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Strategies to enhance the removal of the persistent pharmaceutically active compound carbamazepine by membrane bioreactors

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ABSTRACT

Carbamazepine, which is an anti-epileptic drug, is ubiquitously present in municipal wastewater. Owing to its recalcitrant chemical structure, carbamazepine is not significantly removed during conventional biological treatment or even by membrane bioreactor (MBR). With the ultimate aim of providing insights into the strategies to enhance carbamazepine removal, the effect of key operational parameters, namely, loading rate (2–750 μg/L·d), pH (5–9), mixed liquor suspended solids (MLSS) concentration (1–15 g/L) and dissolved oxygen (DO) (<0.5–5 mg/L) on the removal of carabamazepine by MBR was systematically studied. Results obtained in this study revealed negligible influence of pH and of MLSS concentration (beyond 5 g/L) on the removal of carbamazepine. The removal rate, however, was significantly enhanced under a DO concentration of less than 0.5 mg/L, suggesting that an alternating anoxic-oxic environment in MBR would achieve high removal. Significantly enhanced (287 mg/g vs. 0.02 mg/g) adsorption of carbamazepine on powdered activated carbon (PAC) as compared to MBR sludge indicated that simultaneous PAC adsorption in MBR may achieve enhanced removal.

Keywords: Carbamazepine; Enhanced removal; Membrane bioreactor; Pharmaceutically active compound; Dissolved oxygen; Wastewater

1. Introduction

There is an increasing concern about the presence of pharmaceutical compounds in the environment due to the potential risk to the aquatic environment. A large volume of pharmaceuticals are used per year with different purposes such as prevention, diagnosis and treatment of diseases in humans and animals. Due to the incomplete human metabolism and discharge into the waste stream, pharmaceuticals are frequently found in environment. In the last decade, researchers have detected numerous pharmaceuticals in the aquatic environment [1].

Effluents from wastewater treatment plants (WWTPs) can be considered to be one of the most important sources of pharmaceuticals in the environment [2]. Conventional WWTPs are not specifically designed to remove pharmaceuticals and other micropollutants. As a result of ineffective removal, they pass through WWTPs and are widely detected in downstream water bodies, with concentrations cascading from WWTP effluents, to surface waters, to groundwater.

Carbamazepine, which is an anti-epileptic drug, is composed of two benzene rings fused to an azepine group, which in turn is connected to an amide group. It is ubiquitously present in municipal wastewater and due to its chemical stability it is not significantly removed during conventional biological treatment. Accordingly, this compound has been frequently detected in the effluents of wastewater treatment plants at concentration of up to tens of μg/L [3]. In a survey conducted by Ternes [1], carbamazepine was detected in all 30 WWTP effluents with a 90 percentile of 3700 ng/L and in 24 of 26

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samples from 20 rivers with a 90-percentile of 820 ng/L. The maximum concentration of carbamazepine in WWTP effluents was 6300 ng/L, which was also the maximum detected concentration of all 32 drugs in the survey. In surface waters, carbamazepine usually occurs at relatively low concentrations (tens of ng/L). The highest detected concentration (1075 ng/L) of carbamazepine in surface water was found in Berlin [4]. It has been also detected in sea water, although at a very low concentration (2 ng/L) [5]. Pharmaceutical residues can be introduced into groundwater through surface water filtration, leakage, and groundwater recharge. Carbamazepine has been detected in the groundwater at concentrations from few tens [6] up to 610 ng/L [7].

Due to its persistence in WWTPs, carbamazepine has been proposed as an anthropogenic marker to assess effluent quality. Even the combination of conventional activated sludge treatment, sand filtration, and ozonation could not achieve more than 60% removal of carbamazepine [8]. In addition to chemical stability, their poor removal has been partly attributed to their hydrophilic nature (log Kow < 3). Membrane bioreactor (MBR) is a proven technology to achieve better levels of typical water quality parameters like total organic carbon (TOC) and total nitrogen (TN). However, to date both laboratory scale and pilot scale MBR plant studies have reported negligible to moderate removal (usually less than 10%) of carbamazepine. Even the application of a sludge retention time (SRT) of as long as 500 d did not improve carbamazepine removal in a study conducted by Clara et al [9]. Studies have heavily reported the limited extent of carbamazepine removal, but to date fewer studies have attempted to investigate the governing reasons. Consequently no definitive strategy to solve this problem has been reported to date.

In this study, we investigated the effect of different operational parameters namely carbamazepine loading, pH, dissolved oxygen (DO) and mixed liquor suspended solid (MLSS) concentration on the removal of carbamazepine in laboratory scale MBRs. Based on the results from our study coupled with a comprehensive literature review we provide insights into the strategies to enhance the removal of carbamazepine in MBR. According to our knowledge, this is the first study which comprises investigation into a set of important factors, rather than a single factor.

2. Materials and methods

2.1. Synthetic wastewater

A synthetic wastewater simulating municipal sewage was used to ensure a stable feeding rate throughout the experiment. Concentrated stock solution was prepared and stored in a refrigerator at 4°C. It was then diluted with MilliQ water on a daily basis to make up a feed solution containing glucose (400 mg/L), peptone (75 mg/L), KH_2PO_4 (17.5 mg/L), $MgSO_4$ (17.5 mg/L), $FeSO_4$ (10 mg/L), and sodium acetate (225 mg/L). This composition was based on a previous study [10]. A concentrated stock solution of carbamazepine was prepared in pure methanol. The trace organic stock solution was kept in a freezer and was used within less than a month. A specific amount of stock solution was mixed with the synthetic wastewater to achieve the required influent carbamazepine concentration. All chemicals used were of analytical grade.

2.2. Laboratory scale MBR system

Two laboratory-scale MBR systems were used in this study. Detailed description of the first MBR system is available elsewhere [11]. The system consisted of a glass reactor, a continuous mixer, two air pumps, a pressure sensor, and influent and effluent pumps. Two ZeeWeed–1 (ZW–1) submerged hollow fibre ultrafiltration membrane modules supplied by Zenon Environmental (Ontario, Canada) were used in this set-up. The membrane has a nominal pore size of 0.04 μm. Each module has an effective membrane surface area of 0.047 m^2. The hydraulic retention time was set at 24 h, corresponding to a permeate flux of 4.3 L/m^2h. The MBR pH, temperature and dissolved oxygen (DO) content were kept constant at 7, 20.0 ± 0.1°C and 2 ± 1 mg/L, respectively. The MBR was seeded with activated sludge from the Wollongong sewage treatment plant, NSW, Australia. After the initial start-up process, which lasted about 2 months, a small amount of sludge was regularly extracted from the reactor to keep the sludge age at approximately 70 d. Performance of the MBR system with regard to basic water quality parameters was then monitored for an extended period of more than four weeks, after which the investigation on the effect of carbamazepine loading (2–6 μg/L·d) and pH (5–9) of the reactor, respectively on removal were conducted. The MLSS concentration in the reactor during this part of the investigation was around 15 g/L. A similar MBR system was then inoculated by the sludge taken from the first MBR. The second MBR was subject to high carbamazepine loading (750 μg/L·d) and was operated under a DO of less than 0.5 mg/L from the beginning. The effect of MLSS of this MBR on removal was studied as the MLSS increased from the initial level of only 1 to 11 g/L. The MLSS concentration remained fairly stable beyond this period. The effect of DO concentration on removal was subsequently studied by operating the MBR under a DO of 0.5 mg/L for further 30 d and then under higher DO levels (2–5 mg/L).

2.3. Analytical techniques

The analysis of the model trace organic was based on a previously reported method [11,12]. The target compound was extracted using 5 ml, 500 mg hydrophilic/lipophilic balance (HLB) cartridges (Waters, Millford, MA, USA). After elution the analyte was separated using an Agilent (Palo Alto, CA, USA) 1200 series high performance liquid chromatography (HPLC) system equipped with a 150 x 4.6 mm, 5 μm particle size, Luna C18 (2) column (Phenomenex, Torrence CA, USA). Mass spectrometry was performed using an API 4000 triple quadrupole mass spectrometer (Applied Biosystems, Foster City, CA, USA) equipped with a turbo-V ion source employed in both positive and negative electro-spray modes. When high concentration of carbamazepine (750 μg/L) was used in the feed solution, a Shimadzu HPLC system equipped with an UV-Vis detector was used for the analysis.

Conductivity and pH were measured using an Orion 4-Star Plus pH/conductivity meter. Total organic carbon (TOC) and total nitrogen (TN) were analysed using a Shimadzu TOC/TN-V_{CSH} analyser (Tokyo, Japan). TOC analysis was conducted in non-purgeable organic carbon (NPOC) mode. Samples were kept at 4°C until analysed and calibrations were performed in the range between 0 and 1000 mg/L and 0 to 100 mg/L for TOC and TN, respectively. MLSS and MVLSS contents in the MBR were measured in accordance to the Standard Methods for the Examination of Water and Wastewater [13].

3. Results and discussion

3.1. Effect of loading rate

The basic water quality parameters such as TOC and TN were continuously monitored to confirm biological stability. Apart from the trial on the effect of pH (Section 3.2) the TOC and TN removal rates were stable throughout the operation period (data not shown). Carbamazepine removal rate in our study ranged from 3–22% depending on the loading rate (Table 1). The low removal efficiency in general is in line with the literature reports and demonstrates once again the hardly biodegradable nature of carbamazepine. Löffler et al. [14] found that carbamazepine was highly recalcitrant to elimination in a water/sediment system at laboratory scale. The time required for a 50% reduction of its initial concentrations (100 μg/ L) was 328 d, as calculated by first-order elimination kinetics. Stamatelatou et al. [15] conducted a biodegradability test of carbamazepine in sodium acetate cultured activated sludge in both sea and fresh water. They observed no biodegradation of carbamazepine at an initial concentration of 0.5 mg/L in either sea or freshwater. Carbamazepine was classified in biodegradability group of below 0.1 $L/kg_{ss}/d$ when considering a first order degradation constant (k_{biol}) in WWTPs [16]. Apart from the batch studies, to date both laboratory and pilot scale MBR plant studies have reported negligible [17–19] to moderate [20–23] removal, usually less than 10%. The low removal rate observed in our study is, hence, in close agreement with the prior reports.

Table 1
Carbamazepine removal rare under different loading

Loading rate (μg/L·d)	Removal efficiency	
	In percentage (%)	In mass (μg/L·d)
2–6	22	0.44–1.32
750	3	22.5

In our study, although the percentage removal efficiency was better in case of the lower loading rate (2–6 μg/L·d) operation as compared to the higher loading rate (750 μg/L·d) operation, the removal efficiency (in μg/L·d) was in fact lower in case of the lower loading rate (2–6 μg/L·d). This can be explained by the fact that if the concentration of a pollutant decrease below a certain threshold level, biodegradation may be hindered due to lack of enzyme induction [24,25]. The results here indicate that carbamazepine is extraordinarily persistent to biodegradation at low concentrations.

3.2. Effect of bioreactor pH

As can be seen in Fig. 1, a small decrease in biological performance with regard to TOC removal efficiency was observed as the mixed liquor pH was reduced to 5. A sharp decline in TOC removal efficiency was also observed when the mixed liquor pH was increased beyond 8. While investigations explicitly studying the effects of pH on the treatment efficiency of an MBR system remains very limited [22,26,27], results reported here are in fact consistent with previous studies on conventional activated sludge treatment processes. Lower biological performance at either acidic or basic condition can be attributed to complex changes in the microorganism fauna of the reactor in response to the mixed liquor pH. In contrast to the TOC removal rate, negligible effect of mixed liquor pH on carbamazepine removal was observed. An apparent improvement in removal efficiency of certain acidic trace organics such as ibuprofen, ketoprofen, and diclofenac was observed in case of MBRs operated under acidic conditions [11,22]. This phenomenon was explained by the speciation of the compounds from hydrophilic ionic forms to much more

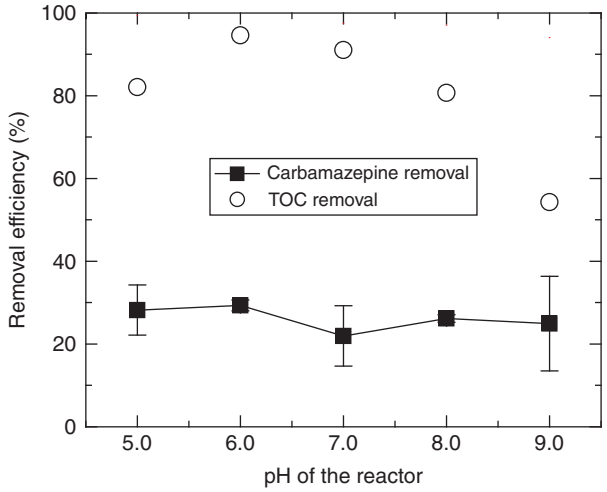

Fig. 1. Effect of bioreactor pH on TOC and carbamazepine removal. Error bars show the standard deviation of 4 measurements.

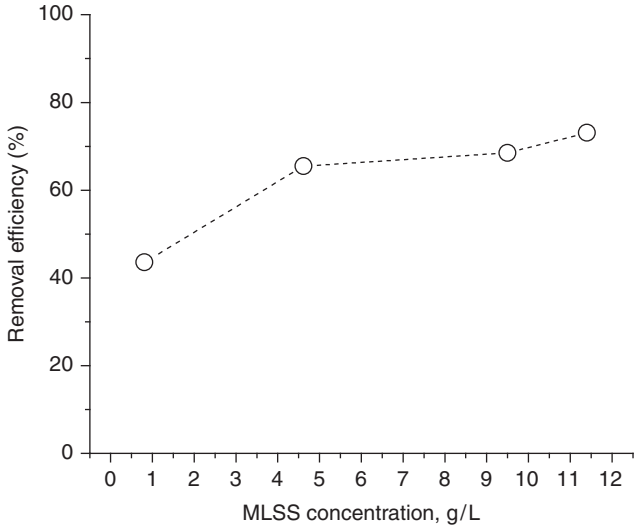

Fig. 2. Effect of MLSS concentration on carbamazepine removal (under anoxic condition with DO < 0.5 mg/L).

hydrophobic forms at pH lower than their pK_a values which allowed them to adsorb to the activated sludge quite readily. However, carbamazepine used in this study did not speciate as the mixed liquor pH varied from pH 5 to pH 9. Consequently, its removal efficiency remained relatively constant and independent of the mixed liquor pH. Carbamazepine contributed a negligible portion of the TOC; hence, mismatch between TOC and carbamazpeine removal profile is not surprising.

3.3. Effect of DO

In this study, the effect of DO was studied under the higher loading (750 μg/L·d) condition. A dramatic effect of operating DO on removal rate was observed (Table 2). In a short-term study conducted by Zwiener and Frimmel [28] diclofenac was better degraded in an anoxic biofilm reactor (62–66% of its initial concentration). While previous studies have demonstrated relationship of nitrifying condition with carbamazepine removal [29], no literature report could be found which mentions the effect of denitrifying (anoxic) condition on its removal. Our result suggests that anoxic environment promotes carbamazepine degradation. In addition to the possible enhanced biodegradation under anoxic condition, abiotic (chemical conversion) degradation may also be responsible for the observed high removal rate. Further investigation is underway to ascertain the governing reason.

Table 2
Effect of DO on carbamazepine removal

DO, mg/L	Removal efficiency (%)
<0.5	67
2–5	3

3.4. Effect of MLSS concentration

The effect of MLSS concentration was studied under near-anoxic (DO < 0.5 mg/L) condition when the loading rate was 750 μg/L·d. The removal efficiency rate of carbamazepine did not increase much beyond a MLSS concentration of 5 g/L or so (Fig. 2). This indicates that due to the insignificant affinity of carbamazepine towards adsorption onto sludge, biodegradation, in contrast to biosorption, played the main role in carbamazepine removal in the MBR. In our study, however, under a low MLSS concentration of approximately 1 g/L the removal rate of carbamazepine was the lowest. This underscores the importance of maintenance of adequate amount of biomass in the reactor to achieve satisfactory degree of recalcitrant pollutant degradation.

3.5. Adsorption on to activated carbon

Adsorption onto sludge may facilitate enhanced biodegradation in MBR due to complete sludge retention [30]. The data from our MBR study, however, suggested limited sorption of carbamazepine onto sludge. Accordingly the intrinsic biodegradation rate governed the overall removal of carbamazepine, and due to the hardly biodegradable nature of carbamazepine the extent of removal was rather limited. In an attempt to promote adsorption of carbamazepine and subsequently reap enhanced biodegradation, a strategy of direct addition of adsorbent (e.g., powdered activated

Table 3
Comparative adsorption of carbamazepine on MBR sludge and PAC

Media	Unit adsorption of CBZ (mg/g)
MBR sludge	0.02
PAC	287

carbon, PAC) into MBR may be proposed. In fact, a preliminary batch test demonstrated many fold higher adsorption of carbamazepine onto PAC as compared to MBR sludge (Table 3). Hai et al. [31] previously demonstrated enhanced removal of recalcitrant dyes in a PAC-enhanced MBR. The efficiency of a PAC-enhanced MBR in carbamazepine removal is currently under investigation. Preliminary results indicate that facilitated adsorption can indeed substantially improve the overall carbamazepine removal in MBR (negligible and around 90% removal without and with PAC addition in MBR).

4. Conclusions

Our results indicate that carbamazepine is extraordinarily persistent to biodegradation at low concentrations. Application of slightly acidic pH may facilitate removal of certain ionizable trace organics which transform to more hydrophobic species under such pH; however, carbamazepine, being a non-ionizable compound, such strategy would be of little significance. In contrast, manipulation of reactor DO appears to be an effective means to achieve high carbamazepine removal. An MBR with alternating anoxic-oxic environment may achieve high removal. On the other hand, negligible sorption of carbamazepine onto sludge implies that maintenance of high MLSS concentration in MBR would not yield significant improvement in overall removal. However, our batch test indicates that enhanced adsorption achieved by powdered activated carbon dosing directly into the MBR may result in enhanced overall removal.

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