

Coarsening of Pharmaceutical Lactose Powders Monitored by Sample-Spinning SWAXS

Overview

Lactose powders of defined microcrystalline morphology are widely used as excipients in pharmaceutical formulations. Their physical properties are critical quality determinants. Storage, particularly under conditions of high temperature and humidity may lead to relevant alterations. Unlike BET measurements, small- and wide-angle X-ray measurements (SWAXS) can be performed directly on conditioned

samples, i.e. under the conditions of their storage, without drying. Such measurements can provide precise information on changes in specific inner surface and in crystal morphology. A crucial factor in such experiments is the avoidance of artefacts that arise from crystal particle orientation. The present note describes how this can be prevented by sample spinning.

Experimental

Two different batches of generic drugs (inhaler powders based on crystalline lactose monohydrate) were incubated under identical conditions: (a) desiccated under room temperature (18-22 °C), and (b) under 75% relative humidity (RH) at 40 °C. Samples were taken at intervals and transferred to 2 mm i.d. X-ray capillaries, sealed and mounted to the spinning accessory of a Hecus SWAX System-3 camera (Hecus X-ray Systems, Graz, Austria), attached to a sealed X-ray tube generator (Cu-target, wavelength $\lambda = 0.154$

nm), operating at a power of 2kVA. The SAXS curves were analyzed in the q -range up to 3 nm⁻¹, by checking the log-log linearity and thus the validity of Porod's law and by extracting the Porod constant k and the invariant Q from the respective plots with the data evaluation program PS (HECUS). Simultaneously, the wide-angle diffraction patterns between 18 – 26 ° (2 θ) were measured.

Results

Figure 1 shows representative small and wide-angle X-ray patterns of the two lactose preparations at 1-10 days intervals under conditions (b). The wide-angle powder patterns revealed no significant changes, while the quantitative evaluation of specific inner surface from the SAXS curves showed decreasing tendency. The decay was observed for both drugs, but stronger (-5%) for the

Buventol than for the Beclomet sample (-3%). The controls (condition a) did not show such changes during that time. At longer 2 periods (up to 5 weeks) also the samples stored under condition a revealed a decrease of the specific inner surface, i.e. coarsening.

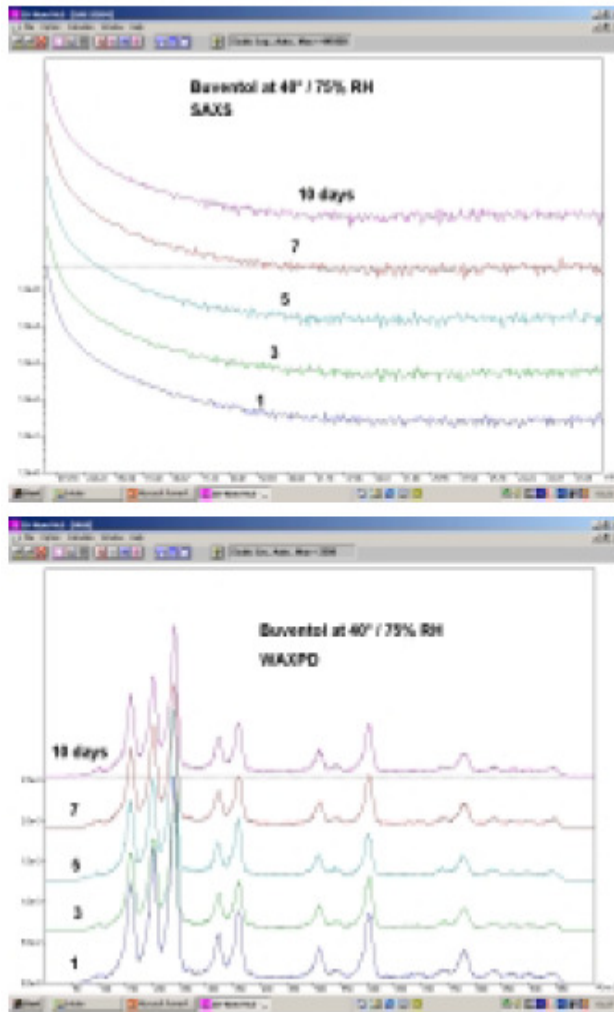


Figure 1: SAXS (top) and WAXS (bottom) patterns

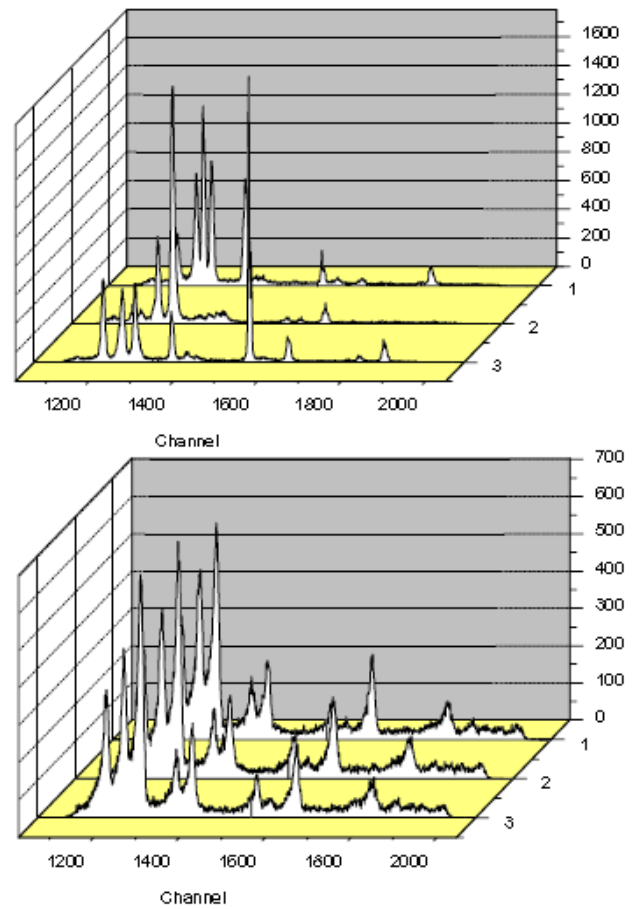


Figure 2: WAXS patterns without (top) and with (bottom) rotation. Speed 1Hz.

Conclusion

It was found essential to rotate the capillaries during measurement to avoid spurious orientation effects. In fact, without rotation

there was no reproducibility in the WAXS patterns. This is demonstrated in Figure 2.