**Taste Masking of Naproxen Sodium**

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**INTRODUCTION**

Most active pharmaceutical ingredients (APIs) have an undesirable taste which leads to problems if they are incorporated into mouth dissolving drug delivery dosage forms, such as orally disintegrating tablets (ODTs). Patients would even accept a longer disintegration time if the tablet tastes favorable. Therefore it is very important to mask the very strong and undesirable taste of naproxen sodium which is incorporated along with a triptan into an ODT for migraine therapy. Studies emphasized the benefits of the combination of an analgesic and a triptan for the treatment of migraine. There are several ways of taste masking, for example flavors and sweeteners, inclusion complexation (cyclodextrins), ion-exchange resins and coating or encapsulation of the API. The aim of the present work was to develop an appropriate taste masking of naproxen sodium by fluid-bed coating. Eudragit® E was the polymer used to form a non-water-soluble film.

**MATERIALS & METHODS**

**Fluid-bed Coating**: The fluid-bed coating of naproxen sodium granules was performed on a Myroclab® laboratory fluid bed coater (Hüttlin, Schopfheim). An inlet temperature of 40°C and a mid air flow of 5.5 m³/h were maintained during the process. A three component nozzle was applied at a spray pressure of 1.0 bar and a microclimate of 0.4 bar. Before the coating process the naproxen sodium powder (Sigma Aldrich, Germany) was granulated through a 500 µm sieve after mixing it with a 20 % w/w Eudragit® E solution. The fraction ≥ 250 µm was used for the taste masking. The preparation of the coating suspension was as follows: Eudragit® E (Evonik Industries, Germany) was dissolved in ethanol 96 %, after that talcum (50 % w/w dry polymer) and double distilled water were added. Subsequently the coating process, the product was dried at 40°C for 2 hours in an air oven. In total 15 batches were produced under equal conditions.

**In-Vitro Taste Masking**: The in-vitro taste masking was determined according Bora et al. 1, 25 mL of phosphate buffer pH = 6.8 were filled into a volumetric flask and then taste masked granules according to 219.02 mg of incorporated naproxen sodium (≥ 200 mg naproxen) were added. Then the flask was shaken for 5 minutes. The unpleasant taste was determined using UV/Vis-spectroscopy (Perkin Elmer, Rodgau). The samples exhibited a linear increase in liberated naproxen sodium from 1 to 5 minutes (data not shown).

**Residual Moisture**: A Karl-Fischer Moisture Analyzer (Metrohm, Filderstadt) equipped with a 832 KF Thermoprep oven was used for determination of the residual moisture. Measurements were conducted at 110°C oven temperature. Three samples of each batch were analyzed.

**Particle Size**: Additionally the particle size distribution of all batches was determined using a Mastersizer Zetasizer equipped with a Zetasizer 5000 S dispersion unit (Malvern, Herrenberg). Particles were dispersed in a 0.5 % (w/v) Tween 80 solution and a speed of 3500 rpm was applied during measurement to prevent sedimentation.

**RESULTS & DISCUSSION**

The coating process consisted of three steps. As depicted in Figure 1 the first step was the warming phase until a constant inlet temperature of 40°C was obtained. After that point the peristaltic pump was started and the fluid was sprayed onto the granules. During the spraying process the last step belonged to a short drying phase (15 to 20 minutes). Furthermore the polymer has good taste masking properties because it is insoluble at a pH ≥ 5.6. Hence the applied mass of Eudragit® E is adequate to guarantee an effective taste masking for more than 5 minutes. The samples exhibited a linear increase in liberated naproxen sodium from 1 to 5 minutes (data not shown). In Figure 2 it can be seen that for all batches a monomodal distribution was obtained with a reproducible most frequent value.

<table>
<thead>
<tr>
<th>Intensity of the taste</th>
<th>Not perceivable</th>
<th>Very slight perceivable</th>
<th>Slight perceivable</th>
<th>Perceivable</th>
<th>Pronounced</th>
<th>Strong</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bitter</td>
<td>9</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sour</td>
<td>11</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salty</td>
<td>12</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweet</td>
<td>9</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adstringent</td>
<td>9</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**REFERENCES**