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in Continuous Manufacturing and Crystallisation

# An Investigation into Fused Filament Fabrication for Pharmaceutical Manufacturing

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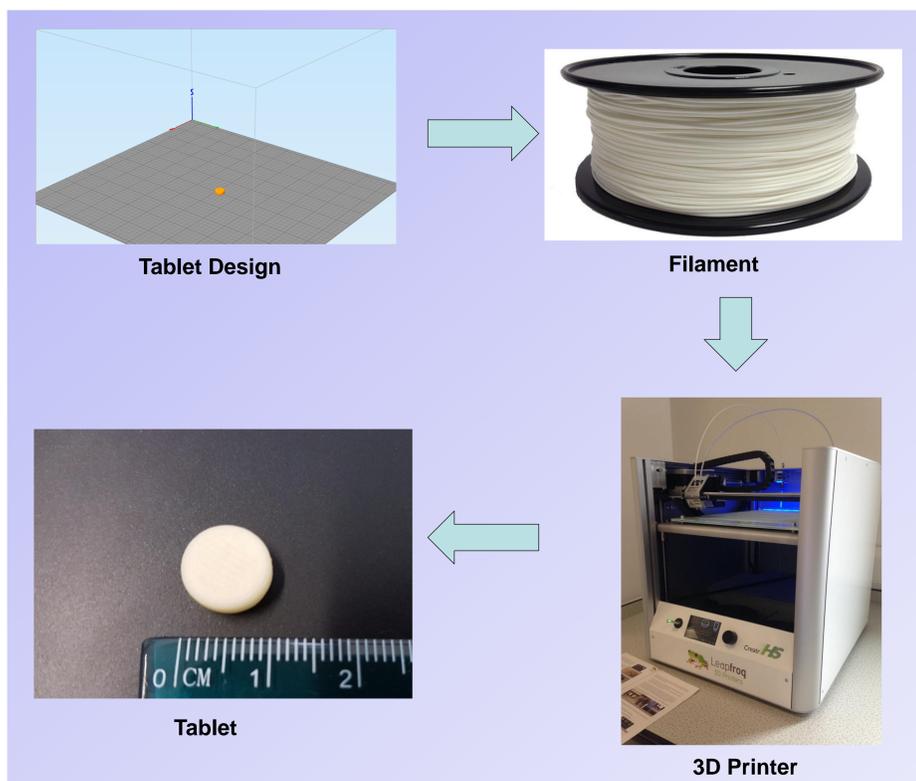
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## Introduction

In a modern world, what is the best way to deliver medicines to the patient? Human beings are an extremely diverse species with many different factors that can influence the behaviour of a drug within the body. Children are a perfect example of such variety. Doses are often prescribed based on body weight, and can vary greatly from infants to adolescents. With current 'traditional' manufacture of oral dose pharmaceuticals, generally only a limited number of doses are produced, leading to difficulties with appropriate dosing. The ability to manufacture personalised doses for these patients would be of great benefit both practically and financially, and may even lead to 'point of care' manufacture.

## Materials and Methods

Fused Filament Fabrication (FFF) is a technique which allows for the creation of a 3D object, layer by layer, by melting a polymer.



There are two different ways to load a selected polymer with drug:

- Extrude the drug and polymer together using a hot-melt extruder (shown below) to produce a filament, then transfer this to the 3D printer.<sup>1</sup>



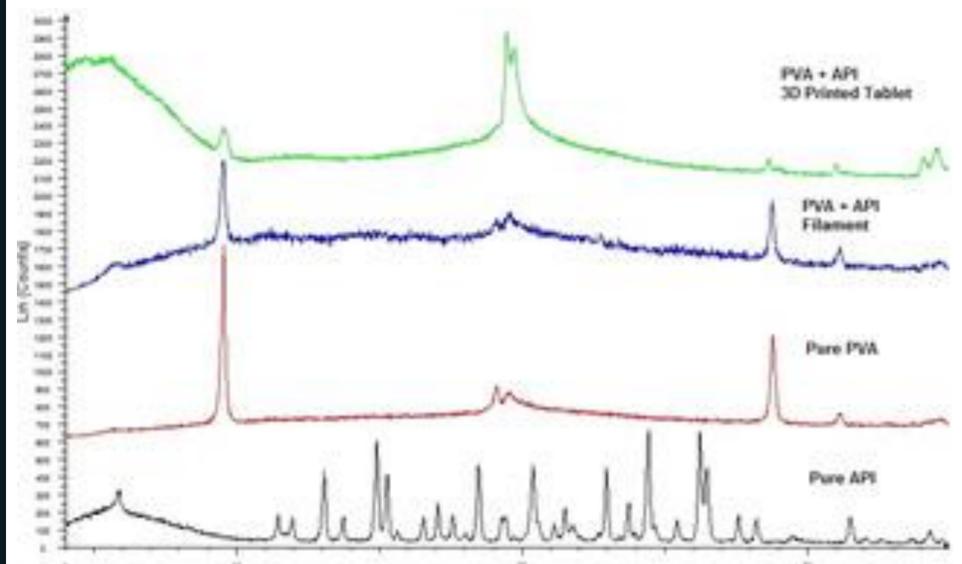
- Obtain a polymer which is already in a filament form and load this with drug by submerging in a solution containing the API of choice. Evaporate the remaining solvent by heating in an oven, then transfer this to the 3D printer.<sup>2</sup>

Both have advantages and limitations. The work presented here was carried out using the latter technique.

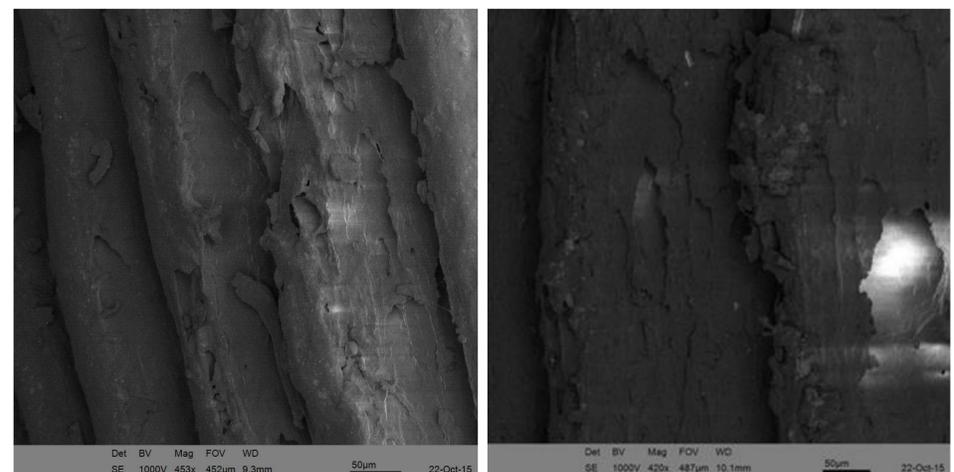
## Results

HPLC was used to determine drug content of both filament and printed tablets (n = 3).

- 3.58 %w/w  $\pm$  0.06 filament.
- 9 mg  $\pm$  0.5 mg 30% infill tablet.



xRPD showed no peaks corresponding to the API in the final product, it is thought the API is amorphous.



SEM analysis was carried out on blank (left) and drug loaded (right) tablets. Both show evidence of residual solvent as seen by rough edges and pores.

While TOF-SIMS analysis also provided data on drug content, it is not possible to ascertain the exact depth to which the API penetrates. It is hoped future analysis with nanoCT can provide a better idea of the distribution of API with the polymer.

## Conclusions and Future Work

While fused filament fabrication is still in its infancy, it is clear that there is potential for this technique to be used as a way of manufacturing personalised medicine. The work presented here only demonstrates doses which can be achieved by printing one particular size of tablet with an infill percentage of 30%. By altering the size of this tablet, or the infill percentage, a larger range of doses could potentially be manufactured in a reproducible manner. Varying the length of time for submersion of the filament would not only alter the drug distribution, but could potentially provide increased or decreased doses compared to those reported here. If the drug is present in an amorphous state, this technique also offers the benefit of potentially improving the dissolution rate of a BCS Class II drug. Further studies will focus on increasing and decreasing the size and infill percentage of printed tablets in order to further investigate the reproducibility.

## References

- <sup>1</sup> Goyanes A. *et al.* Effect of geometry on drug release from 3D printed tablets, *Int. J. Pharm.* 494, 657-663 (2015)..
- <sup>2</sup> Goyanes A. *et al.* Fused-filament 3D printing (3DP) for fabrication of tablets, *Int. J. Pharm.* 476, 88-92 (2014).