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IMPACT AND APPLICATIONS OF CHITOSAN POLYMER IN VARIOUS DRUG DELIVERY SYSTEMS

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ABSTRACT

Chitosan is a versatile natural polymer. Many polymers have been used for delivery systems among them chitosan seems to be a better polymer because of remarkable properties such as non-toxic, biocompatible, biodegradable, high charge density, mucoadhesive properties, nonimmunogenic and noncarcinogenic. Therefore, chitosan has wide applications in biomedicine, wastewater treatment, cosmetics, and pharmaceuticals. This review highlight that research on chitosan-based systems containing various drugs for various therapeutic applications has increased in recent years. This short review is an attempt to emphasize the pharmaceutical applications of chitosan polymer in brief and satisfied the requirement of a review on this naturally derived polymer in the present scenario.

Keywords*:* - Chitosan, Natural polymer, Delivery systems, Therapeutic applications.

INTRODUCTION

In controlled release technology, biodegradable polymers offer probable advantages for prolonged effects of drugs, vaccines and biological. Polymers are useful for a large number of medical applications: as a 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 the delivery system. Since the method by which a drug or vaccine or biological is delivered can have a significant effect on its efficacy. The growth of novel biopolymer materials has been underway for several 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 to overcome instability and increase efficacy.[1]

Chitin is a mucopolysaccharide, derived naturally and found to be produced abundantly through biosynthesis. Chitins are characterized as white, nonelastic, hard, nitrogenous polysaccharides that have been estimated to be synthesized in approximately one billion tons annually. Chitosan is the major elements derived from the shells of arthropods such as crabs, shrimps, lobsters, and insects, also produced extracellularly by the cell walls of fungi and brown algae.[2] Different kinds of methods have been extensively studied to develop micro and nanoparticles of chitosan for drug delivery purposes including emulsion cross-linking, spray drying, emulsion droplet coalescence method, ionic gelation, reverse micellar method, as well as sieving methods. Furthermore, colon-targeted, mucosal, cancer, gene, topical and ocular deliveries have been extensively studied with chitosan.[3]

In current decades there has also been considerable interest in the pharmaceutical field in using chitosan as an excipient, in various applications. The mucoadhesive properties of chitosan, illustrated by its ability to adhere for instance to porcine gastric mucosa in vitro could allow site-specific drug delivery.[4]

Significant amount of research has been conducted on chitosan biomaterial for drug delivery. Chitosan can be used to deliver drugs into various administration routes such as oral, buccal, nasal, transdermal, parenteral, vaginal, cervical, intrauterine, and rectal. Chitosan can be modified into nanoparticles, microspheres, sponges, membranes, and rod shapes reported the

preparation of chitosan microparticles using tripolyphosphate (TPP) by an ion cross-linking method with particle range from 500 to 710 mm. It is reported that with decreasing molecular weight and concentration of chitosan solution, release behavior was increased.[3]

Chemical Properties of Chitosan Polymer:

The chemical properties of chitosan are as follows:

1. Linear polyamine
2. Reactive amino groups
3. Reactive hydroxyl groups available
4. Chelates many transitional metal ions

Biological Properties of Chitosan Polymer:

Following are the biological properties of chitosan:

1. Biocompatible

a. Natural polymer

b. Biodegradable to normal body constituents

c. Safe and non-toxic

2. Binds to mammalian and microbial cells aggressively
3. Regenerative effect on connective gum tissue
4. Accelerates the formation of osteoblast responsible for bone formation
5. Hemostatic, Fungistatic, Spermicidal, Antitumor, Anticholesteremic
6. Accelerates bone formation
7. Central nervous system depressant
8. Immunoadjuvant[5]

Specification of Chitosan[6]:

Table No. 1: Specification of Chitosan Polymer

Parameter	**Description**
Appearance (powder or flake)	White or yellow
Particle size	Less than 30 µm
Viscosity (1% solution/ 1% acid)	Less than 5 cps
Density	Between 1.35 to 1.40 g/cm
Molecular weight	50,000 to 2,00,000 Da
pH	6.5 to 7.5
Moisture content	More than 10 %
Ash value	More than 2 %
Loss on drying	Less than 10 %
Glass transition temperature	203°C

General Pharmaceutical Applications of Chitosan Polymer:

Due to its good biocompatibility and low toxicity properties in both conventional excipient applications as well as in novel application, chitosan has received considerable attention as a pharmaceutical excipient in current decades. Some of the general applications of chitosan in pharmaceutical fields are: [7]

1. Slow-release of drugs from tablets and granules
2. Bioadhesive polymer
3. Disintegrant and biodegradable polymer (implants, microparticles)
4. Binder in wet granulation
5. Diluents in direct compression of tablets
6. Films controlling drug release
7. Carrier about vaccine delivery or gene therapy
8. Site-specific drug delivery (e.g. to the stomach or colon)

9. Absorption enhancer (e.g. for nasal or oral drug delivery)

Permeation Enhancing Properties:

It is enhanced due to the effect of chitosan-based on the positive charge of polymer, which results in interaction with the cell membrane. Chitosan of a high degree of deacetylation and high molecular mass exhibit comparatively highest increase in epithelial permeability.[8]

Mucoadhesive:

Improved therapeutic advantages can be obtained by prolonging the residence period of the drug at its critical absorption site; hence adhesion of the delivery system to the absorption membrane represents a prerequisite for an enhanced drug uptake. The bioadhesivity of various materials is expressed by their ability to bind mucopolysaccharide.[9]

Interaction with Acidic Drug/Excipients:

At acidic pHs, chitosan amino groups are protonated and interact with oppositely-charged drug ions. They can act as release retarding agents, which are useful in the manufacture of prolonged-release tablets. This was largely observed in the case of anti-inflammatory acidic drugs, such as salicylic acid, ibuprofen, diclofenac sodium.[10, 11]

Absorption Promotion:

Chitosan can promote transmucosal absorption of small polar drugs, improving the transport of drugs across mucosal membranes by a combination of bioadhesion and a transient structural reorganization of the tight junctions in the cell membranes, which improves the paracellular route of absorption and allows polar drugs to pass through.[12, 13]

Hydrogels:

Hydrogels are hydrophilic polymer networks that can retain a large amount of water. Absorption of water by dried gelified structures usually occurs with a notable increase in volume, as a function of the extent of cross-linkages present in the polymer, and its nature. A gelation mechanism operates in polymer solutions when some parameters are changed, such as concentration or temperature, ionic strength, or due to the addition of nonsolvent or

counterions. This is how the formation of junction zones or points of electrostatic contact facilitates the gel aggregation of the chains.

Tablet Excipients:

Chitosan can be used as a tablet excipient, for both direct compression and standard wet granulation. Nonetheless, chitosan has not been widely adopted as a pharmaceutical excipient in tablets since virtually all formulations developed to date require the addition of other ingredients to facilitate compression. This reflects the fact that commercially available chitosan, as supplied, lacks good flow properties and compressibility. Chitosan (CO), as a kind of natural carbohydrate polysaccharides, has attracted much attention as an excipient for the preparation of micelles due to the desirable properties like bioavailability, non-toxicity, biodegradability, stability, and affordability. At present, micelles are assumed to be delivered via several targeting mechanisms, particularly extravasation. Blood cells including monocytes, macrophages, and dendritic cells express glycoprotein receptors such as mannose receptors, Dectin 1 receptors, Toll-like receptors 2 and 4. The subsequent travel of these cells resulted in a considerable proportion of COSA accumulation in the tumor. These delivery mechanisms can afford new strategies to improve tumor targeting by increasing monocytes homing to tumors. Overall, the delivery mechanism identified in this work is directional for enhancing tumor.[14] It was reported that FCNGs showed toxicity to melanoma (A375) in the concentration of range 0.4-2 mg/ml, but less to human dermal fibroblast by MTT assay. It was concluded that 5 fluorouracil loaded with chitin nano gels can be a good option for the treatment of skin cancer.[15]

Chitosan was used in following routes of drug administration:

1. Ophthalmic Delivery
2. Buccal Delivery
3. Nasal Delivery
4. Oral Delivery
5. Transdermal Delivery
6. Colon Delivery

7. Vaginal Delivery

Interpenetrating Polymer Network (IPN):

Interpenetrating polymer networks (IPNs) are also composed of two or more polymer systems but they are not a simple physical blend. Semi-IPNs or semi-interpenetrating polymer networks are prepared by dissolving a polymer into a solution of another monomer. An initiator, as well as a cross-linker, is added into the solution and the monomer is polymerized and cross-linked in the presence of the dissolved polymer. The result will be a structure in which one cross-linked polymer interpenetrates into a non–cross-linked polymer system. With fully interpenetrated structures, two different monomers and their corresponding cross-linkers are polymerized and cross-linked simultaneously. This results in a doubly cross-linked polymer system that interpenetrates into one another. Alternatively, conducting the cross-linking reaction on a semi- interpenetrated product can form a full-IPN structure. The non–cross-linked phase of the semi-IPN product will be further cross-linked with a chemical cross-linker or via physical complexation.[16, 17]

It was found that blend microspheres of chitosan and gelatin were prepared by the emulsion cross-linking method using glutaraldehyde for the controlled release (CR) of isoniazid (INH), an antituberculosis drug. Various evaluation test was conducted in in-vitro drug release showed the dependence of drug release on the cross-linking, blend ratio of the IPN matrix as well as stearic add coating. The variations in the IPN blend ratio and cross-link density controlled the drug release up to 30 h, but the coated microspheres could reduce the burst release in the gastric stomach media while enhancing in intestinal pH 7.4 media.[18]

CONCLUSION

Polymers have been used as the main tool to control the drug release rate from the formulations. They are also increasingly used as taste-masking agents, stabilizers, and protective agents in oral drug delivery. Biologically degradable polymers can be insecurely distinct as a class of polymers, which degrade to smaller fragments due to chemicals present inside the body. Natural polymers are always biodegradable because they undergo enzymatically promoted degradation. Chitosan is one of them which shows biodegradability, scrawny antigenicity, and better quality biocompatibility compared with a supplementary natural polymer. Chitin is one of the most important polysaccharides taking from nature,

meeting chitosan an abundant and moderately economical product. Chitosan has great usefulness in controlled release and targeting studies of almost all classes of bioactive molecules.

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