APPLICATION NOTE

Thermal Analysis

Measurement of the Tg' in 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 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 Diamond DSC (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.

Tg' is another measurement that can also be approached by using HyperDSC. HyperDSC is the Diamond DSC's unique capability to heat and cool, in control, at rates up to 500 ˚C/min. The Diamond's 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 Diamond DSC 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.

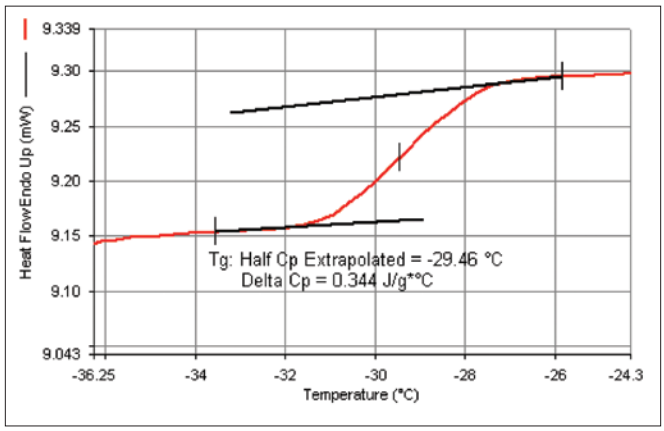

Figure 2. The Tg' of a protein-excipient formulation run as described above.

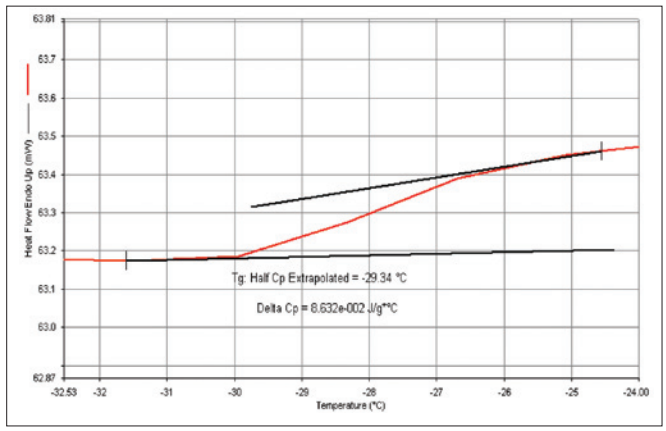

Figure 3. The same formulation as in Figure 2 but run using HyperDSC.

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