Application Note

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Determination of Ethylene Oxide and Ethylene Chlorohydrin in Medical Devices using the Agilent 8890 GC and 7697A Headspace Sampler

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Abstract

This application brief describes an analytical method for determining ethylene oxide and ethylene chlorohydrin in medical devices. An Agilent 8890 series GC equipped with a split/splitless inlet and flame ionization detector (FID) was used to determine the two compounds simultaneously. The DB-Select 624 UI column demonstrates great peak shape and resolution for the analysis, indicating a highly inert flow path from inlet to detector.

Introduction

Sterilizing medical devices with ethylene oxide (EO) is a common practice due to its extensive material compatibility. The main side effect of using EO as a sterilization agent is that it can leave a residue on the devices being processed. These residues include: ethylene oxide (EO), the residue that may remain after processing has been completed; ethylene chlorohydrin (ECH), the residue that may form when EO comes into contact with free chloride ions; ethylene glycol (EG), the residue that may form when EO comes into contact with water. There are three residue levels based on exposure categories: limited (daily), prolonged (monthly), and permanent. The residues can be harmful to the end user, so it is important to set an allowable limit for medical devices. The International Organization for Standardization (ISO) set allowable limits for residual EO and ECH in individual EO-sterilized medical devices and procedures for the measurement of EO and ECH.[1]

China has also released a series of regulations for EO-sterilized medical devices. For example, GB/T 16886.7-2001 is equivalent to ISO 10993-7:1995 Part 7: EO sterilization residuals.[2] GB 19083-2010 specifies the technical requirements for protective face masks in medical use.[3] GB 19082-2009 shows the technical requirements for single-use protective clothing for medical use.[4] The allowable limit of EO in those GB methods is less than 10 µg/g, and the GB/T 14233.1-2008 method is recommended as the reference for sample pretreatment and determination of EO in those GB methods.[5] Although mandatory testing of ECH is not required by many standards, ECH has the same environmental concerns as EO, so many industries are asking for reports on the testing of ECH. This application brief uses GB/T 14233.1-2008 as a reference and develops an analytical method for determining EO and ECH simultaneously.

Experimental

Instrumentation

The EO and ECH analysis were performed using an Agilent 7697A headspace sampler and Agilent 8890 GC. Headspace was involved for the extraction of analytes from solvent by heating the samples. The extracted analytes were then transferred to the GC/FID system for separation and quantitative analysis. Instrument conditions are shown in Table 1.

Table 1. Instrument conditions.

Parameter	Value
Agilent 7697A Headspace Sampler Conditions	
Loop Size	1 mL
Oven Temperature	60 °C
Loop Temperature	90 °C
Transfer Line Temperature	100 °C
Vial Equilibration Time	30 min
Vial Size	20 mL
Fill Pressure	15 psi
Loop Final Pressure	13 psi
GC Cycle Time	14 min
Agilent 8890 GC Parameters	
Inlet	Split/splitless Temperature: 200 °C Split mode, split ratio: 3:1 Liner: straight, nondeactivated (p/n 5183-4709)
Column	Agilent DB-Select 624UI 30 m × 0.53 mm, 3 µm (p/n 125-0334UI)
Carrier	Nitrogen, 5 mL/min, constant flow
Oven	40 °C (1 min), then 15 °C/min to 130 °C (1 min)
FID	250 °C, Air: 400 mL/min, hydrogen: 30 mL/min, makeup and column: constant flow 30 mL/min

Calibration solution preparation

- Two stock solutions of EO and ECH in water (respectively) at a concentration of 10,000 mg/L were used to prepare calibration standards for the study. The stock solutions were from the customer's lab.
- The intermediate stock solutions were prepared at concentrations of 20 and 200 mg/L for EO, and 40 and 400 mg/L for ECH.
- Water was used as the solvent for preparing the calibration standards.
- Five calibration levels were made in headspace vials. Final concentrations were approximately 1, 2, 5, 10, 20 mg/L for EO, and 2, 4, 10, 20, 40 mg/L for ECH. Table 2 shows an example of the dilution process for EO calibration solutions.
- EO is a highly volatile compound due to its low boiling point of 10.8 °C. Special attention should be paid when preparing the calibration solutions and samples. Freezing all EO containers or tools used for transferring EO in advance is recommended, and the stock solution could be treated in an ice bath.

Table 2. Example of dilution series for EO in the preparation of calibration solutions.

Concentration of EO in Stock Solution or Intermediate Stock Solution (mg/L)	The Volume Transferred to Vials from Stock Solution or Intermediate Stock Solution (mL)	Water Added to Vials (mL)	Final Volume in Headspace Vials (mL)	Calibration Solution Concentration (mg/L)
200	0.1	0.9	1	20
200	0.05	0.95	1	10
20	0.25	0.75	1	5
20	0.1	0.9	1	2
20	0.05	0.95	1	1

Results and discussion

GB/T 14233.1-2008 describes two residue extraction methods: simulated-use and exhaustive extraction. Exhaustive extraction is recommended in this method, with water as the solvent. In this brief, water was used for preparing the stock solution and calibration solutions. Purchasing an EO standard solution with methanol as the solvent is not recommended, because methanol may interfere with the analysis of the target compounds on DB-624 column. If an EO standard solution in methanol was purchased, other columns of different polarity could be selected.

Figure 1 shows an example GC/FID chromatogram of EO and ECH. This GC system, installed with an Ultra Inert DB-Select 624 column, demonstrates great peak shapes and resolution.

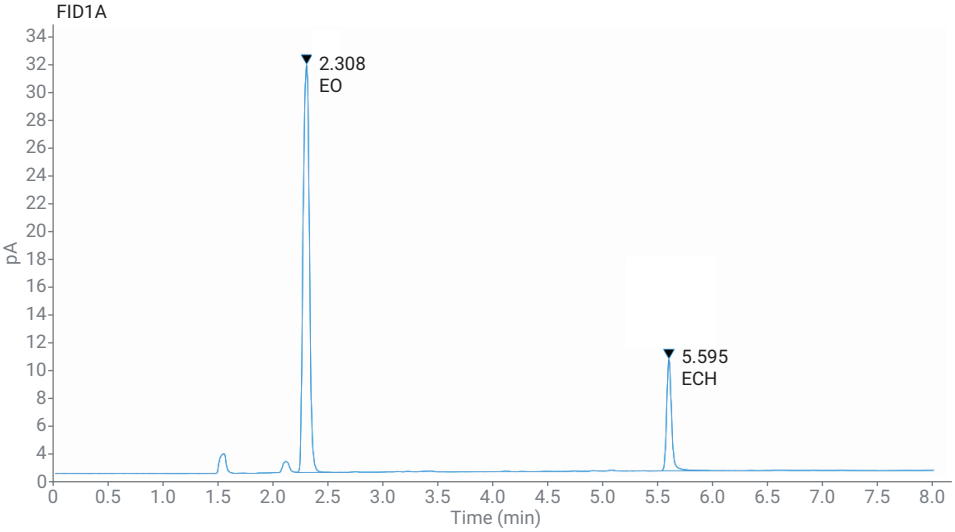

Figure 1. GC/FID chromatogram of EO (20 mg/L) and ECH (40 mg/L).

Calibration curves for EO and ECH showed excellent results. Calibration coefficients (R^2) value for the two compounds were above 0.999. Figures 2A and 2B display the calibration curve information obtained on this instrument. Table 3 shows eight consecutive injections at a concentration of 2 mg/L for EO and 4 mg/L for ECH. The area %RSD for EO and ECH were below 3.5% and the retention time %RSD was less than 0.014%. If poor linearity or repeatability were found during the test, it is good practice to confirm that you have done thorough sample pretreatment: keep the calibration solutions, containers and tools in low temperature. Signal-to-noise (S/N) ratio was used for method detection limit (MDL) calculation. A standard solution with a concentration of 1 mg/L EO and 2 mg/L ECH was used to test the MDL. The MDL of EO is 0.013 mg/L, while the MDL of ECH is 0.11mg/L, as shown in Table 4.

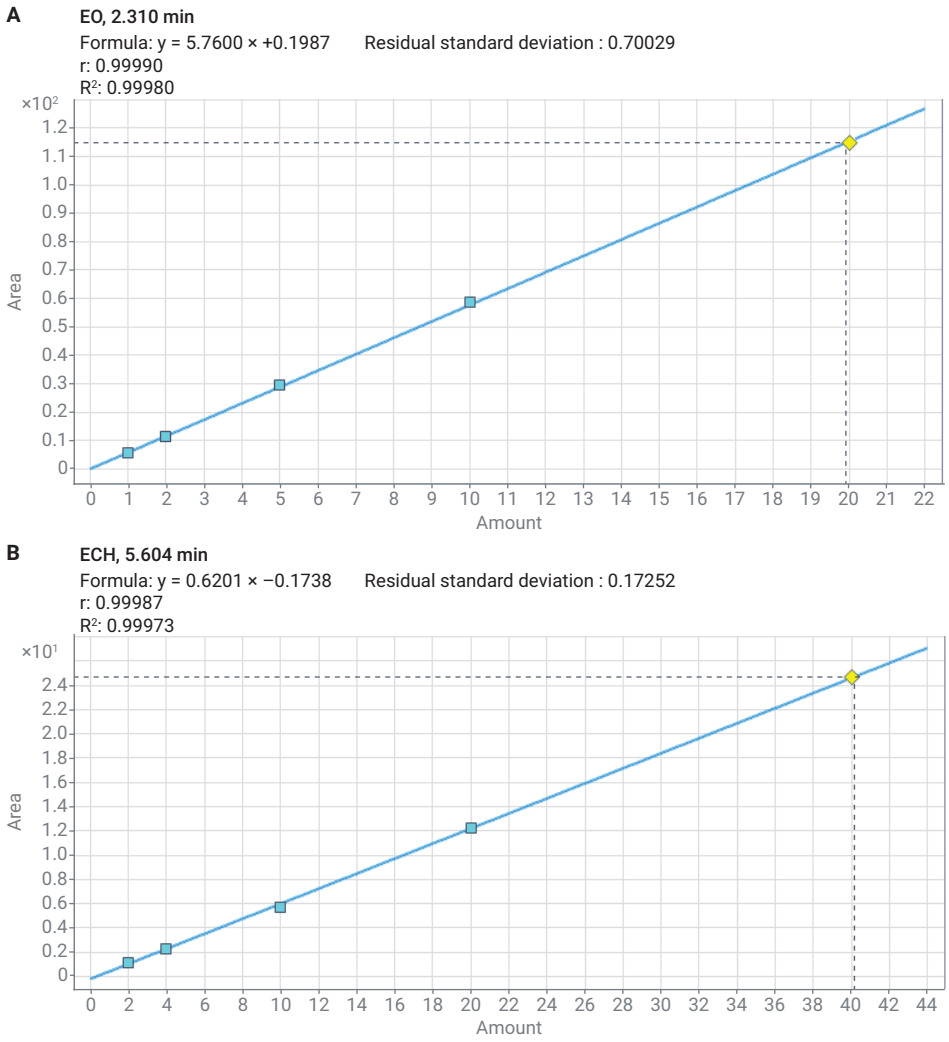

Figure 2. (A) Calibration of EO from 1 to 20 mg/L. (B) Calibration of ECH from 2 to 40 mg/L.

Table 3. Retention time (RT) and area precision of eight consecutive injections at a concentration of 2 mg/L for EO and 4 mg/L for ECH.

	EO		ECH	
Injections	RT (min)	Area	RT (min)	Area
1	2.308	11.263	5.601	2.227
2	2.308	11.807	5.601	2.358
3	2.308	11.612	5.601	2.329
4	2.309	12.13	5.601	2.269
5	2.309	12.342	5.601	2.228
6	2.309	12.054	5.601	2.358
7	2.309	11.608	5.601	2.311
8	2.309	12.482	5.602	2.348
Mean	2.309	11.912	5.601	2.303
SD	0	0.413	0.001	0.055
RSD	0.014	3.463	0.009	2.384

Table 4. The results of linearity and MDL for EO and ECH.

No.	Name	RT	CF R^2	MDL (mg/L)
1	EO	2.308	0.9998	0.013
2	ECH	5.601	0.9997	0.11

Conclusion

This application brief demonstrates the capability of the 8890 GC and 7697A headspace sampler system to analyze EO and ECH simultaneously. Excellent sensitivity, repeatability, and linearity are shown, illustrating the robust and reproducible performance of the system. Correlation coefficients were found to be better than 0.999. EO and ECH yielded area RSDs of 3.5% or better for eight replicate vials. The MDL of EO and ECH is 0.013 mg/L and 0.11 mg/L, respectively.

References

1. ISO 10993-7:2008 Part 7: EO sterilization residuals.
2. GB/T 16886.7-2001 Part 7: Ethylene oxide sterilization residuals (ISO 10993-7: 2008, IDT)
3. GB 19083-2010 specifies the technical requirements for protective face mask for medical use.
4. GB 19082-2009 Technical requirements for single-use protective clothing for medical use.
5. GB/T 14233.1-2008 Test method for infusion, transfusion, injection equipment for medical use – Part 1: Chemical analysis methods.

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DE.5752199074

Printed in the USA, July 30, 2020
5994-2183EN

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