Application Note 52813

Attenuated Total Reflection FTIR Imaging of "Soft Chew" Formulations

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Key Words
ATR, FTIR, Imaging, Microscopy, Formulations

Thermo Scientific Solution
Thermo Scientific™ iN™10 MX Infrared Microscope, Imaging ATR accessory, Thermo Scientific™ OMNIC™ Picta™ software

Figure 1: Imaging ATR accessory (left) and Nicolet iN10 MX infrared microscope (right)

Introduction

In recent years, the pharmaceutical formulation type in which the active ingredients are dispersed in a "soft chew" matrix has become increasingly popular for a number of over-the-counter (OTC) dosage forms. The sticky and oily nature of these dosage forms, however, poses a particular challenge in sample handling for FTIR measurements. For example, it is often difficult to cut these samples sufficiently thin for transmission analysis, while simply pressing them flat would destroy the innate component distribution within the samples. Reflectance spectra, on the other hand, tend to be of poor quality. The Attenuated Total Reflectance (ATR) measurement of a sample cross section could offer a potential solution since this technique would expect to yield high quality spectra regardless of sample thickness. The "stickiness" of these samples, however, leads to "sample carry over" and complicates single point ATR mapping. In addition, maps acquired by ATR typically require longer measurement times due to the time required to raise and lower the sample stage at each measurement point.

In this note, we demonstrate the use of an imaging ATR accessory that's well suited for the analysis of these samples. The accessory makes contact with the sample just once, while still permitting measurements across the sample surface. Additionally, germanium ATR microscope measurements offer the benefit of a four times magnification due to presence of germanium (refractive index n=4) instead of air (n=1) at the sample interface, resulting in enhanced spatial resolution compared to non-ATR measurements.

Experimental

Spectra were measured using a Nicolet iN10 MX infrared imaging microscope (Figure 1), configured with the following detectors: a room temperature DTGS, a single point MCT-A and a linear array MCT-A detector. Each sample cross section was cut to a size of approximately 5 x 5 x 2 mm (l x w x h) and was placed on the sample post of an imaging ATR microscope accessory (Figure 1) and raised to make contact with the germanium ATR crystal for measurement. Unless otherwise indicated, spectra were collected using the array detector in "ultra-fast" mode where a single scan per step at 16 cm^{-1} resolution was collected at each map point at a spatial resolution of 6.25 microns. Sample and background maps of about 625 x 625 microns consisting of about 11,000 spectra were measured in approximately 1.5 minutes each.

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Results

Antacid Product Component Distribution

Representative map spectra and their comparison to the library spectra of pure materials are shown in Figure 2. Examination of individual map spectra showed that each spectrum was dominated by features of a specific sample component, although weaker features of the other major components can also be seen. Maps of the active material (calcium carbonate), and two of the main non-active components, oil and corn syrup based on baseline corrected peak heights at 872, 1746, and 1020 cm^{-1}, respectively are shown in Figure 2. It is clear from the similarities in the active component and corn syrup maps that the calcium carbonate is found primarily in the corn syrup regions.

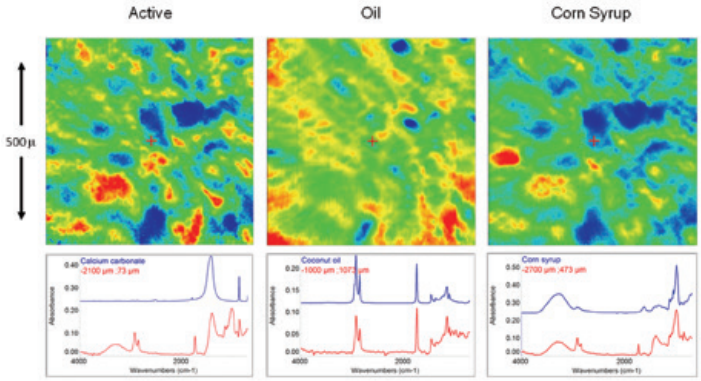

Figure 2: Maps showing distribution of main components of antacid product (top) and representative spectra shown in red, compared to library spectra shown in blue (bottom)

In Figure 3, the quality of the maps created from array spectra is verified by comparing two maps of the same sample measured with array and single point MCT-A detectors, respectively. Each map shows the intensity of the calcium carbonate peak at 872 cm^{-1} and contains approximately 2000 spectra. The array map of single scan spectra at 16 cm^{-1} collected in just 18 seconds shows the same features as the single point detector map collected at 8 cm^{-1} resolution and 16 scans per spectrum that required about two hours to collect.

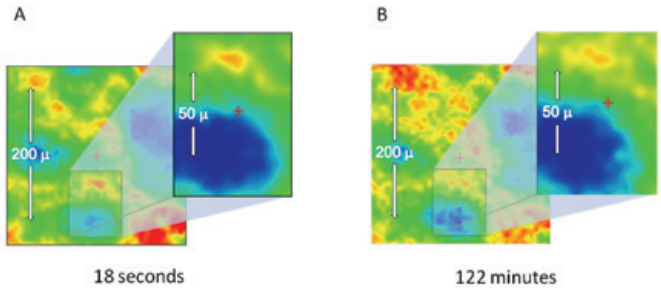

Figure 3: Comparison of maps of active component measured using an array (A) and single point detector (B)

Joint Health Supplement Component Distribution

Due to the low spectral intensity of the glucosamine in this product, a multivariate curve resolution (MCR) analysis was performed which readily extracted the spectra of glucosamine and, as expected, the more obvious oil and corn syrup features. The resulting maps are shown in Figure 4, along with the comparison of the MCR components and pure spectra. The minor presence of glucosamine in the measured spectra is demonstrated in Figure 5, using principal component reconstructed spectra. A map spectrum of mostly corn syrup is subtracted from a map spectrum that MCR analysis indicated contained both glucosamine and corn syrup, resulting in spectral features that compare well to the reference spectrum of glucosamine.

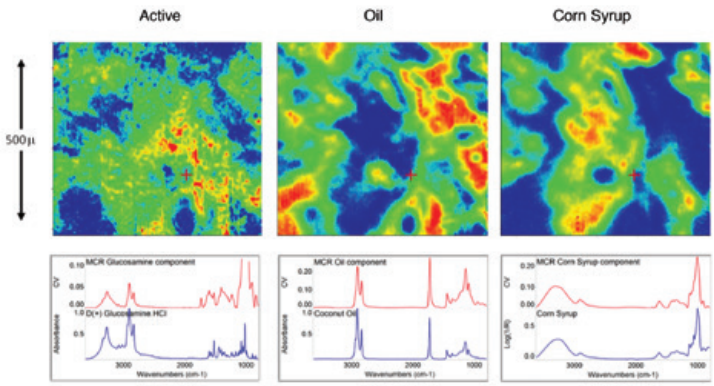

Figure 4: Maps of components obtained with MCR Analysis (top) and MCR components shown in red, compared to library spectra shown in blue (bottom)

Conclusions

In this note, the measurement of the key component distribution in two "soft chew" products by ATR FTIR imaging is described. Maps of sample components with relatively intense features were created by straightforward peak-height methods, while significantly weaker features were readily mapped by using MCR techniques. For each sample, the maps were collected in just a few minutes. The improvement in analysis speed was accomplished through the use of an array detector and a "fit-for-purpose" accessory that eliminates the need to raise and lower the microscope stage at each measurement point. The described methodology should have general applicability for QA/QC and analytical laboratories in pharmaceutical, food and associated industries performing similar analyses.

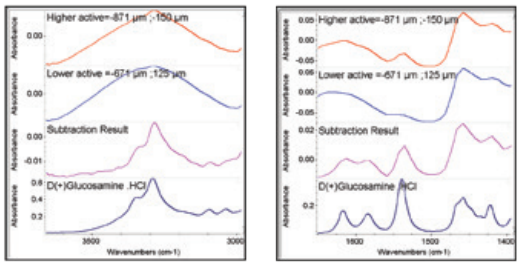

Figure 5: Spectral subtraction confirming the presence of glucosamine as found by MCR analysis

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