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REVIEW PAPER

# Quantitative study on the fate of antibiotic emissions in China

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**Abstract** China, the largest producer and user of antibiotics in the world, discharges excessive amounts of these substances into the environment, without prior treatment. This results in ubiquitous distribution of these substances, as well as increased levels of drug-resistant bacteria, that will eventually cause unimaginable consequences to the environment and to humans. However, most of the research on antibiotics has focused on residue analysis of single medium such as wastewater and landfills. There is paucity of research that systematically investigates the fate of antibiotics after excretion, and specifically of end-treatment processes. In this paper, the fate of antibiotic emissions is systematically calculated. The results show that human and livestock feces account for 57.6% and 42.6% of the discharge of medicinal antibiotics and veterinary antibiotics, respectively. Of these feces types, pig feces accounted for 98.7% of antibiotic residues in livestock feces. The above conclusions can be used to clarify the direction of the tracking and supervision of antibiotic residues and provide new ideas for the treatment of antibiotics, especially their terminal removal.

**Keywords** Antibiotic use · Excrement · Removal process · Antibiotic restriction · Antibiotic regulation

## Introduction

Antibiotics, substances that selectively inhibit biological activities of certain organisms at low concentrations, began to be widely used in agriculture and livestock to fight and prevent the flu after the second half of the twentieth century. Despite the undisputed advantages in health care, the biological toxicity of antibiotics should have attracted more attention (Santos et al. 2010).

The abuse of antibiotics in China is very serious. In 2011, when the Chinese Ministry of Health started to reform the human medical system, the DID (average daily antibiotics used per 1000 residents) was 157 g, which was more than five times higher than that of the USA (28.8 g) and the UK (27.4 g) (Zhang et al. 2015). In 2013, a total of 92,700 tons of 36 most common antibiotics were used in China, the largest producer and consumer of antibiotics, as shown in Fig. 1 (Zhang

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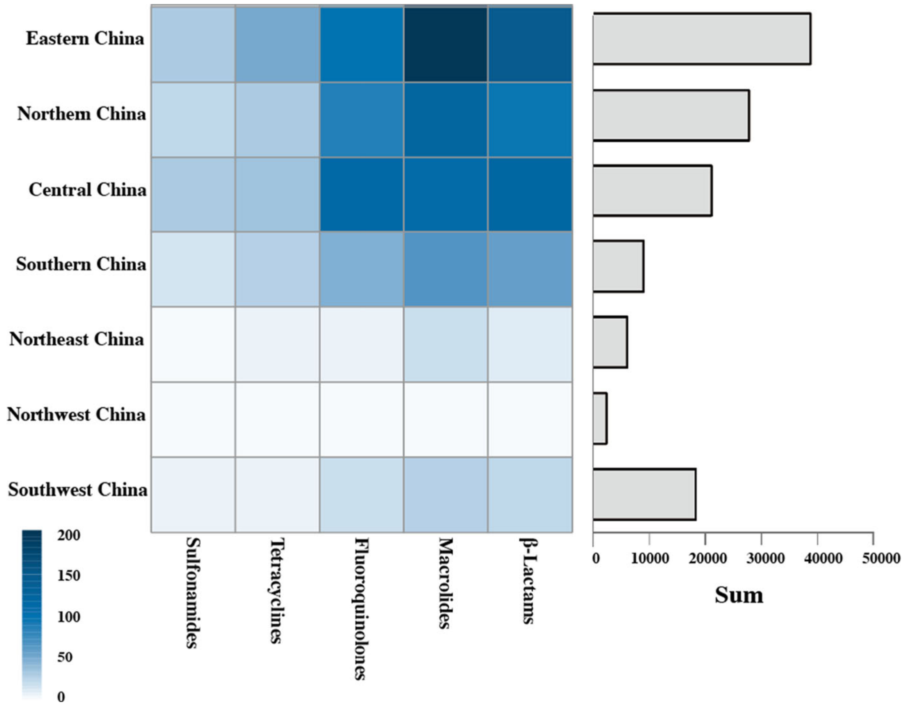


**Fig. 1** Distribution of antibiotic use density and dosage in China in 2013 (tons)

et al. 2015). The extensive use of antibiotics has led to the spread of antibiotics in the environment throughout the country, which has caused a series of potential hazards, such as the biotoxicity of antibiotics themselves and the emergence of drug-resistant bacteria, which have attracted more attention (Martin 2011; Wollenberger et al. 2000; Robinson et al. 2010; Peltzer et al. 2017; Rahube and Yost 2010).

Since the overuse of antibiotics is bound to put undue stress on the environment, the biological toxicity of antibiotics and their trace amounts in the environment have attracted more attention (Martin 2011). However, current research only describes the level of antibiotic usage and residual quantity in the medium. However, the lack of quantification of antibiotic fate in the environment leads to the lack of targeted antibiotic terminal treatment. At present, many types of antibiotics can be detected in aqueous environments around the world due to the widespread use of antibiotics and point source discharge (Kim and Carlson 2007; Dinh et al. 2011; Chen and Zhou 2014). Antibiotics can be divided into medicinal antibiotics and feeding antibiotics according to the applicable objectives. After being used by human beings, livestock and poultry, antibiotics mainly enter into solid waste landfills, sewage treatment plants and septic tanks through domestic garbage, wastewater and feces, which can be roughly represented by Fig. 2 (Wang et al. 2007). Incomplete removal of antibiotics from sewage treatment plants and the infiltration of antibiotics with precipitation in solid waste landfills are also considered as secondary sources of contamination from antibiotics.

At present, the content of antibiotics in various carriers in the environment is not accurately quantified, resulting in the lack of targeted end removal of antibiotics, unable to minimize the entry of antibiotics into the environment. The fate of antibiotics in the environment has been reported through the previous literature, but so far, no literature has collated data to determine the proportion of antibiotic residues in carriers. By calculating and determining the main storage sites of antibiotics in the environment, we can effectively determine the direction for the centralization of terminal treatment of antibiotics. Antibiotics are herein divided into two categories in this paper: medical antibiotics and veterinary antibiotics. The carriers that each antibiotic may go to are analyzed separately. The residual amount in the carrier is calculated by multiplying the pollutant amount

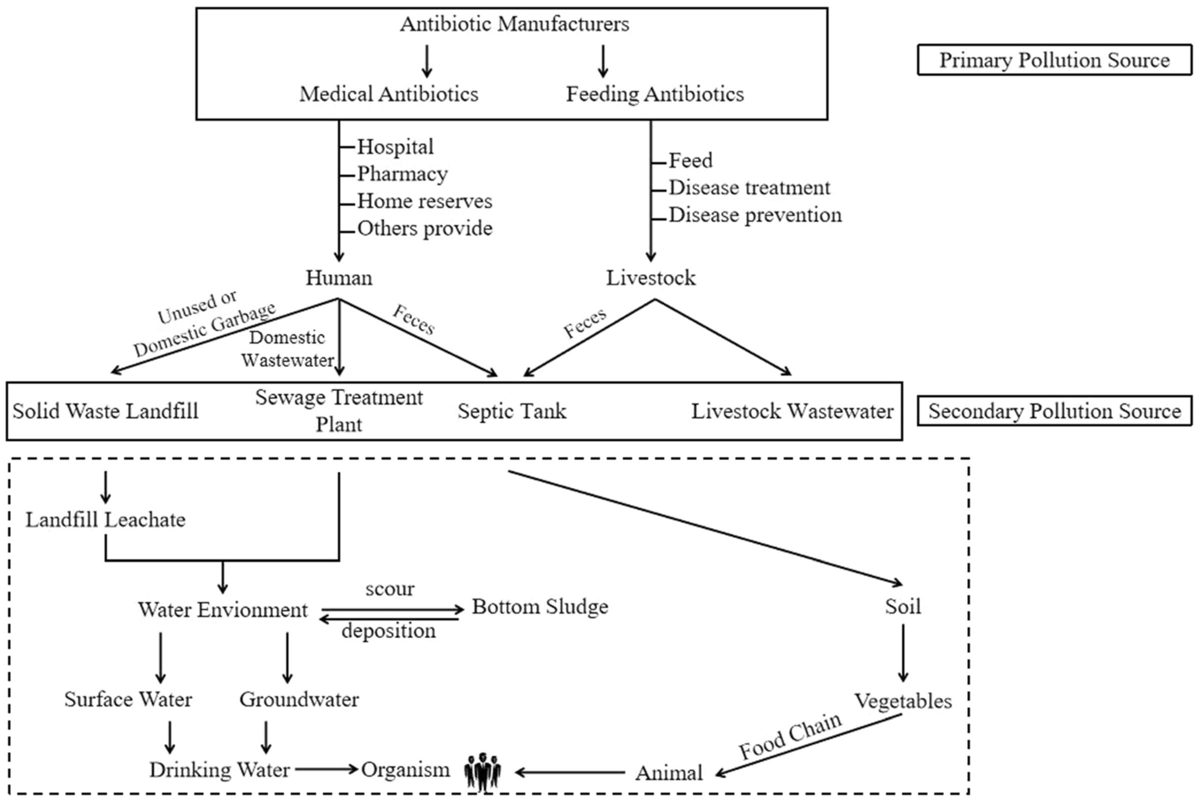


**Fig. 2** Emission sources of antibiotics and their migration routes in the environment

accepted by the carrier within a certain period of time by the average concentration. Then, according to the proportion of the residue of each carrier in the total theoretical emissions, the main destinations of medical antibiotics and veterinary antibiotics can be obtained.

## Analysis and calculation methods

Antibiotics for human use are mainly distributed through hospitals, pharmacies, home stores or others. Antibiotics for animal use are mainly introduced through feed, disease treatment and disease prevention. After use, antibiotics can enter the environment mainly through the flow of feces and sewage into septic tanks, through domestic sewage and livestock and poultry wastewater, through antibiotic disposal in landfills and through precipitation and other forms depositing antibiotics into the leachate. Subsequently, domestic sewage, livestock and poultry wastewater and leachate are treated and then enter the aquatic environment (Heberer 2002; Watkinson et al. 2007). The antibiotics entering the aquatic environment are easily settled on the bottom mud. The rest will enter surface water, groundwater and even drinking water sources through water circulation and ultimately enter the human body (Hu et al. 2010; Du et al. 2017; Lau et al. 2017). Further, excrement can enter the soil as fertilizer after septic tank processing and enter human body through plants and animals in the food chain (Tasho and Cho 2016).

In this regard, we can further conduct a quantitative analysis of the direction of antibiotics. The proportion of antibiotics entering the sewage treatment plant ($P_{STP}$) can be calculated from the daily antibiotic handling capacity of the sewage treatment plant ($HC_j$, g) and by the daily dosage of humans ($D_{H,\ j}$, g). The proportion of antibiotics in domestic garbage ($P_{DG\text{-}Anti}$) is calculated from the proportion of the daily yield of antibiotics in domestic garbage ($Y_{DG}$, g) of the daily dosage of humans ($D_{H,\ j}$, g). The proportions of antibiotics in livestock wastewater ($P_{LW}$) and livestock feces ($P_{LF}$) are calculated from the amount of antibiotics in poultry ($j$) wastewater ($A_{j,\ W}$) and feces

($A_{j, PF}$), respectively, and from the daily dosage of poultry antibiotics ($D_{V, j}$, g) using Eqs. (1)–(4):

$$P_{STP}(\%) = \frac{HC_j}{D_{H,j}} \times 100\% \quad (1)$$

$$P_{DG}(\%) = \frac{Y_{DG-Anti}}{D_{H,j}} \times 100\% \quad (2)$$

$$P_{LW}(\%) = \frac{A_{j,W}}{D_{V,j}} \times 100\% \quad (3)$$

$$P_{LF}(\%) = \frac{A_{j,PF}}{D_{V,j}} \times 100\% \quad (4)$$

The amount of antibiotics used by people ($D_{H, j}$, g) can be obtained by dividing the amount of antibiotics used in medical institutions ($D_{H,MI, j}$, g) by their proportion ($R_{MI}$). The proportion of antibiotics absorbed by human beings and poultry is set as 30% (Hirsch et al. 1999). The dosage of antibiotics used per day per person in medical institutions is calculated by multiplying the number of people in that year ($P_i$) and the intensity of use (AUD, antibiotic use density, DDD/100 people/d, where DDD is the defined daily dose, g) of the selected antibiotics in total use ($R_j$), where *i* represents the year and *j* represents the type of antibiotics. The amount of veterinary antibiotics discharged is expressed by $D_{V, j}$, which is calculated by multiplying the total amount of antibiotics ($C_k$) used by the corresponding total amount of livestock and poultry ($N_k$), where (*k*) represents the livestock and poultry species (pigs, chickens and cattle are used as the main sources of livestock and poultry) using Eqs. (5)–(7):

$$D_{H,j} = \frac{D_{H,MI,j}}{R_{MI}} \quad (5)$$

$$D_{H,MI,j} = P_i \times AUD \times R_j \times 70\% \quad (6)$$

$$D_{V,j} = \sum_k C_k \times N_k \times 70\% \quad (7)$$

The daily antibiotic treatment handling capacity of sewage treatment plants and the amounts of antibiotics in effluent from livestock and poultry are represented by $HC_j$ and $A_j$, respectively. $HC_j$ is mainly calculated by the daily amount of treated wastewater ($Q_1$) in the sewage treatment plant multiplied by the total amount of influent concentration ($C_{j1}$) of a certain class of antibiotic (*j*) in the sewage treatment plants. $P_{DG\text{-}Anti}$ is calculated by multiplying the daily production of domestic garbage ($P_{DG}$) and the average concentration of antibiotics ($C_{j2}$) in domestic garbage of a certain class of antibiotic (*j*). $A_j$ is also calculated from the quantity of livestock and poultry wastewater ($Q_2$) multiplied by the concentration ($C_{j3}$) of antibiotics. The amount of antibiotics in poultry feces ($A_{PF}$) can be multiplied by the number of each poultry ($N_k$), the amount of feces discharged by each poultry ($A_{per, k}$) and the average concentration of antibiotics in the feces ($C_{j4}$) using Eqs. (8)–(11):

$$HC_j = \sum_j Q_1 \times C_{j1} \quad (8)$$

$$Y_{DG-Anti} = \sum_j P_{DG} \times C_{j2} \quad (9)$$

$$A_j = \sum_j Q_2 \times C_{j3} \quad (10)$$

$$A_{PF} = \sum_{k,j} N_k \times A_{per,k} \times C_{j4} \quad (11)$$

## Route calculation

### Route calculation of medical antibiotics

From the above formulas, taking Beijing in 2009 as an example, we can approximate the fate of antibiotics by calculating and analyzing the use of medicinal antibiotics and the possible residual amount of antibiotics discharged into sewage treatment plants, landfills and septic tanks. The results can be seen from Fig. 3, and the details are shown in Table 1 from the supplementary materials. The calculated results showed that the daily discharge of antibiotics after use was approximately 11,720 kg, of which 18.8% went to sewage

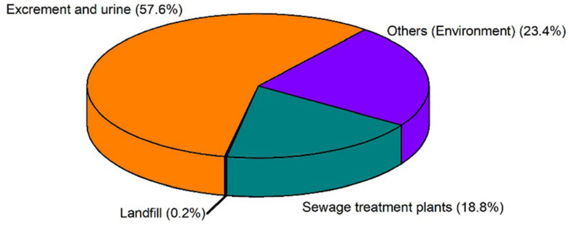


**Fig. 3** Proportion of route of human antibiotics after discharge

**Table 1** Specific parameters of human antibiotics

| Parameter symbol | Correlation parameter value |
|---|---|
| AUD | 70 g/100 people/d (51% of total use) |
| $P_{\mathrm{i}}$ | 18.6 million |
| $j$ | Cephalosporins, penicillins, fluoroquinolones, macrolides, etc. (65.6% of the distributed antibiotics) |
| $D_{\mathrm{H,MI,\ j}}$ | 11,720 kg |
| $Q_1$ | 300,000 m$^3$ |
| $C_{\mathrm{j1}}$ | The total of sulfonamides, tetracyclines, fluoroquinolones, macrolides and β-lactams were 4070 ng/L |
| $P_{\mathrm{DG}}$ | 18,400 tons |
| $C_{\mathrm{j2}}$ | 194 μg/kg |

treatment plants and 0.2% went to landfills. It can be seen from the results that after the use of medicinal antibiotics, only a small amount enters into the sewage treatment plants, landfill leachate and refuse landfills (less than 20%), and the remainder of antibiotics is likely to exist in the feces in the environment, which will be treated in the septic tank in a unified form. At present, there is a lack of research on antibiotics in human feces or septic tanks. If the average concentration of antibiotics in livestock and poultry feces (75 mg/kg) is converted, and each person produces 500 g of excrement and urine every day, then human excrement and urine in Beijing will contain 6750 kg of antibiotics, accounting for 57.6% of the total use of medicinal antibiotics. It follows that septic tanks may be regarded as serious antibiotic enrichment locations, as they will have large amounts of antibiotic discharge to process each day. Therefore, the fate of antibiotics in septic tanks and the role of septic tanks in the efficient removal of antibiotics are particularly important. In addition, the remaining portion of antibiotics will persist in the environment, accounting for 23.6% of the total use of medicinal antibiotics. Antibiotics in the environment will enter and persist in the aqueous environment and in the soil, which will be used by microorganisms or carrier exchanged via strong adsorption of the carrier, such as bottom mud adsorption. Consequently, the antibiotics used by organisms can hardly be treated uniformly with the wastewater flowing into the sewage treatment plants; that is, most of the antibiotics are still in the environment, which will lead to the formation of corresponding resistance genes.

The results suggest that there may be significant amounts of excreted antibiotics in human feces that have been overlooked in previous studies. At present, there is still a lack of research on antibiotic residues in the uniform treatment of human excrement. At the same time, the treatment process of septic tanks for the removal of residual antibiotics is also in urgent need of research. Currently, the removal process for septic tanks is mostly sedimentation and anaerobic fermentation, and relevant literature shows that the removal efficiency of sedimentation for antibiotics is extremely poor (Le-Minh et al. 2010). Furthermore, anaerobic fermentation is a biological method, which cannot effectively remove antibiotics with poor biodegradability. Therefore, at present, the septic tank method may be a serious disaster area that leaves most of the discharged antibiotics intact, and it is necessary to set up an efficient removal processes for related antibiotics in the septic tank to strictly control the concentration of antibiotics at the outlet.

Route calculation of veterinary antibiotics

Similarly, we take Beijing in 2009 as an example in the field of veterinary antibiotics. Then, we set pigs, chickens and cows as the main organisms comprising livestock and poultry and calculated the proportion of veterinary antibiotic residues in each medium. The results are detailed in the supplementary materials. Table 2 and Fig. 4 show the specific parameters and results through calculation. It can be concluded by calculation that the total amount of antibiotics discharged by livestock and poultry metabolism reaches 5000 kg per day, of which approximately 80 kg of antibiotics is contained in livestock and poultry wastewater per day, accounting for 1.6%, and approximately 2128 kg of antibiotics is contained in

**Table 2** Specific parameters of veterinary antibiotic

| Parameter symbol | Correlation parameter value |
|---|---|
| $N_k$ | 186,5700 pigs, 228,354,200 chickens and 220,600 cows |
| $D_{V,\ j}$ | 695 g, 4.755 g and 1091 g of antibiotics were used per pig, chicken and cow per year, respectively |
| $Q_2$ | Per 1000 chickens and 43.5 $m^3$ per 100 cows |
| $C_{j3}$ | 340 μg/L |
| $A_{per,\ k}$ | Each pig, chicken, cow produces 5.3, 0.12, 34 kg of feces every day |
| $C_{j4}$ | Pig feces (212.4 mg/kg), chicken feces (9.66 mg/kg) and (cattle dung) 0.27 mg/kg |

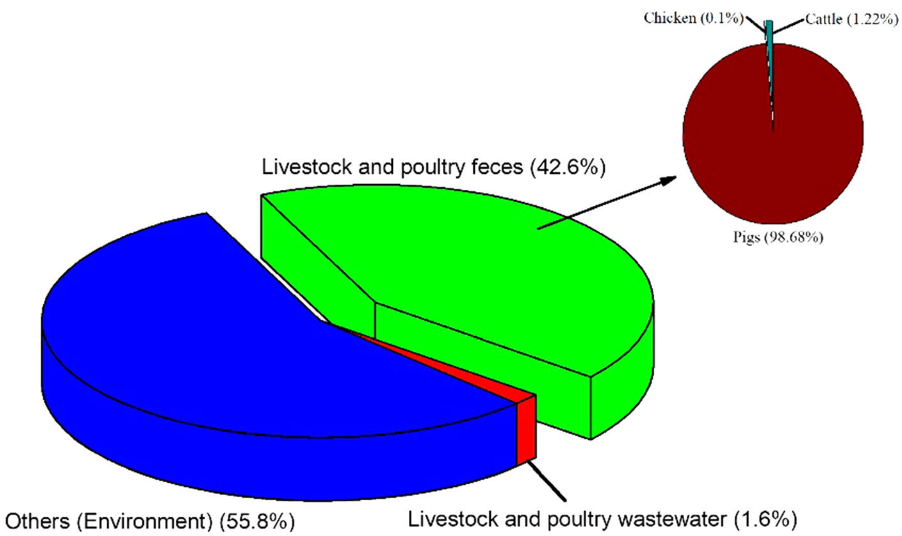


**Fig. 4** Proportion of route of veterinary antibiotic after discharge

livestock and poultry feces per day, accounting for 42.6%. After classifying livestock and poultry excrement according to pig excrement, chicken excrement and cow excrement, it can be clearly found that most antibiotics in livestock and poultry excrement are concentrated in pig excrement, accounting for 98.7%. Further, approximately 55.8% of the remaining antibiotics are excreted in the environment by livestock and poultry, which may enter the water environment with precipitation or be absorbed by other media such as soil in the process of water infiltration or decompose in the environment due to their own degradability.

It can be clearly seen from the veterinary antibiotics discharge channel calculation results that the concentration of antibiotics actually discharged through livestock wastewater is not high. Antibiotic residues in livestock and poultry manure account for a large proportion of the amount of veterinary antibiotic emissions; moreover, the antibiotic residues in pig manure were particularly severe. This may be due to low feed additions to chickens, while cattle, as ruminants, consume food that has been partially digested in the stomach and returned to the mouth to rechew over time, which reduces feed usage. Therefore, the treatment of animal antibiotic discharge should be more focused on the treatment of livestock manure, especially pig manure. At present, the treatment of livestock and poultry excrement in China is mainly carried out by two steps of solid–liquid separation. The liquid excreta are mainly transformed by anaerobic fermentation into biogas slurry, while the solid excreta are aerobically composted into fertilizer. Biogas slurry and fertilizer will eventually be used for fertilization; however, the antibiotics in biogas slurry have not been quantified during the treatment process and subsequent fertilization. Therefore, whether there are excessive quantities of antibiotics in biogas slurry remains to be investigated, which may be due to the formation of corresponding resistance genes (Pu et al. 2017).

### Summary

Through the above systematic calculation of medicinal antibiotics and veterinary antibiotics, we can preliminarily draw the following conclusions. After discharge, 23.4% of medicinal antibiotics and 55.8% of veterinary antibiotics remained in the environment, and these antibiotics were difficult to achieve centralized treatment and could only rely on their own natural degradation. Fecal, environmental and sewage treatment plant discharges account for the majority of the medicinal antibiotics, while veterinary antibiotics are more concentrated in the environment and feces. Pig manure contains 98.68% of the antibiotics in feces, while chicken and cow manures contain very little. Therefore, strengthening the removal of antibiotics from human and pig manure can effectively prevent a large number of antibiotics from entering the environment.

## Future development strategies and the prospects of antibiotics

The persistence of antibiotic residues leads to the formation of resistance genes, which, through migration in an aqueous environment and transmission through the food chain, will cause greater direct or indirect harm to organisms. The conclusions can be drawn as follows: First, 20–45% of residual antibiotics remain in the environment, and excessive use of antibiotics will increase the residual concentration of antibiotics in the environment, leading to the increase in bacterial resistance. Therefore, the most effective path forward is to reduce the use of unnecessary antibiotics to solve the problem at the source. Second, among the antibiotics that have been used, we must specifically remove carriers with larger antibiotic residues to minimize their entry into the environment. It can be clearly seen from the calculation and analysis results that the majority of antibiotics enter sewage treatment plants and septic tanks after being metabolized by an organism. Therefore, future antibiotic tail treatment should place emphasis on sewage treatment plants and septic tanks.

Regarding restricting the use of antibiotics, although China has introduced a series of regulations and strategies to reduce the use of antibiotics in the past few decades, these are still somewhat misguided in China, particularly in rural medical sites (Sun et al. 2015). The government has carried out reforms in recent years to restrict the sources of antibiotics by reducing the use of antibiotics in humans and livestock in China, which is a significant means to control pollution by antibiotics. On the other hand, due to the lack of a proper understanding of the use of antibiotic feed in livestock and poultry breeding, the use of antibiotics has increased with the increase in feed usage. At the same time, compared with veterinary antibiotics, there are systematic medical institutions that limit the purchase and record the use of medicinal antibiotics; however, whether the abuse of veterinary antibiotics has seen real progress is still unknown. Further, the contents of antibiotics in animal feed should be controlled and monitored. The total amount of antibiotics used in animals was estimated roughly by the amount of feed used in all kinds of livestock and poultry to more intuitively determine whether a strategy of restricting antibiotics used in animals has been effective. Antibiotic restriction is currently the only and most effective way to reduce antibiotic residues in the environment. Therefore, the government should continue to strictly implement and supervise the use of medicinal antibiotics and veterinary antibiotics, adjust the policy by comparing the changing antibiotic dosage trend in a timely manner and popularize the relevant methods for scientific with end users so that they can use antibiotics effectively.

Through the conclusion of this study, feces was identified as the main storage place for the discharge of antibiotics. The amount of antibiotic residues in livestock and poultry feces is relatively large, and the analysis results show that, in livestock and poultry feces, the antibiotics from animals are mostly found in pig feces because the amount of feed used for chickens and cows is less than that for pigs. It can be found from the above results that in the limitation of antibiotics in the future, priority should be given to tracking and attending to the fate of antibiotics in feces, and the removal process of antibiotics in septic tanks should be added to lower the antibiotic content to an acceptable concentration range in fertilizers (Huber et al. 2005; Radjenovic et al. 2009). Regarding veterinary antibiotics, because the majority of antibiotics remain in pig manure, the treatment can be more targeted. On this basis, the removal of antibiotics should be carried out mainly for feces. Establish relevant systems for centralized treatment of feces, and increase the efficient antibiotic-related removal process in septic tanks (Dolar et al. 2009; Kosutic et al. 2007), and strictly control the concentration of exported antibiotics. At the same time, the pig breeding industry should be strictly controlled from the source, and the discharge of pig manure should be systematized to ensure the elimination of antibiotics in pig manure, so as to minimize the possibility of the source entering the environment.

Currently, the majority of studies on the fate of antibiotic emissions in China's environment focus only on sewage treatment plants, landfills, livestock and poultry wastewater and livestock and poultry manure. From the calculated results, it can be seen that the current study ignores the residues of antibiotics in human feces, which account for the majority of medicinal antibiotics used. Therefore, the residual carriers of antibiotics should mainly focus on feces (including human feces and livestock and poultry feces) in future studies. Fertilizer actually has a great environmental risk after septic tank treatment. Therefore, it is necessary to focus on antibiotic residues in septic tanks and then add a corresponding antibiotic removal process to septic tanks to ensure that the antibiotic residues in fertilizer can ultimately reach a safe level to prevent the reintroduction of antibiotics into the environment as much as possible, which has consequences for the environment and human health. From the above, antibiotic use should be avoided as much as possible to avoid transfer into the environment, which endangers human and environmental health.

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