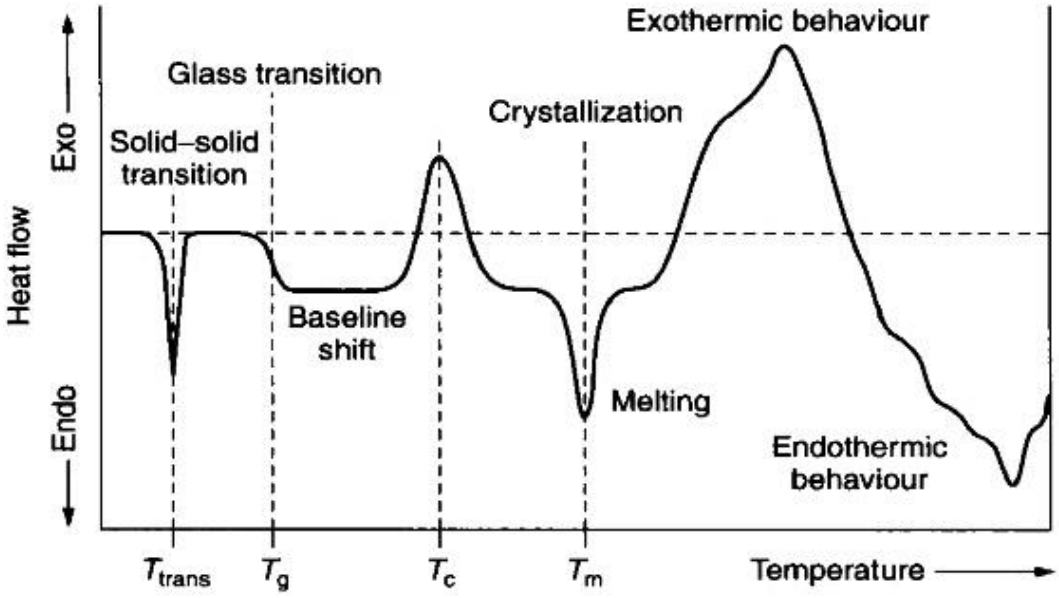
Differential Scanning Calorimetry (DSC)

PharmDr. Eva Šnejdrová, Ph.D.

DSC is a technique in which the difference in the amount of heat required to increase the temperature of a sample and reference are measured as a function of temperature. Both the sample and reference are maintained at nearly the same temperature throughout the experiment. Generally, the temperature program for a DSC analysis is designed such that the sample holder temperature increases linearly as a function of time. The reference sample should have a well-defined heat capacity over the range of temperatures to be scanned. The difference in heat flux is usually plotted against temperature (Fig. 1). The output is a dependence between the thermal properties and the molecular structure of the material, its morphology.

The method is widely used to determine melting points, glass transition and crystallization of various materials, including drug substances and pharmaceutical excipients. DSC is the most widely used thermal method of polymer characterization.

Figure 1: Schematic representation of the DCS graph showing T_g (glass transition temperature), T_c (crystallization temperature) and T_m (melting point)



DSC Applications

The technique is widely used across a range of applications, both as a routine quality test and as a research tool. Differential scanning calorimetry can be used to measure number of characteristic properties of a sample. Using this technique, it is possible to observe fusion and crystallization events as well as **glass transition temperatures T_g**. DSC can also be used to study oxidation, as well as other chemical reactions. The ability to determine transition temperatures and enthalpies makes DSC an invaluable tool in producing phase diagrams for various chemical systems.

- Glass transition
- Melting points
- Crystallization times and temperatures
- Heats of melting and crystallization
- Percent crystallinity
- Oxidative stabilities
- Compositional analysis
- Purities
- Thermal stabilities
- Polymorphism

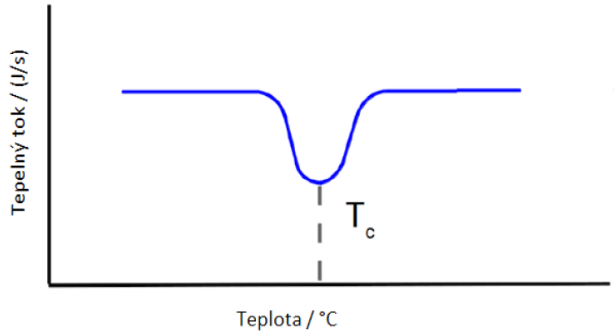
Glass transitions may occur as the temperature of an amorphous solid is increased. These transitions appear as a step in the baseline of the recorded DSC signal. This is due to the sample undergoing a change in heat capacity; no formal phase change occurs.

As the temperature increases, an amorphous solid will become less viscous. At some point the molecules may obtain enough freedom of motion to spontaneously arrange themselves into a crystalline form. This is known as the **crystallization temperature** (**Tc**). This transition from amorphous solid to crystalline solid is an exothermic process, and results in a peak in the DSC signal. As the temperature increases the sample eventually reaches its **melting temperature** (**Tm**). The melting process results in an endothermic peak in the DSC curve.

Crystallization temperature (Tc)

Crystallization is an exothermic process, thus reducing the heat supplied to the system, resulting in a negative peak on the curve (Fig. 2). The crystallization temperature (Tc) is determined at the local minimum of the peak, and the crystallization heat can be obtained by integrating the peak.

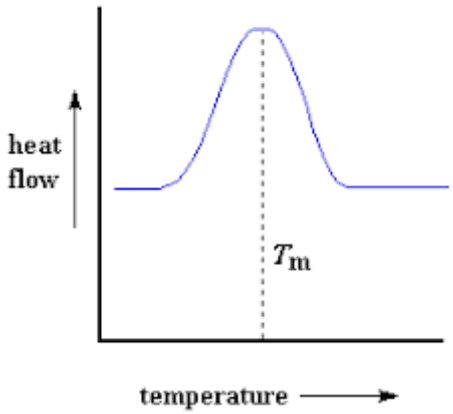
Figure 2. Course of DSC curve during crystallization



Melting temperature (T_m)

Melting of the material is an endothermic process. The temperature of the material remains constant despite continuous heating, so that heat is absorbed into the sample and this energy is converted to melting. On the DSC curve, this phenomenon is reflected by the same peak shape as crystallization, but in the opposite direction (Fig. 3). The melting point (T_m) is declared as the peak of the peak and the energy consumed by the melting is obtained by integrating the peak.

Figure 3. Course of DSC curve during melting



The glass transition temperature (T_g)

The glass transition is associated with a change in the internal structure of the materials, which is particularly reflected in the mechanical properties. Below the T_g, the material is brittle and hard, above the T_g the material becomes elastic. The glass transition usually changes not only the mechanical properties of the material, but also the thermal capacity, which we use for measurement. A typical glass transition is shown in Fig. 4 as a continuous increase in heat flow. The glass transition temperature is the value in the middle of this transition, the inflection point of the curve. Tg is read on the second heating curve. The **heating rate** is important and should be **10 K/min** when determining the T_g.

Figure 4. DSC curve during glass transition – determination of T_g

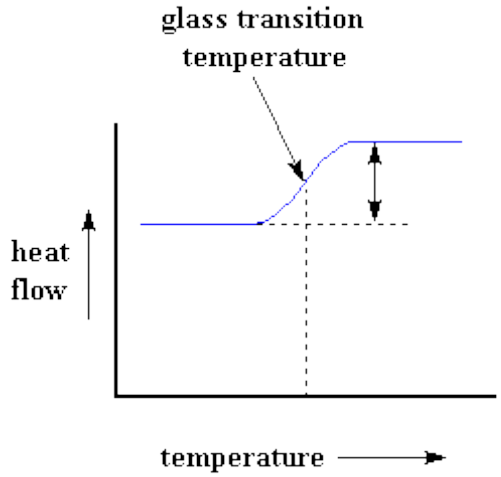
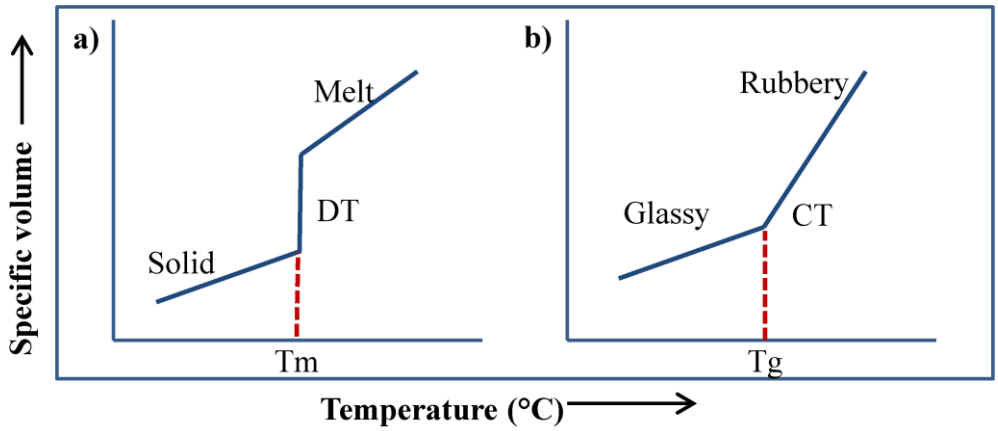


Figure 5. The difference between T_m and T_g



Sample preparation for DSC analysis

Samples for DSC measurements are inserted into the apparatus in pressed aluminium crucibles. Handling of the sample or crucibles should be done with tweezers and do not touch them by hand! Remove one cup and one lid from the storage cartridges. The crucible is taller than the lid, so it can be easily distinguished. Weigh both parts together (to four decimal places) and write down the total weight. Check that you do not weigh more crucible parts.

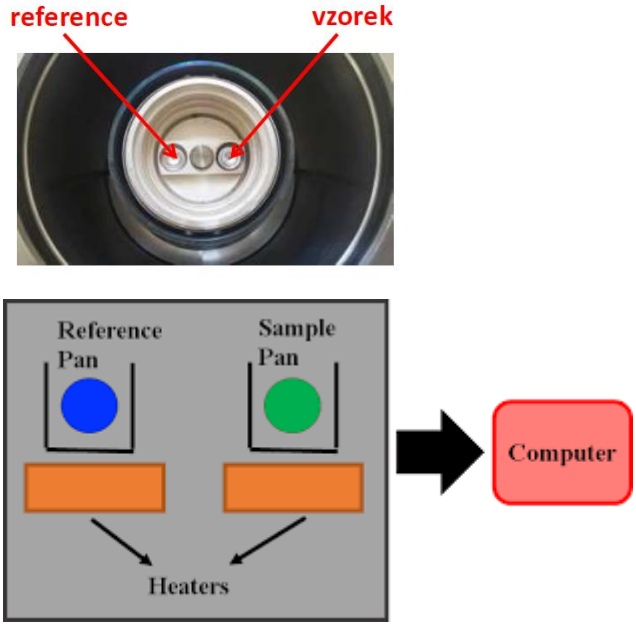
Spread a small amount of sample (ideally 4 to 10 mg) at the bottom of the crucible and weigh. Close the lid and press on the press. Finally, use two tweezers to insert two small holes into the cap. Consider the sealed crucible and check the weight, sometimes part of the sample may stick to the tweezers when punctured. You will fill in the empty crucible weight and sample weight into the measuring program.

Place the sample crucible in the right part of the cell, place the empty reference crucible in the left part (Fig. 6). Make sure that neither cup is touching the wall of the measuring cell.

watch this instructional video

https://www.youtube.com/watch?v=aTWVCfRlMX8

Figure 6. View of the inside of the measuring cell (vzorek = sample)



Examples of real DSC scans

Figure 7. DSC scans of excipients

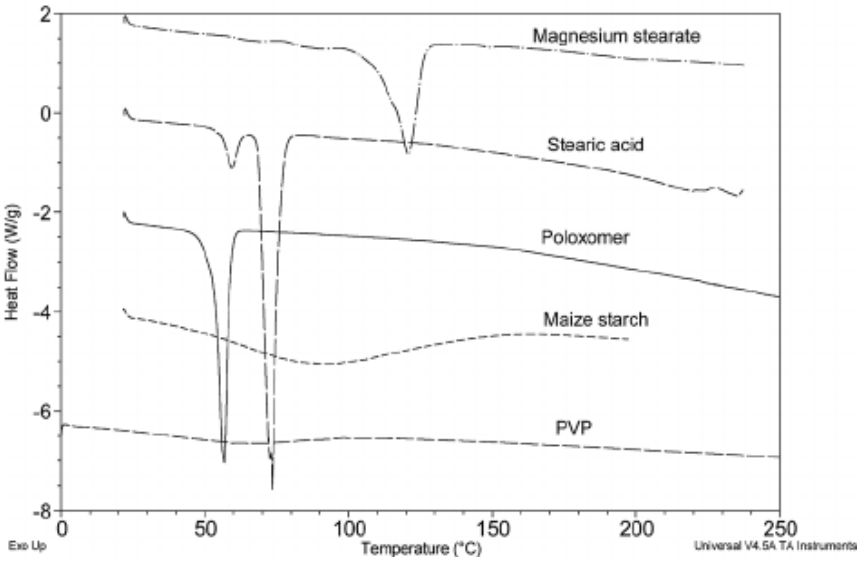


Figure 8. DSC scans of drug-loaded nanospheres and materials for formulation

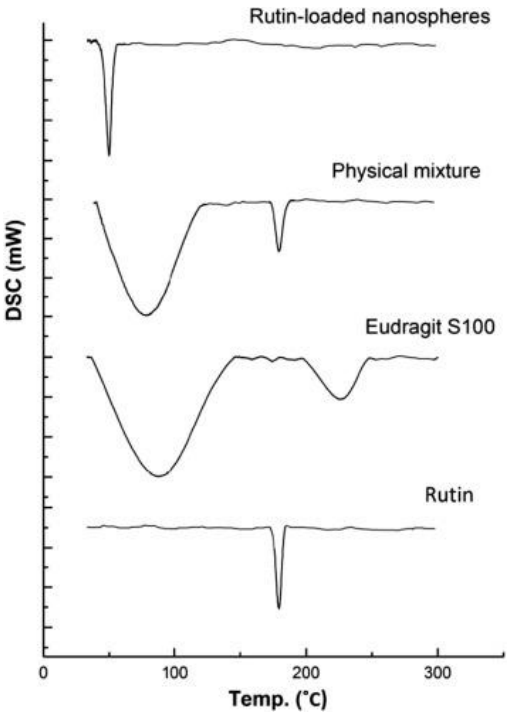
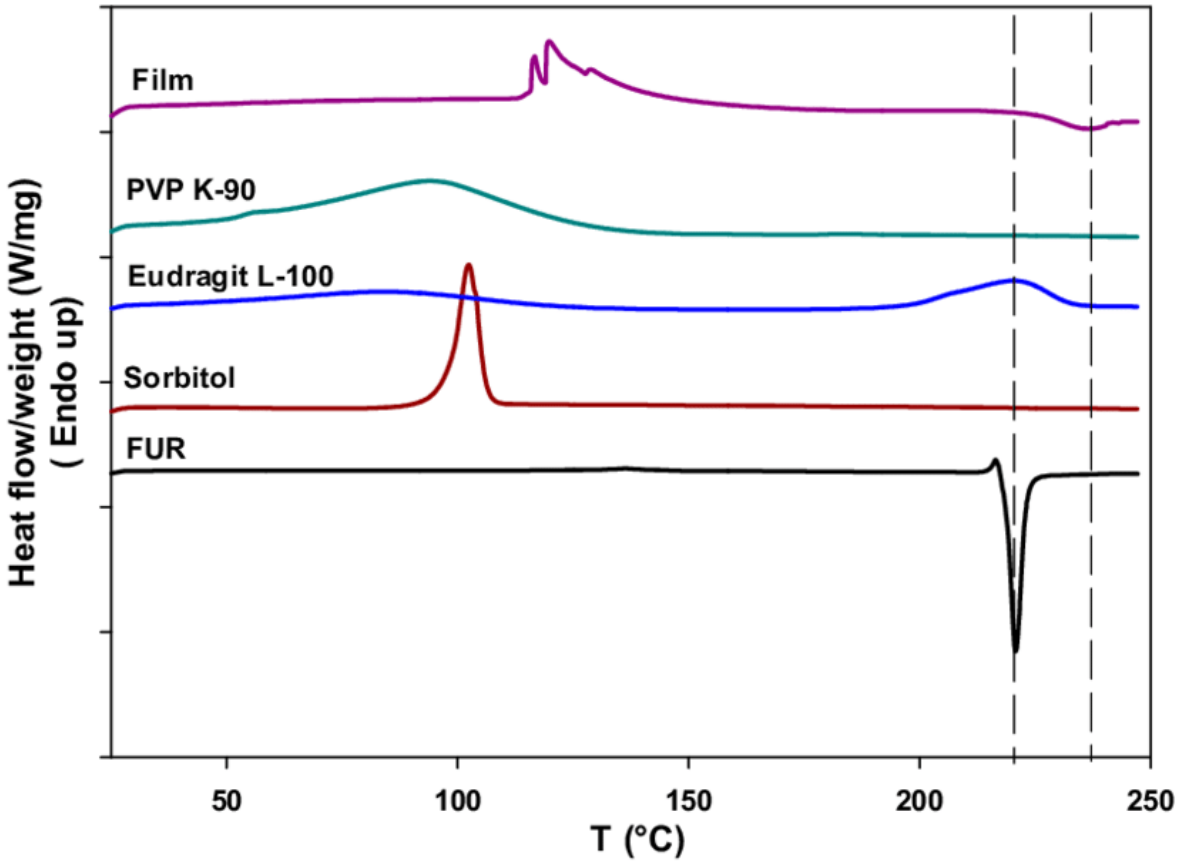


Figure 9. DSC scans of thin film and materials for formulation



More information

https://www.azom.com/materials-video-details.aspx?VidID=2683

http://instrument-specialists.com/thermal-analysis-applications/differential-scanning-calorimetry-dsc/

https://www.toray.jp/plastics/en/torelina/technical/tec_013.html

Measuring by DSC and evaluating the results - videos

https://www.youtube.com/watch?v=QlD3H_s5sZ8

https://www.youtube.com/watch?v=EjAzWwrBz7M