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Chitosan Nanoparticles: Synthesis and Their Applications

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Abstract—*Chitosan nanoparticles (CHNP) are determined as particulate dispersions or solid particles with size in the range of 1-100 nm. Over the past decades, there has been a considerable research interest in the area of using chitosan nanoparticles as adsorbent. Nanoparticles have emerged as one of the most exciting tools, due to the increased surface-to-volume ratio, which provides interaction with the surfaces. In this review, explained of methodsemployed to produce chitosan nanoparticle is provided, along with explained different types of the procedures. In this paper introduced of methods such as, micro emultion, ionotropic gelation, poly electrolyecomplexe (PEC) and also discussed in detail of these methods. The main aim of the present review deals withthe chitosan nanoparticles, which is a bio-degradable and natural polymer. In this review considered research interest in the many areasusing nanochitosan. We include the application of chitosan and its nanoparticles. Chitosan nanoparticles have attracted and gain attention for their wide applications in, for example, controlled drugs release, waste water treatment. Keeping in view importance of chitosan nanoparticles in many different areas, this review article was written. The review focuses on the preparation techniques, Fig. out and applications of chitosan nanoparticles.*

1. INTRODUCTION

Nanotechnology is not a new technique concept; it has gained more attention in past few years. The nano technique has been more attractive for their application in many other fields. Nanoparticles materials are materials within the range smaller than the 100 nm size, which have unique applications and properties due to its size effect. Most of paper authors assumed that nanoparticles will be capable for as adsorbent and enhanced the interaction with metal, protein, cell membrane and many other areas which are used particularly [1]. Within past few years, rapidly developments use nanoparticles in a vast of applications in various fields such as medical, pharmaceutical, waste water treatment etc.

Many author reported about chitosan and its nanoparticles. In the past decade, the synthesis of chitosan nanoparticles has been intensively developed but not only its scientific interest but also for many technological areas applications: gene delivery in shrimp [2], factorial designs [3], adsorption of heavy metals and also adsorption of dyes etc. the control of the nano size is very important because the nanoparticle properties strongly depend upon the size and dimension of nanoparticles. To understand its behavior and to improve application and develop new once, control the surface area, particles size, physical and chemical behavior. In this, we have reviewed preparation, characterization and application of chitosan nanoparticles.

In thisre view, we summarized different methods for the synthesis of chitosan nanoparticles (Ioninc gelation method, micro emulsion, emulsification solvent diffusion and polyelectrolyte complex), All these methods have their own benefits as well as drawbacks, in relation to the properties of the nanoparticles and the different technique structural and physical characterization. Chitosan is a deacetylated unit of chitin. Chitin is polysaccharides found in shrimp, crab and lobster basically the main source of chitin is in the cell wall of fungi. It is very cost effective and it is also available very easily because of seafood companies, huge amount wastes of crab and shrimp shell.

The primary unit in the chitin polymer is 2-deoxy-2-(acetylamino) glucose. These units combined by β-(1, 4) glycosidic linkages, forming a long chain linear polymer [4]. Chitin or chitosan do not dissolved in neutral water. Chitosan dissolve in organic acid. Basically, the solubility of chitosan decrease with molecular weight (MW) increases. The degree of deacetylation is one of the fundamental parameters that can affect the properties and functionality of chitosan.

Chitosan nanoparticles have complete power over its own physical, chemical, and morphological characteristics that actually determine their applications. Some researchers are interested in the other applications of chitosan for pharmaceutical and medical purposes.

2. METHODS OF PREPARATION OF CHITOSAN NANOPARTICLES

Various methods have defined for preparation of chitosan nanoparticle. Few of them are as follows:

Chitosan are hydrophilic natural polymers and have been used to synthesize biocompatible NPs by the ionic gelation method.

2. 1 Inotropic Gelation Method

Chitosan naoparticles have prepared by Ionic Gelation technique. This technique was first reported in 1997 [5]. In this method chitosan is dissolved in acetic acid of appropriate concentration. As cross-linking agent used Sodium tripolyphosphate(TPP) is most of research. The interaction of chitosan and sodium tripolyphosphate (TPP) because of oppositely charged particles can be controlled by pH of the solution.

*Sudha. P. N. et al*prepared nanochitosan by this technique;1gm of chitosan dissolved in 200ml. of 2% acetic acid solution was stirred for 15 min. to get a homogeneous viscous gel. Then add. 8 gm of TPP dissolved in 170 ml. of conductivity water was added drop wise. Milky solution obtained ,this solution allow to rest and settled as suspension by adding conductivity water in excess for 24 hr. chitosan naoparticles were obtained [6]. In *S. Vimal et al*described in paper same technique but nanoparitclesseparated by using centrifugation at 12,000 rpm for a period of 30 min at 14^{o}c.

*Kuo-Shien Huang*used low molecular weight chitosan for preparing chitosan nanoparticles. In his paper author reported amount and processure of preparation ,0. 5 g of LWCS was dissolved in 1000 ml of 2%acetic acid. Then, 100 ml of eachsolution was added to 40 ml of TPP, stirred for 2 h at 25^{o}C and thencentrifuged. Author showed a data list of zeta potantial, the nanochitosan have positive zeta potential. when add TPP solution zeta potential decreases. Because of addition of TPP positively charged chitosan particle surface was neutralised by negatively charged phosphate grroup of TPP. In this reaction it was gradually reduce because of forming inter and intra molecular cross-links.

Author described in his paper The good cross-linking occurredwhen the mass ratio of LWCS+TPP was approximately 5:2,at which the measured zeta potential was also minimal at7. 8[7].

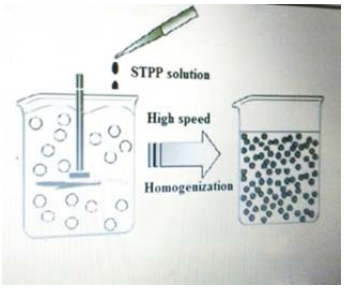

Fig. 1: Schematic representation of ionic gelation method

A mentioned above one technique but used different process for finding chitosan naoparticles. The author's experience in this field and other works available in the literature, have concluded that the properties of chitosan nanoparticles obtained throughinteraction between chitosan and TPP are dependent on many parameters inherent to the preparation method. When increases the addition of cross-linking agent (Tpp) increases the adsorption capacity of chitosan. The author *S. vimal* mentioned in their paper reaction performing under 14^{0}C, the fact that increasing hydrogen bonding between chitosan polar group and water when reducing temperature that's by the probability of nanoparticles collision decreased.

2.2. Micro Emulsion Method

Chitosan nanoparticles prepared by micro emulsion technique were first developed by Maitra. Basically it is based on involvement of chitosan in the aqueous core of reverse micellar droplets and followed by cross-linked through glutaraldehyde. In this technique involvement of surfactant is must to n-hexane. Then prepared chitosan/acetic solution and glutaraldehyde mix with the surfactant/hexane mixture and continuously stirring at room temperature. One author describe the use of surfactant, these molecules are amphiphilic in nature. Which are in the presence of water or any organic solvent form a spherical aggregate. [8]. The final solution is kept overnight, for removal of organic solvent used a low pressure. Many author describedin their papers, the excess surfactant which is used particularly in experiment was removed by precipitating with $CaCl_2$ and found precipitate, this precipitance was removed by centrifugation. The final nanosphere suspension was dialyzed before lyophilization. By this technique found a narrow size distribution of less than 100 nm [9].

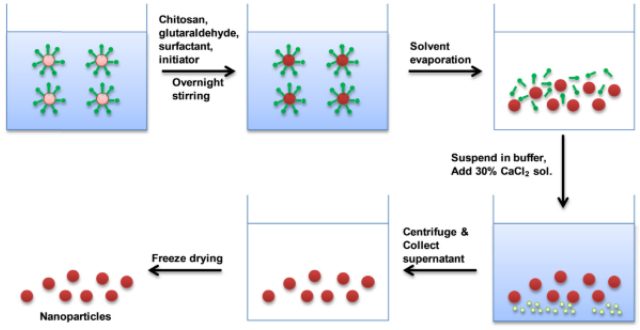

Fig. 2: Schematic representation of Micro emulsion method [8]

2.3. Polyelectrolyte Complex (PEC)

Polyelectrolyte complex is very simple technique for preparations of nanoparticles since no tough condition are involved. It formed by interaction between anionic and cationic charged polymer, followed by charge neutralization see in figure. *Surendra nimesh* described in his paper the

reason of interaction, Due to the charge neutralization, polyelectrolyte complex are self-assembled and it leads to the rise in hydrophilicity. So nano formulated can be sizes from 50 to 700 nm. Many cationic polymers (i. e. gelatin, chitosan, polyethylenimine) also give this property. One author explains this method with the chitosan. The nanoparticles were spontaneously formed after addition of alginate solution into chitosan which was priorly dissolved in acetic acid solution, under mechanical stirring at room temperature. The complexes size range from 50 nm to 700 nm [10].

These polyelectrolyte complexes are used for delivery of proteins, peptides, drugs, and plasmid DNA. [11].

Another study was done where author *Nam et al.* used low molecular weight water soluble chitosan (LMWSC) nano carriers were developed by the similar

methods for insulin delivery [12]. The above method reported size of nanoparticles approximately 200 nm.

Effects of pH, MW, and concentration participate main role while observingthe size and yield of nanoparticles. In above study it observed when pH is low and moderate molecular weight favored more complexation.

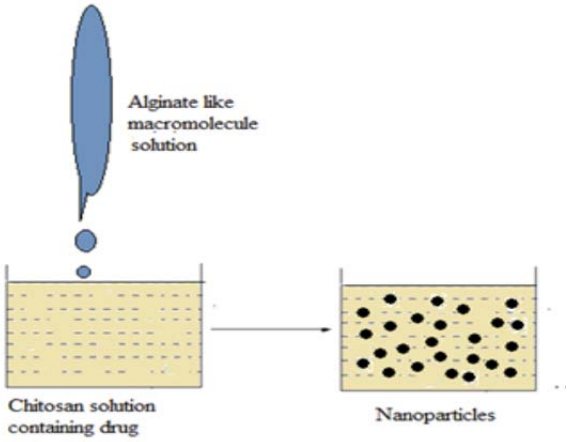

Fig. 3: Schematic representation of Polyelectrolyte complex technique [13]

2.4. Emulsification/solvent Diffusion (ESD)

This is also another method for preparing chitosan nanoparticles. This method originally developed by *Niwaet al.* employing PLGA. This is a modified solvent diffusion method. This is the specific method for preparation of chitosan nanoparticles. In this method the addition involves of water-miscible solvent (e. g. methylene chloride and acetone) along with organic solvent (e. g. dichloromethane or chloroform) are used. According to its boiling point, solvent is eliminated by evaporation or filtration.

The limited number of studies available by using this method, parameters such as molecular weight and reaction time (period of diffusion). This method has proven to be suitable for encapsulating hydrophobic drugs. Authors' research on several drug- loaded nano particles were produced by the technique, but in this review motioned one, mesotetra

(hydroxyphenyl) porphyrin-loaded PLGA (p-THPP) nano particles prepared by *Vargas*[14].

All method has some advantages and also some disadvantages, in this method also have, *Advantages:*

In this technique there isno need for homogenization. Several advantages present, such as

Advantage:
1) reproducibility
2) simplicity, and narrow size
3) easy to scale-up

Disadvantages:
1) Eliminating of high volumes of water from suspension.
2) During emulsification leakage of drug which is water soluble into the saturated-aqueous external phase.

3. APPLICATIONS OF CHITOSAN NANOPARTICLES

Chitosan nanoparticles have wide and rapidlyincreasing applications in the food and biochemicalindustries.

3.1. Peroral Administration

The nanoparticles might protect labile drugs from enzymatic degradation in the gastrointestinal tract (GIT) generate to the development of nanoparticles as oral deliverysystems for macromolecules, proteins and polynucleotides [4]. Chitosan nanoparticles have attractive carriers for oral deliveryvehicle as they promote absorption of drug. Several research groups have studied the absorption promoting effect of chitosan and founded, in mucosal cell membrane, a combination of mucoadhesion and transient opening of tight junctions [15].

3.2. Industrial Importance

In waste water treatment for removal/recovery of heavy metal ions from wastewaters such as copper, chromium, cadmium, lead, nickel, mercury, iron, silver, zinc, cobalt and arsenic and also removal and binding of dyes, sludge treatment and dehydration agent, biological denitrification.

3.3. Controlled Drug Release

Various anticancer drugs have been delivered to cancer cells by chitosan nanoparticles. By varying degree of deacetylation of chitosan, different types of nanoparticles can be prepared with different drug release.

4. CONCLUSION

The main goal of this review was to describe the different preparation techniques available for production of chitosan nanoparticles. It was observed that preparing chitosan nanoparticles is a technology that requires a suitable technique

among the various methods. Chitosan nanoparticles offer many advantages. Chitosan is a safe natural polymer material because of its two main properties: biocompatibility and biodegradable. Chitosan nanoparticles are suitable broad area of drugs including labile drugs and macromolecules. for use on an industrial scale, the emulsion-solvent diffusion method is superior due to its simplicity and its suitability. Chitosan nanoparticles offer many routes of administration especially, peroral. This review paper gives an overview about the applications of nano chitosan in many areas and also describes different type of method for preparing nano chitosan.

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