Crystal properties impacting on milling induced disorder

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Milling of pharmaceuticals is an important unit operation in the preparation of many dosage forms. It is often employed to ensure good blend uniformity and in the case of inhalation dosage forms to ensure correct deposition in the lung. The milling process is extremely inefficient (1) and due to the high energy input, the milled powder may be of reduced crystallinity and may contain disordered regions (2), on the surface of particles which can be considered amorphous (3). The amorphous phase is thermodynamically unstable. When sufficient energy is provided so that the energy barrier to crystallisation is overcome, the stable crystalline product may have different properties to that of the starting material i.e. different polymorphic form. This can have a significant effect on product performance. Based on results from several model compounds including ibuprofen, p-aminosalicylic acid and succinic acid (4) the effect of salt form and initial starting habit on milling induced solid-state property change will be presented. Using techniques such as solution calorimetry, DSC, PXRD, IGC and molecular modelling, the results obtained indicate that salt selection and habit modification are useful tools to overcome process-related problems of pharmaceutical materials.

References

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