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Original Article

Preparation of Chitosan Nanoparticles Loaded by Dexamethasone Sodium Phosphate

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Abstract

Biodegradable nanoparticulate carriers, have important potential applications for administration of therapeutic molecules. Chitosan based nanoparticles have attracted a lot of attention upon their biological properties such as biodegradability, biocompatibility and bioadhesivity. The aim of the present investigation was to describe the synthesis and characterization of novel biodegradable nanoparticles based on chitosan for encapsulation of dexamethasone sodium phosphate. To achieve this objective, ionic gelation method were used. Drug containing nanoparticles were prepared with different amounts of drug. The mean size and size distribution of nanoparticles were measured by dynamic laser light scattering. The mean particle size, varied in the range of 250-350 nm. Values of loading capacity and loading efficiency varied between 33.7%-72.2% and 44.5%-76.0% for prepared nanoparticles.

Keywords: Chitosan; Dexamethasone; Ionic gelation; Nanoparticles.
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1. Introduction

The hydrophilic nanoparticles have received considerable attention to deliver therapeutic peptide, protein, antigen, oligonucleotide and genes by intravenous, oral, and mucosal administration [1]. The information has emphasized the importance of size, and revealed the advantages of nanoparticles over the microspheres [2]. It has bean observed that the number of nanoparticles that cross the epithelium is greater than the number of microsphers. Chitosan is a biodegradable, biocompatible and bioadhesive polysaccharide. It has been shown that chitosan is non-toxic and soft tissue compatible in a range of toxicity tests [3]. It has been widely used in pharmaceutical research and in industry as a carrier for drug delivery and as biomedical material [4]. Chitosan was selected for nanoparticles because of its recognized mucoadhesivity and ability to enhance the penetration of large molecules across mucosal surface [5]. Chitosan nanoparticles are obtained by the process of ionotropic gelation based on the intraction between the negative groups of sodium tripolyphosphate (TPP) and the positively charged amino groups of chitosan. This process has been used to prepare CS nanoparticles for the delivery of peptides and proteins including insulin [6] and

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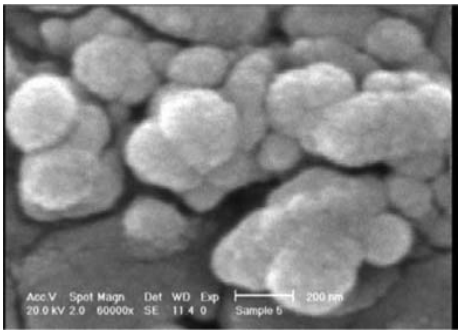

Figure 1. Morphology of chitosan nanoparticles.

cyclosporine [7]. To our knowledge, there have been no reports on the preparation of chitosan nanoparticles containing dexamethasone sodium phosphate (DSP). Therefore, the aim of this work was to encapsulate appreciable quantities of DSP in chitosan nanoparticles made by ionotropic gelation with TPP.

2. Materials and methods

2.1. Materials

Chitosan with a molecular weight of 200 KD and tripolyphosphate of sodium (TPP) were purchased from Aldrich, Canada. TPP was used as received. The minimum degree of deacetylation of chitosan was 85% (the data provided by the company). Dexamethasone sodium phosphate (DSP) was supplied by Atra Co. (Iran).

2.2. Preparation of chitosan nanoparticles

Chitosan nanoparticles were prepared according to the ionotropic gelation process [8]. Blank nanoparticles were obtained upon the addition of a TPP aqueous solution (1 mg/ml) to a chitosan solution (2 mg/ml) stirred at room temperature (rate of 400 rpm). The formation of nanoparticles was a result of the interaction between the negative groups of TPP and the positively charged amino groups of chitosan. The ratio of chitosan/TPP was established according to the preliminary studies. DSP loaded nanoparticles were obtained according to the same procedure and the ratio of chitosan/TPP remained unchanged. Variable amounts of DSP were incorporated to the chitosan solution prior to the formation of nanoparticles in order to investigate the effect of initial DSP concentration on the nanoparticle characteristics and *in vitro* release profiles. Nanoparticles were collected by centrifugation at 10000 rpm for 40 min. and supernatant were discarded.

2.3. Characterization of the nanoparticles

Measurement of physical size and polydispersity (size distribution) of DSP containing nanoparticles, were performed using dynamic laser light scattering (Sem-633, Sematech, France).

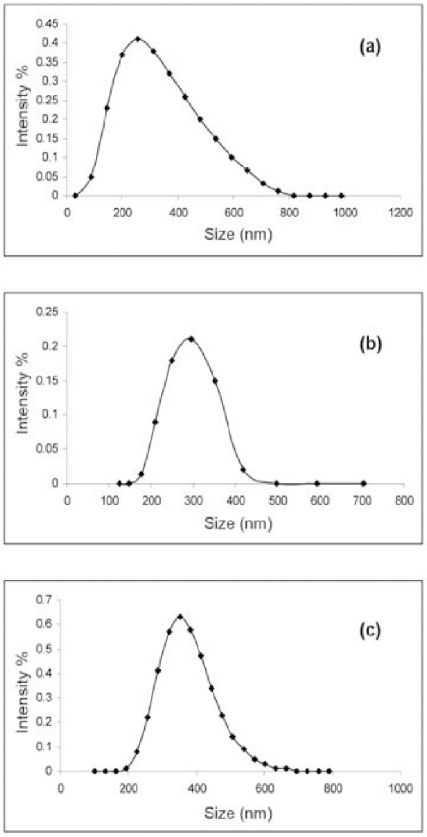

Figure 2. Size distribution for chitosan nanoparticles with different amounts of LC%: a) 33.7, b) 47.5, and c) 72.2.

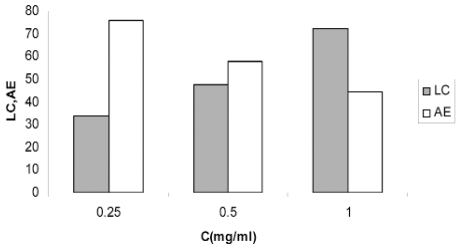

Figure 3. Values of LC and LE based on initial drug concentration.

2.4. Determination of DSP loading capacity and efficiency of nanoparticles

Loading efficiency and loading capacity of nanoparticles with different formation were determind by ultra-centrifugation of samples at 30000×g and 10 °C for 30 min. The amount of free DSP was determined in clear supernatant by UV spectrophotometry at 243 nm using supernatant of non-loaded nanoparticles as basic correction. The DSP loading capacity (LC) of nanoparticles and DSP loading efficiency (LE) of the process were calculated from Equations 1 and 2 indicated below:

$$LC=(A-B)/C\times100 \qquad \text{Equation (1)}$$

$$LE=(A-B)/A\times100 \qquad \text{Equation (2)}$$

Where, "A" is the total amount of DSP; "B" is the free amount of DSP; "C" is the nanoparticles weight.

3. Results and discussion

3.1. Physicochemical characterization of nanoparticles

Spherical nanoparticles were formed spontaneously upon the incorporation of TPP solution to the chitosan solution under magnetic stirring as observed by SEM (Figure 1). The particle diameter (z-average) ranged from approximately 256-350 nm as seen in Figure 2. It is noteworthy that the hydrodynamic diameter of the particles measured by light scattering is higher than the size estimated from microscopy particularly because of the high swelling capacity of chitosan nanoparticles. It indicates that by increasing the DSP concentration, the size of nanoparticles increased. Variation of LC and LE vs the initial concentration of drug in polymer solution is shown in Figure 3. The formulation with the initial DSP concentration of 0.75 mg/ml provided the highest loading capacity (72.2%). However, regarding the particle size and LC%, larger particles were observed in higher association cases. By increasing drug loading, LC increased but LE decreased. Decreased LE with increasing drug content in the initial mixture of polymer and drug is due to the increased chemical potential of drug for diffusion into the external solution. Increased LC with increasing drug content is due to the increased ratio of drug to carrier in the mixture of polymer and drug.

4. Conclusion

Corticosteroid containing chitosan nanoparticles were efficiently produced via ionic gelation method. Particle size of nanoparticles was in the range of 250-350 nm. Because of the safety of the preparation method, prepared naoparticles can be use as suitable drug carriers in aphta treatment in the form of mucoadhesive.

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