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Hand Sanitizer Analysis: Application Notebook

Solutions for

Hand Sanitizer Analysis

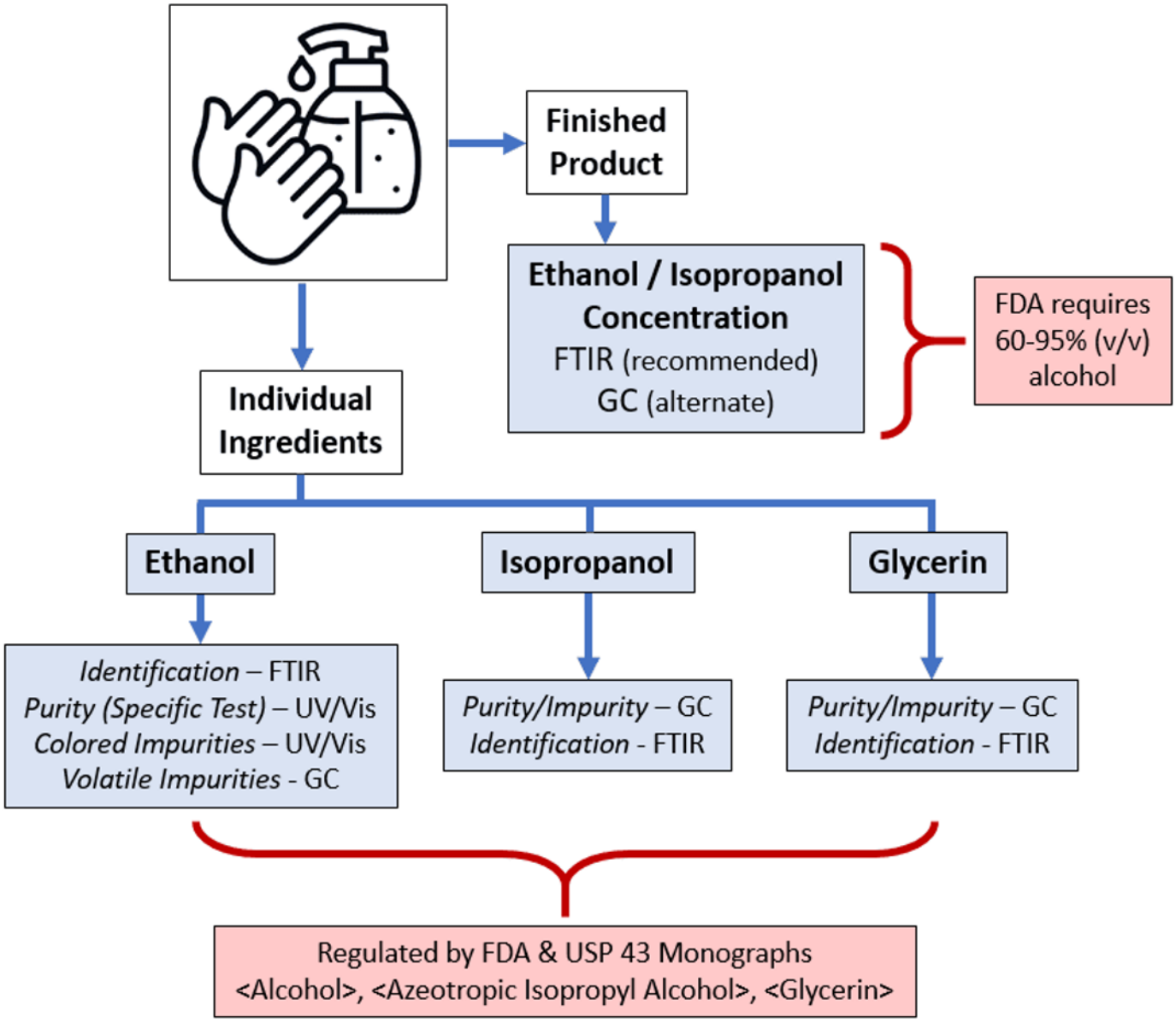
Application Notebook

The Covid-19 pandemic has led to an increase in usage of hand sanitizers as emphasis on disease prevention focuses on cleanliness and personal hygiene. Ensuring the purity and potency of hand sanitizers is paramount to their safety and efficacy. As a result, laboratories are seeking methods and techniques for analyzing hand sanitizers and their common ingredients, including ethanol and isopropanol. This workbook serves as a compendium of Shimadzu's methods for analysis supporting this industry and the fight against Covid-19.

Table of Contents

Which technique is right for my needs?

This flow chart outlines recommended methods and instrumentation for purity and potency of alcohols and finished hand sanitizers. First, determine if you are analyzing finished products or individual ingredients. Then, determine which parameter(s) you need to assess.



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Application News

No. G331

Gas Chromatography

Analysis of Volatile Impurities in Anhydrous Ethanol and Ethanol for Disinfection in Accordance with the Purity Test set by the Pharmacopoeias (JP, USP, EP)

Ethanol has antimicrobial properties and is sold as a disinfectant product at optimized concentrations. Quality control of the alcohol as a medical product is carried out through verification testing procedures as stipulated in each monograph of the Pharmacopoeias. Guided by the International Council for Harmonization on Technical Requirements for Pharmaceuticals for Human Use(ICH), the Japanese (JP), United States (USP) and European (EP) pharmacopoeias share roughly the same verification testing procedures for anhydrous ethanol and ethanol for disinfection. The Chinese Pharmacopoeia (ChP) also adopts a similar testing method.

Methanol, acetaldehyde, acetal and benzene are among the volatile impurities to be monitored. An instrument is required to detect benzene down to the specified 2 vol ppm limit or lower and also obtain a good resolution between acetaldehyde and methanol. This article presents the analysis of volatile impurities in accordance with the purity test (3) of the Japanese pharmacopoeia.

A. Miyamoto, T. Wada

Testing Method

The sample solution and standard solutions (1) – (4) *1 were prepared in accordance with Supplement I to the Japanese Pharmacopoeia Seventeenth Edition. For ethanol for disinfection, purified water was added to 83 mL of anhydrous ethanol*2 to make up to a total volume of 100 mL.

Analysis Conditions

Table 1 lists the instrument configurations and the analysis conditions used in this experiment.

Table 1 Instrument Configuration and Analysis Conditions

Model	:	Nexis™ GC-2030/AOC-20i Plus
Column	:	ZB-624 (30 m, 0.32 mm I.D., df=1.8 µm)
Column Temp.	:	40 °C (12 min)-10 °C/min-240 °C (10 min) Total：42 min
Detector	:	FID
Carrier Gas Control	:	Constant linear velocity
Carrier Gas	:	He, 35 cm/sec
Injection Temp.	:	200 °C
Detector Temp.	:	280 °C
Injection Mode	:	Split *2
Split Ratio	:	1:20
Injection Volume	:	1 µL

*2: The insert for splitless use for GC-17A (P/N：221-41544) was used. The insert was packed with 10 mg of deactivated glass wool (P/N: 221-48600).

System Suitability Test

When 1 µL of the standard solution (2) is injected into GC under the conditions shown in Table 1, acetaldehyde and methanol should elute with acetaldehyde ahead of methanol and their resolution needs to be no less than 1.5. In this experiment, the resolution of acetaldehyde and methanol was greater than 1.5 (Fig. 1 and Fig. 2). The calculation for the resolution was performed as per the JP, USP and EP Pharmacopoeias.

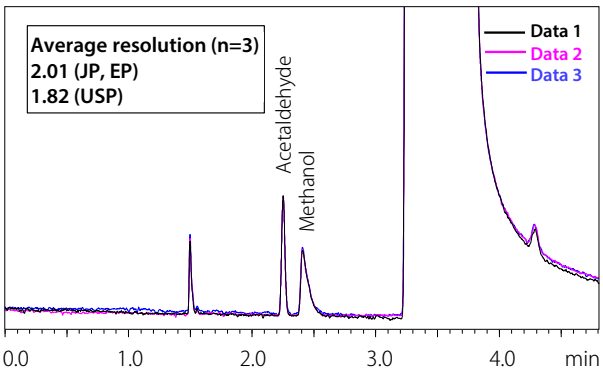

Fig. 1 Chromatogram of Standard Solution (2) for Anhydrous Ethanol (Overlaid Data from Three Continuous Analyses)

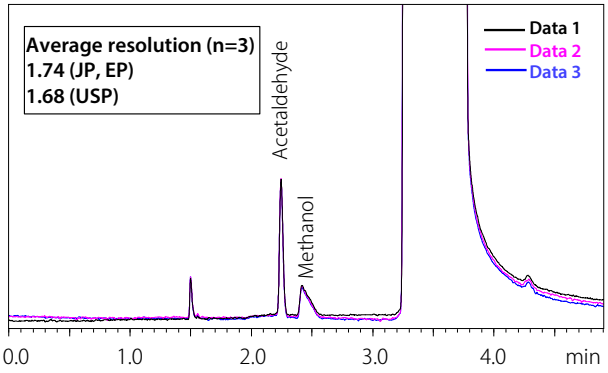

Fig. 2 Chromatogram of Standard Solution (2) for Ethanol for Disinfection (Overlaid Data from Three Continuous Analyses)

*1: This article uses the JP nomenclature. The USP and EP counterparts are as listed below.

JP	USP	EP
Sample	Sample solution A	Test solution(a)
Sample Solution	Sample solution B	Test solution(b)
Standard Solution (1)	Standard solution A	Reference solution(a)
Standard Solution (2)	Standard solution B	Reference solution(b)
Standard Solution (3)	Standard solution C	Reference solution(c)
Standard Solution (4)	Standard solution D	Reference solution(d)

*2: FUJIFILM Wako Pure Chemical Corporation's Japanese Pharmacopoeia-grade ethanol (99.5)

Analysis of Volatile Impurities

Methanol, acetaldehyde, acetal and benzene are analyzed to verify that the volumes of these impurities will not exceed those specified. The chromatograms of the samples (i.e. anhydrous ethanol and ethanol for disinfection), the sample solution and standard solutions (1) – (4) are shown in Fig.3 and Fig. 4. The peak areas and volumes of the volatile impurities are listed in Table 2. The data obtained were confirmed to meet the three purity criteria listed below.

1. The peak area of methanol obtained with the sample be no greater than 1/2 times that of methanol with the standard solution (1).
2. When calculating the amounts of the volatile impurities, the total amount of acetaldehyde and acetal (equation 1) be no more than 10 vol ppm as acetaldehyde and the amount of benzene (equation 2) be no more than 2 vol ppm.
3. The total area of all other impurities peak with the sample solution be no larger than the peak area of 4-methylpentan2-ol[*1].

$$\text{Total amount of acetaldehyde and acetal (vol ppm)} = \frac{10 \times A_E}{A_T - A_E} + \frac{30 \times C_E \times 44.05}{(C_T - C_E) \times 118.2} \quad \textbf{(Equation 1)}\ ^{*2}$$

$$\text{Amount of benzene (vol ppm)} = \frac{2B_E}{B_T - B_E} \quad \textbf{(Equation 2)}$$

*1: Peaks with areas less than 3 % of that of 4-methyl-2-pentanol should not be included. In this experiment, no target peaks were detected in the sample solution.

*2: For abbreviations of A_E, B_E, C_E, A_T, C_T and B_T, see refer to Table 2.

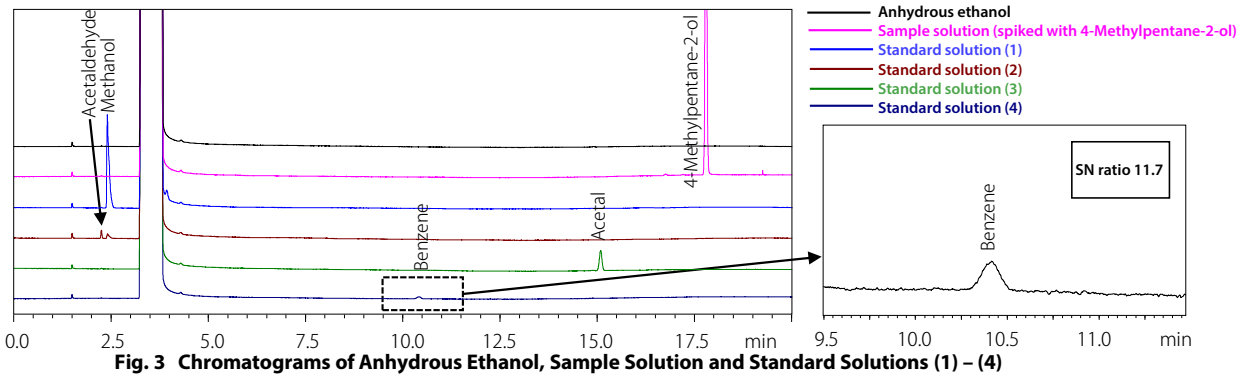

Fig. 3 Chromatograms of Anhydrous Ethanol, Sample Solution and Standard Solutions (1) – (4)

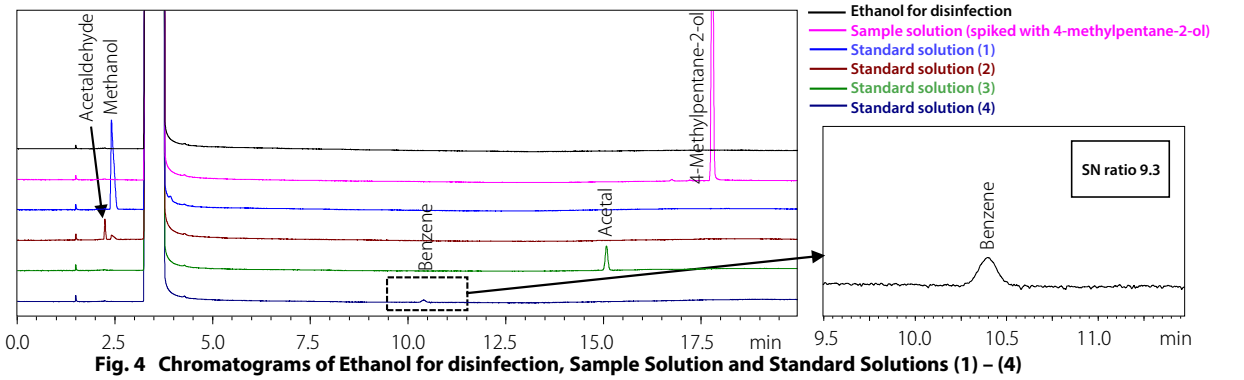

Fig. 4 Chromatograms of Ethanol for disinfection, Sample Solution and Standard Solutions (1) – (4)

Table 2 Average Areas and Amounts of Volatile Impurities (n=3)

	Sample			
	Peak area of methanol	Peak area of acetaldehyde	Peak area of acetal	Peak area of benzene
Sample name		A_E	C_E	B_E
Anhydrous ethanol	0	107	0	0
Ethanol for disinfection	0	107	0	0
	Standard solution (1)	Standard solution (2)	Standard solution (3)	Standard solution (4)
Diluted sample name	Peak area of methanol	Peak area of acetaldehyde	Peak area of acetal	Peak area of benzene
		A_T	C_T	B_T
Anhydrous ethanol	37050	1559	9418	1206
Ethanol for disinfection	34838	3108	8863	1115
Sample name		Total amount of acetaldehyde and acetal (vol ppm)		Amount of benzene (vol ppm)
Anhydrous ethanol		0.73		0
Ethanol for disinfection		0.36		0

Conclusion

System suitability test and analysis of volatile impurities were carried out in accordance with the purity test of ethanol in the JP (USP, EP) using Nexis™ GC-2030 gas chromatograph.

The results met the criteria set for testing anhydrous ethanol and ethanol for disinfection.

Nexis™ GC-2030 equipped with highly sensitive FID-2030 had enough sensitivity to detect even the most demanding volatile impurity like benzene.

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Application News

No. G333

Gas Chromatography

Alcohol Determination of Sanitizer Gel in accordance with USP<611>

United States Pharmacopeia (USP) General Chapters <611> ALCOHOL DETERMINATION stipulates two analytical methods for quantitating ethanol: one with distillation and the other by gas chromatography. The latter (i.e. USP <611> Method II) further gives an option of either using a packed column (Method II a) or a capillary column (Method II b).

This article introduces a quantitative analysis of ethanol in alcohol-based sanitizer gel according to USP <611> Method II b.

N. Iwasa, T. Wada

Preparation of Standard Solution and Sample Solution

5 mL each of 2 %(v/v) ethanol*1 and 2 %(v/v) acetonitrile*1 (internal standard), both in water, were pipetted into a 25 mL volumetric flask, made up to volume with water and vortex to prepare a 0.4 %(v/v) standard solution.

As a sample solution, a commercially available sanitizer gel (ca. 80 %(v/v)) was first diluted with water to ca. 2 %(v/v) ethanol. To further bring down the concentration to ca. 0.4 %(v/v), 5 mL of each of the prepared ca. 2 %(v/v) sample and 2 %(v/v) acetonitrile were aliquoted into 25 mL volumetric flask and mixture was make up to volume with water.

*1 USP<611> specifies the use of USP Alcohol Determination-Alcohol RS (2 %(v/v) ethanol) and USP Alcohol Determination-Acetonitrile RS (2 %(v/v) acetonitrile) to prepare the standard solution.

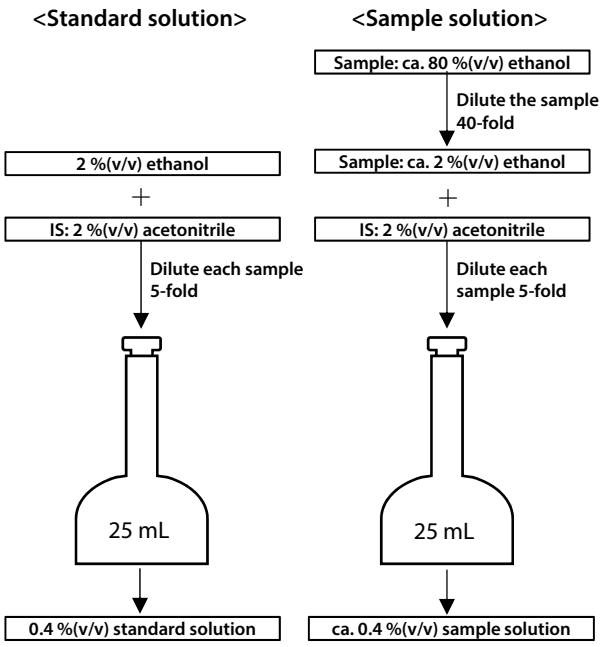

Fig. 1 Sample Preparation Method

Analysis Conditions

Using the gas chromatograph Nexis™ GC-2030, ethanol in the standard solution and the sample solution were quantitated according to USP<611>ALCOHOL DETERMINATION Method IIb. The instrument configuration and analysis conditions for the this experiment are listed below in Table 1.

Table 1 Instrument Configuration and Analysis Conditions

Model	: Nexis GC-2030 + AOC-20i Plus
Detector	: FID-2030 flame ionization detector
Column	: SH-Rtx™-624 (30 m × 0.53 mm I.D., d.f.= 3 µm)
Column Temperature	: 50 °C (5 min) – 10 °C/min – 200 °C (4 min) Total 24 mins
Injection Temperature	: 210 °C
Injection Mode	: Split
Split Ratio	: 1: 5
Carrier Gas Controller	: Linear velocity (He)
Linear Velocity	: 34 cm/sec
Detector Temperature	: 280 °C
FID H_2 Flow Rate	: 32 mL/min
FID Make up Flow Rate	: 24 mL/min (He)
FID Air Flow Rate	: 200 mL/min
Injection Volume	: 0.2 µL
Syringe	: Elastic Syringe, AOC (P/N: 221-49548)*2

*2 When samples in aqueous solution are analyzed with a standard syringe for AOC-20i Plus, the plunger motion may become dull during analysis, which affects repeatability. Using an elastic syringe for AOC (P/N: 221-49548) equipped with a plunger made of titanium enables stable sample introduction.

In this analysis, a glass insert was specifically configured as shown in Fig.2 to meet the requirements for the system suitability test(SST) in USP<611>. 20 mg of deactivated glass wool was packed into a split glass insert at a position 20 mm from the top. Increasing the amount of wool compared to the default amount of 10 mg and placing the wool slightly (i.e. 2 mm) above the default position (i.e. 22 mm from the top) improved reproducibility.

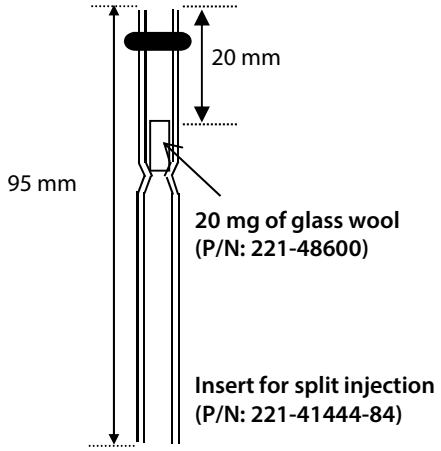

Fig. 2 Position and Quantity of Wool in the Insert

Chromatogram and Calibration Curve of the Standard Solution

The chromatogram and calibration curve of the standard solution are shown in Fig. 3 and 4. The SST results of the standard solution are summarized in Table 2.

The SST criteria include the following:

- The resolution factor, R, between alcohol and the internal standard be not less than 4.
- The tailing factor of the alcohol peak be not greater than 2.0.
- Six replicate injections of the standard solution show a relative standard deviation of not more than 4.0 % in the ratio of the peak of alcohol to the peak of the internal standard.

The results obtained with the standard solution satisfied all three SST criteria. The requirement for reproducibility (i.e. 4 %) was easily met with the RSD of 0.4 %.

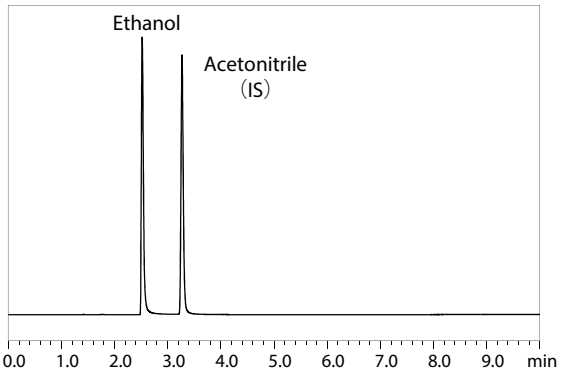

Fig. 3 Chromatograms of Standard Solution

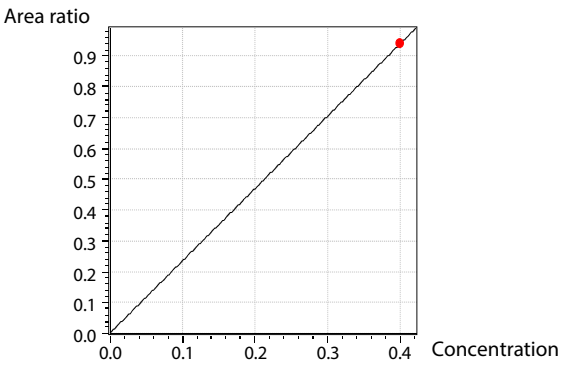

Fig. 4 Calibration Curve

Table 2 System Suitability of Standard Solution (n=6)

Compound	Peak area	Area ratio	Area ratio %RSD	Symmetry (tailing) factor	Resolution (USP)
Ethanol	627440	0.941074	0.405	1.467	---
Acetonitrile (IS)	666723	---	1.255	10.265	10.265

In Table 2, the items specified in the system suitability test are indicated in red.

Note: The values shown are reference values, not guaranteed values.

Chromatogram of Sample Solution and Quantitative Result for Ethanol

The chromatogram of the sample solution is shown in Fig. 5, and the quantitative results and repeatability (n=3) are listed in Table 3.

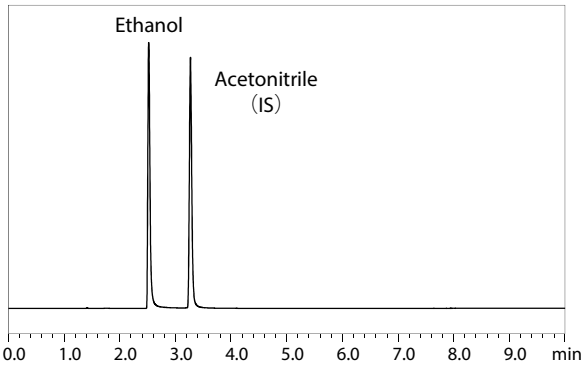

Fig. 5 Chromatograms of Sample Solution

Table 3 Ethanol Quantitative Values and Repeatability (n=3)

	Area ratio	Quantitative value (%)
Data 1	0.929279	78.997
Data 2	0.925411	78.668
Data 3	0.929298	78.998
Average	0.927996	78.888
%RSD	0.241	0.241

Note: The values shown are reference values and not intended to be guaranteed values.

Conclusion

Alcohol concentration in sanitizer gel was determined using a capillary column in compliance with USP <611> Method IIb.

The SST was conducted with a standard solution and satisfied with the resolution of 10.3 (cf. > 4 as a requirement) between ethanol and acetonitrile, the tailing factor of 1.5 (cf. < 2 as a requirement) and the repeatability of 0.4 % RSD (cf. 4 % limit).

The repeatability remained well even with a sample solution, proving the robustness of the gas chromatograph Nexis GC-2030.

Note: The experiment in this article was performed based on the current version of USP-NF as of April 24, 2020.

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Application News

No. GC-2005

Gas Chromatography

Determination of Ethanol and Isopropanol Content in Hand Sanitizers Using Nitrogen Carrier Gas

■ Introduction

The current coronavirus pandemic has created an unprecedented demand for alcohol-based hand sanitizers. The US FDA has provided guidance to allow manufacturing of hand sanitizers using ethanol or isopropanol (IPA) as their active ingredient. The United States Centers for Disease Control (CDC), the World Health Organization (WHO), and the US Pharmacopeia (USP) all have determined that ethanol or IPA concentrations in hand sanitizers must be between 60 and 95% to ensure germicidal and viricidal properties.

We developed a GC FID method to accurately quantify ethanol and IPA concentrations in two hand sanitizer samples. By using nitrogen as the carrier gas, this method is cost-effective and ensures the product compliance with CDC and USP guidelines and regulations.

■ Samples and Analytical Conditions/ Experimental

Ethanol (200 proof) and *n*-butanol (min. 99%) were purchased from Sigma Aldrich. 2-propanol (isopropanol or IPA, min. 99.9%) was purchased from Fisher Scientific. The solutions and samples were diluted in deionized water to specified concentrations.

A Shimadzu GC-2030 chromatograph equipped with split/splitless injector (SPL) and flame ionization detector (FID) was used for this analysis and the data were acquired, analyzed and reported using LabSolutions LCGC software. The method parameters are shown in table 1 below.

Table 1: Instrument Configuration and Analysis Conditions

GC system	Shimadzu GC-2030 with SPL, FID and AOC-20 Plus autosampler
Column	Rxi-624Sil MS, 30m x 0.32mm x 1.8µm
Injector Mode	Split at 1:20 ratio
Injection Volume	1.0 µL
Carrier Gas	Nitrogen (N_2)
Flow mode	Constant linear velocity of 40cm/sec
Column Temperature	30°C, 4min – 30°C/min –120°C, 2min
Injection Port Temperature	250°C
FID Temperature and Gases	250°C, Hydrogen 32mL/min, Air 200mL/min, Makeup (N_2) 24mL/min

■ Results and Discussion

Calibration Curves

Since both ethanol and 2-propanol (isopropanol alcohol or IPA) can be used to prepare hand sanitizer, calibration standards were prepared with both types of alcohol. An internal standard (IS) is commonly used in these assays to improve accuracy. Although acetonitrile is specified in the USP method as the IS for ethanol, it elutes closer to IPA and may cause column/liner deterioration with repeated injections. In comparison, *n*-butanol elutes away from both ethanol and IPA, and is not known to cause degradation to the GC systems. It is commonly used in blood alcohol content assays as an IS for ethanol. Therefore, *n*-butanol was used as the IS in this study.

Nitrogen (N_2) was chosen as the carrier gas to reduce the cost of analysis compared to using helium. As shown in Figure 1, all peaks were well resolved, and no contaminating peaks were found in water blank with IS only.

The calibration standards were diluted to indicated concentrations with 0.5% (v/v) of *n*-butanol in deionized water. Internal standard quantification methods were used, and the calibration curves were fitted to linear regression without forcing through zero.

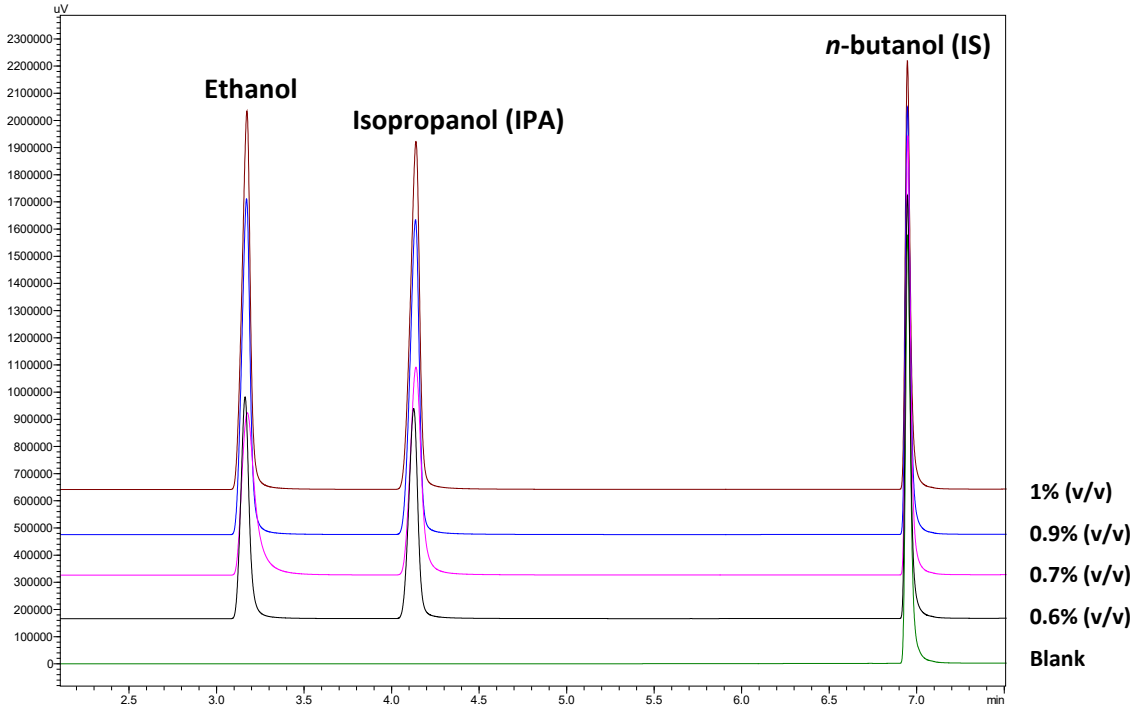

Figure 1: Chromatograms of calibration standards and water blank with IS (*n*-butanol)

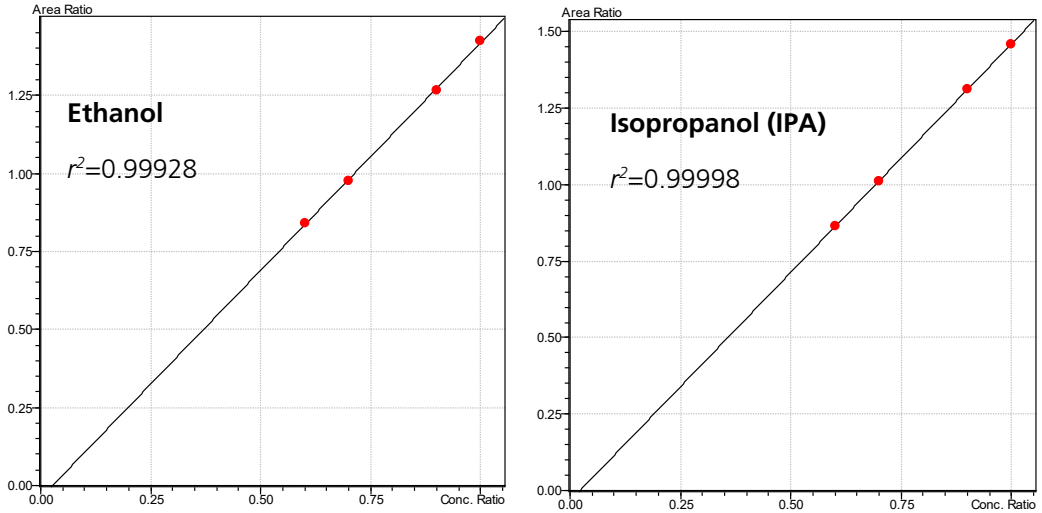

Figure 2: Four-point calibration curves for ethanol and IPA

Hand Sanitizer Samples

Two hand sanitizer samples were analyzed, one containing ethanol and the other IPA. Each sample was diluted 100-fold in IS solution for this analysis. The concentration of alcohol content is calculated by multiplying the concentration reported from the software by 100.

Table 2: Concentration of alcohols in hand sanitizer samples. Results are average of four injections. And the relative standard deviation (RSD) for the repeated injections was also shown for each sample.

	Sample 1	Sample 2
Ethanol conc. (v/v)	59.11	*not detected*
IPA conc. (v/v)	*not detected*	56.40
RSD	2.677%	1.175%

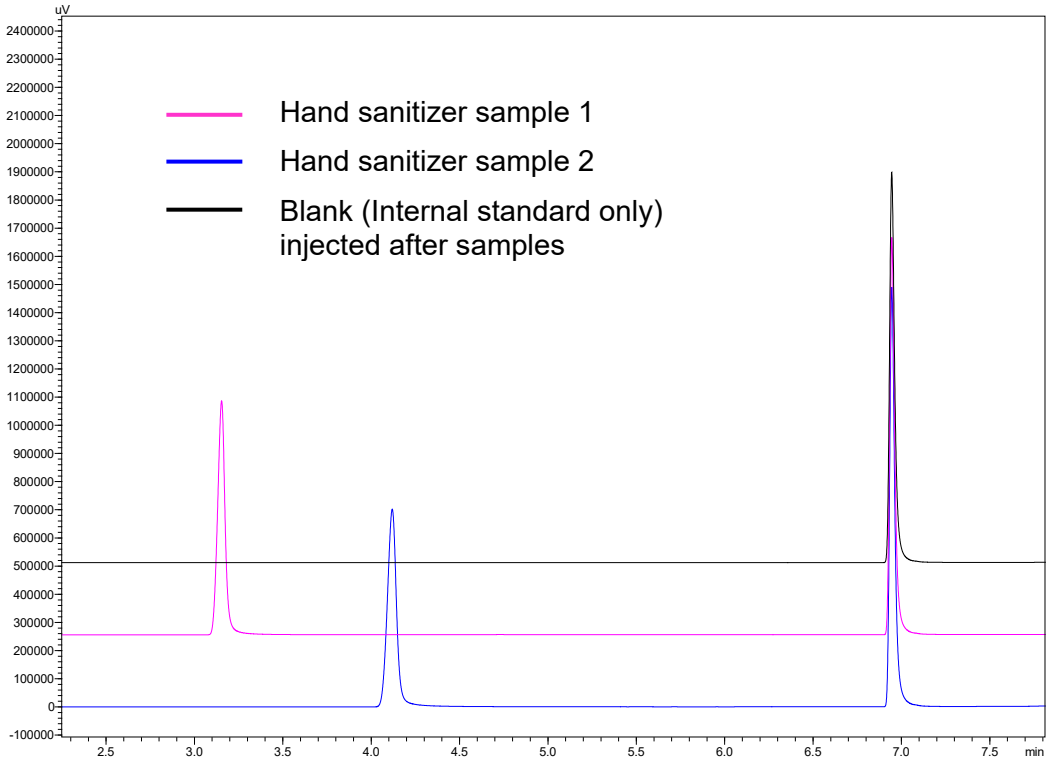

Figure 3: Chromatograms of hand sanitizer samples and a blank injected after the samples. No carryover of analytes was observed

■ Conclusion

Alcohol content in two hand sanitizer samples was successfully analyzed using Shimadzu GC-2030 on a Rxi-624Sil MS column using N_2 carrier gas. One of the samples contains ethanol, while the other contains isopropanol (IPA). The method used in this study was modified from USP standard general chapter 611, alcohol determination. The calibration curves for both ethanol and IPA were linear with $r^2 >$ 0.999, and the analysis was straightforward with very good repeatability (RSD < 3% for both samples). Nitrogen was successfully used as the carrier gas in this assay. Compared to helium, nitrogen is more cost-effective. It is also more inert thus safer than hydrogen, which is another commonly used cost-saving alternative carrier gas. Taken together, both ethanol and IPA content in hand sanitizers can be easily determined using Shimadzu GC-2030 with SPL and FID with nitrogen carrier gas.

■ Reference

1. USP General Chapter 611, Alcohol Determination.

■ Consumables

Part Number	Description	Unit	Instrument
221-76650-01	Septa, Green, Premium Low Bleed	Pk of 25	GC-2030
227-35007-01	Split Liner with Wool	Pk of 5	
221-75597-03	FID jet		
221-81162-02	ClickTek Ferrule 0.5mm	Pk of 6	
221-77155-41	ClickTek Column Connector	each	
221-34618-00	Syringe, 10µL, fixed needle	each	AOC-20i/s
220-97331-31	Sample Vials, 1.5mL Amber Glass with Caps & Septa	Pk of 100	
220-97331-47	Sample Vials, 1.5mL Amber Glass with Caps & Septa	Pk of 1000	
220-97331-63	200µL Glass Silanized Inserts for 1.5mL Vials	Pk of 100	
220-97331-23	Wash Vials, 4mL Amber Glass with Caps & Septa	Pk of 100	
227-36077-01	SH-Rxi-624Sil MS Capillary Column, 0.32 x 1.8 x 30	each	Column
227-36078-01*	SH-Rxi-624Sil MS Capillary Column, 0.53 x 3 x 30	each	

*Column conforms to USP general chapter 611 standard method

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SHIMADZU Corporation
www.shimadzu.com/an/

SHIMADZU SCIENTIFIC INSTRUMENTS
7102 Riverwood Drive, Columbia, MD 21046, USA
Phone: 800-477-1227/410-381-1227, Fax: 410-381-1222
URL: www.ssi.shimadzu.com

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Application News

No. AD-0223

FTIR / IRSpirit / QATR-S / Hand Sanitizer

Quick and Easy Analysis of Alcohol Content in Hand Sanitizer by FTIR Spectroscopy

❑ Introduction

If washing hands with soap and water are not readily accessible, hand sanitizer is the next alternative to prevent the spread of diseases and to kill germs. U.S. CDC have recommended sanitizers with 60–95% alcohol as the most effective composition of sanitizers. Additionally, with concerns over product fraud or fake substances used in the manufacturing of sanitizers, analysis of key active ingredients, such as alcohol, in sanitizers is crucial. This application news investigated the content of two most-commonly-used alcohol [ethanol and isopropyl alcohol (IPA)] in hand sanitizers. This analysis was conducted using Shimadzu FTIR spectrophotometer, IRSpirit^{TM}, equipped with an attenuated total reflection (ATR) accessory, QATR^{TM}-S which enables Fast and Easy set-up for quality testing.

❑ Experimental

Four commercially available alcohol-based hand sanitizers, two of which contains ethanol while the other two contains IPA, were analyzed (Table 2). Ethanol and IPA which were used to prepare the calibration standards were purchased from Merck, Germany, and Fisher Chemical, USA, respectively. The standard solutions, with concentration ranging from 0% to 100%, were prepared by dilution with Type E-1 ultra-pure water (Milli-Q® Millipore system, Germany). The samples were analysed without pre-treatment and dilution.

All standards and samples were measured using Shimadzu FTIR spectrophotometer, IRSpirit, equipped with an ATR accessory, QATR-S with a diamond crystal (Figure 1). The measurement conditions are shown in Table 1. About 20 to 30 µL of the sample amount was placed onto the ATR crystal using a micropipette and covered immediately with a volatile cover to minimize evaporation which could cause its concentration to change (Figure 2). The calibration curves of ethanol and IPA were generated using LabSolutions^{TM} IR Quantitation mode. For ethanol, the baseline was drawn at 1010 cm^{-1} and 1110 cm^{-1} and the calibration curve was created using the height from baseline to peak at 1044 cm^{-1}.

For IPA, the baseline was drawn at 1075 cm^{-1} and 1175 cm^{-1} and the calibration curve was created using the height from baseline to peak at 1127 cm^{-1}.

Table 1: FTIR Measurement Conditions

Instrument	:	IRSpirit^{TM}, QATR^{TM}-S (Diamond)
Wavenumber Range	:	4000 – 400 cm^{-1}
Resolution	:	4.0 cm^{-1}
Accumulation	:	25
Apodization function	:	Happ-Genzel
Detector	:	DLATGS

Fig. 1: IRSpirit^{TM} FTIR with QATR^{TM}-S

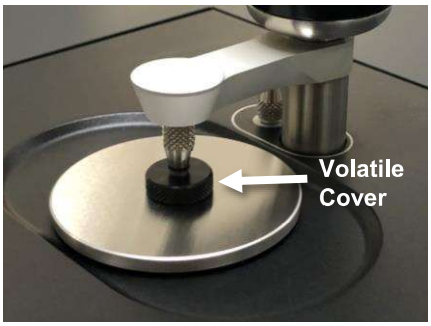

Fig. 2: QATR^{TM}-S with Volatile Cover

❑ Results and Discussion

Figure 3 shows the IR spectra of ethanol standards from 1140 cm^{-1} to 1000 cm^{-1} and IPA standards from 1200 cm^{-1} to 1060 cm^{-1} respectively. The IR spectra of alcohol-based hand sanitizers with 60% and 80% standards are shown in Figure 4. A good coefficient correlation (r^2) of more than 0.999 was obtained for

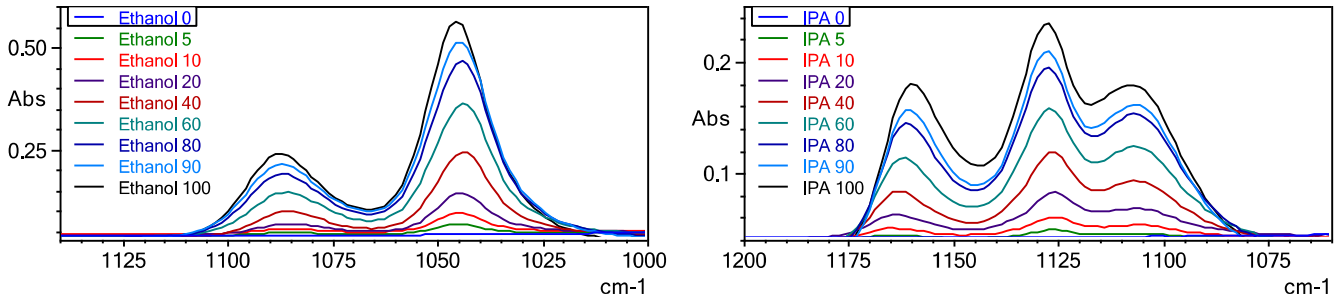

Fig. 3: IR Spectra of Ethanol Standards (left) and IPA Standards (right)

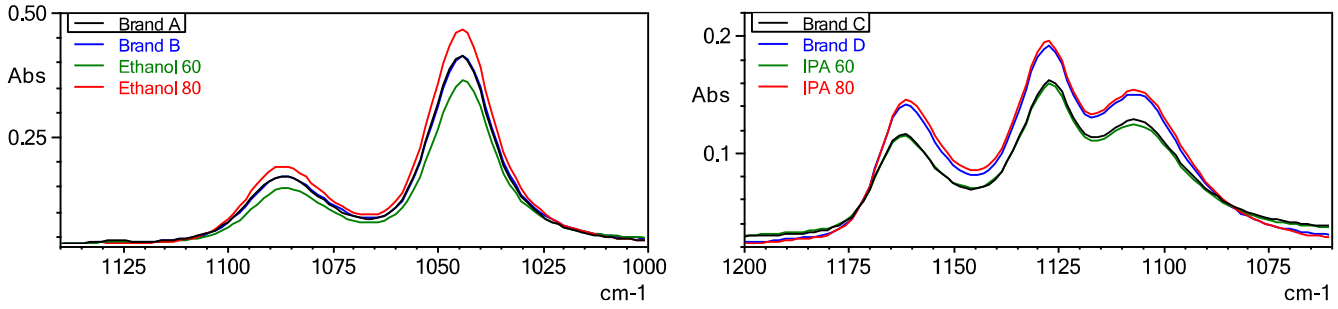

Fig. 4: IR Spectra of Brand A and B with 60% and 80% Ethanol Standards (left) and Brand C and D with 60% and 80% IPA Standards (right)

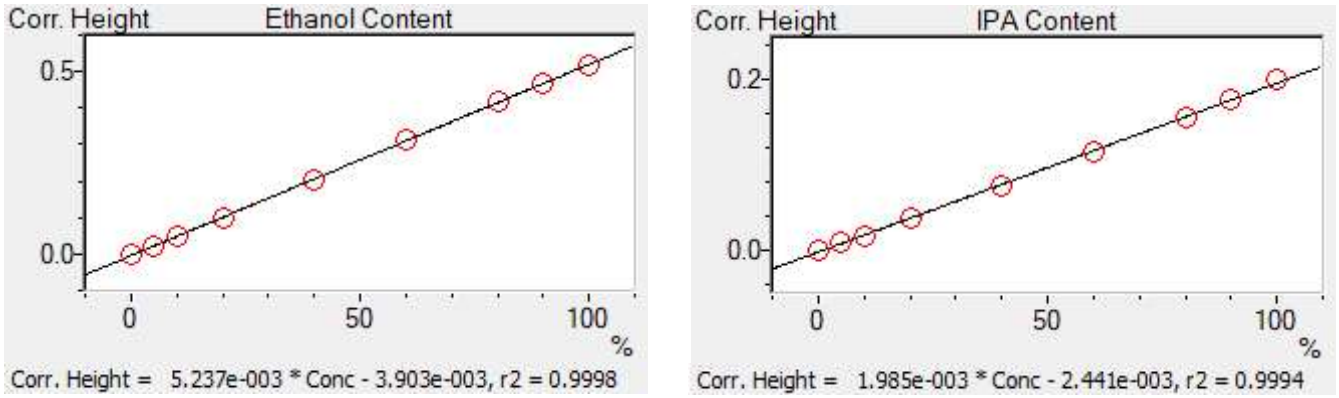

Fig. 5: Calibration Curves of Ethanol (left) and IPA (right)

Table 2 shows the quantitation results of the alcohol content in the alcohol-based hand sanitizers.

Table 2: Quantitative Results of Alcohol Content in Alcohol-based Hand Sanitizers

Sample	Type	Concentration	
		Labelled	Measured
Brand A	Ethanol	70 %	70.2 %
Brand B	Ethanol	66 %	69.4 %
Brand C	IPA	Not Stated	61.2 %
Brand D	IPA	> 70%	77.4 %

❑ Conclusion

With Shimadzu IRSpirit™ and QATR™-S, alcohol content in hand sanitizers are Easily and Accurately determined using just a single drop of sample.

❑ References

1. Todd ECD, Michaels BS, Holah J, Smith D, Greig JD, Bartleson CA. (2010) *Outbreaks where food workers have been implicated in the spread of foodborne disease. Part 10. Alcohol-based antiseptics for hand disinfection and a comparison of their effectiveness with soaps*. Journal of Food Protection 73(11): 2128-2140.
2. Kampf G, Kramer A. (2004) *Epidemiologic background of hand hygiene and evaluation of the most important agents for scrubs and rubs.* Clinical Microbiology Reviews 17(4): 863-893.

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Application News

No. A637

Fourier Transform Infrared Spectrophotometer (FTIR)

Determination of Ethanol Content in and Simple Fail/Pass Judgment of Alcohol Hand Sanitizer by FTIR

Introduction

The effects of alcohol-based hand sanitizers are dependent on type of alcohol used and alcohol concentration. The Center for Disease Control and Prevention (CDC) has recommended sanitizers with 60 - 95% alcohol as the most effective composition of hand sanitizers.

Ethanol, which has bactericidal activity, is prepared at the optimal concentration level for a range of commercially available alcohol-based sanitizers. To measure alcohol concentration, the distillation method or gas chromatography (GC) is stipulated by the United States Pharmacopeia (USP). These methods require more than 20 minutes per sample for analysis. Pretreatment, such as dilution, is also required. In contrast, if the Fourier transform infrared spectrophotometer (FTIR) is used, the preparatory steps can be skipped and the ethanol content in alcohol sanitizers can quickly be determined in approximately one minute.

This report introduces a simple pass/fail judgment of ethanol concentration in a commercially available ethanol sanitizer using the photometric measurement function that comes as standard in LabSolutions™ IR.

S. Iwasaki

Experimental

Dehydrated ethanol was spiked with water to prepare the standards at concentrations of 70 vol% and 82 vol%. The samples were measured using IRSpirit™, a Fourier transform infrared spectrophotometer, equipped with QATR™-S (diamond crystal), a single-reflection ATR accessory, as shown in Fig. 1. The measurement conditions are shown in Table 1. First, 20 to 30 µL of the sample amount was placed onto the ATR crystal using a micropipette and, as shown in Fig. 2, covered immediately with a volatile cover to minimize evaporation, which could cause its concentration to change. Fig. 3 shows the IR spectra of ethanol standards. The figure shows that the heights of peaks from ethanol at 1086 cm^{-1} and 1044 cm^{-1} (green lines) and those from water at 3340 cm^{-1} and 1650 cm^{-1} (blue lines) are dependent on the concentration.

Table 1 Measurement Conditions

Instrument	: IRSpirit, QATR-S (Diamond)
Resolution	: 4 cm^{-1}
Accumulation	: 20
Apodization function	: Sqr-Triangle
Detector	: DLATGS

Fig. 1 IRSpirit™ FTIR with QATR™-S

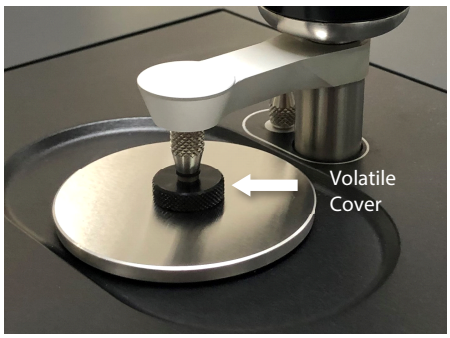

Fig. 2 QATR-S with Volatile Cover

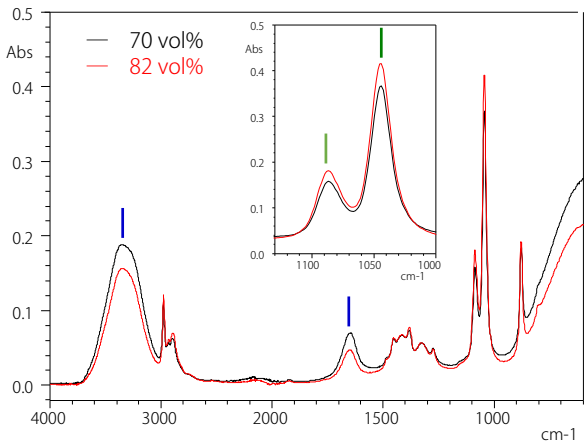

Fig. 3 IR Spectra of Ethanol Standards (70, 82 vol%)

Pass/Fail Judgment Using Labsolutions IR

To maintain the quality of alcohol sanitizers, it is important to control the concentrations of the constituents in these sanitizers. As a general rule, the spectra of a sample of known concentration and the sample to be controlled are analyzed to estimate the concentration of the sample to be controlled based on the height or area of the peak. Additionally, the obtained concentration should be judged by the analyzer as either pass or fail. These steps should be performed carefully because they not only require a lot of time but may also be affected by human error. The photometric measurement function installed as standard on LabSolutions IR can determine the absorbance or transmittance at specific wave numbers/wavelengths, and calculate these results using the formulas for pass/fail judgment. This makes it possible to reduce the operation time significantly.

Using this function, we judged four commercially available ethanol sanitizers (A – D) shown in Table 2. The samples were analyzed without pretreatment and dilution.

The photometric measurement function screen is shown in Fig. 4. The formula for pass/fail judgment is set up in Equation tab (red box) as shown in Fig. 4. In this analysis, the height from baseline to peak at 1044 cm^{-1} (C-O stretching vibration) was used to calculate the ethanol concentration (baseline drawn at 1110 cm^{-1} - 1020 cm^{-1}). The formula for pass/fail judgment was set up so that samples at 70 vol% (height from baseline to peak: 0.301) - 82 vol% (height from baseline to peak: 0.348) are judged Pass and the others are judged Fail. After the measurement of sample spectra, the data are automatically added to the sample table (blue box) shown in Fig. 4 to judge the samples. As shown in Table 2, Samples A and B, for which the concentrations were lower than the set reference concentration, were judged Fail.

Table 2 Labeling and Pass/Fail Judgment of Commercially Available Ethanol Sanitizers

Sample	Ethanol content labeled on the product	Pass/fail judgment
A	58 vol%	Fail
B	65 vol%	Fail
C	70 vol%	Pass
D	76.9 ~ 81.4 vol%	Pass

The measurement results of IR spectra (magnified view) are shown in Fig. 5. Using the peak height from ethanol (black line), the ethanol concentration can also be estimated.

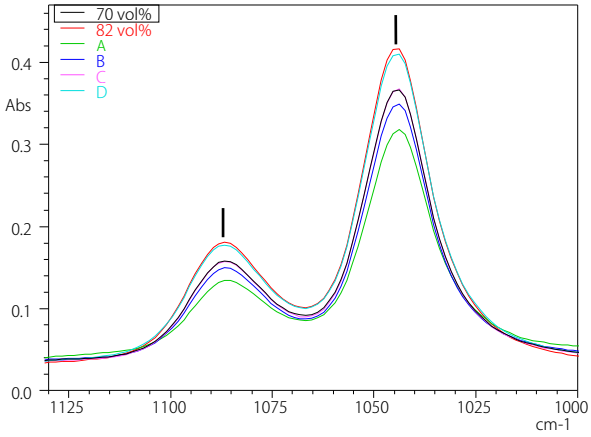

Fig.5 Measurement Results of IR Spectra (Magnified View)

Conclusion

With IRSpirit and QATR-S, ethanol content in sanitizers could be easily determined using just a single drop of sample. Additionally, the ethanol content could be easily and accurately judged for pass/fail by using the photometric measurement function of LabSolutions IR software. The use of this function can reduce the time required for analysis, including judgment. Concerns over product fraud or fake substances can be eliminated by controlling the quality of the major active ingredient (ethanol) in sanitizers.

For an example of quantitative analysis using the program installed as a standard function on LabSolutions IR, see also Application News No. A630 “Quick and Easy Analysis of Alcohol Content in Hand Sanitizer by FTIR Spectroscopy.”

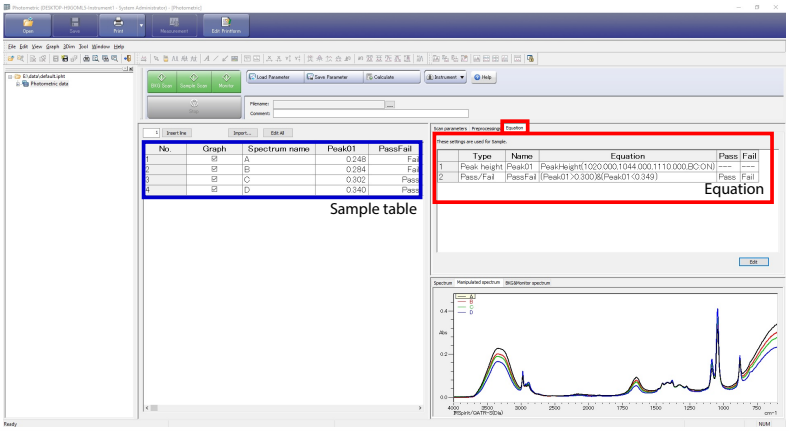

Fig. 4 Photometric Measurement Function Screen

First Edition: Nov. 2020

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Application News

No. A626

Spectrophotometric Analysis

Measurement of Impurities in Ethanol Using UV-Vis Spectrophotometer

At present, demand for ethanol for disinfection is increasing sharply as preventive measure for an infectious disease. When ethanol is to be used as a medical product, identification testing and purity testing conforming to the applicable Pharmacopoeias in each country are necessary. Ultraviolet-visible (UV-Vis) spectrophotometry is used in these tests as one technique for determining whether impurities are present in ethanol.

In the experiment introduced here, measurement of "Other impurities (absorbance)" in ethanols, which is described in the Japanese Pharmacopoeia, European Pharmacopoeia, and United States Pharmacopeia, was conducted using a Shimadzu UV-1900i UV-Vis spectrophotometer, and absorbance, which is specified as an acceptance standard in the Pharmacopoeias, was judged automatically by using the evaluation function of LabSolutions™ UV-Vis.

H. Abo

Test Method for Ethanols

The Japanese Pharmacopoeia (JP) describes the five items "Clarity and color of solution," "Acidity or alkalinity," "Volatile impurities," "Other impurities (absorbance)," and "Residue on evaporation" under "Purity" testing of ethanol, anhydrous ethanol and ethanol for disinfection. Among these, "Other impurities (absorbance)" is measured in order to determine the presence/absence of impurities contained in ethanol based on absorption in the ultraviolet (UV) region.

The European Pharmacopoeia (EP) includes "Absorbance" as one item in "TESTS" and describes similar testing using UV-Vis spectrophotometry.

The United States Pharmacopeia (USP) specifies "ULTRAVIOLET ABSORPTION" in "SPECIFIC TESTS" and also describes testing by UV-Vis spectrophotometry.

The measurement method for "Other impurities" is the same in the three Pharmacopoeias. The absorption spectrum of the sample is measured using a cell with an optical path length of 5 cm and water as a blank, and judgment of acceptability is based on absorbance.

Specifically, the Pharmacopoeias provide that the absorbances at 240 nm, between 250 and 260 nm, and between 270 and 340 nm are not more than 0.40, 0.30, and 0.10, respectively, when the absorption spectrum is measured in the 235 to 340 nm wavelength region. The provision also specify that the absorption spectrum should be smooth and "show a steadily descending curve with no observable peaks or shoulders."

Measurement of Anhydrous Ethanol

Anhydrous ethanol was measured with the UV-1900i UV-Vis spectrophotometer shown in Fig. 1, using a Shimadzu square long-path absorption cell holder and a 50 mm square cell. Table 1 shows the measurement conditions.

Fig. 2 shows the results of spectrum measurement.

Fig. 1 UV-1900i UV-Vis Spectrophotometer

Table 1 Measurement Conditions

Instrument	: UV-1900i
Software	: LabSolutions UV-Vis
Measurement wavelength range	: 235 - 340 nm
Scan speed	: Medium
Sampling pitch	: 0.5 nm
Slit width	: 1 nm (fixed)

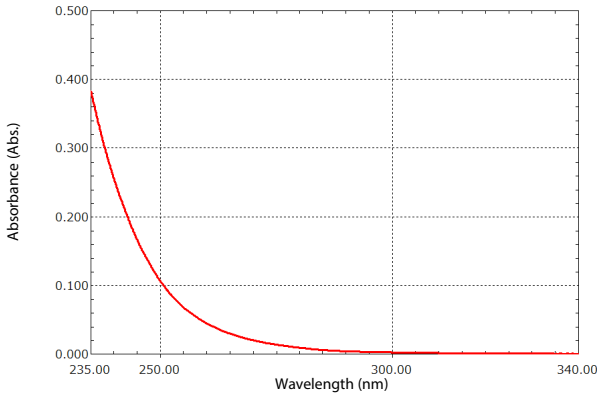


Fig. 2 Result of Measurement of Anhydrous Ethanol

In Fig. 2, it can be confirmed that absorbance is not more than 0.40 at 240 nm, not more than 0.30 between 250 and 260 nm, and not more than 0.10 between 270 and 340 nm, and there are no clear peaks or remarkable shoulders in the absorption spectrum curve.

Pass/Fail Judgment Using LabSolutions UV-Vis

The provisions for "Other impurities (absorbance)" of anhydrous ethanol specify that the absorbances at 240 nm, between 250 and 260 nm, and between 270 and 340 nm are not more than 0.40, 0.30, and 0.10, respectively. However, reading the absorbances of all the measured samples is time-consuming work and judgments must be made carefully, as human error is also possible. The time required for this work can be reduced by the spectral evaluation function of LabSolutions UV-Vis.

The spectral evaluation function features 8 pass/fail criteria and 33 standard evaluation methods, including point pick, maximum value, minimum value, peak, valley, area, statistics, and cutoff, as well as a pass/fail judgment function. Here, a pass/fail judgment for anhydrous ethanol was made using the pass/fail judgment function.

Setting of Pass/Fail Judgment Using LabSolutions UV-Vis

Although there are three judgment conditions by absorbance, in analysis of anhydrous ethanol, judgments are made by using [Point Pick – Single Point] and [Maximum Value – Single Point]. [Point Pick – Single Point] reads the absorbance of a fixed wavelength, and [Maximum Value – Single Point] can read the maximum value in a predetermined wavelength range.

First, absorbance of NMT 0.40 ("not more than 0.40") at 240 nm is set. Fig. 3 shows the Detailed Settings screen for evaluation of [Point pick – Single point]. The setting is made from this screen. The wavelength is set at 240 nm, and the pass/fail judgment criterion is set at NMT 0.40.

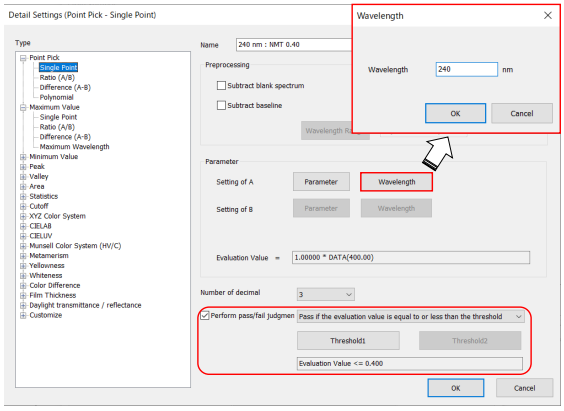


Fig. 3 Detailed Settings Screen for [Point Pick – Single Point] Evaluation

Next, the remaining conditions are set. Fig. 4 shows the Detailed Settings screen for evaluation of [Maximum Value – Single Point]. The wavelength range is designated, and the maximum value of absorbance in that range is read.

Here, two conditions are set. The judgment criteria of NMT 0.30 is set for 250-260 nm, and NMT 0.10 is set for 270-340 nm.

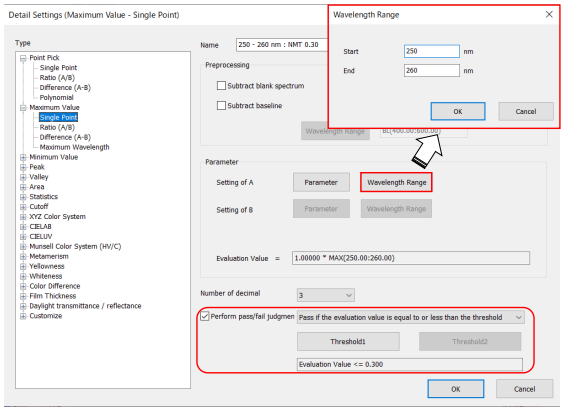
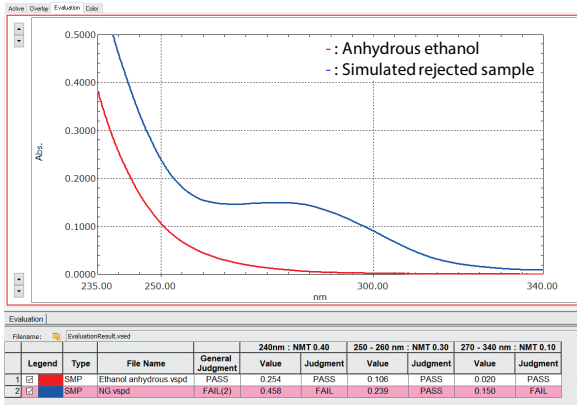


Fig. 4 Detailed Settings Screen for [Maximum Value – Single Point] Evaluation

Results of Pass/Fail Judgment

Fig. 5 shows the results of the pass/fail judgments for the anhydrous ethanol shown in Fig. 2 and a simulated rejected sample. The absorbance values of the anhydrous ethanol are within the pass range for all three wavelength conditions. On the other hand, in case of failure, the result can be understood at a glance, as the evaluation line is colored red. Fig. 6 shows an enlarged view of the evaluation table.

In pass/fail judgments, the data are added to the evaluation table automatically after spectrum acquisition. Therefore, the judgment can be completed simply by measuring the sample.



	Legend	Type	File Name	General Judgment	240nm : NMT 0.40 Value	240nm : NMT 0.40 Judgment	250 - 260 nm : NMT 0.30 Value	250 - 260 nm : NMT 0.30 Judgment	270 - 340 nm : NMT 0.10 Value	270 - 340 nm : NMT 0.10 Judgment
1	☑	SMP	Ethanol anhydrous.vspd	PASS	0.254	PASS	0.106	PASS	0.020	PASS
2	☑	SMP	NG.vspd	FAIL(2)	0.458	FAIL	0.239	PASS	0.150	FAIL

Fig. 5 Results of Pass/Fail Judgment

Conclusion

In this experiment, measurements of anhydrous ethanol were conducted in accordance with the Japanese Pharmacopoeia, European Pharmacopoeia, and United States Pharmacopeia using a UV-1900i, and a pass/fail judgment was made using the spectral evaluation function of the LabSolutions UV-Vis software. Analysis time, including judgment work, can be substantially reduced by using the spectral evaluation function.

	Legend	Type	File Name	General Judgment	240nm : NMT 0.40 Value	240nm : NMT 0.40 Judgment	250 - 260 nm : NMT 0.30 Value	250 - 260 nm : NMT 0.30 Judgment	270 - 340 nm : NMT 0.10 Value	270 - 340 nm : NMT 0.10 Judgment
1	☑	SMP	Ethanol anhydrous.vspd	PASS	0.254	PASS	0.106	PASS	0.020	PASS
2	☑	SMP	NG.vspd	FAIL(2)	0.458	FAIL	0.239	PASS	0.150	FAIL

Fig. 6 Enlargement of Evaluation Table

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Shimadzu Scientific Instruments
7102 Riverwood Drive, Columbia, Maryland 21046, U.S.A.
Phone: 800-477-1227/410-381-1227, Fax: 410-381-1222

www.ssi.shimadzu.com

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