Amorphous Lactose Studied by Rapid Heat-Cool DSC

Introduction

As a technique, interest has been growing in performing differential scanning calorimetry (DSC) at higher than typical (10 °C/min) temperature-scanning rates. This is because a variety of material characterization challenges exist that can benefit dramatically from rapid heating or cooling rate experiments. For example, the investigation of metastable states and time-dependent transitions would profit greatly from fast scanning rates. In general, higher scanning rates will also increase the heat flow sensitivity for subtle transitions although this benefit is usually tempered by the small mass requirement of the rapid scanning rates.

A DSC has been designed specifically for operation at high scanning rates – up to 2000 °C/min in heating with similarly high cooling rates.[1] Key technologies introduced by TA Instruments are essential to, and have been incorporated into the instrument known as Project RHC. For example, Tzero technology improves the resolution and the sensitivity of the measured sample heat flow rates, especially for very weak effects, and improves the instrument baseline. Also, infrared heating, introduced in the Q5000IR TGA, provides a "massless" infrared heat source. Readers interested in further details on the instrument design should refer to reference 1.

This applications note reports on the study of amorphous lactose by rapid heat-cool DSC.

Results and Discussion

The processing of pharmaceutical materials is known to introduce small amounts of amorphous material, which can dramatically affect product stability, compatibility, processing and storage. It is thus critical that pharmaceutical scientists have the ability to accurately and precisely measure amorphous content, particularly at low levels, a task, which can be challenging. Synthetic techniques often result in variations to morphological structure. Further, when crystalline compounds are exposed to mechanical stresses from processes such as grinding and micronization, disturbances can occur in their structure due to the creation of amorphous regions. The physical properties of amorphous structure are quite different from crystalline structure, and can affect the mechanical (flow), physical (solubility), chemical (stability), and pharmacological (bioavailability) properties of the powder. It is thus critical to verify if a drug or drug delivery system has an amorphous component and to quantify the amount.

The most common measurement of amorphous structure involves the analysis of the glass transition by DSC. It is important to examine both the size of the transition in heat flow or heat capacity units and the temperature (T_g) at which it occurs. The size of the transition provides quantitative information about the amount of amorphous structure in the sample, and the temperature identifies the point where there is a dramatic change in physical properties.

Lactose is a semi-crystalline material that is often used as an excipient in pharmaceutical drugs. Amorphous lactose has the ability to spontaneously crystallize if exposed to the proper humidity. Because of this instability, it is critical to be able to

detect and quantify the amount of amorphous material in lactose. Figure 1 shows an overlay of numerous DSC scans from 50 to 2000 °C/min. At each rate, excellent detection of the glass transition is obtained. Previous authors report Tg of pharmaceuticals measured at 500 °C/min results in Limit of Detection (LOD) of <1% amorphous content for lactose[1-3]. With the increased scanning rate of the Project RHC DSC of up to 2000 °C/min a roughly 4x increase in the LOD can be expected.

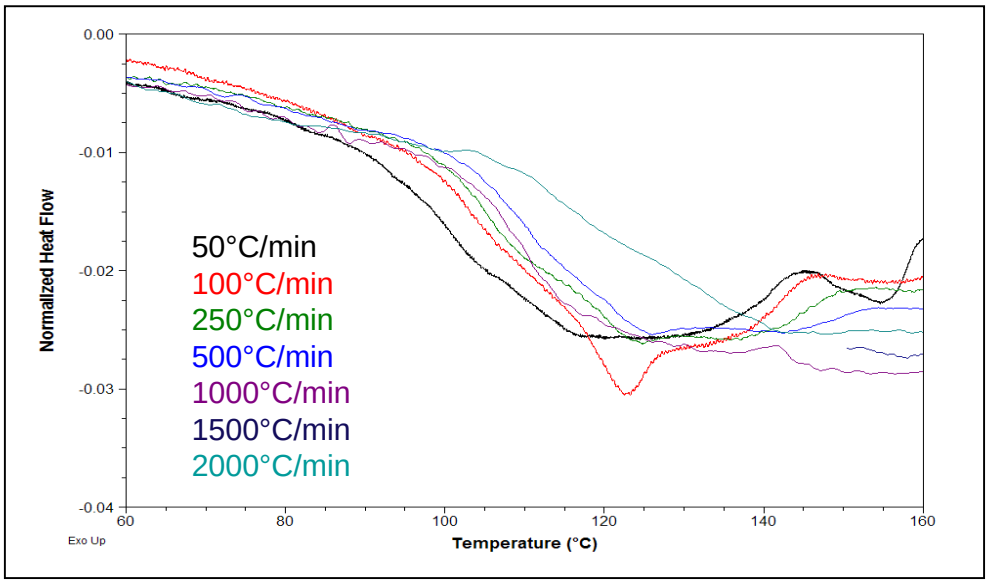

Figure 1 – The glass transition of amorphous lactose detected at rates up to 2000 °C/min.

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