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The Influence of Microspectroscopy on Evaluating and Analyzing Forensic Evidence

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Introduction

The evaluation and analysis of evidence using infrared, Raman, and SEM/EDX microprobe methods has advanced forensic science. Forensic science deals with the interaction of science with the law. This interaction requires that certain standards are met before scientific evidence is admitted in either a civil or criminal case. While the Court's burden of proof is different for a civil case than for a criminal case, the standards of evidence admissibility are not. Forensic scientists must defend their methods and conclusions in Court, regardless of whether they are a trace analyst identifying fibers, a drug analyst determining if the white powder found on a suspected criminal was cocaine, or a pharmaceutical researcher discovering new solid-state forms of a drug. Today, microspectroscopy is a primary technology used within all forensic science disciplines to increase the value of evidence. Modern microbeam methods are extending observations, enhancing documentation, providing additional information, aiding deductions, and testing hypotheses. This increase in value of scientific evidence is pivotal in adjudicating both civil and criminal litigation.

In conducting a scientific examination of evidence, the forensic scientist follows the basic tenets of the scientific method. The mantra: observation, documentation, contemplation, speculation and verification, is followed. In applying microspectroscopy to forensic investigations, microscopy, and spectroscopy are united to detect, document, evaluate, and analyze evidence. Then this evidence must be clearly and convincingly presented to the Court. The forensic scientist must be capable of validating both instrumentation and methods used in their analysis. If expert opinions are presented, then they must meet the standards of reasonable scientific certainty. Each of the following examples shows how microspectroscopy techniques were successfully applied to challenges faced by forensic scientists within different scientific disciplines, as well as within both civil and criminal contexts.

1. Fiber-Residue Transfer Evaluation

Fibers are a common and important type of trace evidence. Dr. Edmond Locard (1877-1966) stated, "It is impossible for a criminal to act, especially considering the intensity of a crime, without leaving traces of this presence." This is the underlying principle for trace evidence. Collection and analysis of these trace materials has historically provided police and prosecutors with the evidence needed to investigate, make arrests, and convict criminals. Developments in infrared microspectroscopy allow forensic scientists to easily and nondestructively identify these materials with little-to-no sample preparation, and to relate this evidence to the environment where they are recovered. The goals of trace evidence examination in criminal cases are to track history of events and establish relationships between victim and perpetrator. Trace evidence evaluation frequently allows for a more complete history of the crime. In the following example, infrared microspectroscopy was applied to an unknown fiber without removing the fiber from the substrate upon which it was adhered (a discharged bullet) at the time of recovery. This evaluation made it possible to not only identify the fiber, but also determine the pathway the bullet took when discharged from a firearm.

Identification of Kevlar® Residue on a Bullet

A few years ago, a Maine State Police officer was shot while patrolling in a wooded area. The bullet passed through the officer's bulletproof vest and his shoulder before exiting and lodging in a nearby tree. No one was seen in the area of the shooting, but a local resident was suspected of committing the crime. When the bullet from the scene was matched to the suspect's gun, the case was thought to be closed. However, the suspect claimed that he frequently went shooting in the area and was not surprised that bullets from his gun could be found in nearby trees. Microscopical examination of the bullet revealed yellow-tinted smears of material. Infrared microprobe analysis of this residue identified these smears as Kevlar®, a DuPont fiber commonly used in bulletproof vests. Confronted with this additional evidence, "the perp copped a plea".

In this example, a discharged bullet recovered from a crime scene was proven to have passed through a bulletproof vest prior to lodging in a tree. The ability to identify microscopic Kevlar® fiber residue adhering to the discharged bullet was of critical importance. This identification validated the claim that this bullet, fired from the suspect's rifle, struck the officer's bulletproof vest.

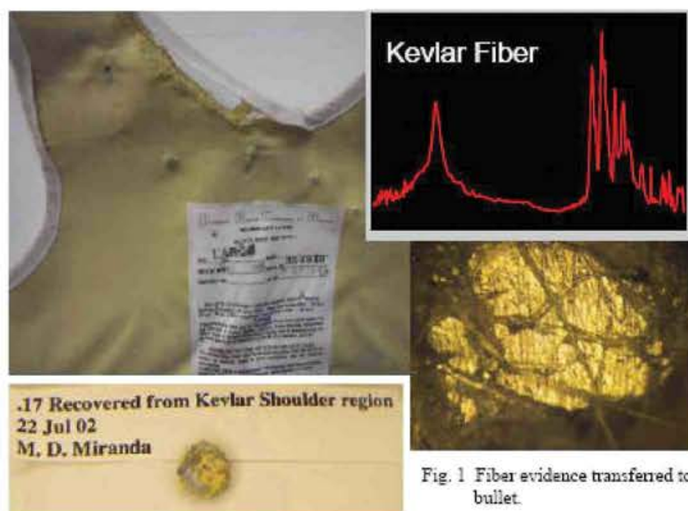

Figure 1. Infrared and Photomicrographic Data Recovered from a Discharged Bullet

The identification of materials transferred to bullets, including Kevlar® residue, using infrared microprobe analysis was the subject of the Master's thesis of Michelle Miranda at John Jay College of Criminal Justice. In this thesis, Miranda demonstrated that residues on bullets recovered at crime scenes can typically be identified using infrared microprobe analysis. These evaluations are easy to perform and can provide a great deal of information about the history of a discharged bullet. Microprobe analysis has detected paint, fiberglass, metals, and building materials residue on bullets.[1]

Microscopical images of fiber residue on a bullet discharged from a firearm and impacted with Kevlar® are displayed in Figure 1. Also included in this figure is the infrared spectrum of the Kevlar® residue adhered to the discharged bullet. Infrared spectra were collected from the residue, and a match was made between these microscopic fibers and a Kevlar® standard.[1]

Prior to the availability of infrared microprobe systems with high-quality imaging capabilities and valid libraries of reference

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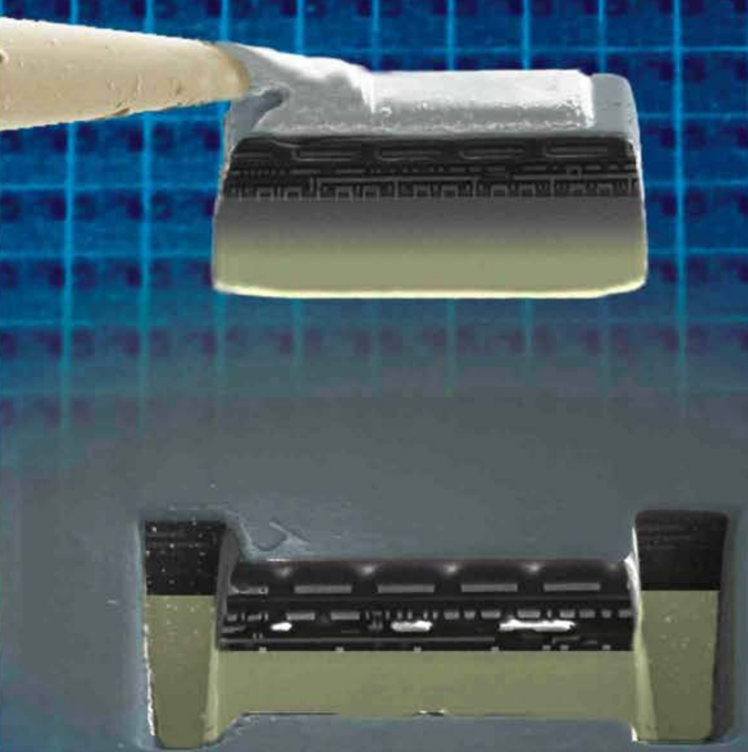

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spectra to identify microscopic particles, this type of evidence evaluation was impractical.

2. Illicit Drug Identification

The illegal use of drugs is a worldwide problem for the criminal justice system. Stopping the flow of drugs, prosecuting both dealers and users, and shutting down clandestine drug laboratories is a gigantic burden on our society. Drug-related crimes generate the largest volume of casework in the criminal justice system.

In 2002, the Michigan State Police Forensic Laboratories reported they analyzed approximately 30,000 drug cases per year, which is 1/3 of their entire Forensic Division caseload. Since each case requires analysis of multiple samples, this state's drug laboratories are estimated to perform over 250,000 analyses each year.

The forensic community continues to improve and standardize the practices used by different laboratories and jurisdictions for identifying illicit drugs. Two peer groups, Scientific Working Group for the Analysis of Seized Drugs (SWGDRUG) and ASTM International, established minimum standards for the forensic identification of commonly seized drugs.[2, 3]

In the SWGDRUG recommendation and ASTM E-2329 Standard, the analytical techniques are divided into three categories. Techniques are listed in order of decreasing discriminating power from A to C (see Table 1). The ASTM Standard requires that laboratories meet the following minimum criteria when identifying illicit drugs:

1. When a validated Category-A technique is incorporated into an analytical scheme, then at least one other technique (from either Category A, B or C) must be used.
   1.1. This combination must identify the specific drug present and must preclude a false positive identification.
   1.2. When sample size allows, the second technique should be applied on a separate sampling for quality assurance. When sample size is limited, additional measures should be taken to assure that the results correspond to the correct sample.
   1.3. All Category-A techniques must have reviewable data.
2. When a Category A-technique is not used, then at least three different validated methods must be employed.
   2.1. These in combination must demonstrate the identity of the specific drug present and must preclude a false positive identification.
   2.2. Two of the three methods must be based on uncorrelated techniques from Category B.
   2.3. A minimum of two separate samplings should be used in these three tests. When sample size is limited, additional measures should be taken to assure that the results correspond to the correct sample.
   2.4. All Category-B techniques must have reviewable data.
3. For the use of any method to be considered of value, the test must be considered "positive". While "negative" tests provide useful information for ruling out the presence of a particular drug or drug class, these results have no value in establishing a drug's identity.
4. In cases where hyphenated techniques are used (*e.g.* gas chromatography-mass spectrometry, liquid chromatography-diode array ultraviolet spectroscopy), they will be considered as separate techniques if the results from each are used. If a hyphenated technique is used as the sole means of identifying a substance, it should be applied to two separate samplings, for quality assurance reasons.

Review of these standards demonstrates how performing analysis using a Category-A method offers advantages over using combinations of only Category-B and Category-C methods. Recent developments in the field of infrared microprobe analysis now enable drug analysts to employ Category-A methods immediately upon positive test results from a presumptive test such as a color test (Category C) or a microcrystalline test (Category B).

Table 1. Categories of Analytical Techniques from SWGDRUG Methods of Analysis

Category A	Category B	Category C
Infrared Spectroscopy	Capillary Electrophoresis	Color Tests
Mass Spectroscopy	Gas Chromatography	Fluorescence Spectroscopy
Near Infrared Spectroscopy	Ion Mobility Spectrometry	Immunoassay
Nuclear Magnetic Resonance Spectroscopy	Liquid Chromatography	Melting Point
Raman Spectroscopy	Microcrystalline Tests	Ultraviolet Spectroscopy
	Pharmaceutical Identifiers	
	Thin Layer Chromatography	
	Cannabis only: Macroscopic Examination Microscopic Examination (Counts as one each)	

Infrared microprobe analysis provides a rapid, reliable and reviewable Category-A method for illicit drug analysis. If all illicit drug samples were pure, and if only infrared spectral analysis were needed for analysis, then the old traditional infrared methods could be used. Street drugs are impure; they are often mixed with cutting agents or impurities. Using an infrared microprobe combines the imaging of the microscope with the analytical power of infrared analysis. Microscopic examination lets the analyst see discrete phases so that infrared spectra can be collected from each phase. There are real advantages and efficiencies in using the infrared microprobe as the primary analytical technique for the identification of illicit drugs.

When drugs are seized and submitted to a laboratory, a presumptive screening test (Category B) is usually the first step. When this test is positive, a specific analysis is made. An infrared microprobe using a carbon (diamond) attenuated total reflection (C_D-ATR) objective enables infrared spectra to be collected from microscopic areas within the sample with no sample preparation. Frequently, and depending upon sample purity, an infrared spectrum consistent with the infrared spectrum of the suspected standard are generated during this analysis. In these instances, sample testing is complete and in accordance with the ASTM standards requirements.

Microcrystalline tests, a Category-B technique, require a microscope to see and record images of the crystals that form with specific test reagents. These tests are very sensitive and specific for the analysis of the most commonly seized drugs.[4] They also provide a means for separating the illicit drug from cutting agents in "street" drug mixtures. When characteristic crystals form, using appropriate microcrystalline test methods,[5, 6, 7] infrared microprobe analysis of these crystals provides a Category-A identification of the suspected compound. Since the infrared spectrum is a Category-A method, identification of the sample is complete, and will meet ASTM standards when duplicate samplings are analyzed.

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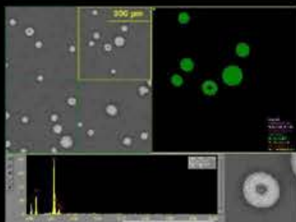

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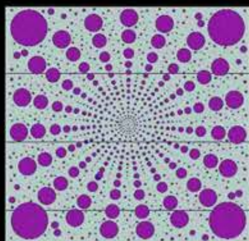

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The ability to identify microcrystal test product using infrared microprobe analysis is an efficient methodology for illicit drug analysis; evaluating samples within minutes. In addition, in cases where it is possible to generate infrared spectra from the neat sample, differentiation amongst cocaine base, cocaine HCl and/or other salt forms is direct and easily performed.

In the following example, testing in accordance with ASTM E-2329 was applied to a street sample of cocaine using infrared microprobe analysis. Analysis of the sample was performed directly on the street sample and the infrared spectrum was consistent with the infrared spectrum of a cocaine base reference standard. Although sample analysis was complete and the sample was positively identified as cocaine, further testing of the sample was performed. This included microcrystal testing in accordance with the ASTM microcrystal test method for the identification of cocaine, followed by infrared microprobe analysis of the resulting microcrystal test crystal complex formed for both the standard and reference samples. This testing, too, identified the sample as containing cocaine.

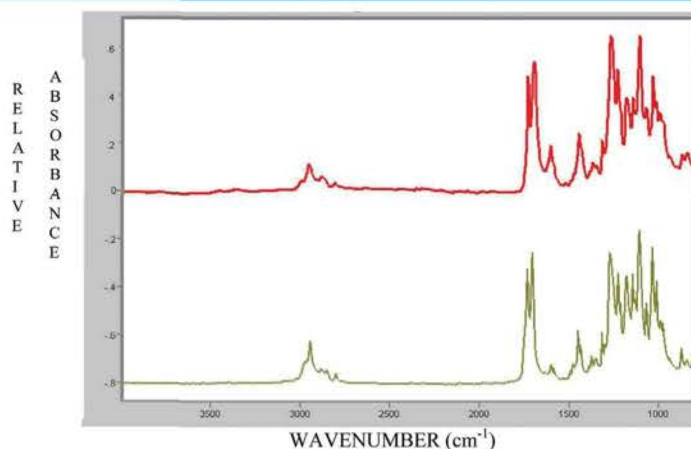

Figure 2. Infrared Spectrum of Street Sample of Cocaine (top spectrum) Compared with Library Spectrum of Cocaine Base (bottom spectrum)

Identification of Cocaine-Gold Chloride Complex Using a C_D-ATR Infrared Microspectroscopy

The ASTM microcrystal test performed to identify cocaine requires that the unknown substance react with gold chloride in an acidic environment to generate characteristic crystals. These crystals are compared with crystals formed from a reference standard prepared in the same manner. When using a C_D-ATR microscope objective, it is possible to isolate these crystals formed and perform an infrared identification of a single crystal. The infrared spectrum of the crystal is compared with the spectrum from the crystal of a similarly prepared reference standard for identification.

In this example, a street sample of cocaine was treated with gold chloride solution in accordance with ASTM Test Method E1968-98(2003). Crystals formed were compared with crystals formed using a reference standard preparation. Photomicrographic documentation of crystals from the reference and sample preparations provides reviewable documentation. Infrared spectra were compared. The infrared spectra were consistent with each other and characteristic of a gold salt form of cocaine.

Figure 3. Characteristic Cocaine-Gold Chloride Crystal Complex

Figure 2 shows the infrared spectra of the street sample of cocaine as well as a reference spectrum of cocaine base. Figure 3 shows characteristic cocaine-gold chloride crystal complexes formed during the microcrystal testing. Figure 4 shows the infrared spectra of the cocaine crystal complexes formed during these microcrystal tests. The spectra of the cocaine crystal complexes are different from the spectra of the neat sample due to differences in solid-state form at the time of the analysis. This ability to differentiate salt (and free base) form adds to the discriminating power of infrared analysis. Chemical identifications, including the ability to differentiate salt forms, are an invaluable capability of this type of analysis.

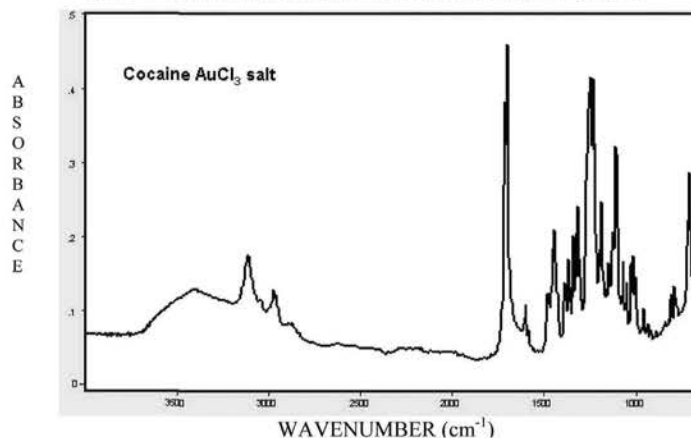

Figure 4. Infrared Spectrum of Cocaine-Gold Chloride Crystal Complex

Infrared microprobe analysis of the characteristic crystals formed by a microcrystal test provides a Category-A identification of the drug. In the previous example, cocaine was identified from the infrared spectrum of the neat sample. However, if this were not the case and only cutting agents or other excipients were identified during the initial analysis of the evidence sample (as is sometimes the case), further testing is required. Although microcrystal tests uniquely identify cocaine,[8] they are still only considered Category-B methods within the established ASTM standards. Identification of the cocaine crystal complexes formed during microcrystal tests, however, confirms the microcrystal test identification while simultaneously offering a Category-A test result to complete the analysis. This identification is supported by a Category-B identification of characteristic crystals and/or the positive results of the Category-C presumptive test.

Prior to advances in infrared microprobe techniques, analysis time and cost were significantly higher. The total time requirement for performing and documenting the testing detailed above, including preparation and evaluation of the cocaine crystal complexes is less than 20 minutes. This time requirement is significantly lower than the total time required for techniques such as gas chromatography/

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mass spectrometry or nuclear magnetic resonance spectroscopy.

3. Identification of Solid-State Form in Pharmaceutical Drug Development

When a new molecular entity is created and deemed to be a viable candidate for development by a pharmaceutical company, years of research will follow before this new molecular entity (NME) reaches the market as a drug product. During this development period, different routes of synthesis of the compound will be evaluated, a variety of dosage forms will be tested, and different drug-product formulations will be compared before, finally, a new drug application (NDA) is filed with FDA. FDA approval is necessary to market the drug within the United States. Evaluations of the compound's solid-state chemistry and structure are performed throughout this process, and these studies range in scope from large-scale polymorph screens performed at earlier stages of NME development, to characterizations of polymorphic form in final drug product as required by FDA. Because vibrational spectra provide direct information on chemical bonding, infrared microprobe techniques are proven to provide information during these assessments that gives unique insight about the solid-state chemistry of the compound.

Modern infrared microspectroscopy systems enable evaluations of the solid-state chemistry and structure of samples on the microscopic scale. Differences in the solid state are important for a variety of reasons. First, different solid-state forms of the same compound, although chemically identical, may behave differently from each other. This ability to exhibit polymorphism is also important from a patent-protection perspective. One solid-state form of a compound may be under patent while another is not. Finally, FDA requires that the polymorphic nature of developed compounds be understood and controlled.[9]

While infrared absorption measurements do not inherently monitor crystal lattice geometry, the infrared spectra of polymorphs are distinguishable because of changes to the local environments of the molecules. These differences are evidenced throughout the mid-infrared spectrum in both the hydrogen-bonding and fingerprint regions. Changes to the fingerprint region are small, but reproducible. Changes in the hydrogen bonding region, on the other hand, are often more dramatic. This combination of small changes in the fingerprint region with more dramatic changes in the hydrogen bonding region helps confirm chemical identity while verifying crystal form.

The ability to perform solid-state characterization on microscopic samples enables scientists to perform these analyses earlier in the drug development life cycle. Early in development, the amount of material available is typically limited and micro scaled methods can speed-up the process. Today, these systems are linked with environment-controlled microscope stages, extending the usefulness of the infrared microprobe in drug substance evaluation.

Infrared Microspectroscopy to Identify Polymorphic Form and Other Solid-State Properties

Ranitidine HCl is the active pharmaceutical ingredient (API) in the over-the-counter medication Zantac®. This compound generated a significant amount of civil litigation as a result of differences observed in its solid state. Two solid-state polymorphic forms of ranitidine HCl were identified and patented. These polymorphic forms were distinguishable using infrared spectroscopy and x-ray diffraction. Their infrared spectra are displayed within Figure 5. During the ranitidine-related litigation, the use of infrared spectroscopy to identify polymorphic form was shown to meet the standards of admissibility of scientific evidence[10] and was used in court to support the identification of Form-I and Form-II ranitidine HCl.

Taking this type of identification one step further, it is now possible to perform infrared microprobe analysis while simultaneously exposing the sample to changes in humidity and/or temperature. The ability to perform this type of evaluation makes it possible to easily identify changes that result from changes in environment. These include hydrate or solvate form, polymorphic conversion, recrystallization from melt, and decomposition.

The affect of exposure to changes in temperature and humidity are critical factors for a variety of reasons. Increases in temperature are common during API and drug-product manufacture. It is necessary to know whether this thermal treatment impacts API and/or formulation stability. In addition, solid-state form of the API may change as a result of thermal treatment. These factors must be considered and evaluated prior to development of the API and drug-product final manufacturing processes.

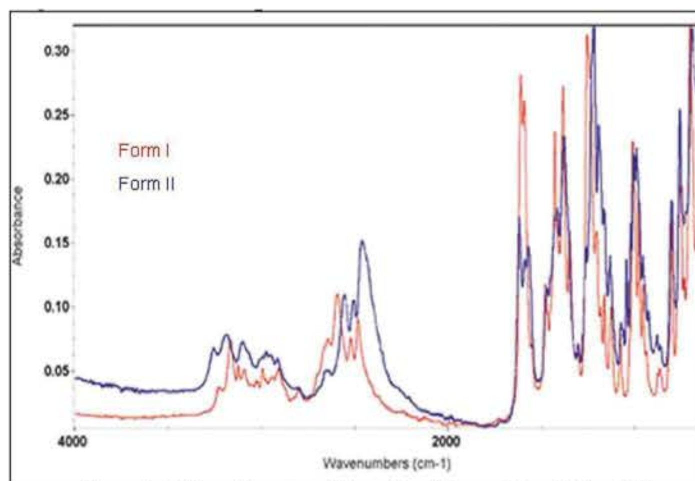

Figure 5. Infrared Spectra of Form-I and Form-II Ranitidine HCl

Understanding the effect of humidity on the API and drug product is also important. Water content of many compounds depends upon the relative humidity of their storage environment. Compounds may change from one crystalline hydrate to another simply by changing the relative humidity within which they are stored. If the same product is manufactured at different sites with different climates, it is necessary to evaluate water content so that product from different locations is the same.

Amorphous compounds, too, can be significantly impacted by exposure to different levels of humidity. Amorphous compounds tend to pick up water at a much faster rate than their crystalline counterparts. In these situations, understanding the water-sorption properties of the sample is of critical importance. Degradation rate was shown to increase in amorphous materials as water content increases.[11] In addition, many amorphous compounds will crystallize at high water-content levels. Typically, this is not a desired activity. It is easy to see how understanding the water sorption of the API and drug product is critical when determining API and product stability, drug load and packaging requirements.

In the following example, a pharmaceutical API was exposed within a variable-humidity microscope stage to three different relative-humidity environments. First, the sample was equilibrated at 0% relative humidity, then at 95%, and then again at 0%. Throughout this environmental exposure, infrared spectra as well as photomicrographs of the sample were collected and reviewed for comparison.

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Comparison of the photomicrographs showed no significant changes in visual appearance. However, the infrared spectra collected at 0% relative humidity using the variable humidity environmental microscope stage were different from each other and showed that two polymorphs of the sample existed. For proprietary reasons, only a portion of the wavenumber region analyzed is displayed within Figure 6. Simply by exposing the sample to high levels of relative humidity and then drying, the solid-state form of the material changed.

Prior to the integration of the infrared microprobe with variable-humidity microscope stages, performing these studies would be difficult or impossible. During this analysis, the sample is never removed from the environmental chamber within which it is being treated. In addition, infrared spectral measurements are collected from a specific region within the sample that can be observed directly using light microscopy for any physical change during environmental treatment.

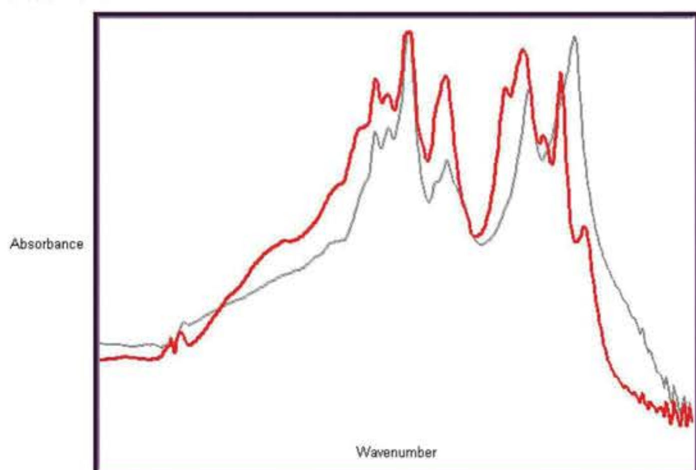

Figure 6. Form-I and Form-II of Anhydrous API

A second example showing the power of this technology uses a variable-temperature microscope stage to control the sample environment. In this experiment, a pharmaceutical API is dried during heating and converted from a crystalline hydrate to an anhydrous form of the same compound. Figure 7 displays the spectral change that occurs in the OH- bonding region as the sample is heated to 100°C. Loss of the peak due to hydrogen-bonded water disappears as the temperature is increased. Changes are observed within the hydrogen- and non-hydrogen-bonding regions of the spectrum, but no significant change is observed in the fingerprint region (not shown for proprietary reasons) during this water-loss event.

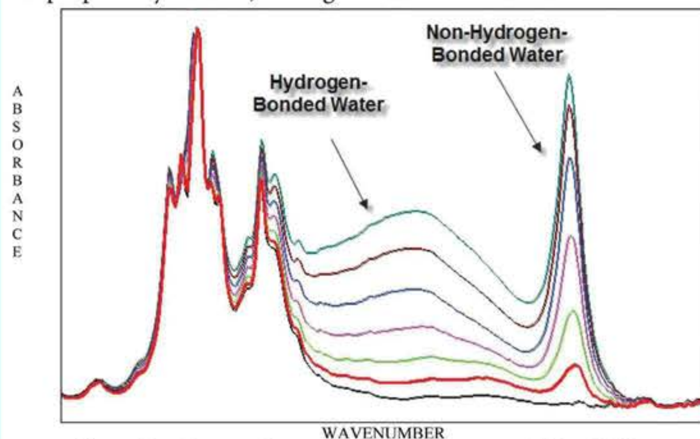

Figure 7. Changes Observed in the Hydrogen and Non-Hydrogen Bonding Regions of the Infrared Spectrum of API Hydrate as Sample is Heated and Water is Removed

This analysis is also significant because it directly relates changes in the spectrum to changes in the -OH stretching region of the sample's water-loss event. The spectral differences displayed above provide information about the manner in which water is removed from the sample during conversion from the hydrate to the anhydrate. It is clear from the change in the ratio of the peak intensities of the non-H-bonded and H-bonded water as temperature is increased that these two water environments are changing at different rates. The hydrogen-bonded water is lost from the sample at a different rate than the non-hydrogen bonded water. This provides insight about the bonding within the molecule. This information is invaluable to the scientist's understanding about their molecules and how these molecules interact with other species in the drug formulation.

Summary and Conclusion

The evaluation and analysis of evidence using microspectroscopy is advancing the field of forensic science. Because infrared microspectroscopy has the greatest utility and importance to both civil and criminal litigation, it was the focus of the applications presented here. SEM/EDX and Raman microprobes have unique applications. Raman microprobes are used in drug-development laboratories to identify solid-state form during development, as well as during prosecution of pharmaceutically relevant patents, but their use within forensic laboratories is not as widespread. This is likely to change over the next few years as a result of accessibility to more moderately priced instrumentation. SEM/EDX systems, too, are frequently encountered within drug-development laboratories to perform a variety of functions including elemental analysis, salt-form identification, and drug distribution within a drug-product matrix. Within the forensic community, SEM/EDX has real value for the analysis of bullet fragments, gunshot residues, paint and other forms of evidence requiring elemental analysis. The bringing together of microscopy and spectroscopy has forever changed forensic investigations. ■

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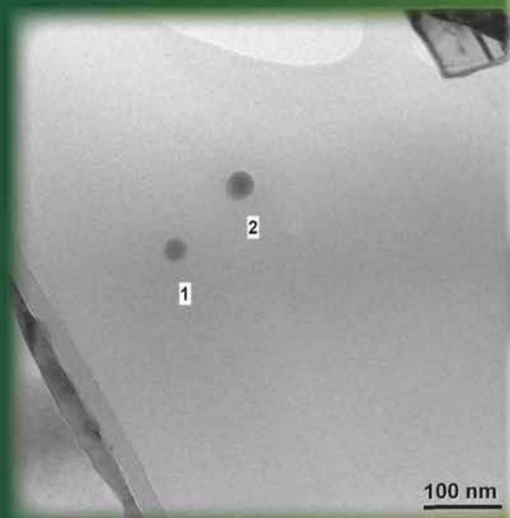

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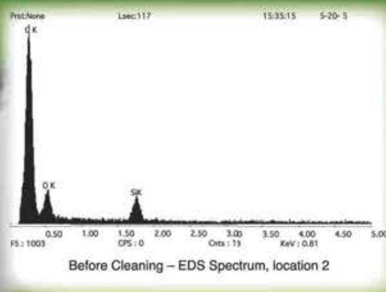
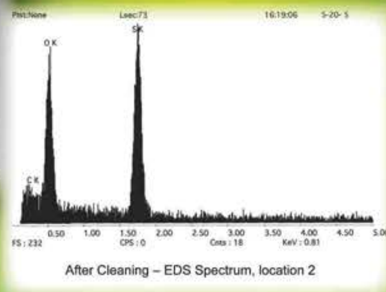


Before Cleaning – EDS Spectrum, location 2



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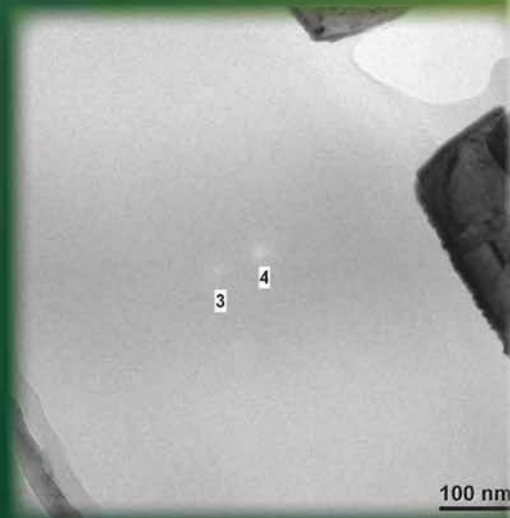
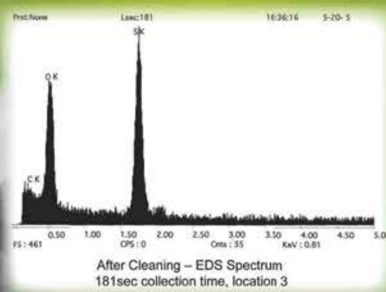
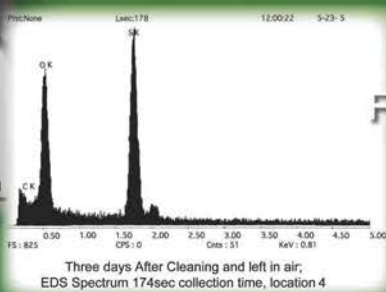


After Cleaning – Location of NEW EDS Spectrum collected over 3 min



After Cleaning – EDS Spectrum 181sec collection time, location 3



Three days After Cleaning and left in air; EDS Spectrum 174sec collection time, location 4

CLEANS TEM/SEM SAMPLES

UNIQUE H_2O_2 CLEANING RECIPE (PATENT PENDING)

SAFE CLEANING OF HOLEY CARBON FILMS

AR/O_2 CLEANING RECIPE

SHORTEST CLEANING CYCLE TIMES

85W RF POWER SUPPLY AND AUTOMATCH RF SYSTEM FOR CONSISTENT RESULTS

TOUCH SCREEN TECHNOLOGY

ONE-TOUCH RECIPE SELECTION

FRONT AND TOP LOADING CHAMBER

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PRECISION PERFORMANCE PRODUCTIVITY

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