Fabrication of solid dispersion based patches using hot melt injection moulding and fused deposition modelling 3D printing

Abstract

The poor aqueous solubility of many APIs, such as felodipine, are significant dissolution rate limiting factors that often lead to poor oral systemic bioavailability. Solid dispersions have been used as a formulation approach to improve drugs dissolution properties. Most of the reported solid dispersion formulations in the literature are binary mixtures with limited functionalities (with enhancing dissolution being the primary function). The aim of this study is to design, characterise and evaluate complex solid dispersions with intentionally designed microstructures (in the form of phase separations). The potential functionalities of these microstructures were explored by this project. In our view, the complex formulations are more representative of real pharmaceutical products in their final forms.

HME-IM is a single processing technique for fabricating formulations with high geometric precision in a rapid, efficient and environmentally friendly way. It was used as the main processing method to produce the solid dispersion based buccal patches in this project. The patches were thoroughly characterised using conventional techniques including DSC, MTDSC, TGA, DVS, ATR-FTIR, PXRD, SEM, EDS, IR imaging, mucoadhesion and in vitro

dissolution testing. In order to address the spatial distribution of the phase separations, two non-conventional characterisation methods, thermal analysis by structural characterisation and X-ray microcomputed tomography, were introduced to provide novel insights into the heterogeneity and phase distribution of these formulations. The results revealed that HME-IM patches with 10% drug loading were unsaturated while those with 20-30% w/w drug concentration were saturated or even supersaturated. HME-IM patches containing TPGS were more solubilising to felodipine and more stable compared to Tween 80 containing systems. Thermal analysis by structural characterisation provided rapid detection of heterogeneity and the thermal dissolution of crystalline drug fraction while XμCT provided microscale spatial distribution of different phases. Having shown the advantages of using polymeric blends to formulate solid dispersions that were demonstrated by the felodipine buccal patches, we further explored the use of polymer blends for improving the FDM 3D printability of pharmaceutical solid dosage forms with the potential applications in personalised medicine.

This project demonstrated the potential and formulation principles of using HME-IM and FDM 3D printing as formulation methods for production of polymer blend based complex solid dispersions for the purposes of enhanced bioavailability of poorly soluble drugs and providing personalised medicines.