

Thermal analysis to be cited in the Japanese Pharmacopoeia

DSC as a method for measurements of fusion, crystal transition etc.

TG as a substitute method for measurement of weight loss by drying test or moisture measurement

Thermal analysis method will be cited as a general testing method in the second annex of the 13th revision of the Japanese Pharmacopoeia. It will describe the principle, general outline of instruments, use, calibration, and analytical conditions in the sections "the first method by differential thermal analysis (DTA) or differential scanning calorimetric method (DSC)" and "the second method by thermogravimetric method (TG)." The following is its outline. (quoted from JP Forum Vol.6, No.4 (1997)).

The first method

Differential thermal analysis method (DTA) or differential scanning calorimetry (DSC)

Instruments applicable to this method are those available in the market (Shimadzu differential scanning calorimeter). Operation procedures, calibration of instrument and items to be specified for analytical conditions are as follows:

Specimens shall be analyzed at a heating rate of 2° C/min in a measuring range to be determined by a preparatory analysis in that α -alumina or a blank cell as a standard sample is heated from room temperature to the temperature of the onset of its decomposition at a rate of 10 - 20° C/min.

The exothermic or endothermic peak of measured specimens shall be analyzed for the change of calories and the temperature at onset, peak, and end of peak. Analytical conditions shall be described in respect of specimen weight, distinction of open or sealed cell for specimen, heating or cooling rate, temperature range, atmospheric gas used and its flow rate. Temperature and calories of heating or cooling device are generally calibrated using the melting point and fusion calories of indium or tin for thermal analysis.

Application examples in pharmaceuticals: melting point, fusion calories, crystallization transition, and polymorphism

The second method

Thermogravimetry (TG)

Just as in the case of DSC, instruments applicable to this method are those available in the market with any one of weighing systems of suspension type, top loading type, and the sliding weight type (Shimadzu thermogravimetric analyzer-TGA and Shimadzu differential thermogravimetric analyzer-DTG).

In case this TG method is used as a substitute method for the drying loss test method or moisture measuring method, measurement shall be exercised in a measuring temperature range starting at room temperature until gravimetric change of moisture, caused by desiccation or volatilization, is over. Specimen shall be linearly heated in dry air or N₂ gas stream with a heating rate of 5° C/min or other appropriate conditions depending on specimen and room temperature.

Temperature shall be calibrated in the same way as that for the first method excepting use of a Curie point of a strongly magnetic substance like nickel. Scale graduation shall be calibrated using balance weights in accordance with the primary level for regular maintenance. Scale graduation shall also be calibrated or checked using the measured amount of dehydration of standard calcium oxalate hydrate as the secondary level. If deviation between the measured moisture amount and the standard value is 0.3% or more, scale graduation shall be calibrated according to the standard value.

Application examples in pharmaceuticals: moisture contents, decomposition temperature, thermal deterioration

Application example, DSC

Difference of crystallization mechanism of pharmaceuticals may result in different fusion speed and different medical effect. That is why polymorphism mechanism of

pharmaceuticals should be clarified.

Fig.1 represents polymorphism of sulfathiazole. The specimen that is of metastable nature at room temperature turns to a stable type at the transition at 169.8° C and fuses at 200.2° C. The specimen becomes a stable type even at room temperature if heat treatment is applied at a temperature of 169.8° C or higher.

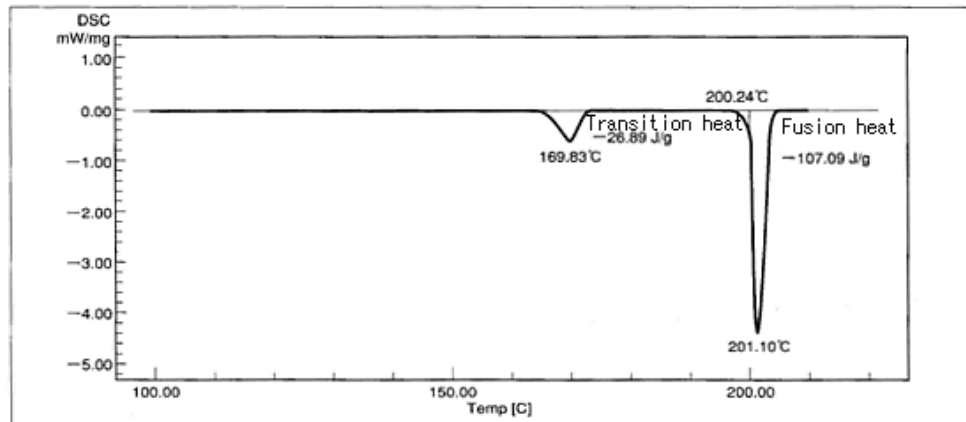


Fig.1 Polymorphism of Sulfathiazole

Table 1 Analytical Conditions for Fig.1

Specimen	Sulfathiazole	Temperature program	
Specimen weight	2.970 [mg]	Heating rate [° C/min]	2.00
Specimen cell	Aluminum	Temperature holding [° C]	210.0
Atmosphere	Air	Holding time [min]	0

Application examples, TG

Fig.2 is a TG measurement of sodium tartaric acid. It is known from the weight loss of 15.5% that the loss is caused by the desorption of crystallized water in single molecules. TG measurement features in small weight of a specimen of 5 to 20mg and a short measuring time within 40 minutes. Loss factor

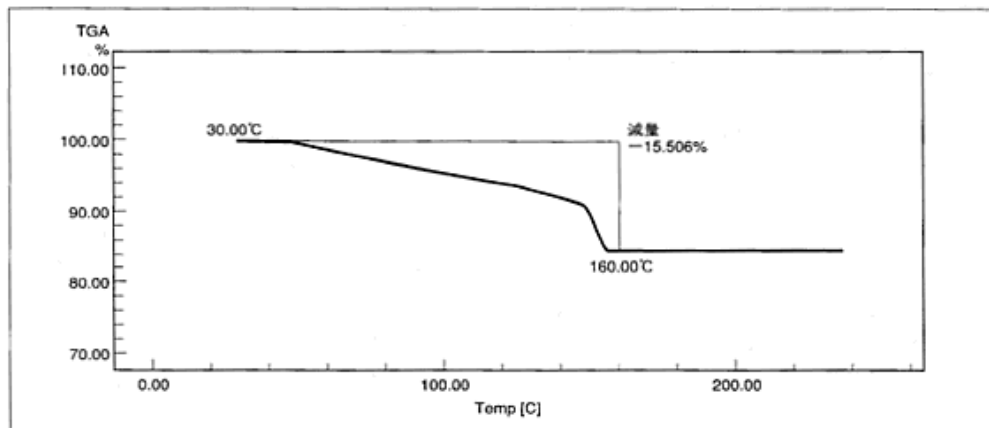


Fig.2 Dehydration of Sodium Tartaric Acid

Table 2 Analytical Conditions for Fig.2

Specimen name	Sodium tartaric acid	Temperature program	
Specimen weight	20.740 [mg]	Heating rate [° C/min]	5.00
Atmosphere	Air	Temperature holding [° C]	300.0
Gas flow	50.00 [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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