Simulation and risk assessment of typical antibiotics in the multi-media environment of the Yangtze River Estuary under tidal effect

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Abstract

Frequent human activities in estuary areas lead to the release of a large number of antibiotics, which poses a great threat to human health. However, there are very limited studies about the influence of the special natural phenomena on the occurrence and migration of antibiotics in the environment. In this study, we simulated the migration and transformation of six typical antibiotics, including oxytetracycline (OTC), tetracycline (TC), norfloxacin (NOR), ofloxacin (OFX), erythromycin (ETM) and amoxicillin (AMOX), in the environmental media from 2011 to 2019 in the Yangtze River Estuary, by using the level III multi-media fugacity model combined with the factor of tidal. The simulation results show that the most antibiotics mainly existed in soil and sediment while erythromycin were found mainly in water. The concentrations of antibiotics in air, freshwater, seawater, groundwater, sediment and soil were 10^{-23}-10^{-25}, 0.1-12 ng/L, 0.02-7 ng/L, 0.02-16 ng/L, 0.1-13 ng/g and 0.1-15 ng/g respectively. Sensitivity analysis showed that the degradation rate (K_m) and the soil-to-water runoff coefficient (K_l) were important model parameters, indicating that hydrodynamic conditions have a significant impact on the migration of antibiotics in various environmental phases in estuarine areas. Tide can enhance the exchange between water bodies and cause the transformation of the antibiotics from freshwater to seawater and groundwater, which improves the accuracy of the model, especially the seawater and soil phase of it. Risk assessments show that amoxicillin, erythromycin, ofloxacin and norfloxacin pose a threat to the estuarine environment, but the current source of drinking water does not affect human health. Our findings suggest that, when one would like to exam the occurrence and migration of antibiotics in environment, more consideration should be given to the natural phenomena, in addition to human activities and the nature of antibiotics.

1. Introduction

As a concentrated area of land and sea activities with tidal current runoff, estuarine area is not only the end point of watershed, but also the starting point of ocean. The remarkable economic and social development, together with and rapid population growth in the Yangtze River Estuary, brought continuous production and import of domestic sewage into the Yangtze River and offshore areas, and the discharge of sewage has been at a high level, which has affected the drinking water safety of cities along the Yangtze River (Jiang et al., 2011; Xu et al., 2007).

The Yangtze River Estuary environmental system has been confirmed to have a certain amount of antibiotic accumulation, and the content of antibiotics in each environmental phase of the Yangtze River Estuary and adjacent sea areas is high. Several types of the antibiotics show a high detection rate in summer (Yan et al., 2015), such as tetracyclines, macrolides and quinolone. The detection rate of fluoroquinolones, in particular, has reached to 100% in a specific period, and the concentration of fluoroquinolones is between 0 and 30.87 ng/g (Chen and Zhou, 2014). Because of the high volatility and strong affinity with organic matter, fluoroquinolones show strong migration activity in the environment, and its impact on ecological environment and human health cannot be ignored. Some typical antibiotics accumulated largely in the soil and sediments of the Yangtze River Estuary. The existing studies on

estuaries mainly focus on Bohai Bay and Zhuhai Bay (Zhang et al., 2020), while the research on the Yangtze River Estuary centers on the determination and source analysis of various pollutants in diverse environmental media. Yu et al., (2020)reported the high content of antibiotics in each environmental phase of the Yangtze River Estuary and adjacent sea areas, as the antibiotics were detected at 27.5 ng/L in livestock farms, aquaculture farms and domestic sewage effluent in the basin studied. Some researchers (Kim and Carlson, 2007; Yan et al., 2013) have detected the content of antibiotics in surface water in Shanghai, finding that pollutions led by tetracycline antibiotics, fluoroquinolones antibiotics and other antibiotics are in fact more serious. However, there are very few studies on the distribution and influential factors of typical antibiotics in sediment-water-soil distribution, multi-medium fate simulation and related areas.

The pollution sources of typical antibiotics are believed to be existing consistently. Therefore, it is necessary to predict the concentration change of the antibiotics in the future and a specific region. With the multi-media environmental fugacity models, researchers can use well-known physicochemical properties, together with the climate data and information on spatial and temporal emissions, to provide a comprehensive picture of the environmental activities of organic chemicals as they transport away from sources (Dale et al., 2015; Di Guardo et al., 2018; Mackay and Paterson, 1991a, 1981). Such models are used to identify the important transport pathways of chemicals in multiple media, provide approximate predictions on the concentrations in environmental compartments, and determine the final fate (Mackay and Paterson, 1991a; Wania and Mackay, 1995; Zhang et al., 2015). In recent years, some progress has been made in the simulation of the long-term trend of persistent organic pollutants in the environment (Zhang et al., 2013; Zhou et al., 2011). Tide effects in estuarine areas can affect antibiotic migration, but few studies take this into account.

Based on the level III multi-media environmental fugacity model, this research on the Yangtze River Estuary aims to simulate the concentrations of oxytetracycline, tetracycline, norfloxacin, ofloxacin, erythromycin and amoxicillin in different environmental media from 2011 to 2019. We imitated the distribution of antibiotics among different phases, analyzed the sensitivities, and explored the main influential factors. The study made an innovative move by introducing the tidal action, an underestimated factor in the previous studies, to simulate the distribution of antibiotics in the estuarine area.

2. Research Method

2.1 Studied area

The studied area is the Yangtze River Estuary and its adjacent sea area, the starting point of which is the Xuliujing River. The Yangtze River Estuary is characterized with crisscrossing waterways and vast beach, which grant the area unique soil and water environment, shipping conditions and ecology and natural resources. The place is also a meeting point of China's "Belt and Road", the Yangtze River Economic Belt and the Yangtze River Delta integration construction. The width of the Xuliujing River is about 5 km, about 90 km from Qidong to Nanhui. The Yangtze River Estuary is divided into the south branch and the north

branch by the Chongming Island. The south branch is divided into south port and north port by Changxing Island and Hengsha Island. And the south port is divided into the south channel and the north channel by the nine sections of sand outside Hengsha.

2.2 Estimate on typical antibiotic emission

Based on the different usage purposes, antibiotics can be classified into two main types: human antibiotics and veterinary antibiotics. The discharge of human antibiotics can be either agricultural or non-agricultural, according to the treatment mode it takes. The estimate on animal antibiotic emissions includes estimate on livestock antibiotic emissions and that on poultry antibiotic emissions, according to the different breeding methods it involves (Celle-Jeanton et al., 2014; Jjemba, 2006). According to the production of regional per capita use and watershed population, the amount of antibiotics used in the basin can be obtained, in which population statistics are mainly converted by official statistics. Emissions of veterinary antibiotics are calculated by breeding scale.

After antibiotics enter the body and animals through various ways, only a very small part of them will be absorbed and utilized, of which about 30%~90% will be excreted through feces (Halling-Sørensen, 2001). By determining the antibiotics excretion of different species and their various ways into the environment, while combining them with the distribution ratio of different environmental phases, Hu et al. (2010) obtained the antibiotic emissions of different environmental phases.

Antibiotic emissions to surface water and soil as follows:

$$T_{02} = \left(n_1 \times p_1 + 0.8 \times n_2 \times p_2 + 0.2 \times n_3 \times p_3\right) \times (1 - c)(1)$$

$$T_{04} = 0.2 \times n_2 \times p_2 + 0.8 \times n_3 \times p_3 + n_4 \times p_4(2)$$

Where T_{02} is emission rate of antibiotics in surface water (mol/h), T_{04} is emission rate of antibiotics in soil (mol/h), n_i (i = 1, 2, 3, 4) and p_i (i = 1, 2, 3, 4) are the number and excretion ratio of urban human, countryman, livestock and poultry, c is removal efficiency.

2.3 Model

The level III multi-media environmental fugacity model was built to simulate the multi-media activities of several typical antibiotics (namely, oxytetracycline, tetracycline, norfloxacin, ofloxacin, erythromycin and amoxicillin) in the Yangtze River Estuary system by considering the estuary as a whole system. Taking the characteristics of the area and the salinity difference existing in the river reach into account, the researchers classified the surface water area into fresh water area and seawater area with Wusongkou as the boundary. The model includes six major phases: air, freshwater, seawater, soil, sediment and groundwater.

The input process of antibiotics in the areas studied includes horizontal flow and sewage discharge. The exchange process among environmental media involves air-water exchange (dry and wet deposition and

diffusion), particulate matter deposition and resuspension in water, diffusion between water and sediment, and so forth. The output process includes degradation in each medium and horizontal flow output. With the exception of a few constants, such as molecular weight and the Henry constant, each parameter is searched from the relevant literature or data manual, and representative data are selected after comparative analysis of similar data in order to exhibit the actual situation of the Yangtze River Estuary as much as possible. By the formula, the fugacity capacity and interphase migration flux of each phase are obtained. The fugacity of each phase is obtained by solving the equation, and the concentrations of oxytetracycline, tetracycline, norfloxacin, ofloxacin, erythromycin and amoxicillin in each phase are obtained by $c = zf$. In addition to that, the interphase migration flux is calculated, in order to analyze the major interphase migration processes.

The mass balance equation is established for each main phase as follows:

Air:

$$T_{01} + D_{21}f_2 + D_{31}f_3 + D_{41}f_4 = (D_{10t} + D_{12} + D_{13} + D_{14} + D_{1M})f_1 \quad (3)$$

Freshwater:

$$T_{02} + T_{02t} + D_{12}f_1 + D_{32}f_3 + D_{42}f_4 + D_{52}f_5 + D_{62}f_6 = (D_{21} + D_{23t} + D_{25} + D_{26t} + D_{2m})f_2 \quad (4)$$

Seawater:

$$T_{23t} + D_{13}f_1 + D_{63t}f_6 = (D_{30t} + D_{31} + D_{32} + D_{36} + D_{3m})f_3 \quad (5)$$

Soil:

$$T_{04h} + D_{14}f_1 + D_{24}f_2 = (D_{41} + D_{42} + D_{46} + D_{4m})f_4 \quad (6)$$

Sediment:

$$D_{25}f_2 = (D_{52} + D_{5m})f_5 \quad (7)$$

Groundwater:

$$(D_{26}f_2 + D_{46}f_4 + D_{36}f_3) = (D_{62} + D_{63} + D_{6m})f_6 \quad (8)$$

where T is the emission rate ($mol \cdot h^{-1}$), D refers to the interphase migration parameters [$mol \cdot (Pa \cdot h)^{-1}$] (as show in **Table S2**). f is the fugacity (Pa), and the subscript t represents the transport process of advection inflow and outflow. The subscript m stands for the pollutant degradation process.

2.4 Process and parameter identification

To use the model to describe the migration of antibiotics in the environment, three types of parameters were collected: physicochemical properties of antibiotics, regional environmental parameters and kinetic

parameters. The physicochemical properties incorporate molar mass, melting point, saturated vapor pressure, half-life of pollutants in each environmental phase and the Henry constant. The environmental parameters include area, height of each phase, rain rate and proportion of organic matter. The kinetic parameters involve diffusion rate, advection rate and sedimentation rate.

According to the relevant literature and field observation of sample areas, the environmental parameters of the areas studied can be set, and the details of the parameters can be found in the **Table.S1**. The simulation results will not be affected as long as the atmosphere height remains at a high level of 1000 m. Considering that the active layer in which the sediment is mainly involved in the dynamic exchange of pollutants is within 0.15 m in the surface layer, the sediment depth parameter value is set as 0.15 m in this study (Chen et al., 2012). In addition to these two parameters, the other parameters are from the relevant literature on the Yangtze River Estuary region (Mackay and Paterson, 1991b; Wania et al., 2006) .

The physicochemical parameters of typical antibiotics (oxytetracycline, tetracycline, norfloxacin, ofloxacin, erythromycin and amoxicillin) are mainly thermodynamic quantities. The basic physicochemical parameters of the typical antibiotics in this study are mainly obtained from environmental manual and published literature. The effects of environmental migration parameters are shown largely in the rate and flux of pollutants in each medium in the model, as well as the time when the system reaches equilibrium. Because the variation among these parameters in different regions is very small and the sensitivity to the model is not high, we adopted the value of the parameters in the Mackay fugacity model.

2.5 Model construction under tidal influence

In order to ensure the integrity of the model, we introduced the estuary tide as an influential factor, mainly by adjusting the environmental parameters and dynamic parameters of the Yangtze River Estuary in the tidal stage to optimize the sensitive parameters of the model and improve the accuracy of the model prediction.

In coastal areas, the salinity of river water in estuarine areas is much higher than that in upstream areas due to saltwater intrusion. Therefore, the following formula is used to make the necessary improvements to the partition coefficient:

$$LogK_{oc} = 2.7 + \frac{1}{3} \times Log\left(\frac{S}{0.032}\right) (9)$$

where K_{oc} is organic carbon - Water distribution coefficient, S is salinity, ‰.

When the tidal current velocity is 0 and the salinity is approximately 0, the saltwater intrusion reaches the maximum length, L_{max}:

$$u_t = 0 (10)$$

$$\frac{\partial s}{\partial t} = 0 (11)$$

$$u = -u_f + u_d (12)$$

$$u_t = -\beta \frac{\delta s}{\delta x} (13)$$

$$L_{max} = \frac{D_X}{u_f} \ln \frac{S_0}{S} + \frac{\beta}{u_f} \left(S_0 - S \right) (14)$$

where u_t is tidal current velocity, m/s; u_f is runoff velocity, m/s; u is total flow rate, m/s; S is average salinity of section, ‰; S_0 is initial salinity of section, ‰; D_X is vertical diffusivity; β is non-uniform coefficient.

Because the study area is the Yangtze River Estuary, the period is dry stage, that is, the salt tide intrusion stage, resulting in the lack of freshwater area in the estuary area. Therefore, when considering the model generalization, the model is divided into five main phases, namely air, seawater, soil, sediment and groundwater.

Air:

$T_{01t} + D_{31}f_3 + D_{41}f_4 = (D_{10t} + D_{13} + D_{14} + D_{1m})f_1$ (15)

Seawater:

$T_{02t} + T_{02h} + D_{13}f_1 + D_{43}f_4 + D_{53}f_5 + D_{63t}f_6 = (D_{30t} + D_{31} + D_{36} + D_{3m})f_3$ (16)

Soil:

$T_{04h} + D_{14}f_1 + D_{34}f_2 = (D_{41} + D_{43t} + D_{46} + D_{4m})f_4$ (17)

Sediment:

$D_{35} f_2 = (D_{53} + D_{5m})f_5$ (18)

Groundwater:

$D_{46} f_4 + D_{36t}f_3 = (D_{63t} + D_{6m})f_6$ (19)

where T is the emission rate (mol·h^{-1}); D is the interphase migration parameters [mol·(Pa·h)$^{-1}$] (as show in **Table S2**); f is the fugacity (Pa); the subscript t represents the transport process of advection inflow and outflow; the subscript m represents the pollutant degradation process.

2.6 Risk assessment

Ecological risk (ER) is a risk assessment against the possible destruction of ecological environment and subsystems with certain numbers and probabilities. Risk quotient (RQs) is the most commonly used ecological risk assessment method (González-Pleiter et al., 2013). Risk assessment based on RQ and acute toxicological data are obtained from United States Environmental Protection Agency (EPA) ECOTOX database (**Table S2** and **S3**).

$$RQ = \frac{PEC}{PNEC} (20)$$

or

$$RQ = \frac{MEC}{PNEC} (21)$$

$$PNEC = \frac{LC_{50}\left(EC_{50}\right)}{AF} (22)$$

PEC is the predicted effect concentration (ng/L); *MEC* is the measured effect concentration (ng/L); *PNEC* is the predicted no-effect concentration (ng/L); EC_{50} is the median effect concentration (ng/L); *AF* is the assessment factor. The risk quotient is divided into three levels. The first one is “low ecological risk” (RQ < 0.1), which means that no pollution exists. The second level is “moderate ecological risk” (0.1 ≤ RQ < 1.0). In this level, some pollution can be found, a status that needs to be alerted and some measures should be taken to reduce the pollution. The third level is “high ecological risk” (RQ ≥ 1.0), where measures should be taken to reduce the pollution concentration of chemicals in the region as soon as possible (Hernando et al., 2006).

Health quotient can be used to evaluate whether the antibiotic concentrations in water go beyond human standards (Kim et al., 2007).

$$HQ = \frac{MEC}{DWEL} (23)$$

$$DWEL = \frac{ADI \times BW}{DWI \times FOE} (24)$$

Here DWEL refers to the drinking water equivalent (μg/L); ADI is the accepted daily intake (μg/(kg·d)); BW is the bodyweight (kg); DWI is the drinking water intake (L/d); FOE is the frequency of the exposure (350 d/a). The BW and DWI data are recommended by EPA (**Table S4** and **S5**).

3. Results And Discussion

3.1 Estimation of antibiotic emissions in the Yangtze River Estuary

Due to the lack of official statistics on the use of antibiotics, we converted them from the permanent population statistics of the Yangtze River Estuary and the breeding scale data of livestock and poultry from 2011 to 2019 (**Table S6**). As shown in **Fig.1a**, the total population in the study area remained stable from 2011 to 2019, the rural population decreased slightly, from 311million to 2.3million, and the urban population increased by 1.5million during the 10 years, with a limited increase relative to the total number. Due to the decrease of agricultural population and the decline of breeding scale in the Yangtze River estuary, the number of breeding livestock and poultry has decreased significantly. In 2011, the number of livestock was 2.67million, and in 2019, it was only 1.17million, which decreased by 60%. The number of poultry breeding has also decreased sharply, from 43million in 2011 to 8.44million in 2019, and the breeding scale has decreased to 20% of the original. Overall, the population of the Yangtze River estuary did not change significantly, but the scale of aquaculture in the region was seriously reduced.

Different types of antibiotics have different retention times after entering the body, resulting in different proportions of final excretion in vitro. Therefore, when considering the total amount of antibiotics entering the environment, antibiotics absorbed by people or animals need to be subtracted (**Table S10 and Table S11**). It can be seen from the rate of T_{02} (**Fig. 1b**) and T_{04} (**Fig. 1c**) of the six target antibiotics released to surface water and soil during 2011–2019 that the amount of these antibiotics released to soil and surface water has been decreasing. In surface water, the emission rate of tetracycline decreased from 0.635 mol/h to 0.272 mol/h, the emission rate of amoxicillin decreased from 0.341 mol/h to 0.154 mol/h, the emission rate of ofloxacin decreased from 0.085 mol/h to 0.038 mol/h, the emission rate of oxytetracycline decreased from 0.023 mol/h to 0.011 mol/h, the emission rate of norfloxacin decreased from 0.019 mol/h to 0.009 mol/h, and erythromycin hardly emitted into surface water. In soil, tetracycline emission rate decreased from 8.125 mol/h to 3.224 mol/h, amoxicillin emission rate decreased from 4.714 mol/h to 1.503 mol/h, ofloxacin emission rate decreased from 4.092 mol/h to 0.988 mol/h, oxytetracycline emission rate decreased from 0.512 mol/h to 0.115 mol/h, norfloxacin emission rate decreased from 0.398 mol/h to 0.121 mol/h, erythromycin emission rate decreased from 1.821 mol/h to 0.407 mol/h. The main reason is that the decrease in the scale of aquaculture has led to the decrease in the amount of veterinary antibiotics. The rate of tetracycline and amoxicillin discharged into the water environment is large, on the one hand because of their large consumption, and on the other hand because the degradation efficiency of these two substances in sewage treatment plants is not high, resulting in a large rate of discharge into the water environment. In addition to high tetracycline and amoxicillin, the rate of ofloxacin directly discharged into the soil was also relatively high because it was mainly used for bacterial and mycoplasma infections in livestock and poultry. Due to the lack of facilities, sewage and feces in rural areas are discharged directly into the outdoor environment and enter the soil, resulting in the rate of these six antibiotics entering the soil environment is much higher than the rate of pollution entering the water phase.

3.2 Model validation

In order to verify the validity of the model, the simulated value of the model was compared with the measured value. The validation data were from the literature (as show in **Table S12**) and the measured

values of this study. Because the predicted antibiotic concentration in the air was lower than the detection limit, the simulated values of the other five environmental phases were compared with the measured values. It can be found in **Fig. 2** that the difference between the simulated concentration and the measured concentration of the six antibiotics in each environmental medium was less than a logarithmic unit, so the model simulation was effective. The simulation results of OTC were also within the allowable range of the model, and the errors in each environmental phase were large compared with other substances. These may be due to the selection of antibiotic emission parameters in this study. Input of OTC in water was from sewage discharge, while the input rate of upstream incoming water was small, which might be the reason for the low simulation value in water. For underground water phase, partition coefficient and degradation rate in environmental medium were very important parameters. The degradation rate of selected antibiotics varied in different environmental media. The values of this study may be different from the actual situation, as the simulation value was higher than the measured value. This is because the hydrodynamic factors of estuary were ignored.

3.3 Interphase distribution

Overall, as the aquaculture area studied shrank **(Fig. 1a)**, the concentrations of those antibiotics in each environmental phase showed a decreasing trend year by year. Among them, the aquaculture area in this region increased by 30% from 2017 to 2018, resulting in the increase of various antibiotic dosage. The predicted ambient concentrations of the six antibiotics (namely, oxytetracycline, tetracycline, ofloxacin, ofloxacin, ofloxacin, erythromycin and amoxicillin) remain extremely low (10^{-23}-10^{-25} ng/L), because of their low volatility.

As shown in Fig. 3a, the concentration of oxytetracycline in freshwater was 0.14 ng/L in 2011 and decreased to 0.06 ng/L in 2019 (a 60% decline), while its concentration in seawater and groundwater was in the order of 10^{-3} ng/L. The concentration of tetracycline in freshwater was higher than that of oxytetracycline, reaching 1.20 ng/L, and its lowest concentration was 0.50 ng/L during 2011–2019 (Fig. 3b). Tetracycline in the seawater phase was up to 0.02 ng/L due to the effects of migration, diffusion and advection. The degree of contamination in the groundwater phase equaled to that of oxytetracycline, because tetracycline itself has a high octanol-water partition coefficient K_{ow} and it tends to be adsorbed by sediments or soils. The concentration of norfloxacin in freshwater, seawater and groundwater was higher than tetracycline antibiotics, and its distribution was more uniform than that of tetracycline antibiotics. The concentration range of norfloxacin in freshwater, seawater and groundwater was 0.10–0.21 ng/L, 0.03–0.06 ng/L and 0.02–0.06 ng/L, respectively (Fig. 3c). The pollution of norfloxacin in seawater and groundwater was more serious than tetracycline antibiotics, but the concentration in freshwater was much lower than tetracycline and was almost the same as that of oxytetracycline. The concentration change of ofloxacin was completely different from that of norfloxacin. From 2011 to 2019, the pollution level of ofloxacin did not change over time, that is, it did not decrease with the decrease of aquaculture. The concentration of ofloxacin in freshwater was maintained at a high level of 12.00 ng/L, and the concentration of ofloxacin in seawater was maintained at 0.28 ng/L, while that in groundwater was about 0.08 ng/L (Fig. 3d). The overall pollution degree was high. The reason is that both the

hydrolysis degree and the degradation rate of ofloxacin are slow, and a certain amount of ofloxacin was imported into the upstream of the river. The concentration of erythromycin in various environmental phases continued to decrease. In 2011, the concentration of erythromycin in groundwater was as high as 16.00 ng/L, but it fell to about 3.00 ng/L in 2019, and the overall concentration decreased by 82.5%. Erythromycin was at a high concentration level in freshwater and seawater. During 2011–2019, its concentration in freshwater was 2.00–8.50 ng/L, and its concentration range in seawater was 2.00–7.00 ng/L (Fig. 3e). However, comparatively, erythromycin pollution was more serious, no matter it was in groundwater, fresh water or seawater. That is because wastewater treatment plants applied better techniques to remove tetracycline and quinolones from water, but they almost failed in addressing the erythromycin issue. (Xu et al., 2007). Amoxicillin concentration peaked at 8.00 ng/L in the freshwater phase, and decreased to 3.00 ng/L in 2019. Amoxicillin concentrations in the seawater and groundwater phases were 0.10–1.00 ng/L (Fig. 3f), and the pollution status was better than erythromycin. The result indicates that beta-lactam antibiotics had not been used on a large scale in the Yangtze River Estuary region. Similar results can be found in the concentration levels of amoxicillin antibiotics in Guangzhou, China (Golet et al., 2003).

As shown in Fig. 4, the pollution of these six antibiotics in soil and sediment was more serious, and the concentrations of tetracycline, norfloxacin, ofloxacin, erythromycin and amoxicillin were basically higher than 0.10 ng/g. The concentration of tetracycline in soil decreased from 14. 00 ng/g to 5. 00 ng/g, and the pollution status improved significantly. Nevertheless, there was still serious pollution. Because the molecules of tetracycline antibiotics contained more polar/ionic functional groups (Chopra and Roberts, 2001), the adsorption ability in soil was strong. The concentration of ofloxacin in sediments has been maintained at about 13. 00 ng/g, with no decrease in recent 10 years. It may be attributed to the higher concentration of quinolones antibiotics in sewage discharge; on the other hand, the adsorption coefficient (K_d) value of quinolones antibiotics is higher, and the quinolones is easy to transfer from the freshwater phase to the sediment phase (Tolls, 2001). Moreover, researchers (Yang et al., 2011) found that sediment adsorption was one of the most important ways to remove quinolones antibiotics from sewage. The molecular structure of quinolones contains positively charged nitrogen atoms or dimethylamino groups. Therefore, under the electrostatic attraction, quinolones antibiotics are easier to be adsorbed than other types of antibiotics in negatively charged sediments (Wang et al., 2010). Quinolones are not easy to be biodegraded, so it is assumed that adsorption removal may be a major approach to remove the quinolones in sewage. Quinolones enter the sediment through adsorption. If they have not been degraded, they will accumulate continuously, pollute the water or soil environment, and then pose threats to human health.

3.4 Sensitivity analysis

The sensitivity of the relevant parameters can determine the source of uncertainty of the model parameters and identify the importance of the parameters to the model. In this regard, a quantitative analysis of the sensitivity of many parameters was carried out and the parameters were calculated with the following formula:

$$S = \frac{X_{1.1} - X_{0.9}}{0.2X_{1.0}} (18)$$

The input of the $X_{1.1}$ was increased to 110% of the original parameter value; the $X_{1.0}$ stands for the original value of the parameter; and the input of the $X_{0.9}$ was reduced to 90% of the original parameter value; S represents the sensitivity coefficient.

After a series of analysis on sensitivity and calculation of the main model input parameters, we found that the two emissions were important parameters for the model, as they had exerted considerable influence on the concentration of six environmental phases, which might be attributable to the uncertainty of the model concentration (**Fig. 5**). The discharge in the soil phase affects that in the groundwater, soil and air phase. Meanwhile, the discharge of freshwater showed an impact on sediment, seawater and freshwater, which was caused by the migration tendency of antibiotics in the environmental phase. Emissions from freshwater had little effect on OFX and AMOX, and this is because that the regional emission volume were much smaller compared to the upstream advection input rate.

Different input parameters demonstrated huge influence on the concentration of each environmental phase. During the sensitivity analysis, we found that the temperature variation had little effect on the six antibiotics. In general, when there was no significant temperature change, the disturbance of the material properties turned to be weaker. The degradation rate (K_m) and the soil-to-water runoff coefficient (K_l) were the main influential parameters. The migration, transformation and fate of the six antibiotics were all affected by these parameters. This also confirms from the model perspective that hydrodynamic conditions are important for the migration and redistribution of typical antibiotics (i.e., oxytetracycline, tetracycline, norfloxacin, ofloxacin, erythromycin and amoxicillin) in various environmental phases of the region.

3.5 Interphase distribution under tidal effect

The tidal action of the Estuary will bring a large number of salt-rich seawater into the area studied. Moreover, the freshwater brought by the upstream runoff changes the salinity distribution of the whole Estuary area. Therefore, when considering the model parameters, we first determined the intrusion length of salt water and the salinity at different intrusion lengths. Combined with the measured data (**Table S13**), the salinity values of water bodies at different distances from the Estuary are calculated (**Fig. 6**).

As shown in **Fig. 7**, after taking the tidal effect into consideration, the results showed that the measured concentrations of six antibiotics in various environmental media and the concentration difference in tidal phase were in a logarithmic unit, in addition to the fact that the logarithmic difference of oxytetracycline and tetracycline in sediment and groundwater environmental phases was slightly greater than 1. The model simulation was generally effective. All of simulated values of all antibiotics in tidal phase are closer to the measured values than in analog state, except amoxicillin in seawater and oxytetracycline in soil. In general, the simulation effect further increased after the introduction of tidal effect, especially the seawater and soil phases.

Concentration distribution of antibiotics in different phases of the Yangtze River Estuary changed greatly after tidal effect was introduced (**Fig.8** and **Fig.9**). The concentration showed a consistently decreasing trend over the time period. Compared with the steady state stage, the occurrence of antibiotics in each phase of the tidal stage increased, and the concentration of some antibiotics rose as well (**Fig.8a**). As one of the main pollutant discharge phases, the overall concentration of seawater remained high in several phases. The concentration of oxytetracycline was 0.26 ng/L in 2011 and decreased to 0.13 ng/L in 2019. The concentration increased a lot compared with that in the steady state, and the concentration of oxytetracycline in groundwater increased to about 0.10 ng/L. The concentration of tetracycline in seawater phase also reached to 0.34 ng/L during 2011–2019 (**Fig.8b**), and the highest value reached 0.80 ng/L, which was an order of magnitude higher than that before, but less than the concentration of freshwater phase at the steady state. The pollution of groundwater environment in the tidal stage was also aggravated, and the highest pollution concentration reached to 0.03 ng/L. The concentration range of norfloxacin in seawater phase was 0.07–0.16 ng/L, and that in groundwater was 0.03–0.08 ng/L (**Fig.8c**). The pollution level in seawater and groundwater in tidal phase was higher compared with tetracycline antibiotics, which was different from that in the steady phase. At the same time, the concentration of seawater phase in tidal phase was also lower than that in the freshwater phase and the seawater phase in the steady phase, indicating that more norfloxacin lost its migration and transformation in the water phase in the tidal phase. Changes in ofloxacin concentrations continued to show the same trend during the period 2011–2019, in other words, not decreasing with the scale of aquaculture in the Yangtze River Estuary, and the ofloxacin concentrations in seawater remained high at 6.80 ng/L (**Fig.8d**). Erythromycin pollution was serious in both groundwater and seawater (**Fig.8e**). Amoxicillin pollution was milder than erythromycin pollution, but more serious than tetracycline antibiotics (**Fig.8f**). On the whole, the pollution in surface water was weakened, but the groundwater was aggravated, indicating that the tides aggravated the pollution of oxytetracycline in groundwater. The possible reason was that the tides increased the exchange between water bodies, causing more oxytetracycline entering into the groundwater.

As shown in **Fig. 9**, the concentrations of these six antibiotics in soil and sediment were still high under tide effect. The concentration of tetracycline in soil decreased from 14.00 ng/g to 5.00 ng/g, and the decreasing trend had not changed, which was consistent with that in the steady state. However, the concentration of ofloxacin in sediment fell to about 8.00 ng/g, a significant decrease. The concentrations of norfloxacin, ofloxacin, erythromycin and amoxicillin in soil and sediment were higher than 0.10 ng/g, and the content of oxytetracycline in sediment was lower than 10^{-3} ng/g. It can be seen that tidal action exerted great influence on the occurrence of stable antibiotics, such as ofloxacin, in the environment.

3.6 Risk assessment

Ecological risks of typical antibiotics in freshwater and soil were evaluated at the Yangtze Estuary in 2019 (**Fig.10a and 10b**). Oxytetracycline, tetracycline and norfloxacin had low risks to the most sensitive aquatic microorganisms (algae) in the area studied, which were all lower than 0.1, indicating that these antibiotics were unlikely to cause adverse effects on algae. Erythromycin and ofloxacin extended

moderate risk to algae, while amoxicillin showed high risk to algae.In soil, erythromycin and ofloxacin demonstrated high risks, and that was especially the case of erythromycin, as its RQ was close to 16, much larger than 1. The risk of norfloxacin was moderate, and tetracycline antibiotics were at a low risk level. Despite that, erythromycin and ofloxacin were two considerable threats to the environment, because the amount of the two antibiotics was large and they were difficult to be degraded. As shown in **Fig.10c**, the HQ of the five selected antibiotics was less than 1, a status that was not threatening to human health. That is to say, the water in the drinking water source had not affect human health. However, the fish resources in the estuary area were relatively concentrated, and the enrichment effect might be harmful to human health. Therefore, it can be concluded that more attention should be paid to the pollution caused by antibiotics.

4. Conclusion

In this study, we analyzed the occurrence and migration of the six antibiotics in the six environmental phases of the Yangtze Estuary under tidal action. The rate of antibiotic emissions in the area studied decreased as the aquaculture scale fell. Tetracycline emission and amoxicillin emission reached their highest level in surface water and soil, while ofloxacin emission peaked in soil. In addition, due to the lack of facilities, sewage and feces in the rural areas were discharged directly to the outdoors and entered the soil, which is the reason why the amount of these six antibiotics entering the soil environment was far higher than that entering the water environment. The traditional level III multi-media environmental fugacity model can well simulate the concentration of antibiotics in different environmental phases, but the simulation value is smaller than the real value, because the hydrodynamic factors of estuary were ignored. The simulation results show that the most antibiotics mainly existed in soil and sediment while erythromycin were found mainly in water. The concentrations of antibiotics in air, freshwater, seawater, groundwater, sediment and soil were 10^{-23}-10^{-25}, 0.1–12 ng/L, 0.02-7 ng/L, 0.02-16 ng/L, 0.1–13 ng/g and 0.1–15 ng/g respectively. The sensitivity analysis shows that degradation rate (K_m) and the soil-to-water runoff coefficient (K_l) were two important contributing factors, which indicates that hydrodynamic conditions were of great significance for the migration and redistribution of antibiotics in various environmental phases in the estuary area. The tides enhanced the exchange between water bodies, resulting in more antibiotics entering seawater and groundwater. Concentrations of antibiotics in soils and sediments remained almost unchanged, but concentrations of ofloxacin in sediments decreased from 13 ng/g to 8 ng/g and remained stable. According to the results of risk assessment, amoxicillin posed a high risk in freshwater; erythromycin and ofloxacin entailed a moderate risk in freshwater and a high risk in soil; norfloxacin exerted a moderate risk in soil. The above four antibiotics had threatened the estuarine environment. At present, the drinking water source will not affect the human health, but antibiotic pollution still needs to be paid attention to. In conclusion, though it is evident that human activities and the nature of antibiotics are influential to the distribution of antibiotics in the environment, the natural phenomena also exert a huge impact on the occurrence and migration of antibiotics.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Competing interests

We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.

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Authors' contributions

Chaomeng Dai: Methodology

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Yan Li: Experiment

Yanping Duan: Conceptualization

Shuguang Liu: Writing- Reviewing and Editing

Yalei Zhang: Supervision

Yaojen Tu: Visualization

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Figures

Figure 1

Scale of resident population and animal farming in the study area (a) and amounts of antibiotics released to surface water (b) and soil (c) from 2011 to 2019.

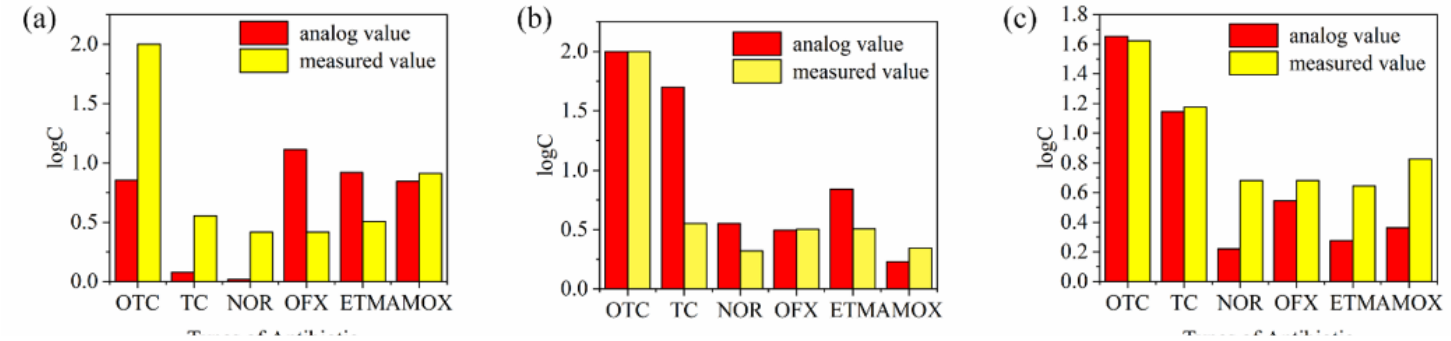

Figure 2

Comparison of freshwater (a), seawater (b), soil (c), sediment (d) and groundwater (e) analog and measured values.

Figure 3

Annual concentration variation of oxytetracycline (a), tetracycline (b), norfloxacin (c), ofloxacin (d), erythromycin (e) and amoxicillin (f) in air, freshwater, seawater and groundwater.

Figure 4

Annual concentration variation of six antibiotics in soil and sediment

Figure 5

Sensitivity analysis of key parameters of OTC (a), TC (b), NOR (c), OFX (d), ETM (e) and AMOX (f) in air, freshwater, seawater, groundwater, sediment and soil.

Figure 6

Relationship between distance from Estuary and salinity.

Figure 7

Comparison of seawater (a), soil (b), sediment (c) and groundwater (d) analog, measured and tidal values.

Figure 8

Annual concentration variation of oxytetracycline (a), tetracycline (b), norfloxacin (c), ofloxacin (d), erythromycin (e) and amoxicillin (f) in air, freshwater, seawater and groundwater.

Figure 9

Annual concentration variation of six antibiotics in soil and sediment.

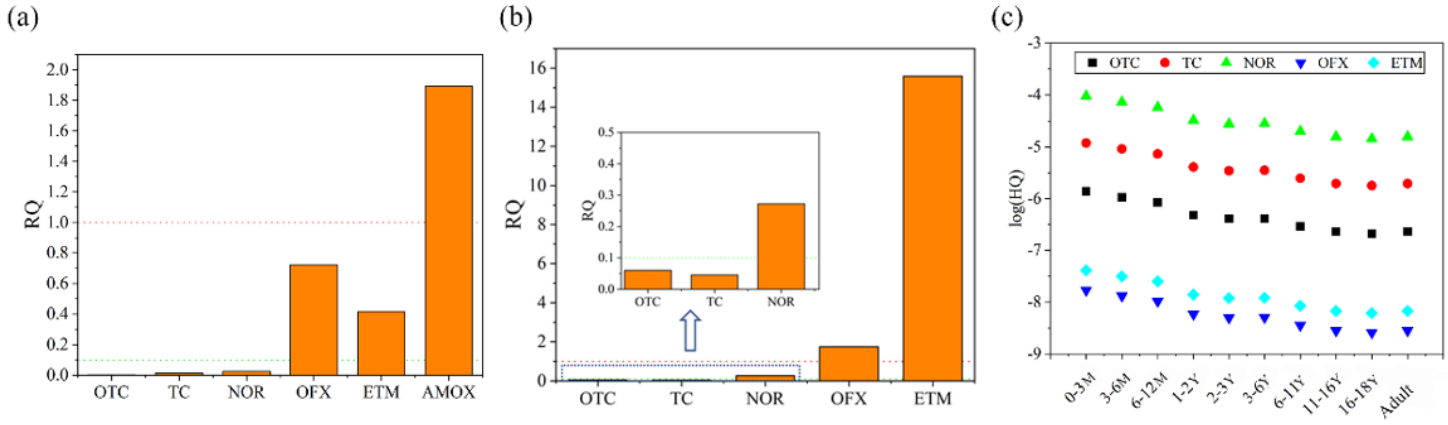

Figure 10

Risk quotient of antibiotics in freshwater (a) and soil (b), and human health risk assessment (c).

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