Microscopy Approaches for Determining the Distribution of Active Pharmaceutical Ingredients in Drugs

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- Chemistry and Chemical Analysis
- Pharmaceuticals

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Researchers at Purdue University have developed label-free autofluorescence-detected photothermal mid-IR (AF-PTIR) microscopy, a technique to determine the distribution of active pharmaceutical ingredients (APIs) in drugs. Mapping the API distribution is critical in designing processes for powdered dosage form manufacturing. High spatial variance of the API can cause variability in both delivered dosage and product efficacy. Infrared (IR) microscopy has been used to map the distribution of APIs; however, this method provides low resolution imaging due to diffraction limits. Photothermal mid-IR (PTIR) microscopy methods measure changes in optical or fluorescence signal because of thermal expansion induced by IR radiation. However, existing PTIR methods are not fully quantitative or require chemical labeling with fluorescent probes. To overcome these limits, the Purdue researchers employed two-photon excited UV-fluorescence microscopy (TPE-UVF), an approach that is sensitive to aromatic compounds, including many APIs, in combination with exposure to IR radiation at wavelengths the API of interest absorbs. The AF-PTIR approach provides for label-free imaging of aromatic APIs with high selectivity and sensitivity in image contrast. AF-PTIR was demonstrated by producing images of the distribution of a small molecule drug, indomethacin, in prepared mixtures of materials designed to reflect the contents of commercially available final dosage forms. Further, AF-PTIR is compatible with instrumentation that supports complementary microscopy techniques.

Recent Publication: Label-Free Autofluorescence-Detected Mid-Infrared Photothermal Microscopy of Pharmaceutical Materials. Anal. Chem. 2022, 94, 6512-6520. https://doi.org/10.1021/acs.analchem.1c05504

Technology Validation: The AF-PTIR microscope could distinguish the API, indomethacin, from a multicomponent mixture with lactose, titanium (IV) oxide, and magnesium stearate.

Advantages:
- High selectivity and sensitivity of aromatic APIs in pharmaceuticals
- Non-invasive method to measure chemical compositions with spatial resolution in 3D
- Expected to enable analysis of macromolecular formulations of protein-based biologics

Applications:
- Drug dosage form manufacturing
- Drug characterization

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