ESRF	**Experiment title:** Kinetics of dehydration of pharmaceutical hydrates and crystallization of anhydrate	**Experiment number**: SC-764
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Shifts: 3	**Local contact(s)**: Dr. Christian Riekel	*Received at ESRF:*

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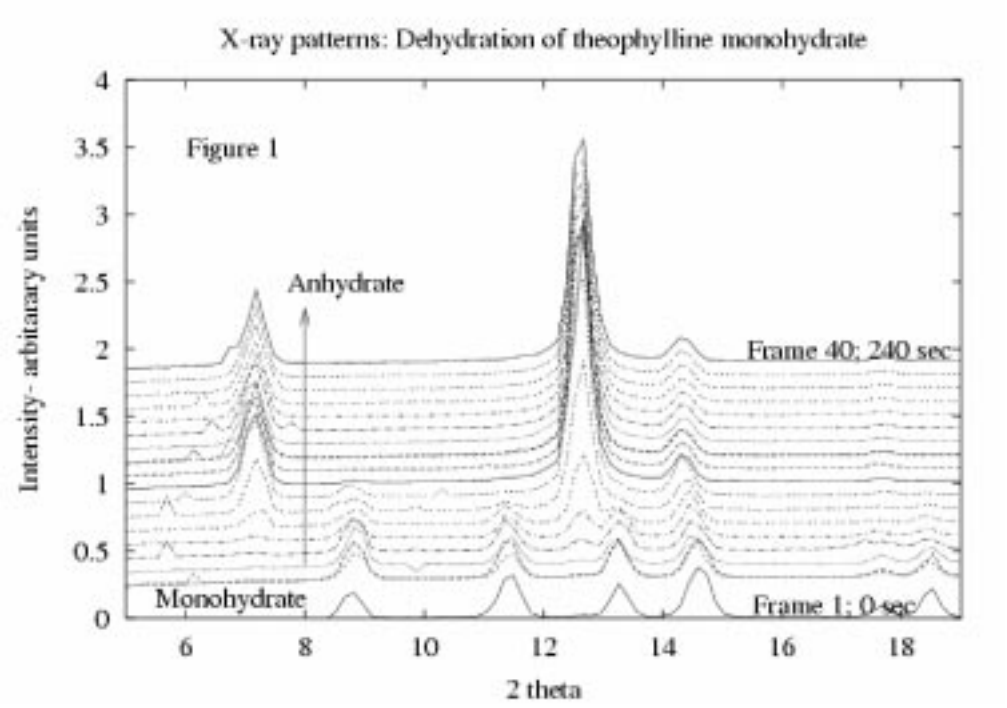
Report:

This report describes the application the time-resolved x-ray diffraction techniques to investigate (i) kinetics of dehydration of crystalline pharmaceutical hydrates and (ii) crystallisation of the amorphous anhydrate.

The temperature of a sample theophylline monohydrate was controlled by purpose built sample cell and two dimensional diffraction data was recorded every 5 seconds on a MAR CCD with one second exposure time while the temperatue of the sample was increased from room temperature to 90^{o}C. The 2D-diffraction data was converted to powder diffraction data format for the phase characterisation of the theophylline monohydrate. A typical thermally induced phase transition of theophylline monohydrate is shown in figure 1. It can be seen that the entire reaction is completed within 4 minutes, with significant changes in the crystal lattice occurring during the first 2 minutes of the reaction. Moreover, both the dehydration and the recrystallisation reactions occur simultaneously. The high brilliance of the ESRF and the availability of a fast electronic detector, meant that we were able to monitor both these

reactions simultaneously with a time resolution of a few seconds. It is important to emphasise that no other analytical technique is suitable for obtaining comparable information from such a rapid solid-state reaction.



The decrease in the concentration of the crystalline hydrate phase was quantified based on the intensity of the reflection at 2θ value of 8.8^{o} while the increase in the crystalline anhydrate was monitored from the variation in the intensity of the reflection at 2θ value 12.6^{o}, as shown in figure 2.

A parallel study of amorphous sucrose anhydrate demonstrated that above a crtitcal temperature of 110^{o}C the crystallisation rate was very fast and appeared to be insensitive to the temperature. One of the reasons for this could be the limitation of the time resolution of data collection. The crystallsation kinetics appear to be first order indicating crystallisation due to random nucleation rather than simple growth. Further simultaneous SAXS/WAXS experiments using the higher time-resolution of the Photonic Science detector are planned to resolve the effects of temperature on crystallisation.