

The effect of anti-solvent addition rate on the behavior of indomethacin-saccharin co-crystallization based on in-line monitoring systems

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On a basis of the pharmaceutical validation guidance recently published by US FDA, in-line monitoring technology or systems for pharmaceutical processes has become very important especially for a study of crystallization and optimization. In this study, two in-line monitoring tools, FBRM (focused beam reflectance measurement) and PVM (particle vision measurement) were employed to investigate the co-crystallization behavior between indomethacin(IMC) and saccharin(SAC) using anti-solvent approach. The injection rate of anti-solvent in this case, the water, was examined as a primary process variable. Resulting crystalline materials were treated suitably and characterized via XRD (x-ray diffraction) and DSC (differential scanning calorimetry). It was found that the pathway of co-crystal formation was significantly dependent upon the addition rate of water. Hence, FBRM and PVM appear to be very valuable in interpreting and understanding the pharmaceutical co-crystallization process as in-line monitoring tools. Detailed experimental procedures and data shall be presented for extensive discussion.