보건학석사 학위논문

Behavioral Characteristics of Mist Containing PHMG Emitted from Ultrasonic Humidifier

가습기 사용시 발생하는

살균제 PHMG의 공기 중 거동 특성

2018년 2월

서울대학교 보건대학원

환경보건학과 산업보건전공

김 유 진

ABSTRACT

Behavioral Characteristics of Mist Containing PHMG Emitted from Ultrasonic Humidifier

Yoojin Kim
Department of Environmental Health Sciences
Graduate School of Public Health
Seoul National University, Korea

Advisor Chungsik Yoon, Ph.D, CIH

Objective After the outbreak of humidifier disinfectant accident in South Korea, most studies have been focused on the toxicological and epidemiological effects of humidifier disinfectants while the behavior of aerosols emitted from humidifier was rarely evaluated. This study aims to identify the behavior characteristics of aerosols emitted from ultrasonic humidifier including polyhexamethylene guanidine (PHMG) as a representing disinfectant substance, and to determine the effect of water among the aerosols.

Methods After selecting the most appropriate condition among the five water vapor

removing conditions using diffusion dryer and thermodenuder, we compared the behavior characteristics of PHMG whether or not the dryer set is used. The scanning mobility particle sizer (SMPS) and the optical particle spectrophotometer (OPS) were utilized to monitor the number concentration and size distribution of aerosols. Filter sampling was conducted simultaneously to confirm the transmission and distribution of PHMG in the air by analyzing with balance and field emission scanning electron microscope with an energy-dispersive X-ray spectrometer (FE-SEM/EDX).

Results The number concentration and the geometric mean of the particles under 10 μm increased as the concentration of PHMG contained in the water tank increased. With the same amount of PHMG added, the number concentration reduced at 1 m, but increased again at 2 m. However, the mean size of the particles continued to increase as the sampling distance is farther from the humidifier outlet. Most of the particles at 0.5 m was nano-sized while 25% of the particles at 2 m measured between 0.3 μm and 10 μm. Through the analysis of FE-SEM/EDX, we observed the aggregated particles containing phosphate in a similar size (40 nm to 70 nm) as measured with real-time monitoring devices.

Conclusion This study aimed to clarify the behavioral characteristics of humidifier disinfectant PHMG. The addition of PHMG in the humidifier water tank produced 10 times more particles in number concentration under 10 μm diameter, compared to the case when only water was added in the humidifier. PHMG was transmitted 2 m from the humidifier, the last measurement distance in the experiment, and remained extensively in the air. The mean size of particles at 2 m was relatively

larger than that at closer distance, but still most of them are less than 10 μm which is considered as respirable fraction.

Keywords: Humidifier disinfectant, PHMG, humidifier mist, aerosol, biocide, active ingredient

Student Number: 2016-24046

Contents

List of Tables

List of Figures

1. Introduction

Humidifier is a device that increase the relative humidity of indoor air by emitting water particles or vapors. Several types of humidifiers are characterized by their mechanism, including the furnace-mounted humidifier or the ultrasonic humidifier which are used domestically. Ultrasonic humidifier increases relative humidity by producing small water particles with the vibration of ultrasonic oscillator (Park, 2007). On the one hand, when ultrasonic humidifier is poorly maintained, microbacteria can grow inside the water tank and can be emitted as a part of particles; on the other hand, furnace-mounted humidifier does not cause this problem because of the temperature. Respiratory diseases, such as humidifier fever (a type of hypersensitivity pneumonitis), related to bacteria multiplication in humidification system have been reported since 1970s. Therefore, poorly maintained humidifiers can pose adverse effects to human health.

As part of maintenance of ultrasonic humidifiers, a humidifier disinfectant was developed in the late 1990s in South Korea. However, the misuse of this disinfectant chemical caused thousands of victims to exhibit significant symptoms of lung fibrosis. Labelled as Humidifier Disinfectant-associated Lung Injury (HDLI), the odds ratio of this disease reached to 47.3 (Kim et al., 2014). Ultrasonic humidifier emits much smaller particles than those from a vaporizer or a furnace-mounted humidifier; hence, such mechanism increases the possibility of particles

smaller than 2.5 μm to reach alveola (USEPA, 1991) if humidifier disinfectant is added. Humidifiers are usually used during winter in Korea when humidity and temperature are relatively low, with barely no ventilation to keep the indoor air condition. As such, the sensitive population who stays indoor for extended period, such as children and pregnant women, has longer and higher exposure.

The number of victims increases, and further investigations and compensations continue. Most studies related to humidifier disinfectants are predominantly animal toxicological assessment or epidemiological studies on humidifier-related lung victims. Studies focusing on particle emission or inhalation emitted from the humidifier were relatively lacking. Korea Centers for Disease Control and Prevention (KCDC, 2011) reported that the mean particle size contained in humidifier disinfectant was about 30 nm–80 nm, with differences due to dilution rate and the kind of disinfectants. Park et al. (2016) calculated the exposure level to humidifier disinfectant considering age and possibility of exposure among the victims and operation patterns. However, this calculation might have potential difference with the actual exposure level since it was based on the assumption that the disinfectant homogenously exists in the indoor air.

Mist emitted from the ultrasonic humidifier can comprise two parts: the humidifier disinfectant as an active ingredient controlling the growth of bacteria and water as a solvent diluting the humidifier disinfectant used in the humidifier. Given that the behavior of particulate matter (PM) differs by size distribution, type of solvent, and chemical interaction between the solvent and the active ingredient,

the distribution status of humidifier-emitted particle should likewise be identified to determine the exposure level; however, to date, such has not been identified.

Therefore, this study aims to investigate the behavior characteristics of particles emitted from ultrasonic humidifiers, especially that of disinfectant substance as an active ingredient, and to clarify the effect of water as a solvent in the aerosol.

2. Methods

2.1. Subject

A domestic ultrasonic humidifier (Worltech H-U977, Ohsung, Korea) which has a large water tank (6.5 L) and a valve to control the emission rate was used during the experiment. Every experiment was conducted with a total of 3 L of water, and the emission rate was fixed at the 'strongest (emission rate in 320 ml/h was measured in this study)'.

Polyhexamethylene guanidine phosphate (PHMG or PHMG-P) was selected as a representative substance which was used in several humidifier disinfectants. Specific amount of PHMG stock solution (25% solution dissolved in water, BOC Sciences, USA) was added to the water tank according to dilution rates, and the rest was filled with water. Considering that the PHMG concentration of the product with the highest sales rate was 1280 ppm, it was diluted into 20:1 as the worst exposure scenario and 200:1 as recommended by the manufacturing company. The exact amount added to the water tank is calculated as shown below. To minimize the effect from water impurities, 3rd distilled water was used to operate the humidifier although the manufacturing company recommends tap water for the operation.

With 20:1 dilution rate and a total of 3 L,

$$1280 \text{ ppm} \div 20 = 64 \text{ ppm}$$

$$64 \text{ ppm} = 64 \ \mu g/l = 192 \ \mu g/3l$$

As the purity of the stock solution is 25%,

$$192 \ \mu g/3l \ \times 4 = 768 \ \mu g/3l$$

Thus, with 20:1 dilution rate, 768 μg of PHMG solution was added in the water tank with a total of 3 L. With 200:1 dilution rate, 76.8 μg of PHMG was mixed with water.

2.2. Experimental Procedure

The overall experimental procedure is described in Figure 1. All the experiments were conducted in a cleanroom (nominal class 1,000) with a volume of 40 m^3 (7.0 m[W] × 2.4 m[L] × 2.4 m[H]) where the background particles can be limited to less than 1,000 particles/ft^3 when measuring under 0.3 μm. The researcher wearing dust-free garments entered to cleanroom after passing through an air-shower to minimize the particles from the outside. The researcher stayed in the cleanroom only when the ventilation system and humidifier needed to be turned on and off.

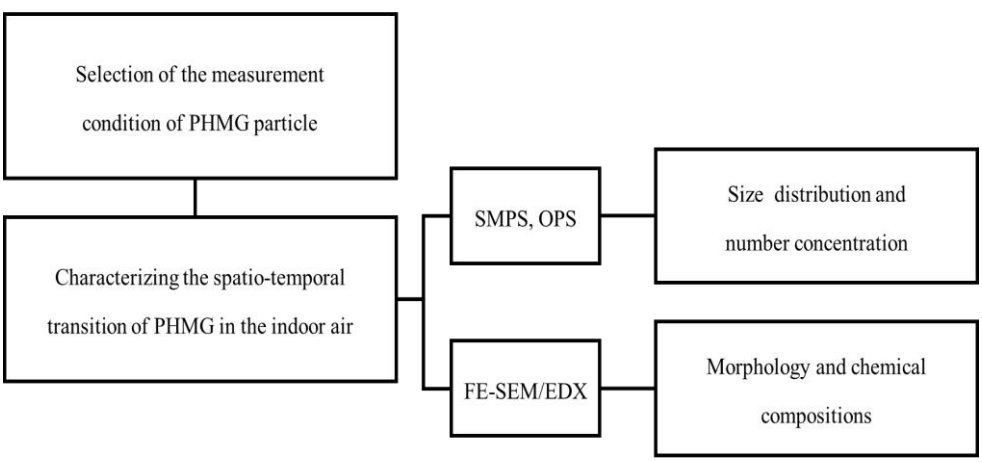


Figure 1. The outline of the study.

2.3. Measurement and Sample Analysis

2.3.1. Selection of pre-dryer for water-free PHMG aerosol measurement

Size distribution and number concentration were expected to differ by options because of the variations on eliminating water among the aerosols. To determine the most appropriate measurement condition in order to characterize the effect of water in humidifier-emitted particles, we compared the size and number distribution of the cases whether or not 64 ppm of PHMG was added. We connected five different options of dryer combination described as below in front of the sampling port and each was measured thrice.

- Option 1: Thermodenuder (T)
- Option 2: Diffusion dryer (D)
- Option 3: Thermodenuder + Diffusion dryer (T+D)
- Option 4: Diffusion dryer + Thermodenuder (D+T)
- Option 5: Without dryers (WO)

The diffusion dryer filled with silica gel evaporates the water vapor from the aerosol and captures large water droplets. Thermodenuder consisting two parts,

namely, heating jacket set to 200 °C and adsorption part filled with active charcoal, is used to remove volatile and semi-volatile compounds. With these differences, the option with less fluctuation and maximum evaporation effect was selected as the most appropriate in characterizing the behavior of PHMG from the humidifier-emitted particles.

Each experiment was divided into three phases according to the state of humidifier. Real-time monitoring was conducted throughout the phase.

1) Pre-operation phase

To remove the background particles to the minimum level, the ventilation system was used for at least 30 minutes (less than 100 particles/cm^3 by SMPS).

2) During the operation phase

The measurement was conducted at 50 cm apart from the outlet part of the humidifier. The humidifier was operated for 2 hours without the ventilation of cleanroom. Integrated sampling was conducted only during the operation.

3) Post-operation phase

After the humidifier was turned off, the measurement continued for 1 hour to monitor the particles remaining in the air.

While the humidifier is operated, the size distribution and number concentration of the emitted particles were monitored with real-time monitoring devices. Scanning mobility particle sizer (SMPS, Model Nanoscan 3910, TSI, USA) and optical particle sizer (OPS, Model 3330, TSI, USA) were used in the range of 10 – 10,000 nm (SMPS: 10 nm – 420 nm, OPS: 300 nm – 10,000 nm) with 1 minute log interval. Thermo-hygrometer (Model TR-72U, T&D Inc., Japan) was also installed at the same location to check the variance of room temperature and relative humidity.

2.3.2. Characterizing the effect of PHMG in the aerosol

After the selection of dryer option in 2.3.1., the experiment was conducted to characterize the spatio-temporal distribution of PHMG particles and variance followed by the difference of concentration. With and without the dryer option selected, sampling was conducted at 0.5 m, 1 m, and 2 m away from the humidifier outlet. The humidifier with 6.4 ppm of PHMG was also tested to obtain the data at the operating condition recommended by the manufacturer. The sampling and analysis process is basically the same with section 2.3.1, except that air collection through filter was conducted for the time-integrated analysis.

A polycarbonate (PC) filter (0.4 μm pore size, 37 mm diameter, SKC Inc., USA) kept in three-piece cassettes was connected to a high pump (ELF-ESCORT, MSA, USA) with 2 l/min flow rate to draw the air. The PC filters were weighed before and after the sampling using a balance (XP6 Microbalance, METTLER TOLEDO, USA). Filters were stored in a desiccator for at least 24 h before the measurement (Temperature: 20 ± 1 °C, RH: 50 ± 5%). PC filters were also analyzed with field emission-scanning electron microscope (FE-SEM, MERLIN Compact, ZEISS Inc., Japan) connected to energy dispersive X-ray spectrometer (EDX, AZtecOneXT, Oxford Instruments Inc., UK). Phosphate was selected as a target element when analyzing the chemical compositions with EDX to clearly discriminate PHMG particles from random particles.

Through this process, the humidifier mist was measured at three different distance options from the outlet and with three different PHMG concentrations mixed in the water tank. Consequently, spatio-temporal variance could be added to 2.3.1., and how PHMG disperses and disappears could be determined by comparing and monitoring the size and the number distributions of humidifier-emitted particles of different disinfectant concentrations and sampling options while identifying whether or not the effect of water is minimized.

3. Results

3.1. Number concentration of humidifier mist

The selection of measurement condition of PHMG particle was conducted as a supporting information prior to identifying the behavioral characteristics of PHMG. This part was added as Appendix 1.

In this section, the size and the number distributions at different sampling locations and different PHMG concentrations were compared to characterize the spatio-temporal differences of PHMG particles behavior in the indoor air. For convenience, option 4 (Diffusion dryer + Thermodenuder) is labeled as the 'dryer set'. As the dryer set is attached in front of the sampling port, the effect of moisture could be minimized and the data could be compared with the cases when the dryer set was not used. Thus, we could determine the effect of water on the mists from ultrasonic humidifier when PHMG was added by determining the differences between the trials.

Temperature and relative humidity mainly affect the behavior of particles, so the monitoring of the two factors was also conducted. As the ventilation fan of cleanroom was turned on before the humidifier was operated, the initial temperature and relative humidity were stable at 25.0 ± 1.53 ℃ and 29.6 ± 3.38%. Temperature was maintained relatively at 25 ℃, but dropped to 20 ℃ in less than 5 mins after the humidifier was turned on only when measured at 0.5 m. Relative humidity

reached 100% in 20 mins at 0.5 m. By contrast, at 1 m and 2 m, humidity reached 40% at maximum in about 40 mins. Once the temperature and relative humidity reached their maximum or minimum level, it was maintained until the humidifier stopped operation. Thus, the transition of real-time monitoring data was conducted while the thermo-hygro condition was stable.

Figures 2 and 3 illustrate the plots of number concentration during the operation at different sampling locations and PHMG concentrations. The two figures differ depending on whether real-time monitoring device was used to obtain data. Figure 2 shows the total number concentration detected from SMPS at the range of 11 nm–420 nm, whereas Figure 3 the total number concentration detected from OPS at the range of 0.3 μm–10 μm. The three boxes represent the distribution of different concentrations (0 ppm/6.4 ppm/64 ppm from the left) at the same distance. The yellow box is an illustration when measured without dryer set in front of the sampling port, while the pink box is when measured with the dryer set.

The concentration of PHMG in water tank increased along with the number concentration, and the moisture dried out with lower efficiency when the dryer set was attached (80.1% at 0 ppm, 40.5% at 6.4 ppm, 25.1% at 64 ppm at 0.5 m) compared to those at the same distance (Figure 2). Thus, as the concentration gets higher, the proportion of particles only consisted of water which can be dried out through dryer set gets lower.

Overall number concentration decreased at 1 m compared to that of 0.5 m,

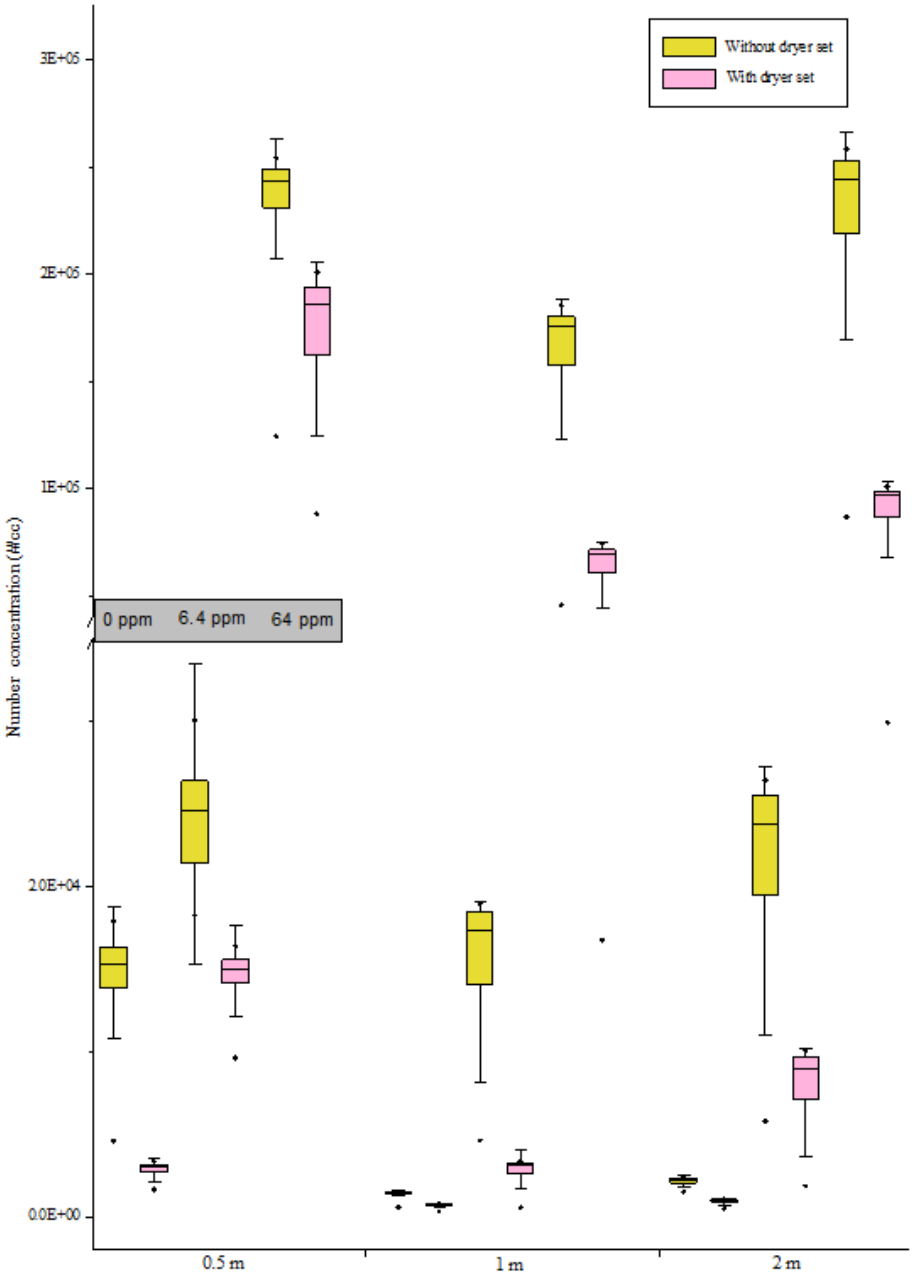


Figure 2. The box plot of particle number concentration during the operation in the range of 11- 420 nm using SMPS. Values shown are median (line within box), 25th and 75th percentiles (bottom and top of box, respectively), 10th and 90th percentiles (lower and upper bars on whisker, respectively), 5th and 95th percentiles (dots and x-marks on bottom and top, respectively)

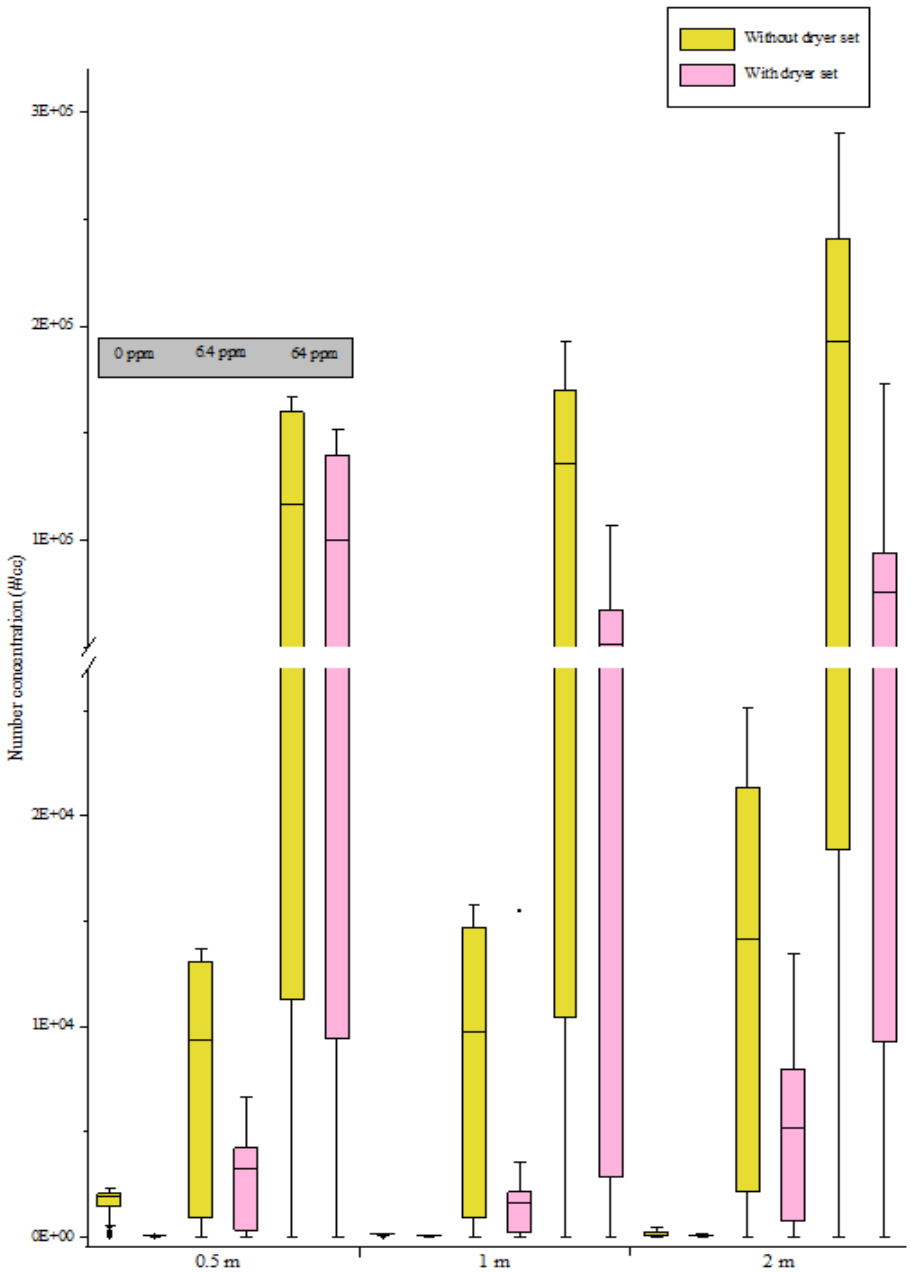


Figure 3. The box plot of particle number concentration during the operation in the range of 0.3 – 10 µm using OPS. Values shown are median (line within box), 25th and 75th percentiles (bottom and top of box, respectively), 10th and 90th percentiles (lower and upper bars on whisker, respectively), 5th and 95th percentiles (dots and x-marks on bottom and top, respectively)

but it increased again at 2 m in every PHMG concentration. The bigger size range and the mean number concentration continued to increase depending on the distance when the dryer set was not used (Figure 3), unlike the data of SMPS. Thus, the growth of particle causes the increased number concentration at 2 m. More discussions on particle size are presented in Section 3.2.

Figure 4 shows the time-varying number concentration of particles measured with SMPS at a different distance. Given that most particles were in the range of SMPS, the graphs for OPS were attached at Appendix 2. The time to reach the maximum number concentration was similar (30 mins) with other experiments. Number concentration slightly decreased as the time passes when only water was put into the humidifier; it was even clearer when wider and bigger size range was monitored at farther distance. However, when PHMG was added, number concentration did not have significant change over time.

After operating the humidifier, the number concentration maintained at almost the same level when humidifier was operated only with water at 0.5 m distance. However, the concentration was about 15.6% of that of phase 2 (during the operation) on the average, while it reduced to 2.3% of phase 2 when PHMG was added. The concentration reduced to an even lower level when the dryer set was attached. As it reaches almost the same level at the same distance, regardless of how high the PHMG concentration, the addition of PHMG induced the production of larger particles, causing rapid elimination of the aerosol after the operation of humidifier.

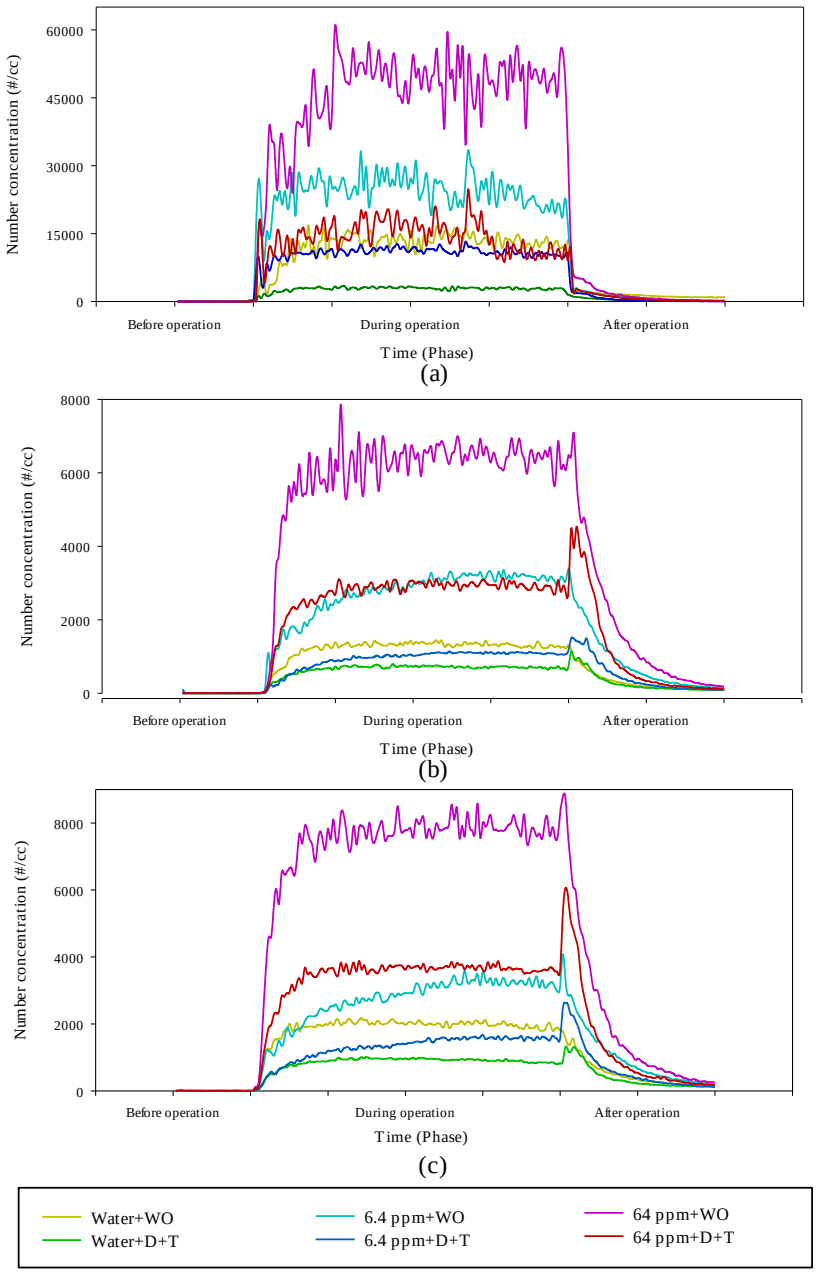


Figure 4. Time-varying number concentration at different distance, dryer option and PHMG concentration ; (a) at 0.5 m, (b) at 1 m, (c) at 2 m

* T: Thermodenuder, D: Diffusion dryer, WO: Without dryers

3.2. Particle size of humidifier mist

Table 1 and Table 2 show the number concentration of particles by size during the operation. Table 1 covered the sized range from nano-scale to 10 μm using SMPS and OPS at the same time, while Table 2 covered larger size range from 0.3 μm with detailed size bin of OPS. The proportion of the particles under 10 μm increases and that of the nano-sized particles decreases as the concentration of PHMG gets higher, regardless whether or not the dryer set was used. Therefore, the addition of PHMG induced the production of larger particles, causing rapid elimination of the aerosols after the operation of humidifier.

The geometric mean (GM) of the particle diameter in each time is shown in Figure 5 with the differences in distance, concentration, and the existence of dryer set. The GM increased as the concentration of PHMG in water tank rose higher, and the distance between the outlet of humidifier and the sampling port was farther. Thus, the addition of PHMG increased the number concentration and the GM at every case. As the distance increased, GM was more stable and almost the same regardless the use of dryer set. Particles existing at farther distance are attached to each other and are aggregated, causing bigger and less evenly distributed particles.

Table 1. The number concentration of particles by size at different distance and concentration during the operations (unit: #/cc)

Concentration	Type of dryers	0.5 m			1 m			2 m		
		~100 nm	100 nm ~ 0.3 μm	0.3 μm ~ 10 μm	~100 nm	100 nm ~ 0.3 μm	0.3 μm ~ 10 μm	~100 nm	100 nm ~ 0.3 μm	0.3 μm ~ 10 μm
0 ppm	WO	11,914 ± 3,129	582 ± 230	1,841 ± 518	1,132 ± 267	88 ± 29	123 ± 27	1,725 ± 338	157 ± 45	231 ± 124
	D+T	2,720 ± 517	85 ± 40	42 ± 7	606 ± 135	56 ± 18	33 ± 8	743 ± 171	109 ± 32	85 ± 48
6.4 ppm	WO	18,884 ± 3,130	5,334 ± 1,465	11,346 ± 3,407	1,867 ± 486	822 ± 241	12,683 ± 3,808	1,774 ± 506	901 ± 272	18,222 ± 5,880
	D+T	8,219 ± 1,088	2,520 ± 401	3,674 ± 1,092	677 ± 200	252 ± 77	1,817 ± 564	861 ± 258	423 ± 134	6,560 ± 2,263
64 ppm	WO	57,355 ± 10,350	30,556 ± 5,643	143,085 ± 34,508	3,285 ± 782	2,659 ± 675	152,968 ± 40,065	3,813 ± 790	3,481 ± 793	214,710 ± 54,373
	D+T	28,027 ± 6,420	17,767 ± 4,136	123,742 ± 30,765	1,549 ± 363	1,128 ± 289	59,070 ± 16,835	1,808 ± 390	1,579 ± 370	83,196 ± 21,874

* T: Thermodenuder, D: Diffusion dryer, WO: Without dryers

Table 2. The number concentration of particles by size at different distance and concentration during the operations using OPS (unit: #/cc)

Distance	Concentration	Type of dryers	0.3 - 0.5 μm	0.5 - 1 μm	1 - 2.5 μm	2.5 - 4 μm	4 - 10 μm
0.5 m	0 ppm	WO	1,698 ± 477	110 ± 31	20 ± 12	13 ± 11	0
		D+T	38 ± 9	3 ± 1	0	0	0
	6.4 ppm	WO	11,185 ± 3,356	159 ± 56	1 ± 1	0	0
		D+T	3,620 ± 1,085	47 ± 14	4 ± 3	2 ± 2	0
	64 ppm	WO	182,289 ± 43,780	8,009 ± 2,291	226 ± 304	130 ± 184	0
		D+T	119,755 ± 29,544	3,847 ± 1,231	87 ± 144	51 ± 89	0
1 m	0 ppm	WO	117 ± 27	5 ± 1	0	0	0
		D+T	30 ± 7	3 ± 2	0	0	0
	6.4 ppm	WO	12,540 ± 3,766	141 ± 44	0	0	0
		D+T	1,802 ± 561	14 ± 4	0	0	0
	64 ppm	WO	142,028 ± 37,007	10,900 ± 3,081	39 ± 12	0	0
		D+T	55,709 ± 15,790	3,356 ± 1,055	5 ± 2	0	0
2 m	0 ppm	WO	223 ± 124	7 ± 2	0	0	0
		D+T	82 ± 48	2 ± 1	0	0	0
	6.4 ppm	WO	17,889 ± 5,777	331 ± 106	0	0	0
		D+T	6,484 ± 2,236	75 ± 28	0	0	0
	64 ppm	WO	199,317 ± 50,268	15,337 ± 4,109	54 ± 13	0	0
		D+T	78,871 ± 20,628	4,319 ± 1,253	5 ± 2	0	0

* T: Thermodenuder, D: Diffusion dryer, WO: Without dryers

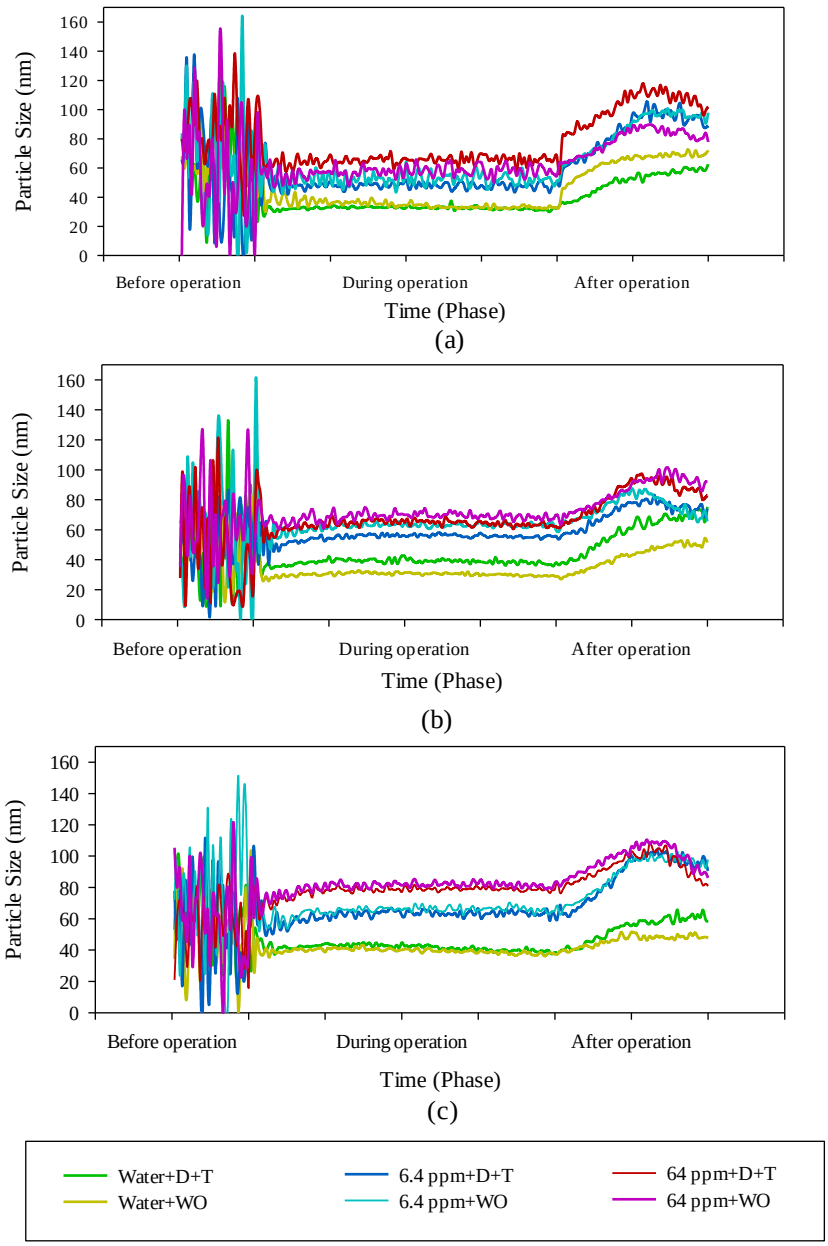


Figure 5. Time-varying geometric mean of particle size at different distance and concentration. (a) at 0.5 m, (b) at 1 m, (c) at 2 m

3.3 Morphology and chemical compositions

Figure 6 is FE-SEM/EDX images collected on PC filters while the ultrasonic humidifier is on operation. We could specify the element through elemental mapping and intensity of phosphate signal. Carbon and oxygen took most of the ingredient, however, particles containing phosphate were significantly observed on PC filters when PHMG was put in humidifier reservoir. Small spherical particles between 40 nm to 80 nm size were mostly aggregated in an irregular form and the size of cluster was between 100 nm to 400 nm. However, the particles were rather easily found at farther distance (2 m).

The waterdrop-like shapes appeared on the filters sampled at the distance of 0.5 m while not many or none of water drops are shown at the distance of 2 m (Appendix 3). This appeared only when PHMG was also added in the reservoir not only water.

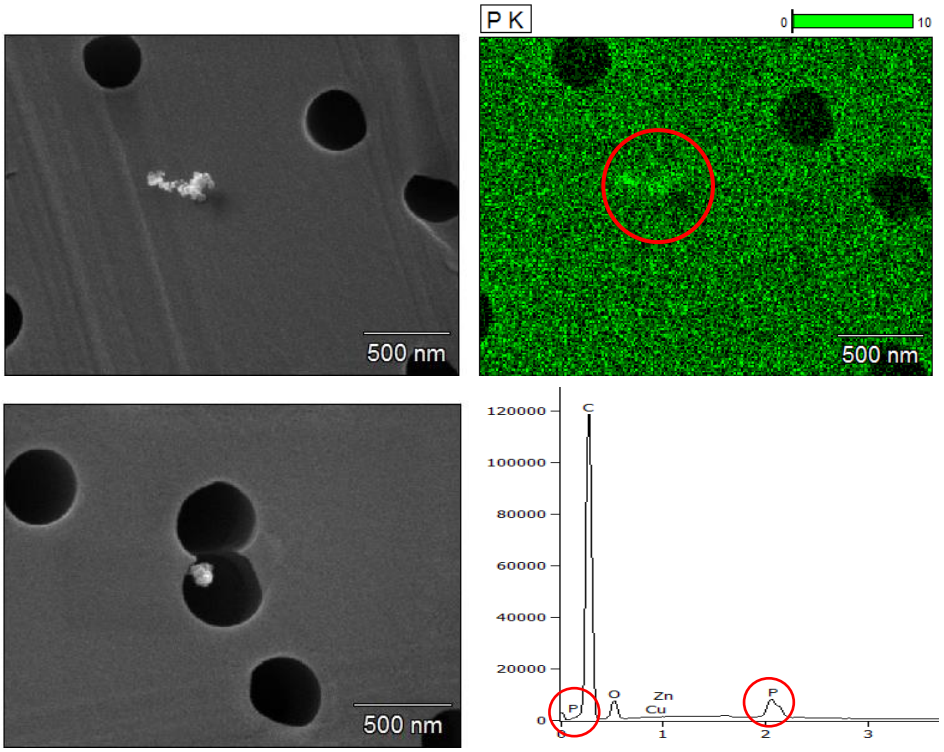


Figure 6. FE-SEM/EDX images collected on PC filters at different sampling condition while the ultrasonic humidifier is on operation.

4. Discussions

Victims of humidifier disinfectant accident proved that chemicals might cause different health effect depending on different usage and exposure route. To date, most of the studies were focused on an epidemiological survey targeting lung disease patients and people around them, or the toxicological studies using different types of animals. However, this study attempted to characterize the behavior of PHMG particles emitted from ultrasonic humidifier, and the variance of exposure level at different distances and concentrations.

This study is pioneering as it intends to observe the behavior characteristics of humidifier disinfectant substance among humidifier mists. Several studies have aimed to measure the concentration of humidifier disinfectant in the air. This study has shown that the trend of the sizes and numbers of distribution transitions were mostly corresponding with other related research even when concentrations were changed. However, variations were noted in overall number and size distribution of the particles when compared to related research because of the differences in sampling conditions. Nevertheless, the problem was that we could not clearly observe the behavior of the humidifier disinfectant, while determining the contribution of water as a solvent. Water takes most of the part in the solution in the water tank, and we needed to minimize the effect of water in order to identify the exclusive behavior characteristics of PHMG. Hence, we utilized dryers to make moisture evaporate before the sampling port and compare

the data to the case when dryers are not used.

Five options were considered in the selection of dryer, and each showed respective results in terms of size distribution and number concentration. When diffusion dryer and thermodenuder were connected individually, they removed less moisture than when both dryers are used simultaneously. However, the result was also different when the order of diffusion dryer and thermodenuder was changed. The reason cannot be explained clearly through this study, but we suppose such is due to the principle that water evaporates differently by type. The thermodenuder on the rear stabilizes the particles once they passed through the diffusion dryer and showed higher water removal efficiency and stable size distribution of the aerosol.

The most noticeable difference resulting from the addition of PHMG was the number concentration of aerosol less than 10 μm although the mist emission rate was constant. The number concentration at 0.5 m can be the highest as it is close to the mist outlet and collects the maximum amount of aerosol among the three distance options. However, at 1 m, the larger particles mostly sank as compared to those at 0.5 m and at 2 m, we assumed the small particles from the humidifier started to aggregate. The number concentration continued to increase when water mists were not eliminated as the distance gets farther. On the other hands, it decreased at 1 m and seemed to increase at 2 m when water mists were evaporated, showing larger gap compared to when the dryer set was utilized. Since the geometric mean size of particles continuously increased by distance, this meant that lighter aerosols from humidifier mostly consisted of water aggregated as they

move through the cleanroom.

Moreover, in terms of PHMG, the number concentration and the mean particles size increase as the PHMG concentration of the water tank increased. It was assumed that the increase in number concentration was derived from the bubbly characteristics of PHMG. Given that PHMG is a kind of surfactant, it produces bubbles when mixed with water. Ultrasonic humidifier produces mists by vibrating water from its bottom. When only the water is put into the water tank, the PHMG-containing water produces more bubbles as the oscillator operates and then produces mists more efficiently. The 10 μm size range was used for convenience as it is the upper detection limit of OPS, not because the particle size actually reaches 10 μm. Even when monitoring at the range under 10 μm, almost 99.9% of the particles were actually under 0.5 μm (Appendix 2).

The ratio of the particles eliminated through dryer set diminished as the PHMG concentration got higher. We assumed that as the concentration got higher, the proportion of particles only consisted of water. This can be dried out through dryer set gets lower. Also, the elimination rate reduced as the sampling distance got further, and this means higher proportion of the particles at further distance contain PHMG.

This study shows that most PHMG particles emitted from the humidifier have less than 100 nm diameter. As the pore size of PC filter used in this sampling was about 400 nm, some of the PHMG particles could have possibly passed by the pore on the surface of the filter. Thus, other filters capturing PHMG were also

observed through sampling to confirm whether PC filter was an ideal option to check the morphology of PHMG.

Factors, such as exact model of humidifier, mist emission rate, and the type of water used in the humidifier, were selected by the researchers. These fixed setting of the study could nonetheless generate limited results. Hwangbo and Chu (2013)'s study showed different results when nanomaterials diffused with tap water, distilled water, and filtered water were nebulized in the air, and they all showed distinctive size distribution and number concentration. The research done by Lee and Yu (2017) is also a relevant comparison to this study in terms of the different humidifier models and water type. Whether the measurement was conducted in cleanroom, the aerosol emitted from the humidifier might show different behavior. The experiments were conducted in the cleanroom to minimize the effect of foreign particles and focus on the humidifier mists. However, at least thousands of invisible particulates exist indoor, and these particulates can encounter the mists from the humidifier. Thus, the measurement from the same ultrasonic humidifier can possibly show a different result compared to this study depending on the different operation factors and measuring environment. Attempts to conduct the same research in actual living space would bring more meaningful outcome because it could reflect more realistic aspects and conditions.

By monitoring the difference by elapsed time and distance, we would be able to understand the various transitions of behavioral characteristics of humidifier mist and PHMG. Furthermore, we can apply this method to other PM consisted of

liquid to understand the effect of solvent to the behavioral characteristics of active ingredient. This would enhance the information on various chemical products in the form of mist to be used in a diversified exposure assessment.

Limitations

The main limitation of this study is that not all the measurements were conducted simultaneously because of the lack of measurement devices. Such has caused minimal deviation of measuring environment (temperature and relative humidity) and resulted in differences among three repeated measurements. Thus, we used arithmetic mean as representative figures of size and number distribution of humidifier-emitted particles.

We utilized OPS and SMPS as real-time monitoring devices during the operation of the humidifier. However, the data were used separately although we could have merged the data of two devices and used them as integrated information. Such decision was mainly due to the notable difference in the number concentration at the similar range of detection. The detection range of OPS is 0.3 μm–10 μm and that of SMPS is 11 nm–420 nm, thus suggesting that the range of 0.3 μm–0.42 μm overlaps in the two devices. The differences were random and not even, but the number concentration of OPS was often about 100 times more than that of SMPS. The reason for the differences could not be clarified, and so the data of two devices were not merged and were showed individually.

One question concerns the peak at the initial part of phase 3 in some of the cases (mostly at 1 m and 2 m). The number concentration suddenly increased and then dropped lower than the average of phase 2 (Appendix 1). Two possible reasons could explain this phenomenon: 1) particles from the outside were brought into the cleanroom when the researcher came in to turn off the humidifier power; 2) laminar flow formed through phase 2 was disrupted because of the researcher's movement. The researcher was always dressed in dust-free clothes, and we expected low possibility of inflow of particles from the outside. The GM of particle size did not fluctuate at the same time, thus we consider this was because of the turbulence when the researcher was moving in and out since the sampling port of 2 m was comparably close to the entrance of the cleanroom. We expect this would not occur if the influence of hinged door were excluded, and that another test needs to be conducted in the clean room with more space and with more careful movement in it.

5. Conclusion

This study aimed to characterize the exclusive behavior of PHMG among the aerosols emitted from ultrasonic humidifier. The dryer set comprising diffusion dryer and thermodenuder was selected to evaporate the water among the mists.

The dispersion characteristics of particles were compared when only water was put into the water tank and when PHMG solution was also added, with and without the dryer set. The addition of PHMG produced more particles under 10 μm; the number concentration and the GM of particle size increased as the amount of PHMG added in water also increased. The number concentration generally decreased by 1 m apart from the humidifier outlet, but increased again at 2 m. However, the aerosol consisted bigger particles (0.3 μm–10 μm) with higher water content at 2 m while most particles were nano-sized at 0.5 m.

Consequently, we confirmed that the addition of PHMG produces larger and more aerosols from the ultrasonic humidifier. Although the possibility that PHMG inhaled by human can vary by conditions, aerosols containing PHMG can reach to 2 m from the humidifier outlet with the size of respirable fraction and can cause adverse effect to human health.

6. References

Allen, E. H., James, F. D., & Jonathan, P. R. (2015). Dynamics of particle size on inhalation of environmental aerosol and impact on deposition fraction. Environmental Science & Technology. 49(24), 14512-21.

An, W. J., Pathak, R. K., Lee, B. H., & Pandis, S. N. (2007). Aerosol volatility measurement using an improved thermodenuder: application to secondary organic aerosol. Journal of Aerosol Science. 38(3), 305–14.

Baker, P. B. (2000). Arizona Agricultural Pesticide Applicator Training Manual for Certification and Continuing Education. III-1 – III-18.

Burtscher, H., Baltensperger, U., Bukowiecki, N., Cohn, P., Huglin, C., Mohr, M., Matter, U., Nyeki, S., Schmatloch, V., Streit, N., & Weingartner, E. (2001). Separation of volatile and non-volatile aerosol fractions by thermodesorption instrumental development and applications. Journal of Aerosol Science. 32(4), 427-42.

Cappa, C. D. (2010). A model of aerosol evaporation kinetics in a thermodenuder. Atmospheric Measurement Techniques. 3(3), 579-92.

Choi, J. E., Hong, S. B., Do, K. H., Kim, H. J., Chung, S. H., Lee, E., Choi, J. H., & Hong, S. J. (2016). Humidifier disinfectant lung injury, how do we approach the issues?. Environmental Health and Toxicology. 31, e2016019.

Choi, Y. Y., Lim, H. K., Lim, S. Y., & Paek, D. M. (2012). Health damages and lessons of the use of humidifier disinfectants in Korea. Korean Society of

Environmental Health. 38(2), 166-74.

Giles, D. K., Welsh, A., Stenke, W. E., & Saiz, S. G. (1995). Pesticide inhalation exposure, air concentration, and droplet size spectra from greenhouse fogging. Health and Safety Report. 38(5), 1321-6.

Hung, D. V., Tong, S., Nakano, Y., Tanaka, F., Hamanaka, D., & Uchino. (2010). Measurements of particle size distributions produced by humidifiers operating in high humidity storage environments. Biosystems Engineering. 107(1), 54-60.

Hwangbo, S. A., & Chu, M. C. (2013). The effect of water droplets on the nano particle size distribution using the SMPS system. Journal of Korean Powder Material Industry. 20(2), 129-33.

Kim, S. K., & Paek, D. M. (2016). Humidifier disinfectant disaster: what is known and what needs to be clarified. Environmental Health and Toxicology. 31, e2016025.

Korea Center for Disease Control & Prevention (KCDC). (2011). Aerozolization of humidifier disinfectants. Public Health Weekly Report. 4(45), 831-2.

Lee, J. H. (2016). What must be done to prevent another humidifier disinfectant disaster?. Environmental Health and Toxicology. 31, e2016024.

Lee, S. K. (2015). Development of risk assessment method of biocide active ingredients. Ministry of Environment.

Lee, J. H., Kang, H. J., Seol, H. S., Kim, C. K., & Yoon, S. K. (2013). Refined

exposure assessment for three active ingredients of humidifier disinfectants. Environmental Engineering Research. 18(4), 253-7.

Lee, J. H., Park, K. H., & Oh, H. B. (2014). Risk assessment for hazardous substances contained in household products.

Lee, J. H., & Yu, I. J. (2017). Human exposure to polyhexamethylene guanidine phosphate from humidifiers in residential settings: cause of serious lung disease. Toxicology and Industrial Health. 33(11), 1–8.

McIntosh, A. H. (1951). Particle size of insecticidal suspensions and their contact toxicity IV. mechanisms of action of different-sized particles. Annals of Applied Biology. 38(4), 881-98.

Park, D. U., Ryu, S. H., Lim, H. K., Kim, S. K., Choi, Y. Y., Ahn, J. J., Lee, E., Hong, S. B., Do, K. H., Cho, J. L., Bae, M. J., Shin, D. C., Paek, D. M., & Hong, S. J. (2017). Types of household humidifier disinfectant and associated risk of lung injury (HDLI) in South Korea. Science of the Total Environment. 596-597, 53-60.

Park, D. U., Ryu, S. H., Lim, H. K., Kim, S. K., Roh, H. S., Cha, W. S., & Park, D. Y. (2016). Estimation of humidifier disinfectant amounts inhaled into the respiratory system. Korean Journal of Environmental Health. 42(3), 141-6.

Park, D. U., Ryu, S. H., Lim, H. K., Kim, S. K., Ahn, J. J., Roh, H. S., Choi, Y. Y., Cha, W. S., Lee, E., Hong, S. B., Do, K. H., Cho, J. L., Bae, M. J., Shin, D. C., Paek, D. M., & Hong, S. J. (2016). Characteristics of exposure to humidifier disinfectant by lung injury patients. Korean Journal of Environmental Health. 42(3),

147-59.

Park, D. U. (2016). Major concerns regarding lung injury and related health conditions caused by the use of humidifier disinfectant. Environmental Health and Toxicology. 31, e2016014.

Park, D. U., Friesen, M. C., Roh, H. S., Choi, Y. Y., Ahn, J. J., Lim, H. K., Kim, S. K., Koh, D. H. Jung, H. J., Lee, J. H., Cheong, H. K., Lim, S. Y., Leem, J. H. Kim, Y. H., & Paek, D. M. (2015). Estimating retrospective exposure of household humidifier disinfectant. Indoor Air. 25(6), 631-40.

Park, J. K. (2007). Effects of ultrasonic humidifier on the change in relative humidity of indoor apartment during wintertime. Korea Society of Environmental Administration. 13(1), 25-34.

Rodes, C., Smith, T., Crouse, R., & Ramachandran, G. (1990). Measurements of the size distribution of aerosols produced by ultrasonic humidification. Aerosol Science and Technology. 13(2), 220-29.

Sain, A.E., Zook, J., Davy, B.M., Marr, L.C., & Dietrich, A.M. (2018). Size and mineral composition of airborne particles generated by an ultrasonic humidifier. Indoor Air. 28(1):80-88.

Shrivastava, A., & Gupta, V. (2011). Methods for the determination of limit of detection and limit of quantitation of the analytical methods. Chronicles of Young Scientists. 2(1), 21-5.

Svetlana, S., Branka, M., Pierre, M., Samuel, C., & Zoran, R. (2015). Characterisation of a commercially available thermodenuder and diffusion drier for ultrafine particles losses. Aerosol and Air Quality Research. 15(1), 357–63.

United States Environmental Protection Agency (1991). Use and Care of Home Humidifiers.

Yoon, J. S., Cho, H. J., Lee, E., Choi, Y. J., Kim, Y. H., Lee, J. L., Lee, Y. J. & Hong, S. J. (2017). Rate of humidifier and humidifier disinfectant usage in Korean children: a nationwide epidemiologic study. Environmental Research. 155, 60-3.

국문초록

가습기 사용시 발생하는 살균제 PHMG의 공기 중 거동 특성

김유진

서울대학교 보건대학원

환경보건학과 산업보건전공

연구목적 : 가습기 살균제로 인한 폐질환 발병 사고 이후, 가습기 살균제의 독성학적 및 역학적 영향에 대한 연구가 꾸준히 진행되어왔다. 그러나 가습기 가동 시 발생하는 입자, 특히 입자 중 유효성분인 가습기 살균제가 보이는 거동 특성에 대한 연구는 상대적으로 부족한 상황이다. 이 연구는 가습기 살균제 성분 중 대표적으로 쓰인 PHMG를 초음파 가습기에 투입하여 이용할 때의 거동 특성을 확인하고, 이를 통해 입자 중 수분의 영향에 대해 파악하는 것을 목적으로 한다.

연구방법 : 먼저 실험을 통해 5가지의 공기 건조 장치 조건 중 PHMG 단독의 거동 특성을 확인하기 위한 최적의 측정 조건을 설정하였다. 선

정된 건조 장치 조건을 이용할 때와 이용하지 않을 때에 가습기에서 발생한 입자들의 거동을 비교하였다. 가습기 중 PHMG 성분의 농도와 시료 채취 거리 등을 달리하여 SMPS와 OPS를 이용한 입도 분포와 공기 중 수농도 분포를 확인하였다. 필터 샘플링을 통해 공기 중 PHMG 입자들을 포집한 후 저울을 통해 중량 분석을 실시하였고, 에너지분산형 X선 분석 장치를 부착한 주사전자현미경을 이용하여 입자의 형태학적 특성 파악 및 성분 분석을 진행하였다.

연구결과 : PHMG의 투입량이 증가할수록 직경 10 μm 이하의 입자 수농도는 증가하였고, 평균 입자 크기 또한 커지는 경향을 보였다. 같은 양의 PHMG를 투입하여 가습기를 가동할 경우에는 거리가 멀어질수록 수농도가 감소하다가 2 m 지점에서 다시 증가하였다. 0.5 m 지점에서 대부분의 입자들이 나노 사이즈였던 데에 비해 2 m 지점에서는 0.3 μm 에서 0.5 μm 사이에 해당하는 큰 입자들이 25% 정도를 차지한다는 차이점을 발견하였다. 그러나 공기 건조 장치를 사용하지 않았을 경우 거리가 멀어질수록 0.3 μm 이상의 입자 수농도는 계속해서 증가하였다. 가습기를 가동하는 동안 입자를 포집한 필터의 중량에는 큰 차이가 발생하지 않았지만, 주사전자현미경을 통한 분석 결과, 실시간 측정기기를 통한 결과와 비슷한 크기의 인 성분을 함유한 입자들이 발견되었으며, 작은 입자들이 한데 모여 엉겨 있는 형태로 분포하고 있는 것을 알 수 있었다.

결론 : 본 연구의 목적은 가습기 살균제 PHMG가 공기 중에서 나타내는 거동 특성을 파악하는 것이었다. 물만 투입하여 가습기를 가동하였을 때와 비교하였을 때 가습기에서 발생하는 0.5 μm 이하 크기의 입자수 농도가 10배 이상으로 나타났다. 가습기에서 2 m 이상 떨어진 지점에서도 PHMG 성분의 입자들이 높은 농도로 측정되는 것을 알 수 있었다. 가까운 지점에서와 비교했을 때에 상대적으로 입자의 크기가 큰 편이며, 수분의 함량이 높은 편이므로 호흡기에 유입되어 건강상 악영향을 끼칠 가능성은 낮아진다. 그러나 여전히 호흡성 입자에 해당하는 10 μm 미만의 크기로 공기중에 존재한다는 데에 집중할 필요가 있다.

주요어 : 가습기 살균제, PHMG, 가습기 입자, 입자상 물질, 살균제, 유효 성분

학번 : 2016-24046

Appendix

Appendix 1. Selection of measurement condition of water-free PHMG particle

Number concentration of humidifier-emitted particles

Table A1 summarizes the number concentration of particles at different size range emitted from ultrasonic humidifier. With option 5 (WO) when the water tank was only filled with 3rd distilled water, 96% of the total particles were with size less than 0.3 μm, and 92% were nanoparticles. Every dryer set shows that majority of particles had size under 100 nm, whereas the overall particle size and number concentration increased when PHMG was also put into the water tank.

Time-varying number concentrations measured with SMPS depending on the options are described in Figure A1. As the humidifier filled with water only is turned on, the number concentration of particles slowly increased by time and reached the maximum level (9,000 #/cc on the average) in about 30 mins without any dryers. Four different options showed distinctive results compared to option 5 in terms of the average number concentration. When each dryer type was used separately, the efficiencies of water removal were relatively lower (of 9,000 #/cc for option 1 (T), 8,000 #/cc for option 2 (D)) than when both of the dryer types were used (4,000 #/cc for option 3 (T+D), 2,000 #/cc for option 4 (D+T)). A difference in water removal efficiencies were noted even when the order of two dryers are changed.

The time to reach the maximum number concentration was almost same when 64 ppm of PHMG is added. However, the scale of number concentration and the average particle size were different. While the number concentration on SMPS barely exceeded 10,000 #/cc when only water was put into the water tank, it reached to 88,000 #/cc on the average and to 180,000 #/cc in maximum with option 5 (WO) during the operation. Moreover, 61% of the total particles were with size less than 0.3 μm, and 39% were nanoparticles. Option 2 ((D) 78,000 #/cc on average) was relatively less efficient than the other options (42,000 #/cc for option 1 (T), 38,000 #/cc for option 3 (T+D), 25,000 #/cc for option 4 (D+T)) when water removal was considered.

Table A1. The number concentration of particles by size at different phases (unit: #/cc)

Concentration	Types of dryer	During operation			After operation		
		~100 nm	100 nm ~ 0.3 μm	0.3 μm ~ 10 μm	~100 nm	100 nm ~0.3 μm	0.3 μm ~ 10 μm
Water	T	8688 ± 1053	355 ± 124 137 - 11,058	350 ± 53	428 ± 625	32 ± 23 103 - 4,964	45 ± 43
	D	7823 ± 1031	287 ± 119 1,473 - 10,105	435 ± 139	398 ± 320	40 ± 23 133 - 1,680	57 ± 41
	T+D	3693 ± 814	236 ± 76 271 - 5,061	34 ± 8	278 ± 366	51 ± 35 132 - 2,717	32 ± 12
	D+T	1996 ± 355	71 ± 29 97 - 2,438	45 ± 8	338 ± 39.16	229 ± 10 213 - 1,143	45 ± 10
	WO	8,432 ± 1,676	511 ± 169 2,449 - 13,428	1,958 ± 517	993 ± 585.76	400 ± 55 2,338 - 6,865	1,685 ± 211
64 ppm PHMG	T	25,360 ± 5,477	16,407 ± 4,354 41,945 - 279,577	191,929 ± 41,666	1,026 ± 1,450	1,168 ± 868 7,163 - 177,092	48,854 ± 40,700
	D	48,702 ± 10,140	29,071 ± 6,237 17,450 - 284,257	161,630 ± 33,129	1,061 ± 2,253	973 ± 1,003 3,016 - 171,283	39,205 ± 41,122
	T+D	22,935 ± 4,662	15,220 ± 3,258 8,832 - 197,611	126,688 ± 33,883	1,301 ± 2,818	1,065 ± 1,663 2,838 - 156,700	34,531 ± 38,311
	D+T	14,474 ± 2,742	10,208 ± 2,093 4,789 - 162,438	103,278 ± 28,163	764 ± 1,342	786 ± 754 3,045 - 128,390	32,138 ± 33,784
	WO	57,444 ± 9,583	30,621 ± 5,294 30,288 - 273,000	143,507 ± 33,786	1,108 ± 2,262	887 ± 1,043 3,164 - 165,225	33,414 ± 36,086

* T: Thermodenuder, D: Diffusion dryer, WO: Without dryers

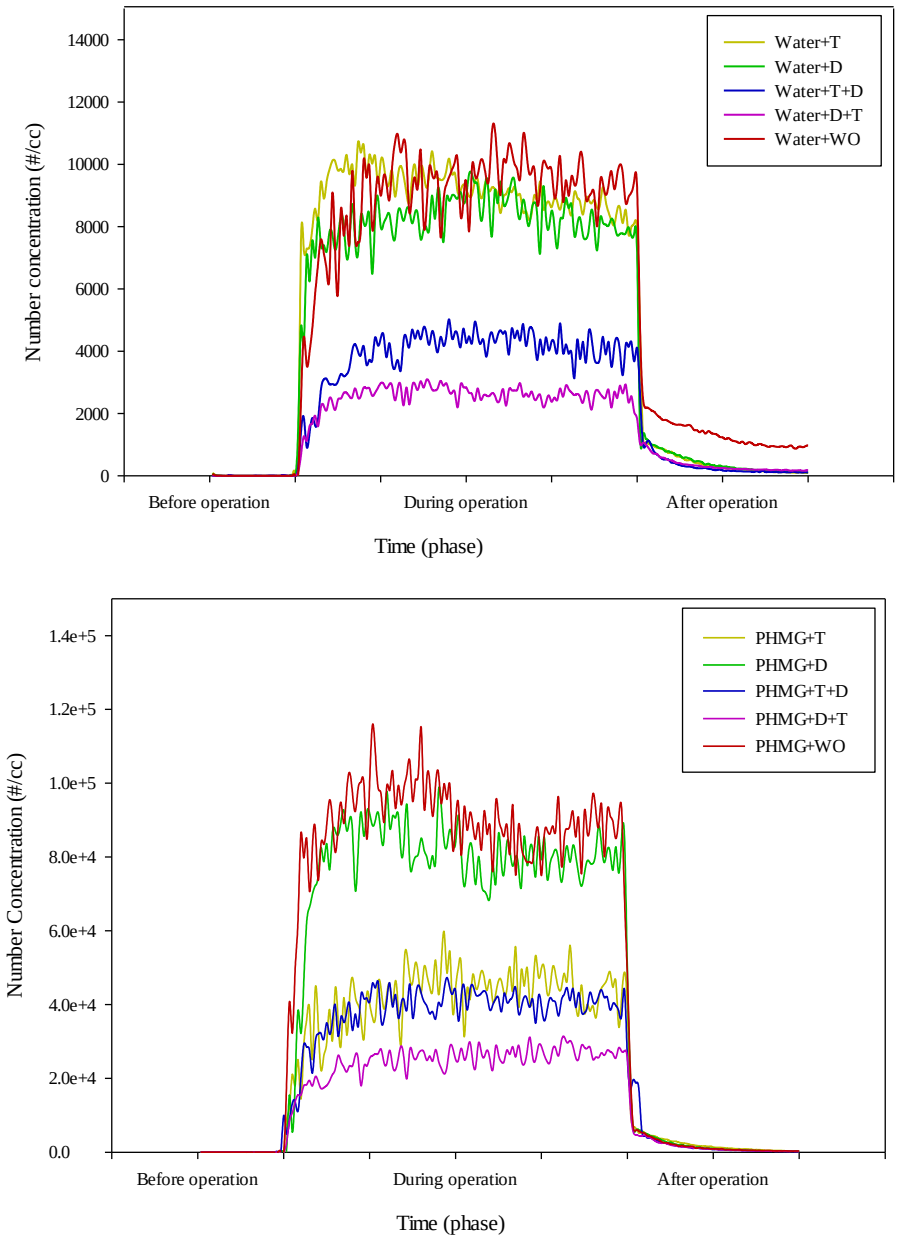


Figure A1. Time-varying number concentration of particles less than 0.3 μm emitted from humidifier by dryer types. (a) without PHMG, (b) with PHMG (64 ppm in solution)

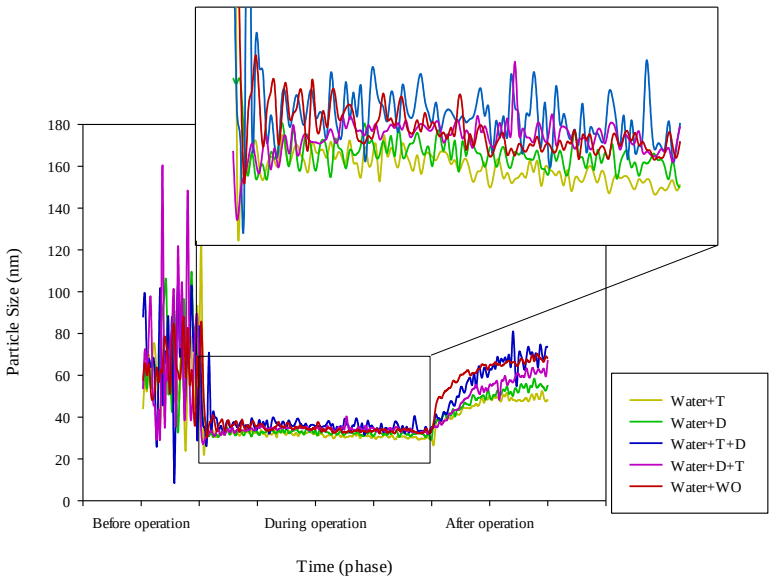
* T: Thermodenuder, D: Diffusion dryer, WO: Without dryers

Size distribution of humidifier-emitted particles

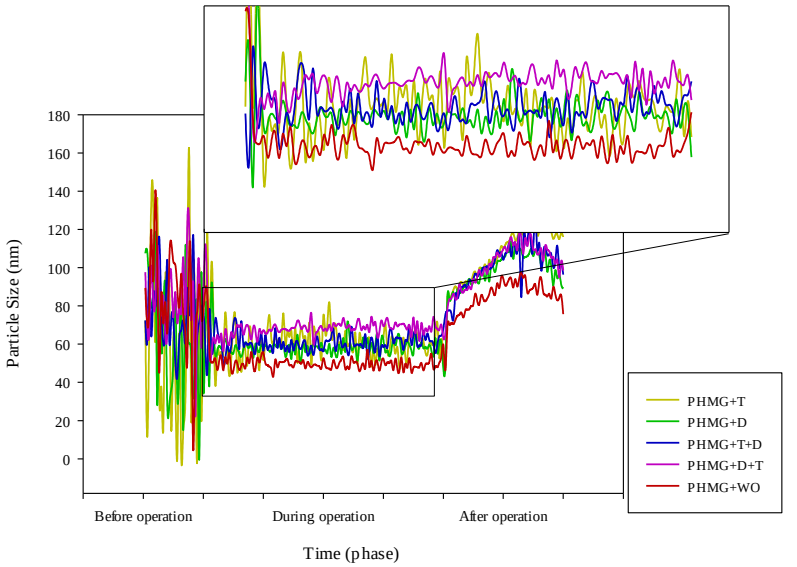
Secondly, we checked the stability of the dryer sets in the aspect of size distribution. Figure 4 shows the time-varying geometric mean (GM) of the aerosol emitted from the humidifier by the options. The GM was fluctuating intensively before the operation since the ventilation fan was turned on. However, during the operation, the GM was kept stable at the size of 30 nm regardless of the dryer set. Overall particle size grew up after the operation.

There was a significant difference when PHMG was also added to humidifier. GM size was between 40 to 80 nm but differ by the options. We could find that GM also increases as the water removal efficiency gets higher (average GM size around 70 nm with option 4 (D+T)). With the combination of two dryers (option 3 (T+D) and option 4 (D+T)), GM did not showed much of fluctuation when compared to the case when each of the dryers were used individually. The trend of GM fluctuation before the operation and growth after the operation was identical when PHMG was added.

We expected that option 4 (diffusion dryer + thermodenuder) would be a proper dryer combination to minimize the effect of water in the air with the basis that the water removal efficiency was high and the mean size of the particles was kept relatively stable. Consequently, we used option 4 at part 3 to figure out the behavior characteristics of water-free PHMG aerosol.



(a)

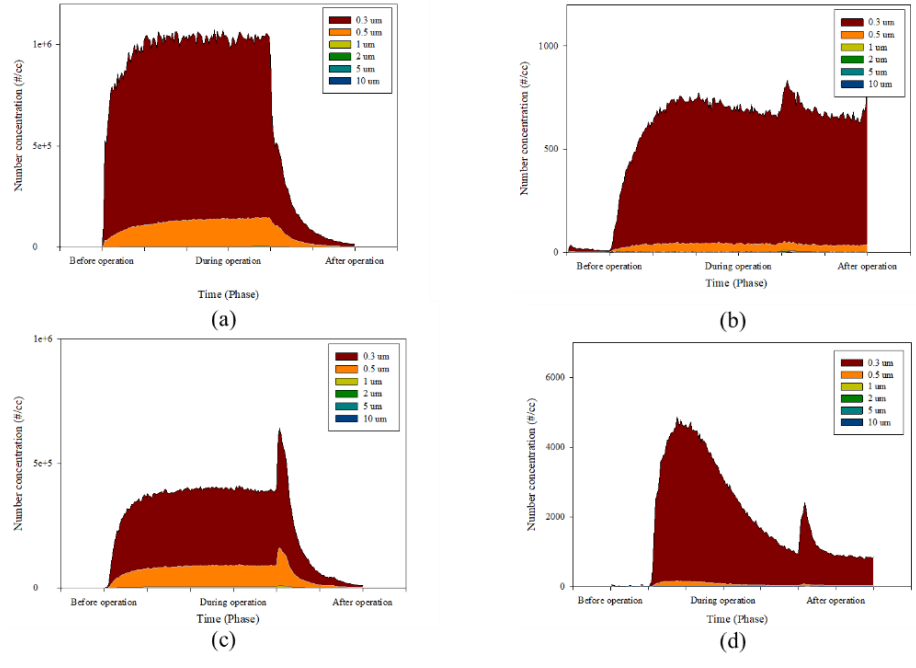


(b)

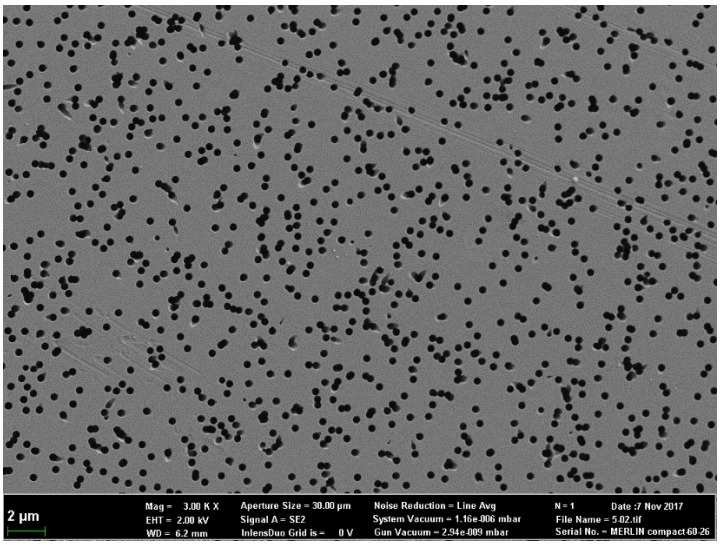
Figure A2. Time-varying geometric mean particle size emitted from humidifier by dryer types. (a) without PHMG, (b) with PHMG (64 ppm in solution)

* T: Thermodenuder, D: Diffusion dryer, WO: Without dryers

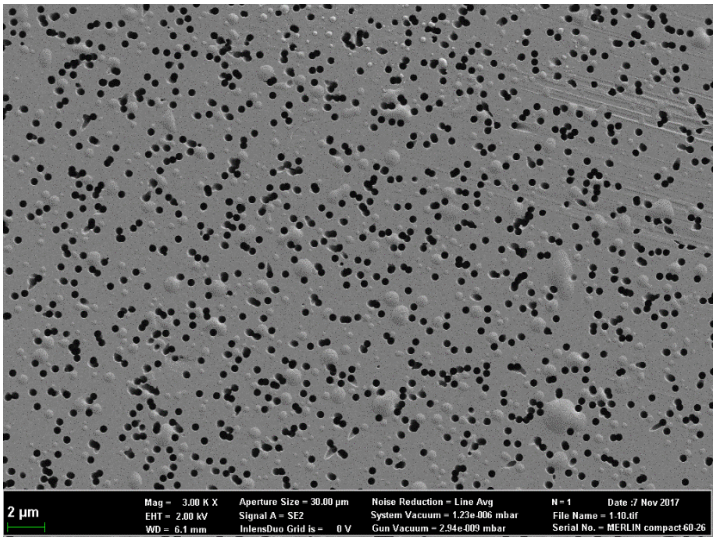
Appendix 2. Time-varying number concentration at different distance from the humidifier when the dryer set was attached. (a) 0 ppm, 0.5 m, (b) 64 ppm, 0.5 m, (c) 0 ppm, 2 m, (d) 64 ppm, 2 m



Appendix 3. The surface of PC filter with and without waterdrops when PHMG was added in reservoir. ; (a) 2 m , (b) 0.5 m



(a)



(b)