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Polymeric nanoparticles for targeted drug delivery system for cancer therapy

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ABSTRACT

A targeted delivery system based on the polymeric nanoparticles as a drug carrier represents a marvelous avenue for cancer therapy. The pivotal characteristics of this system include biodegradability, biocompatibility, non-toxicity, prolonged circulation and a wide payload spectrum of a therapeutic agent. Other outstanding features are their distinctive size and shape properties for tissue penetration via an active and passive targeting, specific cellular/subcellular trafficking pathways and facile control of cargo release by sophisticated material engineering. In this review, the current implications of encapsulation of anticancer agents within polyhydroxyalkanoates, poly-(lactic-co-glycolic acid) and cyclodextrin based nanoparticles to precisely target the tumor site, i.e., cell, tissue and organ are highlighted. Furthermore, the promising perspectives in this emerging field are discussed.

Contents

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1. Introduction

Cancer is the world's deadliest disease of human beings [1]. GLOBOCAN 2012 estimated 14.1 million new cancer cases per year in the world, which would be expected to rise to 19.3 million new cancer cases per year by 2025 [1]. Surgery, radiation, chemotherapy and immunotherapy are the four main methods, which are globally used for cancer therapy. However, the high toxicity, the poor oral bioavailability, the lack of water solubility, low therapeutic indices, inconsistency in circulation, non-specific bio-distribution and delivery of an anticancer drug to both normal and cancer cells are the key shortcomings of the conventional cancer therapies [2,3]. Therefore, the novel, harmless and efficient treatments are immediately needed to restrain these high mortality and morbidity statistics.

Polymeric nanoparticles (PNPs) are submicron-sized colloidal particles. An anticancer agent of interest is adsorbed or encapsulated or conjugated either within or onto the surface of the PNPs. A targeted delivery system is based on drug loaded PNPs and is used for the sustained release of anticancer therapeutics to the site specific targets (Fig. 1). A recent progress in the field of targeted drug delivery system (TDDS) is based upon the rational design of polymer (composition, solubility, crystallinity, molecular weight, backbone stability, hydrophobicity and polydispersity) tailored for a particular cargo (molecular weight and charge of drug).

Several methods are used for synthesis of PNPs [4–6]. A general overview of chemical approaches used for synthesis of PNPs is given in Fig. 2. Emulsification and solvent evaporation/extraction [7,8], nanoprecipitation (solvent-displacement) [9–13], supercritical anti-solvent method [14–16], and salting-out [17] are among the most common techniques, which are widely used for fabrication of PNPs. Emulsification and solvent evaporation/extraction was the first method to synthesize PNP. Polymer (synthetic, semi-synthetic or natural) dissolved in an organic solvent constitutes the organic phase, while, the water along with stabilizer/surfactant is present in an aqueous phase. Chloroform, dichloromethane, and ethyl acetate are commonly used organic solvents. Both single (oil-in-water, o/w) [18,19] and double emulsification (water-in-oil/in-water, w/o/w) [20–22] methods are used for formation of emulsion via high-speed homogenization or ultrasonication followed by solvent evaporation. Solvent evaporation is achieved either by continuous stirring at room temperature or reduced pressure. This method is basically applied to lipophilic drugs. However, high energy requirements for homogenization is a main hindrance in its application on a pilot scale. Nanoprecipitation method is based on drop-wise addition of organic phase (polymer dissolved in water-miscible solvent, i.e., acetone, ethanol, hexane and methylene chloride) into an aqueous phase (with or without stabilizer/surfactant). Likewise emulsification and solvent evaporation/extraction method, only lipophilic drugs can be encapsulated into PNPs via nanoprecipitation. High drug encapsulation efficiency, narrow size distribution, no need of homogenization, and easy scale-up are the main advantages of this method. Technique based on supercritical anti-solvent method is another way to prepare small sized PNPs under mild operating conditions. In this method, the solute containing solution is sprayed in the form of tiny droplets into high pressure vessel containing liquid anti-solvent. The CO_2 is used as anti-solvent. The rapid diffusion of CO_2 into solute containing solution resulted in the formation

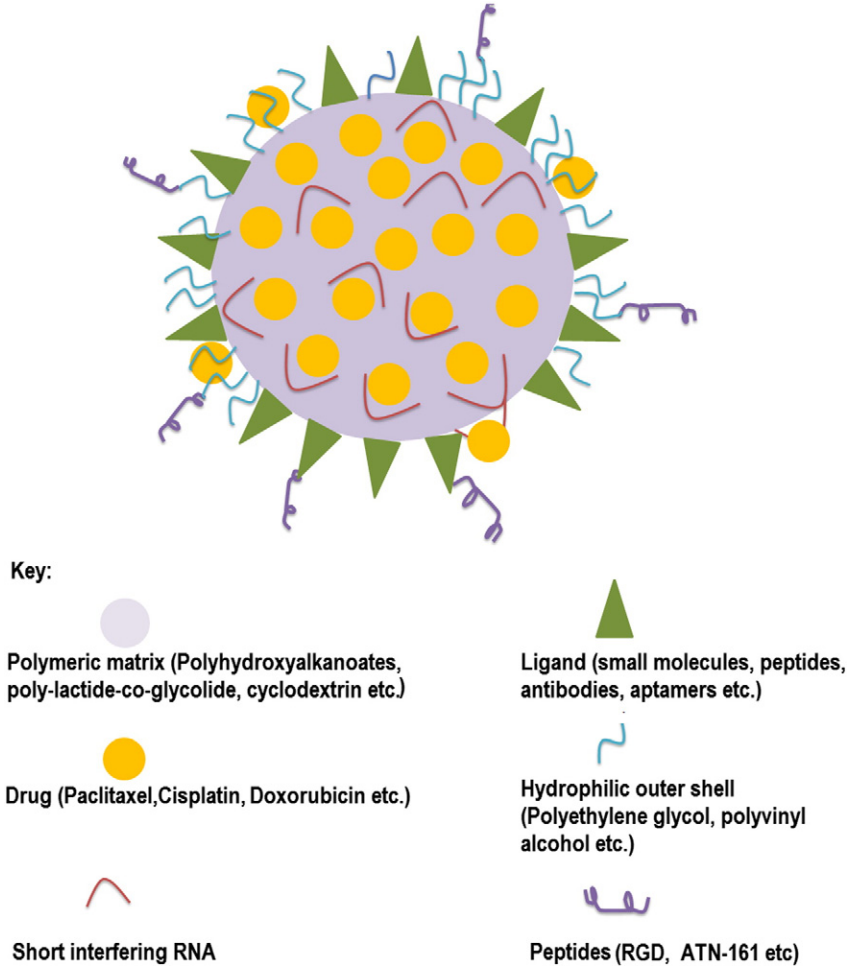

Fig. 1. A schematic representation of structure of polymeric nanoparticle based targeted drug delivery system.