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REVIEW ARTICLE

Performance comparison of different types of constructed wetlands for the removal of pharmaceuticals and their transformation products: a review

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Abstract

This paper presents a comprehensive and critical comparison of four types of constructed wetlands (CWs): free water surface CW (FWSCW), vertical flow CW (VFCW), horizontal flow CW (HFCW), and hybrid CW (HCW) for the removal of 29 pharmaceuticals (PhCs) and 19 transformation products (TPs) using a global data compiled for 247 CWs reported in 63 peer-reviewed journal papers. Biodegradation (aerobic being more efficient than anaerobic) is the major removal mechanism for 16 out of 29 PhCs besides the influence of other processes (e.g., adsorption/sorption, plant uptake, and photodegradation). The HCW performed better followed by VFCW, HFCW, and FWSCW. The comparatively better removal in HCW might be due to the coexistence of aerobic and anaerobic conditions and longer hydraulic retention time considering more than one compartment enhances the removal of PhCs (e.g., diclofenac, acetaminophen, sulfamethoxazole, sulfapyridine, trimethoprim, and atenolol), which are removed under both conditions and adsorption/sorption processes. The augmentation in dissolved oxygen by the application of artificial aeration improved the removal of PhCs, which are degraded under aerobic conditions. Furthermore, the better performance of aerated CWs could be due to the establishment of various microenvironments with different physicochemical conditions (aerobic and anaerobic), which facilitated the contribution of both aerobic and anaerobic metabolic pathways in the removal of PhCs. The removal of some of the PhCs takes place by the formation of their TPs and the nature of these TPs (persistent or non-biodegradable/biodegradable) plays a major role in their removal process.

Keywords Artificial aeration · Constructed wetlands · Pharmaceuticals · Removal efficiency · Removal mechanisms · Transformation products · Wastewater

Introduction

Pharmaceuticals (PhCs), as emerging organic contaminants (EOCs), have provoked rising concern from researchers and public over the last two decades (Daugthon 2004; Zhu and Chen 2014; Li et al. 2017). PhCs are detected in water resources and environment. The various sources of PhCs are domestic wastewater (excretion), hospital and PhCs industrial waste streams, landfill leachate and animal excretion as well as effluent discharge from wastewater treatment plants (WWTPs) (Caliman and Gavrilescu 2009; Daughton and Ruhoy 2009; Zorita et al. 2009; Michael et al. 2013; Luo et al. 2014; Barbosa et al. 2016). Since WWTPs are not designed for their removal (Ternes 1998; Joss et al. 2006; Verlicchi et al. 2012, 2013), many PhCs escape treatment and are released into the environment (Buser et al. 1998; Heberer 2002; Gorito et al. 2017; Gogoi et al. 2018). PhCs enter the environment through a variety of pathways but the human body plays a major role. A portion of each PhCs dose is retained in the human body, and residual parent compound and its transformation products (TPs) are excreted in urine and feces (Daughton and Ternes 1999; Lienert et al. 2007). Although PhCs are found to be in small concentrations (e.g.,

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ng L^{-1} to μg L^{-1}) in water resources (Heberer 2002; Ternes et al. 2004; Kummerer 2010; Ziylan and Ince 2011), their continuous discharge through various sources including WWTPs (as individual compounds, TPs and combined effect of multitude of compounds) could pose risk for human as well as aquatic and terrestrial life (e.g., Caliman and Gavrilescu 2009; Carvalho et al. 2014; Gorito et al. 2017).

Therefore, the development of treatment trains that are more suited for the removal of PhCs by upgrading existing WWTPs or designing new ones are important areas of research and development. Many experimental investigations have been carried out in recent years to test the technologies for their ability to reduce the concentrations of PhCs in the final effluent. For instance, advanced chemical and biological treatment systems have been assessed: ozonation, ozone/ultraviolet irradiation, ozone/hydrogen peroxide (Ternes et al. 2003; Hollender et al. 2009; Benitez et al. 2011; Feng et al. 2013), ultrafiltration, reverse osmosis, granular activated carbon contact (Acero et al. 2010; Michael et al. 2013; Ganiyu et al. 2015), and membrane biological reactors (Radjenovic et al. 2009; Lipp et al. 2012). Modern WWTPs could be equipped with these technologies for a polishing step, as these technologies are proven to be effective in many cases (Huber et al. 2005; Michael et al. 2013; Papaevangelou et al. 2016). However, their capital and operational costs are very high (Ternes et al. 2003; Reif et al. 2011), which highlights the need for cost-effective, sustainable, and efficient wastewater treatment technologies. More details regarding the treatment of PhCs by various conventional and advanced treatment technologies can be found in literature, for instance, in the reviews by Suárez et al. (2008), Caliman and Gavrilescu (2009), Onesios et al. (2009), Michael et al. (2013), Luo et al. (2014), Barbosa et al. (2016), Gogoi et al. (2018), and Kanakaraju et al. (2018).

Next to conventional and advanced WWTPs, constructed wetlands (CWs) are low cost and nature-based treatment technologies that have been extensively investigated for wastewater treatment including the removal of PhCs from wastewater (e.g., Zhang et al. 2014; Gorito et al. 2017; Ekperusi et al. 2019). To date, more than 50 individual case studies have been published in peer reviewed journals, with rapidly growing numbers since last decade. The investigated CWs are free water surface CW (FWSCW), horizontal flow CW (HFCW), vertical flow CW (VFCW), and hybrid CW (HCW). Although the comparative analysis on the performance of different types of CWs has been conducted within the individual studies (also limited number), it has not been done between the studies. For instance, a comparison between FWSCW, HFCW and VFCW (Matamoros et al. 2009; Dan et al. 2013; Liu et al. 2014; Zhang et al. 2018); between FWSCW, HFCW, and HCW (Hijosa-Valsero et al. 2010a, 2011a, 2016; Reyes-Contreras et al. 2012; Dan et al. 2013); between HFCW, VFCW, and HCW (Kahl et al. 2017; Nivala et al. 2019); between FWSCW and VFCW (Matamoros et al. 2007; Rühmland et al. 2015); and between VFCW and HFCW (Sgroi et al. 2018). A comprehensive and critical review of the performance and a comparison of all types of CWs are lacking. Moreover, all of the studies reported in this review considered limited number of PhCs (Supplementary materials 1: Tables S1-S4). Furthermore, a detailed statistical analysis is lacking, for example, a meta-analysis of available studies to establish significant differences in the performance of different types of CWs for a certain PhC. Some recent studies investigated the effect of dissolved oxygen (DO) by the application of artificial aeration (AA) in CWs. For instance, in FWSCW (Li et al. 2017), HFCW (Auvinen et al. 2017a; Kahl et al. 2017; Nivala et al. 2019), VFCW (Ávila et al. 2014a; Kahl et al. 2017; Nivala et al. 2019), and HCW (Auvinen et al. 2017b) (Tables S1-S4). Additionally, the formation and removal of TPs of one or more of the PhCs (diclofenac, ibuprofen, naproxen, ketoprofen, tramadol, sulfamethoxazol, carbamazepine, and venlafaxine) during treatment process in CWs has been discussed by only few studies (Matamoros et al. 2007; Hijosa-Valsero et al. 2011a, 2016; Rühmland et al. 2015; Březinova et al. 2018; Nuel et al. 2018; Petrie et al. 2018) (Tables S1-S4).

In general, a large number of published research studies offer an opportunity to summarize and critically reflect on the existing knowledge on the performance of different types of CWs for the removal of PhCs and their TPs. However, only a few review studies, with specific focus on PhCs removal by CWs, have been conducted in order to summarize current state of knowledge (Imfeld et al. 2009; Carvalho et al. 2014; Li et al. 2014; Verlicchi and Zambello 2014; Zhang et al. 2014; Gorito et al. 2017; Ekperusi et al. 2019). For instance, Imfeld et al. (2009) provided a scientific description on removal processes in CWs, which was further advanced by Zhang et al. (2014) based on (limited) scientific evidence from available studies. Verlicchi and Zambello (2014) provided an overview of the removal of several PhCs by CWs used for the primary, secondary and tertiary treatment purposes. Li et al. (2014) summarized the role of design parameters (e.g., physical configuration, hydraulic mode, and vegetation species) in the removal of PhCs. Similarly, Gorito et al. (2017) discussed the removal processes and influence of design and operation parameters on the removal of four PhCs by CWs (azithromycin, clarithromycin, diclofenac and erythromycin), which are on the priority list of European Union (EU). Carvalho et al. (2014) conducted a comprehensive review on the potential of CWs for phytoremediation. Consistent with that, Ekperusi et al. (2019) only reflected on the role of plants (duckweed-*Lemna minor*) in the removal of PhCs. Most of the previous reviews investigated a small number of PhCs and selection of CWs. The presented synthesis was often constrained by a limited number of available studies on a certain topic. Furthermore, the available knowledge on the formation and removal of TPs of PhCs during treatment process has not been

synthesized. Thus, comprehensive and critical reviews are needed to address abovementioned gaps, especially on the treatment performance of different types of CWs for the removal of PhCs and their TPs in order to instigate evidence-based (general) conclusions.

Therefore, the main objectives of this study are as follows: (1) to critically evaluate and summarize the available evidence on major PhCs removal processes; (2) to conduct a comparative assessment of four types of CWs for the removal of a large number of PhCs; (3) to analyze the effect of AA on the removal of PhCs in different types of CWs; and (4) to synthesize the available knowledge on the formation and removal of TPs during treatment process.

Methodology

The snowball sampling method yielded over 100 journal articles, which were searched from various sources, such as Scopus, Google Scholar, and individual publishers' Web sites. These journal articles were screened for the purpose of this research. The screening was carried out to check the quality of published data. Only peer-reviewed journal papers were selected for this research, which helped to ensure the reliability of given data. The selected studies have used generally accepted and reliable analytical methods such as solid-phase extraction-gas chromatography-tandem mass spectrometry (SPE-GC-MS/MS), SPE-(ultra) high performance liquid chromatography-diode array detector (SPE-(U)HPLC-DAD), liquid-liquid phase extraction-GC-micro electron capture detector (LLPE-GC-μECD), and SPE-rapid resolution liquid chromatography-MS/MS (SPE-RRLC-MS/MS). Instrumental detection and quantification limits described as limit of detection and limit of quantification were in the range of 0.00003–2.8 μg L^{-1} and 0.00006–10 μg L^{-1}, respectively. The samples were analyzed soon after the collection, as the storage time was less than one or two days in most cases. In this way, a global database was compiled containing information of 247 CWs that were reported in 63 peer-reviewed journal publications with case studies from 19 countries (Supplementary materials 1: Tables S1-S4). Since wide range of PhCs are not studied by two or more types of CWs; therefore, this database contains influent and effluent concentrations, removal efficiencies, and removal rates of selected 29 PhCs grouped to 10 categories according to their therapeutic classes and 19 TPs (Table 1). The treatment performance of four types of CWs (FWSCW, HFCW, VFCW, and HCW) was evaluated for the removal of PhCs. In the case of some PhCs, the statistical comparison was made between two or three types of CWs where sufficient data was available. Additionally, the available knowledge on the formation and removal of TPs during treatment process is synthesized and the comparison among different types of CWs was made for their removal.

The information on the physicochemical properties of PhCs was gathered from various sources (e.g., journal papers, reports, and Web sites) for molecular formula/structure/weight, water solubility, dissociation constant (pKa), organic carbon sorption coefficient (Log Koc), octanol-water partition coefficient (Log Kow), and distribution coefficient (Log Dow) (Supplementary materials 2: Table S5).

First, a detailed analysis of the reported PhCs was conducted from the studied literature including the designed database, which focused on therapeutic classes, types of PhCs and identification of the mechanisms responsible for their removal. Second, statistical analysis was conducted to estimate mean and standard deviation of the selected studied variables. The statistical comparison among different types of CWs was done with one-way ANOVA for the significance and z-test for comparison of means (Supplementary materials 3: Table S6-S9).

Results and discussion

Removal mechanisms in different types of CWs for PhC removal

Traditionally, CWs have been designed as FWSCW and subsurface flow constructed wetland (SSFCW). The SSFCW are further categorized into HFCW and VFCW. In all types of CWs, the pollutant removal mechanisms are different, which govern treatment process and resulting performance of CWs. Detailed description on CWs types and dominant removal mechanisms can be found in literature (e.g., Vymazal 2005; Kadlec and Wallace 2009; Ilyas and Masih 2017a, b). Brief information is presented here with specific focus on PhC removal mechanisms in four types of CWs examined in this study. FWSCW consists of open water, floating vegetation, and emergent plants (Kadlec and Wallace 2009). In FWSCW, the main mechanism of PhCs removal is photodegradation, while microbial degradation and plant uptake also contribute to some extent in the removal (Fig. 1). There are only few PhCs such as diclofenac, ketoprofen, naproxen and clarithromycin that are reported to be mainly removed by photodegradation (Table 2).

In HFCW, wastewater stays below the surface of the media and flows horizontally through the bed until it reaches the outlet (Kadlec and Wallace 2009). In this type of CW, anaerobic biodegradation is an important removal mechanism of PhCs besides their removal by the filter media (through sedimentation, adsorption, and precipitation) and plant uptake (Fig. 2). Anaerobic biodegradation was reported as a major removal mechanism for naproxen, sulfamethoxazole, sulfapyridine, trimethoprim, atenolol, and bezafibrate (Table 2). Considering that anaerobic biodegradation is slower than the aerobic one, longer hydraulic retention

Table 1 The studied 29 PhCs categorized according to their therapeutic classes and their TPs

Categories of pharmaceuticals		
No. of categories	Therapeutic classes	PhCs
1	Analgesic/anti-inflammatory drugs	Diclofenac, ibuprofen, ketoprofen, naproxen, salicylic acid
2	Analgesic	Acetaminophen, codeine, tramadol
3	Antibiotics	Clarithromycin, doxycycline, ofloxacin, sulfadiazine, sulfamethazine, sulfamethoxazole, sulfapyridine, trimethoprim
4	Antiallergic drugs	Fexofenadine
5	Stimulants/psychoactive drugs	Caffeine
6	Antihypertensives	Diltiazem
7	Psychiatric drugs	Carbamazepine, mirtazapin, venlafaxine
8	Beta-blockers	Atenolol, metoprolol, sotalol
9	Receptor antagonists	Ranitidine
10	Lipid regulators	Bezafibrate, clofibric acid, gemfibrozil
Transformation products		
No. of PhCs	PhCs	TPs
1	Diclofenac	4-Hydroxydiclofenac
2	Ibuprofen	1-Hydroxyibuprofen; 2-hydroxyibuprofen; carboxyibuprofen
3	Naproxen	O-Desmethylnaproxen
4	Ketoprofen	3-Ethylbenzophenone; dihydroketoprofen
5	Tramadol	O-Desmethyltramadol; N-desmethyltramadol; N,O-didesmethyltramadol
6	Sulfamethoxazole	N-acetylsulfamethoxazole
7	Carbamazepine	10,11-Dihydro-10,11-dihydroxycarbamazepine; 10,11-dihydro-10-hydroxycarbamazepine; 2-hydroxycarbamazepine; 3-hydroxycarbamazepine; carbamazepine 10,11-epoxide
8	Venlafaxine	O-Desmethylvenlafaxine; N-desmethylvenlafaxine; N,O-didesmethylvenlafaxine

time (HRT) is needed to achieve the same removal efficiency (Auvinen et al. 2017b).

In VFCW, the beds are pulse-loaded with a large amount of water to temporarily flood the surface of the bed (Kadlec and Wallace 2009). The aerobic biodegradation is responsible for the removal of PhCs by VFCW among other dominant processes (e.g., sedimentation, adsorption, and plant uptake) (Fig. 3). Several PhCs biodegrade under aerobic conditions; hence,

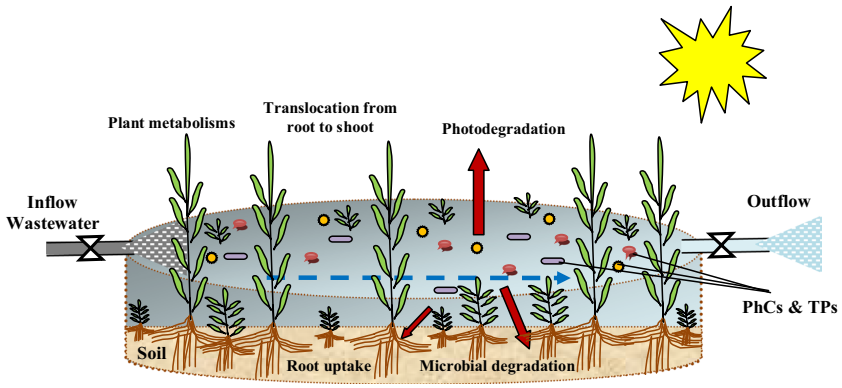

Fig. 1 Free water surface flow constructed wetland and associated removal mechanisms of PhCs and TPs. PhCs pharmaceuticals, TPs transformation products

Table 2 Removal mechanisms of selected 29 PhCs in CWs

Therapeutic class/ pharmaceutical	Possible removal mechanism	References	Dominant removal mechanism *
Analgesic/anti-inflammatory drugs			
Diclofenac	Biodegradation (anaerobic)	Ávila et al. (2010, 2014a); Hijosa-Valsero et al. (2010b); Chen et al. (2016b); Kahl et al. (2017); He et al. (2018); Zhang et al. (2018); Nivala et al. (2019)	Photodegradation; Biodegradation (aerobic)**
	Biodegradation (aerobic)	Hijosa-Valsero et al. (2010a, b, 2011b); Ávila et al. (2013, 2014a); Kahl et al. (2017)	
	Photodegradation	Matamoros et al. (2008a); Matamoros and Salvadó (2012); Ávila et al. (2014b, 2015); Rühmland et al. (2015); Chen et al. (2016b); Francini et al. (2018); Zhang et al. (2018)	
	Plant uptake	Hijosa-Valsero et al. (2010a); Zhang et al. (2011, 2012c)	
Ibuprofen	Biodegradation (aerobic)	Matamoros et al. (2007, 2008b); Hijosa-Valsero et al. (2010a, 2011c); Ávila et al. (2010, 2013, 2014a, b, 2015); Matamoros and Salvadó (2012); Li et al. (2014); Zhu and Chen (2014); Chen et al. (2016b); Vymazal et al. (2017); Březinova et al. (2018); Zhang et al. (2018); Nivala et al. (2019)	Biodegradation (aerobic)
	Sorption	Dordio et al. (2010)	
	Adsorption	Auvinen et al. (2017b)	
	Photodegradation	Reyes-Contreras et al. (2012); Zhang et al. (2014)	
	Plant uptake	Hijosa-Valsero et al. (2010a); Li et al. (2016a, b)	
Ketoprofen	Biodegradation	Hijosa-Valsero et al. (2010a); Zhang et al. (2012a); Chen et al. (2016b); Francini et al. (2018); Zhang et al. (2018)	Photodegradation
	Photodegradation	Matamoros et al. (2008a); Matamoros and Salvadó (2012); Reyes-Contreras et al. (2012); Francini et al. (2018); Zhang et al. (2018)	
Naproxen	Biodegradation (aerobic)	Matamoros et al. (2007, 2009); Hijosa-Valsero et al. (2010a); Matamoros and Salvadó (2012); Zhang et al. (2012b); Chen et al. (2016b); He et al. (2018); Zhang et al. (2018); Nivala et al. (2019)	Biodegradation (aerobic)**; Photodegradation
	Biodegradation (anaerobic)	Matamoros et al. (2009); Ávila et al. (2010); Li et al. (2014); He et al. (2018); Nivala et al. (2019)	
	Photodegradation	Matamoros et al. (2008a); Reyes-Contreras et al. (2012); Hijosa-Valsero et al. (2016); Zhang et al. (2018)	
	Plant uptake	Hijosa-Valsero et al. (2010a); Zhang et al. (2013a); He et al. (2018)	
Salicylic acid	Biodegradation	Hijosa-Valsero et al. (2010a, 2011b); Reyes-Contreras et al. (2012); Zhang et al. (2012a)	Biodegradation (aerobic)**
	Plant uptake	Hijosa-Valsero et al. (2016)	
Analgesic			
Acetaminophen	Biodegradation (aerobic)	Ávila et al. (2013, 2015); Koottatep et al. (2017); Li et al. (2017); Vystavna et al. (2017)	Biodegradation (aerobic)**
	Biodegradation (anaerobic)	Chen et al. (2016b)	
	Photodegradation	Ávila et al. (2015); Li et al. (2017)	
	Adsorption	Ávila et al. (2015); Koottatep et al. (2017)	
	Sorption	Chen et al. (2016b)	
	Plant uptake	Li et al. (2017)	
Codeine	Biodegradation (aerobic)	Rühmland et al. (2015); Petrie et al. (2018)	Sorption; Biodegradation (aerobic)
	Sorption	Petrie et al. (2018)	
Tramadol	Biological transformation	Rühmland et al. (2015); Chen et al. (2016b); Petrie et al. (2018)	Biological transformation
Antibiotics			
Clarithromycin	Biodegradation	Hijosa-Valsero et al. (2011a); Berglund et al. (2014)	Photodegradation; Sorption
	Sorption	Hijosa-Valsero et al. (2011a); Berglund et al. (2014)	
	Photodegradation	Hijosa-Valsero et al. (2011a); Berglund et al. (2014)	
Doxycycline	Biodegradation	Hijosa-Valsero et al. (2011a); Ávila et al. (2014b)	

Table 2 (continued)

Therapeutic class/ pharmaceutical	Possible removal mechanism	References	Dominant removal mechanism *
	Adsorption/ retention processes	Hijosa-Valsero et al. (2011a); Berglund et al. (2014)	Biodegradation (aerobic)**; Adsorption
Ofloxacin	Adsorption	Chen et al. (2016a)	Biodegradation (anaerobic)**; Adsorption
	Biodegradation	Chen et al. (2016a); Yan et al. (2016)	
Sulfadiazine	Biodegradation	Xian et al. (2010)	Biodegradation (anaerobic)**
	Fermentation	Dan et al. (2013)	
Sulfamethazine	Adsorption	Liu et al. (2014); Chen et al. (2016a); Choi et al. (2016)	Biodegradation (aerobic)**; Plant uptake
	Biodegradation	Xian et al. (2010); Liu et al. (2014); Chen et al. (2016a); Choi et al. (2016)	
	Fermentation	Dan et al. (2013)	
	Plant uptake	Xian et al. (2010)	
Sulfamethoxazole	Adsorption	Choi et al. (2016); Liang et al. (2018)	Biodegradation (aerobic; anaerobic)**
	Sorption	Zhu and Chen (2014)	
	Biodegradation (aerobic)	Conkle et al. (2008); Choi et al. (2016); Sgroi et al. (2018); Button et al. (2019)	
	Biodegradation (anaerobic)	Hijosa-Valsero et al. (2011a), Dan et al. (2013); Rühmland et al. (2015); Liang et al. (2018); Sgroi et al. (2018)	
	Photodegradation	Hijosa-Valsero et al. (2011a)	
	Plant uptake	Xian et al. (2010); Hijosa-Valsero et al. (2011a)	
Sulfapyridine	Biodegradation (aerobic)	Conkle et al. (2008)	Biodegradation (anaerobic)**
	Biodegradation (anaerobic)	Dan et al. (2013)	
Trimethoprim	Biodegradation (aerobic)	Hijosa-Valsero et al. (2011a); Rühmland et al. (2015)	Biodegradation (anaerobic)**
	Biodegradation (anaerobic)	Dan et al. (2013)	
Antiallergic drugs			
Fexofenadine	NA	NA	Adsorption/retention processes**
Stimulants/psychoactive drugs			
Caffeine	Biodegradation (aerobic)	Matamoros and Bayona (2006); Hijosa-Valsero et al. (2010b); Zhang et al. (2014); Chen et al. (2016b); Li et al. (2017); Vymazal et al. (2017); Vystavna et al. (2017); He et al. (2018)	Biodegradation (aerobic)**; Plant uptake
	Biodegradation (anaerobic)	Hijosa-Valsero et al. (2010a); Carranza-Diaz et al. (2014); He et al. (2018)	
	Adsorption onto carbon rich surfaces of the gravel bed	Matamoros and Bayona (2006); Dettenmaier et al. (2009); Wang et al. (2014); Li et al. (2017)	
	Plant uptake	Hijosa-Valsero et al. (2010a); Zhang et al. (2013b); Zhu and Chen (2014); Chen et al. (2016b); Li et al. (2017); Petrie et al. (2018)	
Antihypertensives			
Diltiazem	Plant uptake	Petrie et al. (2018)	Plant uptake
	Sorption	Petrie et al. (2018)	
Psychiatric drugs			
Carbamazepine	Adsorption onto the available organic surfaces	Matamoros et al. (2005, 2008b); Hijosa-Valsero et al. (2011b); Carranza-Diaz et al. (2014); Sharif et al. (2014); Vystavna et al. (2017); Park et al. (2018)	Adsorption; Sorption; Plant uptake
	Sorption	Dordio et al. (2010); Park et al. (2018)	
	Biodegradation (aerobic)	Hijosa-Valsero et al. (2010a)	
	Reductive transformation	Kahl et al. (2017); Nivala et al. (2019)	
	Plant uptake	Hijosa-Valsero et al. (2010a, 2016); Macci et al. (2015); Yan et al. (2016); Petrie et al. (2018); He et al. (2018)	
Mirtazapin	Biodegradation	Breitholtz et al. (2012)	
	Plant uptake	Petrie et al. (2018)	

Table 2 (continued)

Therapeutic class/ pharmaceutical	Possible removal mechanism	References	Dominant removal mechanism *
			Biodegradation (aerobic)**; Plant uptake
Venlafaxine	Precipitation Biological transformation	Breitholtz et al. (2012); Vystavna et al. (2017); Petrie et al. (2018) Rühmland et al. (2015); Petrie et al. (2018)	Plant uptake; Precipitation
	Plant uptake	Petrie et al. (2018)	
Beta-blockers			
Atenolol	Biodegradation (aerobic) Biodegradation (anaerobic)	Conkle et al. (2008); Rühmland et al. (2015) Chen et al. (2016b)	Sorption
	Adsorption	Auvinen et al. (2017b); Park et al. (2018)	
	Sorption	Petrie et al. (2018); Park et al. (2018)	
	Photodegradation	Salgado et al. (2013)	
	Plant uptake	Francini et al. (2018)	
Metoprolol	Biodegradation (aerobic)	Conkle et al. (2008); Rühmland et al. (2015); Chen et al. (2016b); He et al. (2018)	Biodegradation (aerobic)
Sotalol	NA	NA	Biodegradation (aerobic)**
Receptor antagonists			
Ranitidine	Biodegradation Sorption	Breitholtz et al. (2012) Petrie et al. (2018)	Sorption
Lipid regulators			
Bezafibrate	Biodegradation (aerobic)	Rühmland et al. (2015)	Biodegradation (anaerobic)**
	Biodegradation (anaerobic)	Petrie et al. (2018)	
Clofibric acid	Plant uptake	Dordio et al. (2010)	Plant uptake
Gemfibrozil	Biodegradation (aerobic)	Conkle et al. (2008); Yi et al. (2017); Zhang et al. (2018)	Biodegradation (aerobic)

*Authors' own insight based on physicochemical properties, removal mechanisms and limited evidence in the literature

**Authors' own insight based on physicochemical properties and removal mechanisms

VFCW is a suitable system for the removal of these PhCs, for example, ibuprofen, salicylic acid, acetaminophen, codeine, caffeine, metoprolol, and gemfibrozil (Table 2). However, the removal of PhCs that are biodegraded under anaerobic conditions might be limited in VFCW (Table S3).

Furthermore, HCWs are designed to achieve higher performance compared with only one setting of a CW. For example, HCW consisting of VFCW and HFCW was developed to enhance the removal of nitrogen by providing nitrification-denitrification processes (Cooper et al. 1999; Kadlec and Wallace 2009; Vymazal 2013) (Fig. 4). However, the other

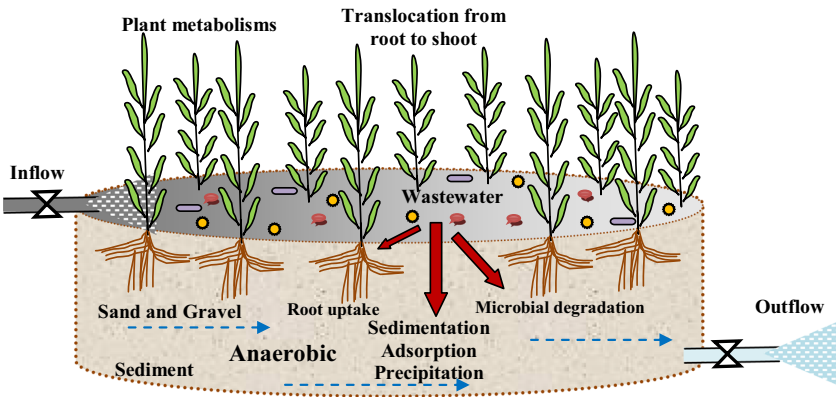

Fig. 2 Horizontal subsurface flow constructed wetland and associated removal mechanisms of PhCs and TPs

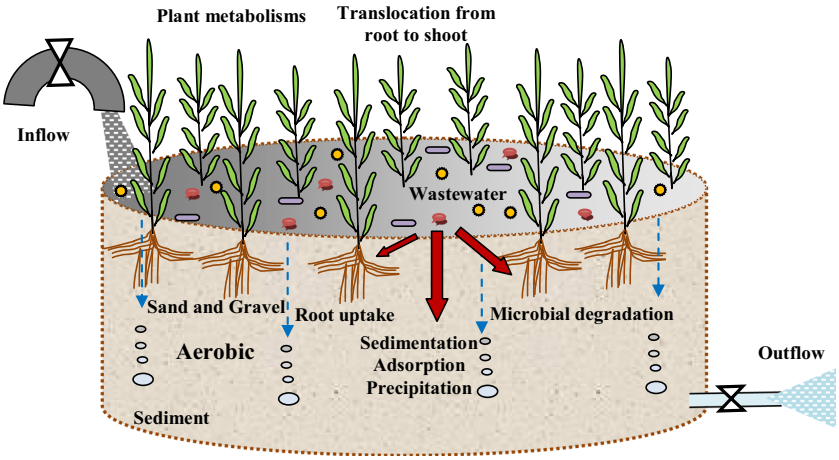

Fig. 3 Vertical subsurface flow constructed wetland and associated removal mechanisms of PhCs and TPs

types of HCWs such as FWSCW combined with VFCW and/or HFCW are also known to enhance the performance (Vymazal 2013). Similarly, the research have been carried out to develop HCW by combining different CWs and hence a range of processes (e.g., reductive and oxidative processes) and different environments (e.g., aerobic and anaerobic) (Fig. 4 and Table S4) to achieve improved performance of CWs for the removal of PhCs and their TPs (Armenante et al. 1992; Master et al. 2002; Vymazal 2005).

The available evidence in the literature and physicochemical properties of PhCs indicate that specific processes are involved in the removal of a certain type of PhC in CWs (Figs. 1, 2, 3, and 4 and Tables 2 and S5), and these complex physical, chemical, and biological processes may occur simultaneously including photodegradation, volatilization, adsorption/sorption, plant uptake and accumulation, as well as biodegradation (aerobic and anaerobic), mainly depending on the design of the CWs (e.g., Zhang et al. 2014; Gorito et al. 2017). Due to the variation in the dominant removal mechanisms of different types of PhCs, their removal efficiency varies in different types of CWs (Table 3). A comparative analysis of PhCs removal by different types of CWs is presented in the following section.

A comparative performance of different types of CWs for PhCs removal

The removal efficiency of 29 selected PhCs with four types of CWs (FWSCW, HFCW, VFCW, and HCW) is presented in Table 3. The results of ANOVA and z-test for comparison of means for statistical significance or non-significance of observed difference among the studied CWs for the removal efficiency of 29 PhCs are given in Supplementary materials 3: Tables S6-S9 and substantiated by Figs. 5, 6, 7, and 8. The removal efficiency of all the studied 29 PhCs did not reveal significant differences in the studied CWs; therefore, in the following section, the statistical results of

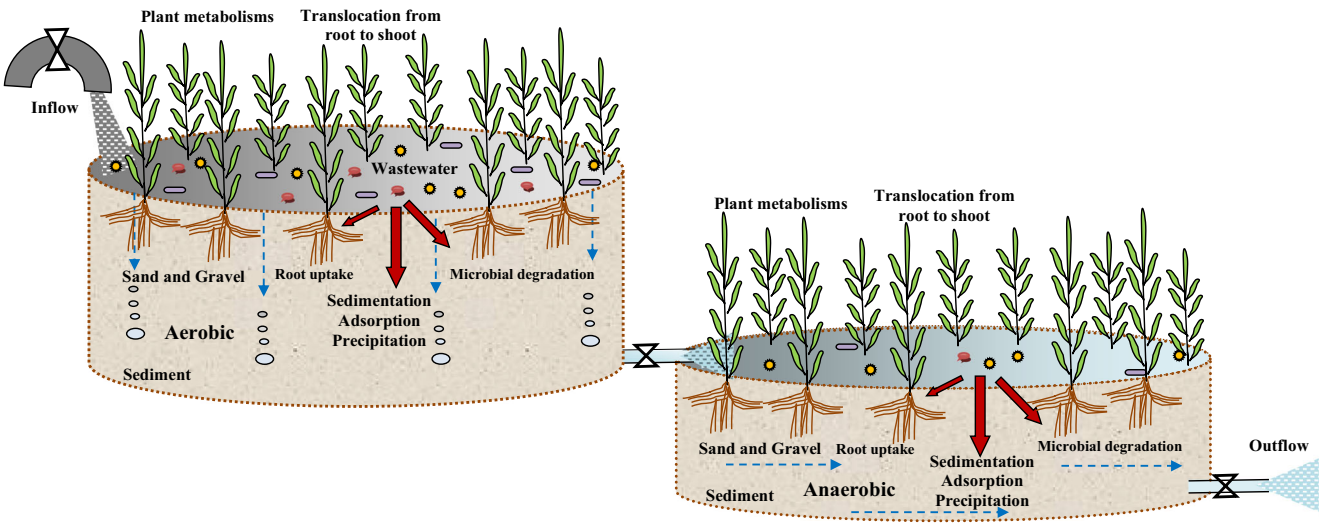

Fig. 4 An example of a hybrid constructed wetland (combination of VFCW and HFCW) and corresponding removal mechanisms of PhCs and TPs

Table 3 Removal efficiency (mean % and standard deviation) of selected 29 PhCs in different types of CWs

Therapeutic class/ Pharmaceutical	FWSCW (*n*)	HFCW (*n*)	VFCW (*n*)	HCW (*n*)	Main findings/statistical results
Analgesic/anti-inflammatory drugs					
Diclofenac	42 ± 24 (22)	39 ± 24 (45)	50 ± 17 (13)	56 ± 32 (25)	The removal efficiency with HCW was significantly higher compared with HFCW
Ibuprofen	57 ± 28 (27)	53 ± 27 (61)	79 ± 24 (10)	62 ± 29 (32)	The removal efficiency with VFCW was significantly higher compared with FWSCW, HFCW and HCW
Ketoprofen	48 ± 30 (22)	47 ± 35 (27)	50 ± 3 (6)	45 ± 28 (17)	Non-significant differences
Naproxen	50 ± 22 (28)	63 ± 26 (42)	75 ± 17 (8)	64 ± 24 (24)	The removal efficiency with VFCW was significantly higher compared with FWSCW, HFCW and HCW
Salicylic acid	76 ± 19 (15)	79 ± 21 (20)	98 (1)	86 ± 17 (15)	Non-significant differences in removal efficiency
Analgesic					
Acetaminophen	99 (1)	70 ± 24 (12)	97 ± 1 (2)	83 ± 25 (11)	Non-significant differences in removal efficiency
Codeine	64 ± 26 (5)	59 ± 18 (4)	95 ± 1 (2)	NA	Non-significant differences in removal efficiency
Tramadol	23 ± 22 (5)	58 ± 42 (11)	46 ± 42 (2)	NA	The removal efficiency with FWSCW was significantly lower compared with HFCW
Antibiotics					
Clarithromycin	41 ± 21 (6)	45 ± 20 (10)	49 ± 57 (2)	46 ± 9 (2)	Non-significant differences in removal efficiency
Doxycycline	73 ± 18 (4)	73 ± 2 (2)	NA	61 ± 15 (3)	Non-significant differences in removal efficiency
Ofloxacin	NA	98 ± 4 (13)	87 ± 10 (3)	NA	Non-significant differences in removal efficiency
Sulfadiazine	61 ± 35 (10)	46 ± 30 (6)	52 ± 22 (12)	NA	Non-significant differences in removal efficiency
Sulfamethazine	48 ± 48 (9)	45 ± 27 (21)	35 ± 30 (12)	74 (1)	Non-significant differences in removal efficiency
Sulfamethoxazole	54 ± 29 (13)	43 ± 24 (10)	54 ± 29 (14)	61 ± 31 (7)	Non-significant differences in removal efficiency
Sulfapyridine	79 ± 4 (6)	84 ± 3 (6)	84 ± 5 (12)	99 (1)	The removal efficiency with FWSCW was significantly lower compared with HFCW and VFCW
Trimethoprim	70 ± 21 (15)	65 ± 31 (12)	69 ± 27 (12)	96 ± 5 (3)	The removal efficiency with HCW was significantly higher compared with FWSCW, HFCW and VFCW
Antiallergic drugs					
Fexofenadine	18 ± 10 (3)	39 ± 26 (3)	NA	NA	Non-significant differences in removal efficiency
Stimulants/psychoactive drugs					
Caffeine	62 ± 29 (17)	84 ± 16 (63)	97 ± 2 (4)	77 ± 25 (26)	The removal efficiency with VFCW was significantly higher compared with FWSCW, HFCW and HCW; The removal efficiency with FWSCW was significantly lower compared with HFCW
Antihypertensives					
Diltiazem	66 ± 25 (4)	68 ± 12 (3)	NA	NA	Non-significant differences in removal efficiency
Psychiatric drugs					
Carbamazepine	31 ± 22 (23)	30 ± 24 (38)	40 ± 20 (11)	27 ± 20 (18)	Non-significant differences in removal efficiency
Mirtazapin	55 ± 23 (3)	8.3 ± 5.0 (3)	NA	NA	The removal efficiency with FWSCW was significantly higher compared with HFCW
Venlafaxine	43 ± 26 (5)	5.1 ± 3.6 (3)	40 ± 21 (2)	63 ± 4 (2)	The removal efficiency with FWSCW was significantly higher compared with HFCW
Beta-blockers					
Atenolol	57 ± 24 (5)	82 ± 19 (7)	79 ± 20 (4)	73 ± 37 (2)	Non-significant differences in removal efficiency
Metoprolol	33 ± 23 (5)	60 ± 32 (15)	74 ± 9 (2)	99 (1)	Non-significant differences in removal efficiency
Sotalol	15 ± 8 (3)	18 ± 12 (3)	NA	82 (1)	Non-significant differences in removal efficiency
Receptor antagonists					
Ranitidine	79 ± 20 (3)	36 ± 8 (4)	NA	NA	The removal efficiency with FWSCW was significantly higher compared with HFCW
Lipid regulators					
Bezafibrate	48 ± 28 (3)	45 ± 13 (4)	56 ± 11 (2)	NA	Non-significant differences in removal efficiency
Clofibric acid	30 ± 9 (4)	49 ± 24 (14)	NA	NA	The removal efficiency with FWSCW was significantly lower compared with HFCW
Gemfibrozil	12 ± 2 (4)	58 ± 23 (8)	45 ± 9 (4)	95 (1)	The removal efficiency with FWSCW was significantly lower compared with HFCW and VFCW

n number of observations, *NA* not available

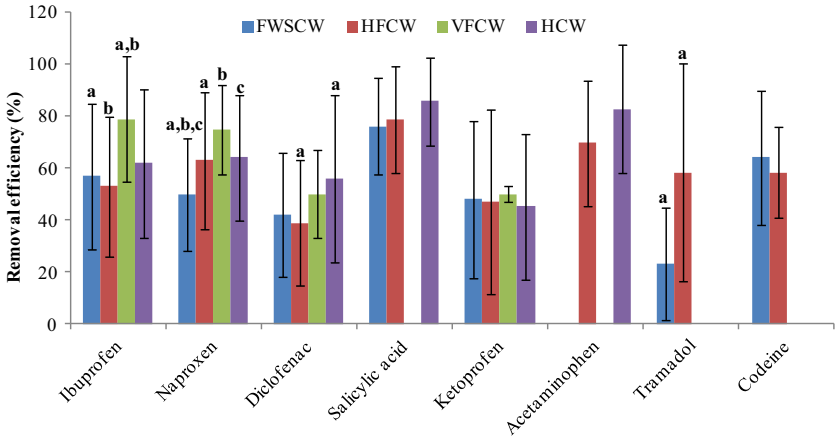

Fig. 5 Removal efficiency (mean and standard deviation) of analgesic/anti-inflammatory drugs with different types of CWs. Ibuprofen: "a" shows that FWSCW exhibit significant difference from VFCW; "b" shows that HFCW and VFCW are significantly different from each other. Naproxen: "a" shows that FWSCW exhibit significant difference from HFCW; "b" shows that FWSCW and VFCW are significantly different from each other; "c" shows that FWSCW exhibit significant difference from HCW. Diclofenac: "a" shows that HFCW exhibit significant difference from HCW. Tramadol: "a" shows that FWSCW exhibit significant difference from HFCW at $\alpha = 0.05$ ($P < 0.05$). The number of observations for studied PhCs in different types of CWs is given in Table 3

12 PhCs are discussed, which exhibited significant differences in their removal efficiency in the studied CWs.

It is important to note that the removal efficiency of the PhCs is influenced by several factors such as physicochemical properties of PhCs, design and operational factors, and physicochemical conditions occurring inside CWs. For instance, Ilyas et al. (2020) noted that the physicochemical properties of PhCs such as, Log Koc, Log Dow and molecular weight are important predictor of removal of PhCs. Similarly, Ilyas and van Hullebusch (2019) highlighted that the removal of PhCs is governed by several design and operational factors with varying degree of influence on a certain PhC; the important factors include area, depth, hydraulic loading rate, organic loading rate, and HRT, and physicochemical parameters including, DO, temperature and seasonality, and pH.

Analgesic/anti-inflammatory drugs

Ibuprofen The removal efficiency of ibuprofen with VFCW was much higher (79 ± 24%) compared with HCW (62 ± 29%), FWSCW (57 ± 28%), and HFCW (53 ± 27%) (Table 3). However, its removal efficiency exhibits significant differences only in the case of FWSCW and HFCW (Fig. 5 and Table S6). Its major removal process in CWs is biodegradation besides plant uptake and adsorption (Table 2). Photodegradation may take place only in unplanted FWS on top of horizontal flow filter (HFF) (Reyes-Contreras et al. 2012) and VFCW are predominantly aerobic compared with anoxic HFCW (Figs. 1, 2, 3, and 4). Although it is easily biodegradable compound (Hijosa-Valsero et al. 2011c), the higher removal efficiency in VFCW can be explained by the fact that the aerobic biodegradation mainly

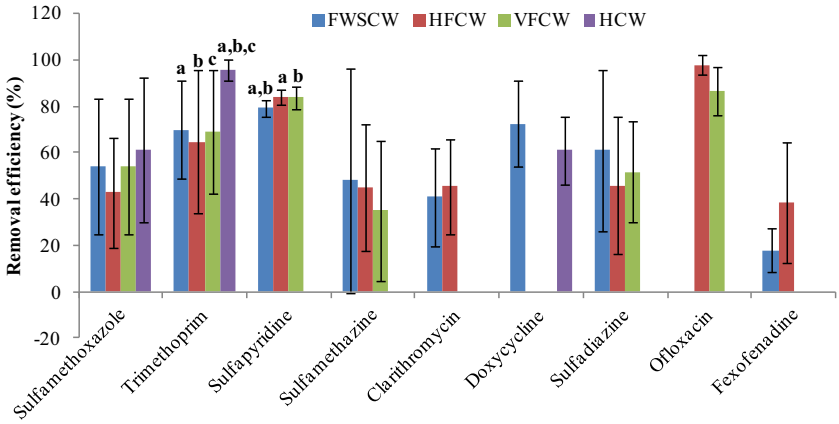

Fig. 6 Removal efficiency (mean and standard deviation) of antibiotics/antiallergic drugs with different types of CWs. Trimethoprim: "a" shows that FWSCW is significantly different from HCW; "b" shows that HFCW is significantly different from HCW; "c" shows that VFCW and HCW are significantly different from each other. Sulfapyridine: "a" shows that FWSCW exhibit significant difference from HFCW; "b" shows that FWSCW is significantly different from VFCW at $\alpha = 0.05$ ($P < 0.05$). The number of observations for studied PhCs in different types of CWs is given in Table 3

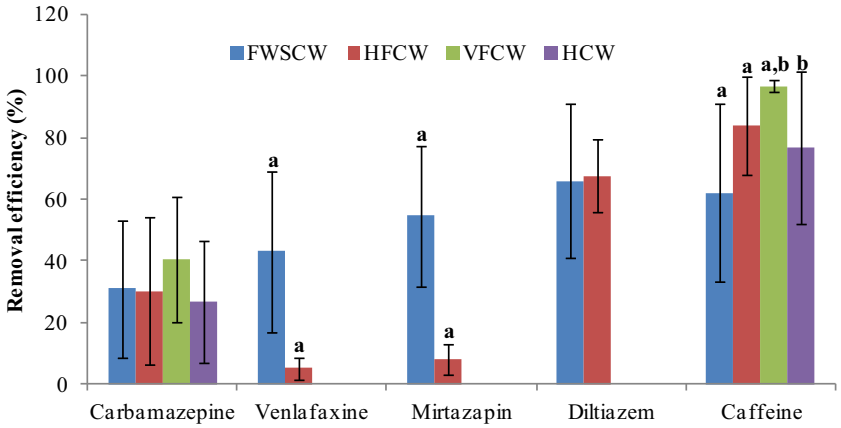

Fig. 7 Removal efficiency (mean and standard deviation) of psychiatric drugs/antihypertensive/psychoactive drugs with different types of CWs. Venlafaxine: "a" shows that FWSCW is significantly different from HFCW. Mirtazapin: "a" shows that FWSCW exhibit significant difference from HFCW. Caffeine: "a" shows that FWSCW, HFCW and VFCW exhibit significant difference from each other; "b" shows that VFCW exhibit significant difference from HCW at $\alpha = 0.05$ ($P < 0.05$). The number of observations for studied PhCs in different types of CWs is given in Table 3

contributes to its microbial degradation process, thus, removal increases under oxic conditions (Table 2).

Naproxen The removal efficiency of naproxen with VFCW was much higher (75 ± 17%) compared with HCW (64 ± 24%), HFCW (63 ± 26%), and FWSCW (50 ± 22%) (Table 3). Nevertheless, its removal efficiency reveals significant differences only with FWSCW. Similarly, the removal efficiency of naproxen in FWSCW was significantly lower compared with HCW and HFCW (Fig. 5 and Table S6). The higher removal efficiency in VFCW might be due to the fact that this compound is readily biodegradable and substrate aeration by the plants is enough for biodegradation (Table 2). Its moderate removal in HFCW indicated that anaerobic biodegradation is also responsible for its removal (Table 2). Nevertheless, Matamoros et al. (2009) reported that its degradation was similar under aerobic and anaerobic conditions. The comparatively low removal efficiency in FWSCW might be due to photodegradation as the main removal mechanism for its removal (Fig. 1 and Table 2).

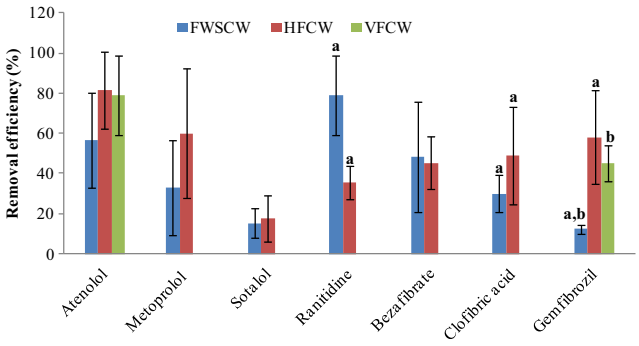

Fig. 8 Removal efficiency (mean and standard deviation) of beta-blockers/receptor antagonists/lipid regulators with different types of CWs. Ranitidine: "a" shows that FWSCW exhibit significant difference from HFCW. Clofibric acid: "a" shows that FWSCW exhibit significant difference from HFCW. Gemfibrozil: "a" shows that FWSCW exhibit significant difference from HFCW; "b" shows that FWSCW and VFCW are significantly different from each other at $\alpha = 0.05$ ($P < 0.05$). The number of observations for studied PhCs in different types of CWs is given in Table 3

Diclofenac The removal efficiency of diclofenac was comparatively better in HCW (56 ± 32%) compared with VFCW (50 ± 17%), FWSCW (42 ± 24%), and HFCW (39 ± 24%) (Table 3) but shows statistical differences only with HFCW (Fig. 5 and Table S6). Its lower to moderate removal efficiency suggested that the presence of chlorine in its structure makes it highly recalcitrant to biodegradation (Kimura et al. 2005). Some studies reported that high redox potential could promote its removal by aerobic biodegradation (Table 2). In contrast, it has also been suggested that its removal efficiency could be enhanced under anaerobic conditions (biodegradation) (Table 2). Its slightly higher removal in HCW might be due to the co-existence of aerobic and anaerobic conditions in HCW (Fig. 4) (Hijosa-Valsero et al. 2010b; Ávila et al. 2014a; Kahl et al. 2017; Nivala et al. 2019). In FWSCW, it is mainly removed by photodegradation (Table 2).

Tramadol The removal efficiency of tramadol in FWSCW is significantly lower (23 ± 22%) than HFCW (58 ± 42%) (Fig. 5 and Tables 3 and S6). It has been suggested that biological transformation was its main removal pathway in CWs (Table 2). Rühmland et al. (2015) reported that different degradation processes can be involved in the degradation pathway of tramadol as well as its N-demethylated TPs. The first degradation reaction (O-demethylation), which is possibly biologically mediated, can occur under aerobic and anaerobic conditions, though anaerobic condition seems to be more favorable. However, the O-demethylated TPs are rather persistent against biodegradation but amenable to photodegradation, which is possible in FWSCW.

Antibiotics/antiallergic drugs

Trimethoprim The removal efficiency of trimethoprim with HCW was much higher (96 ± 5%) compared with FWSCW (70 ± 21%), HFCW (65 ± 31%), and VFCW (69 ± 27%) (Table 3), and also demonstrates significant differences from them (Fig. 6 and Table S7). It is suggested that microbial degradation is its removal pathway in CWs (Table 2), but its contact with the sediment is the prerequisite for biodegradation (Rühmland et al. 2015). Batt et al. (2006) indicated that it is degraded under aerobic conditions by nitrifying microorganisms. However, Dan et al. (2013) ascribed its removal to lower oxidation-reduction potential (ORP) (ranged from − 258 to − 192 mV) and consequently anaerobic degradation, which indicated activity of methanogenic bacteria (Dušek et al. 2008). Its higher removal in HCW might be due to the coexistence of aerobic and anaerobic conditions in these systems (Sgroi et al. 2018).

Sulfapyridine The removal efficiency of sulfapyridine with FWSCW (79 ± 4%) was significantly lower compared with HFCW (84 ± 3%) and VFCW (84 ± 5%) (Fig. 6 and Tables 3 and S7). However, the considerable removal efficiency in all types of CWs indicated that it is easily removable, though contradictory information is available from different studies for its removal. For instance, Dan et al. (2013) reported its removal by anaerobic biodegradation and in the case of HCW, Conkle et al. (2008) reported that the highest removal was achieved in the aeration basin (74% of the total 99% by HCW), which indicates that it is also biodegradable under aerobic conditions.

Psychiatric drugs/antihypertensive/psychoactive drugs

Venlafaxine The removal efficiency of venlafaxine in FWSCW was significantly higher (43 ± 26%) compared with HFCW (5.1 ± 3.6%) (Fig. 7 and Tables 3 and S8). Its removal in HFCW (though poor) was by biological transformation (Petrie et al. 2018). Rühmland et al. (2015) reported that in VFCW, different degradation processes can be involved in the degradation pathway of venlafaxine as well as its N-demethylated TPs. The first degradation reaction (O-demethylation), which is possibly biologically mediated, can occur under aerobic and anaerobic conditions, though anaerobic appears to be more favorable. However, the O-demethylated TPs are rather persistent against biodegradation but submissive to photodegradation, which is possible in FWSCW. On the other hand, its TPs were detected in the sludge of HFCW, which suggests that partitioning into sludge (sorption) might contribute to its removal. Furthermore, the concentration of venlafaxine in the sludge was below the limit of detection, which indicates that particulate bound venlafaxine (molecular weight 277.41 g mol^{-1}) subsequently settle (Petrie et al. 2018). Its removal is attributed to precipitation in FWSCW and HCW (Breitholtz et al. 2012; Vystavna et al. 2017).

Mirtazapin The removal efficiency of mirtazapin was significantly higher in FWSCW (55 ± 23%) compared with HFCW (8.3 ± 5.0%) (Fig. 7 and Tables 3 and S8). In FWSCW, its removal was recognized by microbial degradation (Breitholtz et al. 2012) and in HFCW (though poor) was ascribed to plant uptake (Petrie et al. 2018).

Caffeine The removal efficiency of caffeine in VFCW was significantly higher (97 ± 2%) compared with HFCW (84 ± 16%), HCW (77 ± 25%), and FWSCW (62 ± 29%) (Fig. 7 and Tables 3 and S8). Similarly, the removal efficiency in FWSCW is significantly lower compared with HFCW. Although its removal efficiency is better in HFCW than HCW but does not reveal significant differences. Analogous to that, its removal efficiency is not significantly different in FWSCW and HCW (Fig. 7 and Table S8). However, its moderate to high removal efficiency by all types of CWs indicates that it is readily biodegradable, which has been proved by several studies (e.g., Chen et al. 2016b; Kahl et al. 2017; He et al. 2018; Nivala et al. 2019). Its efficient removal in CWs was credited to aerobic biodegradation (Table 2). However, some studies related its removal to anaerobic biodegradation as well as adsorption onto carbon rich surfaces of the gravel bed or in the plant roots and uptake by the plants (Table 2).

Beta-blockers/receptor antagonists/lipid regulators

Ranitidine The removal efficiency of ranitidine in FWSCW (79 ± 20%) is more than twice the removal efficiency in HFCW (36 ± 8%) (Table 3), and this difference is statistically significant (Fig. 8 and Table S9). Its removal was attributed to microbial degradation in FWSCW (Breitholtz et al. 2012) and partitioning into sludge (sorption) might contribute to its removal in HFCW (Petrie et al. 2018).

Clofibric acid The removal efficiency of clofibric acid in FWSCW is significantly lower (30 ± 9%) compared with HFCW (49 ± 24%) (Fig. 8 and Tables 3 and S9). Its low removal efficiency in CWs is ascribed to its non-biodegradable and refractory nature (Matamoros et al. 2008a; Dordio et al. 2010; Zhang et al. 2012a, b). Nevertheless, in HFCW, plant uptake has been considered as an important removal pathway (Dordio et al. 2010).

Gemfibrozil The removal efficiency of gemfibrozil in FWSCW is significantly lower (12 ± 2%) compared with HFCW (58 ± 23%) and VFCW (45 ± 9%) (Fig. 8 and Tables 3 and S9), which might be due to the reason that in CWs its major removal mechanism is biodegradation. Several studies attributed its removal to aerobic biodegradation, which

is expected in VFCW (Table 2). However, its moderate removal efficiency in HFCW indicated that anaerobic biodegradation is also responsible for its removal.

Redox manipulation to overcome oxygen transfer limitation

The available evidence indicates several benefits of enhanced oxygen availability in CWs such as (1) improved biodegradation; (2) reduced clogging; (3) enhanced removal of organic matter, nitrogen, and phosphorous; and (4) reduced land area requirement (Zapater-Pereyra et al. 2015; Ilyas and Masih 2017a, b, 2018). Matamoros et al. (2008b) revealed that anoxic (−100 mV < RP < +100 mV) and aerobic (RP > +100 mV) conditions favor the biodegradation of PhCs by promoting the biogeochemical reactions. The biogeochemical reactions, which affect the removal of PhCs in CWs, mainly depend on co-existing oxidation-reduction (redox) processes simultaneously occurring at different scales (e.g., wetland system scale and rhizosphere scale) (Imfeld et al. 2009). Several studies indicated that ORP is the main factor affecting PhCs removal (Huang et al. 2004; Matamoros et al. 2005, 2007). The oxygen supply routes and consumption processes in CWs are illustrated in Fig. 9.

For the removal of PhCs in CWs, aerobic biodegradation was thought to contribute more in the microbial degradation process of some PhCs such as ibuprofen, salicylic acid, acetaminophen, codeine, erythromycin, caffeine, and metoprolol (Table 2). On the other hand, anaerobic biodegradation was thought to be responsible for the removal of naproxen, sulfamethoxazole, sulfapyridine, trimethoprim, atenolol, and bezafibrate (Table 2).

In further contrast, for the removal of diclofenac, some studies reported that high redox potential could promote the removal, while several other studies suggested that the removal efficiency could be enhanced under anaerobic conditions (Table 2). Similarly, the removal of some other PhCs is reported to occur under aerobic and anaerobic conditions such as naproxen, acetaminophen, sulfamethoxazole, sulfapyridine, trimethoprim, caffeine, atenolol, and bezafibrate (Table 2).

The oxygen transfer in HFCW occurs through convection and diffusion from air to surface water and the estimated oxygen transfer rates are in the range of 0.3–3.2 g O_2 m^{-2} day^{-1} (Kadlec and Wallace 2009; Tyroller et al. 2010). On the other hand, in VFCW the oxygen transfer rates are much higher (28–100 g O_2 m^{-2} day^{-1}) due to more influx of oxygen under intermittent loading (Cooper et al. 1999; Weedon 2003). The required aerobic and anaerobic environments to achieve efficient removal of PhCs and their TPs necessitate combining reductive and oxidative processes in CWs (Armenante et al. 1992; Master et al. 2002; Vymazal 2005). For that reason, the researchers are investigating the combinations of different types of CWs to establish HCWs (Fig. 4) for the enhanced removal of different categories of PhCs and their TPs (Table S4). Several studies attributed the higher removal of diclofenac in HCW compared with HFCW and VFCW to the coexistence of aerobic and anaerobic conditions in HCW (Hijosa-Valsero et al. 2010b; Ávila et al. 2014a; Kahl et al. 2017; Nivala et al. 2019). For instance, Nivala et al. (2019) reported that the removal of diclofenac in HCW, VFCW, and HFCW was 77%, 53% and 25%, respectively.

Effect of artificial aeration on the removal of PhCs

The removal efficiency of PhCs in CWs is governed by their configuration, operation and ambient environmental conditions. The removal of PhCs in different types of CWs has already been discussed in this paper. DO is among the most significant parameters contributing in the removal of PhCs by CWs. Therefore, to overcome the oxygen transfer limitation and to enhance the removal of PhCs, some recent studies investigated the effect of AA on the performance of FWSCW, HFCW, VFCW, and HCW (Ávila et al. 2014a;

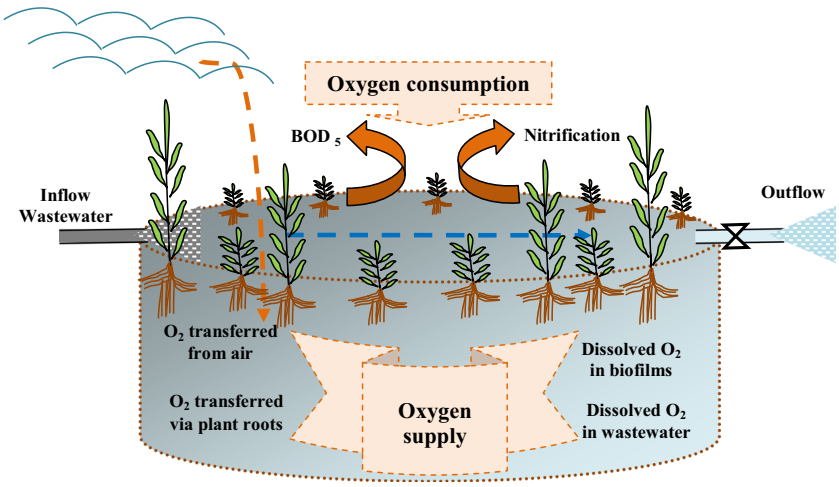

Fig. 9 The oxygen (O_2) supply routes and consumption processes in CWs (adapted from Ilyas and Masih 2017a)

Auvinen et al. 2017a, b; Kahl et al. 2017; Li et al. 2017; Nivala et al. 2019). The removal of studied PhCs in different types of aerated (AA) CWs and non-aerated (NA) CWs (Table 4) is discussed and the comparison is made between the replicates of the same CW system that were designed with and without aeration. Furthermore, the comparative performance of all types of AA-CWs was carried out (Fig. 10).

Diclofenac The removal efficiency of diclofenac in NA-HFCW, NA-VFCW, and NA-HCW was 21 ± 12%, 56 ± 7%, and 56 ± 32%, respectively, which was enhanced in the AA-CWs. Its removal efficiency in AA-HFCW, AA-VFCW, and AA-HCW was 48 ± 22%, 68 ± 9%, and 99%, respectively (Table 4). The enhanced removal efficiency of this moderately biodegradable compound is ascribed to the improved DO level in the AA-CWs (Table 4). In addition to that, the development of various micro-environments in AA-CWs with different physicochemical conditions (aerobic and anaerobic) enabled the contribution of both aerobic and anaerobic metabolic pathways to the removal of PhCs (Ávila et al. 2014a). Although some studies reported that high redox potential could promote the removal, some other studies suggested that the removal efficiency could be enhanced under anaerobic conditions. Furthermore, the higher removal efficiency of diclofenac in AA-HCW compared with AA-HFCW and AA-VFCW (Fig. 10 and Table 4) might not only due to the establishment of aerobic and anaerobic conditions in AA-HCW (Ávila et al. 2014a; Auvinen et al. 2017b; Kahl et al. 2017; Nivala et al. 2019) but also due to longer HRT in HCW considering more than one compartment (Auvinen et al. 2017b).

Ibuprofen The removal efficiency of ibuprofen was significantly enhanced in AA-HFCW (99%) compared with NA-HFCW (23 ± 8%), though its removal efficiency was slightly improved in AA-VFCW (99 ± 1%) compared with NA-VFCW (96 ± 2%). Nevertheless, its removal was almost similar in AA-HFCW and AA-VFCW (Fig. 10). The enhanced removal of this readily biodegradable compound was attributed to the improved DO level in the AA-CWs, which contributed to its microbial degradation under oxic conditions (Ávila et al. 2014a; Kahl et al. 2017; Nivala et al. 2019), which was more explicit in the case of AA-HFCW compared with NA-HFCW (anaerobic) (Kahl et al. 2017; Nivala et al. 2019) (Table 4).

Naproxen The removal efficiency of naproxen was low in NA-HFCW (28 ± 6%), whereas, in AA-HFCW, it was removed up to 99 ± 1%. In contrast, its removal efficiency was slightly improved in AA-VFCW (94 ± 1%) compared with NA-VFCW (89 ± 2%) (Table 4). Nevertheless, the removal of this moderately biodegradable compound in AA-HFCW and AA-VFCW was higher and somewhat similar (Fig. 10), which was attributed to the improved DO level in the AA-CWs, mainly in the case of AA-

Table 4 Removal efficiency (mean % and standard deviation) of PhCs in different types of aerated (AA) and non-aerated (NA) CWs

Parameter/ pharmaceutical	NA-FWSCW/AA-FWSCW	NA-HFCW/AA-HFCW	NA-VFCW/AA-VFCW	NA-HCW/AA-HCW	Major removal mechanism
DO (mg L^{-1})	6.0/na	1.6 ± 1.3/8.9 ± 0.7	4.5 ± 0.7/7.5 ± 1.1	2.3 ± 2.4/11	
Diclofenac	na	21 ± 12/48 ± 22	56 ± 7/68 ± 9	56 ± 32/99	Biodegradation (aerobic/anaerobic)
Ibuprofen	na	23 ± 8/99	96 ± 2/99 ± 1	na	Biodegradation (aerobic)
Naproxen	na	28 ± 6/99 ± 1	89 ± 2/94 ± 1	na	Biodegradation (aerobic/anaerobic)
Acetaminophen	99/97	na	na	na	Biodegradation (aerobic/anaerobic)
Tramadol	na	6.8/1.6	na	na/99.9	Biological transformation
Caffeine	82/94	89 ± 8/99.5 ± 0.7	97 ± 1/99	na	Biodegradation (aerobic/anaerobic)
Carbamazepine	na	12 ± 9/11 ± 11	− 8.5 ± 0.7/− 2.5 ± 2.1	27 ± 20/94	Adsorption/sorption
Atenolol	na	na/96 ± 1	na	73 ± 37/98	Biodegradation (aerobic/anaerobic)
Metoprolol	na	na	na	99/98	Biodegradation (aerobic)
Sotalol	na	24 ± 6/32 ± 13	na	82/99	Biodegradation (aerobic)

Data is taken from: Ávila et al. (2014a); Auvinen et al. (2017a, b); Li et al. (2017); Kahl et al. (2017); Nivala et al. (2019). The enhanced removal is explicit in the case of AA-FWSCW (caffeine), AA-HFCW (diclofenac, ibuprofen, naproxen, caffeine and sotalol), AA-VFCW (diclofenac, naproxen and carbamazepine), and AA-HCW (diclofenac, carbamazepine and sotalol) compared with their corresponding NA-CWs

AA artificial aeration, *NA* non-aerated, *na* not available

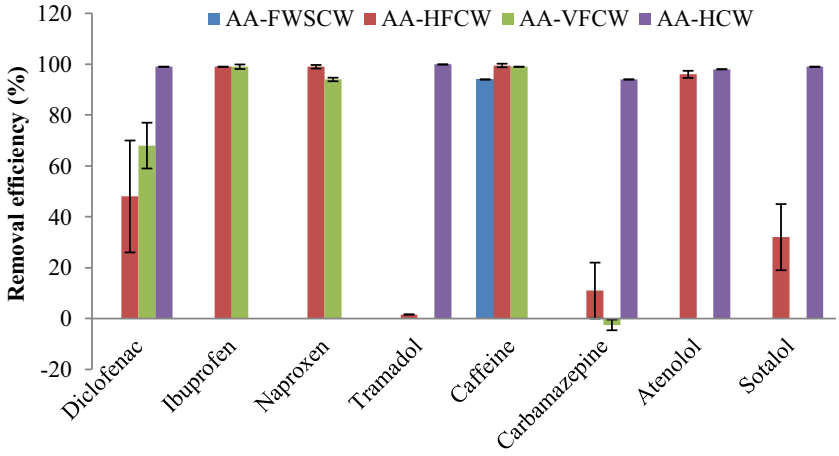

Fig. 10 Removal efficiency (mean and standard deviation) of PhCs in different types of aerated CWs. Artificial aeration (AA). Data is taken from Ávila et al. (2014a); Auvinen et al. (2017a, b); Li et al. (2017); Kahl et al. (2017); Nivala et al. (2019)

HFCW relative to NA-HFCW (anaerobic) (Kahl et al. 2017; Nivala et al. 2019) (Table 4).

Acetaminophen The removal of acetaminophen was almost similar in AA-FWSCW (97%) and NA-FWSCW (99%) (Table 4). This might be due to the fact that it is biodegradable under both aerobic and anaerobic conditions (Li et al. 2017).

Tramadol The removal efficiency of tramadol was very low in NA-HFCW and AA-HFCW (6.8% and 1.6%, respectively) (Table 4). This could be due to daily concentration fluctuations of the influent and the concentrating effect of evapotranspiration, which leads to its low removal (Auvinen et al. 2017a). On the other hand, the almost complete removal of tramadol (99.9%) was achieved in AA-HCW (Fig. 10 and Table 4), which might be due to the establishment of both aerobic and anoxic conditions facilitating the removal of variety of PhCs (Auvinen et al. 2017b) and due to the increase in HRT from 1.0 day in AA-HFCW to 6.0 days in HCW, even when AA was not applied, indicating that the anoxic pathway is preferred but adequate HRT is necessary (Auvinen et al. 2017b).

Caffeine The removal efficiency of caffeine was improved in AA-FWSCW, AA-HFCW, and AA-VFCW (94%, 99.5 ± 0.7%, and 99%, respectively) compared with NA-FWSCW, NA-HFCW, and NA-VFCW (82%, 89 ± 8%, and 97 ± 1%, respectively) (Table 4). The enhanced removal of this readily biodegradable compound was attributed to the higher DO level in AA-HFCW and AA-VFCW (Fig. 10), which might contribute to enhance the biodegradation process, which is one of its major degradation mechanisms (Table 4).

Carbamazepine The removal efficiency of carbamazepine was very low in AA-HFCW and NA-HFCW (11 ± 11% and 12 ± 9%, respectively). However, it was not removed in AA-VFCW and NA-VFCW and negative removal was observed (− 8.5 ± 0.7% and − 2.5 ± 2.1%, respectively) (Table 4). The increase in concentration during biological treatment is attributed to the biotransformation of its TPs (Petrie et al. 2018) as well as the UV irradiation might has the ability to convert its hydroxyl TPs to the parent compound (Miao et al. 2005). The low removal could be due to the fact that in CWs the major fraction of this compound was removed by adsorption onto the available organic surfaces, sorption and reductive transformation (Kahl et al. 2017; Nivala et al. 2019). The poor removal in NA-HCW (27 ± 20%) (Table 4) is attributed to the non-biodegradable and refractory nature of this compound. Its higher removal in AA-HCW (94%) compared with AA-HFCW and AA-VFCW (Fig. 10) might be due to the establishment of both aerobic and anoxic conditions enabling the removal of range of PhCs. Additionally, in AA-HCW the long HRT (10 days) compared with AA-HFCW (1.0 day) and the use of LECA as a substrate material might contribute to its efficient adsorption, which is its major removal pathway in CWs (Auvinen et al. 2017b).

Atenolol The removal efficiency of atenolol in AA-HFCW was 96 ± 1% (Auvinen et al. 2017a). In AA-HCW, its high removal efficiency (98%) was achieved (Auvinen et al. 2017b). In the case of NA-HCW, Conkle et al. (2008) also reported the highest removal efficiency of atenolol in the oxic basin of NA-HCW (80% of the total 99% by NA-HCW). The removal of atenolol was slightly better in AA-HCW and AA-HFCW (98% and 96 ± 1%, respectively) (Fig. 10). The comparatively better removal in AA-HCW than in AA-HFCW might be due to the enhancement in its biodegradation under both aerobic and anoxic conditions. However, the degradation was faster when DO level was higher (Pomiès et al. 2015) (Table 4).

Metoprolol The higher removal of metoprolol (98%) was achieved in AA-HCW (Auvinen et al. 2017b). Its removal is attributed to aerobic biodegradation (Table 2). Also, in the

case of NA-HCW, Conkle et al. (2008) reported its highest removal in the oxic basin of NA-HCW (88% of the total 99% by NA-HCW) (Table 4). Although the application of AA improved the level of DO in AA-HCW compared with NA-HCW (Table 4), its higher and almost similar removal in NA-HCW and AA-HCW might be due to longer HRT in HCW considering more than one compartment (Conkle et al. 2008; Auvinen et al. 2017b).

Sotalol Although the removal efficiency of sotalol was very low, it was improved in AA-HFCW (32 ± 13%) compared with NA-HFCW (24 ± 6%) (Table 4). This compound has been classified among the most resistant to biodegradation (Oulton et al. 2010; Auvinen et al. 2017a). However, its high removal efficiency was observed in AA-HCW (99%), which is consistent with the high removal in the oxic basin of NA-HCW (only 20% in a FWSCW of the total 82% by NA-HCW) (Conkle et al. 2008) (Table 4). Its removal was much higher in AA-HCW compared with AA-HFCW. In AA-HFCW, the high organic load (107 g COD m^{-2} day^{-1}) compared with AA-HCW (22 g COD m^{-2} day^{-1}) might restrict the removal. Its removal efficiency depends on AA and it exhibits positive correlation with the effluent DO. However, its removal was not dependent on AA when HRT was increased from 2.0 to 6.0 days. In general, anoxic biotransformations are considered slower than the oxic ones; therefore, longer HRT is required to obtain the same treatment efficiency (Auvinen et al. 2017b).

Synthesis of available knowledge on TPs

The removal of some PhCs in CWs takes place by the formation of their TPs. Occasionally, the TPs are also removed in CWs leading to the efficient removal of PhCs. However, the removal of all TPs is not possible and sometimes the negative removal is expected, since these are formed in the CWs (Table 5). Thus, with the identification of TPs in different types of CWs, the routes of PhCs biotransformation as well as the involvement of complex conjugation/deconjugation processes in their removal can be determined. Nevertheless, the negative removal of PhCs (parent compounds) could also be due to analytical errors in the case of extremely low influent and effluent concentrations (close to detection limit) (e.g., Breitholtz et al. 2012; Petrie et al. 2018) besides the retransformation of persistent or nonbiodegradable TPs to their parent compounds (e.g., Breitholtz et al. 2012; Vymazal et al. 2017; Petrie et al. 2018).

Diclofenac (4-hydroxydiclofenac) The removal efficiency of 4-hydroxydiclofenac in FWSCW, HFCW, and HCW was very low (29%) and also negative removal was observed (Table 5) (influent concentration: 0.01 μg L^{-1}; effluent concentration: 0.23 μg L^{-1}) (Hijosa-Valsero et al. 2016). It has been reported that the main TPs of diclofenac are its hydroxylated forms, originated in humans and other mammals by hydroxylation reactions (Stierlin and Faigle 1979; Stülten et al. 2008). The detection of 4-hydroxydiclofenac in the effluents designates that the hydroxylation process (aerobic reaction) of diclofenac took place inside the CWs (Hijosa-Valsero et al. 2016). It has been reported that 4-hydroxydiclofenac is one of the most abundant TPs of diclofenac in wastewater effluents (Stülten et al. 2008).

Ibuprofen (1-hydroxyibuprofen; 2-hydroxyibuprofen; carboxyibuprofen) The main TPs of ibuprofen are its hydroxylated forms, originated in humans and other mammals by hydroxylation reactions (Buser et al. 1999). Accordingly, 2-hydroxyibuprofen and 1-hydroxyibuprofen were the most abundant TPs found in FWSCW, HFCW, and HCW, followed by carboxyibuprofen (Hijosa-Valsero et al. 2016; Březinova et al. 2018; He et al. 2018). The removal efficiency of 1-hydroxyibuprofen in FWSCW, HFCW, VFCW, and HCW was 41 ± 24%, 13 ± 24%, 99%, and 12 ± 6%, respectively. The removal efficiency of 2-hydroxyibuprofen in FWSCW, HFCW, and HCW was 40 ± 29%, − 9 ± 24%, and 30 ± 8%, respectively. The removal efficiency of carboxyibuprofen in FWSCW, HFCW, VFCW, and HCW was 84 ± 14%, 67 ± 19%, 99%, and 72 ± 37%, respectively (Table 5). Generally, ibuprofen and its TPs are easily removed in WWTPs and CWs (Onesios et al. 2009; Hijosa-Valsero et al. 2016). However, the higher removal efficiency of ibuprofen (79 ± 24%) and its TPs in VFCW compared with HFCW (53 ± 27%) (Tables 3 and 5) indicates the negative or low removal of its TPs in HFCW, which might retransform to parent compound. This further can be explained by the fact that in VFCW the aerobic biodegradation mainly contributes to the microbial degradation process of ibuprofen, thus, removal increases under oxic conditions (Matamoros et al. 2007; Březinova et al. 2018).

Naproxen (O-desmethylnaproxen) The removal of naproxen was higher in VFCW followed by HFCW, HCW, and FWSCW, which might be that it is readily biodegradable and substrate aeration by the plants is enough for its biodegradation (Tables 2 and 3). However, the removal in HFCW indicated that anaerobic biodegradation is also responsible for its removal (Table 2). The cleavage in naproxen during the mammalian metabolism and transformation reactions caused by fungi under aerobic conditions results in the formation of O-desmethylnaproxen (He and Rosazza 2003), the major TP of naproxen. It was only detected in the influent wastewater of FWSCW, HFCW, and HCW (0.5 μg L^{-1}) (Hijosa-Valsero et al. 2016) and higher removal efficiency was achieved in FWSCW, HFCW, and HCW (96% in all) (Table 5). Lahti and Oikari (2011) reported the complete removal of naproxen under aerobic conditions, after 14 days of incubation, which indicated that O-desmethylnaproxen was possibly formed but was efficiently distorted. In contrast, under anaerobic

Table 5 Removal efficiency (mean % and standard deviation) of 19 studied TPs in different types of CWs

Transformation products	FWSCW (*n*)	HFCW (*n*)	VFCW (*n*)	HCW (*n*)
4-Hydroxydiclofenac	− 924 ± 965 (3)	− 436 ± 657 (2)	NA	− 386 ± 586 (2)
1-Hydroxyibuprofen	41 ± 24 (3)	13 ± 24 (6)	99 (1)	12 ± 6 (2)
2-Hydroxyibuprofen	40 ± 29 (3)	−9 ± 24 (2)	NA	30 ± 8 (2)
Carboxyibuprofen	84 ± 14 (3)	67 ± 19 (6)	99 (1)	72 ± 37 (2)
O-Desmethylnaproxen	96 (3)	96 (2)	NA	96 (2)
3-Ethylbenzophenone	− 1067 ± 289 (3)	− 2650 ± 2475 (2)	NA	− 2400 ± 2121 (2)
Dihydroketoprofen	− 110 ± 156 (3)	− 150 ± 71 (2)	NA	− 150 ± 71 (2)
O-Desmethyltramadol	− 16 ± 6 (2)	11 ± 6 (3)	− 17 ± 39 (2)	NA
N-Desmethyltramadol	33 (1)	12 ± 1 (3)	47 ± 37 (2)	NA
N,O-didesmethyltramadol	− 11 (1)	NA	− 9 ± 34 (2)	NA
N-Acetylsulfamethoxazole	83 ± 17 (4)	96 ± 4 (2)	18 ± 71 (2)	95 ± 4 (2)
10,11-Dihydro-10,11-dihydroxycarbamazepine	18 (1)	NA	19 ± 5 (2)	NA
10,11-Dihydro-10-hydroxycarbamazepine	72 (1)	NA	73 ± 28 (2)	NA
2-Hydroxycarbamazepine	38 (1)	NA	15 ± 1 (2)	NA
3-Hydroxycarbamazepine	42 (1)	NA	19 ± 12 (2)	NA
Carbamazepine 10,11-epoxide	NA	− 33 ± 29 (3)	NA	NA
O-Desmethylvenlafaxine	40 (1)	0.0 (3)	15 ± 8 (2)	NA
N-Desmethylvenlafaxine	59 (1)	NA	32 ± 27 (2)	NA
N,O-Didesmethylvenlafaxine	37 (1)	NA	10 ± 6 (2)	NA

n number of observations, *NA* not available

conditions, O-desmethylnaproxen was detected after 14 days, and after 97 days of incubation, 28% of the initial naproxen was detected as O-desmethylnaproxen, which indicated that under anaerobic conditions O-desmethylnaproxen was relatively persistent.

Ketoprofen (3-ethylbenzophenone; dihydroketoprofen) In FWSCW, the main process is photodegradation for the removal of ketoprofen (Andreozzi et al. 2003; Lin and Reinhard 2005; Pereira et al. 2007). In HFCW, VFCW, and HCW, biodegradation is considered as its main elimination pathway (Tixier et al. 2003; Zhang et al. 2012a; Chen et al. 2016b; Francini et al. 2018; Zhang et al. 2018). The major TP of ketoprofen is 3-ethylbenzophenone, which is formed by its rapid decomposition under UV irradiation (Kosjek et al. 2011). 3-Ethylbenzophenone was only detected in effluent water and in FWSCW, HFCW, and HCW, its concentration was 0.3, 0.9, and 0.8 μg L^{-1}, respectively. Therefore, it shows a negative removal in CWs (Table 5). The highest concentrations of 3-ethylbenzophenone were detected in the unplanted systems, which indicated the occurrence of photodegradation processes when water is exposed directly to sunlight (Hijosa-Valsero et al. 2016). Dihydroketoprofen is another TP of ketoprofen, which was detected in influents of FWSCW, HFCW, and HCW at trace levels (0.1 μg L^{-1}), but its concentrations were generally higher in the effluents (0.3 μg L^{-1}) (Hijosa-Valsero et al. 2016). It has been established that ketoprofen can undergo hydroxylation of the aromatic ring at 3 or 4 positions and reduction of the keto functional group to a hydroxyl group results in the formation of dihydroketoprofen in the human body (Skordi et al. 2004). The similar chemical process might have occurred in CWs (Hijosa-Valsero et al. 2016).

Tramadol (O-desmethyltramadol; N-desmethyltramadol; N,O-didesmethyltramadol) It has been reported that approximately 30% of a tramadol dose is excreted in the urine unchanged and 60% of the dose is excreted as 11 different TPs (Pubchem 2017). O-desmethyltramadol, N-desmethyltramadol, and N,O-didesmethyltramadol are the most studied TPs of tramadol. Wick et al. (2009) suggested that biological transformation was the main removal pathway of tramadol in the conventional wastewater treatment. Rühmland et al. (2015) reported that different degradation processes can be involved in the degradation pathway of tramadol and N-desmethyltramadol. The first degradation reaction (O-demethylation) in which O-desmethyltramadol is formed is possibly biologically mediated and can occur under aerobic and anaerobic conditions, though anaerobic seems to be more favorable. This can be seen by the removal efficiency of tramadol in HFCW (58 ± 42%), VFCW (46 ± 42%), and FWSCW (23 ± 22%) (Table 3). The O-demethylated products are rather persistent against biodegradation but amenable to photodegradation, which is possible in FWSCW. This can be explained by the poor removal of O-desmethyltramadol in HFCW (11 ± 6%) (Table 5) and VFCW (ranged from −

44 to 11%) (Table S3), and negative removal in FWSCW (−16 ± 6%) (Table 5), where the effluent concentration (1.4 ± 0.6 μg L^{-1}) increased compared with influent concentration (1.2 ± 0.4 μg L^{-1}). Similarly, the negative removal (formation) of N,O-didesmethyltramadol was observed in FWSCW (influent concentration 0.9 μg L^{-1}; effluent concentration 1.0 μg L^{-1}) (Table S1) and VFCW (influent concentration: 0.9 μg L^{-1}; effluent concentration: 1.2 μg L^{-1}) (Table S3). This can be elucidated by the removal efficiency of N-desmethyltramadol in VFCW (47 ± 37%), FWSCW (33%), and HFCW (12 ± 1%) (Table 5), which is possibly transformed into N,O-didesmethyltramadol.

Sulfamethoxazole (N-acetylsulfamethoxazole) N-acetylsulfamethoxazole is the major TP of sulfamethoxazole. The removal efficiency of N-acetylsulfamethoxazole was higher in HFCW (96 ± 4%), HCW (95 ± 4%), and FWSCW (83 ± 17%) (Table 5). However, its negative removal to moderate was achieved in VFCW (ranged from − 33 to 68%) (Table S3). Its removal is consistent with the removal of sulfamethoxazole in different types of CWs (Table 3). This indicated that N-acetylsulfamethoxazole undergoes anaerobic degradation more effectively compared with aerobic degradation in CWs (Hijosa-Valsero et al. 2011a; Rühmland et al. 2015).

Carbamazepine (10,11-dihydro-10,11-dihydroxycarbamazepine; 10,11-dihydro-10-hydroxycarbamazepine; 2-hydroxycarbamazepine; 3-hydroxycarbamazepine; carbamazepine 10,11-epoxide) Carbamazepine was poorly removed in VFCW (40 ± 20%), FWSCW (31 ± 22%), HFCW (30 ± 24%), and HCW (27 ± 20%) (Table 3). The lower removal of carbamazepine is attributed to the non-biodegradable and refractory nature of this compound (e.g., Rühmland et al. 2015; He et al. 2018; Nivala et al. 2019). This is also explicit by the low or negative removal of its TPs. For instance, the negative removal of carbamazepine 10,11-epoxide was observed in HFCW (− 33 ± 29%) (influent concentration: 0.2 μg L^{-1}; effluent concentration: 0.3 ± 0.1 μg L^{-1}) as well as low removal of 10,11-dihydro-10,11-dihydroxycarbamazepine in VFCW (19 ± 5%) and FWSCW (18%) (Table 5). The major fraction of removal of carbamazepine in CWs is by adsorption onto the available organic surfaces and aerobic degradation (Table 2). The poor removal or increase in its concentration during biological treatment is attributed to the biotransformation of its TPs into parent compound (Petrie et al. 2018), which can be seen by the moderate removal efficiency of 10,11-dihydro-10-hydroxycarbamazepine in VFCW (73 ± 28%) and FWSCW (72%) (Table 5). It may also be possible that UV irradiation has the ability to convert hydroxyl TPs of carbamazepine to the parent compound (Miao et al. 2005), which can be seen by the comparatively better removal efficiency of 2-hydroxycarbamazepine and 3-hydroxycarbamazepine in FWSCW (38% and 42%, respectively) compared with VFCW (15 ± 1% and 19 ± 12%, respectively) (Table 5).

Venlafaxine (O-desmethylvenlafaxine; N-desmethylvenlafaxine; N,O-didesmethylvenlafaxine) The removal of venlafaxine (though poor) in HFCW and VFCW was by biological transformation (Table 2) and O-desmethylvenlafaxine, N-desmethylvenlafaxine, and N,O-didesmethylvenlafaxine are the TPs of venlafaxine, which indicates that different degradation processes can be involved in the degradation pathway of venlafaxine and its TP, N-desmethylvenlafaxine (Rühmland et al. 2015). The first degradation reaction (O-demethylation) in which O-desmethylvenlafaxine is formed is possibly biologically mediated and can occur under aerobic and anaerobic conditions, while anaerobic condition seems to be more favorable (Gasser et al. 2012). This can be explained by the higher removal efficiency of venlafaxine in HCW (63 ± 4%) compared with FWSCW (43 ± 26%), VFCW (40 ± 21%), and HFCW (5.1 ± 3.6%) (Table 3). The removal efficiency of N-desmethylvenlafaxine was moderate in FWSCW (59%) but poor in VFCW (32 ± 27%) (Table 5). However, the O-demethylated products (O-desmethylvenlafaxine) are rather persistent against biodegradation but submissive to photodegradation, which is possible in FWSCW. This can be seen by the better removal efficiency of O-desmethylvenlafaxine in FWSCW (40%) compared with VFCW (15 ± 8%) and HFCW (0.0%) as well as by the removal efficiency of N,O-didesmethylvenlafaxine in FWSCW (37%) compared with VFCW (10 ± 6%) (Table 5).

Conclusions

A large number of published studies on the removal of PhCs by CWs provided the basis of this comprehensive assessment, which is based on critical review of literature and statistical analysis of available data from peer reviewed studies. The following specific conclusions were inferred from this research:

1. All types of studied CWs have demonstrated a good capacity for removing a variety of PhCs. However, HCW performed better followed by VFCW, HFCW and FWSCW. Various processes are involved in PhCs removal by CWs such as aerobic and/or anaerobic biodegradation, adsorption and/or sorption, plant uptake and photodegradation. Biodegradation is the major removal mechanism in most of the studied PhCs (16 out of 29 PhCs) and aerobic biodegradation, expected in VFCW, is more efficient compared with anaerobic biodegradation taking place in HFCW. In FWSCW, the main removal

pathway is photodegradation and only few PhCs (diclofenac, ketoprofen, naproxen, and clarithromycin) are removed by this process. The comparatively better removal of several PhCs in HCW might be due to the co-existence of aerobic and anaerobic conditions and longer HRT in HCW, which enhance the removal of PhCs (e.g., diclofenac, acetaminophen, sulfamethoxazole, sulfapyridine, trimethoprim, and atenolol), which are removed under both conditions and adsorption/sorption processes.

2. Due to redox manipulation with AA, the improvement in DO enhances the removal of PhCs, which are better removed under aerobic conditions. Generally, anoxic biotransformations are slower than the oxic ones. However, the high performance of aerated CWs could be due to the establishment of various micro-environments with different physicochemical conditions (aerobic and anaerobic) that would allow the contribution of both aerobic and anaerobic metabolic pathways in the removal of PhCs. This is explicit by the enhanced removal of AA-FWSCW (caffeine), AA-HFCW (diclofenac, ibuprofen, naproxen, caffeine, and sotalol), AA-VFCW (diclofenac, naproxen, and carbamazepine), and AA-HCW (diclofenac, carbamazepine, and sotalol) compared with their corresponding NA-CWs.
3. The removal of some of the PhCs in CWs takes place by the formation of their TPs. The removal of eight of the studied PhCs (diclofenac, ibuprofen, naproxen, ketoprofen, tramadol, sulfamethoxazol, carbamazepine, and venlafaxine) through the routes of biotransformation shows that the nature of TPs plays a major role in the removal of PhCs. If the TPs are persistent or non-biodegradable, then they retransform into their parent compound leading to the poor or negative removal of PhCs, which verify the contribution of complex conjugation/deconjugation processes in their removal.

Future research needs

The data and results presented in this research provide a sound basis for comparative analysis and selection of CWs for practical applications for the treatment of wastewater containing PhCs. Furthermore, several new insights propounded in this review could be instructive for improved understanding and guiding future research. The following research needs are identified.

1. The better performance of HCW compared with single settings (e.g., VFCW, HFCW, and FWSCW) demonstrates the high potential for its practical applications for PhCs removal. However, HCW are a combination of different types of conventional CWs such as VFCW+HFCW, HFCW+VFCW, VFCW+VFCW, HFCW+HFCW, HCW including FWSCW, and also multistage of more than two types of CWs. Therefore, further research is needed regarding the evaluation of best possible integrated design of CWs to ensure various removal processes necessary to remove specific PhCs and TPs in a given context.
2. Different sampling strategies could be examined to reflect on the redox conditions across various locations within a CW at different time resolution. This could further help to correlate the redox conditions with the removal efficiency of PhCs and their TPs in different types of CWs. Although ORP emerged as a crucial parameter in assessment of oxic/anoxic conditions in CWs that facilitate in the PhCs removal processes, it was reported by few studies. Therefore, attention should be given to the estimation of ORP of CWs in the future research involving removal of PhCs.
3. It is suggested that the application of AA establishes various micro-environments (aerobic and anaerobic conditions) in CWs, which contributes to both aerobic and anaerobic metabolic pathways in the removal of PhCs. To date, limited research is conducted on the application of AA; therefore, further research is needed to elucidate the type of aeration (e.g., intermittent or continuous) beneficial to generate such conditions while contributing to improve the quality of effluent water.
4. The removal of some of the PhCs takes place by the formation of their TPs and the nature of these TPs (persistent or non-biodegradable/biodegradable) plays a key role in their removal. However, limited research is conducted on the formation of TPs in CWs as well as TPs of only eight PhCs are investigated. Therefore, more studies are needed to affirm the behavior (formation and removal) of TPs in CWs indicated by a limited number of studies. Similarly, more research is required to study the formation and nature of TPs of the examined PhCs.

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