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Size Distribution, Bioaccessibility and Health Risks of Indoor/Outdoor Airborne Toxic Elements Collected from School Office Room

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Abstract: 20 sets of indoor and outdoor size-segregated aerosol (SSA) samples (180 foils) were collected synchronously by using two 8 Stage Non-Viable Cascade Impactor from an office room in the central region of the megacity-Nanjing, China in winter and spring in 2016. The mass size distribution of SSAs was bimodal for outdoor SSAs and unimodal for indoor in both winter and spring. The crustal elements, such as K, Ca, Mg and Fe, were mainly distributed in the coarse fractions of SSAs while toxic elements such as As, Cd, Pb and Sb were enriched more in the fine fractions in both winter and spring. Moreover, indoor/outdoor (I/O) concentration ratios of SSAs and inorganic elements indicated the penetration of outdoor fine fractions of SSAs into indoor air. As, Pb, V and Mn showed higher inhalation bioaccessibility extracted by the artificial lysosomal fluid (ALF); while V, As, Sr and Cd showed higher inhalation bioaccessibility using the simulated lung fluid (SLF), suggesting differences in elemental inhalation bioaccessibility between ALF and SLF extraction. There were similar potential carcinogenic and accumulative non-carcinogenic risks via inhalation exposure to indoor and outdoor particle-bound toxic elements based on their bioaccessible concentrations. Therefore, the potential health risks to human posed by toxic elements in office rooms cannot be neglected via inhalation exposure of the fine airborne particles.

Keywords: chemical composition; size-dependent distribution; inhalation exposure; in vitro inhalation bioaccessibility procedures; risk-based assessment

1. Introduction

It has been well documented that aerosols can result in various acute and chronic health effects to humans via inhalation and oral ingestion exposure [1,2]. These adverse health effects depend not only on the concentrations of particulate matters of different sizes but also on their chemical compositions [3]. Firstly, it is believed that particles of different sizes have different deposition patterns and deposition fractions in lung region, which might result in different health risks to human [1,4]. Secondly, literatures have confirmed that atmospheric particulate matters (APMs) generally contain trace elements, which may result from the abundant anthropogenic sources such as industrial emissions, coal combustion emissions and automotive exhausts [5]. For example, in 44 Chinese cities, the average values of AMP-bound toxic elements were 261, 51.0, 29.0, 85.7, 13.2, 17.9, 425 and 117 ng m^{-3} for Pb, As, Ni, Cr, Cd, V, Zn and Cu, respectively [5]. Moreover, the toxic elements such as As, Cd, Cr, V, Pb and Zn distribute mainly in the fine fractions of size-segregated aerosols (SSAs); while the crustal elements such as Al, Mg, Ca, Fe and Mn occur predominately in the coarse fractions [5,6]. Therefore, investigations about SSAs—bound trace elements are important to understand and manage effects of aerosols on human health in indoor environment.

Recently risk-based assessment that considers linkages between pollution sources, pathways and receptors has been widely used to evaluate the potential hazards of contaminants. "Biological effects are not related to the total concentration of a contaminant in the soil and soil-like materials; Organisms respond only to the fraction that is biologically available (p. 1420)" [7]. Therefore, bioaccessibility (i.e., fraction of a chemical solubilized in simulated human body fluids) and bioavailability (i.e., fraction of a chemical absorbed by internal target tissues and organs) have attracted substantial academic and regulatory attention on the adverse effects of pollutants in environmental media on human health [8,9]. For example, in vitro assays including the physiologically based extraction test (PBET), the Solubility Bioaccessibility Research Consortium (SBRC), in vitro gastrointestinal method (IVG) and the German standard bioaccessibility methodology (Deutsches Institut für Normunge.V., DIN, Berlin, Germany) have been widely used to study the in vitro gastrointestinal bioaccessibility of trace elements in soils and soil-like materials [10,11]. Moreover, in vitro gastrointestinal bioaccessibility and relative bioavailability (RBA) of lead and arsenic in soils have been well documented to be validated by in vitro-in vivo correlation (in vitro data verified by in vivo data) [12,13]. The inhalation bioaccessibility of APM-bound trace elements, that is, the solubility of trace elements in particulate matters in simulated lung fluids, has also been recognized as an important parameter for health risk assessment associated with the inhalation of airborne particles [14,15]. In recent years, some in vitro inhalation bioaccessibility procedures have been developed and compared to investigate the inhalation bioaccessibility of APM-bound trace elements although they are not validated by the in vivo-in vitro correlation [4,14,16]. Risk-based assessment based on the total concentrations of trace elements in outdoor atmospheric particulate matters has been investigated intensively recently [17,18]; however, investigations on indoor airborne particulates have been mainly focused on chemical composition, indoor/outdoor (I/O) ratios and source identification [19,20]. Most people spend plenty of time in the indoor areas (e.g., home and/or office), so the quality of indoor air is very important for risk-based assessment to human health [21,22]. For example, office workers and students spend working or learning time in the indoor areas, where there are no obvious typical indoor sources (e.g., smoking, printing, cooking, etc.) for airborne particulate matters and for AMPs-bound trace elements [21]. Therefore, the comparison of inhalation bioaccessibility and health risks of indoor and outdoor SSA-bound toxic elements is helpful to understand the health risks of toxic elements via inhalation exposure in room without typical indoor sources of particle-bound toxic elements.

Nanjing (118°22′ and 119°14′ E, 31°14′ and 32°37′ N), the capital of Jiangsu Province in eastern China, locates at the lower reaches of the Yangtze River and is surrounded by mountains on three sides. Nanjing, Shanghai and Hangzhou are the three megacities of Yangtze River Delta (YRD) which is an extremely active region of economic development in China. The haze days increased from 40 days in 1980s to 150 days in 2010 in Nanjing [23]. Air pollution in winter and spring is heavier than that in summer and autumn in Nanjing [24]. Therefore, indoor/outdoor SSAs were collected by two Andersen eight stage non-viable cascade impactors (TE-20-800, Tisch, New York, NY, USA) synchronously in an office on the Gulou campus of Nanjing University (118°46′17″ E, 32°3′37″ N), the traditional central region of the megacity-Nanjing, China in winter and spring in 2016. The objectives of this study were to: (a) compare the distribution mode of mass concentrations of SSAs and inorganic elements between indoor and outdoor, (b) investigate the inhalation bioaccessibility of indoor/outdoor SSA-bound toxic elements extracted by using two in vitro inhalation bioaccessibility procedures (artificial lysosomal fluid (ALF) and simulated lung fluid (SLF)) and (c) evaluate health risks posed by indoor/outdoor fine fractions of SSA-bound toxic elements via inhalation exposure based on their inhalation bioaccessibility.

2. Methods

2.1. Sample Collection

Indoor SSAs were sampled in an office room for graduate students located on the fourth floor and outdoor sampling site was set at a platform outside the window of this office room in Gulou campus

of Nanjing University (118°46′17″ E, 32°3′37″ N) which is the traditional center of Nanjing (Figure A1). There were 13 desks for 13 graduate students in this room. The room was 108.1 m^3 (6.8 m long, 5.3 m wide and 3.0 m high) with two windows of 1.3 m^2 (1.2 m wide and 1.1 m high) on one side and a door of 1.7 m^2 (0.9 m wide and 1.9 m high) on the other side. A commuting road is found about 50-m north of the office. Furthermore, the office is surrounded by classroom buildings and laboratory buildings. There was a room air conditioner, which was not running during the sampling periods. The windows were also closed and only four graduate students stayed in this room occasionally during sampling. There was no cooking, printing and smoking, so no obvious indoor sources for airborne particulate matters existed in this room as the common office room. The resuspension of indoor settled dust by human activities may be an indoor source. Moreover, the penetration of outdoor particles through door and/or windows may be the main source for indoor particles [21].

In order to obtain enough SSAs for analysis, 72 h was set for the collection of SSAs according to the pre-experiments. Therefore, consecutive 72-h samples of indoor/outdoor SSAs were collected synchronously using two Andersen eight stage non-viable cascade impactors (TE-20-800, Tisch, New York, NY, USA) with nominal cut-sizes of 0.43, 0.7, 1.1, 2.1, 3.3, 4.7, 5.8 and 9.0 μm at a flow rate of 28.3 L/min in January (from 6th to 15th and 25th to 31st) and April (from 1st to 15th) in 2016. Aerosols' particles of aerosols were thus segregated into 9 size fractions in terms of aerodynamic diameter: >9 μm on the first stage, 5.8–9.0 μm, 4.7–5.8 μm, 3.3–4.7 μm, 2.1–3.3 μm, 1.1–2.1 μm, 0.7–1.1 μm, 0.4–0.7 μm and <0.4 μm on the final back-up stage. Whatman PTFE (polytetrafluoroethylene) filter membranes were used to collect the different fractions of the aerosols. Five sets (5 sets × 9 foil/set = 45 foils) of indoor and outdoor SSA samples were synchronously collected in January and April, respectively. In total, 20 sets of aerosol samples (20 sets × 9 foil/set = 180 foils) were collected in our study.

2.2. Determination of Total Concentrations of Inorganic Elements

To determine the total concentrations of elements in SSAs, a Milestone ETHOS 1 (Milestone, Sorisole, Italy) microwave sample preparation system with temperature control was used to digest the SSAs. A filter was cut into four equal pieces by ceramic scissors. One piece was selected randomly for the determination of total concentrations of elements and the others were used for in vitro assays. The microwave-assisted digestion procedure was seen in our previous report [24]. The resulting digestion solution was stored at 4 °C until analysis. Samples and blanks were prepared in duplicate. Elemental concentrations in the resulting solution were detected by an inductively coupled plasma atomic emission spectrometer (ICP-OES, PerkinElmer SCIEX, Optima 5300, Waltham, MA, USA) and an inductively coupled plasma mass spectrometry (ICP-MS, PerkinElmer SCIEX, Elan 9000, Waltham, MA, USA). Precision and accuracy were verified using standard reference materials available at the National Research Center for Geoanalysis, China (GBW07405, Soil). ICP-MS was optimized using 10 μg L^{-1} Mg, Rh, In, Ba, Ce, Pb and U in 2% HNO$_3$ solution and the internal standard (20 μg L^{-1} In and Bi in 2% HNO$_3$) was added online during analysis of elements.

2.3. Extraction of Bioaccessible Fractions of Toxic Elements

Among in vitro inhalation bioaccessibility procedures, ALF and SLF are often used to simulate the lysosomal fluid in the lysosomal of macrophage of alveolar and interstitial macrophages and neutral interstitial physiological fluids found deep in the human lung (pH 7.4) to investigate the inhalation bioaccessibility of toxic elements [14,15]. The compositions can be found in the previous literatures (e.g., ALF [25] and SLF [15]). It is reported that the fine particles can reach lung, then distribute in alveolar compartment and interstitial spaces as shown in the previous literatures [1], while coarse particles (>5 μm) deposit mainly in the large and medium-sized airways or the distal lung [1,26]. Therefore, bioaccessible concentrations of toxic elements in the <3.3 μm fractions (<0.4, 0.4−0.7, 0.7−1.1, 1.1−2.1, 2.1−3.3 μm) were investigated using ALF and SLF as the previous reports [27,28].

A quarter of the filter membrane was placed in a 10 mL high density polyethylene tube containing 3 mL of the extraction solution. The tubes were incubated at a constant temperature of 37 °C for 24 h

using a water bath shaker at a rate of 200 rpm. The mixture was centrifuged at 8000 rpm for 5 min and the supernatant was filtered through Whatman Grade 42 filter paper. The pH of filtrate should vary within 0.5 pH unites compared with the initial pH, otherwise the procedure had to be redone. Eventually, the resulting solution was stored at 4 °C for analysis, which was conducted within one week after extraction by ICP-OES and ICP-MS mentioned above.

To determine the method detection limits (MDLs) of elements, bioaccessibility experiments with the addition of a spiking solution containing As, Ni, Cu, Zn, Pb, Mn, Sr, Cd, Co and V were conducted on ALF and SLF without sample. The spiking was done by first preparing a spike solution for As, Ni, Cu, Zn, Pb, Mn, Sr, Cd, Co and V using deionized water and standard solution. Then adding it to the test tubes containing SLFs (without a sample), resulting in spiked test samples to contain an additional $0.5 \text{ ng} \cdot \text{L}^{-1}$ and $5 \text{ ng} \cdot \text{L}^{-1}$ of As, Ni, Cu, Zn, Pb, Mn, Sr, Cd, Co and V. Analysis was conducted following spiking. To access the recovery of elements, bioaccessibility experiments with the addition of a spiking solution containing As, Ni, Cu, Zn, Pb, Mn, Sr, Cd, Co and V were conducted on ALF and SLF with and without sample. The spiking was done by first preparing a spike solution for As, Ni, Cu, Zn, Pb, Mn, Sr, Cd, Co and V using deionized water and standard solution. Then adding it to the test tubes containing SLFs (with or without a sample), resulting in spiked test samples to contain an additional $1 \text{ mg} \cdot \text{L}^{-1}$ of As, Ni, Cu, Zn, Pb, Mn, Sr, Cd, Co and V. Analysis was conducted following spiking (after 24 h).

3. Results and Discussion

3.1. Mass Distribution of the Outdoor and Indoor Size—Segregated Aerosols

Figure 1 shows the typical bimodal distribution with strong peaks of 5.8–9.0 μm and 0.4–2.1 μm for the mass concentrations of the outdoor SSAs in both winter and spring, which was similar to those in the previous reports [24]. Figure 1 also shows that a large peak appears in the 0.4–2.1 μm fractions for the indoor SSAs in both winter and spring indicating the significant accumulation of the fine size fractions. The total mass concentrations of the outdoor SSAs in winter and spring were higher than those of indoor SSAs (Figure 1). Average concentrations of the outdoor and indoor <2.1 μm fractions of SSAs (89.8 μg m^{-3} and 64.2 μg m^{-3}, respectively) in winter were higher than those (58.1 and 45.1 μg m^{-3}) in spring, suggesting the heavy pollution of the fine particles in winter. The fine fractions (<2.1 μm fraction) of the indoor SSAs, which account for about 60-70% (70.3% for winter and 61.4% for spring), are the dominant fraction differing from the outdoor SSAs (56.4% for winter and 39.5% for spring). Figure 1 shows that mass concentrations of all fractions of the indoor SSAs were less than them of the outdoor SSAs in both winter and spring, indicating the infiltration of outdoor SSAs. However, the higher percentages of the fine fractions of the indoor SSAs might imply the different infiltration among particles with different sizes.

The mass concentrations of SSAs in Nanjing are higher compared with those obtained in other regions (e.g., 1.9-21.4 and 1.0-3.5 μg m^{-3} for outdoor and indoor PM$_{10}$ in Norway, respectively [29]). They were consistent with those in the previous report in Nanjing [24]. Our results illustrated that the mass concentrations of outdoor SSAs were higher than those of the indoor SSAs (Figure 1), which were consistent with the literatures [30,31]. The bimodal distribution for the mass concentrations of outdoor SSAs and unimodal distribution for indoor particles revealed a significant reduction of the coarse fractions of indoor SSAs. The average concentrations of both indoor and outdoor SSAs exceeded the WHO guidelines and NAAQS (Figure 1) [32], which suggested the potential risks to human health.
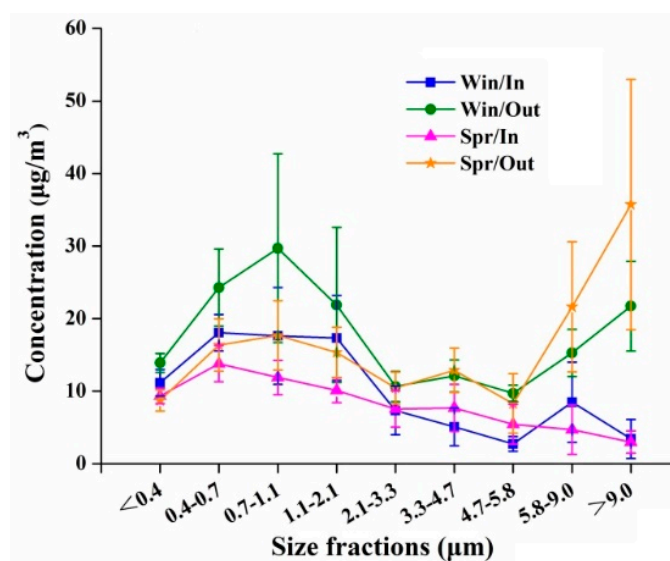
Figure 1. Mass concentrations of indoor/outdoor SSAs in winter and spring (*n* = 5) (Win: Winter; Spr: Spring; In: Indoor; Out: Outdoor).

3.2. Elemental Total Concentrations in the Outdoor and Indoor Size—Segregated Aerosols

Inorganic elements including Al, Ba, Ca, Cr, Fe, K, Mg, Mn, Mo, Na, Ni, Sb, Sr, Ti, As, Cu, Zn, Pb, Cd, Co and V in the outdoor/indoor SSAs were analyzed (Table 1). The mean total concentrations of the studied elements in all fractions are 18.8 and 16.2 µg m^{-3} for the outdoor SSAs in winter and spring, respectively, which were higher than those for the indoor SSAs in winter and spring (8.7 µg m^{-3} for winter and 9.0 µg m^{-3} for spring). The sum of concentrations of the 21 elements increased with the increasing size of SSAs for the outdoor SSAs in winter and spring. However, no similar trend was observed for the indoor SSAs in winter and spring, meaning the different chemical composition between outdoor and indoor SSAs in winter and spring. Moreover, the coarse particles contained higher percentages of crustal elements while fine particles had higher percentages of toxic elements. For example, Ca and Fe were the preponderant crustal elements found in the coarse fraction of the outdoor and indoor SSAs in winter and spring; while Cd was observed as the lowest level in outdoor and indoor SSAs in winter (2.8 and 2.1 ng m^{-3}) and spring (1.2 and 0.7 ng m^{-3}). According to IARC (International Agency for Research on Cancer), lead (Pb), cadmium (Cd), arsenic (As), nickel (Ni) and chromium (Cr) are carcinogenic to humans [33]. European Commission (EC) has issued the threshold values for outdoor Pb, Ni, As and Cd to be 500, 20, 6 and 5 ng m^{-3}, respectively [34]. In the present work, the outdoor/indoor concentrations of As and Ni in winter and spring in the <3.3 µm fractions of SSAs exceeded the EC limit for ambient air quality, suggesting the potential health risks.

Table 1. Average concentrations (ng m^{-3}) of elements in SSAs (*n* = 20).

	<0.4	0.4−0.7	0.7−1.1	1.1−2.1	2.1−3.3	3.3−4.7	4.7−5.8	5.8−9.0	>9.0
Al	75.2	55.4	69.9	113	165	186	146	226	319
Ba	2.7	2.8	4.3	5.8	7.0	7.1	5.0	7.7	10.3
Ca	372	386	372	421	624	686	582	978	1477
Cr	1.8	1.8	2.0	2.1	1.9	1.6	1.5	1.8	2.5
Fe	131	175	176	202	301	275	194	283	471
K	76.3	141	132	94.1	58.3	53.5	40.3	64	86.7
Mg	28.7	31.3	32.7	53.4	70.8	72.2	55.3	86.1	132
Mn	5.7	13.6	14.2	10.6	6.7	6.4	4.2	6.8	9.6
Mo	0.7	0.8	0.6	0.6	0.5	0.5	0.4	0.4	0.5
Na	51.6	43.1	46.2	60.2	64.2	42.2	30	58.1	67.8
Ni	5.8	7.5	5.4	3.9	4.5	4.7	4.8	4.8	5.3
Sb	111	140	134	106	110	117	107	85.2	89.9
Sr	0.7	0.8	0.8	1.2	1.7	1.7	1.2	2.4	3.5
Ti	14.4	13.7	16	19.4	21.6	21.1	21.8	22.6	30.4
As	1.1	1.9	2.3	1.7	0.7	0.4	0.2	0.4	0.4
Cu	3.7	5.3	5.2	4.7	3.4	2.6	1.4	3.4	4.2
Zn	24.2	43.4	63.4	70.3	37.4	21.7	16.8	23.7	20.9
Pb	10.2	15.5	19.1	15	6.8	3.1	2.5	3.1	3.6
Cd	0.2	0.3	0.4	0.4	0.2	0.1	0.04	0.04	0.04
Co	7.4	7.1	9.2	8.1	8.2	8.5	7.6	8.7	8.6
V	1.3	1.2	1.0	0.9	0.6	0.5	0.4	0.6	1.1

SSAs: size-segregated aerosols.

3.3. Indoor/Outdoor (I/O) Ratios for SSAs and Inorganic Elements

3.3.1. Indoor/Outdoor (I/O) Ratios of SSAs' Mass Concentrations

Indoor/outdoor mass concentration ratios for each fraction of SSAs in winter and spring were listed in Table 2. Indoor/outdoor mass concentration ratios for SSAs in winter and spring were 0.6 and 0.5, respectively. Therefore, with the increase of particle size indoor particles decreased greatly. These suggested that mass concentrations of fine fractions of SSAs was similar between indoor and outdoor environment while outdoor coarse fractions of SSAs were greater than indoor. For example, lower ratios were recorded for the >3.3 μm fractions of SSAs (0.4 and 0.3) while higher ratios of 0.7 and 0.8 were observed for the <3.3 μm fractions of SSAs in winter and spring, respectively. Our results concerning the I/O ratios are in good agreement with those reported in the literature, in which I/O ratios lower than unity mean the penetration of outdoor particles into indoor air [35,36]. High I/O ratios for the <3.3 μm fractions of SSAs in winter (0.7) and spring (0.8) are consistent with the previously reports that the penetration efficiency was known to be the greatest for particles in the range of 100-200 nm in which the particle loss from impaction and diffusion was minimal [37]. Furthermore, researchers have suggested that the increasing deposition rate was related to the increasing particle size [35]. Therefore, the different indoor/outdoor concentration ratios for SSAs in winter and spring demonstrated that outdoor fine particles had great influence on their indoor concentrations even when the windows were closed in the cold season.

Table 2. Ratios of mass concentrations of indoor/outdoor fractions of SSAs in winter and spring (*n* = 5).

	<0.4	0.4−0.7	0.7−1.1	1.1−2.1	2.1−3.3	3.3−4.7	4.7−5.8	5.8−9.0	>9.0
Winter	0.8	0.8	0.6	0.9	0.7	0.4	0.3	0.6	0.2
Spring	1.1	0.9	0.7	0.7	0.8	0.6	0.6	0.2	0.1

SSAs: size-segregated aerosols.

3.3.2. Indoor/Outdoor (I/O) Ratios for Elements' Concentrations

I/O concentration ratios for Al, Ba, Ca, Cr, Fe, K, Mg, Mn, Mo, Na, Ni, Sb, Sr, Ti, As, Cu, Zn, Pb, Cd, Co and V were listed in Table A1. The average ratios for total concentrations of all studied elements in SSAs were 0.5 and 0.6 for all fractions, 0.3 and 0.4 for the >3.3 μm fraction and 0.8 and 1.0 for the <2.1 μm fractions in winter and spring, respectively. I/O concentration ratios were generally in the range of 0.3–0.7 for most of the studied elements. Higher I/O ratios (>0.7) were found for Ni (0.8 and 0.9), Sb (0.9 and 1.0), Pb (0.8 and 0.9) and Cd (0.9 and 1.0) in winter and spring in the fine fractions. The values of I/O ratios for inorganic elements decrease generally with the increasing particles' sizes (from <0.4 μm fraction to >9.0 μm fraction). So, outdoor fine particles are easier to penetrate into indoor than the coarse particles, which is confirmed by the I/O concentration ratios of SSAs discussed above.

3.4. Inhalation Bioaccessibility of Toxic Elements

Inhalation bioaccessibility, solubility of SSA-bound toxic elements in the simulated body fluids, is expressed as the percentage of an elemental concentration extracted by an in vitro inhalation bioaccessibility procedure to its total concentration. It is reported that fine and ultrafine particles can reach lung, then distribute in the alveolar compartment and interstitial spaces [4,38] and a 24 h interval time represents the upper limit of inhalation bioaccessibility for particle-bound toxic elements using ALF [27,39]. Therefore, the inhalation bioaccessibility of toxic elements such as As, Ni, Cu, Zn, Pb, Mn, Sr, Cd, Co and V in the <3.3 μm fractions was investigated by using ALF and SLF at 24 h extraction (Table 3). Recovery percentages for trace elements following spiking (after 24 h) were conducted with ALF and SLF (Table A2). For the in vitro tests containing ALF (with or without sample) the overall recovery percentages were satisfactory (within 100% ± 20%). Recovery percentages (with or without sample) for Pb, Zn in SLF were lower than 80%, which may indicate the formation of precipitates in the tubes. It is indicated that pH and composition of SLFs have effects on recovery of elements.

Table 3. In vitro bioaccessibility (%) of toxic elements in the indoor/outdoor <3.3 μm fractions in winter and spring extracted by SLF and ALF (*n* = 5).

	Samples	SLF	ALF		Samples	SLF	ALF
As	Win/In	39.3 ± 7.0	49.1 ± 5.6	Mn	Win/In	5.7 ± 1.2	44.9 ± 2.1
	Win/Out	42.0 ± 6.9	52.2 ± 7.8		Win/Out	22.6 ± 6.5	44.8 ± 3.1
	Spr/In	37.5 ± 4.4	44.2 ± 4.7		Spr/In	19.0 ± 5.1	34.2 ± 2.6
	Spr/Out	39.0 ± 4.6	43.8 ± 4.6		Spr/Out	11.4 ± 1.4	35.9 ± 4.2
Ni	Win/In	26.2 ± 3.0	35.3 ± 3.4	Sr	Win/In	32.6 ± 5.4	34.0 ± 5.5
	Win/Out	24.9 ± 1.9	33.2 ± 4.5		Win/Out	32.0 ± 1.2	35.5 ± 2.1
	Spr/In	18.5 ± 5.3	24.9 ± 3.2		Spr/In	34.0 ± 2.3	36.0 ± 4.8
	Spr/Out	16.3 ± 4.2	24.1 ± 2.2		Spr/Out	32.8 ± 4.3	35.2 ± 3.7
Cu	Win/In	24.3 ± 3.0	27.5 ± 1.3	Cd	Win/In	26.2 ± 4.2	36.3 ± 3.5
	Win/Out	24.3 ± 5.0	23.5 ± 0.5		Win/Out	26.6 ± 5.6	35.5 ± 3.8
	Spr/In	27.2 ± 2.6	26.3 ± 3.2		Spr/In	26.7 ± 3.3	26.3 ± 2.4
	Spr/Out	24.0 ± 4.8	25.2 ± 2.6		Spr/Out	26.6 ± 6.4	25.5 ± 2.2
Zn	Win/In	1.4 ± 0.5	33.9 ± 4.8	Co	Win/In	1.0 ± 0.2	7.9 ± 0.8
	Win/Out	1.5 ± 0.7	34.5 ± 2.0		Win/Out	2.8 ± 0.6	2.9 ± 0.7
	Spr/In	4.5 ± 0.6	44.7 ± 4.6		Spr/In	2.3 ± 0.4	1.3 ± 0.3
	Spr/Out	2.2 ± 1.2	41.9 ± 4.6		Spr/Out	1.4 ± 0.6	1.2 ± 0.3
Pb	Win/In	0.9 ± 0.2	50.0 ± 18.9	V	Win/In	40.1 ± 5.2	44.9 ± 5.3
	Win/Out	0.8 ± 0.3	42.5 ± 13.6		Win/Out	37.0 ± 5.3	45.1 ± 4.1
	Spr/In	4.3 ± 1.2	60.1 ± 12.5		Spr/In	42.7 ± 4.6	45.5 ± 5.0
	Spr/Out	2.1 ± 1.0	58.0 ± 5.3		Spr/Out	39.2 ± 8.6	46.2 ± 5.8

Win: Winter; Spr: Spring; In: Indoor; Out: Outdoor. SLF: simulated lung fluid; ALF: artificial lysosomal fluid. The +/− values are standard deviation.

The average inhalation bioaccessibility extracted by ALF was in the order of As > V > Mn > Pb > Sr ≈ Cd > Zn > Ni > Cu > Co in winter and Pb > V > As > Zn > Mn > Sr > Cd > Cu > Ni > Co in spring (Table 3). Generally, As, Pb, V and Mn showed higher inhalation bioaccessibility (Table 3). Co was the lowest with the mean of 2.9% and 1.2% in winter and spring, respectively (Table 3). The average inhalation bioaccessibility for SLF was in the order of As > V > Sr > Cd > Ni > Cu > Mn > Co > Zn > Pb in winter and V > As > Sr > Cd > Cu > Ni > Mn > Zn > Pb > Co in spring (Table 3). So, V, As, Sr and Cd had higher inhalation bioaccessibility in SLF extraction while Pb showed the lowest solubility (Table 3). Similar inhalation bioaccessibility of toxic elements was found for the indoor SSAs extracted by ALF and SLF (Table 3). Great differences on the inhalation bioaccessibility of the SSA-bound toxic elements in the outdoor and indoor SSAs were observed between ALF and SLF extraction (Table 3). Those may due to the difference on the chemical composition and pH between ALF and SLF extraction.

The inhalation bioaccessibility of Zn and Mn associated with $PM_{2.5}$ in ALF reported previously is similar to our study [28]. Inhalation bioaccessibility of Cd in our study is below the previous reports of Cd in PM_{10} and $PM_{2.5}$ in ALF [28,40]. A particle-size dependent relation for the inhalation bioaccessibility was not obvious in our studied samples extracted by ALF and SLF (Table 3). pH and the chemical compositions of ALF and SLF may be the important factors which influence metal solubility in the simulated body fluids. For example, the solubility of many toxic elements is higher in ALF than in Gamble's solution [28]. pH difference between ALF (pH 4.5) and SLF (pH 7.4) obviously leads to preferential solubility and dissolution is enhanced in ALF [15]. To the near neutral pH of SLF (pH 7.4), the inhalation bioaccessibility of SSA-bound toxic elements for most SSAs' fractions is found to be lower than those extracted with ALF of weak acidity (pH 4.5) (Table 3). The bioaccessible fractions of Pb, Zn and Mn extracted by ALF were higher than those by SLF. However, ALF and SLF had less influence on the extractable Cu and Sr (Table 3). Overall, the inhalation bioaccessibility of toxic elements in SSAs extracted by ALF and SLF is found to be elemental dependence.

3.5. Human Health Risk Assessment

Residents living in this area are potential receptors of airborne metals. The fine fractions of SSAs have more potential to enter into lung than the coarse fractions of SSAs, so toxic elements associated with the fine particles may pose more potential hazards to humans. Therefore, the non-carcinogenic and carcinogenic health risks via inhalation exposure to <3.3 μm fraction were evaluated according to the models from U.S. EPA (Human Health Risk Assessment, https://www.epa.gov/risk/human-health-risk-assessment). According to the human health evaluation manual (Part A) and supplemental guidance for inhalation risk assessment (Part F), the exposure concentration (EC) via inhalation was calculated to assess the health risks posed by airborne toxic elements in the <3.3 μm fractions of SSAs using the following equation. The non-carcinogenic risk was estimated by the hazard quotient (HQ). HQ and carcinogenic risks (CR) posed by toxic elements in the <3.3 μm fractions via inhalation exposure were calculated by the following equations (Human Health Risk Assessment, https://www.epa.gov/risk/human-health-risk-assessment):

$$EC_{inh} = (C \times ET \times EF \times ED)/AT_n \tag{1}$$

$$HQ = EC_{inh}/(R_fC_i \times 1000 \text{ μg/mg}) \tag{2}$$

$$CR = IUR \times C_{inh} \tag{3}$$

where C: the arithmetic mean concentration; EF: exposure frequency (350 days/year for residents); ED: exposure duration (24 years for adults); ET: exposure time (8 h/day for outdoor, 16 h/day for indoor); AT_n: average time (for non-carcinogens, AT_n = ED × 365 days × 24 h/day; for carcinogens, AT_n = 70 year × 365 days/year × 24 h); R_fC_i: inhalation reference concentrations (mg/m^3); IUR: inhalation unit risk $((μg/m^3)^{-1})$. Standard default values for EF, ED, ET and AT_n are cited from the document of U.S. EPA Regional Screening Levels (https://www.epa.gov/superfund).

The hazard index (HI), the sum of HQ, is used to assess the overall potential for non-carcinogenic effects posed by multiple chemicals. A value for HQ and/or HI below one means that there is no significant non-carcinogenic risk; for carcinogens, the acceptable risk range is between 1×10^{-6} (1 in 1,000,000) and 1×10^{-4} (1 in 10,000) by U.S. EPA's risk management (Human Health Risk Assessment, https://www.epa.gov/risk/human-health-risk-assessment).

The non-carcinogenic risks from SSA-bound toxic elements via inhalation exposure to adults are listed in Table 4. The HQ values based on ALF- and SLF-bioaccessible concentrations of toxic elements were lower than the safe level (=1), which indicated that no non-carcinogenic risks exist from the inhalation exposure for a single element (Table 4). HI values for all studied elements were 1.3 for ALF and 0.8 for SLF, suggesting the potential accumulative non-carcinogenic risks for adults. Based on the total concentrations of toxic elements, HQ for Co and HI were higher than the safe level (=1) (Table 4). Due to the differences on ET (16 h for indoor and 8 h for outdoor set for this calculation) and elemental I/O ratios within 0.5~1.0, the health risks for indoor and outdoor were similar (Table 4). Risk-assessment based on the total concentrations over-evaluated the potential health risks (Table 4). The environmental researches have confirmed that the bioavailable concentrations rather than the total concentrations decide the toxicity of metals to organisms [7]. The bioaccessible fraction is generally higher than what is subsequently absorbed into the bloodstream (bioavailable fraction), so in-vitro assessment is thought to generate a "conservative measure of bioavailability" [4]. Therefore, the risk assessment based on bioaccessible concentrations of particle-bound toxic elements will obtain more reasonable results than those based on total concentrations.

Table 4. Non-carcinogenic risks to adults from toxic elements in the indoor/outdoor <3.3 μm fractions (*n* = 10).

		RfCi	EC			HQ		
			Total	ALF	SLF	Total	ALF	SLF
As	In *	1.5×10^{-5}	3.8×10^{-3}	1.8×10^{-3}	1.4×10^{-3}	2.5×10^{-1}	1.2×10^{-1}	9.5×10^{-2}
	Out **	1.5×10^{-5}	3.1×10^{-3}	1.5×10^{-3}	1.2×10^{-3}	2.0×10^{-1}	1.0×10^{-1}	8.0×10^{-2}
Ni	In	9.0×10^{-5}	1.5×10^{-2}	4.3×10^{-3}	3.2×10^{-3}	3.0×10^{-1}	8.7×10^{-2}	6.4×10^{-2}
	Out	9.0×10^{-5}	9.9×10^{-3}	2.7×10^{-3}	2.0×10^{-3}	2.0×10^{-1}	5.4×10^{-2}	4.0×10^{-2}
Mn	In	5.0×10^{-5}	3.1×10^{-2}	1.2×10^{-2}	3.7×10^{-3}	6.2×10^{-1}	2.4×10^{-1}	7.5×10^{-2}
	Out	5.0×10^{-5}	1.7×10^{-2}	6.9×10^{-3}	2.8×10^{-3}	3.4×10^{-1}	1.4×10^{-1}	5.7×10^{-2}
Cd	In	1.0×10^{-5}	8.1×10^{-4}	2.8×10^{-4}	2.0×10^{-4}	8.1×10^{-2}	2.8×10^{-2}	2.0×10^{-2}
	Out	1.0×10^{-5}	5.5×10^{-4}	1.8×10^{-4}	1.4×10^{-4}	5.5×10^{-2}	1.8×10^{-2}	1.4×10^{-2}
Co	In	6.0×10^{-6}	2.4×10^{-2}	1.0×10^{-3}	3.9×10^{-4}	3.9	1.7×10^{-1}	6.5×10^{-2}
	Out	6.0×10^{-6}	1.4×10^{-2}	2.6×10^{-4}	2.7×10^{-4}	2.3	4.4×10^{-2}	4.5×10^{-2}
V	In	7.0×10^{-6}	2.4×10^{-3}	1.1×10^{-3}	9.7×10^{-4}	3.5×10^{-1}	1.6×10^{-1}	1.4×10^{-1}
	Out	7.0×10^{-6}	1.9×10^{-3}	8.5×10^{-4}	6.8×10^{-4}	2.7×10^{-1}	1.2×10^{-1}	9.7×10^{-2}

* In: Indoor; ** Out: Outdoor; RfCi: inhalation reference concentrations; EC: exposure concentration; HQ: hazard quotient. SLF: simulated lung fluid; ALF: artificial lysosomal fluid. A value for HQ and/or HI below one means that there is no significant non-carcinogenic risk (Human Health Risk Assessment, https://www.epa.gov/risk/human-health-risk-assessment).

Carcinogenic risks from toxic elements via inhalation exposure to adults were also calculated (Table 5). The carcinogenic risks based on ALF- and SLF-bioaccessible concentrations of toxic elements via inhalation exposure (As, Pb, Co and V) were beyond the acceptable level (1×10^{-6}), which indicated that the carcinogenic risks posed by these toxic elements to adults via inhalation were unacceptable. Similarly, the potential accumulative carcinogenic risks were beyond the acceptable level (Table 5). The *CR* values based on ALF- and SLF-bioaccessible concentrations were lower than those for total concentrations but they all showed the potential carcinogenic risks via inhalation exposure. Slight differences between indoor and outdoor exposure were found (Table 5) and the reason might be the same as discussed above.

Table 5. Carcinogenic risks to adults from toxic elements in the indoor/outdoor <3.3 μm fractions ($n = 10$).

		IUR	EC			CR		
			Total	ALF	SLF	Total	ALF	SLF
As	In *	4.3×10^{-3}	1.3×10^{-3}	6.2×10^{-4}	4.9×10^{-4}	5.6×10^{-6}	2.6×10^{-6}	2.1×10^{-6}
	Out **	4.3×10^{-3}	1.0×10^{-3}	5.2×10^{-4}	4.1×10^{-4}	4.5×10^{-6}	2.2×10^{-6}	1.8×10^{-6}
Ni	In	2.6×10^{-4}	5.1×10^{-3}	1.5×10^{-3}	1.1×10^{-3}	1.2×10^{-6}	3.6×10^{-7}	2.7×10^{-7}
	Out	2.6×10^{-4}	3.4×10^{-3}	9.3×10^{-4}	6.8×10^{-4}	8.1×10^{-7}	2.2×10^{-7}	1.6×10^{-7}
Pb	In	8.0×10^{-5}	1.2×10^{-2}	6.8×10^{-3}	2.3×10^{-4}	3.2×10^{-6}	1.8×10^{-6}	6.0×10^{-8}
	Out	8.0×10^{-5}	8.5×10^{-3}	4.0×10^{-3}	9.5×10^{-5}	2.2×10^{-6}	1.0×10^{-6}	2.5×10^{-8}
Cd	In	1.8×10^{-3}	2.8×10^{-4}	9.5×10^{-5}	7.0×10^{-5}	5.0×10^{-7}	1.7×10^{-7}	1.2×10^{-7}
	Out	1.8×10^{-3}	1.9×10^{-4}	6.1×10^{-5}	4.6×10^{-5}	3.4×10^{-7}	1.1×10^{-7}	8.3×10^{-8}
Co	In	9.0×10^{-3}	8.1×10^{-3}	3.5×10^{-4}	1.4×10^{-4}	7.3×10^{-5}	3.2×10^{-6}	1.2×10^{-6}
	Out	9.0×10^{-3}	4.7×10^{-3}	9.0×10^{-5}	9.2×10^{-5}	4.3×10^{-5}	8.0×10^{-7}	8.3×10^{-7}
V	In	8.3×10^{-3}	8.3×10^{-4}	3.7×10^{-4}	3.3×10^{-4}	6.9×10^{-6}	3.1×10^{-6}	2.8×10^{-6}
	Out	8.3×10^{-3}	6.5×10^{-4}	2.9×10^{-4}	2.3×10^{-4}	5.4×10^{-6}	2.4×10^{-6}	1.9×10^{-6}

* In: Indoor; ** Out: Outdoor; IUR: inhalation unit risk; EC: exposure concentration; CR: carcinogenic risks. SLF: simulated lung fluid; ALF: artificial lysosomal fluid. The acceptable risk range is between 1×10^{-6} (1 in 1,000,000) and 1×10^{-4} (1 in 10,000) by U.S. EPA's risk management (Human Health Risk Assessment, https://www.epa.gov/risk/human-health-risk-assessment).

4. Conclusions

The present study reported that the concentrations of outdoor coarse particles were significantly higher than those of the indoor coarse particles while no significant differences were observed between the concentrations of outdoor fine particles outdoor and indoor fine particles. The bimodal distribution of the outdoor SSAs and a unimodal distribution of the indoor SSAs were found in both winter and spring. Moreover, indoor/outdoor concentration ratios of SSAs and inorganic elements revealed the penetration of the outdoor fine particles into indoor environment. On the other hand, the inhalation bioaccessibility of toxic elements in the <3.3 μm fractions of SSAs extracted by using ALF and SLF was found to be elemental dependence. The carcinogenic and accumulative non-carcinogenic risks to adults via inhalation exposure cannot be ignored in indoor based on the bioaccessible concentrations. It can be concluded that people in office room without typical indoor sources of particle-bound toxic elements will still be suffered from the health risks from toxic elements via inhalation exposure. The penetration of toxic elements associated with the fine particles from outdoor into indoor may be an important exposure route to indoor residents. Therefore, efficient ways to decrease the indoor airborne fine particles may reduce the potential risks posed by the toxic elements.

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Appendix A

Figure A1. Location of sampling site (red point).

Appendix B

Table A1. Average I/O ratios of elements in indoor and outdoor SSAs' fractions in winter and spring (n = 5).

Elements	Winter	Spring	Elements	Winter	Spring
Al	0.4	0.5	Sb	0.9	1.0
Ba	0.4	0.5	Sr	0.4	0.5
Ca	0.4	0.5	Ti	0.7	1.0
Cr	0.6	0.8	As	0.7	0.6
Fe	0.4	0.6	Cu	0.5	0.6
K	0.6	0.6	Zn	0.8	0.6
Mg	0.4	0.5	Pb	0.8	0.9
Mn	0.5	0.7	Cd	0.8	0.7
Mo	0.6	0.9	Co	0.9	1.0
Na	0.4	0.6	V	0.6	0.6
Ni	0.8	0.9			

Table A2. Recovery percentages (%) for trace elements following spiking (after 24 h) for in vitro bioaccessibility tests conducted with ALF and SLF (n = 8).

Elements	ALF	SLF	ALF	SLF
No sample			With sample	
As	99.0 ± 5.1	96.0 ± 4.7	97.3 ± 8.0	97.0 ± 3.6
Ni	105.4 ± 3.7	95.2 ± 4.9	97.2 ± 5.4	90.4 ± 5.5
Cu	94.7 ± 5.7	95.7 ± 6.6	93.2 ± 7.8	88.8 ± 4.0
Zn	98.6 ± 4.4	34.8 ± 4.8	96.9 ± 6.5	30.1 ± 2.2
Pb	100.7 ± 3.5	15.4 ± 0.9	98.1 ± 4.6	14.2 ± 0.7
Mn	97.3 ± 4.2	87.5 ± 4.2	92.1 ± 5.7	86.8 ± 2.6
Sr	97.4 ± 4.6	98.6 ± 2.8	94.9 ± 6.2	95.3 ± 2.5
Cd	94.9 ± 3.4	87.1 ± 4.4	89.2 ± 4.7	82.6 ± 2.4
Co	95.4 ± 3.7	97.9 ± 6.0	90.2 ± 4.4	90.3 ± 3.2
V	99.1 ± 4.7	93.2 ± 5.3	92.9 ± 6.4	90.3 ± 3.3

SLF: simulated lung fluid; ALF: artificial lysosomal fluid. The +/− values are standard deviation.

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