Greetings!
Welcome. This issue of Fuji's newsletter presents preparation of acetaminophen tablets with Fujicalin and comparison with other similar direct compression excipients.

Direct compression (DC) is the preferred choice to manufacture tablets because it eliminates several steps involved in traditional wet granulation. When formulating DC tablets, the choice of excipient is very critical. The main attributes of a good DC excipient are excellent compressibility, good flowability and particle size distribution that ensures uniform blend. In this newsletter, we compare the tabletting properties of Fujicalin (DCPA), with Dilactose (granulated lactose) and DCPD in formulating acetaminophen (AAP) DC tablets. (Ref: M. Hasegawa, Proceedings of the Standard Formulation Research Association, 2007)

**DC Schematic flow:**

- Excipients for direct compression (54.95%) + Corn starch (14.55%) + MCC (20%)
- AAP (1%) + Corn starch (9%) → mixing → sifting
- *(1)* Anhydrous dibasic calcium phosphate (Fujicalin)
- *(2)* Dibasic calcium phosphate dithydrate (FF-100)
- *(3)* Control: Lactose for direct compression (Dilactose)
- Mixing: V blender, 15 min, 40 rpm
- Lubricant: Mg-st
- Mixing: V blender, 5 min, 40 rpm
- Evaluation of content uniformity: Three samples from the surface and two samples from the inside
- Tablet characteristics: 8 mm R, 180 mg per tablet
- Rotary tablet press AQUISW2A3 (Kikusui Seisakusho LTD)
  - (1) Compression force: 6, 8, 10, 12 kN
  - (2) Tabletting rate: 20, 40, 60 rpm
- Evaluation: Hardness, friability, disintegration time, and content uniformity

**Physical properties of excipients:**

*Excipients for direct compression (54.95%) + Corn starch (14.55%) + MCC (20%)*
Results:
Tablet hardness increased with increased compression force with all three excipients. Fujicalin showed a comparatively higher hardness at all compression forces tested. However, DCPD (FF 100) produced the thinnest tablets followed by Fujicalin and Dilactose (Fig 1).

<table>
<thead>
<tr>
<th>Excipient</th>
<th>Angle of repose (°)</th>
<th>Loose bulk density (g/mL)</th>
<th>Tapped bulk density (g/mL)</th>
<th>Compressibility (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fujicalin</td>
<td>38</td>
<td>0.50</td>
<td>0.63</td>
<td>21.3</td>
</tr>
<tr>
<td>FF-100</td>
<td>38</td>
<td>0.63</td>
<td>0.88</td>
<td>27.9</td>
</tr>
<tr>
<td>Dilactose</td>
<td>39</td>
<td>0.50</td>
<td>0.75</td>
<td>33.4</td>
</tr>
</tbody>
</table>

Tablet hardness at a constant compression force of 10 kN and different tabletting rates were measured by sampling tablets at different time intervals. Fujicalin showed the least variation with increased tablet rate (Fig 2a,b,c). At high tabletting rates, DCPD tended to show variation in tablet weight.
Content uniformity after blending was better when a triturated mixture (AAP 1% + cornstarch 9%) was prepared prior to blending with DC excipients. Friability was less than 0.25% for all three DC excipients tested.

**Summary:**

<table>
<thead>
<tr>
<th>Tablet properties</th>
<th>Fujicalin</th>
<th>FF 100</th>
<th>Dilactose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compressibility</td>
<td>+++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Hardness</td>
<td>+++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Compact thin tablets</td>
<td>++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Tablet hardness at different tabletting rate</td>
<td>+++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Maintain tablet weight at different rate</td>
<td>+++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Content uniformity</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Friability</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
</tbody>
</table>

(+++): Excellent (++): Fair (+): Poor

**Conclusion:**

Although Fujicalin, FF-100 and Dilactose have similar flow properties and behavior, Fujicalin showed less variation for the different characteristics tested resulting in high quality tablets.

**Dosage and Safety:**

**Fujicalin** is manufactured under strict quality control at our FDA-GMP certified facilities. Dibasic calcium phosphate anhydrous is widely used in oral pharmaceutical products and food products. It is generally regarded as relatively nontoxic and nonirritant material.

**Fujicalin:**

Chemical formula: CaHPO₄
Chemical Abstract Service (CAS) Number: 7757-93-9
U.S. Patent No. 5,486,365, Jan 1996
U.S. Drug Master File (DMF) filed, Conforms to USP/NF, EP and JP; and listed as GRAS

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