

## APPLICATION BRIEF

**TA no.79** DSC Measurement of Pharmaceuticals

2007.9

— Crystal polymorphism and crystallinity —

### 1. Introduction

Differential scanning calorimetry (DSC) has been added as a general testing method to the Japanese Pharmacopoeia and is widely used to evaluate the thermophysical properties of pharmaceuticals.

It is known that the organic compounds that compose pharmaceuticals can have different crystalline forms or different crystallinity due to refinement or milling. It is very important to clearly identify these differences when developing pharmaceuticals because crystal polymorphs and crystallinity influence medicinal effects and formulation stability. Crystal polymorphism and crystallinity are influenced by temperature change so DSC is indispensable in understanding the thermophysical properties of pharmaceuticals.

In this brief, we measure Carbamazepine, an antiepileptic drug, and ursodeoxycholic acid, a chol-  
eretic drug, to ascertain the differences of crystal polymorphism and crystallinity.

### 2. Measurement

In one measurement, Carbamazepine, which has different crystalline forms (Form I and III), and its hydrate were measured. In another measurement, ursodeoxycholic acid was measured under three different milling conditions (no milling, milled 5 min, milled 60 min).

The measurements were performed using the DSC6220 differential scanning calorimeter.

For the measurements, a 2mg sample was heated at a rate of 10 ° C/ min in a nitrogen atmosphere.

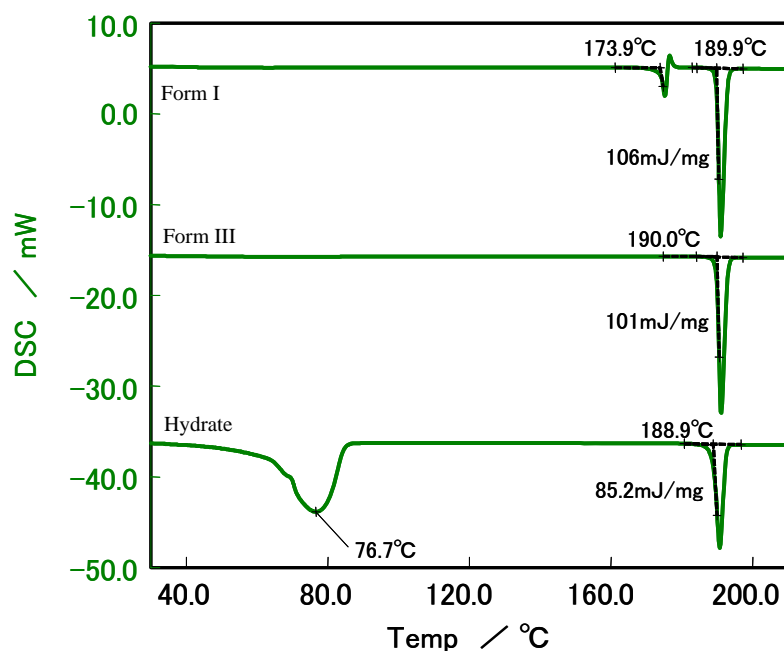


Figure 1. DSC results for Carbamazepine

### 3. Results

#### 3.1 Crystal polymorphism

Figure 1 shows the DSC results for the three conditions of Carbamazepine. All samples showed a sharp endothermic peak at around 190 ° C. From the Form III results, we can see that there was melting of the Form III crystals.

The Form I sample showed an endothermic and an exothermic peak between 170 ° C and 180 ° C. The crystal structure of Form I crystals melts and then recrystallizes into the stable Form III.

The hydrate sample showed an endothermic peak due to crystal water desorption at around 80 ° C. This sample is likely crystal water adhered to Form III crystals. After dehydration, the Form III crystals showed no peaks before melting.

#### 3.2 Crystallinity

Figure 2 shows the DSC results for the three conditions of ursodeoxycholic acid. All samples showed a sharp endothermic peak around 200 ° C, which indicates the melting of ursodeoxycholic acid.

The milled samples showed an exothermic peak at around 110 ° C. The milling process likely broke down the crystal structure of the ursodeoxycholic acid and changed it to an amorphous form, which was cold crystallization by heating.

The longer the sample was milled, the larger the exothermic peak. The longer milling time likely increased the proportion of the amorphous elements.

### 4. Summary

DSC was used to measure the pharmaceuticals Carbamazepine and ursodeoxycholic acid. The results confirmed the presence of crystal polymorphism in Carbamazepine, as well as the polymorphic transition temperature. For ursodeoxycholic acid, the results confirmed that the influence of milling on crystallinity is dependent on milling time.

Using the measurements described in this brief, DSC can be used to investigate the processing and storage conditions of pharmaceuticals.

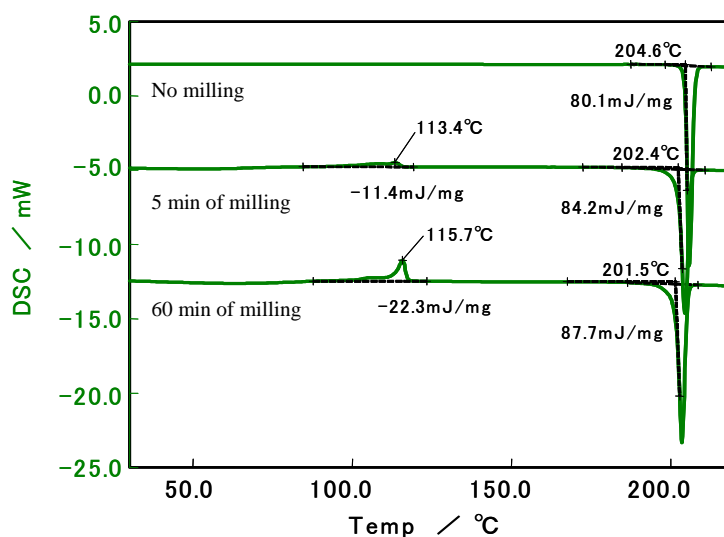


Figure 2. DSC results for ursodeoxycholic acid