Performance Evaluation of Actimask 92S Ibuprofen: A Novel Taste-Masked Ibuprofen for Use in Orally-Dispersible Dosage Forms

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Background

Recently, orally-dispersible dosage forms, including orally-dispersible tablets (ODT) and orally-dispersible powders (ODP) have become increasingly more popular. The numerous benefits of orally-dispersible systems include convenience, improved compliance, increased bioavailability, and is easily dosed to pediatric, geriatric, and debilitated patients.

A major hurdle in developing orally-dispersible dosage forms is the taste profile of API's. Amines and carboxylic acids are common API functional groups, which exhibit sour and bitter taste perceptions, respectively. For this reason it is necessary to develop taste-masked API's to avoid an unpleasant taste from the active ingredient during the ODT or ODP residing time in the mouth.

An ideal taste-masking system should leave no residue, provide a great mouth feel, and resist fracturing during direct compression. The Actimask® 92S Ibuprofen's hydrophilic coating readily wets resulting in pleasing organoleptics. In addition, the coating is shown to be durable in compression up to 30kN in tablets made with SPI Pharma's Pharmaburst 500 ODT system.

The Actimask® taste-masking technology from SPI Pharma provides a barrier to the initial taste of the product, while still exceeding the compendial target of release in 60 min. The smooth hydrophilic coating technology yields a uniform product with a tight particle size distribution, great flow, and a high assay value of 92%. Another significant advantage of the Actimask system is that it is devoid of residual solvents as the entire taste-masking process is aqueous.

Methods

Physical Characteristics: Bulk density, tapped density, and angle of repose were evaluated on a Hosokawa Powder Tester. The PSD of the multi-particulate was determined on a Microtrac particle size analyzer.

Dissolution Characteristics: The dissolution profiles of the raw material and formulated material were determined with a Varian dissolution tester (900ml USP pH 7.2, Apparatus 2; 50rpm, Temperature 37°C (±0.5°C).

Sampling: (1, 5, 15, 30, 60 min) Ibuprofen was assayed by reverse phase chromatography.

Formulated Tablets: Orally disintegrating tablets (ODT) containing 108.7mg taste-masked ibuprofen (equivalent to 100mg IBU) and 217.38mg taste-masked ibuprofen (equivalent to 200mg IBU) were manufactured. Tablet physical characteristics and ibuprofen dissolution profiles were determined for each of these tablets.

Objective

To evaluate the physical characteristics, dissolution characteristics, and in-formulation characteristics of a novel, taste-masked ibuprofen.

Results

Bulk density, tapped density, angle of repose, and PSD were determined.

Actimask® 92S Ibuprofen release in USP pH 7.2 phosphate buffer was as follows: 1min=7.6%, 5min=25.0%, 15min=54.4%, 30min=79.3%, and 60min=97.0%.

100mg and 200mg ibuprofen containing ODT's met USP immediate release dissolution requirements. Manufactured ODTs met USP dissolution requirement (NLT 80% ibuprofen release in 60 minutes) and significantly slowed ibuprofen release at the 1-minute time point compared with ibuprofen IR Tablets per f2 analysis.
Conclusion

Actimask® 92S Ibuprofen was easily incorporated into 100 and 200mg ODT formulations. In manufactured ODT’s, the Actimask delays early-phase release (taste masking) as compared to IR IBU tablets demonstrating taste-barrier characteristics, but meets USP 60min dissolution requirements for IR release of ibuprofen.

Actimask® 92S Ibuprofen is an aqueous based, hydrophilic, uniformly coated taste-masked Ibuprofen.

Durable orally disintegrating tablets can be manufactured from various concentrations of Actimask® 92S Ibuprofen and Pharmaburst 500 ODT system by adjusting compression force in accordance to dilution with active.

Ibuprofen ODT’s manufactured with Actimask® 92S Ibuprofen and Pharmaburst 500 at various compression forces exhibited USP/EP disintegration times of under 30 seconds over the majority of design space.

For all manufactured ODT’s, the release at 1 min (taste-masking period) was significantly less than IR formulations, demonstrating the efficiency of taste-masking provided by Actimask® 92S Ibuprofen in the formulated systems. Conversely, at 15 minutes, active release was complete, demonstrating the ability of Actimask® 92S Ibuprofen to meet USP requirements of Ibuprofen release for IR tablets. Thus, Actimask® IBU provides for both taste-masking and speed to efficacy.

Figures 1 and 2: Actimask® 92S Ibuprofen

Figures 3 and 4: Actimask® 92S Ibuprofen (SEM’s)
### ODT Formulas - Dissolutions

**Figure 5: 100 mg IBU ODT Formula**

**Composition**

<table>
<thead>
<tr>
<th>Composition</th>
<th>% (By Weight)</th>
<th>mg / Tablet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actimask IBU 92S</td>
<td>15.50%</td>
<td>108.70</td>
</tr>
<tr>
<td>Pharmaburst 500</td>
<td>72.10%</td>
<td>504.50</td>
</tr>
<tr>
<td>Crospovidone XL</td>
<td>3.00%</td>
<td>21.00</td>
</tr>
<tr>
<td>Grape Flavor</td>
<td>3.00%</td>
<td>21.00</td>
</tr>
<tr>
<td>SSF</td>
<td>2.50%</td>
<td>17.50</td>
</tr>
<tr>
<td>Tartaric acid</td>
<td>1.50%</td>
<td>2.80</td>
</tr>
<tr>
<td>Sucralose</td>
<td>1.00%</td>
<td>7.00</td>
</tr>
<tr>
<td>Silicon Dioxide</td>
<td>1.00%</td>
<td>7.00</td>
</tr>
<tr>
<td>Colorcon purple</td>
<td>0.40%</td>
<td>10.50</td>
</tr>
</tbody>
</table>

**Final Tablet Weight**: 700.00

### Manufacturing

1. Weigh and screen each ingredient through a #20 mesh (Co-screen color with lubricant).
2. Blend all non-lubricant ingredients in a PK blender (25rpm) for 15 minutes.
3. Add color and lubricant co-screen to blend 2 and blend 5 minutes.
4. Compress 700mg tablets on a GP-8 tablet press outfitted with 0.5” x 0.5” Arc Square - Reduced Cup Depth “D” punches at 25rpm and 600N pre-compression. Compress to a tablet hardness of 5 – 7 kP.

**Physical Characteristics**

<table>
<thead>
<tr>
<th>Formulation</th>
<th>TW (mg)</th>
<th>T (mm)</th>
<th>H (kp)</th>
<th>Fr (%)</th>
<th>USP/EP DT (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100mg IBU ODT</td>
<td>700</td>
<td>6.6</td>
<td>5.3</td>
<td>0.173</td>
<td>13</td>
</tr>
</tbody>
</table>
Manufacturing

1. Weigh and screen each ingredient through a #20 mesh (Co-screen color with lubricant).
2. Blend all non-lubricant ingredients in a PK (25rpm) blender for 15 minutes.
3. Add lubricant and color co-screen to blend 2 and blend 5 minutes.
4. Compress 1200mg tablets on a GP-8 tablet press outfitted with 0.57” x 0.57” Arc Square “D” punches at 25 rpm and 1 kN of pre-compression. Compress to a tablet hardness of 6 – 8 kP.

Physical Characteristics

<table>
<thead>
<tr>
<th>Formulation</th>
<th>TW (mg)</th>
<th>T (mm)</th>
<th>H (kp)</th>
<th>Fr (%)</th>
<th>USP/EP DT (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>200mg IBU ODT</td>
<td>1200</td>
<td>9.1</td>
<td>6.5</td>
<td>0.235</td>
<td>18</td>
</tr>
</tbody>
</table>

Figure 7: Actimask® 92S IBU Dissolution Apparatus 2: 50 rpm
Media: 900ml pH 6.8 Phosphate buffer Temperature: 37 °C
Figure 8: Actimask® 92S IBU Dissolution Apparatus 2: 50 rpm
Medina: 900ml 0.1 N HCl Temperature: 37 °C

Figure 9: Actimask® 92S IBU Dissolution Apparatus 2: 50 rpm Media: 900ml 0.1 N HCl Temperature: 37 °C