High-throughput Screening Using WALDO

The Challenge

Rapid, reliable identification of polymorphs during pharmaceutical drug development is critical for both patent application and discovery purposes. Use of well plates for high-throughput screening (HTS) improves efficiency, however crystallization and form changes can occur within a single well leading to misleading results. Obtaining accurate results is critical to maximize potential financial returns and limit competition.

Traditional Solutions

PXRD is the current standard for quantitative analysis of crystallinity and structural differences but is not suitable for HTS or samples with low crystalline content. ss-NMR is more sensitive to crystallinity, but expensive and slow. Raman spectroscopy is widely used for its minimal sample handling requirements, however the small band shifts exhibited by form and crystallinity changes can be difficult to reliably detect in the traditional fingerprint region (200-1800 cm^{-1}).

Ondax Solutions

Ondax THz-Raman™ systems extend the range of Raman spectroscopy to the THz/low-frequency region (5-200 cm^{-1}), where crystal lattice modes that correspond to molecular structure and phase changes are found. THz-Raman™ provides higher SNR than conventional Raman, resulting in shorter acquisition times, improved detection reliability, and enabling higher throughput workflows.

Ondax's WALDO (Figure 1) can automatically collect high-resolution data regarding both composition and form in both well plates and tablets. As an example, WALDO was used to image an Excedrin tablet (Figure 2). Principal component analysis (PCA) and clustering was used to identify the three constituent compounds (Acetaminophen, Aspirin and Caffeine) plus mixtures in the boundary regions. Polarized light microscopy (PLM) images were concurrently taken for the region then overlaid with the Raman map for visual comparison. The corresponding spectra (Figure 3) are shown to clearly illustrate the high quality, strong magnitude data, demonstrating the ability of WALDO to quickly identify and discriminate between materials or polymorphs, and to capture both visual and spectral data.

Application Field

Raman, High Throughput Screening, Polymorphs, Crystallinity, Polarized Light Microscopy, Pharmaceuticals, Biopharma



***Figure 1**. WALDO is a fully automated THz-Raman™ system, designed for high-through screening and characterization of polymorphs and crystallinity of materials such as active pharmaceutical ingredients (APIs).*

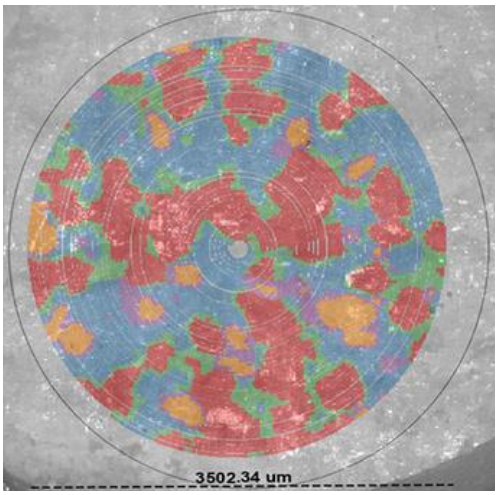


***Figure 2**. Rapid Tablet Mapping image of an Excedrin tablet placed in a well, based on >27k spectral data points collected over a 3.5 mm diameter region of the tablet in 9 mins.*

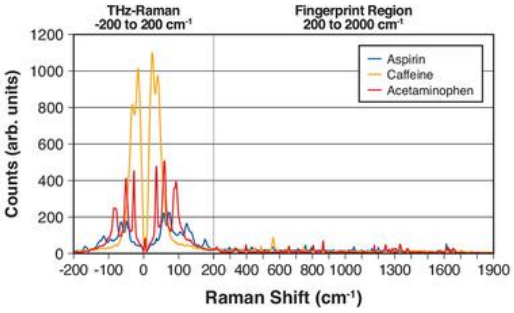


***Figure 3**. Individual Component Spectra of Excedrin Tablet Note the exceptionally strong signals and clear differentiation in the low-frequency/THz-Raman™ region.*

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