A Review of the Distribution of Antibiotics in Water in Different Regions of China and Current Antibiotic Degradation Pathways

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Antibiotic pollution is becoming an increasingly serious threat in different regions of China. The distribution of antibiotics in water sources varies significantly in time and space, corresponding to the amount of antibiotics used locally. The main source of this contamination in the aquatic environment is wastewater from antibiotic manufacturers, large scale animal farming, and hospitals. In response to the excessive antibiotic contamination in the water environment globally, environmentally friendly alternatives to antibiotics are being developed to reduce their use. Furthermore, researchers have developed various antibiotic treatment techniques for the degradation of antibiotics, such as physical adsorption, chemical oxidation, photodegradation, and biodegradation. Among them, biodegradation is receiving increasing attention because of its low cost, ease of operation, and lack of secondary pollution. Antibiotic degradation by enzymes could become the key strategy of management of antibiotics pollution in the environment in future. This review summarizes research on the distribution of antibiotics in China’s aquatic environments and different techniques for the degradation of antibiotics. Special attention is paid to their degradation by various enzymes. The adverse effects of the pollutants and need for more effective monitoring and mitigating pollution are also highlighted.

Keywords: antibiotic contamination, antibiotic resistance, enzyme degradation, water environment, ecosystems

INTRODUCTION

Since Fleming discovered penicillin in 1929, hundreds of other antibiotics have been synthesized, which are being increasingly used to treat infections in humans and animals. Inexpensive and effective antibiotics have become the preferred antibacterial drugs used by pharmaceutical and farming industries to inhibit the growth of bacteria and eliminate pathogens. In the aquaculture industry, antibiotics are used extensively as drugs to prevent bacterial infections and parasitic diseases (Bitchava and Nengas, 2010). Only a small portion of the antibiotics in aquatic products are actually absorbed, with most being discharged into the environment, resulting in antibiotic residues in aquaculture areas in discharged wastewaters and accumulated in the surrounding sediments through adsorption (Kumar et al., 2005; Conkle et al., 2010; Rico et al., 2013). In livestock farming, antibiotics are important for the prevention of infectious diseases and their treatment as well as for promoting the growth of livestock (Yin et al., 2016). Antibiotics applied to livestock and poultry are
not fully absorbed, with most being excreted into the environment through animal feces or urine (Briones et al., 2016). Residual antibiotics enter rivers and lakes through wastewater and accumulate in soil, where they are taken up by plants and animals (as illustrated in Figure 1).

As the world’s most populous country and the largest consumer of antibiotics, China’s antibiotic stewardship is facing significant challenges (Shao et al., 2020). Some of the antibiotics detected have been banned in clinical practice and may seriously impair human immunity (Zhou et al., 2021). In addition, exposure to veterinary antibiotics is associated with childhood obesity (Scott et al., 2016; Park et al., 2020) and liver injury (Mosedale et al., 2014), and the resulting genetic contamination of resistance poses serious threats to human health. China is vast territory with an equally diverse industrial layout. In addition, the levels of economic development vary greatly across the country, and thus the range of antibiotic concentrations in the environment is also broad across different regions. Here, first, we review the distribution of antibiotics in aquatic environments in China and the types of antibiotics, and report the distribution characteristics of antibiotics in China. Secondly, we analyze the potential impacts of antibiotics on the ecological environment in China. Lastly, we review progress in technologies for the degradation and removal of antibiotics in China and abroad, in addition to exploring the underlying principles, as well as their merits and shortcomings. This review provides a basis for risk estimation of antibiotics in ecological systems, an overview of the distribution of antibiotics in the aquatic environment in China, and the current approaches and methods used to eliminate antibiotics from ecological systems.

STATUS OF ANTIBIOTIC CONTAMINATION IN AQUATIC ENVIRONMENTS IN CHINA

Types of Antibiotics in Aquatic Environments in China

The major antibiotics in aquatic environments in China are divided according to their chemical structures and include macrolides, tetracyclines, fluoroquinolones, sulfonamides, and chloramphenicol (Liu et al., 2012). Their structural formulas are listed in Table 1.

Antibiotics in Surface Water

In different regions of China, the spatial and temporal distribution of antibiotics in water sources varies significantly, and this difference is closely related to the local industrial structure, the mode of antibiotic disposal in the pharmaceutical industry, and the mode of antibiotic use in the livestock industry. As shown in Table 2 by the results of a statistical analysis of data from the last five years, the distribution of antibiotics have been found to vary in different areas, and their contamination level also varies from region to region (Zhang et al., 2019). The antibiotic pollution is mainly concentrated in the Yangtze River Basin, and the Bohai Bay and Pearl River Delta, and Xinjiang regions. In the western region, the medical safety standards are relatively poor, and chloramphenicol, a highly effective antibiotic with relatively greater side effects, is a major problem. As a result of its continued use, the detection rate of chloramphenicol in the middle and upper reaches of the Yangtze River is significantly higher than that in the eastern region (Wang, 2020a). The pharmaceutical industry is concentrated in the economically developed eastern region, leading to the discharge of a large amount of antibiotic effluent and thus a high concentration of antibiotic pollution in this region (Bao et al., 2021). In Xinjiang, coastal areas, and other regions, the development of the livestock and aquaculture industries, which use antibiotics, has resulted in significantly higher levels of sulfonamides and tetracycline antibiotics in the environment. (Table 3). Quinolone antibiotics are widely used as broad-spectrum anti-infective drugs in medical treatment, and their presence has been detected in most local drinking water sources (Table 4).

Generally, Chinese rivers and lakes have high concentrations of antibiotics. Sulfonamide and quinolone are the main pollutants in the surface waters of Chinese lakes (Liu et al., 2018).

Antibiotics in the aquatic environment may be influenced by photolysis, temperature, pH, dilution factors, bacterial populations, and hydraulic residence time, leading to inconsistencies in their concentrations (Kümmerer, 2009; Kümmerer, 2009; Zhang et al., 2014; Tang et al., 2015). Based on the results of previous research (Yoshizaki and Tomida, 2000; Loftin et al., 2008; Ben et al., 2013), the concentrations and compositions of the main types of antibiotics in the abundant water period and dry water periods are shown in Figure 2, which show that the concentrations of antibiotics in aquatic environments vary seasonally, with detectable frequencies and average concentrations being higher in winter (dry water period) than in summer (dry water period). Industrial structure, medical level, and climate of different regions have an effect on the distribution of antibiotics in local water bodies, especially pharmaceutical and farming industries have a marked effect on antibiotic discharge. Therefore, strengthening guidance and

![FIGURE 1] Circulation of antibiotics in the environment.
| Type              | Name            | Abbreviation | Structure | CAS No.  |
|------------------|-----------------|--------------|-----------|----------|
| Macrolides       | Roxithromycin   | ROX          | ![Roxithromycin Structure](image1) | 80214-83-1 |
|                  | Erythromycin    | ERM          | ![Erythromycin Structure](image2) | 114-07-8   |
| Tetracyclines    | Tetracycline    | TC           | ![Tetracycline Structure](image3) | 60-54-8    |
|                  | Oxytetracycline | OTC          | ![Oxytetracycline Structure](image4) | 79-57-2    |
|                  | Chlorotetracycl | CTC          | ![Chlorotetracycline Structure](image5) | 57-62-5    |
|                  | Doxycycline     | DOX          | ![Doxycycline Structure](image6) | 209-271-1  |
| Fluoroquinolones | Ofloxacin       | OFX          | ![Ofloxacin Structure](image7) | 82419-36-1 |
|                  | Ciprofloxacin   | CIP          | ![Ciprofloxacin Structure](image8) | 85721-33-1 |

(Continued on following page)
| Type          | Name                  | Abbreviation | Structure | CAS No.  |
|---------------|-----------------------|--------------|-----------|----------|
| Norfloxacine  | Norfloxacin           | NOR          | ![Structure](image1) | 70458-96-7 |
|               | Enoxacin              | ENX          | ![Structure](image2) | 74011-58-8 |
|               | Enrofloxacin          | EFX          | ![Structure](image3) | 93106-60-6 |
| Sulfonamides  | Sulfamethizole        | SMT          | ![Structure](image4) | 144-82-1   |
|               | Sulfathiazole         | STZ          | ![Structure](image5) | 72-14-0    |
|               | Sulfamerazine         | SMR          | ![Structure](image6) | 127-79-7   |
|               | Sulfadiazine          | SDZ          | ![Structure](image7) | 68-35-9    |
|               | Trimethoprim          | TMP          | ![Structure](image8) | 738-70-5   |

(Continued on following page)
TABLE 1 | (Continued) Major classes of antibiotics in aquatic environments in China.

| Type            | Name             | Abbreviation | Structure | CAS No. |
|-----------------|------------------|--------------|-----------|---------|
| Chloramphenicol | CAP              |              | ![CAP Structure](image) | 56-75-7 |
| Thiamphenicol   | TAP              |              | ![TAP Structure](image) | 15318-45-3 |
| Florfenicol     | FF               |              | ![FF Structure](image) | 73231-34-2 |

TABLE 2 | Distribution of antibiotics in different waters of China (From 2015 to 2020).

| Waters                      | Regions                          | The amount of antibiotics detected (ng/L) | References                  |
|-----------------------------|----------------------------------|-----------------------------------------|-----------------------------|
|                             |                                  | Sulfonamides | Fluoroquinolones | Macrolides | Chloramphenicol | Tetracyclines |                                  |
| Songhua river               | Harbin                           | 2.1–92.14  | 0.03–8.14       | 0.26–18.07 | —              | —             | —                             | Wang et al. (2018c) |
| Lancang river               | Lincang                          | 1.51–37.43 | 0.03–1.45       | 0.18–4.46  | —              | ND–12.19     | —                             | Liang (2019) |
| Yarlung zangbo river        | Lasa                             | 2.74–33.94 | <2              | 0.61–33.77 | —              | 0.70–14.07   | —                             | Liang (2019) |
| Huangpu river               | Shanghai                         | 0–22.48    | —               | —          | —              | 9.98–177.28  | —                             | Feng et al. (2017) |
| Yangtze river (nanjing section) | Nanjing                        | 32.42      | 27.25           | 778.49     | 6.48           | 14.55         | —                             | Feng et al. (2019) |
| Moon lake                   | Ningbo                           | 13.68–523.78 | ND–267.0       | 5.88–552.53 | —             | —             | —                             | Wang et al., (2018d) |
| Tahu lake basin (yil-tachang section) | Changzhou-wuxi             | ND–0.58    | ND–0.21         | 0.04–0.94  | —              | ND–17.85     | —                             | Sun et al., (2018) |
| Tahu gonghu bay             | Wuxi                             | ND–47.8    | 14–47.4         | 14–23      | —              | ND–4.720     | —                             | Wu et al. (2016) |
| Tiaoxi (tahu lake basin)    | Huzhou                           | ≤226.6     | ≤36.5           | —          | ND              | ND–106.5     | —                             | Xu et al. (2020) |
| Poyang lake                 | Nanchang                         | 1.3–117    | —               | 3.6–14.8   | 5–16.5         | ND–14        | —                             | Ding (2018) |
| Chishu                      | Heifei                           | ND–189.9   | ND–148.7        | ND–18.48   | —              | ND–14        | —                             | Tang et al. (2014) |
| South lake                  | Wuhan                            | 3.52–20.48 | 70.70–155.52    | —          | —              | 21.41–43.43  | —                             | Xiao et al. (2019) |
| Shahu                       | Wuhan                            | ND–0.81    | 37.85–75.09     | —          | —              | 20.06–29.03  | —                             | Xiao et al. (2019) |
| East lake                   | Wuhan                            | ND–4.17    | 49.49–83.31     | —          | —              | 15.42–24.64  | —                             | Xiao et al. (2019) |
| Datong lake                 | Yiyang                           | 11.56–181.25 | ND–83.53       | —          | ND–18.08       | ND–18.08     | —                             | Liu and Lu (2018) |
| Yangtze river basin (three gorges Section) | Chongqing                       | ND–247     | ND–16.4         | 19.1–223.7 | 11.9–615.8     | —             | —                             | Feng et al. (2017) |
| Namning river               | Guiyang                          | 13.68–523.78 | 1.72–424.37    | 5.88–552.53 | 1.95–235.6     | 0.36–243.25  | —                             | Wang et al. (2018e) |
| Weihe river (Xi’an section) | Xi’an                            | 21.37–60   | 4.7–64.28       | —          | —              | 4.64–129.91  | —                             | Zhu et al. (2018) |
| Pearl river                 | Guangzhou                        | 687.90     | 814.1           | 1112.2     | —              | 643.2         | —                             | Liu et al., (2017) |
| Star lake                   | Zhaoyang                         | 9.27–190.71 | 2.27–9.46      | ND–0.8     | —              | ND            | —                             | Xie et al. (2019) |
| Caohai karst plateau wetland| Weining                          | 50.5       | 43.2            | 22.6       | 15.9           | ND            | —                             | Wang et al. (2020a) |
| Huaihe (shihe district)     | Xinyang                          | —          | —               | 13.1–356.6 | —              | ND–275.1     | Wang and Wang (2020)          |
| Xiaoxinghe (jinan section)  | Jinan                            | DN–196.5   | 11.0–383.9      | 13.16–309.09 | —          | ND–8.91      | —                             | Yan (2018) |
| Ebinur lake                 | Bortala Mongolian autonomous prefecture | 22.50–103.72 | 21.61–83.78   | 0.56–306.75 | —              | ND–15.94     | —                             | Wang (2020b) |
| Bosten lake                 | Bayingoleng Mongolian autonomous prefecture | ND–36.81   | ND–99.32       | —          | —              | ND–43.55     | —                             | Yang (2018) |
| Ebinur lake                 | Alashankou                       | ND–61.01   | 293.78–5144.95 | —          | —              | ND–12.01     | —                             | Qianqian (2016) |
Aquaculture areas and environments can be a significant source of antibiotic discharge into aquatic environments. Antibiotics are detected not only in water bodies such as rivers and lakes but also in sediments, which can contain significant amounts. The level of exposure of sediments to antibiotics is usually higher than that of water because the sediment particles, which have a strong ability to adsorb antibiotics (Lee and Carlson, 2006; Kim and Carlson, 2007; Yang et al., 2010). Antibiotic concentrations in surface water are more susceptible to external environmental influences than those in sediment, including dilution (Cheng et al., 2014; Ding et al., 2017), adsorption of particles (Wang et al., 2017a; Yang et al., 2020), and photodegradation (Chen et al., 2016), all of which can affect the variation of the antibiotic concentrations in water. Compared to the water column, antibiotic levels in sediments are relatively stable because their ability to strongly adsorb antibiotics leads to antibiotic accumulation in the sediments (Mangalgiri and Blaney, 2017). Different water environments lead to different adsorption properties of the sediments, resulting in a both spatially and geographically heterogeneous distribution of antibiotics in sediments, as shown in Table 5. Furthermore, this distribution may also be influenced by the external environment. For example, external currents may flush antibiotics-bearing sediments and thus release adsorbed antibiotics into the aquatic environment, causing secondary pollution (Radke et al., 2009). Sediments can affect the level of antibiotics in water bodies. The components of sediments are highly complex, and there are several differences in the composition of sediments in different water body regions.
TABLE 5 | Antibiotics concentrations in sediment (From 2015 to 2020).

| Waters                        | Regions                     | The amount of antibiotics detected (ng/L) | References |
|-------------------------------|-----------------------------|------------------------------------------|------------|
| Yangtze river/Jialing river   | Chongqing                   | 2.79–23.19, 22.24–33.15, 7.6–14.07       | Wang et al. (2020b) |
| Danjiangkou Reservoir         | Danjiangkou                 | 1.0–15, 1.6–16                         | Hu et al. (2019) |
| Pearl river estuary           | Zhuhai                      | ND–192, ND–157, ND–114                 | Li et al. (2018) |
| Tahu lake                     |                | 0.086–9.169, 0.28–50.1, 0.97–67.39     | Xu et al. (2019) |
| Minjiang estuary              | Fuzhou                      | ND–1.33, 0.03–15.60, 0.02–44.31         | ND         |
| Intertidal mudflat culture areas | Da’ian                      | 0.4312–22.457, 4.682–78.368, 0.963–1.436 | Xuan et al. (2020) |
| Aquaculture area              | ND–71.49                    | ND–13.19                                | Guo et al. (2019) |
| Yangtze estuary (wusongkou)   | Shanghai                    | 2.63, 48.98, 8.54                        | Li et al. (2020b) |
| Yangtze estuary               | Xupu                        | ND–16.28, 2.74                          | ND–10.85   |
| Nanfei river                  | Hefei                       | ND–2.7, ND–311, ND–15.8                 | Lyu et al. (2019) |
| Songhua river                 | Jilin                       | ND–26.9, ND–7.1, 3.0–28.3, ND–15.4      | He et al. (2018) |
| Liao river                    | Jilin                       | ND–5.2, ND–640, ND–512                  | Dong et al. (2016) |
| Mangrove nature reserves      | Hainan                      | 57, 48.8, 28.4                          | Liu et al. (2020c) |
| Mangrove nature reserves      | Hengdong                    | 39.1, 28                          | Liu et al. (2020c) |
| Fengshuba reservoir           | Heyuan                      | 2.91–46.22, 15.8–172.9, 18.9–180.6     | Liu et al. (2020c) |
| Chaobai river                 | Beijing                     | 7.7, 432.9, 12.13                      | Zhang et al. (2020b) |
| East China sea bay            | Zhengjiang                  | 0–25.3, 0.4–45.1, 0.6–60.3              | Li et al. (2020b) |
| Xiangjiang river              | Hunan                       | ND–0.98, 3.73–487, 0.33–9.44, ND–9.03   | Chen et al. (2019) |
environments. The enrichment of antibiotics in sediments and how antibiotics in sediments are released into the water body still need systematic and in-depth research.

EFFECT OF ANTIBIOTICS ON PEOPLE AND ECOSYSTEMS

Antibiotic Hazards to Human Health

Antibiotics have been found in fish from some farming areas and in some cooked foods and crops, and the antibiotics can be enriched in humans after consumption. Antibiotics have a strong inhibitory effect on the entire intestinal bacterial community (He et al., 2014). Antibiotics have a strong inhibitory effect on the entire bacterial community of intestinal microorganisms. The transfer of resistance genes between intestinal endophytes and pathogenic bacteria such as Escherichia coli, Klebsiella, and Enterococcus faecalis leads to an imbalance in intestinal microorganisms, and this in turn causes a variety of bacterial diseases (McInnes et al., 2020) and even intestinal cancer (Sobhani et al., 2019) and experiments have shown that even a small amount of antibiotics rapidly

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**FIGURE 3** | Tetracycline and sulfonamide inhibit algal growth by affecting their chloroplast replication and transcription/translation.

**FIGURE 4** | Antibiotic resistance genes induced by antibiotics and horizontal gene transfer.
changes the diversity of the intestinal flora in a short period of time (Dethlefsen et al., 2007; Fouhy et al., 2012), which may lead to a variety of diseases, especially in newborns. Antibiotic use during pregnancy or in newborns may adversely affect the neonatal gut microbiome and adversely affect the infant’s immune system, leading to childhood atopy, asthma, allergies, and obesity. It increases the probability of epilepsy in children (Kenyon et al., 2008; Neu and Walker, 2011; Madan et al., 2012; Mette et al., 2012; Dik et al., 2016; Koebnick et al., 2019; Milliken et al., 2019; Pronovost and Hsiao, 2019; Tadeusz et al., 2019; Zimmermann and Curtis, 2020; Zhang et al., 2021). Excessive intake of antibiotics can cause damage to the nervous system, kidneys, and other organs (Ramirez et al., 2007). At the same time, germs are prone to develop drug resistance and become super germs that are difficult to cure (Goldman, 2004; Xu et al., 2010). The dose of antibiotics used to treat a disease is controllable, but the enrichment of antibiotics from food into the body is not measurable and assessable. As food is consumed every day, determining the content of antibiotics contained in food is difficult. Therefore, the regulation of antibiotic content in food in the market is important.

Antibiotic Accumulation in the Ecological Chain

Algae are the basis of the food chain, and even a slight decrease in algal populations may affect the balance of the aquatic system (Lanzky and Halling-Sørensen, 1998). Researchers performed relevant cytotoxicity experiments to verify that the presence of antibiotics affects the genetic and normal growth of the genome (Yamaguchi et al., 2003; Yamaguchi and Subramanian, 2003). As shown in Figure 3, tetracycline and sulfonamide antibiotics have been found to inhibit algal growth by affecting their chloroplast

### TABLE 6 | Characteristics of different methods of degrading antibiotics.

| Methods of degrading antibiotics | Stages of application | Advantages | Disadvantages | References |
|---------------------------------|-----------------------|------------|---------------|------------|
| Physical adsorption             | Scaled up applications in industry | Low cost, simple design, and high flexibility | Low efficiency and causes secondary pollution | Dutta and Mala (2020) |
| Membrane filtration             | Applications in drinking water production | Removal of many contaminants | High cost | Yin et al. (2021) |
| Chemical oxidative degradation  | Scaled up applications in industry | Easy to operate, requires short time, and efficient | Environmentally unfriendly and low recycling rate | (Advanced oxidation technology engineering.) |
| Photolysis                      | In the laboratory research stage | Eco-friendly | High cost | Bo (2017) |
| Plant adsorption                | Scaled up applications in industry | Economical, with high efficiency | Selective and diffusion of resistance genes | Liu et al. (2019) |
| Activated sludge and microbial strains | Scaled up applications in industry | Efficient and easy to operate | Susceptible to microbial resistance gene production | Liu et al. (2016) |
| Enzymatic degradation           | In the laboratory research stage | Eco-friendly, efficient, and requires short time | Highly influenced by environment | Bilal et al. (2019) |

![FIGURE 5](Conversion of antibiotics to disinfection byproducts. End products of Norflaxin or Sulfamethoxazole (McInnes et al.) reacts with NaOCl in different water environments.)
Antibiotics and Disinfection Byproducts

In addition to their own toxicological effects and the genetic problem of resistance, antibiotics that remain in the aquatic environment have been found by researchers to be precursors of disinfection byproducts (DBPs) that can react with disinfectants such as chlorine and chlorine dioxide to produce halogenated carbon or nitrogen-containing disinfection byproducts (Wang and Helbling 2016; Zhang et al., 2017; Chuan et al., 2018) (Figure 5). DBPs are the result of the reaction between disinfectants and a special class of organics produced by the reaction of organic precursors in water. Since many antibiotics are nitrogen-containing organics, they contribute significantly to some of the more toxic N-DBPs. These disinfection byproducts, in turn, can be instrumental in inducing antibiotic resistance and resistance genes. DBPs have been shown to significantly increase bacterial resistance to antibiotics (Lu et al., 2015) and the mutagenesis rate of resistance genes (Li et al., 2016) as well as the concentration of resistant bacteria (Lv et al., 2015). The level of DBPs is often overlooked when testing for antibiotics in water, and we need to pay equal attention to the level of DBPs, which can also lead to the development of resistance genes in bacteria.

Antibiotics in Aquatic Organisms

Low concentrations of antibiotics are present in fish; however, they are mainly detected in laboratory studies. The replication, transcription/translation, and metabolic pathways (Brain et al., 2004; Brain et al., 2008; Baran et al., 2011). Fish appear to be less sensitive to antibiotics than algae (Li et al., 2012a). Feeding habits can affect the accumulation of antibiotics in fish, and some studies have shown that carnivorous fish have higher levels of antibiotic enrichment than other fish because they are the top consumers in the food chain in the aquatic environment (He et al., 2014). Zhao et al. showed that the accumulation of antibiotics in different tissues of animals is different, and the accumulated antibiotic levels in different tissues of fish are also different. For example, the accumulation levels of antibiotics in fish bile, plasma, and liver are relatively higher than those in other organs. (Zhao et al., 2016a). Invertebrates and fish that are chronically exposed to antibiotics are enriched in antibiotics, and people who consume these aquatic organisms face a high health risk (Metsälä et al., 2012). The toxicity of antibiotics in water is influenced by their concentration, duration of exposure, aquatic species, and the coexistence of other antibiotics and/or other contaminants (Grenni et al., 2017). Plants can take up multiple antibiotics from soil and water, and while the toxicities of these multiple antibiotics are not superimposed on a single toxicity, they can induce combined toxicity (Brain et al., 2004). Antibiotics are passed up the food chain, resulting in human exposure to antibiotics via the consumption of food containing antibiotics; eventually, the accumulated antibiotics will have negative effects on the human body.

Increase of Potential Novel Antibiotic Resistant Gene Induction by Antibiotics

Genes are mutated and inherited in nature, and antibiotic resistance genes (ARGs) are present in the natural environment. Thus, antibiotics released into the environment exert selective pressure on the microbial community, thereby inducing drug-resistant bacteria and causing widespread bacterial resistance (Wei et al., 2019). Residual antibiotics and ARGs that enter the environment can be taken up by plants and enter the food chain through the migration distribution of the soil-water plant system (Forsberg et al., 2012), where they migrate and accumulate, and eventually enter the human body. There are two main sources of ARGs in the environment (Zhang et al., 2019a): ARGs are present in the environment itself—Antibiotics are mainly derived from secondary metabolites of microorganisms, plants, and animals, and these microorganisms are resistant to the antibiotics they produce (Russell and Yost, 2020); 2) Another source of ARGs is exogenous input (Zhang et al., 2018a). The metabolism rate of antibiotics in animals is very low, and about 25–75% of the antibiotics enter the environment through excreta without having been metabolized, thus inducing the production of resistance genes in the environment. As illustrated in Figure 4, ARGs can be transmitted between microorganisms and vertically between generations through horizontal gene transfer (HGT). As microorganisms evolve, new ARGs may also be produced (Ji et al., 2012; Shi et al., 2015). A wide variety of microorganisms in the environment may even lead to the creation of multidrug resistance genes or superbugs, while also increasing the potential for the induction of novel ARGs. The food chain can enhance the spread of resistance genes (Hu et al., 2016; Johnson et al., 2016). The transfer of ARGs acquired by humans from the environment or from food to gut microbes leads to an increase in gut microbial resistance (Huddleston, 2014), Studies have identified β-lactamase genes in the metabolic genome of human gut flora (Cao et al., 2021), suggesting that human gut microbes can acquire resistance genes from the environment, thereby leading to drug-resistant infections in human (Bengtsson-Palme, 2017).
TABLE 7 | Antibiotic adsorption by plants reported in the literature.

| Antibiotics          | Plant             | Removal (%) | References                  |
|----------------------|-------------------|-------------|-----------------------------|
| Sulfonamides         | Thalia            | 72 ± 6      | Dan et al. (2013)            |
| Sulfadiazine         | Arundo            | 74 ± 6      | Dan et al. (2013)            |
| Sulfadiazine         | Waseyutaka        | 98.7        | Xian et al. (2010)           |
| Sulfadiazine         | Acorus calamus    | 98.4        | Chen et al. (2020a)          |
| Sulfamethoxazole     | Oxytetracycline   | 76.7 ± 4.13 | Kumar et al. (2005)          |
| Sulfamethoxazole     | Dyan              | 91.8        | Xian et al. (2010)           |
| Sulfamethoxazole     | T. angustifolia/P. australis | 60 ± 26 | Hijosa-Valsero et al. (2011a) |
| Sulfamethoxazole     | Acorus/Typha      | 29–52       | Park et al. (2009)           |
| Sulfamethoxazole     | Thalia Dealbata Fraser | 56.9 ± 7.36 | Jun et al. (2016)            |
| Sulfamethoxazole     | Iris tectorum Maxim | 69.2 ± 2.24 | Jun et al. (2016)            |
| Sulfamethoxazole     | T. angustifolia   | 80 ± 42     | Hijosa-Valsero et al. (2011b) |
| Sulfamethoxazole     | Acorus calamus    | 37.81-84.05 | Chen et al. (2020a)          |
| Sulfamethazine       | Waseyutaka        | 88.8        | Xian et al. (2010)           |
| Sulfamethazine       | Tachernasi        | 89.4        | Xian et al. (2010)           |
| Sulfamethazine       | H. pennisetum     | 91–95       | Liu et al. (2013)            |
| Sulfamethazine       | Thalia Dealbata Fraser | 100 ± 0.00 | Jun et al. (2016)            |
| Sulfamethazine       | Iris tectorum Maxim | 100 ± 0.00 | Jun et al. (2016)            |
| Sulfamethazine       | Acorus calamus    | 18.98–65.06 | Chen et al. (2020a)          |
| Sulfadimethoxine     | T. angustifolia   | 99 ± 2      | Hijosa-Valsero et al. (2011b) |
| Sulfadimethoxine     | P. australis      | 99 ± 2      | Hijosa-Valsero et al. (2011b) |
| Trimethoprim         | Thalia            | 31 ± 7      | Dan et al. (2013)            |
| Trimethoprim         | Arundo            | 38 ± 10     | Dan et al. (2013)            |
| Trimethoprim         | Thalia Dealbata Fraser | 84.6 ± 2.26 | Jun et al. (2016)            |
| Trimethoprim         | Iris tectorum Maxim | 84.4 ± 2.28 | Jun et al. (2016)            |
| Clarithromycin       | Thalia Dealbata Fraser | 100 ± 0.00 | Jun et al. (2016)            |
| Clarithromycin       | Iris tectorum Maxim | 100 ± 0.00 | Jun et al. (2016)            |
| Clarithromycin       | Iris tectorum Maxim | 70 ± 0.4  | Jun et al. (2016)            |
| Erythromycin         | P. australis      | 64 ± 30     | Hijosa-Valsero et al. (2011b) |
| Tetracyclines        | Oxietetracycline HCl | 88.4–98.3  | Huang et al. (2015)          |
| Oxytetracycline      | P. australis      | 92.7–99.9   | Gujarathi et al. (2005)       |
| Oxytetracycline      | H. annuus         | 100         | Zhao et al. (2016b)          |
| Oxytetracycline      | Typhoid orientals | 72.43       | Zhao et al. (2016b)          |
| Chlorotetraycline    | Typhoid orientals | 69.0–99.7   | Zhao et al. (2016b)          |
| Chlorodicycline      | Typhoid orientals | 73.84       | Zhao et al. (2016b)          |
| Tetracycline         | P. australis      | 88.4–98.3   | Huang et al. (2015)          |
| Tetracycline         | P. australis      | 99.3 ± 0.4  | Fernandez et al. (2015)      |
| Tetracycline         | Typhoid orientals | 70.85       | Zhao et al. (2016b)          |
| Tetracycline         | H. annuus         | 100         | Gujarathi et al. (2005)       |
| Doxycycline          | T. angustifolia   | 75 ± 40     | Hijosa-Valsero et al. (2011b) |
| Doxycycline          | H. pensiisetum   | 78–84       | Liu et al. (2013)            |
| Ciprofloxacin HCl    | H. pensiisetum   | 78–84       | Liu et al. (2013)            |
| Enrofloxacin         | P. australis      | 98.7 ± 0.3  | Fernandez et al. (2015)      |
| Diclofenac           | P. australis      | >84         | Jun et al. (2016)            |
| Naproxen             | Acorus/Typha      | 52–92       | Park et al. (2009)           |
| Naproxen             | P. australis      | 80 ± 9      | Matamoros and Bayona (2006)  |
| Ibuprofen            | P. australis      | 62 ± 2      | Matamoros and Bayona (2006)  |
| Diclofenac           | Acorus/Typha      | 73–96       | Park et al. (2009)           |
| Carbamazepine        | Acorus/Typha      | 30–47       | Park et al. (2009)           |
| Methyl dihydrojasmonate | P. australis     | 97 ± 1      | Matamoros and Bayona (2006)  |

Concentrations of antibiotics in aquatic organisms are correlated with their habits, their position in the food chain, and vary in fish and shrimp from different pelagic layers, depending on their location in the aquatic environment (Li et al., 2012b). In a previous study, sediments adsorbed with antibiotics were collected and used to construct an ecosystem to cultivate zebrafish (Chen et al., 2017a). The presence of antibiotics was detected in the zebrafish, suggesting bioconcentration of antibiotics in aquatic organisms. Fish in wild water environments were tested for antibiotic levels and antibiotic levels increased progressively from herbivorous to omnivorous to carnivorous, possibly via food chain enrichment (Tang et al., 2020). Antibiotics with different properties showed tissue specificity in aquatic products, suggesting significant differences in bioaccumulation factors between antibiotics (Liu et al., 2014; Zhao et al., 2015; Zhao et al., 2016a). Bioaccumulation and the different metabolic pathways of different aquatic organisms lead to a more complex accumulation of antibiotics in aquatic organisms. With the improvement in living standards, there is an increasing demand for aquatic products. The
government should strengthen the regulation of antibiotic content in aquatic products. There is also a need to strengthen the regulation of fishery drugs and scientific use of drugs and improve the code of practice and standards.

**DEGRADATION OF ANTIBIOTICS**

Antibiotic pollution is becoming increasingly serious globally. Although countries with severe antibiotic pollution have introduced corresponding policies, they have come too late and/or are inadequate to solve the problem (Kara, 2019). Currently, researchers are in the process of developing environmentally friendly alternatives to antibiotics to reduce the use of antibiotics. At the same time, owing to the excessive antibiotic content in the aquatic environment, researchers have developed various antibiotic treatment techniques to degrade antibiotics. These methods can be roughly divided into the following categories: physical adsorption, chemical oxidation, photodegradation, and biodegradation. The general characteristics of various methods of removing antibiotics from water bodies are shown in Table 6.

**Physical Removal of Antibiotics**

The removal of antibiotics from the aquatic environment can be achieved by adsorbing the antibiotics on an adsorbent and then recovering the adsorbent loaded with antibiotics. Existing physical methods include physical adsorption, membrane filtration, and precipitation. However, the physical methods can only separate the antibiotics from the environment but not degrade them, and subsequent treatment is necessary.

### Table 8 | Antibiotic-degrading bacterial strains reported in the recent three years.

| Antibiotics | Bacterial species | Concentration (mg/L) | Removal rate (%) | Sources | References |
|-------------|------------------|----------------------|-----------------|---------|------------|
| β-lactam    | Cephalosporin    | Achromobacter sp. YF-1 | 30 | 92.71 (7 days) | Waste medicine residue | Zhang et al. (2019a) |
|             | Sulfonamides     | Achromobacter sp.     | 10 | 97.9 (3 days) | Laboratory | Mao et al. (2018) |
|             | Sulfamethazine   | Shewanella oneidensis | 10 | 100 (3 days) | Laboratory | Mao et al. (2018) |
|             | Sulfamethazine   | Pseudomonas mandelli  | 50 | 73 (15 days) | Laboratory | Reis et al. (2018) |
|             | Sulfamethazine   | Acinetobacter sp. W1  | 10-240 | 100 (10 h) | Activated sludge | Wang and Wang (2018) |
|             | Sulfamethazine   | Ochrobactrum sp. SMX-PM1-SA1 | 5 | 45.2 (8 days) | Wastewater | Zhang et al. (2019c) |
|             | Sulfamethazine   | Labrys sp. SMX-W11    | 5 | 62.2 (8 days) | Activated sludge | Mulla et al. (2018) |
|             | Sulfamethazine   | Gordonia sp. SMX-W2-SCD14 | 5 | 51.4 (8 days) | Pig manure | Mulla et al. (2018) |
|             | Sulfamethazine   | Achromobacter sp. JL9  | 50 | 79.45 (120 h) | Pharmaceutical wastewater | Liang et al. (2019) |
|             | Sulfamethazine   | Acinetobacter sp.     | 30 | 100 (5 h) | Microbiological culture collection | Wang et al. (2018a) |
|             | Sulfadimidine    | Bacillus cereus J2    | 50 | 100 (36 h) | Municipal sewage | Zhang et al. (2019c) |
|             | Sulfamethazine   | Acinetobacter sp.     | 30 | 100 (10 h) | Microbiological culture collection | Wang et al. (2018a) |
|             | Sulfadiazine     | Acinetobacter sp.     | 30 | 100 (10 h) | Microbiological culture collection | Wang et al. (2018a) |
| Tetracyclines | Tetracycline     | Raoultella sp. XY-1   | 20 | 70.68 (8 days) | Pig farm sediment | Wu et al. (2018) |
|             | Tetracycline     | Klebsiella sp. SQY5   | 10-30 | 67.32 (92 h) | Municipal sludge | Shao et al. (2018a) |
|             | Tetracycline     | Achromobacter sp. TJ-2# | 50 | 63.9 (3 days) | Contaminated soil | Cheng et al. (2017b) |
|             | Oxytetracycline  | Psedomonas sp. T4     | 100 | 26.88 (7 days) | Livestock manure | Meng et al. (2018) |
|             | Oxytetracycline  | Achromobacter sp. TJ-2# | 50 | 58.3 (3 days) | Contaminated soil | Cheng et al. (2017b) |
|             | Oxytetracycline  | Ochrobactrum sp. KSS10 | 30 | 63.33 (4 days) | Municipal sludge | Shao et al. (2018b) |
|             | Aureomycin       | Achromobacter sp. TJ-2# | 50 | 65.5 (3 days) | Contaminated soil | Cheng et al. (2017b) |
| Fluoroquinolones | Norfloxacin    | Staphylococcus caprae | 5 | 92.6 (10 days) | Pharmaceutical wastewater | Fu et al. (2017) |
|             | Ofoxin          | Larbus portucalensis F11 | 0.45 | 34.6 (28 days) | Fluorobenzene | Maia et al. (2018) |
|             | Oxofloxin       | Rhodococcus sp. FR1    | 0.45 | 39.3 (28 days) | Fluorobenzene | Maia et al. (2018) |
|             | Ciprofloxacin   | Thermus thermophiles C419 | 5 | 57 (5 days) | Pharmaceutical sludge | Fan et al. (2017) |
|             | Ciprofloxacin   | Enterobacter sp.      | 5 | 96 (14 days) | Hospital effluent water | Liyanage and Manage (2018) |
|             | Ciprofloxacin   | Lactobacillus gesseri. | 5 | 100 (14 days) | Hospital effluent water | Liyanage and Manage (2018) |
|             | Ciprofloxacin   | Bacillus sp. (KM504129) | 5 | 74 (14 days) | Hospital effluent water | Liyanage and Manage (2018) |
|             | Ciprofloxacin   | Bradyrhizobium sp. GLC_01 | 0.05 | 70.4 ± 7.4 (8 days) | Wastewater | Nguyen et al. (2018) |
|             | Macrolides      | Tylosin               | 50 | 96.06 (56 days) | Spinach soil | Zhang et al. (2018c) |
Physical Adsorption

Physical adsorption is the adsorption of antibiotic molecules on the adsorbent through intermolecular forces. Commonly used adsorbents include activated carbon, modified activated carbon, and other molecular sieve pore structure substances. Ahmed and Theydan (2014) used microwave technology to prepare activated carbon and had high adsorption rates for both ciprofloxacin (CIP) and norfloxacin. Choi et al. (2008) successfully used granular activated carbon. In a different study, Chen and Huang (2010) analyzed the strong adsorption of alumina to three tetracycline antibiotics (chlorotetracycline, oxytetracycline, and tetracycline). The efficiency of an adsorbent is related to the pH of the solution. Adsorbents are widely used in wastewater management because they not only adsorb small molecules, such as antibiotics, but also some heavy metal ions and toxic substances such as dyes. Physical adsorption is a low cost method characterized by simple preparation of the adsorbent, no high technical requirements, simple operation, large specific

### TABLE 9 | Antibiotic-degrading fungi reported in the recent 5 years.

| Antibiotics      | Fungus                        | Concentration (mg/L) | Removal rate (%) | Degradation enzyme | References                      |
|------------------|-------------------------------|----------------------|------------------|--------------------|---------------------------------|
| Sulfonamides     | Sulfdiazine Fusarium solani KS256 | 1.5                  | 18.33 (7 days)   | —                  | Wang et al. (2018b)             |
|                  | Sulfamethoxazole Pyrococcus sanguineus | 10                   | 96.4 (2 days)    | Lac P450           | Gao et al. (2017a)              |
|                  | Sulfamethoxazole Pyrococcus sanguineus | 10                   | 93.6 (3 days)    | Lac P450           | Gao et al. (2017a)              |
|                  | Sulfamethoxazole Phanerochaete Chrysosporum | 10                   | 64.5 (8 days)    | MIP                | Gao et al. (2017a)              |
|                  | Sulfamethoxazole Phanerochaete Chrysosporum | 10                   | 96.4 (2 days)    | Lac P450           | Gao et al. (2017a)              |
|                  | Sulfamethoxazole Trametes versicolor ATCC 42530 | 10                   | 90–94 (30 days)  | —                  | Aydin (2016)                    |
|                  | Sulfamethoxazole Bjerkandera adusta ATCC 28314 | 10                   | 90–94 (30 days)  | —                  | Aydin (2016)                    |
|                  | Sulfamethoxazole Achromobacter denitrificans strain PR1 | 150                  | 91 (51 h)        | —                  | Nguyen et al. (2018)            |
| Fluoroquinolones | Ciprofloxacin Pleurotus ostreatus | 500                  | 95.07            | MnP                | Singh et al. (2017)             |
|                  | Norfloxacin Penicillium janthinum KS272 | 1.5                  | 10.59 (8 days)   | —                  | Wang et al. (2018b)             |
|                  | Ciprofloxacin Pyrococcus sanguineus | 10                   | 98.5 (2 days)    | Lac P450           | Gao et al. (2017a)              |
|                  | Norfloxacin Pyrococcus sanguineus | 10                   | 96.4 (2 days)    | Lac P450           | Gao et al. (2017a)              |
|                  | Ciprofloxacin Phanerochaete Chrysosporum | 10                   | 64.5 (8 days)    | MIP                | Gao et al. (2017a)              |
|                  | Norfloxacin Phanerochaete Chrysosporum | 10                   | 73.2 (8 days)    | MIP                | Gao et al. (2017a)              |
|                  | Norfloxacin Irpea lacteum | 10                   | 100 (10 days)    | Lac P450           | Gao et al. (2017a)              |
|                  | Norfloxacin Trametes versicolor | 10                   | 90 (14 days)     | MIP                | Gao et al. (2017a)              |
|                  | Ofloxacin Irpea lacteum | 10                   | 100 (10 days)    | MIP                | Gao et al. (2017a)              |
|                  | Ciprofloxacin Irpea lacteum | 10                   | 100 (10 days)    | MIP                | Gao et al. (2017a)              |
|                  | Ciprofloxacin Pleurotus ostreatus | 10                   | 60 (14 days)     | Lac                | Čváncarová et al. (2015)        |
| Tetracyclines    | Oxytetracycline Fusarium verticillioides KS248 | 1.5                  | 34.65 (7 days)   | —                  | Wang et al. (2018b)             |
|                  | Oxytetracycline Penicillium janthinum KS272 | 1.5                  | 40.29 (7 days)   | —                  | Wang et al. (2018b)             |
|                  | Oxytetracycline T. harzianum | 250                   | 92 (21 days)     | —                  | Ahumada-Rudolph et al. (2016)   |
|                  | Oxytetracycline T. deliquesens | 250                   | 85 (21 days)     | —                  | Ahumada-Rudolph et al. (2016)   |
|                  | Oxytetracycline P. crustosum | 250                   | 83 (21 days)     | —                  | Ahumada-Rudolph et al. (2016)   |
|                  | Tetracycline Phanerochaete chrysosporum | 10                   | 80 (3 days)      | Lip, mnp           | Qing et al. (2018)              |
|                  | Tetracycline Trichoderma harzianum | 250                   | 92 (21 days)     | —                  | Ahumada-Rudolph et al. (2016)   |
|                  | Tetracycline Trichoderma deliquesens | 250                   | 85 (21 days)     | —                  | Ahumada-Rudolph et al. (2016)   |
|                  | Tetracycline Penicillium crustosum | 250                   | 83 (21 days)     | —                  | Ahumada-Rudolph et al. (2016)   |
|                  | Tetracycline Rhodotorula mucilaginosa | 250                   | 73 (21 days)     | —                  | Ahumada-Rudolph et al. (2016)   |
|                  | Tetracycline Talaromyces atroroseus | 250                   | 72 (21 days)     | —                  | Ahumada-Rudolph et al. (2016)   |
| Beta-lactam      | Oxacillin Leptosphaerulina sp | 16                   | 100 (6 days)     | Lac and mnp and lip | Copete-Pertuz et al. (2018)    |
|                  | Cloxacillin Leptosphaerulina sp | 17.5                  | 100 (6 days)     | Lac and mnp and lip | Copete-Pertuz et al. (2018)    |
|                  | Dicloxacillin Leptosphaerulina sp | 19                   | 100 (6 days)     | Lac and mnp and lip | Copete-Pertuz et al. (2018)    |
|                  | Cephalorxyl Leptosphaerulina sp. CECT20913 | 15.2                  | 100 (15 days)    | Lac and mnp | Pérez Grisales et al. (2019)   |
|                  | Cephalorxyl Trametes versicolor ATCC 42530 | 6                     | 100 (15 days)    | Lac and mnp       | Pérez Grisales et al. (2019)   |

Notes: Lac: laccase; Lip: lignin peroxidase; MnP: manganese peroxidase; MIP: manganese-independent peroxidase; CGMCC: China General Microbiological Culture Collection Center.
surface area, and strong capacity for antibiotic adsorption. However, due to weak intermolecular interaction, the adsorbed antibiotics can easily escape under the influence of the external environment and cause secondary pollution, and is thus limited in its use to cases with low antibiotic concentrations.

**Membrane Filtration**

Membrane separation technology uses micro- and nano-porous membranes to intercept or reverse osmosis of antibiotics in water for purification purposes. In practice, membrane separation is commonly used in conjunction with other methods to remove antibiotics from the aquatic environment. Wang et al. (2017a) studied the removal efficiency and influencing factors of tetracycline in water using a magnetic flocculation-membrane separation technique. Yang et al. (2020) made membrane bioreactors (MBRs) more effective for antibiotic treatment by adding rice straw to improve denitrification. In a study by Pérez and Barceló (2008), a laboratory-scale membrane bioreactor achieved a 56% elimination of diclofenac metabolite 4′-hydroxydiclofenac. The use of membrane filtration is a physical process that does not add any chemical reagents, is green, and has good selective filtration. However, because of the small size of the antibiotic molecule and the tendency of other contaminants to clog the pore size, the membrane module needs to be replaced frequently, which is costly.

**Degradation of Antibiotics by Photolysis**

The separation of electrons and holes generated by semiconductor photocatalysts under light excitation leads to the generation of a large number of oxygen radicals in aquatic environments, thus oxidizing any present antibiotics. Titanium oxide has a high degradation rate for antibiotics in water, however, owing to the narrow spectral absorption of pure TiO<sub>2</sub>, researchers often modify it to efficiently degrade antibiotics in wastewater. Mushtaq et al. (2020) used titanium isopropoxide as a titanium precursor to synthesize peptide-based nanoparticles to study the degradation of NOR. Mountassir et al. (2020) constructed recyclable LDH-TiO<sub>2</sub> nanocomposites to degrade sulfamethoxazole under UV radiation, where TiO<sub>2</sub> can be reused, to reduce the threat to
water resources. Furthermore, researchers are developing new photoelectric systems and explore the use of other metal mineral salts as catalysts to degrade antibiotics. Chang et al. (2017a) constructed a new photoelectric catalytic (PEC) coupled electroenzyme-catalyzed (EEC) oxidation system that degraded up to 98.7% chloramphenicol within 10 h. Eswar et al. (2017) investigated the performance of reticulated CuO photocatalytic degradation of tetracycline in water. Cao et al. (2018) loaded AgPO4-modified BiVO4 on a photoanode on conductive glass, which effectively degraded levofloxacin in water. Photodegradation, a widely used method for the degradation of antibiotics, is green and environmentally friendly, relying on water molecules to provide hydroxyl radicals and oxygen radicals to degrade antibiotics, thus avoiding the possibility of secondary pollution. However, because of the high construction cost of photoelectrodes, it can only be used short-range, which comes with certain limitations. At the same time, some suspended solids and deep pigments in the wastewater obstruct the passage of light and negatively affect the photocatalytic effect.

**Chemical Oxidative Degradation of Antibiotics**

Chemical oxidation is the degradation of antibiotics through free radicals produced by a chemical reaction that react directly with the antibiotic, causing its chemical bonds to break or decompose. However, this type of method produces a large amount of secondary pollution. Ji et al. (2015), Yan et al. (2015) used thermal activation of peroxyxinitrite to produce sulfate radicals to effectively degrade sulfonamide antibiotics, but the effect is not very stable. Gaffney et al. (2015), Nassar et al. (2018) found that chlorination and oxidation selectively removed sulfonamide antibiotics from water, but the degradation effect was greatly influenced by the concentration of the antibiotics and pH.

Compared with earlier oxidative degradation by strong oxidants, Fenton oxidation has greatly reduced the chemical pollution of the environment (Tunç et al., 2012; Tunç et al., 2013; Le et al., 2016; Weng et al., 2020). It can effectively oxidize and remove the difficult-to-degrade organic substances that cannot be removed by traditional wastewater treatment technology. Ioannou-Ttöfá and colleagues (2018) used light illumination combined with the Fenton oxidation technique to degrade ampicillin in water, and showed that the pH had a great influence on the degradation result. The degradation rate of ampicillin increased with an increase in solution pH under acidic conditions.

**Biodegradation of Antibiotics**

Biodegradation of antibiotics is the use of microorganisms, microbes, and enzymes to break down antibiotics in the environment. It generally does not cause secondary pollution, can be used in a variety of environments, and is an environmentally friendly disposal method.

**Plant Adsorption**

Plants take up antibiotics from river water and bottom sediments through roots, stems, and leaves, and then transport them through transpiration or degradation by microorganisms enriched by the roots (Susarla et al., 2002), thus reducing the content of pollutants in the aqueous environment. Plant removal of antibiotics is currently performed mainly by the construction of plant floating beds, artificial wetlands, and other environmental management technologies. Because of their low cost and ease of operation, artificial floating beds are more common than artificial wetlands (Figure 6), even though artificial wetlands can simultaneously deal with a variety of environmental pollution problems and have self-healing functions that can be used for long periods. As shown in Table 7, the type of antibiotic that can be removed from the water column and the antibiotic removal efficiency vary for different plants.

**Degradation of Antibiotics Using Activated Sludge**

Activated sludge is a collective term for communities of microorganisms and the organic and inorganic materials to which they are attached, and is used for biosorption of antibiotics, biodegradation of antibiotics, and flocculation. The complex microorganisms in the activated sludge form a complex food chain with organic nutrients in the wastewater, and the degradation of antibiotics is achieved through the action of the microbial community. Composting with activated sludge removes contaminants through adsorption and microbial biodegradation. Studies have shown (Zhang et al., 2019b; Zhu et al., 2020) that antibiotics can be removed either by microbial nitrification (autotrophic biodegradation) or by microbial chemical oxygen demand (COD) degradation (heterotrophic biodegradation) in activated sludge.

Terzic et al. (2018) found that activated sludge from a municipal wastewater treatment plant was able to degrade three major macrolides (erythromycin, clarithromycin, and azithromycin) and evaluated their toxicity. Their results showed that the harmful effects of the treated effluent were greatly reduced. Radjenovic et al. (2009) found that charged activated sludge influenced the adsorption of environmental quinolone antibiotics. However, while the adsorption was improved, the effect was not stable. Activated sludge for the degradation of antibiotics is generally derived from biopharmaceutical or hospital wastewater and significantly reduces post-degradation toxicity after activated sludge treatment. However, this method is highly dependent on environmental factors such as pH, temperature, dissolved oxygen, nutrients, and toxic substances, as well as the composition and proportion of the microorganisms, which influence the degradation time. Under low dissolved oxygen conditions, irritating gases such as ammonia or sulfur dioxide are easily produced, and the proportion of nutrients in the wastewater needs to be adjusted frequently; otherwise, the degradation efficiency is low.

The use of activated sludge to decompose antibiotics could have some disadvantages. For example, bacterial fermentation in activated sludge may occur to complete the decomposition of antibiotics. The exposure of bacteria to antibiotics may then lead to the production and proliferation of ARGs, resulting in the emergence of novel types of genetic pollutants (Zeng et al., 2019)
Degradation by Microbial Strains

As a result of prolonged exposure to antibiotics, strains of bacteria become resistant to antibiotics and may even break them down. The biodegradation of antibiotics is dominated by microbial decomposition. However, the antibiotic degradation ability of strains is influenced by many factors such as the antibiotic species, strain type, carbon source, nitrogen source, temperature, and wastewater components (heavy metal ions, COD, etc.). In recent years, many bacterial strains with antibiotic degradation abilities have been isolated through screening, enrichment, and domestication, and mainly degrade sulfonamides and tetracyclines. This is most likely due to the fact that these two types of antibiotics are more likely to be adsorbed onto sediment and thus remain in a stationary environment for longer periods (Mulla et al., 2018). Table 8 lists the antibiotic-degrading bacterial strains reported in the literature over the last three years.

The microorganisms that degrade antibiotics can be divided into single and mixed strains, some of which are listed in Martins et al. (2018) demonstrated for the first time that sulfate-reducing flora could remove CIP, and Cordova-Kreylos and Scow (2007) observed that exposing anaerobic sediments to the antibiotic CIP sulfate-reducing bacteria (SRB) is advantageous. In addition, there have been reports that bacteria can degrade antibiotics under sulfate-reducing conditions (Jia et al., 2017) and that nitrate reduction has been used successfully in microbial remediation, where denitrifying bacteria can effectively degrade enrofloxacin and ceftiofur (Alexandrino et al., 2017) as well as CIP. Antibiotic-degrading flora are also present in many estuarine sediments enriched in antibiotics; Chang and Ren (2015) isolated tetracycline antibiotic-degrading flora in sediments of the Eren River estuary, and Harrabi et al. (2018) enriched the flora of the Douro River estuary and achieved a greater than 95% degradation for oxytetracycline and enrofloxacin.

Fungi are more tolerant to high concentrations of pollutants than bacteria and, therefore, are more advantageous in the degradation of antibiotics. Numerous studies have shown that it is feasible to use fungi to degrade antibiotics present in the environment. In Table 9, the antibiotic-degrading fungi reported in the literature during the last 5 years are listed.

Enzymatic Degradation

Microorganisms can produce enzymes that degrade antibiotics, such as β-lactamases, which can cleave the β-lactam rings of cyanotoxins and cephalosporins. Based on the substrate specificity of β-lactamases, they can be roughly divided into three categories: penicillinases, cephalosporinases, and oxime-type cephalosporinases. Penicillin enzymes easily decompose penicillin antibiotics, while cephalosporin enzymes have a higher activity in decomposing cephalosporin antibiotics, and the oxime cephalosporin enzymes have a decomposing effect on both penicillin and cephalosporin, but are especially good at decomposing oxime cephalosporin. To efficiently degrade antibiotics, enzyme systems can be constructed. Table 10 lists the enzyme systems that have been used to degrade antibiotics in recent years.

The construction of various enzyme systems and the use of immobilized enzymes to degrade antibiotics, considered a breakthrough in the field of environmental management, was motivated by the fact that enzymes are easily inactivated in the environment and cannot be used in large quantities in practical applications. Gao et al. (2017b) using magnetic nanoparticles Fe3O4 to immobilize β-lactamase to degrade penicillin, the efficiency remained above 95% after 35 times of reused use; Zhang et al. (2020a) used in situ immobilized laccase to degrade tetracycline and ampicillin and achieved a degradation efficiency in water close to 100%. Simón-Herrero et al. (2019) found that laccase immobilized on polyimide elogels used to remove carbamazepine yielded a degradation efficiency of 74%. In a different study, Zdarta et al. (2019) successfully degraded tetracycline by laccase immobilized with electroporus materials using 1-hydroxybenzotriazole as a medium. For degradation experiments, Becker et al. (2017) constructed an enzyme membrane reactor using a mixture of immobilized laccase and eugenol for the degradation of 38 antibiotics. Their results showed that after 24 h the reactor degraded 32 types of antibiotics with a degradation rate of greater than 50%.

At present, the existing enzymes are mainly β-lactamase types for the degradation of lactam antibiotics, laccase, and other strong oxidative enzymes for the nonselective oxidative degradation of antibiotics. Due to the rapid development of immobilized materials, an increasing number of enzymes are immobilized and are already used in actual sites to manage antibiotics pollution (Shao et al., 2019; Liang and Hu, 2020; Shakerian et al., 2020; Zhang et al., 2020a), resulting in an improvement of the stability of the enzymes and the recycling and reuse of them, thus reducing the cost. Over the past two years, immobilized lacquer enzymes have been applied to the degradation of antibiotics, and some other strongly oxidizing enzymes have gradually entered the view of the general researcher and are applied to oxidative degradation of antibiotics by immobilization.

SUMMARY AND OUTLOOK

Antibiotics have greatly polluted the environment globally. Among the prevalent antibiotic pollution treatments, physical adsorption cannot degrade antibiotics, chemical oxidation is likely to cause secondary pollution, photodegradation is expensive. Biodegradation of antibiotics, however, is attracting increasing attention because of its low cost, easy operation, and lack of secondary pollution. Nevertheless, both microbial degradation and activated sludge degradation will inevitably lead to the proliferation of ARGs. Therefore, using purified antibiotic-degrading enzymes for the degradation of antibiotics poses a good alternative. Synthesizing related enzymes in vitro or constructing engineered bacteria to produce enzymes would reduce the cost of this approach, making it even more attractive. Therefore, enzyme degradation is becoming the future mainstream of environmental management. The main remaining problem is whether the antibiotic degradation products have toxicity. Although the degradation products of
Antibiotics are tested for bacterial toxicity, whether there may be a long-term toxicity problem has yet to be determined. However, it is undeniable that the toxicity of enzymatic antibiotics will be greatly reduced. Once the toxicity problem is solved, antibiotic-degrading enzymes may be used in a variety of wastewater treatments.

Antibiotics in the environment can be enriched in humans through the food chain, and they can be very harmful to young children and pregnant women. In addition, antibiotic contamination increases the development of superbugs. However, there is a lack of mandatory standards for the limits of antibiotic fugitive levels in the surface water. Thus, there is an urgent need to control antibiotics in water bodies. China’s vast territory has a diverse climate, a diverse industrial layout, and unbalanced economic development. All the factors above influence the distribution of antibiotics in China, and these factors make it challenging for governments to control antibiotics. In recent years, China has attached great importance to the issue of antibiotic contamination, and the government has made significant improvements in antibiotic stewardship; however, there are still some shortcomings, such as, the antibiotic regulatory system and antibiotic management-related standards are inadequate to effectively combat antibiotics pollution. In addition, factory emissions do not meet safety standards. Furthermore, there are no institutions specializing in antibiotic use and management to monitor the use of antibiotics and subsequent pollution management. Finally, scientific guidance on drug use is still required to discourage and prevent antibiotic abuse.

**AUTHOR CONTRIBUTIONS**

WT and LM conceived the idea of the review, LZ collected literature, CL and LT wrote the manuscript. All authors contributed to the article.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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