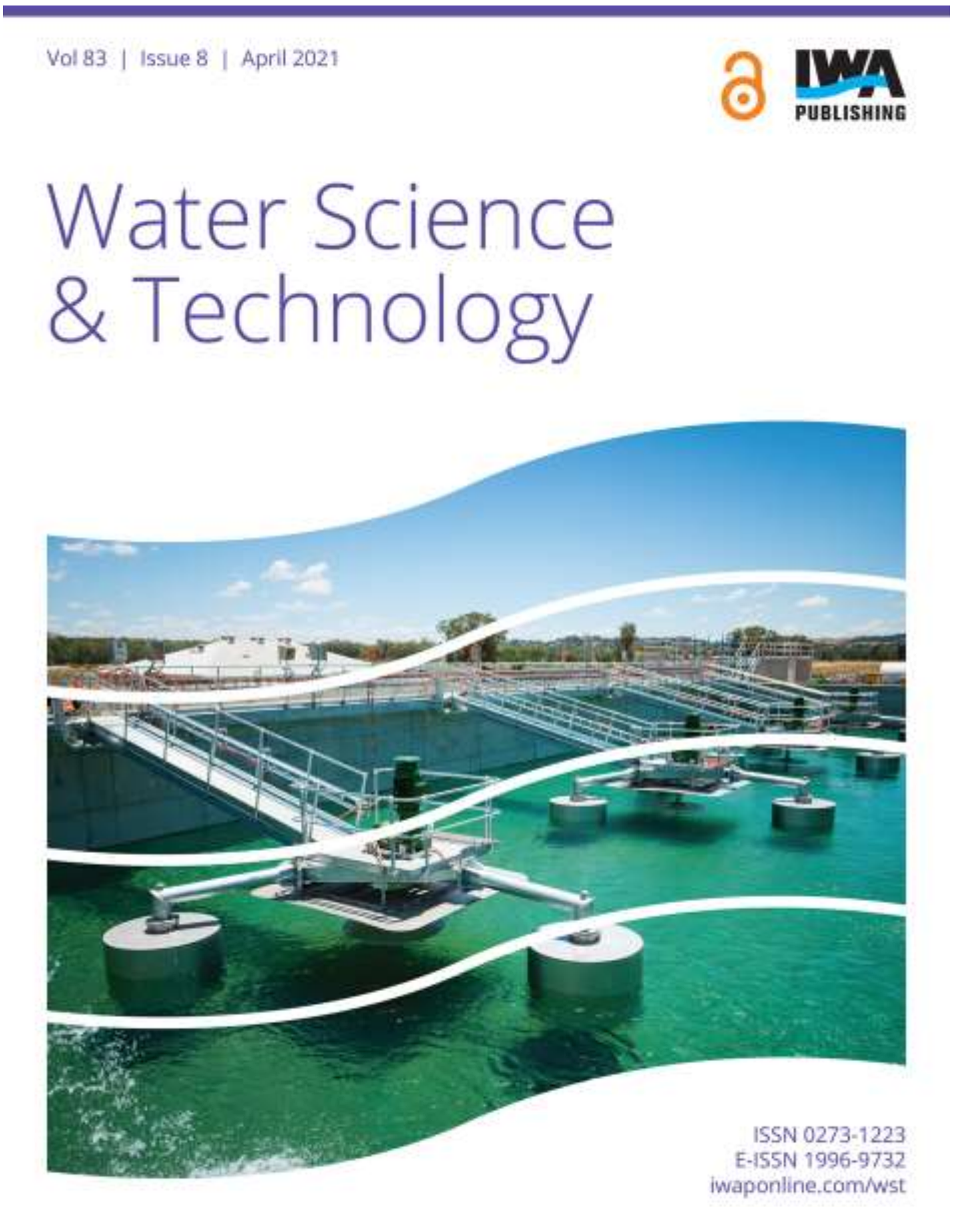

Vol 83 | Issue 8 | April 2021
PUBLISHING
Water Science & Technology
ISSN 0273-1223
E-ISSN 1996-9732
iwaponline.com/wst

Carbamazepine removal from low-strength municipal wastewater using a combined UASB-MBR treatment system

M. J. Moya-Llamas, A. Trapote and D. Prats

ABSTRACT

An Upflow Anaerobic Sludge Blanket reactor combined with a two-stage membrane bioreactor were operated for 193 days in order to evaluate the biological removal of carbamazepine (CBZ) from low-strength municipal wastewater. The system worked in three different organic load stages (0.7 ± 0.1 kg COD·m^{-3}·d^{-1}, 0.4 ± 0.1 kg COD·m^{-3}·d^{-1} and 0.1 ± 0.0 kg COD·m^{-3}·d^{-1}) to assess the impact of the influent OLR on operational parameters such as anaerobic and aerobic sludge retention time (SRT), acidity, volatile fatty acids (VFAs), biomass activity or biogas production. The highest carbamazepine removals were achieved during the anaerobic stage (UASB reactor), reaching averages of 48.9%, 48.0% and 38.2% operating at high, medium and low OLR, respectively. The aerobic treatment (MBR) served as post-treatment, improving the removals, and the global UASB-MBR system reached averages of 70.0%, 59.6% and 49.8% when the influent was at medium and low OLR, respectively. The results demonstrate the potential of combined biological systems on the removal of recalcitrant pharmaceuticals.

Key words | biological treatment processes, carbamazepine, MBR, organic loading rate, UASB

M. J. Moya-Llamas (corresponding author)
Department of Civil Engineering,
University of Alicante,
Carretera de San Vicente del Raspeig s/n, 03690
San Vicente del Raspeig, Alicante,
Spain
E-mail: *mjmoya@ua.es*

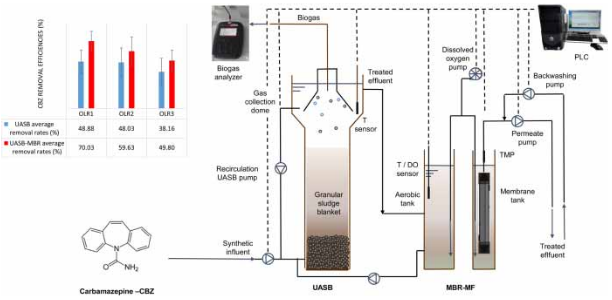
A. Trapote
D. Prats
Institute of Water and Environmental Sciences,
University of Alicante,
Carretera de San Vicente del Raspeig s/n, 03690
San Vicente del Raspeig, Alicante,
Spain

HIGHLIGHTS

- UASB-MBR was proposed for the removal of the anti-epileptic drug carbamazepine.
- The CBZ removal rates of the UASB-MBR combined system were highly dependent on the organic loads of the influent.
- UASB-MBR system proved to be particularly suitable for treating municipal wastewater containing CBZ at OLR above 0.7 kg COD·m^{-3}·d^{-1}.
- UASB reactor was the main contributor to degradation of the pharmaceutical CBZ.

doi: 10.2166/wst.2021.096

GRAPHICAL ABSTRACT

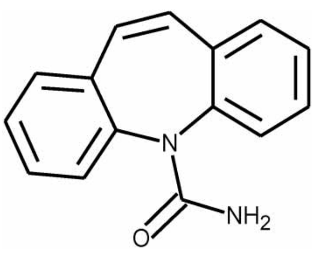


INTRODUCTION

The term emerging contaminants (ECs) is used for chemical and microorganisms that have been identified in water only recently and are under consideration to be regulated (Asano *et al.* 2006). The presence of these ECs in receiving environmental compartments can be a major problem with respect to the long-term protection of public health and the environment, as well as an impediment to water reuse. The persistence of many pharmaceuticals, personal care products and cleaning agents to conventional wastewater treatment plants (Luo *et al.* 2014), generally based on conventional activated sludge processes (CAS) has become an urgent but complex problem for the scientific community.

Carbamazepine (CBZ) (Table 1) is an anti-epileptic and antidepressant drug with anticonvulsant and analgesic properties. It can be used for psychiatric disorders, for relief of trigeminal neuralgia, or for partial seizures (USP 2007; Maan & Saadabadi 2020). Its absorption is slow and occurs almost completely in the intestinal tract. After it is absorbed, carbamazepine is heavily metabolized by the liver (99%) (Zhang *et al.* 2008; Dean 2018) and metabolism removes it primarily by the kidneys, being excreted together with its metabolites and incorporated into wastewater. Its properties include a high persistence to biodegradation in the aquatic environment or in biological processes (Stamatelatou *et al.* 2003; König *et al.* 2016) and a low adsorption onto sludge (Ternes *et al.* 2004; Kim *et al.* 2014). Consequently, carbamazepine and their metabolites remain in the aqueous phase, being one of the most widely detected compounds in raw wastewater (Verlicchi *et al.* 2012; Kim *et al.* 2014).

Table 1 | Chemical structure and main physico-chemical properties of CBZ (National Center for Biotechnology Information 2019)

Chemical structure	Physico-chemical properties	
	Molecular formula:	$C_{15}H_{12}N_2O$
	CAS No:	298-46-4
	Usage:	Analgesic, antiepileptic
	Log K_{ow}(octanol/water partition coefficient):	2.45
	Log $K_{d:}$	1.2–2.3
	Water solubility (mg/L):	17.7
5H-Dibenz[b,f]azepine-5-carboxamide (Carbamazepine-CBZ)	Molecular weight (g/mol):	236.274
	Henry's Law constant at 25 °C (atm m^3/mol):	$1.08{\cdot}10^{-10}$

The recalcitrant behavior of carbamazepine to conventional biological treatments has been highly reported, being only removed in percentages below 10% by municipal wastewater treatment plants (WWTPs) (Ternes 1998; Heberer 2002; Clara *et al.* 2005; Suárez *et al.* 2005; Radjenović *et al.* 2009; Alvarino *et al.* 2014). Therefore, it is incorporated into water bodies where it has been detected in the groundwater at concentrations up to 600 ng·L^{-1} (Drewes *et al.* 2002; Kaiser *et al.* 2014). The implications of the increasing presence of CBZ and its metabolites on human health and the environment are still poorly understood and hardly addressed in the literature. The European Chemicals Agency (ECHA) (www.echa.europe.eu; accessed on December 15, 2020) includes carbamazepine in its databases, mentioning potential adverse effects such as carcinogenesis, teratogenesis and/or mutagenesis, bioaccumulation and toxicity. In this sense, a relevant European regulation regarding micropollutants is the new Swiss water protection act (Gewässerschutzgesetz GSchG), implemented in that country since January 2016, which includes CBZ among twelve active substances selected to evaluate due different criteria such as their presence in all large Swiss WWTPs, not being eliminated by biological treatments and being detectable with a reliable and ready to use analytical method. In addition, relevant research such as that conducted by Paltiel *et al.* (2016) provides concerning results about the real potential for unwitting human exposure to CBZ via reclaimed wastewater.

Advanced aerobic treatment technologies as MBRs have proven to be more effective than conventional activated sludge (CAS) treatment systems in the removal of certain micropollutants (Cases *et al.* 2011). Nevertheless, in the case of persistent pharmaceuticals such as carbamazepine, Hai *et al.* (2011) addressed only a removal efficiency around 20% by a MBR flat plate under anoxic and aerobic conditions operating at low inlet concentration of CBZ (2–5 μg/L), close to the 28% reached by Gurung *et al.* (2017) using the same MBR configuration. Kreuzinger *et al.* (2004) informed only a removal efficiency around 11% with a MBR pilot plant equipped with an ultrafiltration membrane, and no removal was reported by Clara *et al.* (2004) and Radjenović *et al.* (2009). Moreover, according to an exhaustive revision carried out by Simon *et al.* (2021), MBR processes have not been found to be significant in the removal of CBZ. Regarding other technologies such as advanced oxidation processes (AOPs), based on the production of hydroxyl radicals by different mechanisms, these have proven to be highly effective in the degradation of ECs that are refractory to biodegradation. However, its high operating costs and the generation of numerous intermediates and degradation subproducts, such as epoxy-carbamazepine or the carcinogenic compound acridine, constitute a major obstacle to its use (Rivera-Utrilla *et al.* 2013). Consequently, new strategies must be developed in order to decrease the discharged concentration of this persistent and xenobiotic compound.

Anaerobic treatment processes have been well known for decades in the treatment and removal of biodegradable organic matter from wastewater. They are mainly based on a high retention of active biomass on the reactor (Kato 1994). Although they have traditionally been used for the treatment and removal of easily biodegradable organic matter from slaughterhouses, breweries, dairies, distilleries or paper industries, recent research has demonstrated their effectiveness in the removal of certain persistent compounds, such as the analgesic naproxen or the antibiotics sulfamethoxazole and roxythromycin from urban wastewater (Carballa *et al.* 2007). In this sense, previous research such as Schwarzenbach *et al.* (2005) reported that anaerobic degradation favors biodegradation of the persistent ECs through hydrolysis of amide and urea groups of carbamazepine and atenolol, which demonstrates that degradation efficiency depends on the structure and functional group of the compounds (Tiwari *et al.* 2017).

Upflow anaerobic sludge blanket (UASB) reactor has proven to be a competitive low-cost system for the direct treatment of municipal wastewater (Rizvi *et al.* 2015), being also capable of removing certain compounds, such as estrogens, bisphenol A or caffeine (Froehner *et al.* 2011). Nevertheless, CBZ has proven to be highly persistent to anaerobic based treatments. In this sense, Alvarino *et al.* (2014) reported its recalcitrant behavior, achieving low removal rates of CBZ (<15%) treating municipal wastewater anaerobically and also other authors such as Carballa *et al.* (2007) or Stamatelatou *et al.* (2003) found no significant removal of CBZ under anaerobic conditions. According to this, and with the aim of enhancing its biological removal, two or more biological technologies combining different redox conditions must be implemented. Conkle *et al.* (2012) investigated different redox conditions (aerobic and anaerobic conditions) for the degradation of CBZ, concluding that variations in redox conditions play an important role in the degradation of certain pharmaceuticals such as carbamazepine.

In this context, innovative wastewater treatment systems combining aerobic and anaerobic biological processes are a cost-effective and environmentally sustainable alternative for the removal of ECs in municipal wastewaters (Qiu *et al.* 2013; Alvarino *et al.* 2016; Niwa *et al.* 2018). Their main advantages are low operating and maintenance costs, low rate of sludge production or the generation of biogas with a high content of methane suitable for the energy recovery of the system (Rosa *et al.* 2016). The possible configurations of these systems are many and varied; however, recent studies present a two stage UASB-MBR combined system as a particularly promising configuration for the treatment of municipal wastewater (Qiu *et al.* 2013; Alvarino *et al.* 2016; Moya *et al.* 2018; Niwa *et al.* 2018). The use of the anaerobic UASB reactor as a first stage of organic matter degradation with considerably lower energy consumption than aerobic systems, together with the complementary treatment of the remaining organic matter by means of the MBR, results in a treated effluent of excellent quality, thus optimizing the cost-effectiveness ratio.

The organic loading rate (OLR) is a key parameter in the performance of UASB reactors that indicates their capacity for methanogenic conversion. Although previous studies such as that conducted by Lettinga *et al.* (2001), Álvarez *et al.* (2006) or Buntner *et al.* (2013) have demonstrated the feasibility of anaerobic systems treating low organic loading effluents like domestic, municipal and certain industrial effluents, the OLR of the influent is usually a limiting factor in the performance of biological reactors, particularly anaerobic ones. However, the efficiency of these combined systems treating low OLR urban effluents has not yet been addressed. In this sense, the combination of UASB and MBR systems have generally been applied to treatment of municipal effluents with organic loads above 1 kg $COD \cdot m^{-3} \cdot d^{-1}$, as corroborated by Niwa *et al.* (2018) (1.0–3.3 kg $COD \cdot m^{-3} \cdot d^{-1}$), Farajzadehha *et al.* (2015) (7.2–10.8 kg $COD \cdot m^{-3} \cdot d^{-1}$) or Buntner *et al.* (2013) (4.85 kg $COD \cdot m^{-3} \cdot d^{-1}$). Regarding the influence of OLR on the removal of ECs from municipal wastewater, although it could be expected that an increase in the OLR will encourage the microbial/enzymatic activity of the anaerobic reactors as well as the co-metabolic transformation of ECs, no clear correlation has been found between this operational parameter and ECs removal (Gonzalez-Gil *et al.* 2020).

The aim of this research is to evaluate the effectiveness of a laboratory-scale UASB-MBR combined pilot plant in the removal of the persistent pharmaceutical carbamazepine from low strength municipal wastewater. Additionally, the impact of the organic loading rates of the influent on the removal efficiency of CBZ was analyzed. Furthermore, the influence of the presence of CBZ on main operational parameters such as sludge retention time (SRT), acidity, microbial activity of the sludge or biogas production was also evaluated. In this study, carbamazepine has been chosen as an example of a persistent drug present at trace concentrations in municipal WWTP effluents.

MATERIALS AND METHODS

Experimental set-up

The laboratory-scale system consisted of a UASB reactor followed by a membrane bioreactor (MBR) (Figure 1). The recirculation implemented between both systems allowed the pilot plant to operate effectively as a combined UASB-MBR system. The UASB reactor was designed for a usable volume of 20 L and was equipped with a three-phase bell-shaped device for the separation and conduction of the biogas generated in the methanogenic stage as well as to separate suspended solids in the UASB. Given the slow growth of anaerobic bacterial clusters (several months), and in order to initiate the start-up stage with a well-developed bacterial consortium, 8 L of granular sludge from a local brewery located nearby (Valencia, Spain) were used as inoculum for the start-up stage of the anaerobic reactor. The quality and suitability of this granular sludge was verified by physical-chemical (Table 2) and microbiological characterization. The identification on the microscope confirmed the presence of mature granular macroflocs, some of them polynucleated, as well as the presence of species such as *Zooglea* spp., *Cymbella* spp. and small flagellated protozoa and phytoflagellates.

The MBR was designed in external submerged configuration, by means of a 12 L aerobic tank for biomass growth followed by an 8 L membrane tank. The MBR was equipped with an air supply compressor to maintain the dissolved oxygen (DO) concentration required for the maintenance of the aerobic biomass. The concentration of suspended solids in the mixed liquor was maintained as constant in both tanks by the arrangement of a recirculation peristaltic pump. The filtration was carried out by a PDVF hollow-fiber microfiltration membrane (0.4 μm, 0.2 m^2) (mod. Micronet® R, Porous Fibers, S.L).

The main operating parameters were controlled and recorded continuously by a PLC equipped with a software specifically developed and implemented by the research group. This non-commercial software consisted of a SCADA (supervisory control and data acquisition) designed using Visual Basic Studio as the web interface, with allowed access to pilot-plant information.

The experimental system was designed for the treatment of municipal wastewater. This substrate was reproduced by means of synthetic wastewater prepared in the laboratory. Its composition for a COD reference of 1,200 mg/L consisted mainly of peptone (47.60 g), beef extract (32.59 g) and micronutrients (0.59 g $MgSO_4 \cdot 7\ H_2O$, 1.18 g $CaCl_2 \cdot 2\ H_2O$ and 2.07 g NaCl) (Sigma Aldrich, Steinheim, Germany) and was based on DIN 38 412-L24, which has been used in previous studies (Holler & Trösch 2001). According to Carballa *et al.* (2007), Farajzadehha *et al.* (2015) and Show *et al.* (2012), 1.5 and 3 g of sodium carbonate and bicarbonate respectively were added regularly to the

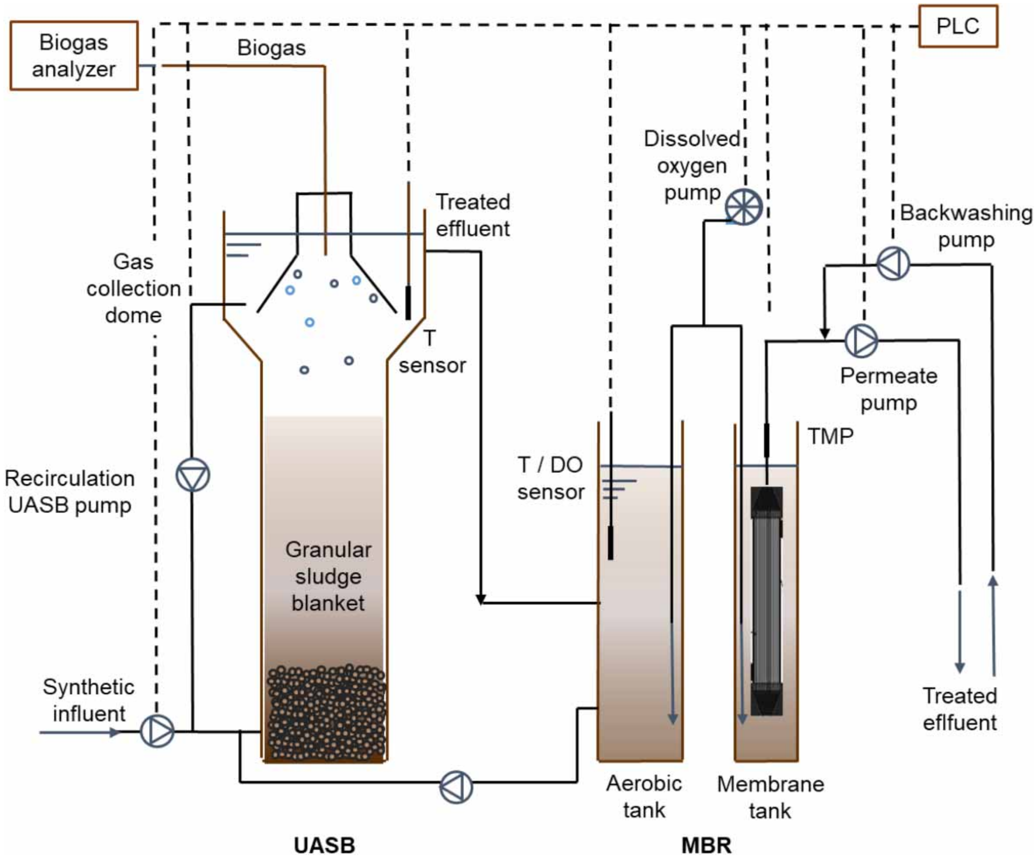


Figure 1 | Combined UASB-MBR laboratory-scale plant scheme.

Table 2 | Characterization of the sludge-inoculum of both reactors

Physico-chemical parameters	Granular sludge (UASB)	Mixed liquor (MBR)	Unit
Total suspended solids	74,200	850	mg/L
COD	6,870	246	mg O_2/L
COD_5	397	93.1	mg O_2/L
pH	7.28	7.07	–
Conductivity	2.43	2.80	mS/cm
Redox potential	– 224	172	mV

substrate to maintain the buffer capacity and bicarbonate alkalinity in the anaerobic reactor. In order to evaluate the impact of different organic loads on the removal efficiency of CBZ, the pilot plant was operated in three stages within the range of municipal wastewaters: high (0.7 ± 0.1 kg COD·m^{-3}·d^{-1}), medium (0.4 ± 0.1 kg COD·m^{-3}·d^{-1}) and low (0.1 ± 0.0 kg COD·m^{-3}·d^{-1}). Consequently, the described substrate was diluted to three different concentrations: COD = 1,200, 600 and 300 mg O_2·L^{-1} respectively.

The average values of the main operating parameters of the UASB-MBR pilot plant during the different stages of the experimental period are included in Table 3.

Concerning the HRT, this is a key operational parameter of UASB reactors, being directly associated with the upward velocity and limited by the hydraulic load applied to the reactor. According to Vassalle *et al.* (2020) and Alvarino *et al.* (2018), HRT is a critical parameter in the removal of certain compounds, since it directly affects their degradation. Taking this into account, and in order to allow high contact time between the sewage and the sludge inside the reactor, the UASB was operated at high HRT (37 hr).

Regarding the temperature, the optimum temperature for the anaerobic digestion ranges from 30 °C to 35 °C (Liu & Tay 2004; Rizvi *et al.* 2015). Its influence on the performance of the UASB reactors is particularly relevant, affecting the hydrolysis processes, the rate of substrate use, the rate of solids sedimentation and gas transfer, and also determining the predominant species in the reactor (Pavlostathis & Giraldo-Gómez 1991; Lettinga *et al.* 2001; Rizvi *et al.* 2015). Nevertheless, several studies have

Table 3 | Operational parameters

Operational parameters	Start-up	Stage 1	Stage 2	Stage 3
Period of time (d)	0–55	56–87	88–125	125–193
UASB reactor				
T (°C)	26 ± 3	29 ± 1	31 ± 1	30 ± 1
HRT (h)	37	37	37	37
SRT (d)	>90	>90	>90	>90
$pH_{synthetic\ influent}$	7.7 ± 0.5	7.7 ± 0.3	7.5 ± 0,4	7.7 ± 0.2
$pH_{supernatant}$	7.2 ± 0.3	7.2 ± 0.1	7.2 ± 0.1	7.4 ± 0.2
MBR				
C_m (kg COD·kg TSS^{-1}· d^{-1})	0.50 ± 0.13	0.47 ± 0.20	0.47 ± 0.21	0.22 ± 0.12
T (°C)	23 ± 2	27 ± 2	29 ± 1	26 ± 2
HRT (h)	30	30	30	30
SRT (d)	90	90	90	90
$pH_{mixed\text{-}liquor}$	6.9 ± 0.2	7.0 ± 0.5	7.4 ± 0.3	7.4 ± 0.2
$pH_{permeate}$	6.8 ± 0.2	6.9 ± 0.3	7.8 ± 0.4	8.1 ± 0.1
DO (mg O_2/L)	6.1 ± 2.0	4.8 ± 2.1	6.0 ± 4.2	6.2 ± 3.1
K (L·m^{-2}·h^{-1})	35.0 ± 6.0	24.4 ± 10.2	87.6 ± 17.7	50.5 ± 7.9

demonstrated the effectiveness of UASB reactors operating at low ambient temperatures (Kato 1994; Buntner *et al.* 2013; Rizvi *et al.* 2015). In this research, the UASB reactor was started up at ambient temperature, with an average value of 23 °C. However, the effects of daily variations on the performance of the reactor were observed in this stage. In order to limit the influence of daily and seasonal variations of temperature and according to previous research (Farajzadehha *et al.* 2015) temperature in the anaerobic reactor was maintained ranging from 29 °C to 31 °C throughout the experimental period (Table 3).

According to Show *et al.* (2012), in order to ensure rapid granulation and a stable treatment process, the start-up stage was completed when COD removal rates of the UASB-MBR combined system remained stable at about 98% and pseudo steady-state conditions were achieved. After that previous stage, CBZ was introduced regularly into the synthetic influent at an inlet concentration of 10 μg·L^{-1} (Sigma Aldrich, Steinheim, Germany). This concentration, similar to those monitored in the influents of the WWTPs, was also sufficient for the fraction not removed to be above the detection limits of the analyzer equipment (Tandem GC-MS equipment GC Agilent 7890 and MS Agilent 5975). In addition, aerobic sludge toxicity tests were performed by respirometric methods (OECD 209, 1993) and no signs of inhibition of aerobic sludge activity were detected at the indicated concentration.

Analytical methods

The control of the main physico-chemical parameters of the combined system was carried out by analyzing samples taken daily from the inflows and outflows of both biological reactors. The periodical determination of the volatile fatty acids (VFAs) present in the fluidized sludge was also carried out (GC Agilent Technologies, 7890A, Palo Alto, CA, USA). To ensure the stability of the UASB reactor and avoid its acidification, the ratio between alkalinity due to VFA and that due to bicarbonate was maintained at values below 0.3 (Ripley *et al.* 1986; Iza 1995), keeping the bicarbonate alkalinity at values between 2,500 and 5,000 mg $CaCO_3$·L^{-1} (Fannin 1987). The production and composition of biogas generated during anaerobic digestion was also used as an indicator of the proper performance of the anaerobic reactor. Samples of the biogas were taken for the subsequent analysis of its composition by the Geotech Biogas-5000 analyzer (Geotechnical Instruments Ltd, U.K.).

With the purpose of detecting a possible decline in aerobic sludge activity due to the presence of CBZ in the synthetic substrate, weekly respirometric tests were carried out (respirometer BM-EVO, Surcis S.L.).

The determination of the outlet CBZ concentrations in the UASB effluent and the MBR permeate were carried out by means of Solid Phase Extraction (SPE) in an acid medium (Thermo ScientificTM DionexTM AutoTrace™ 280). Previously, the compound was derivatized *in situ* according to the methods proposed by Gómez *et al.* (2007) and Hai *et al.* (2011). In order to study the linearity and repeatability of the method, the percentages of recovery, limits of quantification (LOQ) and detection (LOD) of the CBZ were determined. For the analysis of the resulting samples, a tandem GC-MS equipment was used (GC Agilent 7890 and MS Agilent 5975). The MSD ChemStation software was used both for the determination of the sequence and time of appearance of the different compounds analyzed and for the subsequent analysis of the results. By the integration of the chromatograms and their representation on the calibration line of the compound, the concentration of CBZ in the analyzed samples was determined according to the following equation:

$$C = \frac{M_s}{\text{Recovery} \times V} \times 100 \quad (1)$$

where C is the average concentration of CBZ in the sample (%), Ms is the mass retained in the Oasis® HBL cartridge (ng), recovery indicates the percentage of specific recovery of CBZ determined experimentally (%) and V is the total volume that has passed through the adsorbent material.

RESULTS AND DISCUSSION

The combined UASB-MBR pilot plant treating synthetic municipal wastewater was operated for 193 days. The impact of the three different influent OLR stages on the main operational parameters of the combined system for improve CBZ removal rates are reported below.

Operational parameters

- Sludge retention time (SRT)

During the experimental period the combined system operated at high SRT (>90 days) in both reactors, made possible by performing periodical purges and maintaining a low upward velocity (0.1 m/h) inside the UASB reactor (Lettinga & Hulshoff Pol 1991; Alphenaar *et al.*1993). This allowed the development and specialization of communities of slow-growing microorganisms in the MBR and the presence of macroflocs in the mixed liquor, as well as the adaptation of the biomass to the CBZ compound, as previously reported by Judd (2011) and Le-Clech *et al.* (2003). As for the UASB, given the low rate of cell growth of these systems, the high SRT allowed a good development and maturation of the anaerobic granules (Ahn 2000), as corroborated by Figure 2.

- Microbial activity of sludge

Respirometric tests revealed a progressive decrease of the specific oxygen uptake rate (SOUR) coefficient from 4.55 to 1.02 mg O_2 ·g $MLVSS^{-1}$·h, evidencing a slowing down of the aerobic sludge degrading activity. Although further studies related to the response of microbial communities to CBZ must be carried oud, according to Zhang *et al.* (2008), this decrease could be caused by the high SRT in the reactor together with the possible progressive accumulation of CBZ onto sludge due to its moderate potential of adsorption (log $K_{ow} = 2.45$) as well as the disappearance of certain groups of bacteria in the presence of CBZ (Kraigher *et al.* 2008). As expected, the results obtained in relation to the endogenous decomposition constant -k_d indicate that the decay of the biomass was greater in the initial stages of operation, around 3% of the amount of biomass contained in the reactor. This lysis could be mainly caused by the inertia of the sludge-inoculum, which came from an industrial WWTP with high organic loads, and its consequent accommodation at low OLR of the synthetic influent.

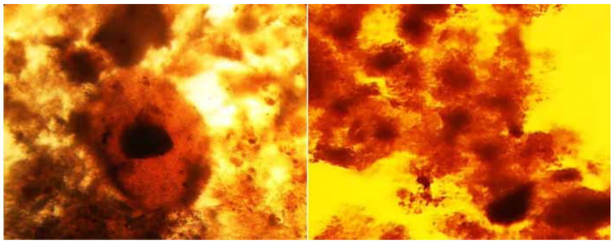


Figure 2 | Structure of anaerobic granular sludge of recent formation in UASB stage (×10).

- Acidity of the medium

In general, most methane-producing bacteria can only function optimally in a pH range of 6.7–7.4 (Bitton 1999; Lorenzo-Acosta & Obaya-Abreu 2005). Agreeing with Show *et al.* (2012), the average values of pH in the UASB reactor (Figure 3) were kept within the optimum range for the anaerobic digestion processes. This corroborates the good control of the bicarbonate alkalinity of the UASB reactor due to the periodical addition of Na_2CO_3 and $NaHCO_3$. The concentration of VFA in the anaerobic medium was very low and the maximum value (437 mg·L^{-1}) was reached during the start-up stage. Acetic acid was the only one present during all stages of the experimental period, with a maximum concentration above 200 mg·L^{-1} (start-up stage), followed by propionic acid (140 mg·L^{-1}) and 4-methylvaleric acid. The concentration of VFA decreased throughout the experimental phase due to its consumption in the different stages of anaerobic digestion, which indicated the

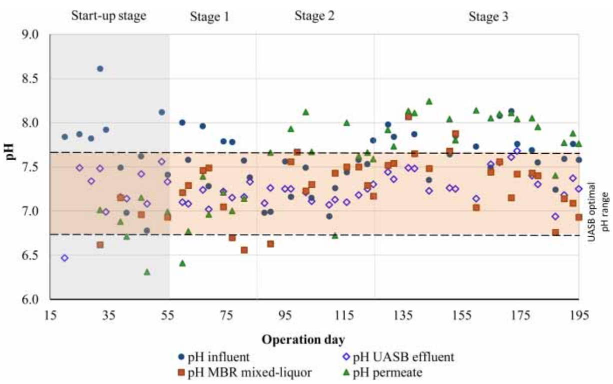


Figure 3 | Evolution of the pH in the inflows and outflows of the individual reactors and the combined UASB-MBR system (UASB optimal pH range according to Lorenzo-Acosta & Obaya-Abreu 2005).

progressive stability of the anaerobic biomass and its accommodation to the presence of CBZ in the influent. Agreeing with Alvarino *et al.* (2014), no VFA accumulation was observed throughout the experimental period.

- Biogas

Regarding the biogas generated in the UASB reactor, the maximum average production was 0.48 m^3 biogas·kg COD^{-1} with an average CH_4 content of 73%, higher than that reported by Carballa *et al.* (2007) and within the acceptable range of 250–350 mL of CH_4· g COD^{-1} (Farajzadehha *et al.* 2015). Given the small size of the pilot plant and the use of low strength synthetic effluents, the results were very successful. This maximum rate was achieved when the influent was in high OLR.

Concerning the presence of H_2S, the average H_2S concentration in the biogas was 2,870 ppm, with a maximum of 4,100 ppm in the start-up stage. Although these values are within the range of the typical biogas composition (Surendra *et al.* 2014; Braun 2007), a H_2S desulfurization treatment could be required to decrease these concentrations below 0.15% (v/v) (<1500 ppm) in order to achieve the minimum requirements for energetic use of biogas (Braun 2007). According to Ali *et al.* (2015), the H_2S concentration in biogas could be significantly minimized in the UASB reactor by adding iron chloride to the influent (1:1 ratio to sulfide concentration).

The high content of methane obtained indicates the good quality of the biogas produced, being suitable for the energy recovery of the combined system (Surendra *et al.* 2014). Considering that pure biogas has a heating value of 35.8 MJ/m^3 (9.94 kWh electricity equivalent) (Metcalf & Eddy 1991) at standard temperature and pressure, the calorific value of the biogas generated in the UASB system (73% of CH_4) was around 22.4 MJ/m^3. According to Gil *et al.* (2010), the main energy requirements of the combined system come from the MBR aeration systems, which represent almost 50% of the total energy requirements of the MBR, being 2–4 times higher than the energy demand of conventional activated sludge process. In this sense, the energy provided through the biogas generated by the UASB reactor, as well as that generated during the digestion of aerobic sludge, becomes a key factor for the sustainability of the UASB-MBR combined system.

Regarding the influence of the operational strategy, in accordance with Farajzadehha *et al.* (2015) a very low recirculation radio from MBR to UASB (0.01 L·h^{-1}) also contributed to a high methane production. Consequently, the anaerobic digestion process in the UASB reactor seemed unaffected by the presence of CBZ in the synthetic influent, as can be seen from the control of VFA or the excellent production of biogas with a high methane content, particularly at high OLR.

Carbamazepine removal

The different redox conditions of both reactor (UASB reactor and aerobic bioreactor (MBR) and their combined operation improved the biological removal of CBZ. Although further studies are required to determine the fraction of CBZ adsorbed onto sludge, the low biodegradation constant of CBZ (<0.1 L·g SS^{-1}-d^{-1}) and its hydrophilic character (log $k_{ow} = 2.45$) suggests a low adsorption rate of the compound, which mainly remains in the aqueous phase (Zhang *et al.* 2008; Reyes-Contreras *et al.* 2011; Alvarino *et al.* 2016; Vassalle *et al.* 2020). In this regard, similar studies such as Arias *et al.* (2018) or Alvarino *et al.* (2018) found the interactions between the positively charged form of the compound with the negatively charged surfaces of the microorganisms (sorption) were not relevant. In this sense, relevant research such as that conducted by Verlicchi *et al.* (2012) and Kim *et al.* (2014) only reported an adsorption percentage around 5%.

- UASB removal rates

The average removal rates of CBZ in the UASB reactor (Figure 4) indicated a high anaerobic degradation efficiency of CBZ, reaching 48.9% and 48.0% in the high and medium OLR stages respectively. According to Wijekoon *et al.* (2015), the presence of nitrogen in the molecular structure of carbamazepine, with two nitrogen atoms, could favor the anaerobic removal of this moderately hydrophilic compound.

At low organic loads of the influent, the average removal percentage of CBZ was 38.2% due to the decrease in the

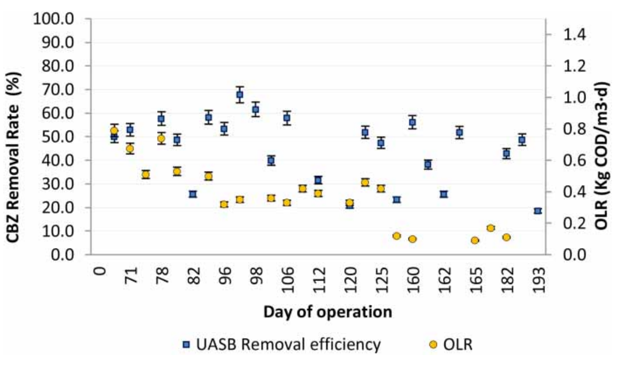


Figure 4 | UASB reactor removal rates at different OLRs.

performance of the UASB reactor at low organic loads of the influent. The low levels of COD in this stage (below 500 mg/L) were not high enough to maintain good conditions for bacterial growth (Show *et al.* 2012) and, consequently, to maintain degradative activity of biomass. Although anaerobic removal of CBZ is poorly reported, the anaerobic degradation rates of CBZ reached in the UASB individual system for all the OLR stages were higher than those reported in previous research (Alvarino *et al.* 2016) for UASB reactors but closer to those reported for other anaerobic technologies such as anaerobic membrane bioreactors (Wijekoon *et al.* 2015).

- UASB-MBR removal rates

The double aerobic and anaerobic biological treatment together with the filtration in the MBR increased the removal rates obtained in the UASB (Figure 5).

The CBZ removal average values achieved by the global UASB-MBR were 70.0% in high OLR and 59.6% and 49.8% when the influent was in medium and low OLR respectively (Figure 6).

The fraction of the compound remaining in the effluent (supernatant) of the UASB was partially removed by aerobic biological treatment and microfiltration of the membrane in the MBR. The processes that took place in the anaerobic reactor served as a first and key treatment stage for the removal of CBZ and, according to Alvarino *et al.* (2016), the previous anaerobic stage enhanced the removal of CBZ, being crucial to improve the removal efficiency in the MBR.

The progressive decrease of the organic load of the influent resulted in a lower CBZ removal efficiency of both the UASB reactor and the UASB-MBR combined system (Figures 3 and 4), confirming that the UASB-MBR combined system reaches its highest performance when subjected to high OLRs.

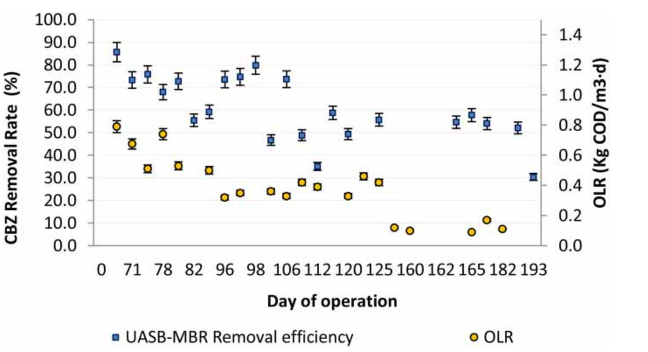


Figure 5 | UASB-MBR combined system removal rates at different OLRs.

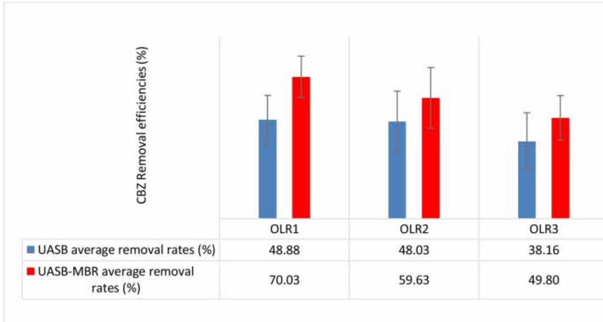


Figure 6 | UASB and global UASB-MBR system removal rates at different OLR stages.

The results indicate the effectiveness of the combined system for the treatment of synthetic wastewater with low OLR. Although OLR could be a limiting factor of the performance of UASB reactor, its combination with the MBR has proven to be efficient in the treatment of low-strength wastewater, also being capable of removing a high rate of certain ECs such as the pharmaceutical CBZ. However, further studies are required in order to analyze the performance of the combined system treating real low-strength municipal wastewater from small WWTPs. In addition, the study of the ECs removal mechanisms in the UASB-MBR pilot-plant is proposed. For this purpose, both the liquid phase and the solid phase (adsorption onto aerobic and anaerobic sludge) should be analyzed.

CONCLUSIONS

The UASB-MBR system proved to be an efficient and cost-effective technology treating low-strength municipal wastewater. The double anaerobic and aerobic biological treatment, together with the membrane filtration, were highly effective in the removal of the pharmaceutical carbamazepine.

- The CBZ removal rates of the UASB-MBR combined system were highly dependent on the organic loads of the influent. The recalcitrant behavior of carbamazepine was demonstrated, being highly persistent to biological treatments at low concentrations. Nevertheless, the UASB-MBR system proved to be particularly suitable for treating municipal wastewater containing CBZ at OLRs above 0.7 kg COD·m^{-3}·d^{-1}.
- The respirometric tests carried out throughout the experimental period showed that high sludge age (SRT) resulted in a significant decrease in biomass activity. However, the presence of mature anaerobic granules and aerobic macroflocs confirmed the development of

slow-growing microorganism communities as well as a good adaptation to the micropollutant CBZ. In addition, the stability of the pH in both reactors together with the moderate rates of VFA in the anaerobic reactor and the generation of excellent quality biogas rich in methane, corroborated the good performance of the UASB-MBR system.

- The anaerobic processes that took place in the UASB reactor were able to partially remove this micropollutant, particularly when the influent presented high and medium organic loads. UASB reactor was the main contributor to degradation of the pharmaceutical CBZ.

ACKNOWLEDGEMENTS

This study was partially funded by the Spanish Ministry of Economy and Competitiveness through the projects 'Removal of emerging contaminants by aerobic and anaerobic processes serially and complementary treatments: 'Combined System UASB + SMEBR + O3/AC (CTM2016-76910-R)' and 'Combined treatments for the degradation and/or elimination of emerging pollutants in water' (CTM2013-46669-R)', which were developed at the University Institute of Water and Environmental Sciences, University of Alicante.

AUTHOR CONTRIBUTIONS

This manuscript was written through contributions of all authors named and all of them have given their approval to the final version of the manuscript.

FUNDING SOURCES

Spanish Ministry of Economy and Competitiveness through the projects 'Combined System UASB + SMEBR + O3/AC (CTM2016-76910-R)' and 'Combined treatments for the degradation and/or elimination of emerging pollutants in water' (CTM2013-46669-R) and University of Alicante.

DATA AVAILABILITY STATEMENT

All relevant data are included in the paper or its Supplementary Information.

REFERENCES

Ahn, Y. H. 2000 Physicochemical and microbial aspects of anaerobic granular biopellets. *Journal of Environmental Science & Health Part A* **35** (9), 1617–1635.

Ali, M., Singh, N. K., Bhatia, A., Singh, S., Khursheed, A. & Kazmi, A. A. 2015 Sulfide production control in UASB reactor by addition of iron salt. *Journal of Environmental Engineering* **141** (6), 06014008.

Alphenaar, P. A., Visser, A. & Lettinga, G. 1993 The effect of liquid upward velocity and hydraulic retention time on granulation in UASB reactors treating wastewater with high sulphate content. *Bioresource Technology* **43** (3), 249–258.

Álvarez, J. A., Ruiz, I., Gómez, M., Presas, J. & Soto, M. 2006 Start-up alternatives and performance of an UASB pilot plant treating diluted municipal wastewater at low temperature. *Bioresource Technology* **97** (14), 1640–1649.

Alvarino, T., Suarez, S., Lema, J. M. & Omil, F. 2014 Understanding the removal mechanisms of PPCPs and the influence of main technological parameters in anaerobic UASB and aerobic CAS reactors. *Journal of Hazardous Materials* **278**, 506–513.

Alvarino, T., Suárez, S., Garrido, M., Lema, J. M. & Omil, F. 2016 A UASB reactor coupled to a hybrid aerobic MBR as innovative plant configuration to enhance the removal of organic micropollutants. *Chemosphere* **144**, 452–458.

Alvarino, T., Suarez, S., Lema, J. & Omil, F. 2018 Understanding the sorption and biotransformation of organic micropollutants in innovative biological wastewater treatment technologies. *Science of the Total Environment* **615**, 297–306.

Arias, A., Alvarino, T., Allegue, T., Suárez, S., Garrido, J. M. & Omil, F. 2018 An innovative wastewater treatment technology based on UASB and IFAS for cost-efficient macro and micropollutant removal. *Journal of Hazardous Materials* **359**, 113–120.

Asano, T., Burton, F. L., Leverenz, H. L., Tsuchihashi, R. & Tchobanoglous, G. 2006 *Water Reuse: Issues, Technologies and Applications*.

Bitton, G. 1999 *Water and Wastewater Disinfection. Wastewater Microbiology*. Wiley-Liss, Inc., New York, NY, pp. 137–168.

Braun, R. 2007 Anaerobic digestion: a multi-faceted process for energy, environmental management and rural development. In: *Improvement of Crop Plants for Industrial end Uses*. Springer, Dordrecht, The Netherlands, pp. 335–416.

Buntner, D., Sánchez, A. & Garrido, J. M. 2013 Feasibility of combined UASB and MBR system in dairy wastewater treatment at ambient temperatures. *Chemical Engineering Journal* **230**, 475–481.

Carballa, M., Omil, F., Ternes, T. & Lema, J. M. 2007 Fate of pharmaceutical and personal care products (PPCPs) during anaerobic digestion of sewage sludge. *Water Research* **41** (10), 2139–2150.

Cases, V., Alonso, V., Argandoña, V., Rodriguez, M. & Prats, D. 2011 Endocrine disrupting compounds: a comparison of removal between conventional activated sludge and membrane bioreactors. *Desalination* **272** (1), 240–245.

Clara, M., Strenn, B., Ausserleitner, M. & Kreuzinger, N. 2004 Comparison of the behaviour of selected micropollutants in a membrane bioreactor and a conventional wastewater treatment plant. *Water Science and Technology* **50** (5), 29–36.

Clara, M., Kreuzinger, N., Strenn, B., Gans, O. & Kroiss, H. 2005 The solids retention time – a suitable design parameter to evaluate the capacity of wastewater treatment plants to remove micropollutants. *Water Research* **39** (1), 97–106.

Conkle, J. L., Gan, J. & Anderson, M. A. 2012 Degradation and sorption of commonly detected PPCPs in wetland sediments under aerobic and anaerobic conditions. *Journal of Soils and Sediments* **12** (7), 1164–1173.

Dean, L. 2018 Carbamazepine therapy and HLA genotype. In: *Medical Genetics Summaries [Internet]*. National Center for Biotechnology Information, USA.

Drewes, J. E., Heberer, T. & Reddersen, K. 2002 Fate of pharmaceuticals during indirect potable reuse. *Water Science and Technology* **46** (3), 73–80.

Fannin, K. F. 1987 Start-up, operation, stability, and control. Elsevier Applied Science, London. https://www.cabdirect.org/cabdirect/abstract/19882438833.

Farajzadehha, S., Shayegan, J., Mirbagheri, S. A., Farajzadehha, S. & Hazrati, H. 2015 The combined UASB and MBR system to COD and TSS removal and excess sludge reduction for the treatment of high strength wastewater in various operational temperatures. *Desalination and Water Treatment* **53** (2), 352–359.

Froehner, S., Piccioni, W., Machado, K. S. & Aisse, M. M. 2011 Removal capacity of caffeine, hormones, and bisphenol by aerobic and anaerobic sewage treatment. *Water, Air, & Soil Pollution* **216** (1–4), 463–471.

Gómez, M. J., Bueno, M. M., Lacorte, S., Fernández-Alba, A. R. & Agüera, A. 2007 Pilot survey monitoring pharmaceuticals and related compounds in a sewage treatment plant located on the Mediterranean coast. *Chemosphere* **66** (6), 993–1002.

Gonzalez-Gil, L., Carballa, M. & Lema, J. M. 2020 Removal of organic micro-pollutants by anaerobic microbes and enzymes. In: *Current Developments in Biotechnology and Bioengineering*. Elsevier, London, pp. 397–426. https://doi.org/10.1016/B978-0-12-819594-9.00016-4. Retrieved from https://www.sciencedirect.com/science/article/pii/B9780128195949000164.

Gurung, K., Ncibi, M. C. & Sillanpää, M. 2017 Assessing membrane fouling and the performance of pilot-scale membrane bioreactor (MBR) to treat real municipal wastewater during winter season in Nordic regions. *Science of the Total Environment* **579**, 1289–1297.

Hai, F. I., Tessmer, K., Nguyen, L. N., Kang, J., Price, W. E. & Nghiem, L. D. 2011 Removal of micropollutants by membrane bioreactor under temperature variation. *Journal of Membrane Science* **383** (1–2), 144–151.

Heberer, T. 2002 Tracking persistent pharmaceutical residues from municipal sewage to drinking water. *Journal of Hydrology* **266** (3), 175–189.

Holler, S. & Trösch, W. 2001 Treatment of urban wastewater in a membrane bioreactor at high organic loading rates. *Journal of Biotechnology* **92** (2), 95–101.

Iza, J. M. 1995 I Curso de Ingeniería Ambiental. Tractament anaerobi d aigües residuals i residus de forta càrrega : paràmetres de disseny i tecnolo. Paperkite, Lleida, pp. 175–202.

Judd, S. 2011 *The MBR Book: Principles and Applications of Membrane Bioreactors for Water and Wastewater Treatment*, 2nd edn. Elsevier Science Ltd, Oxford, UK.

Kaiser, E., Prasse, C., Wagner, M., Bröder, K. & Ternes, T. A. 2014 Transformation of oxcarbazepine and human metabolites of carbamazepine and oxcarbazepine in wastewater treatment and sand filters. *Environmental Science & Technology* **48** (17), 10208–10216.

Kato, M. T. 1994 *The Anaerobic Treatment of Low Strength Soluble Wastewaters*. Kato.

Kim, M., Guerra, P., Shah, A., Parsa, M., Alaee, M. & Smyth, S. A. 2014 Removal of pharmaceuticals and personal care products in a membrane bioreactor wastewater treatment plant. *Water Science and Technology* **69** (11), 2221–2229.

König, A., Weidauer, C., Seiwert, B., Reemtsma, T., Unger, T. & Jekel, M. 2016 Reductive transformation of carbamazepine by abiotic and biotic processes. *Water Research* **101**, 272–280.

Kraigher, B., Kosjek, T., Heath, E., Kompare, B. & Mandic-Mulec, I. 2008 Influence of pharmaceutical residues on the structure of activated sludge bacterial communities in wastewater treatment bioreactors. *Water Research* **42** (17), 4578–4588.

Kreuzinger, N., Clara, M., Strenn, B. & Kroiss, H. 2004 Relevance of the sludge retention time (SRT) as design criteria for wastewater treatment plants for the removal of endocrine disruptors and pharmaceuticals from wastewater. *Water Science and Technology* **50** (5), 149–156.

Le-Clech, P., Jefferson, B. & Judd, S. J. 2003 Impact of aeration, solids concentration and membrane characteristics on the hydraulic performance of a membrane bioreactor. *Journal of Membrane Science* **218** (1), 117–129.

Lettinga, G. & Hulshoff Pol, L. 1991 UASB-process design for various types of wastewaters. *Water Science and Technology* **24** (8), 87–107.

Lettinga, G., Rebac, S. & Zeeman, G. 2001 Challenge of psychrophilic anaerobic wastewater treatment. *TRENDS in Biotechnology* **19** (9), 363–370.

Liu, Y. & Tay, J. H. 2004 State of the art of biogranulation technology for wastewater treatment. *Biotechnology Advances* **22** (7), 533–563.

Lorenzo-Acosta, Y. & Obaya-Abreu, M. C. 2005 La digestión anaerobia. Aspectos teóricos. Parte I. ICIDCA. Sobre los Derivados de la Caña de Azúcar, 39, 35-48.

Luo, Y., Guo, W., Ngo, H. H., Nghiem, L. D., Hai, F. I., Zhang, J., Liang, S. & Wang, X. C. 2014 A review on the occurrence of micropollutants in the aquatic environment and their fate and removal during wastewater treatment. *Science of the Total Environment* **473**, 619–641.

Maan, J. S. & Saadabadi, A. 2020 Carbamazepine. In: *StatPearls*. StatPearls Publishing, Treasure Island, FL.

Metcalf & Eddy 1991 *Wastewater Engineering: Treatment, Disposal and Reuse*, 3rd edn. McGraw Hill Inc., New York, NY.

Moya-Llamas, M., Trapote, A. & Prats, D. 2018 Removal of micropollutants from urban wastewater using a UASB reactor coupled to a MBR at different organic loading rates. *Urban Water Journal* **15** (5), 437–444. doi:10.1080/1573062X.2018.1508599.

National Center for Biotechnology Information. PubChem Database. Carbamazepine, CID = 2554. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/Carbamazepine (accessed 29 May 2019).

Niwa, T., Yamashita, T., Mitsumizo, M., Takahashi, M., Hatamoto, M., Yamaguchi, T., Kekre, K. A., Lin, L. L., Tao, G. & Seah, H. 2018 Pilot-scale test of industrial wastewater treatment by UASB and MBR using a ceramic flat sheet membrane for water reuse. *Journal of Water Reuse and Desalination* **8** (4), 490–496.

OECD Method 209 1993 *Activated Sludge, Respiration Inhibition Test. OECD Guidelines for Testing of Chemicals*. OECD, Paris, France.

Paltiel, O., Fedorova, G., Tadmor, G., Kleinstern, G., Maor, Y. & Chefetz, B. 2016 Human exposure to wastewater-derived pharmaceuticals in fresh produce: a randomized controlled trial focusing on carbamazepine. *Environmental Science & Technology* **50** (8), 4476–4482.

Pavlostathis, S. G. & Giraldo-Gomez, E. 1991 Kinetics of anaerobic treatment: a critical review. *Critical Reviews in Environmental Science and Technology* **21** (5–6), 411–490.

Qiu, G., Song, Y., Zeng, P., Duan, L. & Xiao, S. 2013 Combination of upflow anaerobic sludge blanket (UASB) and membrane bioreactor (MBR) for berberine reduction from wastewater and the effects of berberine on bacterial community dynamics. *Journal of Hazardous Materials* **246–247** (0), 34–43.

Radjenović, J., Petrović, M. & Barceló, D. 2009 Fate and distribution of pharmaceuticals in wastewater and sewage sludge of the conventional activated sludge (CAS) and advanced membrane bioreactor (MBR) treatment. *Water Research* **43** (3), 831–841.

Reyes-Contreras, C., Matamoros, V., Ruiz, I., Soto, M. & Bayona, J. M. 2011 Evaluation of PPCPs removal in a combined anaerobic digester-constructed wetland pilot plant treating urban wastewater. *Chemosphere* **84** (9), 1200–1207.

Ripley, L. E., Boyle, W. C. & Converse, J. C. 1986 Improved alkalimetric monitoring for anaerobic digestion of high-strength wastes. *Journal (Water Pollution Control Federation)* **58** (5), 406–411.

Rivera-Utrilla, J., Sánchez-Polo, M., Ferro-García, M. Á., Prados-Joya, G. & Ocampo-Pérez, R. 2013 Pharmaceuticals as emerging contaminants and their removal from water. A review. *Chemosphere* **93** (7), 1268–1287.

Rizvi, H., Ahmad, N., Abbas, F., Bukhari, I. H., Yasar, A., Ali, S., Yazmeen, T. & Riaz, M. 2015 Start-up of UASB reactors treating municipal wastewater and effect of temperature/sludge age and hydraulic retention time (HRT) on its performance. *Arabian Journal of Chemistry* **8** (6), 780–786.

Rosa, A., Conesa, J., Fullana, A., Melo, G., Borges, J. & Chernicharo, C. 2016 Energy potential and alternative usages of biogas and sludge from UASB reactors: case study of the Laboreaux wastewater treatment plant. *Water Science and Technology* **73** (7), 1680–1690.

Schwarzenbach, R. P., Gschwend, P. M. & Imboden, D. M. 2005 *Environmental Organic Chemistry*. John Wiley & Sons, Hoboken, NJ.

Show, K. Y., Lee, D. J. & Tay, J. H. 2012 Aerobic granulation: advances and challenges. *Applied Biochemistry and Biotechnology* **167** (6), 1622–1640.

Simon, M., Kumar, A., Garg, A. & Manisha 2021 Biological treatment of pharmaceuticals and personal care products (PPCPs) before discharging to environment. In: *Fate and Transport of Subsurface Pollutants. Microorganisms for Sustainability*, Vol. 24 (P. K. Gupta & R. N. Bharagava, eds). Springer, Singapore. https://doi.org/10.1007/978-981-15-6564-9_14.

Stamatelatou, K., Frouda, C., Fountoulakis, M. S., Drillia, P., Kornaros, M. & Lyberatos, G. 2003 Pharmaceuticals and health care products in wastewater effluents: the example of carbamazepine. *Water Science and Technology: Water Supply* **3** (4), 131–137.

Suárez, S., Ramil, M., Omil, F. & Lema, J. M. 2005 Removal of pharmaceutically active compounds in nitrifying-denitrifying plants. *Water Science and Technology* **52** (8), 9–14. doi:10.2166/wst.2005.0214.

Surendra, K. C., Takara, D., Hashimoto, A. G. & Khanal, S. K. 2014 Biogas as a sustainable energy source for developing countries: opportunities and challenges. *Renewable and Sustainable Energy Reviews* **31**, 846–859.

Ternes, T. A. 1998 Occurrence of drugs in German sewage treatment plants and rivers. *Water Research* **32** (11), 3245–3260.

Ternes, T. A., Herrmann, N., Bonerz, M., Knacker, T., Siegrist, H. & Joss, A. 2004 A rapid method to measure the solid–water distribution coefficient (Kd) for pharmaceuticals and musk fragrances in sewage sludge. *Water Research* **38**, 4075–4084.

Tiwari, B., Sellamuthu, B., Ouarda, Y., Drogui, P., Tyagi, R. D. & Buelna, G. 2017 Review on fate and mechanism of removal of pharmaceutical pollutants from wastewater using biological approach. *Bioresource Technology* **224**, 1–12.

USP, DI 2007 *Volume 1: Drug Information for the Health Care Professional*. Thomson Micromedex, Greenwood Village, CO, p. 703.

Vassalle, L., García-Galán, M. J., Aquino, S. F., Afonso, R. J. d. C. F., Ferrer, I., Passos, F. & Mota, C. R. 2020 Can high rate algal ponds be used as post-treatment of UASB reactors to remove micropollutants? *Chemosphere* **248**, 125969. https://doi.org/10.1016/j.chemosphere.2020.125969.

Verlicchi, P., Al Aukidy, M. & Zambello, E. 2012 Occurrence of pharmaceutical compounds in urban wastewater: removal, mass load and environmental risk after a secondary treatment – a review. *Science of the Total Environment* **429**, 123–155.

Wijekoon, K. C., McDonald, J. A., Khan, S. J., Hai, F. I., Price, W. E. & Nghiem, L. D. 2015 Development of a predictive framework to assess the removal of trace organic chemicals by anaerobic membrane bioreactor. *Bioresource Technology* **189**, 391–398.

Zhang, Y., Geißen, S. & Gal, C. 2008 Carbamazepine and diclofenac: removal in wastewater treatment plants and occurrence in water bodies. *Chemosphere* **73** (8), 1151–1161.

First received 3 January 2021; accepted in revised form 3 March 2021. Available online 16 March 2021