High-throughput Polymorph Screen of Cimetidine and Clarification of its Nomenclature

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Polymorphism evaluation as a part of preformulation studies of a candidate drug is a critical step in the drug development process. The progress of high-throughput experimentation in recent years has led to a significant reduction of the amount of time and the quantity of the active pharmaceutical ingredient needed to perform these studies. In order to investigate the effectiveness and efficiency of a rational high-throughput polymorph screen (HTPS) the compound cimetidine was used as a case study for the formation of its polymorphic forms under different crystallization conditions.

The characterization of the various forms that occurred after crystallization was realized by means of X-ray powder diffraction experiments, differential scanning calorimetry and thermogravimetric analysis. As it turned out the HTPS was an effective means for obtaining all of the commonly reported solid-state forms of cimetidine (A, B, C, D, M1) and led to the formation of a new solid form (F). An analysis of the results will be given and the influence of the various crystallization conditions on the formation of the various solid forms will be discussed.

In order to assess the obtained results a literature investigation was carried out revealing a large confusion with respect to the nomenclature of the various cimetidine forms. A general and unifying nomenclature is proposed and compared with the older literature.

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