Investigation of the processing window for Affinisol™ and Plasdone™ - S630 polymers during Hot-melt extrusion (for 3D printing by fused deposition modelling)

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INTRODUCTION

In recent years, the use of 3D printing (3DP) for formation of custom dose forms has received increasing research interest for pharmaceutical applications. To date limited API loadings have been achieved. Current fused deposition modelling (FDM) approaches utilise a formulated filament (e.g. polymer and active) as a feedstock which can be made by hot-melt extrusion (HME). One key purpose of this work is to explore methods of achieving developing a viable routes to establishing wider ranging API loading using HME as a filament former.

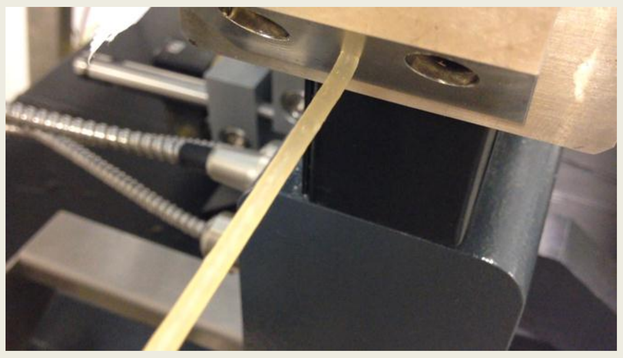
During hot-melt extrusion establishing a viable operating space for subsequent formulation and processing is essential. This processing space must avoid conditions resulting in degradation by thermal or mechanical energy and deliver extruded filament with suitable properties for subsequent processing (e.g. 3D printing)

As a first step, two pharmaceutical polymers, have been processed across the full operating range of a twin screw extruder (TSE) in order to identify processing space where degradation is likely to occur and where it can be avoided.

As a second step, the HME process was further developed to produce up to 50:50 wt/wt API loaded HPMC based filament of suitable character for 3DP)f dose forms by FDM.

Establishing viable operating space for polymers

Affinisol™ 15LV (HPMC, Dow Chemical Co.) and Plasdone™-S630 (copovidone, Ashland) were extruded using a 16mm co-rotating TSE (Thermo Scientific, Karlsruhe, Germany) at 1.0kg/hr through a die to produce an extrudate strand. Three barrel temperatures (150, 180 and 210°C) were used and the screw speed was adjusted between 100-1000 rpm.



Observations of extrudate formed

The physical appearance of the extrudates of both polymers at different processing temperatures (150, 180 and 210°C) and operating range of extruder speed (100 – 1000 rpm) are shown in Figures 1. Specific mechanical energy calculated from torque produced during extrusion as a function of extruder speed is shown for information in Figure 2. It can be seen from the physical appearance of Affinisol™ was degraded/discoloured by a combined effect of screw speeds and temperature whereas Plasdone™ doesn't show any immediate discolouration.

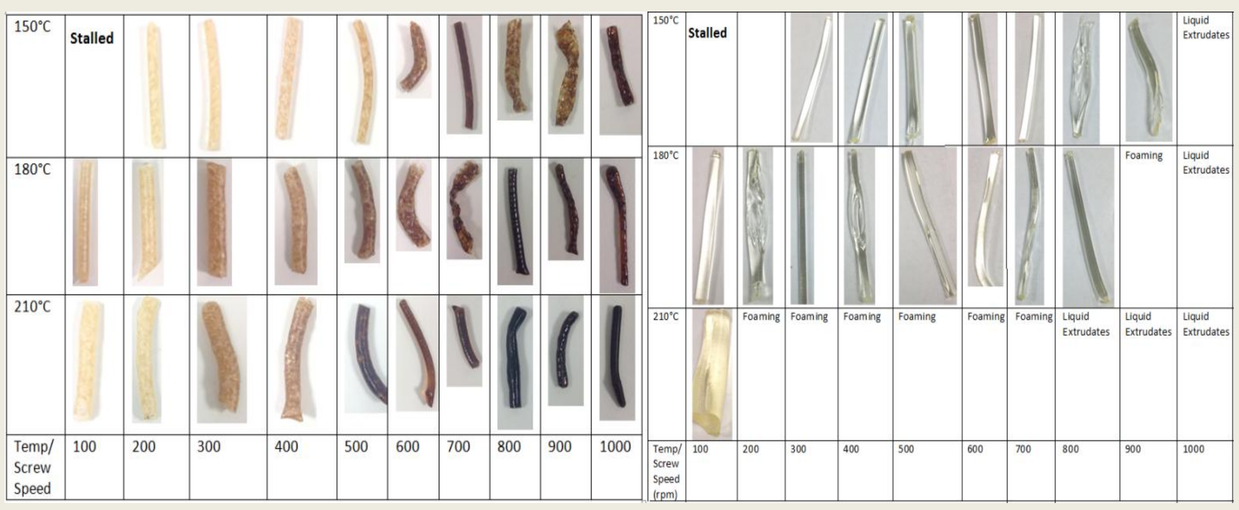


Figure 1: Physical appearance of Affinisol™ 15LV and Plasdone S-630 polymer extrudates

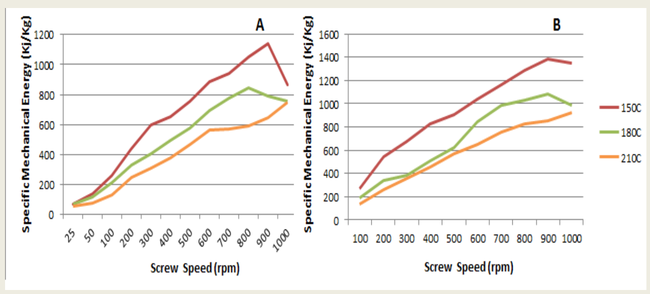


Figure 2: Specific mechanical energy curve for A) Affinisol™ and B) Plasdone™ S630

Although, Affinisol™ 15LV showed discoloration at higher temperature and/or extruder speed compared with Plasdone™-S630, but Plasdone™ starts foaming at similar conditions.

From the initial experiments, it was concluded that both the Affinisiol™ 15LV polymer and Plasdone™ were limited to lower processing speeds and temperature wrt both degradation in the case of Affinisiol™ and successful filament formation in the case of Plasdone™. The next stage of the work focussed upon the use of Affinisol™ for formulating API loaded filaments for subsequent printing by FDM.

For successful printing, filaments of Ø = 1.75 mm ±0.05 mm, must be formulated.

To produce Affinisol™ filaments for 3DP using HME, variables such as die type, extruder speed and downstream conveyor speed were varied to develop knowledge and enable some degree of process optimisation.

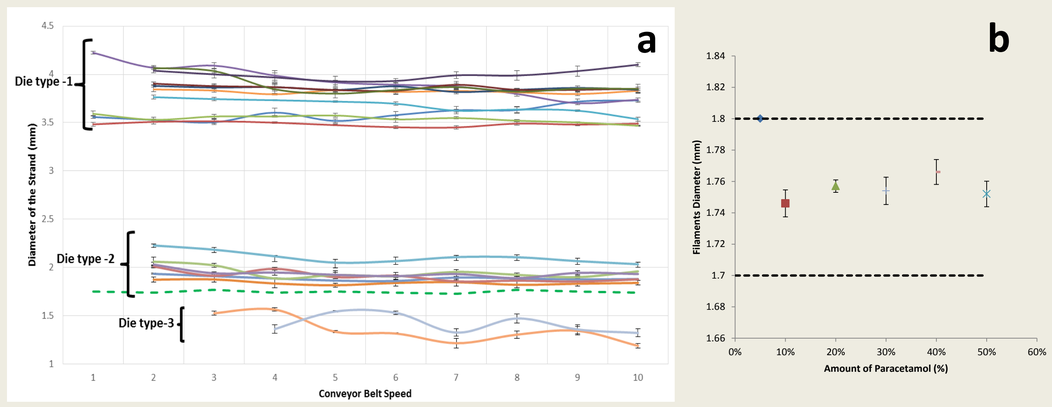
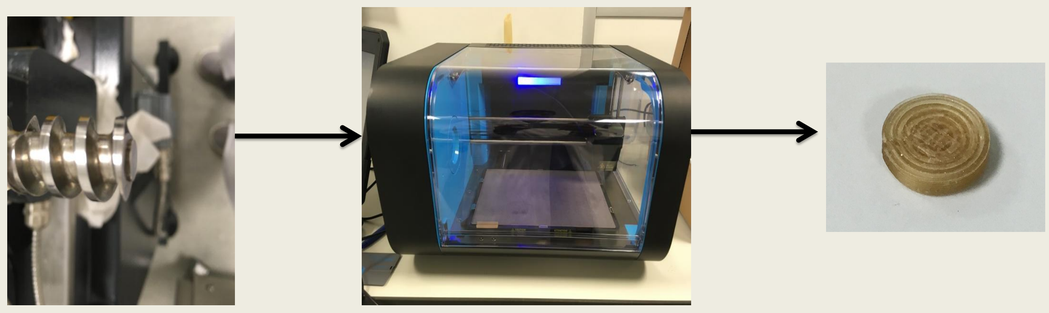


Figure 3: a) Diameter of HPMC Affinisol™ extruded filaments using various die types. b) Diameter of the filament in addition with API (%) during extrusion

Figure 3a shows examples of the overall range of filament sizes of Affinisol™ that can be produced within the viable operating space (i.e. temp and mechanical energy) developed earlier. Figure 3b shows examples of the level of filament diameter control across a range of polymer : API formulations which were then subsequently printed.

Examples of some basic analysis of 10-50% API loaded 3D printed dose forms are shown below.



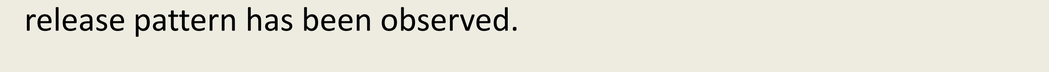


Figure 4: a) X-ray diffractogram of the 3D printed tablets in comparison with extrudates and physical blend of the bulk API and polymer, b) Drug release studies

Amorphous state of the API was observed in all 3D printed tablets and also in the extruded pellets (Figure 4a) except the higher API loaded tablets and from the dissolution studies (Figure 4b), extended drug release pattern has been observed.

CONCLUSIONS

Viable operating space for HME of Affinisol™ 15LV and Plasdone™-S630 has been established.

Methods to produce filaments with a broad range of API loading suitable for 3D printing by FDM has been shown.

ACKNOWLEDGEMENT

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