Different Types of Lactose Fines Have an Impact on Different Dry Powder Inhaler Properties

**Introduction**

The excipient of choice for dry powder inhalers (DPI) is lactose monohydrate. It plays an important role in the whole formulation process from bulking the dose chamber in the devices to facilitate dose delivery by the respiratory action of a patient [1, 2]. A number of scientific papers and opinions have been devoted to the respiratory action of a patient [1, 2]. A number of lactose formulations have been investigated in-vitro and in-vivo with varying amount of fines. In a Quality by Design environment, control of critical attributes of DPI formulations is essential [8]. In this investigation we will demonstrate that, as different sized lactose fines are available with varying amount of fines, the effects of different types of lactose fines affect different properties, the definition of what we consider ‘fines’ is of utmost importance.

**Materials and methods**

Pre-blends of coarse lactose with 2.5, 5, 10, and 20 wt-% of fine type of lactose were prepared in 100g quantities by sandwiching the fines between three layers of LH100 in an earthed 500 mL stainless steel vessel and blended using a Turbula T2F mixer (Glen Creston Ltd, Englewood, N.J.). The excipient of choice for dry powder inhalers (DPI) is lactose monohydrate. It plays an important role in the whole formulation process from bulking the dose chamber in the devices to facilitate dose delivery by the respiratory action of a patient [1, 2]. A number of scientific papers and opinions have been devoted to the respiratory action of a patient [1, 2]. A number of lactose formulations have been investigated in-vitro and in-vivo with varying amount of fines. In a Quality by Design environment, control of critical attributes of DPI formulations is essential [8]. In this investigation we will demonstrate that, as different sized lactose fines are available with varying amount of fines, the effects of different types of lactose fines affect different properties, the definition of what we consider ‘fines’ is of utmost importance. The type of fines, i.e. fine (%<4.5 µm) or very fine (%<30 µm) or very fine (%<4.5 µm) or very fine (%<30 µm) or very fine (%<4.5 µm) or very fine (%<30 µm) or very fine (%<4.5 µm) or very fine (%<30 µm), is of utmost importance in designing a DPI formulation. In this investigation it has been demonstrated that flow of powders is dominated by lactose very fine particles smaller than 30 µm, and that drug deposition is dominated by lactose very fine particles smaller than 4.5 µm. By using combinations of different types of fine grade lactose with coarse grade lactose, a formulation can be fine-tuned on all relevant properties.

**Results and discussion**

The data shows that adding more fines resulted in an increased Carr index, indicating a decreased powder flow. The effect is more pronounced for blends with LH300 and LH230, compared to LH210. Addition of more fines resulted in a significant increase in FPF. The formulations were in vitro tested for aerosol performance using a Next Generation Impactor (NGI) equipped with a pre-separator (Copley Scientific, Nottingham, UK). Hydroxypropyl methylcellulose capsules, filled with 12.5 mg of the desired formulation, were adjusted to 52 L/min for Handihaler with 4 kPa pressure drop. Fine Particle Fractions (FPFs) of particles less than 5 µm were determined in triplicate.

The data shows that adding more fines resulted in an increased Carr index, indicating a decreased powder flow. The effect is more pronounced for blends with LH300 and LH230, compared to LH210. Addition of more fines resulted in a significant increase in FPF. The formulations were in vitro tested for aerosol performance using a Next Generation Impactor (NGI) equipped with a pre-separator (Copley Scientific, Nottingham, UK). Hydroxypropyl methylcellulose capsules, filled with 12.5 mg of the desired formulation, were adjusted to 52 L/min for Handihaler with 4 kPa pressure drop. Fine Particle Fractions (FPFs) of particles less than 5 µm were determined in triplicate.

**Materials and methods**

Pre-blends of coarse lactose with 2.5, 5, 10, and 20 wt-% of fine type of lactose were prepared in 100g quantities by sandwiching the fines between three layers of LH100 in an earthed 500 mL stainless steel vessel and blended using a Turbula T2F mixer (Glen Creston Ltd, Englewood, N.J.).

<table>
<thead>
<tr>
<th>Size fraction</th>
<th>Carr’s index</th>
<th>FPFED (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>%&lt;4.5 µm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>%&lt;30 µm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>%&lt;4.5 µm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>%&lt;30 µm</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2:** Pearson Correlation coefficients (R²) for linear correlation of Carr’s index as function of fraction amount of fines added (%).

Inhalation

**References**