

Simulated Inhalation Levels of Fragrance Materials in a Surrogate Air Freshener Formulation

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This study measured postapplication exposure levels of fragrance materials in a surrogate air freshener formulation in an environmentally-controlled exposure room (ECER). A five-s spray was released to simulate normal consumer use conditions. Time-course airborne fragrance material levels were sampled with Tenax tubes, and aerosol size distributions were monitored with a TSI 3320 aerodynamic particle sizer. Triplicate experiments were performed for each of the control/test substances. The control substance (unfragranced formulation) experiments indicated that the airborne fragrance materials were not detected, suggesting that the base propellant formulation did not interfere with the sampling procedure or analytical results. The test substance experiments found that the higher the volatility of the fragrance material, the higher the airborne fragrance concentration within the ECER. In the adult breathing zone height, the maximum concentrations of the nine fragrance materials ranged from 108 to 347 $\mu\text{g}/\text{m}^3$ during the first minute postapplication. In the child breathing zone height, the maximum fragrance material concentrations ranged from 125 to 362 $\mu\text{g}/\text{m}^3$ during 2–6 min post-application. Particle size distributions indicated that approximately 60–70% of the generated aerosols were less than 1 μm aerodynamic diameter. Initial peak particle mass concentrations ($<5 \mu\text{m}$) were 800–1000 $\mu\text{g}/\text{m}^3$ during the first minute postapplication. Following initial peak concentrations, there was approximately 10–15 min of fluctuation, and then particle levels decayed gradually and exponentially to near background levels. Exposure to the test formulation would originate from two components: particle-bound and vapor-phase fragrance materials. Particle-bound fragrance exposure accounted for approximately 47% and 72% of the total exposures during the first minute postapplication period in the adult and child breathing zone heights, respectively.

Introduction

Many consumer products used in homes contain fragrance materials, including cosmetics, toiletries, and household air

care and laundry products. Although considerable information exists on the dermal effects of exposure to fragrance materials (1–3), relatively little information exists on inhalation exposure to these substances and what does exist suggests that inhalation is a minor route of exposure (4). Numerous anecdotal reports suggest that fragrance materials may elicit a variety of adverse health effects including headaches, dizziness, shortness of breath, difficulty in concentrating, and exacerbation of allergies and asthma (5–10). Some researchers argue that individuals with idiopathic environmental intolerances (IEI) experience symptoms that are triggered by fragrances (11–13). This line of argument has been the source of considerable debate in scientific and nonscientific circles. It is clear that more controlled research is needed to better elucidate the inhalation exposure levels that an individual might encounter. This paper presents results of triplicate application experiments designed to characterize potential inhalation exposure levels of nine fragrance materials and associated particle size distributions and concentrations following release from a pressurized surrogate air freshener that one might use in their home. The results will be used to conduct further research on potential health effects of fragrances on asthmatic and nonasthmatic human subjects.

Materials and Methods

This study was designed to characterize potential consumer inhalation exposure to a surrogate air freshener formulation. The surrogate formulation contained nine fragrance materials, and was released for approximately 5 s from a pressurized aerosol spray can during each experiment. The nine fragrance materials in the surrogate formulation included (at 0.06% each by weight): benzyl acetate (BA), eugenol (EU), α -hexyl cinnamic aldehyde (HCA), 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylcyclopenta- γ -2-benzopyran (HHCB), hydroxycitronellal (HO-C), β -ionone (β -I), *d*-limonene (*d*-L), linalool (LL), and methyl dihydrojasmonate (MDJ). The fragrance materials were selected for their importance in fragranced products, physicochemical properties, and known irritant or sensitization potential. The airborne concentrations of the nine fragrance materials and associated particles were measured up to 2 h postapplication in the adult breathing zone (ABZ) and child breathing zone (CBZ), which were approximately 1.5 and 0.5 m above the floor, respectively.

An unfragranced control formulation was tested to verify whether the inert ingredients in the formulation contributed any background interference. This control formulation was the same as the test formulation except without these nine fragrance materials. Triplicate experiments were performed on each control/test substance formulation.

Test, Control, and Reference Substances. The test and control substances were supplied by Takasago International Corporation (Rockleigh, NJ) in pressurized aerosol spray cans.

The test substance was composed of 0.06% each of the BA, EU, HCA, HHCB, HO-C, β -I, *d*-L, LL, and MDJ fragrance materials, 0.2% BHA (antioxidant/stabilizer), 0.5% Witconol (food grade emulsifier; polyglycerol ester of oleic acid), 29% hydrocarbon propellant (~20% propane and 80% isobutane), and 69.76% water.

2. Composition of the Control Substance (Unfragranced Base). The control substance was the same as the test substance, except that the fragrance materials were replaced with water.

Givaudan Fragrances Corporation (Cincinnati, OH), Firmenich Inc. (New York, NY), and International Flavors and Fragrances, Inc. (New York, NY) supplied the reference

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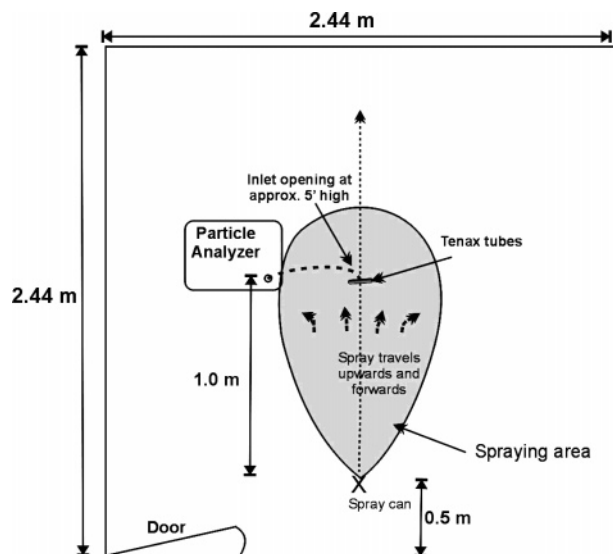


FIGURE 1. Plan view of experimental layout within the environmentally controlled exposure room (ECER).

fragrance materials. The reference substances were used to prepare fortification samples for quality control purposes.

Test Room. All experiments were conducted in a 2.44 m \times 2.44 m \times 2.44 m (14.5 m³) environmentally controlled exposure room (ECER). Figure 1 illustrates a schematic diagram of the ECER. Its dimensions were determined from a local survey of typical residential bathrooms. The ECER was housed within a simulated residential exposure room (SRER) at the Toxcon HSRC Inc. facility in Edmonton, AB. This room was 4.88 m \times 4.88 m \times 2.44 m (58.0 m³). The environmental conditions of the SRER were controlled automatically by a facilitator ventilation management system (Johnson Controls, Inc., Milwaukee, WI) to simulate typical residential conditions (14). The target environmental conditions within the ECER were 72 \pm 4 $^{\circ}$ F, 50 \pm 10% relative humidity (RH), and 0.6 \pm 0.1 air changes per hour (ACH). The air exchange rate was determined using a sulfur hexafluoride (SF₆) tracer decay method (15). During the study period, air exchange rate was checked every week to ensure a consistent ventilation rate. ECER temperature and humidity were monitored with a NIST (National Institute of Standards and Technology)-certified thermohygrometer (digital thermohygrometer, Control Company, Friendswood, TX) during each application experiment.

Sampling Equipment. This study used Tenax TA thermal desorption tubes (Supelco, Oakville, ON) to collect airborne fragrance samples. The sampling tubes were thermally preconditioned at 340 $^{\circ}$ C for 40 min with a model 60 Dynatherm six-tube conditioner (CDS Analytical Inc., Oxford, PA) before use. During conditioning, nitrogen was continuously purged through each tube to remove desorbed fragrance materials. After thermal conditioning, the tubes were cool-purged with nitrogen for 9 min to ambient temperature.

Each tube was assigned to a designated sampling location in every replicate experiment so as to minimize any variation due to sampling position, duration, or the tube itself. For background air sampling, two sampling tubes were connected via 1/4-in. Tygon tubes to two personal air sampling pumps (SKC Inc. PCXR series, Eighty Four, PA) for the ABZ and CBZ.

Two sets of 11 sampling tubes for the ABZ and CBZ were used for each application experiment. Air was drawn through the sampling tubes by a GAST vacuum pump (0323-101Q-G582DX, GAST Manufacturing Inc., Benton Harbor, MI) via 1/4-in. Tygon tubes. Sampling flow rate was controlled and monitored by six precalibrated rotameters. Three-way valves

were used to switch from one sample tube to another according to a designated time-course sampling schedule, as shown in Table 1. Figure 1 illustrates the air sampling locations inside the ECER.

Airborne aerosols were monitored using an aerodynamic particle sizer (APS 3320, TSI Inc., St. Paul, MN). The APS is a time-of-flight laser-based spectrometer that measures aerodynamic diameter of particles. The instrument can measure airborne particles from 0.5 to 20 μ m. For particles from 0.3 to 0.5 μ m, the APS can detect them without size resolution. The lower detection limit of the APS is 0.3 μ m. The APS's sampling inlet was extended to ABZ or CBZ with a conductive rubber tube. The direction of the sampling tube was approximately perpendicular to the direction of the aerosol spray path. It was approximately 0.3 m from fragrance sampling tubes to minimize the interference of aerosol sampling flow. Particle data were collected before, during, and after each application up to 2 h postapplication.

Application of Test and Control Substances. Three replicate experiments were performed on separate days for each of the control/test substances by the same research team. Prior to each application, the aerosol spray can was shaken vigorously for approximately 10 s. Aerosol spray was then released upward through the nozzle on top of the spray can for approximately 5 s. The spray was delivered approximately 1.2–1.4 m above the floor with a slight sweeping motion (within a width of 0.3 m from the center line). Spray application was conducted through a small window on one side of the ECER wall to minimize the applicator's impact. Following each application, the window was closed to ensure a minimum disturbance. The initial and final weights of the spray can were recorded to determine the actual mass of formulation released.

Sample Collection and Storage. Airborne fragrance material samples were collected following the EPA TO-17 sorbent tube sampling method for volatile organic compounds (16). Both background air samples and postapplication samples were collected to construct time-course fragrance material concentration decay curves.

Collection of Background Fragrance Air Samples. Two background air samples were collected on the same day immediately prior to each control or test substance application in ABZ and CBZ. Background air samples were collected at approximately 100 mL/min for 30 min using one SKC personal sampling pump (SKC Inc. PCXR Series, Eighty Four, PA) for each sampling tube. The sampling flow rate was precalibrated with a mini-BUCK flow calibrator (model M-5, A.P. Buck Inc., Orlando, FL). Background samples were handled, stored, and analyzed in exactly the same manner as test samples.

Collection of Postapplication Fragrance Air Samples. For each control/test substance application experiment, air samples were collected at postapplication times $t = 0-1$, $0-2$, $0-3$, $0-4$, $0-5$, $0-6$, $8-18$, $20-40$, $45-65$, $65-95$, and $95-125$ min at a flow rate of approximately 100 mL/min. For each time interval, air samples were collected at ABZ and CBZ simultaneously. The sampling flow rate was calibrated with the same mini-BUCK flow calibrator. For each control/test substance application experiment, 22 test samples and 2 background samples were collected. Three replicates were performed for each control/test substance. A total of 144 samples were collected in the study.

After sampling, each sample tube was sealed in an airtight cylinder supplied by the manufacturer. The cylinders were stored in airtight containers with activated charcoal. Samples were kept in a refrigerator (4 \pm 2 $^{\circ}$ C) until analysis. Following sample analysis, the tubes were again conditioned by the model 60 Dynatherm six-tube conditioner with the procedures described previously.

TABLE 1. Sequential Average Airborne Fragrance Material Concentrations Following Test Substance Applications

sampling time (min)	averaging time (min)	average airborne fragrance material concentrations (μg/m ³) ^{a,b}								
		d-L	LL	BA	HO-C	EU	β-I	MDJ	HCA	HHCB
Sampling Zone Height: ABZ										
0–1	0.5	347 ± 87	339 ± 102	318 ± 87	264 ± 26	339 ± 78	227 ± 57	114 ± 13	109 ± 10	108 ± 13
1–2	1.5	77 ± 44	49 ± 60	44 ± 44	70 ± 40	83 ± 28	151 ± 37	12 ± 16	43 ± 12	38 ± 14
2–3	2.5	110 ± 27	77 ± 28	79 ± 13	113 ± 54	85 ± 78	102 ± 71	36 ± 9	55 ± 7	55 ± 10
3–4	3.5	62 ± 30	75 ± 45	47 ± 46	245 ± 179	229 ± 241	284 ± 216	18 ± 33	29 ± 42	39 ± 47
4–5	4.5	124 ± 35	75 ± 39	77 ± 42	88 ± 45	-6 ± 101	56 ± 50	35 ± 36	79 ± 38	55 ± 30
5–6	5.5	78 ± 34	93 ± 56	95 ± 44	18 ± 144	122 ± 89	128 ± 117	37 ± 39	57 ± 53	65 ± 40
8–18	13	134 ± 10	103 ± 6	91 ± 6	72 ± 12	57 ± 8	62 ± 6	36 ± 13	55 ± 17	54 ± 15
20–40	30	91 ± 3	71 ± 3	61 ± 5	47 ± 1	37 ± 2	40 ± 2	18 ± 5	26 ± 8	30 ± 10
45–65	55	57 ± 5	42 ± 4	34 ± 4	29 ± 2	21 ± 4	24 ± 0	10 ± 4	13 ± 5	18 ± 8
65–95	80	37 ± 2	27 ± 1	21 ± 0	19 ± 1	14 ± 2	15 ± 1	6 ± 1	6 ± 2	8 ± 5
95–125	110	29 ± 2	20 ± 1	15 ± 0	14 ± 1	10 ± 2	11 ± 1	4 ± 1	4 ± 1	5 ± 2
Sampling Zone Height: CBZ										
0–1	0.5	186 ± 104	155 ± 82	154 ± 81	182 ± 72	191 ± 81	126 ± 74	118 ± 62	128 ± 71	128 ± 77
1–2	1.5	262 ± 93	193 ± 55	184 ± 72	160 ± 56	123 ± 15	112 ± 58	78 ± 70	116 ± 64	138 ± 72
2–3	2.5	362 ± 115	300 ± 100	307 ± 90	156 ± 75	217 ± 69	242 ± 76	62 ± 69	128 ± 59	151 ± 63
3–4	3.5	330 ± 95	264 ± 67	271 ± 82	266 ± 65	213 ± 70	224 ± 81	122 ± 29	160 ± 62	179 ± 74
4–5	4.5	290 ± 73	263 ± 61	259 ± 60	181 ± 68	211 ± 34	131 ± 30	35 ± 25	143 ± 6	134 ± 16
5–6	5.5	340 ± 99	277 ± 72	265 ± 82	321 ± 70	239 ± 87	179 ± 53	125 ± 11	207 ± 61	230 ± 66
8–18	13	190 ± 17	161 ± 14	156 ± 17	137 ± 14	122 ± 14	114 ± 11	52 ± 10	85 ± 12	90 ± 12
20–40	30	54 ± 3	41 ± 5	36 ± 7	35 ± 9	24 ± 5	31 ± 7	10 ± 5	13 ± 6	14 ± 6
45–65	55	32 ± 10	23 ± 5	17 ± 4	18 ± 3	10 ± 2	14 ± 3	5 ± 1	4 ± 1	5 ± 2
65–95	80	27 ± 4	18 ± 3	14 ± 2	15 ± 2	9 ± 0	10 ± 1	4 ± 1	4 ± 1	4 ± 1
95–125	110	21 ± 5	14 ± 3	10 ± 2	12 ± 1	7 ± 1	7 ± 1	4 ± 1	3 ± 1	3 ± 1

^a $n = 3$, data are normalized to 5 g of spray mass. ^b Data are presented as mean \pm standard deviation.

Aerosol Monitoring. Sequential aerosol size distributions were collected in the ECER immediately prior to, during, and up to 2 h after each control/test substance application. The APS was started 15 min prior to each control/test substance application for background monitoring. Sampling frequency was one sample per minute. The APS counts particles in 52 size channels on a logarithmic scale. Raw data were converted to particle size distributions (on a count basis) to examine the sequential changes in particle sizes. In addition, sequential particle count concentrations, mass concentrations, and mean aerodynamic diameters were analyzed to examine the mechanisms affecting particle deposition behavior inside the ECER.

Test Fragrance Sample Analysis. Tenax desorption tubes were analyzed using an ACEM 900 thermal desorption system (CDS Analytical, Inc., Oxford, PA), coupled to an Agilent 6890 gas chromatograph and an Agilent 5973N mass selective detector (GC/MSD, Agilent Technologies, Palo Alto, CA). Prior to the analysis, the analytical method was validated to determine the minimum quantifiable level (MQL), recovery, and reproducibility of the method for each fragrance material.

Laboratory fortification samples were analyzed with test samples. The fortified sample was prepared by injecting 1 μL of a standard solution (prepared as a liquid standard in methanol) onto the sampling end of the tube, while being purged with approximately 100 mL/min of nitrogen gas (Zero-Gas, Praxair Inc). The fortified tube was then dry-purged for 10 min with nitrogen to remove solvent from the sorbent tube. A total of 12 laboratory-fortified quality control (QC) samples were analyzed to validate the calibration curves and to calculate method recovery. The mean recoveries ranged from 97 to 110%.

Results and Discussion

The target application time for each substance was 5 s to mimic the upper range of consumer usage in typical homes. Due to slight differences associated with applicator's manual release of the control/test substances, variation in application time occurred. The average amounts of control/test substances released into the ECER were 4.92 ± 0.90 g and 5.37 ± 0.63 g for the control and test substance experiments,

respectively. Because experimental results indicated that fragrance material and particle concentrations were related to the mass of test substance spray, concentration data presented in this paper were normalized so that the triplicate experiments were compared on the same basis. The measured fragrance material or particle concentrations (C) were normalized to 5 g of spray application mass with respect to the actual application mass (w), i.e., $C_{\text{normalized}} = C \times 5/w$.

Airborne Fragrance Material Concentrations. Triplicate experiments were conducted for each control or test substance. For control substance experiments, most fragrance materials were not detected or were less than their respective minimum quantifiable levels (MQLs). The results suggested that the base propellant formulation did not interfere with the sampling procedure or analytical results. Control substance experiments also suggested that background fragrance material concentrations in the ECER were negligible.

Test substance experiments indicated that airborne fragrance material concentrations were correlated with their volatility. Table 1 and Figure 2 present time-course mean concentrations ($n = 3$) of the nine fragrance materials. For each time-course sample, the results indicated that the airborne concentrations of the nine fragrance materials covered a wide span even though their concentrations in the surrogate test formulation were the same (0.06%). In general, the airborne concentrations of the nine fragrance materials increase from left (d-L) to right (HHCB) of Table 1. This trend is correlated with their volatility. Generally, the higher the volatility, the higher airborne concentrations were sampled. The volatility of d-L, LL, BA, HO-C, EU, β -I, MDJ, HCA, and HHCB at 20 $^{\circ}\text{C}$ were 1.2, 0.05, 0.10, 0.02, 0.009, 0.006, <0.001, <0.001, <0.001 mm-Hg, respectively.

In ABZ, the maximum fragrance material concentrations were observed immediately following test substance application. The maximum concentrations of the nine fragrance materials ranged from 108 to 347 $\mu\text{g}/\text{m}^3$ (average of triplicate experiments) during the first minute postapplication. The maximum concentrations occurred immediately postapplication due to direct spray plume contribution. This study applied test formulation approximately from 0.3 m toward the ABZ sampling tubes. Visual observation indicated that

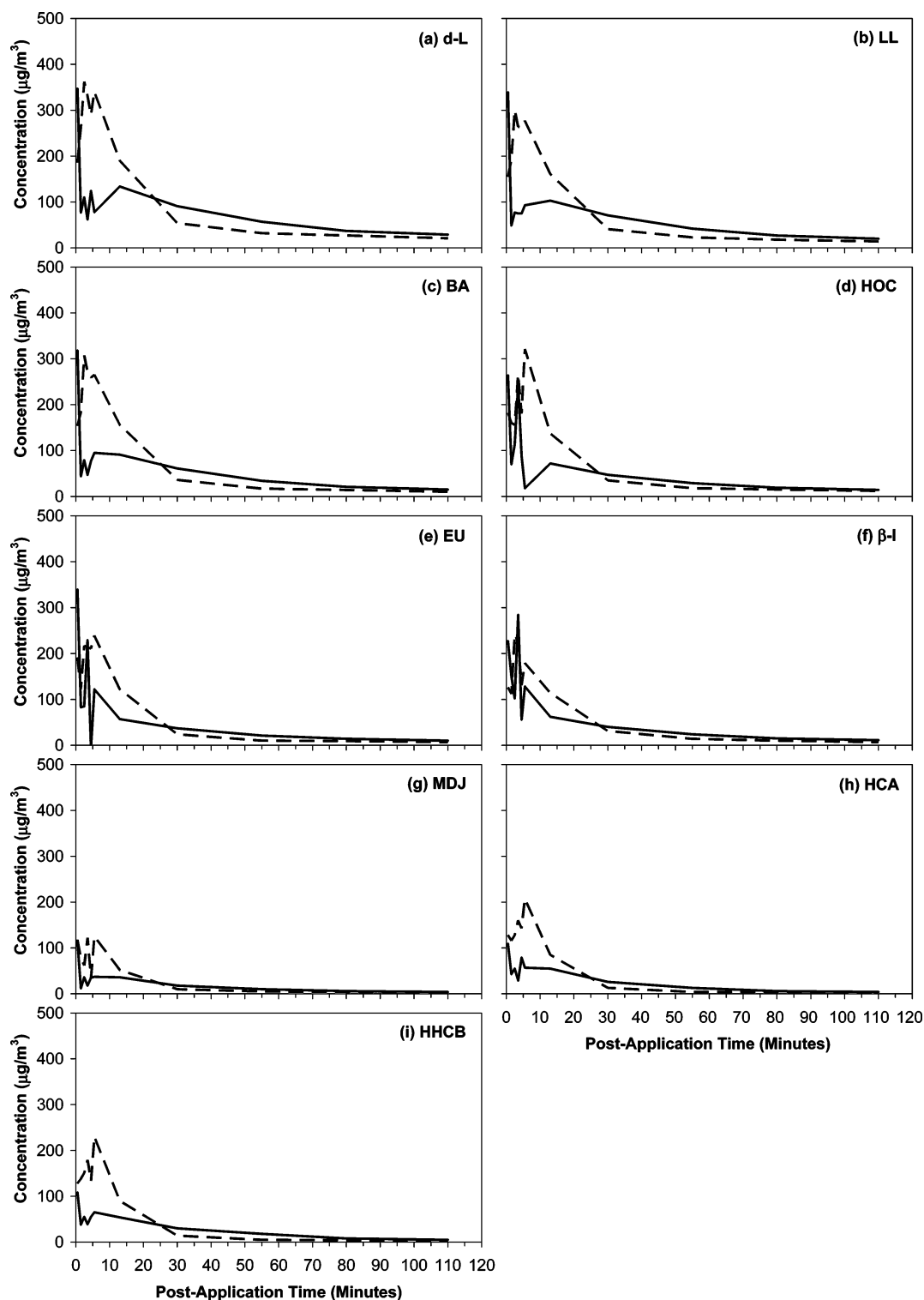


FIGURE 2. Sequential airborne fragrance material concentrations following test substance applications. Symbols: solid and dashed lines represent average concentrations ($n = 3$) in ABZ and CBZ, respectively.

the aerosol plume covered ABZ sampling tubes during spray application, causing maximum exposure levels during the first minute postapplication.

For CBZ, a 2–6 min time delay was observed between application and the attainment of peak concentrations. The maximum average concentrations of each of the nine fragrance materials ranged from 118 to 295 $\mu\text{g}/\text{m}^3$ ($n = 3$). The time delay could be explained by gravitational sedimentation of the spray plume. In this study, test substance was applied toward ABZ sampling tubes. After release, spray

plume settling downward gradually to CBZ. The maximum concentration in CBZ thus was delayed. Due to turbulent mixing of the spray jet, the exact time of maximum concentrations for each fragrance material varied run-to-run. The maximum concentrations of the nine fragrance materials generally were observed 2–6 min post-application.

Airborne Particle Analysis. Figure 3a illustrates sequential particle size distribution histograms (on a particle count basis) in ABZ for the first test substance experiment. The histograms

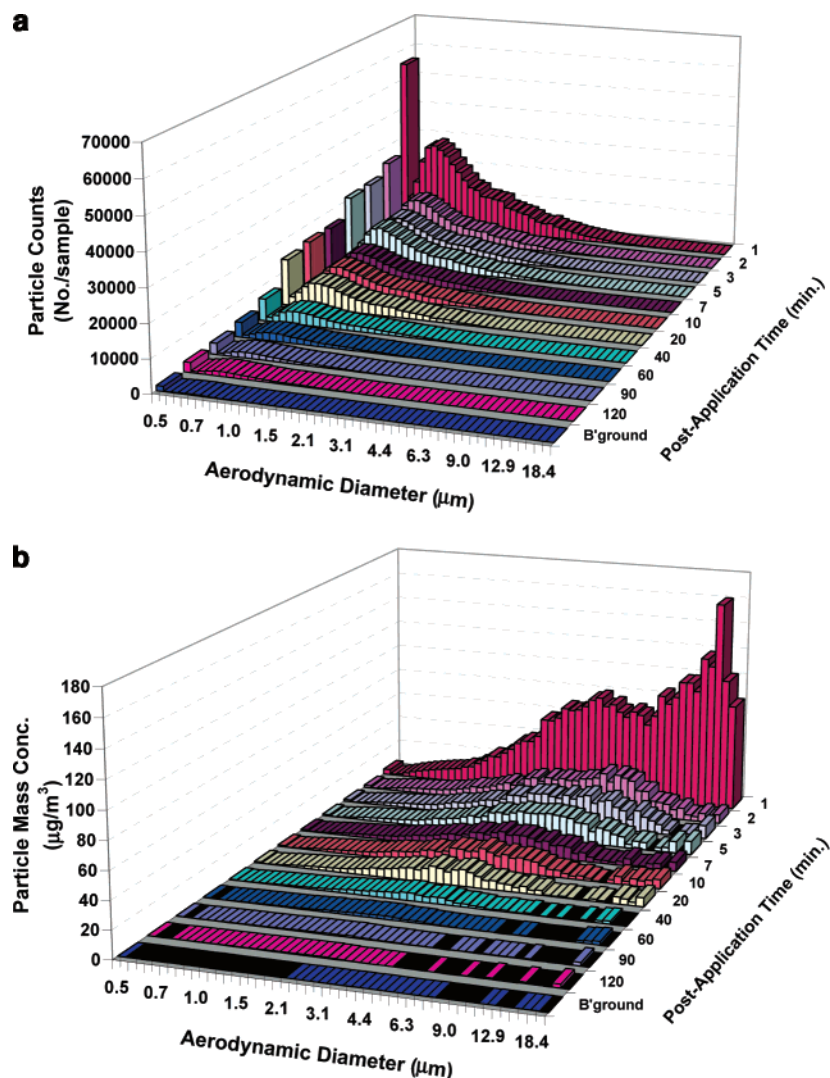


FIGURE 3. Representative particle size distribution histograms for the control and test substance application experiments (normalized to 5 g of spray mass): (a) particle count size distribution, (b) particle mass size distribution.

were representative of the sequential particle size distributions for control and test substance experiments in ABZ and CBZ. The sequential trends indicated that particle levels increased to a maximum immediately postapplication, and then decreased gradually at a slower rate. This decreasing trend was likely to be induced from ventilation, sedimentation, and coagulation. These size distribution histograms indicated that most of the aerosols were in the submicron-sized range ($<1 \mu\text{m}$). For example, 64% of the particles were smaller than $1.0 \mu\text{m}$ in the first minute sample. Throughout the postapplication periods, submicron-sized aerosols were predominant (i.e., 60–70%) at the designated sampling locations.

While particle count histograms indicated that most spray aerosols were in the submicron-sized range, they only comprised minor mass concentrations because particle mass is proportional to the cube of diameter. Figure 3b presents the corresponding particle mass distribution histograms for Figure 3a. Of the total particle mass, 62% was comprised of particles greater than $5 \mu\text{m}$ for the first minute postapplication sample. Then, the weight percentage of $>5 \mu\text{m}$ particles decreased sharply due to a higher terminal settling velocity than small particles. Until 30 min postapplication, the weight percentage of $>5 \mu\text{m}$ particles decreased to approximately 20%.

Figure 4 illustrates the sequential mean aerodynamic diameters (MADs) of particles in ABZ and CBZ. The results

indicate that the particles generated from the control substance were very similar to those generated from the test substance. During the testing periods, MADs ranged from 0.9 to $1.2 \mu\text{m}$ for control substance experiments, and 0.9 to $1.1 \mu\text{m}$ for test substance. The average MADs of background particles were slightly less than $0.8 \mu\text{m}$.

Figure 5 illustrates sequential particle mass concentrations (MCs, $\mu\text{g}/\text{m}^3$) for the control/test substance application experiments in ABZ. Upon initial release, particle MCs reached approximately $800\text{--}1000 \mu\text{g}/\text{m}^3$. The maximum of mean MCs ($n = 3$) were 933 and $950 \mu\text{g}/\text{m}^3$ for the control and test substances, respectively. The peaks were followed by approximately 10–15 min of fluctuation due to nonhomogeneous aerosol distribution in the ECER, which was caused by turbulent mixing induced from the force generated from spray jet. Following initial fluctuations, MCs decayed gradually. This decreasing trend was likely to be induced from ventilation, sedimentation, and coagulation. At the end of the 2-h testing period, MCs ranged from 13 to $21 \mu\text{g}/\text{m}^3$, which were higher than background MCs ($2\text{--}3 \mu\text{g}/\text{m}^3$).

Figure 6 illustrates the sequential particle MCs for the control/test substance experiments in CBZ. During the initial 10-min postapplication period, the fluctuations were similar to those of ABZ due to nonhomogeneous aerosol distributions. The maximum of mean MCs ($n = 3$) were 793 and $977 \mu\text{g}/\text{m}^3$ for the control and test substances, respectively. The maximum MCs occurred during the first minute postappli-

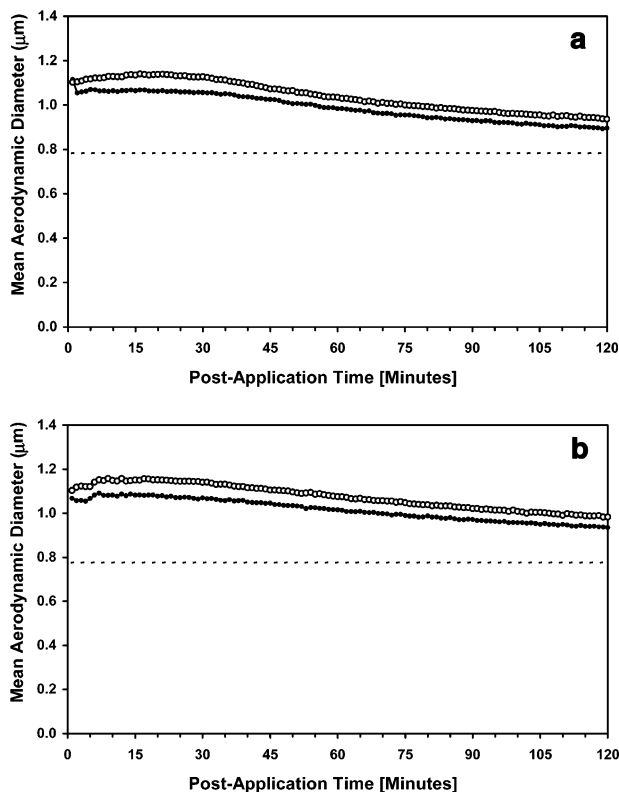


FIGURE 4. Sequential mean aerodynamic diameters (MADs) following control and test substance applications ($n = 3$): (a) ABZ, (b) CBZ. Symbols: ● and ○ represent the control and test substance runs, respectively. The dashed lines represent average MAD of background particles.

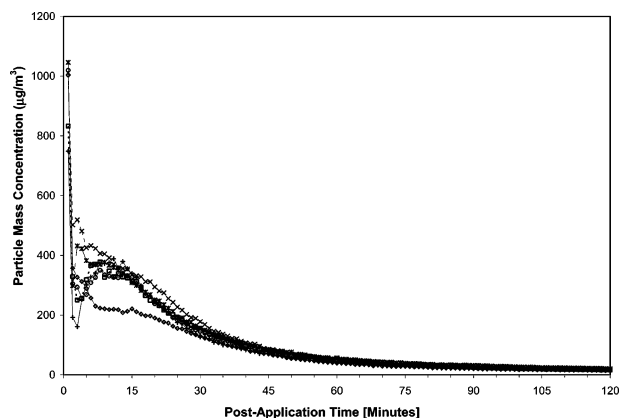


FIGURE 5. Sequential particle mass concentrations following control and test substance applications in ABZ. Symbols: ◇, □, and ○ represent the test substance runs 1, 2, and 3, respectively; +, ×, and * represent the control substance runs 1, 2, and 3, respectively.

cation. It was followed by approximately 10 min of fluctuations. Following this period, MCs decayed gradually to 23–31 $\mu\text{g}/\text{m}^3$, which were higher than background MCs (1–2 $\mu\text{g}/\text{m}^3$).

Implication to Clinical Study Design. Figure 7 presents sequential total fragrance concentrations (TFC) and particle MCs ($<5 \mu\text{m}$) in ABZ and CBZ. TFC is defined as the total concentrations of the nine fragrance materials collected in a Tenax sampling tube. This concentration is assumed the total particle-bound and vapor-phase fragrance materials. During the initial 6 min postapplication, TFC fluctuated intensely due to spray jet mixing. In CBZ, TFC decreased sharply from the maximum of 2029 to 258 $\mu\text{g}/\text{m}^3$ during the initial 30 min postapplication, while in ABZ, the concentra-

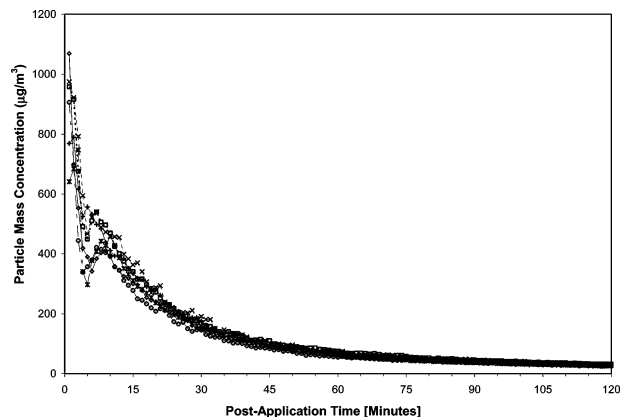


FIGURE 6. Sequential particle mass concentrations following control and test substance applications in CBZ. Symbols: ◇, □, and ○ represent the test substance runs 1, 2, and 3, respectively; +, ×, and * represent the control substance runs 1, 2, and 3, respectively.

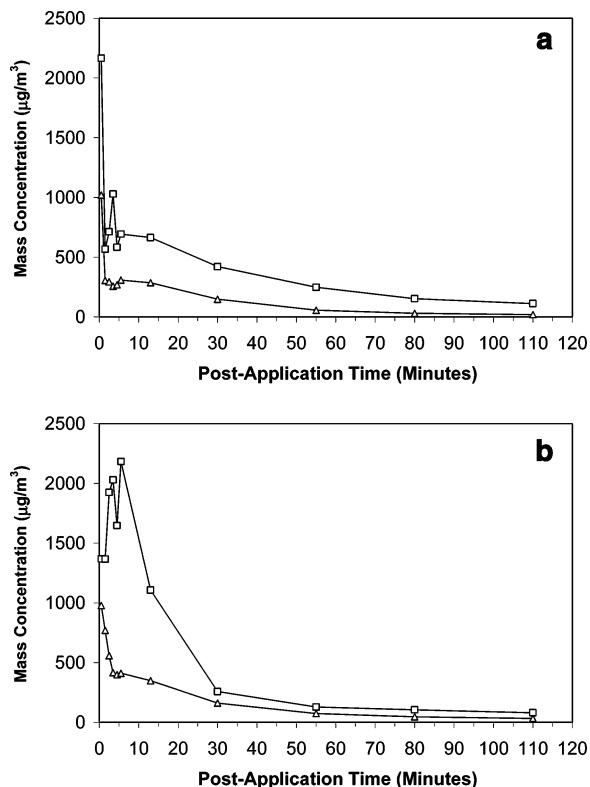


FIGURE 7. Sequential total fragrance concentrations and particle mass concentrations post test substance application in (a) ABZ and (b) CBZ. Symbols: □ and △ represent total fragrance concentrations and particle mass concentrations, respectively.

tions decreased from 693 to 421 $\mu\text{g}/\text{m}^3$. TFC then decreased gradually during the next 1.5-hour testing period to 112 and 81 $\mu\text{g}/\text{m}^3$ in ABZ and CBZ, respectively.

For particulate exposure, the maximum MCs occurred immediately postapplication, and then decreased sharply in both ABZ and CBZ. In ABZ, particle MCs decreased abruptly from 1019 to 305 $\mu\text{g}/\text{m}^3$ during the first minute postapplication, and maintained at the 300 $\mu\text{g}/\text{m}^3$ level for the following 5 min. Then, particle MCs decreased gradually to 148 $\mu\text{g}/\text{m}^3$ at 30 min postapplication. At the end of the tests, particle MCs was 19 $\mu\text{g}/\text{m}^3$. In CBZ, particle MCs decreased from 978 to 416 $\mu\text{g}/\text{m}^3$ during the initial 3 min, and maintained at the 400 $\mu\text{g}/\text{m}^3$ level for the following 3 min. Then, particle MCs decreased gradually to 161 $\mu\text{g}/\text{m}^3$ at 30 min postapplication. At the end of the tests, particle MCs was 33 $\mu\text{g}/\text{m}^3$.

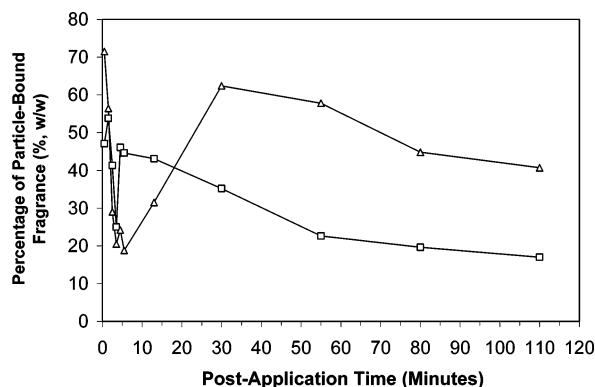


FIGURE 8. Percentage (w/w) of particle-bound fragrance materials. Symbols: \square and \triangle represent ABZ and CBZ, respectively.

The sequential trends of TFCs and particle MCs indicated that the 2-hour total exposure could be categorized as two sections with the division at 30 min postapplication. The initial 30-minute exposure comprised the high exposure period, and the remaining 1.5-hour exposure comprised a lower exposure period. The initial 30-minute time-weighted-average (TWA) TFCs were 638 and 930 $\mu\text{g}/\text{m}^3$ in ABZ and CBZ, which accounted for 57% and 75% of the 2-hour total exposure, respectively. The following 1.5-hour TWA TFCs were 161 and 102 $\mu\text{g}/\text{m}^3$, which only accounted for 43% and 25% of the 2-hours total exposure in ABZ and CBZ, respectively.

The above analysis suggested that an exposure up to 30 min postapplication will cover an acute exposure period (occurred 0–6 min immediately postapplication) and a higher TWA TFC. A follow-up clinical exposure thus selected initial 30-minute exposure to investigate whether residential use of air fresher will cause objective irritant responses in volunteer human subjects.

Particle-Bound and Vapor-Phase Fragrance Exposure.

Figure 8 illustrates sequential percentage of particle-bound fragrance materials with respect to total fragrance concentrations in ABZ and CBZ. In ABZ, except for the 4th-minute exposure, approximately 41–53% of the total exposure was from particle-bound fragrance materials during the initial 20 min postapplication. Then, the percentage decreased gradually. At the end of the 2-hour testing period, the percentage of particle-bound fragrance materials decreased to 17%.

In CBZ, particle-bound fragrance exposure was much greater than in ABZ during the first minute postapplication; 72% of the total fragrance exposure was from particle-bound fragrance materials. The initial high percentage of particle-bound fragrance materials in CBZ may be explained by gravitational sedimentation of spray aerosols. When test substance spray was released, large micron-sized particles settled rapidly to CBZ, while vapor-phase fragrance materials tended to remain airborne in the upper atmosphere. The percentage of particle-bound fragrance materials in CBZ then decreased to 19% during the initial 6 min postapplication, and again increased to 58% during the 45–65 min post-application period. While there was no definitive explanation for the increased particulate exposure, it might be induced from floor rebound when the aerosol plume hit the floor. The percentage of particle-bound fragrance materials then decreased gradually to 40.7% until the end of the 2-hour testing periods.

Figure 8 indicates that the percentage of particle-bound fragrance materials remained higher in the CBZ after 30 min postapplication. In addition, the percentage decreased in a similar rate and trend for ABZ and CBZ. These evidences indicated that gravitational sedimentation gradually brought

particles downward to CBZ, while vapor-phase fragrance materials tended to remain airborne in the upper ABZ area. The air near the floor always contained a higher percentage of particle-bound fragrance materials than the upper atmosphere.

Simulated Exposure Versus Actual Exposure. This study was conducted in a nondisturbing atmosphere and the test substance was applied toward the ABZ sampling zone. These conditions do not occur in typical residential applications. In actual air freshener application, air freshener will not be applied directly in the subject's breathing zone and the atmosphere is mixed by the residents causing enhanced dilution. Thus, the simulated exposure conditions represent a worst-case exposure scenario. If the follow-up clinical exposure study does not reveal significant increase of irritant responses, residential use of air freshener products could be concluded to be safe.

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