Effect of Binders on the Formation of Pellets.\textsuperscript{1)} II.
Polyvinylpyrrolidone

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The effect of polyvinylpyrrolidone (PVP) powder on the formation of pellets of lactose, paracetamol and phenacetin was studied. The high water-solubility and affinity of lactose for water affect pellet growth and properties. Lactose pelletised with PVP powder resulted in some non-wetting of the PVP powder and hence pellet growth was restricted. In the case of phenacetin, a hydrophobic material, pellet growth increased markedly with PVP concentration. This is also attributed to the large viscosity build-up in some regions of the feed material in the pelletiser dish, giving rise to large pellets being formed. Balling of the feed material occurs resulting in an increase in pellet growth. Pelletisation of mixtures of varying proportions of the feed materials showed that the properties of pellets assumed those of the major component.

Keywords——pelletisation; polyvinylpyrrolidone; lactose; paracetamol; phenacetin; lactose-paracetamol; lactose-phenacetin

In an earlier paper,\textsuperscript{1)} water, alcohol and water-alcohol mixtures were used to pelletise lactose, paracetamol and phenacetin. It was found that the high water-solubility of lactose and the greater wetting of lactose particles by alcohol in water-alcohol mixtures affected pellet growth and properties. Paracetamol pellets formed with water were smaller and of lower strength than those formed with alcohol or water-alcohol mixtures. Phenacetin, pelletised with these binding liquids were fragile. In the present study, polyvinylpyrrolidone (PVP) was employed as a binder, the aim being to determine the effect of a binder with adhesive properties on the pelletisation of feed materials. Such a binder can contribute significantly to agglomerate strength and impart cohesive qualities to powdered material through particle-particle bonding.

Experimental

Materials——Lactose, paracetamol and phenacetin used for the formation of pellets were of B.P. grade. The mean particle size and bulk density of these powders have been determined previously.\textsuperscript{1)} Polyvinylpyrrolidone (Plasdone K25, GAF Chemicals U.S.A.) of average particle size 46.3±27.2 μm were used to pelletise the powders.

Formation of Pellets——Pellets were prepared using an inclined dish pelletiser (Erweka, Germany) as described previously.\textsuperscript{2)} It consists essentially of a shallow cylindrical dish rotating about an inclined axis. The operating conditions were: feed load, 200 g; residence time in the pelletiser, 15 min; angle of inclination of the pelletiser, 45° and agitation speed, 31.66 rpm. The PVP powder was added directly to the feed material, mixed thoroughly and then a fixed amount of water was sprayed onto this mixture to form pellets. The pellets were dried at 60°C for 4 h.

The size analysis, bulk density, angle of repose, crushing strength and friability of pellets as well as the viscosity of PVP solutions were determined as described earlier.\textsuperscript{3)} Size fraction of pellets studied was 2.0—2.8 mm.

Results and Discussion

Lactose

The concentrations of PVP powder used to pelletise lactose were 1.5, 3.0 and 4.0%. 
Moistening of the lactose-PVP powder was achieved with water and the amount incorporated was maintained at 20% for all lactose pellets. The mean pellet diameter of lactose pellets decreased and then increased with PVP concentration (Table I). Pellets formed with 1.5% PVP were observed to tumble with ease in the pelletiser, without the pellets sticking to the dish pelletiser. However, with 3% PVP, balling of the pellets occurred. In the regions where water was sprayed directly, it was observed that these regions became overwetted, whilst there was limited distribution of the water to the other regions of the lactose-PVP mixture. This is due to the high viscosity that is developed when PVP comes in contact with water. The viscosity of PVP solutions increases with concentration (Table II). Coalescence of the pellets was slow and small pellets were produced. In addition, lactose being very water-soluble (22.22 g/100 ml)\textsuperscript{1)} may be preferentially dissolved in the water and thus not all the PVP present will go into solution.

With a higher PVP concentration, 4%, the incidence of overwetting regions increased. Although this slowed down the spread of water further, the greater viscosity achieved as a consequence of more PVP being present promotes the formation of large pellets. The viscous nature of PVP in contact with water allows greater rate of coalescence and thus the mean pellet size increases (Table I).

The crushing strength of lactose pellets increased whilst friability values decreased with PVP concentration (Table III). The bulk density was also greater with higher PVP concentrations.

<p>| TABLE I. Effect of Varying Concentrations of PVP on Average Diameter of Lactose, Paracetamol and Phenacetin Pellets |</p>
<table>
<thead>
<tr>
<th>PVP conc. (%)</th>
<th>Average pellet diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5</td>
<td>2.08</td>
</tr>
<tr>
<td>3.0</td>
<td>1.75</td>
</tr>
<tr>
<td>4.0</td>
<td>2.13</td>
</tr>
<tr>
<td>Lactose</td>
<td>0.55</td>
</tr>
<tr>
<td>3.0</td>
<td>0.75</td>
</tr>
<tr>
<td>1.88</td>
<td></td>
</tr>
<tr>
<td>Paracetamol</td>
<td>2.78</td>
</tr>
<tr>
<td>3.40</td>
<td></td>
</tr>
<tr>
<td>Phenacetin</td>
<td>3.83</td>
</tr>
</tbody>
</table>

<p>| TABLE II. Viscosity of PVP Solutions at 30 ºC |</p>
<table>
<thead>
<tr>
<th>PVP conc. (%)</th>
<th>Viscosity relative to water</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.0</td>
</tr>
<tr>
<td>3.75</td>
<td>1.9</td>
</tr>
<tr>
<td>6.66</td>
<td>2.8</td>
</tr>
<tr>
<td>7.50</td>
<td>2.9</td>
</tr>
<tr>
<td>8.57</td>
<td>3.3</td>
</tr>
<tr>
<td>11.25</td>
<td>4.8</td>
</tr>
</tbody>
</table>

<p>| TABLE III. Properties of Lactose Pellets Formed with Different Amounts of PVP |</p>
<table>
<thead>
<tr>
<th>PVP conc. (%)</th>
<th>Bulk density (g/ml)</th>
<th>Mean angle of repose (°)</th>
<th>Crushing strength (g)</th>
<th>Friability index</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5</td>
<td>0.603 ± 0.01</td>
<td>38.38</td>
<td>125.81 ± 3.66</td>
<td>15.81 ± 1.07</td>
</tr>
<tr>
<td>3.0</td>
<td>0.627 ± 0.004</td>
<td>37.39</td>
<td>130.62 ± 2.91</td>
<td>9.93 ± 1.54</td>
</tr>
<tr>
<td>4.0</td>
<td>0.636 ± 0.001</td>
<td>37.42</td>
<td>143.05 ± 5.01</td>
<td>7.18 ± 0.85</td>
</tr>
</tbody>
</table>

Pellet size fraction 2.0—2.8 mm.

<p>| TABLE IV. Properties of Paracetamol Pellets Formed with Different Amounts of PVP |</p>
<table>
<thead>
<tr>
<th>PVP conc. (%)</th>
<th>Bulk density (g/ml)</th>
<th>Mean angle of repose (°)</th>
<th>Crushing strength (g)</th>
<th>Friability index</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5</td>
<td>0.392 ± 0.06</td>
<td>39.51</td>
<td>137.17 ± 2.45</td>
<td>30.14 ± 1.47</td>
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<tr>
<td>3.0</td>
<td>0.425 ± 0.004</td>
<td>38.62</td>
<td>144.33 ± 2.11</td>
<td>25.10 ± 1.16</td>
</tr>
<tr>
<td>4.0</td>
<td>0.456 ± 0.004</td>
<td>38.64</td>
<td>173.70 ± 6.24</td>
<td>23.95 ± 4.99</td>
</tr>
</tbody>
</table>

Pellet size fraction 2.0—2.8 mm.
concentration. Generally, there was a reduction in the angle of repose of lactose pellets, indicating a tendency towards improved flow properties.

**Paracetamol**

Similar amounts of PVP were used for the pelletisation of paracetamol. Preliminary experiments showed that the amount of water required to form pellets of paracetamol with PVP was 30%, but after tumbling in the pelletiser for 10 min, the pellets became very wet and large clusters were formed, resulting eventually in lump formation. This constitutes overwetting of the feed material. With 27.5% of water, the feed material appeared dry within the first 5 min of tumbling in the pelletiser, after which time the pellets produced were satisfactory i.e. neither too dry nor too wet. It was found that when the PVP concentration was increased from 1.5 to 3.0% there was only a relatively small increase in mean pellet size (Table I) but at 4% PVP there was a marked change in the mean pellet size. This corresponds with the formation of large pellets when balling occurs.

Paracetamol is hydrophilic but less soluble in water (1.42 g/100 ml) than lactose. The wetting of this feed material by water is not hindered. However, PVP is more soluble in water (4.1 g/100 ml) and therefore has a greater affinity for water. This brings about an increase in the mean pellet size with increasing PVP concentration (Table I). This is attributed to the build-up in viscosity of PVP at locations in the feed material where water was sprayed. Consequently, this leads to the formation of large pellets, balling is also more evident resulting in layering of feed material on to the pellets. Higher PVP content gives rise to greater adhesiveness between feed material particles.

The crushing strength and bulk density of paracetamol pellets increased with PVP concentration (Table IV).

Phenacetin is hydrophobic with a very low solubility in water (0.096 g/100 ml). Phencetin pellets are “plastic” in nature and resist fragmentation on tumbling in the pelletiser as indicated by their low friability values (Table V). The pellets appeared to deform and flatten when subjected to a high load in the measurement of the crushing strength of pellets. The pellets are not brittle and do not break into smaller particles under increasing loads. It is noted that with 1.5 and 3% of PVP there was an increase in the crushing strength of the pellets (Table V) followed by a slight decrease at 4% PVP. This is believed to be due to the formation of fragmented and irregular pellets as a result of balling of pellets at high PVP concentration. PVP helps to increase the binding capacity of the pellets. This enhances pellet growth and also produces less friable pellets.

**Lactose–Paracetamol Mixtures**

The amount of water required to pelletise lactose–paracetamol mixtures containing 3% of PVP powder was 17.5% for mixtures with ratios of 90:10, 75:25 and 50:50 for lactose and paracetamol respectively. From Table VI, it is seen that the mean pellet size for 90:10, 75:25 and 50:50 lactose–paracetamol mixture was intermediate between those formed when either

<table>
<thead>
<tr>
<th>PVP conc. (%)</th>
<th>Bulk density (g/ml)</th>
<th>Mean angle of repose (°)</th>
<th>Crushing strength (g)</th>
<th>Friability index</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5</td>
<td>0.478 ± 0.004</td>
<td>35.73</td>
<td>24.27 ± 1.86</td>
<td>15.14 ± 1.87</td>
</tr>
<tr>
<td>3.0</td>
<td>0.499 ± 0.006</td>
<td>33.54</td>
<td>43.51 ± 3.25</td>
<td>6.00 ± 1.70</td>
</tr>
<tr>
<td>4.0</td>
<td>0.470 ± 0.005</td>
<td>35.87</td>
<td>42.66 ± 4.87</td>
<td>5.40 ± 0.74</td>
</tr>
</tbody>
</table>

Pellet size fraction 2.0—2.8 mm.
Increasing the paracetamol content caused a reduction in pellet size (Table VI), which approached that of pellets formed with paracetamol alone. The maximum crushing strength was obtained for pellets of 75:25 lactose-paracetamol mixture (Table VII). The reason is that with decreasing lactose content, more water could be utilised by both PVP and paracetamol, resulting in a greater amount of liquid bridges or pendular bonds. It is noted that with a higher paracetamol content, friability of the pellets increased and bulk density values decreased. Paracetamol particles are relatively large rod-like crystals which tend to form less round pellets. This is further evident by the larger angle of repose (Table VII) as the proportion of paracetamol is increased.

Lactose–Phenacetin Mixtures

Pellets were prepared using similar ratios as those of lactose–paracetamol with the same amount of PVP, 3% being incorporated. For each mixture, 20% of water sprayed on to the
feed materials.

The mean pellet size for these pellets was also intermediate between those formed when each of the components was pelletised separately. Similarly there was a reduction in pellet size with an increase in the phenacetin content of the mixture, but the mean pellet size of phenacetin alone was much larger than that of the mixture studied (Table VI).

It was found that the 90:10 and 75:25 lactose-phenacetin pellets had bulk density values higher than that of either lactose or phenacetin when pelletised separately (Table VIII). This is because of the part dissolution of lactose in water. The crushing strength of the pellets generally decreased with increase in the amount of phenacetin present in the mixture. This indicates that with more phenacetin, this hydrophobic component of the mixture exerts a dominant influence on the properties of the pellets.

**Conclusions**

Affinity or hydrophilicity of the feed material for water is an important factor affecting pellet growth and its properties. In the case of lactose pelletised with PVP powder, the affinity of lactose for water resulted in some non-wetting of the PVP powder. With phenacetin, a hydrophobic material, pellet growth increased markedly with increasing concentration of PVP.

The mean pellet size of pellets studied increased with PVP concentration, due to the large viscosity build-up at certain regions of feed material in the pelletiser, giving rise to large pellets being produced.

Pelletisation of mixtures of feed materials of different water-solubility and hydrophilicity produces pellets with mean pellet size that is between those of the individual components of the mixture. With lactose-paracetamol and lactose-phenacetin mixtures, increasing the proportion of one component greater than 50%, the properties of the pellets assumed that of the major component.

**References**