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Application News

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Gas Chromatography

Analysis of Residual Ethylene Oxide in Medical Devices by Headspace Gas Chromatography

Ethylene oxide gas (EOG) is a flammable and colorless gas commonly used in a medical device sterilization. Its permitted maximum residual levels are set by a range of international and local organizations, including the International Organization for Standardization (i.e. ISO 10993-7:2008) and Japanese Industrial Standards (i.e. JIS T 0993-7:2012). In these standards, extraction can be either exhaustive or simulated-use. The exhaustive extraction entails a solvent extraction and allows a choice between the following two instrument configurations: the gas chromatograph (GC) and the headspace (HS) -GC.

In this article, exhaustive extraction of residual EO by the HS-GC was performed in reference to the JIS and ISO section K.4.4 "Exhaustive Extraction with Ethanol Followed by Headspace Gas Analysis of the Ethanol Extract".

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Instrument Configuration and Analytical Conditions

In this experiment, the headspace gas sampler HS-20 was connected to the Nexis™ GC-2030 for effective sample introduction. The analytical conditions for GC and HS were in accordance with JIS T 0993-7:2012 as listed in Table 1 and 2.

Table 1 GC Analytical Conditions

Model	: Nexis GC-2030
Detector	: FID-2030 flame ionization detector
Headspace Sampler	: HS-20
Analytical Column	: SH-Stabilwax™ (30 m × 0.53 mm I.D., d.f.= 2.00 µm)
Column Temperature	: 40 °C (5 mins) – 30 °C/min – 200 °C (20 mins) Total 30.33 mins
Injection Mode	: Split 20
Carrier Gas Controller	: Constant Linear Velocity
Linear Velocity	: 30 cm/sec (N_2)
Detector Temperature	: 250 °C
Detector Gas	: H_2 32 mL/min, Air 200 mL/min
Make up Gas	: N_2 24 mL/min
Injection Volume	: 1 mL

Table 2 HS-20 Analytical Conditions

Oven Temperature	: 70 °C
Sample Line Temperature	: 75 °C
Transfer Line Temperature	: 75 °C
Vial Volume	: 10 mL
Vial Shaking Level	: 3
Vial Equivalating Time*	: Standard) 30 mins Sample) 180 mins
Vial Pressurizating Time	: 1 min
Vial Pressure	: 100 kPa
Loading Time	: 1 min
Needle Flush Time	: 8 mins

*The vial equivalating time listed in the Table 2 is an example only and varies depending on the type of samples.

Preparation of Standards and Samples

The standards and the samples used in this experiment were prepared in conformance with JIS T 0993-7:2012.

For the standards, a 100 µg/mL EO solution and a 100 µg/mL propylene oxide (PO) internal standard solution were prepared from purchased neat solutions. 5 calibrator points were prepared by diluting the 100 µg/mL EO stock solution with ethanol to 0.4, 0.8, 1.2, 1.6 and 2.0 µg/mL. Each calibrator solution also contained PO internal standard at 0.5 µg/mL. For a calibration curve, 5 mL of a calibrator solution was aliquoted into a 10 mL HS vial and hermetically sealed prior to analysis.

For the samples, EOG-sterilized bandage and suction catheter were selected to represent sheet and tube types of samples respectively. The extraction solution was prepared by diluting the 100 µg/mL PO stock solution with ethanol to 0.5 µg/mL. The bandage was cut into 10 mm square pieces while the suction catheter was trimmed into 5 mm long pieces. Ca. 0.5 g of sample pieces was placed in a 10 mL HS vial along with 5 mL of the 0.5 µg/mL PO extraction solution and hermetically sealed for analysis.

It should be noted that all the above-mentioned solutions and lab apparatus (e.g. volumetric flasks) used to handle those solutions were kept at a sub-ambient temperature during the preparation to suppress an evaporative loss of EO.

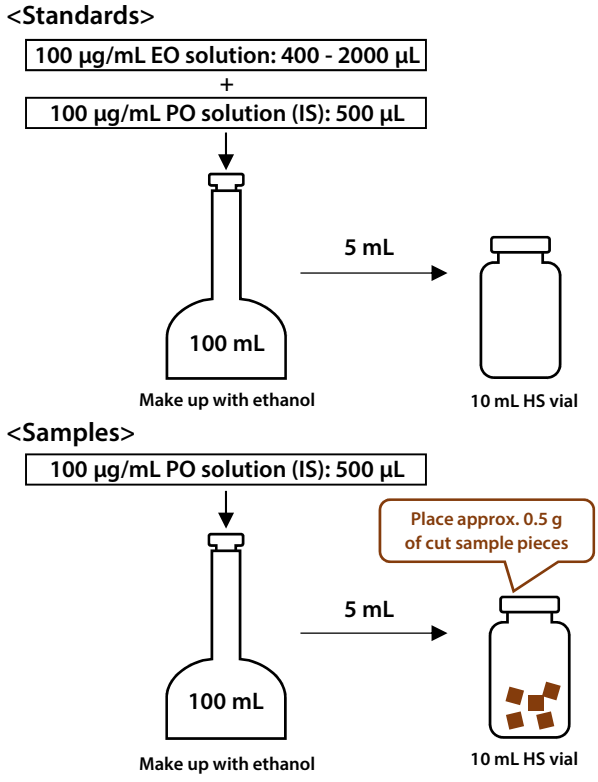

Fig. 1 Sample Preparation Method

System Requirements Test

JIS T 0993-7:2012 contains the following statements with respect to system requirements.

- Resolution between EO and PO be not less than 2.0
- Tailing factor for EO be not more than 1.8
- Relative deviation of the standard curve (RSD) does not exceed 5 % for the range of standards used
- %RSD of the EO peak area does not exceed 5% for the range of the standards used
- Correlation coefficient of the calibration curve be greater than 0.95.

The results obtained in this experiment satisfied all the above 5 criteria.

The detailed analytical results are summarized in Table 3. The chromatograms and a calibration curve are shown below in Fig. 2 and 3 respectively.

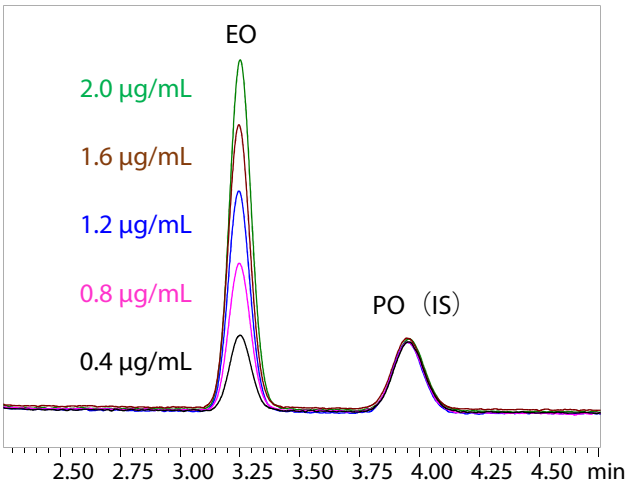

Fig. 2 Standard Chromatograms

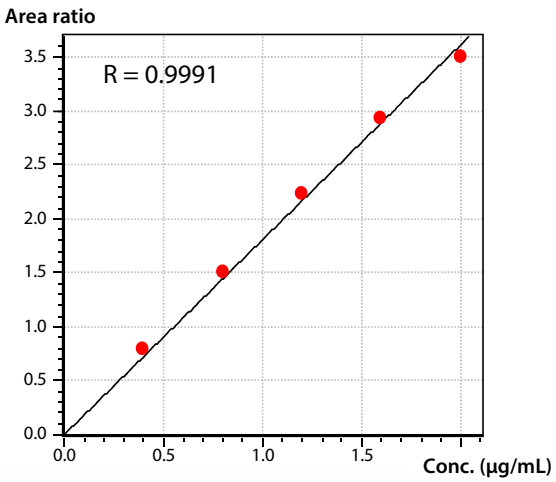

Fig. 3 Calibration Curve

Table 3 System Requirements Test Results (n=6)

Concentration (µg/mL)	0.4	0.8	1.2	1.6	2.0
Mean area value	2930	5614	8324	11054	13433
Area value %RSD	2.285	0.948	1.560	1.130	3.435
Mean area ratio	0.786	1.508	2.234	2.926	3.509
Area ratio %RSD	1.686	1.652	1.223	0.695	2.034
Resolution	3.393	3.380	3.384	3.372	3.371
Tailing factor	1.058	1.058	1.052	1.050	1.051
Limit of detection (µg/mL)*	0.048	0.049	0.048	0.048	0.049
Limit of quantification (µg/mL)*	0.159	0.163	0.161	0.162	0.162

* The limit of detection and the lower limit of quantification were calculated at S/N=3 and S/N=10 respectively.

Note) The chromatograms and quantitative results are for reference purposes only and should not be regarded as guaranteed values.

Sample Results

Fig. 4 are the overlaid chromatograms of the bandage and the suction catheter. The quantitative results are listed in Table 4.

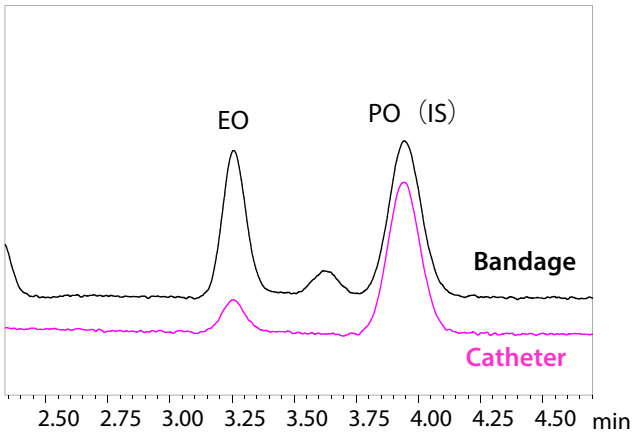

Fig. 4 Sample Chromatograms

Table 4 Quantitative Values of EO in 0.5 g of Samples (µg/0.5 g)

	Bandage	Catheter
Data 1	1.987	0.370
Data 2	2.026	0.412
Data 3	1.903	0.378
Mean	1.972	0.387

Note) The chromatograms and quantitative results are for reference purposes only and should not be regarded as guaranteed values.

Conclusion

Quantitation of residual ethylene oxide in bandages and suction catheters was conducted by HS-GC in accordance with JIS T 0993-7:2012 and ISO 10993-7:2008.

The Shimadzu GC-2030 + HS-20 system satisfied the system requirements and is considered an excellent instrument for measuring residual ethylene oxide in a medical device.

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