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Removal Processes of Carbamazepine in Constructed Wetlands Treating Secondary Effluent: A Review

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Abstract: It is widely believed that constructed wetlands (CWs) own great potentiality as polishing wastewater treatment methods for removing carbamazepine (CBZ). Although the typical CBZ removal efficiencies in CWs are quite low, the CBZ removal performance could be improved to some extend by optimizing the CW design parameters. A comparison of current relevant studies indicates that horizontal sub-surface flow CWs (HSSF-CWs) and hybrid wetlands are attracting more interest for the treatment of CBZ wastewater. According to CBZ's physicochemical properties, substrate adsorption (25.70–57.30%) and macrophyte uptake (22.30–51.00%) are the two main CBZ removal pathways in CWs. The CBZ removal efficiency of CWs employing light expanded clay aggregate (LECA) as a substrate could reach values higher than 90%, and the most favorable macrophyte species is *Iris sibirica*, which has shown the highest total CBZ assimilation capacity. Several methods for enhancement have been proposed to optimize CBZ removal in CWs, including development of hydraulic models for optimization of CW operation, introduction of extra new CBZ removal ways into CW through substrate modification, design of combined/integrated CW, etc.

Keywords: constructed wetlands; carbamazepine; removal mechanisms; enhancement approaches; photocatalytic oxidation

1. Introduction

Pharmaceuticals' existence in the environment was first reported at the end of 1970s [1]. Since then, concerns about the environmental pollution of pharmaceuticals have increased. Discharging treated wastewater with pharmaceuticals is strictly connected with drinking water and public health [2,3], especially many pharmaceuticals themselves have been designed to have particular acute effects on the patients [4]. Among numerous pharmaceuticals, carbamazepine (CBZ) as an effective antiepileptic drug is a current focus of research. Mohapatra et al. indicated that CBZ accounts for the proportion of 96.00% in the global annual pharmaceutical market [5]. CBZ mainly penetrates into the water environment in the form of municipal waste and biological agents. Because it is a benzazazine derivative with an olefin double bond in the central heterocycle, CBZ as an environmental pollutant, has always attracted great concerns for its high persistence characteristic in diverse environmental substrates [6–8]. In addition, bioassays in microbes, algae and micro-crustacean confirmed that CBZ is one of the most dangerous compounds in aquatic environment [9,10]. Many previous studies have indicated that microbial processes could result in a minimal reduction of CBZ in the process of activated sludge treatment [11,12]. Insufficient removal of chemical, biological and mechanical processes leads to fairly high levels of CBZ, ranging between 6.60 ng/L and 11.50 μg/L in surface water or wastewater [13,14] and occurring at 1.4–1250 ng/L values in drinking water [15].

CBZ is one of the most currently detected drugs in municipal wastewater treatment plants (WWTPs). Zhang et al. indicated that CBZ's removal efficiencies in WWTPs are mostly below 10% [8]. This is because WWTPs are not specifically designed to eliminate such chemically stable pollutants [16–18]. To address the above problems, many researchers have optimized the design of WWTPs. For instance, a multi-fence way employing Nano filtration (NF) and osmosis (RO) subsequent to membrane bio-reactor (MBR) showed remarkable removal for CBZ [19]; near-anoxic conditions of MBR treatment is an advantageous operating mechanism for the removal of the persistent contaminant CBZ [20]. However, due to the cost and complexity of operation, and technical feasibility, many improvement measures cannot be effectively applied. Hence, the cost-efficient CBZ removal from WWTP effluents is important.

Through physical, chemical and biological interactions, constructed wetlands (CWs) have been proven to be containable technologies and operating alternative ways to WWTPs effectively eliminate various kinds of pollutants, involving biochemical oxygen demand (BOD_5), total suspended solids (TSS), phosphorus, nitrogen and heavy metals [21–23]. Recently, increasing interest has been paid to the application of CWs in pharmaceutical elimination [24–26]. Generally, it has been found that the pharmaceutical removal efficiencies in CWs are higher than that reported in WWTPs [27,28]. Moreover, Zhang et al. found that some pharmaceuticals removal efficiencies are more effective than 70.00% [29]. However, for CBZ, the removal efficiencies are considerably low [30–32], which is mainly attributed to the recalcitrance of CBZ. Moreover, complex removal mechanism of CWs hinders the further improvement of CBZ removal efficiencies. Hence, much more attention should be paid to these issues in future research studies.

In this review, the research status of CBZ removal by CWs is summarized, and the evaluation of the key mechanisms and impact factors of CBZ removal are emphasized. Finally, some enhancements of CBZ removal technologies such as substrate modification and combination/integration of advanced oxidation process with CWs are proposed to urge more researchers to find new solutions.

2. CBZ Removal Performance in CWs

At present, the typical efficiencies of CBZ in CWs were up to 60.00%. In order to improve CBZ removal performance in CWs, it is very essential to find out the better design plan of CWs from the current treatment status. Table 1 summarizes the results of the present studies. It can be seen from Table 1 that the main parameters affecting CBZ removal performance in CWs include (1) the configuration of CWs; (2) macrophytes; (3) substrate; (4) operating parameters; and (5) environmental conditions.

Table 1. Design parameters of the reported constructed wetlands as an alternative secondary wastewater treatment system for the removal of carbamazepine (CBZ).

Size	Removal Efficiencies	Initial CBZ Concentrations	Type of CWs	Design Parameters	Reference
Full-scale	38.00%	13.80 μg/L	HSSF-CW	Area: 400.00–500.00 m^2; Substrate: N.A.; Macrophytes: N.A.; HRT: N.A.; Operation mode: batch	[33]
	21.00%	1900.00 ng/L	HSSF-CW	Area: 18,000.00 m^2; Substrate: gravel; Macrophytes: *Phragmites australis*; HRT: N.A.; Operation mode: continuous	[34]

Table 1. *Cont.*

Size	Removal Efficiencies	Initial CBZ Concentrations	Type of CWs	Design Parameters	Reference
	0.00–18.00%	0.71–5.60 µg/L	Hybrid CWs	SF-CW: Area: 75.00 m^2; Substrate: gravel; Macrophytes: *Juncus effusus*; HRT: 55 h; Operational mode: batch HSSF-CW: Capacity: N.A.; Substrate: gravel; Macrophytes: *Juncus effusus*; HRT: 55 h; Operational mode: batch	[35]
Mesocosm-scale	5.00%	25.00 µg/L	HSSF-CW	Capacity: 0.93 m × 0.59 m × 0.52 m; Substrate: gravel; Macrophytes: *Phragmites australis*; HRT: N.A.; Operational mode: batch	[25]
	16.00–26.00%	4.70 µg/L	HSSF-CW	Capacity: N.A.; Substrate: gravel; Macrophytes: *Phragmites australis*; HRT: N.A.; Operational mode: batch	[36]
	26.70–28.80%	25.00 µg/L	HSSF-CW	Capacity: 1.20 m × 0.60 m × 0.60 m; Substrate: gravel; Macrophytes: *Typha angustifolia*; HRT: 2 or 4 days; Operational mode: batch	[28]
	27.00–28.00%	25.00 µg/L	HSSF-CW	Capacity: 1.20 m × 0.60 m × 0.60 m; Substrate: gravel; Macrophytes: *Typha angustifolia*; HRT: 2 or 4 days; Operational mode: batch	[37]
	24.00–28.00%	25.00 µg/L	HSSF-CW	Capacity: 1.20 m × 0.60 m × 0.60 m; Substrate: gravel; Macrophytes: *Typha angustifolia*; HRT: 2 or 4 days; Operational mode: batch	[37]
	88.20–96.70%	2.50 µg/mL	VSSF-CW	Capacity: 0.60 m × 0.50 m × 0.40 m; Substrate: LECA; Macrophytes: *Typha angustifolia*; HRT: N.A.; Operational mode: batch	[38]
	60.00–70.00%	0, 10, 30, 100 and 500 µg/L	VSSF-CW	Capacity: 0.60 m × 0.50 m × 0.60 m; Substrate: ceramsite and gravel; Macrophytes: *C. alternifolius*; HRT: 1 days.; Operational mode: batch	[39]
	15.00–48.00%	1.36–1.52 µg/L	Hybrid CWs	SF-CW: Capacity: 1.30 m × 0.80 cm × 0.50 cm; Substrate: gravel; Macrophytes: *Typha angustifolia* and *Phragmites australis*; HRT: 2.1 days, 5.1 days, 2.9 days; Operational mode: batch HSSF-CW: Capacity: N.A.; Substrate: gravel; Macrophytes: *Phragmites australis*; HRT: 2.5 days; Operational mode: batch	[40]
	18.00–95.00%	0.30–1.50 µg/L	Hybrid CWs	SF-CW: Capacity: 1.30 m × 0.80 m × 0.50 m; Substrate: gravel; Macrophytes: *Typha angustifolia* and *Phragmites australis*; HRT: 2.1 days, 5.1 days, 2.9 days; Operational mode: batch HSSF-CW: Capacity: N.A.; Substrate: gravel; Macrophytes: *Phragmites australis*; HRT: 2.5 days; Operational mode: batch	[35]
	0.00–59.00%	0.99 µg/L	Hybrid CWs	SF-CW: Capacity: 1.30 m × 0.80 m × 0.50 m; Substrate: gravel; Macrophytes: *Typha angustifolia* and *Phragmites australis*; HRT: 2.1 days, 5.1 days, 2.9 days; Operational mode: batch HSSF-CW: Capacity: N.A.; Substrate: gravel; Macrophytes: *Phragmites australis*; HRT: 2.5 days; Operational mode: batch	[41]
	10.12–13.30%	25.00 µg/L	Hybrid CWs	Capacity: N.A.; Substrate: ground tezontle; Macrophytes: *Zantedeschia aethiopica*, *Iris sibirica, and Typha latifolia*; HRT: 3 days; Operational mode: batch	[42]
	8.00–56.00%	4.00–24.00 ng/L	Hybrid CWs	Capacity: HSSF-CW: 1.00 m × 2.00 m × 0.30 m; VSSF-CW: 1.00 m × 1.50 m × 1.30 m; SF-CW: 1.00 m × 2.00 m × 0.50 m; Substrate: gravel; Macrophytes: *Phragmites australis*; HRT: 21 days; Operational mode: batch	[43]

Table 1. *Cont.*

Size	Removal Efficiencies	Initial CBZ Concentrations	Type of CWs	Design Parameters	Reference
	2.00%	3.00 μg/L	HSSF-CW	Area: 5.60 m^2; Substrate: gravel; Macrophytes: *Phragmites australis*; HRT: 2 days; Operation mode: batch	[44]
	2.00%	3.00μg/L	VSSF-CW	Area: 6.20 m^2; Substrate: gravel; Macrophytes: *Phragmites australis*; HRT: 2 days; Operation mode: batch	[44]

N.A.: not available; HRT: hydraulic retention time; SF-CW: surface flow-constructed wetland; VSSF-CW: vertical subsurface flow-constructed wetland.

2.1. Configuration of CWs

The configuration of CWs is an important parameter affecting the remediation of CBZ. CWs vary distinctly in layout, involving primary types (SF-CWs: surface flow-constructed wetlands and SSF-CWs: subsurface flow-constructed wetlands) and current configuration (HSSF-CWs and VSSF-CWs), as well as substrate in different types and depths of wetland beds. In addition, the use of hybrid wetlands to process CBZ has gradually drawn the attention of many researchers.

In Table 1, the CBZ removal efficiencies of different configuration types of CWs are compared. SSF-CWs own preferable macrophyte root effects and superior surface uptake in the rhizosphere compared with SF-CWs; hence, CBZ removal situation of SSF-CWs is superior than that of SF-CWs. Moreover, Hijosa-Valsero et al. estimated different configurations of mesocosm-scale CWs to eliminate pharmaceuticals and covered that the CBZ removal efficiency of HSSF-CWs was about 16.00% higher than that of SF-CWs [40]. Although VSSF-CWs seem to be more effective and credible in eliminating other pharmaceutical pollutants than other types of CWs due to their low sensitivity of unsaturated flow to overload conditions, VSSF-CWs have not shown better removal performance (20.00–26.00%); on the contrary, HSSF-CWs can simultaneously provide aerobic and anaerobic environment for CBZ degradation, which show better elimination situation (16.00–40.00%). Moreover, diverse types of CWs can be combined or integrated (called hybrid CWs) to exploit the individual benefits of the respective systems, since single-stage CWs could not reach high CBZ elimination efficiencies. So far, most studies have been confined to mesocosm-scale CWs. Therefore, more studies in the future need to focus on full-scale CWs to provide a stronger basis for research in this field.

2.2. Macrophytes

Because macrophytes can greatly affect the CBZ elimination rates in CWs, it is very important to evaluate CBZ removal effects by different macrophyte species. So far, three types of macrophytes have been mainly used to remove CBZ in CWs, i.e., *Typha angustifolia*, *Eichhornia crassipe* and *Phragmites australis* [32,45–47]. From Table 1, *T. angustifolia* exhibited better removal performance compared with *E. crassipe* and *P. australis* (*T. angustifolia*: 62.50 ± 4.50%; *E. crassipe*: 36.2 ± 07.20%; *P. australis*: 34.30 ± 5.90%). These results also concluded by Zhang et al., who found *T. angustifolia* could metabolize many pharmaceuticals to other products easily compared with other macrophyte species [48]. Nevertheless, Tejeda et al. found that CBZ assimilation by *Iris sibirica* is seven times greater than that by *T. angustifolia* and *Zantedeschia aethiopica* [42]. Simultaneously, Tejeda et al. evaluated the tolerance performance of three ornamental species (*T. angustifolia*, *Z. aethiopica* and *I. sibirica*) spiked with CBZ to an ultimate concentration of 25.00 μg/L, and *T. angustifolia* had the lowest tolerance biomass [42]. This result was reasonable because when being exposed to CBZ, *T. angustifolia* appeared more indications of stress [42]. Thus, *I. sibirica* would be the most recommendable species, which exhibited the highest general assimilation ability because of the high yield of biomass is combined with the excellent assimilation ability of CBZ.

In addition to direct uptake, macrophytes also promote CBZ removal through root exudates released into the root zone [28]. The root exudates secreted from macrophytes are a series of low-molecular-weight carbonaceous compounds, involving organic acids and sugars. Root exudates themselves interact with CBZ, which further affects the substrate adsorption process of CBZ. Among 15 organic acids, succinic acid and fumaric acid were found to co-crystallize with CBZ [49]. Root exudates can also offer organic carbon and diverse nutrient origins to microbes in the root zones and advance microbial degradation [50]. Zhang et al. testified that root exudates worked an immediate function in the biodegradation of some pharmaceuticals and acted as surfactants or transports to increase the bioavailability of pharmaceuticals [28].

2.3. Substrate

Substrate is a significant component in CWs, particularly in SSF-CWs. The substrate in CWs not only interrelates directly with pollutants by sorption processes, but also offers support for development of macrophytes and microorganisms. Thus, it is very important to choose a substrate with adsorption capacity.

The most common substrates used in CWs are soil, sand and gravel because of their high efficiency, low cost, by-product reduction and easy availability. In particular, it was found that CBZ adsorption of gravel is effective due to the adsorption and accumulation of CBZ on the biofilm formed on the gravel [26]. At present, due to the existence of the surface interaction between CBZ and amended substrates, amended substrates are arousing sizable attention. The amended substrates applied in CWs include biochar, zeolite, light expanded clay aggregate (LECA), and fly ash. Ayoub et al. found that iron-impregnated zeolite had greater CBZ removal performance, which owned a large affinity for the surface of the iron-impregnated faujasite [51]. Dalahmeh et al. indicated that CBZ was removed efficiently by biochar [52]. Styszko et al. found that the acid treatment of fly ash improved the adsorption performance of CBZ and an augment of unburned carbon added the adsorption situation of CBZ to fly ash [53]. Although the substrates mentioned above have excellent removal of CBZ, they are all based on modification measures. Dordio et al. indicated that LECA-based microcosm wetlands showed high CBZ removal efficiencies (97.00%) [38]. Thus, the application of LECA as substrate in CWs can achieve the best CBZ removal efficiencies.

2.4. Operation Parameters

2.4.1. Operation Mode

In general, intermittent operation mode of CWs relates to alternating drainage and overflow of wetlands, which leads to entrainment of air in the substrates microspores. This air entrainment increases the oxidation of carbon and nitrogen in CWs, so this mode can be implemented more effectively than continuous operation mode. However, Zhang et al. found no statistically distinct difference between intermittent and continuous operation mode for the CBZ removal [37]. This was mainly because studied CWs were supplied by secondary effluent from a WWTP for two weeks to allow extensive root zone and biofilm form on the substrate before CWs operation; the studied CWs did not have specific CBZ-degrading bacteria. Thus, intermittent operation mode could not enhance CBZ removal performance in these studied CWs. If CBZ biodegradation pathways can be properly introduced into CWs, intermittent operation mode would be better than continuous operation mode.

2.4.2. Temperature

Generally, the ability of microorganism or macrophyte to degrade CBZ in outdoor CWs is strongly influenced by air temperature. At 25 °C, the ability of *Starkeya* sp. C11, *Rhizobium* sp. C12 and *Streptomyces* MIUG 4.89 to degrade CBZ was higher [54,55]. In addition, common thermophilic macrophytes (e.g., *Arundo donax* and *P. australis*) are aging at low temperature, resulting in a weak metabolism of CBZ [56]. Nevertheless, Li et al. isolated a cold-resistant CBZ-degrading bacteria called *Pseudomonas* sp. CBZ-4 at 10 °C from activated sludge; these bacteria could be able to biodegrade CBZ at lower temperatures, as moderate eliminate efficiencies of almost 50.00% at primary concentrations of 10.00–160.00 mg/L [57].

3. CBZ Removal Mechanism in CWs

The contributions of different degradation pathways to CBZ degradation in CWs are shown in Figure 1. An overview of the physicochemical properties of CBZ and the frequently investigated CBZ metabolite DiOH-CBZ in CWs is presented in Table 2.

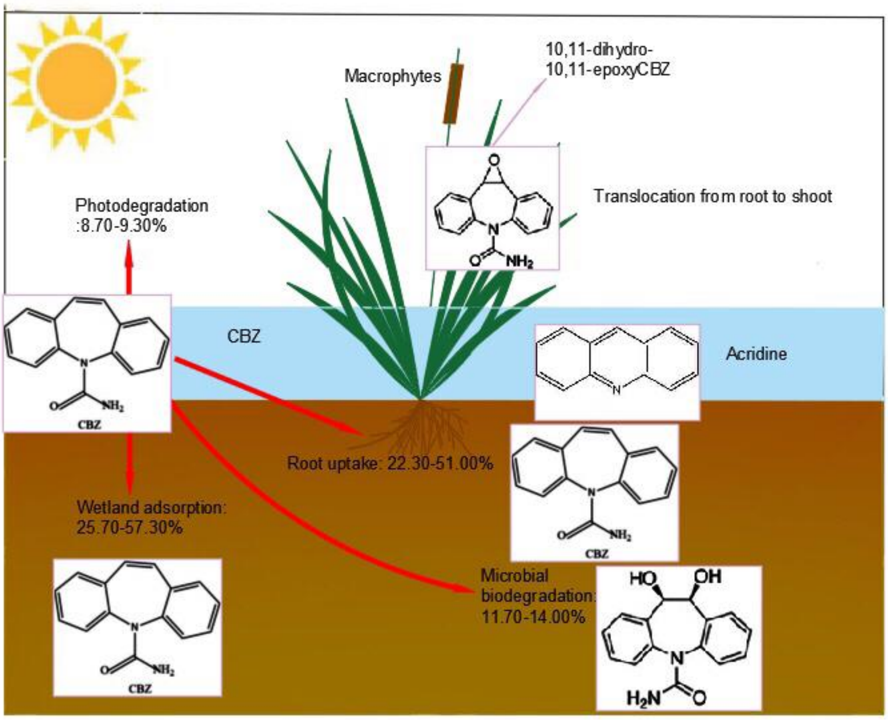
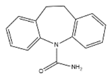
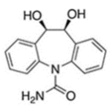


Figure 1. The contribution of different degradation pathways to CBZ degradation in constructed wetlands (CWs).

Table 2. Overview of the physicochemical properties of CBZ and frequently investigated CBZ metabolites in CWs.

Compound	Chemical Structure	Physicochemical Properties								
		MW [1]	S_w [2]	pK_a [3]	K_d [4]	Log K_d	Log K_{ow} [5]	Log D_{ow} [6]	Log K_{oc} [7]	H [8]
CBZ		236.28	17.70	13.90	1.20	0.09	2.45	2.77	3.59	1.08×10^{-10}
DiOH-CBZ		270.10	N.A.	−1.5	0.94	N.A.	0.81	N.A.	1.50	N.A.

N.A.: not available; [1] Molecular weight; [2] Water solubility (25 °C); [3] Ionization constant (pK_a); [4] Solid-water distribution coefficient (K_d); [5] Octanol-water partition coefficient (log K_{ow}); [6] Octanol-water distribution coefficient (log D_{ow}); [7] Organic carbon partition coefficient (log K_{oc}); [8] Henry's law constant (25 °C); DiOH-CBZ: 10,11-dihydro-10,11-dihydroxy-carbamazepine.

3.1. Substrate Adsorption

The highest contribution to CBZ degradation in CWs was exhibited by the substrate adsorption process (25.70–57.30%). The ability to estimate the adsorption of CBZ on various substrates has been discussed. Subsequently, many researchers have explored the adsorption behavior of CBZ in substrates and linked this behavior to the physicochemical properties of CBZ.

The partition coefficient log K_{ow} is a basic measurement of hydrophobicity characteristic of a compound. It is the concentration ratio of a non-ionized compound between octanol and water [32]. Numerous hydrophobic pharmaceuticals, such as CBZ, could be efficiently adsorbed onto the organic substance consist in granular media and get more resistant to degradation, which leads to high aggregation on the substrate within CWs. However, the hydrophobicity of a compound alone is not enough to evaluate the adsorption and distribution behavior of CBZ. Water solubility, chemical structure and acid/base properties also influence the adsorption process. Yan et al. indicated that the high polarizability of CBZ results in strong van der Waals interactions with the substrates in wetlands; furthermore, the water solubility of CBZ is considerably low, which favors its transportation into substrates in CWs [39].

3.2. Macrophyte Uptake

Contaminants' direct adsorption, accumulation treatment and migration through macrophytes have been deemed to significant mechanisms for phytoremediation technology. Macrophyte uptake accounts for 22.30–51.00% in the overall CBZ removal processes. The most widely used methods of estimating the root adsorption potential is related to pharmaceuticals' physicochemical properties, such as log K_{ow}. Previous investigations have shown that pharmaceuticals' direct uptake through macrophytes is an amazing effective elimination mechanism for pollutants with log K_{ow} ranging from 0.50 to 3.00, such as CBZ [46]. However, Yan et al. found the distinctly higher accumulation of CBZ than that of roxithromycin despite their similar log K_{ow} values [39]. Thus, the macrophyte uptake behavior of CBZ alone is insufficiently explained by log K_{ow}. Pharmaceuticals with different molecular masses (MWs), polarity and ionization states also work together to influence macrophyte uptake [39]. Generally, both root and leaves uptake by macrophytes have a well correlation with MWs. Low-MW pharmaceuticals (MW < 500.00), such as CBZ, are more easily adsorbed into the roots and then transferred into the shoots [39]. CBZ is a nonionic pharmaceutical that can easily pass through the membrane and transport from xylem to phloem, thus transposed by transpiration and accumulated in macrophyte leaves [39].

Afterwards, CBZ may experience sectional or entire biodegradation or it could be translated or metabolized into less poisoning compounds and constraint in macrophyte tissues. Because of direct volatilization and phytovolatilization, the expectation of hydrophilic compounds or volatile hydrophobic compounds is moderate [58], thus phytovolatilization in CBZ removal is very weak. In a research by Zhang et al., the removal pathways of CBZ in *Scirpus validus* wetland ecosystem were studied [59]. These results showed that in nutrient solution, the mass percentage of CBZ (22.00%) directly presented in the macrophyte tissues was distinctly lower than the general CBZ elimination rate (64.00%) [59]. This indicates that CBZ must be transformed into other catabolic products. In Dordio et al.'s study, MS^2 and LC-ESI-MS analysis were performed to seek proof of CBZ metabolism products in macrophyte tissues. The results pointed that CBZ epoxides' final existence existed in *T. augustifolia* leaves indicated that 10,11-dihydro-10,11-epoxyCBZ is one of direct metabolism products, which is an excellent explanation for the CBZ reduction observed in the *T. angustifolia* tissues [46].

3.3. Photolytic Degradation

Photolysis can irreversibly alter the reactants and strongly affect the current of certain contaminants in the water environment. Photolysis processes can be divided into three categories: the first type is called direct photolysis, which is the decomposition reaction of the compounds induced directly by solar energy. The second type is called indirect photolysis, in which natural substances are excited by sunlight in water (such as humus), and energy of the excited state is transferred to the compound, which leads to the decomposition reaction. The third type is the oxidation reaction. Free radicals (also known as singlet oxygen) are produced from the naturally occurring substances. The transformation of the compound is radiated to produce these intermediates. The photolysis of CBZ will be discussed according to the three processes mentioned.

Photolysis play a minor role (8.70–9.30%) in the removal of CBZ from CWs. The light intensity of solar radiation to the water surface varies with wavelength, especially in the near-ultraviolet

(290.00–320.00 nm) region, where the light intensity varies greatly, and this part of ultraviolet light often causes the photodecomposition of many organic compounds. Because molar extinction coefficients have been extrapolated for CBZ from spectrum at wavelengths ranging from 297.50 to 330.00 nm, CBZ can use sunlight for photolysis. In addition, the quantum yield of CBZ photolysis varies between 2.00×10^{-6} and 3.50×10^{-4} [60,61], which indicates CBZ would need 1–4 weeks of sunny weather to be removed by photodegradation from surface water [61]. Wang et al. showed that the photodegradation rate constants of CBZ in secondary effluent were significantly higher than in Milli-Q water, which indicated that indirect photolysis had a crucial function in the CBZ elimination [62]. The indirect photolysis process of CBZ is influenced by the presence of hydroxyl radical (·OH), singlet oxygen ($^1O_2$) and wastewater compounds. First of all, in secondary effluent, ·OH accounts for 47.00% of the total degradation of CBZ. Then, Lee et al. showed that CBZ was impressible to ^{3}DOM* (the triplet excited state of dissolved organic matter), compared with $^1O_2$, with *T. angustifolia* wetland NOM (natural organic matter) under deoxygenated conditions [63]. In addition, nitrate can absorb radiation in the ultraviolet range ($\lambda < 350.00$ nm) in an aqueous environment with a maximum at 302.00 nm and react to produce ·OH, thus enhancing the indirect photolysis of CBZ [64]. Acridine is a common product, known as mutagenesis and carcinogenic activities due to direct photodegradation of CBZ [65]. Further investigation should emphasize the requirement to think about toxicologically relevant transformation products related to mixture toxicity and the formation and persistence when evaluating the environmental risks spiked with CBZ.

3.4. Microbial Degradation

Pharmaceuticals' chemical structure can explain their biodegradability or recalcitrability, including the existence of secondary, tertiary or quaternary carbon atoms, along with functional groups, such as those found in CBZ. Microbial degradation accounts for 11.70–14.00% in the overall CBZ removal processes. Therefore, it is important to explore specific bacteria that can degrade CBZ. Li et al. separated a bacterial strain from activated sludge called *Pseudomonas* sp. CBZ-4 with the capacity to biodegrade CBZ [57]. When the compound's initial concentration ranging between 10.00 and 160.00 mg/L, the average removal rate is approximately 50.00%; however, *Pseudomonas* sp. CBZ-4 couldn't degrade CBZ at lower concentrations [57]. Ungureanu et al. isolated the bacterial strain called *Streptomyces* MIUG 4.89 to biodegrade CBZ under aerobic condition in the underwater systems, reaching a 30.00% bioconversion of CBZ spiked with 0.20 mg/L [54]. Bessa et al. showed that when 10.00 mg/L of CBZ was a sole carbon source, CBZ was degraded 30.00% by the strain *Starkeya* sp. C11 and *Rhizobium* sp. C12 [55]. On the other hand, in spite of the widespread microorganism consortiums occur in influent, it is impossible that pharmaceuticals render as micropollutants could be effectually degraded by microorganisms alone in the influent. In this case, the deficiency of biodegradation is attributed to the comparatively pharmaceuticals' low concentration compared with other contaminants within wastewater influent, which may not be sufficient to induce enzymes that can degrade pharmaceuticals. Thus, pharmaceuticals are not likely to be beneficial nutrient or carbon sources for existed microorganisms.

Previous studies on biodegradation performance of pharmaceuticals only focus on maternal compounds' elimination rates, and do not study the generation of metabolites, which may be durable and have analogous exotoxicological functions as well. The evaluation of CBZ biodegradation intermediates in CWs is of great significant for better comprehend of microbial elimination mechanisms. Lee et al. concluded that compared with high log K_{ow} values parent compounds, pharmaceutical metabolites with relatively low log K_{ow} values lead to lower removal efficiencies [63]. Thus, as shown in Table 2, CBZ and the most frequently studied CBZ metabolite 10,11-dihydro-10,11-epoxyCBZ should be assessed to determine their fate in CWs in the future.

4. Enhancement of CBZ Removal with CWs

Although many researchers have tried to improve CBZ removal efficiencies by changing the influence parameters of CWs, these changes are all hollow. The hotspots of future studies should engage in the removing mechanism in CWs. Hydraulic model of CWs, new integrated or combined CW types and treatment technologies have arouse much attention recently.

4.1. Hydraulic Model of CWs

The treatment mechanism in CWs is usually considered to be a metaphor black-box [66,67]. Definite comprehension of CW function is advisable owing to a great deal of physical, chemical and biological processes exist simultaneously and interact mutually. The developed hydraulic model of CWs can solve this problem well in the future.

At first, most designers and researchers tended to use the widely known first-order k-c^* model [68], which are simple regression equations. However, this analysis is explained by two parameters, the background concentration c^* and the first-order decay rate k, which is a distinct over-simplification of complicated wetland treatments. Recently, in a research by Hijosa-Valsero et al. pharmaceutical elimination in different types of CWs was studied using statistical analysis such as stepwise regression model, regression tree, cluster tree graph and direct gradient analysis (especially RDA: redundancy analysis) [69]. These four statistical analysis confirmed the significance of physicochemical parameters, macrophytes existence, chemical structure and environment parameters (e.g., dissolved oxygen concentration, pH, temperature, and etc.) in eliminating most pharmaceuticals [69]. Multitudinous evaluations of pharmaceutical removal efficiencies in CWs are provided by multiple regression equations and CHAID (Chi-square Automatic Interaction Detector) trees. From the current studies, it is strongly suggested that a process based model (CW2D: PC progress, http://www.pc-progress.com; 2D mechanical model: Technical University of Catalonia, Catalonia, Spain; CWM1 modelling software/simulation tool: University of Natural Resources and Applied Life Sciences, Vienna or Stella, France) can be used to explain the various CBZ removal processes in CWs.

4.2. Modification of CW Substrates

Based on CBZ removal mechanisms, adsorption to substrates is the main removal pathway in CWs. Apart from selecting appropriate substrates that have a high adsorptive capacity for CBZ removal, the modification of CW substrates is also a high-profile approach. Such modifications may include the introduction of a new CBZ biodegradation pathway in substrates.

Oxidoreductase, such as laccase, is an environmentally benign substitute for CBZ degradation [70–72]. Jelic et al. found after 6 days, 94.00% of CBZ was degraded by laccase [73]. Moreover, four metabolites, such as acridine, acridone, 10,11-epoxy CBZ and 10,11-dihydroxy CBZ were detected, which exhibited non-toxic through acute toxicity tests [73]. Thus, laccase process might be an excellent strategy for CBZ degradation. However, using free laccase results in a successive reduction of enzyme in the treated effluents, which adds the practical cost. Laccase immobilized onto solid supports is a promising way to conquer this challenge [74]. Naghdi et al. explored immobilized laccase to degrade CBZ and observed 97.00% removal efficiencies in secondary effluent [75]. Therefore, analogous to the papers mentioned above, it is feasible to improve CW substrates with laccase from the perspective of implementation. However, the contribution of laccase biodegradation to CBZ removal in CWs still needs to be explored. In addition, it is not known whether laccase affects the function of macrophytes and microorganisms in CWs.

4.3. Integrated or Combined CWs

Previous studies have reported that the CBZ elimination performance in CWs is macrophyte-reliant and alternative because of the lower biodegradation of CBZ. Recently, combinations or integration of some innovative technologies with economical CWs would boost the removal performance of CBZ and concurrently diminish the cost.

4.3.1. CWs Combined with Photocatalytic Oxidation

UV/TiO_2 photocatalytic technologies combined with CWs can be an interesting selective to treat toxic and non-biodegradable contaminants, converting them into less toxic compounds with less-refractory substances. Figure 2 shows the degradation of CBZ in CWs combined with photocatalytic oxidation. Effluent from WWTPs is first treated with ·OH produced by photocatalytic oxidation. Mena et al. indicated that photocatalytic oxidation was found to increase the conversion of CBZ to more than 95% in 2 h [76]. Furthermore, the photodissociation of CBZ can also occur directly under UV light, as mentioned above. Additionally, CBZ reacts with ·OH radical to produce hydroxyl CBZ as an intermediate [77,78]. Intermediate products such as 10,11-epoxy CBZ could be further oxidized to acridone through ·OH produced in advanced oxidation processes [77]. By combining such process with CWs, all the identified intermediates could be further degraded by CWs, yielding a large number of oversimplified substances, which would be mineralized through further oxidation. For example, under aerobic and anoxic conditions, acridine can be mineralized 40% and 23%, respectively [77]. These results showed that this system could detoxify CBZ and all the identified intermediates effectively, while the photocatalytic oxidation treatment or CW treatment itself could not achieve the emission standards.

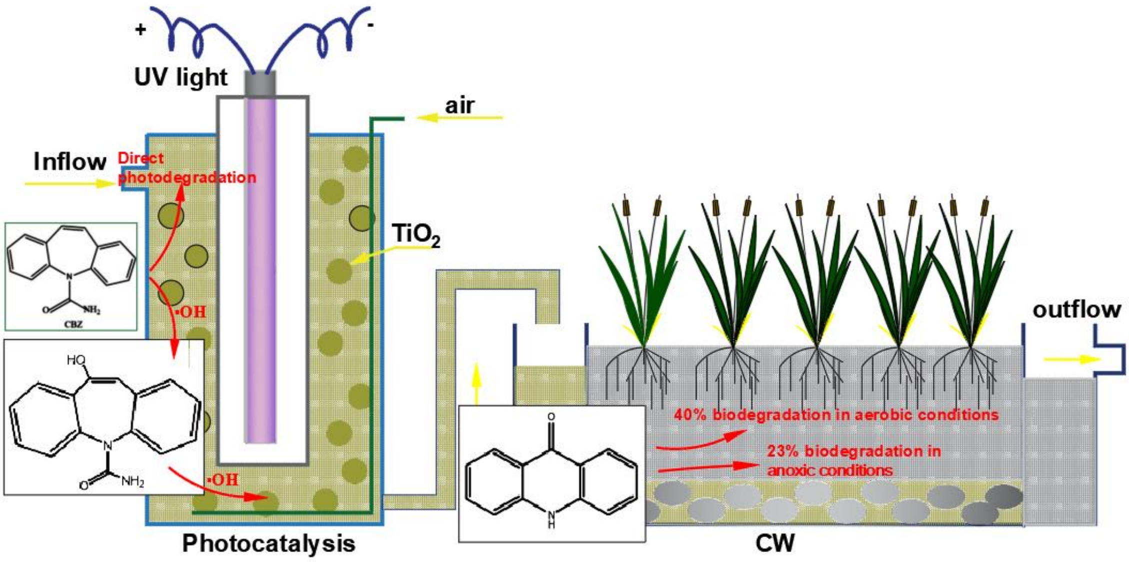


Figure 2. CBZ degraded by CWs combined with photocatalytic oxidation.

4.3.2. CWs Integrated with Microbial Fuel Cells (MFCs)

MFC-CWs can not only convert solar energy and chemical energy into electricity directly, but also achieve better degradation efficiencies of pollutants. In the past studies, MFC-CWs have been exploited in domestic sewage treatment, and the research on promoting pollutant degradation based on closed cycles shows that disposal efficiencies are better than that of CWs [79–81]. Nevertheless, few studies have evaluated the ability of MFC-CWs to process bio-resistant wastewater [82,83]. Through optimizing the design parameters of MFC-CWs, Fang et al. triumphantly realized the highest azo dye decolorization and COD removal values in a MFC-CW because of electric power generation, which indicating that it is likely to enhance the CBZ degradation by MFC-CWs [84]. The schematic diagram of CBZ degradation by a MFC-CW is shown in Figure 3. To achieve CBZ degradation in MFC-CWs, two basic conditions must be satisfied. The first is adequate co-substrate and microbial biomass. Effluent from a WWTP is pumped into MFC-CW from the bottom, which intends that co-substrate (i.e., Glucose) concentration, which is fundamental to CBZ degradation and microbial growth, is greater in the bottom layer than in the middle class; consequently, the removal efficiencies of the bottom layer is superior than that of the middle layer. Moreover, the direct improvement of CBZ degradation performance and COD removal efficiencies in the bottom layer may be attributed to the slow influent flow velocity, which leads to the fresh wastewater is diluted by effluent in the reactor. The second is the appropriate redox potential. Study showed that CBZ can be degraded under near-anoxic conditions [20]. In the middle and cathode classes, CBZ cannot be reduced because breaking CBZ bonds requires near-anoxic conditions. The cathode layer of MFC-CWs is open to the air; the O_2 in the air improves the redox potential of the cathode and middle classes. However, degradation products of CBZ are further reduced by the cathode. Acridine can be generated during ·OH oxidation of hydroxyl CBZ. And the anodic biofilm can then be used to mineralize acridone. Therefore, this system is supposed to accomplish the efficient CBZ degradation. Further investigations are needed to enhance the treatment performance of MFC-CWs and study the degradation mechanism of resistant pollutants.

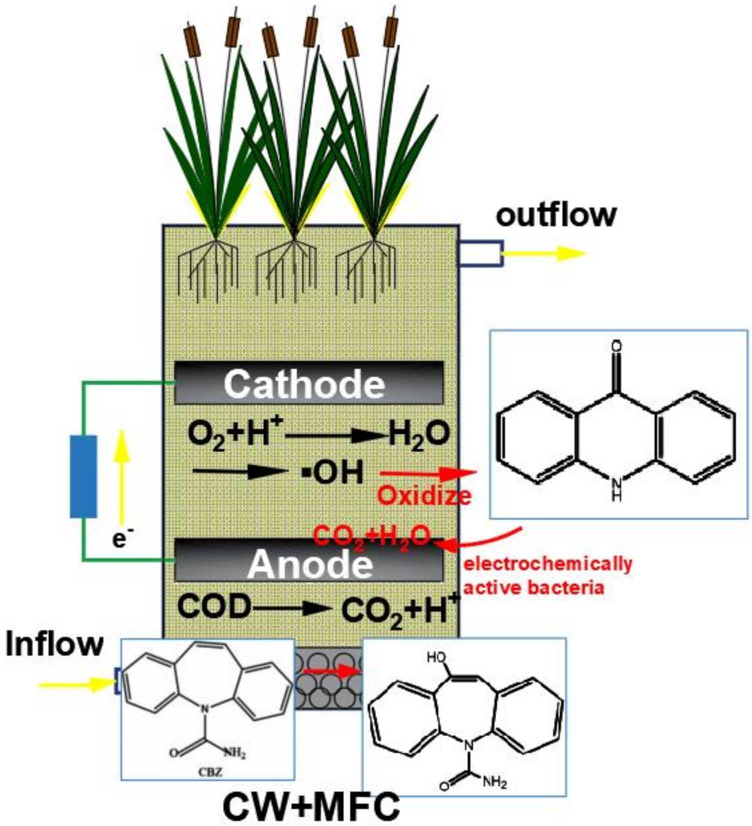


Figure 3. CBZ degradation by a MFC-CW.

5. Conclusions

As polishing wastewater treatments, CWs have attracted more and more attention for the elimination of persistent pharmaceuticals such as CBZ from wastewater. Through selecting CW configurations, macrophyte species and substrate, the CBZ removal performance in CWs could be enhanced by about 20.00–40.00%. The significance of the four main components of CWs (substrate adsorption: 25.70–57.30%, macrophyte uptake: 22.30–51.00%, microbial degradation: 11.70–14.00% and photodegradation: 8.70–9.30%) for CBZ removal on the basis of its physicochemical properties was analyzed to illuminate the potential removal mechanisms involved. Novel research analysis such as building hydraulic models and several new technologies such as laccase degradation, photocatalytic oxidation and MFC can be applied in CWs to achieve efficient degradation of CBZ.

Future studies should focus on more enhancement approaches applied in full-scale CWs to achieve better CBZ treatment.

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