A review on chitosan nanoparticles for cancer treatment

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Abstract
Cancer remains one of the dreadful disease still today. Chemotherapy, radiotherapy and surgery are effective treatments available for treatment of cancer but have serious side effects. Due to advancement in nanomedicine, several drug carriers have become popular. But chitosan for anticancer drug delivery has become popular due to its easy availability, less cytotoxicity and biodegradability. Research has been done on chitosan as a carrier of several anticancer drugs. This review article covers introduction, methods of preparation of chitosan nanoparticles, characteristics of chitosan nanoparticles and various anticancer drug encapsulated in chitosan nanoparticles.

Key words: Chitosan, chemotherapy, radiotherapy, surgery, nanomedicine.

1. Introduction
Cancer is the leading cause of mortality in economically developed countries and the second among developing countries [1]. Despite of lot of research in treatment of cancer, chemotherapy and radiotherapy are major treatment methods for cancer. Although these two methods are effective in the treatment of cancer, these can have serious side effects such as loss of hair, irritation in stomach and low counts of blood cells. Nanotechnology particularly nanomedicine has emerged as hope for treatment of cancer because anticancer drug can be targeted to diseased site by various nanomedical approaches such as lipid based nanoparticles, polymeric nanoparticles etc. Out of these, polymeric nanoparticles have attracted the attention of researchers for targeted drug delivery major being chitosan. Chitosan is obtained from deacetylation of chitin from the shells of crustaceans and mollusks as shown in Figure 1. Chitosan have low toxicity, better stability and biodegradability and can be administered through oral, nasal and other routes. Anticancer drug can be targeted at diseased site by joining various ligands such as folic acid. Thus chitosan is ideal carrier for anticancer drug. In recent past lot of research has been done on chitosan as a carrier of anticancer agent. Keeping in view importance of chitosan in anticancer drug delivery, this review article was written.

2. Methods of preparation of chitosan nanoparticles
There are various methods of preparation of chitosan nanoparticles. Some of them are as follows:

2.1. Ionic gelation method
Ionic gelation method is most commonly used for preparation of chitosan nanoparticles. This method was first reported in 1997 [3]. In this method appropriate concentration of chitosan is dissolved in acetic acid. Sodium tripolyphosphate is most commonly used cross-linking agent. Both of these phases are dissolved in separate glass bottles and mixed under stirring leads to formation of chitosan nanoparticles due to inter and intra molecular interaction between chitosan and sodium tripolyphosphate. Anticancer drug can be loaded in these chitosan nanoparticles during mixing between chitosan and sodium tripolyphosphate. Anticancer drug can be loaded in these chitosan nanoparticles during mixing between chitosan and sodium tripolyphosphate. Size of nanoparticles can be varied by changing degree of deacetylation of chitosan.

2.2 Desolvation method
In this method, desolvating agents are used to produce chitosan nanoparticles. This method was first reported in 1997 [3]. In this method appropriate concentration of chitosan is dissolved in acetic acid. Sodium tripolyphosphate is most commonly used cross-linking agent. Both of these phases are dissolved in separate glass bottles and mixed under stirring leads to formation of chitosan nanoparticles due to inter and intra molecular interaction between chitosan and sodium tripolyphosphate. Anticancer drug can be loaded in these chitosan nanoparticles during mixing between chitosan and sodium tripolyphosphate. Size of nanoparticles can be varied by changing degree of deacetylation of chitosan.
most commonly used precipitating agents. Chitosan nanoparticles are formed by dropwise addition of sodium sulfate into chitosan solution. Due to greater affinity of salt to water, water surrounding chitosan get eliminated results in precipitation, inducing desolvation of chitosan. So chitosan nanoparticles are produced.

2.3. Spray-drying
Spray-drying becomes a good technique to improve the stability of colloidal nanoparticles. Optimization and evaluation of spray dried chitosan nanoparticles containing doxorubicin have been reported [5]. Preparation of lomustine loaded chitosan nanoparticles by spray drying and in vitro cytostatic activity on human lung cancer cell line L132 have been reported [6]. Effect of crosslinking agents (sodium tripolyphosphate (TPP) and sodium hexametaphosphate (HMP) were studied on the drug leaching, water uptake of hydrogels, drug release from matrix and its mechanism.

2.4. Covalent cross-linking
Chitosan nanoparticles can be prepared by covalent cross-linking method. In this method, covalent bond form between chitosan chain and a functional cross-linking agent. The covalent cross linking occurs between reactive amino groups of chitosan with the aldehyde groups of glutaraldehyde, which is added in solution after the emulsion formation and leads to nanoparticle production [7]. Anticancer drug 5-fluorouracil has been encapsulated by cross-linking glutaraldehyde with amino groups in the molecular chain of chitosan [8].

3. Characteristics of chitosan nanoparticles

3.1. Targeting of chitosan nanoparticles
Chitosan possess positive charges so have selective adsorption and neutralizing effects on the cancer cell surface. Hence it can be targeted to various organelles such as liver, spleen, lung and colon. Cancer cells express folate receptor on its surface so folic acid can be conjugated to chitosan nanoparticles for targeted delivery to cancer reported. Chitosan polymeric micelles loaded with doxorubicin had excellent drug-loading properties, were suitable for targeting the liver and spleen, and significantly reduced drug toxicity to the heart and kidney [9].

3.2. Controlled drug release
Anticancer drug encapsulated in chitosan nanoparticles can be released at controlled/sustained manner. By varying degree of deacetylation and molecular weight of chitosan, different types of nanoparticles can be prepared with different drug release. Preparation and characterization of chitosan nanoparticles for the controlled release of anticancer drug paclitaxel have been reported [10].

4. Anticancer drugs encapsulated
Various anticancer drugs have been delivered to cancer cells by chitosan nanoparticles. Some of them are given in Table 1.

5. Future Prospects
Chitosan has attracted attention of researchers working in the field of nanomedicine worldwide as effective drug delivery system. Chitosan nanoparticles have biodegradability, low toxicity and can be administered through various routes such as oral, nasal etc. Chitosan nanoparticles can be readily modified for target specific anticancer drug delivery at controlled/sustained rate. But there are some limitations such as chitosan has poor solubility. Hydrophilic drugs can be encapsulated in unmodified nanoparticles. Biocompatibility is main question when hydrophobic drugs are encapsulated in the chitosan. Biggest challenge is approval of drug based on chitosan nanoparticles from Food and Drug Administration (FDA). More and more research is needed in this area so that lives of cancer patients can be saved worldwide.

References


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