APPLICATION NOTE

Thermal Analysis

Measurement of Tg in Lyophilized Formulations

Figure 1. DSC 8500

In designed formulations for lyophilized drugs, it is important to know the collapse temperature of the cake. If the collapse temperature is exceeded, the cake will collapse and the batch will be ruined. The collapse temperature is often associated with the glass transition temperature (Tg) of the frozen material and measuring this transition is the best way to approximate it. In addition, it is useful to know the amount of non-frozen water, which can be estimated as the enthalpy of melting (ΔH). Both of these necessary values may be obtained with PerkinElmer's DSC 8500 (Figure 1).

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Measurement of the Tg is a basic analysis necessary for formulation development, as the temperature of freeze-drying needs to occur below the collapse temperature. As an example a sample of protein-excipient formulation (0.4 µg plasmid DNA, 588 µg polyethylenimine (PEI) and 200 µg sucrose in 20 µL of buffered water) was loaded into a hermetically sealed aluminum pan. The sample was cooled to -50 ˚C in a Diamond DSC using an Intercooler II with nitrogen purge and then heated to room temperature at 20 ˚C/min. The run shows a clean glass transition at -29.46 ˚C as shown in Figure 2.

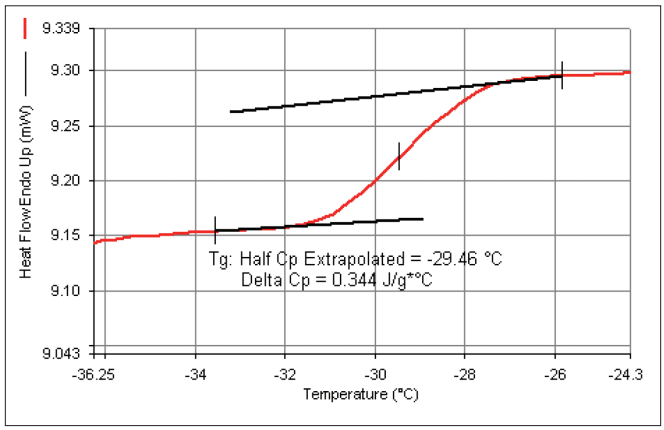

Figure 2. The Tg of a protein-excipient formulation run as described above.

Tg is another measurement that can also be approached by using HyperDSC. HyperDSC is the Double Furnace DSC's unique capability to heat and cool, in control, at rates up to 750 ˚C/min. The ability to heat and cool rapidly with high accuracy allows us to cool the sample at 100 ˚C/min, hold for 2 minutes, and reheat at 100 ˚C/min. While this permits substantial time savings, especially when used with an autosampler, the quality of the data is not compromised. Figure 3 shows the results of that the HyperDSC run. The Delta Cp measurement for the faster scan is 8.6 J/g/˚C compared with 0.34 J/g/˚C for the slower scan so the glass transition is measured with much greater sensitivity. This means that hard to find transitions can be more easily measured.

The DSC 8500 can provide necessary Tg and enthalpy data for the development of protein formulations, as well as providing the capability for both HyperDSC and StepScan techniques.

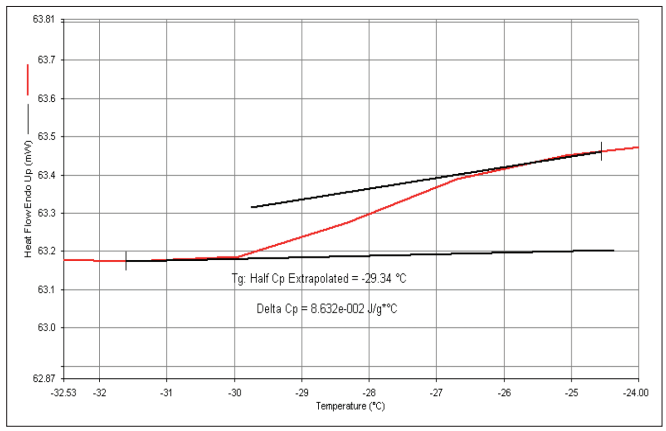

Figure 3. The same formulation as in Figure 2 but run using HyperDSC.

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