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Fused Deposition Modelling 3D Printed Immediate Release Tablets: Understanding the Impact of Printer Parameters

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SUMMARY

The aim of this study was to prepare tablets that offer an immediate release (IR) of the loaded active ingredient using fused deposition modelling (FDM) 3D printing. Hydrochlorothiazide (HCTZ) was used as a model drug, with polyvinyl alcohol (PVA) as the primary polymeric carrier and sorbitol as a plasticizer. The impact of printer parameters, including infill density, roof and floor (R&F) thickness and nozzle size, on the drug release properties of printed tablets was investigated. The results support the use of FDM-3DP as an approach to manufacture IR tablets and highlighted the importance of the printing design on drug release properties.

INTRODUCTION

Fused deposition modelling (FDM) 3D printing has gained attention in providing an option for the development of patient-centric dosage forms [1]. The 3D printer melts deposit an extruded matrix on a heated build plate, layer-by-layer, until for example, a solid dosage form has been constructed. Interestingly, previous studies have shown that resultant tablets are firmer and less prone to disintegration than conventionally compacted tablets. Hence, drug release is often retarded rendering the manufacture of IR tablets challenging.[2]

This study aimed to generate HCTZ-loaded IR tablets and to investigate the impact of printer parameters on the drug release profile. This study also provides insight into coupling hot melt extrusion with FDM-3DP building an attractive and versatile platform for the manufacture of complex dosage forms with multiple drugs, e.g., in the management of cardiovascular disease.

MATERIALS AND METHODS

Parteck®MXP (PVA) and Sorbitol were purchased from Sigma-Aldrich (U.K.). HCTZ was purchased from Kemprotec (U.K.). Pharmacopoeia grade HCl purchased from Fluka Honeywell (U.K.)

***Table 1**. Effect of variables on the tablets apparent volume*

No	Infill density, %	R&F, mm	Nozzle size, mm	Density, mg/mm³
P1	100	1.0	0.45	1.23±0.04
P2	50	1.0	0.45	1.04±0.04
P3	30	1.0	0.45	0.92±0.05
P4	30	0.8	0.45	0.85±0.05
P5	30	0.4	0.45	0.71±0.05
P6	30	0.4	0.2	0.62±0.02
P7	30	0.4	0.6	0.72±0.03

A physical mixture of formulation with 19% w/w plasticizer was processed through a twin-screw extruder (Rondol Industries SAS, France) with full conveying elements at 220°C and 60 rpm. Filaments were then fed into a Replicator 2X (MakerBot Inc. USA) with a pre-set round tablet of 10mm diameter

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and 5mm height. FDM 3DP was carried out using pre-defined (Table 1) with various infill densities, R&F thickness and nozzle sizes. The dimensions and weight of each tablet were measured with digital callipers and an analytical balance respectively. The crystallinity of both raw and processed materials was assessed using Powder X-Ray Diffraction (Rigaku Corporation, England). Filaments and tablets were milled into fine powder using an MM200 miller (Retsch GmbH & Co. KG, Germany) for a period of 5 mins at 20 s^{-1} frequency. Drug release studies were conducted at pH 1.2 under sink conditions with aliquots analysed using a UV-Vis Spectrophotometer (Cary 60, Varian, Ireland) at 272 nm wavelength. To account for the tablet density variability, drug release percentage has been normalised. All results were statistically analysed using one-way analysis of variance (ANOVA) and Post hoc tests.

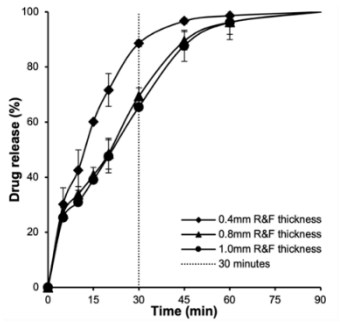

Fig. 1. *Effect of the R&F thickness on the HCTZ-drug release from the tablet (at constant: 0.45mm Nozzle size, 30% infill density)*

RESULTS AND DISCUSSION

It was confirmed that decreasing the infill density resulted in faster drug release, once the outer shells dissolved away, evidently owing to a loose structure of the sandwich layer. Tablets with thinner R&F layer appeared to offer less support in maintaining the tablet dimensions, hence, resulted in more significant swelling upon water ingress. This swelling notably accelerated the drug release process (Fig. 2). As the nozzle size gradually reduced from 0.6, 0.45 to 0.2 mm, the tablet density subsequently decreased. Despite P6's low density of 0.62 mg/mm^3, the dimensions are within the pre-set confidence interval, and the tablet structure's form was preserved. The large gap between the infill contributed to the formation of pores in tablets. Thus, the porous structure allowed drug release media to penetrate the shell and expand the contact surface, accelerated the disintegration of the tablet, and the rapid release of the drug was achieved.

Pure HCTZ exhibited a series of sharp diffraction peaks, the most significant at 17.06° 2θ, signifying the crystalline nature of the drug. At the tested drug loading, peaks characteristic of HCTZ crystallinity were also evident in the physical mixture of the formulation. The absence of sharp diffraction peaks for powdered filaments and tablets containing HCTZ confirmed the amorphous nature of HCTZ (Fig 2).

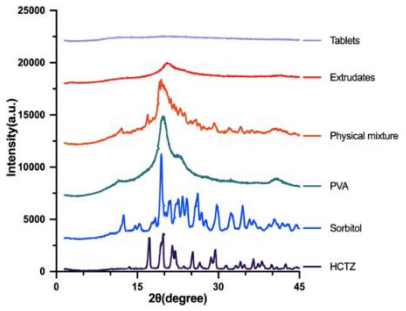

Fig. 2. *X-ray diffraction profiles of the raw material, physical mixtures, extrudates and tablets.*

CONCLUSION

The feasibility of using FDM-3DP as an approach for the manufacture of IR tablets with HCTZ was investigated in this work. The results showed that HCTZ was converted to the amorphous form during extrusion processing and remained amorphous following printing. This study highlighted the importance of adjusting the settings of the printer prior to manufacture and demonstrates the impact of each parameter upon the drug release behaviour of the printed tablet. The drug release profile is not only formulation dependent but is strongly influenced by the tablet design and printing parameters used during manufacture.

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