Characterization of Heterogeneity and Spatial Distribution of Phases in Complex Solid Dispersions by Thermal Analysis by Structural Characterization and X-ray Micro Computed Tomography

Abstract

Purpose: This study investigated the effect of drug-excipient miscibility on the heterogeneity and spatial distribution of phase separation in pharmaceutical solid dispersions at a micron-scale using two novel and complementary characterization techniques, thermal analysis by structural characterization (TASC) and X-ray micro-computed tomography (XμCT) in conjunction with conventional characterization methods.

Method: Complex dispersions containing felodipine, TPGS, PEG and PEO were prepared using hot melt extrusion-injection moulding. The phase separation behavior of the samples was characterized using TASC and XμCT in conjunction with conventional thermal, microscopic and spectroscopic techniques. The in vitro drug release study was performed to demonstrate the impact of phase separation on dissolution of the dispersions.

Results: The conventional characterization results indicated the phase separating nature of the carrier materials in the patches and the presence of crystalline drug in the patches with the highest drug loading (30% w/w). TASC and XμCT where used to provide insight into the spatial configuration of the separate phases. TASC enabled assessment of the increased heterogeneity of the

dispersions with increasing the drug loading. XμCT allowed the visualization of the accumulation of phase separated (crystalline) drug clusters at the interface of air pockets in the patches with highest drug loading which led to poor dissolution performance. Semi-quantitative assessment of the phase separated drug clusters in the patches were attempted using XμCT.

Conclusion: TASC and XμCT can provide unique information regarding the phase separation behavior of solid dispersions which can be closely associated with important product quality indicators such as heterogeneity and microstructure.