The prolonged release of active pharmaceutical ingredients is widely used to achieve long lasting therapeutic effects combined with the patient’s advantage to take his medication less often and reduce the possible risks of adverse effects. Most methods for retardation used in industrially manufactured dosage forms cannot be applied in case of individual preparations manufactured in pharmacies. The addition of a gelling agent such as hypromellose in capsule production could serve as promising possibility for small scale productions. Aim of this investigation was to compare the dissolution characteristics of capsules containing 20 mg Ketamine-HCl and either a mixture of lactose and hypromellose or lactose alone. As there is no clear recommendation considering the optimal lactose-hypromellose-ratio one established formulation was investigated.

Capsules containing Ketamine and lactose dissolve rapidly and liberate 100% of Ketamine within approximately 7 min. Those capsules containing hypromellose as well release only 70% active ingredient within 2 hours (figure 1). Within this period the release is almost linear. Full liberation is obtained in about 3 hours.

Hypromellose has an enormous effect on the liberation characteristics of a gelatine capsule when used as an excipient. It swells in aqueous solutions and prolongs the liberation of Ketamine out of the matrix and contributes to very a consistent release. Hypromellose is therefore a promising excipient for individual pharmaceutical preparations with prolonged release.

This different behaviour can be explained by the different physical properties of lactose and hypromellose. Lactose serves as filling agent. Thus the content of the capsules containing only lactose as excipient is immediately released after dissolution of gelatine (figure 2). In contrast hypromellose is forming a gel when coming into contact with stomach fluid. Ketamine is released out of the gel primarily by diffusion. Consequently the dissolution of ketamine is significantly prolonged (figure 3).

Hypromellose Prolongs the Dissolution of Ketamine-HCl out of Gelatine Capsules

Objective

The prolonged release of active pharmaceutical ingredients is widely used to achieve long lasting therapeutic effects combined with the patient’s advantage to take his medication less often and reduce the possible risks of adverse effects. Most methods for retardation used in industrially manufactured dosage forms cannot be applied in case of individual preparations manufactured in pharmacies. The addition of a gelling agent such as hypromellose in capsule production could serve as promising possibility for small scale productions. Aim of this investigation was to compare the dissolution characteristics of capsules containing 20 mg Ketamine-HCl and either a mixture of lactose and hypromellose or lactose alone. As there is no clear recommendation considering the optimal lactose-hypromellose-ratio one established formulation was investigated.

Results and Discussion

Capsules containing Ketamine and lactose dissolve rapidly and liberate 100% of Ketamine within approximately 7 min. Those capsules containing hypromellose as well release only 70% active ingredient within 2 hours (figure 1). Within this period the release is almost linear. Full liberation is obtained in about 3 hours.

Material and Methods

Capsule composition:

<table>
<thead>
<tr>
<th></th>
<th>Conventional</th>
<th>Prolonged release</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketamine</td>
<td>20 mg</td>
<td>20 mg</td>
</tr>
<tr>
<td>Lactose-monohydrate</td>
<td>330 mg</td>
<td>85 mg</td>
</tr>
<tr>
<td>Hypromellose</td>
<td>-</td>
<td>200 mg</td>
</tr>
</tbody>
</table>

Placebo capsules with hypromellose + lactose and with lactose alone were used as a reference for quantification. Dissolution was simulated in an experimental setup with 200ml 0.1M hydrochloric acid with stirring at a controlled temperature of 37±1°C. Depending on the capsule type and its dissolution profile samples were taken at defined intervals. Five dissolution tests on each capsule type were conducted. Quantification is performed by UV/VIS spectrophotometry at 268nm. Dissolved placebo capsules containing lactose or lactose/hypromellose alone were used as reference. The method was validated regarding linearity, accuracy, precision and repeatability.

Conclusion

Hypromellose has an enormous effect on the liberation characteristics of a gelatine capsule when used as an excipient. It swells in aqueous solutions and prolongs the liberation of Ketamine out of the matrix and contributes to very a consistent release. Hypromellose is therefore a promising excipient for individual pharmaceutical preparations with prolonged release.

References: