B196 X-Ray Powder Diffraction (XRPD) Method Development and Validation for the Identification of Counterfeit Pharmaceuticals

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After attending this presentation, attendees better understand the method development and validation for analyzing suspect counterfeit pharmaceuticals with the Bruker® D2 PHASER desktop X-ray powder diffractometer. Attendees will also understand how this method of analysis could be beneficial compared to other popular methods such as Fourier Transform Infrared (FTIR).

This presentation will impact the forensic science community by providing information on an additional method of analyzing and distinguishing counterfeit pharmaceuticals from authentic pharmaceuticals.

Counterfeit pharmaceuticals are illegally manufactured and widely distributed throughout the world, which is a major threat to public health. Counterfeit pharmaceuticals are unapproved and unregulated products which may contain dangerous or harmful ingredients or insufficient amounts of the Active Pharmaceutical Ingredient (API) the patients require to stabilize or improve their health.[1] Historically, counterfeit pharmaceuticals have been found to not contain the correct amount of API, to contain a different API, no API, or the incorrect excipients within the counterfeit product.[1,2] Fast, easy-to-use, and reliable techniques are required to screen and identify a suspected counterfeit product from an authentic product, ensuring the safety of the public's health.[2]

XRPD is a technique often used in forensic science to analyze various types of trace evidence. XRPD has been shown to be a useful technique in the analysis of suspect counterfeit pharmaceutical products.[3] Previous work has shown that the X-ray diffraction spectra of authentic products can be compared to those of suspect counterfeit products to differentiate authentic products from counterfeit products. In some cases, this technique can be used to determine the presence or absence of an API or other excipients within a dosage form, and ascertain whether the correct API is present within that dosage form.[1] This study describes the method development for analyzing authentic pharmaceutical solid-dosage forms, APIs, and excipients to be used to identify suspect counterfeit pharmaceuticals using the Bruker® D2 PHASER diffractometer at the Food and Drug Administration's Forensic Chemistry Center (FCC).

First, an XRPD spectral library was built by analyzing excipients and active pharmaceutical ingredient standards using the Bruker® D2 PHASER instrument. Next, authentic pharmaceutical dosage forms were analyzed and compared to the corresponding API and excipient standard XRPD spectra to determine if the standards could be observed within the dosage form pattern. The XRPD spectral variability between authentic tablets and different lots of a product were determined to assess the product changes between tablets and lot numbers of the product. Counterfeit dosage forms were then analyzed and compared to the authentic dosage form XRPD spectra to determine if the counterfeit products could be differentiated from the authentic products. The information provided in the United States Pharmacopeia (USP®) General Chapter <941> was used as a guide for the method validation.[4]

The APIs, excipients, and authentic pharmaceutical products chosen for the method development were based on pharmaceutical products for which the FCC has known examples of counterfeits. XRPD spectra of the APIs and excipients were collected first, then the authentic dosage forms were collected. A series of experiments were conducted to determine the optimum sampling and measurement parameters for the standard powders (APIs, excipients) and the dosage forms. The initial results showed that peaks in the XRPD spectra of the APIs were not easily distinguishable in the authentic dosage form XRPD spectra. This was determined to be attributed to the concentration of the API present in the dosage forms and the manipulation of the API during the manufacturing process. The manipulation of the API during the manufacturing process may change the crystallinity of the API in such a way that the XRPD spectrum of the API in the dosage form is different than that of bulk powder API. Based on this result, absence/presence of API could not be used to distinguish authenticity.

Instead of looking for the absence/presence of the API to determine authenticity, it was found that overall differences in the counterfeit formulation compared to the authentic product formulation could be used to determine authenticity. It was also determined that counterfeit products contain various excipients with different crystalline structures than the authentic product. In cases where the counterfeit tablet formulation was similar to the authentic product, the difference in the crystalline structure of the excipients in the counterfeit products resulted in peak shifts greater than 0.2° at the 2θ-diffraction angle for a given peak in the XRPD spectra. This would

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indicate a counterfeit product.[4] This method can be used to distinguish counterfeit pharmaceuticals from authentic pharmaceuticals by looking at the overall XRPD spectral differences (additional peaks, missing peaks, and peak shifts). This presentation will discuss the method development and validation work conducted at the FCC in using XRPD to differentiate counterfeit pharmaceutical products from authentic products.

The mention of specific products/instruments in this presentation is for information purposes only and does not constitute an endorsement by the Food and Drug Administration and/or the Forensic Chemistry Center.

Reference(s):

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XRPD, Counterfeit Pharmaceuticals, X-Ray Diffraction