Poster Presentation

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Fast PDF screening of amorphous pharmaceuticals with a Bruker D8-ADVANCE

Michael Evans[1], Christina Drathen[1], Arnt Kern[1]
[1]*Bruker AXS GmbH, Karlsruhe, Germany*
E-mail: michael.evans@bruker.com

X-ray diffraction (XRD) is a powerful tool used in the pharmaceutical industry to characterize solid pharmaceutical active compounds during drug discovery, development and production.
To increase the binding specificity to protein targets APIs are becoming more complex. This complexity decreases the solubility of the API, reducing their capability of entering into cells and actually reaching their targets. Increasing the solubility would enhance the availability of the API and consequently reduce the dose required. One route to increased solubility is polymorph screening: different molecular packings may have different dissolution properties.
A different approach is to reduce the crystallite size of the API, possibly even to an amorphous state. In those cases, the long-range crystal structure breaks down, resulting in broad features in the diffraction pattern that are not easily interpretable.
Fortunately, a diffraction pattern of an amorphous compound still contains valuable information in the diffuse scattering. This information can be accessed thru the Fourier transform of corrected and normalized diffraction data, which gives the pair distribution function (PDF). Experimentally, the PDF requires good counting statistics to a high Q-range, which generally necessitates the use of hard radiation (Mo, Ag) and long measurement times on laboratory instruments, making this technique less suitable for screening.
To considerably reduce the measurement time, we have used a PILATUS3 R 100K-A 2-dimensional detector in combination with a focusing Goebel mirror on a Bruker D8 ADVANCE diffractometer. Data suitable for extracting the PDF was collected at different measurement times ranging from 30 minutes to a few hours on a series of weakly diffracting pharmaceutical compounds. The obtained PDF data was modelled with DIFFRAC.TOPAS (v6).
Here we will discuss the feasibility of using fast laboratory-PDF data for the characterization of APIs, both in crystalline and amorphous forms. In addition to the fingerprinting of pure substances, we also discuss the usefulness of this approach for quantification of phase mixtures via pattern-scaling.

Keywords: Pair distribution function (PDF), amorphous, fingerprinting of pharmaceuticals