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Research paper

An investigation into the use of polymer blends to improve the printability of and regulate drug release from pharmaceutical solid dispersions prepared via fused deposition modeling (FDM) 3D printing

Muqdad Alhijjaj [a,b], Peter Belton [c], Sheng Qi [a,*]

[a] School of Pharmacy, University of East Anglia, Norwich, Norfolk NR4 7TJ, UK
[b] Department of Pharmaceutics, College of Pharmacy, University of Basrah, Basrah, Iraq
[c] School of Chemistry, University of East Anglia, Norwich, Norfolk NR4 7TJ, UK

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ABSTRACT

FDM 3D printing has been recently attracted increasing research efforts towards the production of personalized solid oral formulations. However, commercially available FDM printers are extremely limited with regards to the materials that can be processed to few types of thermoplastic polymers, which often may not be pharmaceutically approved materials nor ideal for optimizing dosage form performance of poor soluble compounds. This study explored the use of polymer blends as a formulation strategy to overcome this processability issue and to provide adjustable drug release rates from the printed dispersions. Solid dispersions of felodipine, the model drug, were successfully fabricated using FDM 3D printing with polymer blends of PEG, PEO and Tween 80 with either Eudragit E PO or Soluplus. As PVA is one of most widely used polymers in FDM 3D printing, a PVA based solid dispersion was used as a benchmark to compare the polymer blend systems to in terms of processability. The polymer blends exhibited excellent printability and were suitable for processing using a commercially available FDM 3D printer. With 10% drug loading, all characterization data indicated that the model drug was molecularly dispersed in the matrices. During in vitro dissolution testing, it was clear that the disintegration behavior of the formulations significantly influenced the rates of drug release. Eudragit EPO based blend dispersions showed bulk disintegration; whereas the Soluplus based blends showed the 'peeling' style disintegration of strip-by-strip. The results indicated that interplay of the miscibility between excipients in the blends, the solubility of the materials in the dissolution media and the degree of fusion between the printed strips during FDM process can be used to manipulate the drug release rate of the dispersions. This brings new insight into the design principles of controlled release formulations using FDM 3D printing.

1. Introduction

An encouraging trend of using 3D printing in pharmaceutical manufacturing has been established by the approval of Spritam®, which is the first FDA approved 3D printed oral dosage form. This first 3D printed commercial drug product used ZipDose® technology, which is a wet power deposition 3D printing method. There is a wide range of 3D printing technologies that operate via thermal or solvent evaporation mechanisms. FDM 3D printing is a thermal based 3D printing technique and has recently attracted the interest of researchers in many fields including pharmaceutical formulations design [1–3], food technology [4], and tissue engineering [5]. For pharmaceutical applications, this technique has been identified as holding future promise for developing individualized oral medicines [1–3,6,7]. FDM 3D printing can play an important role in reducing the complexity of drug regimens through incorporation of multiple drugs into a 'polypill' type of formulations. It may also allow different release profiles of the drug to be obtained through changing the exposed surface area or the

Abbreviations: FDM, fused deposition modeling; 3D, three dimensional; PVA, polyvinyl alcohol; PLA, polylactide; PCL, polycaprolactone; HPC, hydroxypropyl cellulose; PEG, polyethylene glycol; PEO, polyethylene oxide; DSC, Differential Scanning Calorimetry; MTDSC, Temperature Modulated Differential Scanning Calorimetry; ATR-FTIR, attenuated total reflectance Fourier transform infrared; PXRD, powder X-ray diffraction; SEM, Scanning Electron Microscopy; HME, hot melt extrusion; BCS, biopharmaceutics classification system; T_g, glass transition temperature; TGA, Thermal Gravimetric Analysis; USP, United State Pharmacopoeia; APIs, Active Pharmaceutical Ingredients; UV–VIS, ultraviolet–visible.

* Corresponding author.
E-mail address: sheng.qi@uea.ac.uk (S. Qi).

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