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FTIR TALK LETTER

Vol. 20

In Celebration of FTIR TALK LETTER Vol. 20

General Manager, Global Application Development Center, Analytical & Measuring Instruments Division, Naoki Hamada

This is Vol. 20 of FTIR TALK LETTER. The first volume was published in 2003. It has continued this long thanks to the support of our readers, for which we are extremely grateful.

Looking back, globalization has now become a major trend. In Vol. 12, published in 2009, our local staff explained the state of business in India, a developing nation exhibiting remarkable economic growth. In the four years since then, growth in the economies of the developing nations remains as high as before. Markets continue to expand not only in the BRIC nations but also in the so-called Next Eleven (N-11) nations. As our customers have become more multinational in recent years, Shimadzu has been providing them with global support through collaboration with our support centers in each country.

Contaminant analysis is an FTIR application that has seen a large demand in recent years. It is extremely important for avoiding possible customer complaints and enhancing product quality. The ingress of contaminants greatly inconveniences consumers and seriously reduces faith in the supplier. It is therefore desirable to quickly and accurately determine the conditions that can create contaminants and take appropriate measures against them. To ensure contaminant analysis is performed in a reliable manner, materials and waste generated in the manufacturing environment that could become contaminants in products must be investigated in advance and registered in a database. FTIR provides an extremely powerful tool for this purpose.

FTIR analysis is extremely effective for the identification and qualification of substances in contaminant analysis; however, FTIR alone is often unable to identify contaminants or determine the cause of defects. Such cases require multifaceted evaluation using additional information from other analytical methods. Analytical instruments frequently used for contaminant analysis include the scanning electron microscope - energy dispersive X-ray spectrometer (SEM-EDX, offering electron micrographs and elemental information); the energy dispersive X-ray fluorescence spectrometer (EDX, easily providing elemental information under atmospheric pressure); and the confocal laser scanning microscope (CLSM). The following URL introduces a database for the analysis of contaminants in tap water that was created using FTIR and EDX:
http://www.shimadzu.com/an/spectro/ftir/tapwater.html

We analyzed organic contaminants by FTIR and inorganic contaminants by EDX, which significantly improved the identification accuracy. In addition, FTIR TALK LETTER Vol. 16 introduces the TG-FTIR system that incorporates a thermal analyzer connected to an FTIR. This system permits the online measurement of the sample heating temperature and changes in generated gas composition for gas analysis by FTIR. This is an example of how Shimadzu Corporation strives to combine different types of analytical instruments to develop total analysis methods that meet the needs of the customer.

Shimadzu will continue to deliver instruments, application systems, and options based on an understanding of our customers' needs. We hope for your continued support in the future.

Easy Macro Function Automates Routine LabSolutions IR Operations

Spectroscopy Business Unit, Analytical & Measuring Instruments Division, Yasushi Nakata

1. Outline

Shimadzu has released LabSolutions IR software, which updates the functions of the IRsolution software for FTIR that has been in popular use for a long time.
In addition, LabSolutions IR offers several new functions that were not available in IRsolution and is easier to use.
One new function is the "Easy Macro" function, which makes the macros in IRsolution even easier to use. Easy macros allow you to automate routine tasks, such as spectral measurement, data processing, and printing.
This FTIR TALK LETTER introduces the easy macro function included as standard with LabSolutions IR.
Note that LabSolutions IR also offers an optional VB macro function similar to the one available in IRsolution to automate complex tasks that cannot be handled by easy macros.
However, since specialist knowledge is required to create VB macros, this function is only available on a custom-order basis.

2. What Is the Easy Macro Function?

Macros, available in Microsoft Excel and other software programs, allow repeated, frequently performed operations to be registered in a single file, which can subsequently be loaded and run automatically. The commands for the sequence of operations are written in a text file according to certain rules. The text file, known as a "macro" or "macro program," is difficult to create without special knowledge.
However, the easy macro function offered in LabSolutions IR requires no programming knowledge and allows anyone to create macros easily. To create a macro program, simply drag and drop the symbols (macro items) representing commands on the screen and arrange them in operational sequence.
Using the macro function to automate LabSolutions IR operations eliminates errors during complex operations and cuts the time required to perform repeated tasks.

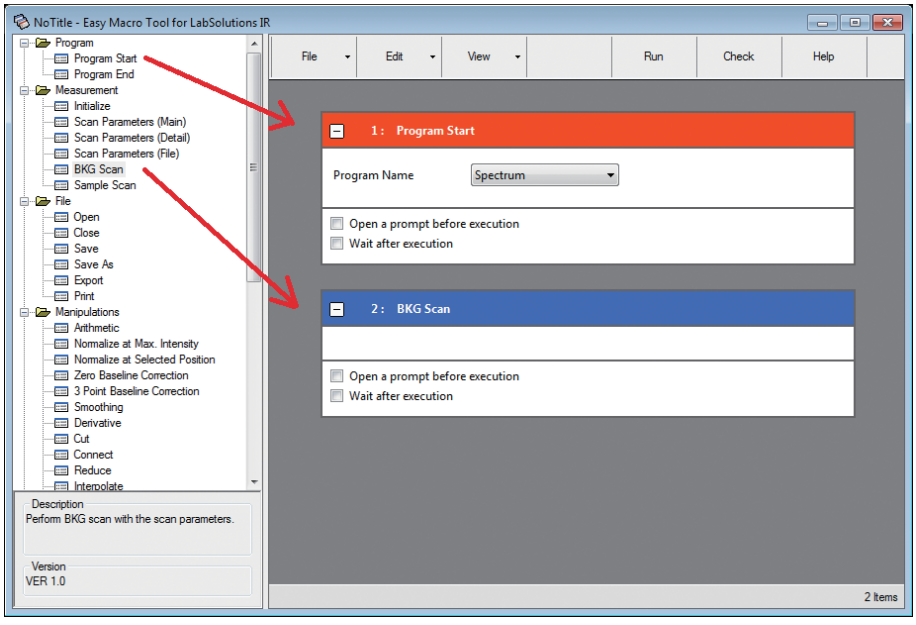


Fig. 1 Easy Macro Editing Window

3. What You Can Do with Easy Macros

Dedicated commands are set for operations such as background measurement and sample measurement, and these are known as "macro items." A macro program can be configured by dragging and dropping the macro items and then setting parameters such as the name of the file to be saved. The easy macro function includes a macro item that loads previously measured and saved spectral data as well as those for data processing, searching, and printing spectral data. All these macro items can be arranged using the easy macro function to automate manual procedures performed in LabSolutions IR. The available macro items are displayed in the tree view at the left of the easy macro editing window (*see* Fig. 1).
The easy macro function helps repeat operations such as measurement or data processing the required number of times.

4. Creating a Basic Easy Macro Program

To create a macro program using the easy macro function, run the easy macro editing program. Click the [Easy Macro] icon in the LabSolutions IR launcher (Fig. 2) to open the easy macro editing window, shown in Fig. 1.

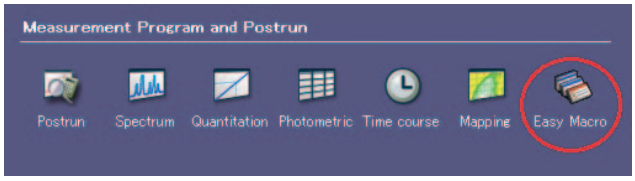


Fig. 2 Launching [Easy Macro] from the LabSolutions IR Launcher

Macro items corresponding to each LabSolutions IR operation are arranged by function at the left of the easy macro display window.
To create a macro program, drag and drop these macro items to the program space at the right of the window in the sequence they are to be used and then add the required parameters.
For example, to create a macro program that simply performs spectral measurements, drag and drop the four macro items [Program Start], [BKG Scan], [Sample Scan], and [Program End] in sequence and then specify the name of the file to be saved (*see* Fig. 3).

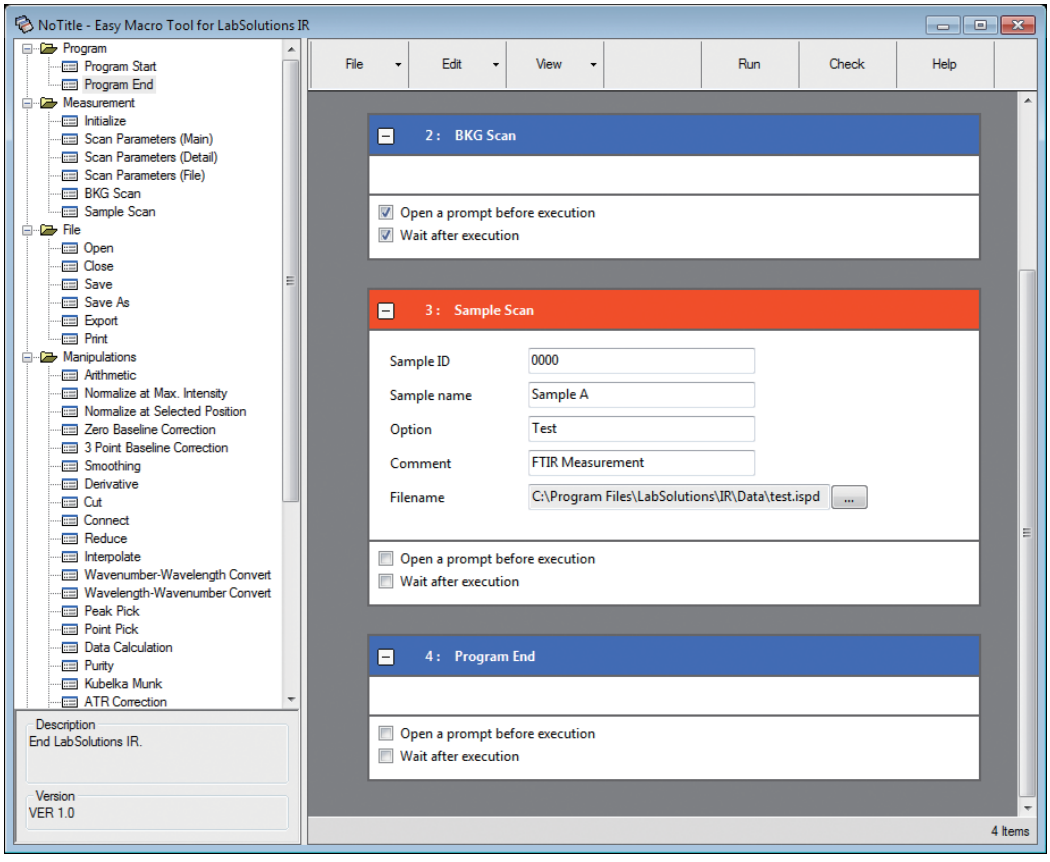


Fig. 3 Sample Program for Spectral Measurement

To repeat the same operation multiple times, enclose the steps to be repeated between the [Start of Repeat] and [End of Repeat] macro items (*see* Fig. 4). The macro items to repeat are enclosed in a blue frame.

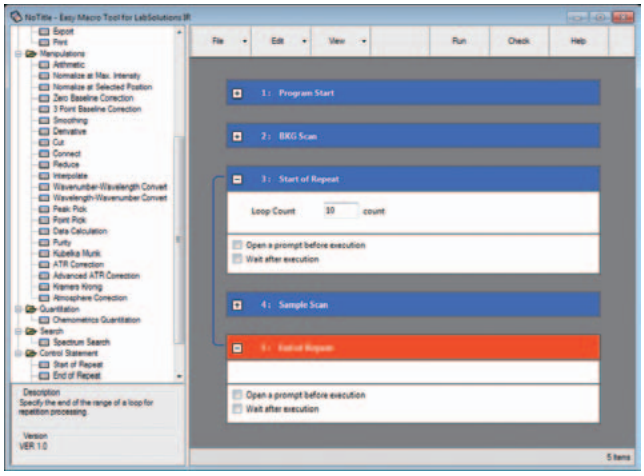


Fig. 4 Macro Program Repeating Sample Measurement Ten Times

5. Registering and Running Easy Macro Programs

Use the save command in the menu to save the created macro program file and register it in the LabSolutions IR launcher. Select the name of a registered macro program in the launcher to automatically start LabSolutions IR and run the series of operations.
A macro program file can also be copied to the Windows desktop and double-clicked to run the macro.

Fig. 5 Macro Programs Registered in LabSolutions IR Launcher

6. VB Macro Function

Easy macros can be used to automate LabSolutions IR operations, but they do not support the input or output of complex text and numeric values or data processing with proprietary formulas.
However, the sophisticated VB macros support such processing to automate LabSolutions IR operations. VB macros are supplied as custom programs to meet customers' requirements. Contact your Shimadzu representative for details.

7. Conclusions

The easy macro function is a convenient function that allows anyone to automate LabSolutions IR tasks. To improve the efficiency of your analysis work, make use of easy macros together with VB macros (custom programs) that help handle more complex tasks.

Raw Materials Identification Testing by NIR Spectroscopy and Raman Spectroscopy

Global Application Development Center, Analytical & Measuring Instruments Division,
Shoko Iwasaki

This FTIR TALK LETTER compares NIR spectroscopy and Raman spectroscopy while introducing their respective features and some examples of sample measurements. These methods make analysis easy and are attracting attention for acceptance testing on all raw materials as required by PIC/S GMP guidelines, verification and identification of received raw materials, intermediate and final product inspections, and counterfeit drug detection. The PIC/S GMP guidelines are outlined below.

1. PIC/S GMP Guidelines

International trends in the quality assurance of drugs have changed dramatically in recent years. There is now a demand for overseas quality assurance measures to also be implemented in Japan. The increased need for international cooperation and information exchange with regard to GMP*1 brings a demand for more advanced business implementation systems.
Under these circumstances, Japan's Ministry of Health, Labour and Welfare applied for membership of PIC/S*2 in March 2012. As future GMP inspections will be based on the PIC/S GMP guidelines, analytical laboratories must comply with them as rapidly as possible.
The PIC/S GMP guidelines require acceptance testing on all raw materials. NIR spectroscopy and Raman spectroscopy, are attracting attention as inspection methods suitable for efficient on-site identification testing. Currently, the Japanese Pharmacopoeia (JP) prescribes NIR spectroscopy. On the other hand, the US Pharmacopoeia (USP) and European Pharmacopoeia (EP) prescribe Raman spectroscopy. Almost all major pharmaceutical corporations in countries other than Japan use Raman spectroscopy for the identification of received raw materials

***1 GMP**
This is the acronym of Good Manufacturing Practice. GMP offers manufacturing control and quality control guidelines for drugs and quasi drugs. It is a standard enacted by government and other public organizations to ensure safety and reliability. The GMP Ministerial Ordinance prescribes validation standards related to the manufacture of drugs and quasi drugs and the conditions to be observed by manufacturers.

***2 PIC/S**
This is the acronym of Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme. As of January 2013, 41 countries were members, predominantly European countries. PIC/S is intended to provide an internationally harmonized standard and devise a quality assurance system for the continuous implementation of GMP compliance for pharmaceuticals. The PIC/S GMP Guidelines have been published as part of these activities.

2. Comparison of NIR Spectroscopy and Raman Spectroscopy

As near-infrared (NIR) spectroscopy and Raman spectroscopy obtain spectra based on molecular vibrations, they both permit qualitative analysis.
The term "near infrared" indicates light with wavelengths between 800 nm and 2500 nm (12500 to 4000 cm^{-1} wavenumber). Absorption appearing in the near-infrared region involves overlaid harmonic and combination tones from normal vibrations and therefore produces wider and more complex peaks than does absorption in the mid-infrared region. Also, since the absorption intensity is lower than in the mid-infrared region, samples can be measured directly without being diluted with KBr or other agents. Furthermore, cells made of glass or quartz, which are chemically stable and easy to use, can be used for NIR spectroscopy because they exhibit virtually no absorption in the near-infrared region. For details on NIR spectroscopy, refer to "Near-Infrared Region Measurement and Related Considerations" in FTIR TALK LETTER Vol. 9 and Vol. 10.
In this example of near-infrared analysis, we used the IntegratIR NIR integrating sphere shown in Fig. 1. Table 1 shows the measurement conditions. All sample types, including powder, pill, liquid, and paste samples, can be placed on the stage for measurement. Samples can also be measured when contained in a plastic bag or glass bottle.

Fig. 1 IntegratIR Integrating Sphere

Table 1 Instrument and Analytical Conditions

Instrument:	IRPrestige-21, IntegratIR
Resolution:	16.0 cm^{-1}
Accumulation:	20
Apodization:	Sqr Triangle
Light Source:	Tungsten lump
Beam Splitter:	CaF_2
Detector:	InGaAs

Meanwhile, Raman spectroscopy uses visible or near-infrared laser light. It measures the light scattered from the sample when it is illuminated with light of a certain wavelength. Raman spectra are plotted with the scattering intensity on the vertical axis and the wavenumber difference between the incident light and scattered light (the so-called Raman shift) on the horizontal axis. The horizontal axis units are cm^{-1}, the same as for IR spectra. In this example, we used an excitation wavelength of 785 nm and a resolution of 6.0 cm^{-1} as measurement conditions. Raman spectroscopy can measure samples contained in a plastic bag or glass container that allows light to pass through it, without the need to unseal the sample. However, measurement may not be possible with certain container materials and material thicknesses.

For details on the differences between Raman spectroscopy and infrared spectroscopy, refer to Q&A in FTIR TALK LETTER Vol. 17 as well.

Table 2 summarizes the features of NIR spectroscopy and Raman spectroscopy. So far, we have touched on items (1) and (2). Section 3 below covers items (3) to (6) and introduces measurements of actual samples.

Table 2 Comparison of NIR Spectroscopy and Raman Spectroscopy

Item	NIR Spectroscopy	Raman Spectroscopy
(1) Pharmacopoeia support	Japanese Pharmacopoeia (JP), US Pharmacopoeia (USP), European Pharmacopoeia (EP)	US Pharmacopoeia (USP), European Pharmacopoeia (EP)
(2) Light used	Near-infrared light	Visible or near-infrared laser light (Requires measures related to using laser light.)
(3) Spectral shapes	For samples with similar structures, wide peaks make differences hard to see.	For samples with similar structures, sharp peaks clearly show differences.
(4) Samples unsuited to measurement	Samples with weak NIR absorption (inorganic compounds etc.)	Samples with weak Raman scattering Samples susceptible to effects of fluorescence Samples that decompose or burn due to visible or NIR laser light
(5) Effects of particle size	Separate standard data registration required for different particle sizes	None
(6) Effects of container	Separate standard data registration required for each container type and thickness.	A container transparent to visible or NIR laser light has little effect.

3. Examples of Sample Measurement by NIR Spectroscopy and Raman Spectroscopy

1) Spectral Shapes and Samples Unsuitable for Measurement (Table 2 (3)(4))

We analyzed titanium dioxide anatase (TiO_2 anatase) and calcium carbonate ($CaCO_3$) as examples of inorganic compounds. The measured results are shown in Fig. 2. Inorganic compounds exhibit weak absorption in the near-infrared region and produce wide peaks. Be aware that, while not shown here, hydroxyl-group-derived peaks may appear in the spectrum when the sample has absorbed moisture. On the other hand, Raman spectroscopy produces sharp peaks, even for inorganic compounds. Another feature of Raman spectroscopy is that hydroxyl-group-derived peaks are not easily detected.

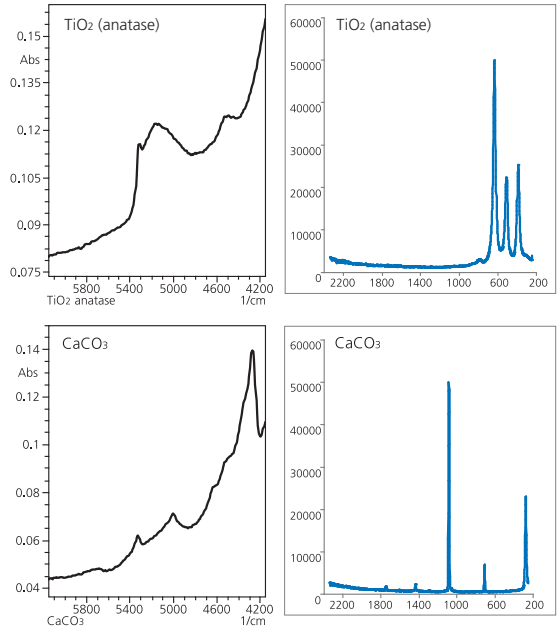


Fig. 2 Analysis of Inorganic Compounds (TiO_2 anatase and $CaCO_3$)
Left: NIR Spectroscopy; Right: Raman Spectroscopy

Next, we measured lactate monohydrate and microcrystalline cellulose as examples of organic compounds. The measured results are shown in Fig. 3. Comparatively strong NIR absorption was detected for the organic compounds but the broad peaks and varying shapes made evaluation difficult. On the other hand, Raman spectroscopy produced sharp peaks but may result in an ascending baseline for fluorescent samples, such as lactate monohydrate. Care is required with the evaluation of fluorescent samples with low peak intensity and few peaks, such as microcrystalline cellulose.

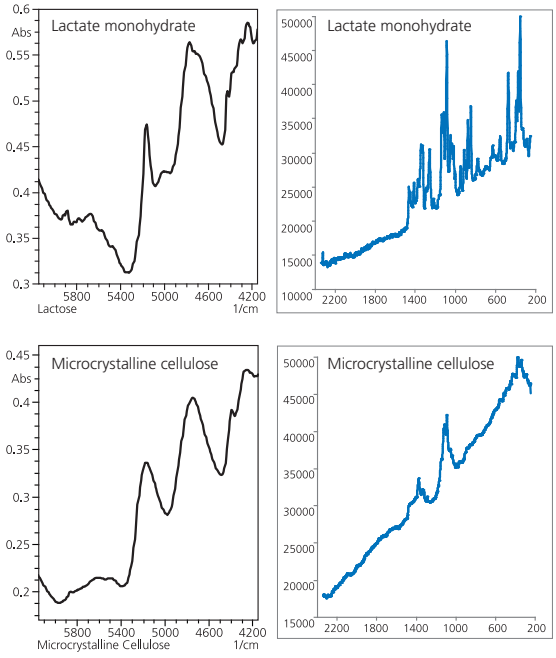


Fig. 3 Analysis of Organic Compounds
(Lactate Monohydrate and Microcrystalline Cellulose)
Left: NIR Spectroscopy; Right: Raman Spectroscopy

2) Effects of Particle Size (Table 2 (5))

To investigate the effects of particle size, we measured stearic acid with different particle sizes. The measured results are shown in Fig. 4. With NIR spectroscopy, the characteristic changes in spectral shape due to the effects of physical properties can be used not only for qualitative analysis but also to obtain information on particle size. NIR spectroscopy is therefore used to monitor all stages of pill manufacture (raw materials acceptance, pulverization, mixing, granulation, drying, tableting, and coating). In this example of stearic acid measurements, Raman spectroscopy, which produces clear peaks, is more effective for component identification than NIR spectroscopy. However, NIR spectroscopy works better to determine differences in particle size.

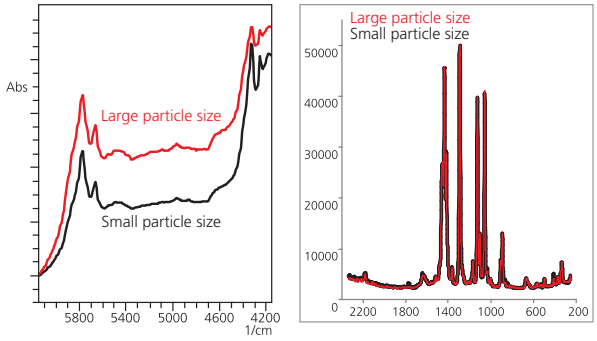


Fig. 4 Effects of Particle Size (Stearic Acid)
Left: NIR Spectroscopy; Right: Raman Spectroscopy

3) Effects of Containers (Table 2 (6))

We next measured talc [$Mg3(Si_4O_{10})(OH)_2$] sealed inside polyethylene (PE), polypropylene (PP) and polyethylene terephthalate (PET) plastic bags. The NIR spectroscopy measurement results are shown in Fig. 5, where the spectral shape varies according to the container material. For this reason, to perform acceptance testing of raw materials using NIR spectroscopy, standard data for pass/fail criteria must be registered for each container material. Also, interference fringes can be seen in the NIR spectrum for the PP bag. These may appear due to the condition and thickness of the bag and how the sample is packed, and may impair peak identification.

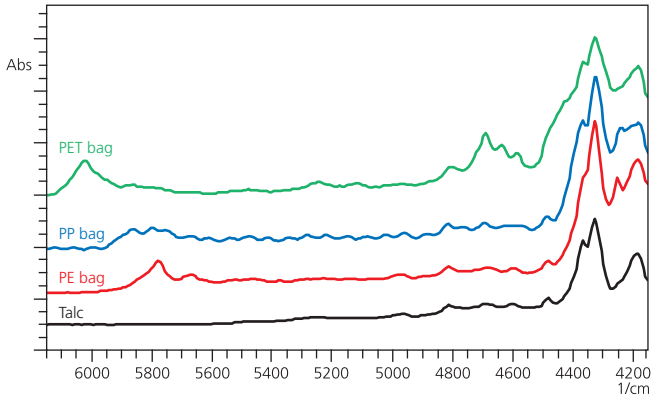


Fig. 5 Effects of Containers on NIR Spectroscopy
(Talc in PE, PP, and PET Bags)

We subsequently analyzed lactose contained in polyethylene (PE) bags of different thicknesses. The measurement results are shown in Fig. 6. In the NIR spectroscopy results, peaks derived from PE are observed and the spectral shape changes according to the container thickness as well. Raman spectroscopy, on the other hand, is hardly affected by the material or thickness of the container, provided that the material is transparent to visible or near-infrared laser light.
Table 3 shows the suitability of different containers to NIR spectroscopy and Raman spectroscopy measurements.

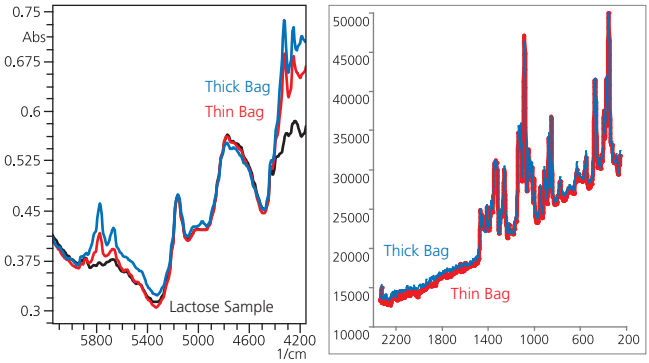


Fig. 6 Effects of Containers (Thick Bag/Thin Bag, Lactose Sample)
Left: NIR Spectroscopy; Right: Raman Spectroscopy

Table 3 Suitability of Containers to Each Measurement

Item	NIR Spectroscopy	Raman Spectroscopy
Glass bottle (colorless)	Good	Good *3
Glass bottle (brown)	Good	Good *3
Plastic bag	Good	Good
Plastic container	Fair	Good
Paper container	Poor	Poor
Metal	Poor	Poor

*3 Some components contained in the glass may prohibit measurements.

4. Conclusions

We measured various samples by NIR spectroscopy and Raman spectroscopy to determine the pros and cons of each method.
Acceptance testing by NIR spectroscopy involves selecting peaks from a smooth spectrum and basing the evaluation on very small differences between them, which makes method creation difficult when an instrument is introduced. Although NIR spectroscopy offers some advantages, such as determining differences in particle size, Raman spectroscopy often makes it easier to evaluate the spectra. However, it is unable to measure samples that fluoresce under laser light. Take these factors into account when selecting the most suitable inspection method for actual samples.

References

- Administrative Circular "**Practical Application of the PIC/S GMP Guidelines**," issued by the Ministry of Health, Labour and Welfare, Feb. 1, 2012
- ***NIR and Raman Spectroscopy***, edited by the Spectroscopical Society of Japan and published by Kodansha

Question

What methods are available to measure strong acids or strong alkalis?

Answer

Methods to measure such solutions include the ATR method and transmission method. The ATR method is commonly used to measure various samples. However, the samples that can be measured differ according to the prism used. A diamond prism is able to withstand strong acids and alkalis*) but the metal (usually stainless steel) fixtures for the prism often have poor resistance. For this reason, measurement of strong acids or alkalis with a normal ATM prism is not recommended.
To handle the measurements of such solutions, special prisms with the surrounding metal parts made of Hastelloy rather than stainless steel are commercially available. However, Hastelloy comes in various types, each with different resistance to strong acids and alkalis.
The most common type of measurement is transmission measurement with an infrared spectroscopy window plate made of KBr. Since the sample to be measured is strongly acidic or alkaline, use extra care when washing the window plate after the measurement.
For those who wish to make measurements even easier, IR cards—single-use KBr window plates for infrared spectroscopy—are helpful (*see* Fig. 1). They are extremely easy to use, as shown below.

Fig. 1 IR Cards

(1) Insert the IR card into the sample chamber and measure the background (BKG).
(2) Remove the IR card and apply the sample to the sample area.
(3) Re-insert the IR card into the sample chamber and measure the sample.
(4) Dispose of the used IR card.
Caution: Dispose of the IR cards according to local laws and regulations.

Figs. 2 and 3 show examples of a strong acid (methanesulfonic acid) and strong alkali (ethanolamine) measured using IR cards made of KBr.

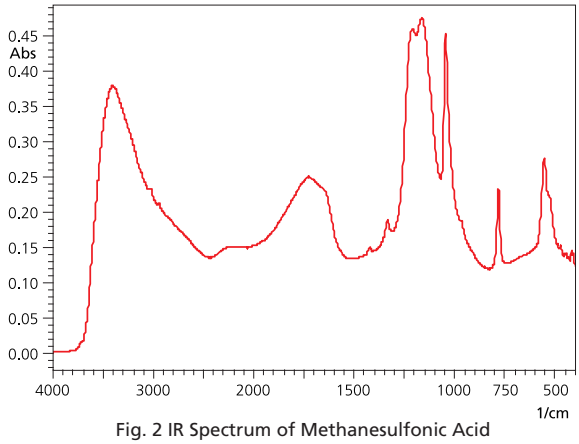


Fig. 2 IR Spectrum of Methanesulfonic Acid

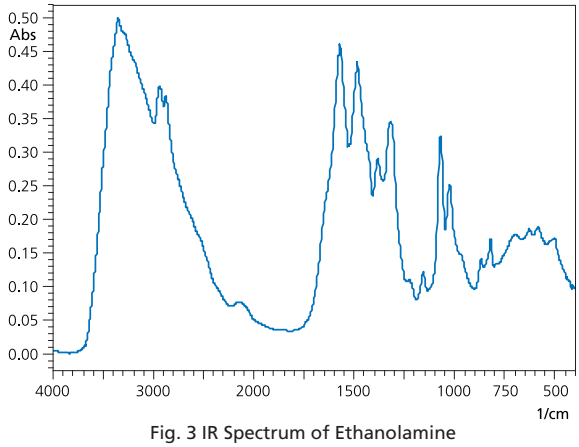


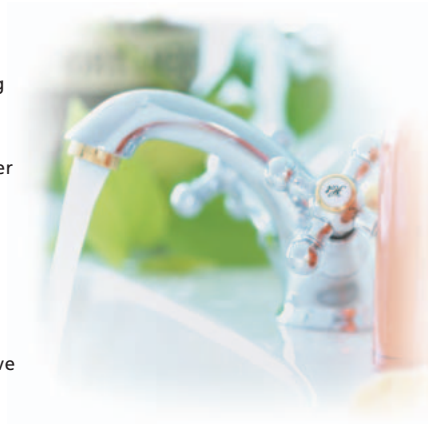
Fig. 3 IR Spectrum of Ethanolamine

As the KBr IR cards introduced here are slightly deliquescent, they are not suitable for the measurement of aqueous samples. However, other IR cards that are not deliquescent are commercially available. For details, refer to Shimadzu Application News No. A448. For details on the chemical resistance of the ATR prisms and infrared spectroscopy window plates, refer to the "FTIR Series Accessories" handbook.

*) "Strong acid" indicates an aqueous solution with a hydrogen ion concentration (pH) of 3.0 or less; "strong alkali" indicates a pH of 11.0 or more.

FTIR/EDX Tap Water Contaminant Search System for LabSolutions IR/IRsolution

Inquiries from organizations involved in public water supply systems reflect a wide range of issues, such as objectionable mold, chlorine, or other tastes or odors; trihalomethane or other environmental pollutants; and the inclusion of other contaminants. Possible substances causing contamination include the various rubber and metal gaskets, packings, and sealing materials used in public water systems, minerals, and microorganisms.
A major cause of contaminants revolves around the aging, servicing, or installation of the water system infrastructure as well as the fixtures and other equipment involved in delivering the water. While eliminating these causes is difficult, identifying the contaminants as quickly as possible helps to ease the concerns of users.

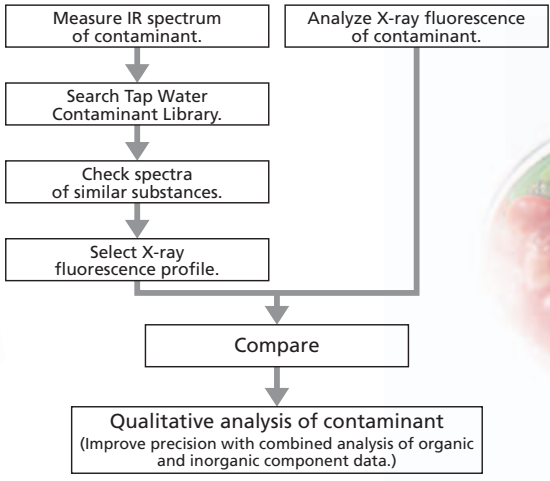


Infrared spectrometry and X-ray fluorescence spectrometry provide an effective way to identify contaminants.
The Tap Water Contaminant System is a comprehensive search system that incorporates both techniques.

IRAffinity-1

EDX-800HS

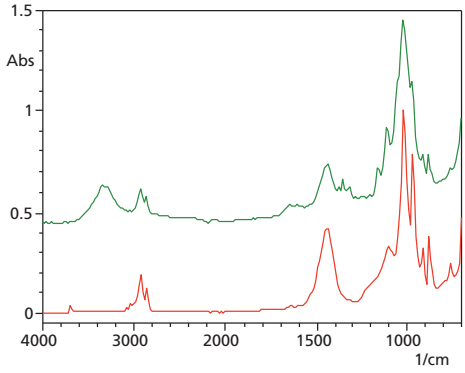
Procedure for Qualitative Analysis of Contaminants



Features of Search System

- Shimadzu's proprietary and state-of-the-art contaminant library, compiled specifically for public drinking water, was prepared with cooperation from organizations in the public water supply industry.
- Includes information from actual contaminant samples and commercially-available service parts used in public water systems.
- Includes both an infrared spectral library and X-ray fluorescence profiles (in PDF file format), which significantly improves precision of contaminant searches.

Infrared Spectral Search Results



Detailed information:

Green (measured IR spectrum):

Infrared spectrum from contaminant detected in public drinking water

Red (specialized Tap Water Contaminant Database):

Interior residue (gray) on fitting seal for 32 mm diameter water drain pipe

Material	: Styrene butadiene styrene (SBS), calcium carbonate ($CaCO_3$), and magnesium silicate (talc - $3Mg_4SiO_2H_2O$)
Color	: Gray
Shape	: Plastic ring
Hardness	: Pliable
Metal shine	: None
Measurement method	: ATR (Diamond)

Infrared spectral search results indicated the contaminant is identical or similar to the metal fitting seal material from the water drain pipe (principal component: styrene butadiene styrene [SBS]).

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