**Evaluation of Pilot Scale High Shear Granulation for Extended Release Tablets Containing Carbopol® 971P NF Polymer**

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**INTRODUCTION**

Carbopol® 971P NF polymer is an efficient controlled-release tablet excipient due to its crosslinked nature and high molecular weight. Traditionally, Carbopol® 971P NF polymer is used in aqueous systems such as oral liquid dosage forms or in polymer-based hydrogels. With the advent of extended release tablets containing Carbopol® 971P NF polymers have been investigated in various lab studies, however, no pilot scale aqueous granulation has been previously conducted.

**METHODOLOGY**

**Materials**

Guiafenesin (Delta Synthetic Co., Ltd, Tokyo), Carbopol® 971P NF polymer (Lubrizol Advanced Materials, Inc., Cleveland, OH), Emcocel® 50M microcrystalline cellulose (JRS Pharma LP, Patterson, NY), Lactose monohydrate (Kerry Bio-Science, Norwich, NY), and magnesium stearate (Ferris Corporation, Watertown, MA).

**Equipment**

Pilot-scale bottom-drive high shear granulator (Freund-Vector GMXB-Pilot equipped with a 25-L vessel by Freund-Vector Corp.), CoMill® MC200 (Model U10 by Quadro Engineering Corp.), fluidized bed dryer (Freund-Vector VFC-15M equipped with a 20-L bowl by Freund-Vector Corp.), and automated tablet press (Piccola 469 Tablet Press by SMI).

**Methods**

Guiafenesin, a non-ionic water soluble drug (Solubility 1.35 g/L), was chosen as a model drug. Guiafenesin tablets were developed using 75.00% w/w of the tableted weight, Carbopol® 971P NF polymer was investigated at a 20% and 10% w/w inclusion level – Table 1.

**RESULTS**

**Granule Distribution**

The granules manufactured under different impeller speeds had similar particle size distributions. The particle size distributions of granules before and after sizing through an 18-mesh screen are summarized in Fig. 1-2.

**Table 2. Granulation conditions for guiafenesin formulations**

<table>
<thead>
<tr>
<th>Impeller speed (m/s)</th>
<th>Target weight (%)</th>
<th>Processing/Formulation</th>
<th>20% 971P NF</th>
<th>10% 971P NF</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.2</td>
<td>7.77</td>
<td>20% 971P NF</td>
<td>806.75</td>
<td>805.58</td>
</tr>
<tr>
<td>3.3</td>
<td>5.00</td>
<td>10% 971P NF</td>
<td>805.78</td>
<td>806.00</td>
</tr>
<tr>
<td>4.4</td>
<td>7.21</td>
<td>20% 971P NF</td>
<td>799.77</td>
<td>799.77</td>
</tr>
<tr>
<td>5.5</td>
<td>0.03</td>
<td>10% 971P NF</td>
<td>799.77</td>
<td>799.77</td>
</tr>
</tbody>
</table>

**Table 3. Composition (%) w/w of Guiafenesin ER Tablets**

<table>
<thead>
<tr>
<th>Component</th>
<th>20% 971P NF</th>
<th>10% 971P NF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guiafenesin</td>
<td>75.00</td>
<td>75.00</td>
</tr>
<tr>
<td>Carbopol® 971P NF</td>
<td>10%</td>
<td>20%</td>
</tr>
<tr>
<td>Lactose monohydrate</td>
<td>9.50</td>
<td>4.50</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>0.50</td>
<td>0.50</td>
</tr>
<tr>
<td>Emcocel® 50M</td>
<td>4.50</td>
<td>5.00</td>
</tr>
<tr>
<td>Total</td>
<td>90.00</td>
<td>90.00</td>
</tr>
</tbody>
</table>

**Table 4. Physical properties of guiafenesin tablets manufactured under 10-kN compression force at 30 rpm**

<table>
<thead>
<tr>
<th>Compression force (kN)</th>
<th>Tablets manufactured under 10-kN compression force at 30 rpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.5</td>
<td>3.63 0.07 6.97 0.05 18.51 1.48 0.190 failed</td>
</tr>
<tr>
<td>10.0</td>
<td>3.63 0.07 6.97 0.05 18.51 1.48 0.190 failed</td>
</tr>
<tr>
<td>15.0</td>
<td>3.63 0.07 6.97 0.05 18.51 1.48 0.190 failed</td>
</tr>
<tr>
<td>20.0</td>
<td>3.63 0.07 6.97 0.05 18.51 1.48 0.190 failed</td>
</tr>
</tbody>
</table>

**CONCLUSION**

Extended release guiafenesin tablets containing mid and high levels of Carbopol® 971P NF polymer (70% or 20%) as a matrix forming polymer was produced by high shear granulation in a pilot scale granulator. The polymer impregnated binding properties to improve the tablets’ dissolution profiles.

The generation could be conducted with low amount of water (7% w/w). This should be beneficial during granulation (avoid over-drying and drying bottle time needed).

The industrious of the formulations in terms of physical properties and drug release was demonstrated under different processing conditions and compression force levels. The high compression force imposed a significant effect on granule performance, tablet physical properties, and drug release. The similar granulation conditions could be used for the two polymer levels. Increasing the compression force in tableting speed did not have a major impact on the drug release. Addition of a pre-compression force up to 750 N significantly improved tablet properties (failure and weight variability) in the case of high compression forces.

**Table 5. Physical properties of formulations obtained at 3.3 m/s impeller speed (effect of compression force, tableting speed, pre-compression force)**

<table>
<thead>
<tr>
<th>Compression force (kN)</th>
<th>Tablets manufactured under 3.3 m/s impeller speed (n=6 ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.5</td>
<td>3.63 0.07 6.97 0.05 18.51 1.48 0.190 failed</td>
</tr>
<tr>
<td>10.0</td>
<td>3.63 0.07 6.97 0.05 18.51 1.48 0.190 failed</td>
</tr>
<tr>
<td>15.0</td>
<td>3.63 0.07 6.97 0.05 18.51 1.48 0.190 failed</td>
</tr>
<tr>
<td>20.0</td>
<td>3.63 0.07 6.97 0.05 18.51 1.48 0.190 failed</td>
</tr>
</tbody>
</table>

**REFERENCES**


**Figures**

- Fig. 1. Particle size distribution of Guiafenesin granules before using different impeller speeds.
- Fig. 2. Particle size distribution of Guiafenesin granules after using different impeller speeds.
- Fig. 3. Effect of impeller speed on drug release in pH 6.8 phosphate buffer and 0.1N HCl (at 100 rot).
- Fig. 4. Effect of impeller speed on drug release in pH 6.8 phosphate buffer and 0.1N HCl (at 300 rot).
- Fig. 5. Effect of compression force on drug release in pH 6.8 phosphate buffer and 0.1N HCl (at 100 rot).
- Fig. 6. Effect of compression force on drug release in pH 6.8 phosphate buffer and 0.1N HCl (at 300 rot).