PREPARATION AND CHARACTERIZATION OF NATURAL POLYMERS LOADED CLINDAMYCIN NANOPARTICLES FOR TOPICAL DELIVERY OF ACNE TREATMENT.

Kanagambikai. R¹, Jaya Raja Kumar², Maivizhi Selvi. MVRA¹, Lee Ali Leng¹, Liow Hin Teng¹

¹Research student, Asian Institute of Medicine, Science and Technology (AIMST) University, Bedong 08100, Kedah, Malaysia
²Unit of Pharmaceutical Technology, Faculty of Pharmacy, Asian Institute of Medicine, Science and Technology (AIMST) University, Bedong 08100, Kedah, Malaysia

ABSTRACT

Present study to investigate the treatment of acne and pimples as well as improves the topical application of clindamycin nanoparticles. Clindamycin nanoparticle was prepared by ionic gelation nanoprecipitation method by using guar gum and sodium alginate as biodegradable polymers. The average particle sizes of clindamycin loaded nanoparticles were in the range of 112 to 241 nm. The entrapment efficiency of clindamycin nanoparticles were in the range of 46.2 to 66.8%. The drug release study shows that sustained action over a period of 12 hours. Drug release was 8.62 to 15.43% at 2 h and 62.01 to 72.23% at 12 hr. The results were strongly support the potential application of nanoparticle as drug delivery system in acne treatment.

Keywords: Clindamycin nanoparticles, Topical delivery, Natural polymers

INTRODUCTION

Today, nanotechnology is found in a wide range of applications in the pharmaceutical industry. Due to new advances in nanotechnology, it is now possible to produce drug nanoparticles that can be utilized in a variety of innovative ways. Nanoparticle introduced in 1991 represent an alternative carrier system to traditional colloidal carriers such as emulsions, liposomes and lipid micro and nanoparticles. Nanoparticles are sub-micron colloidal carriers ranging from 1 to 1000 nm, composed of natural or synthetic polymers and dispersed in aqueous surfactant solution. Nanoparticles offers unique properties such as small size, large surface area, high drug loading and the interaction of phases at the interface and are attractive for their potential to improve performance of pharmaceuticals [1].

Nanoparticles are at the fore-front of the potential applications in drug delivery, clinical medicine and research as well as in other allied sciences. They are manufactured from synthetic/natural polymers and ideally suited to optimize drug delivery and reduce toxicity. In monodisperse systems, nanoparticles are the new generation of nanoparticulated active substance carriers and are attracting major attention as novel drug carriers [2].

Acne is caused by bacteria named Propionibacterium acne (P. acne). The P. acne bacteria live deep within follicles and pores, away from the surface of the skin. In these follicles, P. acne bacteria use sebum, cellular debris and metabolic by-products from the surrounding skin tissue as their primary sources of energy and nutrients. Elevated production of sebum by hyperactive sebaceous glands or blockage of the follicle can cause P. acne bacteria to grow and multiply. In this present research, we investigated nanoparticle loaded clindamycin for treatment of Acne [3].

EXPERIMENTAL

Material:

Clindamycin was purchased from Kotra Pharma (M) Sdn. Bhd. Malaysia. Guar gum and sodium alginate were purchased from Essex chemicals, UK. Sodium bicarbonate and calcium chloride were
purchased from Suka chemicals, SDN BHD, Malaysia and all other chemicals used were of analytical grade.

**Method of preparation of Clindamycin nanoparticle:**

Clindamycin nanoparticles were synthesized via the ionotropic nanoprecipitation method [4]. Required quantity of guar gum and sodium alginate were dissolved in deionized water at various ratios. Required quantity of drug was dispersed in the polymeric solution. In another beaker sodium bicarbonate and calcium chloride was dissolved in deionized water (Table 1). The drug polymeric solutions were spontaneously fabricated with the drop-wise addition of the polymeric solution to calcium chloride solution under magnetic stirring (1000 rpm, 1 hour) at room temperature. The opalescent suspension was formed under the same above mentioned conditions. The nanoparticles were separated by centrifugation at 20,000 g and 14°C for 30 minutes, freeze-dried and stored at 5±0.3°C. The weights of freeze-dried nanoparticles were also measured.

**Table-1: Composition of clindamycin phosphate nanoparticle**

<table>
<thead>
<tr>
<th>Ingredients (w/v)</th>
<th>A1</th>
<th>A2</th>
<th>A3</th>
<th>A4</th>
<th>A5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clindamycin (g)</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Guar gum (g)</td>
<td>0.1</td>
<td>0.2</td>
<td>0.3</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Sodium alginate (g)</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Deionized water (ml)</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>NaHCO₃ (g)</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Calcium chloride (g)</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Deionized water (ml)</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
</tbody>
</table>

**Drug polymer compatibility:**
The drug polymer compatibility studies were analyzed by FTIR and DSC spectrums. The pure drug and mixture of drug and polymers spectrums were compared with standard spectrums.

**Surface morphology:**

Surface morphology of nanoparticles loaded clindamycin was observed by Scanning electron microscope (SEM). A small amount of nanoparticle was taken in metal stub. The stub was coated with conductive gold by Hitachi 1010 ion sputter and observed under Hitachi 3000 N Scanning electron microscope (JSM 5610 LV SEM, JEOL, Japan) chamber. The image was scanned at an acceleration voltage of 20 kV with a chamber pressure of 0.8 mmHg.

**Particle size analysis:**

Particle size of nanoparticles was determined using malvern particle size analyzer (Zetasizer 4000S, Japan). For particle size analysis, nanoparticles were suspended in double distilled water and one drop was placed on clean slide and the particle size was observed. The average particle size was calculated and significant value (P<0.05) was calculated by using graph pad prism5.1 software [5].

**Quantification of drug entrapment efficiency:**
The entrapment efficiency was calculated by using 100 mg of nanoparticles dissolved in 20 mL of dichloromethane and the solution was centrifuged at 12000 rpm. The supernated fluid was collected and passed through membrane filter. The quantity of drug in the solution was measured by ultra violet spectroscopy at 195 nm.

**In-vitro release study:**

In-vitro release of clindamycin loaded nanoparticles was placed in donor compartment containing phosphate buffer (pH 7.4) at (37±2°C). Drug release was assessed by intermittently sampling the receptor medium (5 mL) and fresh phosphate buffer saline solution was replaced. The samples were filtered in membrane filter (0.22 μm) and the amount of drug released was quantified by a U.V. Spectrophotometer at 195 nm.

**RESULTS AND DISCUSSION**

The clindamycin nanoparticles were prepared by ionic gelation nanoprecipitation method, guar gum and sodium alginate as biodegradable polymers were used for these preparation. Calcium chloride was used as ionic precipitating agents for nanoparticles formation. The particle size of clindamycin nanoparticles were in the range of 112 to 241 nm. This particle size was best suit for topical delivery of clindamycin. The morphology of prepared nanoparticles was uniform and cube shape, which can facilitate the penetration of drug via topically (Fig 1).
The entrapment efficiency of clindamycin nanoparticles were in the range of 46.2 to 66.8%. The drug polymer compatibility was analysis by using FTIR. The FTIR spectrums were clearly indicated the compatibility between drug and polymers (Fig 2).

(D) Guar gum+ Sodium Alginate (E) Guar gum+ Sodium Alginate + Clindamycin Phosphate

The DSC thermogram of clindamycin phosphate showed a long and sharp characteristic endothermic peak at 201.11°C. The DSC thermogram of guar gum showed endothermic peak at 112.20°C corresponding to the evaporation of moisture and a poorly resolved change in the baseline of guar gum. The DSC thermogram of sodium alginate showed endothermic peak at 119.29°C and exothermic peak at 257.73°C. The DSC thermograms of physical mixtures of polymer combination showed endothermic peaks at 118.15°C. The DSC thermograms of physical mixtures of polymer and drug combination showed endothermic peaks at 218.76°C. The DSC spectrums were clearly indicated the compatibility between drug and polymers (Fig 3).

The in vitro diffusion studies conducted through the diffusion cell membrane from the formulae A1, A2, A3, A4 and A5 drug released 65.09%, 63.15%, 62.01%, 72.23% and 60.74% respectively at the end of 12th hour (Fig.4).
The clindamycin nanoparticles were successfully prepared by using biodegradable polymers like guar gum and sodium alginate. Drug loaded nanoparticle showed narrow colloidal size range, good loading capacity and drug release. Result was strongly supporting the potential application of clindamycin nanoparticle for topical treatment of acne.

**CONCLUSION**

In this study, the potential of nanoparticle dispersion as carrier’s delivery of clindamycin was exploited. Nanoparticles were prepared by the ionic gelation nanoprecipitation method by using biodegradable polymers such as guar gum and sodium alginate. Drug loaded nanoparticle showed narrow colloidal size range, good loading capacity and drug release. Result was strongly supporting the potential application of clindamycin nanoparticle for topical treatment of acne.

**REFERENCES:**


