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Removal of pharmaceuticals from wastewater by biological processes, hydrodynamic cavitation and UV treatment

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ABSTRACT

To augment the removal of pharmaceuticals different conventional and alternative wastewater treatment processes and their combinations were investigated. We tested the efficiency of (1) two distinct laboratory scale biological processes: suspended activated sludge and attached-growth biomass, (2) a combined hydrodynamic cavitation–hydrogen peroxide process and (3) UV treatment. Five pharmaceuticals were chosen including ibuprofen, naproxen, ketoprofen, carbamazepine and diclofenac, and an active metabolite of the lipid regulating agent clofibric acid.

Biological treatment efficiency was evaluated using lab-scale suspended activated sludge and moving bed biofilm flow-through reactors, which were operated under identical conditions in respect to hydraulic retention time, working volume, concentration of added pharmaceuticals and synthetic wastewater composition. The suspended activated sludge process showed poor and inconsistent removal of clofibric acid, carbamazepine and diclofenac, while ibuprofen, naproxen and ketoprofen yielded over 74% removal. Moving bed biofilm reactors were filled with two different types of carriers i.e. Kaldnes K1 and Mutag BioChip™ and resulted in higher removal efficiencies for ibuprofen and diclofenac. Augmentation and consistency in the removal of diclofenac were observed in reactors using Mutag BioChip™ carriers (85% ± 10%) compared to reactors using Kaldnes carriers and suspended activated sludge (74% ± 22% and 48% ± 19%, respectively). To enhance the removal of pharmaceuticals hydrodynamic cavitation with hydrogen peroxide process was evaluated and optimal conditions for removal were established regarding the duration of cavitation, amount of added hydrogen peroxide and initial pressure, all of which influence the efficiency of the process. Optimal parameters resulted in removal efficiencies between 3–70%. Coupling the attached-growth biomass biological treatment, hydrodynamic cavitation/hydrogen peroxide process and UV treatment resulted in removal efficiencies of >90% for clofibric acid and >98% for carbamazepine and diclofenac, while the remaining compounds were reduced to levels below the LOD. For ibuprofen, naproxen, ketoprofen and diclofenac the highest contribution to overall removal was attributed to biological treatment, for clofibric acid UV treatment was the most efficient, while for carbamazepine hydrodynamic cavitation/hydrogen peroxide process and UV treatment were equally efficient.

Abbreviations: WWTP, wastewater treatment plant; MBBR, moving bed biofilm reactor; AOP, advanced oxidation process; HC, hydrodynamic cavitation; AC, acoustic cavitation; HC/H_2O_2, hydrodynamic cavitation with addition of hydrogen peroxide; CLA, clofibric acid; IB, ibuprofen; NP, naproxen; KP, ketoprofen; DF, diclofenac; CBZ, carbamazepine; IB-d_3, (±)-ibuprofen-d_3 (α-methyl-d_3); CBZ-d_{10}, carbamazepine-d_{10} (rings-d_{10}); KP-d_3, (±)-ketoprofen (α-methyl-d_3); MEC-d_3, mecoprop-d_3; MTBSTFA, *N*-(*t*-butyldimetylsilyl)-*N*-methyltrifluoroacetamid; SPE, solid phase extraction; GC-MS, gas chromatography-mass spectrometry; LOD, limit of detection; ASR, activated sludge reactor; ASR0, control suspended activated sludge reactor (without addition of pharmaceuticals); ASR1, ASR2, two parallel suspended activated sludge reactors (with addition of pharmaceuticals); K0, control moving bed biofilm reactor filled with Kaldnes carriers (without addition of pharmaceuticals); K1, K2, two parallel moving bed biofilm reactors filled with Kaldnes carriers (with addition of pharmaceuticals); M0, control moving bed biofilm reactor filled with Mutag Biochip™ carriers (without addition of pharmaceuticals); M1, M2, two parallel moving bed biofilm reactors filled with Mutag Biochip™ carriers (with addition of pharmaceuticals); COD, chemical oxygen demand; PE, population equivalent.

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1. Introduction

New emerging pollutants like pharmaceuticals have been in the spotlight of the scientific community for some time [1–5]. These compounds are currently not, but may in the future become part of routine monitoring programmes, depending on an assessment of their environmental impact [6]. Pharmaceuticals are used for human and veterinary purposes and in animal husbandry [2] and after accomplishing their mission in target organisms they are excreted in faeces or/and urine as either parent compounds or as metabolites, which can then enter the aquatic environment *via* treated or even untreated wastewater discharge [7].

Studies have proven that some pharmaceuticals are resistant to conventional biological treatment processes used by municipal wastewater treatment plants (WWTPs) and are subsequently found globally in treated wastewater effluents in concentrations from low ng L^{-1} to μg L^{-1} [8–11]. In addition, poor removal of carbamazepine (<16%) [3], [12,13] clofibric acid (<35%) [14,15] and inconsistent removal of diclofenac (3–70%), [9,12,16,17], during conventional biological treatment are reported. Researches also reveal the detrimental effects that these compounds can have on aquatic organisms [18–20]. Diclofenac, for example, causes cytological changes and bioaccumulates in the liver, kidneys and gills of the rainbow trout (*Oncorhynchus mykiss*) [21]. Similar effects are also observed in carp (*Cyprinus carpio*) after exposure to carbamzepine [22]. Such studies confirm the need to upgrade conventional biological wastewater treatment. One option is to replace suspended activated sludge with an attached-growth biomass process, such as moving bed biofilm reactor (MBBR) technology, where biomass grows on specially designed "carriers" that move freely within the reactor's water volume providing a much greater surface area on which a biofilm can grow [23,24]. The advantages of the MBBR include its simplicity, compactness, growth of aerobic and anaerobic organisms in the same system and negligible hydraulic headlosses [24,25]. Fålas and co-workers [26] report higher removal efficiencies of pharmaceuticals using a process comparable to a suspended activated sludge process albeit Joss et al. [27] conclude that no significant difference exists between them. Despite these contradictory results we believe this technology is worthy of further investigation.

Further improvement to biological wastewater treatment can also be obtained by adopting novel treatment technologies that may prove more efficient and less time consuming. Nowadays, attention has turned to special oxidation techniques known collectively as advanced oxidation processes (AOPs) [28]. These include technologies based on UV, Fenton, cavitation (acoustic and hydrodynamic), radiation and wet air oxidation [28,29]. In an AOP, powerful oxidizing species e.g. hydroxyl radicals (·OH) are formed. Compared to other oxidants like O_3,·H_2O_2 and $KMnO_4$, ·OH are among the strongest oxidizing species commonly used for water and wastewater treatment (Table 1). They readily and non-selectively attack organic compounds present in effluent waters and accelerate the rate of contaminants oxidation, preferably resulting in their complete mineralisation [28,30].

AOPs can be used for treatment of different water matrices including groundwater, industrial and municipal wastewater, drinking water, landfill leachate and surface water. They are used to remove bio-refractory and toxic compounds in waters with CODs from 0 to 3000 mg L^{-1} and effluent flow rate from 0.5 to 1000 m^3 h^{-1} (see Supplementary data Suppl. 1). Studies regarding AOPs are usually performed on either bench or pilot scale, but there are some commercial full-scale applications (see Supplementary data Suppl. 2)

Cavitation, which is another AOP, is a physical phenomenon, where the formation, growth and subsequent collapse of small bubbles and bubble clusters in a liquid releases high amounts of energy [28]. In hydrodynamic cavitation (HC), bubble inception and collapse is the result of an increase in fluid velocity and accompanied decrease in static pressure. This phenomenon can occur when the fluid passes through a constriction – e.g. valves [28,31], or gets a rotational impulse as in the case of hydraulic machines. High local temperatures of 5000 K, which are generated during the process, lead to the formation of ·OH after homolytic cleavage of water molecules [32]. The destruction of organic compounds in the liquid can therefore occur *via* two pathways: (i) free radical attack that can take place in the cavitation bubble, on the interface between the bubble and the surrounding area and in the bulk solution or (ii) pyrolysis inside or near the bubble [28,30]. Which of the two mechanisms predominates depends on the properties of the compound and cavitation pattern and intensity [28]. An AOP combed with HC and the use of different sources of radicals (i.e. hydrogen peroxide or ozone), can augment the amount of radicals formed during cavitation [33], which can influence removal, if pharmaceuticals are removed *via* the first pathway. When compared to acoustic cavitation (AC), Braeutigam et al. [32] state that HC has several advantages over AC including lower investment costs and easier scale-up. Its cost-effectiveness compared to other treatment technologies requires further cost benefit analysis. In addition, studies optimising the removal of pharmaceutical residues with HC are still needed. To our knowledge only one published study [32] exists regarding the removal of pharmaceuticals, e.g. carbamazepine using HC, where 27% removal was achieved.

Some recalcitrant pharmaceuticals are also susceptible to photo degradation. For example more than 90% removal efficiencies were achieved for clofibric acid and diclofenac by UV irradiation in wastewater effluents [34]. Further improvements are possible by combining UV irradiation with H_2O_2. For carbamazepine removal efficiency of up to 95% were achieved by adding H_2O_2 as compared to less than 10% without H_2O_2 [35].

The compounds investigated herein include four nonsteroidal anti-inflammatory drugs: ibuprofen, naproxen, ketoprofen and diclofenac, the antiepileptic carbamazepine and the active metabolite of the lipid modifying drugs clofibric acid. Our main objectives were to: (i) improve the removal efficiencies of selected compounds during biological treatment by attached-growth (biofilm) processes; (ii) study HC/H_2O_2 process as a possible technology for upgrading wastewater treatment; and (iii) improve removal efficiency by sequentially coupling biological treatment, HC/H_2O_2 and UV treatment.

Table 1
Oxidation potentials of different oxidants used in water treatment (adapted from [29]).

Oxidizing agent		Oxidation potential (V)
Fluorine	F_2	3.03
Hydroxyl radical	·OH	2.80
Atomic oxygen	O	2.42
Ozone	O_3	2.07
Hydrogen peroxide	H_2O_2	1.78
Perhydroxyl radical	·OOH	1.70
Permanganate	MnO_4^{2-}	1.68
Hypobromus acid	HBrO	1.59
Chlorine dioxide	ClO_2	1.57
Hypochlorus acid	HClO	1.49
Chlorine	Cl_2	1.36

2. Materials and methods

2.1. Standards and chemicals

Clofibric acid (CLA), ibuprofen (IB), naproxen (NP), ketoprofen (KP) and diclofenac (DF) were purchased from Sigma–Aldrich

(Steinheim, Germany). All compounds were of high purity (>97%). Carbamazepine (CBZ) (99%) was purchased from Acros Organics (New Jersey, USA). The isotopically labelled internal standards (±)-ibuprofen-d_3 (α-methyl-d_3) (IB-d_3), carbamazepine-d_{10} (rings-d_{10}) (CBZ-d_{10}) and (±)-ketoprofen (α-methyl-d_3) (KP-d_3) were obtained from CDN Isotopes (Quebec, Canada), while mecoprop-d_3 (MEC-d_3) was obtained from Dr. Ehrenstorfer (Augsburg, Germany). *N*-(*t*-butyldimetylsilyl)-*N*-methyltrifluoroacetamid (MTBSTFA), used for derivatisation, was supplied by Acros Organics (New Jersey, USA). Analytical grade methanol, acetonitrile and ethyl acetate were purchased from J.T. Baker (Deventer, the Netherlands). The same applies for 37% hydrochloric acid (AppliChem, Darmstadt, Germany), 96% sulphuric acid (Carlo Erba, Milan, Italy), sodium hydroxide-pellets (AppliChem, Darmstadt, Germany) and 30% hydrogen peroxide (Merck, Darmstadt, Germany). Potassium dichromate was purchased from Riedel-de-Haën, Hannover, Germany. All standard solutions were prepared in methanol, except for the HC/H_2O_2 process when methanol was replaced by acetonitrile. The composition of synthetic wastewater is described elsewhere [36].

2.2. Sample preparation and instrumental analysis

Prior to analysis, 200 mL samples were filtered through glass microfiber filters (Machery Nagel, Dueren, Germarny), 1.2 μm cellulose nitrate filters (Whatman, Kent, UK) and acidified to pH 2–3 with HCl. Internal standards were then added to give final concentrations of 0.15 μg L^{-1} IB-d_3, 1 μg L^{-1} CBZ-d_{10}, 0.5 μg L^{-1} KP-d_3 and 0.75 μg L^{-1} MEC-d_3. Solid phase extraction (SPE) was performed using 60 mg/3 mL Oasis®HLB cartridges (Waters Corporation, Massachusetts, USA) preconditioned with 3 mL of ethyl acetate, methanol and acidified water. After enrichment, the cartridges were vacuum-dried and eluted with ethyl acetate (3 × 1 mL). The extracts were reduced in volume to approx. 0.5 mL, quantitatively transferred to GC-vials, dried under a gentle flow of nitrogen and re-dissolved in ethyl acetate (0.5 mL). Prior to analysis 30 μL MTBSTFA was added to the samples and derivatisation was performed at 60 °C for 15 h.

The samples were analysed by gas chromatography–mass spectrometry (GC–MS). The instrument was a HP 6890 (Hewlett–Packard, Waldbronn, Germany) gas chromatograph with a single quadrupole mass detector. Separation was achieved on a DB-5 MS (30.0 m × 0.25 mm × 0.25 μm) capillary column (Agilent J&W, CA, USA) with helium as the carrier gas (37 cm s^{-1}). 1 μL samples were injected in splitless mode at 250 °C. The temperature programme of the GC oven was initially set at 65 °C held for 2 min and then ramped at 30 °C min^{-1}–180 °C, at 10 °C min^{-1}–240 °C, at 4 °C min^{-1}–249 °C, held for 3 min, ramped at 5 °C min^{-1}–254 °C, at 40 °C min^{-1}–300 °C and held for 2 min with 1 min post run. The MS was operated in EI ionisation mode at 70 eV. Identification of pharmaceutical derivatives was made in SIM mode by monitoring the following ions: *m/z* **271**,185, 143 for CLA, *m/z* **263**, 205 for IB, *m/z* **287**, 185, 272 for NP, *m/z* **311**, 295 for KP, *m/z* **193**, 293, 250 for CBZ, *m/z* **352**, 354, 214 for DF, *m/z* **274**, 231 for MEC-d_3, *m/z* 266 for IB-d_3, *m/z* **314**, 298 for KP-d_3 and *m/z* **203**, 303 for CBZ-d_{10}. Quantification was performed using ions written in bold text. The data was processed using Chemstation software.

2.3. Analytical method validation

Method validation involved determining SPE efficiency, limits of detection (LOD) and linearity. SPE efficiency was performed at concentrations of 1 μg L^{-1}. Limits of detection were calculated as 3-times the standard deviation of the base line of six blank samples while linearity was assessed in terms of the coefficient of determination (r^2). Effluents from the control bioreactors (ASR0, K0 and M0) were used as matrices and the matrix effect was assessed by comparing the results to those obtained using deionised water.

2.4. Biological treatment

2.4.1. Suspended activated sludge reactors (ASRs)

Experiments were performed in two 4 L flow-through rectangular reactors (ASR1 and ASR2) into which test compounds were continuously added in concentrations relevant for wastewater effluents (1 μg L^{-1}). A control bioreactor (ASR0) was also set up. Each bioreactor was divided into anoxic (0.725 L), aerated (2.55 L) and a settlement (0.725 L) compartment. From the settlement tank the biomass was re-introduced into the anoxic compartment using an aquarium water pump. The aeration and mixing of the biomass were achieved using an aquarium air pump (Airfizz 259 200, Ferplast, Castelgomberto, Italy, 100 L h^{-1}) and a porous stone. More detailed design is described elsewhere [36]. After start-up, the reactors were initially fed with 2 L of synthetic wastewater per day without the addition of test compounds for 6 months to allow biomass growth to stabilize at approximately 6.5 g L^{-1}. Afterwards, a mixture of the test compounds was continuously added into the reactor influents. Hydraulic retention time was 48 h. The biomass used in the experiments originated from a real wastewater treatment plant and a one month period of adaptation to the addition of pharmaceuticals was allowed prior to sampling.

2.4.2. Moving bed biofilm reactors (MBBRs)

Experiments were performed in aerated 4 L cylindrical reactors. Two types of carriers (shown in Supplementary data Suppl. 3), differing in shape, structure, size and surface area were investigated separately. Polyethylene Kaldnes K1 carriers (10 mm in diameter and 7 mm wide), with an effective specific surface area of 500 m^2 m^{-3}, were manufactured by Kaldnes Miljøtehnologi AS, Norway. Mutag BioChip™ carriers, made of polyethylene and with an effective specific surface area of 3000 m^2 m^{-3}. These were kindly donated by Multi Umwelttechnologie AG (Sachsen, Germany). According to manufacturers recommendations the carriers occupied approx. 30% and 5% of the reactor volume, giving a specific surface area of 150 m^2 m^{-3}. The aeration and homogeneous mixing of carriers in the entire water volume was achieved by aquarium air pump and a porous stone. Loss of carriers was prevented by a sieve arrangement at the outlet of bioreactors. The excess sludge produced during the experiments was not returned to the bioreactor as was the case with the ASRs. The same biomass as mentioned in Section 2.4.1 was used. All experiments were performed in parallel (K1 and K2 for Kaldnes carriers and M1 and M2 for Mutag BioChip™ carriers). For each type of carrier control reactors were set up (K0 for Kaldnes carriers and M0 for Mutag BioChip™ carriers). The operational conditions including biomass adaptation, hydraulic retention time, concentration of added pharmaceuticals and composition of synthetic wastewater are described in Section 2.4.1.

Removal efficiencies, in both ASRs and MBBRs, were determined as the difference between concentrations of the target compounds in the influent and effluent samples using Eq. (1):

$$\text{Removal}\,(\%) = \left(1 - \frac{C_{eff1}}{C_{inf1}}\right) \times 100 \quad (1)$$

where removal (%) is the removal efficiency, C_{eff1} is the concentration of the pharmaceutical in the effluent and C_{inf1} is the concentration of the same pharmaceutical in the influent. Comparisons of removal efficiencies of all tested pharmaceuticals between different reactors were evaluated with an independent Student's *t*-test.

2.4.3. Determination of nitrogen species, chemical oxygen demand, dissolved oxygen, pH and biomass concentrations

Besides determining the removal of target pharmaceuticals, the performance of the bioreactors was also assessed by observing the decrease in chemical oxygen demand (COD) and after filtration, the concentrations of NO_3-N, NO_2-N and NH_4-N were measured to confirm the nitrification process. To take into account the hydraulic retention time, influent samples were taken 48 h prior to the corresponding effluents. All samples were analysed immediately after sampling. In addition pH, temperature, dissolved oxygen and biomass concentration (i.e., suspended solids for ASRs and attached solids for MBBRs) data were also collected. In the case of ASRs dissolved oxygen is given as an average concentration of measurements in all three compartments.

The COD and nitrogen species were determined using a DR/2800 spectrophotometer and Dr. Hach-Lange cuvettes (Hach-Lange, Düsseldorf, Germany), LCK514, LCK 339, LCK341 and LCK302 in the case of influents and LCK314, LCK340, LCK342 and LCK303 in the case of effluents. Where necessary, samples were appropriately diluted. Dissolved oxygen levels and temperature were measured simultaneously using a HQ30d probe (Hach, Düsseldorf, Germany). The pH was measured using a pH meter (Thermo Fisher Scientific, Waltham, USA).

The biomass concentration in the ASRs was determined by filtering 15 mL of sample through previously dried and weighed filters (glass microfiber filters), heated to constant weight at 105 °C and calculated as the difference in weight prior to and after heating.

The biomass concentration in the MBBRs was determined according to the recommendations of manufacturers. In the case of Kaldnes carriers, 3 carriers were dried at 40 °C for 12 h and then allowed to cool in a desiccator before being weighed. Afterwards they were soaked in Cr–H_2SO_4 for 12 h and rinsed with deionised water, dried and weighed. In the case of the Mutag Biochip™, 3 carriers were dried for 12 h at 80 °C, allowed to cool in a desiccator and weighed. Afterwards, they were soaked for 36 h in 5% NaOH at 70 °C and then rinsed with deionised water, dried for 12 h at 80 °C and reweighed. In both cases the amount of attached biomass was determined as the difference between the two measured weights.

2.5. Hydrodynamic cavitation

The hydrodynamic cavitation reactor (HC reactor) shown in Fig. 1, consists of a 3-way valve, two 2 L reservoirs, and a symmetrical Venturi pipe with a constriction of 1 mm height and 5 mm width, connecting both reservoirs. The HC reactor is operated in cycles. Water is introduced into the right reservoir, while the left one remains empty (state 1 in Fig. 1). By opening the valve, compressed air at high pressure flows into the right reservoir and forces the water to flow through the Venturi constriction into the left reservoir, where constant pressure is maintained at 1 bar. As the flow passes through the constriction, it accelerates, causing a drop in the static pressure which results in cavitation (state 2 in Fig. 1). The valve is electrically controlled – when a signal that the right tank is empty is received, it closes (state 3 in Fig. 1.) and then opens the path for the compressed air to flow to the left reservoir and for water to flow in the opposite direction and consequently cavitation is achieved (state 4 in Fig. 1). It is worth noting that in our experiments we added hydrogen peroxide in the treated water before the start of the cavitation pulses to augment the oxidation potential of the cavitation phenomena.

A typical cavitation structure behind the Venturi constriction (state 4 in Fig. 1) is presented in Fig. 2.

Transfer of the reactor contents takes about 10 s. Operating the HC reactor in cycles allows a more accurate evaluation of the cavitation phenomena after the preset number of pulsations (cycles). The described set-up was used for detailed studies of how and to what extent the cavitation contributes to the removal of pharmaceuticals. This is why a pump was not included in the test loop, but pressure was used to force the treated water from one reservoir to the other. In this way possible cavitation or shear forces developed inside the pump cannot influence the results – thus all removal of pharmaceuticals can be contributed to cavitating conditions developed in the Venturi constriction.

To optimise the cavitation process, preliminary experiments were performed on spiked deionised water (1 $\mu g\,L^{-1}$ of target pharmaceuticals) and by varying the added amount of H_2O_2, the pressure difference between the reservoirs and the number of cycles. As a compromise between energy consumption, cost-effectiveness and the efficiency of the cavitation process the operational conditions were: addition of 20 mL 30% H_2O_2 per 1 L sample, an initial pressure of 6 bar (5 bar pressure difference) and one hundred 20 s long cycles (30 min overall length) per experiment. The process was then tested on more complex matrices, e.g. biologically treated wastewater from K1, K2 and M1, M2 bioreactors. The performance of the HC/H_2O_2 process was evaluated by the efficiency of the removal of pharmaceuticals.

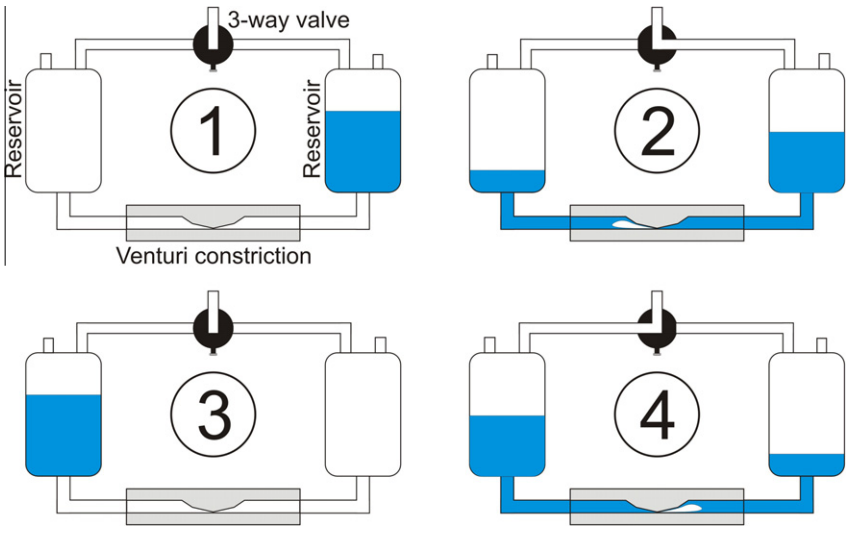

Fig. 1. Cyclic operation of the HC reactor.

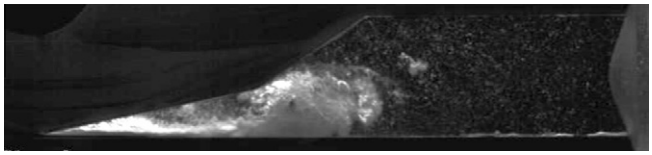

Fig. 2. A typical cavitation structure developed during the experiments.

2.6. UV treatment

UV experiments were performed in a cylindrical glass reactor with 760 mL effective volume (Suppl. 4). The UV source was a monochromatic low pressure mercury lamp (254 nm, 6 W) purchased from Photochemical Reactors Ltd. (Great Britain). Homogenous mixing of the samples was achieved using a magnetic stirrer (400 rpm). Temperature during the experiments was maintained at 21–23 °C in a water cooled immersion well. Experiments were performed on biologically treated effluents (K1, K2 and M1, M2) from the MBBR, which were cavitated under optimised operational parameters (6 bar, 30 min; 20 mL 30% H_2O_2). Similarly, as for the biological treatment and cavitation, the performance of UV treatment was evaluated by determining removal efficiency of pharmaceuticals. The duration of the UV experiment was 30 min, which was selected based on our preliminary experiments (data not shown).

3. Results and discussion

3.1. Analytical method validation

The SPE efficiency was >81% for all tested compounds in all matrices and the linearity was $r^2 \geqslant 0.98$. Considering the linearity and the SPE efficiency the bioreactor effluents are comparable to deionised water. The same goes for most determined LODs except in the case of CLA, where lower LOD was determined in deionised water. Results are presented in Table 2.

3.2. Removal of pharmaceuticals during biological treatment

3.2.1. Performance assessment of the bioreactors

In the suspended activated sludge reactors (ASR1, ASR2) the concentrations (Table 3) of COD declined from approx. 970 mg L^{-1}–50 mg L^{-1}. Slovene guideline (2012) [37] for wastewater treatment plants (WWTPs) for PE $\geqslant$ 100.000, sets upper limit for COD in discharges at 100 mg L^{-1}. According to the guidelines, COD values in ASR1 and ASR2 effluents are acceptable for discharge. However, with exception of M0, the COD in MBBRs effluents exceed 100 mg L^{-1} thus not being acceptable for discharge. Also, a relatively high variability of COD is observed in the reactor effluents (Table 3), which can be attributed to inconsistent discharge of dead biomass. To avoid discharging of dead biomass either a settlement tank or a filter should be installed after treatment, as in the case of ASR bioreactors [36], thus achieving a lower COD. Concentrations of NO_3-N and NO_2-N in the effluents increase, while concentrations of NH_4-N decrease in all the reactors confirming the nitrification process. According to an independent Student's *t*-test significantly higher NO_3-N concentrations in MBBRs effluents were observed as compared to ASRs, which can be contributed to denitrification process, which can occur in ASRs because of bioreactor design. Also, significantly higher concentrations of NO_3-N and lower concentrations of NH_4-N were determined in the K1, K2, M1 and M2 effluents as compared to K0, M0 effluents, which signifies that the addition of pharmaceuticals also affects biomass composition [38]. A study of the microbial community in K0, M0, K1, K2, M1 and M2 bioreactors is currently in progress and may give some explanation to observed results.

Higher concentrations of dissolved oxygen ($\geqslant$8.4 mg L^{-1}) were present in the MBBRs compared to ASRs ($\geqslant$3.5 mg L^{-1}). Temperature remained constant in all types of reactors at 19° C and the pH ranged from 6.3 to 7.8. The amount of biomass in the parallel ASRs is comparable, as is the amount of attached biomass between the parallel MBBRs (Suppl. 5). The highest average amount of biomass was determined in ASRs (6.65 g L^{-1}) as compared to MBBRs (0.5 g L^{-1} for Kaldnes carriers and 0.2 g L^{-1} for Mutag Biochips™ carriers) which is contrary to expectation. Based on the data from the literature [26] there should be more biomass in the MBBRs.

Table 2
Results of analytical method validation.

Matrix used pharmaceutical	Effluent (ASR0, K0, M0)						Deionised water					
	CLA	IB	NP	KP	CBZ	DF	CLA	IB	NP	KP	CBZ	DF
SPE efficiency (n = 3, c = 1 μg L^{-1}) (%)	90–107	81–94	83–91	83–94	84–95	82–86	90	90	90	95	93	81
LOD (ng L^{-1}) (n = 3)	7–19	0.2–4	2–6	0.5–5	0.5–5	0.6–5	3.3	0.4	1	1.6	0.9	1.9
Linear range (ng L^{-1})	10–1200 (7 points)						10–1200 (6 points)					
r^2 (Calibration curve)	$\geqslant$0.98						$\geqslant$0.98					

r^2: Coefficient of determination; n: number of samples.

Table 3
Measurements of COD, NO_3-N, NO_2-N, and NH_4-N in bioreactor influents and effluents expressed as average values ± stdev and statistically significant difference obtained by independent Student's *t*-test (α = 0.05).

Bioreactors		Suspended activated sludge (ASR1, ASR2)/Kaldnes (K0, K1, K2)/Mutag biochips™ (M0, M1, M2)											*t*-Test (α = 0.05)			
Samples		Influent			Effluent								Effluents			
	n	A	B	C	ASR1	ASR2	K0	K1	K2	M0	M1	M2	A/C	B/C	D/E	
COD (mg L^{-1})	6	976 ± 39	707 ± 14	929 ± 14	47 ± 48	54 ± 55	131 ± 38	187 ± 110	104 ± 52	92 ± 48	120 ± 31	128 ± 45	–	–	–	
NO_3-N (mg L^{-1})	6	2.3 ± 1.9	2.4 ± 0.4			15 ± 6	15 ± 16	65 ± 15	80 ± 3	81 ± 5	65 ± 9	70 ± 8	80 ± 6	YES	YES	NO
NO_2-N (mg L^{-1})	6	0.2 ± 0.1	0.04 ± 0.01			0.8 ± 0.8	2.3 ± 1.8	1.9 ± 0.4	1.5 ± 0.6	0.5 ± 0.4	3.9 ± 2	3.4 ± 1.3	1.2 ± 0.6	–	–	–
NH_4-N(mg L^{-1})	6	83 ± 7	68 ± 4			4 ± 3	17 ± 11	10 ± 6	3 ± 3	6 ± 7	13 ± 8	4 ± 3	4 ± 1	–	YES	NO

n = Number of measurements; A: ASR1, ASR2; B: K0, M0; C: K1, K2, M1, M2; D: K1, K2; E: M1, M2.

Still, according to our experience with plastic carriers on different occasions, the biomass is somehow reluctant to adhere onto the plastic and much more biomass is adhered to inorganic carriers like expanded clay, glass or mineral foam, slag, etc.

3.2.2. Removal of pharmaceuticals

Our results from the ASRs are in accordance with the literature [3,9,12–17] and demonstrate that average removals of CLA, CBZ and DF by suspended activated sludge process are poor and inconsistent ranging from 9% for CLA to 48% for DF (Table 4) whereas the average removals for IB, NP and KP are all higher than 74%.

The results from MBBRs also show zero removal of CBZ, poor removal of CLA (5–28 %) and high average removals of IB, NP and KP (63–94 %). In the case of Mutag Biochip™ carriers high and consistent average removal of DF (85%) was achieved.

Zwiener and Frimmel [15] investigated removals of pharmaceuticals in lab-scale aerobic biofilm systems and obtained results in accordance with ours for CLA and IB, but did not observe any removal of DF. Results obtained by Falås and co-workers [26] using carriers from full-scale WWTP are also in agreement with our results for IB, NP, KP and DF, but opposite in the case of CLA. CBZ once again proved to be recalcitrant to biological agreeing with Joss and co-workers [27].

With the use of independent Student's *t*-test significantly different removals between the ASRs and MBBRs were demonstrated in the case of IB, KP, CBZ and DF, whereas no significant difference in removal was observed in the case of CLA and NP (Table 4). Higher removals of IB and DF and lower removals of KP and CBZ were determined in MBBRs. Our results are in accordance with the study performed by Falås and co-workers [26] in the case of DF and opposite in the case of KP. According to Joss and co-workers [39] the discrepancy in the results is due to several reasons, such as the different concentrations of investigated pharmaceuticals, different operational conditions and biomass properties i.e., origin, sludge age and biomass adaptation.

Our results show that the removal efficiencies of individual compounds can be influenced by using different biological treatments. Also, from the data (Table 4) the efficiency of MBBR, based on the biomass concentration per litre, is higher than that in the ASR. The reason is not well understood, but it could be that the biofilm that developed in the MBBR consists of microorganisms that are able, to a much higher degree, exploit pharmaceuticals as organic substrates. Even though little is known about the efficiency of removal of pharmaceuticals by biofilm systems, we can state that the composition and capacity of the biofilm formed in MBBRs favours the removal of certain compounds.

To exclude adsorption as an elimination mechanism, a parallel experiment was performed with carriers and no biomass. Results show that for the investigated compounds adsorption onto the carriers and based on available solid-water distribution coefficients [27,40] sorption onto sludge, are not important removal mechanisms. From this we can conclude that removal of investigated compounds is a result of interactions of investigated compounds with the biomass.

3.3. Removal of pharmaceuticals by HC/H_2O_2 process in different water matrices

To evaluate the performance of the HC/H_2O_2 process, experiments were initially performed using 1 L of deionised water. Table 5 shows that cavitation time, initial pressure and the addition of H_2O_2 all play a role in removing pharmaceuticals, which can occur *via* pyrolysis or free radical attack [28,30]. Results in Table 5 show that addition of H_2O_2 enhances removal efficiencies, suggesting that degradation of pharmaceuticals is driven by ·OH radicals. The amount of H_2O_2 added is clearly important [28], since highest removal efficiencies were obtained with 20 mL 30% H_2O_2

Table 4
Removal efficiency of selected pharmaceuticals with ASRs and MBBRs expressed as average removal ± stdev, statistically significant difference obtained by independent Student's *t*-test ($\alpha = 0.05$) and the average amount of biomass concentration in parallel bioreactors.

		Removal (%) ± stdev (%)			*T*-test ($\alpha = 0.05$)			
	n	ASR1, ASR2	K1, K2	M1, M2	ASR/K	ASR/M	K/M	K + M/ASR
Clofibric acid	12	9 ± 28	28 ± 16	5 ± 12	No	No	Yes	No
Ibuprofen	12	86 ± 10	94 ± 8	94 ± 4	Yes	Yes	No	Yes
Naproxen	12	74 ± 8	70 ± 27	80 ± 13	No	No	No	No
Ketoprofen	12	78 ± 10	73 ± 17	63 ± 17	No	Yes	No	Yes
Carbamazepine	12	21 ± 25	1 ± 11	0 ± 15	Yes	Yes	No	Yes
Diclofenac	12	48 ± 19	74 ± 22	85 ± 10	Yes	Yes	No	Yes
Average biomass concentration ($g\,L^{-1}$)		6.65	0.49	0.21				

n = Number of measurements; ASR/K: statistically significant difference in removal efficiencies between ASR1, ASR2 and K1, K2; ASR/M: statistically significant difference in removal efficiencies between ASR1, ASR2 and M1, M2; K/M: statistically significant difference in removal efficiencies between K1, K2 and M1, M2; K + M/ASR: statistically significant difference in removal efficiencies between K1, K2, M1, M2 and ASR1, ASR2.
All the results are given as the average removal of 12 samples 6 from each reactor ASR1, ASR2, K1, K2, M1 and M2.

Table 5
Removal of selected pharmaceuticals by HC/H_2O_2 process in deionised water under different operational conditions.

	Initial pressure (bar)	6									5	4
	Time of cavitation (min)	15			30			60			30	30
	Addition of 30% H_2O_2 (mL)	0	20	40	0	20	40	0	20	40	20	20
	n	1	1	1	1	10	1	1	1	1	1	1
Removal of pharmaceuticals (%)	Clofibric acid	10	19	16	18	45 ± 16	9	27	23	20	21	14
	Ibuprofen	6	10	8	11	48 ± 15	20	14	19	19	18	13
	Naproxen	49	77	52	74	86 ± 7	74	81	99.9	91	79	74
	Ketoprofen	0	24	20	13	52 ± 14	28	26	29	15	34	29
	Carbamazepine	1	24	10	20	72 ± 10	3	24	89	24	41	35
	Diclofenac	32	35	36	45	77 ± 9	47	53	99.9	64	32	31

n = Number of measurements.

Table 6
Removal of pharmaceuticals in experiments without cavitation (non cavitating/H_2O_2 and H_2O_2) *vs.* cavitation and H_2O_2 (HC/H_2O_2).

	Non cavitating/H_2O_2	H_2O_2	HC/H_2O_2
Pharmaceutical	Removal (%)	Removal (%)	Removal (%)
n	2	1	10
CLA	11 ± 1	5	45 ± 16
IB	10 ± 4	8	48 ± 15
NP	41 ± 3	38	86 ± 7
KP	12 ± 3	11	52 ± 14
CBZ	6 ± 3	4	72 ± 10
DF	33 ± 3	28	77 ± 9

n = Number of repeated experiments.

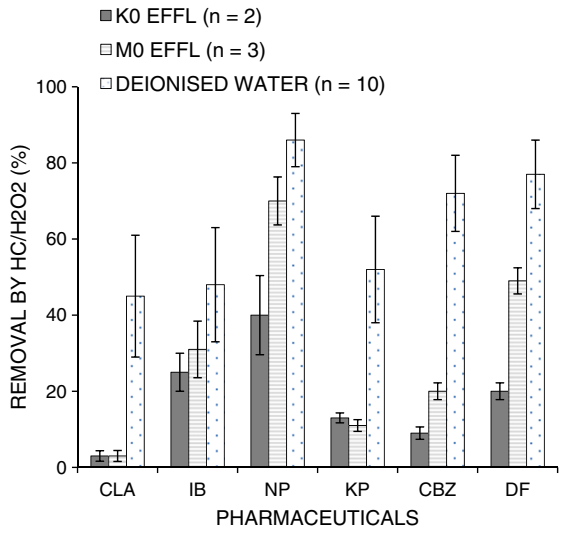

Fig. 3. Removal of pharmaceuticals with HC/H_2O_2 process in K0 and M0 effluents and deionised water as an average removal ± stdev.

per 1 L sample, whereas higher concentrations showed a negative effect on removal (Table 5). One possible reason is that excess H_2O_2 amounts can act as a radical scavenger for hydroxyl radicals generated during treatment [28]. To confirm that formation of hydroxyl radicals during cavitation is the driving force behind the removal of pharmaceuticals, we made two control experiments without cavitation. In the first experiment (Table 6, non-cavitating/H_2O_2) the pressure difference between the reservoirs was lowered to 0.75 bar to prevent cavitation. All other variables remained the same. In second experiment (Table 6, H_2O_2) 1 L of deionised water containing 1 μg L^{-1} of selected pharmaceuticals and 20 mL of 30% H_2O_2 was stirred with magnetic stirrer for 30 min. Both experiments are described in details in the Supplementary data (Suppl. 6). Table 6 shows that experiments performed without cavitation are less effective than HC/H_2O_2 and confirms that ·OH radicals produced during cavitation are primarily responsible for pharmaceuticals removal.

Higher pressures and longer duration of cavitation both influenced the removal of selected pharmaceuticals. Based on these results (Table 5), the following optimal operational parameters were selected: an initial pressure of 6 bar, a cavitation time of 30 min and the addition of 20 mL 30% H_2O_2 per 1 L sample. Experiments were conducted in 10 parallels, where a high removal of NP (86% ± 7%), poor removals of CLA, IB and KP (from 45% to 52%) and substantial removals of CBZ (72% ± 10%) and DF (77% ± 9%) were achieved (Table 5). This is important since CBZ and DF are both biologically persistent (Table 4), and we can assume that coupling biological treatment with HC/H_2O_2 can substantially improve the total treatment efficiency.

To evaluate the effect of matrix complexity on the performance of HC/H_2O_2, wastewater effluents (K0 and M0 effluents) were spiked and the values obtained during HC/H_2O_2 process were compared to those obtained for deionised water samples under optimal conditions (Table 5). Fig. 3 shows how removal efficiencies in the effluents are lower than those determined in deionised water. Clearly, matrix composition affects the efficiency of the HC/H_2O_2 process and since the effluents were not filtered, dead biomass and other organic and inorganic compounds present in K0 and M0 effluents can compete for ·OH [6]. The removal efficiencies for IB, NP, CBZ and DF were higher in M0 effluent compared to K0. This may also be a result of matrix complexity; the COD of the K0 effluent (131 ± 38 mg L^{-1}) is higher than that of M0 effluent (92 ± 48 mg L^{-1}).

3.4. Removal of pharmaceuticals by coupling biological treatment, HC/H_2O_2 process and UV treatment

To further augment the removal of persistent pharmaceuticals CLA and CBZ, the attached-growth biological treatment was coupled to the HC/H_2O_2 process and UV treatment. The results are presented in Fig. 4 and confirm our findings for IB, NP, KP and DF, where the highest contribution to overall removal is made by biological treatment. In the case of CLA highest removal was obtained during UV treatment, whereas for CBZ HC/H_2O_2 and UV treatment

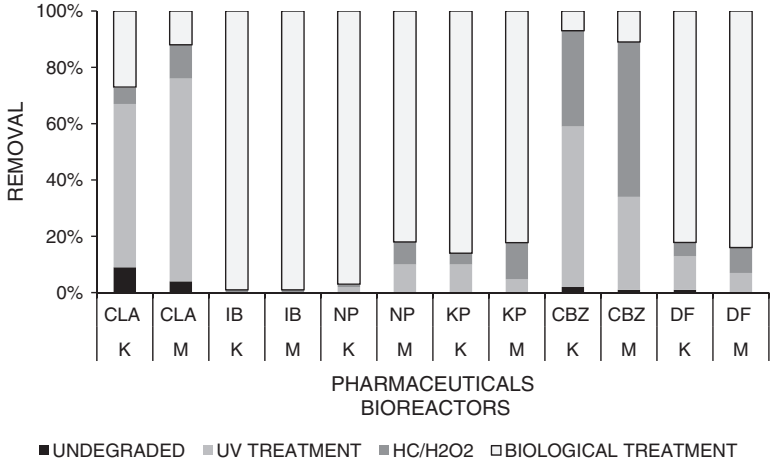

Fig. 4. Contributions of sequentially coupled biological, HC/H_2O_2 and UV treatment on overall removal of pharmaceuticals (*K* = K1, K2 effluent; *M* = M1, M2 effluent).

stages give similar results. Concentrations under LOD were achieved for IB, NP and KP and a total removal higher than 98% was determined in the case of CBZ and DF. High overall removal of >90% was observed for otherwise very recalcitrant CLA. The average COD values determined in K1, K2 effluent (145 ± 93 mg L^{-1}) were higher than those determined in M1, M2 effluent (124 ± 37 mg L^{-1}), which is in accordance with higher observed removal of pharmaceuticals in the effluent with lower initial COD concentration.

4. Conclusions

This study evaluates the removal efficiencies of clofibric acid, ibuprofen, naproxen, ketoprofen, carbamazepine and diclofenac by diverse treatment processes, i.e.: biological treatment (suspended activated sludge and moving bed biofilm process), hydrodynamic cavitation with addition of H_2O_2 and UV irradiation. Our results are in agreement with literature data in the case of conventional biological treatment (continuous flow suspended activated sludge). Poor and inconsistent average removals of recalcitrant clofibric acid, carbamazepine and diclofenac and removals higher than 74% for ibuprofen, naproxen and ketoprofen were observed. For the moving bed biofilm process, poor and inconsistent removals were demonstrated for clofibric acid while obtained removals for ibuprofen, naproxen, ketoprofen and diclofenac were high. In the case of diclofenac, consistent removals of up to 85% were achieved using bioreactors filled with Mutag BioChip™ carriers. Recalcitrant nature of carbamazepine was confirmed with almost no observed removals. Comparison of removal efficiencies between suspended activated sludge and moving bed biofilm reactors, with the use of the Student's *t*-test, showed significantly different removals in the case of ibuprofen, ketoprofen, carbamazepine and diclofenac.

The efficiency of the hydrodynamic cavitation/H_2O_2 process depended on several factors: the amount of added H_2O_2, duration of cavitation (number of cycles) and cavitation intensity. Optimal parameters for cavitation (20 mL 30% H_2O_2, 30 min, 6 bar) were determined based on experiments performed in deionised water. Such settings resulted in removal efficiencies ranging from 72% to 86% in the case of naproxen, carbamazepine and diclofenac, and from 45% to 52% in the case of clofibric acid, ibuprofen and ketoprofen.

To evaluate the effect of matrix composition on the efficiency of the hydrodynamic cavitation/H_2O_2 process, the optimal operating conditions were used in effluents from bioreactors and compared to those determined in deionised water. Higher removal efficiencies of all tested compounds in deionised water show a matrix composition effect on hydrodynamic cavitation/H_2O_2 process efficiency. The results were supported by lower removal efficiencies of pharmaceuticals in effluents with higher COD.

The highest overall removals of all investigated compounds were achieved when biological treatment (MBBR), HC/H_2O_2 process and UV treatment were coupled consecutively, where carbamazepine and diclofenac removal was >98%, while the remaining amounts of ibuprofen, naproxen and ketoprofen were below the LOD. In the future different coupling of demonstrated treatment processes such as AOPs coupled prior to biological treatment will be investigated to determine the most successful sequence of treatments in terms of time and energy consumption and removal efficiency.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ultsonch.2012.12.003.

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