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Research Article

Preparation of diclofenac nanoparticles by desolvation technique using acetone as desolvating agent

A. KRISHNA SAILAJA[1], M. NANDINI [2]

RBVRR Women's College Of Pharmacy, Affiliated to Osmania University, Hyderabad

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ABSTRACT

The aim of the present investigation is to prepare diclofenac loaded BSA nanoparticles by desolvation technique using acetone as desolvating agent. Two formulations were prepared by using continuous addition method and intermittent addition method. Process parameters such as stirring speed and stirring time were optimized. Both the formulations were evaluated for particle size, zeta potential, drug content, entrapment efficiency and loading capacity. Intermittent addition method was showing less mean particle diameter, high drug content, highest entrapment efficiency and loading capacity than continuous addition method. Based on the results it was concluded that intermittent addition method was found to be better than continuous addition method for preparing diclofenac nanoparticles.

INTRODUCTION

The field of nanotechnology is one of the most active research areas in modern materials science. Nanoparticles exhibit new or improved properties based on specific characteristics such as size, distribution and morphology [1]. There have been impressive developments in the field of nanotechnology in the recent past years, with numerous methodologies developed to synthesize nanoparticles of particular shape and size depending on specific requirements. New applications of nanoparticles and nanomaterials are increasing rapidly [2].

Nanotechnology can be termed as the synthesis, characterization, exploration and application of nanosized (1-1000nm) materials for the development of science [3]. It deals with the materials whose structures exhibit significantly novel and improved physical, chemical, and biological properties, phenomena, and functionality due to their nano scaled size. Because of their size, nanoparticles have a larger surface area than macro-sized materials. Nanoparticles, because of their small size, have distinct properties compared to the bulk form of the same material, thus offering many new developments in the fields of biosensors, biomedicine, and bio nanotechnology.

Author for Correspondence:
Email: shailaja1234@rediffmail.com

Nanotechnology is also being utilized in medicine for diagnosis, therapeutic drug delivery and the development of treatments for many diseases and disorders. Nanotechnology is an enormously powerful technology, which holds a huge promise for the design and development of many types of novel products with its potential medical applications on early disease detection, treatment, and prevention [4].

Non steroidal anti inflammatory drugs such as naproxen, ibuprofen and diclofenac sodium are the first line agents in the treatment of rheumatoid arthritis, ankylosing spondylitis. The half life of diclofenac sodium is 1.5-2hours. It acts by inhibiting COX_1 and COX_2 enzymes. By inhibiting COX_1 enzyme it causes severe gastrointestinal bleeding and peptic ulcers. By inhibiting COX_2 enzyme it causes cardiovascular problems. Rheumatoid arthritis patients require this drug for prolonged period of time[5]. On regular usage of this drug causes peptic ulcer, G.I bleeding and tachycardia. The normal dose of the drug is 500mg and the dosing frequency is 3-4 times a day. So, there are more chances for missing the dose of the drug. As the drug exhibit short biological half lifer the dosing frequency is more there is need to develop sustained release dosage form such as diclofenac sustained release tablets. But upon prolonged usage of oral sustained release tablets it cause GI bleeding and ulcers. In order to avoid the adverse effects of

oral sustain release dosage forms nano drug delivery system has been designed [6].

MATERIALS

Diclofenac sodium was obtained as gift sample. BSA (1%) was procured from SD Fine Chemicals Limited, Mumbai. Acetone as desolvating agent was purchased from SD Fine Chem Limited, Mumbai. Glutaraldehyde (25%) as cross linking agent was procured from SD Fine Chem Limited, Mumbai.

METHODOLOGY

Desolvation technique was adopted for the preparation of diclofenac loaded BSA nanoparticles . The processing parameters like concentration of the drug and polymer, speed of rotation were optimized. 1 % drug-polymer solution was prepared and its pH was adjusted to 7. The desolvating agent used was acetone. The addition of desolvating agent to the drug-polymer solution was done by two methods, i.e ; continuous and intermittent, in which the solvent was added at the rate of 1ml/min and 1ml/ 5 min respectively. The appearance of turbidity in the solution was considered as the end point. Then, 3-4 drops of 25% glutaraldehyde was added. For complete cross linking, the stirring was continued for 12 hours. The solvent and water were removed from the resultant solution by means of rotary evaporator. The obtained free flowing powder was then characterized for particle size distribution to ensure that they were within nano size range. Further, it was evaluated for following parameters like zeta potential, entrapment efficiency and loading capacity [7].

Characterization of the nanoparticles [8,9]:

Determining the size and morphology of the nanoparticles

Scanning Electron Microscopy is used to determine the shape, size and surface morphology of the nanoparticles. Nanoparticulate suspension is made to obtain Photomicrographs of the drug loaded BSA nanoparticles using this SEM. The obtained particles were found to be spherical in shape [10].

Particle Size Analysis and Zeta Potential Measurement [11]

The average particle size and size distribution of Diclofenac sodium loaded BSA nanoparticles were determined by dynamic light scattering (DLS), using Horiba Zeta sizer. The mean particle diameters of F1 and F2 formulation were found to be 230 nm and 180 nm. Mean particle diameter of intermittent addition method was found to be less than continuous addition method.

The Zeta potential (Surface Charge) which indicates the stability of the NP's can be defined as electrokinetic potential that is determined by electrophoretic mobility. Samples were prepared by diluting with water and corresponding zeta pontential were measured using Horiba Zeta Sizer.The zeta potential value of F1 and F2 formulation was found to be -43.5mv and 52.5 mv respectively.

Drug content [12]

50 mg of the prepared drug loaded BSA nanoparticles both by continuous and intermittent addition method, were dissolved in 50 ml of methanol and kept for stirring at 600 rpm for 3 hours respectively. The total amount of the drug in the nanoparticles was determined spectrophotometrically. The drug contents of F1 and F2 was found to be 50 % and 60 %. On comparison F2 formulation was showing high drug content when compared to F1 formulation.

Entrapment efficiency and Loading capacity

50 mg of the prepared drug loaded BSA nanoparticles both by continuous and intermittent addition method, were dissolved in 50 ml of 7.2 pH phosphate buffer and was kept for ultracentrifugation for 40 minutes respectively. Entrapment efficiency and loading Capacity of the nanoparticles were determined using the formula:

$$\text{Entrapment Efficiency} = \frac{\text{Total amount of the drug entrapped}}{\text{Total amount of the drug initially taken}} \times 100$$

$$\text{Loading Capacity} = \frac{\text{Total amount of the drug entrapped}}{\text{Total weight of the nanoparticles taken}} \times 100$$

The entrapment efficiency of F1 and F2 was found to be 75.6 % and 80.4 %. On comparison F2 formulation was showing high entrapment efficiency when compared to F1 formulation. The loading capacity of F1 and F2 was found to be 40 % and 48.4 % respectively. On comparison F2 formulation was showing high loading capacity when compared to F1 formulation

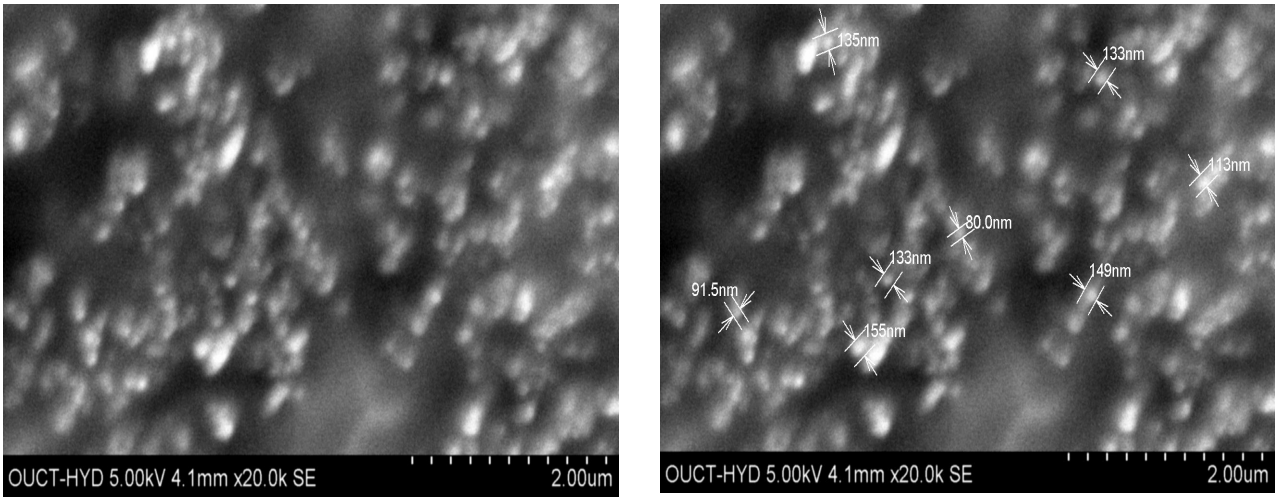

Figure 1: SEM images of F2 Formulation

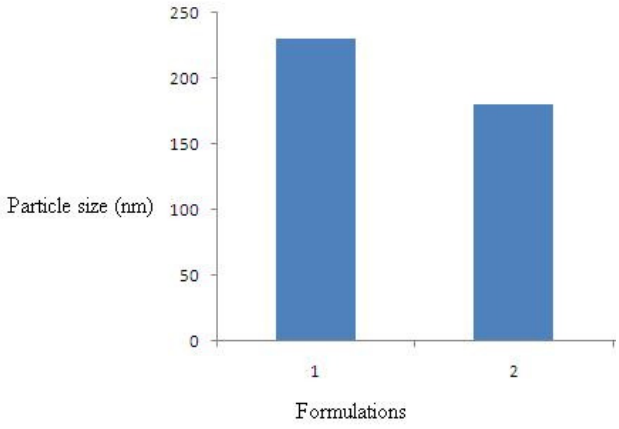

Figure 2: Comparison of Mean particle diameter of F1 and F2 formulations

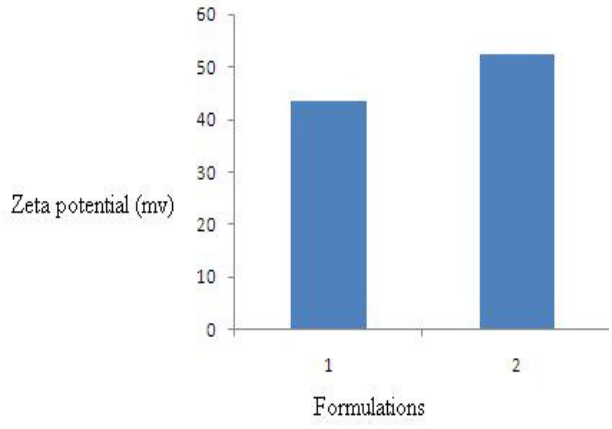

Figure 3: Comparison of Zeta potential value of F1 and F2 formulations

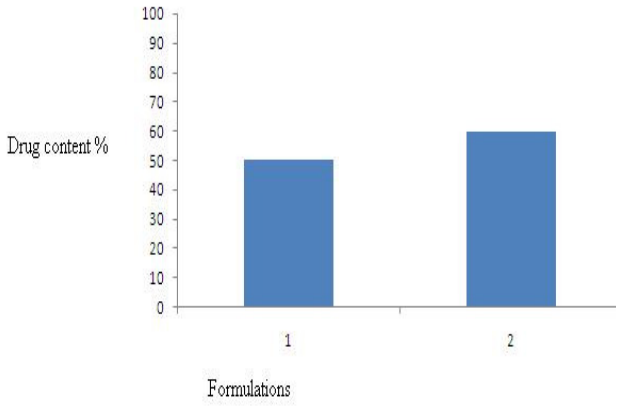

Figure 4: Comparison of Drug content of F1 and F2 formulations

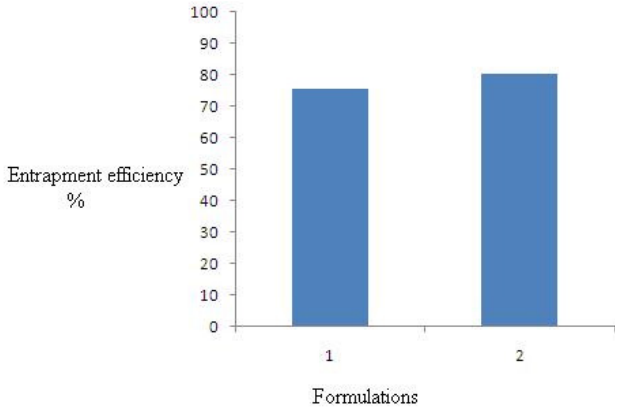

Figure 5: Comparison of entrapment efficiency of F1 and F2 formulations

RESULTS AND DISCUSSION

Diclofenac sodium is a non steroidal anti inflammatory agent used in the treatment of rheumatoid arthritis, ankylosing spondylitis. On prolonged usage it causes GI bleeding and ulcers. Its biological half life is 1.5-2hours. Dosing frequency is 3-4 times a day. In order to reduce the dosing frequency and adverse effects of the drug in this study novel approach has been implemented to prepare diclofenac dosage form. First of all diclofenac nanoparticles has been prepared by desolvation technique using acetone as desolvating agent. Two methods were followed for the addition of desolvating agent. In continuous addition method desolvating agents was added at the rate of 1ml/1min. In intermittent addition method desolvating agents was added at the rate of 1ml of every 5 minutes. Both the formulations were compared for particle size, drug content, entrapment efficiency, loading capacity and drug release studies profiles. On comparison intermittent addition method was found to be better than continuous addition method because its high practical yield, drug content, entrapment efficiency and loading capacity.

CONCLUSIONS

Based on the results diclofenac sodium loaded BSA nanoparticles can be better prepared by intermittent addition method using acetone as desolvating agent.

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