APPLICATION NOTE

FT-IR Imaging

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FT-IR Imaging Capabilities in Pharmaceutical and Biopharmaceutical Segment for Impurity Characterization Studies

Introduction

Mid-infrared (MIR) microscopy, based on a Fourier Transform infrared (FT-IR) spectrometer, has been the infrared micro spectroscopy technique most readily available up to now. It is a broadly employed chemical identification tool that is used to complement traditional light microscopy. Since the first description of the coupling of an infrared (IR) spectrometer to a microscope, the method has enjoyed widespread use in a variety of research and industrial applications. In practice, the method couples light microscopy and chemical identification of a spatially defined area. Typically the light microscope is used to locate the region of interest, and then it is non-invasively and non-destructively sampled with infrared radiation to provide chemical identification of the desired microscopic area within the sample. Infrared mapping techniques provided the first step toward bringing the methodology closer to imaging by translating the sample under the microscope while simultaneously recording infrared spectra.

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In recent years we have seen an explosive growth in the applications of the FT-IR Imaging Microscope and the data resulting from these imaging systems. From materials research to the imaging of cancer cells and disease as well as uses as a quality control tool for polymers and pharmaceuticals. FT-IR imaging microscopes are now used in many different laboratories around the globe. As new challenges emerge for the analysis of samples, the FT-IR imaging system must provide a solution for these types of analyses. The FT-IR imaging system with a linear array (LA) detector provides a rapid, powerful tool for the examination of a wide array of samples and combining this flexible imaging system with advanced image processing software can easily provide visually relevant data. Imaging studies have been performed on Pharmaceutical products for the detection of solid materials (foreign material) observed in Injectibles. FT-IR Imaging has been found to be useful for the rootsource of such impurities.[1-3]

Experimental 1

Solid Materials (Foreign Material) Observed in Injectibles:
Samples were filtered on to Whatman filter papers and dried in an oven. Small particles (Black, White and shiny) were spotted onto a filter paper and analyzed through ATR imaging.

Figure 1. Spotlight 400 with Frontier.

Figure 2. ATR imaging accessory.

Instrument Parameters:

- Accessory used: ATR imaging
- Scan range: 4000 cm^{-1} – 750 cm^{-1}
- No. of scans: 16 per pixel
- Resolution: 4 cm^{-1}
- Area :200 um x 200 um / 150 um x 150 um
- Pixel: 6.25 um

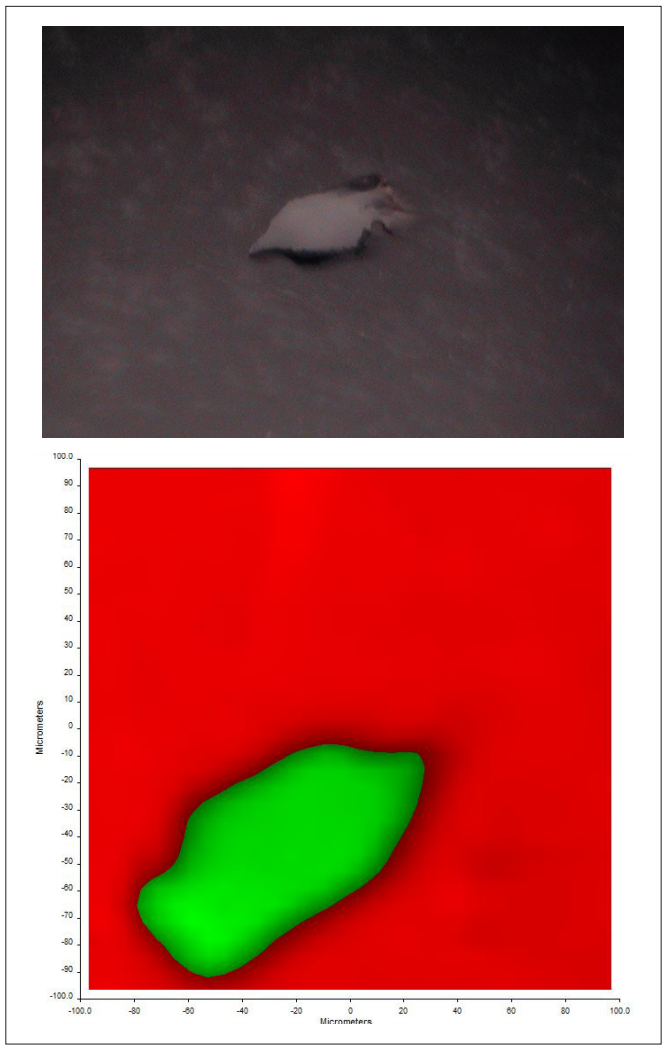

Figure 3. Visible and chemical Image of foreign particle 1.

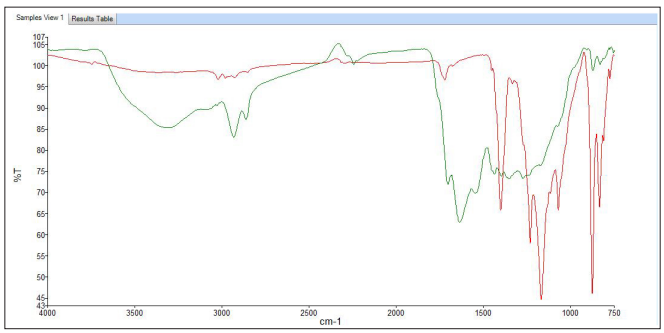

Figure 4. Graph 1 – Overlay spectra of green and red area in chemical image.

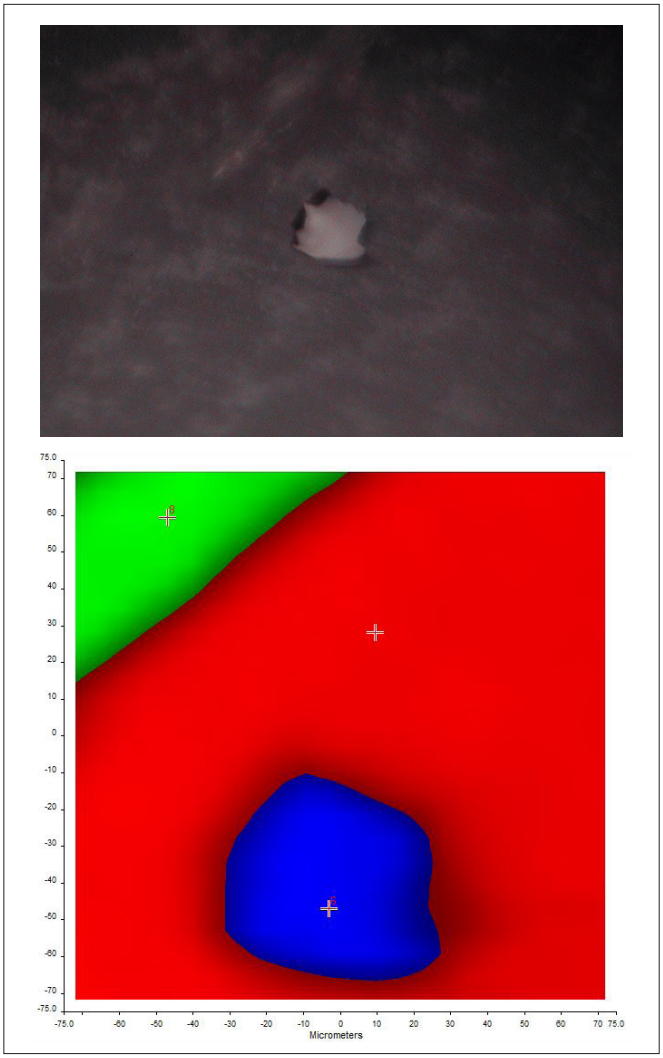

Figure 5. Visible and chemical image of foreign particle 2.

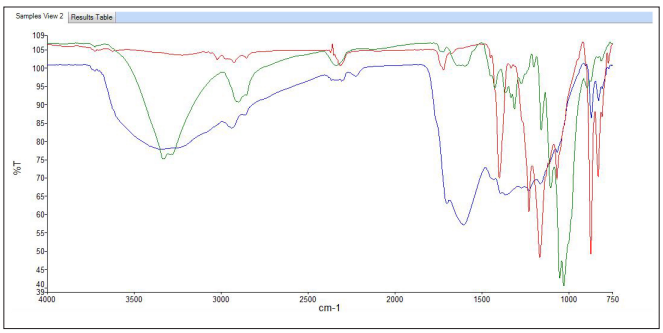

Figure 6. Graph 2- Overlay spectra of blue, red and green area.

The spectrum of the solid foreign particle is cleary indicative of its different functionality, found to be an amide based compound probably added as impurity while in production.

Experimental 2

Needle shaped particles observed in Parental formulations: Parental formulations showed some particles visible to the human eye. Samples were filtered (Vacuum filter) through 0.22 micron pore size filter papers and dried in an oven. Needle shaped particles were spotted onto filter paper and analyzed through ATR imaging.

Instrument Parameters:

- Accessory used: ATR imaging
- Scan range: 4000 cm^{-1} – 750 cm^{-1}1
- No. of scans: 16 per pixel
- Resolution: 4 cm^{-1}
- Area :200 um x 200 um / 150 um x 150 um
- Pixel: 6.25 um

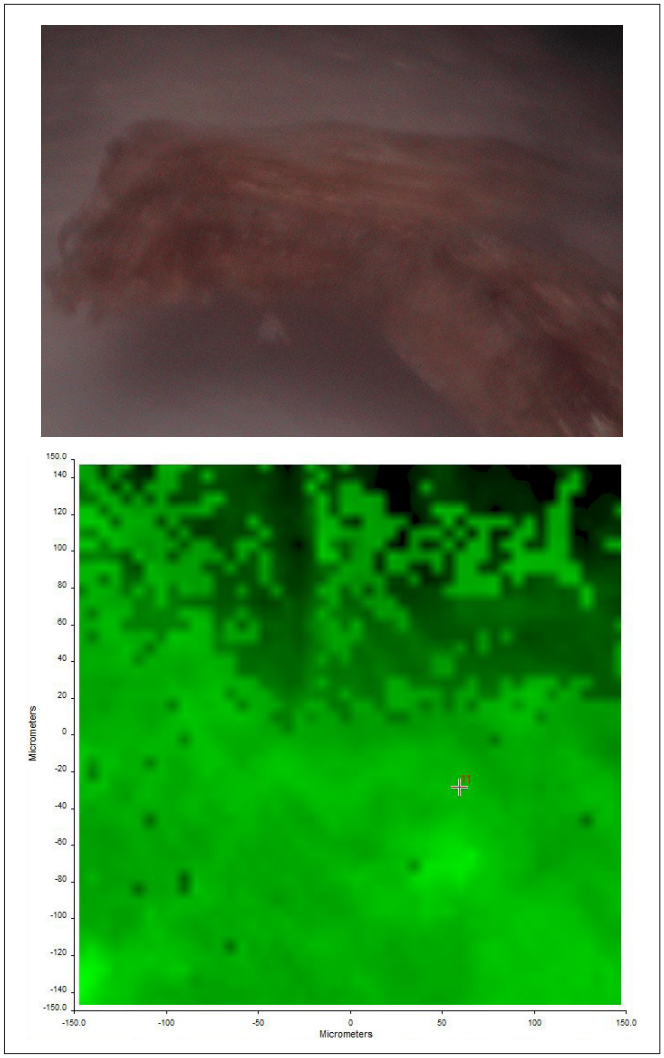

Figure 7. Visible and chemical images of needle shaped material.

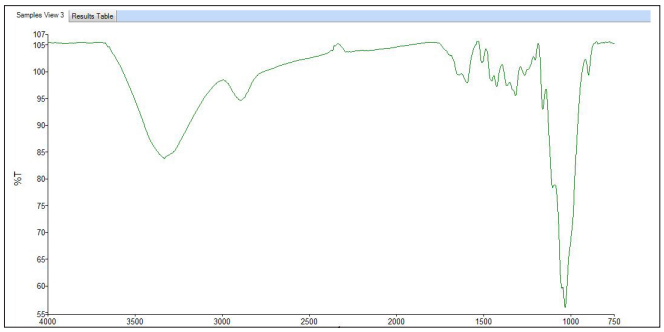

Figure 8. Graph 3- Spectra of green area.

Table 1. Interpretation of Green spectra through KnowItAll BIORAD software.

Name	Value
Resultin HQI	97.59
Database Abbreviation	BWX
Database Title	ATR-IR - Polymers and Monomers (Basic) 1 - Bio-Rad Sadtler
Record ID	303
Name	Cellulose (100 micron)
CAS Registry Number	9004-34-6
Catalog Number	659
Comments	White Powder
Instrument Name	Bio-Rad FTS
Lot Number	290501005
Refractive Intex	1.54
Source of Sample	Scientific Polymer Products, Inc.
Source of Spectrum	Forensic Spectral Research
Technique	ATR-Neat (DuraSamplelIR) II

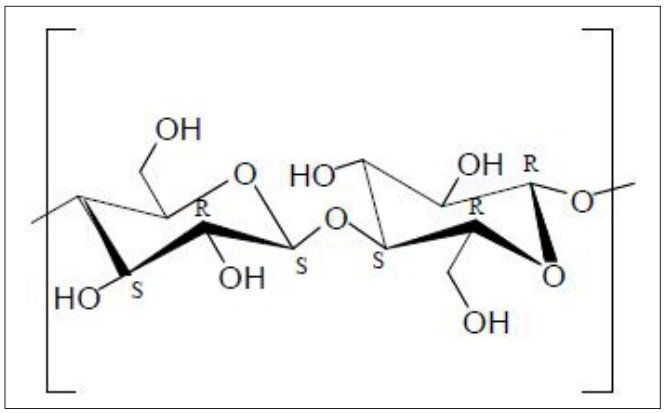

Figure 9. Interpretation of green area.

Interpretation of the Needle shaped particle spectra predicts the presence of cellulosic material. The company R&D team suspected the cellulosic material been added in Injectibles during the filtration process while the active solution passes through the series of filters.

Spotlight 400 FT-IR Microscope

PerkinElmer provides a full line of innovative IR Microscopy and Imaging Systems, software, sampling accessories and services to laboratories worldwide, improving product quality, productivity and analytical processes. Our spotlight 400 is capable of achieving very high spatial resolution down to within the accepted diffraction limit. Our instruments feature optics designed specifically for infrared applications and, because minimal manual adjustment is required, ease-of-use is greatly increased.

Very high sensitivity providing high quality data down to the accepted diffraction limits.

Rapid-scan IR imaging

- Spatial Spotlight 400 connected to frontier FT-IR is capable of operating in MIR, NIR or dual range as per spectral range desired from the sample analysis.
- Thus FT-IR microscope is capable of achieving resolution up to either of 3 pixel resolutions.
- Option of using microATR improved the spatial resolution by down to 1.56 microns.

Conclusion

One of the key advantages of ATR-FT-IR imaging is that it requires minimal or no sample preparation prior to spectral measurements. In this case the sample just needs to be filtered. This is due to the fact that the penetration depth of IR light in the sample for ATR measurements is independent of sample thickness.

FT-IR Imaging has excellent potential in sample characterization within the Injectibles segment of Pharma and Biopharma sector for impurity identification.

References

1. Applications of ATR-FT-IR spectroscopic imaging to biomedical samples http://www.sciencedirect.com/science/article/pii/S0005273606000630.
2. Lewis, E.N.; Schoppelrei, W.; Lee, E.; Kidder, L.; in 'ProcessAnalytical Technology' Blackwell, 2005. ISBN-10 1-4051-2103-3.
3. Canas, A.; Carter, R.; Hoult, R.; Sellors, J.; Williams, S.;' Spatial resolution in mid-IR ATR Imaging: Measurement and Meaning' FACCS conference, 2006.

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