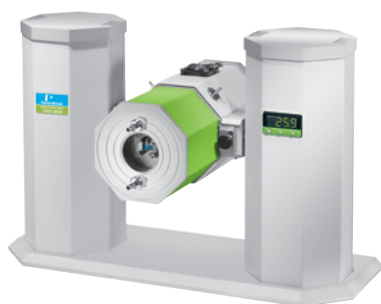


Thermal Analysis



Quantitation of the Amorphicity of Lactose Using Material Pockets



Summary

Lactose is a very important pharmaceutical excipient used in tablet and inhalation products. It is prone to forming amorphous regions on processing however, and can be problematical to characterize the exact amount of amorphous material in a sample. This application note describes a DMA method for quantitatively determining the amorphous content of lactose using the PerkinElmer® Material Pocket. The complex $\tan \delta$ response will be interpreted and an indication of the detection limits of the technique will be discussed.

Introduction

Dynamic Mechanical Analysis (DMA) is one of the most appropriate methods to investigate relaxation events. This fact, until now, has not been exploited for powdered materials due to the difficulty in handling them in mechanical tests. The Material Pocket was developed to allow powdered materials to be investigated in a DMA 8000. The size of the observed glass transition in the $\tan \delta$ response is directly proportional to the amount of amorphous material in the sample. As the crystalline component has no glass transition, it has no contribution to the result obtained.

DMA works by applying an oscillating force to the material and the resultant displacement of the sample is measured. From this, the stiffness can be determined and the modulus and $\tan \delta$ can be calculated. $\tan \delta$ is the ratio of the loss modulus to the storage modulus. By measuring the phase lag in the displacement compared to the applied force it is possible to determine the damping properties of the material. $\tan \delta$ is plotted against temperature and glass transition is normally observed as a peak since the material will absorb energy as it passes through the glass transition.

Experimental

Temperature scan of Lactose.

Approximately 50mg of lactose was loaded into a Material Pocket and the pocket was mounted in the DMA 8000.

Equipment	Experimental Conditions	
DMA 8000 1L Dewar	Sample:	Spray dried lactose
	Geometry:	Single Cantilever Bending
	Support:	Material Pocket
	Temperature:	25 °C to 250 °C at 5 °C min ⁻¹
	Frequency:	1.0 Hz

Results and conclusion

Figure 1 shows a typical DMA response from both a fully crystalline and a fully amorphous sample of lactose. The amorphous sample shows various regions of interest in the $\tan \delta$ corresponding to loss of water, the glass transition, recrystallization of the amorphous material and loss of hydration and finally melting. The crystalline material has no peak corresponding to the initial loss of water as it is significantly less hygroscopic and contains less latent water. It obviously has no glass transition due to the lack of any amorphous material present. The latter peaks correspond to the loss of hydration water and then melting.

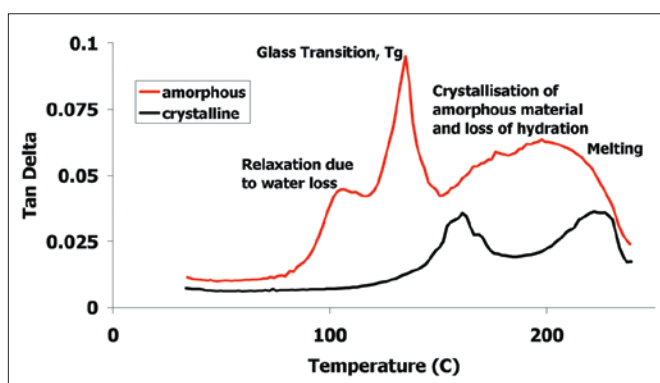


Figure 1. DMA response from a lactose sample.

The peak of main interest is the glass transition which exclusively represents the amorphous material in the sample. The magnitude of $\tan \delta$, as stated previously, is proportional to the amount of amorphous material in the sample. After mass and baseline corrections, the data can be plotted against amorphicity of known samples to achieve a calibration curve.

A plot of relaxation strength against amorphicity is shown in Figure 2. Relaxation strength is defined as 1 minus the glass transition peak value of the $\tan \delta$. The calibration curve shows a good correlation of fit. It was calculated that this technique has a theoretical limit of detection of 2.8% w/w for amorphous lactose. This is comparative to other techniques that have been used to quantitate amorphous lactose. A more comprehensive description of both the technique and the data can be found in the publication by Royall et al. (International Journal of Pharmaceutics, 301, (2005), 181-191.)

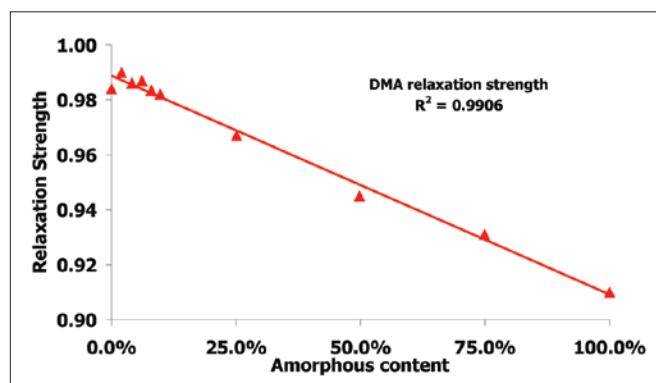


Figure 2. Relaxation strength vs. amorphicity.