NEWSLETTER OF *eurostar-science*

NO 5 – February 27, 2003

CONTENT

5.1 EDITORIAL

PhandTA 7 - the **7th International Conference on Pharmacy and Applied Physical Chemistry** - will be held from Sunday, September 7 to Thursday, September 11, 2003 at the University of Innsbruck. The location of our Conference is the so-called **SOWI - Sozial- und Wirtschaftswissenschaftliche Fakultät** - a very modern and ideally located building. Even more important is the structure of this building in all respects, extremely practical for our activities such as the communications, the poster presentations, the workshops, the exhibition of instruments and also for meetings and discussions during lunch time.

The start of the Conference is planned for Sunday afternoon, approximately at 4 pm with 3 to 4 major communications.

The Scientific Program is anticipated in our usual way in presenting of quite large subjects within our Conference Sections and with extensive discussions. The percentage of scientifically active participants in our preceding conferences was rather high which is the base for a Conference on an outstanding level.

You will find all necessary information in the Circular we distributed already, in this Newsletter and in detail on our Conference website (http://www.eurostar-science.org).

I would like to invite you all in the name of the Members of the Organization Committee to participate at the **PhandTA 7 in Innsbruck**. The Pharmaceutical Institutes of Innsbruck represent an rather old tradition and are with Professor Ulrich Griesser among others Scientists on the way to make the important scientific steps in the direction of the demands in our rather young century.

Erwin Marti, President

5.2 NEWS

PhandTA 7

As already announced and mentioned above, the preparation of PhandTA 7, the 7th International Conference on Pharmacy and Applied Physical Chemistry, has started. The venue will last 3 and a half days followed as during PhandTA 6 by a one-day workshop whereby its subject will be announced later. All necessary information on this event will ongoingly be completed and is available at the conference website:

- Organizing and Scientific Committee
- Timetable
- Exhibtion
- Workshop
- Abstracts
- Details for registration
- Information for authors
- Information on the location and travelling

The organization on an accomodation is on your own responsibility. A list of recommendable hotels will be available by end of March.

Registration is possible either online on the website or by fax/mail. Payment of the registration fee is appreciated beforehand the conference.

To be ongoingly informed on all relevant news and changes, you may register at the website for our electronical Conference Newsticker.

Announcements

- Mettler-Toledo GmbH
  - New pressure DSC for e.g. influence of CO2 on glass transition of PVP
    http://www.mt.com/documents/Brochures/51724328.pdf
  - Latest UserCom on the website: 1/2002
    http://www.mt.com/mt/resourcedetail/userCom.jsp?%20=%20&key=Uy_Tc4NjM1Nz
  - Fachseminar Thermische Analyse in der pharmazeutischen Forschung und Produktion
    http://www.mt.com/mt/resourcedetail/evtSeminar.jsp?%20=%20&key=E3MDg4NjM1_D

5.3 OUR SPONSORS. METTLER-TOLEDO GMBH

Investigation of spray-dried substances. Drying and glass transition using IsoStep™

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Introduction

If several thermal events occur simultaneously in a DSC measurement, the problem is then how to separate the different processes involved. Often, a change in heat capacity is overlapped by exothermic or endothermic peaks, e.g. through chemical reactions, crystallization or vaporization. One possible way to separate the different processes is to vary the measurement conditions in the conventional DSC. For example, heating and cooling measurements can be performed at different rates and in different temperature ranges using different types of crucible. This is of course relatively time-consuming.

IsoStep™ is a new technique that can be used to distinguish between such overlapping processes. It provides both the heat capacity curve and the non-reversing curve simultaneously.

In this article, the separation of different thermal events is demonstrated by measuring the glass transition of a spray-dried pharmaceutical substance. The measurement of a similar compound to determine the change of heat capacity during the vaporization of water has been described in a previous article [1]. As an extension of this, the relationship between the water content and the glass transition temperature is analyzed quantitatively using IsoStep™. Knowledge of this relationship is important for processing the powder because it can become sticky if the glass transition temperature is below the processing temperature.

Experimental details

The DSC measurements were performed with a DSC822^e equipped with an IntraCooler. The STAR^e software with the IsoStep™ option was used for the evaluation.

In the IsoStep™ method, a conventional heat capacity measurement is combined with a quasi-isothermal kinetic evaluation. The temperature program consists of a series of isothermal segments and heating steps. The parameters (length of the isothermal segments, heating rate and step height in the heating step) are not restricted in any way. They can even be different during a measurement depending on the actual task or thermal event investigated.

The heat capacity as a function of temperature is obtained from the heat flow during the heating step, and the non-reversing curve from the heat flow during the isothermal step [2]. The measurements described here used temperature steps of 1 K at 2 K/min. The isothermal period at the beginning of the measurement was 30 s. The measuring cell was purged with nitrogen.

The sample used was a spray-dried pharmaceutical product consisting of two amorphous components. The water content of the starting material was analyzed by TGA/SDTA851^e and found to be 6.08%. Samples of about 8 mg were sealed in 40-µl aluminum crucibles with a 50-µm hole in the lid. The samples were dried each time in the DSC at 80 °C for different periods of time before measurement in order to obtain different water contents. The advantage of this procedure was that the sample did not have to be transported after drying. The small hole in the lid restricts the evaporation of the water so that drying proceeds in a defined way. The moisture content before the beginning the measurement, w_{ini}, was determined by measuring the decrease of the water content during the storage of the crucibles with the TGA/SDTA851^e [3]. Trial experiments in the DSC and TGA showed that the samples did not change chemically during the predrying step at 80 °C.

Results and interpretation

Figure 1 shows a typical IsoStep™ measurement curve as a function of the temperature. The upper limit of the curve corresponds to the heat flow during the isothermal segments, from which, the non-reversing curve is calculated.

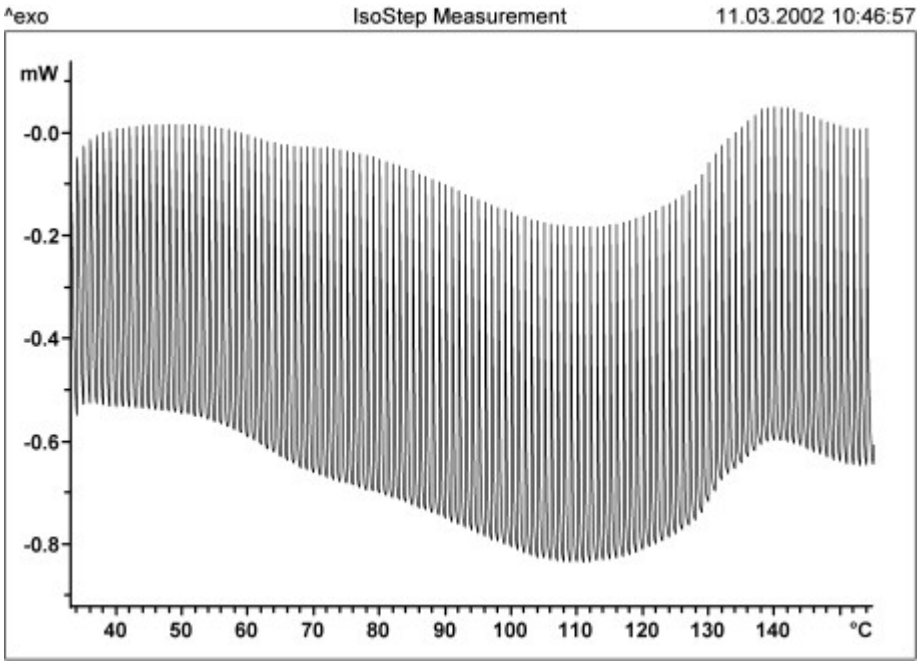

Fig. 1. *IsoStep™ measurement as a function of the temperature of a sample that had been preheated at 80 °C for 20 min*

Figure 2 shows the heat capacity and the non-reversing curves of the material that had been heated beforehand for 20 minutes. In the heat capacity curve, two glass transitions can be seen at about 70 °C and 125 °C. The broad vaporization peak observed in the non-reversing curve overlaps both glass transitions. This peak is so large that the glass transitions are not resolved in a conventional DSC curve. The first glass transition depends on the water content and is responsible for the powder sticking. Its glass transition temperature, T_g, was therefore investigated as a function of water content. In the heat capacity curves (Fig.3), one can see the shift of the glass transition temperature to higher temperature after longer drying times.

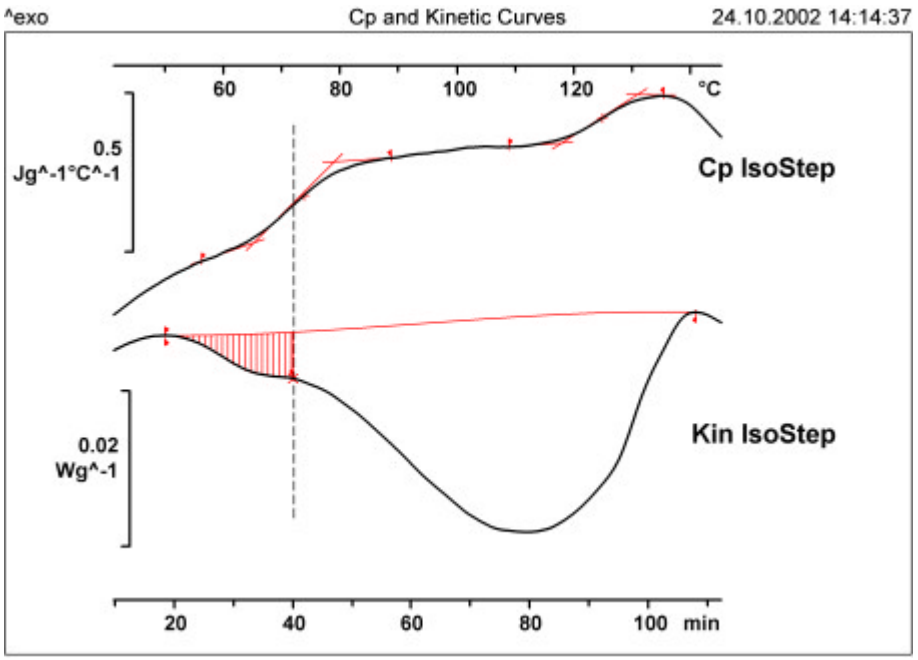

Fig. 2. *Specific heat capacity and non-reversing curves as a function of the temperature or measurement time, calculated from the measurement in Figure 1. The hatched area shows the amount of water vaporized up to the glass transition temperature.*

The water content before the measurement, w_{ini}, is of course not the same as the water content at the glass transition temperature, w_{Tg}, because water escapes continuously from the sample during the measurement. This loss of water can be determined from the non-reversing curve by evaluating the partial peak area up to T_g. The relevant partial peak area, Δh_p, is shown by the hatched area in Figure 2. If the specific heat of vaporization of water, Δh_w, is known, the water content up to T_g can be determined from the equation

$$w_{Tg} = w_{ini} - \frac{\Delta h_p}{\Delta h_w} \cdot 100\,\% \qquad (1)$$

Δh_w can be determined from the total peak area on vaporization, ΔH, and the loss of mass during the measurement, Δm, (determined by re-weighing): $\Delta h_w = \Delta H / \Delta m$ [4]. A value of 2500 J/g was obtained for Δh_w [1]. This is somewhat greater than the value for free water (2400 J/g).

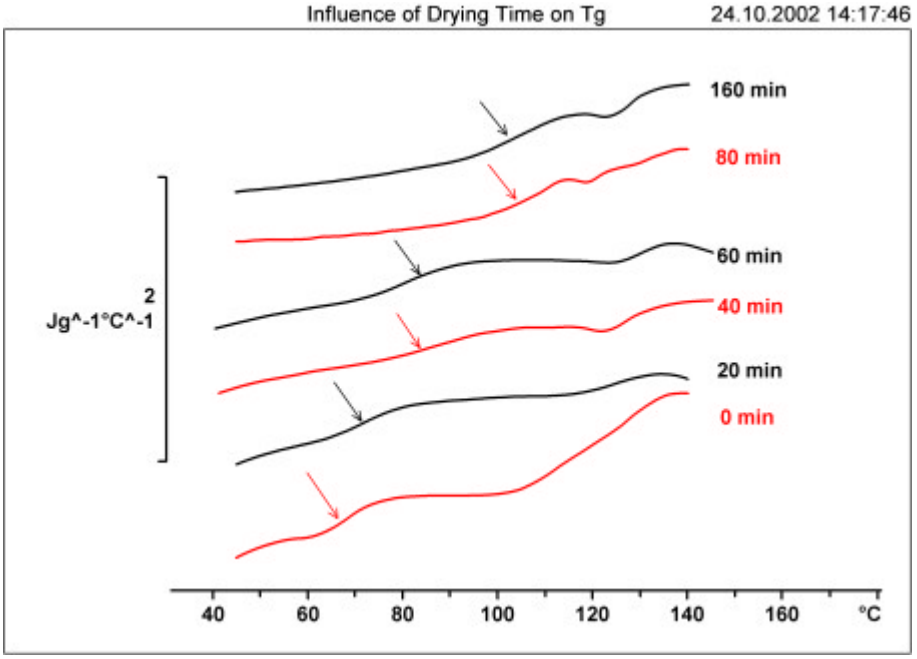

Fig. 3. *Heat capacity curves measured after different drying times at 80 °C. The parameter is the drying time. The arrows point to the glass transition temperatures.*

The glass transition temperatures determined from the curves in Figure 3 are displayed in Figure 4 as a function of the water content, w_{Tg} (Eq. (1)). This diagram can be used to optimize the processing conditions for the material.

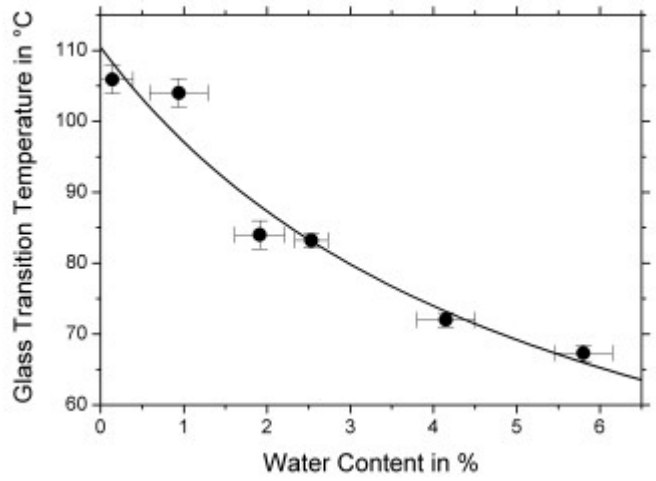

Fig. 4. *Glass transition temperature as a function of water content at T_g*

Summary
With IsoStep™, the heat capacity and the non-reversing curve can be determined simultaneously in one measurement. This allows glass transition and vaporization processes to be separated. With a spray-dried pharmaceutical substance, it has been shown that the method can be used to quantitatively determine the effect of moisture on the glass transition temperature. The measurement procedure features easy sample preparation, direct measurement and high accuracy.

Literature
[1] M. Schubnell, J.E.K. Schawe, Int. J. Pharm., 192 (2001) p.173
[2] U. Joerimann, UserCom 15, Mettler-Toledo (1/2002) p. 8
[3] J.E.K. Schawe, U. Hess, J. Thermal Anal. Cal., 68 (2002) p. 741