Impact of Formulation of Drug-Containing Blends on 3D Printing by Fused Deposition Modelling

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ORIGINAL ARTICLE

ABSTRACT

Introduction: Fused Deposition Modelling (FDM) is paving the way for the digitally-enabled on-demand production of personalized medicines. The thermoplastic polymer matrix determines the mechanical and rheological properties of HME filaments[1], and ultimately the quality and performance of the 3D printed dosage forms[2]. An inappropriate combination of drug and excipients affects these properties and can preclude successful HME-FDM integration[3]. The impact of the physicochemical properties of drug (e.g. melting point, m.p.), and use of excipients, was investigated in this work.

Materials & Methods: Hydroxypropylcellulose (HPC) was used as matrix; the model drugs considered (covering a wide m.p. range) were paracetamol (PCT), paroxetine (PAR), and theophylline (TEO), at 30% w/w drug load. The lowest temperature settings required for HME-FDM coupling were determined and the need for processing aids evaluated. Extrusion and printing temperatures were maintained below drug degradation point. Extrudability and printability were evaluated respectively through the ability to produce (A) drug-loaded filaments with adequate dimensions and rheology and (B) tablets (batches of 10-20 units) with simple and more complex geometries, meeting Eur. Pharm. requirements for mass and content uniformity. For printability, each formulation required the addition of plasticizers to lower the melting temperature (e.g. Soluplus, 7.5-15% or trietylcitrate, 5%) and lubricants (e.g. magnesium stearate, 1-3%) to achieve adequate feeding of the filaments to the printer.

Results & Discussion: The work failed to establish a direct relationship between drug melting point and temperature required for filament production and printing (Table 1), indicating the influence of other factors, such as solubility, hydrophilicity, or ability to establish drug/matrix molecular interactions. Over-plasticization, by water, of HME filaments exposed to ambient relative humidity, affected rheological properties and prevented subsequent printing. Although TEO (highest m.p.) required more drastic conditions, PRX (lowest m.p.) was more demanding than PCT (medium m.p.). However, the temperature ranking followed a similar pattern for HME and FDM. The addition of excipients in the fraction range considered did not impact the temperature required for HME-FDM. The double application of heat resulted in solid-state interactions and amorphization of drugs. It appears that processing settings need to be adjusted on a case-by-case basis but further studies with other drugs are required to substantiate these findings.

Table 1. Characteristics of the model drugs and minimum processing conditions required for integrated HME-FDM

Drug	MW (Da)	Melting point (°C)	Water solubility at 25°C (mg/mL)	HME Temp. (°C)	FDM Temp. (°C)
PRX	374.84	120-138	1.13	120	200
PCT	151.16	168-172	14.00	100	180
TEO	180.17	270-274	7.36	130	220

Keywords: 3D Printing, hot-melt extrusion, fused deposition modelling, extrudability, printability.

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