

TWO-DIMENSIONAL XRD FOR PHARMACEUTICAL

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Applications of two-dimensional X-ray diffraction for pharmaceutical research and discovery have dramatically increased since the first high-throughput XRD screening system was introduced in 2000. It has been well recognized that two-dimensional x-ray diffraction is ideal for analyzing samples of limited quantity, which is a typical case for pharmaceutical samples, with better data quality and fast data collection. A two-dimensional diffraction pattern contains information for phase identification, polymorphous structures, crystallinity, particle size and distribution, phase transformation, melting point, and preferred orientation. Any one or group of these parameters can be used as criteria for high-throughput screening.

The geometry and configuration of an X-ray diffractometer is an important consideration in terms of samples preparation, data quality, productivity, and easy of operation. For instance, the conventional Bragg-Brentano parafocusing geometry may be suitable for a sample prepared with large quantity of powder, but most pharmaceutical samples have limited quantity or special form not suitable for making a conventional powder sample. In this case, a parallel point focus beam geometry with linear or area detector is more suitable. The pharmaceutical samples for high-throughput screening are normally packed in a 96-well plate and 2θ measuring range of a typical pharmaceutical compound is within 2 to 60° . In this case, transmission geometry may be a better choice to avoid the defocusing effect and cross contamination associated with reflection mode diffraction. The defocusing effect can also be reduced by a proper data collection strategy in reflection mode. The addition of Raman probe to a two-dimensional XRD system further enhances the power of high-throughput screening process. Raman spectroscopy measures the characteristic vibration frequencies determined by the chemical composition and chemical bond. Both XRD and Raman are non destructive methods that require virtually no special sample preparation, thus, very suitable to analyze samples in a combined screening process.

This presentation covers some basics and recent development in geometry and configuration of XRD systems for pharmaceutical study. Comparisons between two-dimensional diffraction and the conventional diffractometry are also given with application examples.