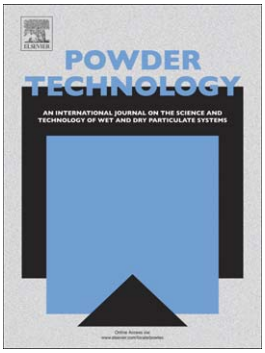

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Amorphization of Crystalline Active Pharmaceutical Ingredients via Formulation Technologies

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ABSTRACT

Amorphous Solid Dispersions (ASDs) were formulated to stabilize amorphous Active Pharmaceutical Ingredients (APIs). We investigated the feasibility of using spray-drying (SD) to generate ASD of indomethacin (IDMC) with a water-soluble polymer excipient poly(vinylpyrrolidone) (PVP), and compared the physicochemical properties of SD IDMC-PVP ASD to IDMC-PVP generated from our previous works via Co-milling (COM) and Supercritical Anti-solvent (SAS) processes [1-3]. Various percentage weight mixtures of IDMC and PVP were dissolved in a mixed solvent (acetone:dichloromethane = 80:20 vol/vol.%) and spray-dried to generate SD samples. The SD samples were then characterized via Scanning Electron Microscopy (SEM, morphology), Thermogravimetric Analysis (TGA, composition), Powder X-ray Diffraction (PXRD, crystallinity), accelerated physical stability testing, dissolution testing, Fourier-Transform Infrared Spectroscopy (FTIR, drug-polymer interaction) and Raman Spectroscopy (amorphous spatial distribution). X-ray amorphous SD IDMC-PVP solid dispersions with up to 80wt.% of IDMC and 20wt.% of PVP were successfully generated, while SAS and COM generated ASDs only up to 60wt.% of IDMC. SD, COM and SAS ASD particles were agglomerated spheres, multi-faceted blocks and agglomerated rounded fines, respectively. SAS and SD samples up to 60wt.% of IDMC