Characterization of Water of Hydration of Pharmaceuticals Using the Pyris 6 DSC

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INTRODUCTION

One important aspect of pharmaceuticals is the water(s) contained in the material. The amount of water is important as it can be related to the product shelf lifetime as well as the tablet properties.

The water contained in pharmaceutical materials can be free or bound. Free water refers to water that is absorbed from the environment and is not chemically attached to the material. Bound water refers to water(s) of hydration that are chemically bound to the substance. Bound waters will have a significant affect on the molecular structure and physical appearance (e.g., color) of the material.

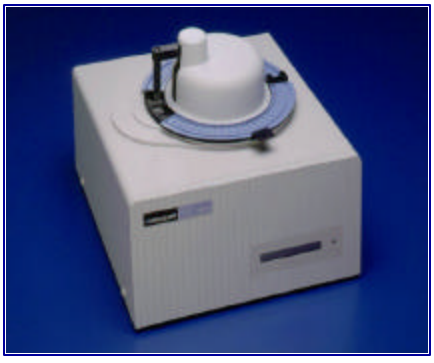
It is desired to have an easy to use test to characterize the properties associated with the waters in a pharmaceutical material. One of the most commonly used techniques for assessing the properties of waters in pharmaceuticals and foods is TGA (thermogravimetric analysis). With TGA, a 'wet' sample or a sample containing bound waters is heated and the resulting mass loss, due to water loss, is quantitatively measured. The PerkinElmer Pyris 1 TGA with its automated sample pan puncturing accessory (Accupik) is ideal for the study of free and bound waters in pharmaceuticals and foods. The high sensitivity of the Pyris 1 TGA allows even minute quantities of water to be accurately measured. In addition, the Accupik accessory provides the highest possible quality results on 'wet' pharmaceuticals or on materials that need to be kept dry until analysis.

An additional means of characterizing hydrated pharmaceuticals materials is DSC, differential scanning calorimetry.

DIFFERENTIAL SCANNING CALORIMETRY

DSC measures heat flow into or from a sample under heating, cooling or isothermal conditions. The PerkinElmer Pyris 6 DSC is a heat flux DSC instrument which offers high performance in terms of:

- Baseline stability
- Resolution
- Sensitivity
- Autosampler operation
- Built-in purge gas switching accessory and flow rate control



With its outstanding baseline stability, resolution and sensitivity, the Pyris 6 DSC instrument is ideal for the characterization of the waters of hydration associated with pharmaceutical materials. The high degree of resolution provided by the Pyris 6 DSC ensures that the waters of hydration are separated or resolved for the best characterization information.

EXPERIMENTAL

In this study, the thermal properties of copper sulfate pentahydrate, lactose monohydrate and epsom salt were measured using the Pyris 6 DSC instrument. The following experimental conditions were used.

Experimental Conditions

Instrument	Pyris 6 DSC
Thermal Program	Heat from room temperature at 10 C/min
Sample mass	Approximately 4 mg
Sample pan	30 µL aluminum holes with holes (BO14-6644)
Purge gas	nitrogen

PerkinElmer™ instruments.

The Pyris 6 DSC was calibrated for temperature and heat flow responses using high purity indium and tin standards.

RESULTS

Displayed in Figure 1 are the DSC results obtained by heating a sample of CuSO4•5H2O at a rate of 10 C/min with the Pyris 6 DSC. Copper sulfate pentahydrate gives off its waters in the follow relative sequence: 2-2-1. The Pyris 6 DSC yields excellent, well-resolved dehydration endothermic peaks. In particular, the temperature difference between the dehydrations for the first two sets of waters is not very much (about 30 C). A DSC instrument with a high degree of resolution, such as the Pyris 6 DSC, is required to separate out the two dehydration peaks at 87 and 116 C. The temperatures at which de-hydration occur provides valuable information as to the thermal stability of the hydrates.

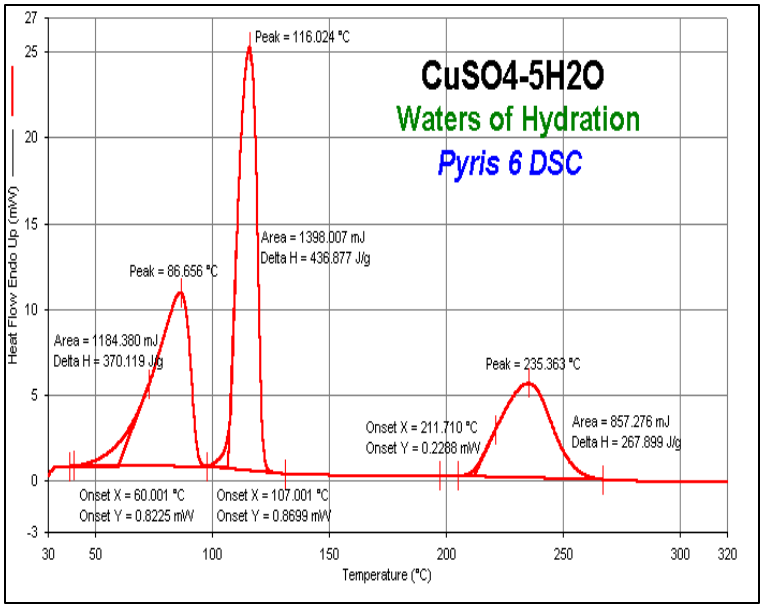


Figure 1. DSC results on dehydration of copper sulfate pentahydrate

A sample of lactose monohydrate was analyzed for its dehydration properties using the Pyris 6 DSC. Lactose is a very common excipient used in pharma-ceutical tablets. The lactose monohydrate loses its water with a well-defined endothermic peak at 144 C (onset temperature). Upon further heating, the lactose sample undergoes sublimation and this is observed as another endothermic peak with an onset temperature of 211 C. The Pyris 6 DSC provides valuable dehydration and thermal stability information on the lactose excipient material.

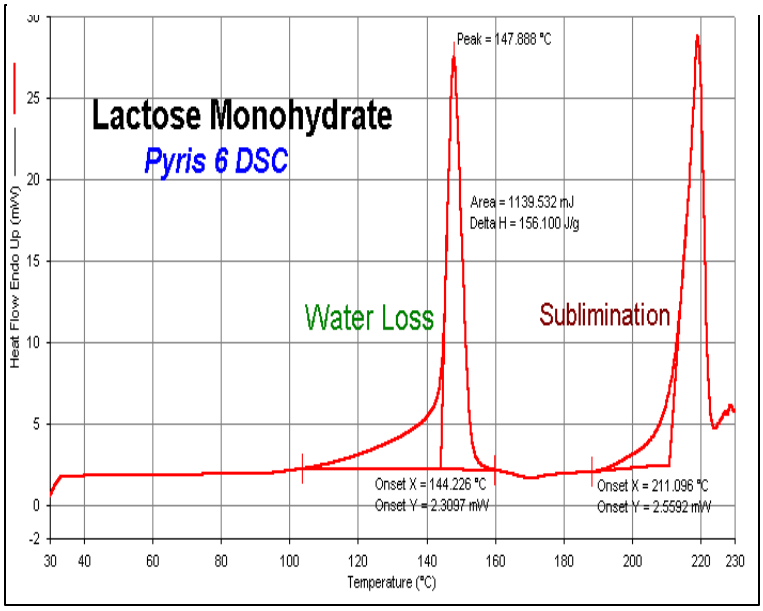


Figure 2. DSC results for dehydration and sublimation of lactose monohydrate

A sample of epsom salt (hydrated magnesium sulfate) was characterized to examine its multiple dehydration transitions. Epsom salt is MgSO4• 7H2O and several dehydration events will be observed on a high performance DSC instrument. Displayed in Figure 3 are the DSC results generated on the sample of epsom salt.

PerkinElmer™ instruments.

These results demonstrate the outstanding ability of the Pyris 6 DSC to yield high resolution and to separate out the multiple dehydration transitions associated with epsom salt.

SUMMARY

Thermal analysis provides valuable characterization information on the hydrates associated with pharmaceutical materials. Knowledge of the evolution of the water from a pharmaceutical material is important as this is related to production of a tablet as well as shelf lifetime of the final product.

The successful characterization of the waters associated with a pharmaceutical material requires a DSC instrument with high resolution and high sensitivity. The Pyris 6 DSC meets both of these requirements and provides outstanding results on the dehydration of pharmaceutical materials.

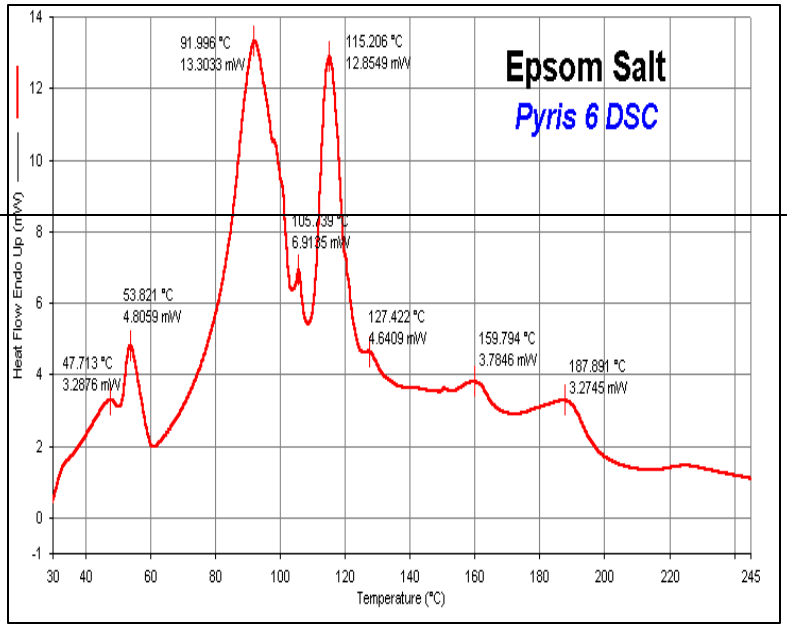


Figure 3. DSC results of multiple dehydration steps for epsom salt (magnesium sulfate heptahydrate)

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