Original article

Development of new passive sampler for measurement of glutaraldehyde in indoor air employing CNET as reactive adsorbent

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Abstract

Routine exposure to glutaraldehyde, which has been in widespread use in hospitals to sterilize instruments, is known to cause adverse health effects for workers in endoscopy, dentistry and other medical departments. Authors have developed a new passive sampler for the determination of glutaraldehyde in air at ppb level and evaluated the performance. The sampler simply consists of porous polyethylene cylinder uniformly packed with *O*-(4-cyano-2-ethoxybenzyl) hydroxylamine (CNET) coated silica gel as a reactive adsorbent. The sampling duration of this device was set at 8 hours to apply to field measurements in workplace. After sampling, CNET derivatives were eluted by acetonitrile and subsequently determined by HPLC. In the HPLC chromatogram, three isomers of CNET-glutaraldehyde (*E-E*, *E-Z*, and *Z-Z*) were found. A sampling rate of the sampler was determined by chamber experiments. The collected amount of glutaraldehyde by the passive sampler showed good linearity against air concentrations in the chamber. Therefore, the sampling rate was derived from the slope of a linear regression analysis and resulted in 24mL/min. The performance of the sampler was then tested in a model laboratory in which glutaraldehyde gas was emitted from a sterilizing solution. The diffusion sampler was successfully used for determination of 0.005～0.149 ppm of glutaraldehyde and gave similar results to the active sampling method. In a dental clinic, personal exposure and indoor air concentrations of glutaraldehyde were determined by the new sampler and found much smaller than the exposure guideline value (0.05ppm)

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《**Key words**》 glutaraldehyde, passive sampler, sampling rate, indoor air quality, CNET

Ⅰ. 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

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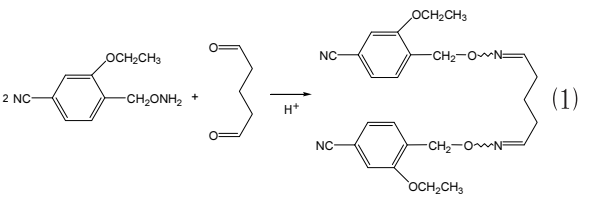
for workers in endoscopy, dentistry and other medical departments within hospitals[1]. The American Conference of Government Industrial Hygienists (ACGIH) has set ceiling exposure limit (TLV-C) for glutaraldehyde in workplace atmosphere to be 0.05ppm. In the UK, Maximum Exposure Limit (MEL) has been set at 0.05ppm for both long-term (8h) and short-term (15min) 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 0.05ppm is recommended[2].

Passive air sampling has been recognized as an efficient alternative to pumped sampling in air according to its ubiquitous, cost-effective and use-friendly properties[3]. Passive samplers, which are taking samples of gases from atmospheric air at a rate controlled by a diffusion process based on Fick's law through a static air layer or a porous material and hence do not involve the active movement of air by pump, are suitable for monitoring personal exposure or indoor concentrations of air pollutants in the living and occupational environment. Solid adsorbents coated with 2,4-dinitrophenylhydrazine (DNPH) have been widely used for the determination of glutaraldehyde in the active[4~6] and passive sampling modes[7~9]. However, several problems were pointed out in the use of DNPH, including its hazardous property, unstable property in storage and influence of artefacts from DNPH in GC analysis[10].

Then, we have developed a new passive sampler (CNET-P) employing *O*-(4-cyano-2-ethoxybenzyl) hydroxylamine (CNET) as a reactive adsorbent of aldehydes. The CNET (I), which is stable in storage and less hazardous, reacts with glutaraldehyde (II) and gave the CNET-glutaraldehyde (III) as follows[11]:



(1)

(I) (II) (III)

Using such passive samplers, sampling rate, α is a dominant factor for analytical liability. The sampling rate shows a magnitude of diffusive uptake rate of analyte in the passive sampling process and has dimensions of volume per unit time (m^3/h or ml/min) which is equivalent to sampling volumetric flow rate which would apply for an active sampler[3]. As shown in Eq. (2), collected amount of glutaraldehyde on adsorbent, W (μg) could be converted to air concentration, C ($\mu g/m^3$) using exposure time, t (h) and α (m^3/h).

$$C = \frac{W}{\alpha t} \qquad (2)$$

The sampling rate could be estimated form a diffusion coefficient of the given analyte and the geometry of the diffusion layer of the passive sampler, 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[3]. However, the sampling rate should be practically determined in advance, because it often depends on the property of adsorbent used[12~13]. In this study, the sampling rate of the CNET-P against glutaraldehyde was determined by small chamber experiments, validated in a model laboratory and applied to field measurements in a dental clinic.

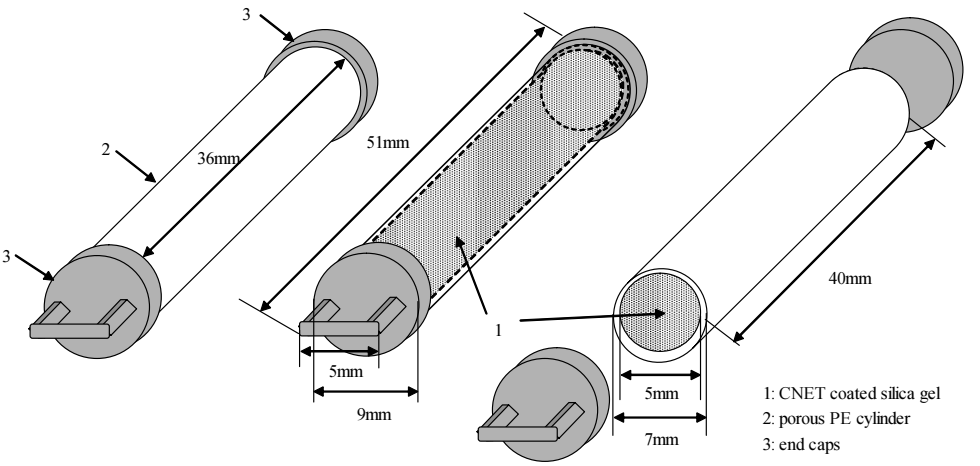


Fig. 1 Schematic view of the passive sampler, CNET-P

Ⅱ. Methods

1. Passive sampler

The passive sampler simply consists of porous polyethylene (PE) cylinder (length: 36 mm, OD: 7mm, ID: 5mm), end caps and CNET coated silica gel inside the PE cylinder, as shown in Fig.1. The porous cylinder made of sintered PE particles works as a diffusion filter. Amount of impregnated CNET is 1.0～1.1mg per sampler.

2. Determination of sampling rate by small chamber experiments

The sampling rate was investigated using a small chamber (32L) 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[13] at a flow rate of 2L/min. 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 CNET coated solid cartridge[11] (Sumika Chemical Analysis Service, CNET-A) connected with air pump (Sibata Science., MP-Σ30) at a flow rate of 0.3L/min for 8 hours. The collection efficiency of the single cartridge was 100% under given sampling condition. The exposure time was set at 8 hours.

3. Validation of sampling rate in a model laboratory

To validate the sampling rate determined, experiments in a model laboratory were conducted in a school facility of Tokai University. The dimension of the model room was approximately 7.9m (length) ×3.0m (width) ×3.8m (height). About 1L of 3w/v% glutaraldehyde solution, generally used for sterilizer (Maruishi Pharmaceutical, Steriscope®) was poured in a plastic bucket (32cm×25cm×11.5cm) and set on a self-standing chair 90cm above from the floor. Sampling condition was static except when a fan thoroughly mixed the air resulting in approximately 0.1m/s of wind speed at the surface of the passive sampler. Air ventilation system was not operated during the samplings. The passive sampler was deployed at a height of 1.2 m above the floor for 8 hours at the center of the room alongside the active sampling apparatus. The 8h-sampling was conducted once a day for 14 days in the same laboratory.

4. Field measurements of glutaraldehyde in a dental clinic

Field measurements were also conducted in a dental clinic located in Kanagawa, Japan, where the glutaraldehyde solution is normally employed for sterilizing tools and equipments, using both CNET-P and previous passive sampler employing DNPH as collection media (Sigma-Aldrich Japan, Supelco, DSD-DNPH[7]). In the hospital, the sterilizer was stand in a plastic bucket (32cm×25cm×11.5cm) loosely covered by a plastic cover at the side of the examination room. Measurements were carried out from 9:30 to 17:30, 16 May 2005, when the clinic was open.

5. Analytical procedure

After sampling, the adsorbent of the passive sampler was placed in a vial. CNET derivatives were eluted by adding 5mL of acetonitrile with mild shaking, stand for 30min and subsequently determined by High Performance Liquid Chromatography (HPLC). The HPLC system consists of Hitachi L-2130 pump with Hitachi L-2400 UV-Vis detector. The following conditions were used: column, 4.6mm×250mm, 5 μm, SUMIPAX ODS D-211 (Sumika Chemical Analysis Service); eluent, 60/40 acetonitrile/distilled water at 1.0mL/min (isocratic); detection, 240 nm; Injection volume, 20 μL. Diluted CNET-glutaraldehyde (Sumika Chemical Analysis Service) was used as analytical standard. Duplicate injections were made for standards, samples and blanks. Analytical procedure of active sampler, CNET-A followed described here. Samples collected by DSD-DNPH were determined by HPLC, following the method described in ref [7].

Ⅲ. Results and discussions

1. HPLC analysis

HPLC analysis of the CNET coated silica gel yields the number of CNET derivatives corresponds to the number of the carbonyl compound collected on the adsorbent. In the HPLC chromatogram (Fig.2), peaks of the CNET derivatives were well separated even in the isocratic mode and CNET-glutaraldehyde gave three peaks corresponding to its possible isomers (*E-E*, *E-Z* and *Z-Z*). Since only small amount of CNET is eluted in acetonitrile, CNET does not interfere in HPLC analysis. As absorption spectra of each glutaraldehyde isomer showed similar curves with a maximum absorption wavelength at 237nm, we then added up the three peaks of CNET-glutaraldehyde for the calibration and determination.

Using DNPH as collection media, it had been known that the peak area varied with time after elution from the solid adsorbents for both active and passive sampling uses, because of unstable properties of DNPH derivatives of certain carbonyl compounds. As for DNPH-glutaraldehyde, Sekine et al.[7] had reported the peak response of DNPH-glutaraldehyde, particularly in the sample solution of active sampler was not stable after elution (the sample solution was stored at 25℃); The peaks gradually increased by 3hours after elution and became constant. Then, to investigate the stability of the peak response of the CNET-glutaraldehyde, the CNET derivatives were immediately eluted just after exposed in the chamber and time-series analysis was made for eluted solutions of both passive and active samplers. Fig.3 shows typical time courses of peak response for eluted CNET-glutaraldehyde in acetonitrile stored at 25℃. The peak responses showed good stablility for at least 25 hours after elution.

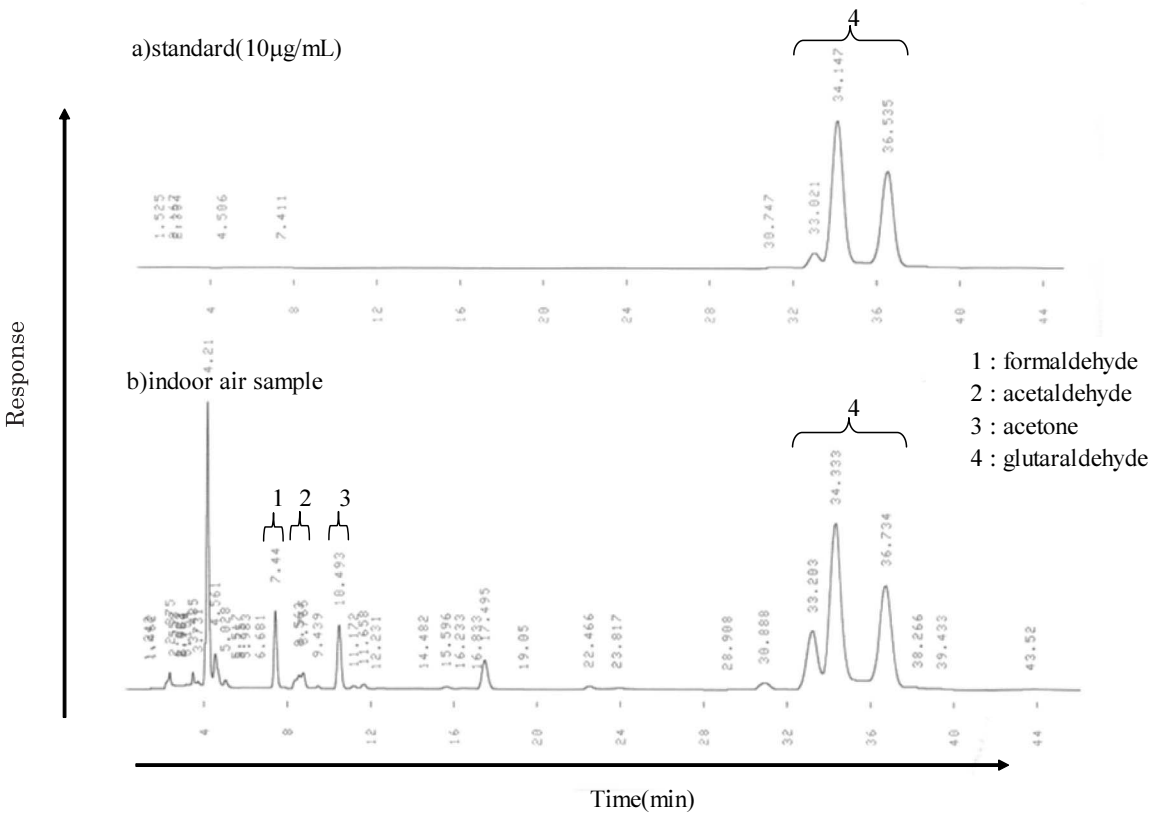


Fig. 2 Typical HPLC chromatogram of CNET-glutaraldehyde analysis, a) standard solution b) indoor air sample.

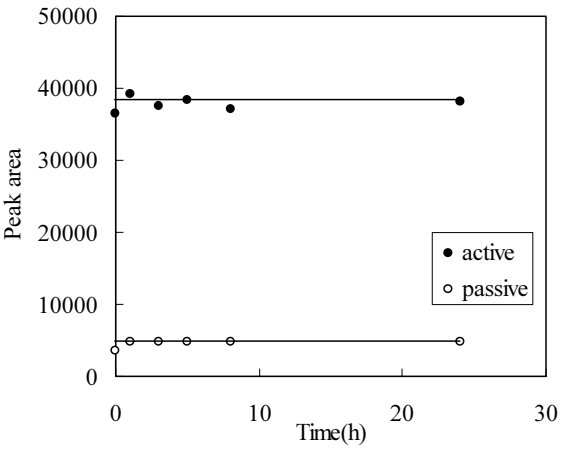


Fig. 3 Variations of peak areas after elution of CNET-glutaraldehyde derivatives from the passive and active samplers. Eluted solutions were stand at 25℃.

2. Determination of sampling rate by small chamber experiments

Sampling rate of the passive 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.

$$\alpha_v(\mu g/ppm/h) = \frac{W(\mu g)}{C_v(ppm)t(h)} \quad (3)$$

$$\alpha_w(\mu g/(mg/m^3)/h) = \frac{W(\mu g)}{C_w(mg/m^3)t(h)} \quad (4)$$

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

Fig.4 shows relationship between air concentration, C_v (ppm) measured by the active sampling method and collected amount of glutar-

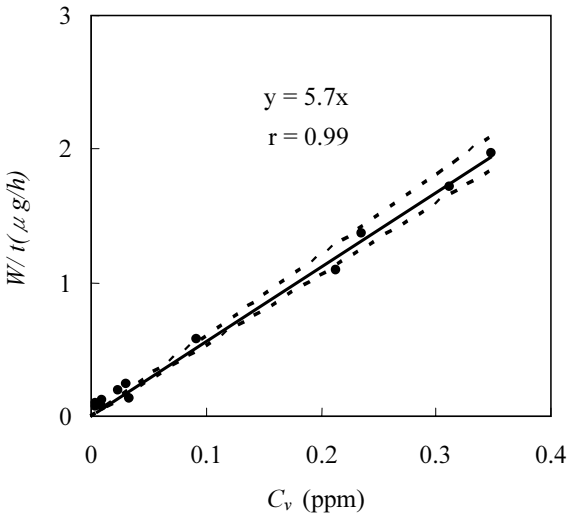


Fig. 4 Scatter diagram between air concentration, C_v and collection amount of glutaraldehyde per hour, W/t (chamber experiment, temp.25℃,RH 22-79%, sampling duration 8hrs, n=12). The least squares linear regression yielded a slope of 5.7 with a standard deviation of 0.18 (shown by dashed lines).

aldehyde per hour, W/t by the passive sampler at 25℃. Even though the simultaneous exposure tests were conducted with varying relative humidity from 22 to 79%, the collected amounts of glutaraldehyde by the passive samplers showed good linearity against air concentrations in the chamber. This means sampling rate of glutaraldehyde was constant under the given condition and independent on the relative humidity. By adapting Eq.(2)-(4) to this relationship, the sampling rate of passive sampler can be derived from the slope of a least squares linear regression analysis and resulted in 5.7 (μg/ppm/h) with a standard deviation of 0.18 for glutaraldehyde. Similarly, the rate resulted in 1.5 ± 0.056 (μg/(mg/m^3)/h) using mass concentrations. Alternatively, the sampling rate can be written in 24mL/min, which is 4 times greater than that of the badge type DNPH passive sampler[9] and 5.4 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[15], and smaller than that of the tube type DNPH passive sampler evaluated by Sekine et al. (40ml/min)[7].

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 CNET derivatives. Then, temperature tests were performed at 15, 25 and 40℃, which seems to be realized in a hospital atmosphere. The sampling rates derived at each temperature were plotted in Fig.5. The results showed effect of temperature was not apparent on the sampling rate of the CNET-P under the given condition. This tendency was similar to the results of previous study of the CNET-P on formaldehyde, acetaldehyde and acetone[16].

3. Validation of sampling rate in a model laboratory

The sampling rate was then validated in a model laboratory. Indoor air concentrations of glutaraldehyde were measured by the passive sampler and co-located pumped samplings in the model laboratory with static and turbulent atmosphere. Fig.6 illustrates good agreement of the passive sampler response with that of the active method for the determination of 0.005～0.149 ppm of glutaraldehyde using the sampling rate derived from the chamber ex-

periment. Even though the sampling conditions included a turbulent atmosphere made by a mixing fan, the wind effect was not apparent. This is because the porous PE cylinder works a good draft shield; the previous tests of CNET-P showed the sampling rates for formaldehyde, acetaldehyde and acetone were independent on wind speed up to 2.5m/s[16]. 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.

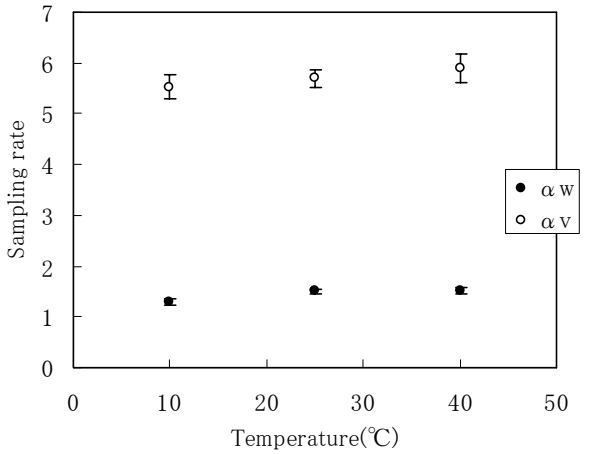


Fig. 5 Derived sampling rates plotted against temperature. Bars show standard deviations of slopes obtained by linear regression analysis between *C* and *W/t*.

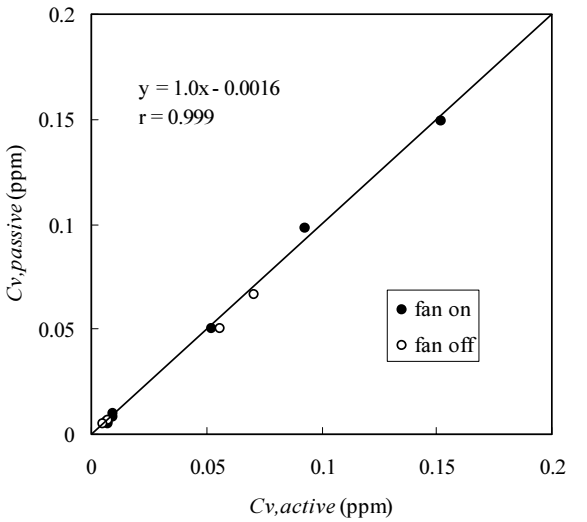


Fig. 6 Comparison of indoor air concentrations of glutaraldehyde measured by passive and active sampling methods with and without operation of mixing fan in the model laboratory (temp.10–27 ℃, RH 18–48%, sampling duration 8hrs, n=14).

4. Limit of detection and determination

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 0.7ppb of glutaraldehyde in air for 8h-sampling duration following the analytical procedure described above. Similarly, limit of quantitation (LOQ) was defined as 10 times the noise (S/N=10) and 2.3ppb of LOQ was obtained.

5. Field measurements in a dental clinic

Based on the results, distribution of indoor air concentration of glutaraldehyde was measured by the CNET-P and DSD-DNPH in the examination room, reception and waiting room of the dental clinic. Samplers were deployed at a height of 1.2m above the floor, because a breathing zone of Japanese adult usually exists around the height. Personal exposure concentrations were also determined by wearing the samplers at doctor's and nurse's throats. Results were illustrated in Fig.7. Similar results were obtained by both samplers. Relatively higher concentrations were observed in the examination room where the sterilizer was usually used, while glutaraldehyde was not detected in the waiting room partitioned from the emission source. Personal exposure concentrations of the nurse, who often handles the solution, showed relatively higher levels with 0.011ppm, but much smaller than the exposure

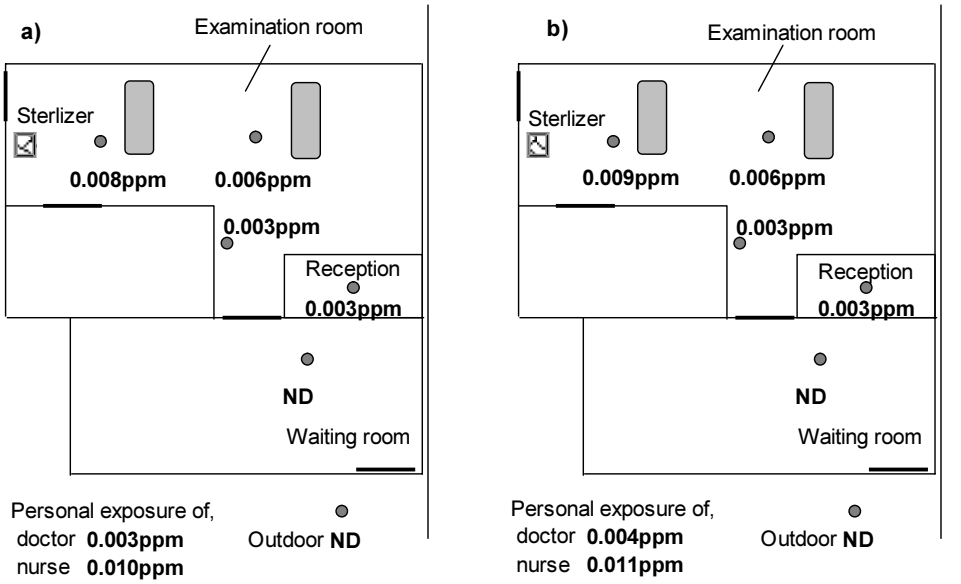


Fig. 7 Distribution of indoor air glutaraldehyde concentrations at the dental clinic in Kanagawa, Japan (16 May, 2005, sampling duration 8hrs), measured by a) DSD-DNPH, b) CNET-P.

guideline value (0.05ppm).

Ⅳ. Conclusion

A sampling rate of CNET-P was determined by chamber experiments and resulted in 24ml/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 passive sampler was successfully used for determination of glutaraldehyde and gave similar results to active sampling in indoor air.

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要約

グルタルアルデヒドは医療器具等の消毒殺菌に広く使用されているが、皮膚や気道等に刺激性を有することから、室内空気を通じて医療従事者に健康障害を与える可能性がある。筆者らは新規誘導化捕集剤*O*-(4-cyano-2-ethoxybenzyl) hydroxylamine (CNET) を用いたパッシブ・サンプラーを開発し、空気中グルタルアルデヒド濃度の受動的測定方法を検討した。用いたサンプラーは多孔質ポリエチレン管にCNETをコーティングしたシリカゲルを充填したものであり、グルタルアルデヒドはCNET誘導体として捕集後、HPLC法により定量される。小型チャンバーにて気中グルタルアルデヒド濃度と本サンプラーによる捕集量の関係を調べたところ両者には良好な直線関係が見出され、直線回帰式の傾きよりサンプリング・レート24mL/minが得られた。グルタルアルデヒドを揮発させたモデル実験室内でアクティブ・サンプリング法と同時測定した結果、パッシブ法による気中濃度測定値は、アクティブ法の値と良い一致を示した。また本サンプラーを用いて歯科医院における個人曝露および気中濃度の実測調査を行なったところ、いずれも曝露指針値（0.05ppm）未満であった。

（臨床環境15：19〜27, 2006）