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Solid Oral Dosage Form Manufacturing Using Injection Moulding

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Overview:

Dosage Unit Manufacturing

Injection Moulding (IM):

- Injection of molten material under pressure
- Product cools in mould then removed
- Commonly used for:
  - Packaging
  - Biomedical devices
- Create solid oral dosage forms
- Makes use of polymers
- Dosage shape dependent on mould design
- Injection parameters:
  - Injection pressure
  - Cylinder temperature
  - Mould temperature
  - Post-injection pressure

Advantages

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soluble</td>
<td>Degradation of materials</td>
</tr>
<tr>
<td>Stability</td>
<td>Drug release</td>
</tr>
<tr>
<td>Mould design not easy</td>
<td></td>
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<tr>
<td>Solvents not required</td>
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</tbody>
</table>

Paracetamol and Affinisol™ formulations:

<table>
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<tr>
<th>Formulation</th>
<th>5%PCM-powder mix</th>
<th>10%PCM-HME</th>
<th>20%PCM-powder mix</th>
<th>50%PCM-Powder Mix</th>
<th>Complete Release</th>
</tr>
</thead>
</table>

Figure 1: Dosage forms produced using HME-IM using the polymer affinisol and paracetamol (PCM) concentrations 5, 10, 20 and 50% (left to right), followed by 50% PCM formulation which recrystallised during storage.

Figure 2: Chart showing the XRD results for dosage forms containing 50% paracetamol measured 1 week post manufacture and after the colour changed to white 4 weeks later. The diffractograms on the top show that both the dosage forms manufactured using IM and HME-IM (blue and red respectively) contain no distinctive peaks associated with powder paracetamol (black) suggesting that the drug is amorphous.

Figure 3: Chart showing the DSC curves for samples of the same formulation (before and after the colour change). Both brown dosage forms (top) observe solid-solid transition events around 91-96 °C that do not appear in the DSC traces for the white dosage forms (bottom). As the XRD results suggest the white dosage forms contain crystalline paracetamol, it can be assumed that the heightened temperatures during DSC analysis accelerate the transition from amorphous to crystalline material observed after 4 weeks storage.

In the XRD and DSC traces for formulations containing 5, 10 and 20% paracetamol are not shown however they suggest the drug is amorphous and remains so after 4 weeks storage time.

Dissolution Profiles:

Figure 4: Chart showing dissolution profiles for Affinisol™ dosage forms produced from IM only and HME-IM containing 5, 10, 20 & 50% PCM.

The data suggests that the polymer due to its slowly eroding properties hinders drug release.

It is also evident that using HME prior to IM is required in order to control the resulting dosage.

Effects of Disintegrant type on Disintegration when using BCS II drug:

Figure 5 shows the contour maps produced using a DoE approach to analyse the effect of disintegrant type and concentration on the mass remaining of strands consisting of Affinisol containing extruded filaments than larger polymers which hindered the breakdown of the affinisol containing extruded filaments than larger polymers which hindered the process.

It can also be concluded that as the API used for that study was a BCS class II drug the concentration of drug was the most important factor affecting mass remaining and not the concentration of disintegrating agent.

Future work will continue looking at disintegrating agents focusing on small molecules. Dosage forms will also be produced for each formulation using IM.

Conclusion & Future Work:

- It is possible to load Affinisol™ with various drug concentrations however at 50% stability issues are introduced
- Due to the slow eroding properties of polymers other agents are required to help facilitate drug release
- The disintegration agent analysis showed that small molecules are more effective at enhancing the breakdown of the affinisol containing extruded filaments than larger polymers which hindered the process.
- It can also be concluded that as the API used for that study was a BCS class II drug the concentration of drug was the most important factor affecting mass remaining and not the concentration of disintegrating agent.
- Future work will continue looking at disintegrating agents focusing on small molecules. Dosage forms will also be produced for each formulation using IM.

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References: