**INTRODUCTION**

Individual dosing and appropriate delivery devices are key topics in paediatrics [1, 2] as well as in personalised medicine [3]. Recently, the Solid Dosage Pen (SDP) was introduced for individual dosing of medicines [4-6]. In this work, a carbamazepine (CBZ) formulation for children with immediate-release characteristics was realised by hot melt extrusion (HME). The drug-loaded rods were investigated for the mechanical properties, the dissolution behaviour and the application of the SDP.

**MATERIALS AND METHODS**

**Materials:**
- 10 % or 30 % (w/w) CBZ (modification III) was used as a model drug.
- Polyethylene glycol (Mw = 2,000 g/mol) and mannitol were utilized as excipients.

**Production of the hot melt extrudates:**
- The extrudates were produced using a Mikro 27GL-8D (Leistritz) with a die plate of 2 x 3.5 mm x 7 mm at 46/47°C.
- A conveyor belt transported the extrudates while cooling.

**Mechanical properties and dissolution behaviour:**
- The maximum cutting force was determined using Hess Test Apparatus H10KM (n = 10).
- The tensile strength [Eq. 1] was assessed via a three point bending test utilizing a texture analyzer (n = 10). Then, the flexural modulus [Eq. 2] was calculated.

\[
\sigma = \frac{F_{\text{max}} \times l}{\pi r^3}
\]

\[
E = \frac{4 \times \text{slope}}{3 \times \pi \times d^4}
\]

- Dissolution testing was performed with a basket apparatus (USP) at 75 rpm (n = 5) and detection via UV-Vis spectroscopy (λ = 285)

**Application of the Solid Dosage Pen:**
- The drug-loaded rods were cut individually by the SDP and mass [mg] and yield [%] of the cut doses were determined.

**RESULTS AND DISCUSSION**

Hot melt extrusion with a screw speed of 25 rpm, a powder feed rate of 10 g/min and adequate barrel and die temperatures (46 and 47°C, respectively), resulted in straight and stable extrudates [Fig. 1].

**CONCLUSION**

An immediate-release formulation with the model drug carbamazepine was produced via hot-melt extrusion. Drug-loaded rods with 10 to 30 % (w/w) API and 55 to 75 % (w/w) matrix exhibited mechanical properties which enabled a practical handling, insertion into the SDP and cutting off in dosage units.

**Figure 2:** Dissolution profiles of hot melt extrudates (mean ± s)

The three formulations containing 10 to 30 % (w/w) CBZ and 55 to 75 % (w/w) binder [Tab.1] showed immediate release characteristics according to USP with 15% of 18, 25 and 28 min., respectively.

The maximum cutting forces (≤ 20 N) [Tab.1] were in the range of Kircher [8] and enabled cutting off in dosage units using the device [Fig. 4]. 3, 5 and 8 dosage units (DU) were cut exemplarily for the formulation 30 % CBZ 70 % PEG 2000 [Tab. 2]. The coefficient of variation decreased from 9.0 % (3 DU) to 3.5 % (8 DU) for the masses of the cut doses. The other two formulations showed similar results.

**Figure 4:** The SDP filled with a drug-loaded rod and a detail of its cutting mechanism

<table>
<thead>
<tr>
<th>formulation</th>
<th>tensile strength [N/mm²]</th>
<th>flexural modulus [N/mm²]</th>
<th>maximum cutting force [N]</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 % CBZ 15 % mannitol 75 % PEG 2000</td>
<td>9.6 ± 0.3</td>
<td>337.5 ± 15.8</td>
<td>18.2 ± 1.1</td>
</tr>
<tr>
<td>30 % CBZ 15 % mannitol 55 % PEG 2000</td>
<td>10.1 ± 0.3</td>
<td>362.5 ± 17.0</td>
<td>18.8 ± 1.4</td>
</tr>
<tr>
<td>30 % CBZ 70 % PEG 2000</td>
<td>9.5 ± 0.4</td>
<td>351.2 ± 16.5</td>
<td>20.4 ± 1.1</td>
</tr>
</tbody>
</table>

**Table 2:** Mass [mg] and yield [%] of the formulation 30 % CBZ 70 % PEG 2000 for 3, 5 and 8 DU (mean ± s)

<table>
<thead>
<tr>
<th>DU</th>
<th>mass [mg]</th>
<th>yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 DU</td>
<td>12.8 ± 1.1</td>
<td>101.0 ± 9.7</td>
</tr>
<tr>
<td>5 DU</td>
<td>18.5 ± 1.0</td>
<td>100.7 ± 5.6</td>
</tr>
<tr>
<td>8 DU</td>
<td>32.8 ± 1.2</td>
<td>102.5 ± 5.3</td>
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