Injection Moulding: A novel approach to the manufacture of homogenous immediate release solid oral dosage forms

EPSRC Centre for Innovative Manufacturing in Continuous Manufacturing and Crystallisation

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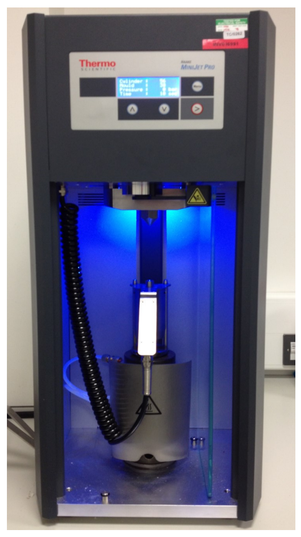
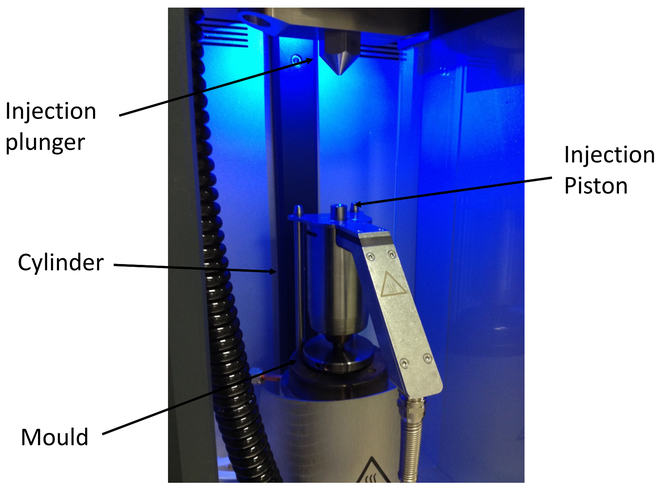
Injection Moulding:

- 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
- Scalable
- Dosage shape dependent on mould-designable
- No solvents needed





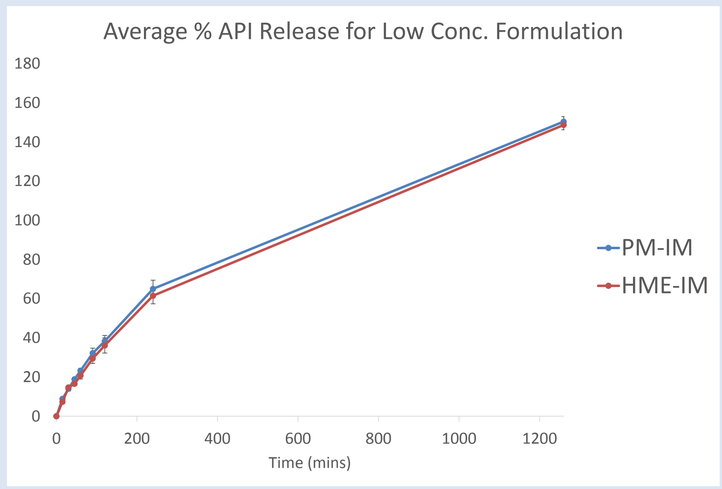
IM conditions:

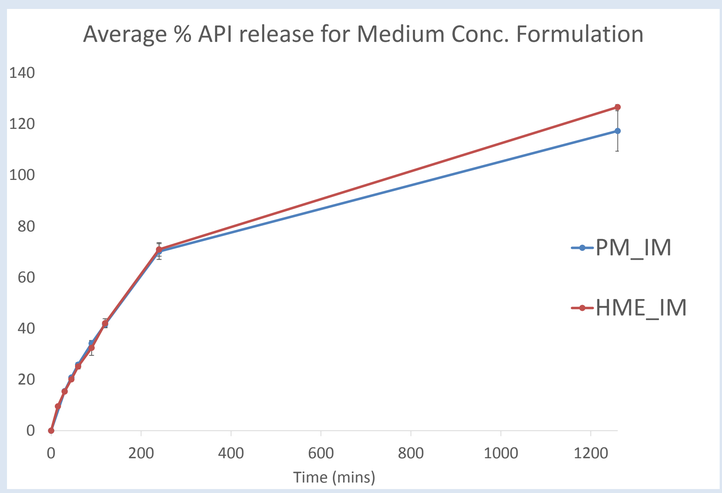
	CYLINDER TEMP (°C)	MOULD TEMP (°C)	INJECTION PRESSURE
Low API conc.	175	70	500 bar
Medium API conc.	175	70	500 bar
High API conc.	175	70	500 bar

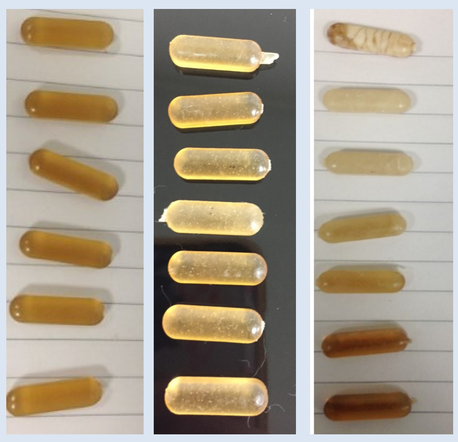
Material extruded using same temperature profiles to form a strand which was then pelletized

Aim: to produce a solid oral dosage form that is immediate release using Injection Moulding and Hot Melt Extrusion

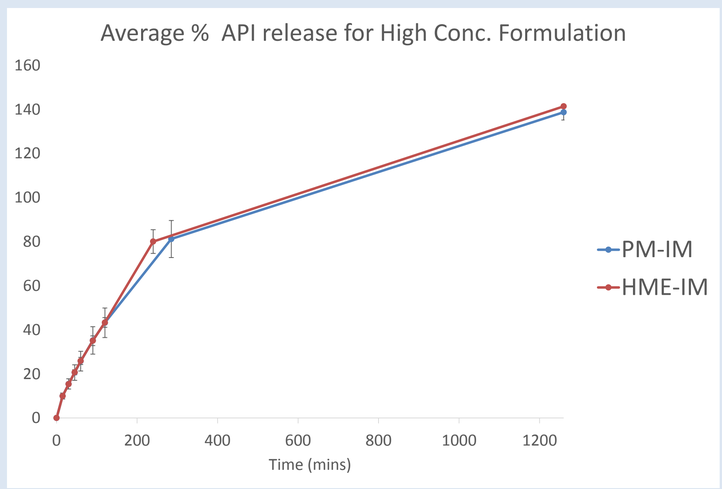
Dissolution studies:







Images of IM dosage units, from left to right: low, medium & high concentration of API



- The dissolution profile show that an immediate release of the API is not achieved. This is most likely due to the polymer hindering drug release as the main mechanism of achieved release of drug is through polymer erosion.
- Most drug release occurs during the first few hours of dissolution when the concentration of drug is at its highest. It then slows down as the effects of the slowly eroding polymer take over.
- Drug release between samples of the same formulation are very similar showing that both methods of production are reproducible. However more analysis of the extrudates used is required to determine their true concentration to give a more accurate HME-IM drug release

Dissolution profiles above show the drug release for dosage forms produced from powder mixtures (PM-IM) and from the extrudates formed from these powder mixtures via Hot Melt Extrusion (HME-IM)

Solid State Analysis:

DSC

- The melting point for the drug is not present in the DSC traces (not shown) for low and medium API concentration formulations which suggests the drug is present in the amorphous form. This is to be expected as the drug has been melted and the polymer is preventing recrystallisation.
- The high concentration API dosage units show a recrystallisation event and in storage the units turned white. This suggests that the polymer is saturated and can no longer prevent the crystallisation of API.

XRD

- X-ray diffraction confirmed that the API in the low and medium concentration solid oral dosage forms is amorphous due to lack of distinct peaks corresponding to the drug (diffractograms not shown).
- The data also confirmed that as the dosage forms containing the high concentration of API turned white recrystallisation was occurring.

High concentration dosage forms turning white after storage

Conclusion:

- Release profiles not immediate- almost 100% of drug should be released within 1 hour however in this case a fraction of that is released and full dissolution occurs between 4 and 17 hours
- Drug release after the first few hours is hindered due to the slow erosion properties of the polymer
- Further optimisation of formulation and process is required as well as more representative analysis

Further Work:

- Full investigation into polymer and disintegrant compatibility and effect of disintegrant on polymer break up
- Altering formulation to contain disintegrants allowing for immediate release of drug
- Analysis of extrudates to determine exact API release
- New mould design to control API distribution

Acknowledgements:

The author would like to thank Dr. Tariq Islam, Elanor Brammer, Eleanor Lawson, Dr. John Robertson and Prof. Gavin W. Halbert for their work and expertise on this project. Also a thank you to the EPSRC Doctoral Training Centre for Innovative Manufacturing in Continuous Manufacturing and Crystallisation for funding this work.

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