PERaME: Personalised polypills with programmable release made by 3D printing

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INTRODUCTION

Personalised, segmented-release polypills fabricated via additive manufacturing (also known as 3D Printing) offer a promising strategy to mitigate issues of polypharmacy and poor medication adherence [1]. However, their implementation requires feedstock materials that balance printability, dose precision, and programmable dissolution profiles. The Personalised Adaptive Medicine (PERaME) project aims to develop a range of bespoke feedstock filaments that can be used to 3D print capsule shells that can be used to host powder/granulated drug formulations.

Feedstock materials for the PERaME system were developed to enable tailored dissolution kinetics, covering immediate, controlled, and pH-dependent release profiles. A pH-dependent polymer blend and fluorescein sodium salt (FSS) were used as model excipient and hydrophilic drug, respectively, to investigate the influence of tablet geometry, including wall thickness, diameter, and layer height, on dissolution behaviour.

MATERIALS & METHODS

Feedstock preparation: Hypromellose acetate succinate (HPMCAS)-based filaments were extruded using the HAAKE MiniLab II. The extrusion temperature was maintained at 140 °C, with a mixing time of 5 minutes and a screw speed of 100 rpm. The extruded filaments were stored in a desiccator for 24 hours prior to the feedability test and 3D printing.

Thermal characterisation: The filament samples were characterised by differential scanning colourimetry (DSC2500, TA Instruments) using a heat-cool-heat cycle with a temperature range of -90°C to 160°C at 10°C/min. The measurement was done in triplicate.

Feedstock feedability: A slightly modified feedability test was used to evaluate the risk of filament breakage within the FDM printhead [2]. Filament segments measuring 5 mm in length (N=3) were compressed at 5 mm/s to mimic the feeding action between the extruder gears and nozzle. Three commercial filaments composed of different materials served as benchmarks (N=3).

Tablet fabrication: Dual-compartment tablets were fabricated at Loughborough University using a Raise3D Pro2 3D printer (0.4 mm nozzle) at 190 °C with a 60 °C bed temperature, designed via FullControl GCODE Designer [3]. Each tablet contained 20 mg of FSS, with wall thickness, diameter, and layer height (Figure 1) varied to investigate their effects on the FSS release time.

In vitro dissolution testing: *In vitro* dissolution testing was conducted using a USP II paddle apparatus at 37 °C and 50 rpm (n = 3) to find out the initial release time and cumulative release of FSS. Tablets were first exposed to 0.2 M HCl for 2 hours with hourly sampling, followed by phosphate buffer solution (PBS, pH 6.8) with 30-minute sampling intervals until complete dissolution. Continuous video recording beneath the vessels captured the initial FSS release. UV–Vis spectrophotometry was used for quantification at 438 nm (acidic phase) and 490 nm (basic phase), with calibration curves constructed for each wavelength.

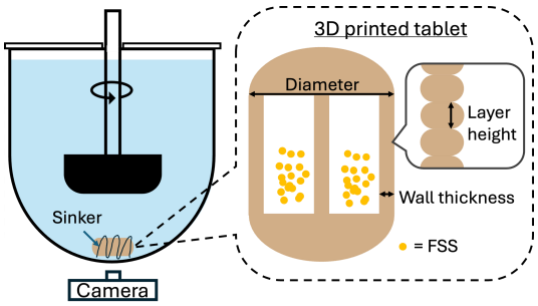

Figure 1. Dissolution testing setup used to monitor initial FSS release, alongside schematic illustrations of tablet geometry variables investigated: wall thickness, tablet diameter, and layer height. Yellow spheres represent the model drug (FSS) within each compartment (not to scale).

RESULTS & DISCUSSION

All filament samples exhibited a single glass transition temperature (Table 1), indicating a homogeneous mixture between HPMCAS and the plasticiser and confirming the amorphous nature of the filaments. Increasing the plasticiser content led to a gradual reduction in Tg, consistent with enhanced plasticisation.

Filament	HPMCAS	plasticiser	T_g (°C)
PD 1	90	10	85.6 ± 0.4
PD 2	80	20	59.8 ± 1.9
PD 3	70	30	27.7 ± 4.1

Table 1. Formulation of the HPMCAS-based filaments.

The feedability test assessed the mechanical robustness of the filament formulations to prevent breakage within the printhead, which is a common challenge in FDM

printing of pharmaceutical filaments. As shown in Figure 2, PD1 fractured during compression, indicating brittleness, while PD2 and PD3 withstood significant compression without breaking. However, during the tablet printing process, PD3 tended to buckle within the printhead due to its softness. Therefore, PD2 was selected for subsequent printing experiments.

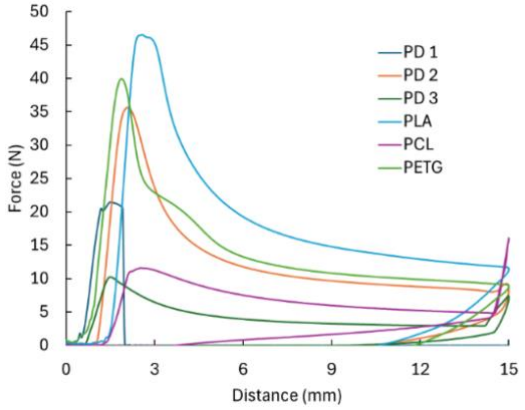

Figure 2. Feedability test results of HPMCAS-based filaments compared with commercially available filaments.

Figure 3 shows an example tablet under different pH conditions. The 3D-printed tablets exhibited no detectable drug release in pH 1.2 and initiated dissolution only after the pH was increased to 6.8.

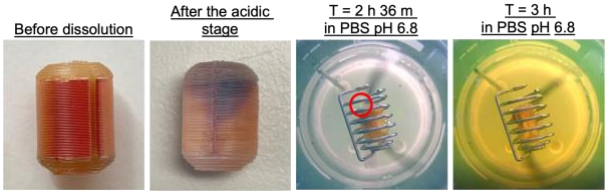

Figure 3. Representative images of the delayed-release tablet showing no drug release in acidic medium (pH 1.2) and subsequent dissolution in basic medium (pH 6.8). The red circle highlights the initial release of FSS.

Tablet geometry influenced dissolution behaviour in distinct ways. Increasing wall thickness delayed the initial release of FSS, potentially prolonging intestinal transit time; however (Figure 4A&B) , the maximum wall thickness was limited to 1.2 mm to maintain acceptable tablet size for swallowing. Changes in tablet diameter had minimal effect on dissolution time (Figure 4C&D) but increased internal volume, enabling incorporation of higher drug doses without affecting release kinetics. Layer height did not measurably influence FSS release or the overall dissolution profile (Figure 4E&F), although higher layer heights enhanced manufacturing efficiency by reducing print time and minimising cumulative printing errors.

ACKNOWLEDGEMENT

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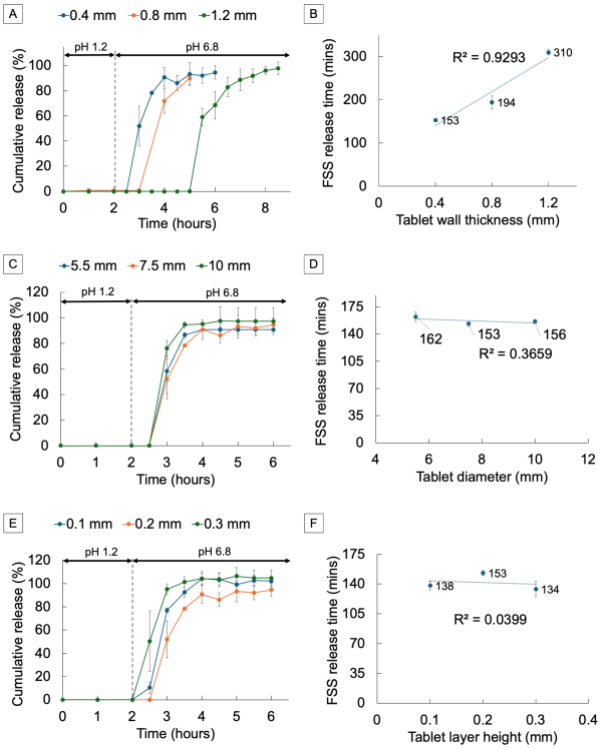

Figure 1114. Impact of tablet geometry on FSS dissolution. (A) Wall thickness, (C) tablet diameter, and (E) layer height.

CONCLUSIONS

The work with the pH-dependent polymer established a reference dataset correlating dissolution time with key physical parameters of 3D-printed tablets. Wall thickness was identified as the primary determinant of FSS release time, whereas variations in diameter and layer height had minimal impact.

Ongoing work includes long-term stability testing of feedstock materials under clinically relevant conditions, expansion of the range of drug candidates, and further system integration. Future studies will investigate the dissolution kinetics of immediate- and controlled-release formulations using the same experimental approach, with the goal of building a comprehensive reference database for the PERaME system.

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