High-Brilliance Laboratory SWAXS Coupled to Calorimetry. A New Tool for Pharmaceutical Analytics

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Structural changes of materials are associated with characteristic modifications of the thermodynamical parameters. Understanding and control of pharmaceutical product properties hence requires both, structural and thermal analysis. The relevant analytical methods are X-ray diffraction and calorimetry which, until today, are independent and separated technologies. This often complicates a conclusive assessment, especially in cases where samples are sensitive on history, pre-treatment, and scan rates.
The diffraction techniques of small- and wide-angle X-ray scattering (SWAXS) are important analytical tools in pharmaceutical solid-state characterization1). Questions of polymorphism in crystalline materials, stability and nanostructure of amorphous states, inner surface, stability and ageing of formulations can be addressed, among others. The information exceeds that of conventional powder diffraction, as it includes the nanoscale up to > 100 nm. A particular advantage lies in the simultaneous observation of the nanoscale (SAXS) and atomic/molecular scale (WAXS), respectively. Calorimetry, in scanning (DSC) or isothermal mode, allows the characterization of the changes of state, and more generally the reversibility of the phenomena involved in phase transitions between condensed states. Initial efforts by Ollivon et al. 2) towards combining these two analytical strategies have shown great promise during the past decade, mostly however on synchrotron X-ray sources.
With the development of high-brilliance laboratory SWAXS systems (Hecus S3-MICROpix) the speed for diffraction analysis has been greatly increased, and hence the combination with microcalorimetry within one laboratory-based instrument is becoming technically feasible. This combination allows to measure simultaneously the thermal events associated with the structural modifications. The new apparatus works between –30 and +200°C at scanning rates between 0.01 and 2°C min–1 with high sensitivity in both measurements using a single sample of small volume (from about 1 to 20 µL). Moreover, scanning SWAXS can now can be applied to routine quality screening and process analytical technology (PAT).
The capabilities of this instrument and its ease of use will be illustrated by examples of thermal and structural analysis for technologically relevant systems, such as polymorphic forms of an API or of an excipient, respectively, inhaler powders, micro-spheres, and amorphous formulations.

References

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