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Application News

No. M315

GCMS-QP™ 2020 NX GC-MS

Analysis of Impurities in Alcohol-Based Hand Sanitizers by GC-MS

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User Benefits

- This method can quantify impurities and alcohol (ethanol or isopropanol) in hand sanitizers.
- It is possible to measure listed impurities in a wide range of concentrations from low to high under a single analysis condition.
- FASST (Fast Automated Scan/SIM Type) analysis can identify compounds other than the listed impurities in hand sanitizers.

■ Introduction

Recently, various types of hand sanitizers have been produced to meet increasing demand due to the spread of infectious diseases, and the U.S. Food & Drug Administration (FDA) has announced a "Direct Injection Gas Chromatography Mass Spectrometry (GC-MS) Method for the Detection of Listed Impurities in Hand Sanitizers" (hereinafter, FDA hand sanitizer analysis method) for quality assessment of hand sanitizers. This method allows the evaluation of sanitizers with ethanol or isopropanol and can also be used in screening for "listed impurities" regulated under the FDA's "Guidance for Industry" on alcohol-based hand sanitizer products. Moreover, it is also possible to assay for % alcohol under the same analysis conditions as in the impurity analysis.

In this article, the quantitative analysis of impurities and alcohol concentration in ethanol-based sanitizers was conducted using a Shimadzu GCMS-QP2020 NX single quadrupole GC-MS, referring to the FDA hand sanitizer analysis method. The analysis conditions described in this article can be used to measure impurity and alcohol concentration in alcohol-based sanitizers. Furthermore, the listed impurities can be detected over a wide concentration range, and the system requirements were satisfied. It is also possible to identify compounds other than the listed impurities by a FASST analysis using high speed switching between the Scan mode and the SIM mode.

■ FDA Listed Impurities in Hand Sanitizers

The impurities listed in the FDA Guidance for hand sanitizer products are classified as Level 1 or Level 2, depending on the toxicity of the impurities in the sanitizer. The concentration of impurities should be below the FDA guideline limits. Table 1 shows the Level 1 and Level 2 impurities, their limit values and the concentration ranges for each of the measured target compounds which can be detected under the analysis conditions described in this article.

Table 1 FDA Listed Impurities and Detectable Concentration Ranges

Compound Name			Interim Limit Listed in FDA Guidances (ppm)	Concentration Ranges for this Method (µg/mL)
Impurity	Level 1	Methanol	NMT 630	15.82 - 791
		Benzene	NMT 2	0.044 - 2.2
		Acetaldehyde	NMT 50	1.178 - 58.9
		1, 1-diethoxyethane	NMT 50	1.245 - 62.25
	Level 2	Acetone	NMT 4400	15.8 - 790
		1-Propanol	NMT 1000	16.08 - 804
		Ethyl Acetate	NMT 2200	18.04 - 902
		2-Butanol	NMT 6200	16.16 - 808
		Isobutanol	NMT 21700	16.06 - 803
		1-Butanool	NMT 1000	16.2 - 810
		3-Methyl-1-Butanol	NMT 4100	16.18 - 809
		Amyl Alcohol	NMT 4100	16.22 - 811
Alcohol		Ethanol	-	39.45 - 1972.5
		Isopropyl Alcohol	-	39.25 - 1962.5

■ Analysis Conditions

The analytical conditions for GC and MS were listed in Table 2, 3 and 4.

Table 2 Instrument Configuration

Model	: GCMS-QP2020 NX
Auto Injector	: AOC™-20i Plus
Auto Sampler	: AOC-20s Plus
Column	: SH-Rtx™-624 (30 m × 0.25 mm I.D., d.f. = 1.4 µm)

Table 3 Analysis Conditions

GC	
Injection Temp.	: 250 ˚C
Injection Mode	: Split
Sprit Ratio	: 50
Carrier Gas	: He
Carrier Gas Control	: Constant column flow rate (1 mL/min)
Column Temp.	: 40 ˚C (5 mins) - 30 ˚C/min - 240 ˚C (4 mins)*1 Total 15.67 mins
Injection Volume	: 1.0 µL
MS	
Ion source Temp.	: 230 ˚C
Interface Temp.	: 240 ˚C
Ionization method	: EI
Measurement mode	: Scan/SIM (FASST mode)
Scan Range	: *m/z* 29 to 300
SIM Ions	: Table 4
Event time	: Scan 0.2 sec, SIM 0.3 sec

*1 Under this oven heating condition, a high power oven model is necessary.

Table 4 MS Table

Time (min)	Compound Name	Target	Ident 1	Ident 2
1.5 – 2.56	Acetaldehyde	44.0	29.0	-
	Methanol	31.0	29.0	-
2.56 – 4.00	Ethanol	31.0	45.0	-
	Acetone	43.0	58.0	-
	Isopropyl Alcohol	45.0	59.0	-
5.00 – 6.65	1-Propanol	31.0	42.0	59.0
	Ethyl Acetate	43.0	61.0	-
	2-Butanol	45.0	59.0	-
6.65 – 7.20	Isobutanol	43.0	42.0	-
	Benzene	78.0	77.0	-
7.20 – 10.00	1-Butanool	56.0	41.0	31.0
	1, 1-diethoxyethane (Acetal)	45.0	73.0	103.0
	3-Methyl-1-Butanol	55.0	42.0	70.0
	Amyl Alcohol	42.0	55.0	41.0

* The detector voltage was set to a relative value based on tuning.

■ Preparation of Standards and Samples

The FDA hand sanitizer analysis method describes methods for a spiked recovery test, impurities determination, and alcohol %assay.

The standards and samples were prepared in accordance with the FDA hand sanitizer analysis method. To represent the liquid and gel types of samples, the following three samples were employed in this study: two ethanol-based sanitizers, one commercially available off a store shelf (sanitizer ①) and the other produced by a sake brewer (sanitizer ②) both to represent the liquid form of sample and an ethanol-based sanitizer gel (sanitizer ③) to represent the gel form. The ethanol concentration of all of the sanitizer samples was approximately 80 % (v/v).

■ Spiked Recovery Test

The FDA method specifies a spiked recovery test for verification of the condition of the instruments and measurement samples. Therefore, measurement samples were prepared, and the analysis was carried out in specified injection order/number of measurements in accordance with the FDA hand sanitizer analysis method.

In evaluating the method precision, the system suitability criteria is that the %RSD of the peak area for each listed impurity for all injection (n=6) of the spiked recovery standard solution should be no more than 10 %. In evaluating the method's accuracy, the % Recovery for impurities should be within the range 80-120. The results of all measured target compounds satisfied these requirements.

As the results of the spiked recovery test, Table 5 shows the repeatability results of the spiked recovery standard solution and the spiked recovery test results for the three sanitizer samples.

Table 5 System Suitability and Spike and Recovery Test

Compound Name	Peak area %RSD (n=6)	Recovery rate (%)		
	Spiked recovery standard solution	Sanitizer ①	Sanitizer ②	Sanitizer ③
Acetaldehyde	1.633	96.3	91.8	107.9
Methanol	1.889	107.8	99.1	103.1
Ethanol	1.757	-	-	-
Acetone	1.737	107.2	102.9	103.8
Isopropyl Alcohol	1.755	109.7	104.8	105.7
1-Propanol	1.802	105.7	107.1	100.3
Ethyl Acetate	2.035	107.3	101.9	100.8
2-Butanol	1.956	104.3	102.6	101.7
Isobutanol	1.889	105.5	109.2	101.7
Benzene	8.014	106.0	90.2	104.7
1-Butanool	2.255	105.7	103.3	100.4
1, 1-diethoxyethane	1.700	110.9	104.4	103.7
3-Methyl-1-Butanol	2.485	105.1	94.6	101.5
Amyl Alcohol	2.203	103.9	104.8	100.6

* Due to the high concentration of ethanol in the sanitizer samples, the recovery rate was not calculated.

■ Impurities Determination

Determination of the impurities (Level 1 and Level 2) specified in the FDA Guidance was conducted. Measurement samples were prepared and the analysis was carried out by the specified injection order/number of measurements, in accordance with the FDA hand sanitizer analysis method.

As system suitability criteria, the %RSD of the peak area for each listed impurity for all injections of standard solution should be no more than 10 %. System suitability was satisfied for the all compounds subject to measurement.

The detailed analytical results of impurities determination are summarized in Table 6. The chromatogram of the standard solution and the SIM chromatograms of each compound are shown in Fig. 1 and 2 respectively.

Table 6 Results of Impurities Determination

Compound Name	Standard solution		Impurities in 100 mL of sanitizer (ppm)			FDA limit value NMT (ppm)
	Concentration (µg/mL)	Peak area %RSD (n=6)	Sanitizer ①	Sanitizer ②	Sanitizer ③	
Acetaldehyde	11.78	0.521	32.5	49.6	ND	50
Methanol	158.2	0.481	ND	31.4	ND	630
Ethanol	394.5	0.488	-	-	-	-
Acetone	158	0.290	ND	ND	ND	4400
Isopropyl Alcohol	392.5	0.265	ND	ND	ND	-
1-Propanol	160.8	0.438	ND	827.8	ND	1000
Ethyl Acetate	180.4	0.537	16.0	168.1	ND	2200
2-Butanol	161.6	0.549	ND	ND	ND	6200
Isobutanol	160.6	0.610	ND	648.6	ND	21700
Benzene	0.44	1.045	ND	ND	ND	2
1-Butanool	162.0	0.432	ND	33.9	ND	1000
1, 1-diethoxyethane	12.45	0.850	40.6	135.8	ND	50
3-Methyl-1-Butanol	161.8	0.472	ND	1580.8	ND	4100
Amyl Alcohol	162.2	0.610	ND	ND	ND	4100

■ Alcohol Determination

Alcohol can also be assayed under the same analysis conditions as in the spiked recovery test and impurities determination. Measurement samples were prepared and the analysis was conducted by the specified injection order/number of measurements, in accordance with the FDA hand sanitizer analysis method.

Table 7 shows the %alcohol (v/v) results for ethanol in the three sanitizers.

* The FDA method states as follows: "If the ethanol or isopropanol peak for the impurity sample is more than 5x greater than the ethanol or isopropanol peak in the standard, dilute the impurity sample so that the resulting peak area should be approximately 0.5x the standard's peak area for those alcohols." In this article, the sanitizer samples were diluted 100 times with distilled water.

* Verification of system suitability criteria differs depending on whether verification is conducted on the same day as the impurity test or on a different day. For details, please refer to the FDA hand sanitizer analysis method.

Table 7 Determination of %Alcohol

Quantitative value of ethanol (%)		
Sanitizer ①	Sanitizer ②	Sanitizer ③
70.5	77.6	78.0

■ Calibration and Quantification

The FDA hand sanitizer analysis method includes the concentration range of each compound for this method shown in Table 1. Analysis conditions which enable analysis in this concentration range are necessary.

Six samples were prepared/measured by diluting the stock standard solution by 2, 5, 10, 20, 50, and 100 times. The linearity of calibration curves confirmed that measurement is possible over a wide range of concentrations.

Fig. 3 shows the calibration curves of each target compound.

* When saturating a high concentration sample or when the sensitivity of a low concentration sample is insufficient, adjust the detector voltage by approximately ±0.1.

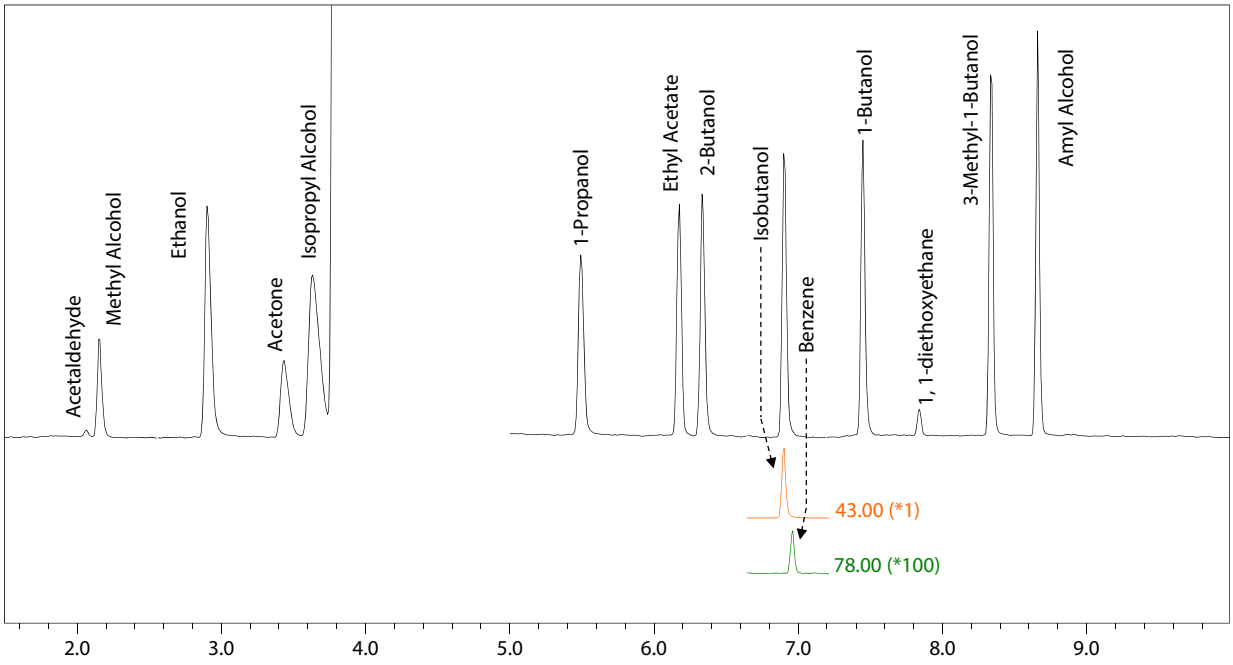

Fig. 1 TIC Chromatogram of Standard Solution (Isobutanol and Benzene: SIM Chromatogram)

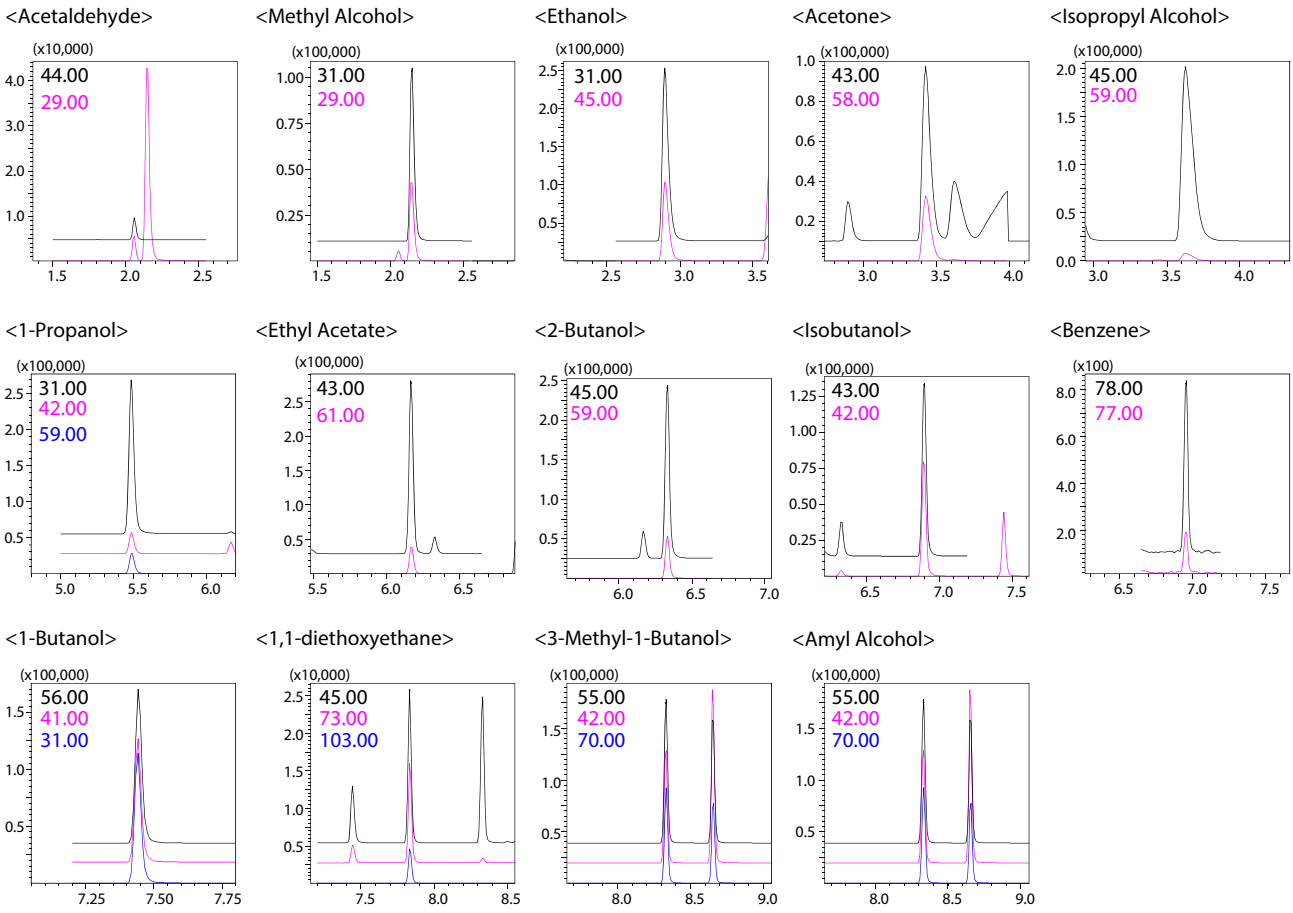

Fig. 2 SIM Chromatograms of Standard Solutions

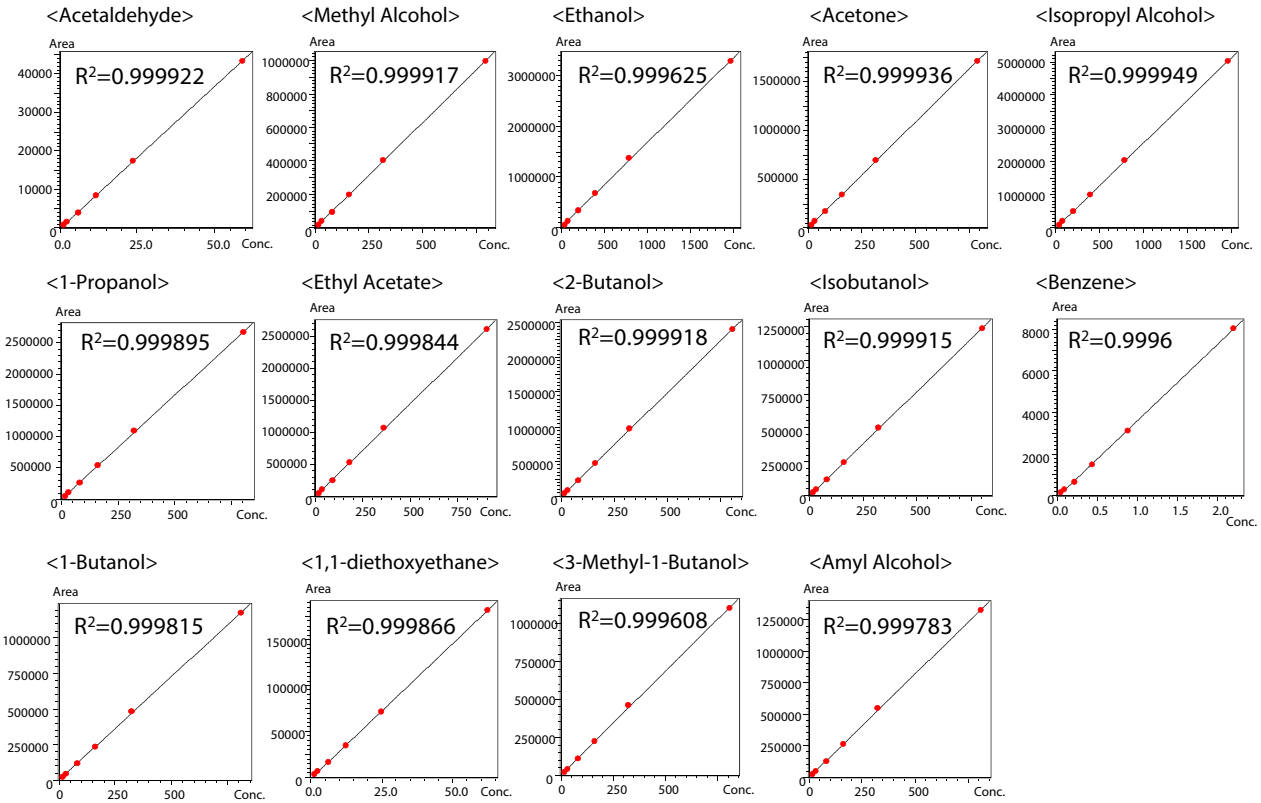

Fig. 3 Calibration Curve of Each Measured Compound

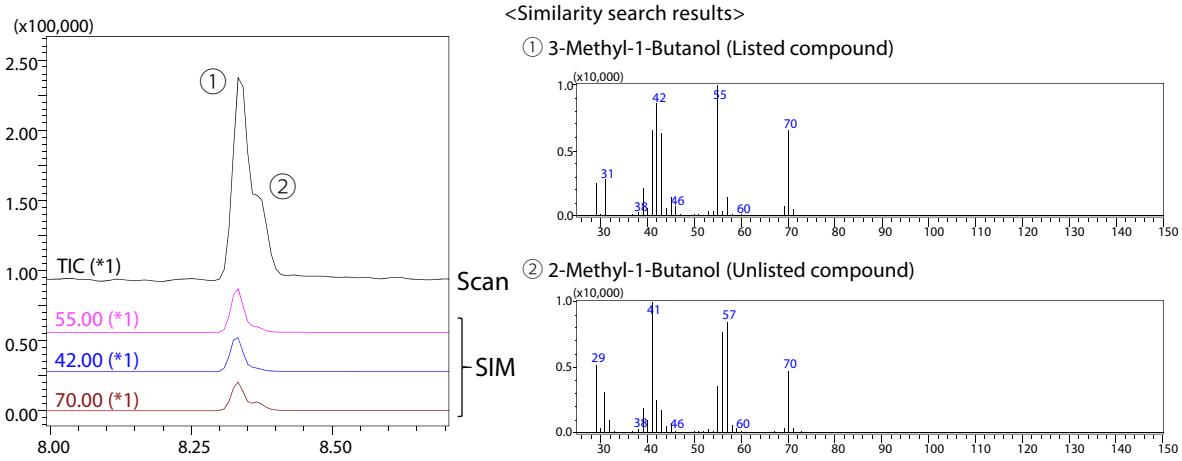

Fig. 4 Identification of Eluted Compounds other than Listed Impurities by FASST Mode

■ Identification by FASST

Using FASST (Fast Automated Scan/SIM Type) analysis, eluted compounds other than listed impurities can be identified. Among the sanitizer samples used in this experiment, a peak for a compound other the listed impurities was detected in the sanitizer produced by a sake brewer (Sanitizer ②). This compound could be identified as 2-Methyl-1-Butanol from the Scan data.

The results are shown in Fig.4.

■ Conclusion

GCMS-QP2020 NX can be used to quantify impurities and alcohol concentration in hand sanitizers. Identification of elution peaks not associated with listed impurities is also possible by FASST analysis.

First Edition: Mar. 2021

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