Application News

SHIMADZU

THERMAL ANALYSIS T126

Application to Medical and Pharmaceutical Products of Multiple Crystallization

What is most important for a medicine is that its medical effect surely works on the symptomatic part. It is known that solubility and solving rate are important factors for medicines in the form of powder and tablet and these properties differ depending on the type of crystallization. According to a report, for example, the dissolving rate as well as the absorption speed of chloramphenicol palmitate in alkali solution is about 30 times faster in a metastable state than in a stable state; in other words, its density in blood can be greater in a metastable state than in a stable state. Accordingly, it is important to measure the existence of polymorphism that causes a significant difference in solubility and resolving rate of medicines.
Polymorphism is divided into two types of a reciprocally convertible types in that the order of the two crystallization processes is reversibly inverted and a simply convertible type in that the crystallization process only proceeds from a metastable type to a stable type. This polymorphism is measured for important information with thermal analysis as well as x-ray diffractometry and infrared absorption spectrometry.
Among thermal analysis methods, DSC is most useful because specimens are quickly analyzed without pretreatment.
The following is a result of measurements of sulfathiazole, known as a substance having multiple crystallization, with Shimadzu scanning calorimeter, DSC.

Analysis of original sulfathiazole

Fig.1 shows a DSC curve of sulfathiazole of 99.9% purity usually used for food analysis. There is an endothermic peak at 166.8°C and another sharp one at 201.7°C. The first one is for the transition from Form I to Form II (from metastable to stable type), while the second one represents the fusion of Type II. It is known that these processes differ according to the recrystallization solvent and the state of pulverization of specimens.

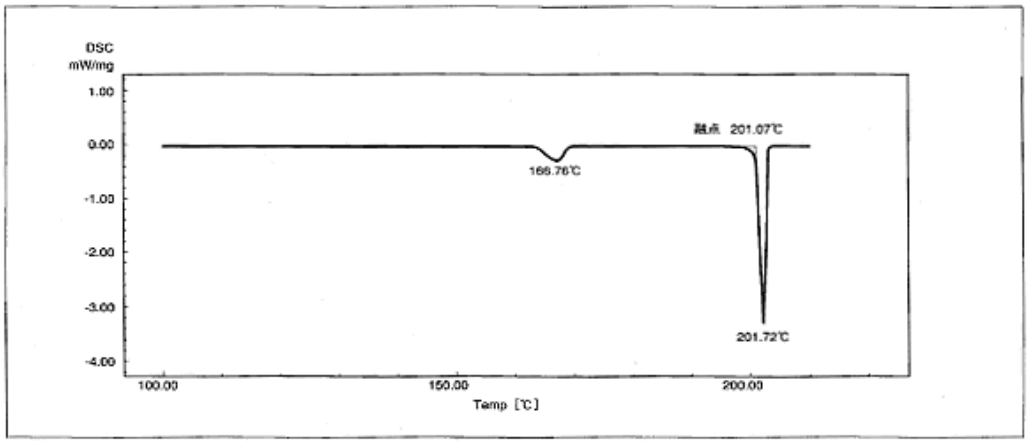

Fig.1 DSC Curve of Sulfathiazole (Original)

Table 1 Analytical Conditions for Fig.1

		Temperature program	

Specimen name	Sulfathiazole	Initial temperature [˚C]	100.0
Specimen weight	2.230 [mg]	Heating rate [˚C/min]	2.00
Atmosphere	N_2 gas	Temperature holding [˚C]	220.0
Gas flow	50.00 [mL/min]	Holding time [min]	0

Analysis of pulverized and recrystallized sulfathiazole

It is known that the state of crystallization of sulfathiazole differs depending on physical treatments like pulverization and solvents for recrystallization. Fig.2 shows a result of measurements of two sulfathiazole specimens pulverized in an agate mortar and recrystallized in acetone solvent.
The peak temperature at transition from Form I to Form II differs between the two specimens. In addition, the endothermic peaks shifted by 8˚C in the pulverized specimen and by as much as 14˚C in the recrystallized specimen, both toward lower temperature side than that of original sulfathiazole. Fusion peaks also shifted, but slightly toward lower temperature direction than that of the specimen of original sulfathiazole.
Pulverized specimen
Recrystallized specimen with acetone

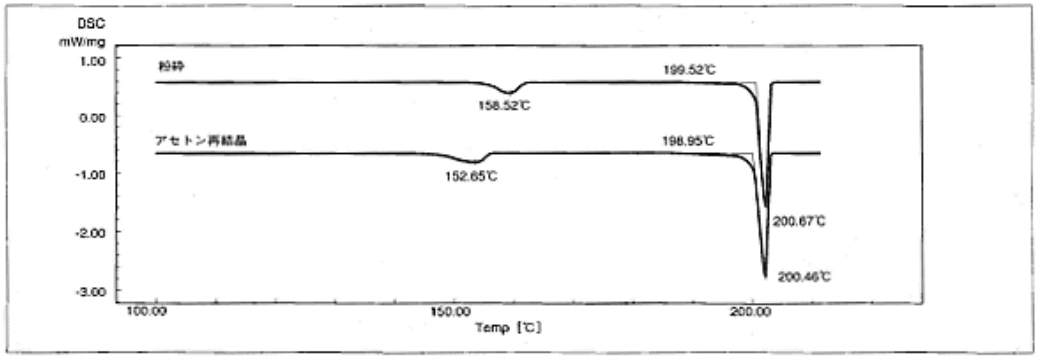

Fig.2 DSC Curve of Sulfathiazole (Pulverized and Recrystallized)

Table 2 Analytical Conditions for Fig.2

Specimen name	Sulfathiazole(pulverized)	Specimen name	Sulfathiazole(acetone)	Temperature program	
Specimen weight	2.340 [mg]	Specimen weight	2.840 [mg]	Initial temperature [˚C]	100.0
Specimen cell	Sealed aluminum cell	Specimen cell	aluminum cell	Heating rate [˚C/min]	2.00
Atmosphere	N_2gas	Atmosphere	N_2 gas	Temperature holding [˚C]	220.0
Gas flow	30.00 [mL/min]	Gas flow	30.00 [mL/min]	Holding time [min]	0

Sulfathiazole after heat treatment

Fig.3 is a result of a measurement of sulfathiazole heated up to 190˚C for heat treatment. An endothermic peak for fusion is only observed on the curve of the heat treated specimen, which otherwise has another peak at 150 to 170˚C for transition from Form I to II, that is, from a metastable state to a stable state. This means that the state of crystallization has already proceeded to Form II as the result of heat treatment.

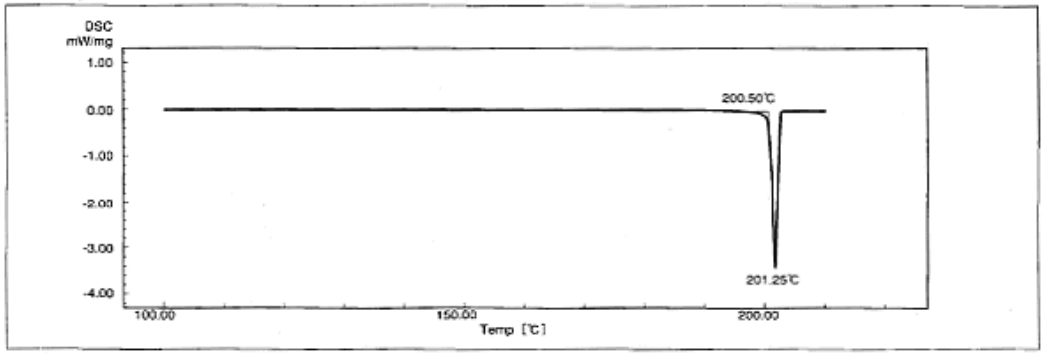

Fig.3 DSC Curve of Sulfathiazole (heat-treated at 190°C)

Table 3 Analytical Conditions for Fig.3

		Temperature program	
Specimen name	Sulfathiazole (heat-treated at 190° C)	Initial temperature [° C]	100.0
Specimen weight	2.470 [mg]	Heating rate [° C/min]	2.00
Atmosphere	N_2 gas	Temperature holding [° C]	220.0
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.

SHIMADZU CORPORATION International Marketing Division
3,Kanda-Nishikicho 1-chome, Chiyoda-ku,Tokyo 101-8448,
JapanPhone: 81(3)3219-5641 Fax: 81(3)3219-5710
Cable Add,;SHIMADZU TOKYO

SHIMADZU SCIENTIFIC INSTRUMENTS, INC.
7102, Riverwood Drive, Columbia, Maryland 21046, U.S.A.
Phone: 1(410)381-1227 Fax: 1(410)381-1222 Toll Free:1(800)477-1227

SHIMADZU DEUTSCHLAND GmbH
Albert-Hahn-Strasse 6-10, D-47269 Duisburg, F.R. Germany
Phone: 49(203)7687-0 Fax: 49(203)7666-25

SHIMADZU (ASIA PACIFIC) PTE LTD.
16 Science Park Drive #01-01,Singapore Science Park, Singapore 118227, Republic of Singapore
Phone: 65-778-6280 Fax: 65-779-2935

SHIMADZU SCIENTIFIC INSTRUMENTS(OCEANIA)PTY. LTD.
Rydalmere Business Park, Unit T, 10-16, South Street Rydalmere, N.S.W. 2116, Australia
Phone: 61(2)9684-4200 Fax: 61(2)9684-4055

SHIMADZU DO BRASIL COMERCIO LTDA.
Rua Cenno Sbrighi, 25 CEP 05036-010 Agua Branca, Sao Paulo, BRAZIL
Phone: 55(11)3611-1688 Fax: 55(11)3611-2209

SHIMADZU (HONG KONG) LIMTED.
Suite 1028, Ocean Centre, Habour City, Tsim Sha tsui, Kowloon, HONG KONG
Phone: 852(2375)4979 Fax: 852(2199)7438

Overseas Office
Istanbul,Beijing,Shanghai,Guangzhou,Shenyang,Chengdu,Moscow