DEHYDRATION AND RE-HYDRATION OF TREHALOSE STUDIED BY HUMIDITY CONTROLLED SIMULTANEOUS MEASURING INSTRUMENT FOR X-RAY DIFFRACTOMETRY AND DIFFERENTIAL SCANNING CALORIMETRY(XRD-DSC)

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Pharmaceutical hydrates, the most popular substances of pharmaceutical solvates, have different physical properties, stability and bioavailability from those of anhydrates. In recent years pharmaceuticals under development tend to have larger molecular weights and to be more sensitive to humidity. Therefore the study on hydration, dehydration and re-hydration process of pharmaceuticals and related compounds, and their polymorphic changes under various temperature and humidity conditions have essential importance. These experiments, however, are laborious tasks even at present. We have developed a humidity controlled simultaneous measuring instrument for XRD and DSC which allows to measure from -40 to 350°C and in the humidity range of dry to 90%RH at 60°C. This instrument allows rapid measurements to clarify the above mentioned behavior under various temperature and humidity conditions with 5-10mg sample without taking out the sample from the DSC chamber.

The dehydration behavior and polymorphic phase change at elevated temperature in high humidity conditions such as 75%RH at 45°C are sometimes different from those measured in dry or low humidity conditions. Here we will show the dehydration and re-hydration behavior after dehydration of α,α-trehalose dihydrate, a non-reducing disaccharide, in various humidity conditions as examples of the application of the humidity controlled XRD-DSC. Results show that the dehydration in dry nitrogen atmosphere yields a mixture of amorphous and intermediate phase of anhydrate followed by the formation of complete amorphous phase. Around an exo-thermic DSC peak at 175-200°C this amorphous phase changes into a crystalline anhydrate, then begins to melt at 210°C. On the other hand, the dehydration in a high humidity condition such as 77%RH at 55°C gives a well crystallized anhydrate at 110°C. It was also revealed that the speed and the water vapor pressure required for the re-hydration after the dehydration depend on the vapor pressure during the dehydration.