The combination of thermoanalytical and crystallographic investigations for a complex polymorphism problem

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Characterization and monitoring of solid state properties of the active ingredients and excipients are fundamental elements of the pharmaceutical development since batch to batch inconsistency can cause crucial problems in the manufacturing of the pharmaceutical dosage form, the quality of the formulation, the bioavailability and drug stability.

Extensive research is required to characterize a new chemical entity. An example from pharmaceutical industry with complex pseudopolymorphic behaviour will be presented. Typical methods for the solid state characterization are X-ray powder diffraction, thermal analysis, solubility and dissolution measurements, water sorption and desorption behaviour and IR or Raman spectroscopy.

During the development of this substance, different crystalline impurities were detected.

The process of characterization and identification of nine different crystalline forms could only be performed by the combination of experimental and computational work. All solid state properties of a substance are based on their molecular packing and molecular interactions in their single crystal structure.

The determination of single crystal X-ray structures and their computational analysis was therefore of great value for the identification of the new crystalline forms and for the analysis of crucial causes and reasons for certain properties. Based on the obtained results a controlled chemical and pharmaceutical manufacturing process could be achieved.

Reference

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