Impact of the amorphisation routes on physical properties of amorphous materials

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So far, substances of pharmacy (active pharmaceutical ingredients and excipients) are most often prepared in the crystalline state (ordered) for obvious reasons of stability. Many pharmaceuticals, either by accident or design, may also exist in a total or partially amorphous state (disordered). This situation is encountered more and more frequently due to the increasing complexity of synthesized molecules. The amorphous state has a lower stability but a higher solubility than the corresponding crystalline forms. The formulation of active substances in the amorphous state, has thus motivated a strong interest in the last decade to increase the solubility of poorly soluble drugs[1].

In this study, the amorphisation process and the amorphous state of lactulose ($C_{12}H_{22}O_{11}$), a disaccharide of pharmaceutical interest, have been investigated by combining a wide range of experimental and numerical techniques in order to probe structural, dynamical and thermodynamical physical properties. The amorphous compounds obtained by milling were compared to other amorphous forms designed by alternative amorphisation routes such as melt-quenching, freeze-drying, spray-drying[2]. Recently, neutron diffraction with polarization analysis has been developed on D3 and successfully applied to mixtures of light and heavy water[3]. For the first time, we were able to experimentally obtain the coherent structure factor of highly hydrogenated lactulose samples using D3 and D7 neutron diffractometers available at ILL. In addition, differences between the amorphous samples due to thermal degradations and chemical changes have been clarified aiming to unravel the true impact of the amorphisation mechanism itself. In this lecture, the observed structural differences between the amorphous samples will be presented.

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