Injection Moulding- A novel method of solid oral dosage form manufacturing

Sarahjane Wood [1] , Alastair Florence[1] & Gavin W. Halbert[1,2]

[1]Doctoral Training Centre in Continuous Manufacturing and Crystallisation, University of Strathclyde, Glasgow, UK

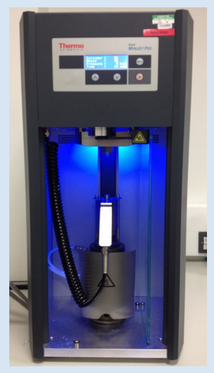
[2]The Cancer Research UK Formulation Unit, the Strathclyde Institute of Pharmacy and Biomedical Sciences, the University of Strathclyde, Glasgow, UK

Overview:

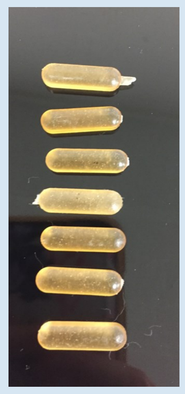
Powder blends

Hot Melt Extrusion

Extrudate



Injection Moulding



Dosage forms

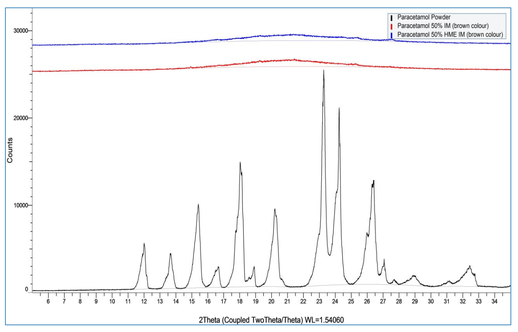
Aim: to produce a solid oral dosage form that is both immediate release and has a homogeneous API dispersion

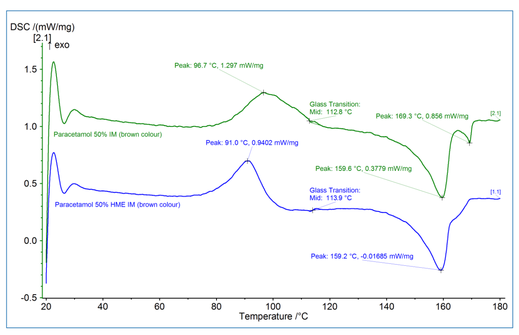
Injection Moulding (IM):

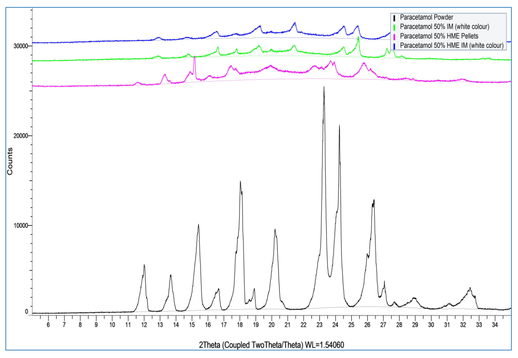
- Injection of molten material under pressure
- Product cools in mould then removed
- Commonly used for
  - Packaging
  - Biomedical devices
- Create solid oral dosage forms
- Makes use of polymers
- Dosage shape dependent on mould design

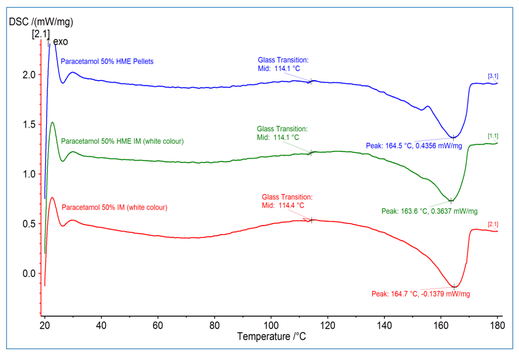
Advantages	Disadvantages
Scalable	Stability issues
Drug in amorphous form	Degradation of materials
Potential for continuous manufacture	Use of polymers can hinder drug release
Dosage unit shape can be designed	Mould design not easy and quick to alter
Solvents not required	

Paracetamol and Affinisol™ formulations:

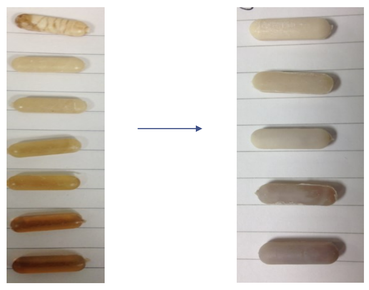






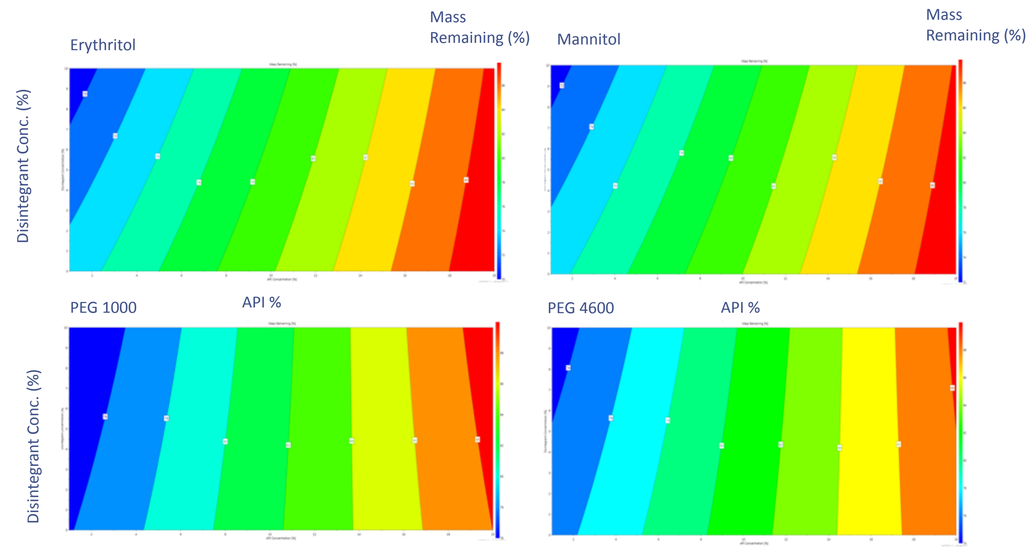


Figures 2 (left) shows the XRD results for dosage forms containing 50% paracetamol measured 1 week post manufacture and after the colour changed to white 4 weeks later. Peaks appear suggesting the drug has crystallised over time. The DSC to the right (fig.3) shows a solid-solid transition which only occurred for 'brown' tablets containing 50% drug which agrees with the XRD data. This did not occur for lower drug concentrations of 5, 10 and 20% paracetamol.



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

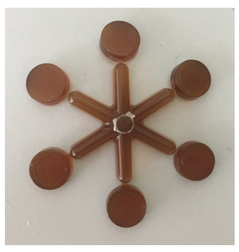
Figure 5 shows the contour maps produced using a DoE approach to analyse the effect of small molecules as disintegrating agents and their concentration on mass remaining of IM dosage forms consisting of Affinisol™ and BCS II drug. The results show that the most influencing factor is API content and concentration of disintegrant is less significant. However the disintegration process could be hindered by injection pressure. A higher pressure would result in a more dense dosage form creating a barrier to disintegration.

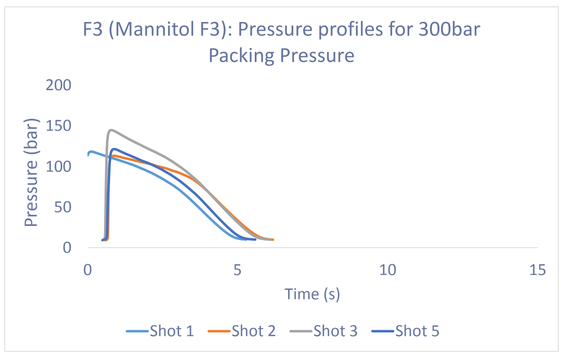


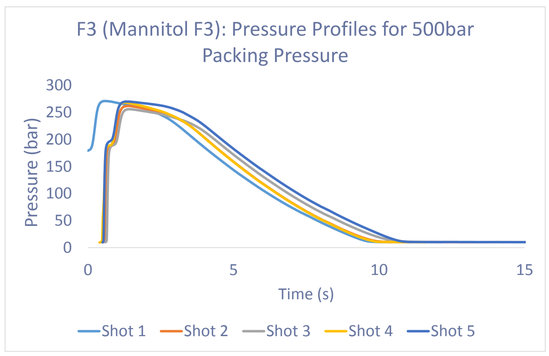
Effects of Packing Pressure on Solid Oral Dosage Forms:

Figures 6 below show that the applied packing pressure is not reached as some pressure is lost to the surroundings.

Analysis of the dosage form weights are consistent per formulation per pressure showing a stable process. There is a small increase in mass when a higher pressure is used.





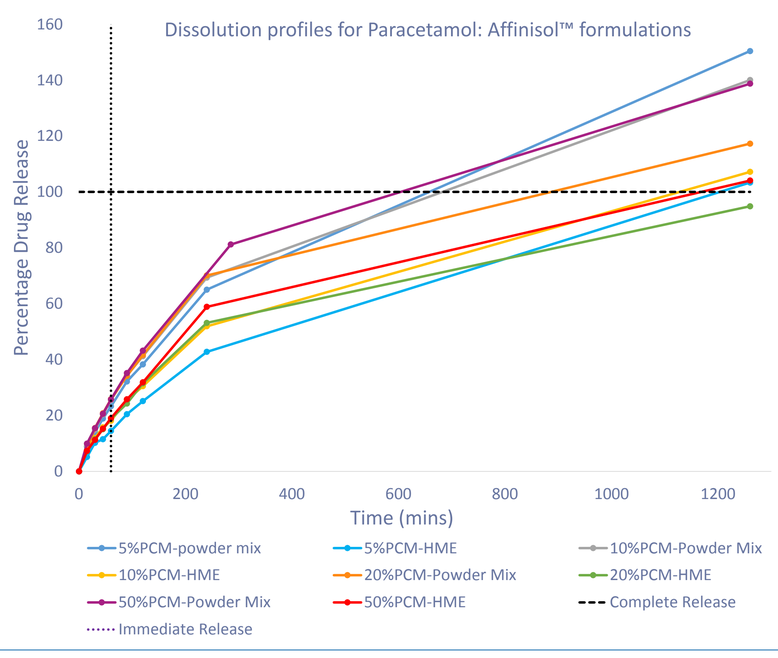


Dissolution Profiles:

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.



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™ as filament but as dosage forms less effective. The API concentration becomes more influential.
- Pressure studies show that a lot of pressure is lost to the surroundings and what is applied is not necessarily experienced by the formulation.
- Future work will include analysing drug release behaviour to investigate the effect of pressure

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