Review

A review on removing pharmaceutical contaminants from wastewater by constructed wetlands: Design, performance and mechanism

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HIGHLIGHTS

- We review the application of constructed wetlands for pharmaceutical removal.
- We summarize and analyze the design parameters of the reported wetlands.
- Constructed wetlands show great potential for treatment of pharmaceuticals.
- Substrate, plants and microbes in wetlands account for the removal mechanisms.
- Relevant research is still limited and requires further work.

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ABSTRACT

This paper presents a comprehensive review of the current state of research activities on the application of constructed wetlands for removing pharmaceutical contaminants from wastewater. The focus of the review was placed on the application of constructed wetlands as an alternative secondary wastewater treatment system or as a wastewater polishing treatment system. The design parameters of the reported constructed wetlands including the physical configuration, hydraulic mode, vegetation species, and targeting pharmaceuticals were summarized. The removal efficiencies of pharmaceuticals under different conditions in the wetlands were evaluated at the macroscopic level. In addition, the importance of the three main components of constructed wetlands (substrate, plants and microbes) for pharmaceutical removal was analyzed to elucidate the possible removal mechanisms involved. There is a general consensus among many researchers that constructed wetlands hold great potential of being used as an alternative secondary wastewater treatment system or as a wastewater polishing treatment system for the removal of pharmaceuticals, but relevant reported studies are scarce and are not conclusive in their findings. Current knowledge is limited on the removal efficiencies of pharmaceuticals in constructed wetlands, the removal mechanisms involved, the toxicity to constructed wetlands caused by pharmaceuticals, and the influences of certain important parameters (configuration design, hydraulic mode, temperature and seasonality, pH, oxygen and redox potential, etc.). This review promotes further research on these issues to provide more and better convincing evidences for the function and performance of larger laboratory-scale, pilot-scale or full-scale constructed wetlands.

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1. Introduction

Pharmaceuticals of different therapeutic classes are consumed in large number annually around the world to prevent, diagnose, mitigate or cure diseases in humans as well as animals (Jones et al., 2001, 2007; Uslu et al., 2013; Zhang et al., 2008). In recent years, with the advancement in analytical techniques of trace pharmaceutical residues, many studies have demonstrated the widespread occurrence of pharmaceuticals in water environment (Fent et al., 2006; Jiang et al., 2013; Jones et al., 2001; Uslu et al., 2013; Verlicchi et al., 2012; Yang et al., 2011). Increasing concern has been raised on this issue to investigate the source, behavior, fate, risk, and control of such emerging pollutants (Jiang et al., 2013; Pal et al., 2010; Richardson, 2007; J. Zhang et al., 2013).

The main route of pharmaceuticals brought into water environment is through the municipal wastewater. Many pharmaceuticals are not completely metabolized and ingested in the body of humans and animals, as a result, pharmaceutical metabolites, conjugates and their native forms are excreted with urine and feces into sewage system (Carballa et al., 2004; Jones et al., 2002; Zhang et al., 2008). In households, the unused and expired pharmaceuticals are usually disposed with normal household waste or discarded into sink or toilets (Zhang et al., 2008). Those pharmaceuticals flushed down the sink or toilets are introduced to the sewage system. Besides, to a minor but relevant extent, the wastewater from hospitals or pharmaceutical manufacturers also contributes to the total loads of pharmaceuticals in municipal wastewater (Fent et al., 2006; Jones et al., 2001; Santos et al., 2013; Sausseureau et al., 2013). In the municipal wastewater treatment plants (WWTPs) where the conventional treatment technologies are not specially designed for elimination of pharmaceuticals, it is found that most pharmaceuticals cannot be readily and fully removed (Carballa et al., 2004; Jiang et al., 2013; Joss et al., 2006; Lindqvist et al., 2005; Paxéus, 2004; Petrie et al., 2013; Repice et al., 2013; Sim et al., 2010; Uslu et al., 2013; Vidal-Dorsch et al., 2012). Consequently, various kinds of pharmaceuticals and their metabolites are released into surface water, ground water, coastal water, and even drinking water via WWTPs' effluent (Jelic et al., 2011; Kim et al., 2007; Lindqvist et al., 2005; Uslu et al., 2013; Vidal-Dorsch et al., 2012; Vieno et al., 2005).

In addition to the municipal wastewater as the major pathway of pharmaceutical compounds entering fresh or marine water environments, there exist some other direct pathways including the household wastewater from small communities, the runoff or wastewater effluent from animal feedlots, and the rural wastewater (Anderson et al., 2013; Carvalho et al., 2013; Focazio et al., 2008; Matamoros et al., 2009a).

Upon entering the water environment, the pharmaceutical compounds and their metabolites became potential risks to the health of aquatic life and human beings even at trace levels in the water environment (Carlsson et al., 2006; Corcoran et al., 2010; Farré et al., 2008; Fent et al., 2006; Gagné et al., 2006; Pomati et al., 2006; Zuccato et al., 2006). The adverse effects on aquatic communities include the feminization of male fish (Corcoran et al., 2010; Fent et al., 2006), impairment of renal, gill and liver in fish (Fent et al., 2006;

Gagné et al., 2006), development of pathogen resistance (Zuccato et al., 2006), and decrease in plankton diversity (Farré et al., 2008). In the case of the toxic impacts on human health, the degenerative and inflammatory reactions have been found in the liver of humans when exposing to diclofenac. (a type of analgesic/anti-inflammatory pharmaceutical) (Fent et al., 2006). In addition, the proliferation inhibition effects were observed for the growth of human embryonic cells under the injection of a pharmaceutical mixture (consisting of atenolol, carbamazepine, ciprofloxacin, furosemide, ibuprofen, sulfamethoxazole, etc.) (Pomati et al., 2006). At present, the information available on the ecotoxicology of pharmaceuticals is weak and the potential risks associated with the presence of pharmaceuticals in water environment are still under debate (Jones et al., 2004). Application of the precautionary principle, therefore, is required to give rise to more stringent controls on treatment of pharmaceuticals in wastewater.

In recent years, certain advanced technologies such as advanced oxidation processes (ozonation, photolysis and heterogeneous photolysis, Fenton and photo-Fenton, sonolysis, electrochemical oxidation, etc.), activated carbon adsorption, membrane separation, and membrane bioreactor have been investigated to assess their effectiveness for the removal of pharmaceuticals from wastewater (Klamerth et al., 2010; Martínez et al., in press; Mestre et al., 2009; Molinos-Senante et al., 2013; Naddeo et al., 2009; Rossner et al., 2009; Singh et al., 2008; Sipma et al., 2010; Trinh et al., 2012). However, these advanced treatment processes are expensive making the large-scale application cost-prohibitive. Thus, selecting low-cost alternative technologies for pharmaceutical treatment is of great significance, especially in poor regions. For this purpose, constructed wetlands which are low-cost in construction, operation and maintenance are attracting great concern on their application for the removal of pharmaceutical contaminants from wastewater.

In the past decades, constructed wetlands have been demonstrated to be efficient for treatment of conventional pollutants in a variety of wastewaters such as domestic wastewater, agricultural wastewater, industrial effluent, mine drainage, leachate, contaminated ground water, and urban runoff (Choudhary et al., 2011; Cooper et al., 1996; Davies et al., 2008; García et al., 2010; Kadlec and Wallace, 2009; Stottmeister et al., 2003; Sundaravadeivel and Vigneswaran, 2001; Vymazal, 2009; Vymazal et al., 1998). However, for the treatment of pharmaceutical contaminants in wastewater using constructed wetlands, it is really a fresh application field. The feasibility of constructed wetlands to eliminate pharmaceuticals in wastewater is requiring comprehensive understanding on the removal efficiencies, the removal mechanisms, the influences of design and environmental factors, and the toxicity risks. Hence, much more attention is needed to pay for these issues in future research studies.

The objective of this paper is to present the state of the research activities on the application of constructed wetlands for the removal of pharmaceutical contaminants from wastewater. The review focuses on the application of constructed wetlands as an alternative secondary wastewater treatment system or as a wastewater polishing treatment system. The design parameters of constructed wetlands

were summarized to provide an understanding about the target pharmaceuticals, configuration, hydraulic mode and vegetation species of the reported constructed wetlands. The removal efficiencies of pharmaceuticals in constructed wetlands were also summarized in this paper in order to evaluate the performance of constructed wetlands in a macroscopic level. In addition, the possible removal mechanisms of pharmaceuticals related to the three important components of constructed wetlands (substrate, plants and microbes) were analyzed. The overall goal of this paper aims to be able to offer help for the further research in future.

2. Design and performance of constructed wetlands for the removal of pharmaceuticals from wastewater

2.1. Reported pharmaceuticals and constructed wetlands

115 pharmaceuticals grouped to 18 categories (according to their therapeutic classes) have been reported in 38 published papers in relation to their removal using constructed wetlands (including both the applications as a secondary wastewater treatment system and a polishing wastewater treatment system). The chemical structures and the physico-chemical properties of these pharmaceuticals can refer to the appendix form on the website of Maritime Research Centre in Nanyang Technological University (<http://mrc.ntu.edu.sg/RD/Pages/default.aspx>). In the form on this website, the pharmaceutical compounds are presented in terms of their chemical formula, chemical

structure, molecular weight (MW), dissociation constant (pK_a), solubility (S_w , 25 °C), octanol–water partition coefficient as $\log K_{ow}$, and octanol–water distribution coefficient as $\log D_{ow}$ ($pH = 7.4$). These data were collected from relevant internet databases such as ChemIDplus Advanced, ChemSpider, DrugBank, Hazardous Substances Data Bank and Wikipedia. In addition, the number and details of the literature references reviewed are also indicated in the form. As deduced from the number of the references, the commonly investigated pharmaceuticals in constructed wetlands are diclofenac, ibuprofen, ketoprofen, naproxen, salicylic acid, sulfamethoxazole, triclosan, atenolol, clofibrate acid, carbamazepine and caffeine.

The constructed wetlands used for the removal of pharmaceuticals from wastewater can be classified into surface free water constructed wetlands (SF-CWs), horizontal subsurface flow constructed wetlands (HSSF-CWs), vertical subsurface flow constructed wetlands (VSSF-CWs) and hybrid constructed wetlands (hybrid CWs). The SF-CWs are composed of shallow channels or basins planted with vegetation (including rooted and floating plants) in which free wastewater flows at relatively shallow depth over the impermeable bottom liner or the packed substrate layer (Fig. 1a). In the HSSF-CW systems, wastewater is fed into the wetland at the inlet zone and flows horizontally through the substrate under the surface of wetland bed which is planted with vegetation (Fig. 1b). After the treatment of wetland, the wastewater effluent is collected at the outlet zone. For the VSSF-CW systems, wastewater is dosed onto the surface of wetland bed and then flows vertically from the planted layer down through the substrate

Fig. 1. Structures of constructed wetlands. (a) SF-CW; (b) HSSF-CW; (c) VSSF-CW.

until it reaches the outlet zone (Fig. 1c). The hybrid CW systems are the combination of two or more wetlands or the combination of wetlands with other pond systems such as lagoons and facultative ponds in parallel or in series. Such hybrid systems are normally laid out in two or three stages in order to realize the improvement of treatment efficiencies.

2.2. Constructed wetlands as a secondary treatment for pharmaceutical removal

Constructed wetlands working as an alternative secondary wastewater treatment system to remove pharmaceutical contaminants from wastewater are being paid with increasing concern in many countries such as Canada, China, Denmark, Italy, Portugal, Singapore, Spain and USA. The main design parameters of the constructed wetlands reported in research work are summarized in Table 1. The removal efficiencies of the investigated pharmaceuticals by the secondary treatment of constructed wetlands are listed in Table 2. The comparison between the removal efficiencies of constructed wetlands and that of conventional WWTPs is shown in Fig. 2. The removal performance of pharmaceuticals in different types of constructed wetlands is compared in Fig. 3.

2.2.1. Design parameters of constructed wetlands

As reported in Table 1, the size of the investigated constructed wetlands was defined in this paper as microcosm-scale (surface area < 0.5 m²), mesocosm-scale (surface area in the range of 0.5 to 5 m²), pilot-scale (surface area in the range of 5 to 100 m²) and full-scale (surface area > 100 m²), of which the mesocosm-scale attracted the most attention. Various kinds of wastewater were fed into constructed wetlands, for example, urban wastewater from sewers or WWTPs, rural wastewater from rural communities, household wastewater from sparsely populated regions, swine wastewater from pig farms, and synthetic urban or agricultural wastewater. Except for the synthetic wastewater, most wastewater was preliminary or primary treated by screen, coarse solid tank, septic tank, homogenization tank, settling tank, aerobic reactor, or hydrolytic upflow sludge bed (HUSB). The target pharmaceutical contaminants in wastewater mainly covered analgesic/anti-inflammatory drugs, antibiotics, beta-blockers, diuretics, lipid regulators, psychiatric drugs, stimulants/psychoactive drugs and veterinary drugs. The analgesic/anti-inflammatory drugs including diclofenac, ibuprofen, ketoprofen, naproxen and salicylic acid were of great concern.

Water depth is one of the important parameters for designing constructed wetlands. As shown in Table 1, the water depth in SF-CWs was usually maintained no more than 30 cm, but larger in the gravel SF-CW beds where 10–25 cm of free water was over the gravel layer (25–60 cm deep). In HSSF-CW systems, the water depth was commonly maintained 5 cm under the surface of substrate (30–60 cm deep). However, Hussain et al. (2011) designed the water depth as 20 cm below the surface of substrate (60 cm deep), and Ranieri et al. (2011) and Reyes-Contreras et al. (2011) maintained the water depth same as the level of substrate as 60–65 cm and 50 cm, respectively. For the VSSF-CW systems, the water depth was controlled just below the surface of substrate in the study of Carvalho et al. (2013), but no more data could be obtained from a very small number of other literatures.

Different constructed wetland systems reported in the literatures were designed using different hydraulic retention time (HRT): 2 to 6 days for the SF-CWs, 2 to 4 days for the HSSF-CWs, 1 to 2 days for the VSSF-CWs, and 2 to 15 days for the hybrid CWs (Table 1). Under these different HRT conditions, both the batch and continuous operation modes were selected for research and both the planted wetland beds and the unplanted beds were investigated. In the planted wetland beds, various types of plants were applied, among which the most popular vegetations were *Typha* spp. and *Phragmites*

spp. In some studies, the plant initial density was selected as 10 to 50 plants m⁻².

Regarding the substrate in constructed wetlands, gravel was the most common aggregate with design D₆₀ of 3 mm to 8 mm, D₁₀ of 0.5 mm to 4 mm, C_u of 0.8 to 2, and initial porosity of 40%–45% (Table 1). In addition, other substrates including stone, lava rock, volcanic rock, zeolite, soil/red soil, sandy soil and sandy clay loam were also found to be applied in some constructed wetlands. Hussain et al. (2011, 2012) used sandy soil or sandy clay loam soil in SF-CWs and sandy soil in HSSF-CWs. Ranieri et al. (2011) filled the HSSF-CWs with three layers including 10 cm layer of soil, 20 cm layer of stone, and 30 to 35 cm layer of gravel. Carvalho et al. (2013) built the VSSF-CW bed with three layers consisting of 10 cm layer of roots' substrate, 2 cm layer of lava rock and 4 cm layer of gravel (from upper to lower). Liu et al. (2013a) constructed the VSSF-CW bed in a different way for layer distribution (from upper to lower) as: 20 cm layer of red soil, 30 cm layer of volcanic rock or zeolite and 10 cm layer of gravel.

2.2.2. Removal performance of pharmaceuticals in constructed wetlands

The removal efficiencies of pharmaceuticals by the secondary treatment of constructed wetlands are important criteria to evaluate the performance of constructed wetlands in a macroscopic level. In Table 2, the removal efficiencies of 36 investigated pharmaceuticals are listed for different constructed wetland systems including SF-CW, HSSF-CW, VSSF-CW and hybrid CW systems, as well as the conventional WWTPs. The other investigated pharmaceuticals whose concentrations in wastewater were frequently below the limit of detection are not included in this Table. Considering the possible influences of plant, seasonality, configuration, operation mode and flow's saturation situation, some removal efficiencies of pharmaceuticals are presented in details, for example, efficiency (plant/unplanted), efficiency (winter/summer), efficiency (low water depth/high water depth), efficiency (continuous/batch) and efficiency (saturated flow/unsaturated flow).

As shown in Table 2, the removal efficiencies of ciprofloxacin HCl, oxytetracycline HCl, nadolol, cotinine, enrofloxacin, monensin, narasin and salinomycin in conventional WWTPs have not been reported. Thus the comparison between the performance of constructed wetlands and conventional WWTPs for elimination of these pharmaceuticals is not premature at this stage. With reference to Table 2, it can be seen that the removal efficiencies of ciprofloxacin HCl, oxytetracycline HCl, nadolol, cotinine and enrofloxacin in constructed wetlands are high (mean removal efficiency > 70%), while the removal efficiencies of monensin, narasin and salinomycin in constructed wetlands are relatively low in the range of 20% to 50%. For the other pharmaceuticals listed in Table 2, most of their removal efficiencies in constructed wetlands appear to be as good as or even better than those in conventional WWTPs (graphically shown in Fig. 2). It can be deduced that constructed wetlands have good potential of being used as an alternative secondary wastewater treatment to remove pharmaceutical contaminants from wastewater.

According to the mean removal efficiencies of pharmaceuticals in constructed wetlands (calculated from Table 2), the pharmaceuticals can be categorized to the readily removed, moderately removed, low removed, and hardly removed. The pharmaceuticals that are readily removed by constructed wetlands (mean removal efficiency > 70%) are acetaminophen, salicylic acid, sulfadiazine, sulfadimethoxine, sulfamethazine, sulfamethoxazole, sulfapyridine, trimethoprim, atenolol, metoprolol, furosemide, caffeine and tetracycline. The pharmaceuticals that are moderately removed by constructed wetlands (mean removal efficiency between 50% and 70%) include ibuprofen, naproxen, doxycycline and gemfibrozil. The pharmaceuticals that show low removal efficiencies in constructed wetlands (mean removal efficiency between 20% and 50%) are diclofenac, ketoprofen, amoxicillin, clarithromycin, triclosan, sotalol, clofibrilic acid and carbamazepine.

Table 1

Design parameters of the reported constructed wetlands as an alternative secondary wastewater treatment system for the removal of pharmaceuticals.

References	Size	Target pharmaceuticals	Influent water	Preliminary/primary treatment	Types of CW systems	Configuration and hydraulic conditions	Plants
Anderson et al. (2013)	Full-scale	Carbamazepine, Gemfibrozil, Sulfamethoxazole, Sulfapyridine	Rural wastewater from the Rural Municipality of St. Clements near Grand Marais, Manitoba, Canada	Septic tank	Hybrid lagoon and SF-CW in series	Two lagoons in series: 134 m long, 134 m wide and 2.3 m deep each; water depth was 1.5 m; storage volume was 29,400 m ³ each. Connecting channel: 0.7 km long between lagoon and SF-CW. SF-CW: Five channel rows in a snaking configuration; water depth was 15 to 30 cm. Effluent discharge: Lake Winnipeg.	<i>Typha</i> spp.
Ávila et al. (2013)	Mesocosm-scale	Acetaminophen, Diclofenac, Ibuprofen	Urban wastewater from a municipal sewer in Spain (84 L d ⁻¹ and 6 g BOD m ⁻² d ⁻¹ for each treatment line)	Coarse screen followed by a hydrolytic upflow sludge bed (HUSB) or a conventional settling tank	Hybrid HSSF-CWs	Three treatment lines: 1) Control line: settler-wetland permanently saturated; 2) batch line: settler-wetland operated with saturated/unsaturated phases; 3) anaerobic line: HUSB-wetland permanently saturated. Layout of each treatment line: Two small wetlands in parallel (0.95 m long, 0.7 m wide and 0.45 m deep each) and connected to a big wetland in series (1.5 m long, 1.1 m wide and 0.5 m deep). Water depth: 25 cm. Substrate (gravel): 30 cm deep; D ₅₀ = 7.3 mm; C _u = 0.83; initial porosity was 40%. HRT: 2.5 d per treatment line.	<i>Phragmites australis</i>
Ávila et al. (2010)	Mesocosm-scale	Diclofenac, Ibuprofen, Naproxen	Urban wastewater from a municipal sewer in Spain (84 L d ⁻¹ and 4.7 g BOD m ⁻² d ⁻¹)	Coarse screen followed by a HUSB	Hybrid HSSF-CWs	Layout: Two small wetlands in parallel (0.65 m ² each) and connected to a big wetland in series (1.65 m ²). Water depth: 25 cm. Substrate (gravel): 30 cm deep; D ₅₀ = 5 mm; initial porosity was 40%. HRT: 3.5 d.	<i>Phragmites australis</i>
Carvalho et al. (2013)	Microcosm-scale	Enrofloxacin, Tetracycline	Swine wastewater from a pig farm in Portugal	– ^d	VSSF-CW	Sixteen microcosms: Seven were planted and nine were left unplanted (0.4 m long, 0.3 m wide and 0.3 m deep for each container). Substrate (from upper to lower): 10 cm layer of roots' bed substrate; 2 cm layer of lava rock; 4 cm layer of gravel. Water depth: Just below the substrate surface (100% flooding). Loading mode: In batch. Plant initial density: 40 plants per microcosm.	<i>Phragmites australis</i>
Conkle et al. (2008)	Full-scale	Acetaminophen, Atenolol, Caffeine, Carbamazepine, Cotinine, Fluoxetine,	Urban wastewater from Mandeville, Louisiana, USA	–	Hybrid aerated lagoon and SF-CW in series	Three aerated lagoon in series: 183 m long, 61 m wide and 3 m deep each; HRT was 9 d each. SF-CW: Water distribution was evenly across CW width by percolation through a	<i>Phragmites australis</i> , <i>Hydrocottle</i> spp.

		Gemfibrozil, Ibuprofen, Metoprolol, Nadolol, Naproxen, Propranolol, Sotalol, Sulfamethoxazole, Sulfapyridine				crushed gravel bed; HRT was 1 d. Effluent discharge: 60% was recycled, 40% was pumped into a ultra-violet irradiation channel for disinfection and then pumped into adjacent natu- ral forested wetland for polishing be- fore discharge into lake.	
Hijosa-Valsero et al. (2011a); Hijosa-Valsero et al. (2011c); Hijosa-Valsero et al. (2010b); Reyes- Contreras et al. (2012)	Mesocosm-scale	Hijosa-Valsero et al. (2010b, 2011c) and Reyes-Contreras et al. (2012): Caffeine, Carbamazepine, Diclofenac, Ibuprofen, Ketoprofen, Naproxen, Salicylic acid Hijosa-Valsero et al. (2011a): Amoxicillin, Ampicillin, Clarithromycin, Doxycycline, Erythromycin, Lincomycin, Sulfamethoxazole, Sulfadimethoxine, Trimethoprim	Urban wastewater from the primary clarifier of León WWTP in Spain	Homogenization tank	SF-CW (soilless)	Container: 130 cm long, 80 cm wide and 50 cm deep; no gravel bed with floating macrophytes. Water depth: 30 cm. Effluent pipe: At the top. HRT: 2.1 d. Plant initial density: 50 plants m ⁻² . Container: 130 cm long, 80 cm wide and 50 cm deep; 25 cm of free water was over 25 cm layer of gravel (D ₁₀ = 4 mm). Effluent pipe: At the top. HRT: 3.3 d. Plant initial density: 50 plants m ⁻² . Container: 130 cm long, 80 cm wide and 50 cm deep; 25 cm of free water was over 25 cm layer of gravel (D ₁₀ = 4 mm). Effluent pipe: At the bottom. HRT: 5.1 d. Plant initial density: 50 plants m ⁻² . Container: 130 cm long, 80 cm wide and 50 cm deep; 25 cm of free water was over 25 cm layer of gravel (D ₁₀ = 4 mm). Effluent pipe: At the bottom. HRT: 6.1 d. Container: 130 cm long, 80 cm wide and 50 cm deep; no gravel bed with floating macrophytes. Water depth: 30 cm. Effluent pipe: At the top. HRT: 2.9 d. Plant initial density: 50 plants m ⁻² . Container: 130 cm long, 80 cm wide and 50 cm deep. Substrate (gravel): 45 cm deep; D ₁₀ = 4 mm. Water depth: 40 cm. Effluent pipe: At the bottom. HRT: 2.5 d. Plant initial density: 50 plants m ⁻² . Container: 130 cm long, 80 cm wide and 50 cm deep. Substrate (gravel): 45 cm deep; D ₁₀ = 4 mm. Water depth: 40 cm. Effluent pipe: At the bottom. HRT: 2.6 d.	<i>Typha angustifolia</i>
					SF-CW (with gravel)		<i>Typha angustifolia</i>
					SF-CW (with gravel)		<i>Typha angustifolia</i>
					SF-CW (with gravel, unplanted)		Unplanted
					SF-CW (soilless)		<i>Phragmites australis</i>
					HSSF-CW		<i>Phragmites australis</i>
					HSSF-CW (unplanted)		Unplanted
	Mesocosm-scale				Hybrid HSSF-CWs		<i>Phragmites australis</i>

(continued on next page)

Table 1 (continued)

References	Size	Target pharmaceuticals	Influent water	Preliminary/primary treatment	Types of CW systems	Configuration and hydraulic conditions	Plants
Hijosa-Valsero et al. (2011b); Hijosa-Valsero et al. (2011c)		Caffeine, Carbamazepine, Diclofenac, Ibuprofen, Ketoprofen, Naproxen, Salicylic acid	Urban wastewater from Barcelona or León in Spain (84 L d ⁻¹ , 6 g BOD ₅ m ⁻² d ⁻¹)	Settling tank (ST) or HUSB		Five treatment lines: Two CW tanks in series in each line. First CW tank: Two parallel compartments, each 93 cm long, 55 cm wide and 45 cm deep. Second CW tank: 134 cm long, 100 cm wide and 80 cm deep. Gravel depth: 30 cm. Water depth: 25 cm. HRT: 3.5 d. Plant initial density: 50 plants m ⁻² . FP	
Hijosa-Valsero et al. (2011c); Hijosa-Valsero et al. (2010a)	Full-scale	Caffeine, Carbamazepine, Diclofenac, Ibuprofen, Ketoprofen, Naproxen, Salicylic acid	Urban wastewater from Cubillas de los Oteros in Spain (184 inhabitants, 20 m ³ d ⁻¹)	Bar screen and septic tank	Hybrid facultative pond (FP), SF-CW and HSSF-CW in series	<i>Lemna minor</i> SF-CW	Surface area: 1073 m ² . Water depth: 1.6 m. HRT: 7.59 d. Surface area: 44 m ² . Gravel depth: 30 cm. Gravel size: 6–8 mm. Water depth: 40 cm. HRT: 1.2 d.
			<i>Typha latifolia</i> HSSF-CW	Surface area: 585 m ² . Gravel depth: 55 cm. Gravel size: 6–8 mm. HRT: 5.7 d.	<i>Salix atrocinerea</i>		
			Urban wastewater from Bustillo de Cea in Spain	Bar screen and coarse solid tank	Hybrid facultative pond (FP), SF-CW and HSSF-CW in series	FP	Surface area: 230 m ² . Water depth: 1.5–2 m. HRT: 4.21 d.
n.a. ^e SF-CW	Surface area: 210 m ² . HRT: 3.53 d.	<i>Typha latifolia</i>					
HSSF-CW	Surface area: 362.5 m ² . HRT: 3.16 d.	<i>Salix atrocinerea</i>					
Hussain et al. (2012) Hussain et al. (2011)	Mesosocsm-scale	Monensin, Salinomycin, Narasin	Synthetic agricultural wastewater in Canada (1 L min ⁻¹)	–	Hussain et al. (2012): SF-CW Hussain et al. (2011): HSSF-CW	Container: A high-density polyethylene half-pipe, 6.1 m long, 1.5 m wide and 0.75 m deep; 9.29 m ² ; 4.17 m ³ . HRT: 1) SF-CW: 4.1 d; 2) HSSF-CW: 2.2 d. Water depth: 1) SF-CW: 0.15 m of water was over 0.6 m of substrate; 2) HSSF-CW: 0.2 m of water was below substrate surface (0.6 m) at the outlet. Inlet zone: An inflow distribution manifold and a transverse deep zone without plants in 2 m length; Treatment zone: A shallow zone (4.1 m long) vegetated with alternate bands of plants. Outlet zone: A tipping bucket and a	<i>Phalaris arundinacea</i> , <i>Typha latifolia</i>

Liu et al. (2013a)	Mesocosm-scale	Ciprofloxacin HCl, Oxytetracycline HCl, Sulfamethazine	Swine wastewater from a pig farm in Xiamen, China (3 cm d ⁻¹)	Aerobic reactor	VSSF-CW	<p>sump.</p> <p>Substrate: 1) In the six SF-CWs: three were filled with sandy clay loam soil; the other three were filled with sandy soil; 2) in the three HSSF-CWs: sandy soil.</p> <p>Two VSSF-CWs: 1 m² each.</p> <p>Substrate (from upper to lower): 20 cm layer of red soil; 30 cm layer of volcanic rock or zeolite; 10 cm layer of gravel.</p> <p>Plant initial density: 15 plants m⁻².</p> <p>HRT: 30 h.</p>	Hybrid <i>pennisetum</i>
Matamoros et al. (2009a)	Full-scale and Pilot-scale	Caffeine, Carbamazepine, Diclofenac, Furosemide, Ibuprofen, Ketoprofen, Naproxen, Salicylic acid	Household wastewater from sparsely populated regions in the eastern part of Jutland peninsula of Denmark	Settling tank	HSSF-CW, VSSF-CW	<p>Five HSSF-CWs' surface areas: 500 m² (180 inhabitants); 470 m² (80 inhabitants); 940 m² (220 inhabitants); 1800 m² (213 inhabitants); 4000 m² (280 inhabitants).</p> <p>Four VSSF-CWs' surface areas: 16 m² (4 inhabitants); 15 m² (2 inhabitants); 15 m² (variable inhabitants); 15 m² (4 inhabitants).</p>	n.a.
Matamoros et al. (2008a)	Mesocosm-scale	Carbamazepine, Clofibric acid, Ibuprofen	Synthetic urban wastewater (two organic carbon sources: One was starch; the other was glucose)	–	HSSF-CW	<p>Container: 0.93 m long, 0.59 m wide and 0.52 m deep.</p> <p>Substrate (gravel): 35 cm deep; initial porosity was 40%; D₆₀ = 3.5 mm; C_u = 1.7.</p> <p>Water depth: 30 cm.</p> <p>Operating mode: In batch.</p>	<i>Phragmites australis</i>
Matamoros et al. (2007)	Pilot-scale	Caffeine, Carbamazepine, Diclofenac, Ibuprofen, Naproxen, Salicylic acid	Urban wastewater from vicinity of Århus, Denmark (loading rates: 13, 30, 70, 160 mm d ⁻¹)	Three chamber settling tank	VSSF-CW	<p>Surface area: 5 m².</p> <p>Bottom gravel layer: 8–16 mm (size); 0.2 m deep.</p> <p>Top gravel layer: 0–4 mm (size); 0.8 m deep; D₁₀ = 0.55 mm; D₆₀ = 3.1 mm.</p> <p>Water distribution: Four 40 mm perforated pipes.</p>	<i>Phragmites australis</i>
Matamoros and Bayona (2006) Matamoros et al. (2005)	Pilot-scale	Matamoros and Bayona (2006): Caffeine, Diclofenac, Ibuprofen, Ketoprofen, Naproxen, Salicylic acid Matamoros et al. (2005): Carbamazepine, Clofibric acid, Ibuprofen	Urban wastewater from a housing development in Barcelona, Spain (200 inhabitants, 36 mm d ⁻¹)	Screen and Imhoff settling tank	HSSF-CW	<p>Two parallel CW beds for comparison: 1) Water depth was 0.5 m, aspect ratio was 2:1, slope was 1%; 2) water depth was 0.3 m, aspect ratio was 2.5:1, slope was 2.5%.</p> <p>Substrate (gravel): D₆₀ = 3.5 mm; C_u = 1.7; porosity was 40%; depth was 5 cm above the water surface.</p> <p>Surface area for each bed: 54–56 m².</p> <p>Plant initial density: 3 plants m⁻².</p>	<i>Phragmites australis</i>
Ranieri et al. (2011)	Pilot-scale	Paracetamol	Wastewater near Lecce, Italy	–	HSSF-CW	<p>Three HSSF-CWs: <i>Phragmites</i> bed, <i>Typha</i> bed, and unplanted bed (3 m wide, 5 m long, 9.4 m³ each).</p> <p>Water depth: 0.6 m–0.65 m.</p> <p>Substrate (upper to lower): 0.1 m of soil layer; 0.2 m of stones layer; 0.30–0.35 m of gravel layer.</p> <p>Side banks: 45° inclination.</p>	<i>Phragmites australis</i> , <i>Typha latifolia</i>

(continued on next page)

Table 1 (continued)

References	Size	Target pharmaceuticals	Influent water	Preliminary/primary treatment	Types of CW systems	Configuration and hydraulic conditions	Plants
Reyes-Contreras et al. (2011)	Pilot-scale	Caffeine, Carbamazepine, Ibuprofen, Ketoprofen, Naproxen, Salicylic acid, Triclosan	Wastewater from a municipal wastewater plant in Santiago de Compostela, Galicia, Spain (17–20 m ³ d ^{−1})	Upflow anaerobic sludge blanket (UASB)	Hybrid SF-CW and HSSF-CW in series	Bottom slope: 1%. Bottom liner: Bentonite liner (including three layers: an upper geo-textile, a lower geo-textile, and sodic powdered bentonite). Effluent discharge: Lagoon. Surface area: 75 m ² each. Plant density: 2 plants m ^{−2} . Substrate (gravel): 6–8 mm (size); initial porosity was 0.45; 0.3 m deep for the SF-CW and 0.5 m deep for the HSSF-CW. Water depth: 0.5 m. HRT: 55 h.	<i>Juncus effusus</i>
Xian et al. (2010)	Microcosm-scale	Sulfadiazine, Sulfamethazine, Sulfamethoxazole	Swine wastewater from a concentrated swine feeding plant located in Nanjing, China	–	SF-CW	Container: 0.5 m long, 0.4 m wide and 0.4 m deep. Working depth: 0.3 m. Capacity volume: 60 L. Foam plate for macrophytes floating: 0.5 m long, 0.4 m wide and 0.015 m thick, with 16 rounded holes (4 × 4, 2 cm diameter). Eight treatment systems (with replications): Two Dryan beds, two Waseyutaka beds, two Tachimasari beds, and two unplanted beds.	Ryegrass (<i>Lolium</i>); Dryan, Waseyutaka, Tachimasari
Zhang et al. (2012a) Zhang et al. (2012b) Zhang et al. (2011)	Mesocosm-scale	Zhang et al. (2012a, 2012b): Caffeine, Carbamazepine, Clofibric acid, Diclofenac, Ibuprofen, Ketoprofen, Naproxen, Salicylic acid Zhang et al. (2011): Carbamazepine, Diclofenac, Ibuprofen, Naproxen	Synthetic urban wastewater in Singapore	–	HSSF-CW	Container: 1.2 m long, 0.6 m wide and 0.6 m deep. Gravel depth: 30 cm. Water depth: 25 cm. HRT: 2 d or 4 d. Plants initial density: 14 plants m ^{−2} .	<i>Typha angustifolia</i>

Notes: ^a D₆₀: the diameter at which 10% of material can pass through sieve. ^b D₁₀: the diameter at which 10% of material can pass through sieve. ^c C_u: D₆₀/D₁₀, uniformity coefficient. ^d – : no existence. ^e n.a.: not available.

The pharmaceuticals that are hardly removed by constructed wetlands (average removal efficiency < 20%) include ampicillin, erythromycin and lincomycin.

In Fig. 3, the removal efficiencies of different types of constructed wetland systems for the elimination of pharmaceuticals are compared. The VSSF-CW appears to be more efficient and reliable for the elimination of diclofenac, ibuprofen, naproxen, salicylic acid and caffeine than the CWs with other configurations. It can be attributed to their less sensitivity to overloading conditions, shorter hydraulic retention time (HRT) and better oxygenation in unsaturated flow (Matamoros et al., 2007; Matamoros et al., 2009a). However, only a very small number of studies have been conducted on VSSF-CW for the treatment of pharmaceutical contaminants. Thus the superiority of VSSF-CW for pharmaceutical removal over other types of constructed wetlands is still inconclusive.

The constructed wetland investigated most often is the HSSF-CW which has been applied separately or associated in hybrid CW system (together with lagoons, ponds, SF-CWs or other HSSF-CWs). As shown in Fig. 3, in comparison with the SF-CW, the HSSF-CW is more efficient for the removal of ketoprofen, naproxen, salicylic acid, doxycycline, sulfadimethoxine, trimethoprim, caffeine, monensin, narasin and salinomycin. Moreover, the HSSF-CW is comparably efficient for the removal of diclofenac, clarithromycin, sulfamethoxazole and carbamazepine, whereas less efficient for the removal of ibuprofen and amoxicillin. In addition, compared with the HSSF-CW for separate application, the hybrid CW system provides better removal efficiencies for acetaminophen, diclofenac, ibuprofen, naproxen and sulfamethoxazole, while lower removal efficiencies for ketoprofen, salicylic acid, carbamazepine and caffeine.

In summer, high temperature and strong sunlight irradiation were found to enhance the activities of plants and microorganisms in constructed wetlands, resulting in increased elimination of diclofenac, ibuprofen, ketoprofen, naproxen, salicylic acid, triclosan, carbamazepine and caffeine. The mean removal efficiencies of these pharmaceuticals were 23%, 53%, 30%, 61%, 82%, 48%, 25% and 90% during summer, in comparison to those of 20%, 38%, 22%, 39%, 56%, 7%, 16% and 53% correspondingly during winter (calculated from Table 2).

Hijosa-Valsero et al. (2010a) found that their most target pharmaceuticals, except for caffeine, ibuprofen and naproxen, were remarkably eliminated during the first stage regardless of the system design (a full-scale hybrid facultative pond, SF-CW and HSSF-CW system). Hussain et al. (2012) observed that the removal efficiencies of their target pharmaceuticals (monensin, salinomycin and narasin) in a mesocosm SF-CW system were significantly affected by the influent concentration levels. Matamoros and Bayona (2006) calculated the zero- or first-order areal rate constants for caffeine, ibuprofen and naproxen in a pilot-scale HSSF-CW system. They noted that the first-order kinetics fitted well with the decay of caffeine and ibuprofen. Zhang et al. (2012a) evaluated the first-order rate constants for caffeine, carbamazepine, clofibric acid, diclofenac, ibuprofen, ketoprofen, naproxen and salicylic acid in a mesocosm HSSF-CW system. They observed that the removal of caffeine, clofibric acid and ketoprofen followed the first-order decay kinetics. As stated above, within a certain period of residence time, the removal performance of certain pharmaceuticals in constructed wetlands would be related to the influent concentrations, resulting in variable removal efficiencies under different concentration levels.

Ávila et al. (2013) and Zhang et al. (2012b) observed the significant enhancement of the elimination of pharmaceuticals when feeding in batch mode due to the higher redox status caused by the alternating cycles of saturation and unsaturation. However, Hijosa-Valsero et al. (2011b) noted very little difference when using a batch flow or a continuous flow strategy. In addition, the hydraulic loading rate (HLR) or the hydraulic retention time (HRT) was suggested as another important hydraulic parameter influencing the removal efficiencies of pharmaceuticals in constructed wetlands. Ranieri et al. (2011) observed that the removal efficiency of paracetamol in a pilot-scale HSSF-CW

system decreased as the HLR was increased. Zhang et al. (2012a) found that the removal efficiencies of all the target pharmaceuticals in a mesocosm HSSF-CW system were linearly proportional to the HRT. However, the difference was not obvious when the HRT was long enough for the treatment of pharmaceutical contaminants (Zhang et al., 2011).

2.3. Constructed wetlands as a polishing treatment for pharmaceutical removal

Constructed wetlands applied as a wastewater polishing treatment system to remove pharmaceutical contaminants from wastewater have been investigated in Denmark, Korea, Portugal, Sweden, Spain, UK and USA. In comparison to the publications on the application of constructed wetlands as an alternative secondary wastewater treatment system for the removal of pharmaceuticals, the number of the research studies on this application is relatively low. The design parameters of the reported constructed wetlands are summarized in Table 3. The removal efficiencies of the investigated pharmaceuticals in different types of constructed wetland systems are listed in Table 4.

2.3.1. Design parameters of constructed wetlands

As reported in Table 3, the size of the investigated constructed wetlands involved microcosm-scale (surface area < 0.5 m²), pilot-scale (surface area in the range of 5 to 100 m²) and full-scale (surface area > 100 m²), of which the full-scale constructed wetlands attracted the most attention. The wastewater fed in the constructed wetlands included the secondary or tertiary effluent water from urban or rural WWTPs and the water from the rivers which received the effluent discharge of WWTPs. The target pharmaceutical contaminants in wastewater mainly covered analgesic/anti-inflammatory drugs, antiallergic drugs, antibiotics, antidiabetics, antidiarrhetics, antifungals, antihypertensives, anti-senile dementia drugs, barbiturates, beta-agonists, beta-blockers, diuretics, hormone inhibitors, lipid regulators, psychiatric drugs, receptor antagonists, stimulants/psychoactive drugs and veterinary drugs. Among these pharmaceuticals, diclofenac, ibuprofen, ketoprofen, naproxen, sulfamethoxazole, triclosan, atenolol, clofibric acid, carbamazepine and caffeine were the commonly investigated pharmaceuticals.

The constructed wetlands selected for wastewater polishing treatment (Table 3) included SF-CWs, HSSF-CWs, VSSF-CWs and hybrid CWs, of which the most popular wetlands were the SF-CWs and the hybrid SF-CWs. The SF-CWs reported by Llorens et al. (2009); Matamoros et al. (2012a); Matamoros et al. (2008b); and Zarate et al. (2012) were designed with surface area of 0.2 to 100 ha. and water depth of 0.05 to 2 m. The target wastewater was retained in these SF-CWs for 3 to 30 days and was finally discharged into the surrounding lake or river. In the hybrid SF-CW system used by Breitholtz et al. (2012); Gross et al. (2004); Lee et al. (2011); and Park et al. (2009), two or more stages of wetland basins were laid out in parallel or in series covering a planar area of 0.36–130 ha. with water depth in the range of 0.1 to 1 m. The wastewater was typically retained in the system for 6 h to 14 days and was finally discharged into the surrounding lake, river or sea. Moreover, SF-CWs could also include ponds to form a hybrid system for wastewater polishing treatment. Matamoros and Salvadó (2012) conducted a study on such kind of hybrid system which consisted of two parallel ponds (2 ha. area and 1 m water depth for each) followed by three parallel deep SF-CWs (0.8 ha. area and 0.5 m water depth for each) and a large shallow SF-CW (4.5 ha. area and 0.2 m water depth). The wastewater was retained in the ponds and the SF-CWs (including both the deep and shallow SF-CWs) for 4 days and 8.5 days, respectively, and was finally pumped to an 18 ha. artificial pond in order to maintain the flooding of the marshlands.

For the HSSF-CWs, Dordio et al. (2010); Dordio et al. (2009a); and Verlicchi et al. (2013) evaluated the performance of HSSF-CWs for the removal of pharmaceuticals from the secondary effluent of

Table 2

Removal efficiencies of pharmaceuticals in constructed wetlands applied as an alternative secondary wastewater treatment system.

Pharmaceutical compounds	Removal efficiencies (%)				
	SF-CW	HSSF-CW	VSSF-CW	Hybrid CW system	Conventional WWTPs
<i>Analgesic/anti-inflammatory</i>					
Acetaminophen (paracetamol)		47 to >99 (14)		>99(19); >95 (20)	>90 (39); 98 to >99 (40); 70–90 (41); 96 (43); 72–97 (44); >99 (46)
Diclofenac	20–40 (winter, 1, 2, 3); 0–50 (summer, 1, 2, 3)	10–15 (winter, 1, 2, 3); 0–35 (summer, 1, 2, 3); 21 (7); 0–11 (0.5 m depth, 8); 0–45 (0.3 m depth, 8); 41–44 (continuous, planted, 9, 10); 48–55 (continuous, planted, 11); 24–32 (continuous, unplanted, 9); 41–47 (continuous, unplanted, 11); 49–55 (batch, planted, 10)	73 (unsaturated flow 16); 53 (saturated flow 16)	32–70 (20); 0–22 (winter, 21); 0–71 (summer, 21); 78–87 (22)	17 (24, 25); 69 (27); 22 (29); 7–63 (30); 0–70 (31); 33 (35); 49 (38); 17–33 (41); 39–75 (42); 35 (43); 0–80 (44); 31 (46); 42 (47)
Ibuprofen	45–75 (winter, 1, 2, 3); 55–95 (summer, 1, 2, 3)	25–40 (winter, 1, 2, 3); 5–55 (summer, 1, 2, 3); 65 (7); 17–52 (0.5 m depth, 8); 48 (0.5 m depth, 13); 62–80 (0.3 m depth, 8); 81 (0.3 m depth, 13); 68–72 (continuous, planted, 9, 10); 71–80 (continuous, planted, 11); 52–61 (continuous, unplanted, 9); 57–60 (continuous, unplanted, 11); 72–83 (batch, planted, 10); 52 (12)	99 (unsaturated flow 16); 55 (saturated flow 16); 89 (7)	>99(19); 52–85 (20); 0–47 (winter, 21); 35–99 (summer, 21); 42–89 (22); 98–99 (23); 3 (winter)–42 (summer) (48)	60–70 (26); 90 (22, 27, 28); 96 (29, 35); 99 (30); 87 (38); 87–93 (41); 100 (42); 88(43); 56–85 (44); 80–87 (45); 94 (46); 98 (47)
Ketoprofen	35–50 (winter, 1, 2, 3)	10–20 (winter, 1, 2, 3); 90 (7); n.r. ^a (0.5 m depth, 8); 0–69 (0.3 m depth, 8); 91–96 (continuous, planted, 9); 91–92 (continuous, planted, 10); 90–94 (continuous, unplanted, 9); 94–95 (planted, batch, 10)		4–27 (winter, 21); 0–37 (summer, 21); 77–81 (22); 5 (winter)–42 (summer) (48)	23 (25); 30 (28); 65(29); 68 (38); 70–84 (41); 83–89 (42); 72–97 (44); 52–72 (45); 85 (46); 55 (47)
Naproxen	40–65 (winter, 1, 2, 3); 25–75 (summer, 1, 2, 3)	25–45 (winter, 1, 2, 3) 55–85 (summer, 1, 2, 3); 45 (7); 0–47 (0.5 m depth, 8); 80–90 (0.3 m depth, 8); 81–93 (continuous, planted, 9, 10); 83–91 (continuous, planted, 11); 52–78 (continuous, unplanted, 9); 50–52(continuous, unplanted, 11) 82–91(batch, planted, 10)	89 (unsaturated flow 16); 62 (saturated flow 16); 92 (7)	98(19); 0–41 (winter, 21); 60–95 (summer, 21); 73–82 (22); 99 (23); 30 (winter)–53 (summer) (48)	82 (24, 25); 40–55 (6); 66 (27); 83 (28); 89 (22); 93 (29, 38); 91–95 (42); 67 (43); 72–97 (44); 43–71 (45); 86 (46); 64 (47)

Salicylic acid	35–85 (winter, 1, 2, 3); 85–90 (summer, 1, 2, 3)	50–60 (winter, 1, 2, 3); 85 (summer, 1, 2, 3); 95 (7); 77–97 (0.5 m depth, 8); 92–98 (0.3 m depth, 8); 86–90 (continuous, planted, 9); 88–89 (continuous, planted, 10); 88 (continuous, unplanted, 9); 93–94 (batch, planted, 10)	98 (unsaturated flow 16); 85 (saturated flow 16); 87 (7)	0–97 (winter, 21); 41–89 (summer, 21); 94–97 (22); 53 (winter)–70 (summer) (48)	80 (22); 88 (25); 95 (28); 99 (32, 38); 94 (43); >99 (46)
<i>Antibiotics</i>					
Amoxicillin	27–45 (4)	6–21 (4)			35 (4);
Ampicillin	0–32 (4)	n.r. (4)			7 (4); n.r. (44)
Ciprofloxacin HCl			82–85 (17)		
Clarithromycin	11–50 (4)	31–32 (4)			18 (4)
Doxycycline	47–75 (4)	71–79 (4)			61 (4)
Erythromycin	n.r. (4)	0–64 (4)			n.r. (4); 25 (35); – 17 to 50 (40)
Lincomycin	n.r. (4)	n.r. (4)			24 (4); 64–80 (40)
Oxytetracycline HCl			91–95 (17)		
Sulfadiazine	98–99 (5)				20–82 (44)
Sulfadimethoxine	67–99 (4)	99 (4)			53 (4); 20–82 (44)
Sulfamethazine	>99 (5)		68–73 (17)		7–17 (41); 20–82 (44)
Sulfamethoxazole	59–80 (4); 89–92 (5)	73–87 (4)		91 (19)	32–66 (30); 24 (35); 60 (4); 66 (38); 0–88 (44); 83 (46)
Sulfapyridine				76 (19)	95 (28)
Triclosan				7 (winter)–48 (summer) (48)	58 (29); 91–93 (42)
Trimethoprim	65–96 (4)	95–99 (4)			14 (4); 49 (29); 69 (35); 74 (38); 67–80 (40); 67–89 (41); 22–56 (44); 70 (46)
<i>Beta-blockers</i>					
Atenolol				93 (19)	50–80 (29); 84 (35); 73–79 (36); 58 (37); 83–87 (41); 71–77 (44)
Metoprolol				92 (19)	83 (27); 30–65 (29); 65 (35); 29–31 (36); 17 (37); 3–67 (44)
Nadolol				77 (19)	
Sotalol				30 (19)	48 (35); 26–27 (36); 66 (37); 58–76 (44)
<i>Diuretics</i>					
Furosemide		71 (7)			77 (46)

(continued on next page)

Table 2 (continued)

Pharmaceutical compounds	Removal efficiencies (%)				
	SF-CW	HSSF-CW	VSSF-CW	Hybrid CW system	Conventional WWTPs
<i>Lipid regulators</i>					
Clofibric acid		34–39 (continuous, planted, 9, 10); 33–34 (continuous, unplanted, 9); 33–34 (batch, planted, 10); n.r. (0.5 m depth, 13); n.r. (0.3 m depth, 13)			51 (27); 52 (35); 49 (38); 0–81 (44); 50 (47)
Gemfibrozil				61 (19)	69 (27); 75 (29); 65 (38); 56 (43); 0–81 (44)
<i>Psychiatric drugs</i>					
Carbamazepine	0–35 (winter, 1, 2, 3); 10–50 (summer, 1, 2, 3)	20–25 (winter, 1, 2, 3); 0–40 (summer, 1, 2, 3); 38 (7); 27–28 (continuous, planted, 9, 10, 11); 24–26 (continuous, unplanted, 9); 28–29 (continuous, unplanted, 11); 27–28 (batch, planted, 10); 5 (12); 26 (0.5 m depth, 13); 16 (0.3 m depth, 13)	26 (unsaturated flow 16); 20 (saturated flow 16)	0–9 (winter, 21); 0–58 (summer, 21); 5 (winter)–18 (summer) (48)	7 (27); 8 (24, 25, 33); 15 (22); 30 (29, 38); —43 to 14 (30); 0–30 (31); —13 (43); 0–40 (44); 7–11 (45); 13 (46)
<i>Stimulants/psychoactive drugs</i>					
Caffeine	25–60 (winter, 1, 2, 3); 80–99 (summer, 1, 2, 3)	60–65 (winter, 1, 2, 3); 99 (summer, 1, 2, 3); 97 (7); 85–94 (0.5 m depth, 8); 94–99 (3 m depth, 8); 84–90 (continuous, planted, 9, 10); 82–84 (continuous, unplanted, 9); 86–93 (batch, planted, 10)	99 (unsaturated flow 16); 82 (saturated flow 16); 99 (7)	>99 (19); 14–84 (winter, 21); 98–99 (summer, 21); 95–96 (22); 55 (summer)–60 (winter) (48)	86 (22); 93 (28); 94 (29); 99 (24, 25, 33); >99 (34); 87–93 (40); 83–90 (41); 89 (43); 85–100 (44); 44–75 (45)
Cotinine				99 (19)	
<i>Veterinary drugs</i>					
Enrofloxacin			94(18)		
Monensin	27–34 (6)	37–43 (15)			
Narasin	29–36 (6)	42–57 (15)			
Salinomycin	30–32 (6)	41–56 (15)			
Tetracycline			98(18)		66–90 (44)

Notes: ^a n.r.: not removed.

1: Hijosa-Valsero et al. (2010b); 2: Hijosa-Valsero et al. (2011c); 3: Reyes-Contreras et al. (2012); 4: Hijosa-Valsero et al. (2011a); 5: Xian et al. (2010); 6: Hussain et al. (2012); 7: Matamoros et al. (2009a); 8: Matamoros and Bayona (2006); 9: Zhang et al. (2012a); 10: Zhang et al. (2012b); 11: Zhang et al. (2011); 12: Matamoros et al. (2008a); 13: Matamoros et al. (2005); 14: Ranieri et al. (2011); 15: Hussain et al. (2011); 16: Matamoros et al. (2007); 17: Liu et al. (2013a); 18: Carvalho et al. (2013); 19: Conkle et al. (2008); 20: Ávila et al. (2013); 21: Hijosa-Valsero et al. (2011b); 22: Hijosa-Valsero et al. (2010a); 23: Ávila et al. (2010); 24: Heberer (2002a); 25: Heberer (2002b); 26: Carballa et al. (2004); 27: Ternes (1998); 28: Camacho-Muñoz et al. (2012); 29: Bendz et al. (2005); 30: Clara et al. (2005); 31: Zhang et al. (2008); 32: Ternes et al. (2004); 33: Heberer et al. (2002); 34: Ternes et al. (2001); 35: Ternes et al. (2007); 36: Maurer et al. (2007); 37: Vieno et al. (2007); 38: Miège et al. (2009); 39: Matsuo et al. (2011); 40: Li et al. (2011); 41: Tewari et al. (2013); 42: Samaras et al. (2013); 43: Kosma et al. (2010); 44: Lin et al. (2009); 45: Santos et al. (2009); 46: Kasprzyk-Hordern et al. (2009); 47: Kimura et al. (2007); 48: Reyes-Contreras et al. (2011).

Fig. 2. Comparison between the mean removal efficiencies of pharmaceuticals in CWs and conventional WWTPs.

WWTPs. Their investigated HSSF-CWs were designed with a surface area of 0.3 m² and 28 m², respectively, and with a water depth of 0.3 m and 2.2 m, respectively. Regarding the VSSF-CW, Reif et al. (2011) studied a pilot-scale VSSF-CW in batch operating mode for purifying the wastewater effluent from a WWTP in USA. In their research work, they designed the substrate layers of the wetland from top to bottom as: 0.15 m of filter grade sand, 0.15 m of 10 mm pea gravel, 0.05 m of 20 mm gravel and 0.6 m of 40–50 mm gravel.

In all the reported constructed wetlands, there were various types of vegetations, among which the most popular plants were *Typha* spp. and *Phragmites* spp.

2.3.2. Removal performance of pharmaceuticals in constructed wetlands

As shown in Table 4, the data on the removal efficiencies of the investigated pharmaceuticals for each kind of constructed wetland are very limited. Thus the comparison among the different types of constructed wetlands is not feasible to date. For the commonly investigated pharmaceuticals, except for the low or inconsistent removal efficiencies obtained by Matamoros et al. (2012a); Breitholtz et al. (2012); and Verlicchi et al. (2013), the readily removed pharmaceuticals by constructed wetlands (mean removal efficiency > 70%) are diclofenac, ibuprofen, ketoprofen, triclosan and atenolol. The moderately removed pharmaceuticals by constructed wetlands (mean removal efficiency

Fig. 3. Mean removal efficiencies of pharmaceuticals in different CW systems.

between 50% and 70%) include naproxen and caffeine; while the pharmaceuticals with low removal efficiencies in constructed wetlands (mean removal efficiency between 20% and 50%) are sulfamethoxazole, clofibric acid and carbamazepine. Breitholtz et al. (2012) investigated four full-scale hybrid SF-CWs systems with different design configurations to remove pharmaceutical compounds from four sewage treatment plants. They detected that some pharmaceuticals were at higher levels in effluent water compared to that in the influent water (shown as negative removal efficiencies in Table 4). This phenomenon could partly be attributed to the numerical variations caused by the occurrence of pharmaceuticals close to the detection limit and the daily concentration fluctuations of pharmaceuticals induced by intermittent usage. In addition, it could also be possible because many pharmaceuticals were metabolized as glucuronides or other conjugated metabolites and then after a period of time were converted to the parent compounds by enzymatic processes.

Dordio et al. (2009a, 2010) found that the removal kinetics of atenolol, carbamazepine, clofibric acid and ibuprofen was a fast initial step in which more than half of the initial pharmaceuticals were removed within the first 6 h and followed by a first-order kinetics during the next period of 6–96 h. Matamoros et al. (2008b) observed that higher removal efficiencies of their target pharmaceuticals were obtained during the first part of system compared to the latter part of system, showing a spatial trend of the removal efficiencies. This phenomenon demonstrated that the first-order removal kinetics was appropriate for the removal of carbamazepine, diclofenac, flunixin, ibuprofen and ketoprofen. As stated above, within a certain period of residence time, the removal efficiencies of certain pharmaceuticals in constructed wetlands would be related to their influent concentrations.

3. Removal mechanisms related to the substrate, plants and microbes in constructed wetlands

3.1. Substrate

Substrate (also known as support matrix) is an important component in constructed wetlands, especially in subsurface flow constructed wetlands. The substrate in constructed wetlands not only provides support for the growth of plants and microorganisms, but also interacts directly with contaminants through sorption processes. Sorption of pollutants onto the surface of substrate involves different mechanisms such as hydrophobic partitioning, van der Waals interaction, electrostatic interaction, ion exchange, and surface complexation (Dordio and Carvalho, 2013; Haberl et al., 2003; Pei et al., 2012; Reddy and DeLaune, 2008; Tolls, 2001). Non-polar organic pollutants can be preferentially adsorbed to the substrate materials that are especially rich in organic matter such as soil, compost and agricultural wastes via hydrophobic process. Polar or ionic pollutants are dominantly adsorbed to the substrate materials (e.g. some kinds of clay) by electrostatic interactions or ionic exchange.

According to Table 1 and Table 3, the most frequently used substrate for pharmaceutical removal in constructed wetlands is gravel which did not show any negative effects on the performance of constructed wetlands. The gravel substrate was found efficient for sorption removal of the pharmaceuticals which are refractory to biodegradation but with relatively high hydrophobicity, for example, carbamazepine. However, at present, very few data are available on comprehensive understanding of the sorption performance of gravel and the associated mechanisms for the removal of pharmaceuticals from wastewater using constructed wetlands.

It has been reported in laboratory batch experiments that light expanded clay aggregate (LECA) is a good sorbent for the acidic pharmaceutical compounds such as clofibric acid and ibuprofen as well as the neutral pharmaceutical compounds such as carbamazepine (A.V. Dordio et al., 2009b). Dordio et al. (2007) compared three different substrate materials including LECA, expanded perlite, and sand for the removal of clofibric acid from water in laboratory. Their research results

indicated that LECA exhibited a high sorption capacity for the removal of clofibric acid, while the expanded perlite only had a very limited sorption capacity and the sand did not show any sorption capacity at all. Considering the alkaline nature of LECA, electrostatic interactions in the case of the acidic pharmaceuticals have been hypothesized as being responsible for the affinities of these compounds towards LECA's surface. For the neutral compounds, van der Waals interactions may be more relevant. Dordio et al. (2009a) found that LECA also showed strong sorption for atenolol which was alkaline and positively charged. Electrostatic interactions cannot explain this phenomenon, but perhaps ion exchange may be responsible to some extent for the removal of atenolol by LECA.

Soil is another kind of popular substrate in constructed wetlands. Hussain et al. (2012) undertook some laboratory batch experiments to investigate the removal efficiencies of three antibiotics (monensin, salinomycin, and narasin) in two SF-CWs with different soil substrates. Higher removal efficiency was observed for the sandy soil when compared with the sandy loam soil. They explained that the higher relative hydraulic conductivity of the sandy soil could facilitate water movement within the soil profile resulting in a greater opportunity of soil-to-contaminants interactions. Whereas, the sandy clay loam soil which contained higher organic matter content showed a lower infiltration rate in the soil medium. However, their experimental results didn't indicate that the sorptive capability of the sandy soil was better than that of the sandy clay loam soil. Lertpaitoonpan et al. (2009) demonstrated that higher coefficient values (K_d) could be found for the soils with higher organic carbon during the batch sorption process of sulfamethazine onto five soils (organic carbon content ranged from 0.1% to 3.8%).

Recently, certain biosorbents such as rice husk, pine bark, and granulated cork have been considered as interesting alternatives to the common substrate materials in constructed wetlands due to their low cost, economical value of reuse, and easy disposal by incineration. A.V. Dordio et al., 2011b evaluated the sorption capacity of granulated cork to remove ibuprofen, carbamazepine and clofibric acid from water. Their laboratory experiments showed that the granulated cork presented good sorption qualities and the three pharmaceutical compounds were removed in the order of efficiency as: ibuprofen > carbamazepine > clofibric acid. In comparison with LECA, granulated cork had a much larger specific sorption capacity for all the target compounds.

Sorption kinetics and isotherms have been studied to describe the sorption process of pharmaceutical compounds to certain kinds of sorbent materials. Dordio et al. (2009a, 2010), A.V. Dordio et al., (2011b) observed that within the initial stage of 6 h, more than half of the initial atenolol, carbamazepine, clofibric acid and ibuprofen could be removed via adsorption. Their laboratory experiment results indicated that the Freundlich equation modeled the experimental data better than the Langmuir equation. It reflected the significant role of the heterogeneity of the sorbent material as well as the possible lateral interactions between the sorbed molecules. Xu et al. (2009) also found that the Freundlich equation could well describe the adsorption process of their target pharmaceuticals in agricultural soils. The degradation of the target pharmaceuticals followed first-order exponential decay kinetics with the adsorption affinity order as follows: triclosan > clofibric acid > naproxen > diclofenac > ibuprofen. Moreover, Yu et al. (2013) confirmed that the Freundlich equation and the first order decay kinetics fitted well the adsorption process of carbamazepine, gemfibrozil and triclosan onto three different sorbents such as Palmdale sand, Imperial Valley clay and Washington Palouse loam.

The pH of substrate materials could play an important role in the sorption capacity of substrate for pharmaceutical removal. Vasudevan et al. (2009) demonstrated that the overall sorption efficiency of ciprofloxacin could be influenced by a difference in soil pH. Hussain and Prasher (2011) observed an inverse relationship between the substrate pH and the sorption of three antibiotics (monensin, salinomycin, and narasin). Sassman and Lee (2007) also found an inverse correlation

between the soil pH and the sorption coefficient of monensin and lasalocid. Lertpaitoonpan et al. (2009) explained that the pH of soil inversely influenced the sorption process of sulfamethazine due to the different ionization states of sulfamethazine under different pH conditions. At pH less than 7.4, hydrophobic partitioning was possibly responsible for the removal of the non-ionized form of sulfamethazine. At pH above 7.4, the decrease in sorption of sulfamethazine was probably due to the predominance of the anionic form of sulfamethazine. Similar trend was also found for sulfonamides that the conversion of the neutral/cationic form of sulfonamides to the anionic form of sulfonamides above pH 7.5 led to a lower sorption to soils (Kurwadkar et al., 2007).

Competitive sorption phenomenon might take place if multiple pharmaceutical compounds and other wastewater pollutants are present in the water at the same time (Conkle et al., 2010; A.V. Dordio et al., 2009b). The sorption capacity of one pharmaceutical compound may be decreased by another pharmaceutical compound or/and other contaminants due to competition for preferred binding sites on the solid matrices in constructed wetlands. Therefore, this competition effect may be of concern in constructed wetland systems which are loaded with a wide range of pharmaceutical compounds.

3.2. Plants

Plants in constructed wetlands play a significant role in direct uptake of many organic pollutants in wastewater. In the cell membranes of plant roots, there are no specific transporters for the xenobiotic organic compounds like pharmaceuticals to move into the plants tissues, but the uptake and translocation of these compounds within plants can be simply driven by diffusion (Dietz and Schnoor, 2001; Dordio et al., 2011a; Dordio and Carvalho, 2013).

The diffusion process of pharmaceuticals into plant tissues is dependent on the physico-chemical characteristics of the compounds including the hydrophobicity (as expressed by logarithm octanol/water partition coefficient $\log K_{ow}$), water solubility and concentration (Dordio and Carvalho, 2013; Stottmeister et al., 2003). In general, the pharmaceutical compounds characterized by a $\log K_{ow}$ in a moderate range of 0.5 to 3.5 are lipophilic enough to move through the lipid bilayer of plant cell membranes and also water soluble enough to travel into the cell fluids of plants (Dietz and Schnoor, 2001; Dordio and Carvalho, 2013; Schröder and Collins, 2002; Stottmeister et al., 2003). For instance, carbamazepine with a $\log K_{ow}$ of 2.45 has been reported to be readily taken up by the roots of *Typha* spp. and then transported from roots to stems and leaves, ultimately showing the largest extent of accumulation in leaves (A.V. Dordio et al., 2011a). In contrast to carbamazepine, for diclofenac whose $\log K_{ow}$ is 4.51 higher than 3.5, Zhang et al. (2012c) demonstrated that the compound had limited ability to be taken up and translocated within the roots and shoots of *Scirpus validus*.

For the nonionizable, polar, highly water soluble organic compounds, Dettenmaier et al. (2009) found that caffeine could be taken up by plant roots and translocated to shoots, which is in agreement with the findings of Matamoros et al. (2012b) and D.Q. Zhang et al., 2013. Liu et al. (2013b) also observed a similar phenomenon for three antibiotics (ciprofloxacin HCl, oxytetracycline HCl and sulfamethazine) which have the $\log K_{ow}$ values below 0.5. The authors suggested that such highly water soluble organic compounds were most likely to be driven by the transpiration water stream in the plant uptake and the translocation within plant tissues. Further, they also found the positive correlation between the antibiotics concentrations and the accumulation levels of antibiotics inside the plants.

After being taken up into plant tissues, the internal pharmaceutical compounds might be degraded via the metabolism processes (phytodegradation). The metabolism processes might include a series of biochemical reactions such as transformation of parent organic pollutants, conjugation of metabolites with macromolecules, and incorporation of conjugated products into plant cell walls and vacuoles (Dordio and Carvalho, 2013; Reinhold et al., 2010). A.V. Dordio et al., 2011a

detected a metabolite (10, 11-dihydro-10, 11-epoxycarbamazepine) of carbamazepine in the leaf tissues of *Typha* spp. indicating the occurrence of carbamazepine metabolism inside the plant tissues. Liu et al. (2013b) found the conversion of ciprofloxacin HCl and oxytetracycline HCl to their epimers such as tetracycline, chlortetracycline, enrofloxacin and ofloxacin in plants.

Plants in constructed wetlands play another important role in stimulating the development and activities of microbial populations which are supported by the rhizodeposition products (exudates, mucigels, dead cell material, etc.), causing various biological processes to occur in the rhizosphere (Calheiros et al., 2009; Cronk, 1996; Stottmeister et al., 2003). Matamoros et al. (2012b) found that the predominant removal process of ibuprofen was microbial degradation which was very possibly associated with the biofilms on the surface of plant roots. In addition to the biological processes, certain plant exudates may also function as catalytic agents for the degradation of organic compounds (Dordio and Carvalho, 2013). Most plant species in constructed wetlands are able to release oxygen around their root tips and on young laterals (Stottmeister et al., 2003). The oxygen released in rhizosphere can also promote the oxidative chemical processes of contaminants in wastewater (Sundaravadivel and Vigneswaran, 2001) and favor the development of aerobic microorganisms in the rhizosphere inducing more efficient biodegradation processes (Cronk, 1996; Dordio and Carvalho, 2013). The continuous release of oxygen from the root zones of plants might counterbalance the chemical and biological oxygen consumption in the rhizosphere.

It has been reported that the presence of plants in constructed wetlands played a positive role in the removal of some certain pharmaceuticals such as diclofenac, ibuprofen, ketoprofen, naproxen, salicylic acid, amoxicillin, ampicillin, erythromycin, sulfadiazine, sulfamethazine, sulfamethoxazole, atenolol, clofibrilic acid, carbamazepine and caffeine (Dordio et al., 2010, 2009a; Hijosa-Valsero et al., 2011a, 2011b, 2010b, 2011c; Xian et al., 2010; Matamoros et al., 2012a, 2012; Zhang et al., 2012a; Zhang et al., 2012b, 2011). Several plant species have been reported for use in pharmaceutical wastewater treatment wetlands (Table 5) among which the most popular plants are *Phragmites australis*, *Typha* spp. *Typha angustifolia* and *Typha latifolia*. The experiment results of Hijosa-Valsero et al. (2010b, 2011c) indicated that *P. australis* had a better performance than *T. angustifolia*. However, Dordio et al. (2009a) observed the superiority of *Typha* spp. compared to the *P. australis* due to the higher transpiration rate of *Typha* spp. Zarate et al. (2012) investigated the accumulation of triclosan inside the plant tissues (roots and shoots) and their results showed the species-specific differences among different vegetations (*Pontederia cordata* and *Sagittaria graminea*), indicating the important influences of plant species on the pharmaceutical removal.

Toxicity to plants caused by pharmaceuticals is an important issue when considering the functions of plants for pharmaceutical removal. The toxicity can be evaluated through analyzing the root activity, the relative growth rate (RGR) of plant and the concentrations of photosynthetic pigments such as carotenoid and chlorophyll in plants tissues (Dordio et al., 2011a, A.V. Dordio et al., 2011a, 2009a; Liu et al., 2013b). In addition, the alteration of antioxidant enzyme activities in plant tissues can also serve as an indication of the phytotoxicity caused by pharmaceutical compounds. The antioxidant enzymes like catalase (CAT), superoxide dismutase (SOD), guaiacol peroxidase (GPX) and ascorbate peroxidase (APX) have been reported for the plants which are subjected to pharmaceutical stress (Dordio et al., 2011a, A.V. Dordio et al., 2011a, 2009a; Liu et al., 2013b).

3.3. Microbes

Microbes in constructed wetlands usually play the main role in the processes of transformation and mineralization of nutrients and organic pollutants (Kadlec and Wallace, 2009; Sundaravadivel and Vigneswaran, 2001; Truu et al., 2009; Zhu et al., 2010, 2011, 2013). Biodegradation of organic compounds by microbes in constructed

Table 3

Design parameters of the reported constructed wetlands as a wastewater polishing treatment system for the removal of pharmaceuticals.

References	Size	Target pharmaceuticals	Influent water	Types of CW systems	Configuration and hydraulic conditions	Plants	
Breitholtz et al. (2012)	Full-scale	92 target pharmaceuticals, of which 54 were detected: Alfuzosine, Alprazolam, Amitryptiline, Atenolol, Atorvastatin, Azithromycine, Bezafibrate, Bisoprolol, Buprenorphine, Bupropion, Carbamazepine, Citalopram, Clarithromycine, Clindamycine, Clotrimazole, Codeine, Desloratadine, Diclofenac, etc.	Sewage effluents from four Sewage Treatment Plants (Eskilstuna, Nynäshamn, Oxelösund and Trosa) in the south of Stockholm, Sweden	Hybrid SF-CWs	Eskilstuna (sewage from 84,000 p.e. ^a with flow rate of 48,000 m ³ d ^{−1} , using activated sludge biological treatment)	Layout: Five parallel basins — three parallel basins. Covering area: 28 ha. Mean depth: 1 m. Detention time: 6–7 d. Plant coverage: ca. 20%. Effluent discharge: Eskilstuna River and finally Lake Mälaren.	<i>Ceratophyllum demersum</i> , <i>Elodea</i> spp., <i>Glyceria maxima</i> , <i>Myriophyllum spicatum</i> , <i>Nymphaeaceae</i> , <i>Schoenoplectus lacustris</i> , <i>Typha</i> spp.
					Nynäshamn (sewage from 13,000 p.e. with flow rate of 5500 m ³ d ^{−1} , using sequencing batch reactor (SBR) biological treatment)	Layout: Two inflow basins – two parallel CW basins (used alternatively) – 2.7 ha. overland flow area. Covering area: 28 ha. including the overland flow area. Detention time: 1.5–2 weeks. Effluent discharge: Baltic Sea.	<i>Carex riparia</i> , <i>Carex</i> spp., <i>Ceratophyllum demersum</i> , <i>Elodea</i> spp., <i>Myriophyllum</i> spp., <i>Potamogeton</i> spp., <i>Scirpus sylvaticus</i> , <i>Typha</i> spp.
					Oxelösund (sewage from 12,000 p.e. with flow rate of 4000 m ³ d ^{−1} , using SBR biological treatment)	Layout: One inlet basin – two parallel CW systems (each of which consists of two basins which are used alternatively) – a joint basin. Covering area: 24 ha. Detention time: 6 d. Effluent discharge: Baltic Sea.	<i>Carex</i> spp., <i>Elodea</i> spp., <i>Phragmites australis</i> , <i>Potamogeton</i> spp., <i>Typha</i> spp.
					Trosa (sewage from 3400 p.e. with flow rate of 1620 m ³ d ^{−1} , using activated sludge biological treatment)	Layout: 2 ha. overland flow area – a collecting basin – three serial CW basins. Covering area: 6 ha. Detention time: 8 d. Effluent discharge: Trosa River and finally to the Baltic Sea.	<i>Phragmites</i> spp., <i>Scirpus</i> spp., <i>Typha</i> spp.
Dordio et al. (2010) Dordio et al. (2009a)	Microcosm-scale	Dordio et al. (2010): Carbamazepine, Clofibric acid, Ibuprofen Dordio et al. (2009a): Atenolol	Secondary effluent from a WWTP serving for a small rural community (ca. 400 inhabitants) in Portugal	HSSF-CW	Container: 0.6 m long, 0.5 m wide and 0.4 m deep. Substrate: Light expanded clay aggregates (LECA) with depth of 0.3 m. Water depth: Just below the LECA surface. Plants initial density: 20 plants m ^{−2} . Operating mode: In batch.	Dordio et al. (2010): <i>Typha</i> spp. Droid et al. (2009a): <i>Phragmites</i> spp., <i>Typha</i> spp.	
Gross et al. (2004)	Full-scale	Carbamazepine, Gemfibrozil, Ibuprofen, Ketoprofen, Naproxen	Water from the Santa Ana River in California, USA which is predominant tertiary effluent from up-stream WWTPs	Hybrid SF-CWs	Surface area: 130 ha. Layout: Four subsections which each consisted of inter-connected cells: East Cells (22%), North Cells (26%), South Cells (28%) and West Cells (24%). Flow streams: Inlet flow of the East Cells was split to two separate streams for entering North Cells (40%) and South Cells (60%) respectively and then recombined	<i>Scirpus</i> spp., <i>Typha</i> spp., <i>Polygonum</i> spp., <i>Najas marina</i> , <i>Zannichellia palustris</i> , <i>Lemna</i> spp.	

Lee et al. (2011) Park et al. (2009)	Full-scale	Lee et al. (2011): Atenolol, Caffeine, Carbamazepine, Diclofenac, Glimepiride, Ibuprofen, Naproxen, Sulfamethoxazole Park et al. (2009): Atenolol, Carbamazepine, Diazepam, Diclofenac, Dilantene, Sulfamethoxazole, Triclosan, Naproxen	Wastewater effluent from the Damyang wastewater treatment plant in Korea ($1800 \text{ m}^3 \text{ d}^{-1}$)	Hybrid SF-CWs	and passed through the West Cells. Water depth: 0.6 m–0.76 m. HRT: 100 h. Layout: Two basins in series (Acorus wetland and Typha wetland); 30 m wide, 120 m long and 0.13 m deep. HRT: 6 h.	<i>Acorus</i> spp., <i>Typha</i> spp.
Llorens et al. (2009) Matamoros et al. (2008b)	Full-scale	Llorens et al. (2009): Carbamazepine, Clofibric acid, Diclofenac, Ibuprofen, Ketoprofen, Naproxen Matamoros et al. (2008b): Carbamazepine, Clofibric acid, Diclofenac, Flunixin Ibuprofen, Ketoprofen, Naproxen	Part of secondary effluent from the Granollers urban WWTP in Spain ($100 \text{ m}^3 \text{ d}^{-1}$)	SF-CW	Surface area: 1 ha. (maximum length and width of around 189 m and 53 m respectively). Water depth: 0.3–0.4 m for planted shallow zones; 1.5 m for unplanted deep zones. HRT: 1 month. Hydraulic loading rate (HLR): 1 cm d^{-1} . Effluent discharge: Congost River.	<i>Phragmites australis</i> , <i>Typha latifolia</i>
Matamoros and Salvadó (2012)	Full-scale	Caffeine, Carbamazepine, Diclofenac, Ibuprofen, Ketoprofen, Naproxen, Triclosan	Secondary effluent from the Empuriabrava WWTP in Spain ($3700 \text{ m}^3 \text{ d}^{-1}$, seasonally ranging from $2300 \text{ m}^3 \text{ d}^{-1}$ to $6400 \text{ m}^3 \text{ d}^{-1}$)	Hybrid pond and SF- CW in series	Ponds (two parallel cells): 2 ha. each; 1 m deep; HRT was 4 d. SF-CWs (three parallel deep cells and a large shallow cell in series): The deep cells were 0.8 ha. and 0.5 m deep each; the shallow cell was 4.5 ha. and 0.2 m deep; HRT was 8.5 d. Effluent discharge: Pumped into an 18 ha. artificial pond to maintain the flooding of the marshlands.	<i>Phragmites australis</i> , <i>Typha latifolia</i>
Matamoros et al. (2012a)	Full-scale	Caffeine, Carbamazepine, Diclofenac, Furosemide, Ibuprofen, Ketoprofen, Naproxen, Triclosan	Water from two feeding rivers in Denmark: Aarhus River ($0.96 \text{ m}^3 \text{ s}^{-1}$) and Lyngbygaard River ($1.03 \text{ m}^3 \text{ s}^{-1}$) which were subjected to the discharges of the WWTPs located upstream	SF-CW	Surface area: 100 ha. Water depth: 0.05 m to 2 m. HRT: 3 to 20 d (average 7 d). Effluent discharge: Lake Brabrand.	<i>Nymphaea alba</i> , <i>Schoenoplectus lacustris</i>
Reif et al. (2011)	Pilot-scale	Carbamazepine, Diclofenac, Ibuprofen, Naproxen	Sewage effluents from a membrane reactor (MBR) and an activated sludge (AS) system in UK	VSSF-CW	Feeding mode: CW beds were fed 8 times per day for 10 min at 125 mL min^{-1} . Depth: 1 m;	<i>Phragmites</i> spp.

Table 3 (continued)

References	Size	Target pharmaceuticals	Influent water	Types of CW systems	Configuration and hydraulic conditions	Plants
Verlicchi et al. (2013)	Pilot-scale	73 target pharmaceuticals, of which 55 were detected: Acetaminophen, Codeine, Diclofenac, Ibuprofen, Indomethacin, Ketoprofen, Mefenamic acid, Naproxen, Phenylbutazone, Propyphenazone, Salicylic acid, etc.	Effluent from the secondary clarifier in a large municipal WWTP in the Po Valley, northern Italy ($8 \text{ m}^3 \text{ d}^{-1}$)	HSSF-CW	Substrate (from top to bottom): 0.15 m of filter grade sand; 0.15 m of 10 mm pea gravel; 0.05 m of 20 mm gravel; 0.6 m of 40–50 mm gravel. Length: 28 m; width: 1 m; depth: 0.7 m at the influent and to 1.75 m at the effluent. Substrate: gravel (8–10 mm) with porosity of 33%. HRT: 1 d. Feeding mode: Gravity-fed from a 10-m^3 equalization tank which is 3 m above the ground.	<i>Phragmites australis</i>
Zarate et al. (2012)	Pilot-scale	Triclosan	Effluent from the Pecan Creek WWTP in Denton, Texas, USA	SF-CW	Layout: A continuous channel separated by three land berms encompassing a total area of 0.21 ha. ($46 \text{ m} \times 46 \text{ m}$). Storage volume: 570,000 L. HRT: 4.3 d.	<i>Ceratophyllum demersum</i> , <i>Lemna</i> spp., <i>Paspalum</i> spp., <i>Pontederia cordata</i> , <i>Potamogeton</i> spp., <i>Sagittaria graminea</i> , <i>Typha latifolia</i> ,

Notes: ^a p.e.: people equivalent.

Table 4

Removal efficiencies of pharmaceuticals in constructed wetlands applied as a wastewater polishing treatment system.

Pharmaceutical compounds	SF-CW	HSSF-CW	VSSF-CW	Hybrid CW system
<i>Analgesic/anti-inflammatory</i>				
Acetaminophen		45 (12)		
Buprenorphine				– 2956 to 58 (7)
Codeine		57 (12)		29–75 (7)
Diclofenac	85 (1); 3 (2); 96 (summer, 3); 73 (winter, 3)	5 (12)	78–79 (6)	24–36 (7); 86–98 (8); 38–85 (9); 62 (10)
Ibuprofen	96 (1); 19 (2); 96 (summer, 3); 95 (winter, 3)	82–96 (winter–summer, planted, 4); 74–91 (winter–summer, unplanted, 4); 28 (12)	66–72 (6)	5–88 (7); 79–97 (8); 55 (10); 59 (11)
Indomethacin		45 (12)		
Ketoprofen	98 (1); 99 (summer, 3); 97 (winter, 3)	18 (12)		3–56 (16); 97–99 (8)
Mefenamic acid		20 (12)		
Naproxen	72 (1); 4 (2); 92 (summer, 3); 52 (winter, 3)	36 (12)	39–45 (6)	34–75 (7); 72–96 (8); 71–82 (9); 67 (10)
Phenylbutazone		55 (12)		
Propyphenazone		– 19 (12)		
Orphenadrine				– 19 to 54 (7)
Salicylic acid		7 (12)		
Tramadol				– 12 to 26 (7)
<i>Antiallergic drugs</i>				
Desloratidin				47–72 (7)
Diphenhydramine				46–50 (7)
Fexofenadine				– 26 to 28 (7)
<i>Antibiotics</i>				
Azithromycine		86 (12)		– 350 to 2 (7)
Ciprofloxacin		67 (12)		
Clarithromycine		7 (12)		– 58 to 58 (7)
Clindamycine				– 103 to 13 (7)
Enoxacin		38 (12)		
Erythromycin		– 78 (12)		
Metronidazole		100 (12)		
Nifuroxazide		100 (12)		
Norfloxacin		52 (12)		
Ofloxacin		84 (12)		
Roxithromycin		– 43 (12)		
Spiramycin		58 (12)		
Sulfadiazine		– 17 (12)		
Sulfamethazine		100 (12)		
Sulfamethoxazole		16 (12)		– 104 to 12 (7); 28–53 (9); 23 (10)
Tilmicosin		51 (12)		
Triclosan	50 (2)			74–93 (8); 67–99 (9)
Trimethoprim		38 (12)		25–86 (7)
<i>Antidiabetics</i>				
Glibenclamide		23 (12)		
Glimepiride				20 (10)
<i>Antidysenterics</i>				
Loperamide				38 (7)
<i>Antifungals</i>				
Clotrimazol				– 18 (7)
Fluconazole				– 40 to 43 (7)
<i>Antihypertensives</i>				
Diltiazem				30–88 (7)
Dipyridamol				80–100 (7)
Eprosartan				24–75 (7)
Hydrochlorothiazide		63 (12)		
Ibersartan				3–58 (7)
Telmisartan				4–87 (7)
Verapamil				69–84 (7)
<i>Anti-senile dementia drugs</i>				
Memantin				5–32 (7)
<i>Barbiturates</i>				
Butalbital		42 (12)		
Pentobarbital		32 (12)		
Phenobarbital		17 (12)		
<i>Beta-agonists</i>				
Clenbuterol		11 (12)		
Salbutamol		100 (12)		
Terbutaline				– 11 to 83 (7)

(continued on next page)

Table 4 (continued)

Pharmaceutical compounds	SF-CW	HSSF-CW	VSSF-CW	Hybrid CW system
<i>Beta-blockers</i>				
Atenolol		93–95 (planted, 5); 82 (unplanted, 5); 48 (12)		27–53 (7); >97 (9); 77 (10)
Bisoprolol				22–36 (7)
Metoprolol		11 (12)		–3 to 30 (7)
Propranolol		38 (12)		
Sotalol		5 (12)		–21 to 17 (7)
Timolol		–8 (12)		
<i>Diuretics</i>				
Furosemide	52 (2)	35 (12)		
<i>Hormone inhibitors</i>				
Finasteride				–394 to –141 (7)
<i>Lipid regulators</i>				
Atorvastatin		100 (12)		4 (7)
Bezafibrate		27 (12)		–21 to 41 (7)
Clofibrate	34 (1); 36 (summer, 3); 32 (winter, 3)	48–75 (winter–summer, planted, 4); 41–43 (winter–summer, unplanted, 4); 100 (12)		
Fenofibrate		100 (12)		
Gemfibrozil		22 (12)		
Mevastatin		53 (12)		
Pravastatin		52 (12)		
Rosuvastatin				–16 to 60 (7)
<i>Psychiatric drugs</i>				
Alprazolam				–130 to 99 (7)
Amitriptyline				6–84 (7)
Bupropion				–135 to 43 (7)
Carbamazepine	39 (1); 3 (2); 30 (summer, 3); 47 (winter, 3)	88–97 (winter–summer, planted, 4); 87–86 (winter–summer, unplanted, 4); –4 (12)	–0.9 to 26 (6)	–19 to 21 (7); 5–51 (8); –12 to 65 (9); 16 (10)
Citaprolam				45–97 (7)
Dilantin				7–39 (9)
Diazepam				–10 to 0 (9)
Fluoxetine		–1 (12)		
Hydroxyzine				50–75 (7)
Levomepromazine				92 (7)
Lorazepam		12 (12)		
Maprotilin				17 (7)
Mianserin				87 (7)
Mirtazapine				29–72 (7)
Oxazepam				–26 to 21 (7)
Paroxetine		100 (12)		–83 to 74 (7)
Perphenazine				13 (7)
Sertraline				0.1–94 (7)
Venlafaxine				17–65 (7)
Zoldipem				24–52 (7)
<i>Receptor antagonists</i>				
Alfuzosine				55–96 (7)
Cimetidine		24 (12)		
Famotidine		100 (12)		
Loratadine		29 (12)		
Ranitidine		41 (12)		–39 to 92 (7)
<i>Stimulants/psychoactive drugs</i>				
Caffeine	3 (2)			47–86 (8); 53 (10)
Naloxone				–116 to 84 (7)
<i>Veterinary drugs</i>				
Flunixin	0 (summer, 3); 64 (winter, 3)			

Notes: 1: Llorens et al. (2009); 2: Matamoros et al. (2012a); 3: Matamoros et al. (2008b); 4: Dordio et al. (2010); 5: Dordio et al. (2009a); 6: Reif et al. (2011); 7: Breitholtz et al. (2012); 8: Matamoros and Salvadó (2012); 9: Park et al. (2009); 10: Lee et al. (2011); 11: Gross et al. (2004); 12: Verlicchi et al. (2013).

wetlands can occur under both the aerobic and the anaerobic conditions involving the activities of various microorganisms such as heterotrophic bacteria, autotrophic bacteria, fungi (basidiomycetes and yeasts), and specific protozoa (Kadlec and Wallace, 2009).

An important factor strongly influencing the microbial degradation process is the chemical structures of the organic compounds (Dua et al., 2002; Reddy and DeLaune, 2008). For those organic compounds with simple structures possessing high water solubility and low adsorptivity, they could be readily degraded by microorganisms.

It is attributable to the usual similarity of these organic compounds to the naturally occurring compounds which are commonly used as energy sources by microorganisms. In contrast, for those xenobiotic organic compounds (including pharmaceuticals) that have the very different structures from the naturally occurring compounds, they may be slowly degraded by microorganisms possibly due to the lack of suitable degrading genes in microorganisms. However, it does not mean that the non-specific enzymes are not able to help degrade the xenobiotic organic compounds. The degradation of such organic

Table 5

Reported plant species in constructed wetlands for the removal of pharmaceuticals.

Common name	Latin name	Sources
<i>Shrubs</i>		
Grey willow	<i>Salix atrocinerea</i>	Hijosa-Valsero et al. (2011c, 2010a)
<i>Emergent plants</i>		
Arrowhead	<i>Sagittaria graminea</i> ,	Zarate et al. (2012)
Bulrush	<i>Scirpus</i> spp.	Breitholtz et al. (2012); Gross et al. (2004)
	<i>Schoenoplectus lacustris</i>	Breitholtz et al. (2012); Matamoros et al. (2012a)
Common reed	<i>Phragmites</i> spp.	Breitholtz et al. (2012); Dordio et al. (2009a); Reif et al. (2011)
	<i>Phragmites australis</i>	Ávila et al. (2010, 2013); Breitholtz et al. (2012); Carvalho et al. (2013); Conkle et al. (2008); Hijosa-Valsero et al. (2011a, 2011b, 2011c, 2010b); Llorens et al. (2009); Matamoros and Salvadó, (2012); Matamoros et al. (2008a, 2008b, 2007); Matamoros and Bayona (2006); Matamoros et al. (2005); Ranieri et al. (2011); Reyes-Contreras et al. (2012); Verlicchi et al. (2013)
Calamus	<i>Acorus</i> spp.	Lee et al. (2011); Park et al. (2009)
Cattail	<i>Typha</i> spp.	Anderson et al. (2013); Breitholtz et al. (2012); Dordio et al. (2010, 2009a); Gross et al. (2004); Lee et al., 2011; Park et al. (2009)
	Narrowleaf cattail/lesser bulrush	Hijosa-Valsero et al. (2011a, 2011c, 2010b); Reyes-Contreras et al. (2012); Zhang et al. (2012a, 2012b, 2011)
	Broadleaf cattail/common bulrush	Hussain et al. (2012, 2011); Hijosa-Valsero et al. (2011c, 2010a); Llorens et al. (2009); Matamoros and Salvadó (2012); Matamoros et al. (2008b); Ranieri et al. (2011); Zarate et al. (2012)
Dallis grass	<i>Paspalum</i> spp.,	Zarate et al. (2012)
Fountain grass	<i>Pennisetum</i>	Liu et al. (2013a)
Reed canarygrass	<i>Phalaris arundinacea</i>	Hussain et al. (2012, 2011)
Reed mannagrass	<i>Glyceria maxima</i>	Breitholtz et al. (2012)
Ryegrass	<i>Lolium</i>	Xian et al. (2010)
Sedge	<i>Carex</i> spp.	Breitholtz et al. (2012)
	Variegated greater pond sedge	Breitholtz et al. (2012)
Soft rush	<i>Juncus effusus</i>	Reyes-Contreras et al. (2011)
Wood clubrush	<i>Scirpus sylvaticus</i>	Breitholtz et al. (2012)
Pickereelweed	<i>Pontederia cordata</i>	Zarate et al. (2012)
<i>Submergent plants</i>		
Coontail/Hornwort	<i>Ceratophyllum demersum</i>	Breitholtz et al. (2012); Zarate et al. (2012)
Eurasian watermilfoil	<i>Myriophyllum spicatum</i>	Breitholtz et al. (2012)
Horned pondweed	<i>Zannichellia palustris</i>	Gross et al. (2004)
Pondweed	<i>Potamogeton</i> spp.	Breitholtz et al. (2012); Zarate et al. (2012)
Spiny naiad	<i>Najas marina</i>	Gross et al. (2004)
Water milfoil	<i>Myriophyllum</i> spp.	Breitholtz et al. (2012)
Water weed	<i>Elodea</i> spp.	Breitholtz et al. (2012)
<i>Floating plants</i>		
Duckweed	<i>Lemna</i> spp.	Gross et al. (2004); Zarate et al. (2012)
	Common duckweed/lesser duckweed	Hijosa-Valsero et al. (2011c, 2010a)
Pennywort	<i>Lemna minor</i>	Conkle et al. (2008)
Smartweed	<i>Hydrocotyle</i> spp.	Gross et al. (2004)
	<i>Polygonum</i> spp.	
<i>Rooted floating leaves</i>		
Water lily	<i>Nymphaeaceae</i>	Breitholtz et al. (2012)
White lotus	<i>Nymphaea alba</i>	Matamoros et al. (2012a)

compounds by non-specific enzymes may still take place at a slower rate via co-metabolism reactions which do not support the microbial growth (Seffernick and Wackett, 2001). In addition, the degradation of xenobiotic organic compounds by microorganisms in constructed wetlands may also be influenced by the substrate, vegetation, oxygen and redox potential, temperature, pH, nutrient available, and presence of toxic substances (Calheiros et al., 2009; Li et al., 2010; Reddy and DeLaune, 2008; Salomo et al., 2009; Truu et al., 2009).

In the reviewed research work, aerobic biodegradation was thought to be the main contribution to the microbial degradation process of ibuprofen (Ávila et al., 2010, 2013; Hijosa-Valsero et al., 2010a, 2010b, 2011c; Matamoros et al., 2008a, 2005; Reyes-Contreras et al., 2012), salicylic acid (Hijosa-Valsero et al., 2010b, 2011c; Reyes-Contreras et al., 2012) and sulfamethoxazole (Hijosa-Valsero et al., 2011a), whereas anaerobic biodegradation was thought to be responsible for naproxen (Ávila et al., 2010) and caffeine (Hijosa-Valsero et al., 2010b; Hijosa-Valsero et al., 2011c; Reyes-Contreras et al., 2012). However, regarding the biodegradation of diclofenac, there exist two different points of views and they are: 1) high redox potential could promote the removal of diclofenac (Ávila et al., 2013; Hijosa-Valsero et al., 2010b, 2011c); 2) the removal efficiency of diclofenac could be enhanced under anaerobic

conditions (Ávila et al., 2010). All the removal mechanisms stated above were inferred from the reported experiment results and do not include explicit demonstrations. Thus, it is still difficult to describe the actual removal mechanisms of pharmaceuticals to date.

Certain pharmaceutical compounds (for example, ibuprofen) which contain an asymmetric carbon atom (also known as a chiral carbon atom) usually have two enantiomeric forms (S_{form} and R_{form}). The enantiomeric fraction ($EF = S_{form} / (S_{form} + R_{form})$) (Hijosa-Valsero et al., 2010a; Matamoros et al., 2009b) which is compound-dependent can be used for the evaluation on the occurrence of enantioselective degradation in wastewater treatment system through investigating the change in the trend of EF. Enantioselective degradation of ibuprofen was reported by Matamoros et al. (2009b) that the S_{form} ibuprofen was degraded faster than the R_{form} ibuprofen under aerobic conditions (in VSSF-CW) inducing EF to decrease. This phenomenon was in agreement with the findings of Hijosa-Valsero et al. (2010a). However, EF didn't change during wastewater treatment under anaerobic conditions (in HSSF-CW) due to the similar degradation rates of S_{form} ibuprofen and the R_{form} ibuprofen. Owing to the different ibuprofen EF trends under aerobic and anaerobic conditions, it can be deduced which kind of metabolic pathway (aerobic biodegradation or

anaerobic degradation) plays a predominant role in the removal of ibuprofen in constructed wetlands.

Evaluation of the biodegradation intermediates of pharmaceuticals in constructed wetlands is also important for elucidating the microbial degradation mechanisms, but available data are very few at present. Matamoros et al. (2008a) studied the behavior of two biodegradation intermediates of ibuprofen including carboxy-ibuprofen (CA-IBP) and hydroxy-ibuprofen (OH-IBP) in a HSSF-CW system to assess the relative contribution of aerobic and anaerobic pathways to the ibuprofen biodegradation. Their findings indicated that the CA-IBP and OH-IBP only contributed to 5% of the degraded IBP and there was negligible accumulation of these two kinds of intermediates in the microcosms. The observation was possibly due to the similar kinetics for their consumption and formation. However, both CA-IBP and OH-IBP can be produced under aerobic conditions and only CA-IBP can be detected under anaerobic conditions (Zwiener et al., 2002). Through the analysis on the ibuprofen removal percentage attributable to the aerobic and anaerobic pathways using Eqs. (1) and (2), the authors suggested that the aerobic metabolic pathways predominated for the removal of ibuprofen.

$$\text{Aerobic-ratio} = (C_{\text{OH-IBP}} + xC_{\text{CA-IBP}}) / (C_{\text{OH-IBP}} + C_{\text{CA-IBP}}) \quad (1)$$

$$\text{Anaerobic-ratio} = yC_{\text{CA-IBP}} / (C_{\text{OH-IBP}} + C_{\text{CA-IBP}}) \quad (2)$$

where:

$C_{\text{CA-IBP}}$ — Concentration of CA-IBP

$C_{\text{OH-IBP}}$ — Concentration of OH-IBP

x — Percentage of CA-IBP obtained in the aerobic pathways, 0.4%

y — Percentage of CA-IBP obtained in the anaerobic pathways, 1.8%.

Feeding pharmaceutical contaminants to constructed wetland may affect the development and activities of microbes in constructed wetlands. Weber et al. (2011) assessed the influence of ciprofloxacin on the distribution of bacterial communities in some mesocosm-scale constructed wetlands planted with *P. australis*. Their experimental results showed that the presence of ciprofloxacin had an initial adverse effect on the bacterial communities in the constructed wetlands, thereby reducing their ability to assimilate anthropogenic carbon-based compounds. However, after a 2–5 week acclimation period, the bacterial communities could return to their normal functionality. Helt et al. (2012) investigated the effect of ciprofloxacin on the antibiotic resistance of the interstitial bacterial community (total culturable heterotrophs) and the selected fecal indicators (*Escherichia coli* and *Enterococcus* spp.) in the same constructed wetlands as those used by Weber et al. (2011). Helt et al. (2012) found that the antibiotic resistance level of the interstitial bacteria community peaked at 7 days following the ciprofloxacin exposure and then decreased thereafter, and also observed that the antibiotic resistance level of the fecal indicators increased.

4. Conclusions

Constructed wetlands are now attracting increasing attention to their application for the removal of pharmaceutical contaminants from wastewater. Based on the findings of published work on the feasibility of constructed wetlands as a means to treat pharmaceutical contaminants in wastewater, one can deduce that constructed wetlands hold great potential of being used as an alternative secondary wastewater treatment system or as a wastewater polishing treatment system. Nevertheless, it remains true that scarce data at present cannot provide very persuasive demonstrations for the performance and effectiveness of constructed wetlands in these applications. There are knowledge gaps in several aspects including the removal efficiencies of pharmaceuticals in constructed wetlands, the removal mechanisms involved, the toxicity to constructed wetlands caused by pharmaceuticals, and the influences of certain important parameters (configuration design, hydraulic mode,

temperature and seasonality, pH, oxygen and redox potential, etc.). Moreover, most studies were undertaken at a microcosm-scale or mesocosm-scale. Therefore, further research is required to provide more comprehensive and convincing evidences in larger laboratory-scale, pilot-scale or full-scale constructed wetlands. In addition, the current constructed wetlands applied for the treatment of pharmaceutical pollutants in wastewater are mainly the conventional constructed wetlands including SF-CWs, HSSF-CWs, VSSF-CWs, and hybrid CW system. Some novel constructed wetlands such as the tidal flow constructed wetlands, anti-sized constructed wetlands, and the dewatered alum sludge based constructed wetlands can also be investigated.

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