Characterizing the Amorphous State in a Pharmaceutical Powder Using an Automatic Moisture and Organic Vapor Sorption Analyzer

Dan Burnett, Frank Thielmann, Daryl Williams

Surface Measurement Systems, 3 Warple Mews, Warple Way, London W3 0RF

Purpose. Amorphous materials in pharmaceutical formulations yield complex and challenging problems concerning the performance, processing, and storage of these products. The presence of amorphous materials can be wanted or unwanted, depending on the desired or undesired unique properties of the amorphous phase. For these reasons, fully characterizing the amorphous state is critical in the formulation of pharmaceutical powders.

Methods. Dynamic Vapor Sorption (DVS) is a well-established method for the determination of vapor sorption isotherms. It is based on a highly sensitive gravimetric system, which measures the adsorption and desorption of extremely small amounts of probe molecule. In the current studies both water and octane vapor uptakes were collected on a lactose sample with various concentrations of amorphous material. (i) Water sorption experiments were performed to determine the exact onset relative humidity that will cause amorphous lactose to recrystallize. These experiments were combined with *in-situ* video microscopy to correlate features in the moisture sorption profile with visible changes in the sample. (ii) Octane vapor sorption experiments were performed to quantify low levels (below 1%) of amorphous contents.

Results. (i) Amorphous lactose was 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 vapor 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 58.0% RH. Images collected i*n-situ* during the ramping experiments support the physical changes indicated by the moisture sorption profile. (ii) Octane vapor isotherms were collected for a series of known mixtures of 100% amorphous and 100% crystalline lactose. The amorphous material has a significantly higher octane vapor sorption capacity. The octane vapor uptake at 0.95 p/po scales with the amount of amorphous material. The physical mixtures were used to generate a correlation curve to determine unknown amorphous contents. The linearity of the correlation and the error bars in the measurement indicate that amorphous contents can be determined down to +/- 0.3%.

Conclusions. (i) Moisture sorption experiments coupled with *in*-situ video microscopy characterized the water-induced recrystallization of amorphous lactose. (ii) The differences in octane vapor uptake between the amorphous and crystalline materials allow the determination of amorphous contents down to +/- 0.3%.