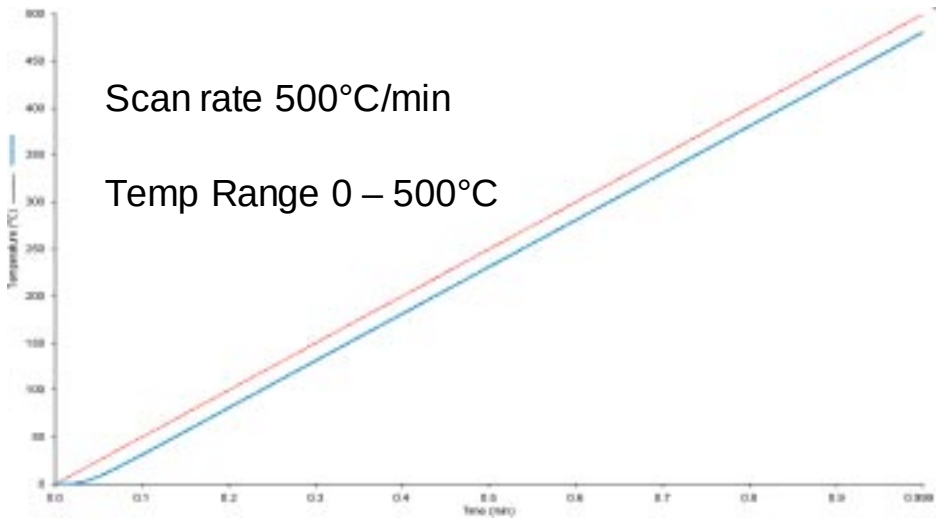
HyperDSC Application Note

The use of HyperDSC in the study of Amorphous lactose- A study of percentage amorphous content

The study of the amorphous content of pharmaceutical materials has been of great interest for many years. It has however, quite often been difficult to quantify very low levels of amorphous content using DSC because of the very low energies associated with this type of glass transition at these low levels. As a consequence other techniques have often been used for this measurement, for example moisture sorption. These other techniques , however, have tended to be be very time consuming.

HyperDSC has been shown previously to greatly enhance the sensitivity of measurement of the glass transition, so it was decided that a study of a model compound with low amorphous content would be made.

HyperDSC allows the use of scan rates upto 500°C/min to analyse the transition behaviour the materials whilst maintaining control of the heating rate. This is shown in the thermogram below



The model compound that was chosen for this study was lactose. Two samples of lactose were provided by Dr Paul Royall of Kings College London for the study. The first sample was a spray dried lactose that would be mostly amorphous , and the second a fully crystalline sample. For the purpose of this study the spray dried lactose was assumed to be fully amorphous.

The thermogram overleaf shows the effect of running a HyperDSC scan on the spray dried sample of lactose at rates up to 500°C/min.

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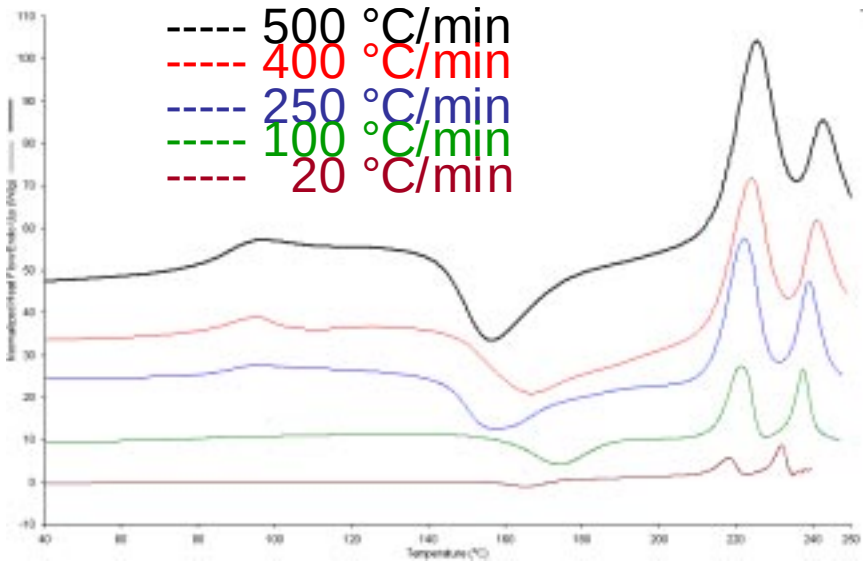
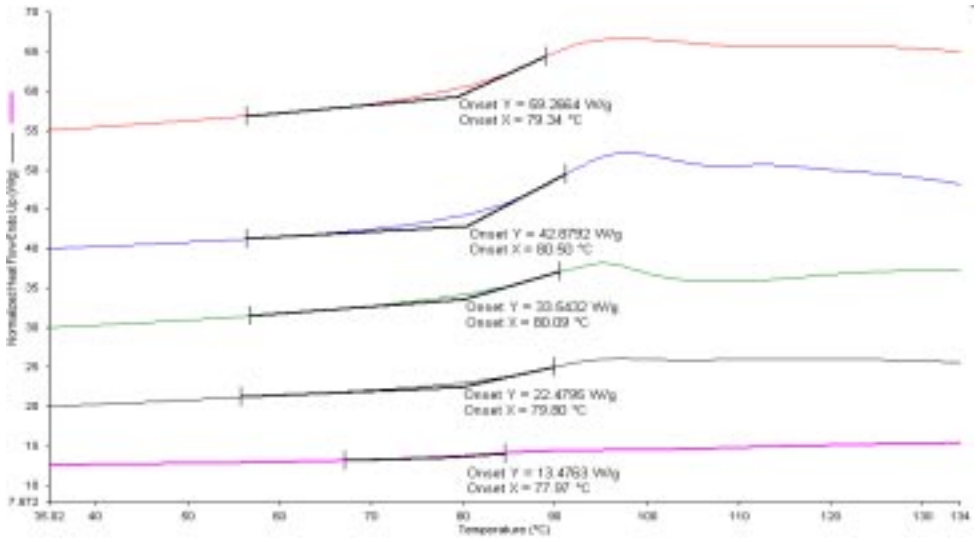


HyperDSC scan of a spray dried lactose

As the thermogram shows, the glass transition of lactose is very difficult to identify at slow scan rates, however at 500°C/min the Tg can be clearly seen. It is also worth noting that recrystallisation of the sample still occurs even at 500°C/min and there is no loss of resolution of the melting of the two forms of crystalline lactose.

If we examine the glass transition area of the thermogram then it can be clearly seem that the use of HyperDSC gives the ability to identify the Tg of lactose simply. The onset of Tg does not vary significantly with the increase of scan rate and shows excellent reproducibility.

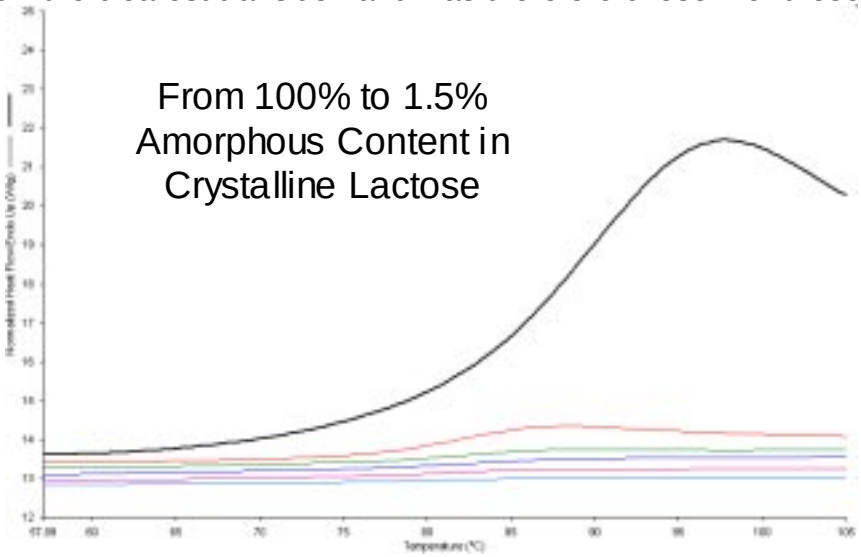


The glass transition area of spray dried lactose

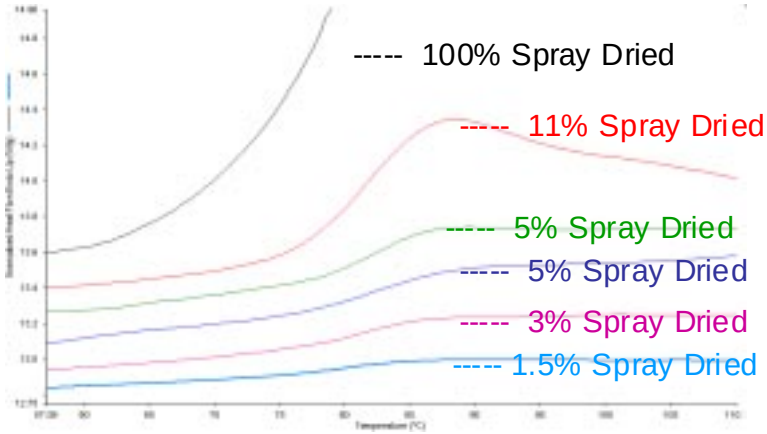
PETA-05

In order to test the sensitivity of HyperDSC for low amorphous content, a series of samples were prepared by mixing a known percentage of spray dried lactose into a sample of fully crystalline lactose. A range of percentages were chosen down to 1.5% spray dried mixed into crystalline.

The following two thermograms show the glass transition region for the samples prepared. A HyperDSC rate of 500°C/min was used for these analyses. This rate was chosen to show the clearest transition and was therefore chosen for these analyses.



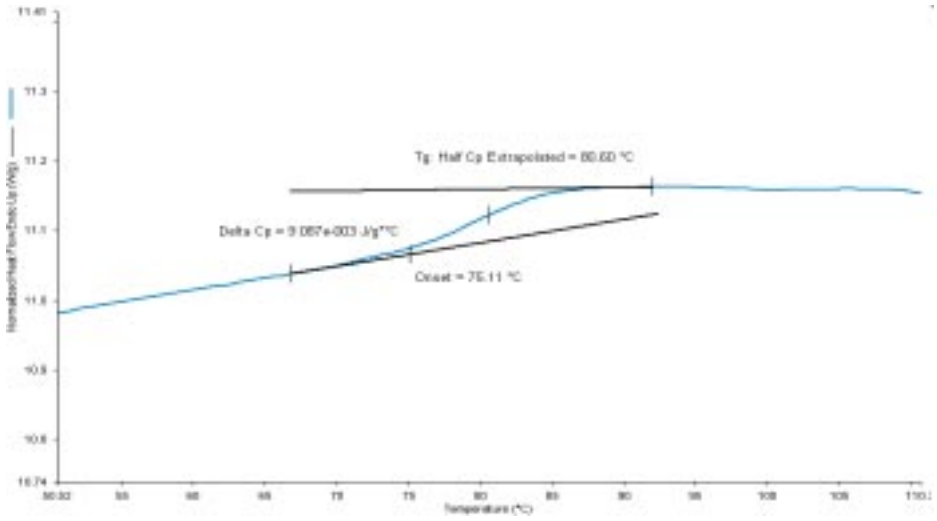
Glass transition of lactose with reducing spray dried content



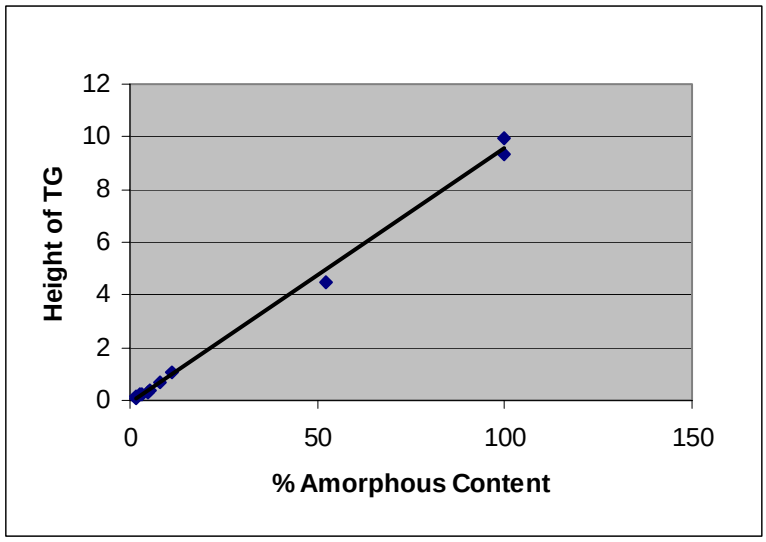
Expansion of the Tg area of the lactose mixtures

The traces shown previously show the ability of HyperDSC to measure very low amorphous content in this system. These results were obtained at 500°C/min giving not only the sensitivity to make this meaurement but also a huge time saving over other methods, on average sample taking 30 seconds to run.

The step height change of the glass transition was measured from the onset to the maximum height for the sample that contained 1.5% amorphous material.



This procedure was carried out for all the samples and it was found, that there is a linear relationship between Tg height and percentage amorphous content, this is shown in the graph below



This means that it is possible to quantitatively measure very low amorphous content. and for lactose this has been shown for levels lower than 1.5%

Conclusions

It has been shown that for the lactose model system it is possible to measure the amorphous content of samples using HyperDSC.

This has many benefits for pharmaceutical research labs because HyperDSC can offer the ability to rapidly screen samples with minimal sample preparation whilst measuring very low levels of amorphous material.

Acknowledements

We would like to thank Prof Jim Ford (Liverpool John Moores University), Mark Saunders (Pharmaterials London School of Pharmacy) and Dr Paul Royall (Kings College London) for many useful discussions on the results. We would especially like to thank Dr Paul Royall for providing the samples used in in this study