



Contribution ID: 112

Type: E-Poster

## Exploring real time amorphization in organic pharmaceutical compounds via in situ ball milling

Amorphization of crystalline powder is known in the pharmaceutical industry to increase the solubility of the Active Pharmaceutical Ingredient (API). Amorphization can be achieved by different routes, among which the mechanical comminution of the powders, which however requires the detailed understanding of mechanochemical processes involved so to gain control on the process and its effect on the API. In situ materials characterization techniques are extensively used, as they offer the advantage to get a description of possible reactive intermediate states in a sample without risk of reaction/relaxation by interrupting the process.

A protocol was developed by Halasz et al. [1] for in situ, real time monitoring of mechanochemical reaction using synchrotron X-ray powder diffraction and later used by Bordet et al. [2] to investigate the amorphization process of a powder with high energy in situ ball milling. However, the ball mill consisting of a Perspex vessel requires to be placed in the path of a high-energy X-ray beam (90keV). Under these conditions, the signal by the extrinsic contribution of the grinding media and outer walls of the vessel strongly interferes with the intrinsic signal from the materials under investigation with the risk of hindering relevant information due to peaks overlapping and high level of background.

A new type of in situ ball mill [3] was developed at the Materials Science beamline (Paul Scherrer Institute, SLS, Switzerland) with a particular geometry allowing one to obtain data with a lower background and much sharper Bragg peaks using Si-based single photon counting detectors operated at lower photon energies (<30keV). This geometry has advantages in the study of the amorphization process of organic pharmaceutical compounds which usually scatter weakly and thus require a fine control of the background.

However, progress in studying in situ amorphization of pharmaceutical compounds was hindered by the tendency of organic compounds to agglomerate while milling, giving rise to inhomogeneous backgrounds and inhomogeneous amorphization processes.

We describe novel strategies allowing improvements in real time monitoring of the amorphization of pharmaceutical compounds. In particular, we present recent results where we show significant improvements for in-situ ball milling using an anti-caking agent to prevent agglomeration of the powder in the ball milling setup. We believe that these improvements could enable systematic and reliable studies of amorphization in pharmaceutical compounds.

[1] Halasz I., Kimber S. A. J., Beldon P. J., Belenguer A. M., Adams F., Honkimäki V., Nightingale R.C., Dinnebier R. E., Friščić T., *Nature Protocols* 2013 (8), 1718–1729

[2] Bordet P., Bytchkov A., Descamps M., Dudognon E., Elkaïm E., Martinetto P., Pagnoux W., Poulain A., and Willart J. F., *Crystal Growth & Design* 2016 16 (8), 4547-4558

[3] Ban V., Sadikin Y., Lange M., Tumanov N., Filinchuk Y., Černý R., and Casati N., *Analytical Chemistry* 2017 89 (24), 13176-13181

**Primary author:** MORIN, Mickael (Excelsus Structural Solutions (Swiss) AG)

**Co-authors:** Dr GRANDEURY, Arnaud (Novartis Pharma AG); Dr JUHNKE, Michael (Novartis); Dr CASATI, Nicola (Paul Scherrer Institute); Dr WILKE, Manuel (Paul Scherrer Institute); Mr LANGE, Michael (Paul Scherrer Institute); Dr POMJAKUSHINA, Ekaterina (Paul Scherrer Institute); Dr WHITFIELD, Pamela; REINLE-SCHMITT, Mathilde (Excelsus Structural Solutions (Swiss) AG); Dr GOZZO, Fabia (Excelsus Structural Solution)

**Presenter:** MORIN, Mickael (Excelsus Structural Solutions (Swiss) AG)

**Session Classification:** E-Poster Session

**Track Classification:** Crystallographic and Spectroscopic Advanced Tools Applied to Pharmaceuticals