High Speed DSC for Greater Sensitivity of Pharmaceutical Materials

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Introduction

Differential scanning calorimetry (DSC) is widely used for the characterization of thermophysical properties of materials. This includes the glass transition temperature (Tg), melting points, crystallization temperatures, heat setting temperatures, polymorphic melts and heats of transitions. Samples are generally heated at rates of 10 or 20 C/min when performing DSC experiments. However, the ability of Power Compensation DSC to achieve much faster linear heating and cooling rates permits real-life DSC experiments to be conducted at rates of 50 to 400 C/min. The application of high heating or cooling rates has been presented by Pijpers and Mathot [1,2] and is known as High Performance DSC or *High Speed* DSC.

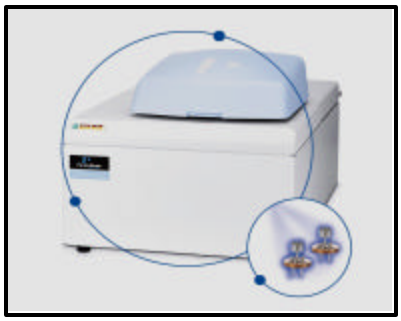
The advantages of the use of high heating or cooling rates for performing DSC experiments are:

- Significantly higher sensitivity since the DSC sensitivity is proportional to the applied heating rate.
- Faster experimental turnaround times where DSC experiments can be conducted in several minutes using the High Speed DSC approach.
- Better simulation or mimicking of processing conditions experienced by a material during production.

In the latter case, materials may experience ballistic heating conditions (microwave heating or laser heating) and High Speed DSC can better mimic the real-life conditions experienced by the material.

Power Compensation DSC

The use of the *High Speed* DSC technique requires a DSC instrument with an extremely fast response time and very high resolution. The one DSC that meets the requirements of the High Speed approach is the PYRIS Diamond Power Compensation DSC from PerkinElmer Instruments.



PYRIS Diamond DSC

Power Compensation DSC uses the Thermal Null principle to apply or remove power from two independently controlled furnaces (sample and reference sides). The Thermal Null approach is true 'temperature zero' where the sample and reference are maintained at the same identical temperature. The Power Compensation system quickly adjusts power to the furnaces to provide this temperature null condition. Power Compensation DSC measures true power or heat flow, Q, rather than a temperature differential via thermocouples.

The Power Compensation DSC employs ultra lightweight furnaces (mass of <1 g), which yields very low thermal inertia and the fastest possible DSC response time. The fast responsiveness of the Power Compensation DSC translates into the ability to obtain very fast linear or controlled heating and cooling ramps (up to 500 C/min). This also provides very high resolution or high definition of DSC transitions.

In marked contrast, most heat flux DSC devices using a single, larger mass furnace, which has higher thermal inertia and provides a much more sluggish DSC response. This yields slower heating and cooling rates and poorer resolution or definition of thermal events. The High Speed DSC approach is not practical or possible using the heat flux DSC instruments. In order to emulate the fast responsiveness of the Power Compensation DSC, some heat flux DSC devices are forced to resort to the use of real-time mathematical modeling equations to alter the displayed DSC heat flow and

PerkinElmer™ instruments.

temperature data. This sort of data alteration is absolutely not required or necessary with the Pyris Diamond Power Compensation DSC.

In this study, the properties of a pharmaceutical material were characterized using standard heating rate (10 C/min) heat flux DSC as well as the High Speed DSC approach of the Pyris Power Compensation DSC.

Calibration

The Pyris Power Compensation DSC was calibrated using the fast heating rate (200 C/min) used to run the sample. The temperature and enthalpic calibrations were performed using high purity indium metal. Displayed in Figure 1 are the High Speed DSC calibration results for the indium standard. Even at the very fast rate of 200 C/min, the Power Compensation DSC provides excellent results on the melting of indium in terms of a well-defined peak shape and accurate onset temperature and heat of melting.

Results

The pharmaceutical sample was analyzed on a heat flux DSC instrument using a heating rate of 10 C/min and these results are displayed in Figure 2. The sample was heated from –30 to 350 C at a rate of 10 C/min under a nitrogen purge. The sample was then cooled back to –30 C and reheated and the results for the first (red curve) and second (blue curve) heating segments are shown in Figure 2.

During the first heat, the sample yields a broad endothermic peak at

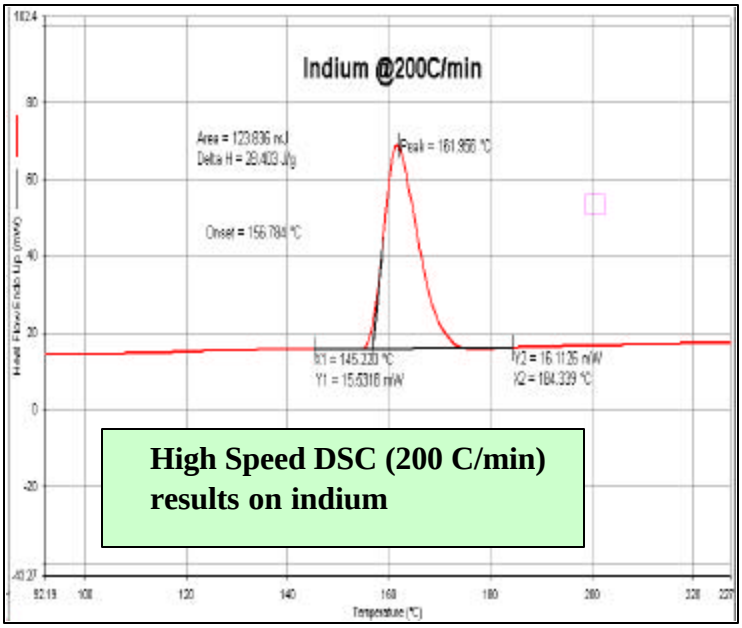


Figure 1. High Speed DSC results obtained for indium standard

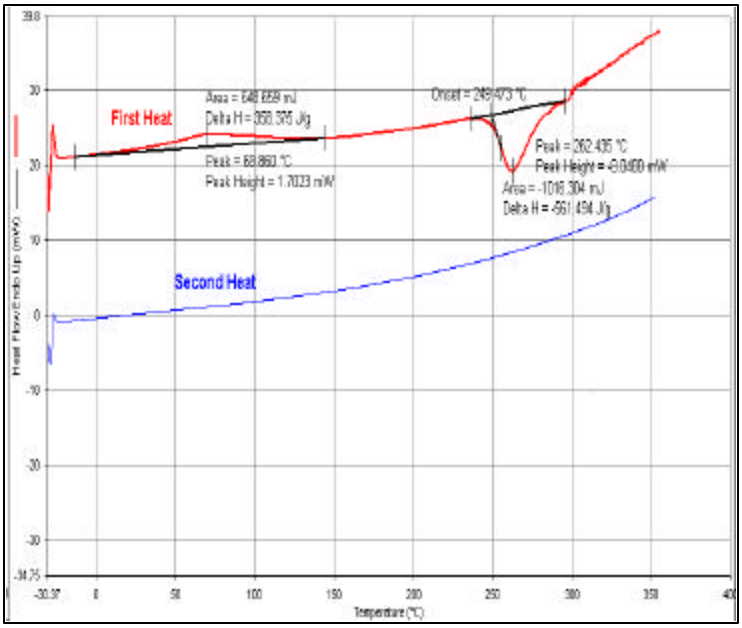


Figure 2. Standard heating rate (10 C/min) heat flux DSC results generated on pharmaceutical sample

PerkinElmer™ instruments.

70 C and this is most likely due to the evolution of water . The sample then yields an exothermic peak with an onset temperature of 249 C. This most likely reflects crystallization of the material. During the reheat experiment, no significant transitions are encountered as would be expected given that the sample evolved its moisture and crystallized during the first heating segment.

The presence of the crystallization peak during the first heating segment would normally indicate that there should be a glass transition at temperatures below the onset temperature. However, no Tg was observed using the standard 10 C/min heating rate with the heat flux DSC.

The pharmaceutical material was then analyzed using the High Speed DSC approach with the Power Compensation DSC. The sample was heated at a rate of 200 C/min between –30 and 350 C, cooled back to –30 C, and then reheated to 350 C at a rate of 200 C/min. The results of the High Speed DSC experiment are displayed in Figure 3. Excellent data is obtained at the very fast heating rate of 200 C/min. In addition, the entire experiment was conducted in a fraction of the time that it took to conduct the standard DSC (10 C/min) experiment.

The High Speed DSC results show the evolution of the moisture at 127 C. The peak is moved to higher temperatures at the faster rate due to the kinetic effects associated with the volatilization. The first heat results reveal the presence of the 'missing' glass transition event, Tg, at 243 C as reflected by the stepwise increase in the heat flow just before the crystallization event at 300 C.

The High Speed DSC technique featured with Power Compensation DSC provides the extra increase in sensitivity required to be able to detect the very weak Tg associated with this particular pharmaceutical material. The identification of the Tg is critical, however, for the complete characterization of the sample.

The reheat results shows that the moisture evolution peak disappears (as would be expected), but that the Tg transition is still observed, although pushed to lower temperatures. This reflects the differences in sample morphology due to the materials given thermal history.

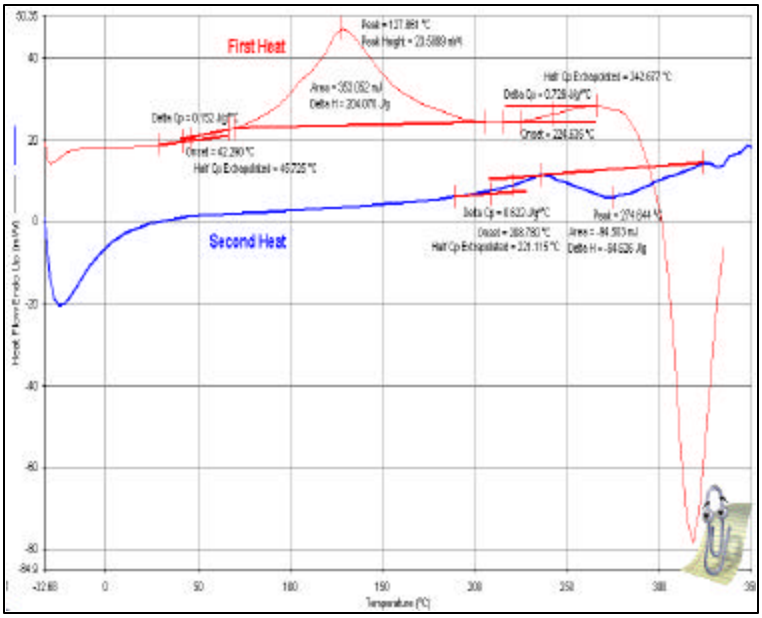


Figure 3. High Speed (200 C/min) DSC results obtained on pharmaceutical material

Summary

The High Speed DSC approach , featured with the Power Compensation DSC, provides a significantly higher level of sensitivity than is obtained using normal (10 or 20 C/min) DSC heating rates. The pharmaceutical material analyzed in this study yielded a previously undetectable Tg using the High Speed DSC approach.

References

1. T. F.J. Pijpers, V.B.F. Mathot, B. Goderis and E. van der Vegte, The Proceedings of the 28th North American Thermal Analysis Society Conference, Orlando, pp. 32-37, 2000.
2. T.F.J. Pijpers, V. Mathot, B. Cassel, The Proceedings of the 28th North American Thermal Analysis Society Conference, Orlando, pp. 860, 2000.