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Chemical characteristics and cytotoxic correlation analysis of $PM_{2.5}$ in Jinan

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Abstract
Atmospheric fine particulate matter ($PM_{2.5}$) can exert a significant impact on human health, especially on causing pulmonary diseases. Inorganic elements and organic compounds are primary toxic components in $PM_{2.5}$ that cause cell death and tissue injury. To study the concentration characteristics as well as cytotoxic effects of $PM_{2.5}$ and chemical components, $PM_{2.5}$ samples were collected in Jinan during 2016. Major inorganic elements and organic components were analyzed and the cell viability of human lung epithelial cells (A549) exposed to $PM_{2.5}$ was examined. The results showed that $PM_{2.5}$ concentrations were higher in Jinan than 90% of cities in China during 2016, and the concentrations of inorganic elements and polycyclic aromatic hydrocarbon (PAHs) in $PM_{2.5}$ were also higher than in other studies. Furthermore, the cytotoxic analysis indicated that cell viability decreased significantly in correspondence with the increase of $PM_{2.5}$ concentrations, which indicated that $PM_{2.5}$ pollution could induce adverse cell injury. The concentrations of most inorganic elements and organic components such as mercury, fluoranthene, anthracene, and dibenzo (a,h) anthracene were significantly negatively correlated with cell viability, indicating that these species were effective chemical toxic components and played a key role in adverse health effects induced by $PM_{2.5}$.

Keywords $PM_{2.5}$ · Inorganic elements · PAHs · Exposure · Cytotoxicity

Introduction

Air pollution caused by particulate matter and its impact on human health has received widespread attention over the decades. The impact of atmospheric particulates on organisms is closely related to their particle size. The particulate matter of aerodynamic diameter (ad) > 10 µm was resisted by nasal cavity structure and cannot enter into the respiratory tract, while inhalable particles (ad < 10 µm, PM_{10}) could be breathed into the respiratory tract, and fine particles (ad < 2.5 µm, $PM_{2.5}$) could be penetrated into the bronchial alveoli, which would cause more serious harm to the respiratory system (Oberdrster 2001; Donaldson et al. 2001; Nemmar et al. 2002). In addition, some studies have further demonstrated that $PM_{2.5}$ exposure can cause cell membrane damage, oxidative stress as well as inflammation and immune disorders, and increase the risk of lung and respiratory diseases, especially lung cancer (Anderson et al. 2011; Ghio et al. 2012; Alexeeff et al. 2021). The mortality rate of lung cancer increased by 15–27% when $PM_{2.5}$ concentration increased 10 µg/m^3 in the US (Dupre et al. 2019). Deaths caused by respiratory diseases increased by 4.71% and the mortality from lung cancer also increased by 9.53% when $PM_{2.5}$ increased 10 µg/m^3 in the Beijing-Tianjin-Hebei region of China (Xie et al. 2019).

The surface of $PM_{2.5}$ could adsorb soluble salts, toxic organic substances such as PAHs, and inorganic elements in the atmosphere due to large specific surface area (Obot et al. 2002; Zou et al. 2016). Some studies have reported

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that the cytotoxicity caused by $PM_{2.5}$ was related to the pollutants on particulate matter surface such as organic composition and inorganic elements (Kelly and Fussell 2012; Prahalad et al. 1999; Bai et al. 2018), which reminds us to pay attention to the adverse effects of the chemical components in $PM_{2.5}$ on human health. Inorganic elements (especially heavy metals) and PAHs in $PM_{2.5}$ can enter into the human body through food intake, skin contact as well as inhalation (Dockery et al. 1992) and exert a significant impact on cell and organ injury, resulting in adverse effects on human health because of their higher toxicity, carcinogenic, and mutagenic effects (Ravindra et al. 2008; Wang et al. 2011). Inorganic elements particularly heavy metal and metalloid elements in $PM_{2.5}$ such as As, Cr, Pb, Mn, Cu, and Ni could adversely affect human health and exert a key role in affecting cytotoxicity by triggering cell apoptosis induced by oxidative stress (Bai et al. 2018; Wang et al. 2013a, b; Choi et al. 2018). PAHs are distributed in the gas phase and particle phase according to different physical properties such as molecular weight and vapor pressure, but most of the highly toxic PAHs exist in the particle phase, accounting for more than 85% of all toxic PAHs (Lai et al. 2017; Pratt et al. 2018). The health risk assessment of PAHs demonstrated that PAHs particularly benzo (a) pyrene, benzo (a) anthracene, benzo (k) fluoranthene, and dibenzo (a,h) anthracene possessed potential health risks and carcinogenic risks to human beings (Chen et al. 2017; Wang et al. 2018; Zhu et al. 2014).

The annual average mass concentration of $PM_{2.5}$ was 52.39 μg/m^3 in China during 2016 (China Statistical Yearbook 2017), which was 5 times higher than the ambient particulate matter standard (10 μg/m^3) of the World Health Organization (WHO). According to a study on the global burden of death attributable to ambient air pollution, China accounted for the highest proportion (≥ 8.6%) of attributable deaths of the global totals (Cohen et al. 2017). $PM_{2.5}$ concentrations in China, especially in Northern China, were at a relatively higher level according to a study published by WHO (2018). Jinan is a typical industrial city located in Northern China with many industrial and coal-burning emissions, resulting in large amounts of particles being emitted into the ambient air. The annual average concentration of $PM_{2.5}$ of Jinan in 2016 was reported at 76 μg/m^3, which was higher than 90% of cities in China (China Statistical Yearbook 2017). More studies about Jinan particulate matter mostly focused on physical and chemical characteristics such as source analysis, concentration characteristics, and chemical composition, but lacked health risk assessment on components of $PM_{2.5}$ (Gu et al. 2014; Zhang et al. 2018, 2019a, b; Sui et al. 2019; Du et al. 2019a, b). Furthermore, there are relatively less in vitro experimental studies on the cytotoxicity of $PM_{2.5}$ collected in Jinan. Therefore, the purpose of this study was to analyze the concentration characteristics of chemical components in $PM_{2.5}$ and investigate the cytotoxicity with the human lung epithelial cell model.

Materials and methods

Sampling

$PM_{2.5}$ samples were collected at Shandong University campus (36°40′41″N, 117°03′50″E) of Jinan, which is located in the middle of Shandong Province in north China. A high-volume particle collector (HVP-4300AFEC) with a flow rate of 1 m^3/min was used for sampling and $PM_{2.5}$ was collected on 8 × 10-inch quartz filters (MUNKTELL, Sweden). $PM_{2.5}$ samples were collected daily from 08:00 in the morning to 07:50 of the next day from January 1 to December 31 in 2016 except for rainy and snowy days, and a total of 236 samples were collected. Meanwhile, un-sampled filters were stored as blank samples at − 20 °C. Before and after sampling, the filters were equilibrated under a constant temperature of 20 °C and relative humidity of 50% for 24 h and then weighed using the electronic balance with an accuracy of 0.1 mg (Mettler Toledo, AL204/01). After sampling, samples were stored in a refrigerator at − 20 °C for subsequent chemical analysis and toxicity testing.

Chemical analysis of inorganic elements in $PM_{2.5}$

For chemical composition analysis, inorganic elements in $PM_{2.5}$ were analyzed as described previously (Du et al. 2019b; Li et al. 2015). The sampling filters were cut into small pieces using ceramic scissors and digested with 10 mL of nitric acid-hydrochloric acid mixed solution (mixing ratio: 1:3) and heated refluxing for 2 h (100 °C). The prepared liquid was saved into the amber bottle for subsequent testing. The glassware used in the whole process was soaked with more than 20% nitric acid for 24 h, rinsed with ultrapure water, and dried before being used to remove trace elements on the surface. The inorganic elements were measured by inductively coupled plasma-mass spectrometry (ICP-MS, Agilent Technologies 7700, Santa Clara, CA 95,051, USA) according to US EPA200.8. Argon was used as carrier gas with a flow rate of 1.04 L/min. The internal standard method was used to eliminate interference and the internal standard substances were scandium (Sc), indium (In), germanium (Ge), and bismuth (Bi). The measured elements are as follows: lead (Pb), arsenic (As), chromium (Cr), manganese (Mn), zinc (Zn), cadmium (Cd), copper (Cu), magnesium (Mg), aluminum (Al), calcium (Ca), vanadium (V), iron (Fe), cobalt (Co), nickel (Ni), selenium (Se), antimony (Sb), molybdenum (Mo), and barium (Ba) were examined. For mercury (Hg) in $PM_{2.5}$, sampling filters were cut into pieces and put into amber high-borosilicate glass bottles, and soaked for 24 h with 5 mL BrCl, and then added 15 mL ultrapure water and shook well. The prepared solutions were stored in a refrigerator until tested. Prior to analysis, 0.1 mL of $NH_2OH{\cdot}HCl$ (30 g $NH_2OH{\cdot}HCl$ was dissolved in 100 mL ultrapure water) was added into the samples to reduce the halogens. Atomic fluorescence spectrometry (Beijing Titian, AFS-830) was applied to analyze the concentrations of mercury after the Hg^{II} was reduced to form Hg^0 by KBH_4. During sampling, storage and chemical analysis, the blank samples were analyzed using the same method to remove the background value.

Chemical analysis of PAHs in $PM_{2.5}$

The 16 priority PAHs confirmed by US EPA were quantified in this study. Naphthalene is difficult to identify in particulates accurately and not discussed in this study due to its low molecular weight and high volatility. The sampling filters were cut into small pieces and extracted with the solvent extractor (ASE 350, Dionex) using the mixed solvent of acetone: n-hexane (v: v = 1:1). The extraction condition was at 100 °C and 1500 psi for 5 min and then concentrated to 1 mL with the sample concentrator (Turbo Vap II, Biotage, Sweden). Then, PAHs were measured using a high-performance liquid chromatography (HPLC) with the chromatographic column SUPEL-COSIL™ LC-PAH (15 cm × 4.6 mm, 5 μm) at 35 °C. Acetonitrile (55%) and water (45%) were used as mobile phases for gradient elution with a flow rate of 1.0 mL/min. The emission wavelength of the fluorescence detector was a multi-wavelength programming program, and the wavelength range of the ultraviolet detector was 190–400 nm. In the analysis process, blank samples were processed using the same steps to remove the background value. The target compounds are as follows: acenaphthylene (ACY), acenaphthene (ACE), fluorene (FLU), phenanthrene (PHE), anthracene (ANT), fluoranthene (FLA), pyrene (PYR), benzo (a) anthracene (BaA), chrysene (CHR), benzo (b) fluoranthene (BbF), benzo (k) fluoranthene (BkF), benzo (a) pyrene (BaP), indeno (1,2,3-cd) pyrene (IcdP), dibenzo (a,h) anthracene (DahA), and benzo (ghi) perylene (BghiP).

Cytotoxicity assay

$PM_{2.5}$ suspension preparation

The suspensions of $PM_{2.5}$ were prepared for cytotoxic analysis. The particle layer was gently peeled off from each sampled filter and tried to make sure that all the particles were collected. Then, the particles were put into centrifuge tubes with 20 mL of saline (Baxter, 0.09%) and 20 μL of antibiotic (Gibco, 100×), and then sonicated for 2 h. Finally, the solution was stored in the refrigerator at − 20 °C for further experiments. The blank filters were treated by the same method for blank control to determine the influence of filter material on the experimental results.

Cell culture

Since $PM_{2.5}$ is mainly released on the lung surface and deposited on the alveoli, human lung epithelial cells are usually considered the main biological targets of particulate matter and are often used to study the cytotoxicity of $PM_{2.5}$ (Ulrich et al. 2002; Müller et al. 1998). A549 cells from ATCC #CCL-185, Manassas, VA, were cultured in RPMI Medium 1640 (500 mL, Gibco, USA) with 10% fetal bovine serum (FBS, 50 mL, Gibco, USA), 1% antibiotic (5 mL, Gibco, USA), and 1% L-glutamine (5 mL, Gibco, USA) at 37 °C with 5% CO_2. When the cells grew to 70–80% adherent in the culture flask, 1 mL of trypsin (Gibco, USA) was added for 3–5 min to digest cells; then, the cells were subcultured for subsequent experiments. Generally, the cells in the 3rd or 4th generation are used for cytotoxic analysis. All laboratory appliances were wiped with 75% alcohol in the whole process, and all cell culture procedures were carried out in ultra-clean workstations sterilized by ultraviolet light for more than 30 min.

Cell viability assay

In order to determine the cytotoxic effect of $PM_{2.5}$ exposure to A549, the cells were exposed to $PM_{2.5}$ and the cell viability was examined using the Cell Counting Kit (CCK)-8 kit (SIGMA, USA) (Akhtar et al. 2014; Yuan et al. 2019). When the cells were passed to 3rd or 4th generation, the cells were digested with trypsin to make uniform cell suspension, and then, the cell suspension was diluted into 5×10^4 cells/mL. For cytotoxicity assay, 100 μL of A549 cell suspensions (5×10^3 cells/well) were transferred to each well of 96-well plate, and the plates were cultured for 24 h in the incubator at 37 °C with 5% CO_2 until cells adhered to the wells. Then, the old medium was removed and dead cells with residual culture medium were washed with PBS (Gibco, USA). Fresh medium and $PM_{2.5}$ suspensions were added into the plates again for incubating 24 h in an incubator at 37 °C with 5% CO_2. Then, 10 μL of CCK-8 solution was added into each well of the plate, and the absorbance was measured at 450 nm using the microplate reader (Multiskan Ascent, Thermo Lab systems) after incubating for 4 h.

Results and discussion

Chemical characteristics of inorganic elements and organic components of $PM_{2.5}$

The $PM_{2.5}$ concentration variations of Jinan during 2016 are shown in Fig. 1. The annual average mass concentration of $PM_{2.5}$ in Jinan was 88.64 ± 56.46 μg/m^3 (11.11–323.96 μg/m^3), which was more than 8 times higher than the $PM_{2.5}$ annual average standard set by the WHO (10 μg/m^3). As shown in Fig. 1, only 14.84% of the samples meet the ambient $PM_{2.5}$ secondary standard (35 μg/m^3) of China, almost 50% of the concentrations exceed 75 μg/m^3, which was considered polluted weather according to the ambient air quality standards of China. According to the China Statistical Yearbook, the $PM_{2.5}$ concentration of Jinan has been among the top 15 cities in the country since 2013. Compared with other cities in China, the $PM_{2.5}$ level of Jinan is slightly lower compared with 96.13 μg/m^3 in the heavily polluted city—Xi'an (Niu et al. 2019), higher than those of 62 μg/m^3 in the open coastal city—Shanghai (Wang et al. 2013b), and 44 μg/m^3 in the coastal city—Fuzhou (Xu et al. 2012). Compared with several foreign cities, the $PM_{2.5}$ concentration in Jinan is much higher than in Houston, USA (10 μg/m^3) (2019a), New South Wales, Australia (5.67 μg/m^3) (Tadros et al. 2018), Veneto, Italy, Europe (33 μg/m^3) (Squizzato et al. 2012), and Yokohama, Japan, East Asia (21 μg/m^3) (Khan et al. 2010). These results indicate that Jinan suffered serious $PM_{2.5}$ air pollution during 2016. Jinan is an industrial city with many steel plants, cement plants, and thermal power plants that mainly depend on coal combustion (Lv et al. 2017), which causes a large amount of ambient particle pollution. Besides, Jinan is surrounded by mountains on three sides, and these special terrain conditions are not conducive to the diffusion and transport of pollutants, which may aggravate ambient air pollution in Jinan. This study also discovered that the concentration of $PM_{2.5}$ (122.23 ± 58.21 μg/m^3) in the heating period (January 1 ~ March 22, November 12 ~ December 31) was significantly higher than the $PM_{2.5}$ concentration (67.92 ± 43.82 μg/m^3) in the non-heating period (March 23 ~ November 11) as shown in Fig. 1, which is mainly related to large amounts of coal combustion happened during the heating period. The higher pollution level of $PM_{2.5}$ in Jinan reminds us that adverse effects on public health cannot be ignored.

The total concentration of inorganic elements in $PM_{2.5}$ was 6.08 ± 3.69 μg/m^3, as shown in Table S1, which accounted for 8.19% of $PM_{2.5}$, while the proportion of elements in $PM_{2.5}$ was usually from 0.3 to 5% (Liu et al. 2018; Qi et al. 2016; Tadros et al. 2018), which indicated that the content of inorganic elements in Jinan particles was relatively high. As shown in Fig. 2a, the predominant inorganic elements were some crustal elements including Ca, Fe, Al, and Mg, with the mean concentrations of 3.47 ± 2.22 μg/m^3, 1.19 ± 0.76 μg/m^3, 0.63 ± 0.50 μg/m^3, and 0.47 ± 0.31 μg/m^3, respectively, and the mass concentrations in $PM_{2.5}$ was respectively 47.47 ± 26.40 mg/g, 15.95 ± 8.28 mg/g, 7.97 ± 4.99 mg/g, and 6.21 ± 3.36 mg/g. The mass concentration of total inorganic elements in Jinan $PM_{2.5}$ was only 81.92 ± 42.52 mg/g, with a range of 6.78–264.51 mg/g. It is worth noting that the annual average concentration of Cr in this study was 5.43 ± 3.60 ng/m^3, exceeding China's Ambient Air Quality Standard by more than 215.2 times (0.025 ng/m^3, GB3095-2012). Liu et al. (2018) reported that the total concentration of 8 elements (Cr, Zn, Mn, Cd, Ni, As, Cu, and Pb) in a heavily polluted city—Taiyuan—was 8.30 mg/g; Qi et al. (2016) measured the content of 13 heavy

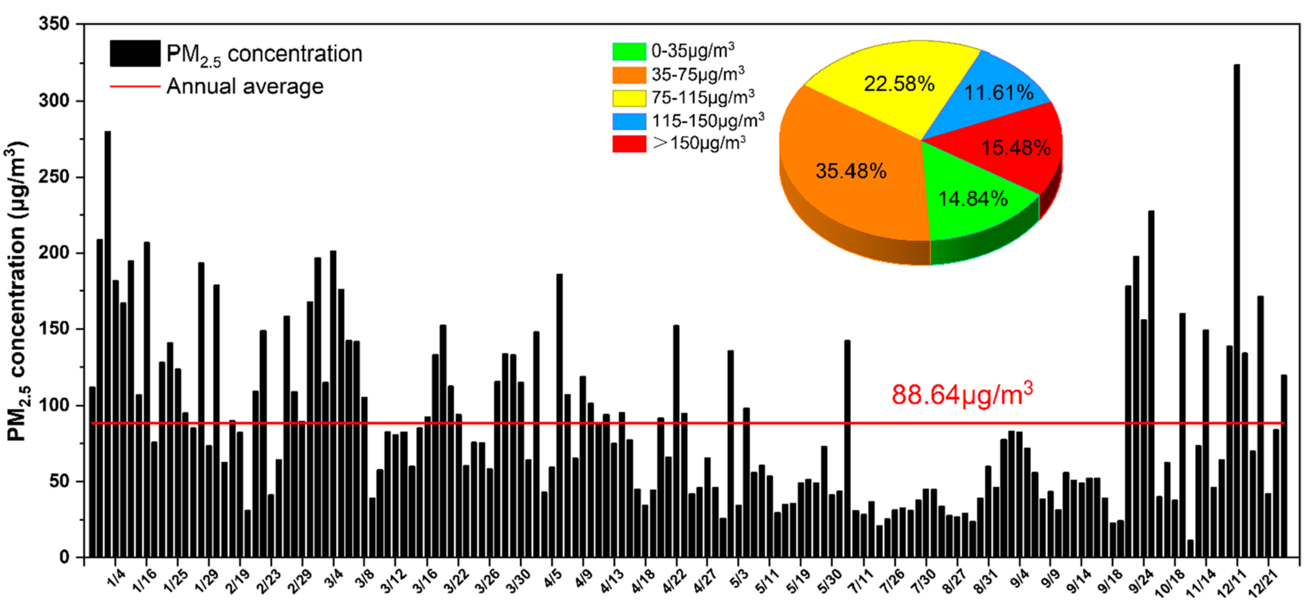

Fig. 1 Time series chart of Jinan $PM_{2.5}$ concentrations (bar graph) and percentage of different $PM_{2.5}$ concentrations intervals (pie chart) in 2016

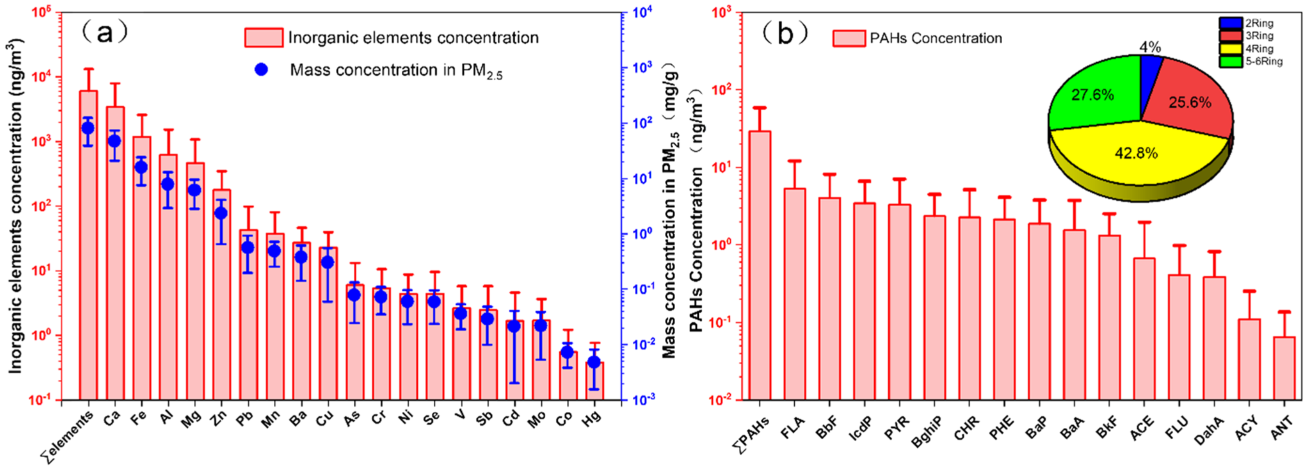

Fig. 2 **a** Volume and Mass concentration of inorganic elements and **b** concentration of each PAHs in $PM_{2.5}$ and percentage of 2 ~ 6-ring PAHs in the total concentration of PAHs (pie chart). The error bar indicates the standard deviation (SD, $n = 154$)

metals (Al, V, Cr, Mn, Co, Ni, Cu, Zn, As, Se, Cd, Ba, and Pb) in $PM_{2.5}$ from Nanjing and found that the heavy metals accounted for 4.74 mg/g; Tadros et al. (2018) found that 12 heavy metals (Al, Ca, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Se, and Pb) accounted for 1.7 mg/g of $PM_{2.5}$ by measuring the content of heavy metals in $PM_{2.5}$ sampled in Australia; Kim et al. (2019) measured $PM_{2.5}$ samples collected in Gwangju, South Korea, and found that 15 elements (Fe, Al, Ca, Mg, Zn, Pb, Mn, Cu, Ba, Cr, V, As, Cd, Mo, and Co) content was 1.65 ± 0.77 μg/m^3. Compared with these studies, the levels of inorganic elements in $PM_{2.5}$ of Jinan are apparently higher except that the content of heavy metals in Taiyuan. Inorganic elements have been proven to cause adverse toxicity and pose threat to human health due to their non-biodegradability and high bioaccumulation characteristics (Zhang et al. 2016a, b; Zhou et al. 2014). Yuan et al. (2019) also have concluded that the contribution of metal elements to particulate-related cytotoxicity is about 22.9% through the cell viability of A549 cells exposed to $PM_{2.5}$. Therefore, the contribution to the cytotoxicity of inorganic elements in $PM_{2.5}$ in Jinan cannot be underestimated.

As shown in Table S2, the total concentration of PAHs in $PM_{2.5}$ of Jinan was 29.42 ± 29.50 ng/m^3, ranging from 2.15 to 122.58 ng/m^3, which was obviously higher than 15.34 ± 8.87 ng/m^3 monitored in background station Tuoji Island (Wang et al. 2018), 7.97 ± 3.55 ng/m^3 measured in Nanjing of eastern China (Chen et al. 2019), 8.22–29.51 ng/m^3 analyzed in Gwangju, South Korea (Kim et al. 2019), and 2.04 ± 0.28 ng/m^3 analyzed in Kuala, Malaysia (Sulong et al. 2018). According to Fig. 2b, the highest concentration is FLA, with an average value of 5.46 ± 6.75 ng/m^3, and the range is 0.19–30.53 ng/m^3. Figure 2b shows the distribution of PAHs with different ring numbers in $PM_{2.5}$. Therein, the highest proportion is 4-ring PAHs with the concentration of 12.59 ± 13.76 ng/m^3, followed by 5–6-ring PAHs and 3-ring with 8.11 ± 7.08 ng/m^3 and 7.54 ± 8.68 ng/m^3, respectively. The lowest is 2-ring PAHs and the concentration is 1.27 ± 1.30 ng/m^3. PAHs with high molecular weight tend to adhere to the particle phase, while PAHs with low molecular weight have a relatively high content in the gas phase (Abdel-Shafy and Mansour 2016). The production of PAHs is mainly related to human activities, including incomplete combustion of fossil fuels and biofuels, while traffic and industrial emissions are also primary sources of PAHs in urban areas (Shen et al. 2013; Zhang et al. 2009). Industrial development and traffic emissions in Jinan may be the main reason for the high concentration of PAHs (Zhang et al. 2019a, b) . PAHs are potential human carcinogens and mutagens, and high toxic PAHs mainly exist on atmospheric fine particles; therefore, PAHs in $PM_{2.5}$ are considered important components that cause harm to the public because of high concentrations and toxicity (Lin et al. 2015; Gao et al. 2016; Zhu et al. 2014). Long-term or chronic inhalation of PAHs can cause health problems such as reduced immune function, respiratory disease, asthma, and abnormal lung function (Abdel-Shafy and Mansour 2016). China is one of the countries with the largest amount of PAHs emissions, and the level of PAHs on $PM_{2.5}$ in North China is higher than that in the east and south of China (Shen et al. 2013; Wang et al. 2018). In China, 1.6% of lung cancer incidence is caused by inhalation of PAHs (Zhang et al. 2009). Therefore, it is necessary to study the effect of PAHs on cytotoxicity.

The cytotoxic effect of $PM_{2.5}$

Given the higher $PM_{2.5}$ concentrations in Jinan, this study conducted cytotoxicity research to figure out the impact of

$PM_{2.5}$ on human health, especially on lung injuries. $PM_{2.5}$ samples collected in Jinan were used to expose to A549 cells for 24 h and cell viability was measured. The scatter plot of $PM_{2.5}$ and corresponding cell viability in Jinan during 2016 was analyzed to determine the relationship between $PM_{2.5}$ concentrations and cytotoxicity as shown in Fig. 3a. The cell viability of A549 cells showed a significant decreasing trend with the increasing $PM_{2.5}$ concentration ($R^2 = 0.96$). In addition, the cell viability was primarily distributed in 60–80%, with an average of 67.3%. An epidemiological study showed that the acute effects of $PM_{2.5}$ are highest in summer and winter (Roosli et al. 2000) and another study showed that the effect of $PM_{2.5}$ on cytotoxicity is more potent in summer in Nanjing (Zhang et al. 2019a). Seasonal differences in $PM_{2.5}$ concentrations and cytotoxicity were also observed in this study, the concentration of $PM_{2.5}$ in the winter heating period (122.23 ± 58.21 μg/m^3) was nearly twice higher than that in the non-heating period (67.92 ± 43.82 μg/m^3), which was caused by the massive combustion of coal during the heating period in Jinan. Different from the studies mentioned above, the cell viability in the winter heating period (63.34%) was significantly lower than that in the non-heating period (72.63%), which indicated that $PM_{2.5}$ in the heating period resulted in more serious cytotoxic effects. $PM_{2.5}$ has been reported to attenuate cell viability of pulmonary bronchial epithelial cells (Duan et al. 2020), especially produced by coal combustion which played a vital role in myocardial toxicity and causing seasonal health risks (Zhang et al. 2016b). Our results also showed that $PM_{2.5}$ could also cause non-negligible damage to the lung cells, and there will exert a more serious effect on the respiratory system due to a large amount of coal burning during the heating period.

The World Health Organization estimated that chronic obstructive pulmonary disease and acute lower respiratory tract infections caused 18% of outdoor air pollution-related premature deaths respectively, and 6% of deaths were due to lung cancer in 2016. In order to further discuss the effects on lung cytotoxicity with variations of $PM_{2.5}$ concentrations, the pollution levels were divided into four concentration groups (clear: 0–75 μg/m^3, light pollution: 75–115 μg/m^3, moderate pollution: 115–150 μg/m^3, and heavy pollution: 150–500 μg/m^3) according to the Chinese Environmental Standards. The analyzed results were presented in Fig. 3b, which showed that the cell viability significantly decreased compared to the control group after A549 cells were exposed to $PM_{2.5}$. Compared with the A549 cells exposed to $PM_{2.5}$ of the clear group, the cell viability after exposure to $PM_{2.5}$ of the light pollution, moderate pollution, and heavy pollution groups significantly decreased. The cell viability of A549 cells exposed to $PM_{2.5}$ of the heavy pollution group was significantly lower than cells exposed to the light pollution group. These gradients indicated that exposure to $PM_{2.5}$ can adversely affect cellular viability and exert more toxic in polluted conditions.

Cytotoxicity of inorganic elements in $PM_{2.5}$

EPA (Environmental Protection Agency) has proposed the toxic effects of heavy metals and listed Cr, Pb, Cd, and As as human carcinogens. Inorganic elements, particularly heavy metals, have been reported to be potentially toxic (Fang et al. 2010; Wei et al. 2010), especially Pb, As, Cr, Cd, and Mn have the highest carcinogenic risk under all the same exposure levels (Sui et al. 2020; Zhang et al. 2016a). This study explored the effect of inorganic elements in $PM_{2.5}$ of Jinan on cytotoxicity to figure out the effective toxic inorganic elements in $PM_{2.5}$. Spearman's correlation coefficients were calculated and determined based on the inorganic element concentrations and cell viability of A549 cells, which are plotted in Fig. 4. The results showed that Hg concentration

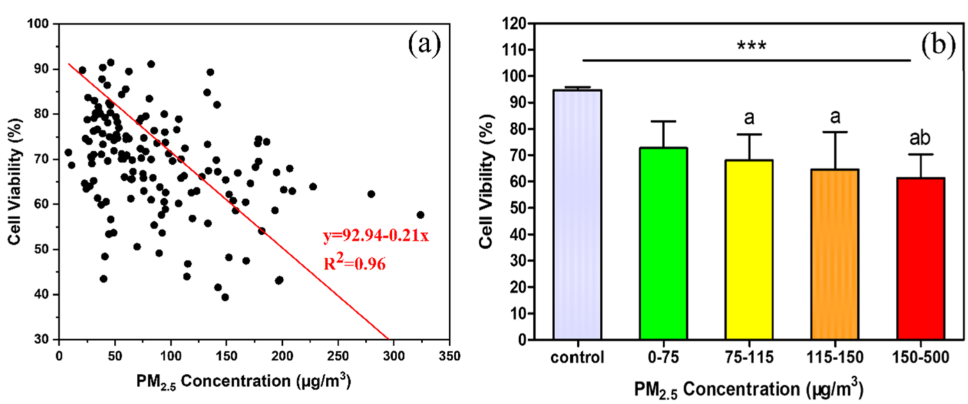

Fig. 3 **a** Relationship between $PM_{2.5}$ concentrations and A549 cell viability and **b** the effect of $PM_{2.5}$ concentrations on cytotoxicity; data were presented as mean ± SD (***$p < 0.001$ implied the significant difference between the treatment group and control group, **a** implied the significant difference between the other three treatment groups and 0–75 μg/m^3, **b** implied the significant difference between the 150–500 μg/m^3 group and 75–115 μg/m^3 group)

was significantly correlated with cell viability ($r = -0.41$, $p < 0.01$), and Pb, Mg, Al, Cr, Mn, Fe, Co, Mo, and Sb were moderately associated with cell viability ($-0.4 < r < -0.2$, $p < 0.01$), while V, Ni, As, Cd, and Ba levels were weakly correlated with cell viability ($-0.2 < r < -0.15$, $p < 0.05$). These results showed that most inorganic elements in $PM_{2.5}$ played an important role in cytotoxicity.

It is interesting that there not exist a significant correlation between cell viability and concentrations of As and Cd that were classified as the carcinogen by EPA, which may be related to low concentration of As (6.05 ± 4.89 ng/m^3) and Cd (1.69 ± 1.34 ng/m^3) in $PM_{2.5}$ of Jinan. Previous studies have also suggested that inorganic elements in $PM_{2.5}$ played important role in the toxic effects, including that Cu, Mn, and Co in $PM_{2.5}$ of Nanjing which played important roles in cytotoxicity (Chen et al. 2018); Cu, Mn, V, and Zn in particulate matter collected in Los Angeles have significant correlation with cytotoxicity (Wang et al. 2013a); Cr, Mn, Fe, Co, Ni, Cu, Zn, Ba, As, and Pb levels were correlated with cell viability in a study about traffic-related air pollution by Chen et al.(2020); toxicity induced by $PM_{2.5}$ was closely related to Mn, Cu, Pb, and Cd in $PM_{2.5}$ of Hangzhou (Zhou et al. 2022). Similar to these studies, this research concluded that toxic inorganic elements such as Hg, Cr, Pb, and Co in $PM_{2.5}$ of Jinan also played important role in the toxicity effect induced by $PM_{2.5}$.

Cytotoxicity of $PM_{2.5}$-bound PAHs

Organic compounds are the major compositions of $PM_{2.5}$ and accounted for 20–60% (Yang et al. 2011; Zhao et al. 2013). PAHs are leading organic toxic components in $PM_{2.5}$, which have adverse effects on human health because of mutagenic, teratogenic, and carcinogenic effects, and different kinds of PAHs have different effects on human health, mainly depending on the structure and inherent toxicity of different PAHs (Franco et al. 2008; Ravindra et al. 2008). PAHs can continuously transport and accumulate in the environment because they are high lipophilic and non-degradable (Yim et al. 2014; Kim et al. 2013). Exposure to PAHs can increase the risk of human disease; previous studies have shown that workers under long-term exposure to PAHs are susceptible to diseases such as lung cancer, skin cancer, and leukemia (Jarvis et al. 2014; Mahler et al. 2012).

This study analyzed the relationship between PAHs with the different number of rings as well as 15 PAHs and cytotoxicity in $PM_{2.5}$ of Jinan to figure out the effective toxic component among them. Spearman's correlation coefficients were calculated to determine whether the PAHs with different ring numbers and each PAHs species were related to the cell viability of A549 cells, which were plotted in Fig. 5. The results showed that cell viability was significantly correlated with PAHs, especially for 3-ring and 4-ring species ($r < -0.46$, $p < 0.01$). Similar results were observed in other studies, for instance, the study has indicated that PAHs of 4–6 ring have more potent effects on cytotoxicity in Gwangju, South Korea (Kim et al. 2013) and the research by Sun et al. (2018) in central China also showed that 3-ring and 4-ring PAHs species in $PM_{2.5}$ exert significant influence on cytotoxicity. As shown in Fig. 5, most PAHs species were significantly correlated with cytotoxicity, the concentrations FLU, ANT, FLA, PYR, BaA, CHR, BbF, BaP, DahA, and IcdP were highly correlated with cell viability ($r < -0.4$, $p < 0.01$), and the concentrations of PHE and BkF were

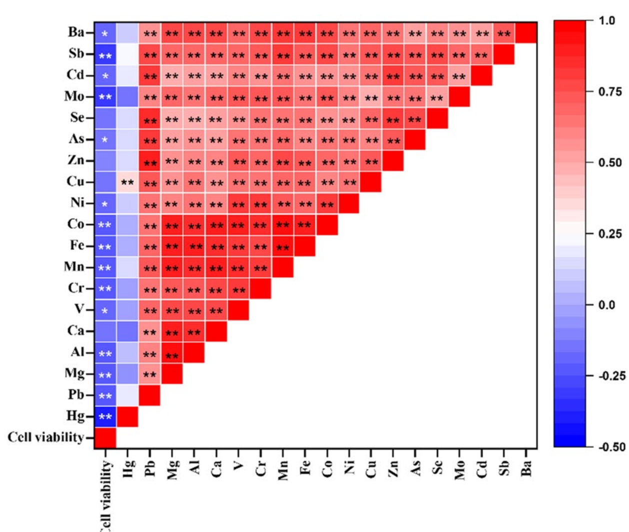

Fig. 4 Correlations of A549 cells viability to concentrations of elements (**$p < 0.01$, *$p < 0.05$ implied the significant difference)

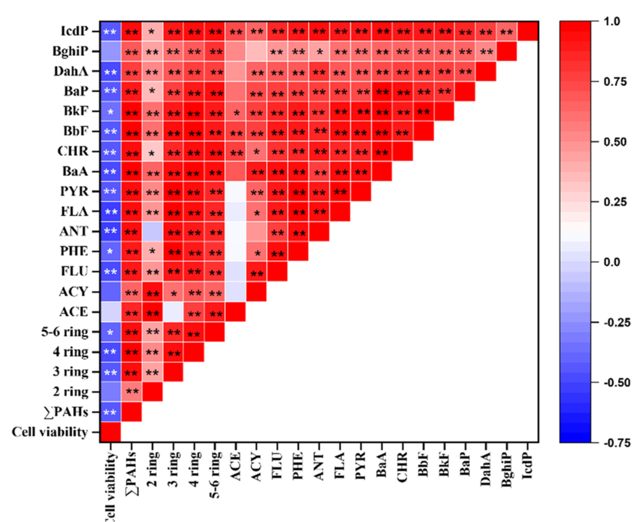

Fig. 5 Correlations between cell viability with different ring number and PAHs species (**$p < 0.01$, *$p < 0.05$ implied the significant difference)

moderately associated with cell viability ($-0.4 < r < -0.3$, $p < 0.05$). The study of Zhou et al. (2022) showed that lung injury induced by $PM_{2.5}$ was closely correlated with ACE, FLA, PYR, BaA, CHR, BbF, BaP, DahA, IcdP, PHE, and BkF in $PM_{2.5}$, and another study has shown that concentrations of ACY, FLU, ANT, PHE, FLT, PYR, CHR, BaP, IcdP, and BghiP in $PM_{2.5}$ were highly correlated with cell viability measured by CCK-8 kits (Song et al. 2020). This research results showed that PAHs especially FLU, ANT, FLA, PYR, BaA, CHR, BbF, BaP, DahA, and IcdP were effective toxic species in $PM_{2.5}$ of Jinan and played important roles in affecting cytotoxicity, which should be paid more attention.

Conclusion

A consecutively atmospheric $PM_{2.5}$ study was carried out during a whole period of 2016 in Jinan and the characteristics of chemical components (inorganic elements and PAHs) in $PM_{2.5}$ were comprehensively analyzed to discuss the effects of chemical components on cytotoxicity induced by $PM_{2.5}$. As a result, the average concentration of $PM_{2.5}$ was 88.64 μg/m^3 and the air pollution of Jinan in 2016 was very severe according to the levels of $PM_{2.5}$ stipulated by the WHO. The concentrations of 19 inorganic elements and 15 PAHs were both at a relatively higher level. The higher species were Ca, Fe, Al, and Mg among inorganic elements and FLA, BbF, and IcdP among PAHs. Cytotoxicity results showed that $PM_{2.5}$ had obvious effects on cell viability which decreased as $PM_{2.5}$ concentration increased. These results provided strong evidence to certify that $PM_{2.5}$ pollution has direct adverse health impacts in Jinan. Correlations between cytotoxicity and chemical compositions revealed that levels of most inorganic elements such as Hg, Pb, and Cr, and PAHs such as FLA, ANT, and DahA were significantly correlated with cell viability and played an important role in cytotoxicity. Collectively, $PM_{2.5}$ and its chemical components could induce cytotoxicity and might result in lung injury, which recommend to pay attention to health risks caused by $PM_{2.5}$.

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Data availability The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code availability Not applicable.

Declarations

Conflict of interest The authors declare no competing interests.

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