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Risk assessment of heavy metal pollution in agricultural soil surrounding a typical pharmaceutical manufacturing complex

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The identification and effective control of pollution sources is essential because heavy metal pollution in agricultural soil is associated with food safety and public health. Industrial wastewater, waste gas, and residues generated from pharmaceutical manufacturing are important sources of heavy metal pollutants in soil, but the research of their risk for surrounding agricultural soil is inadequate. In this study, the typical pharmaceutical manufacturing complex and its surrounding farmland in Hubei Province, China was employed to systematically and comprehensively assess its environmental risk and source apportionment. The results revealed the potential risk of cadmium (Cd), lead (Pb), arsenic (As), and mercury (Hg) from pharmaceutical production for farmland soil around, and among these heavy metals, As and Cd were observed to have the higher pollution level. The accumulated Cd and As had contribution to a series of risks, including comprehensive pollution risk, geo-accumulation risk, potential ecological risk, and the carcinogenic and non-carcinogenic risk. Positive matrix factorization (PMF) source analysis combining with the geographic distribution of heavy metal surrounding pharmaceutical manufacturing confirmed that there were three main heavy metal pollution sources, including pharmaceutical wastewater, traffic, and agricultural chemicals, which had the 52.37%, 16.49%, and 31.14% contributions to the surrounding agricultural soil. The present study provided systematic strategies of environment risk assessment and source apportionment, and can be referred for casual analysis and prevention strategies for farmland soil surrounding pharmaceutical manufacturing complex.

KEYWORDS

heavy metal, soil, pharmaceutical manufacturing, risk assessment, source apportionment analysis

1 Introduction

The heavy metal pollution in soil has been causing great risk for public health. National survey report of China's soil environmental quality in 2014 showed that 16.1% of total soil samples and 19.4% of agricultural soils were polluted by heavy metals, particularly for Cd, Pb, As, Hg, Cr, with over-standard rates of 7.0%, 1.5%, 2.7%, 1.6%, 1.1%, respectively (MEE, 2014). China, with a large population base, has created a huge demand for public medical care (Hu et al., 2019). Pharmaceutical companies scattered throughout China that produce massive amounts of industrial by-products such as wastewater, gas, and residues. Just as previous reported, heavy metals, such as cadmium (Cd) and mercury (Hg), are key potential typical pollutants of the pharmaceutical industry (Wang et al., 2019; Yang et al., 2020; Luo et al., 2021; Duan et al., 2022). Therefore, pharmaceutical manufacturing complex might have potential pollution risk surrounding agricultural soil. Although the emission of industrial by-products has been regarded as the major potential sources of heavy metal pollution in agricultural soil, the potential risk of heavy metal pollution for surrounding agricultural soil during pharmaceutical production has not been systematically explored.

The assessment approaches such as single factors, the Nemerow integrated pollution index, geo-accumulation index, potential ecological risk, and human health risk are commonly employed to evaluate the risk of heavy metal pollution in soil (Kang et al., 2020; Li et al., 2014; Ren et al., 2021; Chen et al., 2022). The Nemerow integrated pollution index reflects the combined pollutive effects of various heavy metals, while the geo-accumulation index reflects the risk of heavy metal accumulation in soil. Moreover, the potential ecological risk assessment determines the ecological risk of heavy metal pollution in soil, and the human health risk assessment focuses on risk to human health caused by heavy metals pollution in soil (Guston et al., 2014; Health, U.S.E.P.A.O.o. and Group, E.A.E.A., 1989; Muller, 1979; Nemerow, 1974; Zhou et al., 2022; Chen et al., 2021). However, the systematic risk of heavy metals cannot be effectively reflected only by referring to a single risk assessment method described above, it is essential to integrate these approaches for evaluating the environmental risk of heavy metals.

Heavy metal pollution risk assessment describes the current status of heavy metal pollution in soil, and pollution source analysis is regarded as necessary to identify and quantify heavy metal pollution sources. Due to the limited data about heavy metal pollution emission sources in China and the difficulty of accurately describing heavy metal migration, the receptor model of pollutants has been widely applied to source analyses of heavy metals in soil because it does not require either information about the composition of various pollution sources or specification of how emission factors are transported (Li et al., 2014; Huang et al., 2018). The reportedly main source analytical methods of the receptor model included chemical mass balance (CMB), positive matrix factorization (PMF), and the UNIX model. Among them, PMF was the most frequently applied to analyze sources of heavy metal pollution in agricultural soil (Lee et al., 2016; Jiang et al., 2017; Liang et al., 2017). In order to fully understand the current pollution level and source of heavy metal in agricultural soil surrounding pharmaceutical manufacturing complexes, it is essential to perform systematic assessment and source analysis in agricultural soil around pharmaceutical manufacturing complexes.

Here, we analyzed the heavy metal contents of soil samples in pharmaceutical manufacturing complexes and its surrounding farmland soil in Hubei Province, China. The main objectives were to determine the accumulation risk and potential ecological risk of heavy metal, characterize the human health risk, and identify the potential sources of heavy metal pollution. We explored the relationship between heavy metal pollution in pharmaceutical manufacturing complexes and its surrounding agricultural soil, and assessed the potential risk of heavy metal pollution to agricultural soil caused by a typical pharmaceutical manufacturing complex. The findings of this study aimed to provide a reference methodology for risk assessment and pollution sources identification of heavy metal in agricultural soil surrounding typical pharmaceutical manufacturing complexes.

2 Materials and methods

2.1 Survey area information and soil sampling

A typical pharmaceutical complex in Hubei Province established in 2009 mainly produced chemical intermediates and active pharmaceutical ingredients (APIs). Due to the poor management of production during the early stage and the lack of environmental monitoring, industrial wastewater and waste residue generated by the complex were not appropriately treated. Surface soil in some areas existed heavy metal pollution. The pharmaceutical plant covers an area of ~188,304 m^2 surrounded by ~ 680,000 m^2 of southwest plain glacial lake tidal soil, where rice paddy fields are irrigated with water from a local river.

In this study, 554 soil samples with different soil depth were collected from 157 soil sites in pharmaceutical complex (Figure 1). For detailed investigation, 40 m × 40 m grid points were used for the soil exceedance areaof preliminary investigation, and 20 m × 20 m grid points were used for the isolated exceedance points and abnormal depths in the results. 38 soil samples were collected from 0 to 20 cm surface layer in agricultural land. The soil samples were air-dried, sieved, and stored at temperature lower than 4°C.

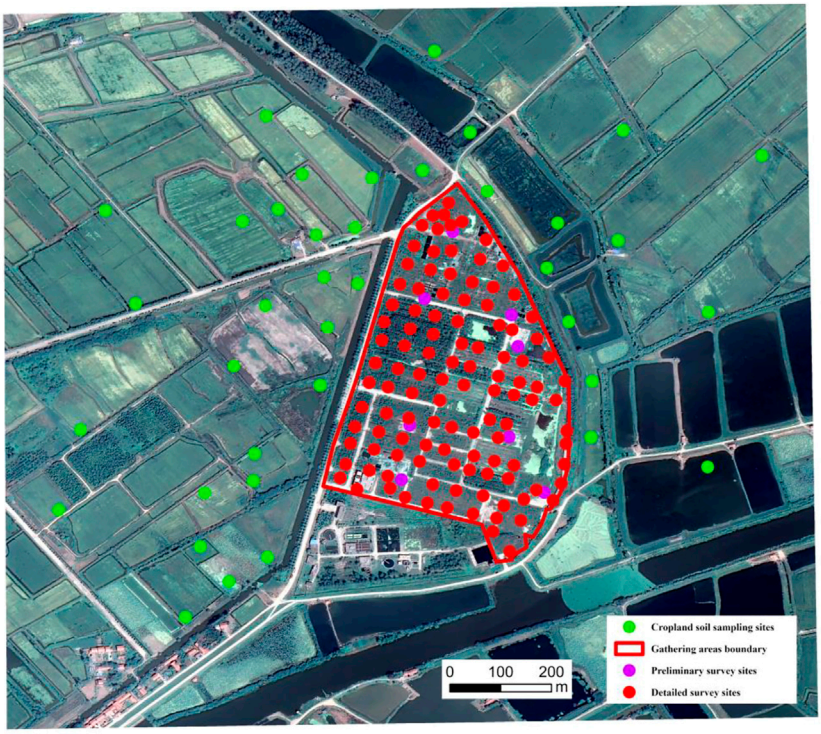

FIGURE 1
Distribution of sampling points within pharmaceutical complex and surrounding agricultural soil.

TABLE 1 Analysis methods and detection limit of heavy metals.

Heavy metals (mg kg-1)	Analysis methods of heavy metals	Detection limit (mg kg-1)
Cd	(Soil quality-Determination of lead, cadmium-Graphite furnace atomic absorption spectrophotometry) (GB/T17141-1997)	0.01
Pb	(Soil quality-Determination of lead, cadmium-Graphite furnace atomic absorption spectrophotometry) (GB/T17141-1997)	0.1
As	(Soil and sediment-Determination of aqua regia extracts of 12 metal elements-Inductively coupled plasma mass spectrometry) (HJ803-2016)	0.01
Hg	(Soil quality—Analysis of total mercury, arsenic and lead contents in soils—Atomic fluorescence spectrometry—Part 1: Analysis of total mercury contents in soils) (GB/T 22,105.1–2008)	0.002

2.2 Soil physiochemical properties analysis

The pH was determined at a soil-water ratio of 1:2.5. Soil samples were digested with nitric-hydrochloride-hydrofluoric acid in a microwave digestion system. Cd and Pb were determined by graphite furnace atomic absorption spectrophotometry. As was determined by inductively coupled plasma mass spectrometry, and Hg was determined by atomic fluorescence spectroscopy. Analysis methods and detection limit of heavy metals are shown in Table 1. To ensure the quality assurance and quality control (QA/QC), certified reference materials and blank samples were included.

2.3 Soil environmental risk assessment

2.3.1 Nemerow integrated multi-factor pollution index

The Nemerow integrated pollution index of multiple heavy metals (Nemerow, 1974) is calculated as follows:

$$P_{Nemerow} = \sqrt{\frac{\overline{P_i}^2 + P_{imax}^2}{2}} \quad (1)$$

where, $\overline{P_i}$ is the average single-factor pollution index of each heavy metal (P_i), P_{imax} is the maximum value of single-factor pollution index (P_i), and $P_{Nemerow}$ is the Nemerow integrated pollution index. The levels of soil Nemerow integrated pollution risk were classified based on the indices shown in Supplementary Table S1.

2.3.2 Geo-accumulation index

The impact of human activity on the environment is identified by the geo-accumulation index with reference to the natural variability of heavy metals (Müller, 1979) calculated as:

$$I_{geo} = log_2\left(\frac{C_n}{K \times B_n}\right) \quad (2)$$

where, I_{geo} is the geo-accumulation index of heavy metal n, C_n is the concentration of heavy metal n in soil, B_n is the background value of heavy metal according to local soil parent material conditions, and K is a coefficient reflecting fluctuating changes for the background value due to differences in parent material across regions. The geo-accumulation index was divided into seven levels of pollution from none to extreme (Supplementary Table S2).

2.3.3 Potential ecological risk assessment

The potential ecological risk index was proposed in 1980 to integrate the potential ecological impact of heavy metals (Hakanson, 1980). It considers the type, toxic effects, concentration, and sensitivity of aquatic organisms to heavy metal pollution and is calculated as:

$$RI = \sum_{i=1}^{m} E_r^i = \sum_{i=1}^{m} T_r^i \frac{C^i}{C_n^i} \quad (3)$$

where RI is the comprehensive potential ecological risk index, E_r^i is the individual potential ecological risk index for heavy metal i, T_r^i is the pollution factor for heavy metal i, C^i is the actual concentration of heavy metal in the sample, and C_n^i is the reference concentration of heavy metal i. The toxicity response factors for Pb, Cd, As, and Hg were taken as 5, 30, 10, and 5 (Yi et al., 2011), respectively.

The intensity of pollution and the magnitude of toxicity are indicated by RI values. Supplementary Table S3 shows the classification criteria for E_r^i and RI.

2.3.4 Assessment of human health risk

We analyzed human non-carcinogenic risk and carcinogenic risk (CR) using the United States Environmental Protection Agency (USEPA)-recommended health risk assessment model (USEPA, 2011; Zhou et al., 2022). The non-carcinogenic hazard quotient and total carcinogenic risk (TCR) were calculated in sensitive populations grouped based on behavioral and physiological differences. Daily intake was calculated using the following equations:

$$HI = \sum HQ = \sum \frac{ADD_{ij}}{RfD_{ij}} \quad (4)$$

$$HI = \sum CR = \sum ADD_{ij} \times SF_{ij} \quad (5)$$

$$ADD_{ingest} = \frac{C \times R_{ingest} \times EF \times ED}{BW \times AT} \times 10^{-6} \quad (6)$$

$$ADD_{dermal} = \frac{C \times SA \times AF \times ABS \times EF \times ED}{BW \times AT} \times 10^{-6} \quad (7)$$

$$ADD_{inhal} = \frac{C \times R_{inhal} \times EF \times ED}{PEF \times BW \times AT} \quad (8)$$

Values >1 for HQ and HI indicates that a population is at potential non-carcinogenic risk. Values for CR or TCR of > 1E-04, 1E-04–1E-06, or < 1E-06 represents carcinogenic, acceptable, and negligible risk to human health, respectively. Supplementary Table S4 shows the values and parameters involved in the equations, and Supplementary Table S5 lists the reference dose (RfD) for chronic disease and slope factors.

2.4 Source apportionment

The major sources of heavy metal pollution and their contributions were identified and quantified using the PMF model based on a weighted least squares iterative calculation with non-negative constraints on the decomposition matrix and standard deviation (SD) for optimization (Norris et al., 2014; Liu et al., 2022). The PMF decomposed the original matrix into three parts by continuously decomposing receptor matrix X to obtain optimal factor scores and loadings of matrices G and F. The criterion for determining the optimal was the minimal value of the objective function Q, which can be calculated as:

$$X_{ij} = \sum_{k=1}^{P} g_{ik} f_{kj} + e_{ij} \quad (9)$$

$$Q = \sum_{i=1}^{n} \sum_{j=1}^{m} \left(\frac{e_{ij}}{u_{ij}}\right)^2 \quad (10)$$

$$U_{ij} = \sqrt{(error\,fraction \times contribution)^2 + (0.5 \times MDL)^2} \quad (11)$$

Where X_{ij} is the content of element j in sample i (mg/kg), g_{ik} is the contribution of source factor k to sample i, f_{kj} is the content of element j in factor k, e_{ij} is the residual for every sample, p is the number of source factors, and U_{ij} is the uncertainty of element j in sample i; MDL is the detection limit, and the error fraction is the ratio (%) of measurement uncertainty. The uncertainty of the PMF model was measured using the classical bootstrap (BS) method, and calculations followed the USEPA PMF 5.0 User Guide.

TABLE 2 Statistical description of heavy metal pollution in agricultural soil.

Heavy metals	pH	Cd (mg kg−1)	Pb (mg kg−1)	As (mg kg−1)	Hg (mg kg−1)
Min	4.19	0.16	23.30	8.26	0.17
Max	6.08	2.22	524.00	6920.00	1.96
Mean	6.56	0.33	52.74	218.50	0.38
Median	6.64	0.25	38.25	22.70	0.32
SD	0.96	0.34	80.37	1,117.90	0.30
CV	0.15	1.04	1.52	5.12	0.79
Background values[a]	—	0.17	26.70	12.30	0.08
Screening values[b]	—	0.30	120	25	0.60

[a]Background values for Hubei Province, China (Chinese soil element background value and CNEMC, 1990).
[b]Soil environmental quality risk control standard for agricultural soil pollution, China (MEEPRC, 2018).

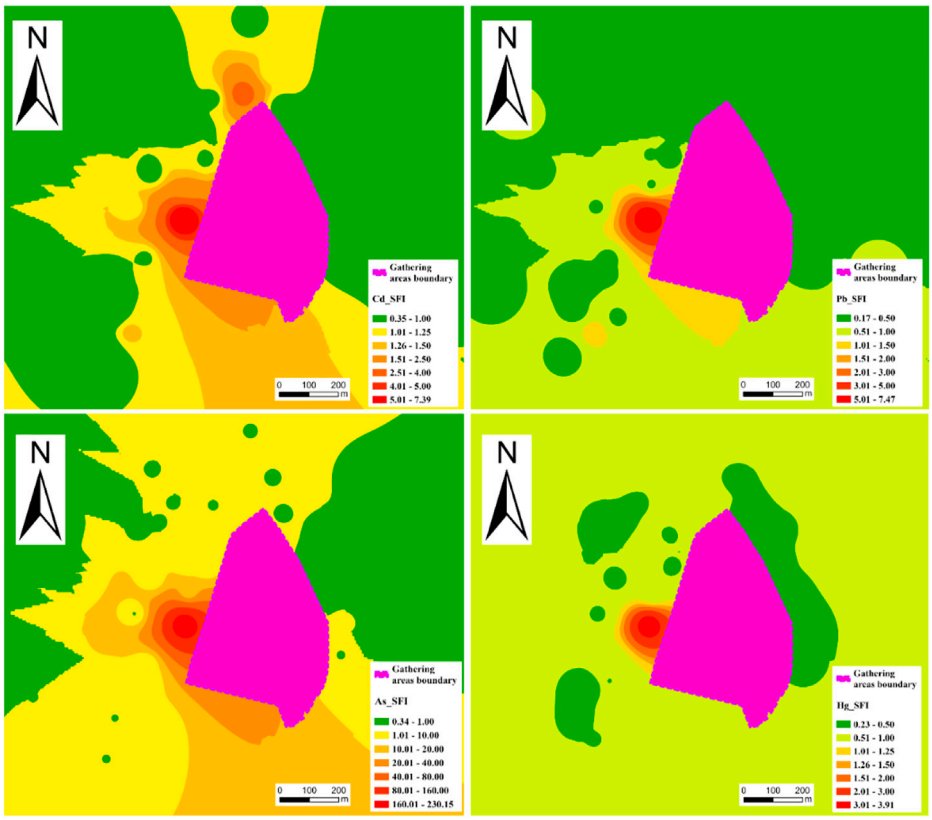

FIGURE 2
Spatial distribution of single-factor pollution index.

2.5 Statistical analysis

Data were statistically analyzed and diagrams were created in *R* language. Positive matrix factorization was calculated by EPA PMF version 5.0 (USEPA, Washington, DC, United States). The spatial distribution of HMs in the study area was produced using ArcGIS pro 3.0 (Environmental Systems Research Institute, Redlands, CA, United States).

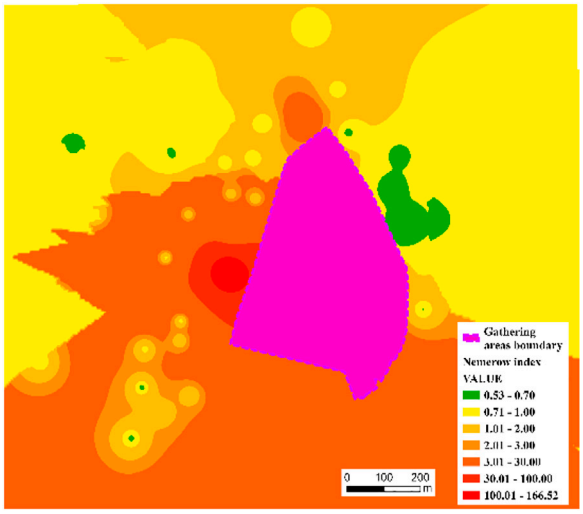

FIGURE 3
Spatial distribution of Nemerow integrated multi-factor pollution index.

TABLE 3 Carcinogenic risk and non-carcinogenic hazard quotient of four typical heavy metals.

Risk	Heavy metals	Children	Adults
HQ	Cd	1.72E-03 ± 1.78E-03	2.17E-04 ± 2.26E-04
	Pb	7.78E-02 ± 1.19E-01	9.86E-03 ± 1.50E-02
	As	3.76E00 ± 1.92E+01	4.77E-01 ± 2.44E00
	Hg	6.47E-02 ± 5.12E-03	8.20E-04 ± 6.48E-04
HI	Total	3.94E00 ± 1.94E+01	4.99E-01 ± 2.45E00
CR	Cd	1.00E-05 ± 1.04E-05	1.02E-06 ± 1.06E-06
	Pb	2.21E-06 ± 5.61E-07	2.26E-07 ± 3.45E-07
	As	1.80E-03 ± 9.22E-03	2.85E-04 ± 1.46E-03
	Hg	—	—
TCR	Total	1.82E-03 ± 9.23E-03	2.87E-04 ± 1.46E-03

3 Results and discussion

3.1 Statistical description of heavy metal pollution in soil

Table 2 shows that the mean pH at the surface of surrounding agricultural soil was 6.56 ± 0.96, with a small coefficient of variation (CV). The mean values for Cd, Pb, As, and Hg in surface soil ranged from 0.16 to 2.22, 23.30–524.00, 8.26–6920.00, and 0.17–1.96, respectively, with CVs of 1.04, 1.52, 5.12, and 0.79, respectively. Among them, the mean values for Cd and As exceeded their corresponding background values, which need to be considered as pollutants of concern. Meanwhile, the CVs of Cd, Pb, and As were higher than 100%, indicating that the existence of influence of anthropogenic activities (Fei et al., 2019).

3.2 Soil heavy metal pollution risk assessment

3.2.1 Assessment of single-factor pollution and Nemerow integrated pollution index

The single-factor and Nemerow integrated pollution indexes reflect the single and comprehensive pollution levels of heavy metals, respectively (Figure 2). The single-factor pollution indices for Cd, Pb, As, and Hg ranged from 0.33 to 7.40, 0.16–7.49, 0.33–230.67, and 0.22–3.92 mg kg^{-1}, respectively, and with the exceedance rate of 5.26%, 23.68%, 34.21%, and 3%, respectively. The Nemerow integrated pollution index ranged from 0.52 to 166.89, with 23.68%, 52.63%, 15.79%, and 7.89% of points, which corresponded to clean, relatively clean, light, and heavy pollution, respectively. The spatial distribution of the single-factor pollution index (Figure 2) indicated a wide distribution of Cd and As pollution, whereas that of Pb and Hg pollution existed lesser extent. Based on the distribution of heavy metals distant from potential pollution sources, the pollution levels of all four heavy metals were closely associated with the pharmaceutical complex. The superimposed Cd and As pollution made Nemerow pollution index a higher level, which was also closely correlated with distance from the pharmaceutical complex (Figure 3). Comprehensively speaking, a pond in the southwest section of the complex was a hotspot for heavy metal pollution. Remarkably, except for Cd and Hg (Wang et al., 2019; Yang et al., 2020), Pb and As were also observed to be the concerned potential pollutant in this study, which were obviously different from previous reports.

3.2.2 Geo-accumulation assessment

The geo-accumulation index reflects the extent of heavy metal pollution in soil by external inputs (Figure 4). As shown in Figure 4, The geo-accumulation indices for Cd, Pb, As, and Hg ranged from −0.69 to 3.11, −0.78 to 3.71, −1.16 to 8.55, and 0.51 to 4.03, respectively, and their corresponding ratios of polluted points were 47.37, 47.37, 78.95, and 100%, respectively. The geo-accumulation indices of heavy metals showed obvious accumulation risk of Cd, Pb, As, and Hg. Among them, Cd and As accumulation were obviously influenced by the distance from the pharmaceutical complex (Figure 4). Hg as a potential pollutant byproduct

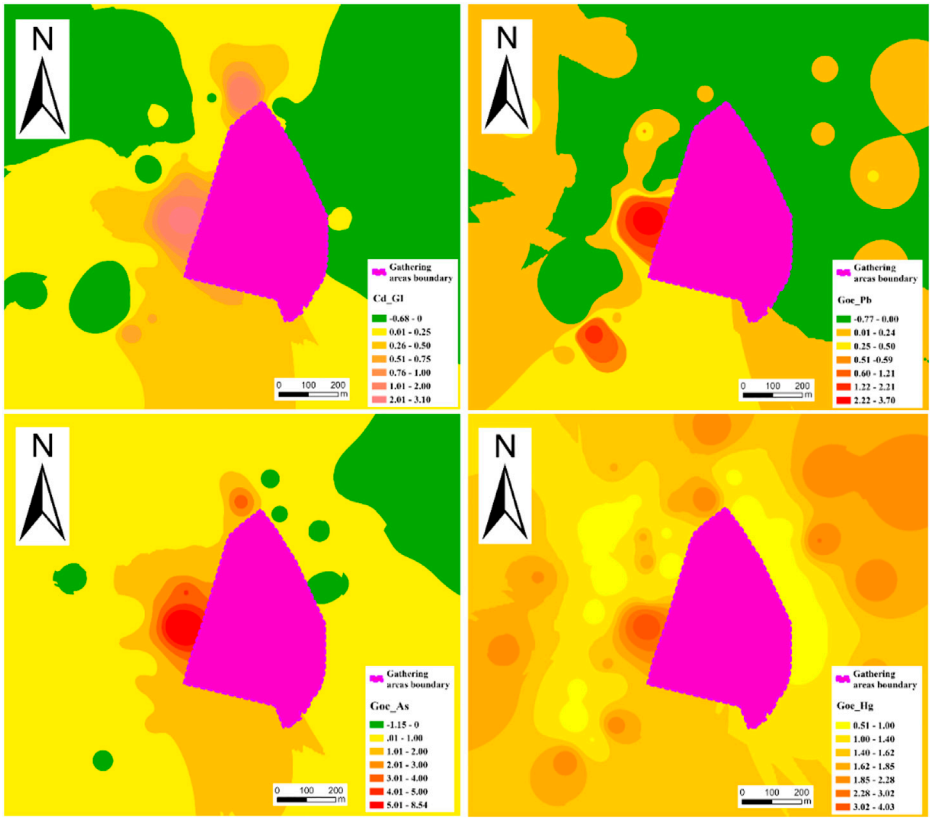

FIGURE 4
Spatial distribution of geo-accumulation index.

of pharmaceutical manufacturing had been proven in previous report (Wang et al., 2019), which was also found herein around the sewage ponds. However, in this study, it was found to have no obvious pollution risk of pharmaceutical Hg byproducts to the surrounding agricultural soil.

3.2.3 Potential ecological risk assessment

The potential ecological risk index (EI) reflects the potential hazard level of heavy metal pollution to soil ecology (Figure 5). The EI of Cd, Pb, As, and Hg ranged from 10 to 222, 0.78 to 37.43, 3.30 to 2,306.67, and 8.76 to 156.80, respectively, and their corresponding ratios (%) of points existing ecological risk were 10.53, 0, 7.89, and 2.63%, respectively. These findings indicated that the accumulation of all four heavy metals might pose a risk to the regional ecosystem (Xiao et al., 2019). Figure 6 shows that Pb and Hg confer potential ecological risk only in the hotspot area, whereas Cd and As have further spillover ecological risk. The geographic distribution of potential ecological risk RI was consistent with the EIs for Cd and As.

3.2.4 Human health risk assessment

The human health risk assessment model recommended by USEPA was applied to assess the non-carcinogenic and carcinogenic risk of heavy metals for children and adults. Table 3 shows that the hazard quotient (HQ) of As was higher than 1, indicating that it existed non-carcinogenic risk for both children and adults, which caused the total non-carcinogenic Hazard Index (HI) value higher than 1. The analysis of carcinogenic risk (CR) revealed that the CR values of both Cd and As were higher than 1×10^{-6}, indicating that these heavy metals had carcinogenic risk. The total carcinogenic risk (TCR) caused by the Cd and As was higher than 1×10^{-6}, while As contribution was predominant. We found that the carcinogenic and non-carcinogenic risk of potentially polluted soils was higher for children than for adults (Table 3), which was agreement with previous literature (Zhou et al., 2022). Human health was reported to be more sensitive to As and Cd (Yang et al., 2019). In this study, Cd and As were identified as the main pollution surrounding pharmaceutical complex, which were also observed to be the sensitivity of human health to As and Cd pollution.

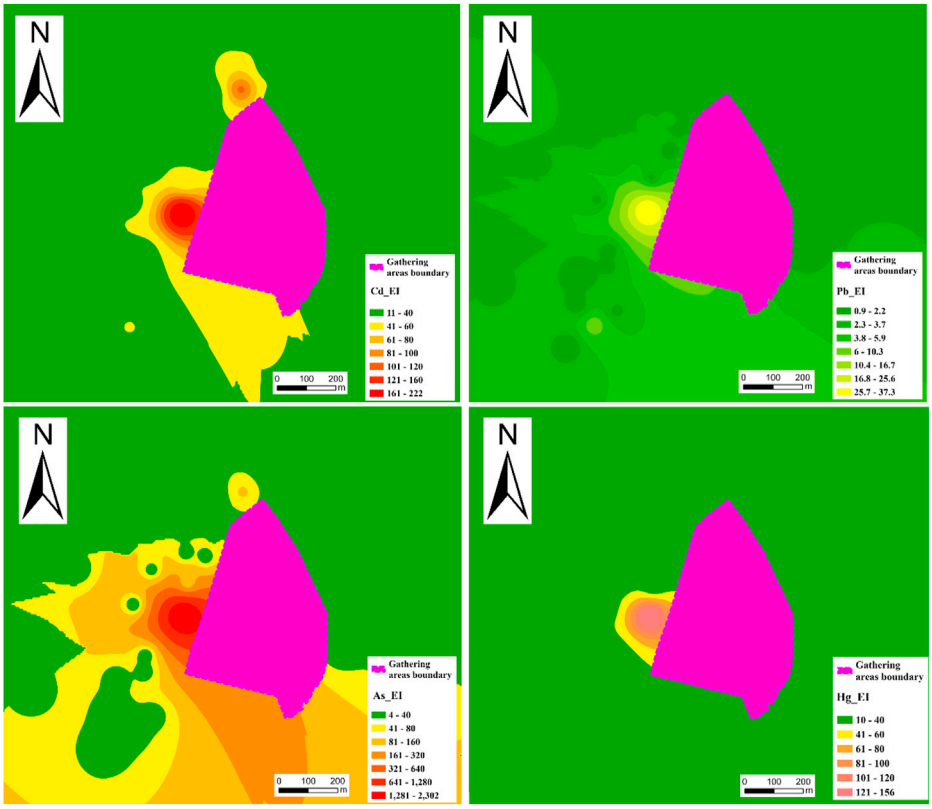

FIGURE 5
Geographical distribution of potential ecological risk (EI) for four heavy metals.

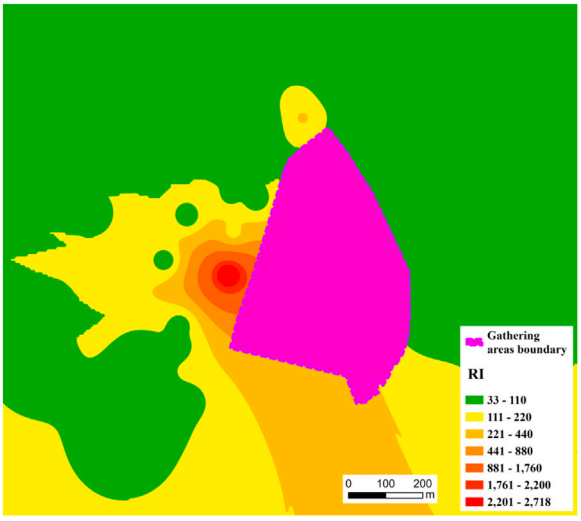

FIGURE 6
Geographical distribution of potential ecological risk RI.

3.3 Source analysis of heavy metal pollution in soil

In this study, the main sources of heavy metal pollution were identified and quantified by combining the spatial distribution of heavy metal concentrations in soil of pharmaceutical manufacturing complex and surrounding agricultural soil using the PMF source analysis. The spatial distribution of heavy metals in agricultural soil was closely associated with the pharmaceutical complex (Figure 7). In addition to the hotspot pond on the southwest of the complex, the risk of Cd and As pollution were significantly related with the pharmaceutical complex. Figure 8 shows that the heavy metals were mainly from three pollution sources. The loading of pollution source 1 mainly contained heavy metals of As, Pb, and Cd, while that of pollution source 2 were Hg, Pb, and Cd. The loading of pollution source 3 mainly included Cd, Pb, As, and Hg. Arsenic was mainly from sources 1 and 3, while Hg was from in sources 2 and 3. Remarkably, Pb and Cd were from all the three sources. Considering the overall contribution of the polluted sources in the study area, sources 1, 2, and 3 contributed 52.37%, 31.14%,

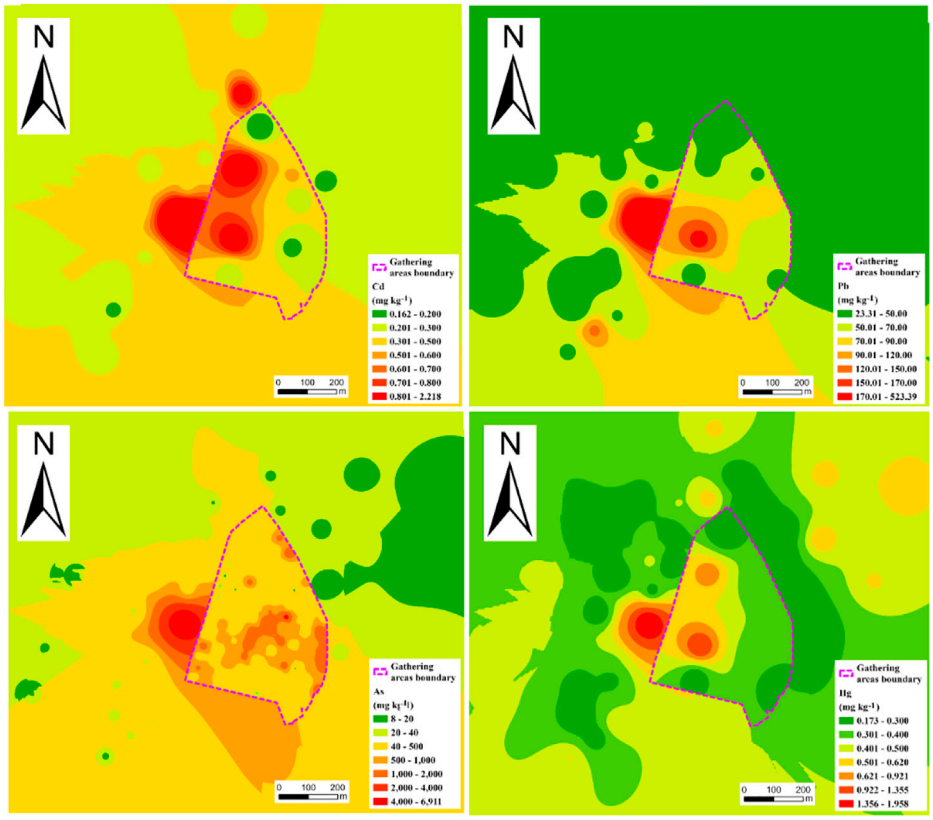

FIGURE 7
Distribution of heavy metal concentrations in pharmaceutical plant cluster and surrounding farmland.

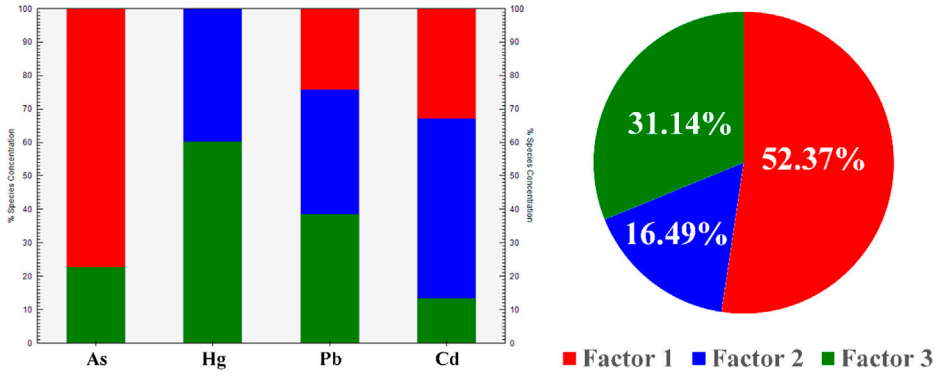

FIGURE 8
Identification of major sources of heavy metal pollution in soil.

and 16.49%, respectively. The composition of heavy metal loadings and the geographic distribution of the pollution sources (Figure 9) indicated that source 1 corresponded to irrigation with pharmaceutical wastewater, while source 2 distribution overlapped with road networks and consists of pollution loadings of Hg, Pb, and Cd, which was presumed as traffic pollution (Chai et al., 2021; Yin et al., 2021). Although source 3 had no direct relationship with the geographic distribution of the pharmaceutical plant cluster, it still contributed to all four heavy metals, which was considered to come from the use of pesticides (Hu et al., 2018).

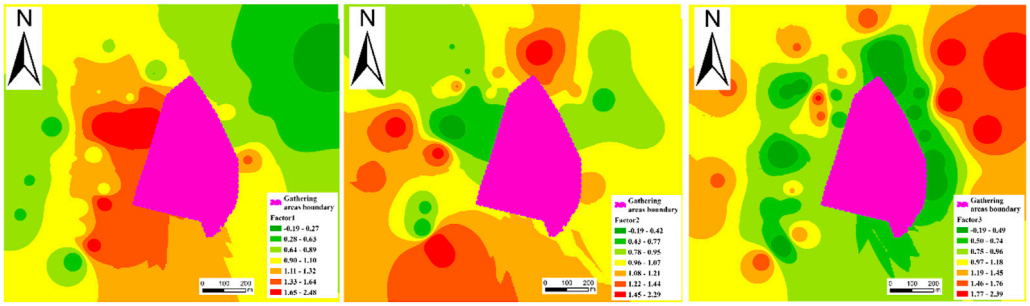

FIGURE 9
Geospatial distribution of three main pollution sources.

4 Conclusion

In summary, the environmental risk and source apportionment in agricultural soil around a typical pharmaceutical manufacturing complex in Hubei Province were comprehensively assessed. The heavy metals of Cd, Pb, As, and Hg were found to be the potential pollutants in manufacturing complex and had pollution risk for surrounding agricultural soil, especially for Cd and As. PMF source analysis revealed that there were three pollution sources including irrigation with pharmaceutical wastewater, traffic, and agricultural chemicals such as pesticides and fertilizers. We combined environmental risk assessment with source analysis to determine the details of soil pollution within and around a defunct pharmaceutical manufacturing complex. Our study provided a reference for analyzing the causes of heavy metal contamination of agricultural soil associated with pharmaceutical manufacturing, which also helped to develop strategies to prevent and control pollution caused by heavy metal by-products of the pharmaceutical industry.

4.1 Suggestions for managing risks

Relevant departments should organize to carry out risk control of soil pollution promptly. Local government should strengthen source management and further establish farmland irrigation management system to guide farmers not to use sewage for irrigation. It is recommended to track the quality of agricultural products through in-depth investigation and routine monitoring of agricultural quality around the pharmaceutical manufacturing complex.

Data availability statement

The raw data supporting the conclusion of this article will be made available by the authors, without undue reservation.

Author contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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Conflict of interest

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fenvs.2022.1105910/full#supplementary-material

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