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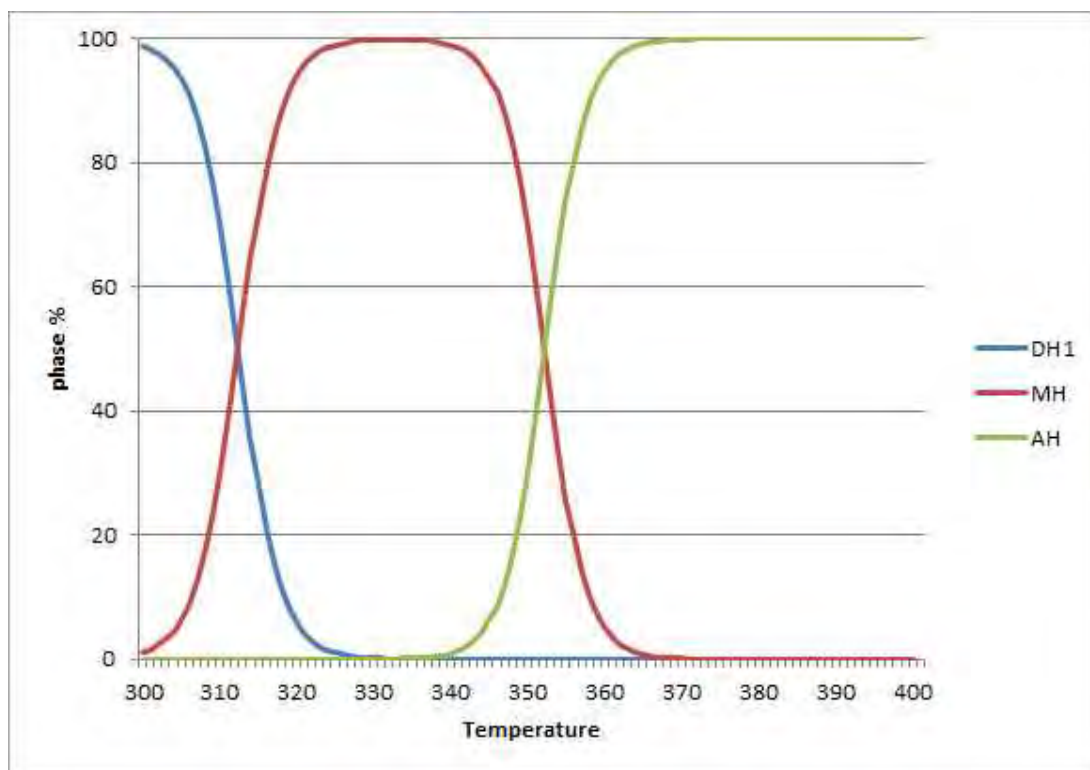
Parametric Rietveld refinement applied to dehydration of sodium naproxen

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The identification of the hydration and dehydration transformations of drugs is vital to establish stable pharmaceutical components. Our aim is to monitor the kinetics of hydration and dehydration processes in pharmaceutical solids, and to relate these to the molecular-level crystal structures. One of the primary tools to achieve this is parametric Rietveld refinement. The dehydration of two dihydrate polymorphs of the non-steroidal anti-inflammatory drug (NSAID) sodium naproxen was monitored using synchrotron powder X-ray diffraction measurements at Beamline I711, MAX IV Laboratory, Lund University. Diffraction patterns were measured in the range 300-400 K at 1 K increments. Both polymorphs dehydrate to form identical monohydrate then anhydrous phases. Independent Rietveld refinements were initially performed for each unique phase in order to establish initial values for the parametric refinement. The refinements were performed using TOPAS-Academic [1]. The structures are molecular and both dihydrate polymorphs display pseudosymmetry, thereby requiring an extensive set of restraints. One of the key advantages of the parametric Rietveld refinement is the possibility to introduce algebraic equations that describe the evolution of various parameters [2]. The kinetics of the dehydration processes were monitored using a sigmoid function applied to the scale factors of the various phases (see Figure). The evolution of the unit-cell parameters and atomic displacement parameters were also treated parametrically, and the influence of using multiple coordinate sets (one model per temperature) or a single common coordinate set for each phase was examined. One dihydrate polymorph shows a smooth and continuous transition to the monohydrate, whereas the other polymorph shows an abrupt transition. These differences are linked to the existence of topotactic or non-topotactic chemical transformations between the dihydrate polymorphs and the monohydrate phase.

[1] TOPAS-Academic Version 5, Alan Coelho, January 31, 2013., [2] G. W. Stinton, J. S. O. Evans, *J. Appl. Cryst.*, 2007, 40, 87-95.



Keywords: parametric Rietveld refinement, dehydration, kinetics