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Application of phytotechnology in alleviating pharmaceuticals and personal care products (PPCPs) in wastewater: Source, impacts, treatment, mechanisms, fate, and SWOT analysis

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ABSTRACT

Pharmaceuticals and personal care products (PPCPs) are over-consumed daily, and are transported along several pathways, including municipal and industrial wastewater to the aquatic environment. PPCPs are considered a type of emerging pollutants and have received alarming concern in recent years. In this review, the available and current methods of conventional and green technology used are summarised and compared with phytotechnology prospective in wastewater treatment field to combat the alarming existence of PPCPs. In applying phytoremediation for PPCPs, the effects of numerous operating parameters, including retention time, concentration, rhizosphere, flow system, and plant species, are considered. The plant mechanism of removing PPCPs from wastewater and the fate of the PPCPs after treatment are also discussed. This review discusses the opportunities to eliminate the negative ecological effects of PPCP pollution and how to sustainably protect environment and life on earth from PPCP pollution through treatment technologies, as well as the challenges in saving ecosystems from PPCP pollution via phytotechnology through the strengths, weaknesses, opportunities, and threats (SWOT) analysis. The results confirmed the concerns about the widespread of PPCPs and the possibility of their transformation into pseudo-persistent pollutants. At the same time, the promising potential of CWs in removing a wide range of PPCPs has been confirmed. Intensifications such as forced aeration have enhanced the removal efficiency of biodegradable PPCPs at subsurface horizontal-flow systems. The influence of plants and hydraulic retention time on the removal process was evident.

1. Introduction

In developing countries, about 80% of domestic sewage is directly released into surface water bodies without prior treatment (World Water Assessment Programme, 2009; Bi et al., 2019), leading to the accumulation of high levels of pollutants including heavy metals, organic matter and nutrients in the receiving ecosystems. Polluted water bodies has lost much of their essential ecosystem roles including water supply, nutrient cycling and recreational values (Bi et al., 2019). In addition, low water quality is the culprit contributes to diseases around the world (Bi et al., 2019), and more than 800,000 mortality annually was recorded due to gastrointestinal illnesses resulting from unsafe drinking water (World Health Organization, 2017; Bi et al., 2019). The safety of drinking water is closely connected to the existence and amounts of various

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micropollutants in water bodies (Xu et al., 2019b). Micropollutants comprise a wide range of classes such as pharmaceuticals, surfactants, personal care products, pesticides, and industrial chemicals, etc. (Sutar et al., 2019). Beside the difficulty of their removal, the occurrences of micropollutants in water sources has become a critical issue for the safety of drinking water due to their adverse health effects, which may extend to neurotoxicity, developmental and reproductive toxicity, and metabolic interference (Xu et al., 2019b).

Pharmaceuticals and personal care products (PPCPs), which cover various groups of organic chemicals (such as antibiotics, hormones and musk fragrances), are a group of emerging organic contaminants (EOCs) (Chopra and Kumar, 2018) that are continuously discharged into the environment due to their extensive consumption in daily life (Ávila and García, 2015). According to the United States Environmental Protection Agency (US EPA), PPCPs are defined as ‘‘any product used by individuals for personal health or cosmetic reasons or used by agribusiness to enhance growth or health of livestock’’ (US EPA, 2012). In fact, this pollutant class comprises thousands of different compounds (Cizmas et al., 2015). Recently, micropollutants, including PPCPs, have received increased interest due to their toxicity and persistence in cells. Prolonged exposure to PPCPs may adversely affect the aquatic environment and human health. PPCPs are released into the environment through several ways such as human excretion, improper disposal and discharge from manufacturing sites and then reach sewage treatment plants, which are considered the major source for PPCPs in waterbodies (Li et al., 2019b).

Most pharmaceutical substances are specifically designed to be sufficiently water soluble since they are usually assumed to function in that medium, and this represents a major difference between pharmaceuticals and other traditional organic pollutants (including pesticides and explosives). Pharmaceuticals commonly pass through digestion system of humans or animals before reaching the environment. The pre-exposure of such substances to a special biotic environment and to biochemical metabolism makes them reach the ecosystem in a more modified and stable form in terms of biotic transformation or degradation. As for pharmaceuticals that remain unchanged at the end of the pathway, they are often greatly resistant to biotic transformation or degradation in ecosystems (Dordio and Carvalho, 2018). The persistent release of PPCPs may lead to a series of individualistic, synergistic, or antagonistic effects, often related to long-term toxicity to human beings and aquatic communities, including carcinogenic or teratogenic and endocrine disrupting effects, in addition to the emergence of antibiotic resistance (Sutar et al., 2019). Pollution generated by pharmaceutical residues has been characterised as a real threat to the environment by various countries, but, unfortunately, to this day, no regulatory levels of these toxic compounds have been set for the effluent discharges from industrial facilities and WWTPs into the ecosystem (Shetty and Gupta, 2019).

Due to the diverse structures and the biological accumulation of most micropollutants, their degradation represents an environmental challenge that may contribute negative impacts on human health and the environment (Sutar et al., 2019). Conventional wastewater treatment plants (WWTPs) are insufficient to remove PPCPs (Ávila and García, 2015; Gorito et al., 2017; Rodriguez-Narvaez et al., 2017; Yang et al., 2017; Kafaei et al., 2018; Tarpani and Azapagic, 2018); additionally, the excreted metabolites and by-products of PPCPs may contribute to the emergence of secondary pollutants that might be subsequently modified in receiving water bodies (Yang et al., 2017). Advanced treatment technologies, including adsorption, membrane filtration, and advanced oxidation, have been confirmed to have high potential for removing residual PPCPs since PPCPs can eventually be eliminated via these processes. However, the excess energy and material requirements, as well as the related potential environmental impacts of advanced wastewater treatment technologies, make quantification of their impacts on the removal of PPCPs in WWTPs necessary (Li et al., 2019b). Thus, despite the promising techniques available for removing PPCPs, there is still a growing need to adopt an effective low-cost alternative method using natural resources for the treatment of wastewater (Kaur et al., 2019).

Phytoremediation fundamentally depends on the naturally occurring processes by which plants and their microbial rhizosphere flora can efficiently degrade and/or segregate both organic and inorganic contaminants (Pilon-smits, 2005; Tripathi et al., 2020). Due to the action of enzymes excreted by the plants, organic pollutants may be converted to less toxic compounds or may be embedded as unattainable forms in plant tissues. Furthermore, during transformation or metabolic degradation, complete mineralisation may be achieved, producing nontoxic inorganic end-products, including CO_2 and H_2O. Phytoremediation is affordable, nonintrusive, and effective technology of remediating soils and wastewater (Sutar et al., 2019). The use of constructed wetlands (CWs) for wastewater treatment has become more significant due to their low cost and environmentally friendly features (Fadhil and Al-Baldawi, 2019; Herath and Vithanage, 2015).

CWs offer a conducive environment to support the growth of living organisms, such as bacteria, yeast, fungi, and algae, which, in turn, lead to the biodegradation process of pollutants in wastewater (Fadhil and Al-Baldawi, 2020; Saeed and Sun, 2012). CWs are complex systems comprising water, substrates, plants, and native microorganisms. Wetland plants are able to grow in wet soil under water (Herath and Vithanage, 2015) and under oxygen deficient conditions (Saeed and Sun, 2012). Triple approach encompassing physical, chemical, and biological processes, via sorption and sedimentation, photodegradation, volatilisation, plant sorption, and microbial degradation, may occur simultaneously, contributing to the remove several types of contaminants (Gorito et al., 2017). This technology has been rapidly developed in recent decades through the utilisation of various designs and augmentations that improve effluent water quality (Wu et al., 2015). Under optimised operating conditions, CWs can attain higher proficiencies by promoting the action of their components (vegetation, microbial communities and support media) (Dordio and Carvalho, 2018), which are mainly influenced by hydraulic, operating, and environmental conditions (Wu et al., 2015).

To date, there are many review articles on PPCPs, but they are mostly focused on each aspect of the process (treatment, design, impact, fate) and not on combining all items under one comprehensive review. Recently published reviews have considered the elimination of PPCPs in CWs in various ways. Ilyas and van Hullebusch (2020a) critically assessed the efficiency of CWs for removing pharmaceutical products, investigated the effect of artificial aeration and touched upon the transformation products formed during treatment. In other studies, the researchers explored the role of design and operational factors in addition to the removal mechanism and the effect of seasonal variation in removing pharmaceutical contaminants (Ilyas and van Hullebusch, 2019) and personal care products (Ilyas and van Hullebusch, 2020b). Ilyas et al. (2020) conducted a comprehensive assessment for the removal of pharmaceutical contaminants in CWs and discussed the available evidence about their removal mechanisms and their environmental risks. Liu et al. (2019b) discussed the performance of CWs for removing antibiotics and antibiotic resistance genes, and also investigated the synchronous removal of nitrogen, phosphorus, COD and antibiotics in CWs. Nguyen et al. (2019) explored the role of plant-bacteria (rhizo- and endophytic) partnerships for the removal of PPCPs. Rabello et al. (2019) studied the relationship between the presence of PPCPs and the operational conditions of CWs. In this study, the authors primarily intend to explore the recent developments related to PPCPs and their potential for elimination by phytotechnology. This review aims to provide more information about PPCPs, their occurrence in aquatic environments around the world, and their potential impact on both humans and ecosystems. This review also covers the available treatment processes, with an intense focus on phytoremediation as a promising and sustainable technology for eliminating PPCPs. Finally, this review provides further insight into the efficiency of CWs, with various scales (lab, pilot or full) for removing PPCPs from wastewater, and we performed the strengths, weaknesses, opportunities, and threats (SWOT) analysis to determine the strengths, weaknesses, opportunities, and threats of the phyto-technological approach in removing PPCPs from the environment.

To achieve these goals and to gather basic knowledge, searches were conducted using Google Scholar and Science Direct databases up to the end of 2020. Search terms have included [sources and pathways of PPCPs in the environment], [occurrence of PPCPs in the environment], [impact of PPCPs on human and ecosystem], [current and advanced technologies to eliminate PPCPs from wastewater], [phytoremediation], [removing PPCPs by phytoremediation], [constructed wetlands], [removing PPCPs in constructed wetlands]. About 138 recent articles (year 2015 to recent) included in this paper out of 162 total articles (85%).

2. Existence and occurrence of pharmaceuticals and personal care products (PPCPs) in the environment

This section will define and categorise PPCPs by giving examples of chemicals or compounds classified under PPCPs. This is followed by an investigation of the main sources of these pollutants and the potential pathways for their transport into the environment. This section will also review the risks of the PPCPs that have been reported in previous studies, in particular, those that have been based on risk quotients (RQs). Finally, this section will address the environmental regulations for the disposal of PPCPs into the ecosystem.

2.1. Categories of PPCPs

PPCPs can generally be categorised into several groups based on the purpose of the consumer product and then according to the individual compounds and properties of the PPCPs (Yang et al., 2017; Dey et al., 2019). Pharmaceutical products basically comprise both prescription and non-prescription medications, illegal drugs, and veterinary drugs, in addition to the subsequent metabolites and conjugates (Cizmas et al., 2015). It is estimated that there are about 3000 substances that are used as pharmaceutical ingredients (Rodriguez-Narvaez et al., 2017). As summarised in Table 1, hormones, antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDS), antidepressants, lipid regulators, and antihypertensives are the major pharmaceutical categories (Cizmas et al., 2015).

Antibiotics are mainly used for inhibiting the growth of pathogenic bacteria (Dey et al., 2019). NSAIDs comprise compounds with antipyretic, analgesic, and anti-inflammatory effects, and can often be obtained without a prescription (Dey et al., 2019). Hormones are used for regulating growth and physical development in organisms (Dey et al., 2019) and are either expressed naturally by humans and animals (such as oestrogen), and herein are not actually considered pharmaceuticals, or they are produced industrially (such as ethinyloestradiol) (Liu and Wong, 2013).

On the other hand, all consumer chemicals that are marketed to enhance living conditions for humans fall under the category of personal care products (PCPs). PCPs are mainly subdivided into preservatives, disinfectants, fragrances, sunlight UV filters, insect repellents, and (Yang et al., 2017). These products are primarily used to promote external senses of taste, odour, appearance, and touch, in addition to maintaining personal hygiene without causing biochemical changes (Dey et al., 2019). PCPs comprise shampoos, hair sprays, synthetic hair dyes, perfumes, deodorants, make-up products, oral hygiene products, sunscreen creams, body lotions, and various other creams (Chopra and Kumar, 2018). Moreover, PCPs also include food additives and supplements, such as flavonoids and colouring agents (Dey et al., 2019). Among the main compounds involved in the manufacturing of PCPs are triclosan and triclocarban as the most frequently monitored antimicrobial agents in wastewater, synthetic musks (including nitro musks and polycyclic musks), N,N-diethyl-m-toluamide (DEET) as the major ingredient in insect repellents, parabens as common preservatives, and sunscreen UV filters such as 2-ethylhexyl 4-methoxycinnamate and 4-methyl-benzilidine-camphor (Ellis, 2006; Liu and Wong, 2013). The concentrations of such compounds in urban runoff and groundwater have increased significantly in recent years (Rodriguez-Narvaez et al., 2017).

Table 1
Classification of PPCPs and examples of each.

Pharmaceuticals and personal care products	Pharmaceuticals	Antibiotics	Amoxycillin, erythromycin, Sulfamethoxazole, and trimethoprim
		Nonsteroidal anti-inflammatory drugs	Ibuprofen, diclofenac, acetaminophen, naproxen, salicylic acid, fluoxetine, and ketoprofen
		Hormones and steroids	Estrone, estriol, 17α-ethinylestradiol, prednisolone, and diethylstilbestrol
		Antihypertensives	Metoprolol, atenolol, timolol, and propranolol
		Lipid regulators	Clofibric acid, gemfibrozil, bezafibrate, fenofibric acid, and etofibrate
		Anticonvulsants	Carbamazepine
		Stimulants	Caffeine
	Personal care products	**Fragrances**	Nitro musks, polycyclic, macrocyclic musks, methyl dihydrojasmonate, phthalates, galaxolide, and tonalide
		Antimicrobials/antifunguls	Triclosan, triclocarban, chlorophene, and methylparaben
		Sunscreen UV filters	Benzophenone and methylbenzylidene camphor
		Insect repellents	N,N-diethyl-m-toluamide
		Food additives and preservatives	Sucralose, benzyl acetate, and propyl paraben

The molecular structures of PPCPs can typically be described as huge and complicated, with differences related to the functional groups (carboxyl, hydroxyl, amine, and ketone) of each compound. It is worth noting that classifying pharmaceuticals according to the active group does not necessarily mean that they may follow a standard chemical behaviour since minor differences in the chemical composition may affect the solubility, polarity, and the other properties of each compound differently (Ávila and García, 2015).

2.2. Potential sources of PPCPs

Most sources of PPCPs in the water bodies are strongly related to human activities (Noguera-Oviedo and Aga, 2016). Several thousand PPCPs are produced annually around the world, and as an inevitable consequence, the PPCPs discharge into the environment continues to be an inevitable by-product of daily lifes (Cizmas et al., 2015). Manufacturing sites, sewage treatment plants (STPs), WWTPs, individual households, landfill sites, and large farms represent the prime sources of the PPCPs that enter various environmental systems (Chopra and Kumar, 2018). As illustrated in Fig. 1, PPCPs are usually discharged into the environment as manufacturing facilities release the untreated or incomplete-treated wastewater to surface water bodies or STPs (Chopra and Kumar, 2018).

In addition, post-use, many PPCPs leak into the environment through different pathways (Ebele et al., 2017). Pharmaceuticals that the body absorbs during the therapeutic period are later excreted and released into septic tanks and sewage systems (Ebele et al., 2017; Dey et al., 2019). It is noted that the amounts of individual PPCPs in sewage is closely affected by various factors, including discharges from local PPCP production sites, the total population, usage patterns, and improper disposal of expired or unused PPCPs. A range of interrelated cultural, social, and institutional factors clearly influence pharmaceutical usage patterns, and the concentrations of PPCPs fluctuate according to region and time (Eggen and Vogelsang, 2015). Due to the complex structure of PPCPs, traditional treatment facilities usually fail to completely remove such compounds (Chopra and Kumar, 2018), and this explains the frequent detection of these pollutants in reclaimed water and surface waterbodies worldwide (Table 2). Moreover, due to multiple reactions during treatment process in WWTPs, the formation of several metabolites and transformed products is also predictable alongside parent compounds (Tarpani and Azapagic, 2018). Both reclaimed water and dried sludge are used for irrigation and fertilisation purposes, and this leads to the accumulation of significant quantities of PPCPs in the form of dissolved and biosorbed compounds in fertile lands (Dey et al., 2019).

Another possible pathway begins with the improper disposal of expired drugs in household solid waste, sinks, and toilets (Hoyett, 2017). Consequently, solid waste is an enduring source of PPCPs, and their biotransformed forms leach into ground water (Dey et al., 2019). In turn, this poses a potential threat to drinking water (Ebele et al., 2017). In addition, aquaculture facilities and animal agriculture are other significant sources of veterinary pharmaceuticals, particularly therapeutic antibiotics and synthetic hormones, which are used to regulate the growth and reproduction of aquaculture (fish, shrimps, crabs) and animals (cow, goat, chicken) (Noguera-Oviedo and Aga, 2016). These pollutants may directly find their path to surface water bodies or may reach the soil via animal faeces and finally seep into groundwater (Dey et al., 2019). On the other hand, PCPs can also be released directly into sewage systems via daily washing activities (Yang et al., 2017). Given that PCPs are usually limited to external use only, the chemical changes caused by metabolic reactions are excluded. Consequently, these compounds are directly released into aquatic environments (Rodriguez-Narvaez et al., 2017).

However, the long-range transport of PPCPs in the environment depends mainly on the physicochemical characteristics of the compounds in addition to the conditions of the receiving environment. For example, transport of PPCPs between different environmental media depends mainly on their ability to adsorb in treatment plants, soil, and the water-sediment system. Accordingly, PPCPs may find their way into the environment either through direct release or by employment of sludge as fertilizer (Ebele et al., 2017). Ngo et al. (2020) pointed out different distribution patterns for several antibiotics, as both azithromycin and quinolones were detected in sediments only, whereas sulfonamides were detected in water samples only. The authors believed that the variation in separation properties of these compounds is the major cause for these differences. For instance, compounds of low octanol-water partition coefficient (K_{ow}), such as sulfamethoxazole (log $K_{ow} = 0.89$), have low tendency for sorption on sediments. In contrast, compounds of high Kow, such as azithromycin (log $K_{ow} = 4.02$) exhibit good affinity for sorption on sediments. Moreover, the high polarity, low volatility, and hydrophilic nature of PPCPs restrict their dispersal in the environment mainly through aqueous medium and food chain dispersions (Ebele et al., 2017).

K'oreje et al. (2018) confirmed that conventional treatment plants,

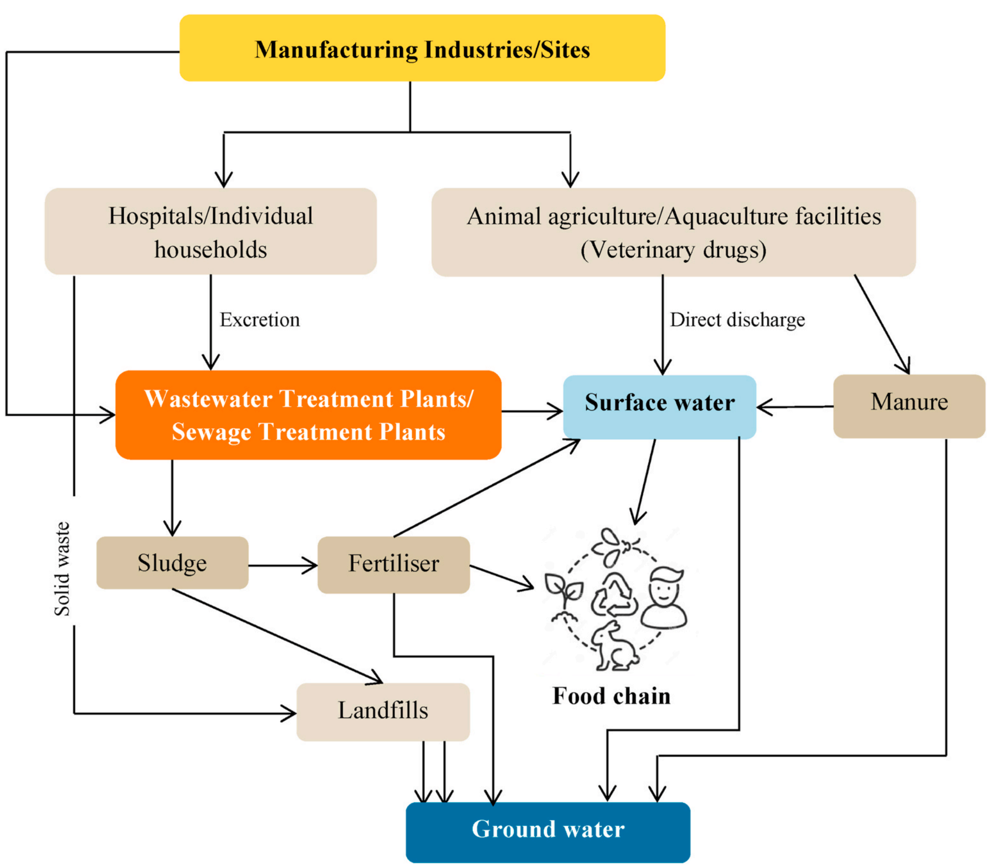

Fig. 1. Sources and pathways of PPCPs in the environment.

Table 2
Concentration of PPCPs in different sources worldwide.

Location	Source	Detected PPCPs	Concentration	Reference
Brazil	Iraı' Reservoir	Paracetamol	69 ng/L	Calado et al. (2019)
		Diclofenac	1,250 ng/L	
		Microcystin-LR	203 ng/L	
Brazil	Surface water (Doce River)	Betamethasone	165 ng/L	Couto et al. (2020)
		Fluconazole	574 ng/L	
China	Surface water (the Three Gorges Reservoir Area [TGRA], Yangtze River)	Ibuprofen	126 ng/L	Junaid et al. (2019)
		Naproxen	297 ng/L	
		Diclofenac	1410 ng/L	
		Methylparaben	11.5 ng/L	
		Propylparaben	3.10 ng/L	
		Musk xylene	206 ng/L	
China	Major watersheds	103 PPCPs (43 non-antibiotic PPCPs, 57 antibiotics, and 3 PCPs)	0.02–333 ng/L	Xu et al. (2019a)
Czech Republic	Inflow concentrations of four full-scale constructed wetlands (CWs) treating municipal sewage	Ibuprofen	14.6 μg/L	Březinova et al. (2018)
		Hydroxyibuprofen	18.3 μg/L	
		Carboxyibuprofen	36.4 μg/L	
Czech Republic	Inflow of four horizontal subsurface flow CWs	Paracetamol	7490–45,600 ng/L	Vymazal et al. (2017)
		Caffeine	2,900–83,000 ng/L	
		Triclocarban	30–259 ng/L	
		Furosemide	3,030–65,100 ng/L	
		Triclosan	169–611 ng/L	
		Hydrochlorothiazine	2,560–12,400 ng/L	
		Ibuprofen	11,300–23,600 ng/L	
		Clarithromycin	<10–2,500 ng/L	
		Tramadol	319–988 ng/L	
		Metoprolol	809–2,310 ng/L	
		Diclofenac	137–3,370 ng/L	
		Warfarin	19–53 ng/L	
		Ketoprofen	45–1,150 ng/L	
		Gabapentin	1,770–20, 200 ng/L	
India	Surface water (Ahar River, Udaipur)	Carbamazepine, antibiotics, and non-steroidal anti-inflammatory drugs (NSAIDs)	Up to 1,900 ng/L	Williams et al. (2019)
		Steroid oestrogens	Up to 124 ng/L	
		Steroid androgens	Up to 1,560 ng/L	
		Caffeine	Up to 37.5 μg/L	
Iran	Seawater (Bushehr coastline)	Six antibiotics (tetracycline, norfloxacin, azithromycin, anhydro erythromycin, cephalexin, and amoxicillin)	1.21–51.50 ng/L	Kafaei et al. (2018)
Korea	Inlet and outlet points of a CW	Sulfamethoxazole	(10.0–11,583 μg/L)-(n/d - 4,780 μg/L)	Choi et al. (2016)
		Sulfathiazole	(1,260–57,800 μg/L)-(201 to 12,800 μg/L)	
		Sulfamethazine	(1,060–30,000 μg/L)-(270 to 1,550 μg/L)	
		Trimethoprim	(1.76–673 μg/L)-(14.3–588 μg/L)	
		Tetracycline	(8.41–69.5 μg/L)-(8.41–69.5 μg/L)	
		Oxytetracycline	(12.3–48.8 μg/L)-(12.3–48.8 μg/L)	
		Chlortetracycline	(4,300–16,100 μg/L)-(4300 to 16,100 μg/L)	
		Enrofloxacin	(34.2–262.1 μg/L)-(34.2–262.1 μg/L)	
Malaysia	Influent of six WWTPs	17β-Estradiol	35.1–1,190 ng/L	Fang et al. (2018)
Malaysia	Drinking water	Caffeine	0.38 ng/L	Praveena et al. (2019)
		Diclofenac	0.14 ng/L	
		17α-Ethynylestradiol	0.02–1.0 ng/L	
Pakistan	Urban drains and canal of Lahore	Acetaminophen	13,900 ng/L	Ashfaq et al. (2019)
Portugal	Raw water	16 Pharmaceuticals	0.010–46 ng/L	Gaffney et al. (2015)
	Drinking water		0.09–46 ng/L	
Saudi Arabia	Influents and effluents of municipal wastewater of Almadinah Almunawarah	Acetaminophen	31.2–38.9 μg/L	Shraim et al. (2017)
		Metformin	3.19–15.2 μg/L	
		Norfluoxetine	7.07–7.25 μg/L	
		Atenolol	0.55–2.0 μg/L	
		Cephalexin	1.53–1.88 μg/L	
Shanghai, China	Tap water from 10 water supply operators and 35 water treatment plants	Thiamphenicol	102 ng/L	Liu et al. (2019a)
		Florfenicol	84.6 ng/L	
		Valsartan	66.8 ng/L	
		Irbesartan	38.4 ng/L	
		Hydrochlorothiazide	33.1 ng/L	
		4-Acetaminopyrine	48.2 ng/L	
		Propylparaben	47.5 ng/L	
		Dicyclohexylamine	42.3 ng/L	

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Table 2 (*continued*)

Location	Source	Detected PPCPs	Concentration	Reference
		Primidone	32.9 ng/L	
		Bisphenol A	31.5 ng/L	
Singapore	Lorong Halus Wetland (different sampling locations)	Caffeine	<1000 ng/L	Wang et al. (2019)
		Carbamazepine		
		Bisphenol A		
		Atrazine		
		Ibuprofen		
		Fluoxetine		
		Triclosan		
		Gemfibrozil		
		Caffeine	6,200 ng/L	
South Africa	Total of 55 emerging contaminants ECs (WWTP influent), 41 ECs (WWTP effluent), and 40 ECs (in upstream and downstream surface waters of the plant)	A set of PPCPs, metabolites, and illicit drugs		Archer et al. (2017)
Spain	Surface water (Llobregat River)	35 Pharmaceuticals and hormones	up to 1,200 ng/L	Huerta-Fontela et al. (2011)
Taiwan	Drinking water	18 PPCPs	<30 ng/L	Pai et al. (2020)
USA	Surface water (Lake Michigan)	32 PPCPs	ng/L level	Blair et al. (2013)
Vietnam	Surface water (Cau River)	36 PPCPs	8.21–529 ng/L	Ngo et al. (2020)

such as wastewater stabilisation ponds (WSPs), act as a considerable point source of PPCPs into waterbodies. Furthermore, the authors pointed to the unavoidable role of nonpoint sources, which exceeds the ability of waterbodies for natural attenuation. For example, pharmaceuticals such as ibuprofen and paracetamol have been completely eliminated during WSP treatment; however, their measured concentrations in Nzoia river exceeded 1000 ng/L (K'oreje et al., 2018).

The prevalence of PPCPs in water bodies worldwide has been frequently recorded in many research works. In China, Liu et al. (2019a) reported that antibiotics and cardiovascular drugs accounted for 58% and 15%, respectively, of the total PPCPs that were monitored in tap water samples in Shanghai. In addition, phenicols were the most detected antibiotic at a percentage of about 94%. According to Xu et al. (2019a), antibiotics were the most frequently detected PPCPs in seven water shades, and quinolones were the predominant antibiotics, namely ciprofloxacin, oxolinic acid, and lomefloxacin, with concentrations exceeding 1000 ng/L. Bisphenol A (oestrogens) was also detected in high concentrations (1286.25 ng/L). Caffeine was reported by Li et al. (2018) to be the predominant compound in the influent of two municipal and industrial WWTPs along Songhua River, with median concentrations of 6870 ng/L and 3360 ng/L, respectively, whilst the effluent was dominated by triclosan (83 ng/L and 17 ng/L, respectively), suggesting the different fates of the selected PPCPs in the WWTPs. Liu et al. (2018a) demonstrated the extensive existence of lipophilic pharmaceuticals (erythromycin, indomethacin, ketoconazole, gemfibrozil, diclofenac, bezafibrate, propranolol, sertraline, carbamazepine, and 17α-ethinylestradiol) in fish tissues (ND–19.6 ng/g), sediment (7.3–11.2 ng/g), suspended particulate matter (25.3–101.5 ng/g), the colloidal phase (10.1–27.7 ng/L), and dissolved phase water (67.0–107.6 ng/L), indicating their high biological availability.

In India, the concentrations of 743 ng/L of caffeine and 107 ng/L of ketoprofen were found to be the highest among the PPCPs detected in the Ganges River (Sharma et al., 2019). In South Africa, 3 illicit drug compounds were detected in surface water, with concentrations of 27.6–147.0 ng/L for cocaine, 35.6–120.6 ng/L for mephedrone, and 270.9–450.2 ng/L for methamphetamine (Archer et al., 2017). Furthermore, K'oreje et al. (2018) linked the high concentrations (>1000 ng/L) of certain PPCPs (lamivudine, zidovudine, sulfamethoxazole, and methylparaben) in rivers with the prevailing patterns of consumption in Kenya and the recalcitrant nature of some pollutants. In Brazil, caffeine was the most commonly found compound in surface water in Anil River and the Bacanga River, as reported by Chaves et al. (2020), with a concentration of 13798 ng/L. Furthermore, high concentrations of ibuprofen, acetaminophen, carbamazepine, diclofenac, and sulfamethoxazole were also detected, whereas benzophenone-3, methylparaben, ketoconazole, and triclocarban were observed in sediments. The data are extremely scarce with regard to the occurrence of PPCPs in Iraq; however, Al-Khazrajy and Boxall (2016) reported the predicted environmental concentrations of both paracetamol (23.99 μg/L) and ibuprofen (0.13–0.8 μg/L) in Iraqi surface water based on consumption data.

2.3. Environmental impacts of PPCPs

The existence of PPCPs in the environment is a concern for many researchers due to the potential toxicological consequences contributing adverse impacts on the environment and public health (Ávila and García, 2015). Knowledge about the ecological toxicity of PPCPs, which are introduced into the environment as a mixture, is still limited, particularly knowledge of prolonged exposure to low levels of non-target species (Noguera-Oviedo and Aga, 2016). Fig. 2 simplifies the main potential impacts of PPCPs in the environment. In addition to toxicity, persistence is another aspect to be looked into when considering the effects of PPCPs in the environment (Dordio and Carvalho, 2018).

2.3.1. Pseudo-persistence

Despite the polar nature of most PPCPs, their relatively short half-lifetime in water, and their very low concentrations, they are considered as pseudo-persistent contaminants (Ávila and García, 2015). Thus,

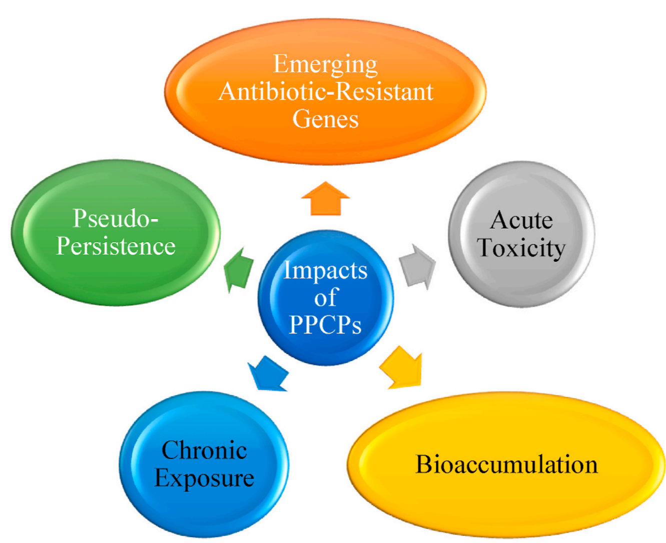

Fig. 2. Main potential impacts of the continuous release of PPCPs into the environment.

even though the bioaccumulation characteristics of some PPCPs are not significant, they may remain persistent due to their continued release into the environment in significant amounts. Accordingly, the persistence of these substances may be associated with prolonged exposure for the aquatic environment rather than a long half-life (Dordio and Carvalho, 2018). This is mainly due to their universal and growing utilisation, which results in continuous discharge into the environment (Ávila and García, 2015).

2.3.2. Bioaccumulation

According to Ebele et al. (2017), many PPCPs are biologically active substances, and their bioaccumulation has been documented in non-target aquatic organisms, such as goldfish, the algae *Pseudokirchneriella subcapitata*, and mosquito fish.

2.3.3. Chronic exposure and acute toxicity

Scientists pay special attention to pharmaceuticals since the effects of chronic exposure to low levels of such compounds are still unknown (Noguera-Oviedo and Aga, 2016). Furthermore, the fact that most PPCPs are designed primarily to have antibiotic, antimicrobial, and/or antibacterial action poses a potential risk to the receiving ecosystem. Some PPCPs can cause acute toxicity effects in an aquatic environment, whilst others may have subtle yet significant effects across various species (Button et al., 2019). By computing the risk quotient (RQ), which is the most widely adopted method by the researchers for assessing the potential risks of PPCPs to the ecosystem based on acute and/or chronic toxicity data for the most sensitive organisms, Liu et al. (2018) emphasized the potential adverse health effects of erythromycin for the most sensitive group of algae near the STP outfall in the receiving river in Nanjing, China. According to the authors, RQ values of erythromycin exceeded 1 for both acute and chronic toxicity data. As a matter of general principle, $RQ > 1.0$ for a compound, indicates high risk level (Yi et al., 2020). Ngo et al. (2020), as well, emphasized the potential risks of several antibiotics to the aquatic life in Cau River. According to the researchers, the potential risks of sulfamethoxazole ranged from high risk for algae ($RQ = 2.469$) to low risk for invertebrates ($RQ = 0.003$). As for lincomycin, its risks ranged from moderate ($RQ = 0.355$) for algae to low for invertebrates ($RQ = 0.001$). However, they pointed out the absence of toxic effects of both trimethoprim (antibiotic) and diclofenac (analgesic) on aquatic life. According to Tamura et al. (2017), the potential toxicity of a set of PPCPs including triclosan and clarithromycin on green alga (*Raphidocelis subcapitata*) was confirmed through chronic or sub-chronic toxicity tests, with these compounds contributing 0.9–69% of the whole toxicity experienced by the algae.

2.3.4. Emerging of antibiotic-resistant genes

The overconsumption of antimicrobial agents causes significant build-up of such compounds in the environment; thus, it would be a mistake to underrate the effect of such accumulation on the occurrence of antibiotic resistance since it makes the environment resemble a reservoir for antibiotic-resistant genes, which constantly feeds on the growing environmental contamination (Roca et al., 2015). Both antibiotic-resistant genes (ARGs) and antibiotic-resistant bacteria (ARB) can be regarded as emerging environmental pollutants, with potential implications for human health, in particular, and the ecosystem as a whole (Nowrotek et al., 2017). In fact, establishing an emission standard for all PPCPs, as well as discharge controls for each contaminant, may involve significant complexities. Therefore, some of the priority PPCPs that are likely to have the greatest potential threats to the environment and human health should be ranked and screened according to certain criteria (Junaid et al., 2019; Lyu et al., 2019).

The conventional method for environmental risk assessment of pollutants is considered a valuable method, but there are some limitations. Such models consider only lethal toxicity on an in vivo level as a risk endpoint, while they highly underrate the impacts of contaminants that cause sub-lethal toxicity to physiological pathways. In fact, it is difficult to draw specific conclusions regarding the potential health effects resulting from the entry of emerging pollutants into the aquatic environment, especially since these contaminants are mostly within complex mixtures with different physiochemical characteristics, requiring more eco-toxicological assessments on the sub-lethal effects of these pollutants (Archer et al., 2017).

As a result of urbanisation and the accompanying shift in lifestyle standards from traditional to contemporary, in addition to the steady increase in population, higher levels of exposure can be expected in the future, unless convenient water and waste management solutions are adopted (Sharma et al., 2019). Currently, there are no discharge guidelines or standards for most PPCPs which are still not included in the list of regulated substances (Ewadh et al., 2017). However, several countries have been proactive in establishing regulations for PPCP management. In the U.S., the assessment of environmental risks by the U.S. Food and Drug Administration (U.S. FDA) under the National Environmental Policy Act (NEPA) has been required since 1969. In 1998, the Center for Drug Evaluation and Research (CDER) published a guideline for a tiered risk-assessment method. The U.S. Environmental Protection Agency (U.S. EPA) also enacted regulations for pharmaceutical industry to control its effluent discharges and air emissions. In the European Union (EU), the European Medicines Agency published the first Guideline for Environmental Risk Assessment of Human Medicines in 2006. It is expected that some PPCPs will soon be included in the updated list for priority organic pollutants of the EU Water Framework Directive (Bartrons and Peñuelas, 2017). In Switzerland, ecotoxicity information about human pharmaceuticals is required, whilst for veterinary drugs, both ecotoxicity and potential environmental risks are used. In China, the Environmental Management Method for New Chemicals was declared in 2010, and in March 2013, the Environmental Management and Registration Method for Hazardous Chemicals was enforced (Liu and Wong, 2013). Setting monitoring limits for micropollutants requires extensive research on the biological response (acute and chronic effects) of these compounds. Likewise, careful consideration must be given to the synergistic, additive, and antagonistic effects, not only the individual effects for these compounds (Ewadh et al., 2017).

3. Recent treatment advancement for PPCPs

The potential impacts of PPCPs to both human health and the environment require effective minimisation in their release (Gorito et al., 2017). Also, using treatment technology that combines low cost and high efficiency for removing PPCPs is a crucial yet challenging task for reinstatement of the environment. Selecting the appropriate technology necessarily requires emphasising several aspects, including the loading to be treated, the concentration of the PPCPs, and, most importantly, the cost of treatment (Morone et al., 2019). Treatment processes for PPCPs in wastewater can be classified into physical, chemical and biological processes, as demonstrated in Fig. 3. These processes can be further categorised into conventional, advanced, or promising technologies based on their complexity, efficiency, and sustainability. On the physical and chemical treatment of PPCPs, it consists of conventional processes including coagulation-flocculation and sedimentation processes (Suarez et al., 2009) and advanced treatment such as adsorption (Bunmahotama et al., 2020; Fu et al., 2019; Paredes et al., 2016), membrane separation (Xu et al., 2019c, 2020; Liu et al., 2018b), and advanced oxidation processes (Lin et al., 2016; Yang et al., 2016). Recently, integration of treatments was conducted by researchers (Yi et al., 2020; Huang et al., 2019). Biological processes, although normally considered slow, offer promising new technologies involving natural resources such as bacteria, fungi, plants and microalgae. Thus, the following section in this review will focus on phytotechnology that utilise plants and their associated microbes to remediate PPCPs.

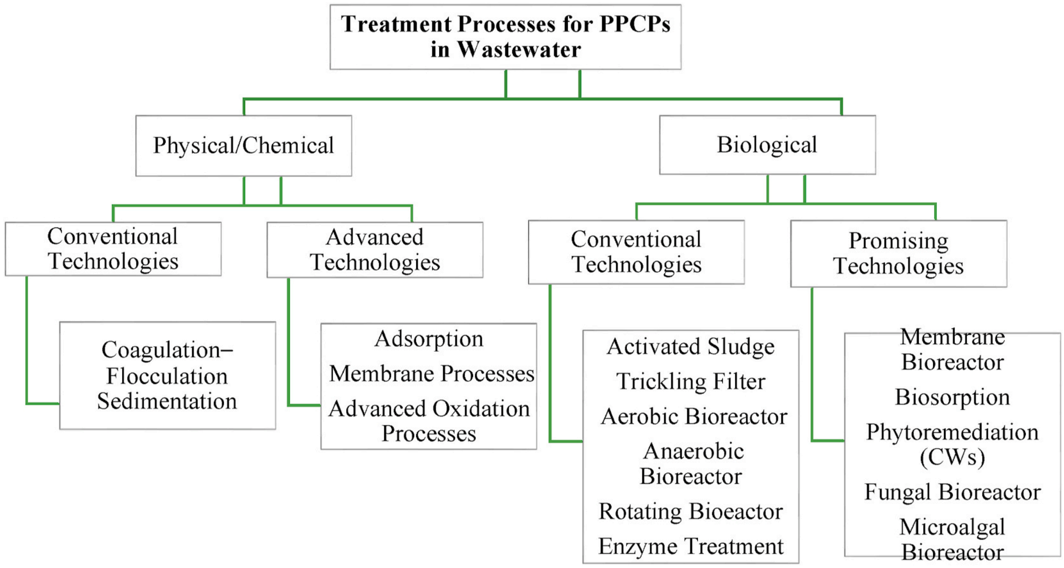

Fig. 3. Treatment processes of PPCPs in wastewater.

4. Phytotechnology for PPCPs removal from wastewater

Phytoremediation encompasses the use of plants and associated rhizosphere microorganisms for reduction or elimination of the pollutants in the soil and water (Abdullah et al., 2020). Plants have been widely exploited for accumulation, sequestering, or metabolisation of organic and inorganic contaminants in soils and wastewaters (Kotyza et al., 2010). The suitability of phytoremediation for removing PPCPs is largely based on the PPCPs physicochemical properties such as hydrophilicity and lipophilicity (Wang et al., 2019). Recently, the reliance on phytoremediation has increased since this technology has become a recognised approach for water and soil treatment. Phytoremediation is a passive technology that also adds aesthetic value to the environment (Zhang et al., 2010). Resorting to the use of plants as a treatment technology can save the environment from the introduction of harmful chemicals (such as solvents and alkali) used in other treatment methods (Kotyza et al., 2010).

4.1. Principles of phytoremediation

The power of phytoremediation originates from the tendency of plants to grow rapidly and to interact with microbiota in the rhizosphere zone. This technology depends on several overlapping and simultaneous processes that utilise the metabolic and hydraulic processes of plants to remove chemicals (Nguyen et al., 2019). Technologies derived from plant metabolic machinery (i.e., phytoremediation) have managed to treat a wide range of contaminants. Phytoremediation processes can be used for complex modification of the environment, including adjustment of the physicochemical characteristics of contaminated soils. Growing root systems have several roles, including increasing the porosity of the soil and improving its aeration, interfering with or slowing down the movement of pollutants in soil or water, and releasing exudations that possibly interact with different pollutants, which reduces the toxicity of these pollutants as a result of conjugation or degradation. Moreover, intensive plant–microorganism interaction may promote the biotransformation of recalcitrant contaminants. Plants may decompose different organic pollutants into low-molecular-weight, non-toxic compounds, which can easily undergo degradation by microorganisms (Kotyza et al., 2010). Several previous studies (Pilon-smits, 2005; Chatterjee et al., 2013; Herath and Vithanage, 2015; Wagner et al., 2018; Tripathi et al., 2020) have extensively discussed the major processes that contribute to control pollutants during phytoremediation, including stabilisation, degradation, extraction, stimulation, rhizofiltration, and volatilisation (Herath and Vithanage, 2015) shown in Fig. 4.

4.2. Fate and phytoremediation mechanisms for PPCPs

Fate of organic pollutants (such as PPCPs) mainly depends on the properties of these pollutants (chemical structure, octanol partition coefficient, acidity constant, etc.) and the condition of the surrounding environment for various treatments. Based on these aspects, several processes may occur including sorption, volatilisation, hydrolysis, oxidation, photodegradation and biodegradation (Gorito et al., 2017). During phytoremediation, micropollutants, including PPCPs, undergo a set of processes, including direct uptake, translocation, and accumulation. The cellular detoxification pathways of plants are described as ‘green liver’ since they counter the phytotoxicity of a wide range of xenobiotics by making use of their versatile detoxification arrangements (Sutar et al., 2019).

Direct accumulation or uptake of contaminants by plants is considered a dominant elimination process for inorganic pollutants such as heavy metals. Whilst regarding a variety of organic contaminants, uptake and translocation of substances by the plant are closely determined by the physico-chemical properties of the pollutants, the concentration, and the type of plant (Dordio and Carvalho, 2018). Indeed, plant cell membranes lack specific transporters for synthetic organic substances of a xenobiotic nature, such as pharmaceutical pollutants; thus, the uptake of PPCPs via the plant and translocation within tissues are passive processes that are entirely driven by simple diffusion (Li et al., 2014; Dordio and Carvalho, 2018; Wang et al., 2019), as demonstrated in Fig. 5. In detail, two main steps are hypothesised to occur initially, namely rapid adsorption of PPCPs onto the surface of the rhizosphere, followed by gradual uptake via the plant rhizosphere (Vo et al., 2018). The passive absorption of soluble organic pollutants from soil water to the plant is principally governed by the transpiration process through the xylem vessels and tracheid.

Water evaporation from the stomata on the leave surface contributes to maintaining a continuous transpiration stream (Madikizela et al., 2018). Accordingly, an organic contaminant must have suitable chemical properties (solubility, partitioning coefficient, and polarity) to be taken up by the plant and to be mobile across cell membranes (Dordio and Carvalho, 2018). Regarding solubility, the water-soluble organic pollutants could be taken up more easily by the plant roots and thereafter translocated to the upper part of shoot tissues, as in the case of

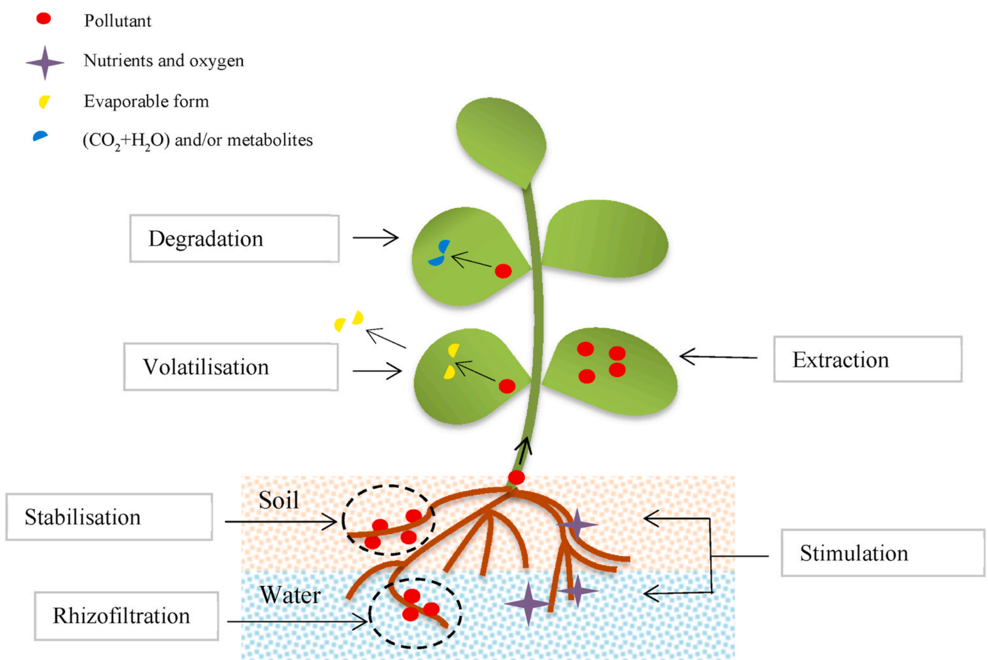

Fig. 4. Major phytoremediation processes.

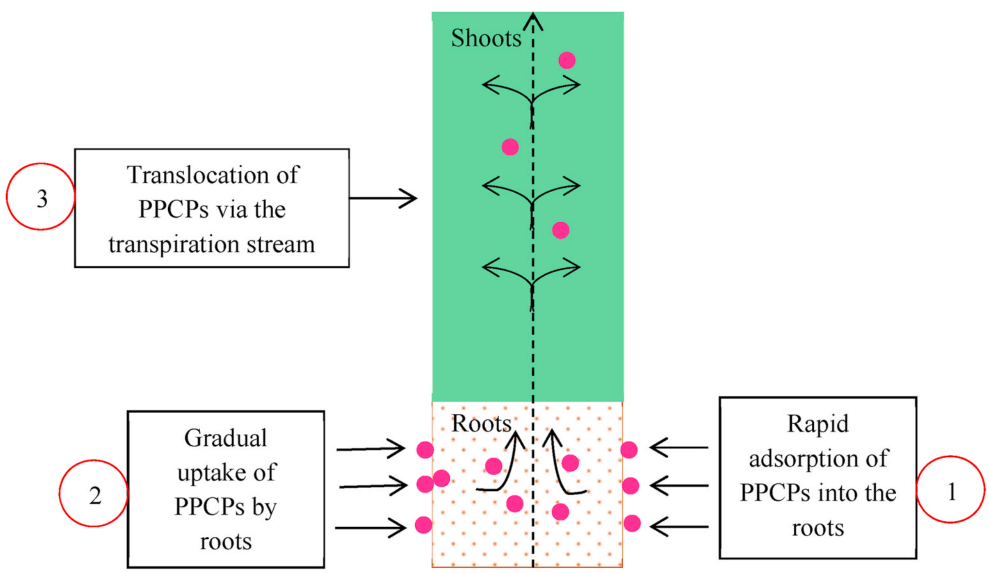

Fig. 5. Uptake and translocation processes of PPCPs by plants.

atenolol (Francini et al., 2018), propylene glycol, and trimethylamine (Ramprasad et al., 2017; Ramprasad and Philip, 2015).

On the other hand, moderately hydrophobic pharmaceutical compounds (Log K_{ow} in a range of 0.5–3.5) have adequate lipophilic characteristics that enhance their movement through the lipid bilayer of plant cell membranes, and they are also soluble allowing to travel into the plant cell fluids (Li et al., 2014). Conversely, organic pollutants with log K_{ow} values that are out of this range are often either too hydrophilic or hydrophobic to be taken up by the plants; therefore, it is more likely that their presence is confined to one type of environment with limited mobility. Regarding very hydrophobic pollutants (log K_{ow}>3.5), the long residence times in the rhizosphere make them vulnerable to phytostabilisation and/or rhizosphere bioremediation (Dordio and Carvalho, 2018). Wang et al. (2019) believed that rhizofiltration was likely to be the dominant approach of remediation for triclosan (Log K_{ow} = 4.76) and ibuprofen (Log K_{ow} = 3.97) during phytoremediation. On the other hand, Marsidi et al. (2016) confirmed the main role of phytostimulation and phytostabilization for naproxen (Log K_{ow} = 3.18) elimination in conjunction with the presence of bacterial activity in the soil around plant roots. However, the plant uptake of PPCPs with log K_{ow} values of −0.92 to 4.8 was observed and is summarised in Table 3.

To convert the organic xenobiotics (including pharmaceutical pollutants) into less toxic compounds, plants expose these pollutants to phytodegradation through a series of metabolic processes that include the transformation of parent organic compounds into smaller molecules (Functionalization phase) and the conjugated metabolites with macromolecules (Conjugation phase). Eventually, the conjugated products are incorporated into plant cell walls and vacuoles (Compartmentalization phase). Functionalization phase includes a set of enzymatic transformations by a group of enzymes (including cytochrome P450

Table 3
Plant uptake of various PPCPs.

PPCP compounds	Plant species	Part of the plant	Concentration/[a]BCF (L/kg)/[b]TF	Log K_{ow}	Reference
Acetaminophen	*M. aquaticum*	Whole plant	138 ng/g	0.46[a]	Calado et al. (2019)
	Scirpus validus		0.119–0.204 μg/g		Vo et al. (2016)
Atenolol	*Phragmites australis*	Leaves	80 μg/g	0.16 [a]	Francini et al. (2018)
	Salix matsudana Koidz.		10 μg/g		
Atrazine	*Typha angustifolia*	Roots	119 L/kg	2.61 [b]	Wang et al. (2019)
		Shoots	3.93		
	Salix exigua	Whole plant	48.6% of the initial concentration		Franks et al. (2019)
Bisphenol A	*Typha angustifolia*	Roots	87.5 L/kg	3.32 [b]	Wang et al. (2019)
		Shoots	1.42		
Caffeine	*Typha angustifolia*	Roots	111 L/kg	−0.07 [a]	Wang et al. (2019)
		Shoots	0.45		
	Echinodorus horemanii	Whole plant	52.0 ± 5.1 L/kg		Pi et al. (2017)
	Eichhornia crassipes		98.4 ± 6.3 L/kg		
	Scirpus validus	Roots	1.35–6.11 mg/g		Zhang et al. (2013)
		Shoots	6.81–13.6 mg/g		
Carbamazepine	*Typha angustifolia*	Roots	1,290 L/kg	2.45 [a]	Wang et al. (2019)
		Shoots	0.82		
	Scirpus validus	Roots	3.33–19.0 mg/g		Zhang et al. (2013)
		Shoots	0.31–0.70 mg/g		
	Lettuces	Whole plant			González et al. (2018)
Carboxylic acid	*Typha angustifolia*	Sheath	1,375 ng/g		Li et al. (2016b)
		Lamina	1,051 ng/g		
Clofibric acid	*Scirpus validus*	Roots	5.44–26.8 mg/g	2.57[c]	Zhang et al. (2013)
		Shoots	7.21–34.6 mg/g		
Diazepam	*Salix exigua*	Whole plant	49.6% of the initial concentration	2.82[c]	Franks et al. (2019)
Diclofenac	*M. aquaticum*	Whole plant	133 ng/g	4.51[a]	Calado et al. (2019)
	Egeria densa		160 ng/g		
	Ceratophyllum demersum				
	Salix matsudana Koidz.	Leaves	15 ng/g		Francini et al. (2018)
	Phragmites australis		7.5 ng/g		
	Echinodorus horemanii	Whole plant	78.9 L/kg		Pi et al. (2017)
	Eichhornia crassipes		19.4 L/kg		
	Scirpus validus	Roots	0.17–1.43 mg/g		Zhang et al. (2013)
		Shoots	0.13–0.49 mg/g		
	Lettuces	Whole plant			González et al. (2018)
Diltiazem	*Salix exigua*	Whole plant	76.2% of the initial concentration	2.70[c]	Franks et al. (2019)
Fluoxetine	*Typha angustifolia*	Roots	658 L/kg	4.63[b]	Wang et al. (2019)
		Shoots	2.25		
Ibuprofen	*Typha angustifolia*	Sheath and lamina	161 ng/g	3.97 [a]	Li et al. (2016b)
	Typha angustifolia	Roots	158 L/kg		Wang et al. (2019)
		Shoots	0.47		
Ketoprofen	*Salix matsudana Koidz.*	Leaves	125 ng/g	3.12 [a]	Francini et al. (2018)
	Phragmites australis		75 ng/g		
Naproxen	*Scirpus validus*	Roots	0.24–2.40 mg/g	3.18 [a]	Zhang et al. (2013)
		Shoots	0.22–2.77 mg/g		
Propylene glycol	*Phragmites australis*	Roots	0.11–0.14 mg/g	0.76–0.88[d]	Ramprasad and Philip (2018)
		Shoots	0.05–0.07 mg/g		
		Leaves	0.31–0.44 mg/g		
		Roots	3.1 μg/g		Ramprasad and Philip (2016)
		Leaves	4 mg/g		
Sodium dodecyl sulphate	*Phragmites australis*	Roots	0.04–0.45 mg/g	3.6[d]	Ramprasad and Philip (2018)
		Shoots	0.04–0.14 mg/g		
		Roots	0.15 mg/g		Ramprasad and Philip (2016)
Triclosan	*Salix matsudana Koidz.*	Leaves	90 ng/g	4.76[a]	Francini et al. (2018)
	Phragmites australis		50 ng/g		
	Typha angustifolia	Roots	1,438.74 L/kg		Wang et al. (2019)
		Shoots	0.20		
	Echinodorus horemanii	Whole plant	4,390 ± 296 L/kg		Pi et al. (2017)
	Eichhornia crassipes		1,050 ± 89.2 L/kg		
	Hornwort	Whole plant	5.7 ± 0.2 μg/g		Liu et al. (2016)
	Lemnaminor		7.2 ± 0.5 μg/g		
Trimethyl amine (N,N-dimethylmethanamine)	*Phragmites australis*	Steam	0.54–1.25 mg/g	0.16[d]	Ramprasad and Philip (2018)
		Roots	5.8 μg/g		Ramprasad and Philip (2016)
		Steam	0.22 mg/g		
		Leaves	30.3 μg/g		
17α-Ethynylestradiol	*Salix exigua*	Whole plant	88% of the initial concentration	3.67	Franks et al. (2019)
1-Hydroxy ibuprofen	*Typha angustifolia*	Sheath	301 ng/g		Li et al. (2016b)
		Lamina	179 ng/g		
2-Hydroxy ibuprofen	*Typha angustifolia*	Sheath	236 ng/g		Li et al. (2016b)
		Lamina	694 ng/g		

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*BCF (L/kg): the ratio of the compound's concentration in the plant's tissues to the concentration in solution (Wang et al., 2017)
**TF: the ratio of the compound concentration (μg/g) detected in stems and roots (Pi et al., 2017).
[a] Chen et al. (2016).
[b] Wang et al. (2019).
[c] National Center for Biotechnology Information (2021)
[d] Ramprasad and Philip (2018).

monooxygenase, peroxidases and peroxygenases). During this phase, the molecules of the hydrophobic compounds acquire a hydrophilic functional group (e.g., hydroxyl, amine, carboxyl, sulphydryl) which contributes to an increase in their polarity and solubility, stimulating further transformation. He et al. (2017) reported the production of two intermediates of ibuprofen in phragmites australis tissues during phase I (Functionalization phase), namely hydroxy-ibuprofen and carboxy-ibuprofen, which (the latter) subsequently was believed to resulted in 1,2-dihydroxy-ibuprofen. The researchers also confirmed that occurrence of these intermediates was strongly correlated with the trend of higher cytochrome P450 monooxygenase activity. During conjugation phase, the xenobiotic metabolites resulting from functionalization phase are conjugated with the endogenous molecules (proteins, peptides, amino acids, organic acids, mono-, oligo- and polysaccharides, pectins, lignin, etc.) to form compounds of higher molecular weight and less toxicity. Several enzymes including glutathione-S-transferases, glucosyl transferase and N-malonyl transferases are responsible for conjugation in this phase. In compartmentalization phase the conjugates are segregated from vulnerable sites in cytosol and transported to sites where they may not interfere with cellular metabolism: soluble conjugates (with peptides, sugars, amino acids, etc.) are accumulated in vacuoles while insoluble conjugates (coupled with pectin, lignin, xylan and other polysaccharide) are taken out of the cell and accumulated in plant cell walls (Dordio and Carvalho, 2018). He et al. (2017) expected that glucopyranosyloxy-carboxy-ibuprofen would be detected in phase II (conjugation phase) as one of the intermediate compounds of ibuprofen.

However, the researcher confirmed that only glucopyranosyloxy-hydroxy-ibuprofen was detected because of glycosyl transferase activity, explaining the absence of ibuprofen-glutathione conjugate in phase III (compartmentalization phase) as the glutathione-S-transferases prefers to catalyse conjugation at electrophilic double bonds or halogen functions.

Once taken up by the roots, pharmaceutical pollutants might be translocated to other parts of the plants where they can be detected in the stem, leaves and edible parts of the plant (AL Falahi et al., 2021; Madikizela et al., 2018). According to González et al. (2018), due to its neutral charge and intermediate hydrophobicity, the carbamazepine concentration (log $K_{ow} = 2.45$, pKa = 13.9) in the leaves of lettuce was found to be 46% more than the roots. On the contrary, diclofenac (log $K_{ow} = 4.5$, pKa = 4.4) was accumulated at higher rates in the roots (89% higher than the leaves) since its high hydrophobicity and low solubility hindered the translocation into the leaves. Li et al. (2016b) believed that the even distribution of ibuprofen that was detected in the lamina and sheath tissues of *Typha angustifolia* clearly indicates the occurrence of direct uptake followed by the phytoextraction process, whereas the uneven distribution of ibuprofen metabolites detected in these tissues can be considered strong evidence of phytotransformation processes within the plant.

Moreover, the secretion of such types of organic compounds creates a favourable microenvironment for attracting chemotactic bacteria, which consume these compounds as a carbon and energy source. The secreted organic compounds may potentially enhance the bioavailability of pollutants, in addition to causing a probable change in the physicochemical properties of soils (Hussain et al., 2018). Biodegradation typically represents a fundamental mechanism for the removal of organic pollutants (Dordio and Carvalho, 2018). Microorganisms contribute significantly to the degradation of a wide variety of environmental contaminants by consuming these substances in their essential physiological and biochemical processes (Singh et al., 2020). As a result of biodegradation, pharmaceutical pollutants may be subjected to the following: a) complete mineralisation or b) transformation to either more hydrophobic compounds (with a high tendency to partition into the solid phase) or to more hydrophilic compounds (with a high preference for the liquid phase) (Zhang et al., 2014). Transformations by microbes can comprise more than one type of mechanism, which explains the repeated detection of different degradation products originated from the same initial compound under different environmental conditions.

Under certain conditions, microorganisms can coordinate with each other for the degradation of pollutants (Singh et al., 2020); thus, biological transformations can occur by one organism or through mixed culture of several species (Dordio and Carvalho, 2018). The availability of oxygen provided by the macophytes in the rhizosphere, together with the existence of other electron acceptors, strongly control the metabolism of pharmaceutical pollutants, where biodegradation varies depending on the type of prevailing conditions, whether aerobic or anaerobic (Dordio and Carvalho, 2018). Basically, both aerobic and anaerobic biodegradation of organic pollutants in CWs can result from the activities of diverse groups of microorganisms, such as heterotrophic and/or autotrophic bacteria, fungi (yeasts and basidiomycetes), and protozoa (Li et al., 2014). The rate of biodegradation and the extent of microbial growth are strongly induced by the chemical structure of the organic pollutants (Dordio and Carvalho, 2018; Sutar et al., 2019). Ideally, ibuprofen is easily biodegradable by virtue of its relatively simple structure which possesses neither chlorine nor double aromatic rings (Li et al., 2019a). In general, organic pollutants that possess simple structures, high water solubility, and a weak adsorptive tendency are good candidates for biodegradation. This is mainly attributed to their similarity to the naturally occurring compounds that are usually utilised as energy sources by microbes. On the other hand, lack of the specific genes required for the degradation of xenobiotic organic pollutants (including pharmaceuticals) causes the degradation of such pollutants by non-specific enzymes in a somewhat slow degradation process, which does not support microbial growth (Li et al., 2014; Dordio and Carvalho, 2018). In addition to rhizobacteria, endophytic bacteria that colonise the internal plant tissues may participate in biodegradation of the pollutant, improving the potential for mineralisation of the targeted pollutants (Tripathi et al., 2020).

4.3. Constructed wetlands (CWs) for PPCPs

Natural wetlands can be described as transitional land between terrestrial and aquatic systems in which the land is covered by low level of water, that is, the water level is usually at the surface of the land or rises slightly near it. Natural wetlands perform an important function in the ecosystem by acting as natural filters that dramatically contribute to the purification and improvement of water quality, and they display various nutrient dynamics. In contrast, CWs are artificial engineered systems that are designed for wastewater treatment purposes under a controlled environment (Herath and Vithanage, 2015). CWs typically comprise substrates, plants, microorganisms, and water; they are properly designed to mimic the natural wetlands, and utilise physical, chemical and biological processes to improve the quality of water (Wu et al., 2015). In a CW unit, vegetation and substrate are employed in properly designed shallow basins, while other components, including microbes and aquatic invertebrates, develop naturally (Ávila and García, 2015). Wetland vegetation facilitates the key mechanisms for removing multiple pollutants; therefore, the employment of CWs for phytoremediation has been widely developed as a cost-effective and environmentally friendly technology (Herath and Vithanage, 2015). The importance of the growth substrate matrix comes from its role in supporting the growth of the plant and enhancing the adsorption of micropollutants (Francini et al., 2018). Hence, substrate selection is one of the key technical issues for CWs, which are mainly based on the biofilm principle for treating wastewater (Yang et al., 2018).

According to the hydrology, CWs can be basically classified into free surface flow constructed wetlands (FS-CWs) and subsurface flow constructed wetlands (SSF-CWs). In turn, subsurface flow CWs can be further subdivided based on the flow path into subsurface horizontal-flow wetlands (SSHF-CWs) and subsurface vertical-flow wetlands (SSVF-CWs). Moreover, to achieve higher removal efficiencies, various categories of CWs may also be integrated in a hybrid system; therefore, the appropriate configuration should be determined based on the characteristics of the targeted contaminants (Gorito et al., 2017; Abdullah et al., 2020). CWs were initially employed to treat municipal wastewater, and then their application was steadily expanded to include treatment of industrial effluents, livestock farm effluents, agricultural wastewaters, landfill leachate, and stormwater runoff, among others (Pascual et al., 2018). CWs may provide a complementary sewage treatment option, especially with the lack of other treatment technologies (Breitholtz et al., 2012). CW systems could be a good choice for polishing partially treated domestic or industrial wastewater due to their success in reducing concentrations of most pollutants, including nitrogen, phosphorus, organic pollutants, heavy metals (Herath and Vithanage, 2015), and PPCPs (Rabello et al., 2019). In addition to improving conventional water quality indexes, CWs can be employed to achieve satisfactory performance in the removal of a variety of organic micropollutants, including reactive oxygen species (ROS), and in the reduction of cytotoxicity and anti-androgen (Ant-AR) activities (Xu et al., 2019b). These systems could be employed for the decentralised treatment of wastewater from different sources (Ávila et al., 2017). Moreover, small CWs provide a brilliant solution for on-site treatment of domestic wastewater in isolated houses, mostly in rural and ecologically sensitive areas where there is no possibility for sewer connection (Gikas and Tsihrintzis, 2012). In this regard, both Jehawi et al. (2020) and Al-Ajalin et al. (2020) confirmed that the hybrid reed bed CWs could be relied upon as a feasible and cost-effective solution to treat domestic wastewater in small communities.

Plants remove micropollutants, such as PPCPs, either through direct uptake and assimilation or through the creation of favourable conditions that are conducive to removal. Micropollutants may be subjected to degradation via metabolic pathways (phytodegradation) as soon as they are taken up by the plants. Moreover, plants support microbial degradation by providing the necessary surfaces (roots) for the growth of microbial biofilms. As a result of the biodegradation process, micropollutants may go through mineralisation or transformation into hydrophobic or hydrophilic compounds (Dhir, 2019). Photodegradation is influenced by light or radiant energy when the functional groups (such as aromatic rings) present in the pharmaceutical pollutants absorb solar radiation. On the other hand, a considerable amount of the pollutants may be retained in the substrate that is present in the wetland. The sorption of pollutants to the substrate is highly related to the characteristics of both compounds and the substrate or soil (Dhir, 2019). The applicability of CWs for the elimination of PPCPs has been widely examined and has been confirmed to be effective (Ferreira et al., 2017), even for compounds that are extremely recalcitrant to conventional treatment methods (Dordio and Carvalho, 2018), such as carbamazepine (Chen et al., 2018).

As an ecological treatment method, CWs outperform other conventional wastewater treatment techniques by many advantages, most notably lower energy requirements, environmentally friendly features, and aesthetic values (Liang et al., 2018). CWs can be constructed out of low-cost local materials (Ávila et al., 2017) with simple requirements for operation and maintenance (Ávila et al., 2017; Rajan et al., 2019), and low carbon-emission (Huang et al., 2013); further, such systems also have the ability to tolerate fluctuations in load which makes them a suitable alternative in wastewater treatment (Ávila and García, 2015). The only by-product in CWs facilities is plant biomass, which is harvested once a year or every few years and exploited for the production of biofuels or compost. On the contrary, conventional treatment plants produce large quantities of sludge that require continuous management and stability on a daily basis (Stefanakis, 2018). However, despite the long list of advantages, the relatively large footprint of these systems is considered a limiting factor that impedes the wide application in areas with high population and scarce land resource (Wu et al., 2015; Ávila et al., 2017). Moreover, the unconsidered design (which does not fit with design criteria) may cause several problems to arise in CWs, including odour-related problems or increase of the water level above the designed surface (Stefanakis, 2018). Phytoremediation in CWs still needs further development, especially as this technology is restricted to some extent with roots depth. Accordingly, phytoremediation commonly requires that the contaminated soil or wastewater be within the rhizosphere. Moreover, phytoremediation often takes longer time and it highly depends on climate dependent. Finally, high initial concentrations of pollutants may adversely affect the growth of wetland plants (Herath and Vithanage, 2015).

4.4. Parameters affecting treatment efficiency

The removal of pollutants in CWs takes place through complex physicochemical and microbial interactions (Ávila and García, 2015). A particular removal mechanism may prevail at the expense of another, depending on the system. The design and operation of CWs systems require consideration of several criteria such as wetland configuration, selection of plant species, selection of substrate, water depth, feeding mode (batch or continuous), hydraulic retention time (HRT) and hydraulic loading rate (HLR); further, all of these factors may have a profound influence on the removal of pollutants (Zhang et al., 2014; Wu et al., 2015; Gorito et al., 2017). The removal efficiency within the CWs is also expected to be influenced by temperature, as well as pH, oxygen levels, presence of toxic substances and nutrients in wastewater to be treated (Dordio and Carvalho, 2018). Proper design and construction of CWs contribute to an efficient and reliable performance, as problems of water runoff from the surface, bed clogging, or limited plant growth that can often accompany the inadequate design or construction can be avoided (Stefanakis, 2018). Under optimised conditions of design and operational factors, CWs can succeed in removing a high rates of PPCP, making it a sustainable solution for wastewater treatment (Kaur et al., 2019). However, a limited number of studies conducted to optimise the design criteria for CWs used in the removal of PPCPs (Zhang et al., 2018). Key data from 39 articles that conformed to the selection criteria were extracted and analyzed. Table 4 summarises reports on CWs with different scales (full-scale, pilot-scale, mesocosm-scale and microcosm-scale), which have been used to remove PPCPs from real or synthetic wastewater.

4.4.1. Retention time

Hydrology is one of the key factors by which the functions of the CWs can be controlled to achieve a satisfactory performance. The optimal HRT and HLR plays a crucial role in CWs performance (Wu et al., 2015). The longer HRT provide an adequate contact period for the microbial community to be established and to remove contaminants. Higher HLR enhances faster flow of wastewater through the substrate, thus limiting the optimum contact time (Saeed and Sun, 2012; Wu et al., 2015; Gorito et al., 2017; Sa'at et al., 2019). In contrast, the increase in HLR causes a significant inhibition of PPCPs removal process, as microbial consortia prefer to consume sucrose in the additional loads as an energy source instead of the targeted pollutants (Ramprasad et al., 2017). Careful monitoring and control of hydraulic loading rates and their potential

Table 4
Design, operational parameters, and significant findings of the reported CWs for the removal of PPCPs.

System/scale/ intensifications	Hydraulic Retention Time (days)	Country	Plant	Target pollutant	Removal (%)	Significant findings	Reference
**Hybrid/full scale	10	Belgium	*Phragmites australis*	Total of 12 pharmaceuticals	>90	• Carbamazepine removal was improved with increasing HRT. • Diclofenac removal improved with increasing HRT as aeration was applied. • On the contrary, tramadol removal improved with increasing HRT as aeration was not applied.	Auvinen et al. (2017a)
**SSF-CW/pilot scale	0.5–2	Belgium	*Phragmites australis*	Total of 10 pharmaceuticals		• Carbamazepine, diclofenac, and sotalol showed recalcitrant behaviour with removal (<50%). • Continuous aeration improved the removal efficiency of the readily degradable compounds (metformin, valsartan).	Auvinen et al. (2017b)
Hybrid/ recirculation flow rate of 50%	21 h	Spain	*Phragmites australis*	Sulfamethoxazole Carbamazepine Tris (2-chloroethyl) phosphate Sucralose Caffeine Fluoxetine Trimethoprim N,N-diethyl-meta-toluamide	Negligible Negligible Negligible Negligible, 80% 27%	• Microbial degradation under aerobic conditions in vertical flow system promoted the removal of trimethoprim, DEET, and sucralose. • Sulfamethoxazole, carbamazapine, TCEP, and sucralose showed overall recalcitrant behaviour.	Ávila et al. (2017)
SSHF-CW/full	6.3–11.6	Czech Republic	*Phragmites australis* *Phalaris arundinacea*	Ibuprofen Hydroxyibuprofen Carboxyibuprofen	44.7% 29.3% 47.5%	• Ibuprofen and its metabolites exhibited limited removal efficiency in anoxic or anaerobic conditions.	Březinova et al. (2018)
SSVF-CW/ mesocosm/ recirculating operation	7	Canada	*Phalaris arundinacea*	Triclosan Sulfamethoxazole	100% 99.9%	• The microbial activity was found to be significantly reduced with exposure to 100 μg/L sulfamethoxazole. Moreover, the severe impacts caused complete cessation of microbial function at the highest dose of 1000 μg/L. In contrast, the highest dose of triclosan (1000 μg/L) did not completely prohibit microbial activity. • Both triclosan and sulfamethoxazole were detected in the biofilm of the CWs following exposure. • Triclosan was more recalcitrant, precisely in the unplanted CWs.	Button et al. (2019)
SSHF-CW/pilot scale	5.5	Germany	*Phragmites australis*	Total of 11 organic micopollutants		• Planted beds showed improved performance compared to the unplanted beds. • Plants supported the removal of fragrances (galaxolide and tonalide) and pharmaceuticals (carbamazepine, diclofenac, ibuprofen, ketoprofen, and naproxen), even under the conditions of high organic load. • Sulphate-reducing bacteria were suspected to be involved in the removal of naproxen and diclofenac since a positive correlation was observed between the removal of naproxen and diclofenac and the sulphide concentration.	Carranza-Diaz et al. (2014)
SSHF-CW/full scale	5.4–12.9	Czech Republic	*Phragmites australis* *Phalaris arundinacea*	Paracetamol Caffeine Naproxen Furosemide Triclosan hydrochlorothiazide Ibuprofen	95–100% 93–99% 73–90% 80–96% 62–91% 18–91% 74–99%	• Low redox conditions in the SSHF-CWs, rhizosphere development and artificial aeration were effective to stimulate the removal of ibuprofen through aerobic degradation.	Chen et al. (2016)

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Table 4 (*continued*)

System/scale/ intensifications	Hydraulic Retention Time (days)	Country	Plant	Target pollutant	Removal (%)	Significant findings	Reference
				Atenolol Tramadol Metoprolol Diclofenac Ketoprofen Gabapentin	58–99% 54–85% 60–93% 63% 47–91% −53 to 88%	• Temperature-dependent biodegradation was suggested to be mainly responsible for ketoprofen removal in the CWs. • The reductive dehalogenation by anaerobic degraders in addition to photodegradation and plant uptake were assumed to be responsible for diclofenac removal given the low redox potentials in the SSHF-CW	
Hybrid/full scale	48.4 h	Republic of Korea	*Phragmites australis* *Miscanthus sacchariflorus*	Sulfamethoxazole Sulfathiazole Sulfamethazine Trimethoprim Tetracycline Oxytetracycline Chlortetracycline Enrofloxacin	49.43% 81.86% 85% <10% – – 29.47% 27.26%	• Plant uptake, biodegradation, and direct adsorption into substrates and plants were the main removal mechanisms in lab-scale studies for sulphonamide antibiotics. • Enrofloxacin was effectively (70%) removed during the photodegradation experiment rather than sulphonamide antibiotics. • The photodegradation rate of trimethoprim was only (8%).	Choi et al. (2016)
SSHF-CW/ mesocosm	1–2	Greece	*Juncus acutus*	Bisphenol A Ciprofloxacin Sulfamethoxazole	76.2% 93.9% –	• *J. acutus* could be efficiently planted in CWs for bioremediation and elimination of emerging organic pollutants. • Ciprofloxacin showed high removal rates in the planted wetland. • The HRT was a significant factor since bisphenol A showed sensitivity with longer HRTs. • Sulfamethoxazole was not significantly eliminated.	Christofilopoulos et al. (2019)
Not specified/pilot scale	4–7	Italy	*Phragmites australis* L. *Salix matsudana Koidz.*	Diclofenac Ketoprofen Atenolol Triclosan		• *Phragmites australis* demonstrated efficient uptake diclofenac and atenolol, whilst *Salix matsudana Koidz.* translocated ketoprofen and triclosan preferentially in the aerial part. • The bacterial biofilms colonising the substrate were suggested to be responsible for the transformation and degradation of the pollutants. • In the unplanted beds, the depletion of the PPCPs was concluded to be associated with both adsorption and transformation of the bacterial community. • In the planted beds, the combined effect of adsorption, degradation, and plant uptake was suggested for PPCP removal.	Francini et al. (2018)
SSHF/mesocosm	1–3	Netherlands	*Phragmites australis*	Caffeine Naproxen Metoprolol Propranolol Ibuprofen Carbamazepine Diclofenac	79–99% 79–99% 79–99% 79–99% 79–99% 46%	• Sorption dominated propranolol removal, whereas other pharmaceuticals were mainly removed via biodegradation and/or phytodegradation. • Carbamazepine was probably sorbed in the first 10 days; thereafter, it underwent a breakthrough, mostly without any removal. • Pre-photocatalysis with a compartment of immobilised TiO_2 was confirmed to be an appropriate approach to improve the removal of diclofenac and carbamazepine after the recalcitrant behaviour demonstrated by both compounds in the SSHF-CW.	He et al. (2018)

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Table 4 (*continued*)

System/scale/ intensifications	Hydraulic Retention Time (days)	Country	Plant	Target pollutant	Removal (%)	Significant findings	Reference
Hybrid/full scale	0.4–75.9	Spain	*Lemna minor* *Typha latifolia* *Salix atrocinerea* *S. atrocinerea*	Ibuprofen Ketoprofen Naproxen Diclofenac Salicylic acid Caffeine Carbamazepine Methyl dihydrojasmonate	42–99% 77–81% 73–85% 65–87% 93–97% 83–96% Not detected ND 81–97%	• Ibuprofen was assumed to be aerobically biodegraded in the CWs. • The FS-CW planted with *T. latifolia* and the SSF-CW planted with *S. atrocinerea* were found to be useful for the degradation of PPCPs in urban wastewater.	Hijosa-Valsero et al. (2010a)
FS-CW and SSF/ mesocosm	2–6	Spain	*Typha angustifolia* *Phragmites australis*	Ketoprofen, Naproxen Ibuprofen, Diclofenac, Salicylic acid, Carbamazepine, Caffeine, Galaxolide, Tonalide, and Methyl dihydrojasmonate		• Ketoprofen degradation was believed to be associated with photodegradation processes. • It had been suggested that carbamazepine was retained or adsorbed inside the CWs. • *Phragmites australis* was more efficient than *Typha angustifolia* for the removal of diclofenac, ibuprofen, caffeine, and methyl dihydrojasmonate.	Hijosa-Valsero et al. (2010b)
FS-CW and SSF-CW/mesocosm	29–71 h	Spain	*Phragmites australis* *Typha angustifolia*	Ibuprofen Ketoprofen Naproxen Diclofenac Salicylic acid Caffeine Carbamazepine Methyl dihydrojasmonate Galaxolide Tonalide		• Biodegradation in the pore water of the CWs was a major removal mechanism for the non-recalcitrant pollutants. • The role of plant uptake/plant adsorption was not essential for PPCP removal in the CWs. • The CW configuration, the presence of macrophytes, or the absence of substrate are key factors affecting the efficiency of the systems due to the contribution of abiotic processes via photooxidation and volatilisation.	Hijosa-Valsero et al. (2016)
(1) SSHF-CW (2) *SSVF-CW (3) [*SSVF-CW + unsaturated sand filter] (4) **SSHF-CW (5) **SSVF-CW/ pilot scale	≥3	Germany	*Phragmites australis*	Caffeine Ibuprofen Naproxen Benzotriazole Diclofenac Acesulfame Carbamazepine		• The CWs exhibited the highest performance in the warm season. • The decreasing dissolved oxygen and positive redox potential enhanced the elimination of moderately biodegradable pollutants, such as naproxen, acesulfame, and benzotriazole. • For pharmaceuticals that are the most difficult to degrade (such as diclofenac), the co-occurrence of high oxygen availability in the subsurface and low carbonaceous biological oxygen demand ($CBOD_5$) content were essential for removal.	Kahl et al. (2017)
SSHF-CW	4	Singapore	*Typha angustifolia*	Ibuprofen		• The presence of plants within the CW significantly promotes the microbial degradation of ibuprofen.	Li et al. (2016a)
**FS-CW/lab scale	7	UK	*spirodela polyrhiza*	N,N-diethyl-meta-toluamide Paracetamol Caffeine Triclosan	43.30% 97.50% 98.20% 100%	• Correlation analysis showed a significant correlation ($p < 0.05$) between the removal of target PPCPs and water parameter removals (COD, nitrate, phosphate).	Li et al. (2017)
SSF-CW/ mesocosm	10	China	*Phragmites australis* *Typha orientalis* *Vetiveria zizanioides* *Canna indica*	Sulfamethoxazole	73.1–74.8% 70.1–76.3%	• The variation in the plant species did not cause any significant changes to the efficacy of sulfamethoxazole removal. • The addition of nutrients and low concentrations of heavy metals generally improved the removal of sulfamethoxazole in the microcosm beds.	Liang et al. (2018)
FS-CW	5	China	*Cattail* *Hornwort* *Lemnaminor*	Triclosan	>97	• Microbial community richness and diversity showed a clear variation with plant type.	Liu et al. (2016)
SSF	56	Malaysia		Naproxen	60.9–81.5		

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Table 4 (*continued*)

System/scale/ intensifications	Hydraulic Retention Time (days)	Country	Plant	Target pollutant	Removal (%)	Significant findings	Reference
			Vetiver zizaniodes			• Phytostimulation and phytostabilisation were responsible for the removal of naproxen. • The effect of naproxen concentration was evident in the treatment area since the dissolved oxygen content was depleted in conjunction with the increase in naproxen concentration.	Marsidi et al. (2016)
(1) SSHF-CW (2) *SSVF-CW (3) *SSVF-CW + unsaturated sand filter (4) **SSHF-CW (5) **SSVF-CW /Pilot scale	1–4	Germany	*Phragmites australis*	Caffeine Ibuprofen Naproxen Benzotriazole Diclofenac Acesulfame Carbamazepine	83–99% 28–99% 32–99% 25–87% 25–77% −5%–62% −9%–13%	• High correlation was observed for system complexity, aerobic conditions, and temperature to overall pollutant removal, including substances of high to moderate biodegradability (caffeine, ibuprofen, naproxen, and benzotriazole). • Carbamazepine removal occurred only under reducing conditions.	Nivala et al. (2019)
Down flow-CW/ microcosm	7	Poland	*Phalaris arundinacea*	Diclofenac Sulfamethoxazole	~50% 24–30%	• The presence of plants had no impact on the removal of diclofenac or sulfamethoxazole.	Nowrotek et al. (2016)
Free surface/field scale	6 h	Republic of Korea	*Acorus* *Typha*	Atenolol Carbamazepine Ibuprofen	50% 50% ~10%	• The electrical charge density of the *Acorus* soil organic matter was twice that of the *Typha* soil organic matter. • Electrostatic interactions represented one of the main pharmaceutical elimination mechanisms in CWs. • Hydrophobic interactions influenced the sorption efficiency, which explains the relatively moderate removal of carbamazepine (log $K_{OW} = 2.77$) compared to the low removal of ibuprofen (log $K_{OW} = 1.68$).	Park et al. (2018)
Hybrid/pilot/ baffled flow	6.5–12.5	India	*Phragmites australis*	Sodium dodecyl sulphate Propylene glycol Trimethyl-amine	94–98% 95–98% 95–99%	• Sodium dodecyl sulphate was removed better during summer compared to winter. • The removal of propylene glycol and trimethyl-amine was affected by the seasons since their predominant removal mechanism is mostly plant uptake and biodegradation.	Ramprasad and Philip (2015)
(1) SSHF-CW (2) SSVF-CW/ pilot	8.9–14.9	India	*Phragmites australis*	Sodium dodecyl sulphate Propylene glycol Tri-methyl amine	85% (1) 89% (2) 90% (1) 95% (2) 95% (1) 98% (2)	• The SSVF-CW was slightly more efficient in removing the pollutants compared to SSHF-CWs. • The removal rates were marginally higher in the summer.	Ramprasad and Philip (2016)
Hybrid/pilot	4–11	Germany	*Phragmites australis* *Lemna* *Iris pseudacorus* *Scirpus* sp. *Carex* sp.	18 Pharmaceuticals		• Low redox conditions within the subsurface flow constructed wetland and the pond with floating plants in summer preferred the anaerobic degradation of some pharmaceuticals, such as sulfamethoxazole and diatrizoate. • The reduction in global radiation and microbial activity in winter reduces the photodegradation and biodegradation processes and the subsequent rates of pollutant removal.	Rühmland et al. (2015)
(1) *SSVF-CW (2) SSVF-CW (3) SSHF-CW (4) FS-CW	3.5	Spain	*Phragmites australis*	Caffeine Trimethoprim Sulfamethoxazole Sucralose N,N-diethyl-meta-toluamide	82 to > 90% 87–99% <30–64% – 25–63%	• The highly biodegradable pharmaceuticals caffeine and trimethoprim were completely eliminated in both SSVF-CWs, exhibiting marginally higher removal in the partially saturated	Sgroi et al. (2018)

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Table 4 (*continued*)

System/scale/ intensifications	Hydraulic Retention Time (days)	Country	Plant	Target pollutant	Removal (%)	Significant findings	Reference
						system compared to the unsaturated system. • The unsaturated vertical unit showed superior performance for removing DEET. • Sucralose and sulfamethoxazole were negligibly removed in all CWs.	
**Hybrid/ mesocosm	161	Czech Republic	*Miscanthus × giganteus* *Iris pseudacorus* *Acorus calamus* *Lythrum salicaria* *Lemna minor* *Myriophyllum aquaticum*	Diclofenac Sulfamethoxazole	77.6% 95.8%	• In the SSVF-CW, sulfamethaxazole exhibited higher removal under non-aerated conditions (about 77%) as compared to aerated conditions (only 26%). • Diclofenac removal was positively influenced by the collective effect of vegetation and aeration in the FS-CW. • The SSVF-CW contributed more to the removal process than the SF-CW, with 56.3% vs 21.3% for diclofenac and 79.2% vs 16.5%) for sulfamethaxazole.	Sochacki et al. (2018a)
SSVF-CW/ microcosm	6–24 h	Czech Republic	*Phalaris arundinacea*	Diclofenac Sulfamethoxazole	47.3–74.2% 52.8–91.2%	• The effect of loading frequency was insignificant in the unplanted beds. • Pharmaceuticals caused a reduction in bacterial diversity within the substrate and rhizosphere zones.	Sochacki et al. (2018b)
FS-CW/laboratory scale	3–5	Thailand	*Scirpus validus*	Acetaminophen	55–99.5%	• Plant uptake was suggested to be a dominant mechanism for acetaminophen removal.	Vo et al. (2016)
SSHF-CW/full scale	6.3–11.6	Czech Republic	*Phragmites australis* *Phalaris arundinacea*	Paracetamol Caffeine Triclocarban Furosemide Triclosan hydrochlorothiazide, Ibuprofen Clarithromycin Tramadol Metoprolol Diclofenac Warfarin Ketoprofen Gabapentin	91% 84% >81% 75% 65% 61% 55% 54% 53% 48% 41% 31% 31% 14%	• The removal of ibuprofen, paracetamol, and tramadol was significantly correlated with temperature. • The removal of triclocarban and hydrochlorothiazide was significantly correlated with the removal of chemical oxygen demand (COD). • The removal of caffeine was significantly correlated with dissolved oxygen, suggesting aerobic biodegradation as the major process in caffeine removal.	Vymazal et al. (2017)
Hybrid/full scale	10–13	Ukraine	*Phragmites australis* *Typha latifolia* L. *Scirpus sylvaticus* L.	Total of 12 pharmaceuticals		• The difference in the removal efficiencies between pharmaceuticals was suggested to be associated with particular physical and chemical properties of the pharmaceuticals.	Vystavna et al. (2017)
Hybrid/full scale	–	Singapore	*Typha angustifolia* *Chrysopogon zizanioides* *papyrus* *Cyperus papyrus* *rush Eleocharis dulcis* *Lepironia articulata* *Phragmites karka* *Cyperus alternifolius* Water lily *Nymphaea* sp.	Atrazine Caffeine Carbamazepine Fluoxetine Gemfibrozil Ibuprofen Triclosan Bisphenol A	88.9–97% −239 to −25% 79.6 to −1588% 93.2 to −229% 97.2 to −29.8% 95.1–47.7% 76.8 to −1777% 93.3–99.9%	• *Typha angustifolia* showed good capability for remediating PPCPs to different extents, with bioconcentration factors of up to 2000. • The suitability for phytoremediation relies on the physico-chemical properties, such as hydrophilicity and lipophilicity, of PPCPs.	Wang et al. (2019)
FS-CW/field scale	20	China	*Phragmites austrails* *Iris pseudacorus*	Total of 45 organic micropollutants		• The fate of the pharmaceuticals in the CW was strongly influenced by their adsorption to soil and sediment.	Xu et al. (2019b)

(*continued on next page*)

Table 4 (*continued*)

System/scale/ intensifications	Hydraulic Retention Time (days)	Country	Plant	Target pollutant	Removal (%)	Significant findings	Reference
SSHF-CW/ mesocosm	4	Singapore	*Zizania caduciflora* *Typha angustifolia*	Ibuprofen	78.5%	• Ibuprofen caused a significant reduction ($P \leq 0.05$) in the bacterial community. • Ibuprofen-enriched wetlands may have selected a special group of bacteria that was able to tolerate and degrade Ibuprofen. • Macrophytes had a vital impact on the microbial community. • Planted systems were more stable against shifts in microbial composition due to Ibuprofen disturbance.	Zhang et al. (2016)
(1) SSVF-CW (2) SSHF-CW (3) **SSHF-CW/ mesocosm	–	Denmark	*Juncus effusus* *Typha latifolia* *Berula erecta* *Phragmites australis* *Iris pseudacorus*	Ibuprofen	29–99%	• Ibuprofen elimination was primarily attributed to microbial degradation by the fixed-bed biofilm. • Plant uptake and degradation within plant tissues were also assumed to participate in ibuprofen removal. • The removal of ibuprofen was positively correlated with the concentration of dissolved oxygen and the removal of nutrients, signifying that degradation could be attributed to co-metabolisation processes.	Zhang et al. (2017a)
Saturated-CW/ mesocosm scale	>1	Denmark	*Typha latifolia* *Phragmites australis* *Iris pseudacorus* *Juncus effusus* *Berula erecta*	Ibuprofen Iohexol	>80% >80%	• Due to the high removal rates, together with the low rates of phytoaccumulation and sorption to the substrate, biodegradation was suggested as the major removal pathway for both ibuprofen and iohexol in the saturated beds. • The removal of ibuprofen and iohexol was found to be stimulated under aerobic conditions and high temperature.	Zhang et al. (2017b)
(1) FS-CW (2) SSHF-CW (3) SSVF-CW/ small scale	2.55 1.27 1.27	China	*Canna indica*	Ibuprofen Gemfibrozil Naproxen Ketoprofen Diclofenac	15.4–79% 15.4–79% 22.1–82.3% 47.9–91.3% 41.7–68.3%	• The removal was higher in both summer and autumn than in winter for all pharmaceuticals. • The removal of pharmaceuticals (ibuprofen, gemfibrozil and naproxen) was positively related to NH^{4+} and dissolved oxygen removal, demonstrating that the nitrification process could be linked to the removal of pharmaceuticals.	Zhang et al. (2018)
Saturated/ mesocosm	–	Denmark	*Typha latifolia* *Phragmites australis* *Iris pseudacorus* *Berula erecta* *Juncus effusus*	Ibuprofen Iohexol	27–94% 76–96%	• Plant presence and plant species contributed to shape the metabolic profiles of the microbial community. • No toxic effects were observed for iohexol or ibuprofen at the concentration of 100 μg/L. • An increase in microbial activity and richness was observed in summer season, particularly in the planted systems. • The removal efficiency was higher in some planted beds, compared to the unplanted beds.	Zhang et al. (2019)

*Partial saturation. **Forced aeration. ND: Not detected.
[a] Ávila et al. (2017).
[b] Chen et al. (2016).
[c] Wang et al. (2019).

[d]Ramprasad and Philip (2018).
[e]National Center for Biotechnology Information (2021)

consequences (such as the accumulation of solid deposits within the bed), can help to avoid clogging of the filter and surface ponding that may reduce the lifetime and efficiency of the wetland, especially non-rested SSVF-CWs, which have been in service for a long time (Ávila and García, 2015).

Based on a recent systematic review by Rabello et al. (2019), the removal of the PPCPs had a positive correlation with the hydraulic retention time of the CWs systems. The improvement of PPCPs removals in conjunction with an increase in HRT, has been demonstrated also by Ramprasad et al. (2017). Vo et al. (2016) revealed that acetaminophen concentrations at effluent were clearly decreased with increasing HRT (0, 3, 5 days). Ramprasad and Philip (2015) reported that the removal rates of sodium dodecyl sulphate (a hydrophobic compound, K_{ow} 3.6) increased from 86% to 96% when the HRT increased from 12.5 days to 16.5 days; whereas changes in HRT have not affected the removal efficiency of water-soluble compounds (propylene glycol and trimethyl amine). The author pointed out that the obvious variation in HRT effect is associated with the difference in physicochemical properties of the compounds, and accordingly their removal mechanisms. The effect of HRT factor appears clearly on amphiphilic compounds that are often subjected to biodegradation or adsorption within wetland systems. Conversely, HRT is not considered influential when it comes to water-soluble compounds that are often directly taken up by plants (Ramprasad and Philip, 2015); since with increasing exposure time, the accumulation of pollutants increases until it reaches a stationary state (Ramprasad and Philip, 2018). Christofilopoulos et al. (2019) reported comparable results for bisphenol A. The authors confirmed that the mean concentration removal of bisphenol A (log $K_{OW} > 3.5$) was 48% at HRT of 1 day and reached 92% when HRT was doubled. Regarding HLR, Zhang et al. (2017a) revealed that the increase in the HLR (1.8, 3.4, 6.9 and 13.8 cm/d).

caused a decline in the removal efficiency of ibuprofen at different influent concentrations (10 and 100 μg/L) and various CW designs (vertical, horizontal, and aerated water saturated) flow systems.

4.4.2. Concentrations of pollutants

Several scientists have investigated the influence of concentration on the PPCP removal process. Vo et al. (2016) revealed that the contribution of removal mechanisms varied with the initial concentration of acetaminophen. At low acetaminophen concentration (1 ppb), the removal mechanism followed the following order: plant uptake (19–68% removal) > microbial and photolytic removal (3–32%) > adsorption, whereas at high concentrations (100 ppb) the following order was observed: microbial and photolytic (approximately 53%) > adsorption (9%) > plant uptake (1–2%). Tai et al. (2017) also revealed that root sorption was obviously related to the concentration of macrolide antibiotics, and the role of exposure concentration was significantly influenced in the removal of tilmicosin, roxithromycin, and anhydroerythromycin A, but not for clarithromycin. Hence, the total removal for macrolides due to rhizosphere processes was about 43.7–67.6% and 44.3–82.2% at 100 and 300 μg/L, respectively.

4.4.3. Rhizosphere community

In wetland systems, the complex microbial communities, which are shaped as a result of the interactions between wetland components, play a major role in wetland systems and contaminant degradation (Zhang et al., 2016). Characterisation of bacterial communities and the associated metabolic pathways cast more light on the degradation mechanisms in CWs, thus assisting in optimising the design parameters and maintenance requirements. However, differences in design, vegetation type, wastewater nature, organic load, physico-chemical conditions, and climatic parameters make establishing general patterns of microbial communities in CWs an extremely complex issue (Hijosa-Valsero et al., 2018).

Despite the extensive research works on the removal of PPCPs by CWs, information on the interaction of plants and bacteria in PPCP biodegradation is still limited (Hussain et al., 2018; Nguyen et al., 2019). Hijosa-Valsero et al. (2018) discovered that the root population associated with *Phragmites australis* exhibited higher microbial richness than that associated with *Typha angustifolia*. However, carbamazepine was more effectively removed by systems with less root microbial richness (*T. angustifolia*). Accordingly, the diversity of the microbial community could be more relevant than the richness as far as removal efficiency is concerned. In a similar context, Liu et al. (2016) confirmed that *Cattail*-CWs showed the highest community richness and microbial diversity compared to both *Hornwort*-CWs and *Lemnaminor*-CWs. This variation was attributed to the difference in the plant root characteristics since Cattail has extensive and fibrous roots, forming a conducive rhizosphere that provides a larger surface area for microorganisms. Furthermore, radial oxygen delivery by the *Cattail* roots enhances the oxygen concentration in sediments.

Hence, understanding the diversity and structure of a microbial community contributes to enhanced performance of a wetland system. Also, characterising the shifts in the structure of the microbial community can be used to predict the microbial populations (Zhang et al., 2016). Li et al. (2016b) referred to the likely role of Dechloromonas sp., the Clostridium sp., the order Sphingobacteriales, and the Cytophaga sp. in the order Cytophagales, in the rhizodegradation of ibuprofen under anaerobic conditions in a SSHF-CW. In another study, Li et al. (2016a) revealed that a variety of microorganisms were responsible for the continuous deterioration in ibuprofen concentration accompanied by the production of the ibuprofen metabolite (2-hydroxy ibuprofen) along the flow path in the SSHF-CW. According to the authors, with an abundance of glucose, the most prospective bacteria to degdrade ibuprofen were the aerobic species of family *Flavobacteriaceae*, family *Methylococcaceae*, and genus *Methylocystis* and the anaerobic species of family *Spirochaetaceae* and genus *Clostridium sensu stricto*. Meanwhile, in the downstream area with low glucose levels, the family *Rhodocyclaceae* and the genus *Ignavibacterium* were the most associated with the ibuprofen degradation.

Nowrotek et al. (2017) believed that the emergence of sulfamethoxazole transformation products linked to glutathione (hydroxy-glutathionyl-Sulfamethoxazole and glutathionyl- Sulfamethoxazole) in the CW effluent indirectly confirmed the occurrence of biotransformation since glutathione is a marker of oxidative stress in bacteria and plants. On the other hand, Button et al. (2019) believed that the continued exposure of intrinsic microbial communities to antibacterial pollutants may theoretically cause a reduction in CW functionality. However, Liu et al. (2016) revealed that several types of bacteria, including beta-Proteobacteria, gamma-Proteobacteria, and Bacteroidetes, were suspected to have a significant role in the CW for triclosan degradation despite the antibacterial characteristics of this substance.

4.4.4. Configuration of the wetland system

The configuration of wetlands has a drastic and prominent effect on the removal of pollutants (Gorito et al., 2017) since the wastewater flow pattern determines the mechanisms prevailing within these systems (Wagner et al., 2018). Furthermore, redox potential conditions and oxygen concentrations are parameters of great importance when degradation follows microbiological pathways (Hijosa-Valsero et al., 2010a). The metabolic function of the microbial community varies greatly depending on the design of the CW (Sgroi et al., 2018). Different wetland configurations promote different conditions, which explains the dominance of certain removal mechanisms in some configurations at the expense of others (Ávila and García, 2015).

According to the data listed in Table 4, SSHF-CWs are the dominant wetlands that have been applied. Studies that dealt with intensified CWs represented 23% of the total studies. The intensifications varied between the use of forced aeration (Auvinen et al., 2017a; Auvinen et al., 2017b; Kahl et al., 2017; Li et al., 2017; Zhang et al., 2017a; Sochacki et al., 2018a; Nivala et al., 2019), re-circulation (Ávila et al., 2017; Button et al., 2019), partial saturation (Kahl et al., 2017; Sgroi et al., 2018; Nivala et al., 2019), and baffled flow (Ramprasad and Philip, 2015). The intensified system improved the removal of ibuprofen (95.5 ± 0.5%), ketoprofen (96.5 ± 2.5%), and naproxen (96.5 ± 2.5%). A total of 48 PPCP substances were repeatedly reported; however, due to the low frequency of some substances, only the most frequent PPCPs were selected for analysis, including seven pharmaceuticals (ibuprofen, caffeine, diclofenac, carbamazepine, sulfamethoxazole, naproxen, and ketoprofen) and four PCPs (sucralose, triclosan, DEET, and propylene glycol).

As illustrated in Fig. 6, FS-CWs offered good performance in removing both ketoprofen and diclofenac. FS-CWs provide favourable conditions for receiving solar radiation, which stimulates photolysis for several PPCPs (Zhang et al., 2018). In a recent review, Ilyas and van Hullebusch (2020a) concluded that the dominant removal mechanism for both ketoprofen and diclofenac is photodegradation, with possible opportunities for biodegradation. However, photodegradation in CWs is strongly influenced by the intensity of light and the amount of light attenuation by the water depth (Francini et al., 2018). Choi et al. (2016) revealed that despite the promising results in removing enrofloxacin during microcosm photodegradation experiments, which exceeded 70%, the limited exposure of sunlight obviously reduced the in situ removal rate (27.26%) of this antibiotic in the CW.

In comparison with SSHF-CWs, SSVF-CWs showed a remarkably high performance and superiority in removing many pharmaceuticals, including readily biodegradable compounds such as ibuprofen (95 ± 0% vs 54 ± 25%), naproxen (89 ± 1% vs 54 ± 29%), and caffeine (94 ± 3% vs 86 ± 9%). Even for the less biodegradable compounds, ketoprofen and diclofenac, the removal efficiencies in the SSVF-CWs were 89% and 58 ± 9%, respectively, vs 35 ± 25% and 35 ± 16%, respectively, in the SSHF-CWs. The prevailing anoxic or anaerobic conditions in the SSHF-CWs may cause the reduction of aerobic degradation for many compounds (Chen et al., 2016). According to Ilyas and van Hullebusch (2020a), aerobic biodegradation was suggested to be the dominant removal mechanism for ibuprofen, naproxen, and caffeine, whereas diclofenac was suggested to be an aerobically/anaerobically biodegradable compound. On the other hand, ketoprofen was reported to be removed via biodegradation in many studies (Chen et al., 2016; Francini et al., 2018; Zhang et al., 2018). However, biodegradation is not the only mechanism responsible for removing PPCPs in SSHF-CWs since both adsorption and/or rhizosphere development enhance the removal of several compounds known for their tendency toward aerobic degradation, such as ibuprofen and metoprolol (Chen et al., 2016).

SSVF-CWs are more functional for the removal of PPCPs than SSHF-CWs, since aerobic pathways that predominate in vertical-flow systems are generally more effective in the degradation of pollutants than the anaerobic pathways prevalent in horizontal systems (Ávila and García, 2015). The design of SSVF-CWs essentially supports aerobic processes where oxygen plays the role of a terminal electron acceptor, while the role of anoxic processes is reduced to a minimum (Sochacki et al., 2018b). In a recent review, Liu et al. (2019b) reported that the removal performance of CWs for antibiotics showed good performance, especially SSVF-CWs with an average value of 80.44%.

The combination of various wetland configurations in hybrid systems contributes to the optimisation of the essential removal mechanisms (physico-chemical and microbiological), attaining an excellent overall removal efficiency of PPCPs (Ávila and García, 2015). As shown in Fig. 6, hybrid CWs offered improved efficiency for removing 77 ± 7% of caffeine and 94.6 ± 6% of diclofenac. However, limited numbers of pharmaceuticals, such as sulfamethoxazole and carbamazepine, show recalcitrant behaviour towards treatment in all types of CWs, which is often due to the nature of these substances, where a variety of characteristics impede their interaction with different removal mechanisms. The average removal of sulfamethoxazole was 38.5 ± 10%, 31.5 ± 31.5%, 65 ± 27%, and 39.7 ± 9% in FS, SSHF, SSVF, and hybrid CWs, respectively, whereas carbamazepine showed negative removals of 16.67 ± 23%, 13.1 ± 14%, −8.5 ± 0.5%, and −126.5 ± 280% in FS, SSHF, SSVF, and hybrid CWs, respectively. Sulfamethoxazole is a low adsorptive antibiotic (Sochacki et al., 2018a), which is likely removed via photochemical and biological processes in CWs, whereas plant uptake can only directly contribute a small portion due to the extremely hydrophilic characteristic (Log Kow 0.89) for sulfamethoxazole (Liang et al., 2018). On the other hand, plant's biomembrane have negative charges, that in turn hinders the absorption of negatively charged compounds (Sochacki et al., 2018a) including sulfamethoxazole (Huang et al., 2019). As for the common anticonvulsant, carbamazepine, although its moderate hydrophobicity (log K_{ow} = 2.3) and neutral charge (Huang et al., 2019), yet the removal rates in CWs were low as reported by several studies (Ávila et al., 2017; Auvinen et al., 2017b; Nivala et al., 2019; Park et al., 2018). Interestingly, the high potential of carbamazepine for bioaccumulation (with bioconcentration factor value

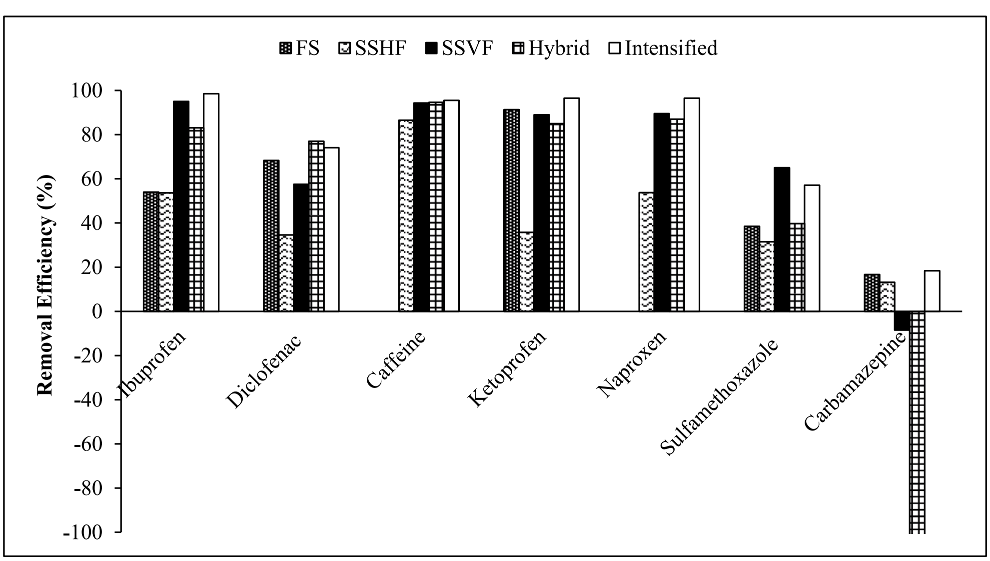

Fig. 6. Removal efficiency of selected pharmaceutical compounds with different types of CWs.

higher than 1000 L/kg) have been confirmed by Wang et al. (2019), however, the authors reported that the overall removal efficiency that was achieved in the study ranged between 79.6 and −1588%. Adsorption is forecasted to be the primary removal mechanism for carbamazepine in CW systems (Ilyas and van Hullebusch, 2020a). In fact, the fate of contaminants that undergo adsorption is limited to removal from the liquid phase with an incoming potential for desorption, leading to contaminant bioavailability at later stages (Wagner et al., 2018).

The difference in feeding patterns (such as continuous, batch, and intermittent) may change the oxidation–reduction conditions as well as oxygen transfer and diffusion in CWs, consequently modulating the treatment efficiency. Unlike continuous feeding, batch operation mode intensifies the performance of wetland systems by promoting the prevailing oxidation conditions (Wu et al., 2015). The 'fill-and-drain' strategy oxygenates the exposed biofilms on the substrate layer as the system is drained, which enhances the treatment efficiency compared to systems with a static water level. Zhang et al. (2012) reported significant removal enhancement for diclofenac, ibuprofen, salicylic acid, caffeine, and ketoprofen under batch operational mode as compared to continuous operation.

The loading frequency is a key operational factor, ensuring that SSVF-CWs provide an effective treatment performance if oxygen replacement and transformation of organic matter are sufficiently allowed. It is preferable to pump wastewater in high-volume batch doses with low loading frequencies since this technique enhances the transport of oxygen into the system by diffusion and convection. Too high of a load volume could reduce the contact time between the wastewater and the biomass and thus decrease the removal efficiency. Also, a highly successive loading frequency reduces the possibility for oxygen renewal that occurs between the pulses, which has a negative influence on the removal of several processes such as nitrification (Ávila and García, 2015). However, the conditions imposed by the loading frequency in the CW are based mainly on the hydraulic properties of the system, as well as the plant presence and type (Sochacki et al., 2018b). Sochacki et al. (2018b) investigated the effect of loading frequency (1 pulse/day and 4 pulses/day) on the removal of diclofenac and sulfamethoxazole in an unsaturated, intermittently fed SSVF-CW. The authors confirmed a deterioration in the removal efficiency of both diclofenac (74.2–47.3%) and sulfamethoxazole (69–52.8%) at the highest loading frequency.

Regarding PCPs, triclosan was moderately eliminated in the classic CWs, with an average removal rate of 61.6 ± 33%, while triclosan was completely removed in the intensified systems. DEET was moderately removed in both classic and intensified CWs at rates of 44 ± 19% and 38.6 ± 4%, respectively. Moreover, propylene glycol was easily removed in all types of CWs, whereas sucralose exhibited a recalcitrant behaviour.

4.4.5. Plant species

It is widely accepted that the prime functions of plants in CWs are related to their physical structures, which uptake nutrients, release oxygen and root exudates, and provide the necessary surface to support microbial growth (Zhang et al., 2017b). Various wetland plants have been employed in CWs to enhance the treatment process by taking advantage of their properties (Kumar and Dutta, 2019). However, the capacity of plant uptake may be strongly correlated with the wastewater types, system configurations, loading rates, retention times, and climatic conditions (Wu et al., 2015). Referring to the data in Table 4, plants were classified according to genus. Fig. 7 shows the percentages of the types of plant used in the CWs. *Phragmites* was the most used genus, with a percentage of 28%, followed by *Typha* (15%), *Irish*, and *Phalaris* (7%), whereas another genus represented about 34%.

Consideration must be taken to select plants with good tolerance to waterlogged-anoxic and hyper-eutrophic conditions, a high capacity for pollutant absorption, and adaption to extreme climates (Wu et al., 2015). The selection of plant species strongly influences the functional profiles of the microbial community in the CWs during treatment for

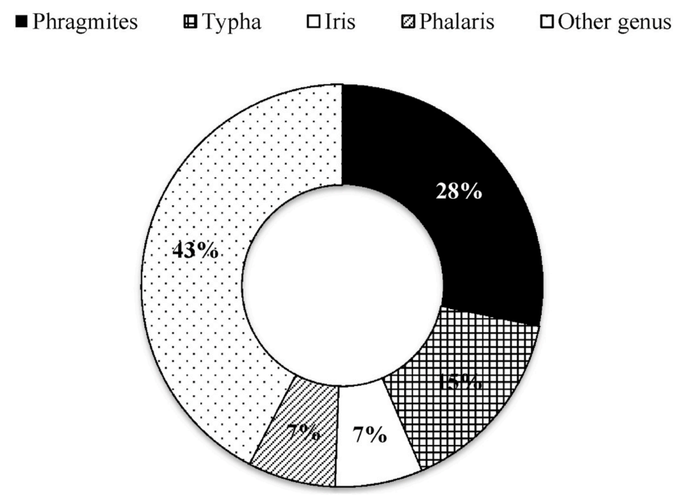

Fig. 7. Percentage of plant species used in CWs.

pharmaceutical compounds. The oxygen and exudations (organic acids, sugars, and enzymes) released by plants in the rhizosphere decide the ecological roles of the attached microbial population. However, the plant exudation profiles vary according to the plant species and shape distinct microbial consortiums. Also, due to the different structures of the plants, including the morphology of the roots, mechanical attachment to the plant root is another conditioning factor that causes subsequent differences in the composition of the microbial community (Zhang et al., 2019). Therefore, not only the presence of the plants but also the plant species shape the microbial function in the CWs (Kraiem et al., 2019; Zhang et al., 2019). Chen et al. (2016) found that CWs with *Phalaris arundinacea* displayed relatively lower removal efficiency (75–76%) for naproxen than two other CWs (76–97% and 69–96%) planted with *Phragmites australis*.

Many studies have confirmed that the presence of plants contributes to the removal of several PPCPs, such as ibuprofen (Zhang et al., 2017a, 2018), gemfibrozil (Zhang et al., 2018), and triclosan (Button et al., 2019). As shown in Fig. 8, planted CWs exhibited improved performance rather than unplanted CWs for removing various pharmaceuticals, including ibuprofen (57.8 ± 27% vs 32.2 ± 26%), diclofenac (38.4 ± 22% vs 28.5 ± 26%), ketoprofen (20 ± 0% vs 12.5 ± 1%), naproxen (46.6 ± 28% vs 32 ± 18%), and carbamazepine (46.1 ± 29% vs 30.7 ± 32%). However, the vegetation was not effective in the removal of caffeine and sulfamethoxazole.

Indeed, the plants did not participate in the removal of PPCPs from wastewater in several studies (Nowrotek et al., 2016; Button et al., 2019); rather, their role was not positive in some cases. For instance, the presence of *Phalaris arundinacea* in the SSVF-CW caused clear deterioration in the removal of diclofenac and sulfamethoxazole (Sochacki et al., 2018b). Likewise, the decomposition of macrophytes in the fall may cause a drastic deterioration in the quality of treated water in FS-CWs, as mentioned by Ávila et al. (2017). The authors reported a clear increase in the concentrations of caffeine, thrimethoprim, DEET, and fluoxetine, which are believed to have resulted mainly from desorption from the sediment/biomass under adverse conditions associated with plant decay. Thus, the pollutants assimilated by the plants during the treatment period may be released later due to the death and decay of the plants during the winter season, which negatively affects the performance of the wetland systems. Therefore, it is necessary to study appropriate strategies for harvesting and recycling plant resources in CWs (Wu et al., 2015).

5. Application of phytoremediation for PPCPs

In recent decades, researchers have been searching for green

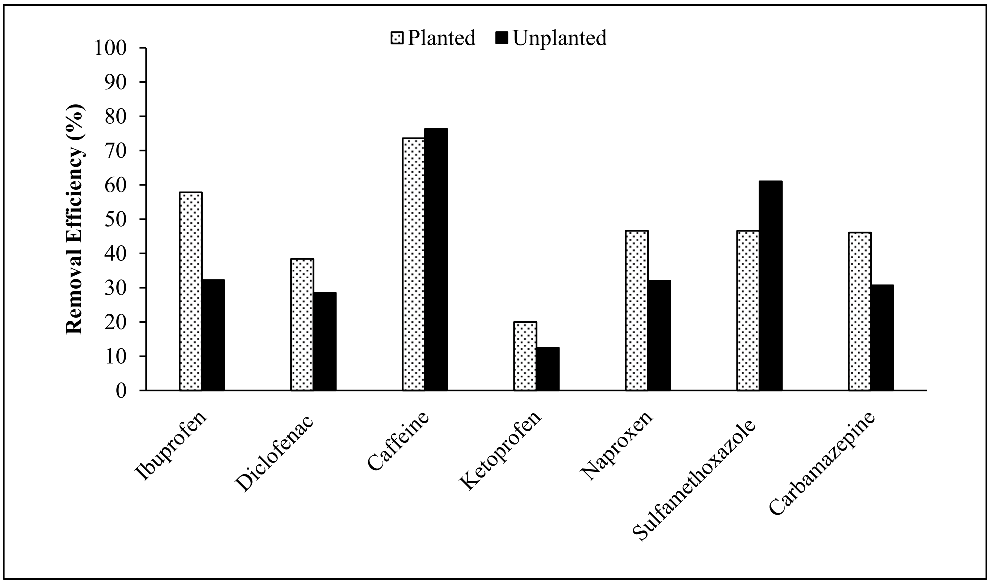

Fig. 8. Removal of pharmaceutical compounds in planted and unplanted CWs.

solutions to treat wastewater by exploiting natural resources, such as microorganisms and plants, to find efficient and cost-effective treatment methods (Kadir et al., 2020). Bioremediation (specifically phytoremediation) offers a solution commensurate with the hydrophilic nature of most PPCPs. In addition, plants are able to tolerate relatively high concentrations of PPCPs, even ones that carry some toxicity to microorganisms. Accordingly, phytoremediation is a fool proof and viable option to combat the increasing concentrations of PPCPs in water sources around the world.

5.1. Success stories of PPCPs removal

Phytoremediation has achieved promising results in removing various PPCPs from wastewater, even for recalcitrant PPCPs. Many phytoremediation projects have been successfully undertaken on a global level. In recent decades, CWs have gone from only being used in empirical research to widespread application in several fields, such as anthropogenic wastewater discharge, sewage treatment, storm water runoff, and land reclamation, which follows mining processes (Ferreira et al., 2017). Large-scale CWs have been widely implemented in several countries, including the Czech Republic (Chen et al., 2016; Vymazal et al., 2017; Březinova et al., 2018), the Republic of Korea (Choi et al., 2016; Park et al., 2018), Singapore (Wang et al., 2019), China (Xu et al., 2019b), Ukraine (Vystavna et al., 2017), Belgium (Auvinen et al., 2017a), and Spain (Hijosa-Valsero et al., 2010a).

Furthermore, large-scale CWs have been found to be an efficient tool in the removal of pharmaceutical pollutants (Vymazal et al., 2017) from municipal wastewaters (Xu et al., 2019b); or at least, offering as good efficiencies as conventional WWTPs for the removal of PPCPs (Hijosa--Valsero et al., 2010a). Nevertheless, it is possible to notice a variation in the performance of these systems, which can be attributed to the influent load, wastewater characteristics, local climate, age of the system, and maintenance status (Chen et al., 2016). It appears that biological treatments will constitute a sustainable approach to dealing with the growing problem of wastewater pollution, and this requires more extensive studies to transfer the promising laboratory results to the applied level.

5.2. SWOT analysis on phyto-technological approach for PPCPs removal

Water quality around the world is decreasing at an alarming rate, and a growing number of water bodies are rapidly losing their ecological role due to climatic changes and population growth (Bi et al., 2019). The SWOT analysis process is an opportunity to explore the possibilities for new technologies or solutions to keep the environment clean. A SWOT analysis is an objective tool for improving strategies through data comparison (Bidhendi et al., 2020). Recently, decision-makers have increasingly relied on SWOT analysis to set priorities in implementing remediation projects. Researchers resort to literature data to analyse environmental, economic, and social trends of environmental remediation techniques, with priority given to environmentally friendly technologies (Kalabić et al., 2019). Thus, in this review, SWOT analysis will focus on strengths, weaknesses, opportunities, and threats of phyto-technological approach to remove PPCPs. The strengths describe positive attributes, which are internal, positive factors. Weaknesses are aspects lacking in a treatment process of PPCPs (internal, negative factors). Opportunities are external, positive factors that represent reasons to concentrate on biotechnology treatment of PPCPs from water. Threats include external negative factors that could affect biotechnological treatment and the ecosystem.

Phytotechnology has appeared as an promising approach for eliminating a wide range of contaminants (Abdullah et al., 2020). The strength of this treatment technology lies in its sustainability, its eco-friendly impact, and its repeated outperformance over conventional WWTPs in removing most PPCPs. Moreover, this phytotreatment is generally easy to manage and represents a low-cost option for reclaiming wastewater contaminated with PPCPs; however, there are limitations. Good management for phytoremediation can provide additional benefits such as exploiting the resulting plant biomass as a raw material for paper and a source of cellulosic feedstock for the production of second-generation biofuels as mentioned by Lin et al. (2020). However, there must be reservation regarding the use of CWs biomass as a raw material in other applications referred to by the authors including fertilizer, compost industries or as a feed supplement for animals, since such products may interfere with the food chain.

The weakness of phytotreatment is due to the fact that its success depends mainly on the nature of the PPCPs being treated. It is worth noting that this technology has achieved impressive results in removing PPCPs, except for a few recalcitrant compounds. Also, this treatment requires more time compared to other treatment technologies. Furthermore, climate conditions and seasonal variations may interfere with or inhibit plant growth (Lee, 2013). To counter time-consuming weakness, enhancement through addition of intermittent aeration system, effective rhizobacteria, enzymes and biosurfactant can expedite the removal process of PPCPs.

In addition, phytotreatment processes are generally limited by the root-depth zone due to the shallow distribution of plant roots; thus, during this treatment process, pollutants are required to be within the root-influence zones for more effective removal or degradation (Herath and Vithanage, 2015). This obstacle can be overcome by applying different types of plants with different root systems (such as tap and fibrous roots) or integration of emergent and submergent or floating plants by knowing the occurrence of PPCPs in the contaminated medium to ensure adequate contact between the roots and the target pollutants (Abdullah et al., 2020). The plant-assisted approach is usually not recommended if pollutants pose a risk to humans or water. It can be applied onsite to remove or mitigate the high levels of PPCPs in sanitary and industrial wastewater for hospitals, medical centres, and related manufacturing facilities.

Additionally, this phyto-approach can also be applied as a tertiary unit in WWTPs to exclude residual PPCPs and to meet water quality standards allowing the treated water to be reused for other purposes such as cleaning or landscaping or even in the manufacturing process. In addition, intensified systems can be employed to improve the removal efficiency and to reduce land requirements to a minimum. The threat related to the treatment of PPCPs via phytotechnology is the possibility of the emergence of transformation by-products during the treatment processes that could be more toxic and may lead and leak to the food chain. Evaluating the performance of CWs over time can provide the fundamental knowledge necessary for refining their design and the overall value to the receiving environment (Tondera et al., 2019).

The age of the filter material (substrate) must also be taken into consideration; thus, to maintain maximum levels of PPCP reduction, an exchange of the filter material or a subsequent filter step is necessary after several years of operation (Tondera et al., 2019). This restriction of phytotreatment is the final fate of contaminant, which is unknown since its disposal may affect the ecosystem (Zhang et al., 2014). This may adversely affect the provision of freshwater to agriculture and, finally, threaten food security (Fig. 9).

Although the phytoremediation technology is frequently employed, the available information regarding the ability of plants to assimilate and translocate PPCPs is still limited to a few types of contaminants and plant species. More comprehensive and intensive research should be promoted and is required to foresee the fate after treatment and to compile concrete evidence on this phytotransformation, phytodegradation/phytostimulation and detoxification so that neither secondary waste will be created, nor the food chain impacted at the end of the phytotreatment. Possibility of reusing the treating plants or converting them to useful by-products such as biogas, feedstock or fertilizer after being used in treatment through CW will be another future research direction.

PPCPs that are directly released into environment can cause a threat to aquatic ecosystems. The current study has reported the occurrence of more than 60 pharmaceutical compounds with concentrations from 10^{-1}–10^{5} ng L^{-1} in aquatic environment, such as waterbodies, groundwater, wastewater, and drinking water. A sustainable approach in wastewater treatment is the use of plants in phytotechnology to eliminate PPCPs. However, there are challenges, particularly in applying large scale constructed wetland because the performance might differ from the performance found in the lab. The most abundant PPCPs discharged into the sewer system are NSAIDs, lipsticks, moisturisers, hair colours, shampoos, deodorants, and toothpastes, which will subsequently be discharged into aquatic systems, such as surface water and groundwater.

In this review, we have assessed the challenges in applying phytotechnology in the removal of PPCPs in wastewater before their release into the environment. Low antibiotic concentrations (ng/L to mg/L) in water can pose major threats to the ecosystem and to human health (Chaves-Barquero et al., 2018). Phytoremediation is an excellent treatment approach in field of wastewater from municipal, industry, and hospital because it can be applied on-site in artificial design with ornamental plants and at same time get good view. In the application of CWs with an availability of natural aquatic plants, physical, chemical, and biological processes, including precipitation, volatilisation, sorption, and degradation, as well as microbial metabolism, are simultaneously involved (Zhang et al., 2014). Phytotechnology is progressing to treat and control micropollutants including PPCPs by interaction between plants and microorganism in CWs as a cost-effective of handling

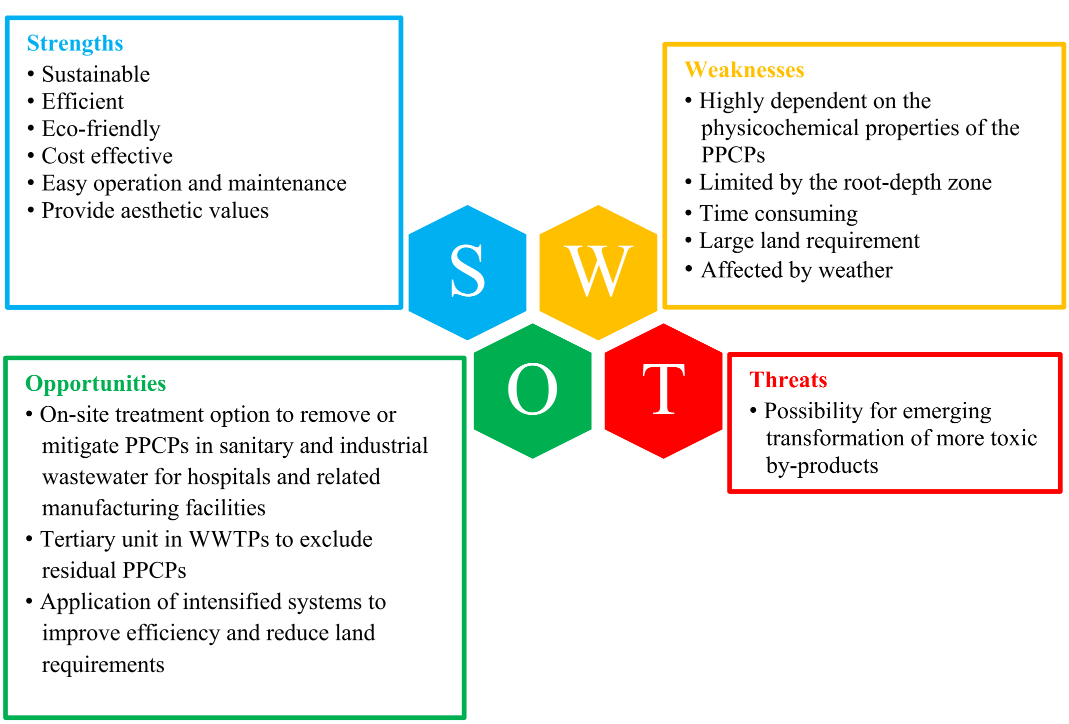

Fig. 9. SWOT analysis presentation of phytoremediation technology to treat PPCPs.

waste (Chaves-Barquero et al., 2018; Riva et al., 2020). To get the best performance of PPCP removal through phytotechnology, plant roots must always be kept in contact with wastewater. The type of plant and the substrate content should be taken into consideration at the design stage of CWs. Native plants should be the best option. More thorough research needs to be extended to look for more native plant species that are capable to treat PPCPs. In addition, in the case of a large volume of contaminated water, the flow rate and retention time should also be considered. For large volume application, it obviously entails more area for the installation of CW system. In terms of large area requirement, consideration on using hydroponic systems or in reed beds in staggered arrangement for wastewater containing PPCPs can be considered. Hybrid system consisting of surface or subsurface flow, horizontal or vertical flow can always offer good combination to remove PPCPs in WWTPs.

Combating PPCPs at their source, such as in hospital wastewater, which typically contains higher concentrations of pharmaceutical residues than other wastewater, would be the best option. Thus, opportunities to separate the treatment of this water will reduce the load of pharmaceuticals on municipal WWTPs, consequently avoiding dilution of the wastewater and thus decrease removal efficiency. Finally, the discharge of pharmaceutical residues to the environment can lead to combined sewer overflows and leakages (Auvinen et al., 2017b). The biggest challenge is how to control non-point sources of PPCPs since they are used daily in human life. Involvement of all parties including government and private sectors, non-governmental organisations (NGOs) and local community are required to increase people's awareness on the issue and impacts of PPCPs through education, active campaign, exhibition, speech or talks, to be more responsible to properly dispose of those expired medicines and not to simply throw or discharge expired medicines into normal bins or into toilets. The hierarchy of waste minimisation (source reduction, reuse/reclaim/recover, treatment, and disposal) should be promoted and applied in human life. Waste separation at source is the best practice that should be campaigned to be applied in day-to-day activities.

6. Conclusions

This review demonstrates the widespread prevalence of PPCPs in aquatic systems around the world. Despite their low concentrations, the continuous discharge of PPCPs may turn them into pseudo-persistent pollutants. A systematic and comprehensive review of the efficiency of phytoremediation (represented by CWs) in removing PPCPs from wastewater was carried out. Overall, CWs showed a moderate to high removal efficiency for removing various PPCPs. Subsurface vertical-flow and hybrid systems offered good performance for removing easily biodegradable PPCPs, such as ibuprofen, caffeine, naproxen, and propylene glycol. Intensifications such as forced aeration and flow recirculation enhanced the efficiency of subsurface horizontal-flow systems, especially for removing aerobically biodegradable PPCPs. On the other hand, free surface-flow systems provided optimum conditions for the removal of photolytically susceptible substances, such as ketoprofen and ibuprofen. The influence of operational factors, such as hydraulic retention time, in the removal process was evident. Moreover, the presence of plants influenced the removal efficiency of the wetland systems. Finally, the feasibility of phytoremediation for PPCP removal was evaluated objectively through SWOT analysis. Sustainability and eco-friendly impacts are the most important strengths of this technology, while large land requirements and more time are the main weaknesses; however, they can be overcome through an appropriate design. This technology has promising opportunities for treating wastewater from medical facilities. As for the threats, they are entirely related to the nature of the PPCPs and the potential for the emergence of by-products. In fact, the future of wastewater treatment is seriously shifting towards sustainable and environmentally friendly solutions since biological tools, such as plants and microorganisms, can be employed to play the primary role in the restoration of ecosystems. Using phytoremediation for wastewater treatment can save massive amounts of energy and reduce carbon emissions. There is still ambiguity regarding the removal mechanism involved; hence, further studies are required to optimise the design and operation conditions and to understand the mechanism.

Declaration of competing interest

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

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References

Abdullah, S.R.S., Al-Baldawi, I.A., Almansoory, A.F., Purwanti, I.F., Al-Sbani, N.H., Sharuddin, S.S.N., 2020. Plant-assisted remediation of hydrocarbons in water and soil: application, mechanisms, challenges and opportunities. Chemosphere 247, 125932. https://doi.org/10.1016/j.chemosphere.2020.125932.

AL Falahi, O.A., Abdullah, S.R.S., Hasan, H.A., Othman, A.R., Ewadh, H.M., Al-Baldawi, I.A., Kurniawan, S.B., Imron, M.F., Ismail, N.I., 2021. Simultaneous removal of ibuprofen, organic material, and nutrients from domestic wastewater through a pilot-scale vertical sub-surface flow constructed wetland with aeration system. J. Water Process Eng. 43, 102214. https://doi.org/10.1016/j.jwpe.2021.102214.

Al-Ajalin, F.A.H., Idris, M., Abdullah, S.R.S., Kurniawan, S.B., Imron, M.F., 2020. Evaluation of short-term pilot reed bed performance for real domestic wastewater treatment. Environ. Technol. Innov. 20, 101110. https://doi.org/10.1016/j.eti.2020.101110.

Al-Khazrajy, O.S.A., Boxall, A.B.A., 2016. Risk-based prioritization of pharmaceuticals in the natural environment in Iraq. Environ. Sci. Pollut. Res. 23, 15712–15726. https://doi.org/10.1007/s11356-016-6679-0.

Archer, E., Petrie, B., Kasprzyk-Hordern, B., Wolfaardt, G.M., 2017. The fate of pharmaceuticals and personal care products (PPCPs), endocrine disrupting contaminants (EDCs), metabolites and illicit drugs in a WWTW and environmental waters. Chemosphere 174, 437–446. https://doi.org/10.1016/j.chemosphere.2017.01.101.

Ashfaq, M., Li, Y., Rehman, M.S.U., Zubair, M., Mustafa, G., Nazar, M.F., Yu, C.P., Sun, Q., 2019. Occurrence, spatial variation and risk assessment of pharmaceuticals and personal care products in urban wastewater, canal surface water, and their sediments: a case study of Lahore, Pakistan. Sci. Total Environ. 688, 653–663. https://doi.org/10.1016/j.scitotenv.2019.06.285.

Auvinen, H., Gebhardt, W., Linnemann, V., Du Laing, G., Rousseau, D.P.L., 2017a. Laboratory- and full-scale studies on the removal of pharmaceuticals in an aerated constructed wetland: effects of aeration and hydraulic retention time on the removal efficiency and assessment of the aquatic risk. Water Sci. Technol. 76, 1457–1465. https://doi.org/10.2166/wst.2017.328.

Auvinen, H., Havran, I., Hubau, L., Vanseveren, L., Gebhardt, W., Linnemann, V., Van Oirschot, D., Du Laing, G., Rousseau, D.P.L., 2017b. Removal of pharmaceuticals by a pilot aerated sub-surface flow constructed wetland treating municipal and hospital wastewater. Ecol. Eng. 100, 157–164. https://doi.org/10.1016/j.ecoleng.2016.12.031.

Ávila, C., García, J., 2015. Pharmaceuticals and Personal Care Products (PPCPs) in the environment and their removal from wastewater through constructed wetlands. Compr. Anal. Chem. 67, 195–244. https://doi.org/10.1016/B978-0-444-63299-900006-5.

Ávila, C., Pelissari, C., Sezerino, P.H., Sgroi, M., Roccaro, P., García, J., 2017. Enhancement of total nitrogen removal through effluent recirculation and fate of PPCPs in a hybrid constructed wetland system treating urban wastewater. Sci. Total Environ. 584–585, 414–425. https://doi.org/10.1016/j.scitotenv.2017.01.024.

Bartrons, M., Peñuelas, J., 2017. Pharmaceuticals and personal-care products in plants. Trends Plant Sci. 22, 194–203. https://doi.org/10.1016/j.tplants.2016.12.010.

Bi, R., Zhou, C., Jia, Y., Wang, S., Li, P., Reichwaldt, E.S., Liu, W., 2019. Giving waterbodies the treatment they need: a critical review of the application of constructed floating wetlands. J. Environ. Manag. https://doi.org/10.1016/j.jenvman.2019.02.064.

Bidhendi, G.N., Zand, A.D., Heir, A.V., Bidhendi, A.N., 2020. Prioritizing of strategies for the ecological design of urban waste transfer stations using SWOT analysis. J. Environ. Soc. Sci. 5, 2665–2672.

Blair, B.D., Crago, J.P., Hedman, C.J., Klaper, R.D., 2013. Pharmaceuticals and personal care products found in the Great Lakes above concentrations of environmental

concern. Chemosphere 93, 2116–2123. https://doi.org/10.1016/j.chemosphere.2013.07.057.
Breitholtz, M., Näslund, M., Stråe, D., Borg, H., Grabic, R., Fick, J., 2012. An evaluation of free water surface wetlands as tertiary sewage water treatment of micro-pollutants. Ecotoxicol. Environ. Saf. 78, 63–71. https://doi.org/10.1016/j.ecoenv.2011.11.014.
Březinova, T.D., Vymazal, J., Koželuh, M., Kule, L., 2018. Occurrence and removal of ibuprofen and its metabolites in full-scale constructed wetlands treating municipal wastewater. Ecol. Eng. 120, 1–5. https://doi.org/10.1016/j.ecoleng.2018.05.020.
Bunmahotama, W., Lin, t., Yang, X., 2020. Prediction of adsorption capacity for pharmaceuticals, personal care products and endocrine disrupting chemicals onto various adsorbent materials. Chemosphere 238, 124658. https://doi.org/10.1016/j.chemosphere.2019.124658.
Button, M., Cosway, K., Sui, J., Weber, K., 2019. Impacts and fate of triclosan and sulfamethoxazole in intensified re-circulating vertical flow constructed wetlands. Sci. Total Environ. 649, 1017–1028. https://doi.org/10.1016/j.scitotenv.2018.08.395.
Calado, S.L. de M., Esterhuizen-Londt, M., de Assis, H.C.S., Pflugmacher, S., 2019. Phytoremediation: green technology for the removal of mixed contaminants of a water supply reservoir. Int. J. Phytoremediation 21, 372–379. https://doi.org/10.1080/15226514.2018.1524843.
Carranza-Diaz, O., Schultze-Nobre, L., Moeder, M., Nivala, J., Kuschk, P., Koeser, H., 2014. Removal of selected organic micropollutants in planted and unplanted pilot-scale horizontal flow constructed wetlands under conditions of high organic load. Ecol. Eng. 71, 234–245. https://doi.org/10.1016/j.ecoleng.2014.07.048.
Chatterjee, S., Mitra, A., Datta, S., Veer, V., 2013. Phytoremediation Protocols: an Overview, Soil Biology. https://doi.org/10.1007/978-3-642-35564-6.
Chaves, M. de J.S., Barbosa, S.C., Malinowski, M. de M., Volpato, D., Castro, Í.B., Franco, T.C.R., dos, S., Primel, E.G., 2020. Pharmaceuticals and personal care products in a Brazilian wetland of international importance: occurrence and environmental risk assessment. Sci. Total Environ. 734, 139374. https://doi.org/10.1016/j.scitotenv.2020.139374.
Chaves-Barquero, L.G., Luong, K.L., Rudy, M.D., Frank, R.A., Hanson, M.L., Wong, C.S., 2018. Attenuation of pharmaceuticals, nutrients and toxicity in a rural sewage lagoon system integrated with a subsurface filtration technology. Chemosphere 209, 767–775. https://doi.org/10.1016/j.chemosphere.2018.06.119.
Chen, X., Hu, Z., Zhang, Y., Zhuang, L., Zhang, J., Li, J., Hu, H., 2018. Removal processes of carbamazepine in constructed wetlands treating secondary effluent: a review. Water (Switzerland) 10, 1–16. https://doi.org/10.3390/w10101351.
Chen, Y., Vymazal, J., Březinová, T., Koželuh, M., Kule, L., Huang, J., Chen, Z., 2016. Occurrence, removal and environmental risk assessment of pharmaceuticals and personal care products in rural wastewater treatment wetlands. Sci. Total Environ. 566–567, 1660–1669. https://doi.org/10.1016/j.scitotenv.2016.06.069.
Choi, Y.J., Kim, L.H., Zoh, K.D., 2016. Removal characteristics and mechanism of antibiotics using constructed wetlands. Ecol. Eng. 91, 85–92. https://doi.org/10.1016/j.ecoleng.2016.01.058.
Chopra, S., Kumar, D., 2018. Pharmaceuticals and personal care products (PPCPs) as emerging environmental pollutants: toxicity and risk assessment. Advances in Animal Biotechnology and its Applications, pp. 337–353. https://doi.org/10.1007/978-981-10-4702-2_19.
Christofilopoulos, S., Kaliakatsos, A., Triantafyllou, K., Gounaki, I., Venieri, D., Kalogerakis, N., 2019. Evaluation of a constructed wetland for wastewater treatment: addressing emerging organic contaminants and antibiotic resistant bacteria. N. Biotech. 52, 94–103. https://doi.org/10.1016/j.nbt.2019.05.006.
Cizmas, L., Sharma, V.K., Gray, C.M., McDonald, T.J., 2015. Pharmaceuticals and personal care products in waters: occurrence, toxicity, and risk. Environ. Chem. Lett. https://doi.org/10.1007/s10311-015-0524-4.
Couto, C.F., Santos, A.V., Amaral, M.C.S., Lange, L.C., de Andrade, L.H., Foureaux, A.F.S., Fernandes, B.S., 2020. Assessing potential of nanofiltration, reverse osmosis and membrane distillation drinking water treatment for pharmaceutically active compounds (PhACs) removal. J. Water Process Eng. 33, 101029. https://doi.org/10.1016/j.jwpe.2019.101029.
Dey, S., Bano, F., Malik, A., 2019. Pharmaceuticals and personal care product (PPCP) contamination-a global discharge inventory. Pharmaceuticals and Personal Care Products: Waste Management and Treatment Technology. Elsevier Inc., pp. 1–26. https://doi.org/10.1016/b978-0-12-816189-0.00001-9
Dhir, B., 2019. Removal of pharmaceuticals and personal care products by aquatic plants. Pharmaceuticals and Personal Care Products: Waste Management and Treatment Technology. Elsevier Inc., pp. 321–340. https://doi.org/10.1016/b978-0-12-816189-0.00014-7
Dordio, A., Carvalho, A.J.P., 2018. Removal processes of pharmaceuticals in ConstructedWetlands. Constr. Ind. Wastewater Treat. https://doi.org/10.5040/9780571261703.0063.
Ebele, A.J., Abou-Elwafa Abdallah, M., Harrad, S., 2017. Pharmaceuticals and personal care products (PPCPs) in the freshwater aquatic environment. Emerg. Contam. 3 (1), 1–16. https://doi.org/10.1016/j.emcon.2016.12.004.
Eggen, T., Vogelsang, C., 2015. Occurrence and fate of pharmaceuticals and personal care products in wastewater. Compr. Anal. Chem. 67, 245–294. https://doi.org/10.1016/B978-0-444-63299-9.00007-7.
Ellis, J.B., 2006. Pharmaceutical and personal care products (PPCPs) in urban receiving waters. Environ. Pollut. 144, 184–189. https://doi.org/10.1016/j.envpol.2005.12.018.
Ewadh, H.M., Abdullah, S.R.S., Anwar, N., Hasan, H.A., 2017. Pharmaceuticals and personal care products : sources , toxicity in the environment, regulations and removal technologies. J. Chem. Pharmaceut. Sci. 10, 1180–1187.
Fadhil, N.M., Al-Baldawi, I.A.W., 2019. Mechanisms of plant-correlation phytoremediation of Al-Daura Iraqi refinery wastewater using wetland plant from Tigris River. J. Eng. 25 October 2019, 20–32. https://doi.org/10.31026/j.eng.2019.10.2.
Fadhil, N.M., Al-Baldawi, I.A.W., 2020. Biodegradation of total petroleum hydrocarbon from Al-Daura refinery wastewater by rhizobacteria. J. Eng. 26 January 2020, 14–23. https://doi.org/10.31026/j.eng.2020.01.02.
Fang, T.Y., Praveena, S.M., Aris, A.Z., Ismail, S.N.S., Rasdi, I., 2018. Quantification of selected steroid hormones (17Β-Estradiol and 17Α-Ethynylestradiol) in wastewater treatment plants in Klang Valley (Malaysia). Chemosphere 215, 153–162. https://doi.org/10.1016/j. Chemosphere.2018.10.032. Elsevier Ltd.
Ferreira, A.R., Ribeiro, A., Couto, N., 2017. Remediation of pharmaceutical and personal care products (ppcps) in constructed wetlands: applicability and new perspectives. In: Phytoremediation: Management of Environmental Contaminants, vol. 5, pp. 277–292. https://doi.org/10.1007/978-3-319-52381-1.
Francini, A., Mariotti, L., Di Gregorio, S., Sebastiani, L., Andreucci, A., 2018. Removal of micro-pollutants from urban wastewater by constructed wetlands with *Phragmites australis* and *Salix matsudana*. Environ. Sci. Pollut. Res. 25, 36474–36484. https://doi.org/10.1007/s11356-018-3582-x.
Franks, C.G., Pearce, D.W., Rood, S.B., 2019. A prescription for drug-free rivers: uptake of pharmaceuticals by a widespread streamside willow. Environ. Manag. 63, 136–147. https://doi.org/10.1007/s00267-018-1120-8.
Fu, J., Lee, W., Coleman, C., Nowack, K., Carter, J., Huang, C., 2019. Removal of pharmaceuticals and personal care products by two-stage biofiltration for drinking water treatment. Sci. Total Environ. 664, 240–248. https://doi.org/10.1016/j.scitotenv.2019.02.026.
Gaffney, V.J., Almeida, C.M.M., Rodrigues, Al, Ferreira, E., Benoliel, M.J., Cardoso, V.V., 2015. Occurrence of pharmaceuticals in a water supply system and related human health risk assessment. Water Res. 72, 199–208. https://doi.org/10.1016/j.watres.2014.10.027.
Gikas, G.D., Tsihrintzis, V.A., 2012. A small-size vertical flow constructed wetland for on-site treatment of household wastewater. Ecol. Eng. 44, 337–343. https://doi.org/10.1016/j.ecoleng.2012.04.016.
González, M., Fernández-lópez, C., Pedrero-salcedo, F., Jose, J., 2018. Absorption of carbamazepine and diclofenac in hydroponically cultivated lettuces and human health risk assessment. Agric. Water Manag. 206, 42–47. https://doi.org/10.1016/j.agwat.2018.04.018.
Gorito, A.M., Ribeiro, A.R., Almeida, C.M.R., Silva, A.M.T., 2017. A review on the application of constructed wetlands for the removal of priority substances and contaminants of emerging concern listed in recently launched EU legislation. Environ. Pollut. 227, 428–443. https://doi.org/10.1016/j.envpol.2017.04.060.
He, Y., Sutton, N.B., Lei, Y., Rijnaarts, H.H.M., Langenhoff, A.A.M., 2018. Fate and distribution of pharmaceutically active compounds in mesocosm constructed wetlands. J. Hazard Mater. 357, 198–206. https://doi.org/10.1016/j.jhazmat.2018.05.035.
He, Y., Langenhoff, A.A.M., Sutton, N.B., Rijnaarts, H.H.M., Blokland, M.H., Chen, F., Huber, C., Schröder, P., 2017. Metabolism of ibuprofen by Phragmites australis: uptake and phytodegradation. Environ. Sci. Technol. 51 (8), 4576–4584. https://doi.org/10.1021/acs.est.7b00458.
Herath, I., Vithanage, M., 2015. Phytoremediation in constructed wetlands. In: Phytoremediation: Management of Environmental Contaminants, ume 2, pp. 243–263. https://doi.org/10.1007/978-3-319-10969-5.
Hijosa-Valsero, M., Matamoros, V., Martín-Villacorta, J., Bécares, E., Bayona, J.M., 2010a. Assessment of full-scale natural systems for the removal of PPCPs from wastewater in small communities. Water Res. 44, 1429–1439. https://doi.org/10.1016/j.watres.2009.10.032.
Hijosa-Valsero, M., Matamoros, V., Sidrach-Cardona, R., Martín-Villacorta, J., Bécares, E., Bayona, J.M., 2010b. Comprehensive assessment of the design configuration of constructed wetlands for the removal of pharmaceuticals and personal care products from urban wastewaters. Water Res. 44, 3669–3678. https://doi.org/10.1016/j.watres.2010.04.022.
Hijosa-Valsero, M., Reyes-Contreras, C., Domínguez, C., Bécares, E., Bayona, J.M., 2016. Behaviour of pharmaceuticals and personal care products in constructed wetland compartments: influent, effluent, pore water, substrate and plant roots. Chemosphere 145, 508–517. https://doi.org/10.1016/j.chemosphere.2015.11.090.
Hijosa-Valsero, M., Sidrach-Cardona, R., Pedescoll, A., Sánchez, O., Bécares, E., 2018. Role of bacterial diversity on PPCPs removal in constructed wetlands. Constructed Wetlands for Industrial Wastewater Treatment, pp. 405–426. https://doi.org/10.1002/9781119268376.ch18.
Hoyett, Z., 2017. Pharmaceuticals and personal care products: risks, challenges, and solutions. Risk Assessment, pp. 285–302. https://doi.org/10.5772/57353.
Huang, J., Cai, W., Zhong, Q., Wang, S., 2013. Influence of temperature on micro-environment, plant eco-physiology and nitrogen removal effect in subsurface flow constructed wetland. Ecol. Eng. 60, 242–248. https://doi.org/10.1016/j.ecoleng.2013.07.023.
Huang, Y., Guo, J., Yan, P., Gong, H., Fang, F., 2019. Sorption-desorption behavior of sulfamethoxazole, carbamazepine, bisphenol A and 17α-ethinylestradiol in sewage sludge. J. Hazard Mater. 368, 739–745. https://doi.org/10.1016/j.jhazmat.2019.01.063.
Huang, Z., Gong, B., Huang, C., Pan, S., Wu, P., Dang, Z., Chiang, P., 2019. Performance evaluation of integrated adsorption-nanofiltration system for emerging compounds removal: exemplified by caffeine, diclofenac and octylphenol. J. Environ. Manag. 231, 121–128. https://doi.org/10.1016/j.jenvman.2018.09.092.
Huerta-Fontela, M., Galceran, M.T., Ventura, F., 2011. Occurrence and removal of pharmaceuticals and hormones through drinking water treatment. Water Res. 45, 1432–1442. https://doi.org/10.1016/j.watres.2010.10.036.

Hussain, I., Aleti, G., Naidu, R., Puschenreiter, M., Mahmood, Q., Mahmudur, M., Wang, F., Shaheen, S., Hussain, J., Reichenauer, T.G., 2018. Microbe and plant assisted-remediation of organic xenobiotics and its enhancement by genetically modi fi ed organisms and recombinant technology : a review. Sci. Total Environ. 628–629, 1582–1599. https://doi.org/10.1016/j.scitotenv.2018.02.037.
Ilyas, H., van Hullebusch, E.D., 2019. Role of design and operational factors in the removal of pharmaceuticals by constructed wetlands. Water 11, 2356. https://doi.org/10.3390/w11112356.
Ilyas, H., van Hullebusch, E.D., 2020a. Performance comparison of different constructed wetlands designs for the removal of personal care products. Int. J. Environ. Res. Publ. Health. https://doi.org/10.3390/ijerph17093091.
Ilyas, H., van Hullebusch, E.D., 2020b. The influence of design and operational factors on the removal of personal care products by constructed wetlands. Water 12, 1367. https://doi.org/10.3390/w12051367.
Ilyas, H., Masih, I., van Hullebusch, E.D., 2020. Pharmaceuticals' removal by constructed wetlands: a critical evaluation and meta-analysis on performance, risk reduction, and role of physicochemical properties on removal mechanisms. J. Water Health 18, 253–291. https://doi.org/10.2166/wh.2020.213.
Jehawi, O.H., Abdullah, S.R.S., Kurniawan, S.B., Ismail, N.I., Idris, M., Al Sbani, N.H., Muhamad, M.H., Hasan, H.A., 2020. Performance of pilot hybrid reed bed constructed wetland with aeration system on nutrient removal for domestic wastewater treatment. Environ. Technol. Innov. 19, 100891. https://doi.org/10.1016/j.eti.2020.100891.
Junaid, M., Wang, Y., Hamid, N., Deng, S., Li, W.G., Pei, D.S., 2019. Prioritizing selected PPCPs on the basis of environmental and toxicogenetic concerns: a toxicity estimation to confirmation approach. J. Hazard Mater. 380, 120828. https://doi.org/10.1016/j.jhazmat.2019.120828.
K'oreje, K.O., Kandie, F.J., Vergeynst, L., Abira, M.A., Van Langenhove, H., Okoth, M., Demeestere, K., 2018. Occurrence, fate and removal of pharmaceuticals, personal care products and pesticides in wastewater stabilization ponds and receiving rivers in the Nzoia Basin, Kenya. Sci. Total Environ. 637–638, 336–348. https://doi.org/10.1016/j.scitotenv.2018.04.331.
Kadir, A.A., Abdullah, S.R.S., Othman, B.A., Hasan, H.A., Othman, A.R., Imron, M.F., Ismail, N.I., Kurniawan, S.B., 2020. Dual function of *Lemna minor* and *Azolla pinnata* as phytoremediator for palm oil mill effluent and as feedstock. Chemosphere 127468. https://doi.org/10.1016/j.chemosphere.2020.127468.
Kafaei, R., Papari, F., Seyedabadi, M., Sahebi, S., Tahmasebi, R., Ahmadi, M., Sorial, G. A., Asgari, G., Ramavandi, B., 2018. Occurrence, distribution, and potential sources of antibiotics pollution in the water-sediment of the northern coastline of the Persian Gulf, Iran. Sci. Total Environ. 627, 703–712. https://doi.org/10.1016/j.scitotenv.2018.01.305.
Kahl, S., Nivala, J., van Afferden, M., Müller, R.A., Reemtsma, T., 2017. Effect of design and operational conditions on the performance of subsurface flow treatment wetlands: emerging organic contaminants as indicators. Water Res. 125, 490–500. https://doi.org/10.1016/j.watres.2017.09.004.
Kalabić, D., Dražić, G., Dražić, N., Ikanović, J., 2019. Production of agri-energy crop miscanthus giganthеus on land degraded by power industry: SWOT analysis. Pol. J. Environ. Stud. 28, 3243–3251. https://doi.org/10.15244/pjoes/93745.
Kaur, H., Hippargi, G., Pophali, G.R., Bansiwal, A.K., 2019. Treatment Methods for Removal of Pharmaceuticals and Personal Care Products from Domestic Wastewater, Pharmaceuticals and Personal Care Products: Waste Management and Treatment Technology. Elsevier Inc. https://doi.org/10.1016/b978-0-12-816189-0.00006-8.
Kotyza, J., Soudek, P., Kafka, Z., Vaněk, T., 2010. Phytoremediation of pharmaceuticals-preliminary study. Int. J. Phytoremediation 12, 306–316. https://doi.org/10.1080/15226510903563900.
Kraiem, K., Kallali, H., Wahab, M.A., Fra-vazquez, A., Mosquera-Corral, A., Jedidi, N., 2019. Comparative study on pilots between ANAMMOX favored conditions in a partially saturated vertical flow constructed wetland and a hybrid system for rural wastewater treatment. Sci. Total Environ. 670, 644–653. https://doi.org/10.1016/j.scitotenv.2019.03.220.
Kumar, S., Dutta, V., 2019. Efficiency of constructed wetland microcosms (CWMs) for the treatment of domestic wastewater using aquatic macrophytes. Environmental Biotechnology: for Sustainable Future, pp. 287–307. https://doi.org/10.1007/978-981-10-7284-0_11.
Lee, J.H., 2013. An overview of phytoremediation as a potentially promising technology for environmental pollution control. Biotechnol. Bioproc. Eng. 18, 431–439. https://doi.org/10.1007/s12257-013-0193-8.
Li, J., Zhou, Q., Campos, L.C., 2017. Removal of selected emerging PPCP compounds using greater duckweed (Spirodela polyrhiza) based lab-scale free water constructed wetland. Water Res. 126, 252–261. https://doi.org/10.1016/j.watres.2017.09.002.
Li, W.L., Zhang, Z.F., Ma, W.L., Liu, L.Y., Song, W.W., Li, Y.F., 2018. An evaluation on the intra-day dynamics, seasonal variations and removal of selected pharmaceuticals and personal care products from urban wastewater treatment plants. Sci. Total Environ. 640–641, 1139–1147. https://doi.org/10.1016/j.scitotenv.2018.05.362.
Li, Y., Wu, B., Zhu, G., Liu, Y., Ng, W.J., Appan, A., Tan, S.K., 2016a. High-throughput pyrosequencing analysis of bacteria relevant to cometabolic and metabolic degradation of ibuprofen in horizontal subsurface flow constructed wetlands. Sci. Total Environ. 562, 604–613. https://doi.org/10.1016/j.scitotenv.2016.04.020.
Li, Y., Zhang, J., Zhu, G., Liu, Y., Wu, B., Ng, W.J., Appan, A., Tan, S.K., 2016b. Phytoextraction, phytotransformation and rhizodegradation of ibuprofen associated with Typha angustifolia in a horizontal subsurface flow constructed wetland. Water Res. 102, 294–304. https://doi.org/10.1016/j.watres.2016.06.049.
Li, H., Zhang, S., Yang, X.L., Yang, Y.L., Xu, H., Li, X.N., Song, H.L., 2019a. Enhanced degradation of bisphenol A and ibuprofen by an up-flow microbial fuel cell-coupled constructed wetland and analysis of bacterial community structure. Chemosphere 217, 599–608. https://doi.org/10.1016/j.chemosphere.2018.11.022.
Li, Y., Zhang, S., Zhang, W., Xiong, W., Ye, Q., Hou, X., Wang, C., Wang, P., 2019b. Life cycle assessment of advanced wastewater treatment processes : involving 126 pharmaceuticals and personal care products in life cycle inventory. J. Environ. Manag. 238, 442–450. https://doi.org/10.1016/j.jenvman.2019.01.118.
Li, Y., Zhu, G., Ng, W.J., Tan, S.K., 2014. A review on removing pharmaceutical contaminants from wastewater by constructed wetlands: design, performance and mechanism. Sci. Total Environ. https://doi.org/10.1016/j.scitotenv.2013.09.018.
Liang, Y., Zhu, H., Bañuelos, G., Shutes, B., Yan, B., Cheng, X., 2018. Removal of sulfamethoxazole from salt-laden wastewater in constructed wetlands affected by plant species, salinity levels and co-existing contaminants. Chem. Eng. J. 341, 462–470. https://doi.org/10.1016/j.cej.2018.02.059.
Lin, T., Yu, S., Chen, W., 2016. Occurrence, removal and risk assessment of pharmaceutical and personal care products (PPCPs) in an advanced drinking water treatment plant (ADWTP) around Taihu Lake in China. Chemosphere 152, 1–9. https://doi.org/10.1016/j.chemosphere.2016.02.109.
Lin, Y., Zhao, Y., Ruan, X., Barzee, T.J., Zhang, Z., Kong, H., Zhang, X., 2020. The potential of constructed wetland plants for bioethanol production, 2020. Bioenerg. Res. 13, 43–49. https://doi.org/10.1007/s12155-019-10065-y.
Liu, J.L., Wong, M.H., 2013. Pharmaceuticals and personal care products (PPCPs): a review on environmental contamination in China. Environ. Int. 59, 208–224. https://doi.org/10.1016/j.envint.2013.06.012.
Liu, J., Dan, X., Lu, G., Shen, J., Wu, D., Yan, Z., 2018a. Investigation of pharmaceutically active compounds in an urban receiving water: occurrence, fate and environmental risk assessment. Ecotoxicol. Environ. Saf. 154, 214–220. https://doi.org/10.1016/j.ecoenv.2018.02.052.
Liu, J., Wang, J., Zhao, C., Hay, A.G., Xie, H., Zhan, J., 2016. Triclosan removal in wetlands constructed with different aquatic plants. Appl. Microbiol. Biotechnol. 100, 1459–1467. https://doi.org/10.1007/s00253-015-7063-6.
Liu, M., Yin, H., Wu, Q., 2019a. Occurrence and health risk assessment of pharmaceutical and personal care products (PPCPs) in tap water of Shanghai. Ecotoxicol. Environ. Saf. 183, 109497. https://doi.org/10.1016/j.ecoenv.2019.109497.
Liu, X., Guo, X., Liu, Y., Lu, S., Xi, B., Zhang, J., Wang, Z., Bi, B., 2019b. A review on removing antibiotics and antibiotic resistance genes from wastewater by constructed wetlands: performance and microbial response. Environ. Pollut. https://doi.org/10.1016/j.envpol.2019.112996.
Liu, Y., Wang, X., Yang, H., Xie, Y.F., 2018b. Adsorption of pharmaceuticals onto isolated polyamide active layer of NF/RO membranes. Chemosphere 200, 36–47. https://doi.org/10.1016/j.chemosphere.2018.02.088.
Lyu, S., Chen, W., Qian, J., Wen, X., Xu, J., 2019. Prioritizing environmental risks of pharmaceuticals and personal care products in reclaimed water on urban green space in Beijing. Sci. Total Environ. 697, 133850. https://doi.org/10.1016/j.scitotenv.2019.133850.
Madikizela, L.M., Ncube, S., Chimuka, L., 2018. Uptake of pharmaceuticals by plants grown under hydroponic conditions and natural occurring plant species: a review. Sci. Total Environ. 636, 477–486. https://doi.org/10.1016/j.scitotenv.2018.04.297.
Marsidi, N., Nye, C.K., Abdullah, S.R.S., Hassan, H.A., Halmi, M.I.E., 2016. Phytoremediation of naproxen in waste water using vetiver zizaniodes. J. Eng. Sci. Technol. 11, 1086–1097.
Morone, A., Mulay, P., Kamble, S.P., 2019. Removal of Pharmaceutical and Personal Care Products from Wastewater Using Advanced Materials, Pharmaceuticals and Personal Care Products: Waste Management and Treatment Technology. Elsevier Inc. https://doi.org/10.1016/b978-0-12-816189-0.00008-1.
National Center for Biotechnology Information, 2021. Pubchem (accessed. https://pubchem.ncbi.nlm.nih.gov. (Accessed 6 June 2021).
Ngo, T.H., Van, D.A., Tran, H. Le, Nakada, N., Tanaka, H., Huynh, T.H., 2020. Occurrence of pharmaceutical and personal care products in Cau River, Vietnam. Environ. Sci. Pollut. Res. 28, 12082–12091. https://doi.org/10.1007/s11356-020-09195-0.
Nguyen, P.M., Afzal, M., Ullah, I., Shahid, N., Baqar, M., Arslan, M., 2019. Removal of pharmaceuticals and personal care products using constructed wetlands: effective plant-bacteria synergism may enhance degradation efficiency. Environ. Sci. Pollut. Res. 26, 21109–21126. https://doi.org/10.1007/s11356-019-05320-w.
Nivala, J., Kahl, S., Boog, J., van Afferden, M., Reemtsma, T., Müller, R.A., 2019. Dynamics of emerging organic contaminant removal in conventional and intensified subsurface flow treatment wetlands. Sci. Total Environ. 649, 1144–1156. https://doi.org/10.1016/j.scitotenv.2018.08.339.
Noguera-Oviedo, K., Aga, D.S., 2016. Lessons learned from more than two decades of research on emerging contaminants in the environment. J. Hazard Mater. 316, 242–251. https://doi.org/10.1016/j.jhazmat.2016.04.058.
Nowrotek, M., Kotlarska, E., Łuczkiewicz, A., Felis, E., Sochacki, A., Miksch, K., 2017. The treatment of wastewater containing pharmaceuticals in microcosm constructed wetlands: the occurrence of integrons (int1–2) and associated resistance genes (sul1–3, qacEΔ1). Environ. Sci. Pollut. Res. 24, 15055–15066. https://doi.org/10.1007/s11356-017-9079-1.
Nowrotek, M., Sochacki, A., Felis, E., Miksch, K., 2016. Removal of diclofenac and sulfamethoxazole from synthetic municipal waste water in microcosm downflow constructed wetlands: start-up results. Int. J. Phytoremediation 18, 157–163. https://doi.org/10.1080/15226514.2015.1073669.
Pai, C.W., Leong, D., Chen, C.Y., Wang, G.S., 2020. Occurrences of pharmaceuticals and personal care products in the drinking water of Taiwan and their removal in conventional water treatment processes. Chemosphere 256, 127002. https://doi.org/10.1016/j.chemosphere.2020.127002.
Paredes, L., Fernandez-Fontaina, E., Lema, J.M., Omil, F., Carballa, M., 2016. Understanding the fate of organicmicropollutants in sand and granular activated carbon biofiltration systems. Sci. Total Environ. 551, 640–648. https://doi.org/10.1016/j.scitotenv.2016.02.008.

Park, J., Cho, K.H., Lee, E., Lee, S., Cho, J., 2018. Sorption of pharmaceuticals to soil organic matter in a constructed wetland by electrostatic interaction. Sci. Total Environ. 635, 1345–1350. https://doi.org/10.1016/j.scitotenv.2018.04.212.
Pascual, A., la Varga, D. De, Soto, M., Van Oirschot, D., Kilian, R.M., Álvarez, J.A., Carvalho, P., Brix, H., Arias, C.A., 2018. Aerated constructed wetlands for treatment of municipal and food industry wastewater. Constructed Wetlands for Industrial Wastewater Treatment, pp. 65–93. https://doi.org/10.1002/9781119268376.ch3.
Pi, N., Ng, J.Z., Kelly, B.C., 2017. Bioaccumulation of pharmaceutically active compounds and endocrine disrupting chemicals in aquatic macrophytes: results of hydroponic experiments with *Echinodorus horemanii* and *Eichhornia crassipes*. Sci. Total Environ. 601–602, 812–820. https://doi.org/10.1016/j.scitotenv.2017.05.137.
Pilon-smits, E., 2005. Phytoremediation. Annu. Rev. Plant Biol. 56, 15–39. https://doi.org/10.1146/annurev.arplant.56.032604.144214.
Praveena, S.M., Rashid, M.Z.M., Adzima, F., Wee, S.Y., Aris, A.Z., 2019. Occurrence and potential human health risk of pharmaceutical residues in drinking water from Putrajaya (Malaysia). Ecotoxicol. Environ. Saf. 180, 549–556.
Rabello, V.M., Teixeira, L.C.R.S., Gonçalves, A.P.V., de Sá Salomão, A.L., 2019. The efficiency of constructed wetlands and algae tanks for the removal of pharmaceuticals and personal care products (PPCPs): a systematic review. Water, Air, Soil Pollut. 230, 236. https://doi.org/10.1007/s11270-019-4304-9.
Rajan, R.J., Sudarsan, J.S., Nithiyanantham, S., 2019. Microbial population dynamics in constructed wetlands: review of recent advancements for wastewater treatment. Environ. Eng. Res. 24, 181–190. https://doi.org/10.4491/EER.2018.127.
Ramprasad, C., Philip, L., 2018. Contributions of various processes to the removal of surfactants and personal care products in constructed wetland. Chem. Eng. J. 334, 322–333. https://doi.org/10.1016/j.cej.2017.09.106.
Ramprasad, C., Philip, L., 2016. Surfactants and personal care products removal in pilot scale horizontal and vertical flow constructed wetlands while treating greywater. Chem. Eng. J. 284, 458–468. https://doi.org/10.1016/j.cej.2015.08.092.
Ramprasad, C., Philip, L., 2015. Occurrence, fate and removal of emerging contaminates in a hybrid constructed wetland treating greywater. Discov. Journals 41, 59–66.
Ramprasad, C., Smith, C.S., Memon, F.A., Philip, L., 2017. Removal of chemical and microbial contaminants from greywater using a novel constructed wetland: grow. Ecol. Eng. 106, 55–65. https://doi.org/10.1016/j.ecoleng.2017.05.022.
Riva, V., Riva, F., Vergani, L., Crotti, E., Borin, S., Mapelli, F., 2020. ribs. Chemosphere 241, 124843. https://doi.org/10.1016/j.chemosphere.2019.124843.
Roca, I., Akova, M., Baquero, F., Carlet, J., Cavaleri, M., Coenen, S., Cohen, J., Findlay, D., Gyssens, I., Heure, O.E., Kahlmeter, G., Kruse, H., Laxminarayan, R., Liébana, E., López-Cerero, L., MacGowan, A., Martins, M., Rodríguez-Baño, J., Rolain, J.M., Segovia, C., Sigauque, B., Taconelli, E., Wellington, E., Vila, J., 2015. The global threat of antimicrobial resistance: Science for intervention. New Microbes New Infect 6, 22–29. https://doi.org/10.1016/j.nmni.2015.02.007.
Rodriguez-Narvaez, O.M., Peralta-Hernandez, J.M., Goonetilleke, A., Bandala, E.R., 2017. Treatment technologies for emerging contaminants in water: a review. Chem. Eng. J. https://doi.org/10.1016/j.cej.2017.04.106.
Rühmland, S., Wick, A., Ternes, T.A., Barjenbruch, M., 2015. Fate of pharmaceuticals in a subsurface flow constructed wetland and two ponds. Ecol. Eng. 80, 125–139. https://doi.org/10.1016/j.ecoleng.2015.01.036.
Sa'at, S.K.M., Zaman, N.Q., Yusoff, M.S., 2019. Effect of hydraulic retention time on palm oil mill effluent treatment in horizontal sub-surface flow constructed wetland. AIP Conf. Proc. 2124 https://doi.org/10.1063/1.5117075.
Saeed, T., Sun, G., 2012. A review on nitrogen and organics removal mechanisms in subsurface flow constructed wetlands: dependency on environmental parameters, operating conditions and supporting media. J. Environ. Manag. https://doi.org/10.1016/j.jenvman.2012.08.011.
Sgroi, M., Pelissari, C., Roccaro, P., Sezerino, P.H., García, J., Vagliasindi, F.G.A., Ávila, C., 2018. Removal of organic carbon, nitrogen, emerging contaminants and fluorescing organic matter in different constructed wetland configurations. Chem. Eng. J. 332, 619–627. https://doi.org/10.1016/j.cej.2017.09.122.
Sharma, B.M., Bečanová, J., Scheringer, M., Sharma, A., Bharat, G.K., Whitehead, P.G., Klánová, J., Nizzetto, L., 2019. Health and ecological risk assessment of emerging contaminants (pharmaceuticals, personal care products, and artificial sweeteners) in surface and groundwater (drinking water) in the Ganges River Basin, India. Sci. Total Environ. 646, 1459–1467. https://doi.org/10.1016/j.scitotenv.2018.07.235.
Shetty, A., Gupta, G., 2019. Design Methodologies for Eco-Friendly Pharmaceutical Waste Management - A Review. Springer International Publishing, pp. 586–595. https://doi.org/10.1007/978-3-030-02707-0_66.
Shraim, A., Diab, A., Alsuhaimi, A., Niazy, E., Metwally, M., Amad, M., Sioud, S., Dawoud, A., 2017. Analysis of some pharmaceuticals in municipal wastewater of Almadinah Almunawarah. Arab. J. Chem. 10, S719–S729. https://doi.org/10.1016/j.arabjc.2012.11.014.
Singh, P., Singh, V.K., Singh, R., BorthakurAnwesha, Madhav, S., Ahamad, A., Kumar, A., Pal, D.B., Tiwary, D., Mishra, P.K., 2020. Bioremediation: a Sustainable Approach for Management of Environmental Contaminants, Abatement of Environmental Pollutants. Elsevier Inc. https://doi.org/10.1016/B978-0-12-818095-2.00001-1.
Sochacki, A., Felis, E., Bajkacz, S., Nowrotek, M., Miksch, K., 2018a. Removal and transformations of diclofenac and sulfamethoxazole in a two- stage constructed wetland system. Ecol. Eng. 122, 159–168. https://doi.org/10.1016/j.ecoleng.2018.07.039.
Sochacki, A., Nowrotek, M., Felis, E., Kalka, J., Ziembińska-Buczyńska, A., Bajkacz, S., Ciesielski, S., Miksch, K., 2018b. The effect of loading frequency and plants on the degradation of sulfamethoxazole and diclofenac in vertical-flow constructed wetlands. Ecol. Eng. 122, 187–196. https://doi.org/10.1016/j.ecoleng.2018.08.003.
Stefanakis, A.I., 2018. Introduction to constructed wetland technology. Constructed Wetlands for Industrial Wastewater Treatment, pp. 1–21. https://doi.org/10.1002/9781119268376.ch0.
Suarez, S., Lema, J.M., Omil, F., . Pre-treatment of hospital wastewater by coagulation-flocculation and flotation. Bioresour. Technol. 100 (7), 2138–2146. https://doi.org/10.1016/j.biortech.2008.11.015.
Sutar, R.S., Motghare, V.M., Kollur, S.C., Parikh, Y., Asolekar, S.R., 2019. Significance of addressing persistence of pathogens and micropollutants to enhance reuse of treated sewages using constructed wetlands. Advances in Waste Management. Springer Singapore, pp. 355–367. https://doi.org/10.1007/978-981-13-0215-2.
Tai, Y., Tam, N.F.Y., Dai, Y., Yang, Yang, Lin, J., Tao, R., Yang, Yufen, Wang, J., Wang, R., Huang, W., Xu, X., 2017. Assessment of rhizosphere processes for removing water-borne macrolide antibiotics in constructed wetlands. Plant Soil 419, 489–502. https://doi.org/10.1007/s11104-017-3359-x.
Tamura, I., Yasuda, Y., Kagota, K., Yoneda, S., Nakada, N., Kumar, V., Kameda, Y., Kimura, K., Tatarazako, N., Yamamoto, H., 2017. Contribution of pharmaceuticals and personal care products (PPCPs) to whole toxicity of water samples collected in effluent-dominated urban streams. Ecotoxicol. Environ. Saf. 144, 338–350. https://doi.org/10.1016/j.ecoenv.2017.06.032.
Tarpani, R.R.Z., Azapagic, A., 2018. Life cycle environmental impacts of advanced wastewater treatment techniques for removal of pharmaceuticals and personal care products (PPCPs). J. Environ. Manag. 215, 258–272. https://doi.org/10.1016/j.jenvman.2018.03.047.
Tondera, K., Ruppelt, J.P., Pinnekamp, J., Kistemann, T., Schreiber, C., 2019. Reduction of micropollutants and bacteria in a constructed wetland for combined sewer overflow treatment after 7 and 10 years of operation. Sci. Total Environ. 651, 917–927. https://doi.org/10.1016/j.scitotenv.2018.09.174.
Tripathi, S., Singh, V.K., Srivastava, P., Singh, R., Devi, R.S., Kumar, A., Bhadouria, R., 2020. Phytoremediation of organic pollutants: current status and future directions. Abat. Environ. Pollut. https://doi.org/10.1016/B978-0-12-818095-2.00004-7.
U.S. Environmental Protection Agency, 2012. Pharmaceuticals and Personal Care Products (PPCP).
Vo, H.N.P., Koottatep, T., Chapagain, S.K., Panuvatvanich, A., Polprasert, C., Ahn, K.H., 2016. Removal of acetaminophen from wastewater by constructed wetlands with *Scirpus validus*. Environ. Eng. Res. 21, 164–170. https://doi.org/10.4491/eer.2015.132.
Vo, H.N.P., Bui, X.T., Nguyen, T.M.H., Koottatep, T., Bandyopadhyay, A., 2018. Insights of the removal mechanisms of pharmaceutical and personal care products in constructed wetlands. Curr. Pollut. Reports. https://doi.org/10.1007/s40726-018-0086-8.
Vymazal, J., Dvořáková Březinová, T., Koželuh, M., Kule, L., 2017. Occurrence and removal of pharmaceuticals in four full-scale constructed wetlands in the Czech Republic – the first year of monitoring. Ecol. Eng. 98, 354–364. https://doi.org/10.1016/j.ecoleng.2016.08.010.
Vystavna, Y., Frkova, Z., Marchand, L., Vergeles, Y., Stolberg, F., 2017. Removal efficiency of pharmaceuticals in a full scale constructed wetland in East Ukraine. Ecol. Eng. 108, 50–58. https://doi.org/10.1016/j.ecoleng.2017.08.009.
Wagner, T.V., Parsons, J.R., Rijnaarts, H.H.M., de Voogt, P., Langenhoff, A.A.M., 2018. A review on the removal of conditioning chemicals from cooling tower water in constructed wetlands. Crit. Rev. Environ. Sci. Technol. 48, 1094–1125. https://doi.org/10.1080/10643389.2018.1512289.
Wang, Y., Yin, T., Kelly, B.C., Gin, K.Y.H., 2019. Bioaccumulation behaviour of pharmaceuticals and personal care products in a constructed wetland. Chemosphere 222, 275–285. https://doi.org/10.1016/j.chemosphere.2019.01.116.
Williams, M., Kookana, R.S., Mehta, A., Yadav, S.K., Tailor, B.L., Maheshwari, B., 2019. Emerging contaminants in a river receiving untreated wastewater from an Indian urban centre. Sci. Total Environ. 647, 1256–1265. https://doi.org/10.1016/j.scitotenv.2018.08.084.
World Health Organization, 2017. Guidelines for Drinking Water Quality. Interligar, Brazil.
World Water Assessment Programme, 2009. The United Nations World Water Development Report 3: Water in a Changing World. UNESCO. UNESCO and London: Earthscan, Paris.
Wu, H., Zhang, J., Ngo, H.H., Guo, W., Hu, Z., Liang, S., Fan, J., Liu, H., 2015. A review on the sustainability of constructed wetlands for wastewater treatment: design and operation. Bioresour. Technol. https://doi.org/10.1016/j.biortech.2014.10.068.
Xu, M., Huang, H., Li, N., Li, F., Wang, D., Luo, Q., 2019a. Occurrence and ecological risk of pharmaceuticals and personal care products (PPCPs) and pesticides in typical surface watersheds, China. Ecotoxicol. Environ. Saf. 175, 289–298. https://doi.org/10.1016/j.ecoenv.2019.01.131.
Xu, S., Zhou, S., Xing, L., Shi, P., Shi, W., Zhou, Q., Pan, Y., Song, M.Y., Li, A., 2019b. Fate of organic micropollutants and their biological effects in a drinking water source treated by a field-scale constructed wetland. Sci. Total Environ. 682, 756–764. https://doi.org/10.1016/j.scitotenv.2019.05.151.
Xu, R., Zhang, P., Wang, Q., Wang, X., Yu, K., Xue, T., Wen, X., 2019c. Influences of multi influent matrices on the retention of PPCPs by nanofiltration membranes. Separ. Purif. Technol. 212, 299–306. https://doi.org/10.1016/j.seppur.2018.11.040.
Xu, R., Zhou, M., Wang, H., Wang, X., Wen, X., 2020. Influences of temperature on the retention of PPCPs by nanofiltration membranes: experiments and modeling assessment. J. Membr. Sci. 599, 117817. https://doi.org/10.1016/j.memsci.2020.117817.
Yang, X., Sun, J., Fu, W., Shang, C., Li, Y., Chen, Y., Gan, W., Fang, J., 2016. PPCP degradation by UV/chlorine treatment and its impact on DBP formation potential in real waters. Water Res. 98, 309–318. https://doi.org/10.1016/j.watres.2016.04.011.

Yang, Y., Ok, Y.S., Kim, K.H., Kwon, E.E., Tsang, Y.F., 2017. Occurrences and removal of pharmaceuticals and personal care products (PPCPs) in drinking water and water/sewage treatment plants: a review. Sci. Total Environ. 596–597, 303–320. https://doi.org/10.1016/j.scitotenv.2017.04.102.

Yang, Y., Zhao, Y., Liu, R., Morgan, D., 2018. Global development of various emerged substrates utilized in constructed wetlands. Bioresour. Technol. 261, 441–452. https://doi.org/10.1016/j.biortech.2018.03.085.

Yi, C., Qin, W., Wen, X., 2020. Renovated filter filled with poly-3-hydroxybutyrateco-hydroxyvalerate and granular activated carbon for simultaneous removal of nitrate and PPCPs from the secondary effluent. Sci. Total Environ. 749, 141494. https://doi.org/10.1016/j.scitotenv.2020.141494.

Zhang, B.Y., Zheng, J.S., Sharp, R.G., 2010. Phytoremediation in engineered wetlands: mechanisms and applications. Procedia Environ. Sci. 2, 1315–1325. https://doi.org/10.1016/j.proenv.2010.10.142.

Zhang, D., Gersberg, R.M., Ng, W.J., Tan, S.K., 2014. Removal of pharmaceuticals and personal care products in aquatic plant-based systems: a review. Environ. Pollut. https://doi.org/10.1016/j.envpol.2013.09.009.

Zhang, D., Luo, J., Lee, Z.M.P., Maspolim, Y., Gersberg, R.M., Liu, Y., Tan, S.K., Ng, W.J., 2016. Characterization of bacterial communities in wetland mesocosms receiving pharmaceutical-enriched wastewater. Ecol. Eng. 90, 215–224. https://doi.org/10.1016/j.ecoleng.2015.12.043.

Zhang, D.Q., Gersberg, R.M., Hua, T., Zhu, J., Goyal, M.K., Ng, W.J., Tan, S.K., 2013. Fate of pharmaceutical compounds in hydroponic mesocosms planted with Scirpus validus. Environ. Pollut. 181, 98–106. https://doi.org/10.1016/j.envpol.2013.06.016.

Zhang, D.Q., Gersberg, R.M., Zhu, J., Hua, T., Jinadasa, K.B.S.N., Tan, S.K., 2012. Batch versus continuous feeding strategies for pharmaceutical removal by subsurface flow constructed wetland. Environ. Pollut. 167, 124–131. https://doi.org/10.1016/j.envpol.2012.04.004.

Zhang, L., Lv, T., Zhang, Y., Stein, O.R., Arias, C.A., Brix, H., Carvalho, P.N., 2017a. Effects of constructed wetland design on ibuprofen removal – a mesocosm scale study. Sci. Total Environ. 609, 38–45. https://doi.org/10.1016/j.scitotenv.2017.07.130.

Zhang, X., Jing, R., Feng, X., Dai, Y., Tao, R., Vymazal, J., Cai, N., Yang, Y., 2018. Removal of acidic pharmaceuticals by small-scale constructed wetlands using different design configurations. Sci. Total Environ. 639, 640–647. https://doi.org/10.1016/j.scitotenv.2018.05.198.

Zhang, Y., Lv, T., Carvalho, P.N., Zhang, L., Arias, C.A., Chen, Z., Brix, H., 2017b. Ibuprofen and iohexol removal in saturated constructed wetland mesocosms. Ecol. Eng. 98, 394–402. https://doi.org/10.1016/j.ecoleng.2016.05.077.

Zhang, Y., Lyu, T., Zhang, L., Button, M., Arias, C.A., Weber, K.P., Shi, J., Chen, Z., Brix, H., Carvalho, P.N., 2019. Microbial community metabolic profiles in saturated constructed wetlands treating iohexol and ibuprofen. Sci. Total Environ. 651, 1926–1934. https://doi.org/10.1016/j.scitotenv.2018.10.103.