Evaluation of Passive Sampler for Measurement of Glutaraldehyde in Occupational Indoor Air

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(Received January 24, 2005; Accepted September 14, 2005; Published online September 27, 2005)

Glutaraldehyde has been in widespread use in hospitals to sterilize instruments. Routine exposure to glutaraldehyde is, however, known to cause adverse health effects. Authors have applied and evaluated a passive sampler (DSD-DNPH) for the determination of glutaraldehyde in air at ppb level. The sampler consists of porous polyethylene tube uniformly packed with 2,4-dinitrophenylhydrazine (DNPH) coated silica gel as a reactive adsorbent. The sampling duration of this device was designed for 8 hr to apply to field measurements in workplace. After sampling, DNPH derivatives were eluted by acetonitrile and subsequently determined by HPLC. A sampling rate of the sampler was determined by chamber experiments and resulted in 40 ml/min for glutaraldehyde. Effects of temperature and humidity on the rate were not apparent. No significant effect of exposure time, air concentration and back diffusion on the sampling performance was suggested by dynamic adsorption model. The sampling rate was then validated in field measurements comparing with a previous active sampling. The diffusion sampler was successfully used for determination of 4–180 ppb of glutaraldehyde and gave similar results to active sampling in indoor air. Limit of quantitation (LOQ) of the diffusion sampler resulted in 3.9 ppb for 8-hr exposure in air.

Key words ——— glutaraldehyde, passive sampler, sampling rate, indoor air quality

INTRODUCTION

Glutaraldehyde has been in widespread use in hospitals to sterilize instruments which are not suitable for heat sterilization. Routine exposure to glutaraldehyde is, however, known to cause adverse health effects such as eye irritation, sore throats, skin irritations, dermatitis, short-term memory loss and fatigue, especially for workers in endoscopy, dentistry and other medical departments within hospitals.[1)] The American Conference of Government Industrial Hygienists (ACGIH) has set ceiling exposure limit (TLV-C) for glutaraldehyde in workplace atmosphere to be 0.05 ppm. In the U.K., Maximum Exposure Limit (MEL) has been set at 0.05 ppm for both long-term (8 hr) and short-term (15 min) exposure as an occupational exposure limit. In February 2005, the Ministry of Health, Labour and Welfare of Japan has given a notice on the glutaraldehyde usage, in which the monitoring of indoor concentrations of glutaraldehyde is encouraged in sterilization workplaces, and the maximum concentration of 0.05 ppm is recommended.[2)]

A solid adsorbent coated with 2,4-dinitrophenylhydrazine (DNPH) was previously used and evaluated for the determination of glutaraldehyde in air: DNPH-impregnated glass fiber filters,[3,4)] DNPH coated XAD-2[5)] and DNPH coated silica gel.[4,6,7)] DNPH-glutaraldehyde derivatives formed when the aldehyde is pumped over the collection media is desorbed by adding acetonitrile and subsequently determined by high performance liquid chromatography (HPLC). Such active sampling methods were also employed as a reference method for evaluating sampling performance of passive samplers developed for monitoring personal exposure and indoor air concentrations.

Passive samplers, which employ diffusion process based on Fick's law and hence do not require power supply or other services, are suitable for monitoring personal or indoor exposure concentrations of glutaraldehyde in the occupational environment.

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Then, authors have applied and evaluated a previous passive diffusion sampler for aldehydes and ketones (DSD-DNPH)[8,9] for the determination of glutaraldehyde in air at ppb level. The sampler is capable of taking samples of glutaraldehyde gas from the atmosphere at a rate controlled by porous polyethylene tube. In the tube DNPH coated silica gel is uniformly packed as a reactive adsorbent. Glutaraldehyde permeating through the tube is deposited on the adsorbent surface and collected as DNPH derivatives. The sampling duration of this device was set for 8 hr to apply to field measurements in workplace.

Using such passive samplers, sampling rate, α is a dominant factor for analytical liability. As shown in Eq. (1), collected amount of glutaraldehyde on adsorbent, *W* could be converted to air concentration, *C* using exposure time, *t* and α, if the adsorbent reduces the concentration of the given analyte at the end of diffusion layer ideally to zero due to sorption or chemical reaction.[10]

$$C = \frac{W}{\alpha t} \quad (1)$$

The Occupational Safety and Health Administration (OSHA) has previously determined the sampling rate of the DSD-DNPH in a test chamber containing 0.02 or 0.2 ppm of glutaraldehyde vapor.[11] However, the sampling rate should be determined in the wide range of air concentrations by establishing relationship between *C* and *W*, because the performance of the adsorbent could affect on the relationship when showing non-ideal behavior (the concentration at the end of diffusion layer, *i.e.* at the surface of the adsorbent is not zero). Furthermore, the rate should be also evaluated in the field where the sampler is practically applied, because the chamber atmosphere does not always reproduce the workplace atmosphere.

In this study, the sampling rate of the DSD-DNPH against glutaraldehyde was determined in a test chamber by establishing relationship between *C* and *W*, and then evaluated in field tests.

MATERIALS AND METHODS

Passive sampler used in this study, DSD-DNPH is commercially available from Supelco, Japan. The sampler consists of three parts: porous polyethylene (PE) tube, reservoir made of PE tube and DNPH coated silica gel (Fig. 1). The porous tube is made

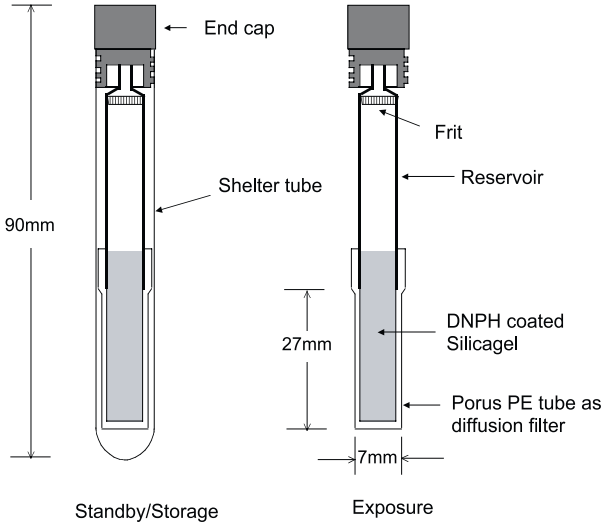

Fig. 1. Schematic View of the DSD-DNPH

of sintered PE particles with 34.5% of porosity and work as a diffusion filter. Amount of impregnated DNPH is 1 mg per sampler.

The sampling rate was investigated using a small chamber (32 l) with a constant gas generation system under controlled temperature. Diffusion samplers were hanged at the center of top of the chamber inside, and glutaraldehyde gas was constantly introduced from a gas generator[12] at a flow rate of 4 l/min (air exchange rate = 7.5/hr). A fan thoroughly mixed the air in the chamber. As a reference to passive sampler, active sampling was simultaneously carried out by pulling air through DNPH coated solid cartridge (Supelco, Tokyo, Japan, LpDNPH) connected with air pump (Shibata Science., Tokyo, Japan, MP-Σ30) at a flow rate of 0.3 l/min for 8 hr. The collection efficiency of the single cartridge was 100% under given sampling condition.

To evaluate the sampling rate determined, field tests were conducted at two sites. At first, a model laboratory in Tokai University was used. The dimension of the room was approximately 7.9 (length) × 3.0 (width) × 3.8 m (height). About 1 l of 3%(w/v) glutaraldehyde solution, generally used for sterilizer (Maruishi Pharmaceutical, Tokyo, Japan, Steriscope®) was poured in a plastic bucket (32 × 25 × 11.5 cm) and set on a self-standing chair 90 cm above from the floor. Sampling condition was static except when a fan thoroughly mixed the air resulting in approximately 0.1 m/sec of wind speed at the surface of the passive sampler. Air ventilation system was not operated during the samplings. Secondary, the simultaneous measurements were conducted

in a dental clinic located in Kanagawa, Japan, where the glutaraldehyde solution is normally employed for sterilizing tools and equipments. The sterilizer was stand in a plastic bucket (32 × 25 × 11.5 cm) loosely covered by a plastic cover at the side of the examination room. Measurements were carried out in July 2003 and January 2004, on the days the clinic was closed. Therefore, sampling condition was static (wind speed: < 0.01 m/sec). Sampling duration was set at 8 hr.

After sampling, the adsorbent of the passive sampler was placed in the reservoir tube. DNPH derivatives were eluted by passing 10 ml of acetonitrile in 5 min, and determined by HPLC. The HPLC system consists of Shimadzu LC-6A pump with SPD-6A UV-visible (Vis) detector. The following conditions were used: column, 4.6 × 150 mm, 5 μm, Inertsil ODS-80A (GL sciences); eluent, 60/40 acetonitrile/distilled water at 1.5 ml/min (isocratic); detection, 360 nm; Injection volume, 20 μl. Diluted DNPH-glutaraldehyde (0.1 mg/ml in acetonitrile, Supelco) was used as analytical standard. Duplicate injections were made for standards, samples and blanks. Analytical procedure of active samplers followed described here.

RESULTS AND DISCUSSION

HPLC Analysis

HPLC analysis of the DNPH coated silica gel yields the number of moles of DNPH-glutaraldehyde derivative and hence the number of moles of glutaraldehyde collected on the adsorbent. Glutaraldehyde reacts with DNPH and gives possible three geometric isomers of hydrazone: *E,E*, *E,Z* and *Z,Z*. However, two peaks were seen in the HPLC chromatogram obtained for standard and sample solutions as previously reported by Levin *et al.*[13] The two peaks may correspond to *E,E* and *E,Z*, deducing from the predominant formation of those isomers in the reactions between glutaraldehyde and DNPH solution.[14,15] The ratios between major and minor peak areas were not constant: 5.2 ± 0.14 in the standard solution (0.05–0.15 μg/ml, n = 4), 3.2 ± 0.23 in eluted solutions from active samplers (n = 16) and 3.4 ± 0.25 in eluted solutions of passive sampler (n = 16) collected at chamber and field measurements. The absorption coefficients of those isomers at the detection wavelength may be slight different. However, separate determination is impossible because there are no standard reagents of each isomer. Therefore, we added up the two peaks for calibration and determination, following the way of Levin *et al.*[13]

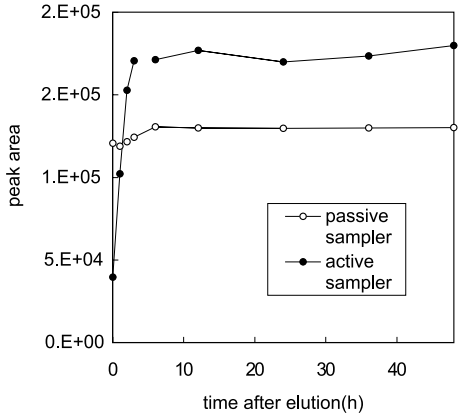

Fig. 2. Variations of Peak Areas after Elution of Glutaraldehyde-DNPH Derivatives from the Passive and Active Sampler
Eluted solutions were stand at 25°C.

Coefficient of variations for repeated injections of 1 μg/ml of standard solution were 2.3% in peak area and 1.1% in retention time (n = 4).

It had been known that peak area varied with time because of unstable properties of DNPH derivatives of certain carbonyl compounds after elution.[16] Then, just after passive and active sampling in the chamber, DNPH derivatives were immediately eluted and time-series analysis were made for both samplers. As shown in Fig. 2, for example, the peak response of the active sampler gradually increased and became constant by 3 hr after elution (the sample solution was stored at 25°C). However, such an increase was not found for the passive sampler. This suggests that the active sampler or sample solution should be stand at least 3 hr at room temperature before analysis.

Sampling Rate

Sampling rate of the sampler was determined by chamber experiments. As air concentration, C can be described in volume basis (ppm) or mass basis (mg/m^3), the rates were expressed as follows.

$$\alpha_v(\mu\text{g/ppm/hr}) = \frac{W(\mu\text{g})}{C(\text{ppm})t(\text{hr})} \quad (2)$$

$$\alpha_w[\mu\text{g}/(\text{mg/m}^3)/\text{hr}] = \frac{W(\mu\text{g})}{C(\text{mg/m}^3)t(\text{hr})} \quad (3)$$

These expressions are useful when the collection amount of glutaraldehyde will be converted to ambient air concentration.

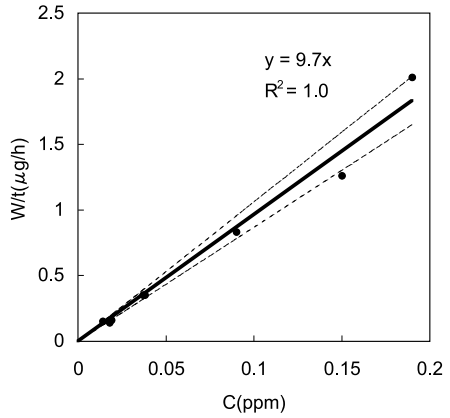

Fig. 3. Scatter Diagram between Air Concentration, *C* and Collection Amount of Glutaraldehyde per hour, *W*/*t* (Chamber Experiment, 25°C, r.h. 35–71%, *n* = 8)

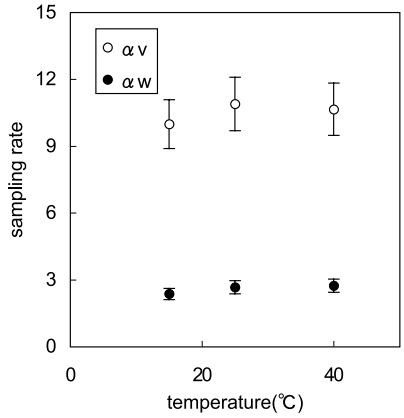

Fig. 4. Derived Sampling Rates Plotted against Temperature
Bars show standard deviations of measurements of triplicate samples.

Figure 3 shows relationship between air concentration, *C* (ppm) measured by the active sampling method and collected amount of glutaraldehyde per hour, *W*/*t* by the passive sampler at 25°C. Even though the simultaneous exposure tests were conducted with varying relative humidity from 35 to 71%, the collected amounts of glutaraldehyde by passive samplers showed good linearity against air concentrations in the chamber. This means sampling rate of glutaraldehyde was constant under the condition and independent on the relative humidity. By adapting Eq. (2) to this relationship, the sampling rate of passive sampler can be derived from the slope of a linear regression analysis and resulted in 9.7 ± 0.38 (μg/ppm/hr) for glutaraldehyde. Similarly, the rate resulted in 2.4 ± 0.11 [μg/(mg/m^3)/hr] using mass concentrations. Alternatively, the sampling rate can be written in 40 ml/min, which agrees to the rate determined by OSHA (41 ml/min[11]), and is 6.8 times greater than that of the badge type passive sampler[3] and 9 times greater than that of a cylindrical passive sampler using *o*-(2,3,4,5,6-pentafluorobenzyl) hydroxylamine hydrochloride — TENAX TA pellet as a solid adsorbent.[17]

The sampling rate of this sampler is potentially depends on temperature; diffusion coefficient usually increases to the absolute temperature raised to the 1.66–1.83 power, air concentration varies inversely with absolute temperature according to the ideal gas law, increase in temperature decreases physical adsorption efficiency of the gas molecule, and heterogeneous reaction rate increases exponentially with absolute temperature obeying an Arrhenius law, if the gas molecule could be first trapped on the surface of silica gel and then fixed as DNPH derivatives. Then, temperature tests were performed at 15, 25 and 40°C, which seems to be realized in a hospital atmosphere. Effect of temperature was not apparent on the rates under given conditions as shown in Fig. 4. This tendency was similar to the result of previous study of DSD-DNPH on formaldehyde.[9]

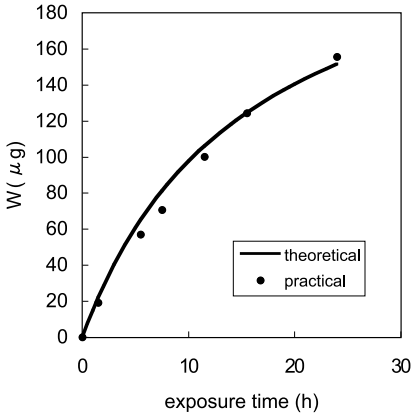

Fig. 5. Relationship between Exposure Time and Collection Amount of Glutaraldehyde by DSD-DNPH (*C* = 2 ppm, 25°C, r.h. 54%)
Theoretical curve was drawn by dynamic adsorption model inputting *s* = 0.8 and *k* = 0.00001.

Dynamic Adsorption Model

Effect of exposure time on the collection amount of glutaraldehyde was investigated. As shown in Fig. 5, time course of collection amount of *W* was not linear with exposure time, *t*. This means sampling rate depends on exposure time and deposition

flux of glutaraldehyde on the adsorbent. Then, change of W with exposure time, t and air concentration, C was described by employing dynamic adsorption model based on Langmuir adsorption theory.[18,19] When sorption of glutaraldehyde on the surfaces of the adsorbent is restricted to uni-molecular layer formation, deposition rate depends on t because the rate of sorption is proportional to the fraction of surface available. This model describes change of W with t on the collection media as follows,

$$\frac{dW(t)}{dt} = sF - \left(\frac{sF}{Q} + k\right) W(t) \tag{4}$$

where s is sticking probability (s = 1; completely fixed, s = 0; reflected), k is desorption rate constant (/hr), Q is saturated sorption amount and F (mg/hr) is mass transfer rate of glutaraldehyde onto the surfaces by diffusion. Thus, $W(t)$ can be given as a function of t.

$$W(t) = \frac{(X+Y)[1-\exp(Yt)]}{Z\left[1-\frac{X+Y}{X-Y}\exp(Yt)\right]} \tag{5}$$

$$X = \frac{2s^2F}{Q} + sk + k \tag{6}$$

$$Y = \sqrt{\frac{4s^2kF}{Q} + k^2(s+1)^2} \tag{7}$$

$$Z = 2\left(\frac{s^2F}{Q^2} + \frac{sk}{Q}\right) \tag{8}$$

Since it is difficult to determine s and k theoretically, these parameters were derived from Fig. 5. Introducing s = 0.8 and k = 0.00001/hr into Eq. (5) with try and error efforts, calculated W showed good agreement to experimental ones, using Q = 250 μg deduced from amount of coated DNPH on the silica gel. The mass transfer rate under the condition was 25 μg/hr approximately calculated from a product of C, D and A/L; D is a diffusion coefficient of glutaraldehyde in air, 0.030 cm^2/sec, A/L is ratio of diffusion cross section and diffusion length of the porous PE filter, 9.7 cm (A/L = 1.53 cm^2/0.157 cm). Then, relationship between t and W/C with different air concentrations was figured out in Fig. 6 using Eq. (5). Even though W/C changed with time, the values were almost constant in the wide variety of air concentration setting the exposure time at 8 hr.

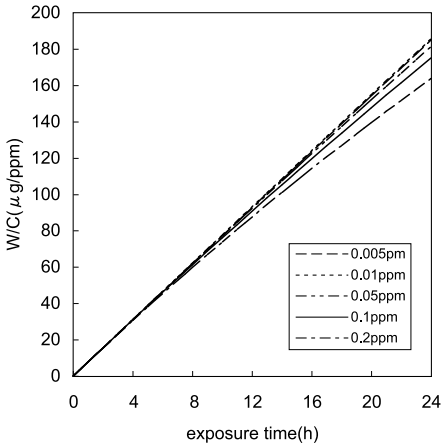

Fig. 6. Effect of Exposure Time and Air Concentration on the W/C, Estimated by Eq. (5) at 25°C

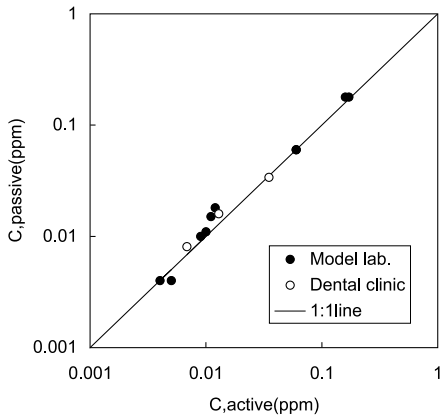

Fig. 7. Scatter Diagram of Field Measured Concentrations between Passive and Active Sampling Methods

This is consistent with the linear relationship between W and C as shown in Fig. 3.

Back diffusion of the analyte is a potential problem in storage of the sampler.[10,20] When taking desorption rate constant, k into consideration, however, the back diffusion will not show significant effects. This is because the reaction between glutaraldehyde and DNPH is irreversible.

Field Evaluation

The sampling rate was then validated in the field measurement. Indoor air concentrations of glutaraldehyde were measured by the passive sampler and co-located active samplers in two fields.

Figure 7 illustrates good agreement of the passive sampler response with that of the active method for the determination of 4–180 ppb of glutaralde-

hyde using the sampling rate derived from the chamber experiment. The results show excellent linearity of the technique and suggest that reasonable accuracy can be expected after establishing the sampling rate under given exposure conditions. The porous PE tube is a good draft shield; previous tests of DSD-DNPH showed the sampling rate for formaldehyde was independent on wind speed between 0.2 to 4 m/sec.[9] Effect of wind speed in the model laboratory was not found on the conversion of collected amount of glutaraldehyde to air concentration.

Quality Assurance

The precision of the passive sampling method was assessed by field quintuplet measurements conducted in the university laboratory. Relative standard deviations (RSD) were 0.78% for 4.0 ppb of air concentration and 0.17% for 180 ppb. Since significant contamination by field handling and during storage was not detected in transport and storage blanks, limit of detection (LOD) of the sampler was defined as 3 times HPLC baseline noise level (S/N = 3) and resulted in 1.2 ppb of glutaraldehyde in air for 8 hr-sampling duration following the analytical procedure described above. Similarly, limit of quantitation (LOQ) was defined as 10 times the noise (S/N = 10) and 3.9 ppb of LOQ was obtained.

Distribution of Glutaraldehyde in Dental Clinic

Based on the results, distribution of indoor concentration was measured by the passive sampler in the examination room, reception and waiting room of the dental clinic at a height of 1.2 m above the floor. A breathing zone of Japanese adult usually exists around the height. Results were illustrated in Fig. 8. The glutaraldehyde concentrations shown in this figure were obtained using 8 hr-sampling period at 5 sites in 26 February 2004. Indoor air concentrations of glutaraldehyde ranged from ND to 16 ppb. Relatively higher concentrations were observed in the examination room, where the sterilizer usually used by dentist, while glutaraldehyde was not detected in the waiting room partitioned from the emission source.

In conclusions, a sampling rate of DSD-DNPH was determined by chamber experiments and resulted in 40 ml/min for glutaraldehyde. Effects of temperature and humidity on the rate were not apparent. The sampling rates were then validated in the field measurements comparing with a previous active sampling method. The diffusion sampler was successfully used for determination of glutaraldehyde and gave similar results to active sampling in indoor air.

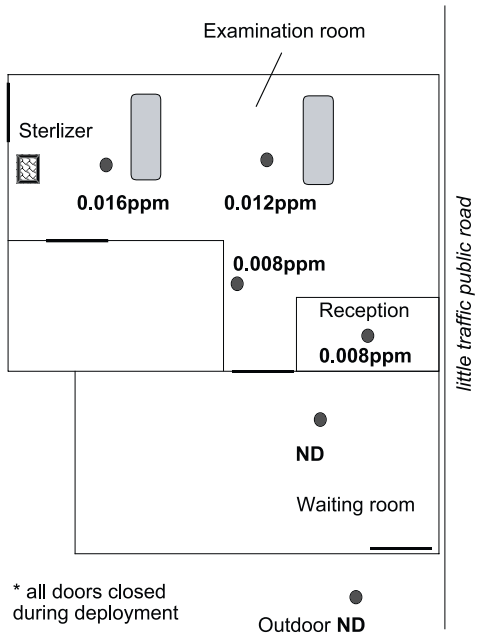

Fig. 8. Distribution of Indoor Air Glutaraldehyde Concentrations at the Dental Clinic in Kanagawa, Japan (26 Feb., 2004)

Acknowledgements Authors awfully thank Mr. M. Machida, TSL Incorporated and Mr. M. Onishi, Tokai University for their great helps in sampling and analysis.

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