ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Review of Chitosan and Its Relevance in Pharmaceutical Sciences.

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ABSTRACT

Chitosan has wide range of applications in biomedicine, pharmaceuticals, cosmetics, agriculture etc. Due to non toxic, biocompatible, biodegradable, high charge density and muco adhesion properties has been found potential applications in pharmaceuticals. Polymers used in controlled drug / biological delivery system have become more sophisticated. Over the past few decades there has been increase in progress of developing controlled delivery system in order to reduce systemic toxicity and to improve patient compliance. Chitosan polymer has emerged as an one of the potential natural polymer to fabricate nanoparticles, microparticles, hydrogels, tablets, implants etc. This review article is an attempt to highlight the applications of chitosan polymer in pharmaceuticals in brief.

Keywords: Chitosan polymer; Pharmaceutical applications; Delivery systems

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ISSN: 0975-8585

INTRODUCTION

The concept of drugs and vaccine delivery system has been developed tremendously during the past few decades. In controlled release technology, biodegradable polymers offer potential advantages for prolonged release of drugs, vaccines and biologicals. Polymers are applied for a large number of medical applications: as medical supplier, as support or replacement of malfunctioning body parts or as a drug reservoir providing a local therapeutic effect. Currently, biodegradable polymers represent a class of ubiquitous materials and are being used for a multitude of purposes, because of increased interest being shown by the pharmaceutical industry for the fabrication of delivery system. Since the method by which a drug/vaccine/ biological is delivered can have a significant effect on its efficacy. The development of novel biopolymer materials has been underway for a number of years, and continues to be an area of interest for many scientists across the world. However, the selection of applicable carriers for controlled delivery is a challenge for researchers in order to overcome instability and increase the efficacy [1]. According to BCC research, the global market for advanced drug delivery systems amounted to $134.3 billion in 2008 and 2009 to $139 billion. The estimate for 2014 is $196.4 billion, for a compound annual growth rate (CAGR) of 7.2% in the 5-year period [2]. A variety of natural and synthetic polymers have been investigated for sustained release of drugs and vaccines in general and particularly chitosan, because of abundant in nature next to cellulose, cost effective when compared to synthetic polymers, nontoxic, biocompatible and biodegradable properties [3]. According to a report from San Jose, CA-based Global Industry Analysts (GIA), the current and future potential for crustacean shell-derived chitin and chitosan in biomedicine, nutrition and food processing are vast and exciting. A Global Strategic Business Report is forecasting that the global chitosan market will reach more than $21 billion by the year 2015 [4]. The Asia-Pacific region (including Japan) was the leading chitosan market with 7.8 thousand metric tons in 2010 and a projected 12 thousand metric tons by 2015. The United States represented the second biggest market for chitosan, with an estimated market size of 3.6 thousand metric tons in 2010. According to GIA, the chitosan market have been impacting in recent years due to high production cost, lack of quality, production shortages and heavy pollution during the production process [4]. Even though, chitosan have been useful in biomedical, cosmetic and Pharmaceutical industries. Hence we are inclined to focus about the various aspects of application of chitosan that related to pharmaceuticals.

About the polymer

Chitosan is the *N* – deacetylated product of chitin mainly composed of poly – β – glucosamine [5-6]. Chitosan is composed of residues of glucosamine and N – acetyl glucosamine linked with (1 – 4) linkage and the ratio of these two is refereed as degree of deacetylation (DDA) [7]. The degree of chitosan polymer depends upon DDA and the distribution of glucosamine units [8]. Chitosan is a week base and insoluble in water and organic solvents but soluble in dilute acid solutions (pH< 6.5) and gets precipitated with alkaline solution [9]. Due to its cationic properties of this polymers afford numerous physiological and biological properties

such as biodegradability, low toxicity and good biocompatible that become suitable for numerous drug delivery applications.

Chitosan Polymer and various applications

As a Pharmaceutical excipients

Chitosan have been used as safe excipients by the pharmaceutical industries in the formulation of drug dosage forms. Chitosan has been reported to have useful pharmaceutical applications in different drug delivery systems. It is used as an excipient for direct tableting of pharmaceuticals to improve the dissolution properties of some drugs and to prepare the sustained release drugs [10 - 14]. The DDA regulates the moisture absorption of a tablet [15]. In combination with other excipients the chitosan is used in controlled release dosage form to get zero – order release profile [16]. It has been demonstrated as a granulating agent [17], disintegrant [18], as a binder [19] in the formulation of tablet.

Antimicrobial properties

Recent reports have been showing that chitosan can be used as antimicrobial agent that can target various group of microorganisms [20 - 21]. Some of the reports suggested that the chitosan is a cationic polymer, which can interact with anionic groups of the cell membrane and form a layer around the microbial cell that prevents the transport of essential solutes [22 - 23]. Another mechanism is penetration of chitosan in to the microbial cell and inhibits the protein synthesis by blocking RNA function [24]. However, antibacterial activity of chitosan is influenced by its molecular weight, degree of deacetylation, concentration in solution, and pH of the medium [24].

Antiulcer, antioxidant, anticholesterolemic and antiobesity properties

Earlier reports displayed that chitosan possesses acid binding capacity and showing anti-ulcer activities [25 - 26]. Antioxidants are the molecules that prevent the oxidation process and scavenging the free radicals that can prevent pathological condition such as arteriosclerosis, heart diseases, cancer, arthritis etc. Chitosan has shown a good scavenging capacity that could well compared with commercial antioxidants and the property improves with higher DDA [27]. The antioxidant may be due to the chelating property of chitosan with metal ions [28]. Chitosan possesses anticholesterolmic activity and absorb large quantity of dietary fat that inhibit fat absorption that used to treat obesity [29 - 31].

Anticoagulant, wound healing, antitumor and analgesic effect

The anticoagulant effect of chitosan is due to the presence of positive charge that reacts readily with negatively charged red blood cells [32]. The anticoagulant activity is greatly influenced by the molecular weight of chitosan [33]. The wound healing development involves the composition of complex interactions among cells, extracellular matrix components and

signaling compounds. Chitosan shows wound healing property is due to the enhancing the function polymorphonuclear (PMN) leukocytes, macrophages and fibroblast growth [34 - 35]. Chitosan bandages hold wound edges, adherent and reduce inflammatory cell infiltrate. Therefore this clamping effect is beneficial because it prevents initial wound expansion. Moreover, it also possesses antibacterial effect and has an overall beneficial effect on wound healing [36]. Chitosan has antitumor activity because it inhibits growth of tumor cells due to immune enhancing effect [37]. Some researchers have reported that chitosan demonstrates analgesic effect [38].

Chitosan as delivery system

The controlled drug delivery systems offer many advantages when compared to conventional immediate release drug delivery methods like maintaining the drug concentration within the targeted therapeutic window range at quantified time [39 – 40]. In recent years, the advancement of technology resulted in the development of appropriate carriers for controlled or sustained release of drugs and it is a great challenge for researchers because the release kinetics of drug molecule from polymeric carriers is greatly influenced by physical, chemical or biochemical processes. However, some proteins, peptides, drugs and oligo nucleotide are unstable compounds that need to be protected from degradation in the biological environment [41]. Proteins and DNA's have become valuable as potent drugs. However, such water soluble macromolecules are very unstable in the body because of their enzymatic hydrolyses. It is also very important for researchers target to develop delivery systems for proteins protecting them from enzyme hydrolysis [42]. There has long been interested in the use of biodegradable polymers for controlled delivery of drugs parenterally. Microspheres and implants based on poly lactic acid – co – glycolide have been investigated in detail and products containing peptides such as leutenizing hormone have been introduced successfully to the market [43]. Due to properties such as non toxicity and polycationic has proved that chitosan as a good polymer for various drug delivery system. Some of the reports showed that chitosan polymer is successful in the production of implants system of chemotherapeutic agents [44 – 45]. In the contest of drug delivery Chitosan has been used as a stabilizing agent for liposomes [46]. Research studies showed that Chitosan has been used as excipient in direct tablet compression for the improvement of dissolution and controlled release of drug [10]. Due to the muco adhesive properties of Chitosan extensive studies were carried out for many years and shown promising results for therapeutic proteins and vaccines especially through mucosal route [47]. Though chitosan polymer considered as an excellent polymer in drug/ biological delivery system but due to the natural properties some disadvantage such as poor solubility at physiological pH was recognized. Thus chemically modified chitosan give new properties such as carboxy methylation of chitosan enhanced the solubility of chitosan in water [48]. Some of the earlier reports proved that chitosan can be used to deliver nucleic acid in effective manner [49 – 51]. Various novel applications of chitosan and its graft copolymers have been under investigation and reportedly the global market of chitosan is growing tremendously.

ISSN: 0975-8585

CONCLUSION

The potentiality of chitosan in pharmaceuticals is well known across the world. The global research strategy forecasting that near future is the “era” of chitosan in Pharmaceuticals.

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