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Laboratory and field validations of a solid-phase microextraction device for the determination of ethylene oxide

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Abstract

Laboratory and field evaluations were performed to validate a solid-phase microextraction (SPME) device that was used as a diffusive sampler. Hydrogen bromide (HBr) was loaded onto the carboxen–polydimethylsiloxane (CAR–PDMS) fiber for the determination of ethylene oxide (EtO) with on-fiber derivatization. For laboratory evaluations, known concentrations of ethylene oxide around the threshold limit values (TLV)/time-weighted average and specific relative humidities (RHs) were generated by syringe pumps in a dynamic generation system. The SPME diffusive samplers and the commercially available 3M 3551 passive monitors were placed side-by-side in an exposure chamber which was designed to allow measurement of face velocities, temperatures, exposing vapor concentrations, and RHs. Field validations with both SPME diffusive sampler and 3M 3551 passive monitors were also performed. The correlations between the results from both SPME device and 3M 3551 passive monitor were found to be linear ($r > 0.9699$) and consistent (slope $\cong 1.12 \pm 0.07$). However, the variations of diffusion coefficients at different temperatures needs to be considered and the adjustment of sampling constant was a must when sampling at temperatures different from 25 °C.

Keywords: Sample preparation; Air analysis; Environmental analysis; Instrumentation; Ethylene oxide; Hydrogen bromide

1. Introduction

Ethylene oxide (EtO; C_2H_4O; epoxyethane; oxirane) is a colorless gas at room temperature with an ether-like odor at concentrations above 895–1253 mg m^{-3} [1]. According to the US Environmental Protection Agency (EPA), EtO is among the top 3% of high-volume chemicals produced in the USA [2]. Ethylene oxide is processed in various applications, for example, in the production of ethylene glycol, or as the starting material for the manufacturing of acrylonitrile and nonionic surfactants [3]. The US National Institute for Occupational Safety and Health (NIOSH) estimated that 270,000 workers in the USA are potentially exposed to ethylene oxide, with the largest concentration being in the health care industry [4]. Exposure to EtO has been reported predominantly on workers occupied in sterilization units [5]. EtO irritates the eyes and skin; it may also cause allergies, adverse reproductive effects, and possibly asthma [1]. EtO is also a known human carcinogen and a potential reproductive hazard [6]. The US Occupational Safety and Health Administration (OSHA) promulgated ethylene oxide health standard with a work-shift 1.79 mg m^{-3} permissible exposure limit and 0.895 mg m^{-3} action level in 1984 [7] and revised in 1988 to add a 8.95 mg m^{-3} short-term excursion limit [8] while the American Conference for Governmental Industrial Hygienists (ACGIH) has set up a threshold limit value (TLV) of 1.79 mg m^{-3} EtO for workplace air [9].

For the exposure assessment of ethylene oxide, many air sampling and analysis methods have been developed. For example, charcoal tube was used for sampling and carbon disulfide was used for desorbing EtO [10], acid bubbler filled with ethylene glycol was used for sampling and followed by colorimetric analysis [11], and Ambersorb XE347 coated hydrobromic acid (HBr) was used to collect EtO as 2-bromoethanol [12]. Besides these, a hydrobromic acid-coated charcoal tube method was recommended by both OSHA and the US National Institute for Occupational Safety and Health where the reaction of EtO with HBr to produce 2-bromoethanol is utilized [13,14]. A commercially available 3M 3551 passive monitor which was

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recommended by OSHA as Organic Method No. 49 also utilizes the reaction of EtO with HBr [15].

However, all the methods mentioned above involve complex procedures for sample preparations (solvent desorption, for example) and therefore are very time-consuming. In recent years, a new extraction technique called solid-phase microextraction (SPME) has been developed by Pawliszyn [16,17]. SPME presents many advantages over conventional analytical methods by combining sampling, preconcentration, and direct transfer of the analytes into a standard gas chromatograph [18]. The air sampling and analysis methods with SPME have been applied to time-weighted average (TWA) sampling [19,20]. TWA passive sampling with a SPME device was shown to be almost independent of face velocity, pressure, and relative humidity (RH) [20]. The diffusive sampling with the SPME device has an advantage over other methods because no pumps and solvents are required which reduces the sampling costs and the time for sample analysis. A user-friendly SPME diffusive sampling device has recently also been reported for the analysis of ethylene oxide where HBr was first loaded onto the SPME fiber and direct 2-bromoethanol analysis was performed to determine the amounts of EtO collected [21]. Methodical optimizations with respect to the fiber material used, the HBr coating time, and the desorption time for 2-bromoethanol were all determined [21]. However, more studies were still required, such as measurements in real environments. The research shown here details the information regarding the validations of the new designed SPME diffusive sampler [21] where side-by-side comparisons between the SPME device and the OSHA approved 3M 3551 passive monitor were performed in the laboratory as well as in the field.

2. Experimental

2.1. Materials

Ethylene oxide, 50,000 μg cm^{-3} in methanol, was purchased from Supelco (Bellefonte, PA, USA). Methanol and 2-bromoethanol were purchased from Sigma–Aldrich. Dichloromethane was from Wako (Osaka, Japan). Hydrogen bromide, 48% (w/w) aqueous solution, was from Lancaster (Eastgate, White Lund, Morecambe, UK). Helium for GC–MS was 99.999% purity from Sanfu, Taiwan. A Harvard syringe pump (model 11), rotameters, and Tedlar gas bags were from Fisher Scientific (Tustin, CA, USA). 3M 3551 ethylene oxide monitors with the sampling constant of 49.3 cm^3 min^{-1} were from 3M (St. Paul, MN, USA). A Whatman Zero Air generator was from Balston (Haverhill, MA, USA) and was used to provide the air for a standard gas generation system. A M-5 Mini-Buck Calibrator for air flow rate calibrations was from Buck Scientific (East Norwalk, CT, USA). A calibrated hot-wire anemometer used to monitor face velocity was from Kanamox Instrument Co., Japan. All SPME fibers, holders and molecular sieve were from Supelco. All retracted fiber path length and surface area were measured by inserting a steel tube that had an outer diameter equal to the needle tube inner diameter, then measuring the depth and outer diameter of the inserted tube.

2.2. Instrumentation

All analyses were performed on a Perkin-Elmer Autosystem XL chromatograph equipped with a 30 m × 0.25 mm i.d. 0.25 μm film DB-225 chemically bonded fused-silica capillary column (J&W Scientific, Folsom, CA, USA) linked with the 70 eV electron impaction source of a Perkin-Elmer Turbo mass spectrometer. The carrier gas was helium with flow rate of 1.0 ± 0.1 cm^3 min^{-1} in the 1:4 split mode. The temperature for the injector was 250 °C. The column temperature program was: 60 °C for 3 min, 60–180 °C at 25 °C/min, and hold for 1 min. The temperature of the ion source was 220 °C. A Hamilton 10 mm^3 syringe from Fisher Scientific (Tustin, CA, USA) was used for the injection of 1 mm^3 standard solutions to determine the detector's response factors.

2.3. Sampling

2.3.1. Theory

By retracting the coated fiber into its needle housing during the sampling, the SPME device can be used as a TWA diffusive sampler and the theory has been reported elsewhere [17]. Fick's first law of diffusion is used to model steady-state mass transport through the sampler and to determine the amount of analyte loaded on the fiber coating. The sampling rate (SR) of the sampler can be defined as follows [22]:

$$\mathrm{SR} = D_{\mathrm{AB}} \left(\frac{A}{Z} \right) \quad (1)$$

where SR is sampling rate (cm^3 min^{-1}); Z the retracted fiber path length (cm); A the surface area of the needle opening (cm^2); D_{AB} the diffusion coefficient of the analyte in the gaseous phase (cm^2 min^{-1}).

As shown in Fig. 1, a modified SPME device was used in this research where the SPME fiber was retracted 3 mm into its needle housing. The SPME fiber assembly was inserted into an 11 cm length PTFE tubing (0.48 cm i.d. × 0.64 cm o.d.). The needle was fixed by a PTFE septum and the tubing was capped by two caps lined with PTFE tape to avoid contamination. As reported previously [21], the path length (Z) of the sampler was 0.3 cm, the surface area was 0.00086 cm^2, the theoretical diffusion coefficient of EtO at 25 °C was 9.30 cm^2 min^{-1} and the sampling rate of the sampler for EtO was estimated to be 2.67 × 10^{-2} cm^3 min^{-1}.

As mentioned above, the sampling constant of the 3M 3551 ethylene oxide monitor was 49.3 cm^3 min^{-1}. It was clear that the great differences in dimensions of these two samplers, i.e. tube-type versus badge type, caused the discrepancy between their uptake rates.

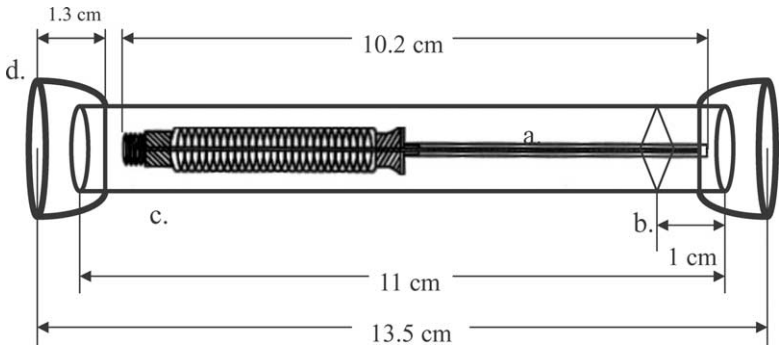

Fig. 1. Perspective view of the passive sampler: (a) SPME fiber assembly, (b) PTFE septum, (c) PTFE tubing, (d) cap/PTFE tape.

2.3.2. Trapping element of the SPME diffusive sampler

Carboxen–polydimethylsiloxane (CAR–PDMS) fiber was selected because it could provide the highest loading and stability of HBr and 2-bromoethanol retention characteristics [21]. For the trapping element preparation, HBr aqueous solution with concentration of 48% (w/w) was placed in a 4 ml PTFE-capped vial with 1 cm stir bar. The solution was stirred at 1100 rpm and the CAR–PDMS fiber was placed in the headspace of the HBr solution for 30 s. After loading with HBr, the SPME fiber was retracted 3 mm into its needle housing and the designed passive sampler was then assembled as mentioned above.

2.3.3. Laboratory validations

Previous laboratory validations have shown that face velocity (0–0.25 m s^{-1}) as well as relative humidities (10–80%) were not expected to have effects on the designed SPME diffusive sampler for EtO [21]. In this research, the effects of different temperatures including 4, 25 and 35 °C were further determined by the gas bag method [21]. To simulate the exposure at 4 °C, the air bag was kept in a refrigerator with the SPME fiber directly inserted into it. For the evaluation at 25 °C, the SPME fiber was inserted into the air bag and stayed still on the lab bench without any movement. For the experiment at 35 °C, the air bag was kept in a laboratory incubator with the SPME fiber also directly inserted into it. For all three temperatures tested, air bags of EtO with concentration equaled 14.38 mg m^{-3} (equivalent to eight times TLV-TWA) and relative humidities of 10 ± 2% were prepared. The samplers were exposed in the air bags for 10–120 min, respectively, and all the experiments were performed in triplicates.

The side-by-side comparisons between the SPME device and the 3M 3551 passive sampler in the laboratory were also performed in this research. The dynamic vapor generation system detailed elsewhere [21] (including vapor generator, air dilution system, and exposure chamber) was used for the evaluation. In brief, the exposure chamber was made by a glass cylindrical vessel (45 cm × 11 cm i.d. × 12 cm o.d.) and a fan was connected to a variac which allowed different fan blade velocities and hence face velocities, as well as adequate mixing. EtO of 0.89, 1.79, 3.58 and 17.9 mg m^{-3} (equivalent to 0.5, 1, 2 and 10 times TLV-TWA) were prepared by the dynamic system, respectively. For each EtO concentration, four SPME diffusive samplers as well as four 3M 3551 ethylene oxide passive monitors were inserted into the chamber simultaneously and were exposed for 6 h. The relative humidities, temperatures, and face velocities during experiments were 11 ± 2%, 23.8 ± 1.4 °C and 0.26 ± 0.03 m s^{-1}, respectively. The concentrations of EtO from dynamic vapor generation system were monitored periodically by collecting the vapors with gas bags followed by the analysis procedures detailed elsewhere [21].

2.3.4. Field validations

The behavior of the designed SPME diffusive sampler in the real environment was validated in Taichung City, Taiwan at a medical device company where EtO was used for the sterilization. The side-by-side comparisons between the SPME device and the 3M 3551 passive sampler in the medical device company were performed by both personal and area sampling for three successive days. As shown in Fig. 2, both SPME diffusive sampler as well as 3M 3551 passive monitor were clipped on the clothes of the workers around the breathing zones. The sampling time was around 30 min that covered the duration when the medical device needed to be moved out from the chamber after sterilization. For area sampling, the samples were collected at six different locations in the company with the SPME device and the 3M 3551 passive monitor side-by-side placed for 6 h. Temperatures, relative humidities, and wind velocities were also measured during the sampling. For each day, the samples were put in a cooler after sampling, shipped back to the laboratory, and stored in a refrigerator before analysis.

2.4. Sample analysis

For field samples, the analysis was performed right after the samples were shipped back to the laboratory for three successive days. The procedures reported elsewhere were followed for the analysis of samples from the 3M 3551 passive monitors [23]. In brief, the 3M 3551 passive monitor was used to collect ethylene oxide at the sampling constant of 49.3 cm^3 min^{-1} [23]. After sampling, 1.5 cm^3

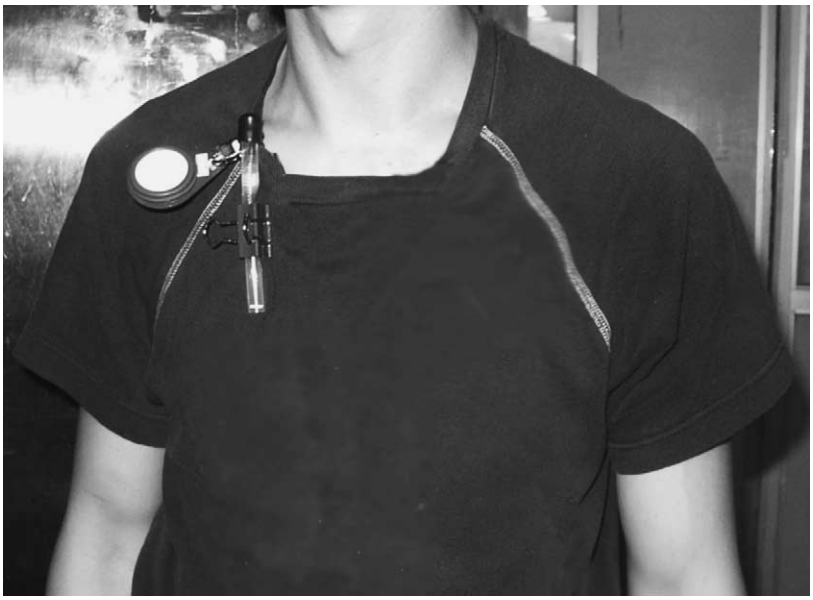

Fig. 2. Side-by-side validations from personal sampling in the fields.

of the desorption solution (10%, v/v, methylene chloride in methanol) was added into each monitor [23]. After 30 min, with occasional gentle agitation, the eluent was decanted into a 4 cm^3 vial and a sample size of 1 mm^3 was injected into the GC–MS system for analysis. For the SPME device, the fiber assembly in the diffusive sampler was removed and assembled with the SPME holder. The needle of the SPME device was then inserted into the GC–MS injector for analysis [21]. To ensure the desorption was complete, the SPME needle was kept in the heated GC injector for 5 min [21]. Chromatographic peak areas and calibration curves obtained through analysis of liquid standards were used for adsorbed 2-bromoethanol quantification.

Compared with 3M 3551 passive monitor where 30 min of desorption with 1.5 cm^3 of 10% (v/v) methylene chloride in methanol was needed, the sample from SPME device was analyzed simply by inserting the needle of the SPME into the GC–MS injector. The cumbersome procedure was omitted obviously.

2.5. Standard 2-bromoethanol solutions in a mixture of methanol and dichloromethane

Standard 2-bromoethanol solutions (3.5–175 $\mu g\,cm^{-3}$) were prepared for GC–MS calibration by dissolving 2-bromoethanol into a mixture of methanol–dichloromethane (9:1, v/v) [21]. Selective ion monitoring utilized *m/z* 31 and 45 while total ion monitoring utilized *m/z* 20–200.

3. Results and discussion

Fig. 3 shows a typical chromatogram and the mass spectrum of a sample from the SPME direct injection with total ion monitoring utilizing *m/z* 20–200. To validate a diffusive sampler, several parameters including face velocity, relative humidity, temperature, shelf life, and sample stability were recommended to be evaluated in the NIOSH protocol [24]. Previous study has shown that face velocity (0–0.25 $m\,s^{-1}$) and RHs (10–80%) were not expected to have effects on the designed SPME diffusive sampler [21]. The recoveries for both shelf life and sample stability were around 100 ± 7% after 7 days storage at 4 °C [21]. In this research, effects of different temperatures were further investigated. By plotting the mass collected versus the magnitude of exposure (in concentration–time units) from the results of laboratory validations [21], the experimental sampling constants of the sampler at 4, 25, and 35 °C were determined to be $(2.37 \pm 0.14) \times 10^{-2}$, $(3.11 \pm 0.08) \times 10^{-2}$, and $(2.94 \pm 0.12) \times 10^{-2}\,cm^3\,min^{-1}$, respectively (from linear regressions). Further statistical analysis on the slopes showed no difference between the sampling constants at 25 and 35 °C ($P \cong 0.45$) while significant differences were observed for the slopes at 4 °C versus 25 and 35 °C ($P \cong 0.007$ and 0.008, respectively).

The changes of diffusion coefficients at different temperatures might explain why the sampling constant was lower at 4 °C. From estimation [25], the theoretical diffusion coefficient at 4 °C for ethylene oxide was 8.16 $cm^2\,min^{-1}$ (around 87% of the diffusion coefficient at 25 °C) while it was 9.90 $cm^2\,min^{-1}$ at 35 °C (around 105% compared to 25 °C). The experimental sampling constant of the SPME device reported previously was $(2.96 \pm 0.09) \times 10^{-2}\,cm^3\,min^{-1}$ at 25 °C [21]. If the variation of diffusion coefficients at different temperatures were considered, the experimental sampling constant at 4 °C was estimated to be $(2.57 \pm 0.08) \times 10^{-2}\,cm^3\,min^{-1}$ (around 87% compared to 25 °C) which showed no statistical difference with what was found in

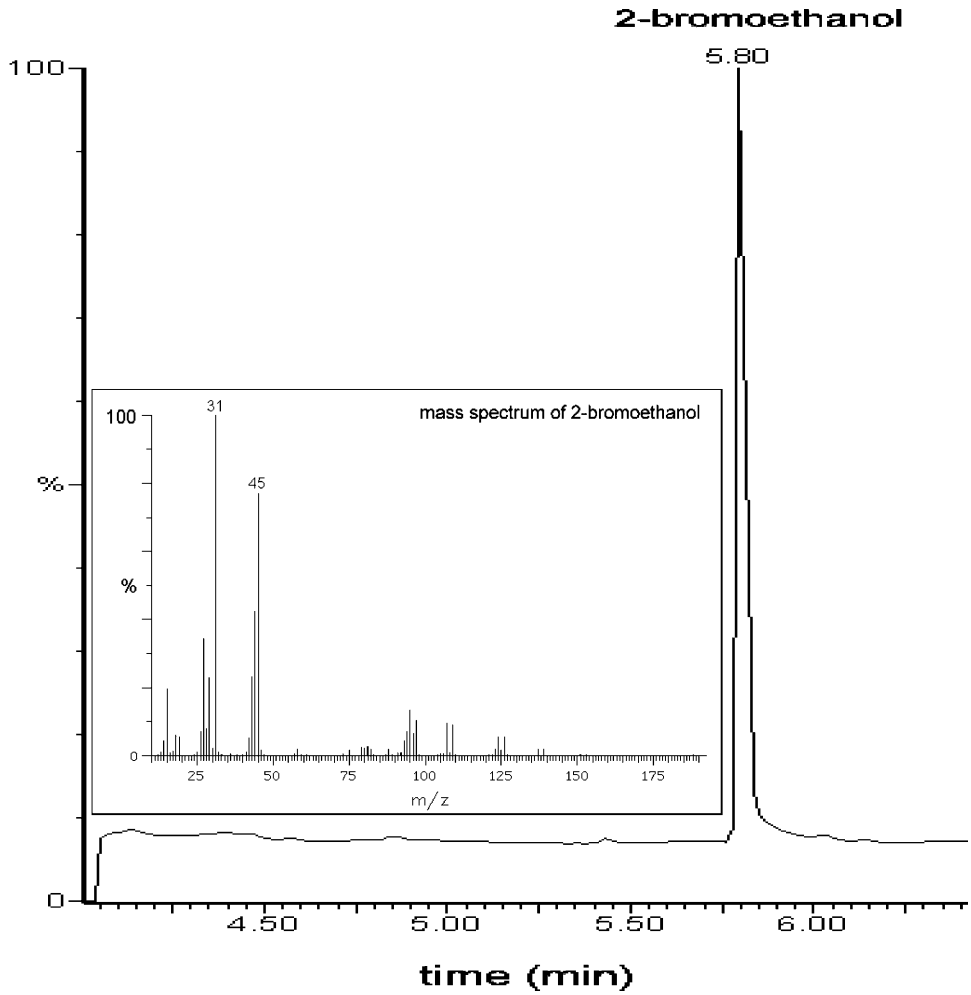

Fig. 3. Chromatogram and mass spectrum of sample injection.

this research ($P \cong 0.11$). On the other hand, the experimental sampling constant at 35 °C was estimated to be $(3.10 \pm 0.09) \times 10^{-2}\,\mathrm{cm^3\,min^{-1}}$ which also showed no statistical difference with what was found in this research ($P \cong 0.14$).

The side-by-side comparisons in the laboratory between the SPME device and the 3M 3551 passive monitor were performed in the study. To calculate the concentrations of EtO that were sampled, $(2.96 \pm 0.09) \times 10^{-2}\,\mathrm{cm^3\,min^{-1}}$ was used as the experimental sampling constant of the SPME device [21] while $49.3\,\mathrm{cm^3\,min^{-1}}$ was used for the 3M monitor [23]. The correlation was linear with $r = 0.9861$ by plotting the results from the 3M 3551 passive monitors versus the results from the SPME devices. The slope is 1.05 ± 0.05 which further suggested that the results from both methods were consistent.

The temperatures and relative humidities during the field validations were 24.5 ± 1.5 °C and 71–80%, respectively. The wind velocities of area samplings were also monitored which showed that the minimum air velocities required for the 3M 3551 passive monitor ($0.076\,\mathrm{m\,s^{-1}}$) [15] and the SPME device (wind velocity had no effects) [21] were both met. For area sampling in the field validations, the correlation was linear with $r = 0.9718$ by plotting the 3 days' results from the 3M 3551 passive monitors versus the results from the SPME devices. The slope is 1.16 ± 0.07 which also suggested that the results from both methods were consistent.

However, when the results of personal and area sampling from the first 2 days were merged together, the correlation ($r = 0.8742$) and consistency (slope $= 2.18 \pm 0.28$) changed. As shown in Fig. 2, the SPME device was originally clipped on the wearer's clothes and was placed in front of the chest. The open-face of the sampler was found very easily to be blocked if the wearer kept moving. This might explain why big variations were observed from the side-by-side personal sampling of the first 2 days. Therefore, the SPME device was placed on the wearer's shoulder at the same side of the 3M 3551 passive monitor to avoid further blocking of the open-face on the third day. When all the data from field validations were merged, except the personal sampling of the first 2 days, the correlation between both methods were linear ($r = 0.9699$) and consistent (slope $= 1.14 \pm 0.07$) again.

4. Conclusions

The research shown here validated the newly designed user-friendly SPME device for the determination of EtO [21]. Both laboratory and field evaluations of the side-by-side comparisons for the SPME device and the 3M 3551 passive monitors were performed. It was shown that the results between the SPME device and the OSHA approved 3M 3551 were linear and consistent. Similar results with good agreement were also observed when the TWA passive sampling with a SPME device was compared with the NIOSH method 1501 for the sampling of volatile organic compounds in the field [20].

A derivatization technique which increased the sample stability and analytical sensitivity was used in this research where simultaneous derivatization and extraction were performed directly on the fiber coating. The designed SPME device could be applied to 1–8 h sampling of ethylene oxide at concentrations equalling 0.5–2 times TLV-TWA as well as only 10–90 min sampling at concentrations equalling eight times the TLV-TWA. Effects of temperatures on the results were not negligible. However, the concentration of EtO could be measured correctly once the variation of diffusion coefficients from different temperatures was considered and the experimental sampling constant was adjusted. On the other hand, special care must be taken to avoid the possible blocking of the open-face when the tube-type SPME diffusive sampler is going to be used.

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References

[1] Preventing Worker Injuries and Deaths from Explosions in Industrial Ethylene Oxide Sterilization Facilities, US Department of Health and Human Services, DHHS (NIOSH) Publication No. 2000–119, 2000.
[2] High Production Volume (HPV) Voluntary Challenge Chemical List, EPA, Office of Pollution Prevention and Toxics, 2001.
[3] S. Budavari (Ed.), The Merck Index, 12th ed., Merck, Whitehouse Station, NJ, 1996.
[4] K. Steenland, L. Stayner, A. Greife, W. Halperin, R. Hayes, R. Hornung, S. Nowlin, New Engl. J. Med. 324 (1991) 1402.
[5] Environmental Health Criteria 55—Ethylene Oxide, World Health Organization, Geneva, 1985.
[6] Ethylene Oxide, IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, vol. 60, Some Industrial Compounds, International Agency for Research on Cancer, World Health Organization, 1994, p. 73.
[7] Occupational Exposure to Ethylene Oxide, Final Standard Federal Register, OSHA, 1984, p. 25734.
[8] Occupational Exposure to Ethylene Oxide, Final Standard Federal Register, OSHA, 1988, p. 11414.
[9] Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices, American Conference of Governmental Industrial Hygienists, Cincinnati, OH, 2000.
[10] A.H. Qazi, N.H. Ketchum, Am. Ind. Hyg. Assoc. J. 38 (1977) 635.
[11] S.J. Romano, J.A. Renner, Am. Ind. Hyg. Assoc. J. 40 (1979) 742.
[12] G.G. Esposito, K. Williams, R. Bongiovanni, Anal. Chem. 56 (1984) 1950.
[13] Organic Method No. 50, OSHA Analytical Laboratory, OSHA, UT, 1985.
[14] Manual of Analytical Methods (NMAM), Method 1614, NIOSH, fourth ed., 1994.
[15] Organic Method No. 49, OSHA Analytical Laboratory, OSHA, UT, 1984.
[16] J. Pawliszyn, Solid-Phase Microextraction—Theory and Practice, Wiley–VCH, New York, 1997.
[17] J. Pawliszyn (Ed.), Applications of Solid Phase Microextraction, Royal Society of Chemistry, Cambridge, 1999.
[18] J.A. Koziel, J. Pawliszyn, J. Air Waste Manage. Assoc. 51 (2001) 173.
[19] P.A. Martos, J. Pawliszyn, Anal. Chem. 71 (1999) 1513.
[20] Y. Chen, J. Pawliszyn, Anal. Chem. 75 (2003) 2004.
[21] S.W. Tsai, K.K. Wu, J. Chromatogr. A 991 (2003) 1.
[22] A. Khaled, J. Pawliszyn, J. Chromatogr. A 892 (2000) 455.
[23] Determination of Ethylene Oxide in Air Using 3M 3550/3551 Ethylene Oxide Monitors, Occupational Health & Environmental Safety Division, 3M Company, St. Paul, MN, 1997.
[24] M.E. Cassinelli, R.D. Hull, J.V. Crable, Diffusive Sampling: An Alternative Approach to Workplace Air Sampling, Royal Society of Chemistry, London, 1987, p. 190.
[25] R.C. Reid, J.M. Prausnitz, B.E. Poling (Eds.), The Properties of Gases and Liquids, fourth ed., McGraw-Hill, New York, 1988, p. 586.