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RESEARCH ARTICLE

Co-contamination of antibiotics and metals in peri-urban agricultural soils and source identification

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Abstract

To identify the dominant sources of contamination in peri-urban land, this study investigated the concentrations and distributions of antibiotics and metals in agricultural soil of this area. An index of landscape development intensity (LDI) was used to characterize the distribution of human disturbance-related land use. The results showed that total antibiotic concentration in the soil reached 395.55 μg/kg and that chlortetracycline was the predominant antibiotic compound, with a relatively high mean concentration of 30.62 μg/kg. In soils, the mean concentrations of Cu, Zn, and Pb were 38.41, 127.88, and 56.61 mg/kg and those of Al, Fe, and K were 83.73, 24.17, and 23.42 g/kg, respectively. A redundancy analysis showed that the landscape pattern in a 300-m buffer zone can well explain the variation in the concentrations of antibiotics and metals (24%, $p < 0.05$). The LDI in the 300-m buffer zone significantly correlated with the concentrations of total antibiotics and total amounts of Cu and Zn in the soil, suggesting that the risk of soil contamination increases with the intensity of anthropogenic activities. A structural equation modeling analysis indicated that Al, Cu, and Zn could significantly aggravate accumulation of tetracycline antibiotics in the soil, whereas there were only significantly direct paths from Cu to ciprofloxacin and norfloxacin. Overall, the results showed that aggravated co-contamination of antibiotics and metals occurs in agricultural soil under intensive human disturbance.

Keywords Landscape development intensity · Land use · Soil contamination · Antibiotics · Metals

Introduction

Urbanization leads to drastic changes in land use/land cover and is associated with soil pollution, land degradation, and other environmental problems. These issues are particularly strong in peri-urban areas with mixed landscapes that provide food security, fertile soil, waste treatment, and other ecosystem services that sustain human well-being and quality of life in urban and rural areas (Raudsepp-Hearne et al. 2010). The excessive demands of urban ecosystems can lead to the degradation and contamination of productive landscapes in peri-urban areas (Grimm et al. 2008; Zhu et al. 2017).

Manures are widely used on agricultural soils to increase soil fertility and crop production, especially in peri-urban areas (Mader et al. 2002). However, antibiotics and heavy metals are added to livestock feeds to increase livestock production and control animal diseases, and their excessive use leads to high levels of antibiotics and heavy metals (especially Zn and Cu) in manures (Nicholson et al. 1999; Qian et al. 2016). The continuous and heavy application of manures can exacerbate the persistence of antibiotics and heavy metals in agricultural soils. In addition, antibiotics and heavy metals may enter and accumulate in agricultural soils through irrigation, atmospheric deposition, or runoff from landfill and livestock farms, further enhancing the risk of co-contamination in food chains (Christou et al. 2017; Du and Liu 2012; Wu et al. 2015).

Klein et al. (2018) reported that global antibiotic consumption increased 65% between 2000 and 2015. Studies have also shown that more than 85% of these drugs are excreted into the environment via human and animal waste (Tasho and Cho

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2016). Based on a survey of national consumption and emissions in China, the total use of the 36 antibiotics most frequently detected in the environment was 92,700 tons in 2013; over time, 11,516 tons of these (54% of total emission) will be deposited into the soil environment (Zhang et al. 2015). Furthermore, more than 100,000 km^2 of arable land (about 8%) are polluted with heavy metals in China (Chen et al. 2015). In the European Union, an estimated 137,000 km^2 of agricultural land (about 6%) contain heavy metals in dangerous concentrations and will need eventual remediation (Toth et al. 2016). It has been estimated that agricultural activities account for 80 and 56% of soil contamination by Cu and Zn, respectively (Teng et al. 2014).

Previous studies showed wide antibiotic contamination in peri-urban agricultural soils. For example, in vegetable greenhouse soils from the peri-urban area of Beijing, the total concentrations of antibiotics range from 28 to 1051 μg/kg, with high-risk proportions of 11~41% for some antibiotic compounds (Li et al. 2015a). In the peri-urban areas of Narok, various antibiotics were detected in all soil samples with high concentration ranging from 14.18 to ~ 98.81 μg/kg, and they posed high ecological risks for more than 50% of the soil samples (Yang et al. 2016). In recent decades, worldwide investigations in countries such as Malaysia, Germany, and Denmark have demonstrated widespread antibiotic contamination (Ho et al. 2014; Pan and Chu 2017; Stuer-Lauridsen et al. 2000; Ternes et al. 2007). Numerous studies have suggested that there is significant heavy metal contamination in peri-urban agricultural soils throughout the world (Carneiro et al. 2015; Chen et al. 2015). The spatial distribution of heavy metals in typical peri-urban agricultural soils reveals that surrounding land use and agricultural activities have a significant influence on heavy metal accumulation in soils (Hu et al. 2018). In particular, organic fertilizers have been identified as an important source of contamination (Huang et al. 2015). Similarly, Nicholson et al. (2003) concluded that livestock manures and sewage sludge could be responsible for 8–17 and 37–40% of Cu and Zn inputs in agricultural soils, respectively. Mantovi et al. (2003) also found that Cu and Zn concentrations in soil were clearly correlated with the intensity of manure applications and were high enough to represent a risk to human health. Notably, approximately 18 and 17% of agricultural soils are polluted by Cu and Zn throughout China (Chen et al. 2015). Moreover, heavy loads and persistent levels of heavy metals have also been observed in the peri-urban soils of India (Singh and Kumar 2006), Algeria (Maas et al. 2010), and Austria (Simon et al. 2013) due to intensive agricultural activities.

Metallic ions (i.e., Cu^{2+}, Zn^{2+}, Pb^{2+}, Al^{3+}, Fe^{3+}, K^{+}) in soils can greatly affect the transport and fate of antibiotics (Jia et al. 2013; MacKay and Canterbury 2005; Zhao et al. 2011). Various sorption mechanisms of antibiotics to soil metals (i.e., complexation, surface-bridging) have been known for decades (Zhang et al. 2011). However, there are many antibiotics with no complex abilities or with complex abilities only under certain pH conditions, and metal ions may suppress their adsorption onto soils (Pei et al. 2014). The combined persistence of antibiotics and metals has synergistic effects on the inhibition of soil organisms (especially microorganisms) (Kong et al. 2006; Zhang et al. 2012). Environmental selection of antibiotic resistance in soils can also be caused by both antibiotic residues and co-selecting metals, and toxic metals in some cases may exert a stronger selection pressure than antibiotics (Song et al. 2017). There is growing evidence that the human use of antibiotics and metals has caused a vast expansion of contamination in agricultural soils. However, most of the previous studies focused on the individual contamination by antibiotics or metals, and there are limited studies concerning on the underlying processes responsible for the co-contamination of antibiotics and metals in soils under reality peri-urban agricultural fields. This also limited our understanding on urbanization and human activities' impact on soils in the changing environment. Simple correlation analysis has shown significantly positive correlations between concentrations of norfloxacin and Cu and between concentrations of ciprofloxacin and Cu and Pb in the urban soils in China (Gao et al. 2015). In the peri-urban agricultural soils of Beijing, significant correlations between sulfamethazine and total Cu and Zn concentrations have also been found (Ostermann et al. 2014). However, few studies have comprehensively evaluated the co-contamination of various antibiotics and metals in peri-urban agricultural soils.

The Yangtze River Delta (YRD) is urbanizing at the fastest rate in China in the last decades. Ningbo City is a typically urbanizing area in YRD, and the rapid urbanization poses intensive environmental pressures to its peri-urban ecosystems. Since there was an increasing demand of agricultural production for urban residents and decreasing demand for chemical fertilizer application, large amounts of manures were applied on the peri-urban agricultural fields to improve soil fertility and productivity. Moreover, peri-urban areas usually are the sites for urban and industrial waste disposal, and the wastewater and solid wastes are important pollution sources for soils. The rapid expansion of human activity in the region over the last several decades has exacerbated soil contamination by antibiotics and metals. Thus, the Zhangxi catchment, a typical peri-urban catchment which has a mixed landscape, was selected as the study area. Previous studies have reported that antibiotics and heavy metals may drive the co-selection and abundance of antibiotic resistance genes (Seiler and Berendonk 2012). In the study area, it has been reported that there were higher levels of antibiotic concentrations and antibiotic resistance genes in arable soils with long-term application of organic fertilizers and surrounding rivers than in pristine landscapes (Xiang et al. 2018; Zhao et al. 2018; Zheng et al. 2018). To further evaluate the environmental risks of antibiotics and metals in peri-urban agricultural soil, it is necessary to identify the process responsible for the co-contamination of antibiotics and metals. Thus, the objectives of this study were as follows: (1) to characterize the spatial variation in soil contamination by antibiotics and metals in a catchment with intensive urbanization and agriculture activities, (2) to evaluate the influence of human disturbance based on surrounding land use on soil contamination by antibiotics and metals in peri-urban areas, and (3) to investigate the potential correlations between antibiotic and metal contaminants. The results provide valuable and insightful scientific guidelines for soil management in similar regions.

Materials and methods

Study area and sample collection

The Zhangxi catchment was selected as the study area. The catchment is located in Ningbo City of YRD, eastern China, and has an area of approximately 89.7 km^2. The catchment has a moderate subtropical monsoon climate, warm and humid during April to October. The mean annual temperature is 17.4 °C and the mean annual precipitation is 1463 mm. The evapotranspiration is about 730 mm, and 45% of that is in summer. Soil types in the study area are mainly yellow soil, red soil, and paddy soil. The main land-use types are forestland, cropland, orchards, rivers, reservoirs, villages, and towns (Fig. 1). There has been a long-term application of manures amounting to about 10~80 t/ha per year in the agricultural fields in the study area.

Soil samples (0~10 cm) were collected from 40 experimental sites in the study area in July, 2016 (Fig. 1). Five to eight subsamples collected from each experimental site were mixed together. All of the samples were transported under cooled conditions to the laboratory and lyophilized. The ≤ 2-mm fraction was separated and stored in a dark environment at − 20 °C before further treatment and analysis of antibiotics. The antibiotics in the soil samples were analyzed by high-performance liquid chromatography tandem mass spectrometry (HPLC-MS/MS). To analyze the physicochemical properties and metal concentrations, the samples were air-dried and also sieved to a particle size of less than 2 mm.

Soil properties

Soil texture (sand, silt, and clay distribution) was determined by the laser diffraction method using a laser particle analyzer. Soil organic carbon was analyzed using the dichromate oxidation method, and soil organic matter (SOM) was calculated from soil organic carbon (Zheng et al. 2009). Soil bulk density, porosity, and pH were also analyzed to determine soil characteristics (Table 1).

Analysis of metals

The acid digestion method was used to obtain the heavy metal concentrations of the prepared soil samples (Rajmohan et al. 2014). First, 1 g of each soil sample was digested with a mixture of concentrated $HClO_4$ and HF. Trace metal concentrations (Cu, Zn, Pb) were then estimated using an inductively coupled plasma mass spectrometer (ICP-MS). The concentrations of Al, Fe, and K were determined by X-ray fluorescence (XRF) spectrometry (McLaren et al. 2012).

The accuracy of the analyses was assessed by using standard samples for standard reference materials (GSS-5, GBW07429, the National Research Center for Certified Reference Materials of China), and reference soil samples and blank samples were used for quality control. The confidence level of the analyzed metals in standard reference material was 90%, and the relative standard deviation of repeated measurement was less than 10%. The limits of detection (LODs) were 0.074, 0.034, 0.043, 153.1, 6.7, and 47.3 mg/kg for Cu, Zn, Pb, Al, Fe, and K, respectively.

Analysis of antibiotics

In this study, the antibiotic concentration values of four tetracyclines (TCs), i.e., tetracycline (TC), oxytetracycline (OTC), chlorotetracycline (CTC), and doxycycline (DXC), and six fluoroquinolones (FQs), i.e., enrofloxacin (ENR), ofloxacin (OFL), ciprofloxacin (CIP), norfloxacin (NOR), perfloxacin (PER), and lomefloxacin (LOM), were obtained. These antibiotics have been shown to be the predominant antibiotic compounds in soils, with contributions of more than 95% in the study area (Zhao et al. 2017).

Extraction procedures for the targeted antibiotic compounds were developed based on the solid-phase extraction (SPE) method (Zhou et al. 2017). The 2.00-g soil samples were initially extracted with 7.5 ml Na_2EDTA-Mcllvaine buffer and 7.5 ml extraction solution in the presence of vortex and ultrasonication, followed by centrifugation. The extraction process was conducted three times, and all the supernatants were sequentially combined and diluted to 500 ml. After dilution, the mixture was filtered through a 0.22-μm glass microfiber (GF/F, Whatman, UK), and then the pH was adjusted to 3.5. The filtrate was subsequently extracted by SPE using HLB cartridges (Waters Oasis HLB, Milford, MA, USA) which have been preconditioned with 6 ml of acetone, 6 ml of methanol, and 6 ml of 0.5 g/l Na2EDTA solution (pH 3.5). Finally, this mixture was diluted with methanol. The eluate was evaporated to near dryness under a gentle stream of nitrogen, and the residue was redissolved to 1 ml. The HPLC-MS/MS analysis (Thermo Dionex Ulitmate 3000, USA) was conducted through testing column (Waters Acquity UPLC BEH C_{18}, USA), and the details are provided in the Supporting information (Section S1).

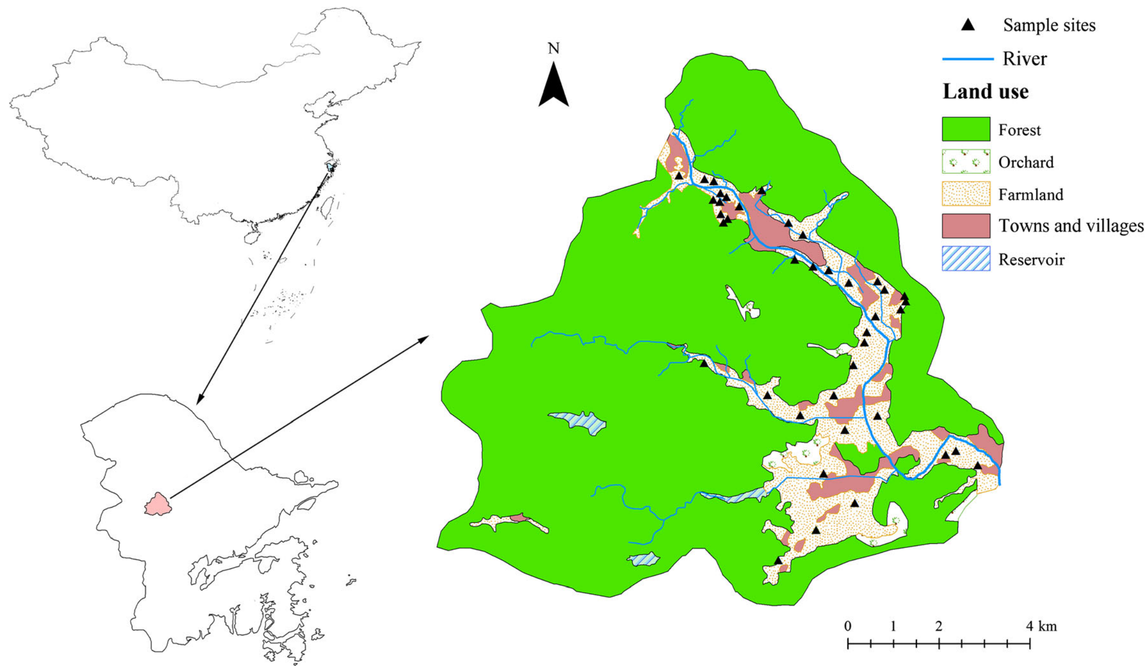

Fig. 1 Location of study area and sampling sites

Quality control and quality assurance A spiked blank, a procedural blank, and a duplicate of soil were processed in parallel in each batch of ten samples. The relative standard deviation (RSD) in the measured concentrations of duplicate samples was less than 20%. The average recoveries of target compounds in the soil samples ranged from 73.1 to 111.7%. The coefficients of determination of the working calibration curve (0.2–300 ng/g) were all > 0.99. The limit of detection (LOD) for antibiotics were calculated and fell in the range of 0.05–2.00 ng/g. Recovery, LOD, and limit of quantification are depicted in Table S1.

Intensity of human disturbance

Land use and its use intensity can have direct, secondary, and cumulative impacts on ecological processes. Landscape development intensity (LDI), as a land-use-based index of the potential human disturbance gradient, measures the level of human impact on the biological, chemical, and physical processes of an area of land or water (Brown and Vivas 2005). In this study, LDI index was used to quantify the intensity of surrounding human-dominated land use to reflect local human activity. This method has been used to evaluate the anthropogenic influence on soils. For example, Margriter et al. (2014) also used LDI to assess the impact of land use on soil quality in Hawai‘i. The LDI can be calculated by using land use/land cover data:

$$\mathrm{LDI} = \sum \%\mathrm{LU}_i \times \mathrm{LDI}_i$$

where $\%\mathrm{LU}_i$ is the area percentage of land-use type i at each sampling site, and LDI_i is the landscape development intensity coefficient for land-use type i, which is shown in Table S2. In this study, the values of LDI at each sampling site were calculated with buffer zones with radii of 50, 100, 300, 500, and 700 m to test the effect of land-use composition on antibiotic concentration.

Table 1 Soil properties in the study area

Soil properties	Minimum	Maximum	Mean	SD
Sand (%)	16.89	80.08	49.88	17.78
Silt (%)	18.80	81.67	48.54	17.46
Clay (%)	0.53	5.09	1.58	0.74
SOM (g/kg)	10.58	124.83	36.29	20.07
BD (g/cm^3)	0.98	1.35	1.13	0.08
pH	4.36	6.91	5.51	0.70
Porosity (%)	48.68	62.92	56.92	3.05

SD standard deviation

Spatial analysis was conducted to calculate the contribution of land use to soil contamination at each sampling site. The proportion of each area covered by five land-use types in each buffer zone was calculated using ArcGIS 10.1. The distances from each sampling site to the road edge and town edge were extracted from Google Earth. The altitudes of the sampling sites were measured using a GPS.

Statistical analysis

The statistical analyses were conducted using SPSS 22. One-way analysis of variance (ANOVA) was used to compare the

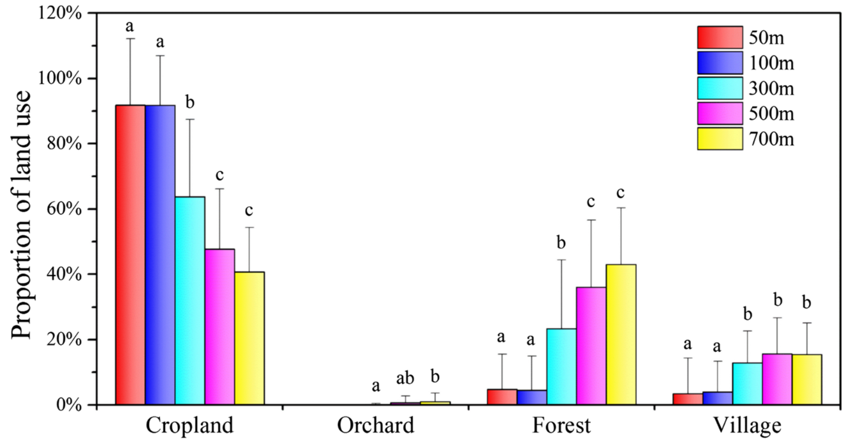

Fig. 2 Land-use proportions in different buffer zones. Different lowercase letters indicate significant differences at the 0.05 level in the same land-use type

proportions of land-use types in the different sample sites. Pearson correlations were used to analyze the correlations between metal concentrations and landscape variables, and Spearman rank correlations were used to explore the correlations between antibiotic concentrations and landscape variables. Redundancy analysis (RDA) was used to evaluate the effects of land-use patterns on the distribution of antibiotics and metals in soils. Variation partitioning analysis (VPA) was used to identify the contribution of soil texture, SOM, and metals to the variation in the concentration of antibiotics. Structural equation modeling (SEM) is a method that can address several of the restrictions common in other methods, providing a robust technique for studying interdependencies among a set of correlated variables; it considers both direct and indirect effects and measurement error (Arhonditsis et al. 2006). SEM was used to identify the effects of metals on antibiotics in soils.

Results and discussion

Landscape variables and human disturbance

The proportions of different land-use types in the buffer zones are shown in Fig. 2. In buffer zones with radii of less than 100 m, cropland was the predominant land-use type with proportions higher than 90%. No significant ($p > 0.05$) differences were found in land-use structures within the 50- and 100-m buffer zones. However, there was a significant decrease in the proportion of cropland in buffer zones with radii larger than 300 m, and a significant ($p < 0.05$) increase in other land-use types was observed. For example, the proportion of cropland in the 500-m buffer zones was significantly lower than in the 300-m buffer zones, and the proportion of forest increased significantly ($p < 0.05$). There were no significant ($p > 0.05$) differences in the land-use structures of the 500- and 700-m buffer zones.

An RDA was performed to test the scale-dependent effects of landscape patterns on soil contamination. The results showed that land-use patterns in the 300-m buffer zones explained 24% of the spatial variation of antibiotics and metals in soils (Table 2). The increased significance values (permutation test results—*p*) in the 700-m buffer zones might be caused by the significant increase in the proportion of land used for orchards. The results indicated that landscape patterns in the 300-m buffer have a better explanation on the variation of soil contamination by antibiotics and metals than the other buffer scales. This has also been demonstrated by studies of the effects of landscape patterns on water quality, where similar 300 m buffers were found to explain variations in water quality (Li et al. 2015b).

The results of the Pearson correlation analysis showed that LDI in the 300-m buffer zones had significant ($p < 0.05$) negative correlations with distance to road, distance to town, and altitude. The values of LDI decreased with increasing distance to road, increasing distance to town, and increasing altitude (Fig. 3). These results are consistent with those of previous studies (Etter et al. 2011; Gombert et al. 2004). These results indicate that LDI in the 300-m buffer zones accurately represent human activities in the study area.

The reasonability of LDI to represent human activities has been reported by many previous studies. For example, Chen

Table 2 RDA analysis of the relationships between landscape pattern and soil contamination by antibiotics and metals

Buffer scales	50 m	100 m	300 m	500 m	700 m
Variation of total explanation (%)	7.72	3.6	23.75	16.64	14.27
Permutation test results—*p*	0.444	0.570	0.018	0.116	0.096

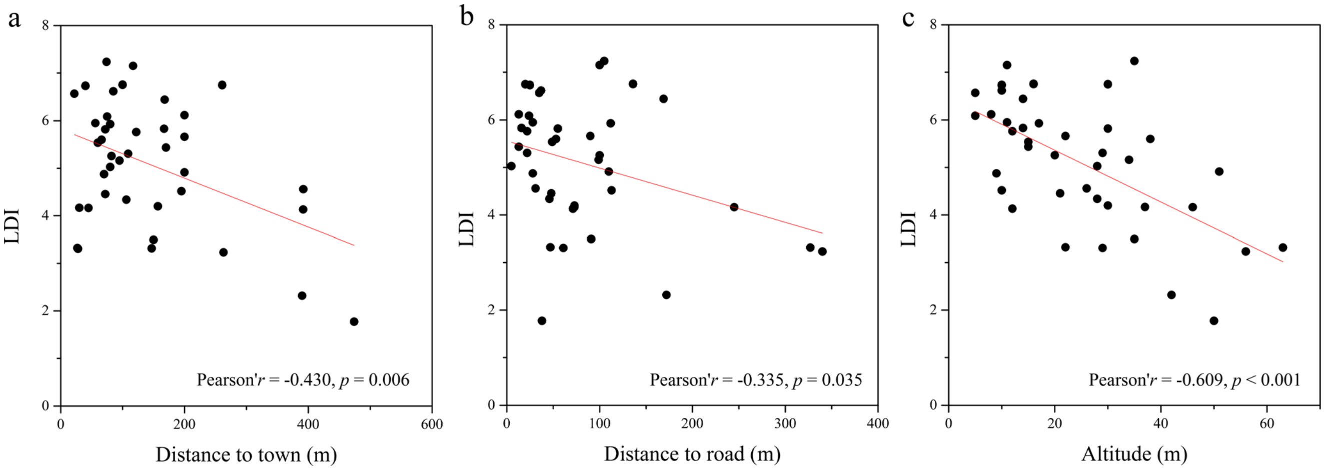

Fig. 3 Correlations between LDI based on land-use pattern in 300 m buffer and **a** distance to town edge, **b** distance to road edge, and **c** altitude

and Lin (2011) found that the LDI index was significantly correlated with the biodiversity status of wetlands in Taiwan, which indicated the index can provide rapid and timely information on landscape development to improve wetland management. The LDI index was also reported to exhibit negative correlations with stony coral colony density, taxa richness, colony size, and total coral cover in Virgin Islands, USA, which is consistent with expectations that higher human land-use activity adversely affects coral condition (Oliver et al. 2011). Moreover, levels of methyl-mercury, which were mainly originated from anthropogenic activities, found in sediments were impacted by the LDI indexes in the Mobile-Alabama River Basin (Bonzongo et al. 2016). Reiss et al. (2014) further proposed that the LDI index can be used to facilitate calculation of wetland mitigation potential. These studies proved that the LDI index is an effective tool to represent human disturbance gradient based on surrounding land uses. It is also demonstrated that the LDI index is more robust than other indicators of human activity by these studies, such as percentage of impervious surface and percentage of natural land (Chen and Lin 2011; Oliver et al. 2011; Reiss et al. 2014).

Impact of human disturbance on soil contamination by antibiotics

This study explored the occurrence of antibiotics including four TCs (OTC, TC, CTC, DXC) and six FQs (OFL, NOR, ENR, PER, CIP, LOM) in soil depths of 0–10 cm. Table 3 shows the summary statistics of the ten antibiotics. In the 40 soil samples, the positive detection frequency for all of the selected antibiotics ranged from 24 to 100%. CTC was the most common antibiotic compound, with a relatively high mean concentration of 30.62 μg/kg. Furthermore, CTC was the most ubiquitous, with a relatively high detection frequency of 62% among the TCs. The relative concentrations and detection frequencies for TCs in the soils had the following order: CTC > DXC > OTC > TC. FQs had a relatively higher detection frequency than TCs. In particular, ENR was detected in all of the soil samples, giving a frequency of 100%. However, the mean concentrations of ENR were much lower than those of CTC and DXC. The concentrations for FQs in the soils decreased in the following order: OFL > CIP > NOR > ENR > PER > LOM.

Table 3 Concentrations of tetracycline and fluoroquinolone antibiotics in soils (μg/kg, dw)

Compound	Frequency (%)	Mean	SD	Minimum	Maximum	Median
OTC	26	2.75	9.78	n.d.	61.06	n.d.
TC	28	2.36	6.21	n.d.	29.82	n.d.
CTC	62	30.62	61.68	n.d.	324.73	6.99
DXC	52	5.71	10.33	n.d.	38.94	1.59
OFL	81	3.20	5.13	n.d.	21.66	0.42
NOR	74	1.54	2.31	n.d.	12.84	0.78
ENR	100	1.04	1.93	<LOQ	10.20	0.38
PER	67	0.37	0.60	n.d.	2.62	0.14
CIP	79	2.28	3.33	n.d.	12.50	0.72
LOM	24	0.35	0.91	n.d.	4.10	n.d.

dw dry weight, *n.d.* not detected. *SD* standard deviation

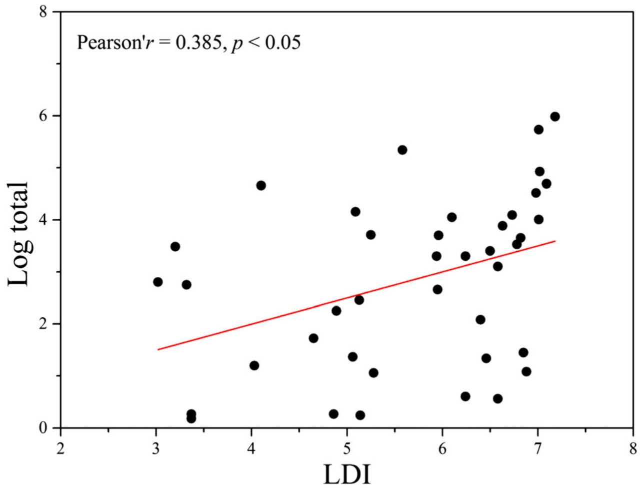

Fig. 4 Correlation between total antibiotic concentrations in soils and LDI based on land-use pattern in 300 m buffer

Previous studies indicated that antibiotic residues in animal excrement were generally detected at extremely high levels in the region where the study area is located (Hou et al. 2015; Li et al. 2015a). It has been reported that manure application and wastewater irrigation are the main sources of antibiotic inputs in agricultural soils of the Yangtze River Delta (Sun et al. 2017; Zhao et al. 2018). The fertilization history and amounts were both correlated with antibiotic concentrations in soils. Rahman et al. (2018) found that long-term pig manure application significantly increased antibiotic concentrations in paddy soils as well as applied manure amounts. The composition and concentration of antibiotics in soils was consistent with those in agricultural soils in Liaoning and Tianjin (Hou et al. 2015). However, vegetable greenhouse soils from Beijing had different levels of FQs, and the mean concentrations of individual compounds decreased in the following order: ENR (47 μg/kg) > CIP (23 μg/kg) > NOR (13 μg/kg) > LOM (2.3 μg/kg) (Li et al. 2015a). A possible explanation for this difference is that the concentrations of antibiotics in agricultural soils are associated with human disturbance such as cultivation strategies and fertilization frequency (Pan and Chu 2017).

Figure 4 shows the correlations between LDI index based on land-use pattern in 300 m buffers and total concentrations of antibiotics in the soils. The total concentration of antibiotics in the soils exhibited a significant ($p < 0.05$) positive correlation with LDI, indicating that the concentration is strongly affected by human activities. The correlations between land-use type and individual antibiotic compounds are shown in Table 4. Most antibiotic compounds were significantly ($p < 0.05$) correlated with the amount of cropland, with the exceptions of OTC, PER, and LOM. All of the antibiotics exhibited positive correlations with orchards, although the correlations were not significant ($p > 0.05$). There were negative correlations between forests and antibiotic compounds. Although most of the antibiotic compounds were negatively correlated with towns and villages, OTC and LOM exhibited slightly positive correlations ($p > 0.05$). OTC and LOM are mainly from human use. The concentrations of OTC and LOM were positively correlated with towns and villages although the correlations were not significant. The results suggested that domestic wastewater and solid waste from towns and villages were probably potential sources of these antibiotics in the soils (Wu et al. 2015). It has been estimated that 16% of antibiotics are used for human disease treatment, and 18 and 18% of OTC and LOM, respectively, are frequently used by humans (Zhang et al. 2015). This is consistent with the results in Li et al. (2016). The results discussed above indicate that human disturbance, especially manure fertilization, is the major source of antibiotics in soils. However, OTC, PER, and LOM did not exhibit any significant positive correlations with our explanatory variables. The other unidentified sources, such as atmospheric particulates and precipitation, might also be responsible for these compounds and impact their environmental fates in soils (Ferrey et al. 2018).

Table 4 Correlation coefficients between antibiotics in soil and land use

Compounds	Area proportion of cropland	Area proportion of orchard	Area proportion of forest	Area proportion of towns and villages	LDI
OTC	0.137	0.032	− 0.277	0.136	0.287
TC	0.420**	0.134	− 0.440**	− 0.104	0.500**
CTC	0.466**	0.299	− 0.363*	− 0.405*	0.404*
DXC	0.434**	0.000	− 0.299	− 0.442**	0.343*
OFL	0.504**	0.099	− 0.530**	− 0.088	0.566**
NOR	0.360*	0.169	− 0.320*	− 0.240	0.329*
ENR	0.507**	0.248	− 0.546**	− 0.151	0.550**
PER	0.211	0.179	− 0.178	− 0.171	0.228
CIP	0.584**	0.207	− 0.580**	− 0.190	0.587**
LOM	0.013	0.258	− 0.028	0.119	0.068

* significant at the 0.05 level; ** significant at the 0.01 level

Table 5 Concentrations of metals in the soils

Elements	Mean	SD	CV	Minimum	Median	Maximum	Background value
Al	83.73	13.14	0.16	64.40	81.10	124.00	–
Fe	24.17	3.06	0.13	16.80	24.35	30.90	–
K	23.42	4.45	0.19	11.70	24.35	32.60	–
Zn	127.88	45.07	0.35	48.40	129.00	245.00	86.6
Cu	38.41	21.24	0.55	12.60	37.95	92.90	23.1
Pb	56.61	21.82	0.39	27.90	52.90	139.00	36.2

The units for Al, Fe, and K are grams per kilogram, and the units for Zn, Cu, and Pb are milligrams per kilogram. Background values were reported by Dong et al. (2007)

SD standard deviation, *CV* coefficients of variation

Impact of human disturbance on soil contamination by metals

As shown in Table 5, the mean concentrations of Pb, Zn, and Cu in soils were significantly higher than the background values, and their maximum concentrations were 3.84, 2.83, and 4.02 times higher than the background values. According to the Environmental Quality Standards for Soils (GB 15618-2018) in China, 18, 5, and 20% of Pb, Zn, and Cu, respectively, in the sampling sites were above the permitted values. Furthermore, the coefficients of variation for the concentrations of the three heavy metals were as follows: Cu (55%) > Pb (39%) > Zn (35%). The distribution characteristics of beneficial elements (Al, Fe, K) had relatively lower variations compared to heavy metals.

Principal component analysis (PCA) was used to explore the relationships between different metal concentrations in the sample soils. The PCA results showed that three common factors accounted for 72% of the variance (Table 6). The first factor grouped the elements by the agricultural activities that produced the deposits of Zn and Cu (Ostermann et al. 2014). The associations between these elements might be attributed to shared anthropogenic sources, in particular fertilization (Qian et al. 2016; Teng et al. 2014). Besides antibiotics, Guo et al. (2018) also observed increased concentrations of heavy metals in soils after long-term manure application, and they also found that a high amount of manure applied on agricultural fields seemed to suggest higher sequestration for both antibiotics and metals in soils than a low amount. Factor 2 grouped elements by deposition methods. Among the elements in this group, Pb has been reported as a marker of atmospheric deposition (Yang et al. 2014). However, there was high loading of K in both factor 1 and factor 2, indicating that the variations in K concentrations in the soil were strongly influenced by both agricultural practices and environmental factors (Blanchet et al. 2017). The association might be attributed to the strong influence of soil properties such as soil pH, SOM, and clay content (Liu et al. 1997; Violante et al. 2010). Thus, factor 2 can be identified as a natural factor. Factor 3 consisted of mineral-crustal elements such as Fe and Al and was identified as a mineral factor (Carneiro et al. 2015). These results indicate that fertilization was the primary source of soil contamination (Toth et al. 2016; Wong et al. 2002).

Correlation analysis showed that there were weak correlations between most of the metals. Significant correlations were only observed between Zn and Cu, Zn and K, Zn and Pb, and Fe and K (Table 7). The relationship between LDI and concentrations of metals also demonstrated the impact of human disturbance on soil contamination (Fig. 5). Only Cu and Zn exhibited significantly ($p < 0.05$) positive correlations with

Table 6 Matrix of loads for the principal component analysis (PCA) with Varimax rotation for the identification of factors related to elemental distribution

	Nonrotated			Rotated		
	Factor 1	Factor 2	Factor 3	Factor 1	Factor 2	Factor 3
Al	0.304	**0.753**	0.324	0.142	0.426	**0.750**
Fe	− 0.215	0.283	**0.799**	− 0.118	− 0.378	**0.780**
K	**0.808**	0.247	− 0.158	0.658	0.548	0.070
Zn	**0.769**	− 0.126	0.272	**0.813**	0.005	0.146
Cu	0.613	− 0.584	0.127	**0.764**	− 0.278	− 0.271
Pb	0.153	0.576	− 0.560	− 0.130	**0.807**	− 0.036
%Var	31	23	18	28	23	21

Significant variables (|values| > 0.7) are in bold

Table 7 Correlations between different metals

	Al	Fe	K	Zn	Cu	Pb
Al	1					
Fe	0.222	1				
K	0.294	− 0.315*	1			
Zn	0.181	− 0.190	0.341*	1		
Cu	− 0.162	− 0.018	0.142	0.443**	1	
Pb	0.034	− 0.169	0.159	0.346*	0.139	1

* significant at the 0.05 level; ** significant at the 0.01 level

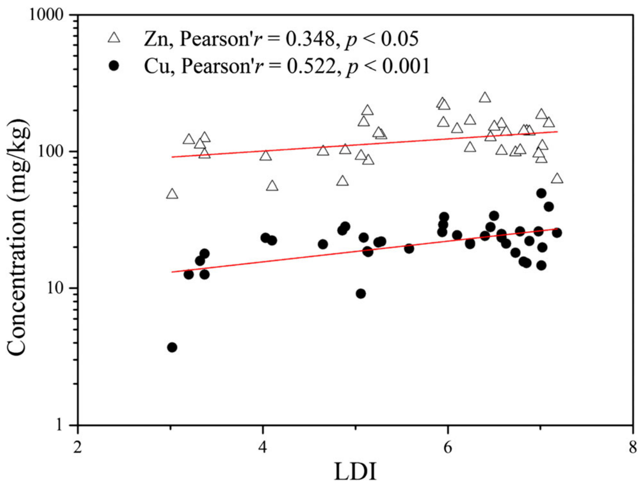

Fig. 5 Correlations between total Cu and Zn concentrations in soils and LDI based on land-use pattern in 300 m buffer

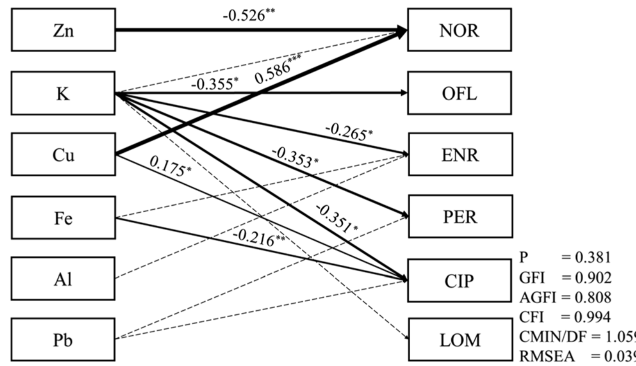

Fig. 7 Structural equation model for the co-contamination of heavy metals and fluoroquinolone antibiotics in soils. Notes: The model fit indices include probability level (*p*), goodness-of-fit statistic (GFI), adjusted goodness of fit statistic (AGFI), comparative fit index (CFI), chi-square/degrees of freedom (CMIN/*DF*), and root mean square error of approximation (RMSEA). $^*p < 0.05$;$^{**}p < 0.01$;$^{***}p < 0.001$

LDI. The results obtained from the correlation analysis were consistent with the PCA results. Probably, K in soil is strongly associated with precipitation and soil properties and, consequently, may be related to natural factors, which is also consistent with the PCA results. Although agricultural practices (i.e., organic and mineral fertilization) were the main sources of K in soil, it showed considerable leaching potential, which was significantly influenced by soil texture (Rosolem and Steiner 2017). It was found that the increase in rates of fertilizer-K application intensified its loss by leaching in sandy clay loam soil, while it did not result in a large amount of leaching in clay soil. Moreover, the spatial distribution of total K content was also influenced by crop type, soil type, soil parent material, and topography (Blanchet et al. 2017; Cassman et al. 1989). Precipitation can also distinctly lead to the spatial variability of K in soils in relation to runoff loss and leaching (Alfaro et al. 2004).

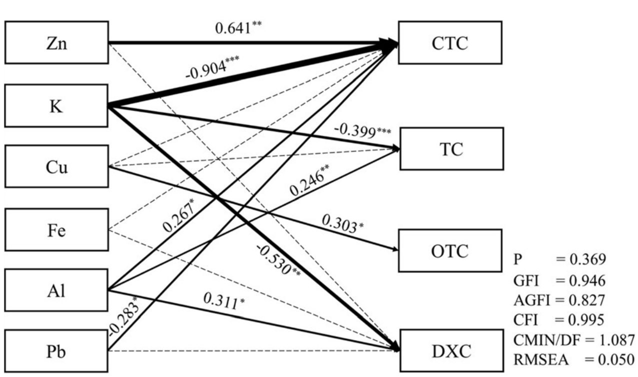

Fig. 6 Structural equation model for the co-contamination of heavy metals and tetracycline antibiotics in soils. Notes: The model fit indices include probability level (*p*), goodness-of-fit statistic (GFI), adjusted goodness of fit statistic (AGFI), comparative fit index (CFI), chi-square/degrees of freedom (CMIN/*DF*), and root mean square error of approximation (RMSEA). $^*p < 0.05$;$^{**}p < 0.01$;$^{***}p < 0.001$

Co-contamination of antibiotics and metals in soil

SEM can explicitly test the indirect effects between two explanatory variables, which may be mediated by another intermediary variable (Arhonditsis et al. 2006). Overall, our conceptual model resulted in an acceptably good fit with the data and provided a plausible interpretation of the environmental processes. The SEM analysis in this study highlighted that Al, Cu, and Zn can significantly aggravate the accumulation of TCs in soil (Fig. 6). The standardized direct effect of Zn on CTC was 0.641 ($p < 0.01$). The standardized direct paths from Al to CTC (0.267), TC (0.246), and DXC (0.311) were significant ($p < 0.05$), although weakly positive, correlations. The correlation ($r = 0.303$) between Cu and OTC was also significant ($p < 0.05$). However, Pb and K were both negatively correlated with TCs ($p < 0.05$), and the standardized direct path from K to CTC had a high negative value ($r = -0.904$, $p < 0.001$). Previous studies have found that the adsorption of antibiotics in soils is affected by metal ions. It has been suggested that the adsorption of antibiotics to organic matter, minerals, and soils is due to the binding of antibiotics to divalent metal cations (Jia et al. 2008). For example, the presence of Cu^{2+} in soil solution increased the adsorption of TC in red soil with a pH > 4.7 by bridging because Cu^{2+} could form strong and specific inner-sphere surface complexes with tetracyclines and clay minerals (Jia et al. 2008). Cu^{2+} can also strongly enhance the sorption of OTC to biochar and soil organic matter due to the formation of water-soluble complexes of Cu^{2+} and OTC with higher adsorption coefficient and the surface-bridging mechanism (Jia et al. 2013; MacKay and Canterbury 2005). In addition, Al^{3+} and Fe^{3+} were found to have clearly positive effects on the adsorption behavior of tetracycline antibiotics in soils through ternary complex formation between tetracyclines, metal cations, and organic matter ligand groups (Wang and Wang 2015). However, some metal ions can compete in adsorption sites with antibiotic

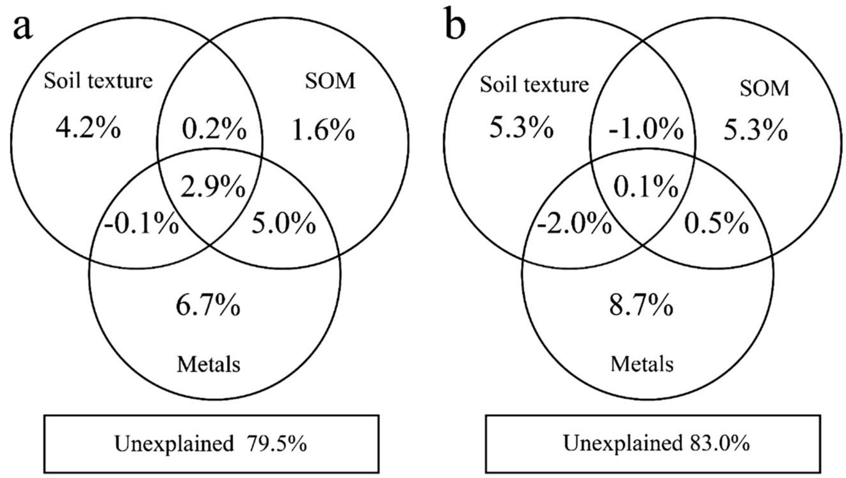

Fig. 8 Variation partitioning analysis differentiating the effects of soil particles, organic matter, and metals on the sorption of **a** tetracyclines and **b** fluoroquinolones in soils

compounds. High Ca^{2+} humic acid showed lower adsorption coefficient for OTC around pH 5 (MacKay and Canterbury 2005). In the presence of K^+, TC adsorption on kaolinite decreased in accordance with the increasing of atomic radius and valence of metal cations, which suggested that outer-sphere complexes formed between tetracycline and kaolinite, and the existence of competitor ions leads to decreasing adsorption (Zhao et al. 2011).

The SEM results showed that the only significantly positive correlations for FQs were between Cu and NOR ($r = 0.586$, $p < 0.001$) and Cu and CIP ($r = 0.175$, $p < 0.05$, Fig. 7). The standardized direct paths from the other metals to the FQs were all negative, especially for K, Zn, and Fe. All of the paths between K and OFL, ENR, PER, and CIP were significantly negative ($p < 0.05$), with standardized direct effects of −0.355, −0.265, −0.353, and −0.351, respectively. In addition, Fe had a weak negative correlation with CIP ($r = -0.216$, $p < 0.01$). The results also showed that metal ions were likely to increase the retention of FQs through cation bridging like TCs. Tan et al. (2015) suggested that the coexistence of divalent cations or soil organic matter can enhance CIP adsorption on goethite surfaces through cation bridging; in particular, Cu can strongly enhance its sorption at pH = 6. However, these ions may compete with antibiotics for adsorption sites under low pH conditions, and they would then restrain the adsorption of antibiotics. Additionally, the properties of FQ antibiotics (amphiphilic and amphoteric) also play an important role during the adsorption of FQs (Wang and Wang 2015). FQ antibiotics occur as cations, zwitterions, and anions at environmentally relevant pH values and also display pH-dependent adsorption on soils. Under lower pH conditions, the carboxyl group of the FQs showed strong interaction with soil oxides, and the FQs remained in zwitterionic form which resulted in the formation of strong complexes with metals of soil (Riaz et al. 2018). However, Cu^{2+} would suppress TC adsorption at pH < 4.7 due to the competition between Cu^{2+} and TC (Jia et al. 2008). The different behaviors between TCs and FQs can be ascribed to their physiochemical properties. The FQs have two different pKa values: carboxylic (p$K a_1$ = 5.90–6.23) and amino (p$K a_2$ = 8.28–8.89) (Riaz et al. 2018). However, p$K a_1$ values for TCs ranged from 3.27 to 3.30, and p$K a_2$ values ranged from 7.2 to 7.68 (Tolls 2001; Gao et al. 2012; Zhao et al. 2018). TCs and FQs have different dissociation constant and pKa values thus impacting the formation of complexes between antibiotics and multivalent cations. Moreover, heavy metals would suppress soil microbial activities, which would in turn reduce the biodegradation of antibiotics. However, nutrient elements, such as K, would enhance the activities of soil organisms and promote the uptake and degradation of antibiotics (Pan and Chu 2017).

Although these contaminates were mainly introduced into soils through human inputs, soil properties also can significantly influence their environmental fates in soils. As shown in Fig. S3, we found that OTC and TC were significantly correlated with soil texture, especially for soil clay content, as well as NOR and Cu ($p < 0.05$). Moreover, PER in soil was significantly influenced by soil pH. Numerous studies have demonstrated that antibiotics and metals can be enriched in clay minerals (Wu 1999; Tolls 2001). For instance, cation exchange is an important mechanism for adsorption of tetracyclines in clay minerals, which depended on the charge of both antibiotic compounds and clay minerals (Pils and Laird 2007). Positive charges are the main forms for tetracycline antibiotics under acidic condition indicating neutralized negative charge sites on the clay surface, and inner-sphere sorption is the main mechanism of adsorption for tetracycline antibiotics on variable charge clay minerals (Aristilde et al. 2010; Zhao et al. 2011). Many metals were also found to be characterized by strong adsorption on clay mineral particles, especially under alkaline conditions due to the carbonate content of soils, and Cu showed higher immobilized amounts than Zn (Sheikhhosseini et al. 2013; Sipos et al. 2008). Moreover, Sheikhhosseini et al. (2013) found that sorption isotherms of Zn declined significantly afterward in the presence of increasing Cu concentration in the case of sepiolite, which indicated competitive sorption among metals on clay minerals. However, there were no significant correlations between the other contaminates and soil properties. That might be caused by the strong effects of human activities on the distribution characteristics of antibiotics and metals in agricultural soils with long-term manure application.

To comprehensively evaluate the contribution of soil texture, metals, and soil organic matter to the distribution of antibiotics, a VPA was conducted. Figure 8 shows that 20.5 and 17.0% of the variance of TCs and FQs, respectively, could be explained by the selected variables. For the TCs, the metals explained the largest variation (6.7%), followed by the interaction between metals and soil organic matter, which accounted for 5% of the variation due to metal bridging (MacKay and Canterbury 2005). Soil texture, soil organic matter, and the interaction between them explained less variation (4.2, 1.6, and 0.2%, respectively). Similar to the TCs, the metals explained the largest variation (8.7%) in FQs, and soil texture and soil organic matter explained the same amount of variation (5.3%). Only 0.5% of the variation was explained by the interaction between metals and soil organic matter. These results showed that metals significantly enhance the sorption of TCs and FQs on soil organic matter.

Conclusions

The distributions of ten antibiotic compounds and six metals in agricultural soils from a typical peri-urban catchment were studied. Land-use composition and LDI were used to analyze the impact of human disturbance on soil contamination by antibiotics and metals. The results showed that the LDI of a 300-m buffer zone is most closely related to soil contamination. Significant correlations between LDI and both types of target antibiotics and metals were observed. The co-contamination of antibiotics and metals in soils was confirmed. Source identification analysis demonstrated that human disturbance, especially agricultural activities, was the dominant source of most antibiotics and of Cu and Zn in soils, whereas the other antibiotics (OTC, PER, and LOM) and metals might come from other unidentified sources. In agricultural soils with long-term fertilization, Al, Cu, and Zn could significantly aggravate the accumulation of tetracycline antibiotics in soil, whereas only Cu exhibited synergistic contamination with ciprofloxacin and norfloxacin. Metals contributed 6.7 and 8.7% of the variance in tetracyclines and fluoroquinolones, respectively. Combining spatial analysis with multivariable statistics, this study provides an effective approach for identifying the sources of antibiotics and metals in soils at a catchment scale and demonstrates that there are multiple diffuse sources. Further study is needed to evaluate the synergetic impact of antibiotics and metals on ecosystem security and public health.

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