C103-E127

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FTIR
TALK LETTER

Vol. 33

European Pharmacopoeia 9.7

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FTIR validation was introduced in FTIR TALK LETTER Vol. 4 (2006) and Vol. 27 (2016). In those articles, the European Pharmacopoeia was introduced as one of the standards. In April 2019, the European Pharmacopoeia was revised to version 9.7, and there were significant changes to the standards. Accordingly, this article describes the changes in European Pharmacopoeia 9.7 and the response with respect to Shimadzu FTIR system.

1. Changes in European Pharmacopoeia 9.7

The changes in European Pharmacopoeia 9.7 are as follows.

(1) Changes to the wavenumber value for the wavenumber accuracy (wavenumber scale) in the transmission method

(2) Addition of standards for the wavenumber accuracy (wavenumber scale) and spectral resolution in the ATR method

There are no changes to the resolution in the transmission method. The details of the respective changes are described below.

(1) Changes to the wavenumber accuracy (wavenumber scale) in the transmission method

The changes to the wavenumber accuracy in the transmission method are listed in Table 1.

In comparison to European Pharmacopoeia 9.6, the wavenumber values 2849.5, 1942.9, 1583.0, and 1154.5 cm^{-1} have been deleted while the wavenumber value 906.6 cm^{-1} has been added.

Wavenumber accuracy is determined by whether the wavenumber indicating the maximum absorbance for the specified peak falls within the permitted range when polystyrene film is used.

Table 1 Changes to the Wavenumber Accuracy in the Transmission Method

European Pharmacopoeia 9.6	European Pharmacopoeia 9.7 (Transmission Method)
3060.0 (±1.0) cm^{-1}	3060.0 (±1.0) cm^{-1}
2849.5 (±1.0) cm^{-1}	-
1942.9 (±1.0) cm^{-1}	-
1601.2 (±1.0) cm^{-1}	1601.2 (±1.0) cm^{-1}
1583.0 (±1.0) cm^{-1}	-
1154.5 (±1.0) cm^{-1}	-
1028.3 (±1.0) cm^{-1}	1028.3 (±1.0) cm^{-1}
-	906.6 (±1.0) cm^{-1}

(2) Addition of standards for the wavenumber accuracy (wavenumber scale) and spectral resolution in the ATR method

Starting from European Pharmacopoeia 9.7, standards have been added for the ATR method in addition to the transmission method.

2. Wavenumber Accuracy

The wavenumber values for the wavenumber accuracy and the pass standard values in the ATR method are listed in Table 2.

A feature of the ATR method is that spectral peaks are shifted toward lower wavenumbers, so the wavenumber values are somewhat different than in the transmission method. Additionally, unlike the transmission method, measurements must be performed with a polystyrene film adhering to the ATR prism; however, the determination method is comparable to that for the transmission method.

Table 2 Standards for Wavenumber Accuracy in the ATR Method

European Pharmacopoeia 9.7 (ATR Method)
3059.7 (±1.0) cm^{-1}
1601.0 (±1.0) cm^{-1}
1027.7 (±1.0) cm^{-1}
906.1 (±1.0) cm^{-1}

3. Resolution

Resolution in the ATR method is standardized as follows.

> Appropriate assessment criteria for the control of spectral resolution according to the specifications of each instrument need to be defined.

Accordingly, clear evaluation standards are not defined in European Pharmacopoeia 9.7 for resolution in the ATR method. LabSolutions IR, the Shimadzu FTIR control software, is equipped with a validation program compatible with European Pharmacopoeia 9.7. It is also configured with the Shimadzu evaluation standards as reference values for resolution in the ATR method.

4. Inspection Details Regarding the Validation Program Compatible with European Pharmacopoeia 9.7

LabSolutions IR Ver. 2.24 is equipped with a validation program compatible with European Pharmacopoeia 9.7.

With regards to the transmission method, just as with the validation program compatible with the Japanese Pharmacopoeia and European Pharmacopoeia 9.6, this program inspects the performance of an instrument on five items: (1) power spectrum; (2) resolution; (3) wavenumber accuracy; (4) wavenumber repeatability; and (5) absorbance repeatability. For the ATR method, it inspects the performance of the instrument on two of these items: (2) resolution and (3) wavenumber accuracy.

(1) Power spectrum

This inspection is not included in European Pharmacopoeia 9.7, but is performed in order to evaluate the most basic aspect of FTIR performance. This is the same as the validation program compatible with the Japanese Pharmacopoeia and European Pharmacopoeia 9.6. The program determines whether the power spectrum at the specified wavenumber is larger than the standard value. The inspection results pass if the standard values are exceeded at all the specified wavenumbers.

(2) Resolution

For the transmission method, the program measures the absorption spectrum of a 0.035 mm polystyrene film. Using the absorption spectrum obtained, the program determines whether the difference between the smallest absorbance in the vicinity of 2870 cm^{-1} and the largest absorbance in the vicinity of 2849.5 cm^{-1} is larger than 0.33; and whether the difference between the smallest absorbance in the vicinity of 1589 cm^{-1} and the largest absorbance in the vicinity of 1583 cm^{-1} is larger than 0.08.

With the ATR method, as noted earlier, the program determines whether the Shimadzu evaluation standards are satisfied.

(3) Wavenumber accuracy

As noted earlier, the results pass if the errors from the measured values for the respective wavenumbers are within the standards.

(4) Wavenumber repeatability

This inspection is not included in European Pharmacopoeia 9.7, but the item is included for uniformity with the Japanese Pharmacopoeia. This is the same as the validation program compatible with the Japanese Pharmacopoeia and European Pharmacopoeia 9.6. Polystyrene film is measured twice, and the peak wavenumbers are compared at three specified points. The program determines whether the difference in the two sets of measurement results is within the permitted range. The results pass if the difference in peak wavenumbers is within the permitted range for all three points.

(5) Absorbance repeatability

This inspection is not included in European Pharmacopoeia 9.7, but the item is included for uniformity with the Japanese Pharmacopoeia. This is the same as the validation program compatible with the Japanese Pharmacopoeia and European Pharmacopoeia 9.6. If the absorbance at the wavenumbers inspected is converted to transmittance, the absorbance permitted range will be on the order of 0.5 %. The program determines whether the difference in the absorbance for the two sets of measurement results at the three peak wavenumbers specified is within the permitted range. The results pass if the difference in absorbance is within the permitted range for all three points.

5. Operating the Validation Program Compatible with European Pharmacopoeia 9.7

This section describes how to operate the validation program compatible with European Pharmacopoeia 9.7 included in Shimadzu LabSolutions IR Ver. 2.24.

Fig. 1 Validation Selection Window

As in Fig. 1, in the LabSolutions IR launcher window, click " EP Validation based on EP 9.7 " to run the validation program. At this point, the previous European Pharmacopoeia validation program can be run by clicking " EP Validation based on EP 9.7 ".

When " EP Validation based on EP 9.7 " is selected, a parameters setting window is displayed (Fig. 2) before the validation measurements start. In this window, the user can select transmission or ATR. With ATR, it is necessary to configure the names of the accessories, the P/Ns of the accessories, and the ATR prism used. The other settings are the same as for the transmission method.

When the settings are complete, simply proceed according to the messages displayed in the window to automatically print a report summarizing the inspection results, as shown in Fig. 3. The inspection takes only about 5 minutes, so it can be used as an alternative to daily inspections.

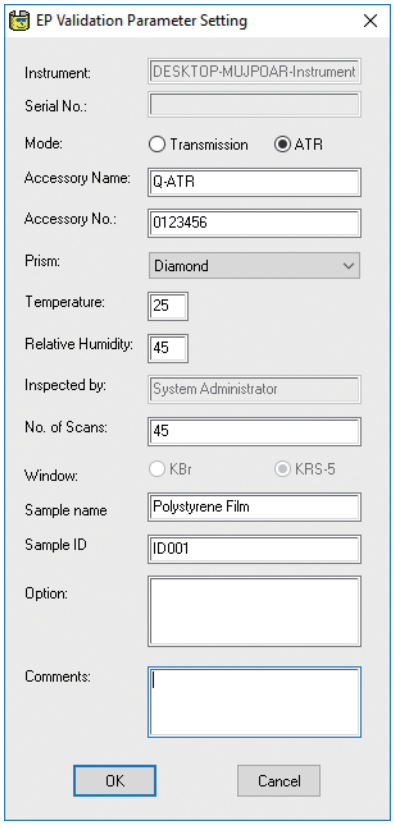

Fig. 2 Parameters Setting Window

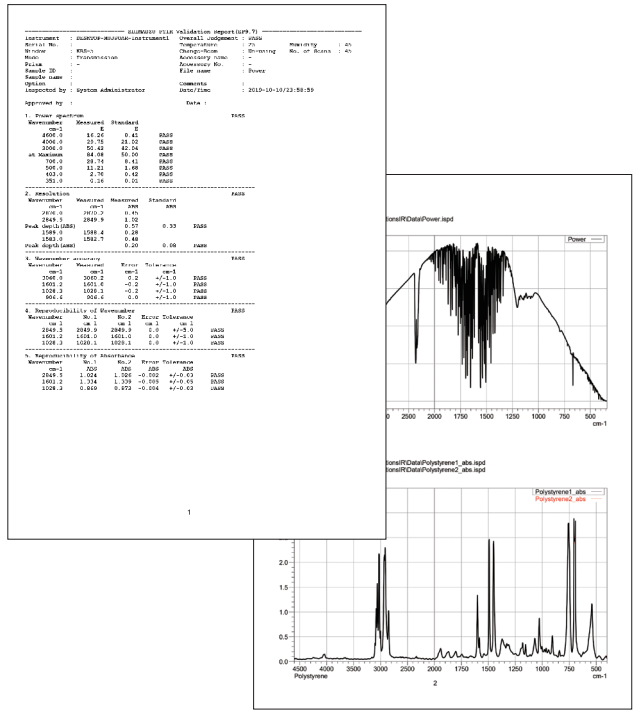

Fig. 3 Inspection Results Report

Reference

- European Pharmacopoeia
  https://www.edqm.eu/

Introduction of Various ATR Measurement Attachments (2)

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In addition to general ATR prism selection methods, FTIR TALK LETTER vol. 32 introduced multiple reflection ATR measurements and heated ATR attachments. This article describes two types of observation-capable ATR attachments.

1. Observation-Capable ATR Attachment (1)

This section describes the MicromATR Vision™, which is equipped with a visible light observation function (Fig. 1). For trace samples or when measuring a specific location, an IR microscope can be used to perform analysis while making observations. However, using this attachment enables analysis to be performed quickly and without pretreatment while observing the measurement position. The MicromATR Vision is equipped with a diamond prism, and can measure across the range of 4,000 to 400 cm^{-1}. Additionally, sample positions and contact status can be observed in real time, simultaneously with measurement, via a built-in interior video camera. The optical layout of the MicromATR Vision is shown in Fig. 2. For this observation, the e-Spot video observation software is used. The software window is shown in Fig. 3. The user can save still images and videos, enlarge the display, insert text, and measure sample size via a scale function.

Fig. 1 MicromATR Vision

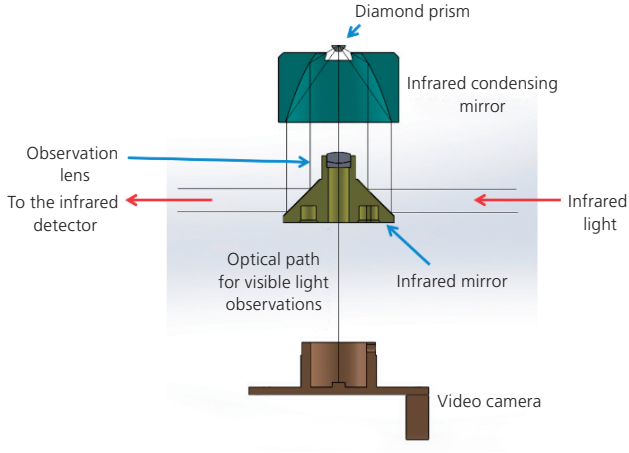

Fig. 2 Optical Layout Diagram for the MicromATR Vision

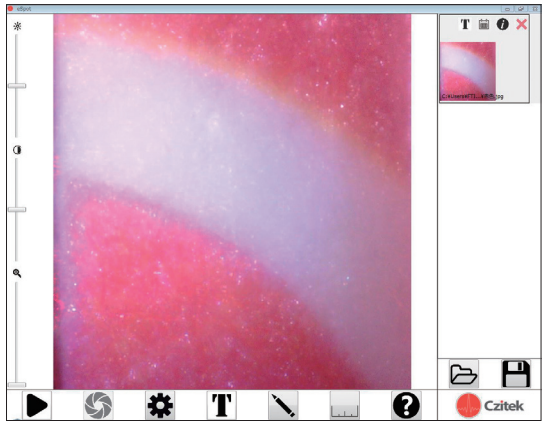

Fig. 3 e-Spot Video Observation Software

A photograph of the sample observed is shown in Fig. 4. A red fibrillary contaminant has adhered to a toy. The fibrillary contaminant has been retrieved and observed with MicromATR Vision. The observation image is shown in Fig. 5. The fiber is on the order of 50 µm. The sample can be placed at the center of the prism while checking via the image.

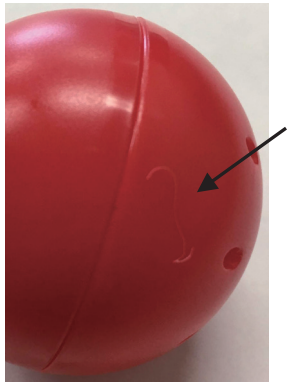

Fig. 4 Measurement Sample

Fig. 5 Observation Image of the Fibrillary Contaminant

An analysis was performed of the fibrillary contaminant and an excised portion of the toy. The ATR spectra for the fibrillary contaminant and toy and their search results are shown in Fig. 6. Both the fibrillary contaminant and the toy are made of acrylonitrile butadiene styrene (ABS). It is surmised that during the manufacturing process, scraps of the material adhered to the toy.

Measurements can be performed while observing the sample. As a result, not only samples that are visible to the naked eye, but also samples 100 to 200 µm or less that require an infrared microscope can be positioned at the center of the prism and analyzed easily.

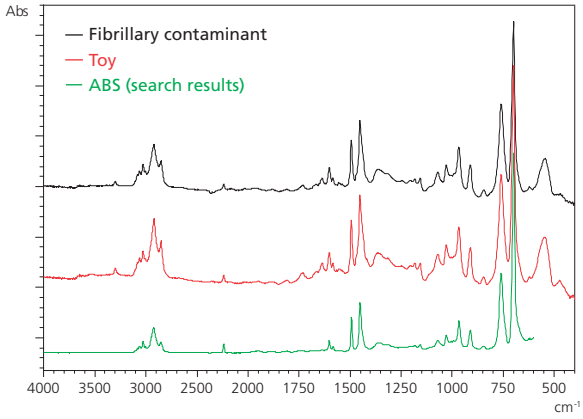

Fig. 6 ATR Spectra and Search Results

2. Observation-Capable ATR Attachment (2)

The GladiATR Vision™ (Fig. 7) is capable of observations through a diamond crystal, and can measure across the range of 4,000 to 400 cm^{-1}. The measurement site can be observed in real time on an LCD monitor making it easy to select the correct measurement position. Even thick opaque samples can be observed through the diamond crystal.

The optical layout of the GladiATR Vision is shown in Fig. 8. Both infrared measurements and visible light measurements can be performed simultaneously. The measurement site on the sample can be enlarged 110× for observation. Trace samples can be optimally positioned at the center of the diamond crystal for measurement. Accordingly, even trace samples on the order of 50 µm can be measured. Additionally, with GladiATR Vision, images can be checked on a monitor making even fine position adjustments easy.

Fig. 7 GladiATR Vision

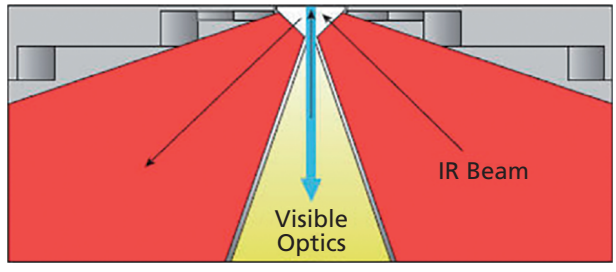

Fig. 8 Optical Layout of GladiATR Vision

A photograph of the sample observed is shown in Fig. 9. The sample consists of material adhering to the surface of filter paper. With an ATR attachment incapable of making observations, the measurement surface faces the prism, so the position of the adhering material cannot be confirmed. With GladiATR Vision, however, observations can be made from below the prism. Accordingly, it is easy to ensure tight contact between the prism and the sites to be measured.

Fig. 9 Measurement Sample

The material adhering to the filter paper was positioned directly on the GladiATR Vision prism before measurement. It was anticipated that the filter paper component will have an effect, so portions of the filter paper without adhering material were also measured for comparison. An observation image of the sample is shown in Fig. 10 and the measurement results are shown in Fig. 11.

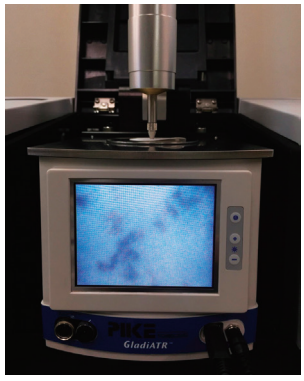

Fig. 10 Observation Image of the Adhering Material

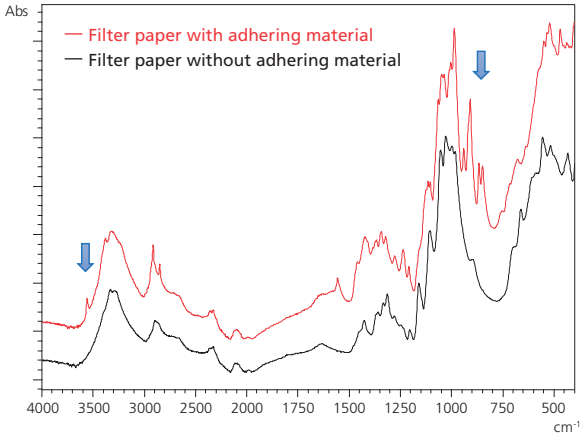

Fig. 11 Measurement Results

In Fig. 11, peak differences can be confirmed in the vicinity of 3600 cm^{-1} or 900 cm^{-1} (blue arrows in the figure). It was anticipated that the filter paper would have an impact on the spectrum of the adhering material. Accordingly, a differential spectrum was calculated from the two spectra shown in Fig. 11, and a search was conducted using the library included as standard in Shimadzu FTIR (Fig. 12). From the results of the search, it was evident that the material adhering to the filter paper is similar to sucrose.

As illustrated here, an observation-capable ATR attachment is effective for samples requiring observations of the measurement surface.

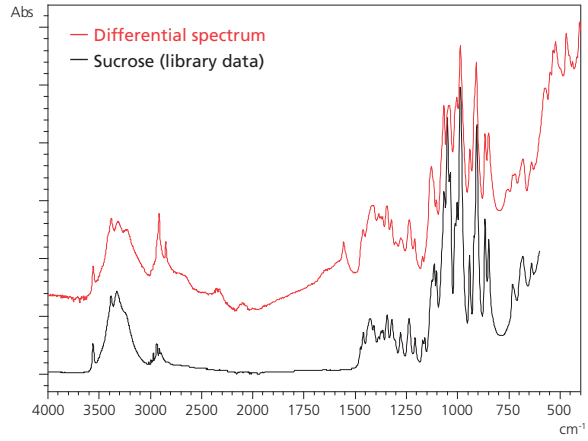

Fig. 12 Search Results

3. Summary

This article introduced two types of observation-capable ATR attachments. Using these ATR attachments makes it easy to confirm the measurement sites on the sample during measurement, so the sites to be measured can be positioned reliably on the prism. Additionally, the observation image can be saved together with the spectral data. Furthermore, various software and monitors are available, so users can select the types they prefer.

At present, a variety of ATR attachments have been developed to suit analysis objectives. For example, when performing an ATR measurement of a silicon wafer, which has a high refractive index, an incidence angle of at least 59° is required, and tight contact with the prism is indispensable. Accordingly, there are ATR attachments designed to ensure that the silicon wafer makes tight contact with the Ge prism under uniform pressure. Additionally, there are instruments that can illuminate samples from below the prism using UV light for tracking chemical reactions. Shimadzu offers a diverse lineup of ATR attachments capable of accommodating the varied needs of our customers, so feel free to contact us.

A Q&A section will not be included in this edition for reasons of the page layout.

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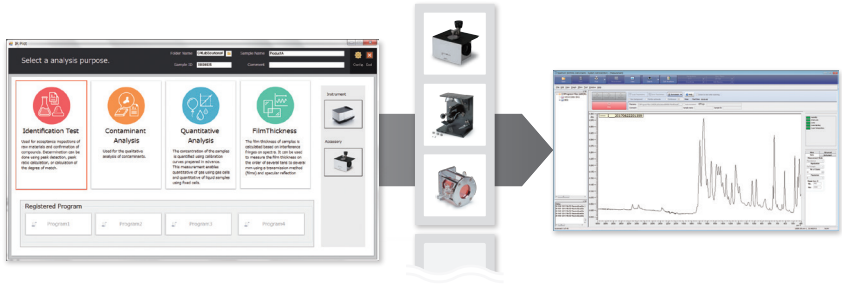

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First Edition: November 2019