Rationals for the Development of Sustained Release Tablets with Kollidon® SR

BASF Aktiengesellschaft

Introduction
Kollidon® SR is a newly developed sustained release matrix excipient based on polyvinyl acetate and povidone. Due to its excellent flow and compression properties it is highly suitable for tablets made by direct compression. This study investigates the correlation between solubility of the active, Kollidon® SR content in the tablet, and the Kollidon® SR time of dissolution.

Experimental Methods

• Materials
Theophylline gran. 0.2/0.7 (Knoll AG), caffeine gran. 0.2/0.5 (Knoll AG); propranolol HCl powder (Knoll AG); indometacin (Synopharm); diclofenac sodium (Ivotec); carbamazepine (Fabrica Italiana AG); propranolol HCl powder (Knoll AG); indometacin (Synopharm); ascorbic acid, 0-24 h: phosphate buffer pH 4.0; 0-2 h: 0.08 M HCl; 2-24 h: phosphate buffer pH 6.8; indometacin, according to the Higuchi equation and the dissolution rate is influenced by the solubility of the active in the dissolution medium (1). Further formulations can be described according to Higuchi’s law showing a quicker release at the beginning and slower at the end, which is characteristic for an inert matrix with pores (2). Povidone and the active are dissolved creating pores through which further active can diffuse.

Methods

All formulations could be compressed easily and resulted in mechanically extremely stable tablets (hardness: 135 N to 325 N). All matrix tablets showed only slight swelling behavior and the drug release was according to Higuchi’s law showing a quicker release at the beginning and slower at the end, which is characteristic for an inert matrix with pores (3). Povidone and the active are dissolved creating pores through which further active can diffuse.

Results and Discussion

All formulations could be compressed easily and resulted in mechanically extremely stable tablets (hardness: 135 N to 325 N). All matrix tablets showed only slight swelling behavior and the drug release was according to Higuchi’s law showing a quicker release at the beginning and slower at the end, which is characteristic for an inert matrix with pores (3). Povidone and the active are dissolved creating pores through which further active can diffuse.

Abstract Summary

Sustained release matrix tablets based on Kollidon® SR could be prepared easily by direct compression. The drug is released according to the Higuchi equation and the dissolution rate is influenced by the solubility of the active in the dissolution medium and the Kollidon® SR content in the tablet.

SEM photo of a fraction of a released tablet

References

1) E. Draganoiu, M. Angheria and A Sakr, Pharm. Ind. 624-629 (2001).
3) W. Fraunhofer and K. Kolter (karl.kolt@basf-ag.de), BASF Aktiengesellschaft, Development Pharma Ingredients, 67056 Ludwigshafen, Germany

Figure 1 and Figure 2

Table 1

Composition of caffeine tablets

<table>
<thead>
<tr>
<th>Formulation</th>
<th>12.5 %</th>
<th>25.0 %</th>
<th>37.5 %</th>
<th>50.0 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caffeine (gran. 0.2/0.5)</td>
<td>125.0</td>
<td>250.0</td>
<td>375.0</td>
<td>500.0</td>
</tr>
<tr>
<td>Kollidon SR</td>
<td>25.0</td>
<td>50.0</td>
<td>75.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>2.5</td>
<td>5.0</td>
<td>7.5</td>
<td>10.0</td>
</tr>
<tr>
<td>Tablet mass</td>
<td>150.0</td>
<td>300.0</td>
<td>450.0</td>
<td>600.0</td>
</tr>
</tbody>
</table>

Table 2

Further formulations

<table>
<thead>
<tr>
<th>Active</th>
<th>Tablet mass</th>
<th>Dispersor</th>
<th>Filter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Theophylline gran. 0.2/0.7</td>
<td>350.0</td>
<td>700.0</td>
<td>SEDANET PD 149</td>
</tr>
<tr>
<td>Caffeine gran. 0.2/0.5</td>
<td>350.0</td>
<td>700.0</td>
<td>SEDANET PD 149</td>
</tr>
<tr>
<td>Propranolol HCl</td>
<td>350.0</td>
<td>700.0</td>
<td>SEDANET PD 149</td>
</tr>
<tr>
<td>Indometacin</td>
<td>350.0</td>
<td>700.0</td>
<td>SEDANET PD 149</td>
</tr>
<tr>
<td>Ascorbic acid cryst.</td>
<td>350.0</td>
<td>700.0</td>
<td>SEDANET PD 149</td>
</tr>
</tbody>
</table>

Figure 3

Release profiles of caffeine tablets according to Higuchi paddle (50 rpm) 0 – 2 h: 0.08 m HCl; 2 – 24 h: pH 6.8, 37 °C

Figure 4

Release profiles of caffeine tablets according to Higuchi paddle (50 rpm) 0 – 2 h: 0.08 m HCl; 2 – 24 h: pH 6.8, 37 °C

Conclusion

• The dissolution profile of tablets with Kollidon® SR can be described according to Higuchi’s law.
• The lower the solubility of the active, the slower the release rate.
• A targeted formulation development is possible when the solubility of the active and the required release rate (t50-time) are known.

Release profiles of caffeine tablets according to Higuchi paddle (50 rpm) 0 – 2 h: 0.08 m HCl; 2 – 24 h: pH 6.8, 37 °C

Dissolution was carried out in a paddle tester at 50 rpm using the following media: caffeine, theophylline, propranolol HCl, 0-2 h: 0.08 M HCl, 2-24 h: phosphate buffer pH 6.8; indometacin, 0-24 h: phosphate buffer pH 6.2; diclofenac sodium, 0-24 h: phosphate buffer pH 6.2; carbamazepine, 0-24 h: SDS - solution (1 % water); ascorbic acid, 0-24 h: phosphate buffer pH 4.0 (1 % cysteine HCl - solution).

SEM photo of a fraction of a released tablet

Table 1

Table 1

Table 2

Table 2

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