Pharmaceutical Characterization using PDF-4/Organics Q&A

Q: Can we analyze an API (active pharmaceutical ingredient on the surface of a nanoparticle?

A: In the 2019 publication on formulation analysis (Formulation analyses of high-volume prescription drugs | Powder Diffraction | Cambridge Core) we analyzed several APIs that were on the surface of microspheres. The microspheres were within plastic capsules and included the formulations of Inderal XL, Linzess, Namzaric, Nexium, and Pradaxa. The spheres ranged in size from ~10 microns to hundreds of microns. API concentrations ranged from 3% to 58%. There were no problems identifying all bulk components (above 1 wt %) in all five formulations with PDF-4/Organics using a benchtop diffractometer with a 300W source and strip detector. The microspheres were either nanocrystalline cellulose or alpha lactose monohydrate. Another formulation used a microchip morphology substrate.

When you go to nanosized materials, the peaks would all broaden for both the API and the substrate. If the sizes were below 100 Å, you should expect severe peak overlap issues. This is where modeling using whole pattern fitting methods that include crystallite size models (as shown in the webinar) might be essential to cleanly identify the nanosized phases. Having a nanosized (~45 Å) reference pattern of cellulose (PDF 00-060-1502) greatly helped in the cases where cellulose was the substrate. Using synchrotron radiation would not help the peak overlap issues since the peak broadening is due to the material. It would help in providing improved signal to noise that helps in fine-tuning the model and enables lower detection limits.

Q: How do we analyze polymers that are used as excipients – does the crystallinity of the polymer make a difference?

A: Several polymers are frequently used as excipients as shown by the USP, European Pharmacopeia, and FDA. Over a period of many years, the ICDD has identified which polymers are used in pharmaceutical formulations and obtained polymer patterns through grants and special projects, to include in the pharmaceutical subfile. Sometimes the chemistry or crystallinity will be varied within a polymer family, for example - povidones, starches, and cellulosics, and multiple reference patterns are collected, each for a specific variation. Common polymeric excipients include cellulose, methylcellulose, hydroxypropyl cellulose, povidone, crospovidone, starch, polyethylene glycol (PEG), polyethyloxazoline (PEOX), dextran and polyacrylic acid (PAA).

Q: In the webinar you mentioned a review article and that it is available for free download?

A: A practical guide to pharmaceutical analyses using X-ray powder diffraction | Powder Diffraction | Cambridge Core

This review article includes ~88 references that cover events in pharmaceutical analysis over the last 20 years. It takes particular focus on the changes made to hardware and software that improve our ability to analyze and detect pharmaceutical materials and challenges old assumptions and some myths found in historic literature.

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