

The Development of Photothermal FTIR Microspectroscopy as a Novel Means of Spatially Identifying Amorphous and Crystalline Salbutamol Sulfate on Composite Surfaces

Louise C. Grisedale¹, Jonathan G. Moffat¹, Matthew J. Jamieson², Peter S. Belton¹,

Susan A. Barker¹ and Duncan Q.M. Craig^{1}*

1 School of Pharmacy, University of East Anglia, Norwich, UK, NR4 7TJ

2 Particle Generation, Control and Engineering, GlaxoSmithKline, Medicines Research Centre, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY, UK.

* Corresponding author: d.craig@uea.ac.uk Fax: +44 1603 592003

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1. Analysis of pure amorphous and crystalline salbutamol sulfate samples with macroscopic techniques

Modulated temperature differential scanning calorimetry was performed using a TA Instruments DSC Q1000 with an attached integrated refrigerated cooling system (TA Instruments, Delaware, US). Temperature calibration was performed with indium and heat capacity calibration was performed using dried aluminium oxide. Samples (3-4 mg) were hermetically sealed in aluminium pans and heated to 200°C with an underlying heating rate of 2°C min⁻¹, a modulation amplitude ± 0.212°C and a period of 40 seconds. Each set of MTDSC experiments were repeated four times to ensure reproducibility.

The (macroscopic) ATR-FTIR studies were carried out using a Bruker Optics IFS66/S spectrometer (Coventry, UK) with a Golden Gate MkII Accessory from Specac Ltd. (Orpington, UK). Spectra were collected from the region 4000 to 400 cm⁻¹ with 200 scans at a resolution of 8 cm⁻¹.

Modulated temperature DSC

Figure 1a shows that the spray dried sample compressed with 1 tonne pressure behaved similarly to the loose (amorphous) powder in that a water loss endotherm is observed at circa 40-80°C followed by a glass transition at approximately 121°C, seen most clearly in the reversing heat flow signal which represents the heat capacity separated from latent heat effects, then followed by a further endothermic signal which represents decomposition. The crystalline material showed the expected melt/decomposition process at circa 160°C for both the powdered and compacted material (data not shown). Overall, therefore, the compression

process used appears not to result in significant alterations to the amorphous or crystalline structure of the material.

ATR-FTIR Spectroscopy

Figure 1b shows a comparison between the ATR-FTIR spectra of loose amorphous and crystalline powder with their respective compacts formed with a 1 tonne force. An assignment of the peaks is available and the spectral differences between amorphous and crystalline materials has been previously discussed^{1, 2}. In brief, the most obvious differences between the absorbance bands for the crystalline and amorphous samples are seen in the 3500 to 2200 cm^{-1} region, which arise from overlapping contributions from NH, OH and CH stretching vibrations. In the 1430 to 1470 cm^{-1} region (CH_2N vibration) changes between the two materials almost certainly reflect changes in hydrogen bonding. The peaks associated with aliphatic CH bending modes also alter, with the peak at 1250 cm^{-1} becoming reduced in intensity and the peak at 1270 cm^{-1} intensifying for the amorphous material. In the 1100 to 800 cm^{-1} region, there are ranges of broadenings and intensity changes which we ascribe to the creation of a range of environments for the amorphous material.

Spectrally the chemical behaviour of the compressed or loose crystalline samples was similar. However, the amorphous samples did show some differences between the two forms; it appeared that there was a marginal increase in crystallinity of the compressed sample with the sample showing more structure in the bands at approximately 1000 cm^{-1} and in the region 3500-3000 cm^{-1} . Overall differences in intensity seen may have been caused by the pressure exerted by the anvil on the ATR window while positioning and securing the samples in place. In summary, the application of 1 tonne pressure to the compacts was found to produce some small effects, which may or may not reflect minor structural change, on the behaviour of amorphous compacts but none on the crystalline salbutamol sulfate.

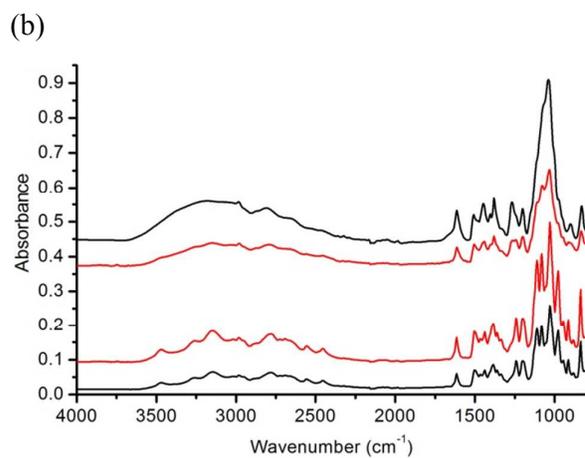
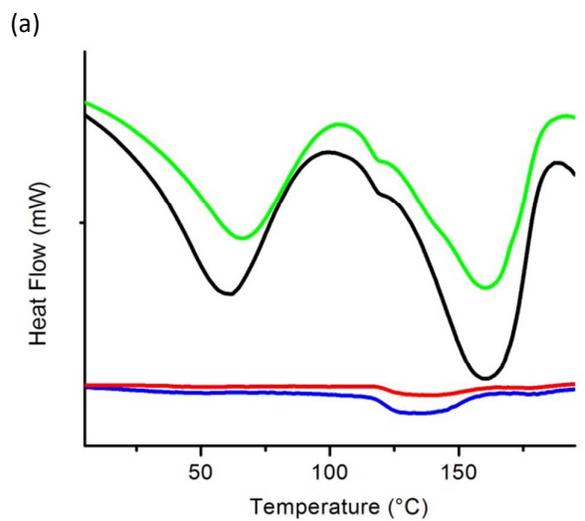


Figure S-1: (a) MTDSC trace of total (black line) and reversing (red line) heat flow signals amorphous sample compressed by a 1 tonne force and the total (green line) and reversing heat flow (blue line) of the loose powder. (b) ATR-FTIR spectra of the loose powder (black lines) and 1 tonne compressed (red lines) amorphous spray dried (top) and crystalline (bottom) salbutamol sulfate samples. Spectra offset for clarity.

2. References

1. Ali, H. R. H., H. G. M. Edwards, J. Kendrick and I. J. Scowen, *Drug Test. Anal.*, 2009, *1*, 51-56.
2. Grisedale, L. C., M. J. Jamieson, P. S. Belton, S. A. Barker and D. Q. M. Craig, *J. Pharm. Sci.*, 2011, *100*, 3114-3129.