The uptake of solvents into drugs and their influence on the stability of polymorphs

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The understanding of the solid state properties of pharmaceutical active ingredients is of uppermost importance for manufacturing and formulation of drug substances. Various techniques can be used to obtain conclusive data about important parameters such as crystalline structure, amorphous content or the existence and influence of solvates. In this work a steroid drug substance DS1 has been studied by means of isothermal microcalorimetry, DSC, DVS, XRPD and Raman to elucidate the stability of amorphous structure and polymorphs under various conditions such as increased temperature, solvent vapour and suspension of the drug.

For the steroid DS1 it could be shown that solvents play an important role in the formation of the crystal lattice. The formation of stable or metastable crystalline forms in slurry experiments was found to be strongly depended on the used solvent. This unexpected behavior was related to an unusual strong interaction of organic solvents with the drug molecules as observed by microcalorimetry.

References

Giron, D. Investigations of polymorphism and pseudo-polymorphism in pharmaceuticals by combined thermoanalytical techniques. Journal of Thermal Analysis and Calorimetry (2001), 64(1), 37-60.

K. Fiebich, M. Mutz. Evaluation of calorimetric and gravimetric methods to qualify the amorphous content of Desferal. J. Thermal. Anal. (1999), 57, 75-85.

Yonemochi, E; Inoue, Y; Buckton, G. Moffat, A; Oguchi, T; Yamamoto, K. Differences in crystallization behavior between quenched and ground amorphous ursodeoxycholic acid. Pharmaceutical Research (1999), 16(6), 835-840.