



Application Note

Nondestructive Analysis of Ingredient Blend Uniformity in Pharmaceutical Tablets Using Wide-Field Raman Chemical Imaging

Introduction

Product quality is critical in pharmaceutical manufacturing. Changes in drug properties during formulation scale-up and manufacturing can adversely affect product performance.

Drug distribution in solid dosage forms (pressed tablets) have been traditionally challenging to measure. Destructive methods such as tablet staining have been used to generate image contrast between the ingredients to visualize the distribution using optical microscopy. While effective, these methods are destructive and lack chemical specificity.

Chemical Imaging provides a methodology for rapid, nondestructive testing and characterization of sample composition, distribution and morphology. The technology has been routinely demonstrated to be a critical tool in determining domain size and distributions in complex mixtures.

Experimental Information

A surface region of a pharmaceutical tablet was characterized using a FALCON II™ Wide-Field Chemical Imaging System to characterize blend uniformity of several excipient compounds (Figure 1). The brightfield reflection image exhibits contrast due only to the rough surface topography and refractive index properties of the pressed tablet. Wide-Field Raman Chemical Imaging (RCI) enables the visualization of component distribution by generating image contrast from the underlying spectroscopic (i.e., chemical) fingerprint of the materials. The relative intensities of characteristic bands change across the surface of the tablet indicating heterogeneous distribution of the materials.

Results & Discussion

Wide-Field RCI adds a spatial element to the sensitivity and specificity of Raman spectroscopy while presenting complex chemical information in a visually accessible format. Faster speed and better image clarity are allowing Wide-Field RCI to displace

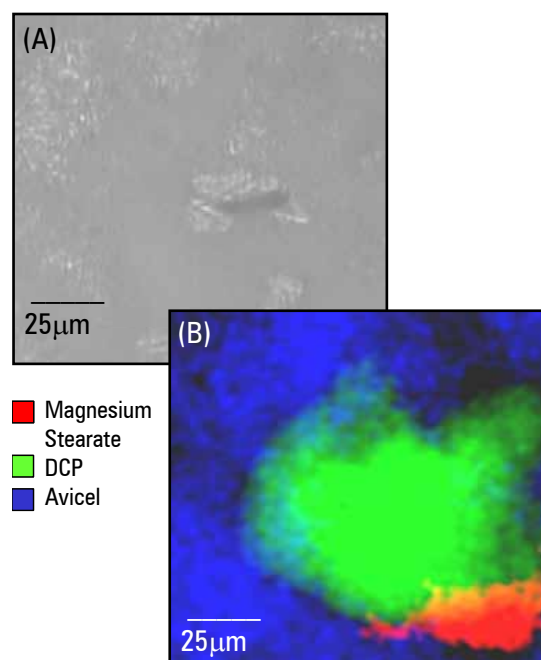


Figure 1. (A) Brightfield reflectance image and (B) false-colored Raman chemical image of an over-the-counter tablet taken on FALCON II System at 20X microscope objective magnification.

conventional microspectroscopy techniques. Typical data acquisition times are on the order of seconds to minutes compared to hours and days spent on traditional Raman mapping instruments. The information obtained from RCI provides feedback to optimize product manufacturing and to ensure product quality. Time savings (often >100X) ultimately lead to drastic cost reduction in manufacturing.

The FALCON II™ System allows data acquisition in Raman, NIR and/or fluorescence modes. ChemImage Xpert™ acquisition and analysis software makes experiment optimization easy. For instance, chemical imaging data may be acquired over discrete wavelengths, specific spectral ranges, or the entire spectrum allowing the data acquisition to be customized to your formulation.

Conclusion

Wide-Field Raman Chemical Imaging:

- Gives you faster speed and better image clarity allowing it to displace conventional microspectroscopy techniques
- Provides feedback to optimize product manufacturing and to ensure product quality
- Provides high quality images with chemical contrast in seconds to minutes

Wide-Field RCI makes routine monitoring of ingredient-specific tablet blend uniformity straight forward. Tablet regions of interest or whole tablets may be quickly scanned with high image fidelity and spatial resolution in a timely and cost-effective manner. Chemical Imaging provides a methodology for rapid, nondestructive testing and characterization of sample composition, distribution and morphology. The technology has been routinely demonstrated to be a critical tool in determining domain size and distributions in complex mixtures enabling the visualization of component distribution through image contrast from the underlying spectroscopic (i.e., chemical) fingerprint of the materials. Faster speed and better image clarity are allowing Wide-Field RCI to displace conventional microspectroscopy techniques while providing feedback to optimize product manufacturing and to ensure product quality.