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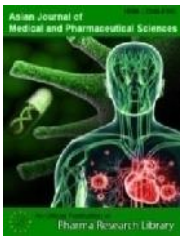

Review Article **Open Access**

A Review on Chitosan Nanoparticles

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A B S T R A C T

Chitin and chitosan are unique and these are standard marine polysaccharides, attracted the interest of many researches. Chitin and its derivatives exhibit a variety of physicochemical and biological properties. In the present study, chitin and chitosan properties will be reviewed and their potentialities as promising biomaterials. Chitosan nanoparticles have gained more attention as drug delivery carriers because of their better stability, low toxicity, simple and mild preparation method, and providing versatile routes of administration. The sub-micron size not only suitable for parenteral application, but also applicable for mucosal routes of administration, i.e., oral, nasal, and ocular mucosa, which are non-invasive route.

Keywords: Chitosan, nanoparticles, chitin, applications

A R T I C L E I N F O

CONTENTS

1. Introduction 94
2. Methods of chitosan nanoparticles. 95
3. Applications of chitosan nanoparticles. 95
4. Conclusion 96
5. References 96

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1. Introduction

Chitosan is a cationic polysaccharide that finds vast applications in medicine and pharmacy because of its excellent biological qualities. It is biocompatible, biodegradable, mucoadhesive and non-toxic and exhibits antimicrobial, antiviral and immunoadjuvant properties. It can be easily processed in diverse forms, such as films, threads, tablets, membranes and micro particles/ nanoparticles, allowing the design of a variety of medical and pharmacological devices adaptable to end purposes. In particular, chitosan nanoparticles have become of great interest as polymeric platforms for the development of new pharmacological and therapeutic drug release systems with

improved bio distribution and increased specificity and sensitivity and by that way reduced pharmacological toxicity. (H. Hosseinzadeh)

Chitosan:

The natural biocontrol active ingredients, chitin/chitosan, are found in the shells of crustaceans, such as lobsters, crabs, and shrimp, and many other organisms, including insects and fungi. It is one of the most abundant biodegradable materials in the world and also Chitin is a cellulose-like biopolymer found mainly in the exoskeleton of marine animals such as shrimp, crabs, or lobsters. Chitin can also be found in mushrooms and yeasts. (Aranaz I)

Nanoparticles:

Nanoparticles are solid colloidal particles with diameters ranging from 1-1000 nm. They consist of macromolecular materials and they can be used therapeutically as adjuvant in vaccines or drug carriers & active ingredient is dissolved, entrapped, encapsulated and adsorbed. In particular, nanotechnology has led to the significant progress in a biomedical field such as controlled drug/gene delivery, tissue engineering, imaging of specific sites and probing of DNA structure. (Fang, H)

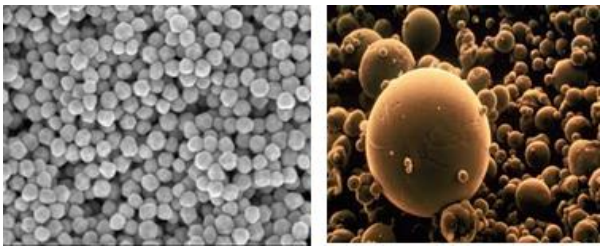

Figure 1: Microscopic structures of nano particles

2. Methods of chitosan nanoparticles

Ionic gelation method:

Ionic gelation method is most commonly used for preparation of chitosan nanoparticles. 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. (Aruna U).

Desolvation method:

In this method, desolvating agents are used to produce chitosan particles. Sodium sulfate and acetone are most commonly used precipitating agents. Chitosan nanoparticles are formed by drop wise 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.

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. Anticancer drug 5-fluorouracil has been encapsulated by cross-linking glutaraldehyde with amino groups in the molecular chain of chitosan. (H. Hosseinzadeh, Lili SH)

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. Preparation of lomustine loaded chitosan nanoparticles by spray drying and *in vitro* cytostatic activity on human lung cancer cell line L132 have been reported. Effect of cross linking agents (sodium tripolyphosphate (TPP) and sodium hexa metaphosphate (HMP) were studied on the drug leaching, water uptake of hydrogels, drug release from matrix and its mechanism.

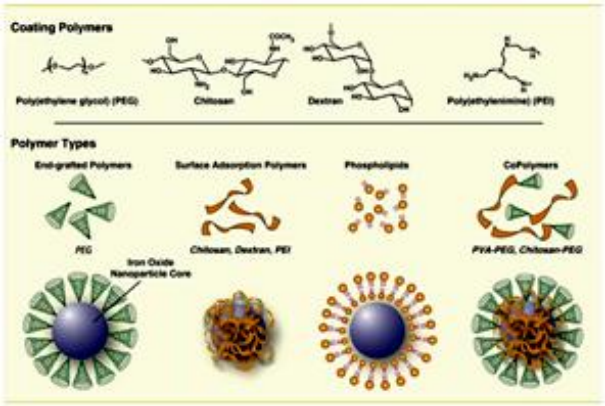

Figure 2: Different type of coating polymers

3. Applications of chitosan nanoparticles

Parenteral administration:

Nano-sized particles can be administered intravenously because the diameter of the smallest blood capillary is approximately 4 μm. Particles greater than 100 nm in diameter are rapidly taken up by the reticulo endothelial system (RES) in the liver, spleen, lung and bone marrow, while smaller-sized particles tend to have a prolonged circulation time. Negatively-charged particles are eliminated faster than positively-charged or neutral particles.

Peroral administration:

Among polymeric nanoparticles, chitosan NP showed to be attractive carriers for oral delivery vehicle as they promote absorption of drug. The mucoadhesive properties of chitosan are due to an interaction between positively charged chitosan and negatively charge of mucin which provide a prolonged contact time between the drug and the absorptive surface, and thereby promoting the absorption. Chitosan mucoadhesion is also supported by the evidence that chitosan increases significantly the half time of its clearance. This property implies that chitosan would be effective as an absorption enhancer only in a limited area of the intestinal lumen where the pH values are below or close to its pKa. (Y. Ohya)

Non-viral gene delivery vectors:
Although viruses can efficiently transfer genes into cells, concerns such as host immune response, residual pathogenicity, and potential induction of neoplastic growth following insertional mutagenesis have led to the exploration of non-viral gene transfer systems. There are usually considered to be five primary barriers that must be overcome for successful gene delivery.

Ocular administration:
Among mucoadhesive polymers explored now, chitosan has attracted a great deal of attention as an ophthalmic drug delivery carrier because of its absorption promoting effect. Chitosan not only enhance cornea contact time through its mucoadhesion mediated by electrostatic interaction between its positively charged and mucin negatively charged, its ability to transient opening tight junction is believed to improve drug bioavailability.

Delivery of vaccines:
Nanoparticles often exhibit significant adjuvant effects in parenteral vaccine delivery since they may be readily taken up by antigen presenting cells. The submicron size of nanoparticles allows them to be taken up by M-cells, in mucosa associated lymphoid tissue (MALT) i.e. gut-associated, nasal-associated and bronchus-associated lymphoid tissue, initiating sites of vigorous immunological responses. (Y. Ohya). Immunoglobulin A (IgA), a major immunoglobulin at mucosal surface, and the generation of B-cell expressing IgA occur primarily in MALT. The B-cell then leave the MALT and reach systemic circulation where they clonally expand and mature into IgA plasma cells. Therefore, providing not only protective IgA at the pathogen entered sites, but also systemic immunity. There are two main administration routes for mucosal vaccine delivery, oral and nasal. (Haider S., park)

Cancer-targeted drug delivery using chitosan and its derivatives: The critical bottleneck of conventional cancer chemotherapeutics includes high toxicity of most anticancer drugs, due to indiscriminate distribution of drugs towards disease and healthy cells. in addition, anticancer drugs often suffer from poor solubility in water and thus need to use organic solvents or detergents for clinical applications, resulting in undesirable side effects such as venous irritation and respiratory distress. Chitosan have low toxicity, better stability and bio degradibility 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. (park k, kim j)

Topical Delivery: During the last three decades, a variety of topical preparations have been developed as topical delivery of drugs provide advantages over conventional oral administration such as convenience, improved patient compliance and elimination of hepatic first pass effect. by increasing the concentration and MW of Chitosan, there was increase in both the rate and extent of drug release and was probably because of the increase in repulsive forces between LC and chitosan cations. (Mei lin tan peter F.M)

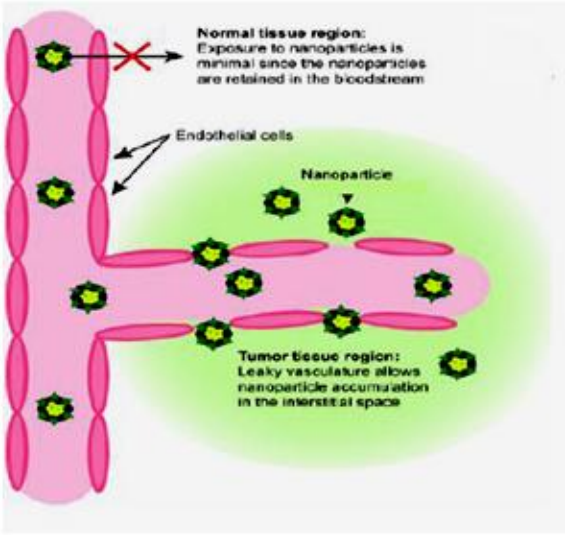

Figure 3: Anti tumour activity of chitosan nanoparticles

Cosmetics:
Chitosan can be tailored to produce different forms for use in different cosmetic fields such as skin- care, hair care and deodorants. It is an essential component in skin-care creams, shampoos and hairsprays due to its antibacterial properties. It forms a protective, moisturizing, elastic film on the surface of the skin that has the ability to bind other contents that act on the skin. (M. T. Isa)

4. Conclusion

Chitosan is a multifunctional biopolymer with many interesting applications. The chitosan with its versatile characteristics like adhesiveness, bio degradable nature and anti-tumour activity acts as a best carrier for the cancer therapy when compared to other natural polymers available. These systems have great utility in controlled release and targeting studies of all class of bio active molecules and chitosan nano particles are used in parenteral, Peroral administration, Non-viral gene delivery vectors, topical delivery & cosmetics.

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