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Chitosan –An Ideal Polymer in Drug Delivery Systems: An Overview

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ABSTRACT

Chitosan is a natural, biologically safe polymer synthesized from chitin by deacetylation reaction. It is a tough, biodegradable, biocompatible, non-toxic linear polysaccharide suitable for various applications in pharmaceutical drug delivery technology. Chitosan has unique physicochemical and biological characteristics demanded for the development of safe and effective drug delivery systems. One of the most properties of chitosan is for chelation. It can selectively bind to desired materials such as cholesterol, fats, metal ions, and protein and tumor cells. It also does not cause allergic reactions and rejection and is biodegradable in nature. It is metabolized into harmless products (amino sugars), which are completely absorbed by the human body. Chitosan being a good cationic polymer for membrane formation; have also been useful as artificial kidney membranes. Along with these properties it also possesses certain medicinal applications such as analgesic, hypocholesterolemic, hemostatic antitumor, anti-oxidant spermicidal, CNS depressant, immunoadjuvant properties, antacid, antiulcer activities, wound and burn healing action and has been found to be suitable for immobilization of enzymes and living cells in ophthalmology 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 systems. This paper discusses the potential of chitosan in the development of drug delivery systems.

Keywords: Chitosan, Structure, Drug delivery, Pharmaceutical applications

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INTRODUCTION

A wide range of materials, such as natural or synthetic polymers, lipids, surfactants and dendrimers, have been employed as drug carriers[1–4]. Among these, polysaccharides have attained greater attention because of their outstanding physical and biological properties[5]. Synthetic polymers are usually non- biocompatible, non- biodegradable and expensive. However natural polymers such as chitin and chitosan are devoid of such problems that makes them a carrier of choice for the development of specific drug delivery systems. Chitosan a cationic polysaccharide, owing to its abundant availability, unique mucoadhesivness, inherent pharmacological properties, and other beneficial biological properties such as biocompatibility, biodegradability, non-toxicity and low-immunogenic have wide range of pharmaceutical and biomedical applications[6–8]. Being a bioadhesive polymer and having antibacterial activity, chitosan has been used as potential carrier for prolonged delivery of drugs, macromolecules and for targeted drug delivery.

The imperative factors of the chitosan- purity, degree of acetylation, viscosity and molecular weight should be taken in to consideration while selecting chitosan for the precise drug delivery. Chitosan nanoparticles, microspheres and beads have been widely accepted for drug delivery. Chitosan microspheres are used to provide controlled release of many drugs and to improve bioavailability of degradable substances such as protein; or to enhance the uptake of hydrophilic substances across the epithelial layers. Magnetic Chitosan microspheres are used in targeted drug delivery to be retained at target site capillaries under the influences of an external magnetic field. Chitosan has been used for the oral delivery of genes and peptides due to its absorption and penetration enhancing properties. The special affinity of chitosan for biomolecules has been utilized for reduced side effects of drugs. Membranes prepared from chitosan have shown greater permeability for acidic drug than basic drugs.

Among pharmaceutical applications chitosan can be exploited as a popular formulation excipient due to its unmatched characteristics in the field of pharmaceutical sciences as –

- Binding agent,
- Disintegrating agent,
- Stabilizing agent,
- Suspending agent,
- Tablet coating and film forming material
- Drug carrier for sustained release formulations

- Co-grinding diluents for the improvement of dissolution rate and bioavailability of water insoluble drugs.
- To improve the therapeutic efficacy of the low molecular weight drug compounds

Chitosan being low chemically reactive has been employed combination with various polymers to achieve desired and controlled release of the drugs. Numerous studies have demonstrated that chitosan and its derivatives (N-trimethyl chitosan, mono-N-carboxymethyl chitosan) are effective and safe absorption enhancers to improve mucosal (nasal, peroral) delivery of hydrophilic macromolecules, such as peptides, proteins, and heparins, antimicrobial, and wound-healing properties. Chitosan itself is haemostatic, some derivatives such as sulfated chitosan are anticoagulants, By utilizing the haemostatic effect, Chitosan bandage and sponges are prepared for surgical treatment and wound protection.

The low toxicity of chitosan coupled with wide applicability makes it a promising candidate not only for the purpose of drug delivery for a host of drug moieties like anti-inflammatory drugs, peptides, etc but also as a biologically active agent. The objective of this article is to review the current and future potentials of chitosan in the pharmaceutical field.[9-11]

Chemical Structure and Preparation

Chitin is widely distributed in nature and found in nature as a renewable bioresource.[12,13,14] Chitin is believed to be the second most abundant biomaterial after cellulose. Chitin is the principal component of protective cuticles of crustaceans such as crabs,shrims, prawns, lobsters and also obtained from bacterial cell walls and some fungi such as aspergillus and mucor. The exoskeleton of crustaceans consists of 15% to 20 % chitin of dry weight. The crystalline structure of chitin has been shown to be similar to cellulose in the arrangements of inter- and intra-chain hydrogen bonding and same biological function.

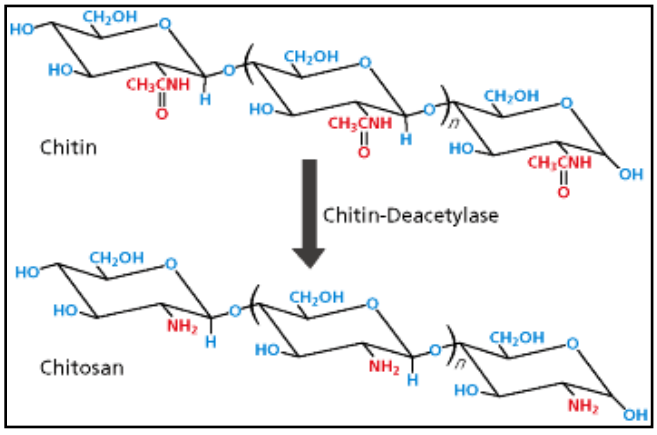

Figure 1. Chitosan from Chitin

Commercial chitin and chitosan consists of both types of monomers. Chitosan is found in nature, to a lesser extent than chitin. Physicochemical and biological properties of chitosan are greatly influenced by its molecular weight and degree of deacetylation.

Chitin is straight homopolymer composed of b-(1-4)-linked N –acetyl-glucosamine units while chitosan comprise of copolymers of gucosamine and N-acetyl glucosamine. Chitosan is polysaccride containing more than 5000glucosamine units, respectively and their molecular weight are over one million Daltons. Chitosan is made by alkaline N-deacetylation of chitin. It consists of two types of monomers; chitin-monomers and chitosan-monomers. Chitin is a linear polysaccharide consisting of (1-4)-linked 2-acetamido-2-deoxy-b-D-glucopyranose. Chitosan is a linear polysaccharide consisting of (1-4)-linked 2-amino-2-deoxy-b-D-glucopyranose. Chitosan has one primary amino group and two free hydroxyl group for each C building unit.

Chitosan carries positive charge due to the easy availability of free amino groups and thus in turn react with many negatively charged surfaces/polymers and also undergoes chelation with metal ions. 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. Chitosan is weak base and is insoluble in water and organic solvents; however, it is soluble in dilute aqueous acidic solution which can convert the glucosamine unit into a soluble form. It gets precipitated in alkaline solution or with polyanions and forms gel at lower pH.

The presence of reactive functional groups in chitosan offers great opportunity for chemical modification, which affords a wide range of derivatives such as quaternized chitosan (N,N,N-trimethyl chitosan;TMC), carboxyalkyl chitosan, thiolated chitosan,sugar-bearing chitosan, bile acid-modified chitosan and cyclodextrin-linked chitosan[5–20]. These chitosan derivatives have been designed to improve specific properties of native chitosan. For example, thiolation of chitosan amazingly improves its mucoadhesive properties because of the formation of disulfide bonds with cysteine-rich subdomains of mucus glycoprotein.

The chemical modification of chitosan imparts amphiphilicity, which is an important characteristic for the formation of self-assembled nanoparticles, potentially suited for drug delivery applications. Conjugation of the targeting moieties to the surface of drug-loaded nanoparticles may improve therapeutic efficiency of the drug[24]. Chitosan has been widely utilized as drug delivery systems for low molecular drugs, peptides and genes. The preparation of chitin and chitosan is given in Figure 3.

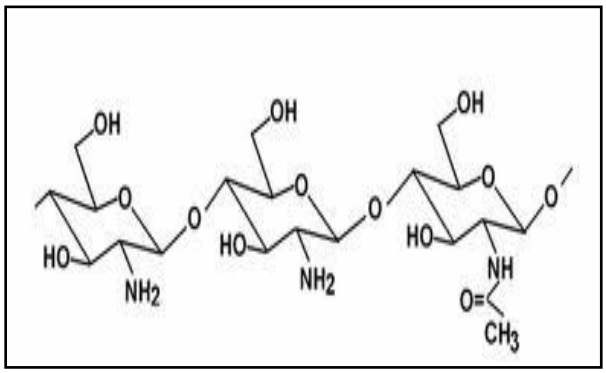

Figure 2. Structure of Chitosan

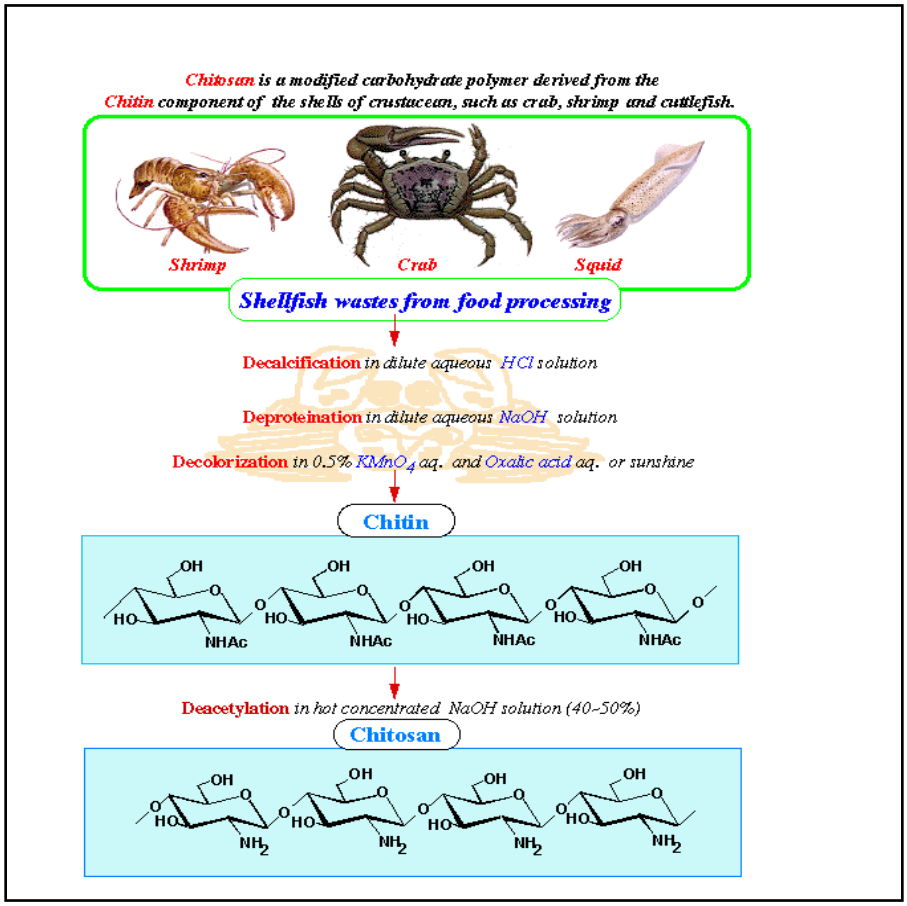

Figure 3. Preparation of Chitosan and Chitin

Properties of Chitosan

The qualities and properties of chitosan products such as purity, viscosity, deacetylation, molecular weight, and polymorphs structure may differ with manufacturing process variables that in turn influence the characteristic of the pharmaceutical formulations

The mucoadhesive properties of chitosan are attributed to its positive charges at neutral pH that enable an ionic interaction with the negative charges of sialic acid residues of the mucus.

In addition to mucoadhesive property, chitosan also posses binding, disintegrating, and tablet coating properties. These properties may be attributed to -

- Strong hydrogen bonding groups like-OH, -COOH
- Strong charges
- High molecular weight
- Sufficient chain flexibility and
- Surface energy properties favoring spreading into mucus.

Commercially, chitosan is available in the form of dry flakes, solution and fine powder. It degrades under the action of ferments; it is nontoxic and easily removable from the organism without causing concurrent side reactions. The polyelectrolyte nature as well as chelating ability of the amine groups of the macromolecule decides the applications of chitosan.

Characterization of Chitosan

Generally Chitosan is described by the following parameters:

- Degree of deacetylation in %,
- Dry matter in %,
- Ash in %,
- Protein in %,
- Viscosity in Centipoises',
- Intrinsic viscosity in ml/g,
- Molecular weight in g/mol, and
- Turbidity in NTU units.

All of these parameters can be attuned to the application for which chitosan is being used. The deacetylation is very important to get a soluble product. In general, the solubility of heteroglucans are also influenced by the distribution of the acetyl groups, the polarity and size of the monomers, distribution of the monomers along the chain, the flexibility of the chain, branching, charge density, and molecular weight (50,000 to 2,000,000 Da) of the polymer. Viscosity (10 to 5000 cp) can be accustomed to each application by controlling the process parameters.[15-16]

Chitosan in Drug Delivery

Ophthalmic Drug Delivery Systems

As stated, chitosan is capable of forming films and therefore has been recommended as a biopolymer of choice for the development of contact lenses that are used as protective devices

for acutely or chronically traumatized eyes. Because of amazing properties of chitosan, it is found to be a unique material for designing ocular drug delivery vehicles. The elastic property of chitosan, dictates chitosan gels to have excellent adhesion to mucin, which coats the conjunctiva and the corneal surface of the eye. Chitosan has been reported to enhance retention and biodistribution of drugs in ocular cavity. It is also reported to be bear ocular tolerability, less or non-toxicity and allergenicity. Several studies have established the potential use of chitosan in ophthalmic drug delivery systems- nanoparticles, microspheres[17;18], gels, colloidal systems coated with chitosan etc.

Further study shows its potential as a right and proper vehicle for ocular drug delivery.[19] In contrast, chitosan-based colloidal systems were found to be suitable for transmucosal drug carriers, for either facilitating the transport of drugs to the inner eye (chitosan-coated colloidal systems containing indomethacin) or their accumulation into the corneal/conjunctival epithelia (chitosan nanoparticles containing cyclosporine). The microparticulate drug-carrier (microspheres) seems a promising means of topical administration of acyclovir to the eye.[20-22]

Nasal Drug Delivery Systems

The basic characteristic of nasal mucosa – large surface area and high vascularity makes it an ideal site for bioadhesive drug delivery systems. Microspheres, beads, liposomes, and gels, have been established to be strong candidate for bioadhesive drug delivery systems. Chitosan possess no toxicity and irritancy, therefore can be applied on to the nasal epithelium. It swells and forms gel like layer in aqueous environment which is favorable for interpretation of polymer and glycoprotein chain into mucus. Chitosan also shows good bioadhesive characteristics and can reduce the rate of clearance of drug from nasal cavity there by increasing the bioavailability of drug incorporated in it.[23-25]

Chitosan has remarkable influence in augmenting the transport of polar drugs. There are two central effects of chitosan delivery systems on nasal mucosa that influence the permeation of drug across it.

- Firstly, clearance of the formulation from the nasal cavity is abridged by the cations present in the chitosan bind to negatively charge sialic residues tenders excellent mucoadhesive properties consequently leads to prolonged contact time.
- Secondly, its reversible and momentary action on epithelial tight junctions between cells steps up the drug transportation paracellularly. Various studies have established the transportation of peptides and proteins across nasal epithelial surfaces by this mechanism.[26-27]

A variety of chitosan salts (chitosan lactate, chitosan aspartate, chitosan glutamate, and chitosan hydrochloride) showed nasal sustained release of vancomycin hydrochloride[28] Diphtheria toxoid (DT) associated to chitosan microparticles results in protective systemic and local immune response against DT, and enhances significant IgG production after nasal administration.[29]

Drug release studies from Chitosan microsphere have generally shown that release of the drug decreases with increase in molecular weight of chitosan. This may be attributed to swelling behavior of Chitosan microspheres. An increase in molecular weight of chitosan leads to increase in viscosity of the gel layer that influences the drug diffusion as well as erosion of the microspheres. Drug release from chitosan microspheres decreases with increase in the polymer concentration.[30-33]

Intranasal systemic delivery of pentazocine has resulted in significantly improved bioavailability with sustained and controlled blood level profiles compared to intravenous, oral administration[34]

The nasal absorption of insulin after administration in chitosan powder has been the most effective formulation for nasal delivery of insulin in sheep compared to chitosan nanoparticles and chitosan solution[35] Different types of nasal vaccine systems have been described to include cholera toxin, microspheres, nanoparticles, liposomes, attenuated virus and cells, and outer membrane proteins (proteosomes). Nasal formulations induced significant serum IgG responses similar to and secretary IgA levels superior to what was induced by a parenteral administration of the vaccine[36-37]

Buccal Drug Delivery Systems

The promising and distinctive mucoadhesive and absorption enhancing quality of chitosan has confirmed its suitability for the buccal drug delivery for efficient buccal drug delivery, prolonged adherence to the buccal mucosa is the vital requirement of an ideal carrier. And release the drug in a unidirectional way toward the mucosa in a controlled- or sustained-release manner. Mucoadhesive polymers extends the residence time of the device in the oral cavity.

Buccal patches, tablets, and gel formulations prepared with chitosan have been reported to effectively deliver the drug unidirectional into systemic circulation through buccal mucosa. In another extensive study the chitosan sponges were developed for buccal administration of insulin. The sponges were reported to exposed efficient unidirectional delivery of insulin and demonstrated its excellent mucoadhesive properties.[38]. Directly compressible bioadhesive tablets of ketoprofen containing chitosan and sodium alginate in the weight ratio 1:4 showed sustained release for three hours on intra oral (sublingual site of rabbits) drug administration[39] Buccal tablets of chlorhexidine diacetate based on chitosan microspheres, for antifungal activity ,showed

a prolonged release of the drug in the buccal cavity. The improvement is particularly high against Candida albicans. Placebo micro particles have an antimicrobial activity due to the chitosan itself.[40]. Bilayered devices ensure the release of the drug in a unidirectional way.[41] The buccal bilayered devices (bilaminated films, bilayered tablets) using a mixture of drugs -nifedipine and propranolol hydrochloride and chitosan, with or without anionic cross linking polymers (polycarbophil, sodium alginate, gellan gum), demonstrated that these devices show promising potential for use in controlled delivery of drugs to the oral cavity.[42] Bioadhesive tablets of nicotine containing 0% to 50% w/w glycol chitosan produced the good adhesion.[43].

Chitosan containing quick-hardening paste was developed as a bone substitute for dental purpose. The use of this paste will minimize the inflammation in gums. A monolayer and multilayered film of chitosan PLGA containing ipriflavone were showed to prolong drug release for 20 days *in vitro*[l].Mucoadhesion developed by a chitosan hydrogel appears to be suitable for prolonging the residence time of the drug and improving the therapeutic effect.[44-47]

Periodontal Drug Delivery System

In periodontal delivery of drug, especially for anti microbial agents the drug concentration needs to be retained beyond the minimum inhibitory concentration (MIC), as it is reduced by food intake and saliva. Systemic administration of these drugs has certain disadvantages, such as the necessity for frequent dosing to maintain the drug concentrations at the therapeutic level in the plasma, poor patient compliance, super infections caused by resistant organisms, and gastrointestinal and systemic side-effects.[48-49] For example, for moderate to severe periodontal diseases, antimicrobial agents are used to eradicate and/or suppress the plaque bacteria.

An ideal formulation should be easy to deliver, have good retention at the target site, and provide sustained release of the drug. This can be overcome by using muco/bioadhesive polymers. These polymers can increase the residence time of the formulation in the oral cavity. This will enhance drug penetration, localize the drug for local therapy, target the diseased tissue, and improve efficacy and acceptability Chitosan based drug delivery systems have been developed to treat the oral mucositis Chitosan is a biologically safe polymer and itself possesses non-toxicity, biocompatibility, biodegradability, antibacterial and antifungal activity. Chitosan also inhibits the adhesion of Candida albicans to human buccal cells .Chitosan gel and chitosan film containing chlorhexidine gluconate for local delivery showed prolonged release. A monolayer and multilayered film of chitosan/PLGA containing ipriflavone have been shown to prolong drug release for period of 20 days Chitosan-nystatin gel and suspension for topical application reduces the difficulty and prevalence of oral mucositis and support in the healing process significantly.[50]

Unmodified chitosan has been proved to display a permeation-enhancing effect for peptide drugs. Chitosan and most of its derivatives strongly reduces the presystemic metabolism of peptides imminent between the dosage form and the absorption membrane. Based on these unique features, the administration of chitosan and its derivatives leads to a strongly improved bioavailability of many perorally given peptide drugs, such as insulin, calcitonin, and buserelin. A protective effect for polymer-embedded peptides toward degradation by intestinal peptidases can be achieved by the immobilization of enzyme inhibitors on the polymer. Serine proteases are inhibited by the covalent attachment of competitive inhibitors, such as the Bowman-Birk inhibitor; metallo-peptidases are inhibited by chitosan derivatives displaying complexing properties, such as chitosan-EDTA conjugates.

The mucoadhesive property of chitosan gel could be enhanced by threefold to sevenfold by admixing of chitosan-glycerylmono-oleate. Drug release from the gel followed a matrix diffusion controlled mechanism. The chitosan-coated nanosphere reduces significantly the blood calcium level compared with uncoated nanospheres, and the reduced calcium level was sustained for a period of 48 hours [51 -53]

Floating Drug Delivery System

Floating systems have a density lower than the density of the gastric juice. Thus, gastric transit time and hence the bioavailability of drugs that are absorbed in the upper part of the GI tract will be improved. Intragastric floating dosage forms are useful for the administration of drugs that have a specific absorption site, area insoluble in the intestinal fluid, or area used for the treatment of gastric diseases. 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 dioctyl sulfosuccinate.

El-GibalyI[55] have prepared Floating drug delivery systems and evaluated sustained release floating tablets using a mixture of sodium bicarbonate, citric acid and chitosan . Bioadhesiveness and floating capabilities of chitosan microspheres 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 microspheres are having capability to stay longer in stomach and facilitate the stomach-specific drug delivery. Floating hollow microcapsules of melatonin produced have an interesting gastro retentive controlled-release delivery system for drugs. Chitosan capsules have been used in the specific delivery of insulin to the colon.[54] Floating hollow microcapsules of melatonin produced have an interesting gastroretentive controlled-

release delivery system for drugs. Release of the drug from these microcapsules was greatly retarded with release lasting for several hours (1.75 to 6.7 hours in simulated gastric fluid), depending on process factors. Most of the hollow microcapsules developed tended to float over simulated biological fluids for more than 12 hours. Chitosan granules having internal cavities were prepared by de-acidification. When added to acidic (pH 1.2) and neutral (deionized distilled water) media, these granules were immediately buoyant and provided a controlled release of the candidate drug prednisolone.[55]

Intestinal Drug Delivery System

Sustained intestinal delivery of drugs, such as 5-fluorouracil (choice for colon carcinomas) and insulin (for diabetes mellitus), seems to be a feasible alternative to injection therapy. A formulation was developed that could bypass the acidity of the stomach and release the loaded drug for long periods into the intestine by using the bioadhesiveness of polyacrylic acid, alginate, and chitosan[56]. Bromothymol blue was taken as a model drug. The formulation exhibited bioadhesive property and released the drug for an 80-day period in vitro. Chitosan/calcium alginate microcapsules containing nitrofurantoin showed sustained release of drug. Drug release into the gastric medium is found to be relatively slow compared to that into the intestinal medium[57]

Colon Delivery System

Chitosan was used in oral drug formulations to provide sustained release of drugs. Recently, it was found that chitosan is degraded by the microflora that is available in the colon. Consequently, this compound could be promising for colon-specific drug delivery. Chitosan was reacted separately with succinic and phthalic anhydrides. The resulting semisynthetic polymers were proved for colon-specific, orally administered drug delivery systems. Systems for colon delivery containing acetaminophen (paracetamol), mesalazine (5-ASA), sodium diclofenac, and insulin have been studied and showed satisfactory results.[58-60]The effect of chitosan tripolyphosphate beads on the absorption of insulin was studied by measuring the decrease of the plasma glucose concentration and the relative pharmacological availability. Chitosan tripolyphosphate showed excellent association with insulin and improved intestinal absorption of insulin to a great extent. Chitosan succinate and chitosan phthalate loaded with sodium diclofenac has been found to resist dissolution under acidic conditioned improved dissolution under basic conditions, suggesting their suitability for colon specific drug delivery systems. [61-62]

Vaginal Drug Delivery System

Anti-infective drugs incorporated mucoadhesive vaginal formulations based on chitosan have

been reported successfully in various literatures demonstrates the best qualities of this polymer for the vaginal drug delivery.[63] Chitosan vaginal tablet containing metronidazole, acriflavine, and other drugs gave adequate release, therapeutic action, and good adhesion properties. Apart from the vaginal tablets and films, pH- or temperature-sensitive delivery systems, nanocarriers, and inserts have 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.[64] 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 clotrimazole and an imidazole derivative showed very promising results in an increased residence time of the drug in the vaginal mucosa tissue ensuring good controlled drug release. In treatment of mycotic infections of the genitourinary tract Vaginal tablets of chitosan containing metronidazole, acriflavine, and other excipients showed adequate release and good adhesion properties.[65-67]

Transdermal Drug Delivery System

Owing to its exceptional film forming capacity penetration enhancing competence without causing much stress to the skin, skin compatibility and good adhesive properties[68] incited the researchers to conduct plenteous studies that have been done extensively and reported on the skin permeation ability of the drugs by using this natural biopolymer chitosan. The drug release from the devices are affected by the membrane thickness and cross-linking of the film 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[69] 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 is reversible. Chitosan-alginate poly electrolyte complex (PEC) has been prepared in situ in beads and microspheres for potential applications in packaging, controlled release systems, and wound dressings.[70] Chitosan gel beads are a promising biocompatible and biodegradable vehicle for treatment of local inflammation. Chitosan gel beads containing the anti-inflammatory drug prednisolone showed sustained release of drug with reduced inflammation indexes that resulted in improved therapeutic efficacy.[71] Chitosan membranes with different permeability to propranolol hydrochloride obtained by controlled cross-linking with glutaraldehyde were used to regulate the drug release in the devices.[72]. Chitosan gel was used as the drug reservoir. The drug-release profiles showed that drug delivery is completely controlled by the devices. The rate of

drug release was found to be dependent on the type of membrane used. A combination of chitosan membrane and chitosan hydrogel containing Lidocaine hydrochloride, a local anesthetic, is a good transparent system for controlled drug delivery and release kinetics.[73-74]

Vaccine Delivery

Various chitosan-antigen nasal vaccines have been prepared. These include cholera toxin, microspheres, nanoparticles, liposomes, attenuated virus and cells, and outer membrane proteins (proteosomes). They induced significant serum IgG responses similar to and secretory IgA levels superior to what was induced by a parenteral administration of the vaccine.[75] Chitosan microparticles are very promising mucosal vaccine delivery systems. Significant systemic humoral immune responses were found after nasal vaccination with diphtheria toxoid associated to chitosan microparticles. Diphtheria toxoid associated to chitosan microparticles results in protective systemic and local immune response against diphtheria toxoid after oral vaccination, and in significant enhancement of IgG production after nasal administration.[76] Chitosan microspheres cross-linked with glutaraldehyde were loaded by bovine serum albumin (BSA) and diphtheria toxoid and showed tissue compatibility with a long-lasting drug delivery system in wistar rats for several days.[76]

CONCLUSION

It is versatile polymer whose application from weight supplement in the market to use in biomedical and pharmaceutical formulations. Being characterized by biocompatibility, non toxicity, lack of allergenicity, biodegradability chitosan is really an attractive biopolymer for delivering a wide variety of drugs in a controlled/sustained manner and can be successfully targeted for site specific drug delivery and in gene drug delivery. Chitosan possess suitable properties as carrier for microsphere drug delivery. Chitosan microsphere are widely studied drug delivery system for controlled release of drugs, antibiotics, antihypertensive, agents, proteins, peptide drugs anti-inflammatory, steroids, antidiabetic, diuretics, amino acid and vaccines.Chitosan has shown marked improvement in the dissolution rate of poorly soluble drugs and thus can be exploited for enhancement of bioaviailitiby of poorly water soluble drug or to enhance drug targeting to specific area of the body. Due to its biocompatibility with living tissues it does not cause allergic reactions and rejection. It down slowly to harmless products (amino sugars), which are completely absorbed by the human body .Fabrication of biosmers as well as delivery of both hydrophilic and lipophilic drugs, problems associated with dose dumping, burst out effect, unavoidable fluctuations in drug concentrations (mostly associated

with conventional dosage form) can be eliminated/reduced by use of such biopolymers resulting in enhanced efficacy and lesser incidences of adverse effects associated with the drugs. Chitosan also have has plentiful applications in the fields of agriculture, textile, nutritional enhancement and food processing, waste water management, cosmetics.

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