Stability, Aging and Release of Drug Products: SWAXS opens new Perspectives

Peter Laggner

Institute of Biophysics and X-Ray Structure Research, Austrian Academy of Sciences, and Hecus X-Ray Systems, Graz, Austria

Combined small- and wide-angle X-ray scattering (SWAX), optionally with integrated calorimetry function (DSC), is arguably the most informative and versatile method to gain structural information on solids or liquids. The accessible length scale of 0.1 to 100 nm covers the powder-crystallographic details to the nano-scale characteristics, i.e. inner surface, long periods, macro- or supramolecular sizes, in amorphous, porous, or liquid-crystalline systems (1,2). With modern instrumentation, including advanced X-ray optics, fast position sensitive detectors, automatization and pattern recognition, developed in this laboratory, typical measuring times for solids have come down to the order of minutes or even seconds, with normal laboratory X-ray facilities. At synchrotron sources, measuring times can reach down to milliseconds and below (3).

To make use of this potential in the investigation of technologically or pharmacologically interesting systems, innovative solutions for sample containment, such as oscillating or, rotating reaction chambers, and flow-through systems have been developed. This opens entirely new perspectives: nano-scale reactions can be studied *in situ* and in real time, temperature- or pressure scans or jumps can be performed, and automated high-throughput investigations of multiple formulations are now possible even without resorting to synchrotron facilities.

In this presentation, representative examples of pharmaceutical interest will be presented. SAXS of different lactose qualities revealed widely varying specific inner surfaces (at the 1-100 nm scale), which is likely to influence the interaction with fine drug particles as used for dry powder inhalers. Similarly, the stability of such formulations upon storage at elevated temperatures and humidity has been monitored, both in terms of the powder crystallographic patterns as well as the amorphous nanostructure. In liposome systems, the interaction with solvent components, e.g. salts or sugars, has been studied. There, the integration of a DSC cell allows to precisely assign the heat capacity changes to the structural processes involved in phase transitions and separations. Finally, as an example of reaction moniotoring, the synthesis pathways to template-molded zeolithic structures have been followed with a time resolution of 5 minutes over several hours.

References:

(1) P. Laggner and H. Mio. 1992. SWAX - A Dual-Detector Camera for Simultaneous Small- and Wide-Angle X-Ray Diffraction in Polymer and Liquid Crystal Research. Nucl. Instr. Meth. in Phys. Res. A323, 86-90.

(2) http://www.hecus.at/

(3) http://www.ibr.oeaw.ac.at/beamline/