Advances in Biological Research 5 (1): 28-37, 2011
ISSN 1992-0067

Applications of Chitosan and Chitosan Derivatives in Drug Delivery

Vipin Bansal, Pramod Kumar Sharma, Nitin Sharma, Om Prakash Pal and Rishabha Malviya

Department of Pharmaceutical Technology, Meerut Institute of Engineering and Technology Baghpat Crossing, NH-58, Meerut-250005, India

Abstract: Chitosan is a versatile natural polymer. This article reviewed different aspects of Chitosan that's including preparation and characterization of Chitosan with their applicability in pharmaceutical formulations. Also, the article included different derivatives of Chitosan and their use in different drug delivery system. This review emphasized that research on Chitosan based systems containing various drugs for various therapeutic applications have increased in recent years. So this article has fullfill the requirement of a review on this naturally derived polymer in present scenario.

Key words: Chitosan · Chitosan derivative · Pharmaceutical applications · Natural polymer

INTRODUCTION

Polymers are macromolecules composed of repeating structural units of monomers connected by covalent chemical bonds and this process is known as polymerization. There are many types of polymers including natural and synthetic moiety. Natural polymers such as proteins (collagen, silk and keratin), carbohydrates (starch, glycogen) are widely used materials for conventional and novel dosage forms. These materials are chemically inert, nontoxic, less expensive, biodegradable, eco-friendly and widely available [1, 2]. The development of new applications for Chitosan and its derivative is mainly due to the fact that these are renewable source of natural biodegradable polymers and also due to chitin and its derivative are the most abundant natural polymers. The main factors which stimulated the interest in chitosan utilization in various fields from fertilizers to pharmaceuticals are its versatility, economical and easily availability. Chitosan is no longer just a waste by-product from the seafood processing industry. This material is now being utilized by industry to solve problems and to improve existing products, as well as to create new ones. Chitosan (CS) is modified natural, biodegradable, biocompatible, non toxic, as well as linear nitrogenous polysaccharides, a basic polysaccharide homo-polymer [2]. CS is produced commercially by deacetylation of chitin, naturally occurring polysaccharides which is the structural element in the exoskeleton of crustaceans (crabs, shrimp, etc.). Due to variable and incomplete deacetylation process, it acts as a copolymer of varying amounts of N-acetyl glucosamine and N-glucosamine repeated units. The presence of reactive primary amino groups renders special property that makes CS very useful in pharmaceutical applications. Commercially available CS has an average molecular weight ranging between 3800 and 20,000 Daltons and is 66 to 95% deacetylated. The solubility of CS depend on the degree of deacetylation, pH and on the protonation of free amino groups. CS is readily soluble in dilute solutions of most of the organic acids such as citric, tartaric acid, while soluble to a limited extent in inorganic acids [3]. CS has a large number of applications in pharmaceutal dosage form; its further application can be exploited by modifications of basic structure to obtain polymers with a range of properties. It can be done by number of approaches such as chemically as well as by enzymatically. CS can be modified in to N-trimethylene chloride, which is a quaternary derivative of CS and has a superior aqueous solubility, intestinal permeability as well as higher absorption of neutral and cationic peptide analogue over a wide pH range [4]. It can be modified in to an ester form such as CS glutamate, CS succinate, CS phthalate. These CS esters have a different solubility profile. These esteric forms were insoluble in acidic condition and provide sustained release in basic condition [5].

Corresponding Author: Vipin Bansal, Department of Pharmaceutical Technology, Meerut Institute of Engineering and Technology, Baghpat Crossing, NH-58, Meerut-250005, India.
Tel: +91 9639435888, E-mail: vipinbansal1986@gmail.com.

This article discussed the structure characteristics, physiochemical and biological properties, its effect on pharmacokinetic release of drugs and its applications in various dosage forms through various routes.

History of Chitosan: The history of CS was started when Rouget discussed the deacetylated form of CS. Different researchers have been discussed the need of understand and studying these materials, from better production, purification methods, to the modifications of basic structure and its applications. CS has been regarded as a source of potential bioactive material, but it also has several limitations to be utilized in biological system, including its poor solubility under physiological conditions. Therefore, to overcome these limitations, researchers focused on the derivatization of CS by chemical modifications and partially hydrolyzed CS by enzymatic actions as it contains various reactive functional groups. Chemical modifications of CS structures results in increased solubility in water as well as in organic solvents have been reported by some researchers. Partially hydrolyzed CS by enzymatic methods results in enhanced significant properties [6].

Further preparation and derivatives of Chitosan are covered by fallowing points given below:

Preparation of Chitosan (CS) from Raw Materials: CS is not a single chemical entity, but varies in composition depending on the source and method of preparation and also on physiological conditions. CS could be defined as sufficiently deacetylation of chitin to form a soluble amine salts. The degree of deacetylation must be 80 to 85% or higher or the acetyl content must be less than 4- 4.5% to form the soluble product. CS is manufactured commercially by a chemical method. Firstly the sources such as crab or shrimp shells are washed and grinded in to powdered form and then it is deproteinized by treatment with an aqueous 3-5% solution of sodium hydroxide. After that it is neutralized and demineralized at a room temperature by treating it with aqueous 3-5% of hydrochloric solution to form a white or slightly pink precipitate of chitin. Then chitin is deacetylated by treatment with an aqueous 40-45% of sodium hydroxide solution and the precipitate is then washed with water. The insoluble part is removed by dissolving in an aqueous 2% acetic acids solution. The supernatant solution is then neutralized with an aqueous sodium hydroxide solution to obtain a purified CS [7].

Derivatives of Chitosan (CS): CS has a large no. of application in pharmaceutal dosage form; its further application can be exploited by modification of basic structure to obtain polymers with a wide range of properties.

N-Trimethylene Chloride Chitosan: N-trimethylene chloride (TMC) is a quaternary derivative of CS and it has a superior aqueous solubility, intestinal permeability as well as higher absorption over a wide pH range. The TMC polymer is designated according to their degree of methylation such as TMC-20%, TMC-40% and TMC-60%. The TMC with high degrees of substitution, decrease in solubility has been observed. Hamman *et al.* [4] demonstrated that quaternization of TMC decreases the transepithelial electrical resistance and thereby influences its drug absorption-enhancing properties.

Chitosan Esters: CS (glutamate, succinate, phthalate) esteric forms have a different solubility profile. These esteric forms were insoluble in acidic condition and provide sustained release in basic condition. CS esters based matrix been used successfully in many formulations such as in colon-specific oral delivery of sodium diclofenac [5].

Chitosan Conjugates: CS can be conjugate with a bioactive excepients for delivery of active ingredients such as calcitonin. CS conjugates such as 5-methylpyrrolidinone chitosan, chitosan-4-thiobutylamidine conjugate have shown enhanced absorption as well as mucoadhesives properties. Guggi and Bernkop [8] attached an enzyme inhibitor to CS. The resulting polymer retained the mucoadhesive properties and furthermore an attached enzyme inhibitor prevents the degradation of drugs by inhibiting enzymes, such as trypsin and chymotrypsin. This conjugated CS demonstrated promise delivery of sensitive peptide drugs, such as calcitonin.

Properties of Chitosan: Chemistry: CS is a linear randomly distributed, hetero polysaccharide consisting of β (1-4) linked 2-acetamido-2-deoxy-β-D-glucopyranose and 2-amino-2-deoxy-β-Dglycopyranose units (Fig. 1). It is prepared by deacetylation of chitin, a linear polymer of β (1-4) linked N-acetyl-D-glucosamine units composed of mucopolysaccharides and amino sugars [7, 9-11].

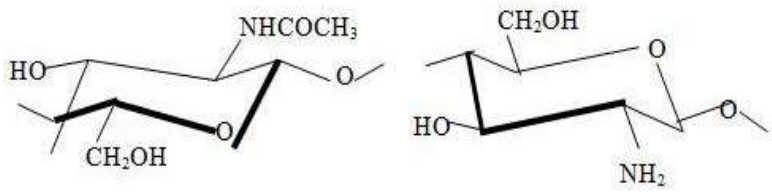

Fig. 1: Structural units of chitosan (right) and chitin (left)

Table 1: Solubility profile of Chitosan and Chitin

Chitosan solublity	Chitin solublity
Para- Toulene sulphonic acid, 10-Camphor sulphonic acid, Dimethylsulfoxide, dilute mineral or organic acids below pH 6.5	Hexafluoroisopropylalcohol, Hexafluoroacetone sesquihydrate, Lithium thiocyanate solution, LiCl in (dimethyl acetamide, diethyl acetamide, N-methyl-2-pyrrolidone

Owing to the removal of acetyl moieties that are present in the amine functional groups, CS is readily soluble in aqueous acidic solution. The solubilization occurs through protonation of amino groups on the C-2 position of D-glucosamine residues whereby polysaccharide is converted into polycation in acidic media.

Physicochemical Properties: Generally commercial natural polysaccharides such as, cellulose, carragenans, dextran, pectin, agar-agar, agarose, heparin, alginic acid and many others are neutral or acidic in nature, whereas chitin and chitosan are highly basic polysaccharides due to presence of primary amino group in its structure. This polymer has some specific properties such as polyoxy salt formation, polyelectrolyte complexation with oppositely charged polymers (guar gum, carragenans etc.), acting as a chelating agent, film forming property and specific structural characteristics. The main factors which may affect the CS properties are its molecular weight and degree of deacetylation (DD). These factors enable the researcher to formulate different grades of CS which differ primarily in molecular weight and degree of deacetylation. During the processing of CS from row material, different conditions such as type and concentration of reagents, time and temperature employed can affect the physical characteristics of CS product. The molecular weight of the CS also depends on viscosity, solubility, elasticity and tears strength. In alkaline or neutral medium, free amino group of chitosan is not protonated and therefore it is insoluble in water, while in acidic pH, it gets solubilized due to protonation of free amino groups and the resultant soluble polysaccharide is positively charged. Chitosan forms water-soluble salts with inorganic and organic acids includes glyoxylate, pyruvate, tartarate, malate, malonate, citrate, acetate, lactate, glycolate, ascorbate. The solubility profile of Chitosan and Chitin is given in the Table 1 [9]. The degree of deacetylation of molecular chain of chitin can also be increased by increasing the temperature or strength of the alkaline solution. The degree of deacetylation can also be determined by its ratio of 2-acetamido-2-deoxy-D-glucopyranose to 2-amino-2-deoxy-D-glucopyranose structural units. When the number of 2-amino-2-deoxy-D-glucopyranose units is more than 50 percent, the biopolymer is said to be Chitosan and when the number of 2-acetamido-2-deoxy-Dglucopyranose units is higher, the polymer is said to be chitin. The pka, solubility of CS can be modified by changing the DD or by modifying the pH and ionic strength of the formulation. In neutral pH, CS molecules losses their charge and get precipitated from the solution. Chemical modification of various reactive (amino, hydroxyl) groups present on the molecule provides a powerful means to promote new biological activities and to modify its mechanical properties. The characteristic features of Chitosan such as being cationic, insoluble at high pH can be completely reversed by a sulfation process which makes the molecule anionic and water-soluble and also introduce anticoagulant properties. Chitosan is a pseudoplastic material and an excellent viscosity-enhancing agent in acidic environments. The viscosity of CS solution increases with an increase in Chitosan concentration and decreases with increase in temperature. The viscosity of Chitosan also influences the biological properties such as wound-healing properties as well as biodegradation by lysozyme. Since Chitosan is hydrophilic in nature, thereby it has the ability to form gels at acidic pH. This type of gels can be used as a slow-release drug-delivery system. The solubility of Chitosan can be decreased by cross-linking it with covalent bonds using glutaraldehyde. Swelling property of the Chitosan decreases with an increase in the concentration of cross-linking agent [6, 11].

Table 2: Specification of Chitosan

Parameters	Description	Instrument
Appearance (powder or flake)	White or yellow	External shape estimation
Particle size	Less than 30 µm	Optical microscopy
Viscosity (1% solution/ 1% acid)	Less than 5 cps	Intrinsic viscosity (Capillary test)
Density	between 1.35 to 1.40 g/cm^3	Densitometer
Molecular weight	50,000 to 2,00,000 Da.	HPLC
pH	6.5 to 7.5	pH meter
Moisture content	More than 10 %	Gravimetric analysis
Ash value	More than 2 %	Gravimetric analysis
Matter insoluble in water	0.5 %	
Degree of deacetylation	66 % to 99.8 %	(FTIR test)
Heavy metal (Pb)	Less than 10 ppm	
Heavy metal (As)	Less than 10 ppm	
Protein content	Less than 0.3 %	Kjeldal method
Loss on drying	Less than 10 %	
Glass transition temperature	203°C	

Biological Properties: During the last two decades, CS has been used as a safe excepient in drug formulations. Due to its bioadhesive property, it can adhere to hard and soft tissues and has been used in dentistry, orthopedics and ophthalmology and in surgical procedures. It adheres to epithelial tissues and to the mucus coat present on the surface of the tissues. It also has a fungistatic or bacteriostatic, anticancerogen and anticholestermic action. Clinical tests of CS has been carried out in order to promote CS-based biomaterials do not report any inflammatory or allergic reactions following implantation, injection, topical application or ingestion in the human body [11].

Specification of Chitosan [12]: Table 2 shows specification concerning Chitosan.

Drug Release and Release Kinetics: The release of drug from CS based dosage form depends upon the morphology, size, density and extent of cross-linking of the particulate system, physicochemical properties of the drug as well as the polymer characteristics such as either it is hydrophilic or hydrophobic, gel formation ability, swelling capacity, muco-adhesive or bioadhesive properties and also on the presence of other excepient present in the dosage form. In vitro release of drug from the prepared dosage form in the dissolution media also depends upon volume of dissolution medium, pH and polarity, rate of stirring, temperature, sink condition and presence of enzyme. The release of drug from CS particulate systems involves three different mechanisms: (a) erosion, (b) by diffusion and (c) release from the surface of particle. The release of drug mostly follows more than one type of mechanism. In case of release from the surface, adsorbed drug dissolves rapidly and it leads to burst effect when it comes in contact with the release medium. He *et al*. [13.] observed that CS based microspheres prepared by spray drying technique have shown burst release of cimetidine. The burst release of drug can be prevented by use of cross linking agents such as glutaraldehyde and formaldehyde or by washing microparticles with a proper solvent. Al-Helw *et al*. [14] observed that a high release of the phenobarbitone in initial hours and drug release rate was dependent on the molecular weight of CS and particle size of the microspheres. The microspheres prepared from high molecular weight CS have shown slow release of drug as compared to those prepared from low molecular weight CS. This is due to the fact that high molecular weight CS has lower solubility and formation of the high viscosity gel layer around the drug particles upon contact with the dissolution medium. Microspheres having the size range of 250-500 µm, the release of drug were 75-95% up to 3h but for particles having the size range of 500-1,000 µm, drug release was 56-90% in 5h. Kweon and Kang [15] prepared the CS-g-poly (vinyl alcohol) copolymer matrix to study the release pattern of prednisolone under various conditions. In this study drug release was controlled by the extent of PVA grafting, heat treatment or cross-link density. He observed that there was a linear relationship between the amount of drug release and square root of time indicating that release was based on diffusion mechanism. Ganza-Gonzalez *et al*. [16] analyzed the controlled release of

Table 3: List of chitosan based formulations prepared by different methods

Types of system	Method of preparation	Drug
Tablets	Matrix	5-ASA, Diclofenac Sodium [26], Theophylline [27], Mesalamine [29], Glipizide [28]
	Coating	Propranolol HCl [30]
Capsules	Capsule shell	Insulin [31]
Microspheres/ Microparticles	Emulsion cross-linking	Gentamicin Sulphate [32], Hemoglobin [33], Diclofenac [34], Clarithromicin [35]
	Coacervation/precipitation	Propranolol-HCl [36]
	Spray-drying	Cimetidine [13], Famotidine [13], Bovine serum albumin.
	Ionic gelation	Bovine serum albumin (BSA) [37]
	Sieving method	Clozapine [38]
Nanoparticles	Emulsion-droplet coalescence	Gadopentetic acid [39]
	Coacervation/ precipitation	Bovine serum albumin [40], Ovalbumin [54, 55]
	Ionic gelation	Ascorbic acid [41], Cyclosporin A [56]
	Reverse micellar method	Doxorubicin [42]
Beads	Coacervation/ precipitation	Bovine serum albumin, Insulin [43]
Films	Solution casting	Ofloxacin [44], Paclitaxel [45]
Gel	Cross-linking	5-Fluorouracil [46]

metoclopramide by using Higuchi equation [17]. Ritger and Peppas [18] has given equation for diffusion-controlled matrix system in which the early time release data can be fitted to obtain the diffusion parameters (equation1),

$$(M_t/M_8) = kt^n \quad (1)$$

M_t/M_∞ is the ratio of drug concentration released at time t, k is a constant characteristic of the drug and polymer interaction and *n* is an empirical parameter characterizing the release mechanisms. Based on the diffusion exponent [19] drug release is classified as Fickian (n=0.5), non-Fickian or anomalous (0.5<n<1), Case II transport (n =1) and super Case II (n>1). Jameela *et al.* [20] observed a linear relationship between amount of drug released and the square root of time, indicating that the release is diffusion-controlled and obeys Higuchi equation.

Role of Chitosan in Various Dosage Forms: Various studies on role of Chitosan in various dosage forms are given below:

Amal El-kamel *et al.* [21] prepared CS based vaginal tablets containing metronidazole by directly compressing the natural cationic polymer CS, loosely cross-linked with glutaraldehyde. The batch containing 6% chitosan, 24% sodium alginate, 30% sodium CMC and 20% MCC showed adequate release properties in both media and gave lower values of swelling index compared with the other examined formulations. It also proved to have good adhesion properties with minimum applied weights. Moreover, its release properties (% dissolution efficiency, DE) in buffer pH 4.8, as well as release mechanism (n values), were negligibly affected by aging. Thus, this formula may be considered a good candidate for vaginal mucoadhesive dosage forms. Tozaki *et al.* [22] utilized CS capsules containing 5-amino salicylic acid (5-ASA) for colon-specific delivery to treat ulcerative colitis. It was observed that CS capsules disintegrated specifically in the large intestines as compared to the control formulation (in absence of CS), which demonstrated absorption of the drug in small intestines. This data is a representative example of utility of chitosan for colon-specific delivery. Patel *et al.* [23] prepared CS based glipizide microspheres by simple emulsification phase separation technique using glutaraldehyde as a cross-linking agent. Microspheres were discrete, spherical and free flowing. The microspheres exhibited good mucoadhesive property in the in vitro wash-off test and showed high percentage drug entrapment efficiency. Naima Zerrouk *et al.* [24] studied the comparison of the effect of Chitosan and polyvinylpyrrolidone (PVP) on properties and analgesic effect of naproxen. Both polymers improved drug dissolution and their performance depended on the drug polymer ratio and the preparation method. It was found that the direct compression property makes CS particularly suitable for developing a reduced-dose fast-release solid oral dosage form of naproxen. Marija Glavas-Dodov *et al.* [25] prepared and evaluated the topical liposomal gels containing 5-flouro uracil (5-FU) which is embedded into a structured vehicle of CS. The release rate of 5-FU from topical liposome gels was affected by the formulation variables. The release rate of liposome-entrapped drug was prolonged as compared to hydrogel type formulation. Other CS based dosage forms are given below in table form:

Role of Chitosan in Colon Targeted Drug Delivery: Chitosan is a well accepted and a promising polymer for drug delivery in colonic part, since it can be biodegraded by the microflora present in the human colon. Jitendra kawadkar *et al.* [47] prepared the CS coated microsphere matrix system for the treatment of ulcerative colitis-A. In these study the microspheres of Chitosan Hcl was directly compressed with the drug 5-aminosalisylic acid (5-ASA), into matrices. These matrices were compressed into tablets or introduced into capsules and coated. The release of 5-ASA from these compressed matrices by the polymer degrading action of the caecal microflora was evaluated *in vitro* using rat caecal microflora in virtue of the similarity with human intestinal microflora and it provides better release of 5-amino salicylic acid in the colon having ulcerative colitis. M.L. Lorenzo-Lamosa *et al.* [48] proposed the design of microencapsulated chitosan microspheres for colonic drug delivery. He prepared the pH-sensitive multicore microparticulate system containing CS micro-cores entrapped into enteric acrylic microspheres. CS micro-cores in which sodium diclofenac was entrapped and then it was microencapsulated into Eudragit (L-100 and S-100) to form a multi reservoir system have been prepared. In vitro release study revealed no release of the drug in gastric pH for 3 h and after the lag-time, a continuous release for 8-12 h was observed in the basic pH.

Chitosan as a Coating Material: Chitosan is used as a coating material in drug delivery applications as it has a good film forming properties and also due to its good mucoadhesive property. CS as a coating material has many advantages such as controlled release of drug for a prolonged period of time, improvement of drug payloads and bioadhesive property over the uncoated particles. Shu and Zhu [49] observed the effect of the novel technique in formulating CS beads for controlled release drug delivery. They prepared the alginate beads coated with CS by three different methods. The release of brilliant blue was not only affected by CS density on the particle surface, but also on the preparation method and other factors. Chiou *et al.* [50] observed the effect of the characteristics of CS on controlling the release of drug from CS coated PLLA microspheres. They used different molecular weight of CS for coating the microspheres. The initial burst release was observed in the first hour with 50% release of lidocaine. But, 19.2% release occurred at 25^{th} hour for the uncoated particles and 14.6% at the 90^{th} hour for the CS-coated microsphere.

Mucosal Delivery: Nowadays nasal, pulmonary drug delivery through mucosal surfaces are receiving a great deal of attention as alternative routes of systemic administration. These surfaces are used to deliver the drug for a prolong period of time at a controlled rate by use of mucoadhesives agent. CS has mucoadhesive properties and it is useful to formulate the bioadhesive dosage forms and can be given through (ocular, nasal, buccal, gastro-enteric and vaginal-uterine) route. Nasal mucosa has high permeability and easy access of drug to the absorption site. CS gets protonated in an acidic solution due to presence of free amino group and the resultant soluble polysaccharide is positively charged, which can bind strongly to negatively charged surface such as cell surface and mucosa. Therefore, CS formulation can greatly improve the residence time of drug on tissues and cells and shows sustained release of drugs there, as a result, the bio-availability of drug can be improved, the administration frequency of drug can be reduced. Chitosan has been found to enhance the drug absorption through mucosa without damaging the biological system. Patil *et al.* [51] prepared the mucoadhesive CS microspheres of amlodipine besylate by simple emulsification cross linking method and optimize parameters like external phase (mixture of heavy and light liquid paraffin in the ratio of 1:1), stirring rate, dioctyl sodium sulfosuccinate concentration, CS: drug ratio, volume of cross linking agent (glutaraldehyde) and time of cross linking. It was found that as the amount of polymer (CS) was increased, the % *in vitro* mucoadhesion also increased. This may be due to the fact that, as the amount of polymer increased, the amino groups available for binding with the sialic acid residues in mucus layer also increase and that results in the increase in the *in vitro* mucoadhesion of microspheres.

Genta *et al*. [52] studied the influence of cross linking agents on drug release and mucoadhesive properties of CS microspheres. A new *in vitro* technique was developed based on scanning microscopy (SEM and TEM) to study the effect of polymer cross-link density on the mucoadhesive properties of CS microspheres and thereby modulating the release rate of theophylline. Akbar Bayat *et al.* [53] studied the effect of insulin-loaded CS nanoparticles on bioavailability of insulin and it was observed that insulin-loaded CS nanoparticles enhanced the nasal absorption of insulin and shown sustained effect. Van der Lubben *et al.* [54] prepared CS microparticles containing ovalbumin protein and demonstrated the increased uptake of ovalbumin loaded CS microparticles by the Peyer's patches of the gut

associated lymphoid tissue (GALT) using confocal laser scanning microscopy. It was observed that CS based nanoparticles enhances both mucosal as well as systemic immune response. In a further study, van der Lubben *et al.* [55] investigated the ability of CS microparticles to enhance both systemic and local immune responses against diphtheria toxoid (DT) vaccine after the oral and nasal administration in mice.

Ocular Delivery: De Campos *et al*. [56] demonstrated the potential of CS nanoparticles in improving the delivery of drugs to ocular mucosa. Cyclosporin A (CyA) was chosen as a model drug. The in vitro release studies, performed under sink conditions, revealed a initial burst release followed by a more gradual drug release during the 24-h period. The in vivo experiments showed that after topical instillation of CyA-loaded CS nanoparticles to rabbits, therapeutic concentrations were achieved in the external ocular tissues (i.e., cornea and conjunctiva) within 48 h while maintaining negligible or undetectable CyA levels in the inner ocular structures (i.e., iris/ciliary body and aqueous humour), blood and plasma. These levels were significantly higher than those obtained following the instillation of CS solution containing CyA and an aqueous CyA suspension. The study indicated that CS nanoparticles could be used as a vehicle to enhance the therapeutic index of the clinically challenging drugs with potential application at the extra ocular level.

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. Jaleh Varhosaz *et al.* [57] prepared the gel containing lidocaine (LC) as a local anesthetic agent with three different molecular weights (MW) and concentrations of Chitosan for prolonging anesthetic effect of this drug for transdermal delivery. Lecithin was used as permeation enhancer. Viscosity, bio-adhesion, drug release from synthetic membranes, drug permeation through the biological barrier (rat skin) was studied. It was found that 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.

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 ingredients that act on the skin. In this way, it can be used in formulating moisturizing agents such as sunscreens, organic acids, etc. to enhance their bioactivity and effectiveness. Its applications includes: maintenance of skin moisture, minimizes acne problems, protect the epidermis, reduces the static electricity in hair, reduces dandruff, improve suppleness of hair, makes hair softer.

It can be concluded from the whole study that Chitosan is an important, versatile, natural polymer, have been successfully used as pharmaceutical excepient in various formulations. This has prompted accelerated research activities worldwide on Chitosan as drug delivery vehicles. These systems have great utility in controlled release and targeting studies of almost all class of bioactive molecules as discussed in this review.

ACKNOWLEDGEMENT

Authors are highly thanks full to Department of Pharmaceutical Technology, Meerut Institute of Engineering and Technology for providing necessary guidance and library facilities.

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