A STUDY OF THE AMORPHIZATION OF LACTOSE MONOHYDRATE FOLLOWING EXTENDED MILLING TIMES

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INTRODUCTION

Milling is known to produce both an amorphous surface phase while converting a proportion of α-lactose to β-lactose (Shariare, de Matas et al. 2011). The aim of present work is to elucidate nano-scale domains of amorphous material in ball-milled lactose.

METHOD

Lactose monohydrate (EP) was used in this study. The sieved sample (with size approximately ≥ 180 μm) was ball milled for extended time intervals (90, 180, 270 and 360 min) and thermal analysis was performed using TGA and DSC immediately after each stage of milling. Dielectric measurements were undertaken in a Solartron 1296/1255 dielectric spectrometer across the frequency range 0.1-10^6 Hz at discrete temperatures from −80 to 100 °C at 5 °C increments.

RESULTS

The dielectric response surface in the frequency and temperature domains for the pre-milled sample (data not shown) has a simple response surface with a single percolation peak (which has been ascribed previously to the percolation of protons in the hydration surface of the particles).

The creation of an amorphous phase is supported by the observations of a new dielectric relaxation that appears on the low temperature side of the original percolation peak (for the 45 min to 360 min samples). This dielectric relaxation process becomes more pronounced as the milling time increases, which is consistent with data obtained from TGA and DSC which show a progressive increase in amorphous content on increasing the milling time up to 180 min.

DISCUSSION

The dielectric relaxation within the amorphous component takes on a saddle-shape (Figure 1) characteristic of that observed for ice-like water clusters in porous silica (Gutina, Antropova et al. 2003). If one assumes that the relaxation time on the low temperature side of this process has an Arrhenius dependency then one gets an approximate value for the activation energy close to that of the α-process reported for dynamic glass transition of amorphous lactose. However, the equivalent static glass transition temperature (equivalent to the calorimetric glass transition temperature) is significantly lower than that in the bulk which is

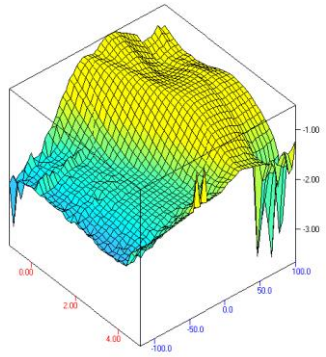

Figure 1: Dielectric spectra of crystalline lactose showing imaginary part of permittivity plotted against temperature and frequency in sample after 180 minute milling.

consistent with the confinement effect seen for polymeric glasses at scale length of tens of nanometres (Liu, Siegel et al. 2010). The approximate scale length (i.e. depth) of the amorphous surface domains for particles at the limiting size of 100 nm was considered to be in the region of 4 nm. This scale length was estimated from the proportion of amorphous material that was derived from the reduction in the dehydration step of α-lactose monohydrate in TGA data). From the reduction in T_g, one can therefore infer that the stability of the amorphous sub-surface phase in micronized particles will be significantly less than that in the bulk material.

CONCLUSION

The development of amorphous phase during milling and the water present in nano-porous structures developed during this process can have a more pronounced impact on the stability of lactose than might at first be expected from conventional measurements on the glass transition of glassy lactose in the bulk.

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