Occurrence and Fate of Antibiotics in the Aqueous Environment and Their Removal by Constructed Wetlands in China: A review

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(Received April 19, 2016; revised November 14, 2016)

ABSTRACT

Overuse of antibiotics has become a serious ecological problem worldwide. There is growing concern that antibiotics are losing their effectiveness due to an increased antibiotic resistance in bacteria. During the last twenty years, consumption of antibiotics has increased rapidly in China, which has been cited as one of the world’s worst abusers of antibiotics. This review summarizes the current state of antibiotic contamination in China’s three major rivers (the Yangtze River, Yellow River, and Pearl River) and illustrates the occurrence and fate of antibiotics in conventional municipal wastewater treatment plants (WWTPs). The analytical data indicate that traditional WWTPs cannot completely remove these concerned pharmaceuticals, as seen in the large difference between the distribution coefficient (Kd) and the uneven removal efficiency of various types of antibiotics. Although constructed wetlands (CWs) offer a potential way to remove these antibiotics from water supplies, knowledge of their mechanisms is limited. There are four main factors affecting the performance of CWs used for the treatment of antibiotics in water supplies, the types and configurations of CWs, hydraulic load rates, substrates, and plants and microorganisms. Further researches focusing on these factors are needed to improve the removal efficiency of antibiotics in CWs.

Key Words: antibiotic contamination, biological degragation, municipal treatment plant, pollutants, water supplies


INTRODUCTION

Abuse of antibiotics, along with the ecological threats posed by such abuse, is a global problem. It affects developed countries such as the USA and the European Union (Homem and Santos, 2011), as well as developing countries such as China (Xu et al., 2007; Zhou et al., 2011; Zhou et al., 2013), India (Abdul Ghafor, 2010), Vietnam (Thuy et al., 2011), and most African countries (Olaniran et al., 2009). It has been shown that the overuse of antibiotics can negatively affect human organs, potentially resulting in metabolic deficiencies (Modi et al., 2013). It can also lead to an increase of the level of antibiotic-resistant human genes (Clemente et al., 2012), thus posing a threat to human therapy due to the potential spread of resistant microorganisms or clones along the food chain (Soulsby, 2005).

China is one of the world’s largest producers of antibiotics, producing approximately 210 000 tons of antibiotics per year (Luo et al., 2010). As the world’s largest developing country, China’s consumption of antibiotics has increased rapidly during the last twenty years. Based on annual sales, 10 of its top 15 pharmaceutical drugs are antibiotics (Li et al., 2005). It is estimated that the average consumption of antibiotics in China totals 138 g person−1 year−1, which is more than 10 times the consumption of the USA (Tong and Wei, 2012). Over half of the antibiotics consumed will be excreted without modification in the form of urine and feces, and a significant fraction eventually enters the water, where toxic emissions could pose severe ecological risks to the aquatic environment (Thuy et al., 2011; Liu et al., 2013).

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Recently, there has been a rapid rise in concern about the environmental safety of antibiotics, and aqueous contamination by antibiotics has become a prominent problem in China (Xu et al., 2009b; Wang et al., 2010; Jiang et al., 2011; Zhou et al., 2013).

Nevertheless, most of the available researches on antibiotics in China usually focus on the occurrence and fate of antibiotics in aqueous bodies (mainly rivers) or wastewater treatment plants (WWTPs). Very few studies have attempted to integrate the antibiotic contamination of aqueous environments with the antibiotic contamination of WWTPs. In particular, there is little information on the antibiotic contamination of China’s three major rivers (the Yangtze River, Yellow River, and Pearl River), which are the main sources of drinking water for over 56% of the Chinese population (ca. 728 million people). Moreover, few studies have explored the feasibility of treating pharmaceuticals found in the secondary effluents of municipal wastewater using constructed wetlands (CWs), despite the fact that CWs are assumed as one of the best ways to reduce aquatic contamination from sewage discharge in developing countries (Cronk, 1996; Yu et al., 2013).

In this context, this review attempts to: 1) integrate the antibiotic datasets for the three major rivers in China to explore the general contamination profiles of antibiotics at a national level; 2) illustrate the antibiotic profiles of the different treatment processes in WWTPs; and 3) analyze the primary factors involved in improving antibiotic removal using CWs.

### OCCURRENCE OF ANTIBIOTICS IN CHINA’S THREE MAJOR RIVERS

Generally, the main sources of aqueous antibiotics are the direct discharge of untreated sewage wastewater (Zhou et al., 2013), effluent of municipal WWTPs (Hijosa-Valsero et al., 2011; Zhou et al., 2013; Yan et al., 2014a), and non-point pollution emitted from agricultural, livestock, and fishery production (Arıkan et al., 2009; Thuy et al., 2011). Given the large consumption and utilization of antibiotics in clinical settings and livestock production (against the background of China’s rapid economic development and massive population), it is not surprising that most of the country’s surface waters are contaminated by these compounds. This includes the three major rivers in China.

Sulfonamides, quinolones, macrolides, tetracyclines, and β-lactams are recognized as the most commonly utilized five groups of antibiotics in China. They are the major pharmaceuticals employed in the agricultural industry (especially for livestock) and the medical industry (Liu et al., 2013; Zhou et al., 2013). Table I shows the antibiotic levels of China’s three major rivers. The average concentrations of quinolones and β-lactams are generally much higher than the other three groups of antibiotics. The mean levels of quinolones and β-lactams are 10.0 and 123.1 ng L⁻¹ in the Yangtze River, 105.3 and 343.5 ng L⁻¹ in the Yellow River, and

### TABLE I

Levels of five groups of antibiotics in the surface waters of China’s three major rivers

<table>
<thead>
<tr>
<th>River</th>
<th>Item</th>
<th>Sulfonamides</th>
<th>Quinolones</th>
<th>Macrolides</th>
<th>Tetracyclines</th>
<th>β-lactams</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yangtze</td>
<td>Mean ± SD(b)</td>
<td>27.3 ± 85.2</td>
<td>10.0 ± 23.1</td>
<td>24.6 ± 46.6</td>
<td>20.5 ± 27.4</td>
<td>123.1 ± 128.2</td>
<td>Jiang et al. (2011),</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>4.1</td>
<td>4.2</td>
<td>6.2</td>
<td>12.2</td>
<td>96.8</td>
<td>Yan et al. (2015),</td>
</tr>
<tr>
<td></td>
<td>Minimum</td>
<td>0.8</td>
<td>1.4</td>
<td>0.1</td>
<td>2.5</td>
<td>0.1</td>
<td>Zhang et al. (2015),</td>
</tr>
<tr>
<td></td>
<td>Maximum</td>
<td>623.3</td>
<td>114.1</td>
<td>166.5</td>
<td>113.9</td>
<td>298.8</td>
<td></td>
</tr>
<tr>
<td>Yellow</td>
<td>Mean ± SD</td>
<td>6.6 ± 14.8</td>
<td>105.3 ± 78.7</td>
<td>22.9 ± 29.1</td>
<td>NA</td>
<td>343.5 ± 345.6</td>
<td>Xu et al. (2009a, b),</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>0.5</td>
<td>115.5</td>
<td>8.0</td>
<td>NA</td>
<td>285.3</td>
<td>Zhang et al. (2015),</td>
</tr>
<tr>
<td></td>
<td>Minimum</td>
<td>0.5</td>
<td>10.0</td>
<td>2.0</td>
<td>NA</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Maximum</td>
<td>56.0</td>
<td>300.0</td>
<td>102.0</td>
<td>NA</td>
<td>803.2</td>
<td></td>
</tr>
<tr>
<td>Pearl</td>
<td>Mean ± SD</td>
<td>48.2 ± 106.8</td>
<td>91.5 ± 144.6</td>
<td>62.7 ± 84.4</td>
<td>6.9 ± 3.2</td>
<td>1606.3 ± 1384.3</td>
<td>Xu et al. (2007),</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>15.0</td>
<td>107.4</td>
<td>69.0</td>
<td>5.9</td>
<td>1519.7</td>
<td>Yang et al. (2011),</td>
</tr>
<tr>
<td></td>
<td>Minimum</td>
<td>1.7</td>
<td>15.3</td>
<td>11.0</td>
<td>4.7</td>
<td>2.0</td>
<td>Liang et al. (2013),</td>
</tr>
<tr>
<td></td>
<td>Maximum</td>
<td>485.0</td>
<td>557.0</td>
<td>266.0</td>
<td>13.1</td>
<td>3383.8</td>
<td>Zhang et al. (2015),</td>
</tr>
</tbody>
</table>

(a)Sulfonamides include sulfadiazine (SDZ), sulfamethazine (SM1), sulfamethoxazole (SMZ), sulfapyridine (SPD), sulfamerazine (SMR), sulfachlorpyridazine (SCP), and trimethoprim (TMP); quinolones include ofloxacin (OFL), norfloxacin (NOR), enrofloxacin (ENR), ciprofloxacin (CIP), fleroxacin (FLE), and sarafloxacin (SAR); macrolides include erythromycin (ERY), roxithromycin (ROX), azithromycin (AZM), and tylosin (TYL); tetracyclines include doxycycline (DOX), tetracycline (TC), oxytetracycline (OTC), and chlorotetracycline (CTC); β-lactams include cephalaxin, amoxicillin, penicillin, and cephalzin.

(b)Standard deviation.

(c)Not available.
91.5 and 1606.3 ng L\(^{-1}\) in the Pearl River, respectively. These observations are in accordance with the use of antibiotics in China, indicating that these two groups are consumed more than the other groups in fighting infections (Tan, 2007).

The total antibiotic concentrations in the surface waters show the following decreasing order: Pearl River > Yellow River > Yangtze River (Table I). The mean levels of the five groups of antibiotics in the Pearl River are higher than those of the Yangtze River, except for tetracyclines. This exception might be partially due to the tendency of tetracyclines to enter sediments (Zhang et al., 2015) and sampling errors. It should be noted that the consumption of \(\beta\)-lactams has been calculated based on market investigation rather than practical detection because \(\beta\)-lactams are easily subjected to hydrolysis and are rarely detected (Zhang et al., 2015). The Pearl River basin is one of the most heavily developed areas in China, with high population density due to its concentration of economic opportunities. However, only 62% of municipal wastewater in Guangzhou, the largest city in the Pearl River basin, is transported and treated in WWTPs, indicating that approximately 600,000 t wastewater is directly discharged into the Pearl River without treatment (Xu et al., 2007; Yang et al., 2011). Yang et al. (2011) detected that up to 176 and 2260 ng L\(^{-1}\) antibiotics were contained in the Pearl River and its tributaries, respectively. Considering the ubiquity of antibiotic abuse and the high population density of the Pearl River Delta, there is an urgent need to alleviate the accelerated deterioration of water quality in the Pearl River. In addition, concentrations of antibiotics show obvious seasonal fluctuations. Compared to the Yellow River and the Yangtze River, a higher flux of antibiotics (in terms of contaminant concentration) is transmitted into the Pearl River ecosystem as a direct result of anthropogenic sources. A temporal distribution of antibiotics in the Pearl River has been reported (Liang et al., 2013), while a similar distribution has not yet been observed in the Yellow River or the Yangtze River. In the dry season (January), concentrations of norfloxacin and sulfonamide were approximately 2- and 3-fold higher compared to the flood season (August) of the Pearl River, respectively (Liang et al., 2013). Moreover, macrolide antibiotics (roxithromycin (RTM) and erythromycin (ETM)-\(H_2\)O) could only be detected at very low frequencies in the Pearl River during flood season, while they are definitely detected in the dry season (Xu et al., 2006, 2007). This variation can partially be explained by the fact that more antibiotics are used and discharged into the aquatic environment during summer because they are utilized to treat higher rates of gastrointestinal infection and diarrhea among both humans and domestic animals. In contrast, levels of antibiotics in waterways increase during the dry season because there is much lower flow runoff in rivers, although the consumption of antibiotics is reduced to some extent due to fewer outbreaks of gastrointestinal infection. Similar results are also reported in China’s urban rivers (Jiang et al., 2011), which are usually highly polluted.

Table II displays the antibiotic levels in the sediment of China’s three major rivers. The descending order of antibiotic levels in these rivers (Pearl River > Yellow River > Yangtze River) is consistent with that in their surface waters, as shown in Table I. However, the antibiotic levels in sediment show much lower fluctuations than those in the aqueous matrices. Overall, the five groups of antibiotics are all detected at high

### Table II

<table>
<thead>
<tr>
<th>River</th>
<th>Item</th>
<th>Sulfonamides</th>
<th>Quinolones</th>
<th>Macrolides</th>
<th>Tetracyclines</th>
<th>(\beta)-lactams</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yangtze Mean ± SD(^{b)})</td>
<td>0.60 ± 1.30</td>
<td>22.90 ± 72.03</td>
<td>5.61 ± 11.71</td>
<td>3.07 ± 4.65</td>
<td>0.66 ± 0.85</td>
<td>Shi et al. (2014), Zhang et al. (2015)</td>
<td></td>
</tr>
<tr>
<td>River Median</td>
<td>0.21</td>
<td>2.39</td>
<td>1.01</td>
<td>0.61</td>
<td>0.37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min</td>
<td>0.02</td>
<td>0.08</td>
<td>0.04</td>
<td>0.12</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max</td>
<td>9.12</td>
<td>458.20</td>
<td>51.50</td>
<td>18.60</td>
<td>1.90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yellow Mean ± SD</td>
<td>0.16 ± 0.11</td>
<td>38.56 ± 58.88</td>
<td>14.51 ± 23.71</td>
<td>33.75 ± 73.96</td>
<td>0.89 ± 1.13</td>
<td>Zhou et al. (2011), Zhang et al. (2015)</td>
<td></td>
</tr>
<tr>
<td>River Median</td>
<td>0.13</td>
<td>5.71</td>
<td>4.04</td>
<td>0.19</td>
<td>0.50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min</td>
<td>0.04</td>
<td>0.03</td>
<td>0.15</td>
<td>0.04</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max</td>
<td>0.33</td>
<td>141.00</td>
<td>49.80</td>
<td>184.00</td>
<td>2.54</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pearl Mean ± SD</td>
<td>26.79 ± 65.18</td>
<td>135.53 ± 379.92</td>
<td>41.18 ± 96.94</td>
<td>30.09 ± 62.19</td>
<td>35.14 ± 39.05</td>
<td>Zhou et al. (2011), Liang et al. (2013), Zhang et al. (2015)</td>
<td></td>
</tr>
<tr>
<td>River Median</td>
<td>1.58</td>
<td>6.58</td>
<td>11.15</td>
<td>5.34</td>
<td>24.92</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min</td>
<td>0.13</td>
<td>1.03</td>
<td>1.33</td>
<td>0.99</td>
<td>0.13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max</td>
<td>248.00</td>
<td>1560.00</td>
<td>385.0</td>
<td>196.00</td>
<td>90.61</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^{a)}\)See Table I for details of five groups of antibiotics.

\(^{b)}\)Standard deviation.
concentrations in the Pearl River, but only three
groups (quinolones, macrolides, and tetracyclines) are
measured at high levels in the Yellow River and
Yangtze River. This also reveals that the highest in-
tensity of anthropogenic effects occurs in the Pearl Ri-
ver, and that the antibiotic levels in the sediment of
the Yellow River are higher than those of the Yangtze
River.

Compared with the Pearl River, the antibiotic le-
vels in the Yellow River and Yangtze River are much
lower due to lower population density and the longer
lengths. However, the quinolone content of the Yellow
River has reached as high as 105.3 ± 78.7 ng L\(^{-1}\), as re-
ported by Xu et al. (2009b). This is much higher than
the levels of sulfonamides and macrolides, suggesting
the serious risk of pharmaceutical contamination in the
Yellow River basin. Moreover, this sampling was con-
ducted midstream and downstream of the Yellow Ri-
ver, indicating that the Yellow River is suffering from
increased pressure on its aquatic environment due to
anthropogenic changes (Xu et al., 2009b). The Yellow
River serves over 100 million people and is the prima-
ry water resource for nine Chinese provinces. Its water
shortages can persist for 100 years. Therefore, extreme
attention should be paid to its weak ecological sta-
tus and the massive population that depends on it,
since accelerated aquatic pollution in the Yellow River
may have an especially severe impact on China’s de-
development. Currently, although the antibiotic contami-
nation of the Yangtze River is relatively low due to its
huge water volume and much lower degree of urbaniz-
ation upstream and midstream, caution should also
be applied to potential sources of antibiotics, including
poultry feeding, which is assumed to be one of the main
sources of antibiotics in the Yangtze River (Jiang et al.,
2011; Yan et al., 2015). It is worth noting that China
has no strict regulations on antibiotics as forage addi-
tives, which are consumed at the rate of approximately
100000 t annually (Zhou et al., 2013). Nevertheless,
this use of antibiotics has been prohibited by the Euro-
pean Commission since 2006 (European Commission,
2005). Overall, data are lacking on the occurrence and
fate of antibiotics in China’s three major rivers, and
further efforts are needed to determine the general sta-
tus of antibiotics in these ecosystems.

REMOVAL OF ANTIBIOTICS IN WWTPS AND BY
CWS

Removal of antibiotics in WWTPs

Under increasingly stringent environmental requi-
rements, a large number of WWTPs have been built
in China since the 2000s. However, these plants are
designed mainly to reduce common organic substrates
and nutrients, rather than antibiotics. Neverthe-
less, WWTPs are still assumed to play a crucial role
in mitigating the negative impacts of antibiotics in the
aquatic environment (Michael et al., 2013; Zhou et al.,
2013). Removal efficiencies of traditional WWTPs in
Southwest China are quite different among the three
groups of antibiotics (Fig. 1) (Gan et al., 2014; Yan
et al., 2014b). The plants’ physical devices, includ-
ing grease and grit chambers and primary clarifiers,
are found to perform poorly when removing antibiot-
ic. The removal efficiency is calculated to be −5.3%–
38.5% for sulfonamides, 16%–25.1% for quinolones,
and 4.3%–27.5% for macrolides. It is worth noting that
the negative removal efficiency for antibiotics based
on grab sampling observed by other researchers may
be partially attributed to diurnal variations in the oc-
currence of antibiotics in traditional activated sludge
WWTPs (Sui et al., 2010; Wang et al., 2014). When
considering biological processes, removal efficiencies
vary greatly for different types of substrates. Specifica-

Fig. 1. Antibiotic concentrations in wastewater (a) and sludge
(b) in conventional municipal wastewater treatment plants (Gan
et al., 2014; Yan et al., 2014b). SDZ = sulfadiazine; SM1 = sul-
famethazine; SMZ = sulfamethoxazole; TMP = trimethoprim;
MOX = moxifloxacin; NOR = norfloxacin; OFL = ofloxacin;
AZM = azithromycin; ERY = erythromycin; ROX = roxith-
romycin.
lly, the removal efficiency of quinolones (ofloxacin (OFL), norfloxacin (NOR), and moxifloxacin (MOX)) in activated sludge processes (62.6%–80.5%) is higher than those of sulfonamides (sulfadiazine (SDZ), sulfamethazine (SM1), sulfamethoxazole (SMZ), and trimethoprim (TMP)), and macrolides (erythromycin (ERY), roxithromycin (ROX), and azithromycin (AZM)), while the removal efficiencies of the latter two groups of antibiotics are similar (22%–69% and 20%–66%, respectively) (Gan et al., 2014; Yan et al., 2014b). For the disinfection unit, its removal efficiencies for all antibiotics (<10%) are substantially lower than those of the biological process. Thus, the biological process is preferred for antibiotic removal, and the removal efficiencies of antibiotics in conventional WWTPs in Southwest China are generally consistent with the values in Northwest Spain reported by Hijosa-Valsero et al. (2011).

The mean values of sulfonamides (1.105 μg L\(^{-1}\)) and macrolides (0.329 μg L\(^{-1}\)) (Fig. 1) in WWTPs in Southwest China are comparable with the concentrations found in WWTPs in Beijing, China (837 and 175.0 ng L\(^{-1}\) for sulfonamides and macrolides, respectively) (Li et al., 2013). In contrast, concentrations of quinolones are much lower than those found in Beijing (1.813 μg L\(^{-1}\) for NOR and 2.794 μg L\(^{-1}\) for OFL) (Li et al., 2013). This difference is attributed to the very different living habits and living standards in western (Chongqing) and eastern (Beijing) China. Moreover, sludge is evidently a sink for antibiotics, as the mean concentrations of antibiotics are 0.459 μg L\(^{-1}\) and 7.6 μg kg\(^{-1}\) for sulfonamides, 0.046 μg L\(^{-1}\) and 109 μg kg\(^{-1}\) for quinolones, and 0.180 μg L\(^{-1}\) and 195 μg kg\(^{-1}\) for macrolides in the secondary clarifiers for effluent and sludge, respectively. This is also consistent with the results observed by Li et al. (2013). The above finding suggests that the dominant removal pathway for antibiotics in conventional WWTPs is adsorption via the transformation of dissolved contaminants into an insoluble solid (sludge), rather than biological degradation.

Adsorption by sludge in conventional WWTPs plays a primary role in the transport and fate of pollutants. It is known that the distribution coefficient (\(K_d\)), defined as an organic compound distributed between the solid (e.g., sludge) and liquid phase (e.g., wastewater) in a specific matrix, is a useful parameter to describe adsorption behavior (Xu et al., 2009a). The \(K_d\) value decreases in the order of OFL (2982 L kg\(^{-1}\)) > RTM (1420 L kg\(^{-1}\)) > ETM (337 L kg\(^{-1}\)) > SMZ (89 L kg\(^{-1}\)) (Xu et al., 2009a), which represents the typical characteristics of quinolones (OFL), macrolides (RTM and ETM), and sulfonamides (SMZ), respectively. Moreover, the high \(K_d\) value of OFL means that quinolones usually have high affinities for absorption by the sludge/sediment matrix. Quinolones are mainly removed by the physical, biochemical, and physico-chemical processes of WWTPs and finally disposed in the form of waste sludge. Roxithromycin and ETM have a moderate degree of adsorption due to their medium \(K_d\) values, and the solubility of macrolide antibiotics would be strongly affected by the specific process between the solid-water interface. The low \(K_d\) value of SMZ indicates a low affinity for solid particles in sewage sludge and sulfonamides will mainly be present in aqueous solution and decomposed by microbes in sewage. The similar biological removal mechanism of quinolones, sulfonamides, and tetracyclines was also reported by Zhou et al. (2013), who assumed that quinolones and tetracyclines were mainly removed by adsorption onto sewage sludge rather than biological degradation, and that the vast majority of sulfonamide and macrolide compounds were decomposed by biodegradation. β-lactams are likely to be hydrolyzed and barely detected in surface waters (Zhang et al., 2015). Conventional WWTPs are insufficient to eliminate pharmaceuticals given the rapid diffusive mass transfer of compounds from wastewater to sludge (ca. 30 min) (Xu et al., 2009a). This is because their design is based on the removal of common biologically active molecules rather than highly resistant and heterogeneous pharmaceuticals.

**Removal of antibiotics by CWs**

**Antibiotic removal performance by CWs.** Constructed wetlands offer a fresh alternative for treating pharmaceutical compounds due to their low construction costs, low operation and maintenance demands, and low operation costs (Hijosa-Valsero et al., 2011; Guan et al., 2015). The removal efficiency of antibiotics varies dramatically in CWs (Table III). The removal efficiencies of sulfonamides, quinolones, macrolides, tetracyclines, and β-lactams range from −78.4% to 100.0%, 13.5% to 100.0%, −25.8% to 100.0%, 47.0% to 97.0%, and 6.0% to 45.0%, with mean values of 83.7%, 29.2%, 70.1%, 15.9%, and 51.1%, respectively. Such wide variations among different studies can be partly attributed to the different kinds of CWs employed, substrate and plant configurations of CWs, operating conditions (mainly hydraulic load rate), and sampling durations. Although CWs provide a method for removal of antibiotics under current conditions, the available reports focus predominantly on the performance evaluation of antibiotic removal by CWs. However, the fa-
### Table III
Removal efficiency of five groups of antibiotics in constructed wetlands

<table>
<thead>
<tr>
<th>Item</th>
<th>Removal efficiency</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sulfonamides</td>
<td>Quinolones</td>
</tr>
<tr>
<td>Mean ± SDb)</td>
<td>73.3 ± 9.4</td>
<td>NAc)</td>
</tr>
<tr>
<td>Median</td>
<td>73.0</td>
<td>NA</td>
</tr>
<tr>
<td>Minimum</td>
<td>59.0</td>
<td>NA</td>
</tr>
<tr>
<td>Maximum</td>
<td>87.0</td>
<td>NA</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>73.0 ± 5.4</td>
<td>90.2 ± 0.8</td>
</tr>
<tr>
<td>Median</td>
<td>73.0</td>
<td>90.2</td>
</tr>
<tr>
<td>Minimum</td>
<td>69.2</td>
<td>89.6</td>
</tr>
<tr>
<td>Maximum</td>
<td>76.8</td>
<td>90.8</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>88.8 ± 2.5</td>
<td>100.0 ± 0.0</td>
</tr>
<tr>
<td>Median</td>
<td>88.8</td>
<td>100.0</td>
</tr>
<tr>
<td>Minimum</td>
<td>87.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Maximum</td>
<td>90.6</td>
<td>100.0</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>12.9 ± 40.2</td>
<td>53.0 ± 46.0</td>
</tr>
<tr>
<td>Median</td>
<td>3.2</td>
<td>49.3</td>
</tr>
<tr>
<td>Minimum</td>
<td>−8.4</td>
<td>13.5</td>
</tr>
<tr>
<td>Maximum</td>
<td>100.0</td>
<td>100.0</td>
</tr>
</tbody>
</table>

a) See Table I for details of five groups of antibiotics.
b) Standard deviation.
c) Not available.

Factors affecting the performance of CWs are still poorly understood. Further study can improve our understanding of the behavior and control of antibiotics in wetlands.

**Perspectives on improving antibiotic removal by CWs.** Since there are few relevant reports on the removal of antibiotics using CWs, integrated support from other disciplines, mainly soil science, botany, environmental chemistry, and chemical engineering, could be applied to this research. In addition, some practical experience of engineering, including the previous researchers’ experience in operating chemical reactors (i.e., CWs and soil filters), can also be employed to enhance the performance of CWs for antibiotic treatment at low cost.

**Types and configurations of CWs.** It was reported that vertical subsurface-flow CWs (VSFCWs) and soil filters (multi-soil layering systems) exhibit better capacities for oxygen diffusion than horizontal subsurface-flow CWs (HSFCWs). This is due to more frequent contact between the solid-liquid interface (Garcia et al., 2010; Guan et al., 2015), which provides more violently oxidized conditions to degrade pharmaceuticals. In contrast, HSFCWs show signs of inferior conditions inside, reflected by poor ammonia-N removal (Healy et al., 2007). Usually, CWs must reduce the contents of organic substances in terms of biological oxygen demand (BOD) or chemical oxygen demand (COD) and nutrients (N and P) while also degrading antibiotics. Therefore, an integrated CW, comprising a VSFCW and a HSFCW, may provide a better balance between the removal of BOD, N, P, and antibiotics by providing more suitable conditions for biodegrading different contaminants. In addition, the CWs with lower water depth were found to have a higher redox value, as increased redox potential close to the surface correlated with the presence of oxygen (Garcia et al., 2010), revealing that greater water volume was subject to the enhanced degradation processes that resulted from more intensified molecular oxygen plus the potential benefit of ultraviolet radiation.

**Hydraulic load rate (HLR).** Although the HLR of CWs is generally lower than that of WWTPs, CWs also can treat aqueous solutions containing antibiotics. The HLR of CWs is still an important parameter to consider. A lower HLR is beneficial for producing a lower effluent concentration but occupies a larger footprint, while a higher HLR indicates less land cover and deterioration of effluent quality, but greater likelihood of being clogged (Pedescoll et al., 2011; Guan et al., 2012, 2014). With regard to the frequent detection of antibiotics in the aquatic environment and the potentially severe risk of antibiotics in the ecosystem (Clemente et al., 2012; Modi et al., 2013), a low HLR may be a conservative but reasonable option to protect the health safety of people and reduce probable environment risk. Currently, few reports consider this issue, and more research on the influence of CW
design characteristics (including HLR, media composition and structure, C/N ratio of substrate, etc.) are needed to determine the proper HLR of CWs under various influent levels of pharmaceuticals, as well as under different temporal and spatial variations.

Substrate. Substrates in CW systems play dual roles: providing a basic environment for growth of plants and microbes and removing pharmaceuticals through the coupled effect of biological degradation and absorption. Previous research has shown that various substrates can be utilized to treat specific antibiotic contaminants. The substrate utilized should absorb the target antibiotics by capturing them towards the substrate surface under the effect of van der Waals interaction, electronic interaction, ion exchange, and surface complexation (Li et al., 2014). Among polar pollutants, quinolones show strong absorption on solid substrates containing rich organic matter (OM) and metal oxides (Al and Fe hydrous oxides, etc.) (Zhou et al., 2011). Sulfonamides and tetracyclines are typical amphoteric compounds and their relative hydrophobicity greatly depends upon the pH and organic content of the substrate (Carda-Broch and Berthod, 2004; Li et al., 2010). It was reported that a substrate with high OM content is helpful in reducing the potential leachability of sulfonamides (Guo et al., 2013) and tetracyclines (Le-Minh et al., 2010; Li et al., 2010). Macrolides with hydroxyl groups present a medium degree of absorption affinity to soil with high mineral content, and their leachability is limited (Qi et al., 2009). The OM content effectively increases the absorption of antibiotics due to the interaction between the organic groups (carboxyl and phenolic groups), ion exchange, and hydrogen bonding of the substrate matrix with the polar groups of the antibiotics. Therefore, substrates with high OM content, such as compost, soils, and compost/soil mixtures, have been applied to remove tetracyclines (Li et al., 2010), salinomycin (Ramaswamy et al., 2010), sulfonamides and quinolones (Selvam et al., 2012), and tylosin (Mitchell et al., 2015). The furnace slag, bentonite, dolomite, and rock gravels (with highly active ions, e.g., Ca$^{2+}$, Al$^{3+}$, and Fe$^{3+}$) are often used to enhance P removal in CWs by absorption and chemical precipitation (Prochaska and Zouboulis, 2006; Li et al., 2008; Garcia et al., 2010). Zeolite is a favorable material for stabilizing and removing the influent N due to its strong affinity with NH$_4^+$-N. Thus, it deserves attention from researchers looking to balance the removal of nutrients and antibiotics in CWs. By far, the available research has usually focused on monocomponent antibiotics or a single type of antibiotic rather than the practical complex system that contains various classes of antibiotics. The different classes of antibiotics often display dramatic diversities of absorption performance. In addition, advantages, deficiencies, economic costs, and efficiencies of antibiotic treatment using CWs should be carefully analyzed. More knowledge is needed to overcome the difficulties of selecting suitable substrates to remove antibiotics under practical conditions.

Plants and microorganisms. Plants and microorganisms are the basic elements of CWs. Although some researchers note that the importance of wetland plants is negligible when treating antibiotics (Tang et al., 2015), we argue that plants can perform multiple functions that strengthen the performance of CWs. Plants directly enhance oxygen transportation by secreting oxygen from their roots, which plays a crucial role in the activity and metabolism of microorganisms around the rhizosphere (Bais et al., 2006). Specifically, the biodegradation of pollutants is improved due to the involvement of plants and microbes in CWs, and it is reported that iron plaque on plant roots contributes over 70% of total root oxygen released (Yao et al., 2011). In treating domestic wastewater, much higher numbers of ammonia-oxidizing bacteria were observed in the rhizosphere than in the non-rhizosphere of the wetland cells, which produced a significantly higher nitrification intensity ($P < 0.01$) (Peng et al., 2014). Regarding the function of wetland plants in the degradation of antibiotics, few studies have touched on the interaction between the plant rhizosphere and microorganisms inside the CWs. Moreover, plants can take up some pollutants as nutrients, although only approximately 8% of antibiotics were removed by plant assimilation directly. Most pollutants are removed via biological decomposition and simply sink inside the CWs (Yan, 2014). Nevertheless, vegetation cover could attenuate the temperature fluctuations of planted CWs, and wastewater temperature is much higher and more constant during winter in planted than in unplanted CWs (approximately 0–4 °C) (Torrens et al., 2009). In attached growth processes such as CWs, the biological reaction rate is positively associated with higher temperatures until reaching an upper temperature limit, and enzyme-catalyzed reactions are most active within the range of optimal temperatures (Rittmann and McCarty, 2002). In addition to encouraging the development of alternative treatment systems such as CWs, Chinese authorities should implement a national campaign to effectively monitor and cut antibiotic overuse. The Swedish experience has confirmed the effectiveness
of antibiotic reduction, which has been in place for 10 years and reduced antibiotic consumption in children aged 5–14 years by 52% compared to 1994 (Mølstad et al., 2008).

CONCLUSIONS

China’s three major rivers, the Pearl River, Yellow River, and Yangtze River, have all been contaminated with antibiotics, with the Pearl River’s contamination being most severe. When treating antibiotics in WWTPs, a large amount of quinolones and sulfonamides are removed by adsorption to solid (sludge) surfaces and biological degradation processes, respectively. The removal of macrolides depends on the specific characteristics of these compounds. Given the insufficient capacity of traditional WWTPs to remove pharmaceuticals, CWs offer a potential way to remove antibiotics from water supplies. Types and configurations, hydraulic load rates, substrates, plants, and microorganisms of CWs are found to affect the antibiotic removal performance of CWs. Further researches focusing on these factors are needed to improve the removal efficiency of antibiotics in CWs.

ACKNOWLEDGMENTS

The research was partially supported by the Major Science and Technology Program for Water Pollution Control and Treatment, China (No. 2012ZX07101-013-02), the Natural Science Foundation of the Jiangsu Higher Education Institutions (No. 15-KJB610011), Top-notch Academic Programs Project (TAPP) of Jiangsu Higher Education Institutions, China, and the Priority Academic Program Development (PAPD) of Jiangsu Higher Education Institutions, China. The first two authors, GUAN Yidong and WANG Bo, contribute equally to this work. We would like to thank the editor and two anonymous reviewers for the helpful comments and suggestions given to this paper.

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