Dynamic Vapor Sorption Characterization of Pharmaceutical Recrystallization

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INTRODUCTION

Materials exist in either amorphous or crystalline forms. Because the processing and end-use properties associated with those two forms are different, it is important to know which form is present, as well as the conditions where conversion of the amorphous to crystalline form occurs. Water, acting as a plasticizer, is one of the factors that affect this conversion. Dynamic vapor sorption (DVS) can be used to detect and study the glass transition and water-induced recrystallization.

EXPERIMENTAL

In DVS measurements, humidity is stepped, ramped, or maintained constant while the material is held at a constant temperature. Stepped and ramped humidity experiments provide information about adsorption / desorption properties of materials over a broad humidity range, and are valuable for determining if the material is amorphous or crystalline and where the glass transition occurs. Once the glass transition conditions are defined, constant temperature / humidity experiments provide additional insights into the recrystallization process and kinetics.

RESULTS and DISCUSSION

Figure 1 is the DVS weight change profile for amorphous lactose obtained while increasing humidity (0.1 %RH/min) at 25 °C. Initially, only surface adsorption occurs but upon reaching the glass transition, molecular mobility increases allowing bulk water absorption to occur. The resultant change in water adsorption rate creates an inflection in the adsorption profile, which is generally designated as the glass transition. As the percent relative humidity increases further, the material starts to rearrange to its more stable crystalline form, at which point the weight change decreases, since the crystalline form has a lower affinity for water than the amorphous form.

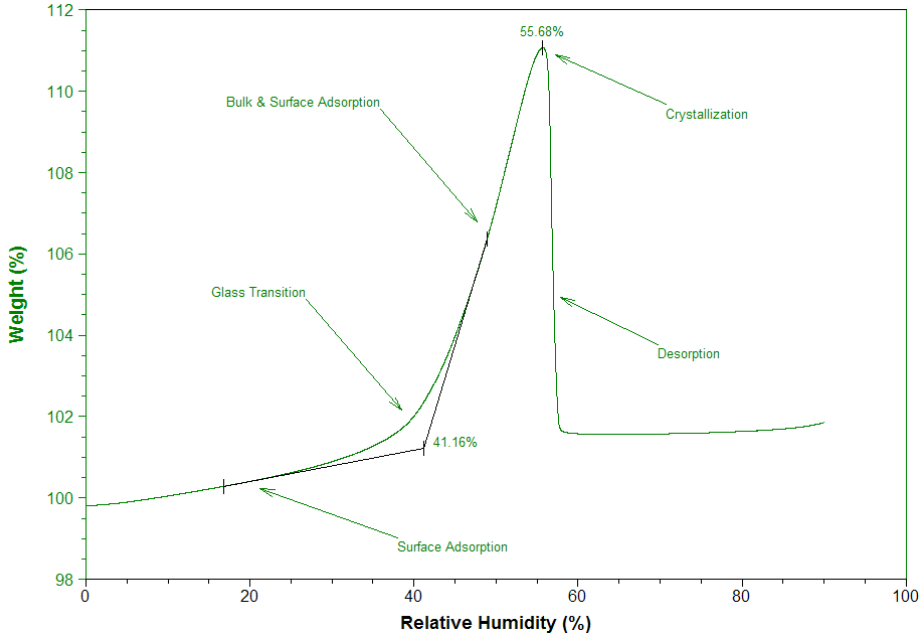

Figure 1. Effect of Increasing Humidity on Amorphous Lactose at 25 °C

Figure 2 shows the constant humidity results for amorphous lactose at between 30 and 58 %RH respectively. Initially, the weight changes fairly rapidly when the relative humidity is stepped from 0 to 55 %RH due to bulk absorption by the amorphous form. With additional time, however, the weight gradually decreases as the structure changes from amorphous to crystalline. The weight finally equilibrates at a level equivalent to that observed for crystalline lactose at 55 %RH and 25 °C. Increasing or decreasing humidity at that point yields only minor weight changes as expected for the fully crystalline material.

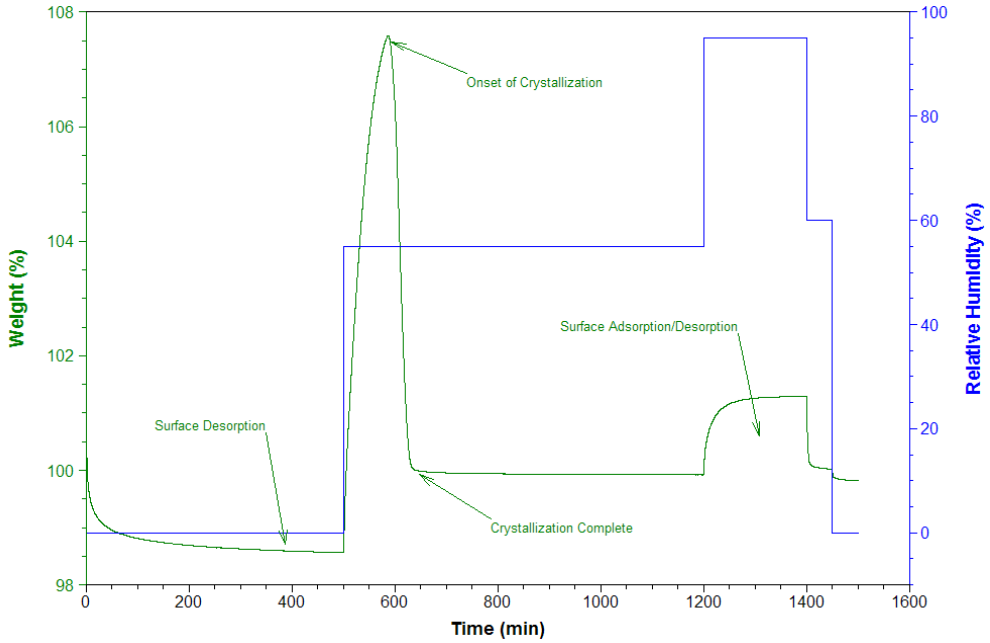

Figure 2. Water-Induced Crystallization of Amorphous Lactose at 25 °C & 55 %RH

Repeating the experiment shown in Figure 2 at several different humidities above the "critical" %RH where the glass transition occurs, and focusing on the region where recrystallization occurs, yields a plot like that in Figure 3. [Note: the x-axis has been normalized so that the onset of recrystallization for each experiment has been shifted to time zero, and the Y-axis has been normalized to reflect the amorphous fraction present. The amorphous fraction in all cases is assumed to be 1.0 at time zero and 0 after recrystallization.] At 55 and 60 %RH, the recrystallization process is a rapid single step process, while at 50 %RH, the process takes longer and appears to contain discreet regions of water uptake.

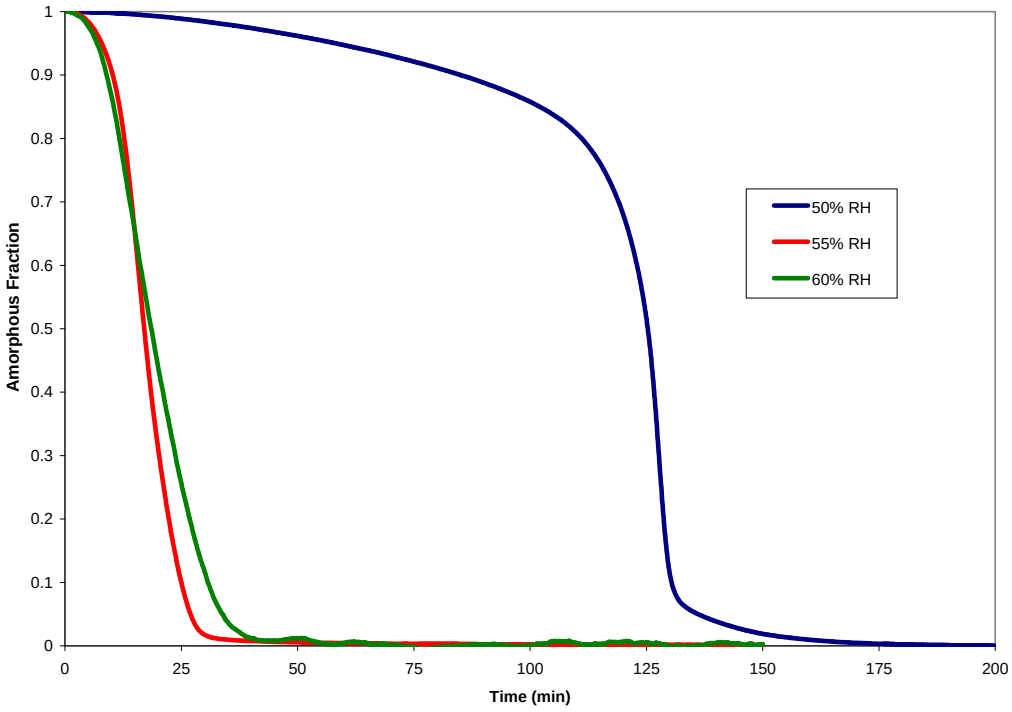

Figure 3. Effect of Relative Humidity on Crystallization of Amorphous Lactose at 25 °C

Similar recrystallization curves are obtained if the humidity is held constant at a value above 30 but below 58 %RH (in the case shown in Figure 4 at 51 %RH) and temperature is varied. At temperatures above 25 °C, the recrystallization occurs in a single rapid step, while at lower temperatures, an apparent more complex profile is observed similar to that seen at 25 °C and lower humidities. This data could indicate that the recrystallization process is different depending on the temperature / humidity combination used, or it may be the result of "poorer resolution" of this DVS experiment when the conditions chosen accelerate the recrystallization process. In the case of lactose, kinetic treatment of this DVS data does not provide an explanation for the apparent single-step versus complex behavior.

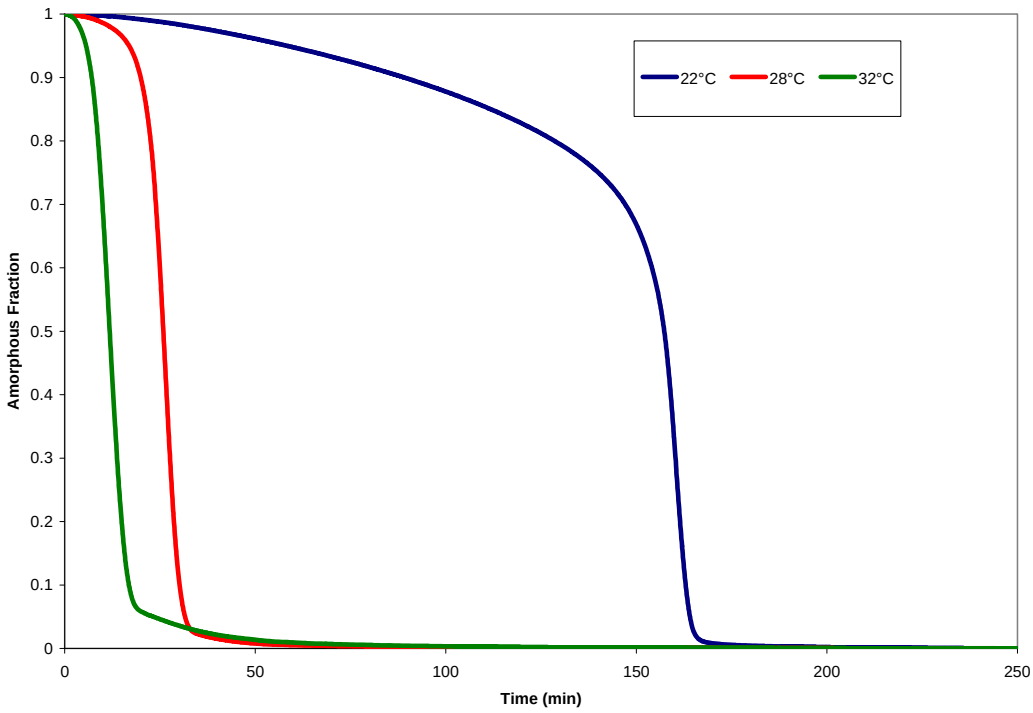

Figure 4. Effect of Temperature on Crystallization of Amorphous Lactose at 51% RH

SUMMARY

Dynamic vapor sorption is a versatile technique for evaluating water adsorption / desorption and related morphology changes in materials, including amorphous to crystalline structural changes.

KEY WORDS

Dynamic vapor sorption, DVS, Adsorption, Desorption, Amorphous, Crystalline

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