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PHARM004: Crystal Structure Change of Tolbutamide Due to Thermal Phase Transition

Introduction

In drug development, differences in crystal polymorphs affect solubility, stability, and absorption, and have a significant bearing on formulation quality and development strategy. Missing polymorphs can lead to serious risks such as re-testing and delays in patent compliance. Especially in the early stages of development, polymorphs must be identified quickly from a limited amount of samples, and in many cases, large crystals cannot be obtained. Here, we introduce an example of single-crystal X-ray structure analysis in which multiple crystal polymorphs were analyzed from crystals several tens of micrometers in size.

Crystalline phase analysis

Analysis:	Active pharmaceutical ingredients
Use:	Pre-formulation (API)
Analyzed materials:	Tolbutamide
Analysis software:	CrysAlis ^{Pro}

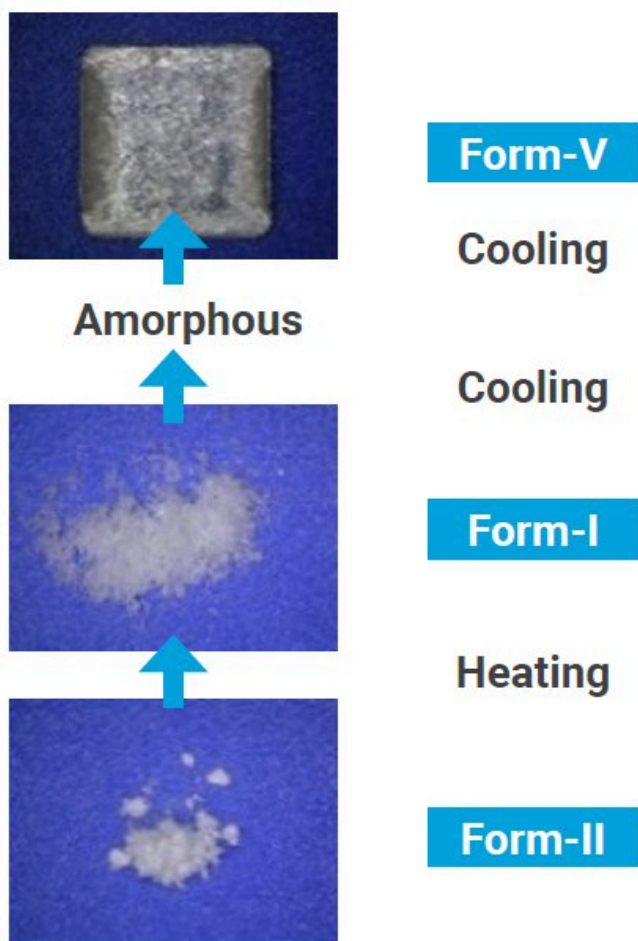


Figure 1: Phase transition

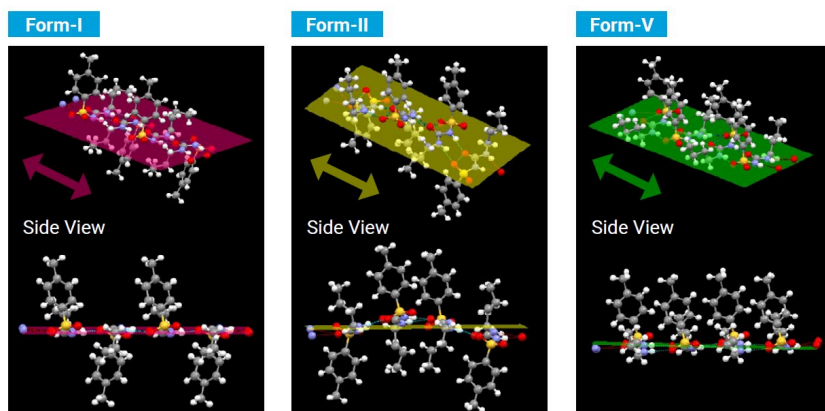


Figure 2: Crystal structure of each polymorph

Conclusion

While monitoring phase transition temperatures by DSC, Form I, II, and V of tolbutamide were prepared, and crystals with a size of several tens of micrometers were analyzed using XtaLAB Synergy-R (Figure 1). The differences in the molecular arrangement of each polymorph were clearly identified in a short time, demonstrating that polymorph evaluation is possible even with tiny crystals (Figure 2). This method is useful for identifying polymorphs in the early development stage, even when it is difficult to grow large single crystals, and for avoiding re-testing and patent risks.

Related products



XtaLAB Synergy-R

Our most popular diffractometer for Protein Crystallography, configured with a high-flux rotating anode X-ray source and an extremely low noise direct X-ray detection detector.



CrysAlis^{Pro}

User-inspired data collection and data processing software for small molecule and protein crystallography.