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Research Article

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Formulation and Characterization of Atenolol Loaded Sodium Alginate Nanoparticles

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ABSTRACT

The aim of the present work is to formulate NPs for ATE drug. ATE is a selective β1 receptor antagonist, a drug belonging to the group of β-blockers, a class of drugs used primarily in cardiovascular diseases. The NPs were prepared by ionotropic pre-gelation method. The concentration of PEI, Sodium Alginate and ATE were taken into consideration. The prepared formulations were further evaluated for characterization like surface morphology,particle size distribution, zetapotential and drug excipient interaction study by FTIR spectroscopy.

Keywords: Atenolol; Polyethyleneimine; Beta blockers; Nanoparticles

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INTRODUCTION

The use of biopolymers especially polysaccharides in drug delivery has attracted particular interest due to their biocompatibility, biodegradability and hydrophilic nature. The interactions between biodegradable cationic and anionic biopolymers form polyionic hydrogels, which have shown favourable characteristics for drug entrapment and delivery. Alginate is a linear anionic polysaccharide composed of alternating blocks of 1,4-linked β-D-mannuronic acid (M) and α-l-guluronic acid (G) residues. Alginate has some advantages in its high mucoadhesiveness, aqueous solubility, and a tendency for gelation in proper condition, biocompatibility and non-toxicity. Alginates which are a group of hemocompatible polymers have not been found to accumulate in any major organs and have shown evidence of *in vivo* degradation [1]. In the presence of Calcium ions, ionic interaction between divalent Calcium ions and the guluronic acid residue cause Alginate to form gels. The properties of Calcium –Alginate gel beads make them one of the most widely used carriers for controlled release systems [2]. Coating of these beads with other polymers including Chitosan has been shown and their half-life in biological fluids. In present work we have tried to form Alginate -PEI (Polyethyleneimine) polyionic complexes through ionic gelation via interaction between the carboxyl groups of alginate and amine group of PEI. It is considered that the complex protects the encapsulant, has biocompatible nature and limits the release of encapsulated materials more effectively than either alginate or PEI alone. Therefore, the purpose of this study was to optimize a method for the preparation of Alginate-PEI nanoparticles.

Atenolol a Beta- blocker is prescribed widely in diverse cardiovascular diseases, like hypertension, angina pectoris and arrhythmias etc. Administration of conventional tablets of this drug has been reported to exhibit fluctuations in the plasma drug levels, resulting in manifestation of side effects or reduction in drug concentration at the receptor site. In this present study an attempt is made to synthesize atenolol, loaded polysachharide nanoparticles to improve absorption and to increase bioavailability, so as to reduce side effects of this drug.

MATERIALS AND METHODS

The polymer Sodium alginate and BaCl2 were purchased from S.K. traders Indore, PEI was purchased from Sigma Aldrich and the distilled water was taken as the solvent.

Nanoparticle Preparation

Nanoparticles of Sodium alginate (SA) were prepared by counter ion induced gelification method [3], Barium Chloride (2 ml, 0.33%), a cross linking agent was added to 10 ml. sodium alginate solution (0.30%) containing ATE (300 µl) under continuous stirring on magnetic stirrer at 1400 rpm. To this added 4 ml. of PEI (0.8 mg/ml.) solution and stirring was continued till one hour at same rpm. Now the prepared nanoparticles were kept overnight for stabilization. Drug loaded nanoparticles were recovered by Ultracentrifugation at 18000 rpm for 30-45 min. and were washed thrice with distilled water to obtain final nanoparticles. This final nanosuspension was kept in freezer at 4°C after addition of cryoprotectant (D-mannitol 30% of total volume).

Characterization of Nanoparticles

The drug loaded nanoparticles were further characterized for determination of size, morphology and zeta potential.

Transmission Electron Microscopy

The morphological observation of drug-loaded nanoparticles was performed by TEM using a negative staining method.

Measurement of Particle Size

The particle size of optimized ATE-SA-PEI nanoparticle formulation was determined by using Malvern zetasizer. Data was analysed by the cumulate method and assuming spherical nanoparticles. Accordingly the results are given as the effective diameter and the polydispersity index (PDI) as a measure for the relative width of particle size distribution [4-7].

Measurement of Zeta Potential

The zeta potential value of optimized ATE-SA-PEI nanoparticle formulation was measured with zetasizer. To determine the zetapotential, optimized formulation was diluted with double distilled water and placed in electrophoretic cell.

Determination of Encapsulation Efficiency

The encapsulation efficiency of nanoparticles was determined by the separation of drug-loaded nanoparticles from the aqueousmedium containing non-associated ATE by ultracentrifugation (REMI High speed, cooloing centrifuge, REMI Corporation, India) at 18000 rpm at 4°C for 30 min. The amount of ATE loaded into the nanoparticles was calculated as the difference between the total amount used to prepare the NPs and the amount that was found in supernatant. The amount of free ATE in the supernatant was measured by spectrophotometer at 226 nm [8-12].
The encapsulation efficiency of the nanoparticles was determined in triplicate well using following formula –

$$\%EE = (\text{Total amount of drug} - \text{total amount of unbound drug} \times 100) / \text{Total amount of drug}$$

RESULTS AND DISCUSSION

TEM Analysis

TEM analysis confirmed that particles with target size and narrower size distribution could be prepared using an ionotropic pre gelation method. Figure 1 showed that ATE-ALG-PEI nanoparticles had spherical shape with size ranging about 100 nm. This was achieved by adapting optimized parameters for the preparation of nanoparticles.

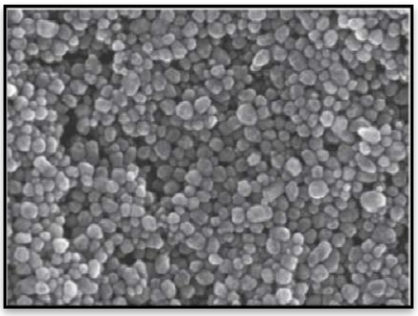

Figure 1: TEM analysis

Particle Size Determination

The particle size of optimized ATE-ALG-nanoparticle formulation is shown in Figure 2. The mean particle size of optimized formulation was found to be 276.7 nm and the PDI value indicates the uniform particle size distribution which may be due to adoption of optimized formulation parameters.

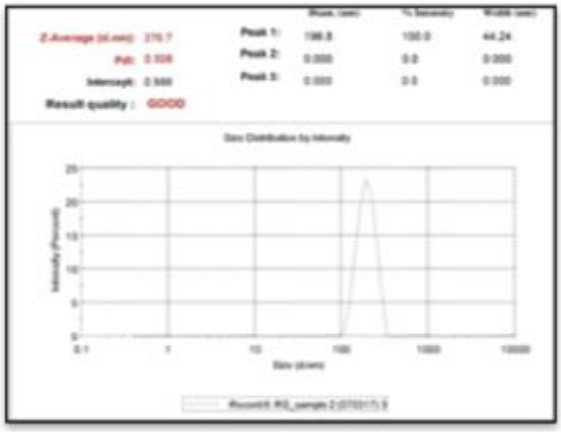

Figure 2: Particle size determination of nanoparticles

Zeta Potential

The zeta potentials of about -31.4 mV showed in Figure 3.

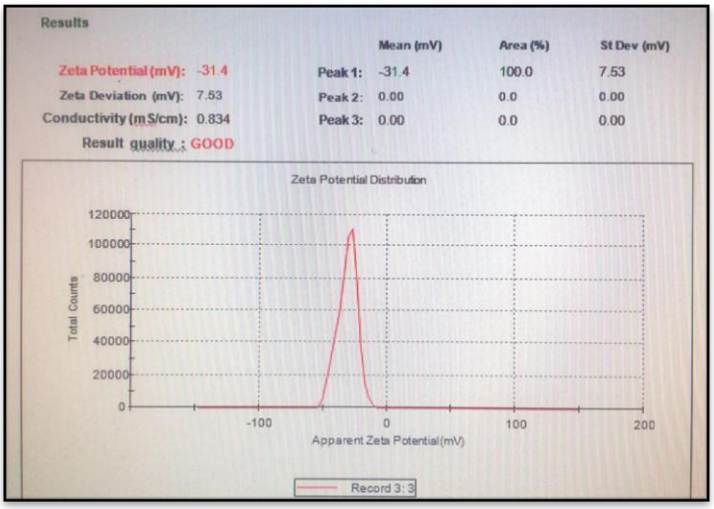

Figure 3: Zeta potential distribution of nanoparticles

CONCLUSION

Atenolol loaded nanoparticles were prepared by the ionotropic pregelation method. The Atenolol used as an antihypertensive drug was successfully formulated in the form of ATE-SA-PEI nanoreservoir system with the optimum particle size, Zeta potential (>30) and maximum entrapment of drug content.

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