Application Note XRD 618

Rapid XRD Analysis of Pharmaceuticals

- Snapshot 1D and 2D Mode with the EIGER2 R 500K

X-ray Powder Diffraction (XRPD) is an essential characterization technique in the pharmaceutical industry for structural analysis of candidate materials, polymorph confirmation, and positive material identification. A specific challenge in the discovery phase, lead optimization and scale-up to production is to run XRPD in high throughput screening mode.

Report Summary

- Rapid 1D and 2D data acquisition on samples with large and small crystallites is demonstrated
- Line beam and 1D mode for large sample amounts
- Point beam and 2D mode for small sample amounts
- Crystallite size impacts data quality in both cases, with increasing effect as sample amount is reduced

Best practices in the pharmaceutical industry dictate task-driven data collection with sample considerations. During discovery and lead identification, samples may consist of a small quantity of large crystallites while in production large quantities of sample may be available with a crystallite size optimized for dosage requirements. To demonstrate rapid data collection on a variety of sample types, coarse and smooth powders were analyzed in capillary transmission with line beam geometry and 1D detector mode and point beam geometry and 2D detector mode.

Experimental

Data were collected on a D8 ADVANCE diffractometer equipped with Cu radiation (40 kV, 40 mA), Göbel mirror, capillary stage, and EIGER2 R 500K detector in 2θ optimized mode. Switching between line and point geometry was accomplished by changing the beam mask, air scatter guard, and software selection of the detector mode. The EIGER2 was positioned at 106 mm distance to the sample, yielding coverage of 2.5˚ to 41.5˚ 2θ in both 1D and 2D modes. All data was collected in a static snapshot mode for 10 sec.

Specimens were prepared from as-received and finely ground ibuprofen powders by loading into a 0.5 mm diameter glass capillaries and flame sealing. A schematic representation of the two samples is shown in figure 1.

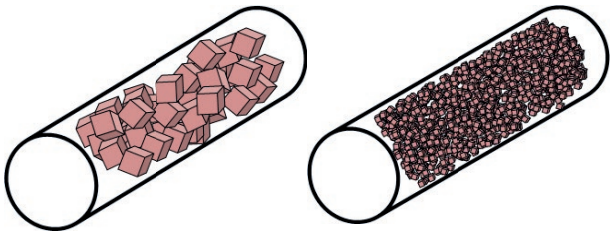


Figure 1. Schematic representation of as-received and ground samples. The as-received sample contains a finite number of diffracting crystallites leading to aberrant peak intensities in the resulting data while the ground sample is constituted by a more random crystallite orientation.

Large Sample Amount (Line Beam / 1D mode)

A 0.6 mm slit and linear scatter guard were used to produce a line beam geometry with the detector set to 1D measurement mode, shown in figure 2. This geometry produces high intensity and improved statistics from a large sample volume (estimated ~3 mg) benefiting applications such as crystalline structure refinement, structure solution, and quantification.

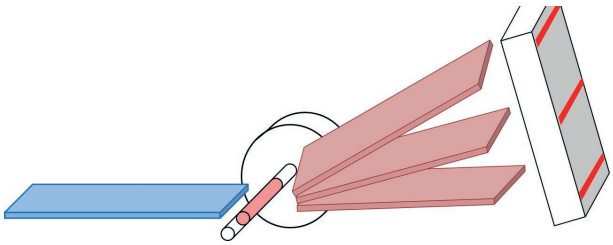


Figure 2. Line beam geometry and 1D detection mode.

Figure 3 shows diffractograms of the as-received and ground samples with a reference pattern of ibuprofen. Data quality including peak shape and relative intensities is noticeably improved when using finely ground powder. In particular, the inset shows more accurate reproduction of the anticipated powder pattern intensity ratios and an increase in peak symmetry for the ground sample.

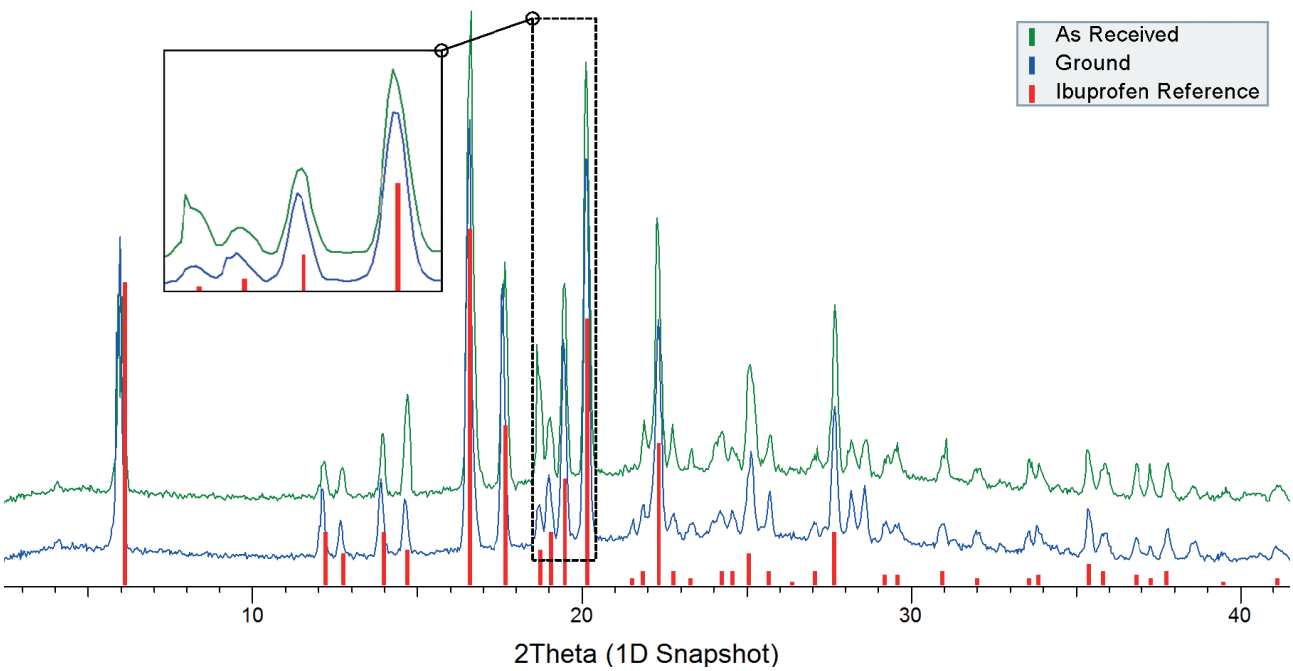


Figure 3. 1D snapshot data with 10 sec collection time collected on the as-received and ground samples.

Small Sample Amount (Point Beam / 2D mode)

A 0.3 mm pinhole slit and magnetic collimator were used to reduce the beam to a small spot. The detector was placed in 2D measurement mode. This geometry (figure 4) benefits from maximum diffracted beam coverage resulting in better statistics from a limited sample volume (estimated ~60 µg). This geometry is useful for applications including HTS well-plate analysis, high potency sample analysis, and tablet mapping.

With 2D data, integration of large sections of Debye rings allow for improved accuracy in peak intensity. Comparison of the 2D frames (figure 5) reveal that data from the coarse sample is spottier than the smooth powder. These spots lead to the aberrant intensities and peak splitting observed in the coarse 1D and 2D data.

Figure 6 shows full frame integration of the frames. The ground sample with smooth diffraction rings results in more accurate peak intensities.

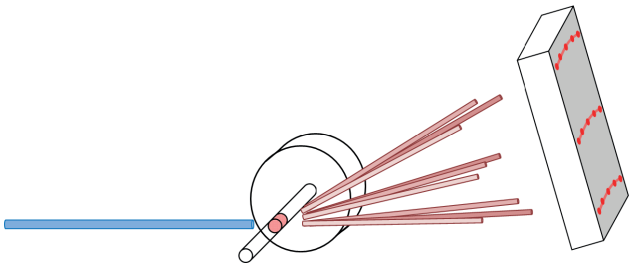


Figure 4. Point beam geometry and 2D detection mode.

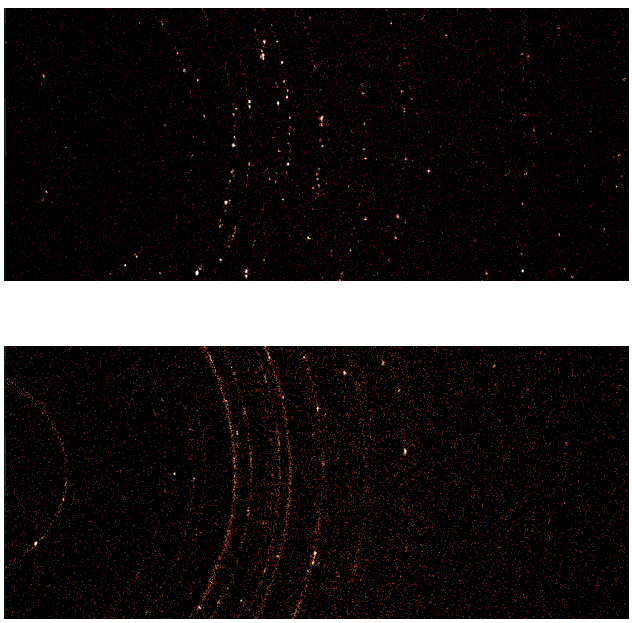


Figure 5. 2D snapshot data with 10 sec collection time collected on the as-received (top) and ground (bottom) sample.

Conclusion

For both 1D and 2D geometries, smaller crystallite sizes lead to higher accuracy in observed peak intensities. Best practice should include grinding specimens to increase the number of diffracting crystallites.

Selecting an optimized measurement geometry is also important in collecting the best quality data. For large amounts of material, line geometry and 1D detection provides high intensity and increased sampling statistics. For samples with limited volume, point geometry and 2D detection is preferred due to wider coverage of the diffracted beam. The D8 with EIGER2 provides simple exchange between both 1D and 2D collection modes.

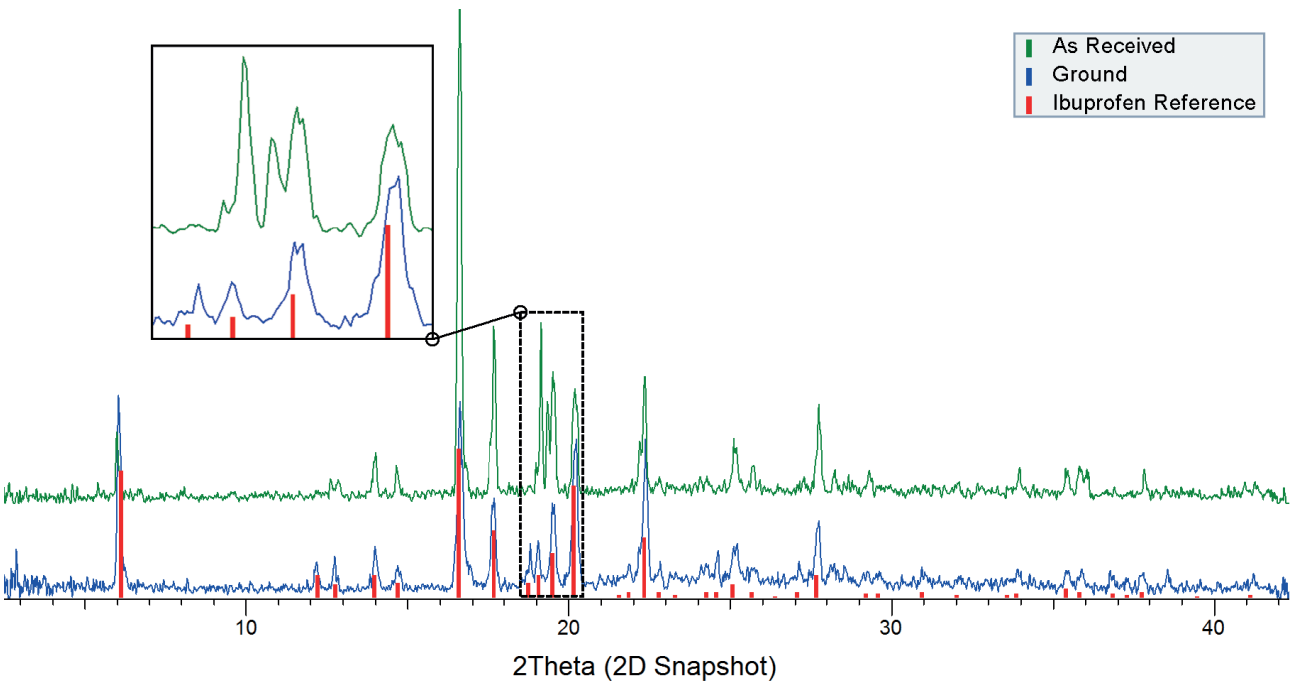
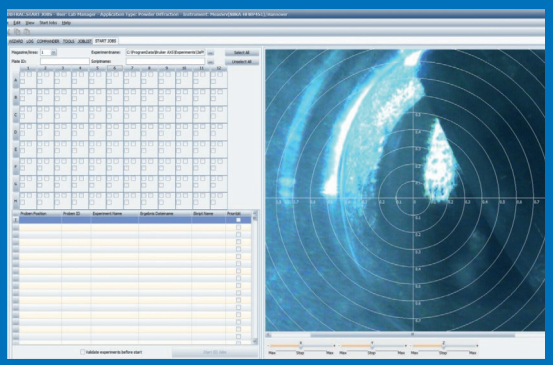


Figure 6. Integrated 1D scans from the 2D snapshot data with 10 sec collection time collected on the as-received and ground samples.

DIFFRAC.SUITE Workflow for Rapid Powder Analysis

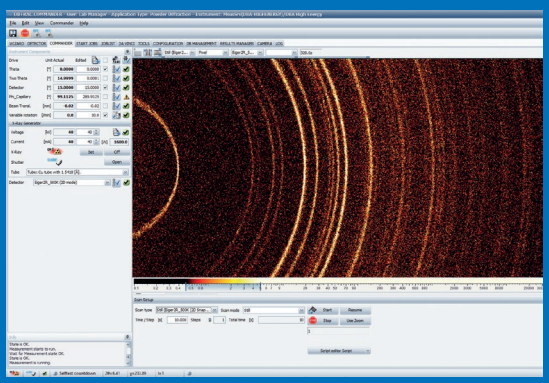
PLAN in DIFFRAC.START JOBS

- Quickly execute a measurement template or queue multiple measurements to run in sequence
- Set up single or multi-spot analyses for high-throughput screening and 96-position wellplates



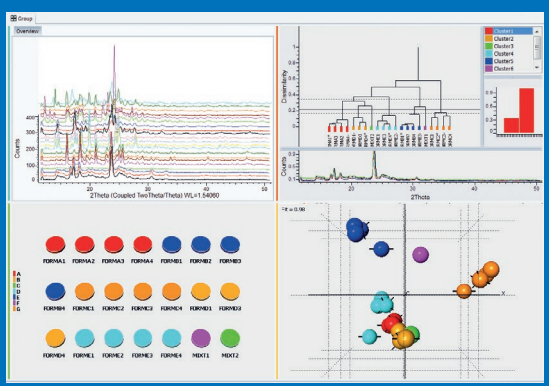
MEASURE in DIFFRAC.COMMANDER

- Direct measurement control or launch pre-defined experiment methods
- Real-time data monitoring in both 1D and 2D detector modes
- Integrated camera plugins for verifying sample positioning



ANALYZE in DIFFRAC.EVA

- Supports 0D, 1D, and 2D data
- Create customized report layouts and templates
- Deploy powerful clustering algorithms to quickly sort through large datasets



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