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Therapeutic Delivery

Polymeric nanoparticles as carrier for targeted and controlled delivery of anticancer agents

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In recent decades, many novel methods by using nanoparticles (NPs) have been investigated for diagnosis, drug delivery and treatment of cancer. Accordingly, the potential of NPs as carriers is very significant for the delivery of anticancer drugs, because cancer treatment with NPs has led to the improvement of some of the drug delivery limitations such as low blood circulation time and bioavailability, lack of water solubility, drug adverse effect. In addition, the NPs protect drugs against enzymatic degradation and can lead to the targeted or/and controlled release of the drug. The present review focuses on the potential of NPs that can help the targeted or/and controlled delivery of anticancer agents for cancer therapy.

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Keywords: anticancer agent • nanocarriers • polymeric nanoparticles • targeted drug delivery

Cancer is the second leading cause of death in the world and was responsible for 8.8 million deaths in 2015. There are many ways for cancer therapy, including chemotherapy, hormone and gene therapy, radiation, surgery, photothermal and immunotherapy [1–3]. These methods in spite of effectiveness have many side effects on patients. In addition, conventional methods are not specific in targeting the drugs to the cancer cells, causing many side effects for healthy tissues. Among cancer therapeutic methods, chemotherapy is the most frequently used one for its high efficiency. However, cancer drugs have low water solubility that considerably reduces their bioavailability and biodistribution [1,4]. In addition, the development of drug resistance causes a significant failure in the treatment of metastasis cancer [5]. Today, these problems can be solved with nanoparticles (NPs) that are capable of carrying drugs with minimum side effects and diminish drug resistance in cancer therapy [6]. The use of nanocarrier also has many advantages such as prolonged plasma half-life [7], different biodistribution profile compared with conventional chemotherapy [8], ability for surface functionalization, targeting drug delivery [9], possibility of multiple drug delivery to achieve synergistic therapeutic response [10], protect drug against enzyme degradation, dissolution of hydrophobic drugs [11] and higher permeability across the biological membranes [12]. Metals [13,14], liposomes [15,16], dendrimers [17,18], micelles [19,20] and polymeric NPs are the most common example of nanocarrier for drug delivery. Biopolymers are used in biomedical applications because of their biocompatibility and biodegradability properties. The NPs according to their applications are 20–200 nm in size and can carry a variety of hydrophilic [21] and hydrophobic drugs [22], proteins [23], peptides [24] and siRNAs [25]. NPs with size ranging from 100 to 200 nm have desirable enhanced permeability and retention (EPR) within tumor vasculature [26,27]. Even though NPs can be passively targeted to tumor tissue with the EPR effect, but there is the ability to become active in various targeting agents and enhance targetability (Figure 1). Polymers like pullulan (Pul) and hyaluronic acid (HA) are used to activate NPs for active targeted drug delivery. Presence of asialglycoprotein and cluster of differentiation 44 (CD44) receptors on the surface of cancer cells and the tendency of Pul and HA to each of them cause to use these polymers as active targeting. Surface characteristics of NPs influence their uptake and clearance *in vivo*. NPs clearance occurs mainly via opsonization and phagocytosis by macrophages following the mechanism of receptor-mediated endocytosis [28–30]. Biopolymers according to their source of extraction are divided into natural and synthetic polymers. Some of the natural polymers include chitosan (CS), alginate (Alg), Pul, dextran (Dex), HA and synthetic polymers include poly-lactic-*co*-glycolic acid (PLGA), polylactic acid (PLA), poly-ε-caprolactone

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