APPLICATION NOTE

Thermal Analysis

Better Characterization of Water in Pharmaceuticals Using the Pyris 1 TGA Accupik Accessory

Introduction

One important aspect associated with many pharmaceutical materials is the water content. Moisture, in the form of free water or hydrate(s) (chemically bound) will affect the properties of the pharmaceutical material including: thermal stabilities, shelf life, plasticizing effects on the glass transition event (Tg), sticking and clumpiness, and the rate of dissolution.

Thermogravimetric analysis (TGA) provides a useful means of characterizing and quantifying the moisture content in pharmaceutical materials. The technique measures sample mass loss and the rate of weight loss as a function of temperature or time. TGA applications for pharmaceutical moisture assessment include:

- Measuring the temperature of dehydration
- Stoichiometry of a hydrate
- Quantification of the amount of hydrate phase in a bulk sample
- Construction of the stability diagram of the hydrate systems as a function of temperature and water vapor pressure
- Dehydration/hydration kinetics

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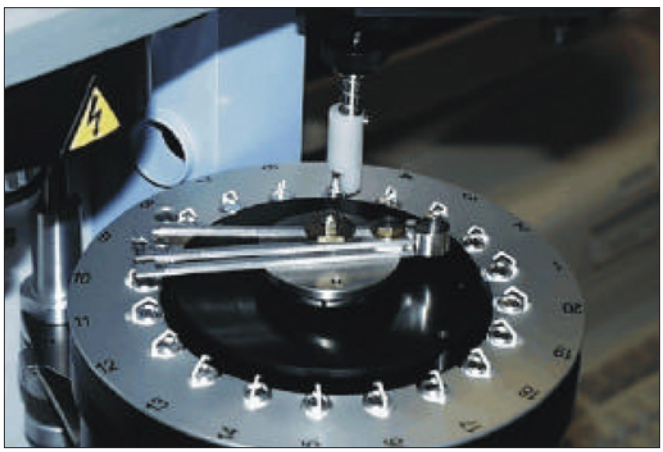
Hydrate and moisture studies can sometimes be difficult to accurately study using TGA, especially when using an autosampler, as the 'wet' samples can tend to dry out when sitting in a queue. The loss of moisture can lead to 'skin' effects due to surface drying of the sample before analysis. Another problem is that dried or desiccated samples can pick up ambient moisture when sitting in a humid environment waiting for analysis. One solution for both of these sample moisture loss or gain problems is to place the sample in a sealed container. However, in order to allow the sample to lose weight during the TGA experiment, the pan must have an opening to permit the unencumbered evolution of volatiles. This can be accomplished using a device, which will puncture a sealed container immediately before the analysis. This is now possible with the *Accupik* accessory (N5370430) offered by PerkinElmer in conjunction with the state-of-the-art Pyris® 1 TGA.

The Accupik accessory will automatically pierce the sealed sample containers immediately before the given sample is analyzed by the Pyris 1 TGA. This ensures that the pharmaceutical material will remain in its desired moisture state without losing or gaining weight due to ambient effects, as the sample sits in the autosampler queue. This provides significantly more accurate volatiles information on pharmaceutical materials and prevents the need to rush the analysis. The Accupik accessory would also provide more accurate compositional information on highly volatile formulations containing alcohol, such as cough syrups or cold medications since the volatile alcohol component would be contained in the sealed pan.

The Accupik automated puncturing accessory is displayed here with the Pyris 1 TGA autosampler:



Pyris 1 TGA Accupik accessory.

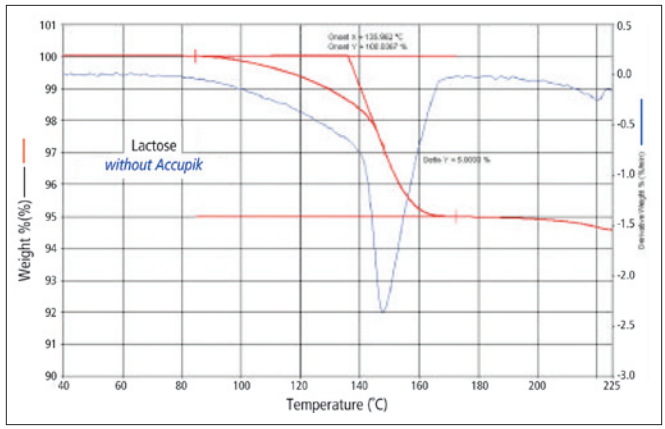


Figure 1. TGA results on lactose hydrate sample without Accupik accessory.

The autosampler tray is rotated and the sample pan is automatically pierced immediately prior to the experiment with the Accupik accessory.

In addition to the Accupik accessory, the Pyris 1 TGA offers many other valuable features:

- Low mass, ultra-light balance for ultra-low noise and outstanding sensitivity
- Separate thermostatically controlled temperature environment of balance to provide highest possible stability
- Iris shutter assembly to isolate balance chamber from sample/furnace
- Automated ion stream to eliminate troublesome static effects
- High performance heat/sensor furnace technology
- Reduced furnace volume for more efficient switching of purge gases and elimination of oxygen during pyrolysis
- 20 position, autosampler accessory for reliable, unattended operation
- Accupik accessory for better handling of volatile samples without uncontrolled and unmeasured weight loss while waiting to run

Results on Lactose Hydrate

To demonstrate the ability of the Pyris 1 TGA with Accupik to provide better results on pharmaceutical hydrate materials, the water loss properties of a sample of lactose were analyzed with and without the Accupik accessory.

Displayed in Figure 1 are the TGA results obtained without the use of the Accupik accessory. The lactose sample was heated at a rate/min of 10 ˚C in a standard, open sample container under a nitrogen purge. The plot shows the percent mass and the derivative, or rate of mass loss (d%/dt) as a function of sample temperature. The derivative is a particularly sensitive indicator of a given transition's resolution.

The sample loses mass over a broad temperature region between 90 and 150 ˚C as the water of hydration is evolved. It should be noted that the derivative trace clearly shows that the water loss is not well-defined as reflected by the occurrence of a low temperature shoulder in the derivative trace.

Displayed in Figure 2 are the TGA generated on the lactose hydrate obtained with the use of the Accupik accessory where the sealed sample container is pierced just before the experiment.

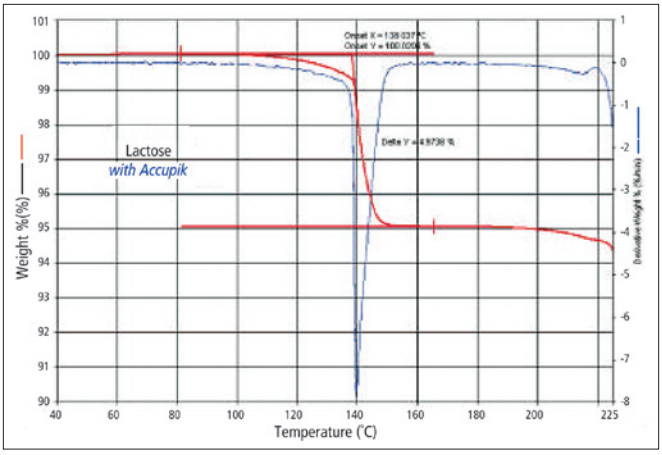


Figure 2. TGA results obtained on lactose hydrate sample with Accupik accessory.

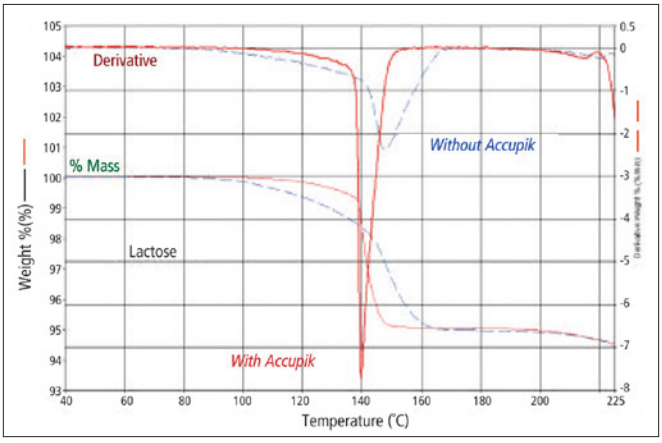


Figure 3. Overlay of TGA results obtained on lactose hydrate with and without Accupik accessory.

These results demonstrate the significant improvement that is obtained on the lactose hydrate weight loss with the use of the Accupik accessory. The moisture in the sealed container remains confined until just prior to the experiment, when the pan is automatically punctured and loaded. Additionally, the small hole that is obtained in the sample pan lid from the Accupik accessory provides for more controlled evolution of volatiles, and retards interfering processes such as sublimation.

The mass loss due to the loss of the water of hydration of lactose is much more well-defined with the use of the Accupik accessory. The derivative peak is very sharp and narrow reflecting the desired high resolution of the hydration transition. No low temperature shoulder is observed in the derivative trace with the Accupik accessory and this indicates that the water comes off in a single, well-defined weight loss step. The shape of the mass loss event with Accupik is more like a step as compared to a diffuse, rounded weight loss seen in Figure 1. This provides a more accurate assessment of the temperature associated with the water loss.

Displayed in Figure 3 is a direct overlay of the TGA results obtained on the lactose hydrate sample with and without the use of the Accupik accessory.

These results demonstrate that the Accupik accessory does provide the much better defined and higher resolution weight loss associated with the evolution of the water of hydration. The sharper weight loss (onset) transition provides for a more accurate hydrate stability temperature and this is important for the proper characterization of pharmaceutical hydrate materials.

Summary

The Accupik accessory featured with the state-of-the-art PerkinElmer Pyris 1 TGA provides enhanced results on ‘wet’ or hydrated pharmaceutical materials. The Accupik device allows for a hydrated sample to be completely sealed and thus retain its moisture (or to keep moisture out) until just prior to the experiment. The Accupik accessory in conjunction with the Pyris 1 autosampler will automatically puncture the pan with a small pinhole before the sample is analyzed. Moisture sensitive materials can remain in a queue without moisture loss or gain with the Accupik accessory. The use of the Accupik device provides a sharper and higher resolution weight loss transition associated with hydrated materials as compared to running the samples in a standard (open) TGA pan.

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