Application News

SHIMADZU

THERMAL ANALYSIS T127

Application to Medical and Pharmaceutical Products (Melting Point and Fusion Heat)

Melting point and fusion heat are major indexes representing nature of substances. Several methods are available for measuring melting point and fusion heat.
According to the Pharmacopoeia, temperature is measured when a specimen is gradually heated in a capillary until it is completely liquefied with nothing remaining in solid state. In thermal analysis method, an endothermic reaction is analyzed of a specimen heated at a constant rate. Its melting point and fusion heat are known from the result of this analysis.
Compared with the method in the Pharmacopoeia, thermal analysis method features the following advantages.

1. Melting process of a substance is observable.
2. Pretreatment is not required for substance that is hard to pulverize.

Thermal analysis for this purpose includes methods of DTA (differential thermal analysis) and DSC (differential scanning calorimetry). In both methods, a specimen and a reference sample are heated at a constant rate in a heating furnace for measurement of the differential temperature, the output of which is monitored in the unit of either μV (differential temperature) for DTA or mW (differential calories) for DSC. DSC is better fitted to measuring melting point and fusion heat as it measures calories directly, though DTA also is suitable for the analysis.
The followings are results of measurements of medicines with Shimadzu Differential Scanning Calorimeter, Model DSC.

Analysis of benzoic acid

Pharmaceuticals contain substances that evaporate or sublimate while undergoing the process of fusion. Measurement of accurate melting point and fusion heat by thermal analysis method is difficult as the overlapping peaks of endothermic reaction for fusion, evaporation and sublimation obstruct the measurement. A sealed cell is used for suppressing evaporation and sublimation for effective measurement of fusion.
Fig.1 shows a measurement using an open cell (crimp cell) for general use and a closed cell (sealed cell).
The melting point is determined by the cross point between a line extended from the baseline at lower temperature side and a tangent line drawn at the maxim inclination point on the lower temperature side of a fusion peak.
Fusion heat corresponds to an area (peak area) enclosed by the branching and joining points of DSC curve from and to the base line respectively.
Fig.1 shows a result of measurement of benzoic acid. In the measurement using a crimp cell, sublimation appearing around 60°C and on overlaps fusion, while an independent clear peak for fusion only appears in the measurement using a sealed cell. The melting point is estimated 121.43°C and fusion calories is 147.82J/g.

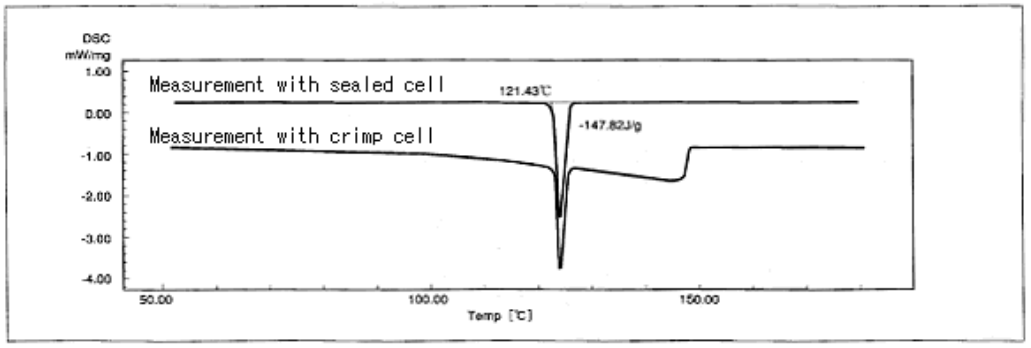

Fig.1 Fusion of Benzoic Acid

Table 1 Analytical Conditions for Fig.1

Specimen name	Benzoic acid	Specimen name	Benzoic acid	Temperature program	
Specimen weight	5.050 [mg]	Specimen weight	5.060 [mg]	Heating rate [˚C/min]	2.00
Specimen cell	Aluminum sealed cell	Specimen cell	Aluminum sell	Temperature holding [˚C]	200.0
Atmosphere	N_2 gas	Atmosphere	N_2 gas	Holding time [min]	0
Gas flow	30.00 [mL/min]	Gas flow	30.00 [mL/min]		

Analysis of aspirin

Melting point and fusion heat of aspirin are measured.

Melting point : 132.8 ˚C
Fusion heat : 190.5 J/g

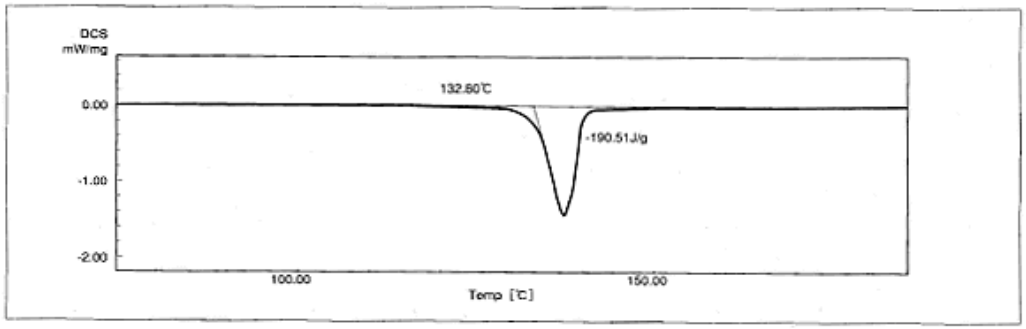

Fig.2 Fusion of Aspirin

Table 2 Analytical Conditions for Fig.2

Specimen name	Aspirin	Temperature program	

Specimen weight	4.820 [mg]	Initial temperature [˚C]	50.0
Specimen cell	Aluminum sealed cell	Heating rate [˚C/min]	2.00
Atmosphere	N_2 gas	Temperature holding [˚C]	200.0
Gas flow	30.00[mL/min]	Holding time [min]	0

Analysis of Caffeine

Caffeine was measured for melting point and fusion heat.

Melting point : 235.0˚C
Fusion heat : 113.1J/g

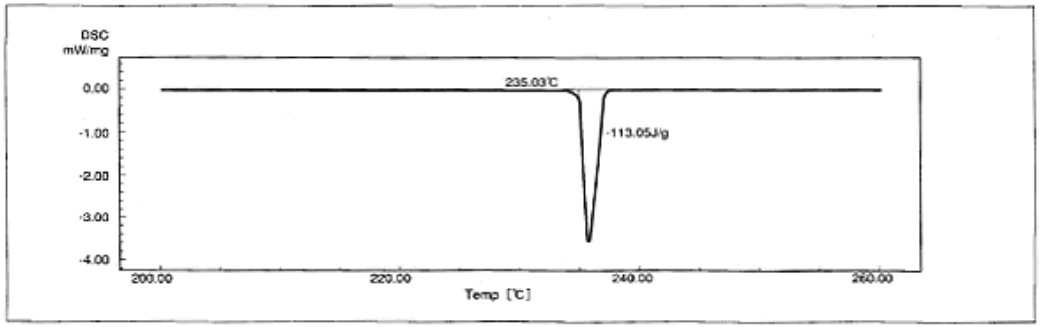

Fig.3 Fusion of Caffeine

Table 3 Analytical Conditions for Fig.3

Specimen name	Caffeine	Temperature program	
Specimen weight	2.510 [mg]	Initial temperature [˚C]	170.0
Specimen cell	Aluminum sealed cell	Heating rate [˚C/min]	2.00
Atmosphere	N_2 gas	Temperature holding [˚C]	280.0
Gas flow	30.00 [mL/min]	Holding time [min]	0

* Please be advised that data obtained before the implementation of the current Weights and Measures Law may be presented in terms of gravimetric unit.

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