Crystal Structure Determination and Phase Identification of Pharmaceutical Material(s) Using Powder Diffraction Techniques

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The International Centre for Diffraction Data (ICDD®) has developed a comprehensive database for identification of pharmaceutical materials. As powder X-ray diffraction is commonly used in phase identification, the necessity for quality reference patterns and software tools continues to evolve. In 2012, a project was initiated to acquire powder X-ray diffraction and crystallographic data for compounds classified as top pharmaceuticals based on U.S. (1) sales and (2) prescriptions. Developed in collaboration with Argonne National Laboratories and Illinois Institute of Technology, synchrotron powder diffraction data collected at APS beamline 11-BM have been used to obtain reference data for these high-volume pharmaceuticals. The diffraction patterns and additional crystallographic information are incorporated into the Powder Diffraction File™ (PDF-4+) for use as references for phase identification, structure analysis, and materials characterization. Since the onset of this project, ICDD and its collaborators have successfully constructed reference entries for over 85 commercial pharmaceuticals. Included in these new entries are new crystal structures determined using a combination of density functional theory and structure refinement techniques. In addition to determining unit cell and atomic coordinate positions, hydrogen bonding is observed and can be used to investigate dissolution rates and efficacy of Active Pharmaceutical Ingredients (APIs). Structure elucidation also allows for Hirschfield calculations, for the prediction of particle shape anisotropy. The project is on-going and continues to generate new pharmaceutical entries annually.

In addition, ICDD has developed software tools to assist in the analysis of pharmaceutical pill and capsule composition(s). The formulation of pharmaceutical drugs incorporates a multitude of chemical constituents that can be organic, inorganic, or polymeric in nature. While the API in a formulation is the key component that provides a drug its functionality, excipients are generally the bulk of the content and proper identification of these frequently amorphous or semi-crystalline excipients, is important in formulation & design. Therefore, it is often necessary to analyze and identify all excipients before one can make an accurate identification of an API. With that in mind, ICDD has developed a total pattern analysis method for formulation analyses of pharmaceuticals. This full pattern analysis method is presented as proof of phase identification (amorphous and crystalline) capabilities using powder X-ray data combined with the comprehensive PDF-4+ database. These new patterns and analysis tools have finally provided a novel method for identification of high profile pharmaceuticals by room temperature powder X-ray diffraction.