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Review Article

Chemical Composition Analysis, Indoor Diffusion Deposition Model and Pathogenic Mechanism of Fine Particulate Matter ($PM_{2.5}$)

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Abstract

In recent years, with a gradual increase of health awareness, society has become more concerned about the frequent occurrence of air pollution. As is known to all, fine particulate matter (particles less than 2.5 micrometers in diameter [$PM_{2.5}$]) is the main cause of haze, which is suspended in the air and generated through a series of physical and chemical changes. Of note, different components and sources of $PM_{2.5}$ cause different kinds of damage. Identification of the components and analysis of the sources have guiding significance for the prevention of $PM_{2.5}$ damage. Indoor $PM_{2.5}$ that is mainly from smoking and biomass combustion also has an adverse influence on human health. The prediction of indoor $PM_{2.5}$ sedimentation and suspension is of great significance for maintaining good indoor air quality. Thus, the present review was conducted to provide a brief overview of new insights into the composition analysis, source analysis, indoor diffusion and deposition model, and the pathogenic mechanism of $PM_{2.5}$, which have been explored with new technologies in recent years. This review will help to provide reference for $PM_{2.5}$ related policy formulation.

Introduction

In recent years, with a gradual increase in health awareness, society has become more concerned about the frequent occurrence of air pollution. As is known to all, fine particulate matter (diameter ≤ 2.5 μm, $PM_{2.5}$) is the main cause of haze, which is suspended in the air and generated through a series of physical and chemical changes.[1] The sources of $PM_{2.5}$ include factories, power plants, motor vehicles, and construction activities, and its composition is subject to a wide variety of natural and human activities.[2]

Many studies have provided hard evidence that $PM_{2.5}$ has an adverse influence on human health. On one hand, some large-scale epidemiological studies have shown that $PM_{2.5}$ is closely related to the morbidity and mortality of patients with respiratory, cardiovascular, and cerebrovascular diseases, especially among the elderly, infants, and high-risk groups suffering from basic chronic diseases. The study from Shah *et al.*[3] concerning the global association of air pollution and heart failure suggested that heart failure hospitalization or death was associated with increases in $PM_{2.5}$ (2.12% per 10 μg/m^3). Another survey indicated that exposure to $PM_{2.5}$ was associated with a notable proportion of mortalities due to numerous diseases, including lung cancer (23.9%), chronic obstructive pulmonary disease (COPD; 18.7%), stroke (40.3%) and ischemic heart disease (IHD; 26.8%).[4] Research from Hayes *et al.* that involved 565,477 men and women in America showed that each increase of 10 μg/m^3 $PM_{2.5}$ was as-

Keywords: Ambient particulate matter; Mass spectrometry; Oxidative stress injuries; Principal component analysis; Source analysis.

Abbreviations: $PM_{2.5}$, fine particulate matter (diameter ≤ 2.5 μm); MS, mass spectrometry; EF, enrichment factor; PMF, positive matrix factorization; PCA, principal component analysis; CMB, chemical mass balance.

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Table 1. Composition analysis methods for fine particulate matter (particles less than 2.5 micrometers in diameter; $PM_{2.5}$)

Author	Method
Palomo-Marín *et al.*[12] and Mitra *et al.*[13]	Inductively coupled plasma mass spectrometry (ICP-MS)
Zhang *et al.*[14]	High resolution aerosol mass spectrometry (HR-AMS)
Chen *et al.*[15]	Inductively coupled plasma atomic emission spectrometry (ICP-AES)
Wang *et al.*[16]	Wavelength dispersive X-ray fluorescence (WDXRF) spectrometry
Warnke *et al.*[19]	Liquid chromatography mass spectrometry (LC-MS)
Kim *et al.*[20]	Gas chromatography mass spectrometry (GC-MS)

sociated with a 16% increase in mortality from IHD and a 14% increase in mortality from stroke.[5]

On the other hand, many *in vivo* animal experiments have indicated that $PM_{2.5}$ can contribute to the acute exacerbation of asthma, heart failure, and COPD through the activation of various signaling pathways, such as adenosine monophosphate (AMP)-activated protein kinase (AMPK) catalytic subunit alpha 1 and signal transducer and activator of transcription (STAT)-1.[6] In addition to the adverse effects of exposure to particulate matter on respiratory and cardio-cerebrovascular systems, studies have shown that it can also damage other organs and DNA. According to Gao *et al.*,[7] exposure to $PM_{2.5}$ at a concentration between 20 μg/mL and 200 μg/mL decreased cell viability and increased lactate dehydrogenase release.[7] Treatment in human corneal epithelial cells with $PM_{2.5}$ remarkably increased DNA double-stand breaks, increased expression of a DNA repair-related protein (phosphorylated H2A histone family member X [γH2AX]), elevated formation of reactive oxygen species, and altered cellular ultrastructure.[7] It was observed that exposure to $PM_{2.5}$ could increase the number of leukocytes in the lung and the liver of $PM_{2.5}$-treated mice. A recent study based on data analysis from 3,080 counties revealed that each 1 μg/m^3 increase in $PM_{2.5}$ causes approximately an 8% increase in the coronavirus disease (COVID)-19 death rate (95% confidence interval [CI]: 2%, 15%).[8] Enkhjargal *et al.*[9] summarized that each 10 μg/m^3 increase of $PM_{2.5}$ led to a 0.65% increase in the hospitalization for cardiovascular disease (CVD) on the day of exposure, and on the second day of exposure, a 10 μg/m^3 growth of the pollutant contributed to 0.66% increase.[9]

$PM_{2.5}$ also imposes a burden on the economy and society. It was estimated that a mean reduction in $PM_{2.5}$ of 3.9 μg/m^3 would prevent 7,978 heart failure hospitalizations and save one-third of a billion US dollars per year.[3] A study based on $PM_{2.5}$ concentration of 338 Chinese cities showed that the national $PM_{2.5}$-attributable mortality was 0.964 (95% CI: 0.447, 1.355), which accounts for approximately 9.98% of total reported deaths in China, and $PM_{2.5}$ exposure led to an economic loss of $101.39 billion, which was 0.91% of the national gross domestic product (GDP) in 2016.[10] According to a report by World Bank,[11] lost income for countries in South Asia due to air pollution totaled more than $66 billion in 2013, the equivalent of nearly 1% of GDP. The magnitude of losses was greatest in East Asia and the Pacific, where premature mortality costs reached the equivalent of 7.5 percent of GDP in 2013, closely followed by South Asia where costs were on the order of 7.4 percent of GDP equivalent.

As scientists deepen their understanding of $PM_{2.5}$, the hazards of particulate matter have become widely known to the public. This article summarizes the progress of source analysis, pathogenic mechanisms, component analysis, and a diffusion deposition model. Relevant studies and publications have been identified using the search terms $PM_{2.5}$, source analysis, component analysis, and indoor $PM_{2.5}$ in the literature databases MEDLINE, Web of Science, PubMed, and Google Scholar.

Composition analysis

Currently, methods to determine the components in $PM_{2.5}$ primarily include inductively coupled plasma mass spectrometry (ICP-MS),[12,13] high resolution aerosol mass spectrometry (HR-AMS),[14] inductively coupled plasma atomic emission spectrometry (ICP-AES),[15] and wavelength dispersive X-ray fluorescence (WDXRF) spectrometry.[16]

ICP-MS has become one of the main approaches to determine the composition of $PM_{2.5}$, which was developed in the 1980s for the measurement of inorganic elements and isotopes.[17] ICP-MS adopted a unique interface technology that combines the high-temperature ionization characteristics of inductively coupled plasma with the sensitivity and high scanning speed of the mass spectrometer to form a highly sensitive analytical technique with the advantages of high sensitivity and rapidity.[18] HR-AMS[14] conducts a quantitative chemical analysis of aerosols by means of thermal evaporation and electron bombardment ionization mass spectrometry, which can also be applied to quantify the compositions of organic matters. Similarly, liquid chromatography mass spectrometry (LC-MS),[19] gas chromatography mass spectrometry (GC-MS)[20] and the other methods can be used to determine the compositions of organic matters in $PM_{2.5}$ as well. Compared to the other approaches, sample derivatization is a necessary procedure in GC-MS, suggesting higher complexity. LC-MS technology, on the other hand, has the most substantial advantage among all methods for its capability to detect unstable thermal organic compounds and polar organic compounds (Table 1).[12–16,19,20]

The particle mass concentration online monitoring technology mainly utilizes the tapered element oscillating micro-balance (TEOM) method,[21] β-ray method[22] and light scattering method,[23] of which TEOM is the most commonly used. Its mechanism is as follows: under the action of an electric field, a hollow conical tube is in a state of reciprocating oscillation, and the oscillation frequency is determined by the characteristics and mass of the conical tube. A change in the mass of the filter leads to an alteration in the oscillation frequency that is inversely proportional to the square root of the mass of the thin head. The mass of the $PM_{2.5}$ particles collected is then calculated from the oscillation frequency. Next, the ambient temperature, air pressure, and the mass concentration of particulate matter during this period can be calculated based on the flow rate.

Prior to composition analysis, the identity of the collected samples needs to be verified as $PM_{2.5}$. In general, dynamic light scattering is used to determine whether the collected particles are $PM_{2.5}$ samples.[24] This technique measures the size of the particle

Table 2. The comparison of the diffusion and receptor models

	Diffusion model	Receptor model
Basic conditions	Emission factor, geographical factors, meteorological data, transportation and diffusion of $PM_{2.5}$	Size distribution, chemical composition
Result	Emission forecast	Contribution rate of pollution sources
Default	Dynamic temporal variation of pollution sources	Cannot be used for prediction

in the suspension sample according to the change in the scattering light intensity. Due to the positive correlation between the change in the fluctuation of the light intensity signal and the speed of the small particle in Brownian motion, the correlation between the light intensity after a slightly longer time and the initial light intensity is lower. However, the behavior of large particles is opposite to that of small particles. Therefore, this method used to distinguish the size of the particulate suspensions. To fully understand the morphology of $PM_{2.5}$, scanning electron microscope (SEM) is usually used for direct observation.

Source analysis for $PM_{2.5}$

Ambient $PM_{2.5}$ mainly comes from nature and human activities. Natural sources include primarily salt water evaporation, natural dust, and volcanic eruption.[25] Human activities principally include stationary sources (such as industrial production and fossil fuel) and mobile sources (such as vehicle emission).[25,26] According to previous research, the proportion of urban ambient $PM_{2.5}$ sources from transportation, civil fuel combustion, industrial activities, and other human activities were 25%, 20%, 15%, and 22%, respectively, whereas Salt water evaporation and natural dust contributed 18%.[27] The components of $PM_{2.5}$ consisted of soluble components, inorganic elements and carbon composition.[28] Soluble components accounted for 20% of the total $PM_{2.5}$ mass, which mainly consisted of SO_4^{2+}, NO_3^-, K^+, NH^+, Na^+, Ca^{2+}, Mg^{2+} and Cl^-. SO_4^{2+} and NH^+ were from motor vehicle exhaust and the secondary conversion process of gas produced by fuel combustion. The ratio of NO_3^-/SO_4^{2+} was usually applied to identify if the pollution source was from a stationery or mobile source. Inorganic elements found in $PM_{2.5}$ included Al, Si, Ca, P, K, Fe, Mn, Cu, Cd, Co, Cs, Au, Hg, Cr, and others.[29] Carbon composition include organic carbon, elemental carbon, and carbonate. Organic carbon is a mixture of hundreds of organic compounds, including polycyclic aromatic hydrocarbons, n-alkanes, phthalates, aldehydes, ketones, and other toxic and harmful substances. Organic carbon can be divided into water-soluble and water-insoluble.

Source analysis models can be divided into diffusion or receptor models.[30] The diffusion model can quantitatively identify a fixed pollution source and pollutant source at a time to calculate the rate of contribution of the pollution source in the fixed location at a certain time.[31] Meteorological conditions and pollution sources can be introduced into the diffusion model, but are not considered in receptor models. The comparison of diffusion and receptor models is presented in Table 2. A weakness of receptor models is that they cannot be used to predict the contribution rate of each pollution source.

Receptor models included enrichment factor (EF), positive matrix factorization (PMF) analysis, principal component analysis (PCA), and chemical mass balance (CMB).[31,32] Source component spectrum is required for CMB and it is sensitive to collinearity issues. Additionally, the complex usage of PMF is a weakness (Table 3).

Diffusion deposition model of indoor $PM_{2.5}$

The concentration and composition of indoor $PM_{2.5}$ are mainly determined by both outdoor infiltration and indoor source emission. A study by Gilbert *et al.* in Australia showed that smoking, frying, and grilling caused $PM_{2.5}$ levels to be three, 30, and 90 times higher than the background value, respectively.[33] It was found that tobacco smoke and cooking are major sources of indoor $PM_{2.5}$ in both residential and non-industrial environments.[34] Nitta *et al.* investigated indoor air pollution in downtown Tokyo and found that smoking increases the concentration of indoor $PM_{2.5}$ by approximately 50–80%.[35] Thus, mass balance model has been proposed to predict the settlement of $PM_{2.5}$. According to Figure 1, the source of indoor $PM_{2.5}$ consists of outdoor air input, re-suspension, and infiltration. Based on this model, three typical $PM_{2.5}$ deposition diffusion models are summarized in this paper.

Indoor $PM_{2.5}$ deposition diffusion model under different ventilation conditions

Based on the mass balance principle, the deposition and diffusion model of indoor $PM_{2.5}$ under different ventilation conditions is proposed.[36] The following conclusions can be drawn: different ventilation modes in residential buildings can lead to different levels of indoor fine particulate matter mass concentration and indoor exposure. The model is as follows:

Table 3. The comparison of receptor models

	CMB	PMF	PCA	EF
Sample size	Less	More	More	Less
Source component spectrum	Yes	No	No	No
Feature identification element	No	Yes	Yes	Yes

CMB, chemical mass balance; PMF, positive matrix factorization; PCA, principal component analysis; EF, enrichment factor.

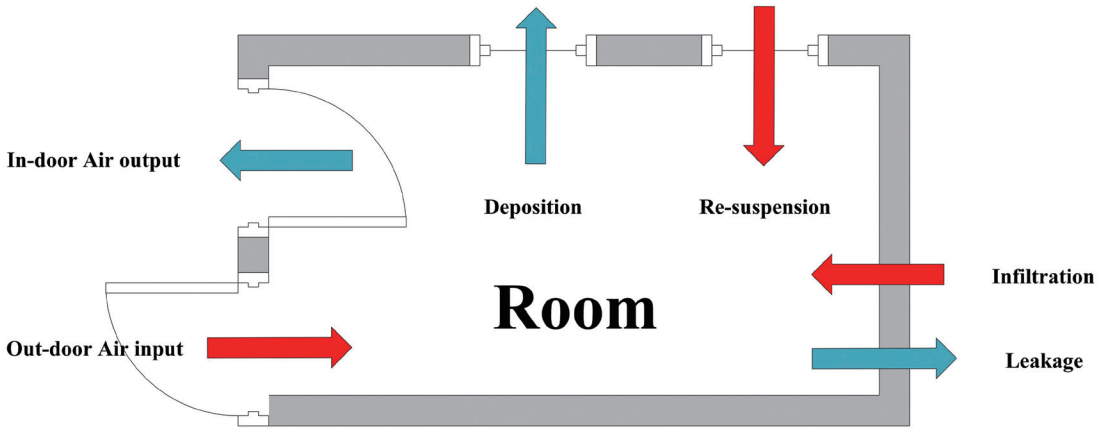

Fig. 1. The main sources and locations of indoor fine particulate matter (particles less than 2.5 micrometers in diameter; $PM_{2.5}$).

$$V\frac{dC}{dt} = Q_v\eta_1 C_o - Q_v C + Q_n P_p C_o - Q_n C_o - Q_c\eta_2 C - v_d AC \quad (1)$$

where V is the residential volume, m^3; C, indoor particle mass concentration, g/m^3; T, time, h; Qv, mechanical ventilation volume, m^3/h; $\eta 1$, the filter efficiency for fine particles in mechanical ventilation system; Co, the concentration of particulate matter in the atmosphere, g/m^3; Qn, natural ventilation rate, m^3/h; Pp, penetration coefficient of fine particles-Pp = 0.8 (closed window)/Pp = 1 (open window); Qc, air purification air volume, m^3/h; $\eta 2$, primary filtration efficiency of air purifier for the fine particles; and Vd, particle deposition rate. For fine particles, the general indoor particle deposition rate K is as follows:

$$K = v_d A / V = 0.09h^{-1} \quad (2)$$

where A is the residential surface area.

Evaluation model of outdoor $PM_{2.5}$ infiltration and settlement characteristics according to the gap ventilation of building exterior windows

Utilizing the concepts of the law of the conservation of mass, mathematical statistics and controlled variables, Wang *et al.* proposed and verified a model of the relationship between the gap ventilation of building exterior windows and indoor $PM_{2.5}$ settlement.[37] The model is as follows:

$$V\frac{dCi,t}{dt} = aPVC_{o,t} + v_i + RL_f A_f - aVC_{i,t} - kVC_{i,t} \quad (3)$$

where V is room volume, m^3; C_i,t, indoor $PM_{2.5}$ concentration at time T, g/m^3; a, the number of air changes, h^{-1}; P, penetration coefficient; C_o,t, outdoor $PM_{2.5}$ concentration at time T, g/m^3; v_i, indoor $PM_{2.5}$ concentration per unit time, μg/h; k, settling rate, h^{-1}; R, secondary suspension rate of $PM_{2.5}$, h^{-1}; L_f, $PM_{2.5}$ mass per unit area, h^{-1}; and A_f, surface area of the room, m^2.

Evaluation model on indoor $PM_{2.5}$ concentration level of building structure based on the influence of infiltration ventilation conditions

Under the condition of ignoring chemical reactions such as coagulation and phase transition of particulate matter without an indoor pollution source, the mass concentration balance equation of indoor particulate matter under permeable ventilation is established based on the principle of mass conservation, specifically as follows:[38]

$$\frac{dC_{in}}{dt} = aPC_o - kC_{in} - aC_{in} \quad (4)$$

where C_o is outdoor $PM_{2.5}$ concentration, $\mu g/m^3$; C_{in}, indoor $PM_{2.5}$ concentration, $\mu g/m^3$; a, ventilation times, h^{-1}; P, $PM_{2.5}$ penetration coefficient; and k, $PM_{2.5}$ natural sedimentation rate, h^{-1}.

Another study demonstrates that, the number of time-related parameters, such as the ventilation frequency of infiltration ventilation as well as indoor and outdoor $PM_{2.5}$ concentration, remain stable with small fluctuation[39] over a relatively short period of time. In formula (4), the left side can be regarded as zero to obtain formula (5).

$$aPC_o - kC_{in} - aC_{in} = 0 \quad (5)$$

Rewriting the above equation, formula (6) can be obtained:

$$I/O = \frac{C_{in}}{C_o} = \frac{aP}{a+k} \quad (6)$$

Then, the concentration ratio of indoor and outdoor PM2.5 particles can be calculated using formula (6).

The pathogenic mechanisms of $PM_{2.5}$

Patients with chronic respiratory diseases are susceptible to damage by $PM_{2.5}$. The mechanisms of lung injury and aggravation caused by $PM_{2.5}$ include oxidative stress, inflammatory reaction, and gene toxicity, as shown in Figure 2.

Oxidative stress

Aerobic metabolism of cells can produce reactive oxygen species (ROS), which participates in the signal transduction and regulation of gene expression. Under normal conditions, the concentration of ROS in the body is low and in a state of dynamic balance. Once the equilibrium state is disrupted, a high concentration of ROS can lead to oxidative damage of large molecules such as DNA, and the degeneration or even necrosis of cells, ultimately resulting in oxidative stress. As $PM_{2.5}$ enters the human body, the copper ions (Cu^{2+}) contained in the $PM_{2.5}$ can lead to an increase in ROS,[40,41]

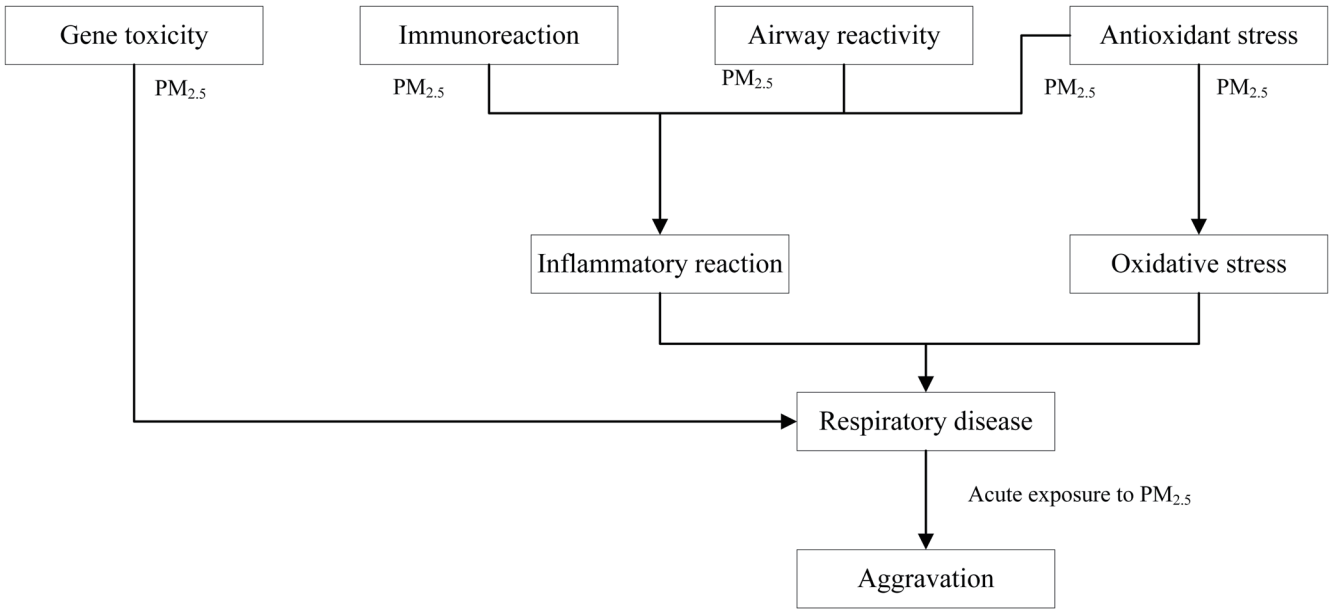

Fig. 2. Schematic diagram of exposure to fine particulate matter (particles less than 2.5 micrometers in diameter; $PM_{2.5}$) and acute aggravation of lung diseases.

resulting in an imbalance between the oxidation and anti-oxidation,[3] which can cause further damage to the respiratory system. Oxidative stress pathways related to $PM_{2.5}$ include the Kelch epoxy chloropropane related proteins 1-nuclear factor E2 related factor 2-oxidation reaction signaling (Keapl-Nrf2-ARE) pathway, phosphatidyl inositol-3-kinase/protein kinase B (PI3K/Akt) pathway, mitogen-activated protein kinase (MAPK) signaling pathway, tyrosine protein kinase/STAT signaling, and nuclear factor (NF)-kB signaling pathways.[42,43]

Inflammatory response

$PM_{2.5}$ exposure can also lead to inflammatory cell infiltration by releasing inflammatory factors such as interleukins, which causes damage to the trachea and lungs. Relevant studies have demonstrated that $PM_{2.5}$ turbidity increases the concentration of interleukin (IL) 6, tumor necrosis factor-alpha (TNF-α), and the activation level of inflammatory responses in the body.[41] It has been illustrated that $PM_{2.5}$ has the potential to cause lung fiber hyperplasia and proliferative inflammation.[44] For COPD patients who have alveolar macrophage phagocytosis defect, exposure to $PM_{2.5}$ exacerbates the situation since macrophages are one of the most important cells involved in the inflammatory response. Moreover, it was also shown that $PM_{2.5}$ exposure can exacerbate the phagocytic dysfunction of alveolar macrophages in a mouse model of COPD.[45]

Gene toxicity

One study has shown that, compared with a control group, the expression level of repair genes (such as apurinic/apyrimidinic endonuclease 1 [APE1]) in cells exposed to $PM_{2.5}$ is significantly higher, which indirectly proves DNA damage caused by $PM_{2.5}$.[46] When exposed to 300 $\mu g/m^3$ of $PM_{2.5}$ over a short term, approximately 2,800 sites in the DNA of human peripheral blood mononuclear cells may be hypomethylated, thus inhibiting the normal expression of around 400 genes.[47]

Future directions

Research focusing on $PM_{2.5}$ has made considerable progress as detailed above, but it is believed that there is still room for improvement.

Components and biological effect

Due to different regions, levels of economic development and economic pillars, the concentration and composition of $PM_{2.5}$ are greatly varied, which leads to different results among scholars. The human exposure level to air pollution is a low dose exposure, and it is not a simple linear cumulative effect, so it is difficult to determine the effective relationship between exposure dose and health in the short term. In addition, the mobility of the population makes it even more difficult to monitor human exposure quantitatively. The complexity of the factors affecting human health status make it difficult to identify and monitor the exposure level in a certain target or a certain class of objects, and while some researchers investigate the effect of $PM_{2.5}$ based on certain components, this might lead to the neglect of some critical adverse components. Differences between individual populations make it difficult to apply specific research results to other populations effectively.

Prediction for $PM_{2.5}$

$PM_{2.5}$ concentration prediction is meaningful and important to guide the travel of high-risk and sensitive groups. Factors affecting the variations in $PM_{2.5}$ concentration include the source and diffusion factors. Sudden events often lead to a sharp change in $PM_{2.5}$ concentration and warning with a delayed effect. Current studies

regarding $PM_{2.5}$ are limited to a certain city, and should be coordinated between regions, taking into account monsoons and other factors that accelerate $PM_{2.5}$ diffusion between different regions.

Conclusion

The present review aims to provide a brief overview of new insights into the composition analysis, source analysis, indoor diffusion and deposition model, and the pathogenic mechanism of $PM_{2.5}$, which have been explored with new technologies in recent years. This review will help to provide reference for $PM_{2.5}$ related policy formulation.

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Conflict of interest

The authors declare no conflict of interest.

Author contributions

All authors have participated in this study, and consent to publish this article. Guarantor of integrity of entire study (CC), study concepts (CC, YS), study design (CC, YS), literature research (YS, JA, ZM), manuscript preparation (YS, XM), manuscript definition of intellectual content (CC, YS), manuscript editing (CC, YS, QL), manuscript revision/review (XL, QL, CC, YS).

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