Solid Oral Dosage Form Manufacturing Using Injection Moulding

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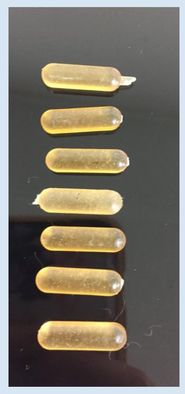
Overview:

Powder blends

Hot Melt Extrusion

Extrudate

Injection Moulding



Dosage forms

Aim: to produce a solid oral dosage form that is both immediate release and has a homogeneous API dispersion

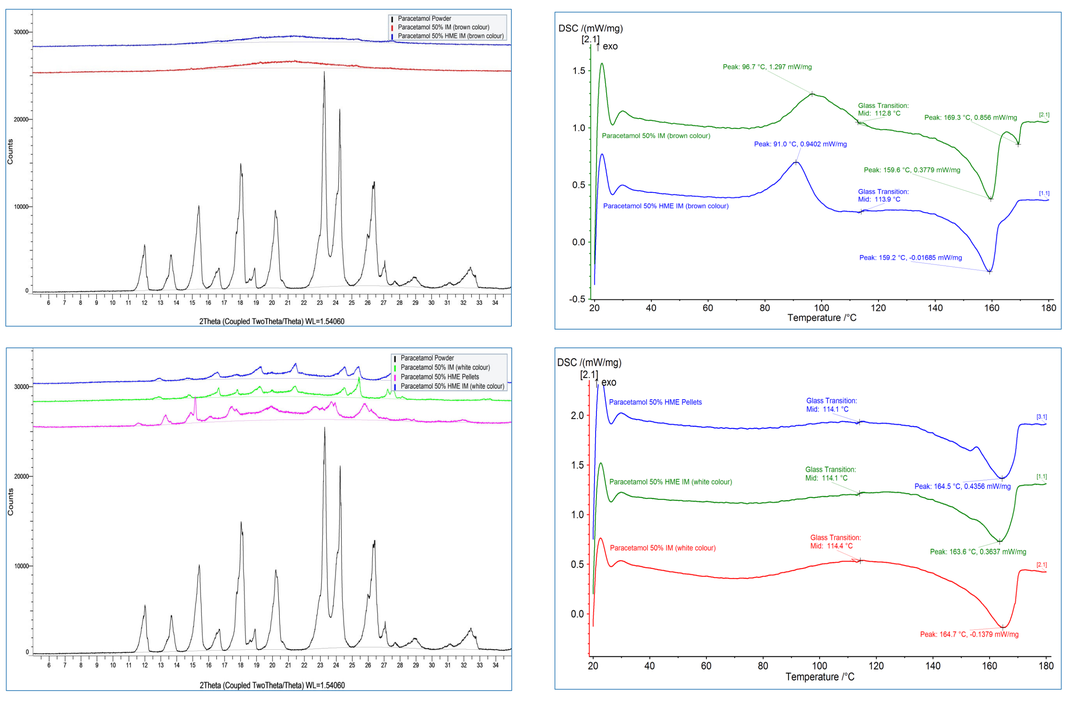
Injection Moulding (IM):

- 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	Disadvantages
Scalable	Stability issues
Drug in amorphous form	Degradation of materials
Potential for continuous manufacture	Use of polymers can hinder drug release
Dosage unit shape can be designed	Mould design not easy and quick to alter
Solvents not required	

Paracetamol and Affinisol™ formulations:

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



Figures 2 (left) shows 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 (right) shows 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.

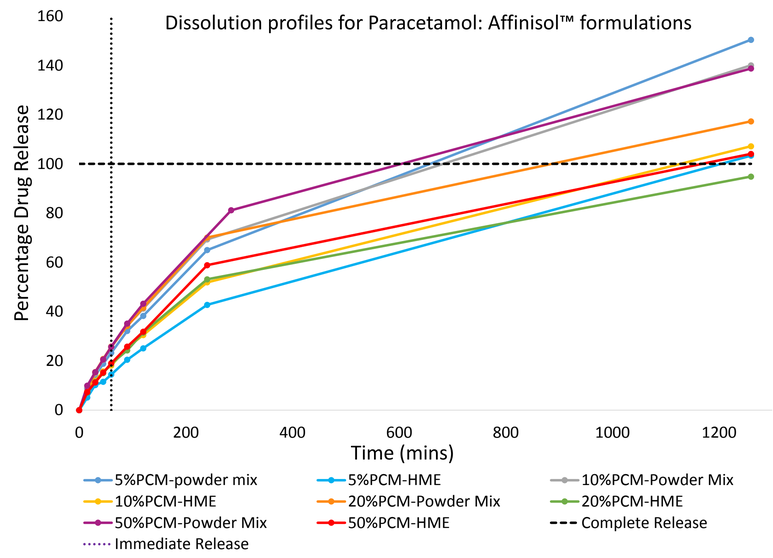
The XRD and DSC traces for formulations containing 5, 10 and 20% paracetamol are not shown however they suggest the drug is amorphous and remains so after 4 weeks storage time.

Dissolution Profiles:

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

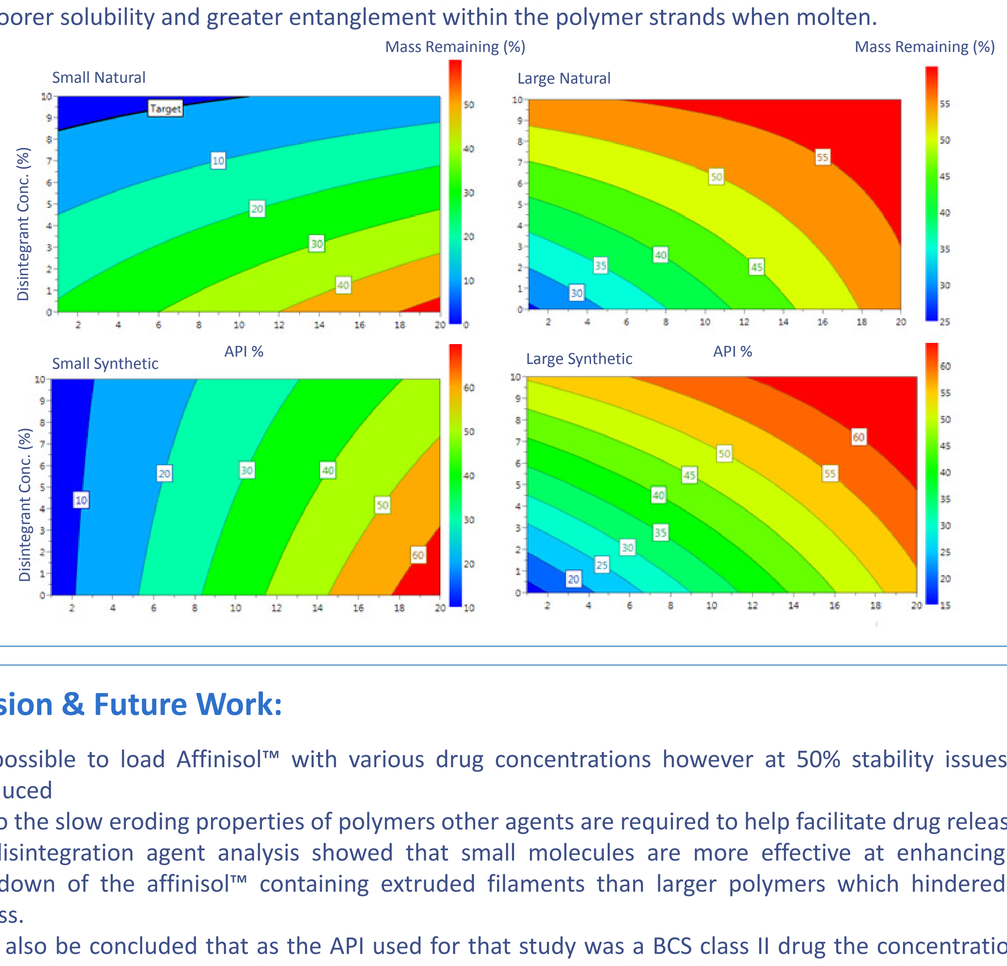
The data suggests that the polymer due to it's slowly eroding properties hinders drug release.

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™ and BCS II drug. The results show that the most influencing factor is API content. For all disintegrants a low drug concentration produced the smallest mass remaining. There seems to be no significant effect on mass remaining caused by disintegrant concentration except for when a small natural disintegrating agent is used. This suggests that for these formulations small natural molecules should be more effective disintegrating agents whereas larger molecules hinder disintegration due to poorer solubility and greater entanglement within the polymer strands when molten.



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 focussing on small molecules. Dosage forms will also be produced for each formulation using IM

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