Environmental antibiotic pollution and resistance in China: pollution status, degradation methods and control strategies

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Abstract: Antibiotics and antibiotic resistance genes (ARGs) which are closely related to human activities and life are globally recognized as emerging pollutants in the 21st century. China is one of the largest producers and consumers of antibiotics in the world, is also one of the countries most severely polluted by antibiotics. Antibiotics and ARGs are widely present in surface water, soil, animal excreta and wastewater treatment plants in China. When the concentration exceeds the risk quotient ($RQ \geq 0.01$), they pose a threat to human health. This review systematically combed the relevant research literature on antibiotics in China in recent years, and made a key summary from four aspects: 1) The current situation of antibiotic pollution in various environmental medium in China; 2) The pollution sources and abundance levels of ARGs in the seven administrative regions of China; 3) The potential risks and hazards of antibiotics and their resistance; 4) The latest and most representative antibiotic degradation methods for the management of antibiotics. Finally, this review brings forward suggestions for future antibiotic supervision, including strictly implementing relevant laws and regulations, formulating specific supporting measures, encouraging the research and development of antibiotic alternatives. It is believed that in the near future, the problem of antibiotic pollution in China can be improved to the greatest extent.

Key words: misuse of antibiotics; antibiotic resistance genes; environmental pollution; degradation; regulatory strategies

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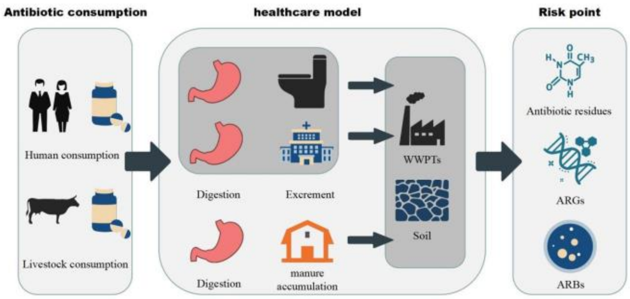
Graphical Abstract

Fig. 1 Sources of antibiotics and resistance in the environment



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INTRODUCTION

Since A. Fleming discovered penicillin in 1929, it has produced and used a variety of antibiotics worldwide to treat humans, animals and plant diseases caused by pathogenic bacteria. Antibiotics are secondary metabolites produced by microorganisms (bacteria, fungi, and threading bacteria) in their growth metabolic activities. It can also be artificially synthesized by chemical methods. The main antibiotics to be reviewed in this article is shown in Table 1. This review is based on similar scientific research and review papers published during 2012-2022 with the purpose to introduce the use of China's emerging pollutants antibiotics, pollution assessment, resistance gene dissemination, degradation methods and relief strategies. This paper will provide the overall viewpoint of antibiotic residual health risk assessment in the environment, and bridge the main reality gap and the reality with emphasize on future research needs.

Table 1 The basic information of the main antibiotics in this review

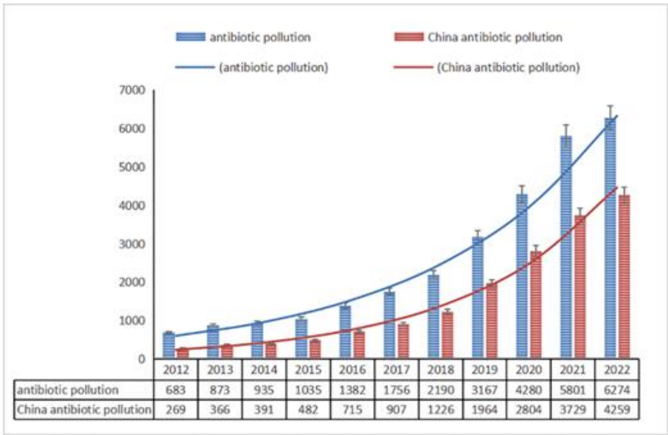
Class	Antibiotic (Acronym)	Molecular formula	Molecular weight	PKa	Water solubility
Tetracyclines（TCs）	Chlortetracycline（CTC）	$C_{22}H_{23}ClN_2O_8$	478.88	2.99/9.04	0.295
	Doxycycline（DXC）	$C_{22}H_{24}N_2O_8$	444.43	3.27/8.33	0.630
	Oxytetracycline（OTC）	$C_{22}H_{24}N_2O_9$	460.43	2.84/7.41	1.400
	Tetracycline（TC）	$C_{22}H_{24}N_2O_8$	444.43	3.26/9.25	1.330
Fluoroquinolones（FQs）	Ciprofloxacin（CIP）	$C_{17}H_{18}FN_3O_3$	331.34	5.56/8.77	1.350
	Levofloxacin（LEV）	$C_{18}H_{20}FN_3O_4$	361.37	5.35/6.72	1.440
	Norfloxacin（NOR）	$C_{16}H_{18}FN_3O_3$	319.33	5.58/8.77	1.010
	Ofloxacin（OFL）	$C_{18}H_{20}FN_3O_4$	361.37	5.35/6.72	1.440
Macrolides（MLs）	Azithromycin（AZI）	$C_{38}H_{72}N_2O_{12}$	748.98	12.34/9.57	0.514
	Clarithromycin（CLA）	$C_{38}H_{69}NO_{13}$	747.95	12.46/9	0.217
	Roxithromycin（ROX）	$C_{41}H_{76}N_2O_{15}$	837.04	12.45/9.08	0.187
	Erythromycin（ERY）	$C_{37}H_{67}NO_{13}$	733.92	12.45/9	0.459
β-Lactams（BLs）	Amoxicillin（AMO）	$C_{16}H_{19}N_3O_5S$	365.40	3.23/7.22	0.958
	Ampicillin（AMP）	$C_{16}H_{19}N_3O_4S$	349.40	3.24/7.23	0.605
	Cephalexin（CEP）	$C_{16}H_{17}N_3O_4S$	347.38	3.26/7.23	0.297
	Cefazolin（CEF）	$C_{14}H_{14}N_8O_4S_3$	454.50	2.84/0.26	0.487
	Penicillin（PEN）	$C_{16}H_{18}N_2O_4S$	334.39	3.53/-2.8	0.285
Sulfonamides（SFs）	Sulfadiazine（SDZ）	$C_{10}H_{10}N_4O_2S$	250.277	6.99/2.01	0.601
	Sulfamerazine（SMR）	$C_{11}H_{12}N_4O_2S$	264.30	6.99/2	0.304
	Sulfamethazine（SMT）	$C_{12}H_{14}N_4O_2S$	278.33	6.99/2	0.230
	Sulfamethoxazole（SMX）	$C_{10}H_{11}N_3O_3S$	253.27	6.16/1.97	0.459
	Sulfapyridine（SPY）	$C_{11}H_{11}N_3O_2S$	249.28	6.24/2.14	0.235

Note: Data retrieved from https://www.drugbank.ca.

The antibiotics antibacterial agent has a bacteriostatic or bactericidal effect, it contains 4 core action mechanisms, namely to inhibit bacterial cell wall synthesis, enhance bacterial cell membrane permeability, interfere with bacterial protein synthesis, and inhibit bacterial nucleic acid copy transcription (Laxminarayan 2014). Although antibiotics can treat human and animal diseases, only a few are consumed in the body, and most antibiotics are excreted from the body, and they are detected in urine and feces (Lyu et al. 2020). These excess antibiotics through sewage treatment plants (WWTPS) (Wang et al., 2021a)、medical wastewater (Walia et al. 2016)、home wastewater and animal husbandry waste (Nõlvak et al. 2016; Gros et al. 2019; Marti et al. 2020) are discharged into the environment. The abuse of antibiotics will increase the environmental pressure of bacteria, stimulate the production of antibiotic resistance bacteria (ARB), accelerate the transmission of antibiotic resistance gene (ARGS), reduce the effectiveness of antibiotic drugs, and form "super bacteria" (Wright 2010; Qiao et al. 2018). Countries in

Asia, Europe and Africa has also been reported with contamination of antibiotics (Gros et al. 2021). In the past ten years, a large number of publications (including research articles, review articles, and scientific research series) had reported the problem of antibiotic pollution particularly, prominent in China (Li et al., 2020), as about 46 % of the world's similar articles are shown in Fig. 2 (CHINA Antibiotic Pollution and Antibiotic Pollution entry search in Elsevier ScienceDirect).

Fig. 2 Number of antibiotic literature searches from 2012 to 2022



Note: Data retrieved from https://www.sciencedirect.com

THE CURRENT SITUATION ON THE USE OF ANTIBIOTICS IN CHINA

The abuse of antibiotics use has become a global public health issue (Laxminarayan et al. 2013), and it has increased the cost of treating infectious diseases and ARB for low and middle -income countries (Alsan et al. 2015). China is the largest antibiotic consumer country in the world. It was reported that the antibiotic raw materials consumed in China in 2013 was about 92700 tons (which include 36 types of antibiotics)(Qiao et al. 2018). The amount was 87.5 times than the British (1060 tons) (Klein et al. 2018), 6.3 times the United States (14600 tons), which were MLs (42200 tons), BLs (34100 tons) and FQs (15300 tons) (Zhang et al. 2015). Among them 48 % were used for human medical and consumption, while the rest as additives for animal and plant feed and fertilizer (Cai et al. 2022). The defined daily dose (DDD) of antibiotic per 1,000 residents of China is 157g, which far exceeds the daily dose of Britain (27.4G), the United States (28.8g), Canada (20.4g) and Europe (20.1g). (Zhang et al. 2015). According to reports, 70 % of the world's antibiotic consumption in Asia, was mostly consumed by the Chinese. Among the top 100 drugs in China, more than half of them are antibiotic drugs, but there are no antibiotics in the top 100 of European and American medicines. (Shao et al. 2021).

"The Lancet Infectious Diseases" published an article revealing that there are inappropriate prescriptions for China's high proportion of antibiotics. In the outpatient clinic of 139 public hospitals, more than 51% of the antibiotic prescriptions (nearly 2 million pieces per year) were reported to be inappropriate, where the proportion considered appropriate is only 15.3%(Zhao et al. 2021). Currently, there are 12,436 public hospitals in China. According to the calculation of the total amount of antibiotic prescriptions that are not appropriate each year, the total number may exceed 173 million (Liu 2021). This overprescribing problem may be caused by the fact that the vast majority of hospital revenue comes from drug sales, and that outpatient bonus income is directly linked to these sales, so that antibiotics, which are dispensed under the incentive system was become mandatory prescriptions (Currie et al. 2014). Since 2009, China government has introduced a series of related policies to curb antibiotics abuse. The measures taken include restrictions and intervention in primary health care and hospital departments, the prescriber must comply with the results of the clinical examination (Tang et al. 2018), nonetheless this approach has little effect. In 2016, the Chinese government released the " the National Action Plan to Contain Antimicrobial Resistance (2016-2020)", which strengthened its determination to control bacterial resistance (Shen et al. 2022).

ANTIBIOTIC POLLUTION OF THE ENVIRONMENT IN CHINA

As early as 2014, the existence of antibiotics was detected in residents' tap water major rivers, and antibiotic pollution has become a serious public health problem in China (Huang et al. 2015).

Antibiotic in aquatic environment

Aquatic environment is the main way to spread antibiotics and antibiotics resistance genes (Yang, et al., 2018). In the past ten years, the existence of antibiotics has been detected in China's main rivers, surface water, groundwater and sediments. (Zhou et al. 2022; Shi et al. 2022). Many experts and scholars have reported the antibiotic pollution in the seven major rivers and the four ocean water bodies and sediment in China. The 12 most commonly detected antibiotics were three Sulfonamides (SFs), two Tetracyclines (TCs), four Fluoroquinolones (FQs), and three Macrolides (MLs). (Li et al. 2022b). In addition, almost all other inland lakes and sediments have detected the footprint of antibiotics (Wu et al. 2022). For example, a total of 14 antibiotics were detected in 63 sampling points of surface water of Chaohu Lake and its tributaries, with concentrations up to 892 ng/L (Zhou et al. 2022) ; Lei and coauthors reported 15 detected antibiotic concentrations ranging from 414 ~ 1951 ng/L in the Haihe River basin (Lei et al. 2019). In addition, the Xi 'an section of the Wei River (Wang et al. 2019), Poyang lake (Ding et al. 2017) and Jiaozhou bay (Liu et al. 2020) also found to have the same results. It has been reported that the antibiotic content in the Chinese river has risen from ng/L to μg/L recently (Lei et al. 2019), which push the important to remove or alleviate the problem of water pollution caused by antibiotics.

Sulfonamides and fluoroquinolones are also the most studied antibiotics in surface water and groundwater in China (Li et al. 2020b). Studies have shown that there are 26 types of antibiotics such as SAs, FQs and MLs detected in the surface water in Pudong New District, Shanghai, with the concentration up to 9.73 ng/L, 30 ~ 344 ng/L and 14 ~ 107 ng/L respectively (Pan et al. 2020). This kind of situation was also detected in the Hanjiang River Basin, but the content of TCs in the sediment was dominant (Hu et al. 2018). Before 2015, there were few studies on groundwater antibiotics due to the difficulty of sampling, but with the development of science and technology in recent years, the detection, spatial distribution and risk assessment of groundwater antibiotics have made rapid progress (Shi et al. 2022). Three sulfonamide antibiotics (SMX, SM2, SMP) were detected in groundwater resources of Limin District, Harbin, with concentrations ranging from 7 ~ 30 ng/L (Zuo et al. 2021), The similar situation also happened to groundwater resources in Beijing and Changzhou (Ding et al. 2020).

Antibiotic in the soil

Improper agroecosystem development and soil management will increase the contamination from farmland soil antibiotics and pollute the environment (Li et al., 2022). Antibiotics are introduced into soils through field irrigation, manure application, and sedimentation adsorption. Other soils with high levels of antibiotics are found in medical waste landfills (Chi et al. 2020), large livestock farms (Chen et al. 2014), farmland near river dams (Pan et al. 2021), and wastewater treatment plants (Pazda et al. 2019). Researchers reported that the concentration of antibiotics in northeast black soil varied from 2.56 μg/kg SDZ to 1590.16 μg/kg CTC. More surprisingly, the applied fertilizer contained as much as 143.97 mg/kg of CTC (An et al. 2015). The detection frequency of CTC, OFL, ENR and CIP in the Yangtze River Delta was high in summer and winter (Li et al. 2022e). Soil in the Pearl River Delta region was dominated by TCs, and the content was as high as 557.41μg/kg. The maximum average concentration was in the following order: OTC> CTC> TC (Gu et al. 2021). The highest CTC concentration was reported to be 12.9±0.7mg/kg in a farm near a livestock farm. High levels of antibiotics are almost always found in farmland, probably because of the use of chemical fertilizers and recycled water irrigation.

Antibiotics in livestock waste

More and more reports have shown that the frequency and distribution range of veterinary antibiotics are on the rise in livestock feces around the world (Manzetti and Ghisi 2014), with no exception to China. In 2015, the Chinese government issued the Plan for the Prevention and Control of Water Pollution in Major River Basins (2016-2020), which requires the transformation of coastal river basins from extensive agriculture to intensive agriculture and the control of livestock manure pollution (MEE 2022).

Economic dependence or lack of awareness of antibiotics in rural China has led to the prevalence of antibiotics in livestock manure (Li et al., 2021; Shi et al., 2021; Zhou et al., 2020). Tetracyclines (TCs), sulfonamides (SAs), fluoroquinolones (FQs) and macrolides (MLs) are commonly used antibiotics in animal farms in China (Yue et al. 2021). The SMT and TC concentrations in manure from livestock farms in Jiangsu Province were reported to be 5650 μg/kg and 1920 μg/kg respectively (Zhou et al., 2020). The main antibiotics in animal feces of farms in Ningxia were TCs (CTC and DOC), with the highest concentrations of 21796.7 μg/kg and 25767.5 μg/kg, respectively (Peng et al. 2022). Dali City in Yunnan Province is dominated by family farms, the highest concentrations of CTC in livestock wastewater and soil reached 25,000 μg/kg and 305.56 μg/kg, respectively (Zhi et al. 2020). The accumulation of antibiotics in aquaculture also poses a potential risk to food safety (Liu et al. 2017). For example, the total concentration of antibiotics in aquaculture farms in Guangdong Province is as high as 25697ng/L (Zhong et al. 2018). Therefore, the abuse of veterinary antibiotics in China has been one of the difficult problems to solve.

Antibiotics in Wastewater Treatment Plants (WWTP)

Wastewater from urban and rural sewage treatment plants is discharged directly into surface water or soil, which undoubtedly increases the pressure of antibiotics in the environment (Chen et al. 2020). Many reports have confirmed high antibiotic concentrations in incoming and outgoing water from sewage treatment plants in China (Bao et al., 2021; Wang et al., 2021). Both classes of antibiotics, TCs and FQs, were detected in WWTPs nationwide (Li et al. 2013). TC, OTC, NOR and OFL were the major antibiotics used in wastewater treatment plants in Guangdong Province, with total concentrations as high as 5800 ng/L (Zhou et al. 2013). Some studies reported that the removal efficiency in WWPTs followed the order of TCs (87.9%) >SAs (11.6%) >FQs (1.06%) (Xu et al. 2015). Therefore, the antibiotic removal rates of different WWPTs are also different, which may be due to the physical and chemical properties of antibiotics, daily inflow, removal means and removal conditions, and other factors. In addition, rainwater input also affects the removal efficiency (Qiao et al. 2018). However, it is known that among all antibiotics, TCs and FQs drugs have relatively higher removal efficiency, which may be due to their adsorption by sludge (Bao et al. 2021).

THE OCCURRENCE OF ANTIBIOTIC RESISTANCE GENES IN CHINA

Survival strategies of antibiotic-resistant microorganisms

Environmental microorganisms, especially bacteria, develop resistance under long-term stress of low concentration of antibiotics (Wistrand-Yuen et al. 2018), The principle is that microbes increase their tolerance to the minimum inhibitory concentration (MIC) of antibiotics, a mechanism that microbes must evolve in order to survive (Trinh et al. 2018). In this way, microorganisms can develop antibiotic resistance by evading target drugs, controlling antibiotic entry and exit through osmotic pumps in the cell wall, and modifying enzymes to modify antibiotics and their metabolites (Sharma et al. 2018). These antibiotic modifying enzymes are assisted by many substrates, such as ATP, which can transfer functional groups and covalently modify antibiotics through acetylation, phosphorylation, adenylation, nucleotide, ribosylation and glycosylation (Camotti et al., 2018), lead to modification of cell surface receptors, damage of REDOX mechanism, hydrolysis, and eventually lead to multidrug resistance (MDR) (Rajivgandhi et al. 2018). Different kinds of resistance genes will be activated under long-term antibiotic stress and eventually become part of the microorganism itself, so resistance enzymes will be produced even under controlled conditions (Kumar et al. 2019).

Antibiotic resistance genes (ARGS) not only exist in clinical pathogens, but also in other pathogenic bacteria, symbiotic bacteria and environmental bacteria, and along with mobile genetic elements (MGEs) and phages formed a reservoir of ARGs which spreads widely between bacteria (D. Sun et al., 2019). There is a strong positive correlation between different ARGs or between ARGs and MGEs, these results suggest that ARGs are at risk for horizontal gene transfer (Peng et al. 2022). The "drug resistance" system of drug-resistant bacteria is formed by the combined expression of genes such as channel proteins, DNA spinase mutant proteins, drug efflux pump proteins and degradation enzymes (Li et al., 2021). Three efflux pump genes (tet A, tet C, and tet G), four ribosomal protection protein genes (tet M, tet O, tet Q, and tet W), and one enzyme modifier gene (tet X) appear to be the most common tetracycline resistance genes in WWPTs from China (Du et al. 2014).

Environmental ARGs pollution in seven administrative regions of China

According to data from the Global Antibiotic Resistance Surveillance System 2020, 66 countries have problems with antibiotic resistance contamination (Hu et al. 2021). ARGs can be detected in major rivers, surface water and soil in China. It has become a new pollutant in China and seriously damages public health (Wang et al. 2020).

The water environment is the main vessel for ARGs transmission. sul (sul 1, sul 2 and sul 3) and tet (tet A, tet B, tet C, tet M, tet O and tet W) genes were detected in Poyang Lake, the largest freshwater lake in China (Liang et al., 2020). Almost all FQs drugs in the Dongjiang River Basin were found to be at risk of drug resistance (Zhang et al. 2020), Similar problems have also been found in the Pearl River Basin (Xu et al. 2013). Fisheries and aquaculture are also being polluted by ARGs (Wang, et al., 2022), sul and tet family genes were detected in six main seawater cage culture areas in Hainan Province, China (Wu, et al., 2019). Tab. 2 shows the abundance and content of ARGs and ARBs detected in different environmental media in seven administrative regions of China.

Table 2 Antibiotic resistance genes and antibiotic-resistant bacteria in seven administrative regions of China

Administrative division	**Sources of pollution**	**Types of pollution sources**	**Manifestation of antibiotic resistance**	**Reference**
North China	Western Inner Mongolia	Surface water	Fourteen ARGs were detected, and *bla* $_{\mathrm{TEM}}$ gene was the main ARGs	(Shi et al. 2019)
	Beijing, Tianjin two chicken farms	Waste water and soil	*tet* M was the major ARGs in all samples and in all resistant subtypes	(Song et al. 2022)
Northeast China	The three northeast provinces	Soil	The resistant bacteria associated with ARGs are *Anaerolineae*, *Planctomycetia* and *Solibacteres*.	(Wang et al. 2022a)
	Liaohe river basin	River	164 ARGs and 10 MGEs were detected.	(Gao et al., 2022)
East China	Wangyu River west bank	River	*sul* I was the most abundant (1.28×10^5 copies/mL). Followed by *sul* II and *tet* O .	(Zhang et al., 2022)
Central China	Large pig farm near Poyang Lake in Jiangxi Province	Animal husbandry waste	Major ARGs, including aminoglycosides, β-lactamase, flufenicol, MLSB, vancomycin resistance genes and so on.	(Fu et al., 2022)
South China	five major rivers in Shenzhen	Surface water	8 ARGs (*sul*1, *sul*2, *sul*3, *Ere*A, *Ere*A2, *tet* G, *AAC* (6′)-*IIa*, *ScEmcrte*) were found.	(Qiu et al. 2019)
	Guangdong Province	Aquaculture	The ARGs family genes total relative abundance of *sul* > *tet* > *erm*	(Wu et al., 2019)
Southwest	26 family farms in Erhai Lake, Yunnan province	Soil, untreated wastewater	The abundance of detected ARGs including *tet* O, *tet* Q and *tet* W were all $10^{-2} \sim 10^{0}$ copies/16 S copies.	(Gu et al. 2020)
	Mianyang landfill in Sichuan province	Soil	*mex* F and *sul* gene had the highest average abundance.	(Li, et al., 2022)
Northwest China	10 breeding farms in Shaanxi province	Soil	There were high concentrations of tet X, *sul* 1, *sul* 2 and *tet* G.	(Duan et al. 2019)
	28 livestock and poultry farms in Ningxia	Animal husbandry waste	There were 54 ARGs and 15 MGEs, and the highest abundance was *erm* F (87.02).	(Peng et al. 2022)
Chinese ocean	Bohai Sea and Yellow Sea	Sediment	*qnr* S, *qnr* B, *qnr* A, *erm* T, *erm* F, *tet* X, *tet* G, *tet* B, *sul* 2, *sul* 1 and other genes were detected.	(Lu et al. 2019)

Note: data from https://www.sciencedirect.com and https://www.scopus.com retrieved

METHODS TO MITIGATE THE HARM OF ANTIBIOTIC CONTAMINATION

The harm caused by antibiotics to people

Antibiotic residues have become a serious threat to global public health security (Chua et al. 2021), A total of 10 million people are expected to die by 2050 if no action is taken. Antimicrobial resistance could push up to 24 million people into extreme poverty by 2030 (World Health Organization 2019). Although efforts have been made to curb the overuse of antibiotics worldwide, they have had little effect. Currently, at least 700,000 people die each yearly from drug-resistant diseases, including about 230,000 from MDR-TB. More and more common diseases, including respiratory infections, sexually transmitted infections and urinary tract infections, are becoming incurable, life-saving medical procedures are becoming more dangerous, and our food systems are becoming less safe (World Health Organization 2019). According to a report on antibiotic resistance released by the World Health Organization (WHO) in 2014, Methicillin-Resistant Staphylococcus Aureus (MRSA) infections accounted for 80% of the total disease infections in Africa and 90% in the Americas(World Health Organization 2014). Based on the above risk identification, the Chinese government has recognized the threat of antibiotic abuse to ecosystems and human health. Despite a series of bans on antibiotics, standardization of antibiotic use is still far from being achieved (Shao et al. 2021).

A feasible solution to antibiotic contamination

The implementation of antibiotic ban has promoted the research on how to accelerate the degradation of antibiotics. Experts and scholars at home and abroad have published many methods to reduce antibiotic residues, which also brings new development opportunities and challenges to antibiotic research. In this paper, we summarizes the latest and most representative degradation methods and their performance on each antibiotic mentioned (Table 3). Furthermore, Chinese government is focusing on alternatives to antibiotics, which has important implications for the country's animal husbandry, aquaculture and public health safety.

Table 3 Degradation methods and performance on each antibiotic

Antibiotic	Concentration	Substrate	Governance approach	Degradation rates and results	Reference
Chlortetracycline	10 ~ 100 mg/L	Excreta in the cowshed	Anaerobic digestion of sludge	Nearly 19-25% and 18-26% (w/w) of CTCS were converted to ECTC and ICTC, respectively, while only 19-28% remained CTC	(Lee et al. 2020)
Doxycycline	15 mg/kg	Chicken manure	Compost Compound microbial agent was added	The double addition of 0.8% (w/w) compound microbial agent promoted DOX degradation more effectively than single addition	(Liang et al., 2020)
Oxytetracycline	20 mg/L	Distilled water	Photo - Fenton reaction	Under optimal conditions, 99.7% of OTC was eliminated within 80 min	(Wang, et al., 2022)
Tetracycline	20 mg/L	Distilled water	Photocatalytic	Under the condition of adsorption-photocatalysis, the removal rate reached 98% in 20 min	(Jiang et al. 2022)
Ciprofloxacin	10 mg/L	Distilled water	Catalyst	The CIP degradation rates of AM-450 and AM-850 at 60min were 90% and 84%, respectively	(Zhao et al. 2022)
Levofloxacin	30 mg/L	Distilled water	Electrodeposition (VO) - EF	The degradation efficiency of levofloxacin in VO-EF system reached 97.67% within 120 min	(Liang et al. 2022)
Norfloxacin	20 mg/L	Sludge + wastewater	Biodegradable	Biofortification with 2% N215-1 significantly improved the degradation efficiency	(Chen et al. 2022)
Ofloxacin	25 mg/L	wastewater	Electro-Fenton	The degradation efficiencies of ofloxacin and TOC were 100% and 82.4±0.4%, respectively	(Cao et al. 2022)
Azithromycin	10 mg/L	Synthetic wastewater	UASB bioreactor	When the concentration is 10 mg/L, the removal rate is 70%	(Martínez-Polanco et al. 2022)
Clarithromycin	0.16 µg/L	wastewater	Electro-Fenton	The removal rate of CLA was 99.38%	(Basturk et al. 2021)
Roxithromycin	10 mg/L	Ultrapure water	Light conversion	The photolysis rate is stronger when SRHA and SRNOM are added	(Li et al., 2020)
Erythromycin	1 µM	medium	biodegradable	The removal and degradation efficiencies were 77% and 53%, respectively	(Zhou et al. 2018)
Amoxicillin	100 mg/L	Distilled water	Ultrasonic degradation	The combination of H_2O_2 system and nano-zno achieved 99.0% degradation	(Ayanda et al. 2021)
Ampicillin	10 mg/L	Distilled water	Microbial electrofenton	Microbial electrofenton results in 96 - 98% in situ degradation of ampicillin	(Mukhopadhyay et al. 2022)
Cephalexin	10 mg/L	Distilled water	degradation of biochar	$SO_4^{\cdot -}$ and $HO^{\cdot -}$ play a major role in the degradation of CEX	(Song et al. 2021)
Sulfadiazine	50 mg/L	Distilled water	Activated degradation of biological carbon	The SDZ removal rates of sorghum stalk, reed stalk, cotton stalk were 94.4% and 85.1%, respectively	(Feng et al. 2022)
Sulfamerazine	50 mg/L	Distilled water	Pyrolysis coupled	O_2^- and h^+ play a major role in SMZ degradation	(Ke et al. 2022)
Sulfamethazine	10 mg/L	Ultrapure water	Degradation of biochar	NPSB-700 was able to degrade 97.59% of SMX within 40 min	(Xia et al. 2022)
Sulfapyridine	10 mg/L	Distilled water	Degradation of biochar	Under the best conditions, the removal rate is up to 89.6%	(Huang et al. 2020)

Note: data from https://www.sciencedirect.com and https://www.scopus.com retrieved

STRATEGIES AND FUTURE PROSPECTS IN MANAGING ANTIBIOTIC CONTAMINATION

A large number of studies have confirmed that the traces of antibiotics and ARGs can be detected in various environmental media in China. The increasing prevalence of antibiotics and their resistance in the environment has attracted more attention from academia and the government. Over the past few years, the Chinese government has issued a series of regulations in animal husbandry and clinical use to reduce the use of antibiotics. For example, in 2019, the Ministry of Agriculture of China issued the "Announcement on the Cessation of the Use of Three Veterinary drugs including quinolinethanol, carbarsone acid and roxarsone in Food Animals" (Announcement of the Ministry of Agriculture No. 2638). In 2020, the Ministry of Agriculture of China issued a "Comprehensive Ban on the Addition of Antibiotics in animal Feed" (Announcement No. 194) (The People’s Republic of China 2022). However, in some cities in China, inappropriate antibiotic prescriptions have not been effectively curbed, especially in rural primary health centers with underdeveloped economy and relatively backward information, "junior doctors" will inevitably abuse antibiotics in pursuit of benefits and efficacy. Therefore, in order to effectively reduce the abuse of antibiotics in animal husbandry and clinical care, the Chinese government needs to make efforts in the following aspects:

First, law enforcement and supervision should be strengthened to increase the cost of breaking the law. Government regulatory departments should continue to strengthen the implementation of the special file management of antimicrobial drugs, further implement the requirements for the adjustment of antimicrobial drugs supply catalogue and the filing management, restrict the application norms and standards of antibiotics, strictly examine drugs, and improve the regulatory system. Strictly control the types, doses and quantities of antibiotics in clinical application, and achieve standardized use of antibiotics.

Second, the development of low-toxicity, biodegradable alternatives to antibiotics should be encouraged. It is reported that there are active factors with the same efficacy as antibiotics in the traditional Chinese medicine (TCM) with herbs and flowers as raw materials, such as allicin, isatis root, berberine, houttuynia, andrographil inner fat and so on (Shao et al. 2021). The development of animal vaccine is also one of the important ways for the Chinese government to resist infectious diseases and ensure the production and safety of livestock and aquatic products, especially in large farms, vaccination is very important.

Third, Explore practical and affordable antibiotic degradation technology. Residual antibiotics will inevitably be released into the environment and cause bacterial resistance, thus endangering human life and safety. Therefore, it is urgent to find a reliable technology to degrade antibiotics. Both activated sludge and microalgae technologies can effectively degrade antibiotics in wastewater, and the removal mechanism mainly involves the adsorption, biotransformation and degradation, accumulation and hydrolysis of antibiotics (Li et al. 2022a)。 Based on this, the Chinese government can try some practical technologies to improve the environmental status of the soil and water environment that has been stressed by antibiotics.Therefore, the Chinese government still has a long way to go in raising awareness among farmers to reduce antibiotic abuse and pollution.

Author statement

Chao Yang and Baiyan Cai organized the data and wrote the manuscript. Khim Phin Chong was the corresponding author and modify the manuscript. Harry Lye Hin Chong modified the whole manuscript. All contributing authors read and agreed to the final manuscript. The authors declare no competing interests.

Declaration of competing interest

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

Data availability

Data will be made available on request.

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