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# CHITOSAN POLYMER USED AS CARRIER IN VARIOUS PHARMACEUTICAL FORMULATIONS: BRIEF REVIEW

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**ABSTRACT :** Chitosan (CS) is a naturally occurring polymer which finds a wide array of pharmaceutical applications due to its low production costs, biodegradability, biocompatibility, nontoxic nature and mucoadhesion. It has been used in the blueprint of many different types of drug carriers; for various administration rules such as oral, buccal, nasal, transdermal, parenteral, vaginal, cervical, intrauterine and rectal. CS microspheres can be prepared by chemical denaturation process, solvent evaporation method and complex coacervation methods.

**Key words**: Natural polymer, Biodegradable, Drug carrier, Applications.

## INTRODUCTION

Chitosan is a natural cationic biopolymer consequent commencing the hydrolysis of chitin. One perceptible improvement of this substance is that it can be obtained from ecologically sound natural sources, namely crab and shrimp shell wastes. Together with chitin, Chitosan is well thought-out the second most profuse polysaccharide subsequent to cellulose. However contrasting cellulose, the employ of Chitosan as an excipient in pharmaceutical formula is a pretty new development. But Chitosan has been widely premeditated in the biomedical field and has been found to be highly biocompatible. In addition to the good biocompatibility of Chitosan and the abundance of natural sources of the material, Chitosan has a number of enviable properties that put together study of it attention-grabbing. (Janet cuy, et.al., 2004).

## DISCOVERY OF CHITOSAN

Henri Braconnot, director of the botanical garden in Nancy, France, first discovered Chitosan in 1811. Bracannot pragmatic that a definite substance (chitin) set up in mushrooms did not dissolve in sulfuric acid. Some 20 years later, there was a man who authored an article on insects in which he renowned that analogous substance was present in the structure of insects as well as the structure of plants. He then called this amazing substance as “chitin”. Basically, the name chitin is derived from Greek, connotation “tunic” or “envelope”. The perception was further known in 1843 when Lassaigne demonstrated the presence of nitrogen in chitin.

After the discovery of chitin, the name “chitosan” emerged in the scene. Rouget while experimenting with chitin first discovered it. Accordingly, Rouget observed that the compound of chitin could be manipulated through chemical and temperature treatments for it to become soluble. Then, it was in 1878 when Ledderhose identified chitin to be made of glucosamine and acetic acid. It was not actual by the early 20th century; quite a lot of researches took chitosan as their subject of study. They then involved sources of chitin, including crab shells and fungi. Over the last 200 years, the traveling around of chitosan has taken on many different forms. Several other researchers continue to build on the original finding of Bracannot, discovering new uses for chitin as they find different forms of it in nature.(Koide, et.al., 1998),(Gresha A, et.al., 2005).

## ORIGIN OF CHITOSAN

Chitosan (CS) [a (1→4) 2-amino-2- deoxy-β- -glucan] is derived by the alkaline deacetylation of chitin (Figure-1). The primary amine groups render special properties that make CS very useful in pharmaceutical applications. Chitin is an amino polysaccharide (combination of sugar and protein). Most CS in practical and commercial use comes from the production of deacetylated chitin with the shells of crab, shrimp, and krill (the major waste by-product of the shellfish –processing industry).

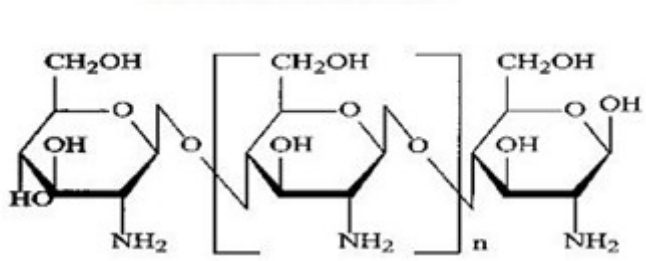

Figure-1 : Structure of Chitin

being the most available source of CS.(Knorr D, et.al., 1984). CS is a polysaccharide polymer containing more than 5,000 glucosamine units, respectively, and their molecular weights are over one million Daltons.CS comprises of copolymers of glucosamine and N-acetyl glucosamine.(Kas H.S et.al., 1997).The increasing use of for CS is due to the fact that the polysaccharide is not only naturally abundant, but it is also nontoxic and biodegradable.

## CHEMISTRY

Chitosan (Poly[-(1, 4)-2-amino-2-deoxy-D-glucopiranose]) has a structure as shown in figure –2.Chitin is isolated from shells of crustacean( for example shrimp, crab and lobster ) by treating the shells with 2.5 N NaOH at $75^0$ C and with 1.7 N HCl at room temperature for 6 hours.(Chang K.C.B, et.al., 1997).

Deacetylation can be done by alkaline treatment or by enzymatic reaction. The alkaline deacetylation is carried out by treating chitin with NaOH at high temperature. The degree of deacetylation increases with increasing temperature or NaOH concentration. Determine the optimum deacetylation is done by mixing 23 ml of 60% NaOH per gram of chitin 170°C (Chang K.L.B, et.al., 1997).

Chitin deacetylation by enzymatic reaction is described by Martinou et.al. Chitin deacetylase isolated from Mucor rouxii has been used successfully to deacetylate chitin almost completely (98%) (Bouritotis V, et.al., 1995).

The polymer differs from chitin in that a majority of the N-acetyl groups in Chitosan is hydrolyzed. The degree of hydrolysis has a significant effect on the solubility and rheological properties of the polymer. The amino group on the polymer has a pKa in the range of 5.5 to 6.5, depending on the source of the polymer. At low pH, the polymer is soluble, with the sol-gel transition occurring at approximate pH 7. The pH sensitivity coupled with the reactivity of the primary amino groups makes chitosan a unique polymer for and drug delivery applications. Chitosan is now available commercially in various molecular weights (50kDa–2,000kDa) and different degree of deacetylation (40% to 90%) (Bhumkar et.al, 2006).

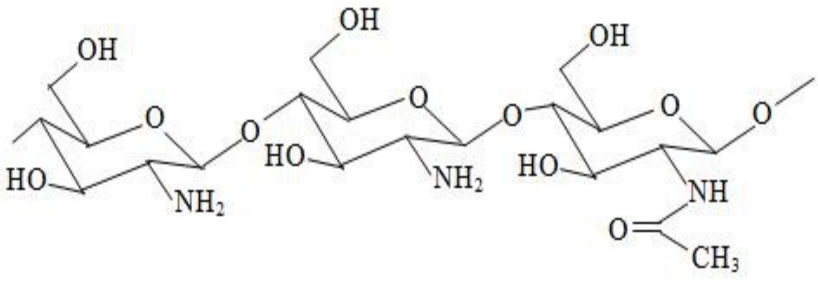

**Figure-2 : Chemical structure of Chitosan**

## PRODUCTION OF CHITOSAN

Production of chitosan was conducted using two Mucoralean strains, Mucor racemosus and Cunninghamella elegans. Chitosan was extracted from mycelia of M. racemosus and C. elegans at different growth phases on YPD medium. In both fungi, chitosan was rapidly produced, while highest yield of extractable chitosan was found in 24h of cultivation in submerged culture. The yield of chitosan isolated from dry mycelia of M. racemosus was about 40% higher than from C. elegans. The degree of N-acetylation of chitosan was 49% in M. racemosus and 20% in C. elegans, and the D-glucosamine contents were about 48% and 90%, respectively.

Disclosed is another process for producing particles of the modified carbohydrate polymer chitosan. Such chitosan particles are "activated" because of the specific steps used in the process. The process involves precipitation of dissolved chitosan from an acid solution thereof by the step-wise addition of neutralizing agent to the solution. A partial neutralization is carried out under shear agitation to form a continuous gel phase having a pH within the range of 5.0 to 6.9. This partially neutralized chitosan gel phase is then further subjected to shear agitation for at least 10 seconds to homogenize the gel phase. The homogenized gel phase is then further neutralized under shear agitation to a pH of above 6.9 to form a gel-like suspension of discrete chitosan particles. (Rosa Valeria, et.al., 2001).

## GENERAL PHARMACEUTICAL APPLICATIONS OF CHITOSAN

a) Chitosan by itself is haemostatic (stops bleeding), some derivatives such as sulphated Chitosan are anticoagulants. By utilizing the haemostatic effect, CS bandages and sponges we prepared for surgical treatment and wound protection. (Kibune K, et.al., 1988).

b) It has a capacity of forming film and has been suggested as a biopolymer of choice for the development of contact lenses (soft and hard contact lenses). (Marky K, et.al., 1996).

c) It has been used for the manufacturing of ocular bandage lenses used a protective device for acutely or chronically traumatized eyes.

d) It is also useful as artificial kidney membranes because of their suitable permeability and high tensile strength. (Amiji M.M, et.al., 1995).

e) Used for hypobilirubinaemic and hypercholesterolemia effects, antacids and antiulcer activities, wound and burn healing properties, immobilization of enzymes and living cell and in ophthalmology. (Felt O, et.al., 1999).

Among the pharmaceutical applications it has been used as a: (Miasakkinen, et.al., 2003).

1. Diluents in direct compression of tablets.
2. Binder in wet granulation
3. Slow-release of drugs from tablets and granules
4. Drug carrier in micro particle systems
5. Films controlling drug release
6. Preparation of hydrogels, agent for increasing viscosity in solutions.
7. Wetting agent, and improvement of dissolution of poorly soluble drug substances
8. Disintegrant
9. Bio adhesive polymer
10. Site-specific drug delivery (e.g. to the stomach or colon)
11. Absorption enhancer (e.g. for nasal or oral drug delivery)
12. Biodegradable polymer (implants, micro particles)
13. Carrier in relation to vaccine delivery or gene therapy

## DIFFERENT STUDIES ON CHITOSAN AND ITS DERIVATIVES

During a study chitosan, nanoparticles including hydroxylpropylcyclodextrins prepared by the ionic cross linking of chitosan with sodium tripolyposphate in the presence of cyclodextrins. Two hydrophobic drugs, triclosan and furosemide, were selected as models for complexation with the cyclodextrin and further entrapment in the chitosan Nano carrier. The resulting Nano systems were thoroughly characterized for their size and zeta potential and also for their ability to associate and deliver the complexed drugs. So this new Nano system with chitosan offers an interesting potential for the transmucosal delivery of hydrophobic compounds. (Francesca Maestrelli, et.al., 2006).

Chitosan capsules for colon-specific delivery to treat ulcerative colitis. A 5-amino salicylic acid was encapsulated into Chitosan capsules and delivered in vivo to Male Wistar rats after induction of colitis. It was observed that Chitosan capsules disintegrated specifically in the large intestines as compared to the control formulation (in absence of Chitosan), which demonstrated absorption of the drug in small intestines. This data is a representative example of utility of Chitosan for colon-specific delivery. (Tozaki H, et.al., 2002).

Microcrystalline Chitosan (MCCh) may be particularly valuable as an excipient. As a highly crystalline grade of chitosan base. One specific property of MCCh is its high capacity for retaining water. This property could be advantageous in relation to the development of slow-release formulations because it might facilitate the formation of gels that would control drug release. The pronounced ability of MCCh to form hydrogen bonds could theoretically result in efficient mucoadhesion by MCCh. The properties of MCCh mentioned made it particularly interesting for study as a hydrophilic excipient-controlling rate of drug release from formulations that were also intended to be mucoadhesive in the stomach. (Miasakkinen, et.al., 2003).

Intratumoral and local drug delivery strategies have gained momentum recently as a promising modality in cancer therapy. In order to deliver paclitaxel at the tumour site in therapeutically relevant concentration, Chitosan films were fabricated. Paclitaxel could be loaded at 31% wt/wt in films, which were translucent and flexible. Chitosan films containing paclitaxel's were obtained by casting method with high loading efficiencies and the chemical integrity of molecule was unaltered during preparation according to study. (Anand Babu D, et.al., 2004).

A quaternary derivative chitosan (N-trimethylene chloride Chitosan) was shown to demonstrate higher intestinal permeability than chitosan alone. The TMC derivative was used as a permeation enhancer for large molecules, such as octreotide, a cyclic peptide. Hamman and co-workers showed that the degree of quaternization of TMC influences its drug absorption-enhancing properties. (Thanou M, et.al., 2000).

Chitosan and randomly methylated b-cyclodextrin (RAMEB) were the most to be studied absorption enhancers for nasal administration recently. From where it has clear that Chitosan and randomly methylated b-cyclodextrin could combine to enhance the absorption and elevate the bioavailability of estradiol after nasal administration. (Wei L Eng., et.al., 2006).

A cationic polymer like chitosan has potential for DNA complexation and may be useful as non-viral vectors for gene therapy application. Chitosan is a natural non-toxic polysaccharide, it is biodegradable and biocompatible, and protects DNA against DNase degradation and leads to its condensation. Hence chitosan can be used to improve the transfection efficiency in vivo and in vitro. (Sania mansouri, et.al., 2004).

Chitosan/tripolyposphate nanoparticles that promote peptide absorption across mucosal surfaces. The main theme of this work was to microencapsulate protein-loaded chitosan nanoparticles using typical aerosol excipients, such as mannitol and lactose, producing microspheres as carriers of protein-loaded nanoparticles to the lung. The results showed that the obtained microspheres are mostly spherical and possess appropriate aerodynamic properties for pulmonary delivery (aerodynamic diameters between 2 and 3 micron, apparent density lower than 0.45 g/cm3). Moreover, microspheres morphology was strongly affected by the content of chitosan nanoparticles. These nanoparticles show a good protein loading capacity (65-80%), providing the release of 75-80% insulin within 15 min, and can be easily recovered from microspheres after contact with an aqueous medium with no significant changes in their size and zeta potential values.(Grenha, et.al., 2002).

Insulin-chitosan nanoparticles were prepared by the ionotropic gelation of chitosan glutamate and tripolyphosphate pentasodium and by simple complexation of insulin and chitosan. The nasal absorption of insulin after administration in chitosan nanoparticle formulations and in chitosan solution and powder formulations was evaluated in anaesthetised rats and/or in conscious sheep. Insulin-chitosan nanoparticle formulations produced a pharmacological response in the two animal models, although in both cases the response in terms of lowering the blood glucose levels was less (to 52.9 or 59.7% of basal level in the rat, 72.6% in the sheep) than that of the nasal insulin chitosan solution formulation (40.1% in the rat, 53.0% in the sheep). The insulin-chitosan solution formulation was found to be significantly more effective than the complex and nanoparticle formulations. The hypoglycaemic response of the rat to the administration of post-loaded insulin-chitosan nanoparticles and insulin-loaded chitosan nanoparticles was comparable. As shown in the sheep model, the most effective chitosan formulation for nasal insulin absorption was a chitosan powder delivery system with a bioavailability of 17.0% as compared to 1.3% and 3.6% for the chitosan nanoparticles and chitosan solution formulations, respectively.(Dyer A M, et.al., 2002).

Effects of chitosan oligomers on pulmonary absorption of interferon-alpha (IFN) were examined by means of an in vivo pulmonary absorption experiment. Chitosan oligomers used in this study were chitosan dimer, tetramer, hexamer, and water-soluble (WS) chitosan. A significant increase in serum IFN concentrations was observed after intratracheal administration of IFN with these oligomers. Of these chitosan oligomers 0.5% w/v chitosan hexamer appeared to be more effective in enhancing the pulmonary absorption of IFN than other oligomers at the same concentration, and the AUC value of IFN with chitosan hexamer increased 2.6 –fold as compared with the control. Therefore these findings indicated that the use of chitosan oligomers would be a promising approach for improving of the pulmonary absorption of biologically active peptides including IFN. (Yamada K, et.al., 2005).

## BONE REGENERATION AND REPAIR

Bone healing involves a sequence of biochemical events that should not be disturbed by the
Presence of a composite or scaffold. The chemical and technological versatility of chitosan enables researchers to prepare elaborated composites: for example, the research works on bone regeneration with the aid of bone cements have recently become more refined in terms of the effects of chitosan composites on the cells involved in the healing process. The use of nano-hydroxyapatite as well as other inorganics in conjunction with variously modified chitosan is greatly contributing to the advancement and exploitation of chitosan composites for bone healing. With the advent of nanotechnology the applications of fairly non-toxic nanocrystalline hydroxyapatite extends from bone repair and augmentation to the delivery of drugs, growth factors and genetic material to the bone: for this purpose, particles of uniform size with controlled morphology can be manufactured by using macromolecules as templates. A number of advantages have become evident, particularly when Nano-hydroxyapatite is crystallized using biomimetic methods, or when the biopolymers are submitted to bio mineralization. The hydroxyapatite nanoparticles influence favourably the morphology of attached cells, as a consequence of the adsorption of extracellular matrix proteins from serum that in turn bind osteoblast precursors. Thus, an additional peculiarity of chitosan emerging from the most recent studies is the capacity to influence both the mineralization and the cell activity. Chitosan, N-carboxymethyl chitosan, fibroin and poly (L-lactic acid) are at the basis of new strategies useful to stimulate stem cells to become osteoblasts, and to make co-cultures of osteoblasts and osteoclasts. (Muzzarelli R.A.A, et.al. 2010).

## WOUND DRESSING

Haemostasis is immediately obtained after application of most of the commercial chitin-based dressings to traumatic and surgical wounds: platelets are activated by chitin with redundant effects and superior performances compared with known haemostatic materials. To promote angiogenesis, necessary to support physiologically ordered tissue formation, the production of the vascular endothelial growth factor is strongly up-regulated in wound healing when macrophages are activated by chitin/ chitosan. The inhibition of the expression of matrix metalloproteinase in primary human dermal fibroblasts by low MW chitosan's prevents or solves problems caused by metalloproteinase-2 such as the hydrolysis of the basement membrane collagen IV. Experimental biocompatible wound dressings derived from chitin are today available in the form of hydrogels, xerogels, powders, composites, films and scaffolds: the latter are easily colonized by human cells in view of the restoration of tissue defects, with the advantage of avoiding retractive scar formation. The growth of nerve tissue has been guided with chitin tubes covalently coated with oligopeptides derived from laminin.

The regeneration of cartilage is also feasible because chitosan maintains the correct morphology of chondrocytes and preserves their capacity to synthesize cell-specific extracellular matrix: chitosan scaffolds incorporating growth factors and morphogenetic proteins have been developed. The introduction of azido functions in chitosan has provided photo-sensitive hydrogels that crosslink in a matter of seconds, thus paving the way to cytocompatible hydrogels for surgical use as coatings, scaffolds, drug carriers and implants capable to deliver cells and growth factors. Recent progress in wound management is mainly in terms of physiologic support of healing. Chitin and chitosan substantially contribute to the advances in this direction, as testified by the sound knowledge of the biochemical mechanisms of healing promoted by various forms of these polysaccharides, and also by the absence of adverse data in the many articles published since the early observations 20 years ago. The modern clinical approach to improving the appearance and functionality of regenerated tissue in the healed wounds finds a valid basis in the versatility, functionality and efficacy of chitosan, whose performances underline the obsolescence of the cellulose-based medical items.(Muzzarelli R.A.A, et.al., 2009).

## PREPARATION OF MICROSPHERES BY DIFFERENT METHODS

### Chemical cross linking

The Process involves the precipitation of the polymer followed by chemical crosslinking. Precipitation can be done by sodium sulphate followed by chemical crosslinking using glutaraldehyde Aqueous solution of CS (3% (w/v) in 4% (v/v) glacial acetic acid) was added into agitating medium and stirring continued to obtain wet microspheres, which were then filtered, washed and finally dried at room temperature.(Aggarwal A, et.al., 2001).The result show that solvent emulsification technique can also be used to prepare microspheres using heat as cross linking agent and avoiding the use of chemical as cross linking agent.

### Solvent evaporation method

The processes are carried out in a liquid manufacturing vehicle. The microcapsule coating is dispersed in a volatile solvent, which is immiscible with the liquid manufacturing vehicle phase. A core material to be microencapsulated is dissolved or dispersed in the coating polymer solution. With agitation the core material mixture is dispersed in the liquid manufacturing vehicle phase to obtain the appropriate size microcapsule. The mixture is then heated if necessary to evaporate the solvent for the polymer of the core material is disperse in the polymer solution, polymer shrinks around the core. If the core material is dissolved in the coating polymer solution, matrix – type microcapsules are formed. The solvent Evaporation technique (Figure 4) to produce microcapsules is applicable to wide variety of core materials. The core materials may be either water soluble or water in soluble materials. Solvent evaporation involves the formation of an emulsion between polymer solution and an immiscible continuous phase whether aqueous (o/w) or non-aqueous. The comparison of mucoadhesive microspheres of hyaluronic acid, CS glutamate and a combination of the two prepared by solvent evaporation with microcapsules of hyaluronic acid and gelating prepared by complex coacervation were made. (Brown M.B, et.al. 2000).

### Complex Coacervation method

Micro particles can also prepared by complex coacervation. Sodium alginate sodium CMC kCarregnan and sodium polyacrylic acid can be used for complex coacervation with CS to form microspheres. These micro particles are formed by interionic interaction between oppositely charged polymers solutions and KCl & CaCl2 solutions. The obtained capsules were hardened in the counter ion solution before washing and drying. (Nishioka Y, et.al., 1990), (Ohya Y, et.al., 1993).

### Ionotropic gelation method

The counter ions used for ionotropic gelation can be divided into 3 categories. Low molecular counter ions like pyrophosphate and tripolyposphate, Hydrophobic counter ions (e.g. Alginate k carragenan), and High molecular weight ion(e.g.: octyl sulphate , lauryl sulphate).
(Skaugrud O et.al., 1991).
The CS solution in acetic acid was extruded drop wise through a needle into different concentrations on aqueous solutions of magnetically stirred tripolyposphate or some other an ion. The beads were removed from the counter ion solution by filtration washed with distil water and dried. (Wan L.S et.al., 1994).

## VARIOUS CLASSES OF DRUGS WHICH HAVE BEEN MICROENCAPSULATED USING CHITOSAN

Microspheres which are prepared using CS are being extensively investigated for various classes of drugs.

### Cardiac agents

### Diltiazem hydrochloride

Casein-CS microspheres containing Diltiazem hydrochloride were prepared by colloidal coacervation technique.(Aydin Z, et.al., 1996).The interaction between CS solution in acetic acid (5%, v/v) and casein solution in 0.5 M NaOH formed the basis of formation of microspheres. Formaldehyde was used as the crosslinking agent. The concentration of casein, CS, drug and stirred speed affected the properties and performance of the micro spheres. (Bayomi M.A, et.al., 1998).

### Nifedipine

Nifedipine and nifedipine cyclodextrin complexes were encapsulated in CS microspheres. More than 70% of drug entrapment efficiency was achieved. (Filipovie-Greiejet, et.al., 1996).

### Isosorbide-5-mononitrate

The formulation and *in-vitro* release profile of the isosorbide-5-mononitrate loaded CS micro spheres, was compared with marketed formulations. (Fariver M, et.al., 1993).

### Anticancer drugs

### Fluorouracil (5-FU)

Anionic polysaccharides, 6-O-methyl-Nacetyl–α-1,4-polygalactosamine, 6-Ocarboxymehtyl-chitin alginate and heparin have also been used to coat CS gel microspheres f 1-(N-(5-aminipentyl)-carbamoyl)-5-flouro uracil by polyelectrolyte complex membrane formation. These microspheres released the drug in a controlled manner and were found to have target ability to specific organs/cells to the presence of polysaccharide chains on the surface of microspheres which are further recognized by the saccharides specific receptors cell surface. Release properties of 5-FU were also influenced by the addition of substances such as chitin, alginic aced, agar, stearic acid and sodium caprylate. (Akbuga J, et.al., 1996).

### Cisplastin

Coated albumin microspheres of cisplastin with chitin and CS have shown to possess sustained release characteristics and have also been found useful in hepatic artery embolization. (Miyazaki M, et.al.,1990).

### Taxol

The possibility of encapsulating taxolloaded polylactic acid (PLA) microspheres with in heparin-CS spheres to develop a prolonged release co-matrix form. (Chandy T, et.al., 2001).

### Anti-inflammatory drugs

### Diclofenac sodium

CS microspheres of diclofenac sodium are prepared with three different crosslinking methods i.e. glutardehyde, $H_2SO_4$ and heat treatment. CS microspheres were produced in a w/o emulsion followed by cross-liking using one of the above methods. (Kumbar S.G et.al., 2002).

### Indomethacin

CS gel beads composed of CS hydro lysate (MW: 25,000) might be suitable for the sustained-release preparation of Indomethacin. (Shivaishi s, et.al., 1993).

### Ketoprofen

Effect of molecular weight of CS on drug loading and drug release was studied. Using ketoprofen as a model drug. CSs with MW between 70,000 and 2,000,000 were found to be suitable carriers for ketoprofen that could modulate drug release within 48 hours. CS microspheres to ketoprofen have also been prepared by a multiple emulsion (o/w/o), which produced satisfactory yield of micro spheres. (Genta I, et.al., 1995).

### Ibuprofen

Spherical pellets of poorly soluble drugs. Micronized griseofulvin, ibuprofen, indomethacin, sulfadiazine ortolbutamide were prepared by dispersing the drug in solutions of the ionic polysaccharides CS or sodium alginate, and then dropping these dispersions into solutions of the respective counter ions tripoly phosphate or $CaCl_2$.(Bodmeir R, et.al., 1989). The droplets instantaneously form gelled spheres by ionotropic gelation.

**Antibiotics**

**Amoxicillin**

Amoxycillin and metronidazole loaded CS microspheres for stomach specific deliveries were prepared for the treatment of Helicobacter pylori infection. (Shah S, et.al., 1999). The micro spheres were prepared by cross-linking in addition to precipitation with sodium tripolyposphate.

**Ampicillin**

A new derivative of CS, methylpyrrolidinone CS was used to prepare ampicillin micro particles by spray drying technique. (Giunchedi P, et.al.,1989). Microbial assays which were conducted using different bacterial strains showed that ampicillin microspheres were able to maintain the antibacterial activity of the drug. (Sinha V.R, et.al.,2004).

**Tetracycline**

Tetracycline loaded CS microspheres prepared by ionic cross-linking and precipitation method. (Hejazi R, et.al., 2003)

**Griseofulvin**

Spherical pellets of micronized griseofulvin were prepared by dispersing the drug in solutions of the ionic polysaccharides CS or sodium alginate. These dispersions were then dropped into solutions of the respective tripolyposphate or $Cacl_2$. Strong spherical heads with a narrow particle size distribution and high drug content (approaching 98%) could be prepared. (Bodmeier R et.al., 1989).

## CONCLUSION

Biologically degradable polymers can be loosely distinct as a class of polymers, which degrade to smaller fragments due to chemical present inside the body. Natural polymers are always biodegradable because they undergo enzymatically promoted degradation. Chitosan is one of them, which exhibits biodegradability, scrawny antigenicity and better-quality biocompatibility compared with supplementary natural polymer. Chitin in fact, is one of the most abundant polysaccharides bringing into being in nature, assembly Chitosan a plentiful and moderately inexpensive product. Chitosan has recently sparked significance in the tissue-engineering field. Chitosan has been used in the blueprint of many different types of drug carriers for various administration rules such as oral, buccal, nasal, transdermal, parenteral, vaginal, cervical, intrauterine and rectal. It can be engineered into poles apart shapes and geometrics such as nanoparticles, micro spheres, membrane, sponge and rods. On drug delivery special preparation techniques are used to put in order chitosan drug carriers by cluttering such parameters as cross linker concentration. Accessibility of different chemical side groups for add-on to other molecules in Chitosan would however be most wanted to further endorse the exploit of the polymer as development of a new Chitosan derivatives. Various therapeutic agents such as anticancer, anti-inflammatory, antibiotics, antithrombic, steroids, proteins, amino acids, ant diabetic and diuretics have been incorporated in CS micro spheres to achieve controlled release as well to enhance bioavailability or for drug targeting to specific areas of the body.

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