

## POWDER DIFFRACTION USING SYNCHROTRON SOURCES FOR PHARMACEUTICAL PROBLEMS

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Synchrotron radiation sources have revolutionized the use of x-rays in many fields of research, and many of these advances are directly applicable to the pharmaceutical industry, especially in the area of powder x-ray diffraction. More than a dozen synchrotron sources worldwide have the capability for users to perform powder diffraction experiments. Synchrotron sources are major facilities, generally built and operated by the governments of one or more countries; they can serve many users at one time, making the scale of individual experiments quite manageable.

While many potential users of synchrotron radiation are concerned about issues of proprietary research, protection of intellectual property, etc., these should not be serious roadblocks to the pharmaceutical community. Many drug companies have large proprietary programs of protein crystallography at synchrotron sources, indicating that the necessary agreements for proprietary access can be negotiated.

In this talk, I will start with the basics of synchrotron radiation compared to laboratory sources, a list of operating facilities worldwide, pathways of access, and what the user should expect from the facility. I will discuss examples of pharmaceutical powder diffraction studies using synchrotron x-rays:

- Identification of phase purity of crystalline materials, based on the ability to index a diffraction pattern. The current state of the art is that essentially any powder pattern collected from a high resolution synchrotron-based diffractometer can be indexed. This is a consequence of the sharper peaks and freedom from sample displacement and transparency aberrations.
- Structure determination from powder diffraction data. Many samples of pharmaceutical interest are not available as single crystals. Structure determination from powder diffraction data is a fairly mature technique, allowing, for example, structure determination of multiple polymorphs. The intensity and resolution from synchrotron data are significant advantages for such projects.
- Detection of a small amount of one phase in a mixture. The resolution and intensity lead to limits of detection that are significantly lower than with conventional laboratory x-ray sources.
- Time resolved experiments. Higher intensity allows data to be collected from transient events such as changes in hydration state with better time resolution.

All of these tasks can be accomplished with a laboratory source, but the brightness and intensity of synchrotron radiation offer compelling advantages for many powder x-ray diffraction problems in the pharmaceutical field.