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SHG Microscopy to Guide Targeted Measurements by Raman Spectroscopy and Synchrotron X-ray Diffraction

A rapid, selective method combining SHG microscopy with Raman spectroscopy and X-ray diffraction significantly improves the detection and quantification of trace crystallinity and composition in pharmaceutical formulations.

Modern drug discovery frequently identifies active pharmaceutical ingredients (APIs) that are highly effective against the disease target, but which are hard to deliver to the body. As a result, second harmonic generation (SHG) has emerged as a complementary technique for the rapid detection and quantification of trace crystallinity within pharmaceutical materials. Despite the low detection limits of SHG microscopy, the SHG intensity itself provides insufficient chemical information about the composition of the SHG-active source. There is unmet need to obtain such information.

Researchers at Purdue University have developed a method utilizing SHG microscopy to identify regions of interest for localized confocal Raman spectroscopy and synchrotron x-ray diffraction (XRD) measurements to quantify crystallinity and identify composition within formulations of pharmaceutical materials. By targeting the Raman and XRD analysis to these localized regions identified by SHG, the corresponding reduction in background, lowered the limits of detection for both Raman and XRD by 2 to 3 orders of magnitude relative to ensemble-averaged measurements. Targeted analysis by XRD and Raman spectroscopy were both consistent with crystalline paclitaxel comprising the insoluble particles. These combined results show the potential benefits provided by the marriage of the rapid and highly selective technique of SHG with information-rich methods such as Raman and XRD.

Advantages:

-Enable targeted analysis by Raman and XRD

-Reduces the time required to perform the Raman measurements

Technology ID

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Category

Pharmaceuticals/Drug Discovery & Development
Biotechnology & Life Sciences/Analytical & Diagnostic Instrumentation

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-Improvements in the detection limits for trace crystallinity

Potential Applications:

-SHG Microscopy

-Spectroscopy

-Synchrotron x-ray diffraction

TRL: 3

Intellectual Property:

Provisional-Patent, 2014-09-28, United States | PCT-Patent, 2015-09-28, WO | NATL-Patent, 2017-03-28, United States

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