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DETERMINATION OF AMORPHOUS CONTENT BY DVS

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Amorphous materials in pharmaceutical formulations yield complex and challenging problems concerning the performance, processing, and storage of these products. For these reasons, fully characterising the amorphous state is crucial.
Dynamic gravimetric vapour sorption (DVS) is a well-established method for the determination of water and organic vapour sorption isotherms. It is based on a highly sensitive gravimetric system, which measures the adsorption and desorption of extremely small amounts of probe molecule. Water vapor can act as a plasticizing agent in amorphous materials, thus lowering the glass transition temperature below room temperatures. Additional water sorption can lead to a crystallization event below the glass transition temperature.
In the current studies water sorption experiments were performed to determine the glass transition as well as the exact onset relative humidity that will cause amorphous sugars to recrystallise. These experiments were combined with *in-situ* video microscopy to correlate features in the moisture sorption profile with visible changes in the sample.
Spray-dried amorphous lactose was chosen as a model sugar and exposed to a linearly ramped humidity profile from 0% to 90% RH. At a critical RH, the amorphous lactose passes through the glass transition due to the plasticizing effect of water. As amorphous lactose passes through the glass transition, it recyrstallizes to form lactose monohydrate, as indicated by the sharp change in vapour sorption capacity. This was performed for a series of ramping rates. A clear relationship exists between the onset glass transition RH and the RH ramping rate, allowing extrapolation to a ramping rate of zero, or the sample's inherent glass transition RH. For this lactose sample at 25.0 C, the inherent glass transition RH was 29.8% and the recrystallisation onset at 58%RH. Moisture sorption experiments coupled with *in*-situ video microscopy collected i*n-situ* during the ramping experiments support the physical changes indicated by the moisture sorption profile. Glass transition and crystallization RH values were also measured at 5, 15, 25, 35, and 45 °C on a spray-dried salbutamol sulfate sample. The glass transition RH values for the salbutamol sulfate sample ranged from 64.5% RH (5 °C) to 32.8% RH (45 °C) while the crystallization RH values ranged from 81.0% RH (5 °C) to 50.4% RH (45 °C). The results clearly show that the glass transition and crystallisation humidity values decrease as the sample temperature increases.

Keywords: amorphous materials, glass transition, moisture sorption

D.J. Burnett, F. Thielmann, J. Booth, "Determining the critical relative humidity for moisture-induced phase transitions", *International Journal of Pharmaceutics* **287** (2004) 123–133.