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Cancer and Polymeric-Carriers

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ABSTRACT

Advances in medicine and pharmacy have saved many lives from death. Researchers and scientists around the world have made great strides with their findings, not only improving public knowledge with their findings but also keeping hope alive in the hearts of some people with incurable diseases. Various sciences accompanied medicine and pharmacy in this development, one of which is polymer engineering. Polymers due to amazing properties can be used as prostheses, drug carriers, gene delivery, etc. Polymers are unique candidates for the release of anticancer drugs. Non-toxicity, and biodegradability are important features of a carrier. This study summarizes cancer statistics and introduces several polymer-carriers.

Keywords: Cancer; Polymer; Carrier; Dendrimer; Micelle; Chitosan

Introduction

The development of human societies has been accompanied by deforestation, environmental pollution, and the destruction of animal habitats, which have put human health at increasing risk. Improper use of pesticides, drought, ozone depletion, surface water pollution, and extinction of many animal species are the gift of modern human life, which have caused many diseases [1-13]. Cancer has been the cause of human death for decades and has become a major public health problem in the world [14,15]. The deaths statistics from cancer in various parts of the world is shocking [16,17]. Unfortunately, this disease is seen at all ages and can be a serious threat to health [18,19]. Breast, prostate, lung, colorectal, and stomach cancers are the most common cancers in the world. Screening tests, changing nutrition patterns and reduced use of cigarettes and alcohol can greatly reduce the incidence of the disease. Unfortunately, despite many advances in cancer, the cost of treatment remains high, so the golden time for early diagnosis and treatment is lost [20-24]. Contrary to popular belief, cancer is not the end of life, and in recent years a wide range of this disease has been cured and human has returned to normal life. Cancer treatment has progressed wonderfully, surgery, radiotherapy, and chemotherapy can destroy tumors and arrest cancer progression. Radiotherapy and chemotherapy are used to destroy or shrink cancerous tissue. In these methods, damage to the deoxyribonucleic acid of cells destroys the target tissue, progress and division become impossible. Although in addition to cancer cells, healthy cells are also damaged, most healthy cells recover again. In conventional chemotherapy drug is distributed as general in the body, and because some drugs have serious side effects, they can also affect normal cells, and that these side effects cause to restrict the frequency and size of dosages [25,26].

Paclitaxel and doxorubicin are two of the most used drugs in the treatment of many cancers. Paclitaxel is a toxoid antineoplastic that interferes with the normal function of microtubule growth. This drug has a wide range of side effects, including risk of infection, closing of the throat, breathlessness and looking pale, bruising and bleeding, allergic reaction, hair loss, muscle and joint pain [27,28]. Doxorubicin is an antineoplastic in the anthracycline class. These compounds are isolated from natural sources and antibiotics, they lack the specificity of the antimicrobial antibiotics and thus produce significant toxicity. Doxorubicin is widely used to treat several types of cancer. Also, doxorubicin has serious side effects such as heart damage [29,30]. As can be seen, drugs have many side effects that can in some cases weaken the patient and thus disrupt the healing process. Nanoparticles have many applications

in medicine and nanocomposites due to their unique properties [31-38]. In recent years, nanoparticles have been used extensively to diagnose and treat cancer [39]. Nanoparticles can penetrate cancer cells and increase the concentration of drugs in them while preventing toxicity in normal cells. However, nanoparticles still have limitations such as instability in circulatory system and toxicity. Polymers due to their amazing properties are used in a wide range of applications, such as batteries, coatings, adhesives, solar cells, drug carriers, and Prosthesis [40-46]. They can be suitable carriers and prevent premature destruction of the drug and improve their stability and prolong the presence of the drug in the circulatory system. The function of polymer-carriers differs in terms of drug release.

Commonly, we can say that drugs are graft to them, and with changes such as temperature, chemical activation (biodegradation), solvent activation, pH, etc., this bond is destroyed and the drug is released. The drug can be loaded on the carrier or the carrier can act as a protective shield and hold the drug in the core. The top polymer-carriers can be classified into three groups: dendrimers, chitosan, and micelles. In recent years, a lot of research has been done on this field. Dehghani, et al. [47] they studied the fabricate new electrolyte/non-electrolyte janus particles with low cytotoxicity as carriers of doxorubicin. For this purpose, seeded emulsion polymerizations of 2-(dimethylamino) ethyl methacrylate (DMAEMA) and methacrylic acid (MAA) were performed in presence of poly (2-hydroxyehtyl methacrylate) particles as seed to fabricate Janus particles. These particles were then used as carriers of doxorubicin in different conditions. All samples showed high loading capacity and long-time release process. The results of cytotoxicity showed PMAA-based particles had no mentionable cell toxicity whereas PDMAEMA-based ones had moderate cytotoxicity. Moreover, all drug-loaded particles prohibited cell growth significantly. Najafi, et al. [48] they studied the new method for the synthesis of Janus dendrimers. The new method has three main stages for the synthesis of Janus dendrimers including synthesis of 5th generation Poly(propylene imine) dendrimer with cystamine core and hydrophobic surface, conversion of disulfide bonds to thiol group using a structure scission approach, and the formation of polyamido amine hydrophilic dendrons with amine end groups. This Janus dendrimers have resulted in significant improvements in drug solubility. Also, solubility of the two hydrophobic drugs in water was increased by increasing concentration and generation of dendrimer. Also, self-assembly of Janus dendrimer in water led to formation of spherical micelles besides cubic ones with sizes almost < 100nm. Xu et al. [49] they studied the poly(ethylene glycol) (PEG)-detachable pH-responsive self-assembled from amphiphilic copolymer poly(ethylene glycol) methyl ether-D_{labile}-poly(β-amino ester)-D_{labile}-poly(ethylene glycol) methyl ether consisting of pH-labile bonds and pH-sensitive blocks. Doxorubicin-loaded polymeric micelles can accumulate at the tumor site via an enhanced permeability.

The Doxorubicin molecules are controlled release from the carriers at specific pH values. The results demonstrate that Doxorubicin-loaded polymeric micelles have the capability of showing high therapeutic efficacy and negligible cytotoxicity compared with free Doxorubicin in vitro and in vivo. polymeric micelles had spherical morphology with an average size of 200nm. Yang et al. [50] they studied a novel polymeric prodrug micellar carrier based on polyethylene glycol (PEG)-derivatized glycyrrhizic acid (GA) (PEG-Fmoc-GA), was developed for co-delivery of doxorubicin as a combined anti-cancer treatment. Polymeric micelles containing doxorubicin ranged in size from 184 to 290nm. Also, PEG-Fmoc-GA conjugated micelles significantly facilitated the intracellular uptake of doxorubicin by HepG2 cells, when compared to a doxorubicin solution alone. In addition, doxorubicin encapsulated in PEG-Fmoc-GA micelles displayed longer blood circulation time, larger drug concentration area under the curve, decreased volume distribution and clearance than doxorubicin solution. Xie et al. [51] they studied the a facile approach was established to fabricate the pH-responsive surface charge reversal carboxymethyl chitosan-based drug delivery system for pH and reduction dual-responsive triggered doxorubicin release, with a reduction responsive sheddable shell via facile organic solvent-free co-precipitation method. For this purpose, doxorubicin was loaded in the pH responsive core of the poly(2-(diisopropylamino) ethyl methacrylate) (PDPA) fragments, which were bio reducibly conjugated onto the PEGylated carboxymethyl chitosan (PEG-CMCS) backbone as reduction responsive sheddable shielding shell. The proposed nanoparticles, with a high drug loading capacity of >36% with drug-loading only in their cores, showed excellent pH and reduction dual-responsive triggered disintegration and doxorubicin release performance with cumulative release >85% in the simulated tumor intracellular microenvironment. Chen et al. [52] they studied the formation and properties of a novel polyelectrolyte complex of drug carrier system for the delivery of doxorubicin, which consists of hyaluronic acid coated hydrophobically modified chitosan. The nanoparticles had an average size between 280 and 310nm. The results showed that doxorubicin could be easily incorporated into the nanoparticles with encapsulation efficiency and kept a sustained release manner without burst effect when exposed to phosphate-buffered saline (pH 7.4) at 37°C. In general, polymers are good candidates for drug carriers, they are commonly used to release drugs such as doxorubicin, paclitaxel, methotrexate, nystatin, vinblastine, cisplatin, rapamycin, fenofibrate, and carvedilol [53-57].

Conclusion

We believe that polymeric carriers are a good method to treat cancer. The growing trend of science promises a successful future. Polymeric carriers can load multiple drugs simultaneously, so the chemotherapy steps can be reduced, thereby causing less damage to healthy cells. It can be said that the best advantage of polymer-

carriers is that the drug is delivered to the target tissue, which prevents other cells from being affected by the drug and minimizes the side effects of the drug.

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