

Thermal Analysis



Investigation of Partially Amorphous Ranitidine HCl



Summary

This application note demonstrates the ability of DMA to investigate the amorphous properties of Ranitidine HCl. As the substance is in powdered form, the Material Pockets were used to hold the sample. Two different polymorphs of crystalline Ranitidine HCl were ball milled for different times and the resultant powders were run in the PerkinElmer® DMA 8000. The amount of amorphous material was variable in each sample and after a glass transition was observed, a second peak in $\tan \delta$ was observed for some samples. This is attributed to the recrystallization of the amorphous component.

Introduction

Dynamic Mechanical Analysis (DMA) is one of the most appropriate methods to study amorphous materials. The glass transition (T_g) is a key process in any material, and can be observed with ease by DMA. This technique provides very revealing information about these relaxations through the $\tan \delta$ vs. temperature data. Most pharmaceutical active materials are in a powder form. Powders can be easily investigated in the DMA 8000 by using the Material Pockets which sandwich the powder in stainless steel prior to measurement.

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. The size of this peak quantifies the amount of amorphous material present in the sample.

Ranitidine HCl is a pharmaceutically important material. It has polymorphic properties and is susceptible to creation of amorphous regions on milling. DMA is a good technique to investigate the amorphous material as it is very sensitive to relaxation events such as Tg and the crystalline part of the sample does not mask the amorphous.

Experimental

DMA Temperature Scan of Ranitidine HCl.

About 20 mg of each sample was weighed into a Material Pocket before being mounted into the DMA 8000 in Single Cantilever Bending geometry. 1 Hz and 10 Hz data were collected over the full temperature range.

Equipment Experimental Conditions

DMA 8000	
1L Dewar	Sample: Ranitidine HCl 2 batches (A and B) Each batch ball milled for different times
	Geometry: Single Cantilever Bending
	Support: Material Pocket
	Frequency: 1 and 10 Hz

Results and conclusion

Figure 1 shows data from three samples prepared from sample A. Line A30 was ball milled for 30 minutes, A120 for 120 minutes and A150 for 150 minutes. Sample A150 shows the tail of a glass transition initially then a second peak. Sample A120 shows a small glass transition peak and A30 no clear peak at all. The magnitude of the peak reflects

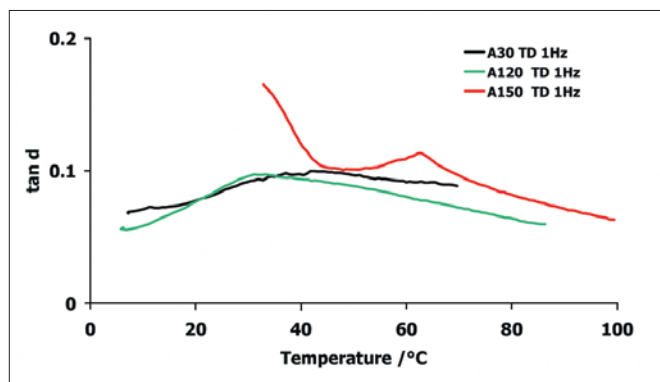


Figure 1. Three samples prepared from Sample A.

the amount of amorphous material in each sample. The longer the sample was milled the larger the tan δ peak. The second peak in the A150 sample corresponds to the recrystallization of amorphous material.

It is not evident in the other samples as the amount of amorphous material was so low. The tan δ peak could be due to the loss of water on crystallization as well as the actual recrystallization process itself.

Figure 2 shows data from three samples prepared from sample B. The numbers 30, 120 and 150 reflect the time spent in the ball mill. Unlike the Figure 1 data, no recrystallization event is observed but the glass transition is quite strong.

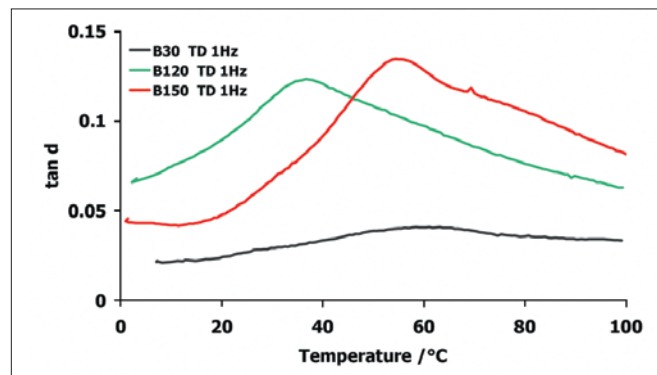


Figure 2. Three samples prepared from Sample B.

There are clearly mechanical and relaxation differences between both polymorphs regarding the amorphous state that is created on ball milling. DMA has shown that it is an excellent technique for investigating small quantities of amorphicity in powdered materials.

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