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Review

Polysaccharide based nanogels in the drug delivery system: Application as the carrier of pharmaceutical agents

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ABSTRACT

Polysaccharide-based nanoparticles have fascinated attention as a vesicle of different pharmaceutical agents due to their unique multi-functional groups in addition to their physicochemical properties, including biocompatibility and biodegradability. The existence of multi-functional groups on the polysaccharide backbone permits facile chemical or biochemical modification to synthesize polysaccharide based nanoparticles with miscellaneous structures. Polysaccharide-based nanogels have high water content, large surface area for multivalent bioconjugation, tunable size, and interior network for the incorporation of different pharmaceutical agents. These unique properties offer great potential for the utilization of polysaccharide-based nanogels in the drug delivery systems. Hence, this review describes chemistry of certain common polysaccharides, several methodologies used to synthesize polysaccharide nanoparticles and primarily focused on the polysaccharide (or polysaccharide derivative) based nanogels as the carrier of pharmaceutical agents.

Contents

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1. Introduction

Cancer is a multi-gene, multi-step devastating disease with an altered DNA sequence (mutation) which grows uncontrollably by disregarding the normal rule of cell division [1]. Nowadays, cancer is a global issue and is a worldwide disease with a leading cause of mortality [2]. Cancer is the second leading cause of death in the United States and a total of 1,685,210 new cancer cases and 595,690 cancer deaths are projected to occur in 2016 [3]. Similarly, cancer is the leading cause of death in developing countries due to adoption of cancer-associated lifestyle choices including physical sedentariness, smoking, and westernized diets [2]. Current treatment tactics of cancers are primarily centered on surgery, irradiation and the systemic administration of chemotherapeutics drugs [4]. However, conventional chemotherapy used nowadays has certain limitations: (a) Low (non) water solubility: Majority of anticancer drugs are hydrophobic which leads to poor aqueous solubility and low bioavailability; (b) Lack of selectivity: Most anticancer drugs lack selectivity toward tumor cells and have significant toxicity mainly to rapidly proliferating normal cells; and (c) Multidrug resistance (MDR): chemotherapeutics resistance is a major problem that limits (cause treatment failure in over 90% of patients with metastatic cancer) the effectiveness of anticancer drugs used to treat cancer. MDR is mainly due to increased efflux pumps of anticancer drugs from the tumor cells via P-glycoprotein (Pgp) which is much more expressed on the cell membrane of many cancer cells [5–7].

Any pharmaceutical agents transported through different routes of delivery, will certainly encounter the physiological, biochemical and chemical barriers before reaching at the site of action, which may reduce the therapeutic effects of drugs [8]. Therefore, understanding physicochemical and biochemical characteristics of molecules is important to know how a pharmaceutical agent interacts with these barriers. It is well recognized that the solubility, permeability and metabolic stability of a drug molecule are major factors in drug delivery systems [9,10].

The microenvironment of a solid tumor has various features like high interstitial fluid pressure, low extracellular pH and low oxygen tension or hypoxia, which discriminate it from the corresponding normal tissue [11]. Blood vessels of tumors have exceptional features that are not usually observed in normal blood vessels like extensive angiogenesis, defective vascular architecture, extensive extravasation (vascular permeability), and impaired lymphatic clearance from the interstitial space of tumor tissues [12,13]. Tumor vascular permeability and impaired lymphatic clearance, i.e., enhanced permeability and retention (EPR) effect, are key points for selective nanoparticles-drug delivery to the tumors (displayed in Fig. 1), which can overcome the devastating side effects of chemotherapeutic drugs to the normal cells [14,15]. Therefore, delivery of these anti-cancer agents with the use of nanoparticles (NPs) can help to overcome certain limitations related to conventional chemotherapy [16].

Drug delivery systems (DDS) are based on interdisciplinary approaches that combine polymer science, bioconjugate chemistry, pharmaceutics and molecular biology [17]. The main objective of DDS is to transport pharmaceutical agents to the systemic circulation based on controlling the pharmacokinetics, pharmacodynamics, non-immunogenicity, non-specific toxicity and bio-recognition of target site to produce a desired pharmacological effect [18,19]. The primary advantages of DDS over traditional systems are the tendency to deliver pharmaceutical agents more selectively to a specific site, eliminate over or under dosing (maintain drug levels in desired range), increase patient compliance, more consistent absorption within the cell of interest and prevention of side effects [20].

Nanoparticles (NPs), within a size range from 10 to 1000 nm in diameter, have unique features (such as; their surface area is high, their quantum properties and their capability to adsorb and carry other compounds) which make them attractive tools in the drug delivery systems [21–23]. As a result of relatively large (functional) surface area, NPs can encapsulate in or immobilize high amount of anticancer drugs either through covalent or non-covalent interactions [24,25]. Hence, NPs composed of biocompatible and biodegradable polymers can be used in DDS [26]. Polymeric nanocarriers may be prepared from natural proteins (such as albumin, collagen, gelatin, etc.) [27–29] or synthetic polymers (such as polyacrylamide (PAA), polylactic acid (PLA), polyglycolic acid (PGA), poly(lactide-co-glycolide) (PLGA), dendrimers, etc.) [30–35].

Nowadays, polysaccharide-based nanoparticles have fascinated attention as a vesicle of different pharmaceutical agents due to their unique multi-functional groups in addition to their physicochemical properties, including biocompatibility and biodegradability [23,36,37]. The multi-functional groups of the polysaccharide backbone permit facile chemical modification to synthesize NPs with miscellaneous structures [38,39]. Certain polysaccharides have the special intrinsic

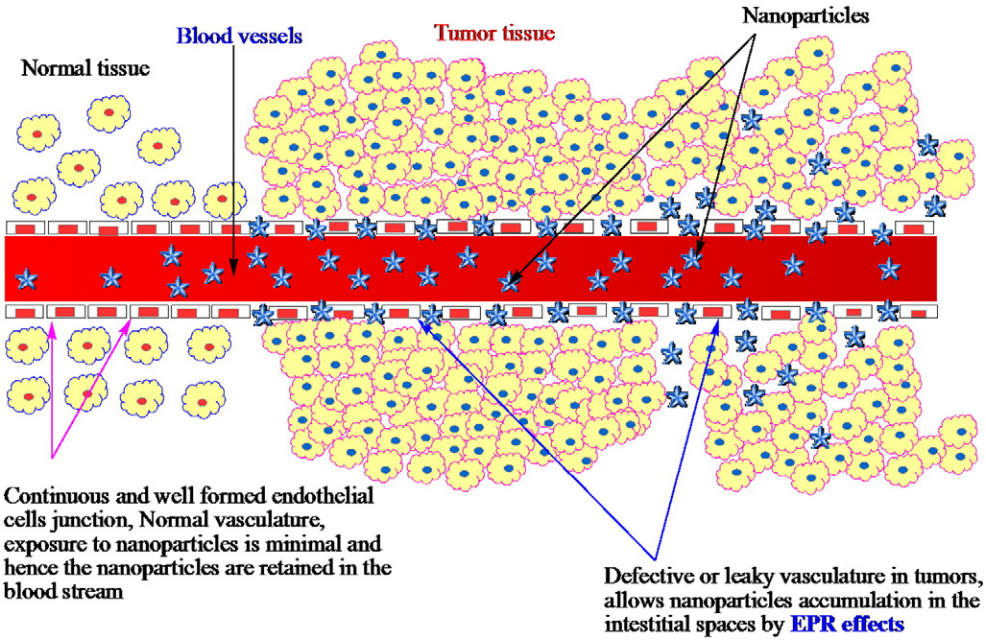

Fig. 1. EPR effects extravasation and release of nanoparticles in tumor interstitial space.