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# Application News

## No.T152

Thermal Analysis

# Polymorphism of Drugs

## Introduction

Polymorphism is the phenomenon of materials with the same chemical structure having different crystalline structures. The different crystal forms of polymorphic materials have different properties, including solubility and stability, so evaluating polymorphism is an important part of drug development. Differential scanning calorimetry (DSC) is an effective technique for investigating polymorphism that requires no sample pretreatment and performs measurements quickly. DSC can be used to evaluate polymorphism based on different crystal shapes having different melting points and heat of fusions. Here, we describe an example use of DSC to analyze polymorphs.

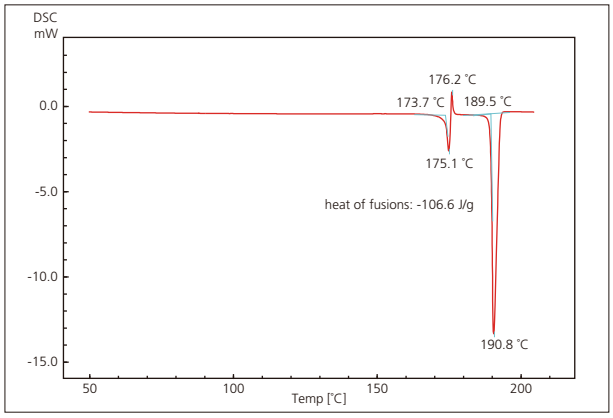


**Fig. 1 DSC Measurement of Carbamazepine Form Ⅰ**

## Measurement of Carbamazepine

Carbamazepine is used as an anticonvulsant and is known to exist in multiple crystal forms. Carbamazepine form Ⅰ (Fig. 1) and form Ⅲ (Fig. 2) were analyzed. A sharp endothermic peak can be observed with both forms at around 190 ˚C. This peak represents the melting of crystal form Ⅲ. An endothermic/exothermic peak is visible between 170 ˚C and 180 ˚C with crystal form Ⅰ. This phenomenon is speculated to be caused by recrystallization of form Ⅰ to stable form Ⅲ following melting.

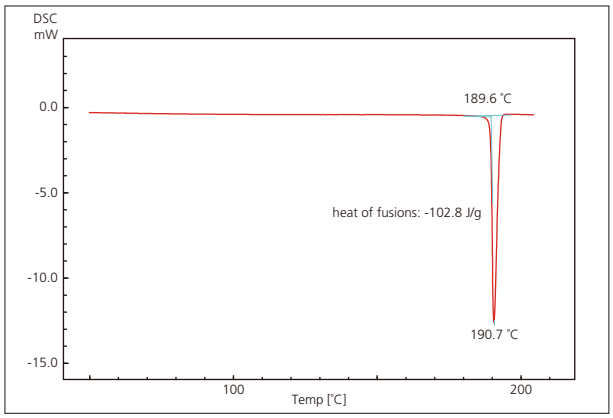


**Fig. 2 DSC Measurement of Carbamazepine Form Ⅲ**

## Measurement of Sulfapyridine

Sulfapyridine was heated to 205 ˚C (first run), then cooled and heated again (second run) (Fig. 3).
During the first run, only the melting peak of a stabilized phase is visible at 192.2 ˚C, while during the second run, there is a glass transition at 54.7 ˚C, a crystallization peak at 101 ˚C, and the melting peak of a quasi-stable phase at 181.9 ˚C.

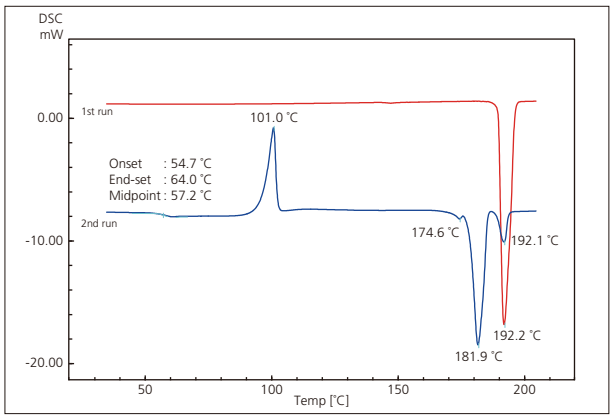


**Fig. 3 DSC Measurement of Sulfapyridine**

## Measurement of Tripalmitin

Tripalmitin is also known to be polymorphic. In Fig. 4, the melting peak seen at 61.6 ˚C during the first run corresponds to melting of stable crystal form $\beta$.
Next, an exothermic peak at 42.5 ˚C is seen during the cooling process. This peak equates to crystallization of quasi-stable crystal form $\alpha$. The exothermic/endothermic peak observed in the region of 45 ˚C to 58 ˚C during the second run equates to melting of form $\alpha$ followed by crystallization of form $\beta$. The heat of fusion of form $\beta$ melting at around 60 ˚C is observed to be smaller due to incomplete crystallization of form $\beta$.

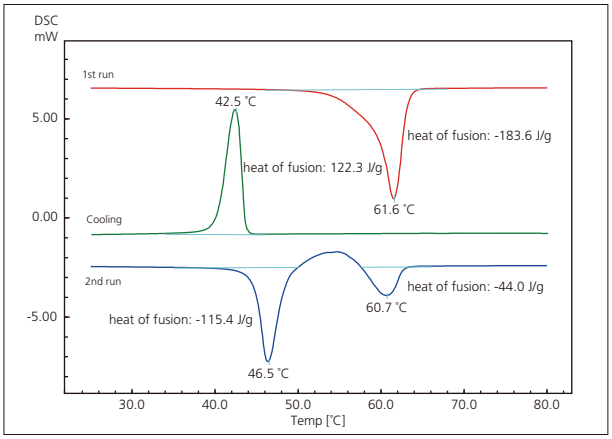


**Fig. 4 DSC Measurement of Tripalmitin**

## Measurement of a Suppository

Fig. 5 shows data from heating (first run), cooling, and reheating (second run) of a commercially available suppository drug. The melting peak shapes are different during the first run and second run. This difference is due to a change in the crystal form of triglyceride present in the suppository drug caused by the heating method used. Because different crystal forms give rise to different melting characteristics and cracking behaviors, optimum heat treatment conditions must be investigated.

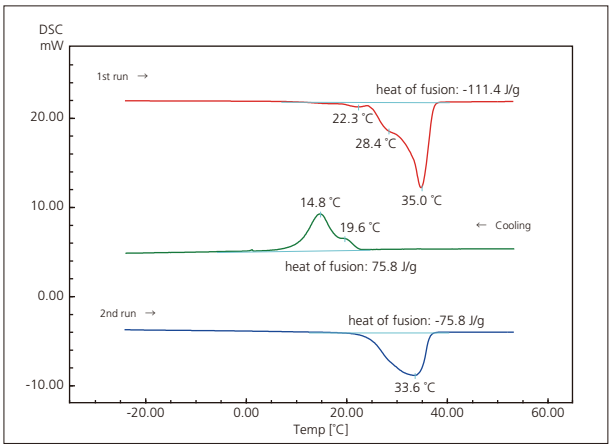


**Fig. 5 DSC Measurement of a Suppository**

## Measurement of Sulfathiazole

Fig. 6 shows the results of analyzing sulfathiazole. The peak at 169.8 ˚C is presumed to represent the transition from a quasi-stable phase to a stable phase, and the peak at 201.1 ˚C is presumed to be melting of the stable phase.

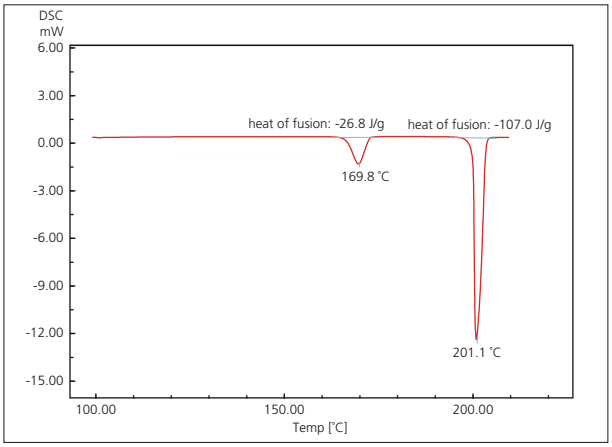


**Fig. 6 DSC Measurement of Sulfathiazole**

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