
Cancer
Anti-inflammatory agents

ABSTRACT

Self-assembled nanoparticles have reached a growing interest for the improvement of cancer diseases and associated inflammation processes. This article describes the most representative types of self-assembling nanosystems, including a detailed review of different methodologies for their preparation. Nanoparticles are commonly formed by self-assembling of amphiphilic polymers in aqueous environment. For that reason, the main strategies for the design of amphiphilic polymeric systems are also reviewed, with an emphasis on the different polymerization techniques of synthetic monomers and several strategies of chemical modification of polysaccharides and proteins. Additionally, most advanced applications of self-assembled nanocarriers for the improvement of treatment of cancer and inflammation diseases are also discussed, focusing on the description of drug-loaded and drug-conjugated systems, active targeted strategies and most recently possibilities for the multimodality treatment of cancer diseases.

Contents

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http://dx.doi.org/10.1016/j.progpolymsci.2015.07.005
0079-6700/

1. Introduction

Nanomedicine is growing in directions of diagnostic, treatment and theranostics (diagnostic, drug delivery and therapeutics), and the participation of systems based on a macromolecular concept is well recognized [1–3]. In fact, we have to learn from nature that most of the activities in the living organism, including the human body, are based on the design and application of bioactive systems and drugs developed in a macromolecular or polymeric concept. Nature shows a lot of examples that we have the opportunity to apply; *i.e.* bioactive systems and macromolecular drugs. Systems such as heparin, chondroitin sulfate, heparan sulfate (polysaccharides), or insulin, growth hormone, fibroblast growth factor, morphogenetic proteins, fibronectin, albumin, fibrinogen (proteins) and other well-known bioactive compounds are designed and fabricated in our organism within a macromolecular architecture.

High molecular weight (MW) polymers with specific molecular architectures present the ability of association and distribution in specific nanodomains, with morphologies and properties depending on the nature of the molecules [4]. The design, composition and morphological assembly of the cells and the extracellular matrix in the human organism are developed on the basis of the interactions and arrangements of long molecules with specific properties. On this way, the cytoplasmic membrane is composed of a bilayer assembled organization of lipid molecules containing a hydrophilic head. These individual and isolated structures develop their activity in a medium of controlled viscosity constituted by a macromolecular hydrogel of unique characteristics (collagen), which allows the development of the cellular activity and at the end, the proliferation of cells and fabrication of tissues and organs.

Macromolecular self-assembly is a spontaneous process based on the ensemble of molecules into 3D supramolecular structures with different morphologies such as polymeric micelles (PM), nanoparticles (NP), polymerosomes, *etc.* [5,6]. This process is possible due to the amphiphilic nature of these structures, containing both hydrophobic and hydrophilic domains. Particularly, in the core–shell organization, the inner core is composed of the hydrophobic part of the amphiphilic polymer and serves as a nanocontainer of poor soluble drugs. This core is surrounded by an outer shell based on hydrophilic polymers [7–9]. The characteristics of self-assembling systems depend on several important factors:

- Design, molecular composition and structure, considering macromolecular size and size distribution.
- Monomeric or co-monomeric sequences arrangement and distribution along the macromolecular chains.
- Functionality and its distribution in the structure of the macromolecular systems.
- Structural and morphological distribution in nanodomains.
- Macromolecular associations of natural and synthetic polymers, and stability in physiological conditions.

The structural characteristics of self-assembling systems have several advantages to improve the effectiveness and safety of cancer and anti-inflammation therapies for clinical use [10–13]. For example, the encapsulation of chemotherapeutic and anti-inflammatory drugs in the core of these assemblies improves their aqueous diffusion and transport, as well as bioavailability, decreasing their toxic side effects [14,15]. Moreover, their hydrophilic surfaces decrease clearance by the reticuloendothelial system (RES),