

Characterization of Hydrates. Case study

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Investigations on polymorphic behaviour of new entities is mandatory for a proper development (ICH tree, Q6). Since water is present in the atmosphere and in most excipients, water sorption-desorption isotherms are also measured. Water can be tightly bound to the active substance or enclosed in channels, resulting in different behaviour.

The example discussed demonstrates the advantage of the use of X-ray diffraction with heating cell or with a humid chamber additionally to classical thermal analysis methods, DSC and TG.

The drug substance was first obtained as solvated form with acetone (called 1A) whereby water replaces easily the solvent. A monohydrate (form 1B) was obtained. By heating the solvate or the monohydrate the same anhydrous form (1A') is obtained.

A second monohydrate, completely different was obtained by crystallization. Water sorption desorption and X-ray experiments demonstrate that this form 2 dehydrates in a different anhydrous form (2').

The single crystal structure of the solvate and the monohydrate 2 were determined and the calculated X-ray diffraction pattern compared to the experimental data. Furthermore molecular packing and interactions were investigated.

Form 2 is chemically less stable than form 1. Equilibration of this new monohydrate in different solvents shows a solvent mediated transition into the form 1.