Formulation and Evaluation of Captopril Sustained Release Microparticles

Amal H. EL-Kamel, Doaea H. AL-shora, Yousry M. EL-Sayed

Department of Pharmaceutics- Faculty of Pharmacy- King Saud University

Introduction:
- Captopril is an orally active angiotensin converting enzyme inhibitor.
- Captopril is the drug of choice for the treatment of essential hypertension.
- The duration of antihypertensive action after single oral dosing is only 6-8 h, So clinical use requires the daily dose of 37.5-75 mg to be taken three times daily.

Objective:
- To formulate captopril sustained release formulations to:
  1. Minimize the fluctuation in blood drug concentration.
  2. Decrease the side effects and frequency of administration.
  3. Increase the patient compliance.

Methodology:
1. Preparation of captopril microparticles:
   - Emulsion-solvent evaporation technique is used.
   - The polymer is acetate propionate of low (15000) and high (75000) molecular weight. The drug polymer ratios are 1:1, 1:1.5 and 1:2.
2. Determination of drug content: HPLC method
3. Particle size determination: Sieve analysis.
4. Determination of flow properties:
   - Bulk density and angle of repose measured according to method reported by Martin, 1993.
5. In vitro release:
   - USPXXIII dissolution procedure are applied using apparatus I.
   - Captopril concentrations is measured using HPLC at 220 nm.

Results and discussion:
1. Drug content of microparticles.

<table>
<thead>
<tr>
<th>Ratio</th>
<th>M.wt 15000</th>
<th>M.wt 75000</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:1</td>
<td>63.938 ± 6.5574</td>
<td>69.504 ± 3.169</td>
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<tr>
<td>1:1.5</td>
<td>67.183 ± 5.391</td>
<td>81.829 ± 2.427</td>
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<tr>
<td>1:2</td>
<td>66.597 ± 4.533</td>
<td>76.096 ± 2.156</td>
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Drug content in formulae containing high M.wt polymer is higher than that containing low M.wt.

2. Particle size determination:
- The formula containing drug polymer ratio 1:2 shows the best flow properties.

3. Flow properties:

<table>
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<th>M.wt 75000</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Angle of repose</td>
<td>Bulk density</td>
</tr>
<tr>
<td>1:1</td>
<td>16.88 ± 0.902</td>
<td>0.31 ± 0.004</td>
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<tr>
<td>1:1.5</td>
<td>16.51 ± 1.100</td>
<td>0.39 ± 0.011</td>
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<tr>
<td>1:2</td>
<td>16.03 ± 0.600</td>
<td>0.37 ± 0.011</td>
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4. Differential thermal analysis and IR Spectrum
- The absence of the characteristic peaks of the drug in the prepared formulations (1:1) indicates the possibility of presence of interaction.

5. In vitro release:
- The initial rapid release rate of drug could be due to untrapped drug particles.
- The release of drug decreases by increasing the polymer ratio.
- The drug release from formulae containing low M.wt polymer is generally faster than that of high M.wt polymer.

Conclusions:
- Sustained release captopril microparticles have been successfully prepared using acetate propionate and employing the solvent evaporation technique.
- Microparticles prepared from mixture of low and high M.wt polymer are being prepared to optimize the rate of release.
- Animal studies are being carried out in rabbit to confirm the sustained release properties of the prepared microparticles in vivo.

References