APPLICATION NOTE

Gas Chromatography

Authors:

Kira. Yang

Yong. Xu

Feixiang. Shen

PerkinElmer, Inc.
Shanghai, PRC

Rapid Analysis of Residual Ethylene Oxide (EO) in Drug Packaging Materials by HS-GC/FID

Introduction

Ethylene oxide (EO) is a highly reactive, toxic and flammable gas which can act as an irritant to humans at room temperature. Since the 1950s, EO has been utilized for the sterilization of medical instruments that cannot be exposed to moisture or high temperatures, including those made of polymers, plastics or those containing electronic components. Although the EO method ensures medical instruments can be sterilized without the deleterious effects of high-temperature sterilization, potentially dangerous side effects are possible, namely owing to the hazardous nature of the chemical. The lethality of EO is driven by an alkylation reaction with DNA, which also accounts for its cancer-causing activity.

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To ensure the safety of medical supplies sterilized with EO, two voluntary consensus standards (ANSI/AAMI/ISO 11135:2014 and ANSI/AAMI/ISO 10993-7:2008(R)2012) were developed to perform the validation of the sterility of the medical supplies sterilized with EO, as well as determine acceptable levels of residual EO left on a product after it has undergone sterilization. According to the standards, the maximum EO dose shall not exceed 4 mg in the first 24 hours for permanent contact supplies and prolonged exposure supplies. The average daily dose of EO to patients shall not exceed 4 mg for limited exposure supplies, 2 mg per day for prolonged exposure supplies, and 0.1 mg per day for permanent contact supplies.

In this application note, a rapid analytical method for the determination of EO in medical supplies was established using a PerkinElmer Clarus® GC/FID with the TurboMatrix™ HS-40. Empower® software was utilized throughout the entire experiment. This method demonstrates results with high efficiency, good linearity, sensitivity and repeatability for EO analysis.

Experimental

Sample Preparation and Extraction

An EO standard was obtained from ANPEL Laboratory Technologies (Shanghai) Inc., and the pure water utilized in the experiment was produced by Millipore Mini-Q. The sample utilized in this experiment is a drug packaging material.

The sample preparation procedure used is as follows:

1. Cut product sample into 5 mm pieces.
2. Weigh approximately 1 g of sample, and place it in a headspace vial.
3. Transfer 5 mL of pure water into the headspace vial.

Method precision was investigated with six injections of the level three standard (Table 1). Reporting limits were determined by analyzing the level one standard.

Table 1. Calibration points employed in this study.

Compound Name	Level 1	Level 2	Level 3	Level 4	Level 5
EO (ppm)	1	5	10	20	50

Instrumentation

A PerkinElmer Clarus GC/FID and TurboMatrix HS-40 were used to perform these experiments, with detailed conditions presented in Table 2. This system ensures that the sample preparation process is very simple, and that non-volatile material doesn't enter the analytical system, thus preventing contamination. A PerkinElmer Elite-624 column (60 m x 0.25 mm x 1.4 µm) was used to separate the eluting compounds. This thick-film column and low original oven temperature provided sufficient retention for EO.

Calibration

The calibration curve was prepared by dissolving the appropriate EO standard, respectively, in 5 mL of pure water (Table 1). Each calibration standard was transferred to a separate headspace vial. All vials were sealed immediately with the PTFE side of the septum facing toward the sample.

Results and Discussion

The chromatogram of a calibration standard is shown in Figure 1. Benefited by the fastest available GC cool-down rate, an initial temperature of 35 °C was used to obtain better peak profile and sensitivity for ethylene oxide. The overlapping thermostatting function of the TurboMatrix HS-40 substantially decreases overall run time, while boosting productivity. Table 3 summarizes the results for retention time (RT), method dynamic range and signal to noise (S/N) at the reporting limit. The calibration curves were plotted as the peak area versus the amount of analyte. The coefficient of determination (r^2) was 0.9999, showing the reliability of the analysis in the range of 1-50 ppm (Figure 2). Area repeatability measured by the relative standard deviation (RSD) was found to be 0.60%. Retention time precision was calculated and found to be 0.02%, showing the tremendous stability of the method.

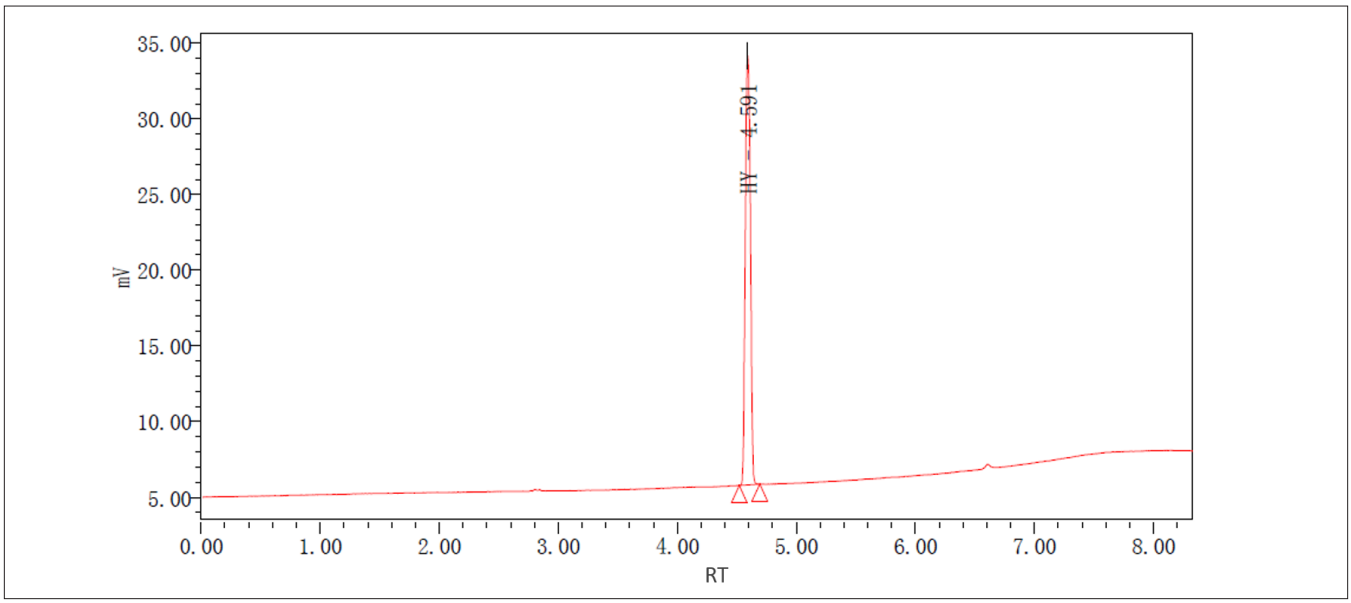

Figure1. The chromatogram of a calibration standard (level 5).

Table 2. Analytical parameters.

HS Parameters	
Needle Temperature	115 °C
Transfer Line Temperature	120 °C
Oven Temperature	60 °C
Thermostatting Time	40 min
Pressurization Time	1 min
Injection Time	0.06 min
Outlet Split	OFF
Column Pressure	25 psi
Vial Pressure	25 psi
Option Mode	Constant
GC Parameters	
Headspace Connector	Split Mode Connection
Inlet Temp	200 °C
GC Injector	PSSI with a 2 mm ID Siltek Deactivated Glass Liner
Carrier Gas	Helium
Carrier Gas Flow Rate	2.0 ml/min
Split Ratio	5:1
Initial Oven Temp	35 °C
Oven Hold	3 min
Ramp	15 °C/min to 100 °C
Oven Hold	1 min
FID Temperature	250 °C
H_2	40 mL/min
Air	400 mL/min

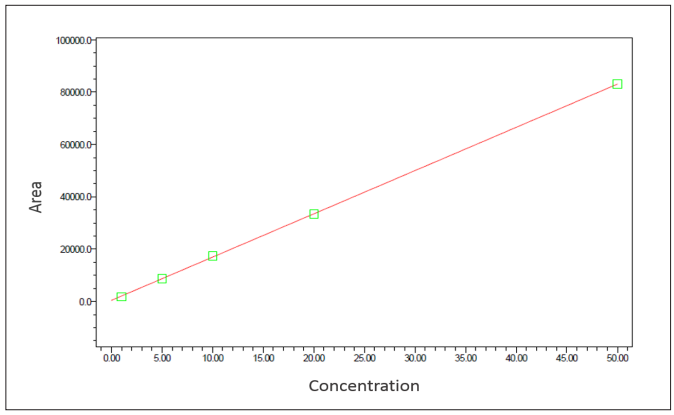

Figure 2. The EO calibration curve.

Summary

The results obtained in this experiment demonstrate the ability of the PerkinElmer Clarus GC/FID and TurboMatrix HS-40 to efficiently quantify ethylene oxide in medical supplies. The methodology has shown good performance with excellent linearity, repeatability and sensitivity, thus satisfying the needs of the medical industry.

Table 3. Results for MDL, repeatability and recovery.

Compound name	Retention Tme	Reporting Limit (S/N at level 1)	Repeatability (RSD%)		Linearity (1 – 50 ppm)		
			RT	Area	Slope	Intercept	r^2
EO	4.59	24.73	0.02	0.60	421.5	1653.6	0.9999

PerkinElmer, Inc.
940 Winter Street
Waltham, MA 02451 USA
P: (800) 762-4000 or
(+1) 203-925-4602
www.perkinelmer.com

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