Creating Drug Solubilization Compartments via Phase Separation in Multicomponent Buccal Patches Prepared by Direct Hot Melt Extrusion-Injection Molding

Abstract

Creating in-situ phase separation in solid dispersion based formulations to allow enhanced functionality of the dosage form, such as improving dissolution of poorly soluble model drug as well as being mucoadhesive, can significantly maximize the in vitro and in vivo performance of the dosage form. This formulation strategy can benefit a wide range of solid dosage forms for oral and alternative routes of delivery. This study using buccal patches as an example created separated phases in situ of the buccal patches by selecting the excipients with different miscibility with each other and the model drug. The quaternary dispersion based buccal patches containing PEG, PEO, Tween 80 and felodipine were prepared by direct hot melt extrusion-injection molding (HME-IM). The partial miscibility between Tween 80 and semi-crystalline PEG-PEO led to the phase separation after extrusion. The Tween phases acted as drug solubilization compartments and PEG-PEO phase had the primary function of providing mucoadhesion and carrier controlled dissolution. As felodipine was preferably solubilized in the amorphous regions of PEG-PEO, the high crystallinity of PEG-PEO resulted in an overall low drug solubilizing capacity.

Tween 80 was added to improve the solubilisation capacity of the system as the model drug showed good solubility in Tween. Increasing the drug loading led to the supersaturation of drug in Tween compartments and crystalline drug dispersed in PEG-PEO phases. The spatial distribution of these phase-separated compartments was mapped using X-ray micro-CT, which revealed the domain size and heterogeneity of the phase separation increased with increasing the drug loading. The outcome of this study provides new insights into the applicability of in situ formed phase separation as a formulation strategy for the delivery of poorly soluble drugs and demonstrated the basic principle of excipient selection for such technology.