CHITOSAN: A PERFECT POLYMER USED IN FABRICATING GENE DELIVERY AND NOVEL DRUG DELIVERY SYSTEMS

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ABSTRACT

Chitosan is a natural, tough, cationic, biodegradable, and biocompatible polymer obtained from chitin by deacetylation. Chitin is a polysaccharide obtained from exoskeletons of crustaceans and sea insects such as crab, krill, shrimp and crawfish etc. Besides the formerly mentioned resources it is also obtained from some fungi and bacterial cell walls. In recent times chitosan has been far and wide used as a popular formulation excipient due to its inimitable characteristics in the field of pharmaceutical sciences as binding, disintegrating, stabilizing, suspending, tablet coating, and film forming material. Chitosan has been comprehensively investigated for its suitability for its controlled release characteristics in various studies. Oral delivery of genes and peptides by means of different formulations based on chitosan was also investigated in various examinations by the capability of its absorption and penetration enhancing properties. It is possessing tremendous mucoadhesive and inherent anti-microbial properties, so that it can be used as a carrier for novel drug delivery. In addition to the above mentioned reasons, tailoring the controlled release and to improve the therapeutic efficacy of the low molecular weight drug compounds can also be achieved by this polymer and moreover in combination with various polymers is feasible due its compatibility i.e. low chemical reactivity. This brief editorial epitomizes the potential applications of chitosan in novel drug delivery systems.

Keywords: Chitosan, Drug delivery, Gene delivery, Pharmaceutical applications

INTRODUCTION

Chitosan is a natural, biologically safe polymer synthesized from chitin by deacetylation (hydrolysis of acetamide groups). It is a tough, biodegradable, biocompatible, non-toxic (depends on the source, method of preparation, molecular weight and degree of acetylation) linear polysaccharide suitable for various applications in pharmaceutical drug delivery technology. Along with these properties it also possesses some medical applications such as analgesic, hypcholesterolemic, hemostatic, antitumor, anti-oxidant, spasmylial, CNS depressant, immunoadjuvant properties. The mechanism of the above mentioned properties of chitosan has been very well comprehended. The exclusive characteristics and analysis of chitosan gave an idea of the accompanying compounds responsible for the aforementioned medical properties, so that then it can be purified and can be used extensively in the field of drug delivery technology as an appropriate drug carrier.

Functions of chitosan in drug and gene delivery

Important applications of chitosan in the pharmaceutical industry are in the development of nasal, vaginal, ophthalmic, transdermal & topical, buccal, parenteral, colon-specific and in implantable drug delivery etc. Purity, degree of acetylation, viscosity and molecular weight are the imperative factors of the chitosan ought to be taken in to consideration while selecting chitosan for the precise drug delivery. For the reason that, these qualities of this polymer decides the selection of an apt grade of chitosan as a material/carrier for a specific drug delivery. This biodegradable polymer can be dissolved in mineral acid and organic acid aqueous solutions at particular conditions i.e. soluble in dilute acidic solutions below pH 6. The polyelectrolytic nature as well as chelating ability of the amine groups of the macromolecule determine the applications of chitosan. The amine groups of chitosan are protonated to NH3+ in acidic solution, and accordingly chitosan's polyelectrolytic and chelating properties are essentially dominated by the acidity of the -NH3+. As a penetration enhancer chitosan disrupts the epithelial tight junctions on the skin and facilitates the drug permeation. This epithelial disruption is very brief and within a diminutive period of time altogether it is reversible.

Ophthalmic Drug Delivery Systems

Enhanced retention and biodistribution of drugs has been reported in numerous studies established the potential use of chitosan-based ophthalmic drug delivery systems such as nanoparticles, microspheres, gels, colloidal systems coated with chitosan etc. Since the various examinations have been firmly established that the

Transdermal Drug Delivery Systems (TDDS)

Owing to its irreplaceable film forming capacity penetration enhancing competence without causing much stress to the skin, skin compatibility and good adhesive properties etc. prompted the researchers to conduct plentiful studies that have been done extensively and reported on the skin permeation ability of the drugs by using this natural biopolymer chitosan. The electrostatic interaction of the positively charged chitosan mediates protracted contact with the epithelium and the negatively charged glycoprotein residues on the cell surface smooth the progress of the passive diffusion results in the successful absorption of drug into the underlying epithelium. As a penetration enhancer chitosan disrupts the epithelial tight junctions on the skin and facilitates the drug permeation. This epithelial disruption is very brief and within a diminutive period of time altogether it is reversible.
chitosan based ophthalmic formulations has admirable bioadhesion and penetration enhancing properties together with appropriate ocular tolerability and less or non-toxicity and allergenicity. In an one more examination, in vitro stability, in vivo fate, and cellular toxicity of the chitosan nanoparticles as new ocular drug delivery systems further shows its potential as a right and proper vehicle for ocular drug delivery.

**Nasal Drug Delivery Systems**

Chitosan, a cationic bioadhesive natural polymer has remarkable influence in augmenting the transport of polar drugs, peptides and proteins across epithelial surfaces was established in various studies. There are two central effects of chitosan delivery systems on nasal mucosa influence the drug permeation. Firstly, clearance of the formulation from the nasal cavity is abridged by the cations present in the chitosan bind to negatively charged sialic residues tenders excellent mucoadhesive properties consequently bids the prolonged contact time. Secondly, its reversible and momentary action on epithelial tight junctions between cells actually steps up the drug transportation paracellarily. Nasal insulin delivery in the chitosan solution has also been successfully reported.

**Buccal Drug Delivery Systems**

Prolonged adherence to the buccal mucosa is the vital requirement of an ideal carrier for efficient buccal drug delivery. Buccal patches, tablets, and gel formulations prepared with chitosan have been effectively delivered the drug unidirectionally into systemic circulation through buccal mucosa. In another extensive study the chitosan sponges were developed for buccal administration of insulin, exposed efficient unidirectional delivery of insulin and demonstrated its excellent mucoadhesive properties. The promising unique mucoadhesive and absorption enhancing quality of this polymer further confirmed its aptness for the buccal drug delivery.

**Chitosan based formulations in treating the oral cavity disorders**

Lots of typical mouth washes containing alcohol or astringents used in treating the several oral cavity problems may have an objectionable taste, which aggravate the diseased state. In addition to this setback the drug concentration needs to be retained beyond the minimum inhibitory concentration (MIC) for the duration of the therapy will be reduced by food intake and saliva. Competent chitosan based drug delivery systems were fabricated in intention to treat the oral mucositis, verified by in vitro and in vivo studies. The interaction of chitosan in delivering the therapeutic active compounds. Chitosan based gel and suspension authenticated the propensity of chitosan in delivering the therapeutic active compounds. Chitosan based gel and suspension meant for topical application containing nystatin diminishes the difficulty and prevalence of oral mucositis and promotes healing significantly.

**Vaginal Drug Delivery Systems**

Anti-infective drugs incorporated mucoadhesive vaginal formulations based on chitosan have been reported successfully in various literatures substantiated the best qualities of this polymer for the vaginal drug delivery. Apart from the vaginal tablets and films, pH- or temperature-sensitive delivery systems, nanocarriers, and inserts are also in the investigation. Mucoadhesive vaginal gel based on chitosan for the delivery of lactic acid was exclusively illustrated the polymer’s mucoadhesive performance and release profiles. In an another study, chitosan was modified by the introduction of thioglycolic acid for a new bioadhesive vaginal drug delivery system in order to deliver clindamycin showed very promising results in treatment of mycotic infections.

**Gastro Retentive Drug Delivery Systems (GRDDS)**

Suitability of utilizing chitosan in making these particular floating drug delivery systems has been successfully achieved by ionic interaction of chitosan and negatively charged surfactant sodium deoxycholate. In an additional endeavor chitosan granules prepared with prednisolone demonstrated good buoyancy and controlled release when it was added to acidic and neutral media provide evidence of its appropriateness in making such category of formulations. Effervescent floating drug delivery systems and Sustained Release floating tablets using a mixture of sodium bicarbonate, citric acid and chitosan were prepared and evaluated effectively. Bioadhesiveness and floating capabilities of chitosan microphers shown to have a high potential in developing GRDDS especially for the drugs which are all poorly soluble in intestinal medium and readily soluble in acidic medium. Chitosan microphers are having capability to stay longer in stomach and facilitate the stomach-specific drug delivery. Chitosan capsules have been used in the specific delivery of insulin to the colon.

**Gene Delivery**

Chitosan’s cationic qualities have the aptitude to interact with negative molecules such as DNA and form complexes, facilitate transfection and inhibit degradation of the same. Chitosan as (safer to other non-viral vectors) non-viral vector for gene delivery put forward quite a few advantages that are not producing endogenous recombination, oncogenic and immunological effects. The molecular mass and deacetylation extent of the chitosan, chitosan to DNA/siRNA charge proportion (N/P ratio) and its strength, the chitosan salt form utilized, pH, serum, additives, chitosan/nucelic acid particles preparation process and routes of administration and diverse formulation allied factors influence the transfection efficiency.

**CONCLUSION**

Chitosan, owing to its vast unique qualities as a natural biopolymer can be widely used in the area of novel drug delivery systems, and in gene delivery has been quiet evident from the numerous reported data related to the chitosan drug delivery.

**REFERENCES**

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