Differences in the amorphous state in differently processed pharmaceutical powders

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Amorphous materials are inherently metastable and therefore tend to revert to a more thermodynamically stable, crystalline form. As this instability has a potentially negative impact on storage and drug potency it is important to understand the thermodynamic properties of the amorphous phase.

In recent years the main attention of research has been focused on the amorphous content of drugs and excipients. However, it has been found that no universal "critical amorphous content" could be defined that is related to a step-change in stability or dissolution rate as a certain amorphous content can have a different relevance for the properties of different compounds. Newer research also suggests that even for a single compound, different amorphous states exist each with variations in the energetic state and these various states can cause differences in product behaviour. If, for example the same crystalline compound is made amorphous using different techniques (e.g. by different processing procedures) a different amorphous state possessing different thermodynamic properties can result.

In this study the impact of processing technologies on the amorphous state of lactose has been investigated. For this purpose the same batch of alpha lactose monohydrate has been transformed into an amorphous state using four techniques: spray-drying, freeze-drying, super-critical fluid (SCF) freeze-drying and high energy milling. The energetic state on the surface of each sample has been explored by Inverse Gas Chromatography (IGC) in terms of the dispersive and specific surface energy. To make results comparable the same particle fractions (45-63 μm) have been used. As different procedures can result in different amorphous contents, the samples have been exposed to humidities just above the glass transition to induce a slow crystallisation. The surface energy was monitored during the crystallisation process.

Results suggest that at higher amorphous contents the surface energies of the same sample remain constant while at lower amorphous contents surface energies decrease, possibly due to an increased contribution of crystalline alpha lactose monohydrate. When samples processed using different techniques but with the same amorphous content are compared significant differences can be found suggesting different energetic states.