

Full length article

Antibiotics in ambient fine particulate matter from two metropolitan cities in China: Characterization, source apportionment, and health risk assessment[☆]



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ABSTRACT

Excessive production and widespread application of antibiotic has led to residues in environmental matrices worldwide. There is limited knowledge of the concentrations of antibiotics bound to ambient fine particulate matter (PM_{2.5}) and their health risks. We investigated the occurrence, sources, environmental driving factors, and health risks of antibiotics in PM_{2.5} samples collected from Beijing and Shijiazhuang, China, during periods of high air pollution. Using ultra-high performance liquid chromatography-tandem mass spectrometry, 25 antibiotics were detected in PM_{2.5} at concentrations ranging from undetectable to 774.7 pg/m³. These compounds were predominantly tetracyclines and macrolides. The positive matrix factorization model was used to pinpoint the main sources of these antibiotics as pharmaceutical and medical waste, sewage treatment plants, and livestock emissions, with contributions of 39.1 %, 31.7 %, and 29.2 % respectively, to the total concentrations. Crucial environmental driving factors were determined using a linear mixed-effects model and random forest model. Most antibiotics showed a positive correlation with gaseous pollutants and a negative correlation with meteorological factors. PM_{2.5}, PM₁₀, and CO had the highest influence. The estimated daily intake and hazard quotient (HQ) were calculated to assess the human inhalation exposure risks for these antibiotics, and children aged 0–6 years had the highest intake of 102.8 pg/kg/day. Although the calculated health risk of antibiotic inhalation was low (HQ < 1), considering that exposure to antibiotics via inhalation occurs over long periods and these compounds accumulate, further attention should be given to health risks associated with this exposure. Our results provide valuable insight for environmental planning and policymaking concerning antibiotic pollution and its associated health risks.

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1. Introduction

Antibiotics, which are classed as pharmaceuticals and personal care products, are widely used globally in both human and veterinary medicine for treating infectious diseases and as animal growth promoters (Wang et al., 2022b). As the world's leading producer and consumer, China annually produces approximately 248,000 tons of antibiotics, with over 50,000 tons being discharged into the environment (Feng et al., 2020; Tiseo et al., 2020; Xu et al., 2021). Because antibiotics are not fully metabolized or assimilated *in vivo*, approximately 40%–90% of antibiotics are excreted through feces and urine into environmental matrices as either the original compounds or metabolites (Pan et al., 2021). Antibiotic residues in the environment can lead to the proliferation of resistant genes and bacteria, and have contributed to a global increase in antibiotic-resistant infections. According to a World Health Organization (WHO) report, antibiotic-resistant bacteria are responsible for 700,000 deaths globally each year, and this number is predicted to rise to 10 million annually by 2050 (WHO, 2019). The pervasive presence of antibiotics in environmental matrices, particularly in aquatic environments where concentrations can reach up to several micrograms per liter, has caused global concern. Therefore, it is important to quantitatively detect antibiotics in environmental matrices to assess their effects on public health.

Air pollution caused by fine particulate matter (PM_{2.5}) poses severe risks to the respiratory and cardiovascular systems, and can lead to mortality. The 2021 Global Burden of Disease study estimated that long-term exposure to PM_{2.5} caused more than 8.1 million deaths worldwide, with 1.4 million deaths occurring in China (Cohen et al., 2017; Wu et al., 2024a). In developing countries, megacities frequently experience intense smog episodes, with daily PM_{2.5} concentrations (150–199 µg/m³) often greatly exceeding the WHO's recommended limits (15 µg/m³) (Fu et al., 2015; Hong et al., 2021; WHO, 2021). The health hazards of PM_{2.5} are closely linked to its chemical composition, which includes harmful inorganic components (e.g., elemental carbon, metals, and major ions) (Liu et al., 2023; Schlesinger, 2007; Zhang et al., 2019). These components can penetrate the alveoli and circulatory system, triggering DNA methylation, inflammatory responses, and other adverse health effects (Chowdhury et al., 2022; Jiang et al., 2021; Zhang et al., 2019). This underscores the need for thorough quantitative assessments of organic components within PM_{2.5} to accurately evaluate their health risks. Recent studies have applied non-parametric tests to analyze the spatiotemporal distribution of antibiotics in various environmental media (Ding et al., 2024). Studies have shown the presence of antibiotics in particulate matter, particularly in areas with severe pollution (Ben et al., 2019). For instance, particulate matter from cattle feed yards in the southern High Plains of the United States were found to contain tetracycline (TC), tylosin (TYL), and sulfamethoxazole (SMX) at concentrations ranging from 0.5 to 4.6 mg/kg (McEachran et al., 2015). Comprehensive reports on antibiotic residues in the air in China are still lacking. Therefore, accurately describing the concentrations of antibiotic residues in PM_{2.5} and their spatial distributions is crucial for health risk assessment. Furthermore, antibiotics entering the environment undergo complex transport and transformation processes, which are regulated by a series of environmental mechanisms, including photolysis, adsorption, and biodegradation (Li et al., 2022a; Mu et al., 2024). Environmental factors, such as particulate matters, gaseous pollutants, and meteorological conditions, significantly affect the distribution and transformation of organic pollutants in the atmosphere (Hong et al., 2021). Previous studies have shown that pollutants such as PAHs and phthalate esters can be transported through particulate matter, with their distribution closely linked to gaseous pollutants such as O₃ and SO₂ (Hong et al., 2021; Zhang et al., 2023). Exploring the major sources and key environmental factors influencing the behavior of antibiotics in ambient PM_{2.5} is vital for improving control measures against antibiotic pollution.

The Beijing-Tianjin-Hebei region, which is a highly developed

economic hub in China, reported gross domestic product of 10.4 trillion RMB in 2023, which accounted for approximately 10% of the national gross domestic product (Statistics, 2024). Despite the implementation of policies since 2013 aimed at improving the air quality and reducing PM_{2.5} concentrations, pollution remains a severe issue (Zhang and Chen, 2022). For instance, in 2023, the annual average PM_{2.5} concentration in Beijing was 32.6 µg/m³, which far exceeded the WHO's guideline (5 µg/m³) (Li et al., 2022b). Concentrations during the heating seasons of winter and spring are approximately 20% higher than the annual average (Huang et al., 2021). Moreover, the Beijing-Tianjin-Hebei region is amongst the areas with the highest antibiotic emission intensities in China (Li et al., 2024). Most research has focused on antibiotic residues in soil, water, and food, and studies on antibiotics in the air, especially during periods of high PM_{2.5} pollution, have been scarce (Chen et al., 2022; Pan et al., 2021). Furthermore, although the potential for human exposure to antibiotics through drinking water, plant-based foods, and meat products has been assessed, the risk of inhaling antibiotics through PM_{2.5} has been largely overlooked (Ben et al., 2020). This oversight limits our understanding of the health risks posed by antibiotic residues in environmental matrices.

We selected the two metropolitan cities of Beijing and Shijiazhuang within the Beijing-Tianjin-Hebei region as research locations to collect PM_{2.5} samples during periods of higher pollution (winter and spring). The main objectives of this study were to 1) characterize the spatio-temporal distribution of antibiotics in PM_{2.5} from cities with relatively high PM_{2.5} pollution levels; 2) analyze the source contributions of antibiotics in PM_{2.5} using the PMF model; 3) investigate the main gaseous pollutants and meteorological factors that might affect the levels of antibiotics in PM_{2.5}; and 4) assess the potential health risks of antibiotics exposure via inhalation across different age groups using toxicological and microbiological parameters, and analyze the effects of extreme weather on health risks.

2. Materials and methods

2.1. Reagents and standards

Information relative to standards and solvents used in this study are provided in the [Supporting Information \(Text S1 and Table S1\)](#).

2.2. Sample collection

Airborne PM_{2.5} samples ($n = 257$) were collected in Beijing and Shijiazhuang from November 2021 to March 2022 and from November 2022 to March 2023. The sampling locations, which were surrounded by hospitals, schools, and numerous traffic arteries, were representative of urban environments ([Fig. S1](#) and [Fig. 1](#)). Before collection, quartz filters (PALL Pallflex Inc., Ann Arbor, MI, USA) were prepared by baking them at 500 °C for 4 h in a programmed furnace (NEY 2–525 Series II, USA) to remove any residual chemicals. Airborne PM_{2.5} samples were then collected over 24 h periods at a constant flow rate of 1.05 L/min using a high-volume PM_{2.5} collector (TH-150C, Wuhan Tianhong Instrument Co., Ltd., China). Following collection, the filters were wrapped in aluminum foil and stored in plastic zip bags at –80 °C until required for further analysis. The average daily meteorological parameters [temperature (TEMP), relative humidity (RH), sunshine duration (SUN), and wind speed (WS)], air quality index (AQI), and the concentrations of particulate matters (PM_{2.5} and PM₁₀) and gaseous pollutants (SO₂, NO₂, CO, and O₃) were recorded. ([Text S3](#)).

2.3. Sample preparation

The sample preparation followed an established method for particulate matter samples (McEachran et al., 2015). Briefly, one-eighth of the quartz filter was placed into a centrifuge tube and extracted using 10 mL of acetonitrile containing 0.1% formic acid (v/v) and 10 mL of 0.1 M

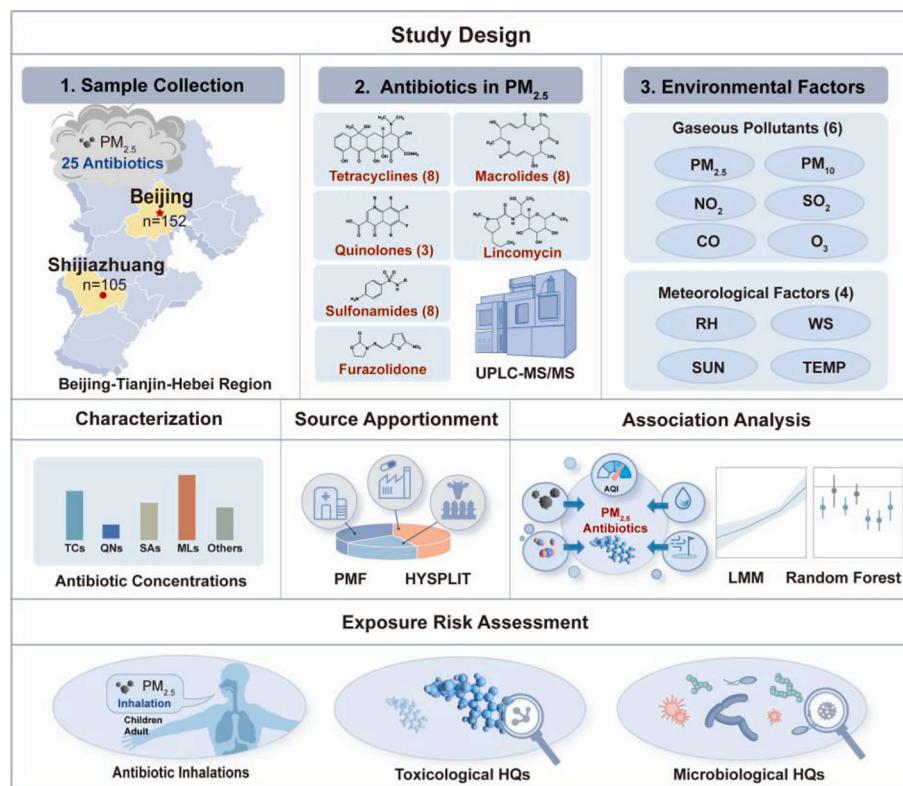


Fig. 1. Overview of the study design. Two hundred and fifty-seven $\text{PM}_{2.5}$ samples were collected along with data on gaseous pollutants and meteorological factors during periods of high air pollution in Beijing and Shijiazhuang. Five classes of antibiotics in $\text{PM}_{2.5}$ were detected using ultra-high performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS). The sources of antibiotics in $\text{PM}_{2.5}$ were analyzed using the positive matrix factorization (PMF) model. Furthermore, the relationships between antibiotics in $\text{PM}_{2.5}$ and environmental factors were revealed using a linear mixed-effects model (LMM) and random forest analysis. Additionally, Monte Carlo simulations were conducted to determine the toxicological and microbiological health risks of antibiotic exposure via inhalation among different age groups. Abbreviations: HYSPLIT, hybrid single particle lagrangian integrated trajectory; RH, relative humidity; WS, wind speed; SUN, sunshine duration; TEMP, temperature; and HQ, Hazard quotient.

Na_2EDTA -McIlvaine buffer solution (pH 4). The mixture was immediately vortexed for 2 min and then extracted by ultrasonication for 30 min. The resulting solution was centrifuged for 15 min at 3500 rpm, and the supernatant was transferred to a clean centrifuge tube. This extraction process was repeated twice, and the extracts were combined and concentrated to reduce the organic phase. Subsequently, 20 mL of purified water was added to dilute the organic volume fraction below 5 %. The samples were then processed through a hydrophilic-lipophilic balanced solid-phase extraction cartridge (Oasis, Waters, USA). The hydrophilic-lipophilic balanced cartridges were preconditioned with methanol and purified water in sequence. The aqueous samples were loaded onto cartridges at a flow rate of 5 mL/min, rinsed with purified water, and then vacuum-dried for approximately 30 min. Analytes were eluted with methanol, and the eluate was evaporated to dryness under a gentle stream of nitrogen and reconstituted in 0.2 mL of methanol/water (30:70 v/v) for instrumental analysis.

2.4. Instrumental analyses

Antibiotics were determined using a triple quadrupole mass spectrometer (TQS, Waters) equipped with a high-performance liquid chromatograph (I Class, Waters). Separation of the target antibiotics was performed on an ACQUITY UPLC HSS T₃ column (100 × 2.1 mm, 1.8 μm , Waters). The mobile phases and elution gradients are summarized in Table S2 and the MS parameters are detailed in Table S3. Quantitative and qualitative ions of the target antibiotics are shown in Table S4.

2.5. PMF model

The PMF model (PMF 5.0, United States Environmental Protection Agency) was used to evaluate the source allocation of antibiotics in $\text{PM}_{2.5}$ from Beijing and Shijiazhuang (Zhang et al., 2023). With the concentrations and uncertainty values of antibiotics as input data, each simulation was run 20 times, and the number of sources was preset to 3–7. The optimum number of sources was determined from the q -values, coefficient of determination (R^2), and protocol values (Text S4).

2.6. Risk assessments

To assess the potential adverse effects of antibiotics on individuals inhaling $\text{PM}_{2.5}$, hazard quotients (HQs) were calculated for each antibiotic. The HQs were calculated as the ratio of the estimated daily intake (EDI, pg/kg/day) to the acceptable daily intake (ADI). To explore the overall risk of total antibiotic exposure, a hazard index (HI) was calculated as the sum of HQs for each antibiotic. In this study, if the value of the HQ or HI was > 1 , it was concluded that exposure to the antibiotic surpassed the tolerable level, which indicated there would be potential effects on residents in the two metropolitan cities. Health risk assessments for antibiotic exposure were calculated for toxicological and microbiological risks separately. Because reference limits for inhalation exposure to antibiotics were unavailable, ADIs for oral exposure (Table S5) derived from toxicological and microbiological data were used to estimate the HQs and HIs for antibiotic exposure. The EDIs, HQs, and HIs were calculated using the following equations (Liu et al., 2023; Zhang et al., 2019):

$$\text{EDI} = \frac{C \times \text{IR} \times T}{\text{BW}} \quad (1)$$

$$\text{HQ} = \frac{\text{EDI}}{\text{ADI}} \quad (2)$$

$$\text{HI} = \sum \text{HQ} \quad (3)$$

where C is the concentration of the antibiotic in PM_{2.5} (pg/m³), IR is the inhalation rate (m³/day), T represents the average exposure time per day (12 h/day) (Wang et al., 2018), BW is the human body weight (kg), and ADI is the acceptable daily intake for each antibiotic (pg/kg/day). All parameters for inhalation exposure used in the calculations are listed in Table S6.

2.7. Quality assurance and quality control

Antibiotics were quantitatively analyzed using an isotope labeling method. For instrument analysis, the calibration curve was established for each batch of samples, and their correlation coefficients were > 0.990. Otherwise, the calibration curve was rebuilt. The middle-concentration standard solution from the calibration curve was determined in duplicate for every 10 samples. The relative error between the measured results and the standard values were within ± 20 % to ensure the consistency and reliability of the instrument performance (Zhang et al., 2023). To ensure the accuracy and reliability of the analysis, blanks (solvents and glass instruments) were determined for every 10 samples, with all blank results less than the limit of detection (LOD). Additionally, parallel sample and spiked blank (standards spiked into solvents) were analyzed for every set of 10 samples, and the relative deviations of the parallel samples' results were < 20 % (Hong et al., 2021).

According to the United States Environmental Protection Agency method (Agency, 2014), the estimated LOD for target antibiotics was determined using a threefold signal-to-noise ratio. The LOD and the limit of quantification were established by analyzing seven fortified replicate samples with concentrations two to five times the estimated LOD in post-extraction matrix samples. The LOD was defined as three times the standard deviation of the seven results, and the limit of quantification was defined as 10 times the standard deviation. The LODs of the target antibiotics ranged from 0.11 to 0.94 pg/m³ (Table S7). Furthermore, the recoveries of these antibiotics at three different spiking levels (0.5, 2.0, and 5.0 ng) were 69.7 %–131.7 %, with relative standard deviations below 11.9 %.

2.8. Data analysis

The analytes were identified and quantified using MassLynx V4.1. For statistical analysis, we included antibiotics with detection frequencies of > 30 %. Samples with results below LOD were given a value of half of the LOD. According to the definitions of marker residue, the concentration of each tetracycline was calculated as the sum of the concentrations of the parent compound and its 4-epimer. For example, the residual concentration of TC was the sum of TC and ETC.

Comparison of target antibiotics concentrations among the two metropolitan cities was performed using the Wilcoxon rank sum test. The Kruskal–Wallis H test was used to explore seasonal variations in the antibiotic concentrations. Spearman's rank correlation was used to investigate the correlations among antibiotics in PM_{2.5}. A linear mixed-effects model was used to analyze the relationships between environmental factors and antibiotic concentrations. A p-value (FDR) of < 0.05 after correction using the Benjamini–Hochberg procedure was considered statistically significant. Environmental factors affecting the concentrations of antibiotics in PM_{2.5} were analyzed using a random forest model (Text S5). To minimize uncertainties arising from interindividual variability in exposure and to evaluate population-wide exposure risks,

we performed Monte Carlo simulations using R (version 4.3.2, R minpack.lm). A total of 10,000 iterations were conducted using the concentrations of antibiotics in PM_{2.5}. The probability distribution of the antibiotic concentrations in PM_{2.5} was described using a log-normal distribution, and the Shapiro-Wilk test was performed on the concentration data, and the judgment rule was set as $p > 0.05$.

3. Results and discussion

3.1. Occurrence and spatiotemporal distributions of antibiotics in PM_{2.5}

3.1.1. Occurrence of antibiotics in PM_{2.5}

This study represents the first quantitative detection of five classes of antibiotics in PM_{2.5} from residential areas in two Chinese metropolitan cities. The detection frequencies (DFs, %) and concentrations of antibiotics in PM_{2.5} are illustrated in Table S8, Fig. 2A and 2B. In PM_{2.5} samples from Beijing and Shijiazhuang, 25 different antibiotics were detected, with at least one type of antibiotic found in each sample. These results showed that antibiotic residues were widespread in PM_{2.5} in the study area. Thirteen antibiotics were detected in more than 30 % of the samples, including four TCs, two quinolones (QNs), two sulfonamides (SAs), four macrolides (MLs), and lincomycin (LCM). Notably, oxytetracycline (OTC), chlortetracycline (CTC), and doxycycline (DXC) had the highest DFs (75.7 %–99.1 %). These three antibiotics are also commonly found in particulate matter in the United States and Germany (Hamscher et al., 2003; McEachran et al., 2015), which is likely because of the greater ease with which tetracyclines (TCs) are absorbed by particles and their persistence in the environment. Like in previous studies, QNs and MLs were detected in our study area (Fig. 2A) and their presence was possibly related to human activities. For instance, OFL and azithromycin (AZM) are commonly used in medical treatment and may enter urban air through improper disposal of medical waste or emissions from nearby pharmaceutical factories.

The total concentration of antibiotics in the PM_{2.5} samples ranged from 0.9 to 774.7 pg/m³, with median concentrations of 27.8 pg/m³ in Beijing and 41.3 pg/m³ in Shijiazhuang (Table S8). TCs and MLs were the predominant antibiotics in PM_{2.5} (Fig. 2C). The mean concentrations of TC (2.0 pg/m³), OTC (11.3 pg/m³), CTC (11.0 pg/m³), and TYL (1.9 pg/m³) detected in PM_{2.5} in the study area were significantly lower than those reported in particulate matter from cattle feed yards in the United States (TC: 0.3×10^6 pg/g, OTC: 0.8×10^6 pg/g, CTC: 1.0×10^6 pg/g, and TYL: 0.3×10^6 pg/g) (McEachran et al., 2015) (Fig. 2A, 2B, and 3A). It should be noted that the difference in units between the antibiotic concentrations in PM_{2.5} from China (pg/m³) and those reported from cattle feed yards in the United States (pg/g) may limit the accuracy of direct comparisons. However, despite the discrepancy in units, the observed general trends still highlight the significantly higher concentrations of antibiotics in particulate matter at cattle feed yards, likely due to the higher usage rates of TCs for disease prevention and growth promotion in livestock management. Additionally, in urban areas, antibiotics are typically degraded or removed by advanced treatment facilities before entering the environment. By contrast, at cattle feed yards, antibiotics can be directly released into the environment through animal feces and urine and are then adsorbed by particulate matter.

3.1.2. Spatial distribution of antibiotics in PM_{2.5}

A total of 24 antibiotics were detected in ambient PM_{2.5} from Beijing (four TCs, three QNs, seven SAs, eight MLs, furazolidone, and LCM), while 18 antibiotics were detected in ambient PM_{2.5} from Shijiazhuang (four TCs, three QNs, five SAs, five MLs, and LCM) (Table S8). Among these compounds, 17 antibiotics (including TC, OTC, and OFL) were found in both cities, which showed they were common in metropolitan cities. The number of antibiotics detected in Beijing's PM_{2.5} was significantly higher than that for Shijiazhuang, which showed that antibiotic pollution was more complex in Beijing. This observation may be attributed to several factors. Firstly, as a megacity with a significantly

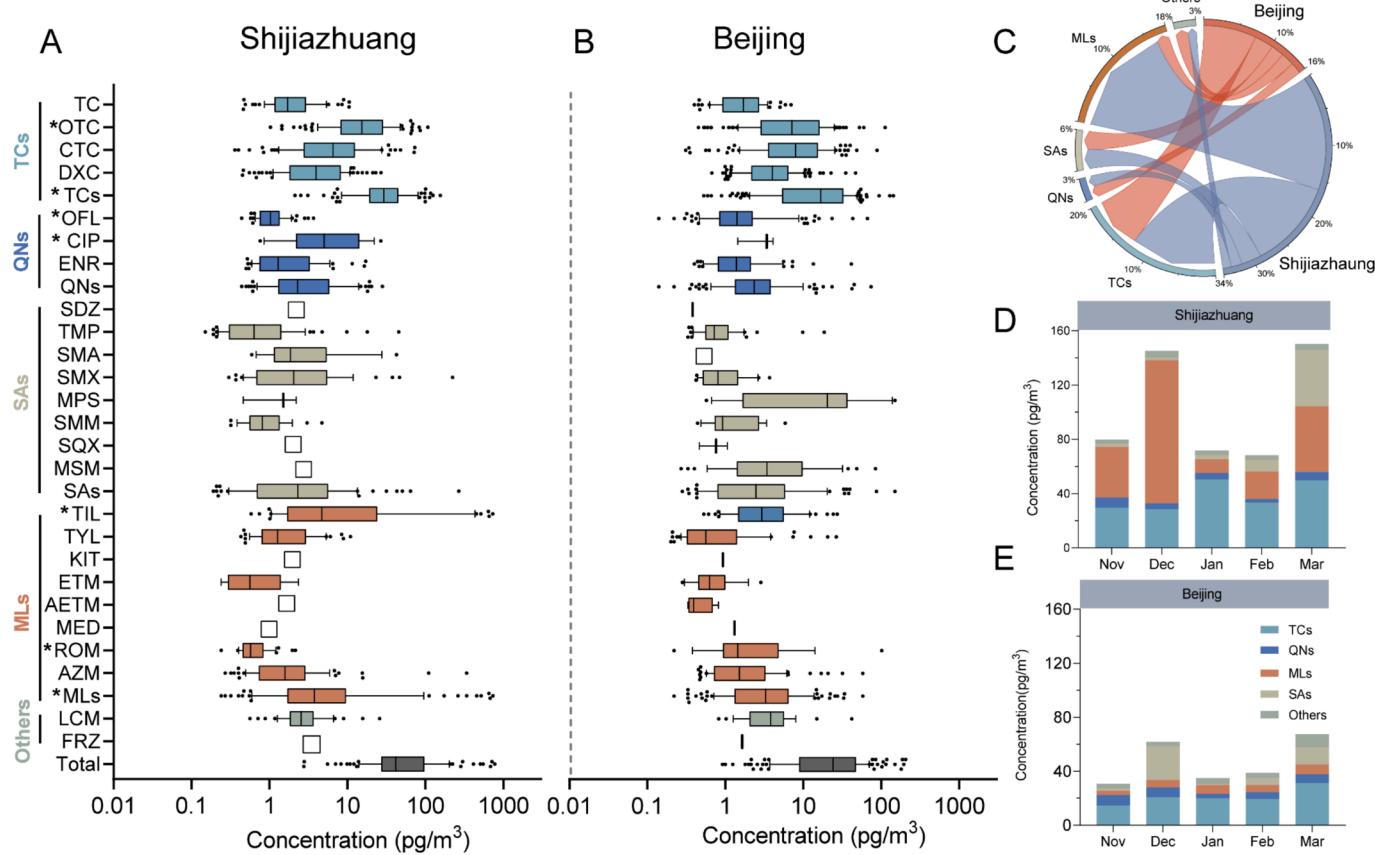


Fig. 2. Antibiotic concentrations and compositions in PM_{2.5}. Box plot depicting the concentrations of detected antibiotics in PM_{2.5} from Shijiazhuang (A) and Beijing (B) (* $p < 0.05$). Chord diagrams illustrating the variations in antibiotic compositions in PM_{2.5} from Shijiazhuang and Beijing (C). Temporal distribution of antibiotic concentrations in PM_{2.5} from Shijiazhuang (D) and Beijing (E). Abbreviations: SAs, sulfonamides; MLS, macrolides; QNs, quinolones; TCs, tetracyclines.

larger population, Beijing experiences a higher consumption of antibiotics across both human and veterinary healthcare sectors, leading to a broader range of antibiotic residues being present in the environment (Luo et al., 2024). Additionally, Beijing's advanced medical infrastructure and extensive pharmaceutical activities may contribute to the release of a more diverse array of antibiotics into the atmosphere. The total antibiotic concentration ranges in PM_{2.5} were 0.9–276.3 pg/m³ in Beijing and 2.8–774.7 pg/m³ in Shijiazhuang. Specifically, the ranges were 0.5–142.4 pg/m³ for ΣTCs, 0.1–73.6 pg/m³ for ΣQNs, 0.2–104.9 pg/m³ for ΣMLS, and 0.3–149.2 pg/m³ for ΣSAs in Beijing, and 2.1–154.9 pg/m³ for ΣTCs, 0.4–28.0 pg/m³ for ΣQNs, 0.2–734.0 pg/m³ for ΣMLS, 0.2–257.0 pg/m³ for ΣSAs in Shijiazhuang (Table S8). Among them, the differences in the concentrations of ΣTCs and ΣMLS between the two cities were statistically significant ($p < 0.05$, Fig. 2A and 2B). TCs and MLS were the most frequently detected antibiotics in PM_{2.5} (Fig. 2C). The high detection rates and concentrations of tilmicosin (TIL) and AZM in Shijiazhuang's PM_{2.5} and the relatively high concentrations of TCs in Beijing's PM_{2.5} showed that there may be regional differences in antibiotic usage and environmental release. TCs are commonly used to treat various infections, and release of substantial quantities in medical wastewater may explain their high concentrations in Beijing, which is a densely populated city with abundant medical resources (Xu et al., 2021). By contrast, the high detection rates and concentrations of TIL and AZM in Shijiazhuang may reflect their more frequent use in local medical practices (Luo et al., 2024). In this study, the comparison of antibiotics between Beijing and Shijiazhuang was limited by the sample size and number of sampling points. Further investigation is necessary to comprehensively assess antibiotic residues in ambient PM_{2.5} across these cities.

3.1.3. Temporal and seasonal distributions of antibiotics in PM_{2.5}

Degradation of antibiotics is reduced in spring and winter because of lower temperatures and reduced sunlight. The prevalence of livestock diseases during these seasons also increases the use of SAs and TCs, which leads to higher concentrations of these antibiotics in summer and autumn (Guo et al., 2023). In this study, we used the Kruskal-Wallis H test to analyze seasonal differences in antibiotic concentrations in PM_{2.5}. The total concentrations of antibiotics in November, December, January, February, and March were 1.8–84.5, 0.9–179.3, 3.9–60.9, 2.1–105.1, and 3.3–276.3 pg/m³ for Beijing, respectively. The corresponding concentrations in these months in Shijiazhuang were 14.1–200.7, 16.0–774.7, 2.8–198.9, 5.6–168.9, and 12.0–411.2 pg/m³ (Fig. 2D and 2E). Significant seasonal differences in the concentrations of TCs, SAs, and total antibiotics in PM_{2.5} were observed, which indicated that these concentrations were influenced by seasonal changes. The concentrations of TCs, SAs, and total antibiotics in PM_{2.5} were significantly higher in spring than in winter ($p < 0.05$). No significant differences were found in the concentrations of QNs and MLS between spring and winter (Fig. 2D and 2E, and Fig. S3). This study suggests that seasonal variations in environmental antibiotics are likely related to natural seasonal changes and terrestrial emissions, with the most significant effects arising from human activities such as antibiotic consumption and the livestock industry. The observed seasonal variations in the concentrations of different types of antibiotics in PM_{2.5} may be associated with antibiotic consumption patterns (Wang et al., 2024a; Wang et al., 2024b). TCs and SAs are widely used in agriculture and livestock farming, particularly for disease prevention and growth promotion in animal husbandry (Pan et al., 2024). Spring marked a peak period for animal breeding in the livestock industry, and antibiotics may be released into the atmosphere through animal waste, agricultural

runoff, and soil interactions (Li et al., 2024).

3.2. Source apportionment of antibiotics

Considering the complexity of antibiotic emissions and their environmental pathways, we conducted a PMF analysis of antibiotic concentrations in $\text{PM}_{2.5}$ from Beijing and Shijiazhuang to identify the potential sources of antibiotic pollution in atmospheric $\text{PM}_{2.5}$. Because of data limitations, source apportionment was performed for the entire study area rather than distinguishing between individual cities. This approach was deemed appropriate because the antibiotic emission sources in $\text{PM}_{2.5}$ are likely consistent across various urban settings, which will minimize the impact of this methodological simplification. Antibiotics with DFs below 30 % were excluded to ensure the robustness of our analysis. Our PMF model identified the sources of 11 antibiotics (TC, OTC, DXC, CTC, OFL, ENR, TMP, SMX, TIL, TYL, and AZM). Three distinct factors were found to influence their concentrations in $\text{PM}_{2.5}$ (Fig. 3B).

Factor 1 was predominantly associated with pharmaceutical and medical waste emissions, which was indicated by high loadings for TIL (56 %), TYL (53 %), AZM (42 %), ENR (41 %), DXC (40 %), OFL (39 %), and OTC (39 %, Fig. 3B). TIL is mainly used to treat and prevent mycoplasma and other bacterial infections and is synthesized from the hydrolysate of TYL. The pharmaceutical manufacturing industry produces a wide range of drugs, and the concentration of TYL in mixed antibiotic wastewater can reach up to 200 mg/L (Chelliapan et al., 2006; Mu et al., 2024). Because of the widespread use of AZM, ENR, and OFL in the treatment of diseases, these compounds are frequently detected in pharmaceutical manufacturing (Guo et al., 2018; Orimolade et al., 2023). Additionally, OTC and DXC are present in high concentrations in pharmaceutical companies (Bavandpour et al., 2020; Scaria et al., 2021). Therefore, Factor 1 was attributed to pharmaceutical factories.

Factor 2 likely represents emissions from sewage treatment plants, as evidenced by high loadings for AZM (42 %), OFL (42 %), CTC (41 %), TC (40 %), and OTC (36 %, Fig. 3B). AZM is widely used to treat various bacterial infections in humans and is frequently detected in sewage

treatment plants because of its low removal efficiency (Hu et al., 2023b). During the COVID-19 pandemic, the concentration of AZM in urban sewage was reportedly 217 times that in previous years (Wu et al., 2024b). OFL, which primarily used for human purposes because its use in animals was banned in 2015, has a detection rate in sewage treatment plant effluent of nearly 100 % (Liu et al., 2024; Ministry of Agriculture and Rural Affairs, 2015). TC was one of the first antibiotics used in clinical medicine and is still used to treat more than 80 % of human diseases in China (Wang et al., 2023; Zhang QQ, 2015). OTC is used to treat human bacterial infections, although the dose for humans is approximately 25 % of that used for animals (Wang et al., 2023; Zhang et al., 2015a, 2015b). Residues of TCs, such as OTC, TC, and CTC, in wastewater from treatment plants typically occur at nanogram per liter levels (Chang et al., 2023). Moreover, studies have highlighted that OFL and OTC pose particularly high ecological risks in sewage treatment plants within the Beijing–Tianjin–Hebei region (Wang et al., 2024a). This indicates that the current treatment processes in most sewage treatment plants are ineffective at removing these antibiotics. Therefore, Factor 2 was closely associated with discharges from sewage treatment plants.

Factor 3 was attributed to livestock emissions, with high loadings for TMP (54 %) and SMX (52 %). SMX is a typical antibiotic used in both humans and animals, with over 90 % being widely used in animals (Hu et al., 2023a). Previous studies have shown that SMX is often added to animal feed to prevent and treat diseases in livestock and aquaculture (Zhang QQ, 2015). Additionally, SMX has been detected in atmospheric particulate matter samples from pig farm, with concentrations reaching up to 2.9 mg/kg (Hamscher et al., 2003). TMP is a synthetic antibiotic with broad-spectrum antimicrobial activity. It is often used in combination with SMX to enhance its effectiveness against pathogens, and is widely used in both humans and animals (Han et al., 2021). High detection rates and concentrations have been reported for TMP in wastewater from pig farms and breeding ponds (Wang et al., 2022a). Therefore, Factor 3 represented aquaculture and livestock industry sources.

We simulated the long-distance transport trajectories of air masses

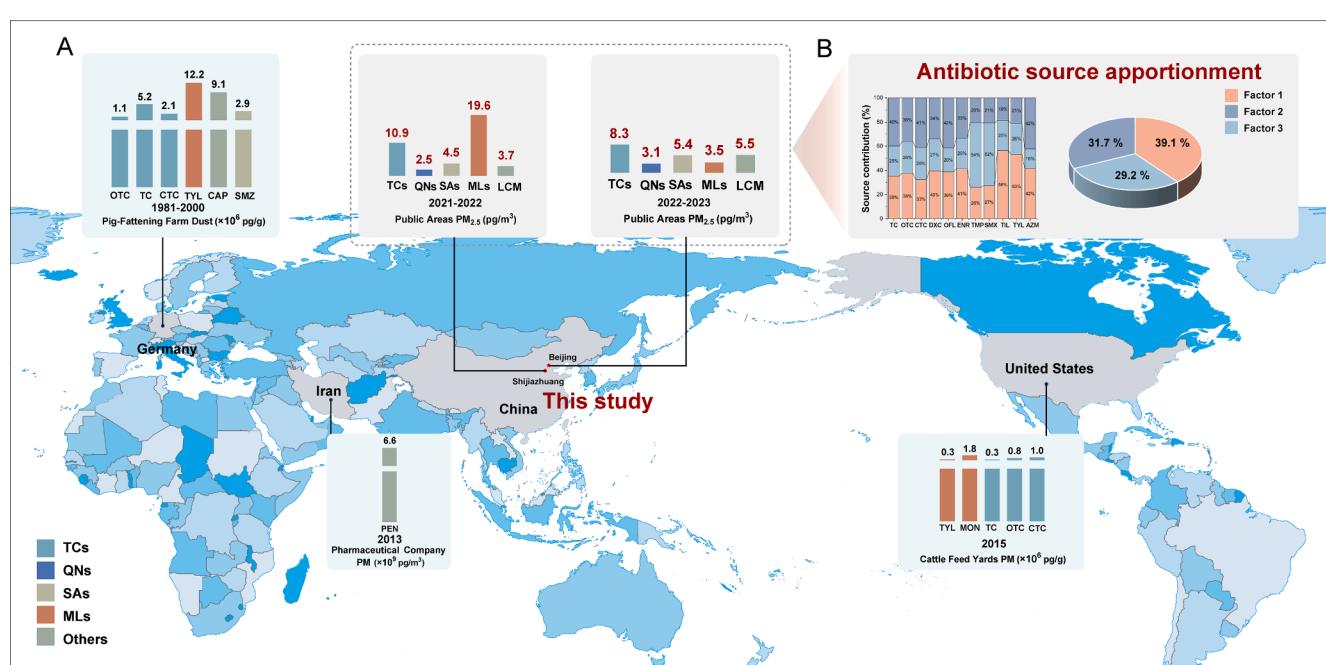


Fig. 3. Comparison and source profiles of antibiotic concentrations in $\text{PM}_{2.5}$. Comparison of mean antibiotic concentrations in airborne $\text{PM}_{2.5}$ from Beijing and Shijiazhuang with literature data (A). Detailed data used in the figure are compiled in Table S9. Source profiles of antibiotics derived from PMF model in airborne $\text{PM}_{2.5}$ (B). Abbreviations: CTC, chlortetracycline; OTC, oxytetracycline; TC, tetracycline; SMX, sulfamethoxazole; TYL, tylosin; CAP, chloramphenicol; MON, monensin; PEN, penicillin; SAs, sulfonamides; MLs, macrolides; QNs, quinolones; TCs, tetracyclines.

above the sampling point using the HYSPLIT model. The results showed that the atmospheric antibiotics in the urban region of Beijing and Shijiazhuang were primarily influenced by local, while the probability (1–10 %) of antibiotics transported from Russia or even farther regions was very low (Fig. S6). The PMF analysis highlights the significant contributions of pharmaceutical and medical waste, sewage treatment plants, and the livestock industry to the antibiotic concentrations in atmospheric PM_{2.5}. Effective management strategies targeting these sources are crucial for mitigating antibiotic pollution in urban environments. In winter and spring, health-related sources, particularly emissions from pharmaceutical factories and hospitals, were key contributors to the concentrations of antibiotics in PM_{2.5} in Beijing and Shijiazhuang, with a contribution of 39.1 % to the total detected antibiotic concentration (Fig. 3B). Urban wastewater and sewage treatment plant emissions were the second largest contributor, accounting for 31.7 % of the total concentration (Fig. 3B). The significant presence of pharmaceutical enterprises and hospitals in the Beijing–Tianjin–Hebei region underscores the regional importance of these sources, especially in urban centers like Beijing and Shijiazhuang, which house approximately 3,900 biomedical institutions. Shijiazhuang is home to China's largest antibiotic production base, North China Pharmaceutical Co., Ltd., which accounts for approximately 15 % of the national production of antibiotic active pharmaceutical ingredients (Zhao et al., 2023). The composition of antibiotics in PM_{2.5} is highly complex, with individual antibiotics having different uses, and this complicates source identification. This complexity necessitates comprehensive source apportionment and targeted mitigation strategies to effectively address antibiotic pollution in urban environments.

3.3. Relationships between antibiotics and environmental driving factors

Given that weather conditions influence phase partitioning,

dispersion, and accumulation of environmental pollutants, they ultimately affect the distribution and concentrations of these substances (Liu et al., 2018; Zhang et al., 2023). In our analysis of antibiotics with DFs of > 30 %, we analyzed correlations between their concentrations and gaseous pollutants (including the AQI, PM_{2.5}, PM₁₀, and SO₂, NO₂, CO, and O₃ mass concentrations) and meteorological factors (including the SUN, WS, RH, and TEMP). For each environmental factor with increasing standard deviations, the EWAS model was used to calculate the corresponding percent changes in antibiotic concentration estimates with 95 % confidence intervals. Additionally, a random forest model integrated these factors into 11 principal components to assess the key environmental factors affecting antibiotic concentrations in PM_{2.5}.

3.3.1. Relationships between antibiotics and atmospheric pollutants

In the present study, the atmospheric pollutants were positively correlated with most antibiotics (Fig. 4A). For instance, PM_{2.5} and PM₁₀ were significantly positively correlated with OTC, DXC, TMP, and TYL ($p < 0.05$). This could be explained by the role of particulate matter as a carrier for antibiotics, facilitating their transport over long distances. Due to its high surface area, particulate matter can adsorb antibiotics, allowing them to remain suspended in the air for longer periods (Wang et al., 2024a). Additionally, NO₂ showed significant correlations with OTC, CTC, DXC, OFL, ENR, TMP, TYL, and AZM ($p < 0.05$), and SO₂ showed similar correlations ($p < 0.05$, Fig. 4B). Although few studies have explored the correlations between antibiotics and gaseous pollutants, research from the Yangtze River Delta and Shanghai found positive correlations between gaseous pollutants such as SO₂, NO₂, and organic compounds attached to particulate matter (Hong et al., 2021; Zhang et al., 2023). These positive correlations may be explained by the affinity of PM's specific surface area to adsorb a wide range of harmful compounds (Zhang et al., 2023). Moreover, antibiotics and gaseous pollutants in the atmosphere may stem from common sources. The

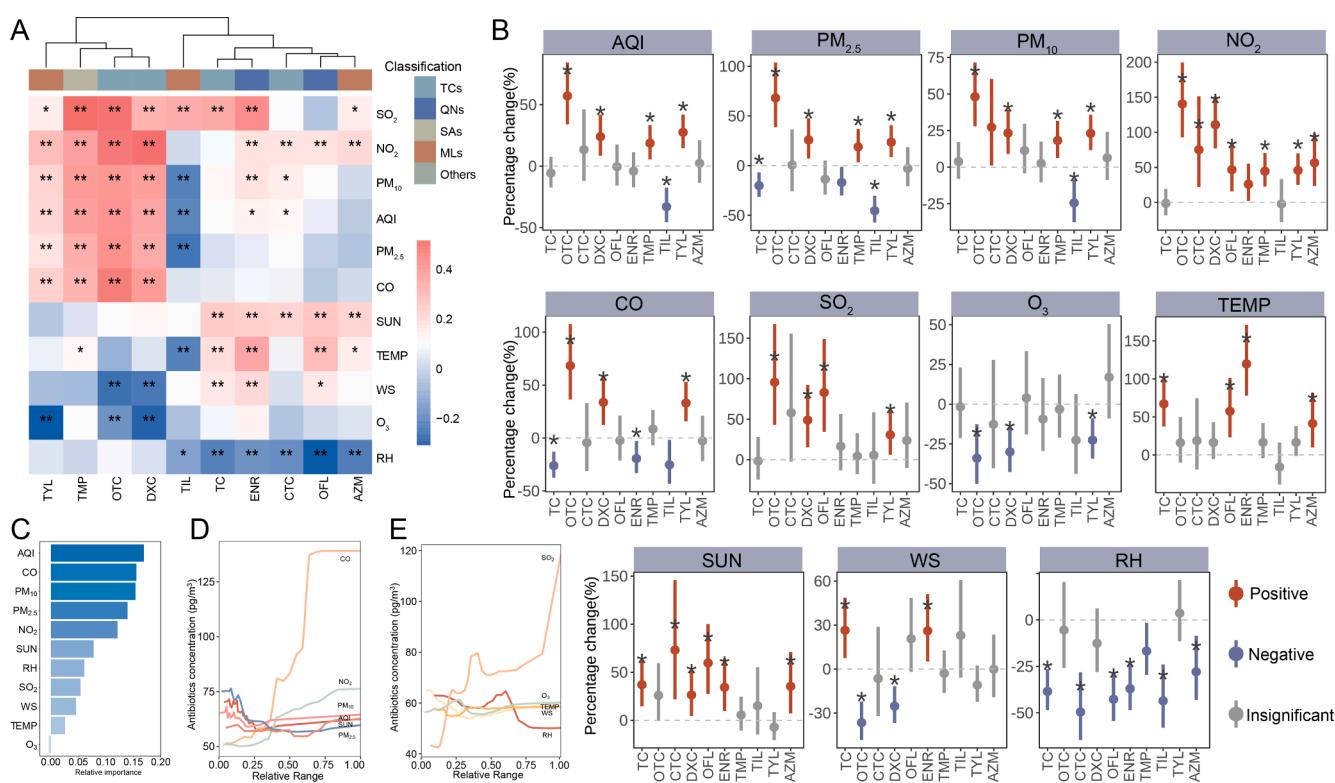


Fig. 4. Effects of environmental factors on antibiotic concentrations in PM_{2.5}. Correlation analysis illustrating the relationship between environmental factors and antibiotic concentrations in PM_{2.5} (A). Association of specific environmental factors with antibiotic concentrations in PM_{2.5} (B). The effects of environmental factors on antibiotic concentrations in PM_{2.5} (C) and the relative importance of principal components. Partial correlation analyses showing the top six (D) and bottom five (E) factors affecting antibiotic concentrations (* $p < 0.05$ and ** $p < 0.01$).

pharmaceutical industry, for example, could emit both antibiotic residues and gaseous pollutants (e.g., SO₂, NO₂, and CO) (Farshad et al., 2016). This suggests that air quality management should implement integrated measures to reduce the emissions of both particulate matter and gaseous pollutants, thereby mitigating the environmental risks of antibiotic contaminations. Interestingly, some antibiotics such as CTC, DXC, and TYL exhibited negative correlations with O₃ ($p < 0.05$, Fig. 4B). This phenomenon was likely due to a low concentration of O₃ caused by weakened photochemical reactions normally observed under conditions of high PM_{2.5} levels (Hong et al., 2021). Particulate matter reduces the photolysis rate by directly scattering or absorbing solar radiation, thereby reducing O₃ production (Chen et al., 2020; Qu et al., 2023). Remarkably, PM_{2.5}, PM₁₀, and TIL were negatively correlated with one another ($p < 0.05$). The Spearman's correlation coefficient between DXC and TIL was $r = -0.19$ ($p < 0.05$, Fig. S4), which suggested that DXC and TIL in PM_{2.5} might originate from different pollution sources.

3.3.2. Relationships between antibiotics and meteorological factors

Meteorological factors generally showed a negative correlation with most antibiotics (e.g., TYL, TIL, OTC, and DXC). Specific factors such as the TEMP, SUN, WS, and RH demonstrated distinct associations with certain antibiotics. The RH was negatively correlated with several antibiotics (e.g., TC, CTC, OFL, ENR, TIL, and AZM; $p < 0.05$) (Fig. 4B), which echoed previous findings that associated high RH with reduced concentrations of polycyclic aromatic hydrocarbons (Khan et al., 2018). RH is often associated with precipitation events, and a rise in RH may increase the probability of precipitation and lead to rain washout depositing large quantities of particulate matter at ground level and reducing airborne antibiotic concentrations (Zhang et al., 2024). Additionally, high RH may facilitate the absorption or adsorption of antibiotics onto particulate matter, potentially reducing the stability of these compounds in the air. The increased moisture could also promote microbial activity, thereby accelerating the degradation of antibiotics through microbial metabolism or hydrolysis processes (Wong, 2024). The concentrations of OTC and DXC presented a negative correlation with WS ($p < 0.05$, Fig. 4B). It revealed that PM_{2.5}-bound OTC and DXC were scavenged by the dilution of air flow under higher WS. By contrast, SUN was positively correlated with TC, CTC, DXC, OFL, ENR, and AZM ($p < 0.05$), and TEMP was positively correlated with TC, OFL, ENR, and AZM ($p < 0.05$). In contrast to some earlier studies, increasing temperature may alter the atmospheric meteorological conditions (e.g., the RH and WS), which will influence the transport and enrichment processes of antibiotics in the atmosphere and affecting their concentrations in PM_{2.5} (Chen et al., 2024).

To further elucidate the relative importance of environmental factors, we used a random forest model to quantify the effects of gaseous pollutants and meteorological factors on the total concentration of antibiotics in urban PM_{2.5}. The variability in the total antibiotic concentration was predominantly controlled by the gaseous pollutant (75.8 %) principal component, which mainly represented the contributions of the AQI, CO, PM₁₀, and PM_{2.5} (Fig. 4C). By contrast, SUN (7.5 %) and RH (5.8 %) had relatively minor effects (Fig. 4C). These findings underscore the complex interplay between air quality and the presence of antibiotics in the atmosphere. The analysis further demonstrated correlations between antibiotic concentrations and most environmental factors (Fig. 4D and 4E). Notably, CO stands out with the highest relative importance, indicating a potential direct or indirect linkage between CO levels and the presence of antibiotics in PM_{2.5} ($p < 0.05$; Fig. 4C and 4D). This might be because CO and certain antibiotics have common sources, such as industrial emissions. These results prompt further investigation into the dynamic interactions between air quality, meteorological factors, and antibiotic distributions, which are crucial for understanding pollution control and environmental health strategies.

3.4. Health risks of antibiotics in PM_{2.5} through inhalation exposure

Exposure to antibiotics through the daily inhalation of PM_{2.5} can lead to long-term exposure to a broad spectrum of antibiotic residues at various concentrations. For the first time, to comprehensively understand the health risks associated with antibiotic exposures via PM_{2.5}, we evaluated the EDIs of antibiotics through inhalation of PM_{2.5} for children (0–6 years, 6–12 years, 12–15 years, and 15–18 years) and adults in Beijing and Shijiazhuang. Using Monte Carlo simulations, we conducted 10,000 simulations to assess the health risks from antibiotic residues by comparing the daily intakes with the ADIs. The EDIs and HIs were consistent across different age groups, yet the median EDIs and HIs for children aged 0–6 years were relatively higher than those for any other age group (EDI: 102.81 pg/kg/day; microbiological HI: 9.38×10^{-5} ; toxicological HI: 3.34×10^{-6} , Fig. 5A, 5B, and 5C). The median EDI for children aged 0–6 years was approximately 2.0 times that for adults. This result suggests that young children are at higher risk from exposure to antibiotics during a critical developmental period. This difference could be attributed to the children's underdeveloped physiology and different behavioral patterns (Ferguson et al., 2017; Wang et al., 2018). Although the ingestion of antibiotics via food and drinking water remains the primary route of human exposure rather than inhalation of PM_{2.5} (drinking water: 4,000–16,000 pg/kg/day; food: 7,300–260,000 pg/kg/day), it is crucial to evaluate the health risks associated with inhaling antibiotics (Ben et al., 2020; Ben et al., 2022). For individual antibiotics, the top three in terms of toxicological HQs were OFL (2.05×10^{-5}), ENR (2.22×10^{-6}), and DXC (2.05×10^{-7} , Fig. S7). Meanwhile, for the microbiological HQs, the top three compounds were AZM (7.21×10^{-6}), ENR (6.61×10^{-6}), and OFL (3.84×10^{-6} , Fig. S8). Like in other studies, the HQs and HIs in our study were well below one, which indicates that, in most cases, residents in Beijing and Shijiazhuang will not face appreciable toxicological and microbiological risks through inhalation of PM_{2.5}.

The correlation between antibiotic concentrations and environmental factors showed that the AQI had the highest relative importance for the antibiotic concentration in PM_{2.5}. Furthermore, we evaluated the impact of the AQI on toxicological and microbiological HIs using the Kruskal-Wallis H test for multiple comparative analyses (Fig. 5D and 5E). The toxicological HIs showed a statistically significant increase at AQI levels of 50–100 and 100–150, with the largest increase occurring at 100–150 ($p < 0.05$). Similarly, the microbiological HIs showed a significant increase at AQI levels of 100–150 ($p < 0.05$). However, no significant increases in either toxicological or microbiological HIs were observed for AQI > 150. These findings indicate that the toxicological and microbiological HIs for antibiotics in PM_{2.5} show significant increases particularly in the AQI range of 100–150. This points to a higher risk of exposure to these substances during periods of moderate air pollution. This pattern suggests a threshold effect, where beyond an AQI of 150, an increase in pollution does not correspond to higher hazard indices, potentially because of a saturation or interference from different environmental factors.

However, considering that exposure to antibiotics through inhalation is lifelong, it is crucial to adequately address the risk of human exposure through this route. This study contributes additional evidence for risk assessment of airborne antibiotics. It should be noted that because of the lack of toxicological and microbiological data on antibiotic inhalation exposure, we used the toxicological and microbiological ADIs for oral exposure to antibiotics in this study. Consequently, the exposure risk may be underestimated. Therefore, further refined and accurate assessments of the potential risks of antibiotic inhalation exposure are warranted.

4. Study limitations

Our study has several limitations. First, the study was conducted within a restricted sampling period, focusing only on winter and spring.

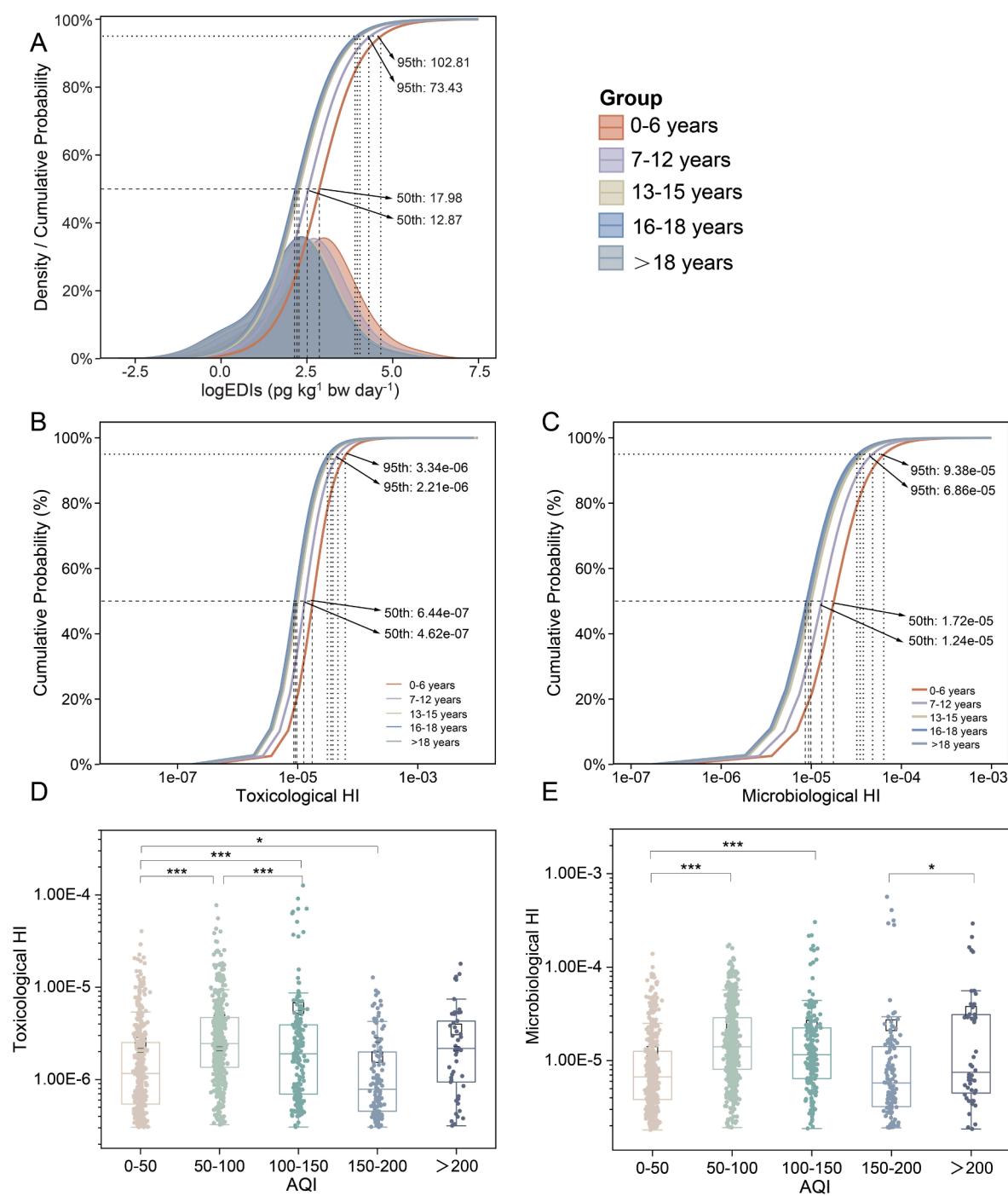


Fig. 5. Estimated daily intakes (EDIs) and hazard indexes (HIs) of antibiotics across different age groups via inhalation of $\text{PM}_{2.5}$. Probability density distribution of the estimated daily antibiotic intake for different age groups (A). Toxicological (B) and microbiological (C) HIs for different age groups resulting from antibiotic inhalation via $\text{PM}_{2.5}$. Effects of the air quality index (AQI) on toxicological (D) and microbiological (E) HIs of children aged 0–6 years (* $p < 0.05$, ** $p < 0.01$ and *** $p < 0.001$).

This narrow timeframe may not fully capture the year-round variations in antibiotic concentrations in $\text{PM}_{2.5}$. Additionally, the limited range of meteorological factors (e.g., TEMP, RH, SUN, and WS) during winter and spring might not have been sufficient to clearly elucidate the relationship between antibiotic concentrations and these atmospheric conditions. Future studies should consider a more comprehensive sampling period to better understand how seasonal fluctuations in meteorological conditions influence antibiotic concentrations in $\text{PM}_{2.5}$. Second, our study did not analyze the influence of other atmospheric components (e.g., sulfates and nitrates) on the occurrence and behavior of antibiotics in

$\text{PM}_{2.5}$, which somewhat limits the identification of key environmental factors affecting atmospheric antibiotic concentrations. Third, while our study identified several common antibiotics in $\text{PM}_{2.5}$, it did not explore the chemical transformations or degradation pathways of these antibiotics in the atmosphere. Future studies should consider investigating the transformation products of antibiotics and their potential environmental impacts. Fourth, potential biases in source attribution due to uncertainties in source profiles and co-emissions may affect the robustness and accuracy of the estimated contributions. Additionally, the limited seasonal coverage of the study restricted the analysis of seasonal

variations in source contributions, introducing further uncertainty in the source apportionment. Future studies should aim to address these limitations by integrating more comprehensive datasets, conducting continuous sampling across different seasons, and applying advanced modeling approaches to improve the accuracy and reliability of source attribution.

5. Conclusions and implications

This study is the first to provide a detailed description of the spatiotemporal distributions, sources, environmental driving factors, and inhalation exposure risks of antibiotics in atmospheric PM_{2.5} from two metropolitan cities in China. The results provide a basis for regional pollution control and development of antibiotic emission policies. A total of 25 antibiotics were ubiquitously detected in PM_{2.5}, with concentrations ranging from 0.9 to 774.7 pg/m³. These compounds were predominantly TCs and MLs. Pharmaceutical factories, sewage treatment plants, and livestock emissions were the main sources, with pharmaceutical factories having the highest contributions. The concentrations of antibiotics in PM_{2.5} were significantly correlated with particulate matters, gaseous pollutants and meteorological factors. More specifically, particulate matters (PM_{2.5} and PM₁₀) and gaseous pollutants (CO, SO₂, and NO₂) showed positive correlations with antibiotic concentrations, while meteorological factors, especially the RH, showed negative correlations with the concentrations. Risk assessment analysis indicated that the EDI of antibiotics for children was higher than that for adults; although, the overall health risks of antibiotic exposure through inhalation of PM_{2.5} remained low. However, the data and knowledge required to comprehensively characterize the overall risks of antibiotic residue exposures are limited. To better understand the potential adverse health effects of such exposure, a systematic approach is needed, particularly for assessing human exposure to antibiotics through different exposure pathways. This study addresses a critical knowledge gap by providing insights into the antibiotic profiles present in PM_{2.5} from Chinese metropolitan cities, which significantly advances our understanding of the contamination status, sources, driving factors, and potential risks of antibiotics within PM_{2.5}. The findings not only provide suggestions for future research but also offer practical guidance and technical references for policymakers and stakeholders in the fields of antibiotic management and pollution control. These insights may inform evidence-based strategies to effectively mitigate the risks posed by antibiotic residues to public health and the environment, ultimately contributing to improved air quality and sustainable environmental practices.

CRediT authorship contribution statement

Juan Liu: Writing – review & editing, Writing – original draft, Software, Formal analysis, Data curation, Conceptualization. **Qiao Yao:** Software, Data curation. **Wenyan Yan:** Writing – original draft, Formal analysis, Data curation. **Ke Fang:** Methodology, Data curation. **Runming He:** Methodology, Data curation. **Xiaona Wang:** Methodology, Data curation. **Yu'e Cha:** Methodology, Data curation. **Xiaoyan Yang:** Methodology, Data curation. **Wen Gu:** Methodology, Data curation. **Chao Wang:** Methodology, Data curation. **Yifu Lu:** Methodology, Data curation. **Mingyu Zhao:** Methodology, Data curation. **Yujie Ben:** Writing – review & editing. **Kai Wang:** Writing – review & editing. **Zhaomin Dong:** Writing – review & editing. **Rong Zhang:** Writing – review & editing. **Hong Chang:** Writing – review & editing. **Song Tang:** Writing – review & editing, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envint.2025.109340>.

Data availability

No data was used for the research described in the article.

References

- Agency, U.E.P., 2014. Definition and Procedure for the Determination of the Method Detection Limit, Revision 2. <https://www.epa.gov/cwa-methods> (accessed 29 December 2024).
- Bavandpour, R., Rajabi, M., Karimi-Maleh, H., 2020. Ultrasensitive electroanalytical sulfisoxazole sensors amplified with Pd-doped ZnO nanoparticles and modified with 1-hexyl-3-methyl imidazolium bis(trifluoromethylsulfonyl)imide. *New J. Chem.* 44, 11125–11130.
- Ben, Y., Fu, C., Hu, M., Liu, L., Wong, M.H., Zheng, C., 2019. Human health risk assessment of antibiotic resistance associated with antibiotic residues in the environment: a review. *Environ Res.* 169, 483–493.
- Ben, Y., Hu, M., Zhang, X., Wu, S., Wong, M.H., Wang, M., Andrews, C.B., Zheng, C., 2020. Efficient detection and assessment of human exposure to trace antibiotic residues in drinking water. *Water Res.* 175, 115699.
- Ben, Y., Hu, M., Zhong, F., Du, E., Li, Y., Zhang, H., Andrews, C.B., Zheng, C., 2022. Human daily dietary intakes of antibiotic residues: dominant sources and health risks. *Environ Res.* 212, 113387.
- Chang, D., Mao, Y., Qiu, W., Wu, Y., Cai, B., 2023. The source and distribution of tetracycline antibiotics in China: a review. *Toxics.* 11, 214.
- Chelliapan, S., Wilby, T., Sallis, P.J., 2006. Performance of an up-flow anaerobic stage reactor (UASR) in the treatment of pharmaceutical wastewater containing macrolide antibiotics. *Water Res.* 40, 507–516.
- Chen, Z., Chen, D., Zhao, C., Kwan, M.P., Cai, J., Zhuang, Y., Zhao, B., Wang, X., Chen, B., Yang, J., Li, R., He, B., Gao, B., Wang, K., Xu, B., 2020. Influence of meteorological conditions on PM_{2.5} concentrations across China: a review of methodology and mechanism. *Environ Int.* 139, 105558.
- Chen, Y.R., Duan, Y.P., Zhang, Z.B., Gao, Y.F., Dai, C.M., Tu, Y.J., Gao, J., 2024. Comprehensive evaluation of antibiotics pollution the Yangtze River basin, China: emission, multimedia fate and risk assessment. *J Hazard Mater.* 465, 133247.
- Chen, Y., Jiang, C., Wang, Y., Song, R., Tan, Y., Yang, Y., Zhang, Z., 2022. Sources, environmental fate, and ecological risks of antibiotics in sediments of Asia's longest river: a whole-basin investigation. *Environ Sci Technol.* 56, 14439–14451.
- Chowdhury, S., Pozzer, A., Haines, A., Klingmüller, K., Münnel, T., Paasonen, P., Sharma, A., Venkataraman, C., Lelieveld, J., 2022. Global health burden of ambient PM_{2.5} and the contribution of anthropogenic black carbon and organic aerosols. *Environ Int.* 159, 107020.
- Cohen, A.J., Brauer, M., Burnett, R., Anderson, H.R., Frostad, J., Estep, K., Balakrishnan, K., Brunekreef, B., Dandona, L., Dandona, R., Feigin, V., Freedman, G., Hubbell, B., Jobling, A., Kan, H., Knibbs, L., Liu, Y., Martin, R., Morawska, L., Pope 3rd, C.A., Shin, H., Straif, K., Shaddick, G., Thomas, M., van Donkelaar, A., Vos, T., Murray, C.J.L., Forouzanfar, M.H., 2017. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. *Lancet.* 389, 1907–1918.
- Ding, F., Li, Y., He, T., Ou, D., Huang, Y., Yin, G., Yang, J., Wu, S., He, E., Liu, M., 2024. Urban agglomerations as an environmental dimension of antibiotics transmission through the “One Health” lens. *J Hazard Mater.* 465, 133283.
- Farshad, A.A., Enferadi, M., Bakand, S., Jamshidi Orak, R., Mirkazemi, R., 2016. Penicillin dust exposure and penicillin resistance among pharmaceutical workers in Tehran, Iran. *Int. J. Occup. Environ. Health.* 22, 218–223.
- Feng, L., Cheng, Y., Zhang, Y., Li, Z., Yu, Y., Feng, L., Zhang, S., Xu, L., 2020. Distribution and human health risk assessment of antibiotic residues in large-scale drinking water sources in Chongqing area of the Yangtze River. *Environ Res.* 185, 109386.

- Ferguson, A., Penney, R., Solo-Gabriele, H., 2017. A review of the field on children's exposure to environmental contaminants: a risk assessment approach. *Int. J. Environ. Res. Public Health* 14, 265.
- Fu, J., Jiang, D., Lin, G., Liu, K., Wang, Q., 2015. An ecological analysis of PM_{2.5} concentrations and lung cancer mortality rates in China. *BMJ Open* 5, e009452.
- Guo, Z.-F., Boeing, W.J., Xu, Y.-Y., Borgomeo, E., Liu, D., Zhu, Y.-G., 2023. A systematic workflow of data mining confirms widespread occurrence of antibiotic contamination in freshwater reservoirs. *Exposure and Health* 15, 889–901.
- Guo, N., Wang, Y., Tong, T., Wang, S., 2018. The fate of antibiotic resistance genes and their potential hosts during bio-electrochemical treatment of high-salinity pharmaceutical wastewater. *Water Res* 133, 79–86.
- Hamscher, G., Pawelzick, H.T., Szczesny, S., Nau, H., Hartung, J., 2003. Antibiotics in dust originating from a pig-fattening farm: a new source of health hazard for farmers? *Environ Health Perspect* 111, 1590–1594.
- Han, Q.F., Song, C., Sun, X., Zhao, S., Wang, S.G., 2021. Spatiotemporal distribution, source apportionment and combined pollution of antibiotics in natural waters adjacent to mariculture areas in the Laizhou Bay, Bohai Sea. *Chemosphere* 279, 130381.
- Hong, Y., Xu, X., Liao, D., Ji, X., Hong, Z., Chen, Y., Xu, L., Li, M., Wang, H., Zhang, H., Xiao, H., Choi, S.-D., Chen, J., 2021. Air pollution increases human health risks of PM_{2.5}-bound PAHs and nitro-PAHs in the Yangtze River Delta, China. *Sci Total Environ.* 770, 145402.
- Hu, J., Li, S., Zhang, W., Helbling, D.E., Xu, N., Sun, W., Ni, J., 2023a. Animal production predominantly contributes to antibiotic profiles in the Yangtze River. *Water Res.* 242, 120214.
- Hu, J., Lyu, Y., Chen, H., Li, S., Sun, W., 2023b. Suspect and nontarget screening reveal the underestimated risks of antibiotic transformation products in wastewater treatment plant effluents. *Environ Sci Technol.* 57, 17439–17451.
- Huang, X., Tang, G., Zhang, J., Liu, B., Liu, C., Zhang, J., Cong, L., Cheng, M., Yan, G., Gao, W., Wang, Y., Wang, Y., 2021. Characteristics of PM_{2.5} pollution in Beijing after the improvement of air quality. *J Environ Sci (china)* 100, 1–10.
- Jiang, X., Han, Y., Qiu, X., Chai, Q., Zhang, H., Chen, X., Cheng, Z., Wang, Y., Fan, Y., Xue, T., Li, W., Gong, J., Zhu, T., 2021. Organic components of personal PM_{2.5} exposure associated with inflammation: evidence from an untargeted exposomic approach. *Environ Sci Technol.* 55, 10589–10596.
- Khan, M.B., Masoli, M., Bruno, C., Pasqualeto, A., Formenton, G.M., Agostinelli, C., Pavoni, B., 2018. Potential sources and meteorological factors affecting PM_{2.5}-bound polycyclic aromatic hydrocarbon levels in six main cities of northeastern Italy: an assessment of the related carcinogenic and mutagenic risks. *Environ Sci Pollut Res Int.* 25, 31987–32000.
- Li, Y., Bai, X., Ren, Y., Gao, R., Ji, Y., Wang, Y., Li, H., 2022b. PAHs and nitro-PAHs in urban Beijing from 2017 to 2018: characteristics, sources, transformation mechanism and risk assessment. *J Hazard Mater.* 436, 129143.
- Li, J., Li, W., Liu, K., Guo, Y., Ding, C., Han, J., Li, P., 2022a. Global review of macrolide antibiotics in the aquatic environment: sources, occurrence, fate, ecotoxicity, and risk assessment. *J Hazard Mater.* 439, 129628.
- Li, S., Zhu, Y., Zhong, G., Huang, Y., Jones, K.C., 2024. Comprehensive assessment of environmental emissions, fate, and risks of veterinary antibiotics in China: an environmental fate modeling approach. *Environ. Sci. Technol.* 58, 5534–5547.
- Liu, L.S., Guo, Y.T., Wu, Q.Z., Zeeshan, M., Qin, S.J., Zeng, H.X., Lin, L.Z., Chou, W.C., Yu, Y.J., Dong, G.H., Zeng, X.W., 2023. Per- and polyfluoroalkyl substances in ambient fine particulate matter in the Pearl River Delta, China: levels, distribution and health implications. *Environ Pollut.* 334, 122138.
- Liu, J., Yang, F., Cai, Y., Lu, G., Li, Y., Li, M., Fan, L., Gao, L., 2024. Unveiling the existence and ecological hazards of trace organic pollutants in wastewater treatment plant effluents across China. *Eco Environ Health.* 3, 21–29.
- Li, Y., Yu, Y., Liu, M., Lu, M., Ge, R., Li, S., Liu, X., Dong, W., Qadeer, A., 2018. Characterization and source identification of PM_{2.5}-bound polycyclic aromatic hydrocarbons (PAHs) in different seasons from Shanghai, China. *Sci Total Environ.* 644, 725–735.
- Luo, X., Han, S., Wang, Y., Du, P., Li, X., Thai, P.K., 2024. Significant differences in usage of antibiotics in three Chinese cities measured by wastewater-based epidemiology. *Water Res.* 254, 121335.
- McEachran, A.D., Blackwell, B.R., Hanson, J.D., Wooten, K.J., Mayer, G.D., Cox, S.B., Smith, P.N., 2015. Antibiotics, bacteria, and antibiotic resistance genes: aerial transport from cattle feed yards via particulate matter. *Environ Health Perspect.* 123, 337–343.
- Ministry of Agriculture and Rural Affairs, P.R., China, 2015. List of the prohibition of drugs and other compounds in food animals. https://www.moa.gov.cn/govpublic/SYJ/201509/20150907_4819267.htm (accessed 1 January 2025).
- Mu, Y., Tang, B., Cheng, X., Fu, Y., Huang, W., Wang, J., Ming, D., Xing, L., Zhang, J., 2024. Source apportionment and predictable driving factors contribute to antibiotics profiles in Changshou Lake of the Three Gorges Reservoir area, China. *J. Hazard Mater.* 466, 133522.
- Orimolade, B.O., Oladipo, A.O., Idris, A.O., Ujisipho, F., Azizi, S., Maaza, M., Lebelo, S. L., Mamba, B.B., 2023. Advancements in electrochemical technologies for the removal of fluoroquinolone antibiotics in wastewater: a review. *Sci Total Environ.* 881, 163522.
- Pan, Z., Yang, S., Zhao, L., Li, X., Weng, L., Sun, Y., Li, Y., 2021. Temporal and spatial variability of antibiotics in agricultural soils from Huang-Huai-Hai Plain, northern China. *Chemosphere.* 272, 129803.
- Pan, Y., Zeng, J., Zhang, L., Hu, J., Hao, H., Zeng, Z., Li, Y., 2024. The fate of antibiotics and antibiotic resistance genes in large-scale chicken farm environments: preliminary view of the performance of national veterinary antimicrobial use reduction action in Guangdong, China. *Environ Int.* 191, 108974.
- Qu, Y., Wang, T., Yuan, C., Wu, H., Gao, L., Huang, C., Li, Y., Li, M., Xie, M., 2023. The underlying mechanisms of PM_{2.5} and O₃ synergistic pollution in East China: photochemical and heterogeneous interactions. *Sci Total Environ.* 873, 162434.
- Scaria, J., Anupama, K.V., Nidheesh, P.V., 2021. Tetracyclines in the environment: An overview on the occurrence, fate, toxicity, detection, removal methods, and sludge management. *Sci Total Environ.* 771, 145291.
- Schlesinger, R.B., 2007. The health impact of common inorganic components of fine particulate matter (PM_{2.5}) in ambient air: a critical review. *Inhal Toxicol.* 19, 811–832.
- Statistics, N.B.o., 2024. Statistical Bulletin of the People's Republic of China on National Economic and Social Development, 2023.
- Tiseo, K., Huber, L., Gilbert, M., Robinson, T.P., Van Boeckel, T.P., 2020. Global trends in antimicrobial use in food animals from 2017 to 2030. *Antibiotics (Basel)* 9, 918.
- Wang, C., Mao, Y., Zhou, W., Li, Y., Zou, G., Chen, B., Wang, Z., 2023. Inhomogeneous antibiotic distribution in sediment profiles in anthropogenically impacted lakes: source apportionment, fate drivers, and risk assessment. *J Environ Manage.* 341, 118048.
- Wang, L., Wang, Y., Li, H., Zhu, Y., Liu, R., 2022a. Occurrence, source apportionment and source-specific risk assessment of antibiotics in a typical tributary of the Yellow River basin. *J Environ Manage.* 305, 114382.
- Wang, Y., Wang, L., Liu, R., Li, L., Cao, L., Jiao, L., Xia, X., 2022b. Source-specific risk apportionment and critical risk source identification of antibiotic resistance in Fenhe River basin, China. *Chemosphere* 287, 131997.
- Wang, X., Wang, J., Niu, Z., 2024b. Modelling based study on the occurrence characteristics and influencing factors of the typical antibiotics in Bohai Bay. *Sci Total Environ.* 906, 167853.
- Wang, B., Xu, Z., Dong, B., 2024a. Occurrence, fate, and ecological risk of antibiotics in wastewater treatment plants in China: a review. *J Hazard Mater.* 469, 133925.
- Wang, P., Zhao, N., Cui, Y., Jiang, W., Wang, L., Wang, Z., Chen, X., Jiang, L., Ding, L., 2018. Short-chain chlorinated paraffin (SCCP) pollution from a CP production plant in China: dispersion, congener patterns and health risk assessment. *Chemosphere* 211, 456–464.
- WHO, 2019. New report calls for urgent action to avert antimicrobial resistance crisis. <https://www.who.int/news/item/29-04-2019-new-report-calls-for-urgent-action-to-avert-antimicrobial-resistance-crisis> (accessed 30 December 2024).
- WHO, 2021. What are the WHO Air quality guidelines? <https://www.who.int/news-room/feature-stories/detail/what-are-the-who-air-quality-guidelines> (accessed 30 December 2024).
- Wong, C., 2024. Antibiotic resistance is a growing threat – is climate change making it worse? *Nature.*
- Wu, H., Bin, L., Guo, P., Zhao, Y., Chen, C., Chen, Z., Tang, B., 2024b. Ecological risk assessment of the typical anti-epidemic drugs in the Pearl River Delta by tracing their source and residual characteristics. *J Hazard Mater.* 463, 132914.
- Wu, C., He, G., Wu, W., Meng, R., Zhou, C., Bai, G., Yu, M., Gong, W., Huang, B., Xiao, Y., Hu, J., Xiao, J., Zeng, F., Yang, P., Liu, D., Zhu, Q., Chen, Z., Yu, S., Huang, C., Du, Y., Liang, X., Liu, T., Ma, W., 2024a. Ambient PM_{2.5} and cardiopulmonary mortality in the oldest-old people in China: a national time-stratified case-crossover study. *Med.* 5, 62–72.e63.
- Xu, L., Zhang, H., Xiong, P., Zhu, Q., Liao, C., Jiang, G., 2021. Occurrence, fate, and risk assessment of typical tetracycline antibiotics in the aquatic environment: a review. *Sci Total Environ.* 753, 141975.
- Zhang, S., Chen, W., 2022. Assessing the energy transition in China towards carbon neutrality with a probabilistic framework. *Nat Commun.* 13, 87.
- Zhang, Q.Q., Y.G., Pan, C.G., Liu, Y.S., Zhao, J.L., 2015. Comprehensive evaluation of antibiotics emission and fate in the river basins of China: source analysis, multimedia modeling, and linkage to bacterial resistance. *Environ. Sci. Technol.* 11, 6772–6782.
- Zhang, X., Wang, Q., Qiu, T., Tang, S., Li, J., Giesy, J.P., Zhu, Y., Hu, X., Xu, D., 2019. PM_{2.5} bound phthalates in four metropolitan cities of China: Concentration, seasonal pattern and health risk via inhalation. *Sci Total Environ.* 696, 133982.
- Zhang, X., Diao, Z., Ma, H., Xie, X., Wang, Y., Liu, X., Yuan, X., Zhu, F., 2023. Multi-class organic pollutants in PM_{2.5} in mixed area of Shanghai: Levels, sources and health risk assessment. *Sci. Total Environ.* 903, 166352.
- Zhang, Q.Q., Ying, G.G., Pan, C.G., Liu, Y.S., Zhao, J.L., 2015b. Comprehensive evaluation of antibiotics emission and fate in the river basins of China: source analysis, multimedia modeling, and linkage to bacterial resistance. *Environ. Sci. Technol.* 49, 6772–6782.
- Zhang, W., Zhou, T., Wu, P., 2024. Anthropogenic amplification of precipitation variability over the past century. *Science* 385, 427–432.
- Zhao, X., Chen, H., Zhao, B., Song, Y., Mengqi, L., Jiansheng, C., Zhang, L., Li, S., 2023. Spatial-temporal Distribution and Risk Assessment of Quinolones Antibiotics in Soil of Shijiazhuang City Environmental Science (China). 44, 2223–2233.