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REVIEW ARTICLE

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# The Classification, Related Hazards and Biomarkers of Particulate Matter

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## ABSTRACT

Particulate matter (PM), a mixture of solids, liquids and gaseous matters, is produced by natural environment or anthropogenic activities. Attribute to their small size and light weight, they could exist in human surroundings for a long time and migrate from long-distance. Particulate matter enters human body through respiratory tract, digestive tract, skin contact and other ways to cause damage to cells and organs, which is called particle disease. This review summarized the particles and their hazards that have attracted attention in recent years, the toxicity of cells and organs after entering human body, and we also concluded the potential markers indicating of cell and/or tissue toxicity. It should be useful for the research in prevention and treatment of the hazard of particulate matter on human health.

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## Introduction

Particulate matter (PM) is a mixture of solids, liquids and gaseous matters commonly contains inorganic components and organic components which is produced by natural sources and anthropogenic activities [1]. According to GBD 2015 Risk Factors Collaborators, 4.24 million people deaths in 2015 were attributed to ambient particulate matter, 2.85 million deaths due to household pollution from solid fuels, 0.25 million deaths due to ambient ozone pollution, 0.49 million deaths due to lead exposure, 0.49 million deaths due to various occupational exposures and 7.16 million deaths due to tobacco smoke [2]. So, it is urgent to recognize the composition of PM and its threat to human health.

While these particles are so common in daily life, human is exposed and ingest these particles through a variety of pathways, including respiration, digestion, direct skin contact, iatrogenic implantation, etc. These particles have a wide variety of physico-chemical components and sources. At present, the research is still using commercial products based on its main components or directly collected from the atmosphere. After entering the human body, particles will cause cell and tissue toxicity and endanger human health. However, particles used in medicine may have some positive effects on human health, such as targeted therapy and drug delivery. The adverse effects of PM on human health mostly are based on mass concentration, particle size and composition, which are important parameters for the prevention and treatment of diseases induced by [3].

On the one hand, PM could be classified into three categories based on their aerodynamic diameter: (I) coarse particulate matter ($PM_{10}$) with an aerodynamic diameter of less than 10 μm or (II) fine particulate matter ($PM_{2.5}$) with an aerodynamic diameter of less than 2.5 μm or (III) ultra-fine particle ($PM_{0.1}$) with a diameter of less than 0.1 μm [4]. "Lung airways and alveoli retain mostly $PM_{2.5}$ rather than $PM_{10}$ [5]." On the other hand, PM should also be classified into natural sources and anthropogenic activities. Natural source includes volcanoes, dust storms, forest fires, living vegetation, and sea spray. Anthropogenic sources are highly variable and include solid-fuel (coal, lignite, heavy oil, and biomass) combustion, industrial and agricultural activities, erosion of the pavement by road traffic, and abrasion of brakes and tires [4].

In this study, we summarized the update studies in particulate matter, including their size, the way to enter the human body, the potential hazard to the human body, the potential biomarkers for detection of particle toxicity and classified into two methods, one based on the diameter of the particle and another based on the source of the particle. All of these will offer an overview of the particulate matter and binging a glimmer of light for the prevention and treatment of particulate matter related disease.

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## Particles Classification According to Size

### $PM_{10}$

The United States Environmental Protection Agency (US-EPA) set up an outdoor air quality standards for $PM_{10}$ in 1987 at 150 μg $m^{-3}$ of 24-h of average concentration. The mainly source of $PM_{10}$ were biomass burning in mainland Southeast Asia and saltation of agricultural soils [6,7]. Among the chemical composition of $PM_{10}$, $SiO_2$, organic carbon, $SO_4^{2-}$, $NO_3^-$ were the major elements, and Cu, Ti, Mn, Ba were trace elements [8]. However, as Roberto Rojano pointed out in another study, the highest content of $PM_{10}$ were crustal elements (Ca, Na, K, Fe, Mg, As, and Co), and those with the lowest levels in $PM_{10}$ were anthropogenic tracers of traffic emissions (Cd, V, Cu, Mn, Ni, Pb, and Zn) [9]. The heavy metals in $PM_{10}$ were related to out of hospital cardiac arrest cases which was one of the most causes of death in developed countries [10]. Long term exposure to $PM_{10}$ was associated to lung cancer development risks modified antiviral factors production of peripheral blood mononuclear cells, and increased viral replication of SARS-CoV-2 [11,12]. Exposure to $PM_{10}$ increased blood triglycerides even at low levels [13]. Anti-inflammatory compound biochanin A could alleviate $PM_{10}$-induced acute pulmonary cell injury in vitro [14].

### $PM_{2.5}$

$PM_{2.5}$ is a major contributor to air pollution and causes various impacts on human organs. $PM_{2.5}$ also has complicated components including secondary ions ($NH_4^+$, $NO_3^-$, $SO_4^{2-}$), organic carbon (OC), elemental carbon (EC), crustal elements (Si, Ca, Al) and trace metals (Fe, Pb, Zn and Cu) and demonstrate, which have significant differences between urban and rural areas [15].

According to exist findings, in respiratory systems, exposure to ambient $PM_{2.5}$ decreased cell viability and elevated cell apoptosis of human bronchial epithelial cells and alveolar type II cells through NLRP3/caspase-1 and NOS2 pathways, inhibited alveolar type II to alveolar type I cell transition, interfered with lung epithelial cell division, induced inflammation and oxidative stress in human nasal epithelial cell, increased mucus production in chronic sinusitis, activated macrophages to mediate angiogenesis in lung cancer participating in lung cancer progression [16-22]. Osteopontin expression was increased in lung tissue, bronchoalveolar lavage fluid, and serum in $PM_{2.5}$ exposure condition and was a candidate for biomarker of $PM_{2.5}$ exposure [23]. In immune systems, $PM_{2.5}$ mediated macrophage autophagy by activating PI3K/AKT/mTOR signaling [24]. $PM_{2.5}$ induced macrophage release proinflammatory mediators by activation of the LPS/MyD88 pathway, but macrophages were more sensitive to LPS present in $PM_{2.5}$ [25]. In circulatory system, $PM_{2.5}$ caused cell death by increasing iron overload, lipid peroxidation, and REDOX imbalance in vascular endothelial cells [26]. Autophagy and apoptosis of endothelial cells were mediated through the endoplasmic reticulum stress system [27]. $PM_{2.5}$ induced proliferation of vascular smooth muscle cells, which was associated to pulmonary vascular lesions [23].

Digestive system: $PM_{2.5}$ interfered with amino acid metabolism, TCA cycle, urea cycle, and purine metabolism in the liver [28]. Nervous system: Exposed to $PM_{2.5}$ caused neurotoxicity including neurodevelopmental and neurodegenerative disorders, such as Alzheimer's disease risk, Parkinson's disease, autism spectrum disorders (ASD) and other forms of dementia. While Astaxanthin attenuated these $PM_{2.5}$ induced neurotoxicity in microglial cells [29-33]. Endocrine system: $PM_{2.5}$ exposure activated the hypothalamic-pituitary-adrenal and sympathetic-adrenal-medullary axes [34]. Prenatal exposure to $PM_{2.5}$ could also lead to behavioral deficits which exacerbated autism symptoms [32]. Exposure to $PM_{2.5}$ was also associated with and weight gain and can be inherited into the third generation [35,36].

### Ultrafine Particles (UFPs)

Ultrafine particles usually refer to particles with an aerodynamic diameter of less than 100 nm, which have significant cell and organ toxicity due to their large specific surface area, high permeability, and ability to produce reactive oxygen species [37]. In European Union, transportation, residential and commercial, industrial combustion, and agriculture composed the total UFPs emissions [38]. Inhaled UFPs could deposit throughout the respiratory tract. The peak deposition occurred at about 4 nm in the tracheobronchial region, whereas it occurred at about 20 nm in the pulmonary region [39]. Exposure to UFPs was associated to high risks to ASD [40]. A reduction in UFPs in exhaled breath condensate may be a marker of exacerbations of chronic obstructive pulmonary disease [41]. In western diet, more than $10^{12}$ UFPs are ingested daily by a single person [42]. Ingested UFPs passed through the gastrointestinal tract and increased intestinal inflammatory cells, decreased cholesterol metabolism in cecum [43].

## Particles Classification According to the Source

### Particles from Natural Source

Particles from natural source including volcanoes, dust storms, forest fires, living vegetation, minerals deposition and sea spray. Potentially toxic metals elements associated with nanoparticles (Ni, Zn, Ag, Cd, Tl, As, Pb, Bi, Te, Hg) may be contained in volcanic ash [45]. Ash from volcanoes hazarded to people over the world due to abundance of inhaled cristobalite, a crystalline silica polymorph and fine sulphate particles (≤ 0.3 μm). Volcanic ash induced the activation of NLRP3 inflammasome in human and murine macrophages, and elicited pro-inflammatory response in TT1 cells [46,47]. Long-term exposure to active degassing volcanic areas had an adverse impact on cardiorespiratory health in adults [48]. Dust storm particles reduced cell viability of human lung epithelial cells, and had a long-term impact on tracheitis hospital admissions [49,50]. The levels of pro-inflammatory cytokines (IL-1β, TNF-α, IL-6), profibrotic factors in serum fibrinogen and blood pressure were higher in dust storms than in normal conditions [51,52].

### Particles from Anthropogenic Source

### Traffic Related Air Pollution

Air pollution caused by vehicle exhaust has gradually become a worldwide respiratory health hazard. Diesel exhaust particles (DEPs) induced a novel and critical SiglecF$^{+}$ neutrophils in lung, which exacerbates airway inflammation [53]. DEPs modulated the immune response by affecting the interaction between lung epithelial cells and macrophages, which leading to changes in macrophage polarity [54]. DEPs exposure led to endothelial cell apoptosis by induction of endothelial cell autophagy, which contributed to cardiovascular disease, and manifested symptoms of anxiety and depression by inducing oxidative stress in the brain [55,56]. Traffic related air pollution was also associated with the increased morbidity of Parkinson's Disease [57]. Magnetite ($Fe_3O_4$) nanoparticles (MNPs) arose as combustion-derived Fe-rich particles from vehicle braking systems which contributed to the mainly of inhalable airborne magnetite particles [58].

### Biomass Burning

Biomass burning emissions are one of the contributors of outdoor air pollution, accounting for at least 10% of ambient particulate matter [59]. Particles emission from biomass burning were depended on the type of fuel and heating conditions, particles smaller than 0.43 μm were major contributors of PAHs [60]. Biomass burning increased the risk or hospital admission of respiratory and cardiovascular disease including asthma, upper respiratory infections, COPD, bronchitis, pneumonia, ischemic heart disease [61-63].

### Cooking

The size of particles from cooking emission covers the range of ultrafine (14.6-100 nm), accumulation mode (100-661.2 nm) and $PM_{2.5}$. In total amount, particles were mainly composed of ultrafine size range while in the kitchen and living room, which were mostly composed of accumulation mode [64]. Oxidatively damaged DNA and the levels of lipids and lipoproteins in blood were increased after exposure to cooking emissions [65].

### Industrial Emissions

Black carbon (BC), a carbon-containing mixture produced from incomplete combustion of biomass or fossil fuels, with diameter ranging from 20 to 150 nm, is a major component of $PM_{2.5}$. It adsorbs other pollutants in the atmosphere to form pollutant complexes, including heavy metals and organics, causing greater toxicity. Its remarkable cytotoxicity includes causing oxidative damage, cellular inflammation, DNA damage cell death, and causing lung damage in vivo [66]. Petroleum coke (PC), a black carbonaceous material, is a byproduct of the oil sands refining process. The open stacking of PC and uncontrolled release of dust have raised health concerns for residents in surrounding communities. 99% of PC was less than 7.2 μm. PC exposure inhibited the secretion of proteins involved in extracellular matrix organization and epithelial differentiation, and increased fibrosis-related marker collagen III [67]. Material 3D printing has been widely used in industry. High levels of crustal metals (e.g., Na, Mg, Al and Si) were detected from the collected particles, among these, Si had the highest concentrations and largest emission yielded for all of the studied filaments. Although the concentrations of heavy metals such as, Cd, Co, Cr, Mn, Cu, Pb, and Zn were relatively low, they also had adverse health effects and could be detected [68].

### Occupational

Most people are exposed to portable electronic devices every day in their daily life. Lithium-ion batteries are routinely used in these devices, and workers producing lithium-ion batteries are exposed to a large number of $LiCoO_2$ particles. $LiCoO_2$ particles are one of the most commonly used cathode materials for lithium-ion batteries. $LiCoO_2$ particles in lithium batteries can cause genotoxicity by affecting the ability of lung cells to form hydroxyl radicals, leading to primary mutations [69]. Co and Ni elements in $LiCoO_2$ particles can stabilize HIF-1α, which caused lung inflammation, to induce lung inflammation. It can also be used as a biomarker to predict lung inflammation [70].

Titanium dioxide ($TiO_2$) is widely used in products such as paints, coatings, plastics, paper, ink, pharmaceuticals, food, cosmetics and toothpaste. The concentrations of titanium compounds in drinking water are generally low. A regular diet can provide 300 to 400 μg $TiO_2$ per day [71]. The $TiO_2$ content in candies and chewing gum was highest in the range of less than 100 nm [72]. $TiO_2$ nanoparticles with a primary diameter of 21 nm could form polymers with two particle sizes of 110 nm and 1500 to 2000 nm in PBS solution and serum [73]. It affected glucose absorption [74]. An oral dose of 50 mg $TiO_2$ nanoparticles per kilogram caused marked hepatocyte steatosis and changes in hepatic metabolites, with quantitative disorganization of the gut microbiota [75]. The current limit for occupational $TiO_2$ particle exposure is 5 mg/m$^3$, while the non-occupational environmental exposure limit is 50 μg/m$^3$. Titanium dioxide nanoparticles are excreted primarily in the urine [76].

Respiratory diseases such as bronchitis, pulmonary fibrosis, and "hot metal smoke" is a common occupational disease of welders [77]. Welding smoke and dust with the aerodynamic diameter of 250 nm, under the concentration of 20 mg/m$^3$ inhaled, causing lung inflammation and reduced sperm production [78]. Among those metals collected from the welding processes, Iron (Fe) had the highest concentration across all range sizes [79]. Increased nasal mucosal lining fluid c-reactive protein is a potential markers for workers' occupational exposure [80].

Silver nanoparticles (Ag-NPs) are considered as potential materials for biomedical applications such as biosensing, antiviral, and anti-cancer. However, the presence of Ag-NPs in toothbrushes, textiles, food packaging, and medical products has raised concerns about health risks. The distribution of Ag-NPs in vivo is related to their particle size and dose [81]. Ag-NPs with the size of 20 nm, caused oxidative stress in hepatocytes by targeting and inhibiting glutathione S-transferase (GST) molecules at 10 μg/ml, but had no significant effect on the expression of GST [82]. Gold nanoparticles (Au-NPs) were divided into nanometer and micrometer sizes, with particle sizes of 40 ± 1 nm and 637 ± 9 nm, respectively. Inhalation caused cerebral edema through the ERK-AQP1 pathway [83].

The average size of nanoparticles of alumina (ANPs) was 160 nm, the human mesenchymal stem cells could be induced to mitochondria mediated cell death [84]. Nano-sized alumina particles are more likely to produce brain neurotoxicity through mitochondrial oxidative damage than microsized alumina particles [85]. Iron oxide nanoparticles (IONPs) are gradually being used in different biomedical fields due to their magnetic properties, including magnetic hyperthermia, targeted drug delivery, and magnetic resonance imaging contrast agents. A dose of 10 mg/kg IONPs produced hepatotoxicity with elevated blood urea nitrogen and direct bilirubin in BALB/c mice [86]. In non-cytotoxic concentration of iron oxide nanoparticles induced endothelial cell endothelial-to-mesenchymal transition [87]. Occupational exposure to nano-sized copper oxide nanoparticles (CuO NPs) could induce cell and organ damage in workers in copper mining and smelting industries. The average particle size of CuO NPs was 28.2 nm. The copper content in the atmosphere ranged from 5 to 20 ng/$m^3$, and the average concentration in natural water was 4 to 10 μg/L, most of which was bound to organic matter [88]. When copper intake exceeded tolerable limits, toxic effects that led to cell death, such as oxidative stress and apoptosis. Methylnicotinamide (MNA) could be used as a marker of apoptosis after exposure to CuO NPs [89]. Zinc oxide nanoparticles (ZnO NPs) are currently used in sunscreens, cosmetics, ceramics, paints, food packaging, solar cells and electronics. The particle size of ZnO NPs ranges from 50 to 70 nm. ZnO NPs in acidic solution would rapidly dissolve and release $Zn^{2+}$ to damage lysosomes, and the lysosomal contents would be released into the cytoplasm to damage organelles [90]. ZnO NPs produced genotoxicity through the generation of ROS with DNA damage and decreased sperm number and activity [91]. After tongue instillation, ZnO NPs were transferred to the central nervous system and mediated neurotoxicity through the activation of $Ca^{2+}$ -dependent NF-κB, ERK and p38 [92]. Nuclear factor-erythroid 2-related factor (Nrf2) alleviated ZnO NPs causing inflammation of the lungs [93].

Multi-walled carbon nanotubes (MWCNT) have been widely used in electronics, sports equipment, protective clothing, aerospace, optical fiber and molecular diagnosis, and other fields, which leading to its potential occupational exposure. Among them, Mitsui-7 MWCNT was defined as a 2B carcinogen by the International Agency for Research on Cancer. The average length of MWCNT is 3.86 μm and its average width is 49±13.4 nm. It is estimated that human alveolar epithelial absorbs 226 μg per square meter per month, causing lung inflammation, pulmonary fibrosis, and penetrate the pleura [94]. The genotoxicity and carcinogenicity of MWCNT include the induction of mitotic aberrations, centromeric disruption, chromosome translocation and chromosome insertion [95]. Porter, D.W. pointed out that after engulfed by macrophages, the MWCNT was discharged by lung lymphatic drainage [94]. The cytotoxicity and organotoxicity of Single-walled carbon nanotubes (SWCNT) were associated with its size. It should be divided into two categories according to the length, 0.40±0.29μm and 2.77±3.22 μm, respectively. Inhalation through bronchial instillation resulted in pulmonary toxicity including lung tissue weight increase and bronchial lavage fluid inflammation, while the shorter carbon nanotubes were more toxic [96]. SWCNT induced autophagy and apoptosis of lung epithelial cells, and activated macrophage P2X7R-mediated signaling promoting exocytosis of SWCNT-containing lysosomes [97,98]. In addition, the SWCNT caused breast tumor shrinkage, and hopefully as a drug carrier targeted therapy [99].

Potassium octatitanate fibers ($K_2O•8TiO_2$, POT) were used as a substitute for asbestos. The average length and width of POT fibers were 6.06 ±1.53 μm and 305 ± 69 nm, respectively. Intra-tracheal intra-pulmonary spraying had a carcinogenic effect to lungs and pleura [100]. Printer-emitted particles in printing houses, with particle sizes ranging from 2.5 to 210 nm, impaired cardiac conduction and hemodynamics [101]. Graphene oxide (GO) was used for cell imaging and drug delivery due to its unique properties. The particle size ranged from 90 nm to 5 mm. Exposure of RAW264.7 macrophages to GO increased the expression of lipoprotein lipase (LPL) and lysozyme 1 (LYZ1), and induced autophagy through the ROS-NRF2-P62 pathway [102]. However, Mukherjee, Kostarelos and Fadeel pointed out that although the GO particles were readily internalized by the primary human macrophages, they had noncytotoxic for primary human macrophages regardless of its lateral size [103].

Amorphous silica nanoparticles ($SiO_2$ NPs) were widely used in coating, adhesive, composite materials, cosmetics, food additives, drug delivery and diagnosis, etc. The researchers calculated the silicon dioxide intake of 124 mg per day according to the food containing $SiO_2$ NPs [104]. $SiO_2$ NPs at concentrations of 100 mg/kg and above increased blood glucose concentration and intracellular ROS levels, activated NF-κB and MAPK signaling pathways, and exhibited insulin resistance [105]. Pulmonary thrombosis, heart wall fibrosis, cerebral infarction and retinal damage were observed in BALB/c mice exposed to $SiO_2$ NPs with the size of 500 nm [106]. Blood biochemical indicators such as albumin, alkaline phosphatase and aspartate aminotransferase activities were significantly increased in mice treated with 10-15 nm $SiO_2$ NPs [107].

Crystalline silica (CS) promoted lung cancer progression and pulmonary aseptic inflammation through LTB4/BLT1 axis [108]. Serum neopterin, malondialdehyde and erythrocyte glutathione can be used as potential biomarkers of oxidative stress induced by inhalation of crystalline silica particles [109]. Silicon carbide (SiC) was a kind of hard brittle ceramic materials, used in refractory material and casting industry, electronic industry and diesel particulate filter, in addition to widely used as abrasive cutting and grinding industry. The SiC NPs showed good biocompatibility with human mesenchymal stem cells, neural stem cells derived from human dental pulp and mouse olfactory ensheath cells [110,111].

Plastic products are widely used in all aspects of daily life. There are two main sources of plastic particles:

(1) Manufactured goods containing plastic particles or powders, such as cosmetics, detergents, sunscreens and drug carriers.

(2) Decomposition of larger plastic sheets by ultraviolet radiation, mechanical wear, and biodegradation in the environment [112].

The massive discharge of microplastics products into the ocean had seriously polluted the marine environment. Microplastic particles could interact with mercury in water, causing neurotoxicity through inhibiting acetylcholinesterase (AChE) and increasing lipid oxidation (LPO) in brain and muscle, and interfered with lipid metabolism [113,114].

Perfluoro Alkyl Substances (PFASs), including persistent ionic perfluorocarboxylates and perfluorosulfonates, refered to a group of fluorinated carbon chain chemicals, known as the "super collection" of more than 90 related chemicals. Its size was less than 0.1 μm and was the ingredients of UFPs. These substances were used in consumer products and industrial applications due to their water, grease, and contamination resistance properties. They can combine with blood protein and accumulation in the liver and gallbladder [115].

## Particles for Medical Use

CoCr28Mo6 particles and alumina matrix composite (AMC) particles with a mean particle size of 500 nm were generated from the particle wear debris of the artificial implant prosthesis. It decreased the viability of fibroblasts and promoted the expression of pro-osteolytic marker MMP-1 in fibroblasts [116]. The blood compatibility and effects of hydroxyapatite on endothelial cells depends on the particle morphology [117]. Among them, the acicular particles have higher endothelial cell toxicity than rod-shaped particles. Beta tricalcium phosphate (β-TCP) were widely used in clinical coating material for bone substitutes and prosthesis. β-TCP played an immunomodulatory role in significantly reducing the antigen absorption of dendritic cells.

## Conclusion

In conclusion, human diseases caused by particulate matter had become a global problem that should not be ignored. Particles hazarded to human body, not only inducing interfering cell metabolism, including the induced cell oxidative damage and even cell death, but also causing, toxicity of tissues and organs including neural toxicity, genetic toxicity, toxicity of the respiratory system, cardiovascular system, digestive system and so on. The timely detection of particulate matter after exposure becomes a direction for the treatment or prevention of damage caused by particulate matter. In recent years, with the research of particulate matter toxicity, more and more tissue damage biomarkers have been found as the first gate to detect particulate matter exposure. We wish that these summarizations could provoke people realize the hazard produced by the particles and further help researchers for further study the prevention and treatment of particle related diseases.

## Author Contribution

Prof. Xiaomian Wu contributed to conceptualization, methodology, investigation, original draft writing, review, revision and writing – editing. Dr. Baoming, Zhang contributed to literature search, methodology, investigation, original draft writing, review, revision and writing – editing.

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## References

[1] Wang F, Liu J, Zeng H. Interactions of particulate matter and pulmonary surfactant: Implications for human health. ADV COLLOID INTERFAC. 2020; 284: 102244.

[2] Global. regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. LANCET. 2016; 388: 1659-1724.

[3] Valavanidis A, Fiotakis K, Vlachogianni T. Airborne particulate matter and human health: toxicological assessment and importance of size and composition of particles for oxidative damage and carcinogenic mechanisms. J Environ Sci Health C Environ Carcinog Ecotoxicol Rev. 2008; 26: 339-362.

[4] Kim K, Kabir E, Kabir S. A review on the human health impact of airborne particulate matter. Environ Int. 2015; 74: 136-143.

[5] Churg A, Brauer M. Ambient atmospheric particles in the airways of human lungs. Ultrastruct Pathol. 2000; 24: 353-361.

[6] Vongruang P, Pimonsree S. Biomass burning sources and their contributions to PM10 concentrations over countries in mainland Southeast Asia during a smog episode. Atmos Environ. 2020; 228: 117414.

[7] Tatarko J, Kucharski M, Li H, Li H. PM2.5 and PM10 emissions by breakage during saltation of agricultural soils. Soil Till Res. 2021; 208: 104902.

[8] Millan-Martinez M, Sanchez-Rodas D, Sanchez DLCA, Alastuey A, Querol X, et al. Source contribution and origin of PM10 and arsenic in a complex industrial region (Huelva, SW Spain). Environ Pollut. 2021; 274: 116268.

[9] Rojano R, Vengoechea AM, Arregocés HA. Indoor/outdoor relationship of particulate matter (PM10) and its chemical composition in a coastal region of Colombia. Case Studies in Chemical and Environmental Engineering. 2023; 8: 100397.

[10] Sielski J, Kazirod-Wolski K, Jozwiak MA, Jozwiak M. The influence of air pollution by PM2.5, PM10 and associated heavy metals on the parameters of out-of-hospital cardiac arrest. Sci Total Environ. 2021; 788: 147541.

[11] Lee HW, Kang S, Kim S, Cho Y, Hwang S. Long-term Exposure to PM10 Increases Lung Cancer Risks: A Cohort Analysis. Cancer Res Treat. 2022; 54: 1030-1037.

[12] Marín-Palma D, Tabares-Guevara JH, Zapata-Cardona MI, Zapata-Builes W, Taborda N, et al. PM10 promotes an inflammatory cytokine response that may impact SARS-CoV-2 replication in vitro. Front Immunol. 2023; 14: 1161135.

[13] Gaio V, Roquette R, Monteiro A, Ferreira J, Lopes D, et al. PM10 exposure interacts with abdominal obesity to increase blood triglycerides: a cross-sectional linkage study. Eur J Public Health. 2022; 32: 281-288.

[14] Li S, Wang J, Yu Y, Zheng B, Ma J, et al. Investigation on the mechanisms of biochanin A alleviate PM10-induced acute pulmonary cell injury. Ecotox Environ Safe. 2021; 228: 112953.

[15] Kundu S, Stone EA. Composition and sources of fine particulate matter across urban and rural sites in the Midwestern United States. Environmental science--processes & impacts. 2014; 16: 1360-1370.

[16] Jia H, Liu Y, Guo D, He W, Zhao L, et al. PM2.5-induced pulmonary inflammation via activating of the NLRP3/caspase-1 signaling pathway. Environ Toxicol. 2021; 36: 298-307.

[17] Zhu XM, Wang Q, Xing WW, Long MH, Fu WL, et al. PM2.5 induces autophagy-mediated cell death via NOS2 signaling in human bronchial epithelium cells. Int J Biol Sci. 2018; 14: 557-564.

[18] Yu H, Lin Y, Zhong Y, Guo X, Lin Y, et al. Impaired AT2 to AT1 cell transition in PM2.5-induced mouse model of chronic obstructive pulmonary disease. Respir Res. 2022; 23: 70.

[19] Longhin E, Holme JA, Gutzkow KB, Arlt VM, Kucab JE, et al. Cell cycle alterations induced by urban PM2.5 in bronchial epithelial cells: characterization of the process and possible mechanisms involved. Part Fibre Toxicol. 2013; 10: 63.

[20] Hong Z, Guo Z, Zhang R, Xu J, Dong W, et al. Airborne Fine Particulate Matter Induces Oxidative Stress and Inflammation in Human Nasal Epithelial Cells. Tohoku J Exp Med. 2016; 239: 117-125.

[21] Renwu Zhao, Zhiqiang Guo, Weiyang Dong, Congrui Deng, Zhijin Han, et al. Effects of PM2.5 on mucus secretion and tissue remodeling in a rabbit model of chronic rhinosinusitis. Int Forum Allergy Rhinol. 2018; 8: 1349-1355.

[22] Li R, Yang L, Jiang N, Wang F, Zhang P, et al. Activated macrophages are crucial during acute PM2.5 exposure-induced angiogenesis in lung cancer. Oncol Lett. 2020; 19: 725-734.

[23] Ho C, Wu W, Chen Y, Liou S, Yet S, et al. Identification of osteopontin as a biomarker of human exposure to fine particulate matter. Environ Pollut. 2019; 245: 975-985.

[24] Pei C, Wang F, Huang D, Shi S, Wang X, et al. Astragaloside IV Protects from PM2.5-Induced Lung Injury by Regulating Autophagy via Inhibition of PI3K/Akt/mTOR Signaling in vivo and in vitro. J Inflamm Res. 2021; 14: 4707-4721.

[25] He M, Ichinose T, Yoshida S, Ito T, He C, et al. PM2.5-induced lung inflammation in mice: Differences of inflammatory response in macrophages and type II alveolar cells. J Appl Toxicol. 2017; 37: 1203-1218.

[26] Wang Y, Tang M. PM2.5 induces ferroptosis in human endothelial cells through iron overload and redox imbalance. Environ Pollut. 2019; 1: 2541-12937.

[27] Wang Y, Tang M. PM2.5 induces autophagy and apoptosis through endoplasmic reticulum stress in human endothelial cells. Sci Total Environ. 2020; 710: 136397.

[28] Shi C, Han X, Mao X, Fan C, Jin M. Metabolic profiling of liver tissues in mice after instillation of fine particulate matter. Sci Total Environ. 2019; 696: 133974.

[29] Younan D, Petkus AJ, Widaman KF, Wang X, Casanova R, et al. Particulate matter and episodic memory decline mediated by early neuroanatomic biomarkers of Alzheimer's disease. Brain. 2020; 143: 289-302.

[30] Thiankhaw K, Chattipakorn N, Chattipakorn SC. PM2.5 exposure in association with AD-related neuropathology and cognitive outcomes. Environ Pollut. 2022; 292: 118320.

[31] Wang Y, Li C, Zhang X, Kang X, Li Y, et al. Exposure to PM2.5 aggravates Parkinson's disease via inhibition of autophagy and mitophagy pathway. Toxicology. 2021; 456: 152770.

[32] Emam B, Shahsavani A, Khodagholi F, Zarandi SM, Hopke PK, et al. Effects of PM2.5 and gases exposure during prenatal and early-life on autism-like phenotypes in male rat offspring. Part Fibre Toxicol. 2020; 17: 18.

[33] Kim RE, Shin CY, Han SH, Kwon KJ. Astaxanthin Suppresses PM2.5-Induced Neuroinflammation by Regulating Akt Phosphorylation in BV-2 Microglial Cells. Int J Mol Sci. 2020; 21: 7227.

[34] Li H, Cai J, Chen R, Zhao Z, Ying Z, et al. Particulate Matter Exposure and Stress Hormone Levels: A Randomized, Double-Blind, Crossover Trial of Air Purification. Circulation. 2017; 136: 618-627.

[35] Wei Y, Zhang JJ, Li Z, Gow A, Chung KF, et al. Chronic exposure to air pollution particles increases the risk of obesity and metabolic syndrome: findings from a natural experiment in Beijing. Faseb J. 2016; 30: 2115-2122.

[36] Xu Y, Wang W, Chen M, Zhou J, Huang X, et al. Developmental programming of obesity by maternal exposure to

concentrated ambient PM2.5 is maternally transmitted into the third generation in a mouse model. Part Fibre Toxicol. 2019; 16: 27.

[37] Li N, Georas S, Alexis N, Fritz P, Xia T, et al. A work group report on ultrafine particles (American Academy of Allergy, Asthma & Immunology): Why ambient ultrafine and engineered nanoparticles should receive special attention for possible adverse health outcomes in human subjects. J Allergy Clin Immunol. 2016; 138: 386-396.

[38] Kwon H, Ryu MH, Carlsten C. Ultrafine particles: unique physicochemical properties relevant to health and disease. Experimental & molecular medicine. 2020; 52: 318-328.

[39] Nazaroff WW. Ten questions concerning indoor ultrafine particles. Build Environ. 2023; 243: 110641.

[40] Allen JL, Oberdorster G, Morris-Schaffer K, Wong C, Klocke C, et al. Developmental neurotoxicity of inhaled ambient ultrafine particle air pollution: Parallels with neuropathological and behavioral features of autism and other neurodevelopmental disorders. Neurotoxicology. 2017; 59: 140-154.

[41] Fireman KE, Adir Y, Krencel A, Peri R, Vasserman B, et al. Ultrafine particles in airways: a novel marker of COPD exacerbation risk and inflammatory status. Int J Chron Obstruct Pulmon Dis. 2019; 20: 557-564.

[42] Powell JJ, Harvey RSJ, Ashwood P, Wolstencroft R, Gershwin ME, et al. Immune Potentiation of Ultrafine Dietary Particles in Normal Subjects and Patients with Inflammatory Bowel Disease. J Autoimmun. 2000; 14: 99-105.

[43] Li R, Yang J, Saffari A, Jacobs J, Baek KI, et al. Ambient Ultrafine Particle Ingestion Alters Gut Microbiota in Association with Increased Atherogenic Lipid Metabolites. Sci Rep. 2017; 7: 42906.

[44] Ermolin MS, Ivaneev AI, Fedyunina NN, Fedotov PS. Nanospeciation of metals and metalloids in volcanic ash using single particle inductively coupled plasma mass spectrometry. Chemosphere. 2021; 281: 130950.

[45] Damby DE, Horwell CJ, Baxter PJ, Kueppers U, Schnurr M, et al. Volcanic Ash Activates the NLRP3 Inflammasome in Murine and Human Macrophages. Front Immunol. 2018; 8: 2000.

[46] Horwell CJ, Baxter PJ, Hillman SE, Calkins JA, Damby DE, et al. Physicochemical and toxicological profiling of ash from the 2010 and 2011 eruptions of Eyjafjallajökull and Grímsvötn volcanoes, Iceland using a rapid respiratory hazard assessment protocol. Environ Res. 2013; 127: 63-73.

[47] Longo BM, Rossignol A, Green JB. Cardiorespiratory health effects associated with sulphurous volcanic air pollution. Public Health. 2008; 122: 809-820.

[48] Ardon-Dryer K, Mock C, Reyes J, Lahav G. The effect of dust storm particles on single human lung cancer cells. Environ Res. 2020; 181: 108891.

[49] Chen CS, Chan YS, Liu TC. Tracheitis hospital admissions are associated with Asia dust storm. Int J Environ Health Res. 2022; 32: 1337-1343.

[50] Badeenezhad A, Parseh I, Veisi A, Rostami S, Ghelichi-Ghojogh M, et al. Short-term exposure to some heavy metals carried with PM10 and cardiovascular system biomarkers during dust storm. Sci Rep-Uk. 2023; 13: 6146.

[51] Cao XJ, Lei FF, Liu H, Luo WY, Xiao XH, et al. Effects of Dust Storm Fine Particle-Inhalation on the Respiratory, Cardiovascular, Endocrine, Hematological, and Digestive Systems of Rats. Chin Med J (Engl). 2018; 131: 2482-2485.

[52] Shin JW, Kim J, Ham S, Choi SM, Lee C, et al. A unique population of neutrophils generated by air pollutant–induced lung damage exacerbates airway inflammation. J Allergy Clin Immun. 2022; 149: 1253-1269.

[53] Ji J, Upadhyay S, Xiong X, Malmlöf M, Sandström T, et al. Multi-cellular human bronchial models exposed to diesel exhaust particles: assessment of inflammation, oxidative stress and macrophage polarization. Part Fibre Toxicol. 2018; 15: 19.

[54] Wang J, Tseng C, Chao M. Diesel Exhaust Particles Contribute to Endothelia Apoptosis via Autophagy Pathway. Toxicol Sci. 2017; 156: 72.

[55] Ehsanifar M, Tameh AA, Farzadkia M, Kalantari RR, Zavareh MS, et al. Exposure to nanoscale diesel exhaust particles: Oxidative stress, neuroinflammation, anxiety and depression on adult male mice. Ecotox Environ Safe. 2019; 168: 338-347.

[56] Ritz B, Lee PC, Hansen J, Lassen CF, Ketzel M, et al. Traffic-Related Air Pollution and Parkinson's Disease in Denmark: A Case-Control Study. Environ Health Perspect. 2016; 124: 351-356.

[57] Ingo GM, Riccucci C, Pisani G, Pascucci M, D'Ercole D, et al. The vehicle braking systems as main source of inhalable airborne magnetite particles in trafficked areas. Environ Int. 2022; 158: 106991.

[58] Corsini E, Marinovich M, Vecchi R. Ultrafine Particles from Residential Biomass Combustion: A Review on Experimental Data and Toxicological Response. Int J Mol Sci. 2019; 20: 4992.

[59] Hata M, Chomanee J, Thongyen T, Bao L, Tekasakul S, et al. Characteristics of nanoparticles emitted from burning of biomass fuels. J Environ Sci (China). 2014; 26: 1913-1920.

[60] Kamal R, Srivastava AK, Kesavachandran CN, Bihari V, Singh A. Chronic obstructive pulmonary disease (COPD) in women due to indoor biomass burning: a meta-analysis.

Int J Environ Heal R. 2022; 32: 1403-1417.

[61] Karanasiou A, Alastuey A, Amato F, Renzi M, Stafoggia M, et al. Short-term health effects from outdoor exposure to biomass burning emissions: A review. Sci Total Environ. 2021; 781: 146739.

[62] Mueller W, Loh M, Vardoulakis S, Johnston HJ, Steinle S, et al. Ambient particulate matter and biomass burning: an ecological time series study of respiratory and cardiovascular hospital visits in northern Thailand. Environ Health. 2020; 19: 77.

[63] Wan M, Wu C, Sze To G, Chan T, Chao CYH. Ultrafine particles, and PM2.5 generated from cooking in homes. Atmos Environ. 2011; 45: 6141-6148.

[64] Laursen KR, Christensen NV, Mulder FA, Schullehner J, Hoffmann HJ, et al. Airway and systemic biomarkers of health effects after short-term exposure to indoor ultrafine particles from cooking and candles - A randomized controlled double-blind crossover study among mild asthmatic subjects. Part Fibre Toxicol. 2023; 20: 26.

[65] Jiang S, Shang M, Mu K, Jiang N, Wen H, et al. In vitro and in vivo toxic effects and inflammatory responses induced by carboxylated black carbon-lead complex exposure. Ecotox Environ Safe. 2018; 165: 484-494.

[66] Caruso JA, Stemmer PM. Petroleum coke exposure leads to altered secretome profiles in human lung models. Hum Exp Toxicol. 2018; 37: 1215-1232.

[67] Zhang Q, Weber RJ, Luxton TP, Peloquin DM, Baumann EJ, et al. Metal compositions of particle emissions from material extrusion 3D printing: Emission sources and indoor exposure modeling. The Science of the total environment. 2023; 860: 160512.

[68] Sironval V, Scagliarini V, Murugadoss S, Tomatis M, Yakoub Y, et al. LiCoO2 particles used in Li-ion batteries induce primary mutagenicity in lung cells via their capacity to generate hydroxyl radicals. Part Fibre Toxicol. 2020; 17: 1-9.

[69] Sironval V, Palmai-Pallag M, Vanbever R, Huaux F, Mejia J, et al. HIF-1α is a key mediator of the lung inflammatory potential of lithium-ion battery particles. Part Fibre Toxicol. 2019; 16: 35.

[70] Shi H, Magaye R, Castranova V, Zhao J. Titanium dioxide nanoparticles: a review of current toxicological data. Part Fibre Toxicol. 2013; 10: 15.

[71] Weir A, Westerhoff P, Fabricius L, Hristovski K, von Goetz N. Titanium dioxide nanoparticles in food and personal care products. Environ Sci Technol. 2012; 46: 2242-2250.

[72] Ekstrand-Hammarström B, Hong J, Davoodpour P, Sandholm K, Ekdahl KN, et al. TiO2 nanoparticles tested in a novel screening whole human blood model of toxicity trigger adverse activation of the kallikrein system at low concentrations. Biomaterials. 2015; 51: 58-68.

[73] Chen Z, Wang Y, Wang X, Zhuo L, Chen S, et al. Effect of titanium dioxide nanoparticles on glucose homeostasis after oral administration. 2018; 38: 810-823.

[74] Chen Z, Zhou D, Han S, Zhou S, Jia G. Hepatotoxicity and the role of the gut-liver axis in rats after oral administration of titanium dioxide nanoparticles. Part Fibre Toxicol. 2019; 16: 48.

[75] Kreyling WG, Holzwarth U, Schleh C, Hirn S, Wenk A, et al. Quantitative biokinetics over a 28 day period of freshly generated, pristine, 20 nm titanium dioxide nanoparticle aerosols in healthy adult rats after a single two-hour inhalation exposure. Part Fibre Toxicol. 2019; 16: 29.

[76] Greenberg MI, Vearrier D. Metal fume fever and polymer fume fever. Clinical toxicology (Philadelphia, Pa.). 2015; 53: 195-203.

[77] Skovmand A, Erdely A, Antonini JM, Nurkiewicz TR, Shoeb M, et al. Inhalation of welding fumes reduced sperm counts and high fat diet reduced testosterone levels; differential effects in Sprague Dawley and Brown Norway rats. Part Fibre Toxicol. 2020; 17: 2.

[78] Chang C, Demokritou P, Shafer M, Christiani D. Physicochemical and toxicological characteristics of welding fume derived particles generated from real time welding processes. Environmental science--processes & impacts. 2013; 15: 214-224.

[79] Baumann R, Brand P, Chaker A, Markert A, Rack I, et al. Human nasal mucosal C-reactive protein responses after inhalation of ultrafine welding fume particles: positive correlation to systemic C-reactive protein responses. Nanotoxicology. 2018; 12: 1130-1147.

[80] Park E, Bae E, Yi J, Kim Y, Choi K, et al. Repeated-dose toxicity and inflammatory responses in mice by oral administration of silver nanoparticles. Environ Toxicol Phar. 2010; 30: 162-168.

[81] Xu M, Yang Q, Xu L, Rao Z, Cao D, et al. Protein target identification and toxicological mechanism investigation of silver nanoparticles-induced hepatotoxicity by integrating proteomic and metallomic strategies. Part Fibre Toxicol. 2019; 16: 1-46.

[82] Chen CY, Liao PL, Tsai CH, Chan YJ, Cheng YW, et al. Inhaled gold nanoparticles cause cerebral edema and upregulate endothelial aquaporin 1 expression, involving caveolin 1 dependent repression of extracellular regulated protein kinase activity. Part Fibre Toxicol. 2019; 16: 37.

[83] Alshatwi AA, Vaiyapuri Subbarayan P, Ramesh E, Al-Hazzani AA, Alsaif MA, et al. Al2O3 Nanoparticles Induce Mitochondria-Mediated Cell Death and Upregulate the

Expression of Signaling Genes in Human Mesenchymal Stem Cells. J Biochem Mol Toxic. 2012; 26: 469-476.

[84] Mirshafa A, Nazari M, Jahani D, Shaki F. Size-Dependent Neurotoxicity of Aluminum Oxide Particles: a Comparison Between Nano- and Micrometer Size on the Basis of Mitochondrial Oxidative Damage. Biol Trace Elem Res. 2018; 183: 261-269.

[85] Salimi M, Sarkar S, Fathi S, Alizadeh AM, Saber R, et al. Biodistribution, pharmacokinetics, and toxicity of dendrimer-coated iron oxide nanoparticles in BALB/c mice. Int J Nanomed. 2018; 13: 1483-1493.

[86] Wen T, Du L, Chen B, Yan D, Yang A, et al. Iron oxide nanoparticles induce reversible endothelial-to-mesenchymal transition in vascular endothelial cells at acutely non-cytotoxic concentrations. Part Fibre Toxicol. 2019; 16: 30.

[87] Gaetke LM, Chow-Johnson HS, Chow CK. Copper: toxicological relevance and mechanisms. Arch Toxicol. 2016; 88: 1929-1938.

[88] Boyles MSP, Ranninger C, Reischl R, Rurik M, Tessadri R, et al. Copper oxide nanoparticle toxicity profiling using untargeted metabolomics. Part Fibre Toxicol. 2016; 13: 49.

[89] Cho W, Duffin R, Howie SEM, Scotton CJ, Wallace WAH, et al. Progressive severe lung injury by zinc oxide nanoparticles; the role of Zn2+ dissolution inside lysosomes. Part Fibre Toxicol. 2011; 8: 27.

[90] Srivastav AK, Kumar A, Prakash J, Singh D, Jagdale P, et al. Genotoxicity evaluation of zinc oxide nanoparticles in Swiss mice after oral administration using chromosomal aberration, micronuclei, semen analysis, and RAPD profile. Toxicol Ind Health. 2017; 33: 821-834.

[91] Liang H, Chen A, Lai X, Liu J, Wu J, et al. Neuroinflammation is induced by tongue-instilled ZnO nanoparticles via the Ca(2+)-dependent NF-kappaB and MAPK pathways. Part Fibre Toxicol. 2018; 15: 39.

[92] Sehsah R, Wu W, Ichihara S, Hashimoto N, Hasegawa Y, et al. Role of Nrf2 in inflammatory response in lung of mice exposed to zinc oxide nanoparticles. Part Fibre Toxicol. 2019; 16: 47.

[93] Porter DW, Hubbs AF, Mercer RR, Wu N, Wolfarth MG, et al. Mouse pulmonary dose- and time course-responses induced by exposure to multi-walled carbon nanotubes. Toxicology. 2010; 269: 136-147.

[94] Siegrist KJ, Reynolds SH, Porter DW, Mercer RR, Bauer AK, et al. Mitsui-7, heat-treated, and nitrogen-doped multi-walled carbon nanotubes elicit genotoxicity in human lung epithelial cells. Part Fibre Toxicol. 2019; 16: 36.

[95] Ema M, Takehara H, Naya M, Kataura H, Fujita K, et al. Length effects of single-walled carbon nanotubes on pulmonary toxicity after intratracheal instillation in rats. J Toxicol Sci. 2017; 42: 367-78.

[96] Ghosh M, Murugadoss S, Janssen L, Cokic S, Mathyssen C, et al. Distinct autophagy-apoptosis related pathways activated by Multi-walled (NM 400) and Single-walled carbon nanotubes (NIST-SRM2483) in human bronchial epithelial (16HBE14o-) cells. J Hazard Mater. 2020; 387: 121691.

[97] Cui X, Wan B, Yang Y, Ren X, Guo LH, et al. Crucial Role of P2X (7) Receptor in Regulating Exocytosis of Single-Walled Carbon Nanotubes in Macrophages. Small. 2016; 12: 5998-6011.

[98] Kavosi A, Hosseini Ghale Noei S, Madani S, Khalighfard S, Khodayari S, et al. The toxicity and therapeutic effects of single-and multi-wall carbon nanotubes on mice breast cancer. Sci Rep-Uk. 2018; 8: 8312-75.

[99] Abdelgied M, El-Gazzar AM, Alexander WT, Numano T, Iigou M, et al. Carcinogenic effect of potassium octatitanate (POT) fibers in the lung and pleura of male Fischer 344 rats after intrapulmonary administration. Part Fibre Toxicol. 2019; 16: 34.

[100] Carll AP, Salatini R, Pirela SV, Wang Y, Xie Z, et al. Inhalation of printer-emitted particles impairs cardiac conduction, hemodynamics, and autonomic regulation and induces arrhythmia and electrical remodeling in rats. Part Fibre Toxicol. 2020; 17: 7.

[101] Yang X, Zhang Y, Lai W, Xiang Z, Tu B, et al. Proteomic profiling of RAW264.7 macrophage cells exposed to graphene oxide: insights into acute cellular responses. Nanotoxicology. 2019; 13: 35-49.

[102] Mukherjee SP, Kostarelos K, Fadeel B. Cytokine Profiling of Primary Human Macrophages Exposed to Endotoxin-Free Graphene Oxide: Size-Independent NLRP3 Inflammasome Activation. Adv Healthc Mater. 2018; 7: 1700815.

[103] Dekkers S, Krystek P, Peters RJ, Lankveld DP, Bokkers BG, et al. Presence and risks of nanosilica in food products. Nanotoxicology. 2011; 5: 393-405.

[104] Hu H, Fan X, Guo Q, Wei X, Yang D, et al. Silicon dioxide nanoparticles induce insulin resistance through endoplasmic reticulum stress and generation of reactive oxygen species. Part Fibre Toxicol. 2019; 16: 41.

[105] Mohammadpour R, Yazdimamaghani M, Cheney DL, Jedrzkiewicz J, Ghandehari H. Subchronic toxicity of silica nanoparticles as a function of size and porosity. J Control Release. 2019; 304: 216-232.

[106] Hassankhani R, Esmaeillou M, Tehrani AA, Nasirzadeh K, Khadir F, et al. In vivo toxicity of orally administrated silicon dioxide nanoparticles in healthy adult mice. Environmental science and pollution research international. 2015; 22:

1127-1132.

[107] Satpathy SR, Jala VR, Bodduluri SR, Krishnan E, Hegde B, et al. Crystalline silica-induced leukotriene B4-dependent inflammation promotes lung tumour growth. Nat Commun. 2015; 6: 7064.

[108] Mohammadi H, Farhang Dehghan S, Tahamtan A, Golbabaei F. Evaluation of potential biomarkers of exposure to crystalline silica: A case study in an insulator manufacturer. Toxicol Ind Health. 2018; 34: 491-8.

[109] Chen F, Li G, Zhao ER, Li J, Hableel G, et al. Cellular toxicity of silicon carbide nanomaterials as a function of morphology. Biomaterials. 2018; 179: 60-70.

[110] Bonaventura G, Iemmolo R, La Cognata V, Zimbone M, La Via F, et al. Biocompatibility between Silicon or Silicon Carbide surface and Neural Stem Cells. Sci Rep-Uk. 2019; 9: 11513-11540.

[111] Deng Y, Zhang Y, Lemos B, Ren H. Tissue accumulation of microplastics in mice and biomarker responses suggest widespread health risks of exposure. Sci Rep. 2017; 7: 46687.

[112] Barboza LGA, Vieira LR, Branco V, Figueiredo N, Carvalho F, et al. Microplastics cause neurotoxicity, oxidative damage and energy-related changes and interact with the bioaccumulation of mercury in the European seabass, Dicentrarchus labrax (Linnaeus, 1758). Aquat Toxicol. 2018; 195: 49-57.

[113] Brandts I, Teles M, Tvarijonaviciute A, Pereira ML, Martins MA, et al. Effects of polymethylmethacrylate nanoplastics on Dicentrarchus labrax. Genomics. 2018; 110: 435-441.

[114] Ge H, Yamazaki E, Yamashita N, Taniyasu S, Ogata A, et al. Particle size specific distribution of perfluoro alkyl substances in atmospheric particulate matter in Asian cities. Environ Sci Process Impacts. 2017; 19: 549-560.

[115] Jonitz-Heincke A, Tillmann J, Ostermann M, Springer A, Bader R, et al. Label-Free Monitoring of Uptake and Toxicity of Endoprosthetic Wear Particles in Human Cell Cultures. Int J Mol Sci. 2018; 19: 3486.

[116] Santos C, Turiel S, Sousa GP, Costa E, Santos-Silva A, et al. Vascular biosafety of commercial hydroxyapatite particles: discrepancy between blood compatibility assays and endothelial cell behavior. J Nanobiotechnology. 2018; 16: 27.

[117] Tai S, Cheng J, Ishii H, Shimono K, Zangiacomi V, et al. Effects of beta-tricalcium phosphate particles on primary cultured murine dendritic cells and macrophages. Int Immunopharmacol. 2016; 40: 419-427.