The effect of various soluble polymers on the dissolution of Cilostazol tablets prepared by different manufacturing techniques

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Abstract

Active Pharmaceutical Ingredients (APIs) with poor solubility still represent a major challenge for the development and introduction of new pharmaceutical products for the treatment of unmet therapeutic needs. With the aim of enhancing the dissolution for poorly soluble drugs, the effect of some hydrophilic polymers such as PEG4000 and Poloxamer 407 at different quantities (5.0%w/w, 10% w/w, and 20.0% w/w) on the dissolution of Cilostazol from tablets was investigated. Moreover, the contribution of the hot melt extrusion (HME) as a promising technique compared to other conventional manufacturing techniques was evaluated. Final powder blends were prepared using different polymers, at different levels, and produced by different techniques. The compressibility and flowability of these blends were investigated thoroughly by the characterization of their bulk and tapped density, Carr's index, Hausner ratio and angle of repose. Additionally, particle size distributions were determined by laser diffraction technique. On the other hand, compressed tablets were characterized for their Hardness, weight, thickness, disintegration, and dissolution. Finally, solid state characterization was carried out using differential scan calorimetry (DSC).

HME showed a remarkable enhancement of the dissolution at 10% w/w of the hydrophilic polymers with superiority to Poloxamer 407 over PEG4000. Higher concentration of the hydrophilic polymers had sustained the disintegration of Cilostazol tablets and thus, the tablets showed slower dissolution profiles. Compared to Direct Compression (DC) method, Wet Granulation (WG) had clear positive outcomes at 5.0% w/w of Poloxamer 407 and to lower extent at 5.0% w/w PEG4000. Dissolution results with significant enhancement were gained at 10% of each of the hydrophilic polymers tested. At higher concentrations of the polymers, the sustained effect on release was again observed for

the WG tablets. However, the dissolution profiles were slower than those from tablets produced by HME. Besides dissolution, HME and WG had great improvement on the physical characteristics of the Cilostazol blends with slight advantage for HME. DSC characterization of the different blends showed no detected changes on the peaks of the API and the different polymers, revealing that no changes on the crystalline state of the Cilostazol had happened during the processing of either manufacturing techniques. In conclusion, the effects of the manufacturing procedure, polymer type and polymer incorporation level on the characteristics and in vitro performance of Cilostazol tablets were successfully revealed.