Experimental Report

23/02/2015

Proposal:	**9-13-519**	**Council:**	10/2012
Title:	Investigation of the dehydration of trehalose dihydrate		

This proposal is a new proposal

Research Area: Soft condensed matter

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Samples: Trehalose C12H26O13

Instrument	Req. Days	All. Days	From	To
D19	6	5	15/07/2013	18/07/2013

Abstract:

The aim of this proposal is to investigate the role of water molecules within the kinetics and mechanisms of the dehydration of disaccharides used as pharmaceutical excipients; specifically: confirmation of the existence of transiently stable, partially hydrated states, and the identification of critical water occupancy fractions which separate crystal phases.

Experiment number: 9-13-519 **Instrument:** D19

Dates of experiment: 15 July 2013 to 18 July 2013

Title: Investigation of the dehydration of trehalose dihydrate

Experimental team (names and affiliation):

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1 Background

Trehalose has widespread industrial application within the food, pharmaceutical and cosmetic sectors. The trehalose system is polymorphic, and the most stable polymorph is the dihydrate ($T{\cdot}2H_2O$). However, on processing, the stability of $T{\cdot}2H_2O$ is threatened, due to the possibility of dehydration. The presence of free water within a product can cause detrimental effects, and causes substantial product destabilisation. Therefore, a scientific knowledge of the dehydration behaviour is imperative for the effective and efficient processing of $T{\cdot}2H_2O$.

Claims of a partially hydrated state of trehalose have been made from a previous study, from the observation of a two-step dehydration process [2]. A neutron diffraction study also reveals that the rehydration kinetics occur similarly as a two-step process [4]. The purpose of this study is to understand the role of water molecules within the dehydration event, and further investigate the possibility of a partially hydrated state.

2 Results

Time and temperature resolved neutron powder diffraction data of $T{\cdot}2H_2O$ were recorded using a 2D detector with a wavelength of 2.4 Å. The data was corrected for the detector response using a vanadium flood field. Dehydration was performed at temperatures of 90, 100, and 110°C, with an approximate sampling time of 2.5 minutes. An example of the time-resolved data is given in Figure 1.

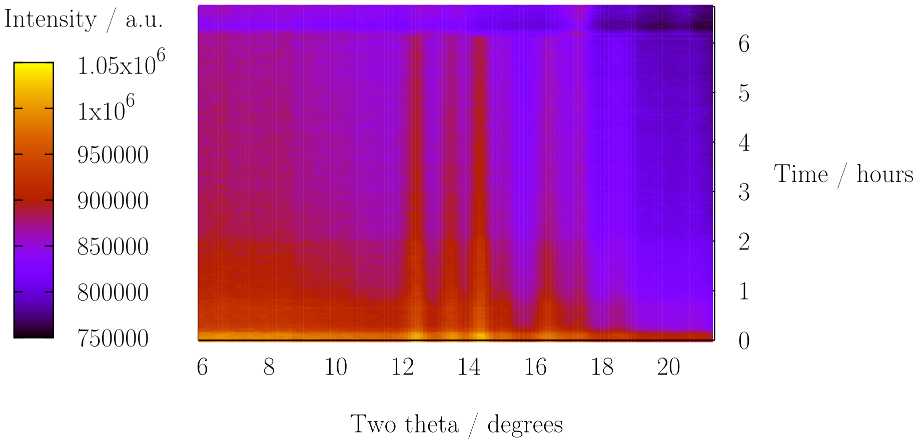

Figure 1: Time-resolved neutron diffraction data following the dehydration of trehalose dihydrate at 90°C. Data includes a heating ramp from 21°C to 90°C at times (t) $0 \leq t \leq 0.25$ hours. The sample remains at 90°C until t = 6 hours. After this time, the temperature is raised to 120°C to prompt dehydration.

Figure 1 shows that at 90°C, the dehydration is a prolonged process. Although the $T{\cdot}2H_2O$ lattice is present until the end of the 90°C conditioning, it is apparent that there is a distinct gradual decrease in the diffuse background scattering. Incoherent hydrogen scattering present within the background of neutron diffraction data can be used as a measure of the hydrogen content within the sample. This approach has been adopted within our data, and the hydrogen background has been fitted using a Gaussian function, in order to estimate the hydrogen content as a function of time, throughout the course of dehydration.

The decreasing behaviour of the hydrogen background is found to mimic that of the total sum of detector counts, indicating that the sampling volume is decreasing, as expected during water removal. The magnitude of the change in the hydrogen background is found to be approximately 12.9%, which is reasonably close to the exact water content of 9.52% in T·2H_2O [2]. As such, it is considered reasonable to associate the change in the hydrogen background with the water content of the sample. Therefore, the integrated intensity of the hydrogen background has been scaled so that it varies between 1 (representing total water occupancy) and 0 (representing anhydrous lattice/zero water occupancy).

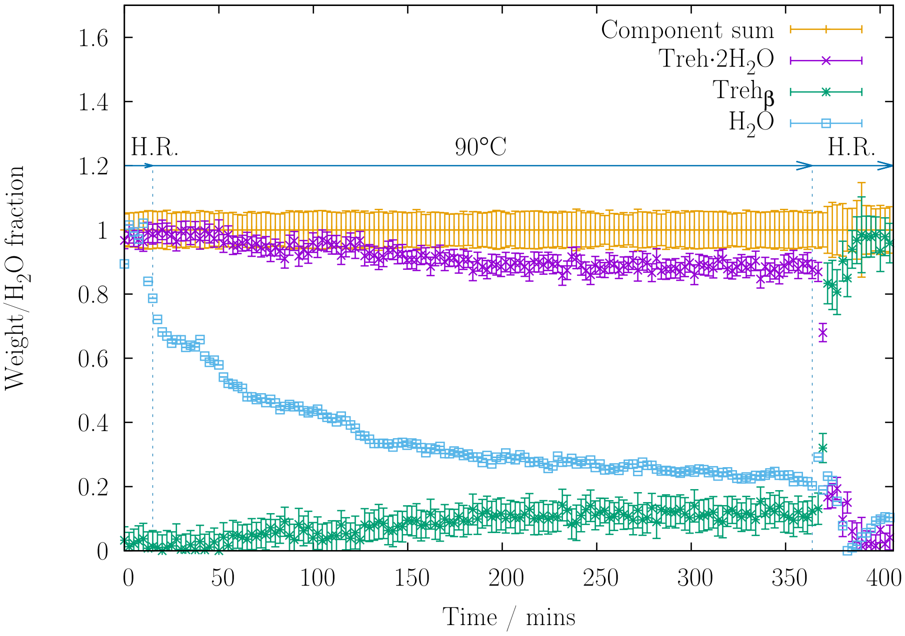

Figure 2: Quantitative phase analysis (QPA) of the thermal dehydration at 90°C of trehalose dihydrate (Treh·2H_2O) to form anhydrous beta trehalose (Treh$_\beta$). Water content (H_2O) of the sample is also shown from the fitting of the diffuse hydrogen scattering. Some portions of data have been collected over heating ramps (H.R.) as shown. Initially, the sample is heated from 21°C to 90°C, and finally, heated from 90°C to 120°C.

Quantitative phase analysis (QPA) has been performed through Rietveld refinement within the General Structure and Analysis System (GSAS) [1, 5]. The QPA for the 90°C dataset is given in Figure 2, and the water volume fraction is also plotted. From this analysis, it is evident that the water content, and the crystalline weight fraction of T·2H_2O are decoupled quantities, i.e. the T·2H_2O lattice can remain stable despite substantial water loss. Furthermore, nearing the end of the 90°C treatment, the water content appears to be approaching a plateau, suggesting convergence to a fractional water occupancy with an associated stability. Due to time constraints, the sample temperature is raised to prompt dehydration. As such, the longevity of the partially hydrated phase (at around 20% H_2O) at 90°C is unknown. Although further testing is required to evaluate the stability of the phase, the results provide clear, supporting evidence of a partially hydrated state of trehalose.

The decoupling between phase fraction and water content is a common feature at each tested dehydration temperature (data not shown). This demonstrates that the passage through the partially hydrated state could be the typical dehydration response of T·2H_2O. We are in the process of comparing the neutron diffraction data with x-ray data, to further the understanding of the dehydration mechanism, and build a comprehensive study of the transition.

This study demonstrates the effectiveness of exploiting the incoherent hydrogen scattering in the measure of the sample water content, resulting in a technique which has similar outcomes to TGA/DTA. Combining these methods with QPA through Rietveld refinement has shown that the T·2H_2O structure does not collapse on the release of water molecules, revealing further evidence of a partially hydrated state of trehalose. In all, the study exposes the diversity of the D19 beamline in the study of powder samples through the use of whole pattern fitting methods, and the developed techniques could be applied to explore the dehydration event in other hydrogenated species.

References

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[2] Sussich F, Princivalle F, Cesaro A. The interplay of the rate of water removal in the dehydration of α,α-trehalose. Carbohyd Res. 1999; 322(1): 113-119.

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[5] Toby BH. EXPGUI, a graphical user interface for GSAS. J Appl Cryst. 2001; 34: 210-213.