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Application News

AIRsight™ Infrared/Raman Microscope

Contaminant Analysis of Pharmaceuticals (Tablets) Using AIRsight Infrared/Raman Microscope

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User Benefits

- Use of AIRsight makes it possible to acquire both infrared and Raman spectra at the same location without moving the measurement target sample.
- Highly accurate qualitative analysis is possible by measuring the infrared and Raman spectra at the same location.
- Even microscopic contaminants on pharmaceuticals (tablets) can be analyzed by simple operation.

■ Introduction

In recent years, consumers have shown heightened concern about contamination of products by foreign matter, and demand for analysis to respond to this problem has also increased. Although news reports that contaminants have been discovered in some foods and pharmaceuticals have appeared from time to time, it is difficult to eradicate this problem completely, as the causes of contamination are assumed to include various processes such as contamination of raw materials at the time of purchase, contamination of the product due to deterioration of component parts of the production line, and contamination of the product by the consumer. The types of foreign matter are also diverse, including not only organic materials such as human hair, plastics, and rubber, but also oxides, metal fragments, and other inorganic substances. For these reasons, higher accuracy is required in qualitative analysis in order to identify the cause of contamination.
The AIRsight Infrared/Raman microscope is a new microscope in which a Raman unit is incorporated in an infrared microscope, making it possible to carry out both Raman and infrared analysis with a single instrument, even though separate instruments had been required until now. Fig. 1 shows the appearance of the AIRsight. Since the infrared spectrum and Raman spectrum can be acquired at the same location, without moving the sample, the accuracy of qualitative analyses of micro regions is dramatically improved. Operation is also simple because both the infrared and Raman measurements can be controlled with one software program, AMsolution.
This article introduces an example of measurement of a contaminant adhering to the surface of a pharmaceutical (tablet) (hereinafter, "tablet") by micro-infrared spectroscopy and micro-Raman spectroscopy.

Fig. 1 Appearance of AIRsight™

■ Infrared Spectroscopy and Raman Spectroscopy

In infrared spectroscopy, infrared light is irradiated on the sample and the amount of light absorbed at each wavelength (wavenumber) is measured. In contrast, in Raman spectroscopy the light scattered by sample when it is irradiated with light of a specified wavelength is measured, and the difference between the incident light and the scattered light (i.e., the Raman shift) is then calculated. Like the infrared spectrum, the Raman spectrum is based on the vibrational spectrum of molecules. Both techniques are used for purposes such as identification of substances by comparison with known spectra and structural determination and quantitative analysis of molecules. However, the intensity and shape of the detected peaks differ in the two methods.

■ Measurement Samples and Conditions

Fig. 2 shows the appearance of a contaminant adhering to the surface of a tablet. The contaminant is reddish-brown and exists in a scattered form over a range of about 100 µm on the tablet surface. With conventional instruments, the single most time-consuming process is the work of setting the tablet on the microscope stage and adjusting the measurement position so that it is in the field of view (FOV) of the microscope. With AIRsight, this work can be completed easily because the wide-field observation camera, which is provided as standard equipment, makes it possible to observe a FOV at a size that is visible to the human eye (10 × 13 mm). The wide-field camera is also equipped with a digital zoom function with a maximum magnification of 5x (2.0 × 2.6 mm). The microscope camera, which is used in the actual measurement, is also equipped with a 10x zoom (0.03 × 0.04 mm) function, so even microscopic contaminants can be observed smoothly. Positional information is shared by the microscope camera and the wide-field camera, ensuring that the FOV does not shift due to switching between the two cameras.
Table 1 shows the measurement conditions.

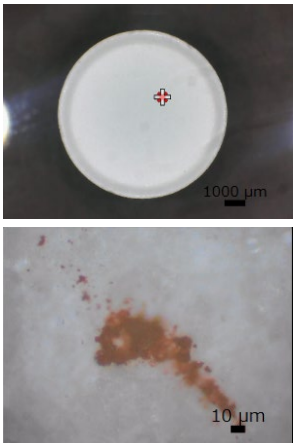

Fig. 2 Appearance of Contaminant on Tablet Surface
Top: Image of Entire Tablet Observed with Wide-Field Camera
Bottom: Image of Contaminant on Tablet Surface Observed with Microscope Camera

Table 1 Measurement Conditions

Instruments	: IRTracer™-100, AIRsight
Infrared Spectrometry	
Resolution	: 8 cm^{-1}
Accumulation	: 100
Apodization Function	: SqrTriangle
Detector	: T2SL
Raman Spectrometry	
Accumulation	: 100
Exposure Time	: 1.0 sec
Objective Lens	: 50x
Excitation Wavelength	: 785 nm
Detector	: CCD

■ Contaminant Analysis by Micro-Infrared Spectroscopy

First, the infrared spectra were acquired. An analysis of the normal area and an area with an adhering contaminant was conducted by micro-ATR measurement. Fig. 3 shows the acquired infrared spectra.

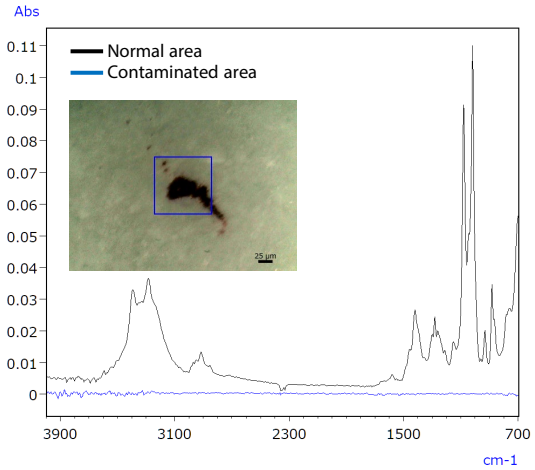

Fig. 3 Infrared Spectra of Normal and Contaminated Areas

The infrared spectrum of the normal area corresponded to the main component (mannitol) of a pharmaceutical product. However, it was not possible to identify the cause of contamination because no peaks were detected from the area with the adhering contaminant.

■ Contaminant Analysis by Micro-Raman Spectroscopy

Next, the Raman spectra were acquired and an analysis of the normal and contaminated areas was carried out by micro-Raman measurement. Fig. 4 shows the measurement results of the Raman spectra. The intensities of the spectra are also shown. The differences between the spectra of the normal area and the contaminated area were clearly evident.

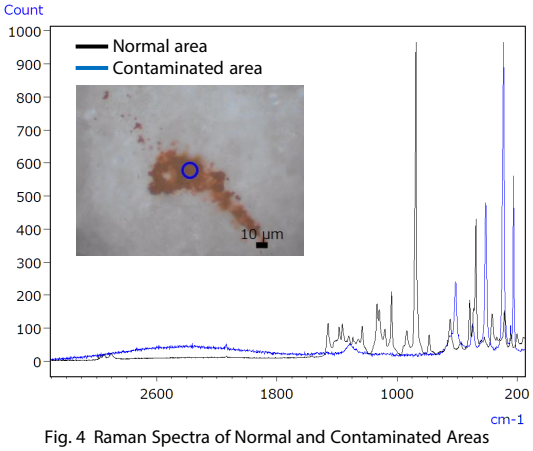

Fig. 4 Raman Spectra of Normal and Contaminated Areas

A Raman spectrum was acquired for iron oxide, which may possibly have adhered to the tablet surface, and the spectra of the contaminated part of the sample tablet and the iron oxide were overlaid, as shown in Fig. 5. Since the two spectra showed close agreement, the contaminant adhering to the tablet surface was inferred to be iron oxide.

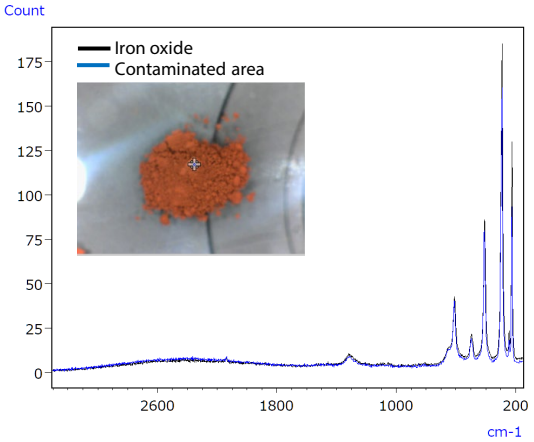

Fig. 5 Raman Spectra of Contaminated Area and Iron Oxide

■ Infrared Spectrum of Iron Oxide

As shown in Fig. 3, it was not possible to identify the cause of the contaminated area by micro-infrared spectroscopy. Fig. 6 shows the infrared spectrum (measurement method: single-reflection ATR) of iron oxide, which was estimated to be the contaminant by micro-Raman spectroscopy.

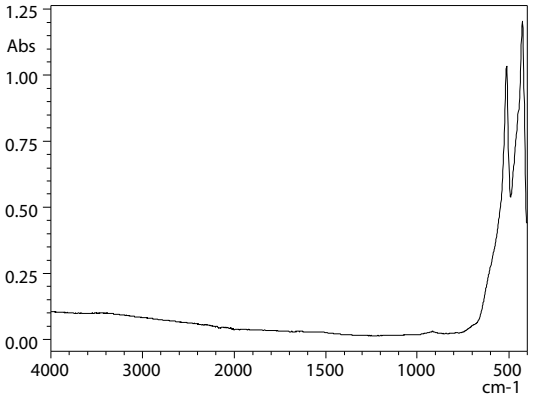

Fig. 6 Infrared Spectrum of Iron Oxide by Single-Reflection ATR Method

Because the characteristic peak in the infrared spectrum of iron oxide was located on the low wavenumber side from 510 cm^{-1}, it could not be detected by micro-infrared spectroscopy using an MCT detector. However, useful data could be obtained by Raman spectroscopy because this technique has higher qualitative capability for inorganic compounds than infrared spectroscopy.

■ Conclusion

As introduced in this article, a contaminant analysis of a pharmaceutical tablet was carried out by micro-infrared spectroscopy and micro-Raman spectroscopy. Although trace amounts of inorganic compounds are difficult to analyze qualitatively by infrared spectroscopy, identification of the inorganic contaminant in this experiment was possible by Raman spectroscopy.

Because the AIRsight Infrared/Raman microscope introduced in this article enables smooth infrared spectrometry and Raman spectrometry of the same location using only one instrument, it is extremely useful for qualitative analyses of unknown samples. In addition, the entire sequence of operations necessary in an analysis, that is, setting the observation and measurement position, measurement, and analysis, can be carried out automatically. We hope that analysts will use this new instrument when analyzing contaminants which high accuracy in qualitative analysis is required and identifying the causes of nonconforming products and other problems.

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