FORMULATION, CHARACTERIZATION AND INVITRO EVALUATION OF MUCOADHESIVE MICROCAPSULES OF PARACETAMOL

Mishra J*, Nayak S.K
College of Pharmaceutical Sciences, Puri, Odisha, India

ABSTRACT

The present study involves the preparation and evaluation of mucoadhesive microcapsules of Paracetamol as the model drug to enhance the residence time in the body. The microcapsules were prepared with sodium alginate and ethyl cellulose using Emulsification-Solvent Evaporation Technique. The morphology and particle size of the microcapsules were detected by optical microscopy and SEM. The drug loading efficiency was found to be 54-75.77%. The mucoadhesion testing was done by using the freshly incised goat intestine. The swelling ability was found to be 6-8.9% and 4-7.9% in distilled water and 0.1N HCl respectively. The invitro release of drug exhibited more than 12 hours duration. The microcapsules prepared were found to be free flowing.

Key Words: Mucoadhesion, Scanning Electron Microscopy microcapsules, Sodium alginate, Ethyl cellulose, Paracetamol.

INTRODUCTION

Paracetamol in the form of oral tablets and gels12 gets rapidly absorbed from small intestine absorbed on administration. Mucosal drug delivery systems increases the retention period of formulation in the body and thus prolongs the drug releases34. Sodium alginate and ethyl cellulose has been used to prepare microcapsules & microspheres individually which gives controlled release for various categories of drugs like zidovudine, glipizide56 etc. Paracetamol is a NSAID has a biological half life of 2-3 hrs only and also shows effects of liver damage and peptic ulceration7. In the present study, microcapsules are prepared by emulsification-solvent evaporation technique by using SA and EC and were evaluated for size, invitro drug release, drug loading efficiency, swelling ability and mucoadhesion.

MATERIALS AND METHODS

Materials

Paracetamol, Chloroform, Sodium alginate (SA) was obtained from Loba pharmaceuticals Ltd. (India). Ethyl cellulose (EC) was obtained from Central drug house Pvt.Ltd. (India). Sodium hydroxide pellets, Potassium dihydrogen phosphate, were obtained from Ranbaxy fine chemicals Ltd. (India). All other chemicals or reagents were of analytical grade.
A UV/ VIS spectrophotometer (Elico India Ltd.) was used for drug analysis.

**Preparation of Microcapsules**

Microcapsules were prepared by Emulsification-Solvent evaporation technique as stated by Simon et al.\(^8\). Two phases were prepared, an aqueous phase comprising of SA maintained at 40\(^\circ\)C for 10min and a dispersed phase comprising of EC in Chloroform containing Paracetamol. The dispersed phase was added to the continuous phase slowly by continuous stirring maintaining temperature at 40\(^\circ\)C till volatile solvent evaporated completely. The formed microcapsules were separated by vacuum filtration, air dried and kept in a dessicator. Various combinations of formulations were prepared varying the polymer ratio (Table 1) but best are reported.

**Evaluation of Microcapsules**

**Size and Shape of Microcapsules**

The particle size was determined using a optical microscope\(^9\) (Olympus NWF 10x, Educational Scientific Stores, India), fitted with an ocular and stage micrometer. The morphology was determined by using SEM (Scanning Electron Microscopy).

**Loading efficiency**\(^10\)

Exactly 100 mg of microcapsules were weighed out and triturated and suspended in a minimal amount of phosphate buffer \(pH\) 7.4 and filtered through a whatman filter no.41. Drug content was analyzed spectrophotometrically at 249nm (Table 1).

**Sorption Studies**\(^11\)

Around 500mg of the fully dried microcapsules were taken and placed in two different media, distilled water and 0.1N HCl for 48 hours at room temperature and measured the increase in weight at the end of 48hours by the following formula,

\[
\text{Percent Water Sorption} = \frac{W_s - W_d}{W_d} \times 100
\]

\(W_s\) is the weight of the Swollen device, \(W_d\) is the weight of Dry Device

**Mucoadhesion Testing**\(^12, 13\)

The mucoadhesive property of the microcapsules was evaluated by an invitro adhesion and compared with that of a non bio adhesive material, ethylene vinyl acetate microcapsules as described by Chowdary et al.\(^13\). Freshly excised piece of goat intestine were mounted onto two glass slides with cyanoacrylate glue with their mucous layer exposed to the external environment and one slide was placed at the base and the other was hung to one arm of the analytical balance. About 50 microcapsules were spread on the lower wet rinsed tissue specimen and placed in a water bath at 37\(^\circ\)C, pressed both the slides together with the microcapsules between them. To the other pan of the balance placed weights in ascending order till both the slides separated from each other. The test was performed for 30min in distilled water (Table 1).

**In vitro release studies**

Dissolution assays were carried out in triplicate for 12 hours at 37±0.5\(^\circ\)C using phosphate buffer, \(pH\) 7.4 as dissolution media for P1,P2,P3,P4 only. The tests were performed in an
apparatus as described in USP which is USPXIII by taking 100 mg of microcapsules in the sample holder. At prefixed time (30min), 5ml of solution were withdrawn and spectrophotometrically assayed for the Paracetamol content ($\lambda = 249$ nm) (Elico India Ltd.).

**RESULTS AND DISCUSSION**

NSAIDS suffers from many disadvantages and to overcome those problems various techniques are applied to prolong the release. Micro encapsulation techniques are most famous in extending the release of NSAIDS\textsuperscript{14}. The particle size increased with an increase in the polymer concentration and found to be 1-3mm(Table1) and shape is exhibited in Fig1. These results are in agreement with the observations made by Kim et al and Jeffery et al, where higher concentration of the polymer results in formation of large microcapsules\textsuperscript{15,16}.

![Fig1.Scanning Electron Microphotograph of Paracetamol Microcapsules](image)

With the increase in SA concentration the drug loading efficiency also increased and was found to 54-75.77%(Table1).These result is in agreement with the observations made by the research groups who have stated that the amount of uncoated drug decreases with an increase in the polymer concentration\textsuperscript{17,18}.

**Table 1: Composition and Characteristic of microcapsules of different composition**

<table>
<thead>
<tr>
<th>Batch Code</th>
<th>Polymer ratio</th>
<th>Particle size ($\mu$m)</th>
<th>Loading efficiency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>1:1.2</td>
<td>1.12±0.05</td>
<td>54.56</td>
</tr>
<tr>
<td>P2</td>
<td>1:1.3</td>
<td>1.3±0.07</td>
<td>63.57</td>
</tr>
<tr>
<td>P3</td>
<td>1:1.5</td>
<td>1.5±0.09</td>
<td>69.67</td>
</tr>
<tr>
<td>P4</td>
<td>1:3</td>
<td>2.1±0.09</td>
<td>75.77</td>
</tr>
<tr>
<td>P5</td>
<td>1:1</td>
<td>1.05±0.05</td>
<td>47.67</td>
</tr>
<tr>
<td>P6</td>
<td>1:1.1</td>
<td>1.1±0.06</td>
<td>52.78</td>
</tr>
<tr>
<td>EVA</td>
<td>-----</td>
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<td>------</td>
</tr>
</tbody>
</table>
As the concentration of SA increased, the swelling ability and mucoadhesion (Table 2) also increased but swelling was more as 6-7.2% in case of distilled water and 4-7% in 0.1N HCl whereas mucoadhesion was highest for 0.1NHCl than in comparison to water and intestinal. This result is in confirmation with the reported study\textsuperscript{11}. The results of mucoadhesion showed that as the pH of the medium was critical for degree of hydration, solubility and mucoadhesion of the polymers as reported by Ch’ng et al\textsuperscript{19}.

Table 2: Mucoadhesion and swelling ability

<table>
<thead>
<tr>
<th>Batch Code</th>
<th>Swelling ability(%)</th>
<th>Mucoadhesion testing (Pressure,N/m\textsuperscript{2})</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Distilled water</td>
<td>0.1N HCl</td>
</tr>
<tr>
<td></td>
<td>W_d (mg)  W_s (mg)</td>
<td>W_d (mg)  W_s (mg)</td>
</tr>
<tr>
<td>P1</td>
<td>500 536 6.7 500 520 4</td>
<td>0.0105 0.0078 0.007</td>
</tr>
<tr>
<td>P2</td>
<td>500 538 7.0 500 527 5.1</td>
<td>0.0149 0.0097 0.0078</td>
</tr>
<tr>
<td>P3</td>
<td>500 544 8.08 500 536 6.7</td>
<td>0.0194 0.0098 0.0084</td>
</tr>
<tr>
<td>P4</td>
<td>500 548 8.76 500 543 7.9</td>
<td>0.024 0.0109 0.0086</td>
</tr>
<tr>
<td>P5</td>
<td>500 515 2.9 500 513 2.5</td>
<td>--- --- --- ---</td>
</tr>
<tr>
<td>P6</td>
<td>500 517 3.2 500 514 2.7</td>
<td>--- --- --- ---</td>
</tr>
<tr>
<td>EVA</td>
<td>----- ----- ---- ----- -----</td>
<td>0.0015 0.0014 0.0011</td>
</tr>
</tbody>
</table>

It is observed that drug release was slow and depended on the composition of the coat (Fig2) i.e. as the amount of polymer increased the drug release decreased significantly\textsuperscript{20}.

Fig.2: Drug Release profiles from Paracetamol-EC/SA microcapsules.
CONCLUSION

Thus, microcapsules with an outer coat of alginate for mucoadhesion over ethyl cellulose as inner core coat entrapping the water soluble/dispersible drugs can be prepared by solvent-evaporation technique. The prepared microcapsules showed good mucoadhesion property in an invitro test. Release of paracetamol from the prepared EC-SA microcapsules was considerably affected by concentration of the polymers used. Moreover the polymer ratio and pH of the medium also affected the mucoadhesion of the device and also the swelling capacity of the microcapsules. These mucoadhesive microcapsules are thus suitable for oral prolonged release of paracetamol.

REFERENCES