

PREPARATION OF CHITOSAN COATED NANOPARTICLES BY EMULSION POLYMERIZATION TECHNIQUEKRISHNA SAILAJA A¹, AMARESHWAR P¹

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ABSTRACT

Nowadays there has been considerable interest in developing new routes alternative to injection for delivering macromolecules such as proteins and peptides. However peptides and protein drugs are degraded before they reach the blood stream and can not cross the mucosal barrier. The mucoadhesive polymer coated nanoparticles can solve these problem. They were prepared by emulsion polymerization. Methyl methacrylate polymerized in the presence of polysaccharide such as chitosan leads to formation of mucoadhesive polymer coated nanoparticles. The mucoadhesive polymers could interact with the mucus glycoproteins which allows the mucoadhesive system to remain adhesive for an extended period of time. Coating nanoparticles with them improved their mucoadhesion. These mucoadhesive polymer coated nanoparticles are suitable for carrying hydrophilic drugs. In present study Chitosan coated nanoparticles are prepared by emulsion polymerization technique. Particle size was measured by Scanning electron Microscope. The effect of polymer concentration and chemical initiator concentration on the resultant nanoparticles was studied.

Keywords: Methylmethacrylate, Chitosan, Ammonium persulphate.

INTRODUCTION

Chitosan is a polysaccharide comprising copolymers of glucosamine and N-acetylglucosamine and can be derived by the partial deacetylation of chitin. It is a biodegradable, biocompatible and hydrophilic polymer of low toxicity. It is a material found in abundance in shells of crustacean such as lobsters, prawns and crabs. It is insoluble under alkaline and neutral conditions, but can react with inorganic and organic acids such as hydrochloric acid, lactic acid, acetic acid and glutamic acid under acidic conditions. It has OH and NH₂ groups that give rise to hydrogen bonding and these groups could act as nucleophilic agent to initiate the polymerization of methylmethacrylate leading to an irreversible attachment between chitosan and methylmethacrylate through different multipoint linkages. The cationic polyelectrolytic nature of chitosan could interact with a negatively charged mucosal surface. It was also confirmed that coating liposomes with chitosan improved their adsorption to mucosal surfaces.

MATERIALS AND METHODS**Materials**

Methylmethacrylate

Chitosan

Ammonium persulphate

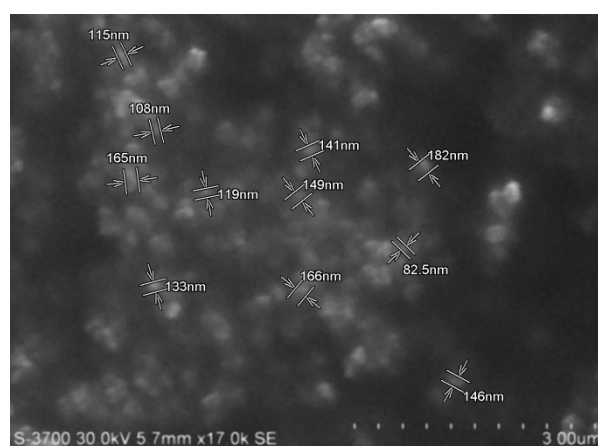
Preparation of chitosan coated nanoparticles

Chitosan coated nanoparticles were prepared by emulsion polymerization technique in a closed 100ml flask. Chitosan was dissolved in 100 ml 1% acetic acid solution under magnetic stirring at 400-500 rpm. The pH value was adjusted to 4-5. One percent (w/v) of the monomer methylmethacrylate was dissolved in the above mixture at 75°C and APS solution was added. The reaction was completed after 5 hrs. Different batches were prepared according to the following reaction conditions. Concentration of chemical initiator (APS) was varied keeping monomer concentration and polymer concentration constant.

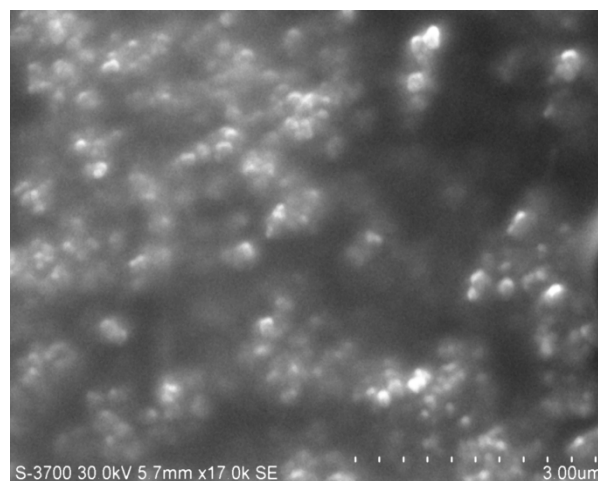
RESULTS AND DISCUSSION

Size of Chitosan nanoparticles was determined by scanning electron microscope. In order to perform the SEM observation, nanoparticle suspension was first diluted with ultrapure water (1/5), and then a drop of the diluted nanoparticle suspension was then directly deposited on a polished aluminum sample holder. Samples were dried in vacuum and subsequently sputter-coated with a carbon layer at 4-6

AMPS for 30 seconds then with a gold layer at 2 AMPS for 30 seconds at 5×10^{-5} Pa (Edwards Auto 306 Vacuum Coater, Edwards, Germany). The morphology of nanoparticles was observed at 3 kV using a scanning electron microscope (SEM; S-4200, Hitachi, Japan).



SEM images of chitosan nano particles (APS3%)



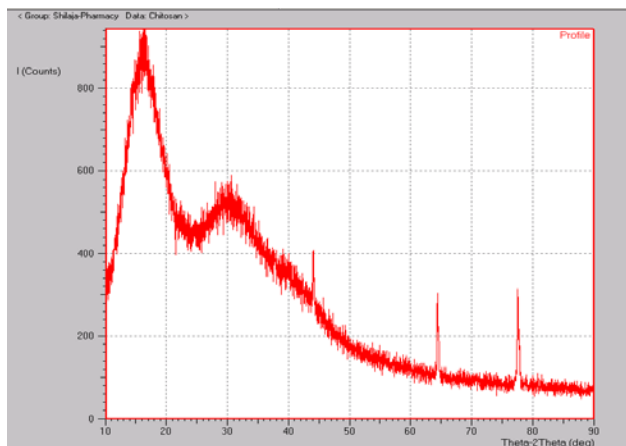
SEM images of chitosan nano particles (APS3%)

Determination of crystallinity of chitosan nanoparticles by X-ray diffraction study

XRD for Chitosan nanoparticles

Physical status of chitosan nanoparticles

An X-ray diffractometer (Philips, Xpert-Pro, The Netherlands) was used to determine the physical status of chitosan in the nanoparticles. The diffraction angle (2θ) was recorded from 3° to 80° with a scanning speed of $5^\circ/\text{minute}$. CuK α radiation was used as the X-ray source at 40 kV and 30 mA.



particle size of chitosan is also conformed by X-ray diffraction study. Particles are found to be crystalline in nature. The mean size of the ordered domains is determined by the following formula

$$T = K\lambda / B \cos\theta$$

K = shape factor

λ = X-ray wavelength

B = FWHM (Half the maximum intensity in radian)

θ = angle

T = mean size of the ordered domains (crystalline)

$K = 0.9$ (typical value) varies with the actual shape of the crystallite

Scherrer equation: - It is not applicable to grains larger than about $0.1 \mu\text{m}$

$$\lambda = 1.5406$$

$$T \text{ value for PMMA (10ml, 3\% APS)} = 0.9 \times 1.5406 / \cos 16.44$$

$$= 1.38654 / 0.959$$

$$= 1.4458 \times 10^{-8}$$

Chitosan nanoparticles were prepared using Ammonium persulphate as an initiator for polymerization reaction. Different batches were prepared using APS at 1%, 2% and 3% concentrations. All the three batches were evaluated for particle size and crystallinity. It was observed that the batches prepared by using 3% APS were shown to fall in a range of 100-200 nm. Uniformity was obtained at 3% APS concentration.

CONCLUSION

The mucoadhesive polymer-coated nanoparticles could be developed through polymerizing methylmethacrylates in the presence of mucoadhesive polymers. The resulting nanoparticle suspension could incorporate the hydrophilic drugs greatly due to the hydrophilicity on the surface of the nanoparticles. They possessed mucoadhesive polymers which interacted with mucus to prolong the residence time of the drug carriers at the drug absorption sites and protected the entrapped drugs from enzymatic degradation. Therefore bioavailability of the drug may be improved. Therefore they are promising for transmucosal drug delivery.

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