Formulation and Evaluation of Sodium Alginate Discs for Prolonged Release of Glipizide

Sodium alginate (SA) discs were developed and evaluated for prolonged release of glipizide. The swelling behavior and drug release rates were dependent upon the crosslinking density. The SA discs were capable of releasing drug up to 24 h. Slow release of drug from the discs was observed with the discs prepared with higher concentration of glutaraldehyde. The drug release profile indicated that the drug release mechanism followed non-Fickian diffusion.

**INTRODUCTION**

The development of sustained-release (SR) or controlled release (CR) drug delivery systems and study of drug transport mechanism have been continued since long time in the pharmaceutical filed. SR matrix systems can be divided into porous and nonporous matrices (1-3). Nonporous matrices are swelling-controlled systems in which the drug could not diffuse out when the polymer is in a dry state, but drug diffusion starts when the polymer swells upon hydration. The oral SR systems containing inert matrices release the drug through either diffusion and/or dissolution controlled mechanism. In such systems, water uptake is an important condition for the release of drug from the inert matrix (4, 5).

Matrix types of drug delivery systems have been used to prolong the drug release. Such systems are simple to prepare and have been in use for many years (6, 7). The alginate matrices are currently prepared by spraying or dropping aqueous alginate solution/ dispersion into calcium chloride solution for cross-linking (8, 9). In this case, the obtained pellets/ spheres may entrap large amounts of calcium chloride, which can make them hygroscopic (10). Given these problems, there is need for an alternative method for the development of crosslinked alginate matrix type of drug delivery system.

Hence the present study was aimed to develop and evaluate the novel sodium alginate discs by chemical crosslinking/ molding method for the prolonged release of glipizide. Glipizide is an oral anti-diabetic drug having a shorter plasma half life of about 3 h and it undergoes first pass metabolism in intestinal wall (11). Hence to conquer these limitations, development of prolonged release systems are desirable for glipizide.

**MATERIALS AND METHODS**

Glipizide was obtained as gift sample from Wallace Pharmaceuticals (Mumbai, India). Sodium alginate (SA), glutaraldehyde (GA; 25% v/v), sodium hydroxide, conc. HCl and methanol were purchased from S.D. fine Chemicals (Mumbai, India). Double distilled water was used throughout the study. All other chemicals were used without further purification.

**Preparation of sodium alginate discs**

SA was accurately weighed and dissolved in distilled water at 50 °C using magnetic stirrer to get 4%, 6% and 10% w/v of SA (formulation codes: SAD1, SAD2 and SAD3, respectively). Glutaraldehyde (20% w/w of dry polymer) was uniformly dispersed in polymeric solution with a continuous stirring for 30 min. Glutaraldehyde at concentrations of 10% and 15% w/w of dry polymer (formulation codes: SAD4 and SAD5) was added to above solution and stirred. Then the mixture was immediately poured in a stainless steel mold and kept for 5 h at 37°C. After the formation of wet discs, excess water was drained out. Obtained discs were taken out from the mold and washed repeatedly with distilled water. The discs were dried at 40 °C for 24 h and stored in a desiccator until further use.

**RESULTS AND DISCUSSION**

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<tr>
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The swelling behavior and drug release rates were dependent upon the crosslinking density. The SA discs were capable of releasing drug up to 24 h. Slow release of drug from the discs was observed with the discs prepared with higher concentration of glutaraldehyde. The drug release profile indicated that the drug release mechanism followed non-Fickian diffusion.
increased; whereas increased concentration of GA decreased the disc size. The drug content of the discs was found to be in the range of 88.48% to 93.04%. As the concentration of the alginate was increased, the drug content was increased. The drug content was decreased as the concentration of GA was increased, as shown in Table 1. The swelling study of the prepared discs was carried out in phosphate buffer of pH 7.4 and the results are shown in Figure 1. The swelling of discs was depending on the concentrations of SA and GA. The swelling of the discs increased with an increasing amount of alginate and decreased with an increasing amount of GA.

Table 1. Thickness, Diameter, Weight, Drug Content and Drug Release Parameters (n) of the Discs

<table>
<thead>
<tr>
<th>Formulations</th>
<th>Average thickness (mm) ± SD</th>
<th>Diameter (mm) ± SD</th>
<th>Weight (gm) ± SD</th>
<th>Drug content (%) ± SD</th>
<th>n</th>
<th>R²</th>
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</thead>
<tbody>
<tr>
<td>SAD1</td>
<td>4.59 ± 0.92</td>
<td>9.23 ± 0.94</td>
<td>0.17 ± 0.75</td>
<td>88.48 ± 0.81</td>
<td>0.520</td>
<td>0.962</td>
</tr>
<tr>
<td>SAD2</td>
<td>4.93 ± 0.82</td>
<td>9.66 ± 0.65</td>
<td>0.18 ± 0.35</td>
<td>91.46 ± 0.48</td>
<td>0.553</td>
<td>0.970</td>
</tr>
<tr>
<td>SAD3</td>
<td>5.52 ± 0.88</td>
<td>9.98 ± 0.15</td>
<td>0.17 ± 0.25</td>
<td>93.04 ± 0.65</td>
<td>0.581</td>
<td>0.984</td>
</tr>
<tr>
<td>SAD4</td>
<td>4.32 ± 0.11</td>
<td>9.35 ± 0.25</td>
<td>0.17 ± 0.16</td>
<td>90.12 ± 0.65</td>
<td>0.681</td>
<td>0.991</td>
</tr>
<tr>
<td>SAD5</td>
<td>4.02 ± 0.18</td>
<td>9.01 ± 0.52</td>
<td>0.18 ± 0.62</td>
<td>89.31 ± 0.86</td>
<td>0.771</td>
<td>0.985</td>
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</tbody>
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CONCLUSIONS

Sodium alginate discs loaded with glipizide were prepared by molding method. Uniform discs were produced with drug content as high as 93%. Swelling of the discs and drug release rates were depending on the extent of crosslinking and amount of sodium alginate used in the formulation. The SA discs slowly released glipizide over a time period of 24 h. The drug release rate was decreased with an increase in amount of GA. The study indicates that the drug release rate could be controlled by formulation composition and extent of crosslinking.

REFERENCES


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