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Vaporization—Condensation Generation of Ultrafine Hydrocarbon Particulate Matter for Inhalation Toxicology Studies

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An evaporation/condensation particle generator produced 30–50 nm count median diameter particles from both pure hydrocarbons and from a complex mixture—used motor oil—at a concentration above $1 \times 10^6/cm^3$. The objective was to generate ultrafine aerosols for inhalation toxicology studies using specified organic components as surrogates for the particulate emissions generated by diesel internal combustion engines. This nanoparticle generation system, assembled from commercially available components, produced smaller particle size and higher particle number concentration than has been previously documented using Sinclair-La Mer condensation generator technology. The paper describes both the experiments used to design and characterize the particle generator and the operating conditions used for a specific inhalation experiment as an example of the system capability.

INTRODUCTION

Diesel engine exhaust is thought to be a major source of ultrafine particulate matter (PM) in urban environments (HEI 1995; Harrison et al. 1996, 1999; Kittelson 1998; Morawska et al. 1998; Hitchins et al. 1999). Diesel engines produce a multimodal particle size distribution that varies with engine speed, load, fuel sulfur content, and exhaust dilution conditions (Abdul-Khalek et al. 1998, 1999; Shi and Harrison 1999; Shi et al. 1999; Brown et al. 2000). Newer low-emissions engines do not produce clouds of black smoke, but can produce a high number concentration of particles smaller than 100 nm, and often show a separate nucleation mode between 20 nm and the smallest size detected by the instruments (Abdul-Khalek et al. 1998). Gasoline-powered engines and compressed natural gas-powered engines also emit high numbers of ultrafine particles. The current opinion is that the particle mode below 100 nm is composed of high boiling point hydrocarbons condensed on soot, sulfuric acid, or metal oxide nuclei (Kleeman et al. 2000; Tobias et al. 2002). The branched alkanes and alkyl-substituted cycloalkanes detected in mass spectra are presumably derived from lubricating oil and unburned fuel.

This project was motivated by a need for an ultrafine organic aerosol that could be used in animal inhalation exposure experiments. Previous studies have shown that inhalation of ultrafine particles can produce inflammation and other responses even when the ultrafine aerosol is a substance that is considered to have low toxicity when inhaled as larger particles, such as TiO_2 or carbon black (Baggs et al. 1997; Li et al. 1999; Elder et al. 2000a, 2000b). The objective was to produce a high number concentration of the smallest possible diameter aerosol from either pure, high-molecular-weight hydrocarbons or from real-world mixtures such as motor oil that were free of gas-phase or solid copollutants. Use of a small diesel engine as an aerosol source was considered (Mokler et al. 1984) but was rejected due to the heat, noise, and vibration of an engine in a biomedical laboratory setting, and the need to remove copollutants such as soot, CO, and NOx. Concurrent efforts to generate a suitable aerosol using an electrospray generator (Rulison and Flagan 1994; Gomez et al. 1998) were attempted. The electrospray requires a conducting fluid, and attempts to operate the electrospray with water-oil emulsions were unsuccessful.

Much of the previous work in laboratory aerosol generation was directed toward generation of either monodisperse supermicron aerosols for instrument calibration (Fuchs and Sutugin 1966; Willeke 1980; Chen and John 2001) or the generation of ultrafine aerosols of metal or salt for nucleation and coagulation studies (Husar 1971). Production of ultrafine metal or salt

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Table 1
Aerosol generator design and operating parameters

	Inhalation exposure setpoint	Characterization tests	Comment
Q1, main flow, Lpm	4	2–6	Argon
Q2, nebulizer flow, Lpm	1–2*	0.5–2.5	Argon
Q3, air flow, Lpm	0–2*	0–3	Breathing quality compressed air
Q4, oxygen flow, Lpm	1.4*		To obtain 20–21%
Syringe pump flow, ml/min	0.1	0.05–0.5	
Motor oil/solvent	1:400	1:50–1:3200	Hexane and ethanol
Gross motor oil flow, μl/h	15	1.9–120	
Net motor oil aerosol, μl/h	0.15		From SMPS volume
T1, NaCl, Furnace 1, K	off	820–935	
T2, organic, Furnace 2, K	623 K	373–673	Controller setpoint
P2, Furnace 2 outlet pressure, cm H_2O	$<$20 cm H_2O		Impinger backpressure
Inhalation chamber pressure, mm H_2O	-2		
Reynolds number in Furnace 2	75		0.025 m diameter, 800 K
Reynolds number in Q3 mixing tee	540		0.01 m diameter, 400 K

Settings used during the inhalation exposure experiment and the range of values used during the system characterization testing are indicated. The asterisk denotes inputs that were used as real-time operating adjustments according to the final procedures for the inhalation study.

aerosol by vaporization/condensation has been reported by multiple investigators (Scheibel and Porstendörfer 1983; Bartz et al. 1987; Muir and Cena 1987; Singh et al. 2002). Wood et al. (1996) used a condensation generator to produce 0.6–1.4 μm diameter cocaine aerosols for animal studies. An extensive keyword literature search, Science Citation Index search, and review of citations contained in papers on organic particle generation (Koch et al. 1993; Dubtsov and Baklanov 1996; Ristovski et al. 1998) revealed no prior report of a laboratory condensation particle generator producing hydrocarbon aerosols smaller than 100 nm.

Scoping calculations suggested that a vaporization-condensation particle generator based on the classical Sinclair-La Mer generator (Sinclair and La Mer 1949; Rapaport and Weinstock 1955) should be capable of generating a suitable organic aerosol. This type of generator uses a two-step process where nuclei of a very high boiling point compound are produced and the lower boiling compound is then condensed on the nuclei. The final particle size distribution depends on the nucleation rate and subsequent particle growth as discussed in texts (Friedlander 2000) and papers (Koch et al. 1993; Barrett and Baldwin 2000; Singh et al. 2002).

MATERIALS AND METHODS

The equipment description and operating conditions in this article include both the final configuration used for an inhalation exposure study and the preliminary experiments used to design and characterize the system. The system geometry, gas flow rates, operating temperatures, and organic feed mixture were arrived at by a combination of rational design calculations and empirical experimentation. Alternatives may give similar or better performance. In an attempt to characterize and optimize performance, a systematic series of experiments was conducted where each major variable was changed in both directions from a base-case setpoint while other inputs were held constant.

Table 1 lists both the operating setpoints used for generating the inhalation study aerosol and the range of variables tested during system characterization experiments. The aerosol generation system used for the inhalation studies is shown in Figure 1. The furnace tubes were 0.025 m inside diameter by 0.56 m long with 0.28 m heated section. For the characterization tests, a 5 L aging flask was installed in place of the inhalation chamber. This allowed more rapid response to setpoint adjustments while still allowing measurement of both the initial aerosol at the exit of Furnace 2 and an aged aerosol.

Both air and argon were tested as the carrier gas through Furnaces 1 and 2, flow Q1. Preliminary experiments with long-chain n-alkanes using air as the furnace atmosphere showed partial oxidation of the hydrocarbon leading to dark, low-volatility deposits, and changes in aerosol size over an hour-long run. Argon was used as the carrier gas for the balance of system characterization and for the inhalation exposure. Oxygen was added between the aerosol generator and the inhalation chamber so the animals were exposed to a 21% oxygen mixture.

Prior investigators have used a range of nuclei sources including gas flame, hot wire, and various salts. A stationary boat containing NaCl in a tube furnace (Lindberg/Blue M, Ashville NC) was found to be reliable and easily controlled. The plan, during system characterization, was to generate a 5–10 nm NaCl nuclei aerosol based on the operating conditions used by Scheibel

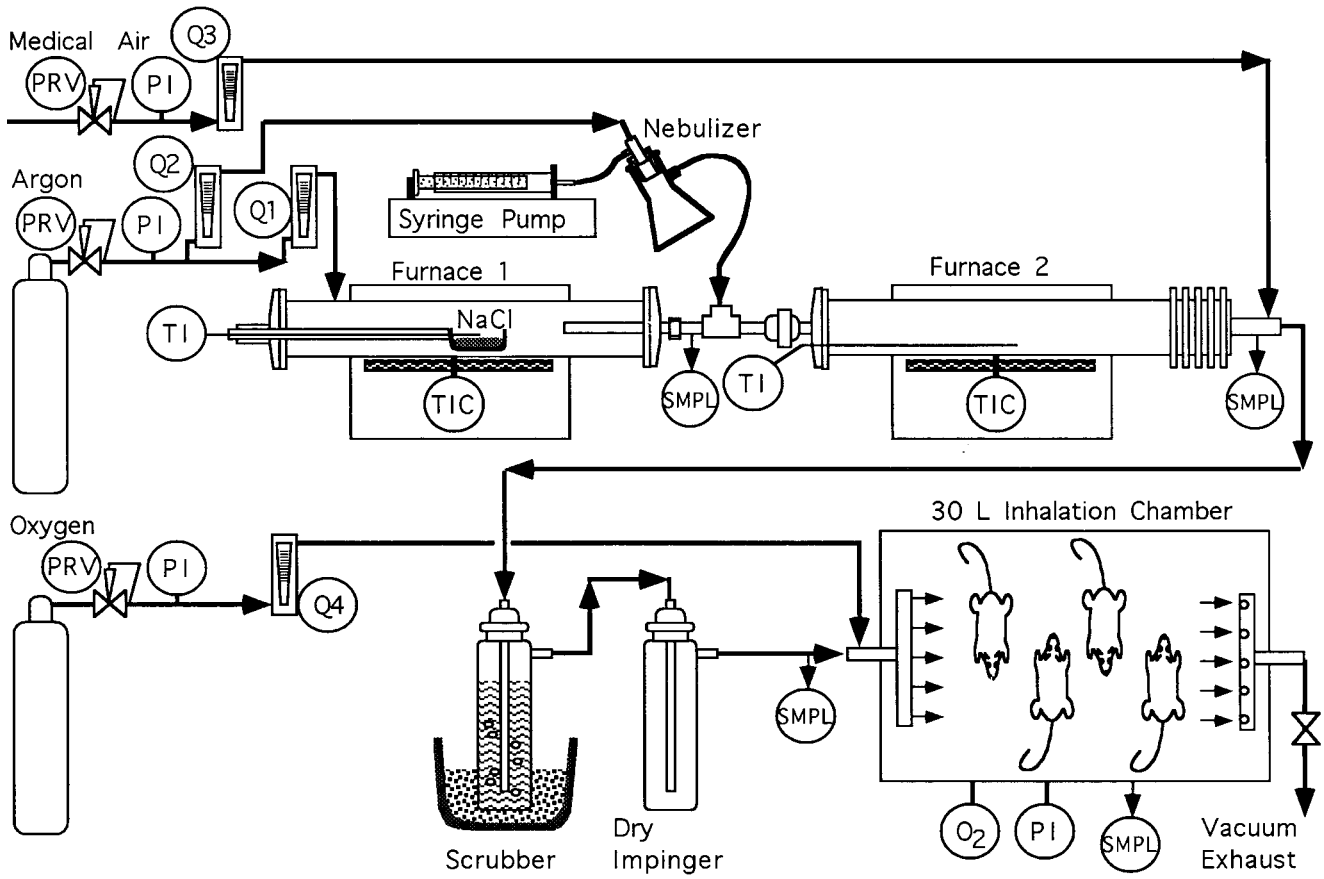

Figure 1. Schematic of the inhalation exposure experiments. Nomenclature: PRV, pressure reducing valve; PI, pressure indicator; TI, temperature indicator; TIC, temperature indicating controller; Q1–Q4, flow indication; SMPL, sample port. An aging flask was used in place of the impingers and inhalation chamber during system characterization testing.

and Porstendörfer (1983), followed by condensation of sufficient hydrocarbon onto the salt nucleus to produce a 15–30 nm final particle.

The test hydrocarbons included the pure n-alkanes $C_{25}H_{52}$ pentacosane, $C_{30}H_{62}$ triacontane, $C_{40}H_{82}$ tetracontane (Aldrich, Milwaukee, WI), a light paraffin oil CAS #8012-95-1 (EMD Chemicals, Gibbstown, NJ), and "used motor oil" collected from an automobile. The used motor oil was opaque and solids settled out over a period of weeks in storage. A pipette was used to remove the motor oil supernatant to obtain the feed material. Complete vaporization of a spray was selected since evaporation from the surface of a stationary pool of an oil mixture in the furnace would result in time-varying aerosol composition due to preferential distillation of the low-boiling components.

The feed rate of hydrocarbon was the main variable that controlled aerosol median diameter and number concentration. A syringe pump (Harvard Apparatus, Holliston, MA) was able to deliver very low flow rates, but the nebulizers tested were unable to generate a fine mist or even maintain a steady flow due to surface tension effects and evaporation at the air-liquid mixing point if the flow was less than 0.1 mL/min. The combination of high dilution of the hydrocarbon in a volatile carrier solvent plus a reduction of effective hydrocarbon flow by impaction removal of large spray droplets prior to introducing the mist into the furnace was the most successful approach. A Sherba (New Port Richy, FL) Model 55007 ceramic nebulizer, sold for use on ICP instruments, was used. The hydrocarbon was dissolved 1:400 in carrier solvent. Hexane was used for initial testing but material balance indicated that the resulting hexane in the inhalation chamber would be unacceptable. Ethyl alcohol was considered preferable since it can be water scrubbed, but motor oil does not dissolve in ethyl alcohol. A mixture of 1 part used motor oil, 9 parts hexane, and 390 parts ethyl alcohol was found to form a stable solution and was used for generating the inhalation study aerosol.

Calculations showed that the residence time and wall temperature in the second furnace (Lindberg/Blue M, Ashville NC) were sufficient to completely vaporize the oil-solvent mixture. Aerosol formed as the gas cooled downstream of the center of the furnace. Temperature in the finned section at the exit of Furnace #2 was 75°C and the gas approached ambient temperature in the metal tubing downstream of the Q3 dilution air addition.

A glass impinger containing deionized water scrubbed the ethyl alcohol from the furnace exit gas. An ice bath was used both to decrease the equilibrium partial pressure of alcohol over

the scrubbing water and to minimize moisture entering the inhalation chamber. A second dry impinger allowed rewarming of the gas. The oxygen content in the inhalation chamber was maintained at 21% by the addition of oxygen upstream of the inhalation chamber (Q4 in Figure 1). The inhalation chamber was maintained under slight (1–2 mm H_2O) negative pressure by adjusting a valve leading to a vacuum vent. The inhalation chamber was a 30 L Plexiglas® gasketed box with distribution manifolds on the inlet and exit. Eight rats were in an individual-compartment wire cage which was placed inside the 30 L box.

The number concentration and size distribution of the aerosol was measured with a TSI, Inc. (St. Paul, MN) Model 3071A scanning mobility particle sizer (SMPS) and Model 3022A condensation particle counter (CPS). A neutralizer (Nuclecel, Grand Island, NY) preceded the SMPS. At various times in the study the SMPS was operated at 2 Lpm aerosol with 20 Lpm sheath flow to obtain resolution from 4.9 to 191 nm. Alternatively, the SMPS was operated at 0.3 Lpm aerosol and 3 Lpm sheath flow so the range from 13 to 778 nm measured both the nucleation and accumulation modes. The instrument was set up according to the TSI operating manual, and flows were checked with a bubble flow meter. The data are reported as electrical mobility diameter as calculated by the TSI software, and this diameter may differ from that obtained by aerodynamic or optical techniques. The mass distribution of particles larger than the SMPS cutoff was determined using a cascade impactor (In-Tox Products, Albuquerque, NM).

A number of alternatives were considered but were not used in the final design. Flame, hot wire, and electric spark processes (Palas Aerosoltechnologie, Karlsruhe, Germany) for generation of nuclei were tested before selecting a stationary bed of NaCl in a laminar flow furnace. A stationary bed of pure alkane, ultrasonic nebulization of hexane solutions, and several different nebulizer designs were tested as alternatives to the selected syringe pump, nebulizer, and impaction chamber configuration. Modifications of the cooling rate including mixing of furnace products and dilutant gas in an eductor (Bartz et al. 1987) and inserting a coaxial exit tube into Furnace 2 (Singh et al. 2002) were unable to achieve a smaller median diameter aerosol for the inhalation experiments.

A coating accumulated on the surfaces of the nebulizer when operating with used motor oil diluted in solvent. Eventually this coating would prevent proper operation of the nebulizer, resulting in a change of feed rate to Furnace 2 and a change in the aerosol size and concentration. During the inhalation exposure the 5 mL syringe was refilled, the scrubber water (250 ml) was replaced, and the nebulizer was cleaned at 45 min intervals. Practice runs had demonstrated that this periodic servicing produced a reasonably consistent gas-phase composition and aerosol size distribution.

RESULTS

The condensation process was able to reliably and reproducibly generate a hydrocarbon aerosol with a number mode between 20 and 100 nm. Figure 2 shows the particle number-based and volume-based size distribution achieved during a 6 h inhalation exposure experiment. The particle number concentration in the 30 L inhalation chamber was $1.1 \pm 0.3 \times 10^6/\text{cm}^3$ and, within the SMPS range from 13 to 778 nm, the integrated particle volume was $1.4 \pm 0.5 \times 10^{11}$ nm^3/cm^3, which is about 110 $\mu\text{g/m}^3$. Table 2 summarizes the aerosol data for the inhalation exposure period. The systematic difference in total number concentration between the number computed by TSI software from the SMPS readings and the total directly measured by a CPC has also been noted in previous work, but the issue remains unresolved.

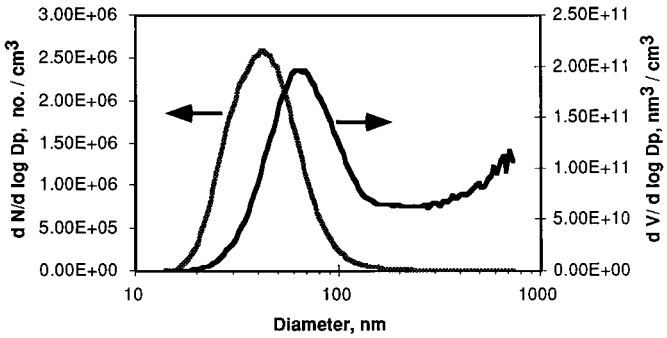

Figure 2. Number-based distribution (left axis) and volume-based distribution (right axis) versus particle diameter during the inhalation experiment. Data are average of SMPS readings at 6 min nominal intervals during the 6 h exposure. A large diameter mode occasionally appeared in the volume distribution, but this mode could be eliminated by increasing dilution flow.

Results from the system characterization testing are documented to aid in the design of similar aerosol generators. The amount of hydrocarbon entering Furnace 2 was the most

Table 2
Aerosol characteristics during a 6 h inhalation exposure experiment

	Average	Standard deviation	Units
Count median diameter	39.9	3.5	nm
Geometric standard deviation	1.46	.02	
Integrated number concentration	1.13E + 6	0.3E + 6	N/cm^3
CPC direct number count	2.84E + 6	0.5E + 6	N/cm^3
Volume median diameter	100.9	10	nm
Integrated volume concentration	1.36E + 11	0.5E + 11	nm^3/cm^3

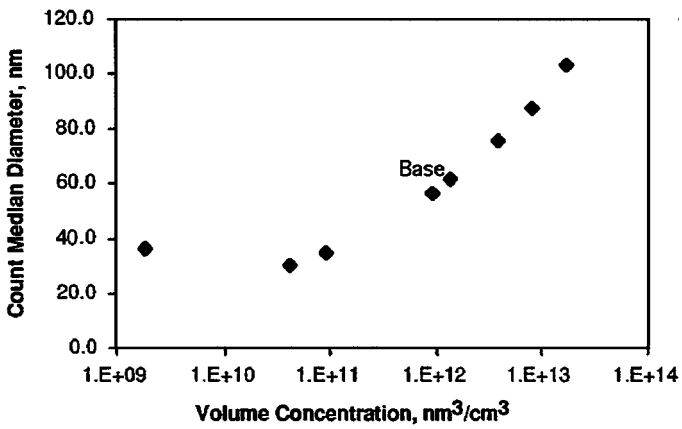

Figure 3. Count median diameter versus total aerosol volume as determined by varying the hydrocarbon feed rate from one-eighth to eight times the base operating feed rate. The far left point is the background aerosol with hexane solvent feed removing hydrocarbons remaining from previous runs.

important variable affecting the aerosol size distribution. The low-volatility hydrocarbon feed rate to the nebulizer could be manipulated by adjusting the volumetric flow rate of the syringe pump or by changing the ratio of hydrocarbon to volatile carrier solvent in the mixture used to fill the syringe. Changing the argon flow to the nebulizer, Q2, changed the net feed rate of hydrocarbon to Furnace 2 by changing the size of the nebulizer spray. Larger droplets resulted in more hydrocarbon being trapped in the impingement flask, thus reducing feed to the furnace. Volumetric flow from the syringe pump and mixture dilution were changed during system characterization testing, but only nebulizer flow, Q2, was used as an operating adjustment during the inhalation exposure experiment.

To quantify the effect of hydrocarbon feed rate on aerosol size, an experiment was conducted where the flow of hydrocarbon to the nebulizer was varied from one-eighth of the base rate to eight times the base rate by varying the concentration of used motor oil in the solvent. All other operating conditions were held constant. Figure 3 shows the observed relationship in the aging flask between the count median diameter of the aerosol and the total aerosol volume per volume of gas. The data were analyzed by fitting with an equation of the form:

$$D_p = D_{\text{ref}}\left(\frac{\phi}{\phi_{\text{ref}}}\right)^p, \qquad [1]$$

where ϕ is the aerosol volume fraction and where the reference diameter and volume fraction were selected so that the curve passes through the base case point ($D_{\text{ref}} = 61.3$ nm, $\phi_{\text{ref}} = 1.4 \times 10^{12}$ nm^3/cm^3). The experimental data is fit by an exponent of 0.2, which is less than the 1/3 exponent predicted by theory assuming the number of nuclei is constant (Perry and Smaldone 1985) and which was observed experimentally by Bartz et al. (1987) with NaCl aerosol. The data show that both

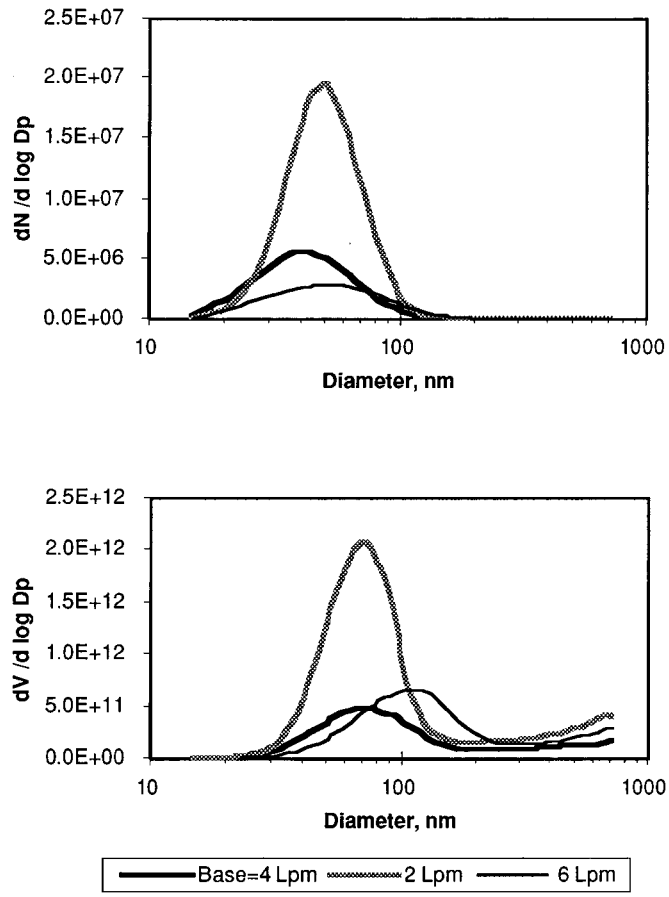

Figure 4. Changing the gas flow shows effect of competing residence time and dilution. The sum of Q1 and Q3 was kept constant as Q1 was varied from 2 to 6 Lpm. Measurements were made downsteam of a 5 L aging vessel. Oil feed and furnace temperature were held constant.

the median size and the number concentration of particles increased with increasing aerosol volume. This suggests that the number of effective nuclei for condensation increased as the supply of hydrocarbon vapor increased. The system blank particle concentration with no NaCl nuclei, hydrocarbon, or solvent feed added to the heated carrier gas was less than 100/cm^3 within the SMPS range.

System performance was also sensitive to carrier gas flow (sum of Q1 and Q2) through Furnace 2. Figure 4 shows that there was an optimum gas flow for achieving the smallest possible aerosol due to the effects of gas flow on the time-temperature pattern, hydrocarbon vapor concentration, and aerosol age at the sampling point. An increase in the number median diameter resulted when the Q1 flow was either increased or decreased from the 4 Lpm base condition.

Adding dilution air, Q3, downstream of Furnace 2 decreased both aerosol number concentration and volume concentration; however, the decrease in aerosol volume was more than predicted by material balance. Comparison of the aerosol sampled

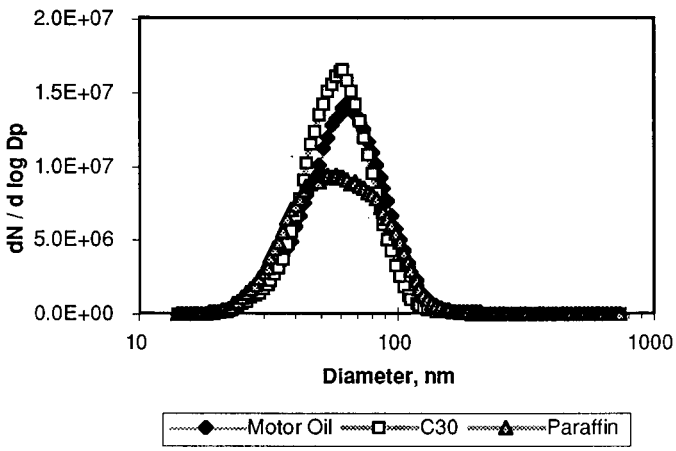

Figure 5. Aerosols produced with different hydrocarbons: used motor oil (diamond), clear paraffin oil (square), and triacontane ($C_{30}H_{62}$) (triangle).

at the exit of Furnace 2 and downstream of the 5 L aging flask showed that both the number of detectable particles and the total volume of aerosol increased during the first 60 s. These observations are consistent with a dynamic aerosol size distribution that depends on gas-particle mass transfer. As expected from standard coagulation theory (Friedlander 2000), the aerosol was sufficiently concentrated that particle coagulation was significant on the scale of 1–5 min. The inhalation chamber residence time was about 5 min, and the aerosol sampled from inside the chamber was larger and had a lower number concentration than the aerosol measured at the chamber inlet.

The system characterizaton experiments showed that the aerosol generator performance was relatively insensitive to (1) the specific high boiling point hydrocarbon and volatile solvent, (2) the supply of nuclei from Furnace 1 when operating Furnace 2 at high hydrocarbon concentration, and (3) the Furnace 2 temperature. Figure 5 shows that aerosols with similar number-based size distribution can be obtained with either a single compound such as triacontane or with mixtures like paraffin oil and used motor oil. Both hexane and ethanol were used as the dilution solvent and the change in hydrocarbon aerosol size distribution was insignificant. Changes in the NaCl nuclei supply, controlled by adjusting Furnace 1 temperature, had no effect on the aerosol size distribution at base condition hydrocarbon feed rates to Furnace 2. At low hydrocarbon feed rates (one-quarter of base condition) the particle number increased and median diameter decreased when NaCl nuclei were supplied. This is consistent with achieving sufficiently high supersaturation to induce homogeneous nucleation, but the effect of nuclei from wall deposits remaining from previous runs was not conclusively ruled out. Nuclei from wall deposits, if present, were below the minimum size detectable by the CPC. At the nominal setpoints used, changes in Furnace 2's temperature over the range from 300–400°C had no effect on aerosol size distribution, consistent with all hydrocarbons being vaporized. Repeated practice runs verified that the generator produced a consistent aerosol from day to day.

Experiments were conducted with increased oil feed to test for the presence of a large particle mode extending above the SMPS size cutoff. Cascade impactor sampling showed that over 98% of the mass was in particles <1 μm aerodynamic diameter. The aerosol mass computed from the 3 h average of the SMPS measurements, assuming 0.8 specific gravity spheres, was 246 μg/m^3, compared to 281 μg/m^3 measured by weight change on Stages 6, 7 and filter of the cascade impactor. The D_{50} cut point for impactor Stage 6 was 0.72 μm.

The cold water impinger reduced the ethyl alcohol concentration from over 6000 ppm to under 100 ppm as determined by gas chromatography. The ultrafine particle number concentration decreased by about one-third through the impinger, but this did not prevent achieving the target concentration in the inhalation chamber. Gas chromatography of the used motor oil feed stock and of filter extracts collected downstream of the aerosol generator did not show major difference, indicating that the passage through the furnaces was not cracking or partially oxidizing feed compounds.

DISCUSSION

The aerosol produced by this vaporization/condensation particle generator can be compared to real-world particulate emission concentrations and ambient exposures. A material balance calculation showed that the concentration of oil aerosol produced by the particle generator is approximately what would be found at the tailpipe of an engine that consumed one quart of oil per 10,000 miles, assuming 95–99% combustion of the oil entering the cylinder. The mass concentration of the $d < 100$ nm oil aerosol achieved in the inhalation chamber was about twice the US EPA $PM_{2.5}$ ambient air quality standard. The maximum test chamber ultrafine aerosol number concentration was limited by both the observed relationship between count median diameter and total particle volume from the particle generator, and by loss of particle number concentration due to coagulation.

An unresolved challenge was laboratory generation of particles comparable to the smallest particle mode reported for diesel engines. Dilution sampling of diesel engines under light load shows a particle mode starting about 10 nm and extending beyond the small-diameter cutoff of the instrument (Abdul-Khalek et al. 1998, 1999). The minimum particle size shown in Figure 3 is consistent with the calculated Kelvin diameter if the supersaturation, P/Psat, is 2-3 at the location where particle formation occurs. The gas cooling rate and the presence of nanometer-sized nuclei of soot, metal oxides, or sulfuric acid are suspected to be important differences between aerosol generation in bench-scale condensation processes and in diesel engines.

The tests with a range of hydrocarbons indicate that the particle generator produces an aerosol size distribution which is not dependent on unique properties of the used motor oil, such as trace contaminants serving as nuclei. The ability of the aerosol

generator to work with both complex mixtures such as used motor oil and with single-component hydrocarbons suggests that future studies can be designed using a range of environmentally relevant organic aerosols. This would include controlled mixtures of relatively benign aliphatic hydrocarbons with known biologically active species such as polycyclic aromatic hydrocarbons (PAHs). Further, the condensation organic particle generator can be combined with a nuclei generator to create mixtures of organic compounds and carbon or metal oxides. This opens the way to a reductionist approach to studying the toxicology of engine emissions by hypothesis-driven inhalation studies of single components and of mixtures of components found in real engine exhaust.

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