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Development of a novel aerosol generation system for conducting inhalation exposures to ambient particulate matter (PM)

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Abstract

In this study, we developed a novel method for generating aerosols that are representative of real-world ambient particulate matter (PM) in terms of both physical and chemical characteristics, with the ultimate objective of using them for inhalation exposure studies. The protocol included collection of ambient PM on filters using a high-volume sampler, which were then extracted with ultrapure Milli-Q water using vortexing and sonication. As an alternative approach for collection, ambient particles were directly captured into aqueous slurry samples using the versatile aerosol concentration enrichment system (VACES)/aerosol-into-liquid collector tandem technology. The aqueous samples from both collection protocols were then re-aerosolized using commercially available nebulizers. The physical characteristics (i.e., particle size distribution) of the generated aerosols were examined by the means of a scanning mobility particle sizer (SMPS) connected to a condensation particle counter (CPC) at different compressed air pressures of the nebulizer, and dilution air flow rates. In addition, the collected PM samples (both ambient and re-aerosolized) were chemically analyzed for water-soluble organic carbon (WSOC), elemental and organic carbon (EC/OC), inorganic ions, polycyclic aromatic hydrocarbons (PAHs), and metals and trace elements. Using the aqueous filter extracts, we were able to effectively recover the water-soluble components of ambient PM (e.g., water-soluble organic matter, and water-soluble inorganic ions); however, this method was deficient in recovering some of the important insoluble components such as EC, PAHs, and many of the redox-active trace elements and metals. In contrast, using the VACES/aerosol-into-liquid collector tandem technology for collecting ambient PM directly into water slurry, we were able to preserve the water-soluble and water-insoluble components very effectively. These results illustrate the superiority of the VACES/aerosol-into liquid collector tandem technology to be used in conjunction with the re-aerosolization setup to create aerosols that fully represent ambient PM, making it an attractive choice for application in inhalation exposure studies.

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Keywords

Ambient PM; re-aerosolization; aqueous extraction; VACES; aerosol-into-liquid collector; inhalation exposures

1. Introduction

Many metropolitan areas of the world suffer from severe air pollution as a by-product of rapid urbanization, industrial, and technological advancements during the past few decades. More than 90% of the world population is exposed to air pollutant concentrations exceeding WHO guideline limits (WHO, 2018). Several epidemiological as well as toxicological studies have well documented the harmful health impacts of exposure to ambient particulate matters (PM), including neurological, cardiovascular, respiratory, and pulmonary diseases (Delfino et al., 2010; Dockery and Stone, 2007; Gauderman et al., 2015; Morgan et al., 2011; Rich et al., 2013; Wai et al., 2015). There is, therefore, a need to conduct *in vitro* and *in vivo* toxicological studies to further evaluate the health effects of exposure to ambient PM, which requires the use of aerosols that are representative of real-world PM. Ambient PM is comprised of several different chemical constituents and varies in size by 5 orders of magnitude from a few nanometers to tens of micrometers; this makes PM a complex pollutant to reproduce in the laboratory (Bladt et al., 2012; Filep et al., 2016; Jacoby et al., 2011; Keskinen and Rönkkö, 2010). There are several aerosol generators that are used for producing particles in the laboratory (Arefin et al., 2017; Hahn et al., 2001; Polk et al., 2016; Shimada et al., 2009; Steiner et al., 2017). For example, nano-objects and their aggregates and agglomerates (NOAA) are being used for nano-aerosol generation (Ahn et al., 2017). Clemente et al. (2018) developed a novel aerosol generator to re-aerosolize target nanomaterials (e.g., TiO and ZuO) with specific chemical composition. However, these laboratory-generated particles are of unique physicochemical characteristics and, therefore, do not adequately represent the physical and chemical characteristics of ambient real-world aerosols (Lippmann and Chen, 2009). In addition, direct use of ambient PM in the lab is not necessarily a viable alternative, as ambient PM concentrations are generally not sufficiently high to induce acute adverse health effects in toxicological studies (Jung et al., 2010; Lippmann and Chen, 2009; Liu et al., 2014).

The development of particle concentrators has resolved several of the above issues, as these instruments are capable of significantly increasing the PM concentration in the inlet of the exposure chamber (Chang et al., 2002; Demokritou et al., 2003, 2002; Gupta et al., 2004a, 2004b; Sioutas et al., 1999, 1997, 1995), reaching levels that can cause responses in toxicological studies. The versatile aerosol concentration enrichment system (VACES) is one of the most widely used aerosol concentrators which employs condensational growth followed by virtual impaction to enrich PM concentrations in the air flow (Kim et al., 2001a, 2001b, 2000; Ning et al., 2006; Pakbin et al., 2011; Sioutas et al., 1999). The VACES is able to effectively concentrate different size fractions of PM (i.e., ultrafine, fine, and coarse PM) by 20–30 times, while preserving the physical and chemical characteristics of ambient particles (Kim et al., 2001a, 2001b; Saarikoski et al., 2014). In addition, VACES can also be used in tandem with a Biosampler™ (SKC Inc, Eighty-Four, PA; Willeke et al., 1998) or the

high-volume aerosol-into-liquid collector to provide highly concentrated liquid suspension, which corroborates its versatility and ability for simultaneous *in vivo* and *in vitro* exposure assessment experiments (Daher et al., 2011; Kim et al., 2001a, 2001b; Wang et al., 2013). Due to the abovementioned advantages, the VACES has been used in several toxicological (both *in vivo* and *in vitro*) exposure studies to supply either of concentrated ambient particles (CAPs) or PM liquid suspensions (Budinger et al., 2011; Maciejczyk and Chen, 2005; Mills et al., 2011; Qiu et al., 2017; Quan et al., 2010; Wang et al., 2018; Xu et al., 2011; Zheng et al., 2015). In spite of the abovementioned advantages, there are some major drawbacks associated with employing aerosol concentrators in exposure assessment studies. For instance, inhalation exposure studies usually span several weeks and require physically and chemically stable PM for the exposure (Cheng et al., 2016a, 2016b; He et al., 2017; Shimada et al., 2009). However, the concentration and chemical composition of the aerosol provided by these concentrators during the inhalation exposure is inevitably variable, as it depends on the variations in the ambient PM. Furthermore, inhalation exposure studies of animals and/or humans to specific pollution sources (e.g., vehicular emissions, biomass burning, power plants, airport or ship emissions) require sophisticated and expensive facilities to house animals in a stationary or mobile laboratory. These are costly logistical issues, which may limit the applicability of aerosol concentrators in exposure assessment studies.

A potential solution to these issues is to decouple the PM collection from the inhalation exposure process, mainly because the former is a lot simpler to conduct in the field alone than in combination with the latter. Therefore, in this study, we developed a new technique for generation of stable aerosols that are representative of real-world ambient PM. In this method, the ambient PM samples are collected on filters, followed by extraction of the filters in Milli-Q ultrapure water to produce a concentrated PM slurry. The PM slurries are then re-aerosolized using a commercially available nebulizer to produce a constant flow and concentration of aerosols that are physically and chemically representative of ambient PM to be used for inhalation studies. In order to ensure the representativeness of the re-aerosolized PM, their physical and chemical characteristics are compared with those of ambient PM collected in parallel. In addition, the results from this method are also compared with those from a potentially superior method, in which ambient PM is captured directly into a suspension of Milli-Q ultrapure water using the high-volume aerosol-into-liquid collector, developed by Wang et al. (2013), followed by re-aerosolization of the suspension to produce the concentrated exposure PM.

2. Methodology

2.1. PM collection

2.1.1. High-volume sampler PM collection and filter extraction—In the first approach, ambient PM samples were collected on PTFE membrane filters (20 × 25 cm, 3.0 µm pore size, PALL Life Sciences, USA) using a high-volume PM sampler; the schematic of the set-up for high-volume sampler is shown in Figure 1(a). As shown in the figure, the high-volume sampler setup is composed of a 180° bend, which serves as a PM₁₀ inlet, and a very high flow rate (i.e., 400 lpm), low pressure drop (i.e., 2 kPa) ultrafine (UFP) slit nozzle

impactor for segregation of accumulation and ultrafine PM modes with a cut point diameter of 0.18 μm (Misra et al., 2002). Prior to the aqueous extraction of samples, the mass loading of collected ambient PM on the filters was determined gravimetrically using a high precision (± 0.001 mg) microbalance (MT5, Mettler Toledo Inc., Columbus, OH), following the equilibration of filters at proper temperature (22–24°C) and relative humidity (40–50%) for 24–48 h. The filters were then divided into half and one half was cut into 16 pieces; the pre-extraction weights of these small filter pieces were quantified using the abovementioned microbalance. Subsequently, vortexing was done for 5 minutes to effectively soak each filter piece in 10 ml of ultrapure Milli-Q water, followed by sonication of the solution for 30 minutes to extract the PM (i.e., water-soluble fraction of PM) from the filter pieces. Following sonication, the filter pieces were dried up and weighed to estimate the extracted PM mass in the slurry. The extracted PM mass was quantified as the difference between the total pre-extraction and post-extraction weight of filters. The efficiency of the extraction was also determined as the ratio of the actual extracted PM mass to the total collected PM mass on the filters before extraction. Finally, it is noteworthy that the unextracted half of the filter was used as the reference ambient $\text{PM}_{0.18}$ sample for chemical analysis, to be compared with the chemical composition of the re-aerosolized PM from filter extractions (see Section 2.2).

2.1.2. PM collection using the VACES/aerosol-into-liquid-collector tandem—

In the second approach, we collected ambient $\text{PM}_{2.5}$ in slurry samples using the VACES/aerosol-into-liquid collector tandem (Wang et al., 2013), the schematic of which is presented in Figure 1(b). As shown in the figure, after passing through the $\text{PM}_{2.5}$ inlet, the ambient air is drawn into a saturation tank that is filled with ultrapure Milli-Q water using a vacuum pump (Model 2067, GAST Manufacturing, USA) working at a flow rate of 300 lpm. The incoming ambient particles are mixed with saturated water vapor inside the tank that is operated at 30°C. The mixture is then drawn through a condensation unit (each line operating at 100 lpm) that is connected to a chiller operating at -5°C . This drops the temperature of the particle-vapor mixture to around 20°C. The supersaturation created by the temperature drop causes the water vapor to condense on the particles, growing them to 3–4 μm droplets. The airstreams from two of the condensation lines are merged, making a total flow rate of 200 lpm, which passes through the impaction nozzles of the aerosol-into-liquid collector, causing the liquid droplets to impact and get collected on the lateral cylindrical surfaces of the collector. These droplets are then drained into the bottom section (i.e., collection stage) of the collector and form the concentrated slurry sample.

The airstream in the third condensation unit (100 lpm) passes through a virtual impactor with a cut point diameter of 1.5 μm , causing the grown droplets to enter into the minor flow (i.e., 5 lpm) and become enriched in concentration by approximately 20 times. Subsequently, the airstream passes through a diffusion dryer (Model 3620, TSI Inc., USA), filled with silica gel, to remove the excess water from the concentrated grown particles, which causes them to return to their original size (Kim et al., 2001a, 2001b). The air stream then passes through filters, on which the particles are collected for chemical analysis. These samples are used as the reference ambient samples, to which the chemical characteristics of the re-aerosolized PM from slurry collection are compared (Section 2.2). Both filter and slurry PM

collections were done at the University of Southern California's particle instrumentation unit (PIU), which is an urban site exposed to a mixture of primary (coming mostly from the I-110 freeway located 150 m upwind of the site) and secondary PM (Shirmohammadi et al., 2018; Sowlat et al., 2016b; Wang et al., 2016).

2.2. Aerosol generation and inhalation exposure

To provide a stable source of concentrated PM for *in vivo* exposure studies, the collected PM slurries (i.e., the PM liquid suspension from both methods) were re-aerosolized using the commercially available HOPE nebulizers (B&B Medical Technologies, USA). As presented in Figure 1(c), a pump (Model VP0625-V1014-P2-0511, Medo Inc., USA) is generating HEPA-filtered compressed air introduced into the nebulizer's suspension to re-aerosolize the PM liquid suspension and produce the concentrated aerosol. Using a vacuum pump (Model VP0625-V1014-P2-0511, Medo Inc., USA) at various dilution flow rates, the re-aerosolized PM is then drawn through a diffusion dryer (Model 3620, TSI Inc., USA) filled with silica gel to remove excess water, and then through Po-210 neutralizers (Model 2U500, NRD Inc., USA) to remove their electrical charges. The particles are then collected in parallel on 37 mm PTFE (Teflon) and Quartz (Pall Life Sciences, 2- μ m pore, Ann Arbor, MI) filters for chemical analysis and compare their chemical composition to that of the corresponding ambient samples. In addition, a scanning mobility particle sizer (SMPS 3936, TSI Inc., USA) connected to a condensation particle counter (CPC 3022A, TSI Inc., USA) was used to evaluate the physical properties (i.e., number and mass size distribution) of the re-aerosolized PM at different pressures (i.e., 80–140 inch H₂O), and dilution air flow rates (5, 10, and 15 lpm). Finally, as shown in Figure 1(c), part of the air flow can also enter the animal exposure chambers for *in vivo* inhalation exposure assessments.

2.3. Chemical analysis

The quartz filters (i.e., ambient and re-aerosolized) were analyzed for polycyclic aromatic hydrocarbons (PAHs), elemental (EC), and organic carbon (OC), while the Teflon filters (i.e., ambient and re-aerosolized) were chemically analyzed for inorganic ions, and metals and trace elements. EC and OC content of the samples was analyzed using a Model-4 semi-continuous OC/EC field analyzer (Sunset Laboratory Inc, USA) following the National Institute for Occupational Safety and Health (NIOSH) Thermal Optical Transmission (TOT) method (Birch and Cary, 1996). The PAHs were also determined using Gas Chromatography/Mass Spectrometry (GC/MS) (Schauer et al., 1999). Ion chromatography (IC) was employed to quantify the concentrations of inorganic ions. Finally, particle-bound metals and trace elements were determined using magnetic sector inductively coupled plasma mass spectrometry (IC-PMS) (Herner et al., 2006). In order to perform multiple chemical analyses on each filter, punches of known surface areas were taken from each filter, and the pertinent chemical analyses were performed on individual filter punches. The results were then extrapolated to the whole filter, based on the ratio of the surface area of the punch to the surface area of the filter.

3. Results and discussion

3.1. Physical properties of the ambient vs. re-aerosolized PM

As mentioned in the Methodology section, a scanning mobility particle sizer (SMPS 3936, TSI Inc.) was used for analyzing the physical characteristics of the re-aerosolized PM at different pressures, and dilution flow rates. The PM slurries used for these experiments were obtained from the filter extractions, with a mass concentration of $40 \pm 2 \mu\text{g/ml}$. Figure 2(a) indicates the changes in the number size distribution of the re-aerosolized particles as a function of compressed air pressure at a constant dilution air flow rate (i.e., 15 lpm). According to this figure, applying higher pressure increases the re-aerosolization of the suspended PM, leading to higher number (and in turn mass concentrations) in the system. For example, increasing the pressure from 80 to 140 inches of H_2O increased the total number and mass concentrations from nearly 44700 particles/ cm^3 and $46.9 \mu\text{g/m}^3$ to almost 262000 particles/ cm^3 and $114 \mu\text{g/m}^3$, respectively (Figure S1). It should be noted, however, that increasing the pressure to levels higher than 130–140 inches of H_2O produces considerable vapor condensation in the mixing chamber, which leads to greater rate of particles losses. Additionally, as presented in Figure 2(a), the generated aerosols have number mode at a diameter of around 50 nm, without significant changes in the mode diameter as the pressure changes.

Figure 2(b) also illustrates the dependency of the number size distribution of the re-aerosolized PM on the flow rate at a constant compressed air pressure (i.e., 80 inches of H_2O). As shown in the figure, a decrease in the flow rate leads to higher number and mass concentrations of the re-aerosolized PM in the system; for instance, the total number and mass concentrations increased from 44100 particles/ cm^3 and $46.9 \mu\text{g/m}^3$ to 133000 particles/ cm^3 and $141 \mu\text{g/m}^3$, respectively, when the flow rate decreased from 15 to 5 lpm (Figure S2). This indicates that in addition to pressure, the number and mass concentration of the re-aerosolized PM can be controlled by changing the flow rate. However, according to figure 2(b), in spite of the changes in the maximum and total number concentrations of the re-aerosolized PM at different flow rates, the number modes were observed at around 50 nm, at all different flow rates. It should be noted that the above discussion on the aerosol concentrations and size distributions pertains to the specific nebulizer characteristics as well as the aqueous PM slurry concentrations employed; for example, a more concentrated slurry suspension would result in a higher aerosol concentration with a larger mean diameter, and vice versa (Hinds, 1999).

In order to evaluate the representativeness of the re-aerosolized PM in terms of the physical characteristics, we measured number size distributions of ambient PM at the same sampling site using the SMPS (connected to CPC) instrument, the results of which are presented in Figure 3. As can be seen in the figure, the measured number size distributions are quite consistent with those reported previously for the same sampling site in year-long sampling campaigns (Mousavi et al., 2018b; Sowlat et al., 2016a), showing a number mode diameter in the ultrafine PM size range (i.e., at 40 nm). In addition, comparison of the ambient number size distributions with those of the re-aerosolized PM indicates that the size distributions of re-aerosolized PM particles are quite consistent with those of the ambient

PM in terms of the shape of the distribution and the mode diameters. This further corroborates the fact that the re-aerosolized PM is quite representative of the ambient PM in terms of the physical characteristics.

3.2. Chemical composition of the ambient vs. re-aerosolized PM

3.2.1. Mass balance for bulk chemical components—Figure 4(a) illustrates the mass balance for the bulk chemical components of the ambient $PM_{0.18}$ (collected by high-volume sampler) versus re-aerosolized $PM_{0.18}$ from the filter-extracted slurry. According to the figure, there is general agreement between the chemical mass balance of ambient and re-aerosolized PM. Water-soluble organic matter (WSOM), sulfate, and metals and trace elements were the major chemical constituents of both ambient and re-aerosolized particles. In this study, a conversion factor of 1.8 was used to calculate water-soluble organic matter (WSOM) from WSOC concentration. This ratio accounts for the contribution of non-carbon atoms (i.e., hydrogen, and oxygen) to the bulk mass of organic matter (Turpin and Lim, 2001).

For the water-soluble ions (i.e., chloride, nitrate, ammonium, potassium, and sulfate), there was a strong association between the mass fractions of the re-aerosolized and ambient $PM_{0.18}$ samples. For instance, the mass fraction of chloride was almost the same in the ambient (i.e., 8.26 $\mu\text{g}/\text{mg}$ of PM) and re-aerosolized (i.e., 8.07 $\mu\text{g}/\text{mg}$ of PM) samples. Similarly, the WSOM mass fraction was also perfectly comparable between ambient (i.e., 355 $\mu\text{g}/\text{mg}$ of PM) and re-aerosolized samples (i.e., 372 $\mu\text{g}/\text{mg}$ of PM). However, due to the water-insolubility of some PM components (e.g., EC, and some metals and elements), these insoluble fractions of PM were not extracted efficiently during the aqueous extraction, which artificially increased the relative contribution of soluble components, such as WSOM, to total $PM_{0.18}$ mass in re-aerosolized (i.e., 53%) versus ambient PM (i.e., 42%) samples. Unlike water-soluble species, the mass fraction of EC was dropped by 75% upon water extraction, since EC is an insoluble species and remains mostly on the filter even after applying the extraction protocol (Azeem et al., 2017; Wallén et al., 2010). Similarly, lower mass fractions were observed for several metals and trace elements in the re-aerosolized samples compared to the ambient samples, which will be discussed in detail in section 3.2.1.

The chemical mass balance for ambient $PM_{2.5}$ (collected on VACES filters) versus re-aerosolized $PM_{2.5}$ (from slurries collected using the VACES/aerosol-into-liquid collector) is shown in figure 4(b). Based on the figure, a virtually excellent agreement was observed between chemical composition of ambient and re-aerosolized samples. Organic matter (OM), sulfate, nitrate, ammonium, and metals were the major contributors to $PM_{2.5}$ composition in both set of filters, substantiating the similarity of ambient and re-aerosolized samples in terms of chemical characteristics. In addition, similar to filter extraction protocol, the mass fractions and relative contributions of water-soluble ions (i.e., chloride, nitrate, ammonium, potassium, and sulfate) were almost the same in ambient and re-aerosolized filters. For example, the ambient and re-aerosolized mass fractions of sulfate were 181 $\mu\text{g}/\text{mg}$ of PM and 161 $\mu\text{g}/\text{mg}$ of PM, respectively. The actual mass fraction of OM was also quite comparable between ambient (i.e., 437 $\mu\text{g}/\text{mg}$ of PM) and re-aerosolized (i.e., 482 $\mu\text{g}/\text{mg}$ of PM) samples. However, unlike aqueous filter extraction, the water-insoluble

constituents of PM were almost completely reconstructed using the VACES/aerosol-into-liquid collector tandem. For instance, the ambient mass fraction of EC was 34.3 $\mu\text{g}/\text{mg}$ of PM which was similar to that of re-aerosolized one (i.e., 31.0 $\mu\text{g}/\text{mg}$ of PM). This shows that VACES/aerosol-into-liquid collector tandem is able to retrieve nearly 90% of ambient EC in collected PM slurries, which is a significant advantage over Particle-Into-Liquid Sampler (PILS), capturing 20% of soot particles (i.e., EC) into pure water (Wonaschuetz et al., 2018). Similar mass fractions were also observed between metal species (i.e., water-soluble and water-insoluble) for both set of samples, which will be discussed in further detail in the following section.

3.2.1. Metals and trace elements—Due to the importance of metals and organic species in driving the toxicity of ambient PM (Daher et al., 2011; Saffari et al., 2015; Samara, 2017; Yang et al., 2014), in this and the following section, we have compared and contrasted the chemical composition of ambient versus re-aerosolized PM samples (from filter-extracted slurries as well as slurries collected using the VACES/aerosol-into-liquid collector) in terms of metals/elements and organic (i.e., PAHs) components in more detail. Figure 5(a) indicates the correlation line between the mass fractions of metals and trace elements in the ambient $\text{PM}_{0.18}$ samples and those in the re-aerosolized PM from filter-extracted samples. As can be seen in the figure, the slope of the correlation line is significantly higher than one (i.e., 1.8). This indicates that metals and trace elements that have lower water solubility (e.g., Fe, V, Cr, Ba and Mn) (Birmili et al., 2006; Saffari et al., 2015) are not effectively extracted into the slurry samples, leading to significantly higher mass fractions of these metals and elements in the ambient $\text{PM}_{0.18}$ samples compared to those in the re-aerosolized PM samples. This point is more clearly illustrated in Figure 6(a) as bar charts comparing the mass fraction of redox-active metals, such as V, Cr, Mn, and Fe (Akhtar et al., 2010; Argyropoulos et al., 2016; Charrier and Anastasio, 2012; Decesari et al., 2017; Gasser et al., 2009; Lovett et al., 2018; Mousavi et al., 2018a, 2018b) in the ambient $\text{PM}_{0.18}$ samples versus re-aerosolized PM samples from filter extracts. Results of the independent t-test also confirmed the significant differences in the mass fractions of V ($P_{\text{value}}=0.062$), Cr ($P_{\text{value}}=0.039$), Mn ($P_{\text{value}}=0.007$), and Fe ($P_{\text{value}}=0.063$) between the re-aerosolized and ambient $\text{PM}_{0.18}$ samples. Since the aerosol generation system is mainly designed to supply concentrated ambient PM for the *in vivo* health exposure studies, the re-aerosolized samples should preserve the toxicological characteristics of ambient PM. However, as can be seen in the figure, the mass fractions of many of these redox-active species are significantly higher in the ambient $\text{PM}_{0.18}$ samples, compared to the re-aerosolized PM samples. In case of Fe, for instance, the pertinent mass fraction was 2460 ng/mg of PM in the ambient $\text{PM}_{0.18}$ samples compared to 307 ng/mg of PM in the re-aerosolized PM samples. This clearly indicates the inability of this filter extraction protocol in preserving the concentration of many of the ambient metals and elements, including the redox-active species, in the re-aerosolized samples.

A similar correlation analysis was also performed between the metal and trace element mass fractions of the ambient $\text{PM}_{2.5}$ samples versus the re-aerosolized $\text{PM}_{2.5}$ from the slurry samples collected using VACES/aerosol-into-liquid collector (Figure 5(b)). As can be seen in the figure, a high correlation was observed between the mass fractions of the ambient

versus re-aerosolized PM in the VACES-collected filter and slurry samples with an R^2 value of 0.99 and a slope of nearly 1 (i.e., 1.15). This is shown more clearly in Figure 6(b), which presents the comparison of the mass fractions of redox-active metals (i.e., V, Cr, Mn, Fe, Ni, Cu, and Ti) for the ambient versus re-aerosolized PM samples collected using VACES as bar charts. For instance, the mass fraction of Fe was 17600 ng/mg of PM in the ambient samples, which is quite consistent with that of re-aerosolized sample (i.e., 15100 ng/mg of PM). In addition, according to the independent sample t-test, there were no statistically significant differences (i.e., $P_{\text{value}} \gg 0.05$) between the mass fractions of the metals in re-aerosolized versus ambient PM samples. This further corroborates the advantages of using the VACES/aerosol-into-liquid collector over the aqueous extraction of filters in preserving the chemical composition (and particularly metal elements) of ambient PM samples, which leads to generating PM for inhalation studies that are far more representative of real-world aerosols.

3.2.2. Polycyclic Aromatic Hydrocarbons (PAHs)—Figure 7(a) illustrates the mass fractions of PAHs in the ambient $PM_{0.18}$ samples against the re-aerosolized PM from filter extracts. Previous studies have indicated that PAHs result from incomplete combustion of fossil fuels and they induce detrimental health impacts (e.g., lung cancer) due to mutagenic and carcinogenic characteristics (Hesterberg et al., 2012; Kam et al., 2013; Lovett et al., 2017; Sauvain et al., 2003; Taghvaei et al., 2018). However, as shown in the figure, there is no recovery of PAHs in the re-aerosolized PM samples from filter extracts, due mainly to the water-insolubility of these organic compounds (Kim et al., 2013; Miller et al., 1998; Tang et al., 2005; Tarafdar and Sinha, 2017). Therefore, given the toxicity of these species and the importance of their inclusion in inhalation studies, this can be considered as another major disadvantage of the filter extraction protocol in reconstructing PM that is well representative of ambient PM.

Figure 7(b) also indicates the comparison of the mass fractions of organic species (i.e., PAHs) in the ambient versus re-aerosolized $PM_{2.5}$ samples collected using the VACES/aerosol-into-liquid collector tandem technology. As can be seen in the figure, unlike the filter extraction protocol, this method was able to recover almost all PAHs in the re-aerosolized PM. For example, similar mass ratios were observed for total PAHs in the ambient (i.e., 105 ng/mg of PM) versus re-aerosolized samples (i.e., 100 ng/mg of PM). Given the toxic properties of PAHs, the almost complete recovery of these species is considered as one of the crucial advantages of using the VACES/aerosol-into-liquid collector tandem technology in collecting ambient PM directly into slurry samples over the aqueous extraction of filters to be used in toxicological inhalation exposure studies.

4. Summary and conclusion

The main objective of this study was to develop a new protocol for generating chemically and physically stable sources of aerosols to be used in inhalation exposure studies that are representative of real-world ambient PM. Results from the present study indicated that the re-aerosolized PM are quite representative of ambient PM in terms of the physical characteristics (i.e., size distributions). The re-aerosolized PM from aqueous filter extracts also showed a rather consistent mass balance to that of ambient samples for the bulk

chemical components, especially in terms of the water-soluble fractions of ambient PM (i.e., WSOM, and inorganic ions), which were recovered efficiently in the re-aerosolized PM samples. However, the major drawback of this protocol was that it produced slurries that were deficient in important redox-active species such as EC, PAHs, and some toxic metals and elements, due mainly to their low solubility in water, leading to less-than-ideal recovery of these species in the re-aerosolized PM. On the other hand, the VACES/aerosol-into-liquid collector tandem technology showed superiority in capturing not only the water-soluble, but also the water-insoluble components of PM directly into aqueous slurries, leading to a very efficient recovery of all components of ambient PM in the re-aerosolized PM. This makes the latter protocol an ideal choice to generate particles for toxicological studies that are well representative of real-world ambient PM.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- We developed a novel method for generating physically and chemically stable sources of PM in inhalation exposure studies.
- Using the aqueous filter extracts, the water-soluble fractions of ambient PM were perfectly recovered.
- Re-aerosolization of aqueous suspensions of PM was deficient in reconstructing water insoluble PM components.
- Results indicated the advantages of VACES/aerosol-into liquid tandem technology in recovering both water-soluble and insoluble fractions of PM.

(c)

Figure 1.

Schematic of: a) high-volume sampler with PM_{10} inlet, and ultrafine (UFP) impactor; b) the VACES, coupled with high-volume aerosol-into-liquid collector; and c) aerosol generation setup for filter collection and inhalation exposure

(a)

(b)

Figure 2.
Number size distributions of re-aerosolized particles as a function of a) nebulizer's compressed air pressure; and b) dilution flow rate;

Figure 3.
Typical number size distribution of ambient PM at central Los Angeles obtained during our field tests

Figure 4.
Chemical composition of re-aerosolized versus ambient a) PM_{0.18}; and b) PM_{2.5}

(a)

(b)

Figure 5.
Correlation analysis between the nebulized and ambient mass ratios of metals and trace elements in a) $PM_{0.18}$; and b) $PM_{2.5}$

(a)

(b)

Figure 6. Comparison of the redox active metals mass ratio in (a) PM_{0.18}; and (b) PM_{2.5}

Figure 7.
Comparison of selected PAHs mass ratios in the ambient versus re-aerosolized: a) PM_{0.18};
and b) PM_{2.5}