CRYSTALLITE SIZES AND MICROSTRAINS DETERMINED BY RIETVELD REFINEMENT : APPLICATION TO MILLED LACTOSE

Vincent Caron[+]*, Jean-Francois Willart[+], Jacques Lefebvre[+], Ronan Lefort[+-], Marc Descamps[+].

+: Laboratoire de Dynamique et Structures des Matériaux Moléculaires, UMR CNRS 8024, Université des Sciences et Technologies de Lille, 59655 Villeneuves d'Ascq Cedex, France
* : Now at School of Pharmacy, Trinity College Dublin, Dublin 2, Ireland
-: Now at the Institut de Physique de Rennes, UMR CNRS 6251, Université de Rennes 1, France

Milling is an operation frequently used in pharmaceutical industry to produce powder with desired micromeritic properties (particle size…). However, it is now widely recognized that milling can also induce physical transformation of matter like amorphization or polymorphic transformation for example. Due to their weak elastic constants, pharmaceutical compounds are particularly sensitive to mechanical perturbations. Therefore, it is important to detect and understand the nature of these transformations in order to avoid unexpected changes in the properties of the pharmaceuticals or, on the contrary, to tune their physical states to enhance some properties like stability, dissolution…

Lactose is a disaccharid widely used as an excipient for its good properties of flowability and compressibility. It has been previously shown that anhydrous stable α-lactose (αL_S) undergoes solid state vitrification upon milling.

1) We have followed in details the microstructural evolutions (i.e. crystallite sizes and microstrains) of lactose during the amorphization process by Powder X-Ray Diffraction (PXRD). The width of the Bragg peaks in a diffractogram is sensitive to the microstructure of a sample i.e. the size and the microstrain of the crystallites. The Rietveld method permits to fit the diffraction pattern as a whole and to extract this information from the profile of the Bragg peaks. The results show a strong decrease of the crystallite sizes concomitant to a strong increase of the microstrains prior to the amorphization.

2) These evolutions have been compared with the ones observed by Differential Scanning Calorimetry (DSC) and 13C Solid State Nuclear Magnetic Resonance (^{13}C SS-NMR). The results show that amorphous content given by PXRD and ^{13}C SS-NMR are higher than amorphous content determined by DSC. These differences are too huge to be attributed to a difference of sensitivity depending on the techniques used. The more plausible interpretation is that these differences are due to the different ways the techniques probe the samples.