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Degradation of pharmaceuticals from wastewater in a 20-L continuous flow bio-electro-Fenton (BEF) system

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Abstract

The bio-electro-Fenton (BEF) technology has proven to be an effective and energy-saving method for treating wastewaters containing a single pharmaceutical in the lab-scale. However, the continuous degradation of pharmaceuticals in a scaled-up BEF has never been reported. In this study, a 20-L dual-chamber BEF reactor was designed and tested for treating six model pharmaceuticals. The effect of key operational factors including applied voltage, cathode Fe^{2+} dosage, initial pharmaceuticals concentration and hydraulic retention time (HRT), were assessed. By implementing 0.1 V voltage, 0.3 mM Fe^{2+} and HRT of 26 h, the six selected pharmaceuticals ($500 \mu\text{g L}^{-1}$ for each) were removed completely. Moreover, transformation products during clofibric acid degradation, such as 4-chlororesorcinol, were detected and the relevant transformation pathway was proposed. Additionally, it successfully removed these pharmaceuticals in the real wastewater matrix. This paper contributes to scaling-up the BEF process for continuous and effective treating pharmaceuticals-contaminated wastewater.

Keywords: Bio-electro-Fenton; Scaling-up; Pharmaceuticals; Wastewater treatment; Transformation pathway

1. Introduction

Over the last few decades, a strong and growing demand for pharmaceuticals has occurred as a result of global population growth and advances in medicine. Although the use of various pharmaceuticals, such as antibiotics, antipyretics, analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), antimicrobials, etc., can bring many benefits such as saving and extending lives, ameliorating suffering and improving quality of life, large amounts of wastewater containing pharmaceuticals have been discharged into the environment with an average treatment ratio (wastewater treatment plant, WWTP) of less than 30% (Hu et al., 2018). Previous studies on environmental hazard assessments have suggested that many pharmaceuticals are environmentally hazardous to aquatic organisms and might pose long-term negative risks to humans (Vandenberg et al., 2012; Wilkinson et al., 2016). Consequently, discharge such inefficiently treated pharmaceuticals-containing effluent by conventional WWTP has turned into a serious contribution to water pollution. However, due to improved analytical chemistry techniques, it is possible to detect compounds at a trace-level concentration (i.e. ng L^{-1}) in natural aquatic environments (Bouissou-Schurtz et al., 2014; Kümmerer, 2001). Since the human health and environmental risks of these pharmaceuticals are high, extensive research efforts have been devoted to finding effective ways to remove them from wastewater. In general, existing removal methods can be classified into three groups, namely physical adsorption, chemical advanced oxidation, and biological degradation. Among the existing treatment technologies, electro-Fenton (EF), which combines traditional chemical Fenton's oxidation with electrochemistry, has a number of unique merits, including high removal efficiency, mild operating conditions and the ability to complete pharmaceutical mineralization (Brillas et al., 2009; Plakas et al., 2016; Sirés et al., 2007). However, the major challenges involved in high electric energy consumption, scaling-up and costly electrodes hinder the widespread application of the technology (Li et al., 2017d; Monteil et al., 2018; Zhou et al., 2017).

More recently, an innovative process, entailing the integration of conventional EF and namely bio-electro-Fenton (BEF), which offers the ability of strong oxidation by EF and the low energy consumption of microbial electrochemical systems biodegradation, has been developed to reduce electrical energy consumption (Feng et al., 2010; Olvera-Vargas et al., 2016; Zhu & Ni, 2009). Compared with the traditional EF technology, much lower electricity input (0.2-0.8 V) is required in the BEF process, due to in-situ electricity generation by anode electroactive bacteria through decomposing of organic matter (e.g. wastewater) and generate electrons, protons, and carbon dioxide. In the cathode chamber, the major electrode reactions can be explained as follows. Firstly, H_2O_2 is in-situ generated via a two-electron oxygen reduction reaction (ORR) (Eq. (1)). Secondly, hydroxyl radicals ($\cdot\text{OH}$) is formed by the reaction between H_2O_2 and Fe^{2+} (Eq. (2)). Thirdly, the regeneration occurs via Fe^{3+} reduction (Eq. (3)).

BEF process has been developed for treating pollutants in diverse wastewaters, like dyes (Li et al., 2017c; Zhang et al., 2015b), pharmaceuticals (Nadai et al., 2018; Wang et al., 2018; Zhang et al., 2015a) and municipal, agricultural and industrial pollutants (Hassan et al., 2017; Yong et al., 2017; Yu et al., 2018). Though promising, most studies have been carried out in labs, with reactor sizes in the hundreds of milliliters and the scaling-up feasibility of these systems has never been explored. Furthermore, previous BEF process studies focused mainly on wastewater containing a single pharmaceutical, while the continuous degradation of pharmaceuticals in wastewater has never been reported, let alone in terms of a 20-L system.

Thus, the core purpose of current work is to develop a 20-L BEF reactor for the continuous treatment of pharmaceutical wastewater containing NSAIDs (diclofenac, ibuprofen, ketoprofen, and naproxen), an anticonvulsant (carbamazepine) and a lipid regulator (clorfibric acid), all of which

have been detected in varying concentrations in urban effluent (Gurke et al., 2015; Laurencé et al., 2014; Papageorgiou et al., 2016). The previous studies regarding pharmaceuticals removal by lab-scale BEF process are shown in Table 1. Therefore, the feasibility of the 20-L BEF process for pharmaceutical containing wastewater treatment was first evaluated. The effects of operational parameters, including initial pharmaceuticals concentration, Fe^{2+} dosage, applied voltage as well as hydraulic retention time (HRT), on system performance were explored. Finally, the transformation products and the corresponding transformation pathway of clorfibric acid were determined. This research provides insights into developing a large-scale BEF system for future commercial applications such as the tertiary treatment facility of traditional WWTP to effectively remove pharmaceuticals.

2. Materials and methods

2.1 BEF system setup and operation

A rectangular, two-chamber BEF reactor ($20\text{ cm} \times 20\text{ cm} \times 25\text{ cm}$ for each chamber) was set up for the experiments (Fig.1). The cathode and anode chambers of the BEF reactor were separated by a cation exchange membrane (CEM, CMI 7001, Membrane International, NJ), which can let the H^+ produced in anode be transported to the cathode as well as prevent the aerated air diffused to the anode. Stainless steel screws and silicone gaskets were used to avoid leakage whilst assembling this 20-L BEF reactor. The total and working volumes of each chamber of the BEF reactor were 10 L and 9 L, respectively. There were 20 electrodes in each chamber, arranged as exhibited in Fig.1. The carbon brush (diameter 5.9 cm, length 6.9 cm, Mill-Rose, USA) was used as the anode, which was pretreated before use as previously described. (Zhang & Angelidaki, 2015). The working electrodes and reference electrode in the cathode chamber of the BEF reactor were commercial graphite plates (projected size of each was $4.5\text{ cm} \times 4.5\text{ cm}$) and Ag/AgCl electrode (+0.197 V vs SHE, Pine Instrument Company, USA), respectively.

The BEF system was first operated as a microbial fuel cell and was fed with domestic wastewater containing 1 g L^{-1} of sodium acetate (Lyngby Wastewater Treatment Plant, Denmark) to cultivate mature anodic biofilms. Domestic wastewater was used as inoculum and sodium acetate was used as carbon source. After one month of operation, when the current output was stable, the BEF system was running as a microbial electrolysis cell, and the anaerobic anode chamber was continuously fed with synthetic nutrient medium. The detailed ingredients of the synthetic nutrient medium are as described in the previous study (Kvesitadze et al., 2012). The HRT of the solution in the anode chamber was set to 58 h, to maintain anode performance (Zhang et al., 2015b). Synthetic wastewater laden with diclofenac, ibuprofen, ketoprofen, carbamazepine, clofibric acid and naproxen, each at different concentrations (250 , 500 and $1000 \text{ } \mu\text{g L}^{-1}$), was used to investigate the effect of initial pharmaceutical concentration on the system performance. The abiotic cathode chamber was fed with Na_2SO_4 (50 mM) solution unless stated otherwise. $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$, as an iron catalyst, was also added into the synthetic pharmaceutical wastewater. The catholyte pH was adjusted by using H_2SO_4 solution (3 M). The catholyte remained in a continuous flow, and the catholyte pH was maintained at 2.8. The cathodic aeration rate was set to 350 mL min^{-1} by using a peristaltic pump (OLE DITCH, Instrument Makers APS, Denmark), corresponding to an equilibrium dissolved oxygen (DO) concentration of about 7.8 mg L^{-1} at $28 \text{ }^\circ\text{C}$, unless stated otherwise. Moreover, different HRTs were also set to test system performance when the catholyte was in continuous flow. For the trials with real wastewater, effluents after secondary biological treatment (Lyngby Wastewater Treatment Plant, Copenhagen, Denmark) with TOC of 25.48 mg L^{-1} were taken. When the system was operating in BEF mode, a $0.1 \text{ } \Omega$ external resistance was connected between anode and cathode. A constant voltage of 0.1 V was supplied by using a potentiostat (CT-4008W, Neware Battery Testing System, China), except for investigating the effect of different voltages (0.05 and 0.2 V). Control experiment conditions were conducted for an open circuit (Control 1), without cathode aeration (Control 2) or no Fe^{2+} addition (Control 3). The

stirring speed of both anolyte and catholyte was set to 200 rpm. All experiments were performed in duplicate at room temperature (20 ± 2 °C).

2.2 Chemicals

A stock solution (1 g L^{-1}) was prepared by weighing 0.1g each of the six selected pharmaceuticals (clofibric acid, diclofenac, carbamazepine, naproxen, ibuprofen, and ketoprofen) and dissolving the mixture in 10 mL of methanol (Merck Darmstadt, Germany), and analytical-grade substances in this regard were purchased from Sigma-Aldrich, Denmark.

2.3 Analytical Methods

The pH value of the treated effluent was determined by a pH meter (PHM 210 pH meter, Radiometer). The potentiostat recorded current and cathode potential every 10 min. The power consumption induced by the pumping and stirring were recorded by a sparOmeter electricity meter (Type NZR230, S.L. Energitekinik, Denmark).

A total of 10 mL of each sample was collected from the cathode chamber at given time intervals, 6 mL of which was used to test immediately the pH and any remaining H_2O_2 concentrations. Then, the concentration of H_2O_2 was determined as described in the previous study (Nadais et al., 2018). Samples collected for pharmaceuticals concentration and transformation products of clofibric acid analysis were kept at -20 °C before analysis. Gas chromatography/mass spectrometry (GC/MS, Agilent GC 6890 N, MSD 5973 N utilizing a CombipAL from CTC analytics as auto-sampler) was used to quantify the concentration of pharmaceutical compounds. The detailed derivatization procedure, chromatography and MS conditions were carried out as previously described (Hey et al., 2012; Nadais et al., 2018). Furthermore, a high-performance liquid chromatography (Agilent 1290 Infinity, USA, HPLC) system with a tandem mass spectrometer (Agilent 6470 series, USA, MS/MS) was used in the experiment set up to identify the degradation of clofibric acid by-products. Detailed operating parameters are described as following: the HPLC system consisted of a pump, a column oven, a degasser, and an auto-sampler all supplied from Agilent 1290 Infinity, USA.

Chromatographic separation was performed using a C18 column (2.1 x 50 mm, 1.8 μm , Eclipse Agilent, USA). The temperature of the HPLC column oven was 35 $^{\circ}\text{C}$, and the constant flow rate was 0.6 mL min^{-1} . The HPLC gradient was formed by changing the mix ratio of Milli-Q water including 0.1% ammonium formate (solvent A) and 90% acetonitrile/10% Milli-Q water including 0.1% ammonium formate (solvent B). A mass spectrometer equipped with the triple quadrupole was from Agilent 6470 series, USA. The gradient was initiated with 0% B, followed by a linear increase of gradient B up to 100% within 20 min. Initial gradient conditions were also re-established for 3 mins. An MS 2 scan, starting from 60 Da to 350 Da in the ESI-ionisation mode, was introduced to identify the clofibric acid by-product. The sheath gas flow was 12 L min^{-1} at a temperature of 400 $^{\circ}\text{C}$, while the gas flow was 10 L min^{-1} at a temperature of 260 $^{\circ}\text{C}$. The injection volume was 10 μL . In addition, the apparent rate constants for removing six selected pharmaceuticals under different operating parameters were determined based on a previous study (Li et al., 2017a; Li et al., 2017c; Nadais et al., 2018).

3. Results and discussion

3.1 Pharmaceuticals elimination in batch mode

As shown in Fig. 2, the six selected pharmaceuticals as a mixture can be completely removed within 18 h with a 0.2 V voltage supply. The increase of removal rate was positively correlated with the applied voltage ranging from 0.05 to 0.2 V. Correspondingly, system current increased as the applied voltage increased, which can be seen in Fig. S1. The above results match up with the findings in previous studies in terms that applied voltage can affect the current in the BEF process and thereby further control the generation of H_2O_2 and its induced $\cdot\text{OH}$ (Li et al., 2017a; Li et al., 2017c; Nadais et al., 2018). Comparatively, in an open circuit condition (Control 1), only 2.6% of clofibric acid, 2% of diclofenac, 3.8% of carbamazepine, 1.4% of naproxen, 2.6% of ibuprofen and 1.8% of ketoprofen were removed. This phenomenon could be explained by the occurrence of sorption between pharmaceuticals and CEM as well as cathode electrodes. Similarly,

pharmaceutical removal efficiencies in those systems without any airflow in the cathode (Control 2), or without Fe^{2+} addition (Control 3), were lower than 26%. Also, the concentration of H_2O_2 progressively raised and achieved 120 mg L^{-1} at 18 h in the system without Fe^{2+} addition, while no H_2O_2 was detected under other conditions (Fig. S1). In line with the observed results, we could draw some basic conclusions as following. First, sorption by CEM and electrode, or H_2O_2 alone and without Fe^{2+} , cannot effectively remove six selected pharmaceuticals. Second, electricity-driven H_2O_2 synthesis followed by a Fenton reaction induced by Fe^{2+} was the main reason for pharmaceutical degradation. Furthermore, based on data from the batch experiment, only a small variation was observed in pH (from 3 to 3.4) with different applied voltages (Fig. S1), which was in the optimum EF and BEF process reaction ranges reported by the previous literature (Laurencé et al., 2014; Sellers, 1980; Zhang et al., 2012). In conclusion, the results demonstrate the feasibility of this novel 20-L BEF process for pharmaceutical-containing wastewater treatment.

3.2 Pharmaceuticals elimination in continuous flow mode with implementations of operational parameters

It is advantageous for industrial applications that the reactor operates in continuous mode. However, most previous studies are carried in batch mode, so testing this scaling-up BEF system for continuous pharmaceuticals removal is important to validate the feasibility of this technology under industrial-scale conditions. In this section, the effects of applied voltage, FeSO_4 dosage, different HRTs and initial pharmaceutical concentration on removal efficiency are investigated. Other operational parameters, such as initial pH, supporting electrolytes as well as air supply, are set based on the optimal operation conditions obtained directly from previous research (Li et al., 2017a; Monteil et al., 2018; Nadais et al., 2018).

3.2.1 Effect of different applied voltages

It has been documented that the in-situ generation of H_2O_2 and further conversion to $\cdot\text{OH}$, can be controlled through circuit current density (Estrada et al., 2012; Li et al., 2017a; Nadais et al., 2018).

Hence, applied voltages with 0.05 V, 0.1 V, and 0.2 V were used to study their effects on pharmaceutical removal. During the tests, 500 $\mu\text{g L}^{-1}$ of each pharmaceutical, initial pH of 2.8, Fe^{2+} of 1 mM, Na_2SO_4 of 50 mM, air flow rate of 350 mL min^{-1} and HRT of 23 h in the cathode was chosen, based on batch experiments. The removal rates for diclofenac, clofibric acid and carbamazepine (see in Fig. 3) increased from nearly 80% to 100% along with increasing applied voltage from 0.05 to 0.1 V over 69 h operation (with HRT of 23 h). There was no apparent observation on the improvement of pharmaceutical removal when 0.2 V of voltage was applied. For ketoprofen and ibuprofen, removal rates reached 100% with an applied voltage of 0.05 V, but when it further increased to 0.1 V or even 0.2 V, the reaction rate of ketoprofen was enhanced significantly. As for naproxen, by increasing the applied voltage from 0.05 to 0.2 V, where the removal rate raised slightly from 87% to 92%. In general, the pharmaceuticals removal rate increased with the increase of the applied voltage. This was due to the increase in electro- H_2O_2 production, which subsequently lead to more $\cdot\text{OH}$ generation. Additionally, it was found that the removal of those pharmaceuticals in the BEF process with tested applied voltage conformed to pseudo-first-order kinetics, and the kinetics constants were showed in Table S1. The rate constant of each pharmaceutical increased first as the applied voltage raised from 0.05 to 0.1 V. But further increasing to 0.2 V, it began to decline (diclofenac, clofibric acid and carbamazepine). It was worth noting that the rate constant of ibuprofen was much larger than the others, probably because ibuprofen was easily removed through the BEF process. Similar results were also obtained that the rate constant rate of ibuprofen was higher than naproxen and ketoprofen in an 80 mL lab-scale BEF process (Nadais et al., 2018). Moreover, Zhao et al explored the removal of ibuprofen and naproxen in a photoelectrochemical process and observed the faster removal rate of ibuprofen due to the complex molecular structure of naproxen (Zhao et al., 2009). Effluent pH (as seen in Fig. S2) showed a slight increase from 2.8 to 3.4 while the applied voltage was changed from 0.05 to 0.2 V after three HRTs.

The above results indicate that any further control of cathodic pH was not necessary for continuous flow mode when an influent pH of 2.8 was applied in the cathode. The current increased in line with increasing the applied voltage (Fig. S2), which was consistent with changes in treatment performance. While an increase in applied voltage can improve treatment performance, it may in turn increase energy consumption, so the applied voltage of 0.1 V was selected for subsequent experiments.

3.2.2 Effect of different initial pharmaceutical concentrations

The previous research has shown that the performance of pollutant removal by the BEF process was independent of the pollutant concentration (Li et al., 2017a). Therefore, the influence on the removal of the six selected pharmaceuticals in continuous flow mode was studied further at three different initial concentrations (250, 500 and 1000 $\mu\text{g L}^{-1}$). The other fixed operational parameters were as following: initial pH of 2.8, Fe^{2+} of 1 mM, Na_2SO_4 of 50 mM, air flow rate of 350 mL min^{-1} and HRT of 23 h. The results presented in Fig. 4 show that pharmaceutical concentrations dropped rapidly in the first 8 h, following which removal rate stabilized after approx. 24 h. For clofibric acid, diclofenac, carbamazepine, ibuprofen and ketoprofen with initial concentrations of 250 and 500 $\mu\text{g L}^{-1}$, approximately 100% of their removal rates were observed after 48 h, while removal rates ranged from 72% to 85% at 1000 $\mu\text{g L}^{-1}$, except for ibuprofen (100%). As for naproxen, the degradation efficiencies stabilized after around 24 h at 100%, 90% and 88% with initial concentrations of 250, 500 and 1000 $\mu\text{g L}^{-1}$, respectively. A similar result, that is, a higher concentration corresponds to a lower removal efficiency, was also found in our group's previous research on the degradation of the orange G by the BEF process with different initial orange G concentrations. This phenomenon can be explained as the constant number of $\cdot\text{OH}$ produced under the given operating condition while the concentrations of pharmaceuticals molecules were increased (Kahoush et al., 2018). Similarly, the removal of those pharmaceuticals in the BEF process with tested initial concentration also followed pseudo-first-order kinetics, and the rate constants can be

seen in Table. S2. It can be found in Table S2 that the rate constants of pharmaceuticals (diclofenac, clofibric acid and naproxen) firstly increased as the concentration of the initial pharmaceutical increased from 250 to 500 $\mu\text{g L}^{-1}$. This may be related to increasing the number of pharmaceuticals molecules participated in the Fenton reaction, which caused $\cdot\text{OH}$ more involved in the desired reaction and thus increased pharmaceuticals removal rate (Kahoush et al., 2018). Thereafter, the rate constant of each pharmaceutical decreased when initial concentration further increased to 1000 $\mu\text{g L}^{-1}$. Similar tendencies have been observed in EF and BEF processes treating dyes (Li et al., 2017c; Zhang et al., 2015b) and pharmaceuticals (Labiadh et al., 2015; Liu et al., 2018). To overcome this saturation issue, and to improve removal efficiencies at higher initial concentrations, it may be necessary to initiate a relatively longer treatment time or a higher applied voltage. Lab-scale BEFs were generally applied to low-concentration pollutants at a range of $\mu\text{g L}^{-1}$ (Nadai et al., 2018; Wang et al., 2017). The results obtained with this 20-L BEF system indicate that BEF technology could also be used for high-strength pharmaceutical wastewater treatment, implying good viability for industrial applications.

3.2.3 Effect of different HRTs

HRT is an important parameter affecting treatment efficiency and capacity (Plakas et al., 2016; Zhang et al., 2012). Thus, the 20-L BEF process was tested under three HRTs (16, 23 and 26 h), with other fixed operational parameters (an initial pharmaceutical concentration of 500 $\mu\text{g L}^{-1}$, pH of 2.8, Na_2SO_4 of 50 mM, applied voltage of 0.1 V, airflow rate of 350 mL min^{-1} and Fe^{2+} of 1 mM). Fig. 5 showed the corresponding degradation efficiency of the six selected pharmaceuticals. There was a clear relationship between HRT and degradation efficiency. The higher degradation efficiency was obtained when the longer HRT was set. The pharmaceuticals (except ibuprofen which reached 100% removal at HRT of 16 h) removal rates ranged from 80% to 85% when HRT was 16 h. The previous study on using moving bed biofilm reactor (MBBR) technology for the removal of six selected pharmaceuticals also obtained the highest removal efficiency of ibuprofen

(94%), followed by diclofenac (85%), naproxen (80%), ketoprofen (63%), clofibric acid (5%), and carbamazepine (0%) (Zupanc et al., 2013). When extending HRT to 23 h, 100% removal of carbamazepine, clofibric acid, ketoprofen, diclofenac and ibuprofen, and 90% removal of naproxen were observed. Finally, all the pharmaceuticals can be completely removed at HRT of 26 h. These results suggest by adjusting the HRT of the BEF reactor, it is possible to achieve adequate removal of pharmaceuticals. The reason can be that there was sufficient reaction time between the generated $\cdot\text{OH}$ and pharmaceuticals, and thus more $\cdot\text{OH}$ was involved in the degradation of pharmaceuticals with the extension of HRT. It is notable that the selected pharmaceuticals were treated without operational problems and can be entirely removed without the addition of other oxidant agents like H_2O_2 and O_3 . The results indicate the suitability of this system to treat pharmaceuticals-containing wastewater. Based on the removal rates, HRT of 26 h was chosen for the following experiments.

3.2.4 Effect of different initial catholyte Fe^{2+} concentration

It has been reported widely in EF and BEF process literature that one of the key prerequisites is the dosing of Fe^{2+} , which is not harmful and can significantly affect the oxidation of organic pollutants, as it can react with H_2O_2 to produce $\cdot\text{OH}$ radicals (Brillas et al., 2009; Nadais et al., 2018).

The influence of initial Fe^{2+} dosage (0.3, 0.5, 1.0, 2.0 and 4 mM) on pharmaceuticals degradation was investigated with a set of defined parameters (initial pharmaceutical concentration of $500\text{ }\mu\text{g L}^{-1}$, pH of 2.8, Na_2SO_4 of 50 mM, applied voltage of 0.1 V, HRT of 26 h and air flow rate of 350 mL min^{-1}). The initial concentration of Fe^{2+} did have an obvious influence on the pharmaceutical removal (see in Fig. 6) because when it was between 0.3 and 0.5 mM, the rapid and complete removal of all six selected pharmaceuticals was observed. However, the removal efficiency and rate of the six selected pharmaceuticals decreased by increasing Fe^{2+} concentrations further (to 1, 2 and 4 mM). For example, removal rate for clofibric acid, diclofenac, carbamazepine, naproxen, and ketoprofen was around 70% on average at an initial Fe^{2+} concentration of 4 mM, while an average

removal rate of 80% was achieved at an initial 2 mM dose of Fe^{2+} . The Fe^{2+} concentration was able to positively affect the organic pollutant degradation performance by EF and BEF process below a certain range, and by increasing Fe^{2+} concentration further, the degradation rate may start to decrease caused by a competitive reaction between excess Fe^{2+} and $\cdot\text{OH}$, and eventually formed Fe^{3+} . (Eq. (6)).

In addition, a side reaction occurred (Eq. (7)) because excessive Fe^{2+} added could produce numerous $\cdot\text{OH}$ instantaneously (Eq. (2)), which could then further promote the consumption of $\cdot\text{OH}$ and H_2O_2 .

These reactions consumed $\cdot\text{OH}$ and H_2O_2 and resulted in the poor performance of pharmaceutical degradation (Monteil et al., 2019).

Since there were no significant differences in pharmaceutical degradation between initial Fe^{2+} dosages at 0.3 and 0.5 mM, 0.3 mM could be chosen for future applications. It has been reported that the optimum Fe^{2+} concentration for the EF process is in the range of 0.1-0.5 mM (Monteil et al., 2018; Oturan & Aaron, 2014; Sirés et al., 2014), and so the result was consistent with traditional EF process. Furthermore, compared with other lab-scale systems, the Fe^{2+} concentration required by this 20-L BEF reactor was lower (Li et al., 2017c; Nadais et al., 2018; Zhang et al., 2015b). Overall, the results imply that the 20-L BEF process could maintain the same or even lower levels of Fe^{2+} consumption.

3.2.5 Energy consumption

Energy consumption is the most expensive part of any EF process. Comparatively, BEF oxidation technology has been proven to be a more energy-efficient way to approach recalcitrant wastewater treatment (Li et al., 2017a; Li et al., 2017c; Nadais et al., 2018). In this 20-L BEF reactor, energy consumption was mainly included in two ways: electricity consumption for providing the applied

voltage, and electricity consumption for stirring and aeration. The first part can be calculated according to Eq. (8):

$$E = \frac{I \times V \times t}{V_s} \quad (8)$$

where E (kWh m^{-3}) represents power consumption regarding the applied voltage, I is the current intensity (A), V is the applied voltage (V), t is the HRT (h) and V_s is the working volume of the cathode (L). Hence, electricity consumption for the first part after one HRT based on the selected operating parameters (applied voltage of 0.1 V, Fe^{2+} concentration of 0.3 mM and HRT of 26 h), was $8.67 \times 10^{-3} \text{ kWh m}^{-3}$.

Energy consumption for the second part was 0.44 kWh after one HRT, equating to $48.889 \text{ kWh m}^{-3}$. Therefore, the final total figure was 48.89 kWh m^{-3} , which means that energy consumption in terms of the 20-L BEF reactor mainly contributed by aeration with a ratio of 99.98%. Our previous studies provided information about reactor cost and electricity price, which were approximately 930 € m^{-3} and 0.13 € kWh^{-1} , respectively (Li et al., 2017b; Nadais et al., 2018). Accordingly, the operating cost for treating 1 m^3 of such pharmaceuticals containing wastewater was 5.84 €. To the best of our knowledge, most previous works have focused only on energy consumption for the first part. For example, in a previous study, using an 80 mL lab-scale BEF reactor for NSAIDs-containing wastewater treatment, energy consumption for applied voltage was $29.875 \text{ kWh m}^{-3}$ (Nadais et al., 2018). Besides, it should be mentioned that the concentration of treated pollutants which was of 40 μg L^{-1} of each four NSAIDs for the lab-scale reactor against 500 μg L^{-1} of each six selected pharmaceuticals including that four NSAIDs for our 20-L reactor. Therefore, assuming the treatment of the same amount of pollutants as the continuous operation, the operation cost of 80 mL lab-scale BEF process in batch mode was as high as 71.25 €. Besides the reactor volume and/or the concentration of the pharmaceuticals, the difference in electricity consumption could be the electrolyte and the type and the effective size of the electrode. Greater effort should there be expended to optimize cathode aeration further and to reduce total energy consumption, thus

reducing overall treatment costs. In addition, some renewable energy sources such as wind energy and solar energy can be used to drive the reactor in the future to further reduce energy consumption. In general terms, the 20-L BEF process could become a competitive and energy-saving technology applied to wastewater treatment when it contains pharmaceuticals.

3.3 The pharmaceuticals transformation pathway in BEF system

Understanding the transformation pathway and intermediate products of pollutants is important, in order to evaluate the treatment process better, especially in a 20-L BEF system. Among the six selected pharmaceuticals, clofibric acid has attracted widespread attention because it was difficult to be degraded by traditional biological treatments and can persist in the aquatic environment. For example, it has been found that the removal rate of clofibric acid by traditional WWTP was only 55%, while the half-life of photolytic clofibric acid in the natural environment can be as long as 250 days in winter (Li et al., 2010). Thus, clofibric acid was selected as an example, and its transformation pathway in the 20-L BEF process was investigated by using the HPLC-MS/MS under MS2 scan. As can be seen from the obtained total ion chromatogram (Fig. S3), two main peaks of the suspected were observed at retention times of 2.73 and 10.85 min, respectively. Furthermore, the mass spectrum of each of the two peaks was studied and exhibited in Fig. S4. Since clofibric acid was analyzed in negative ionization mode ($[M - H]^-$), five main products with molecular ion peaks of m/z 112.9 (2.73 min), 144.8 (2.73 min), 188.9 (2.73 min), 248.8 (10.85 min) and 265.0 (10.85 min) have been found, respectively. Peaks of m/z 112.9, 144.8 and 265.0 were individually elucidated as chlorobenzene, 4-chlorocatechol and 2-(4-chlorophenoxy)-2-methylpropanoic acid compound with methanol and hydrogen peroxide (1:1:1), respectively. Among of which, except for 4-chlorocatechol, the rest of transformation products above mentioned have also been observed in previous studies regarding the removal of clofibric acid by UV/chlorine disinfection, photocatalytic, EF and photo EF processes (Chen et al., 2017; Sirés et al., 2007; Tang et al., 2018).

Based on the MS/MS analysis and previous studies (Chen et al., 2017; Sirés et al., 2007; Tang et al., 2018), two transformation pathways of clofibric acid in the 20-L BEF process were then proposed (Fig. 7). As described by frontier orbital theory, the C-position of clofibric acid with higher values of $FED_{HOMO}^2 + FED_{LUMO}^2$ can be attacked easier by $\cdot OH$, where FED_{HOMO} represents frontier electron densities (FED) of the highest occupied molecular orbital (HOMO) and FED_{LUMO} represents FEDs of the lowest occupied molecular orbital (LUMO) (Chen et al., 2017; Wahab et al., 2009). The previous study has demonstrated that the C-positions of clofibric acid, including the C1, C2, C5, C6 and C7 sites (shown in Fig.7), have higher $FED_{HOMO}^2 + FED_{LUMO}^2$ values (Chen et al., 2017). Both pathways incited an electrophilic adduct reaction by $\cdot OH$, following which multi-hydroxylation intermediate products formed. In pathway 1, the C1 and C7 sites were attacked simultaneously by $\cdot OH$ and formed P1 (m/z 248.8), which was then attacked by $\cdot OH$ via demethylation and decarboxylation processes, thereby forming P2 (m/z 188.9). In addition, the stable byproduct of 4-chlorocatechol (m/z 144.8) formed after further demethylation and decarboxylation processes (Wahab et al., 2009). Ultimately, the 4-chlorocatechol could be oxidized to form small-molecule chlorobenzene (m/z 112.9). 4-chlorocatechol and chlorobenzene were also detected in removing clofibric acid during EF, photo EF and photocatalytic processes (Chen et al., 2017; Sirés et al., 2007). Further verification was performed by comparing mass spectra and retention time of samples to the standard purchased from Sigma-Aldrich (Munich, Germany). The results indicated that the suspected transformation products with the retention time (2.73 min) and mass spectra (m/z=144.8) was confirmed to be 4-chlorocatechol, as a transformation product during clofibric acid degradation in the 20-L BEF process (see SI Fig. S3 for details).

In pathway 2, the C2 site was attacked by $\cdot OH$ and formed P3 (m/z 265). Previous studies have demonstrated that the initial generation of mono-hydroxylation product 2-(4-chloro-3-hydroxyphenoxy)-2-methyl-propionic acid can be achieved by $\cdot OH$ attacks at the C2 site forms initially, which was also detected in current work (Chen et al., 2017; Zhang et al., 2018). Thereafter, the P3

was formed during further oxidation. In summary, these intermediate products were oxidized further by $\cdot\text{OH}$ to form the smaller molecule products and finally mineralized into CO_2 and H_2O .

3.4 Applied to real wastewater

In fact, the discharge of treated effluent from WWTP was the main route for micropollutants to enter the aquatic environment (Luo et al., 2014). Thus, the applicability of the 20-L BEF process for removing the pharmaceuticals in real wastewater after secondary biological treatment was evaluated. The detail characteristics of wastewater can be seen in Table S3. The operation parameters settings were based on the integration of the optimized settings in section 3.2. In addition, applied voltage (0.1 and 0.2 V) and HRT (26 and 36 h) were varied during the test to observe the corresponding changes in the pharmaceuticals removal rate. As shown in Fig. 8, 37-90% of six selected pharmaceuticals were removed in real wastewater matrix at the applied voltage of 0.1 V and HRT of 26 h, which were relatively lower than that achieved removal rates from the laboratory water distribution (100% removal) under the same condition. The reason can be summarized as the following. Firstly, natural organic matters (NOM) in real wastewater may consume the generated $\cdot\text{OH}$ and resulted in a lower removal rate (Nadais et al., 2018). Secondly, the real wastewater had lower ionic strength compared to the synthetic wastewater, which resulted in relatively lower current (Fig. S6) and caused a drop in $\cdot\text{OH}$ production and eventually affected treatment efficiency (Moreira et al., 2017; Nadais et al., 2018; Thiam et al., 2015). Thirdly, the inhibition effect of inorganic ions such as phosphate (Table S3) in real wastewater could also lower the treatment efficiency. The previous study has found that the formation of Fe^{3+} -phosphate complexes led to the reduction in micropollutants removal efficiency during Fenton processes (Antonin et al., 2015; Nadais et al., 2018; Wang et al., 2016).

Considering the low treatment performance observed at 0.1 V, raise the applied voltage further to 0.2 V and exhibited an obviously improved removal rate of six selected pharmaceuticals over two HRTs (Fig. 8). The removal rate of clofibric acid, diclofenac carbamazepine, naproxen, ibuprofen

and ketoprofen increased from 44%, 66%, 37%, 89%, 85% and 58% to 78%, 87%, 76%, 96%, 92% and 86%, respectively. The variation in effluent pH showed the same trend as using synthetic wastewater (Fig. S6), which increased slightly from 2.8 to 3.4 when increasing the applied voltage from 0.1 to 0.2 V after two HRTs. The reason can be attributed to the increase in current with a relatively higher-high voltage which enhanced the $\cdot\text{OH}$ production and improved the removal rate. Furthermore, the removal rate of six selected pharmaceuticals was improved by further extending HRT to 36 h. As also exhibited in Fig. 8, the removal rate of the six selected pharmaceuticals first increased from 78 to 94 h and then significantly decreased in the remaining 20 h. This phenomenon could be due to the rapid rise of cathodic pH. pH in the effluent (as seen in Fig. S6) presented a slight increase (3.4 to 4.0) from 78 to 94 h and then rapidly increased from 4.0 to 6.3 in the remaining 20 h. Previous studies found that optimum pH was ranging from 2.0 to 4.0 for EF and BEF oxidation processes (Fan et al., 2010; Flox et al., 2006; Nadais et al., 2018). Therefore, the reasons for the reduction in removal efficiency obtained after 94 h can be summarized into the following: 1) the rapid rise of pH caused the precipitation of iron; 2) carbonate and bicarbonate can exist when pH was above 5, which can further eliminate $\cdot\text{OH}$; 3) the generated H_2O_2 could decompose to O_2 and H_2O automatically when pH was above 5 (Moreira et al., 2017). Therefore, the removal rate can be increased by further controlling pH in the cathode chamber. In addition, the TOC removal rate was only 35% at 0.1 V, while it increased to 64% at 0.2 V after two HRTs (Fig. S6). When the HRT was extended to 36 h, the TOC removal rate in the first 16 h was 82% and then decreased to 52% in the remaining 20 h. The above results demonstrate the potential of the 20-L BEF process for practical application in real wastewater treatment.

Overall, the pH adjustment and low conductivity in real wastewater could be the key challenges for practical application. In the future, more efforts should be made to develop novel cathodic catalysts that can allow the Fenton reaction under neutral conditions. The conductivity issue could be addressed by combining two different wastewaters of varying conductivity.

3.5 Implications

This study demonstrated the applicability of continuous treatment of pharmaceuticals-contaminated wastewater using the scaled-up BEF process. Compared with the lab-scale BEF process, it has the following advantages: 1) efficient treatment of high-load pharmaceuticals-contaminated wastewater; 2) lower operating costs for treating 1 m³ wastewater with the content of same pharmaceuticals (5.84 € vs. 71.25 €); 3) less addition of iron (0.3 mM vs. 7.5 mM). Though promising, several challenges still need to be addressed: 1) the need for pH adjustment before and after treatment; 2) iron sludge; 3) energy consumption mainly contributed by pumping and stirring.

To address the above challenges, more efforts should be made to develop novel catalysts that can enable the scaled-up BEF process under neutral conditions in the future. Furthermore, it is also possible to increase the gas-liquid mass transfer efficiency by designing the reactor configuration to further reduce the energy consumption of aeration.

4. Conclusions

This work presents that successfully designing and utilizing an innovative 20-L BEF system for continuously removing high concentration pharmaceuticals from wastewater. Six selected pharmaceuticals were completely removed with lower operating cost and followed by the pseudo-first-order kinetics. Moreover, a transformation pathway of clofibric acid was proposed according to the HPLC-MS/MS analysis of transformation products. Finally, the application in actual wastewater also exhibited good performance. The above results highlighted the feasibility of scaling-up BEF process as an efficient and cost-effective technology applied to pharmaceuticals containing wastewater treatment for future commercial application.

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References

- Antonin, V.S., Santos, M.C., Garcia-Segura, S., Brillas, E., 2015. Electrochemical incineration of the antibiotic ciprofloxacin in sulfate medium and synthetic urine matrix. *Water Res.* 83, 31–41. <https://doi.org/10.1016/j.watres.2015.05.066>
- Bouissou-Schurtz, C., Houeto, P., Guerbet, M., Bachelot, M., Casellas, C., Mauclaire, A.-C., Panetier, P., Delval, C., Masset, D., 2014. Ecological risk assessment of the presence of pharmaceutical residues in a French national water survey. *Regul. Toxicol. Pharmacol.* 69, 296–303. <https://doi.org/10.1016/j.yrtph.2014.04.006>
- Brillas, E., Sirés, I., Oturan, M.A., 2009. Electro-Fenton process and related electrochemical technologies based on Fenton's reaction chemistry. *Chem. Rev.* 109, 6570–6631. <https://doi.org/10.1021/cr900136g>
- Chen, P., Wang, F., Zhang, Q., Su, Y., Shen, L., Yao, K., Chen, Z.-F., Liu, Y., Cai, Z., Lv, W., 2017. Photocatalytic degradation of clofibric acid by g-C₃N₄/P25 composites under simulated sunlight irradiation: the significant effects of reactive species. *Chemosphere* 172, 193–200. <https://doi.org/10.1016/j.chemosphere.2017.01.015>
- Estrada, A.L., Li, Y.-Y., Wang, A., 2012. Biodegradability enhancement of wastewater containing cefalexin by means of the electro-Fenton oxidation process. *J. Hazard. Mater.* 227, 41–48. <https://doi.org/10.1016/j.jhazmat.2012.04.079>
- Fan, Y., Ai, Z., Zhang, L., 2010. Design of an electro-Fenton system with a novel sandwich film cathode for wastewater treatment. *J. Hazard. Mater.* 176, 678–684. <https://doi.org/10.1016/j.jhazmat.2009.11.085>
- Feng, C.-H., Li, F.-B., Mai, H.-J., Li, X.-Z., 2010. Bio-electro-Fenton process driven by microbial fuel cell for wastewater treatment. *Environ. Sci. Technol.* 44, 1875–1880. <https://doi.org/10.1021/es9032925>

- Flox, C., Ammar, S., Arias, C., Brillas, E., Vargas-Zavala, A.V., Abdelhedi, R., 2006. Electro-Fenton and photoelectro-Fenton degradation of indigo carmine in acidic aqueous medium. *Appl. Catal. B Environ.* 67, 93–104. <https://doi.org/10.1016/j.apcatb.2006.04.020>
- Gurke, R., Rößler, M., Marx, C., Diamond, S., Schubert, S., Oertel, R., Fauler, J., 2015. Occurrence and removal of frequently prescribed pharmaceuticals and corresponding metabolites in wastewater of a sewage treatment plant. *Sci. Total Environ.* 532, 762–770. <https://doi.org/10.1016/j.scitotenv.2015.06.067>
- Hassan, M., Pous, N., Xie, B., Colprim, J., Balaguer, M.D., Puig, S., 2017. Employing Microbial Electrochemical Technology-driven electro-Fenton oxidation for the removal of recalcitrant organics from sanitary landfill leachate. *Bioresour. Technol.* 243, 949–956. <https://doi.org/10.1016/j.biortech.2017.07.042>
- Hey, G., Ledin, A., Jansen, J. la C., Andersen, H.R., 2012. Removal of pharmaceuticals in biologically treated wastewater by chlorine dioxide or peracetic acid. *Environ. Technol.* 33, 1041–1047. <https://doi.org/10.1080/09593330.2011.606282>
- Hu, D., Li, X., Chen, Z., Cui, Y., Gu, F., Jia, F., Xiao, T., Su, H., Xu, J., Wang, H., 2018. Performance and extracellular polymers substance analysis of a pilot scale anaerobic membrane bioreactor for treating tetrahydrofuran pharmaceutical wastewater at different HRTs. *J. Hazard. Mater.* 342, 383–391. <https://doi.org/10.1016/j.jhazmat.2017.08.028>
- Kahoush, M., Behary, N., Cayla, A., Nierstrasz, V., 2018. Bio-Fenton and Bio-electro-Fenton as sustainable methods for degrading organic pollutants in wastewater. *Process Biochem.* 64, 237–247. <https://doi.org/10.1016/j.procbio.2017.10.003>
- Kvesitadze, G., Sadunishvili, T., Dudaui, T., Zakariashvili, N., Partskhaladze, G., Ugrekhelidze, V., Tsiklauri, G., Metreveli, B., Jobava, M., 2012. Two-stage anaerobic process for bio-hydrogen and bio-methane combined production from biodegradable solid wastes. *Energy* 37, 94–102. <https://doi.org/10.1016/j.energy.2011.08.039>

- Kümmerer, K., 2001. Drugs in the environment: emission of drugs, diagnostic aids and disinfectants into wastewater by hospitals in relation to other sources—a review. *Chemosphere* 45, 957–969. [https://doi.org/10.1016/S0045-6535\(01\)00144-8](https://doi.org/10.1016/S0045-6535(01)00144-8)
- Labiadh, L., Oturan, M.A., Panizza, M., Hamadi, N. Ben, Ammar, S., 2015. Complete removal of AHPS synthetic dye from water using new electro-fenton oxidation catalyzed by natural pyrite as heterogeneous catalyst. *J. Hazard. Mater.* 297, 34–41. <https://doi.org/10.1016/j.jhazmat.2015.04.062>
- Laurencé, C., Rivard, M., Martens, T., Morin, C., Buisson, D., Bourcier, S., Sablier, M., Oturan, M.A., 2014. Anticipating the fate and impact of organic environmental contaminants: a new approach applied to the pharmaceutical furosemide. *Chemosphere* 113, 193–199. <https://doi.org/10.1016/j.chemosphere.2014.05.036>
- Li, W., Lu, S., Qiu, Z., Lin, K. 2010. Clofibric acid degradation in UV254/H₂O₂ process: Effect of temperature. *J. Hazard. Mater.* 176(1-3), 1051-1057. <https://doi.org/10.1016/j.jhazmat.2009.11.147>
- Li, X., Jin, X., Zhao, N., Angelidaki, I., Zhang, Y., 2017a. Novel bio-electro-Fenton technology for azo dye wastewater treatment using microbial reverse-electrodialysis electrolysis cell. *Bioresour. Technol.* 228, 322–329. <https://doi.org/10.1016/j.biortech.2016.12.114>
- Li, X., Jin, X., Zhao, N., Angelidaki, I., Zhang, Y., 2017b. Efficient treatment of aniline containing wastewater in bipolar membrane microbial electrolysis cell-Fenton system. *Water Res.* 119, 67–72. <https://doi.org/10.1016/j.watres.2017.04.047>
- Li, X., Zhang, R., Qian, Y., Angelidaki, I., Zhang, Y., 2017c. The impact of anode acclimation strategy on microbial electrolysis cell treating hydrogen fermentation effluent. *Bioresour. Technol.* 236, 37–43. <https://doi.org/10.1016/j.biortech.2017.03.160>

- Liu, D., Zhang, H., Wei, Y., Liu, B., Lin, Y., Li, G., Zhang, F., 2018. Enhanced degradation of ibuprofen by heterogeneous electro-Fenton at circumneutral pH. *Chemosphere* 209, 998–1006. <https://doi.org/10.1016/j.chemosphere.2018.06.164>
- 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. *Sci. Total Environ.* 473, 619–641. <https://doi.org/10.1016/j.scitotenv.2013.12.065>
- Monteil, H., Péchaud, Y., Oturan, N., Oturan, M.A., 2019. A review on efficiency and cost effectiveness of electro-and bio-electro-Fenton processes: application to the treatment of pharmaceutical pollutants in water. *Chem. Eng. J.* 376, 119577. <https://doi.org/10.1016/j.cej.2018.07.179>
- Moreira, F.C., Boaventura, R.A.R., Brillas, E., Vilar, V.J.P., 2017. Electrochemical advanced oxidation processes: a review on their application to synthetic and real wastewaters. *Appl. Catal. B Environ.* 202, 217–261. <https://doi.org/10.1016/j.apcatb.2016.08.037>
- Nadai, H., Li, X., Alves, N., Couras, C., Andersen, H.R., Angelidaki, I., Zhang, Y., 2018. Bio-electro-Fenton process for the degradation of Non-Steroidal Anti-Inflammatory Drugs in wastewater. *Chem. Eng. J.* 338, 401–410. <https://doi.org/10.1016/j.cej.2018.01.014>
- Olvera-Vargas, H., Oturan, N., Buisson, D., Oturan, M.A., 2016. A coupled bio-EF process for mineralization of the pharmaceuticals furosemide and ranitidine: feasibility assessment. *Chemosphere* 155, 606–613. <https://doi.org/10.1016/j.chemosphere.2016.04.091>
- Oturan, M.A., Aaron, J.-J., 2014. Advanced oxidation processes in water/wastewater treatment: principles and applications. A review. *Crit. Rev. Environ. Sci. Technol.* 44, 2577–2641. <https://doi.org/10.1080/10643389.2013.829765>
- Papageorgiou, M., Kosma, C., Lambropoulou, D., 2016. Seasonal occurrence, removal, mass loading and environmental risk assessment of 55 pharmaceuticals and personal care products

- in a municipal wastewater treatment plant in Central Greece. *Sci. Total Environ.* 543, 547–569.
<https://doi.org/10.1016/j.scitotenv.2015.11.047>
- Plakas, K. V., Sklari, S.D., Yiankakis, D.A., Sideropoulos, G.T., Zaspalis, V.T., Karabelas, A.J.,
2016. Removal of organic micropollutants from drinking water by a novel electro-Fenton filter:
pilot-scale studies. *Water Res.* 91, 183–194. <https://doi.org/10.1016/j.watres.2016.01.013>
- Sirés, I., Arias, C., Cabot, P.L., Centellas, F., Garrido, J.A., Rodríguez, R.M., Brillas, E., 2007.
Degradation of clofibric acid in acidic aqueous medium by electro-Fenton and photoelectro-
Fenton. *Chemosphere* 66, 1660–1669. <https://doi.org/10.1016/j.chemosphere.2006.07.039>
- Sirés, I., Brillas, E., Oturan, M.A., Rodrigo, M.A., Panizza, M., 2014. Electrochemical advanced
oxidation processes: today and tomorrow. A review. *Environ. Sci. Pollut. Res.* 21, 8336–8367.
<https://doi.org/10.1007/s11356-014-2783-1>
- Tang, Y., Shi, X., Liu, Y., Feng, L., Zhang, L., 2018. Degradation of clofibric acid in UV/chlorine
disinfection process: kinetics, reactive species contribution and pathways. *R. Soc. open Sci.* 5,
171372. <https://doi.org/10.1098/rsos.171372>
- Thiam, A., Sirés, I., Brillas, E., 2015. Treatment of a mixture of food color additives (E122, E124
and E129) in different water matrices by UVA and solar photoelectro-Fenton. *Water Res.* 81,
178–187. <https://doi.org/10.1016/j.watres.2015.05.057>
- Tran, N.H., Reinhard, M., Gin, K.Y.-H., 2018. Occurrence and fate of emerging contaminants in
municipal wastewater treatment plants from different geographical regions-a review. *Water
Res.* 133, 182–207. <https://doi.org/10.1016/j.watres.2017.12.029>
- Vandenberg, L.N., Colborn, T., Hayes, T.B., Heindel, J.J., Jacobs Jr, D.R., Lee, D.-H., Shioda, T.,
Soto, A.M., vom Saal, F.S., Welshons, W. V., 2012. Hormones and endocrine-disrupting
chemicals: low-dose effects and nonmonotonic dose responses. *Endocr. Rev.* 33, 378–455.
<https://doi.org/10.1210/er.2011-1050>

- Wahab, H.S., Bredow, T., Aliwi, S.M., 2009. A computational study on the adsorption and ring cleavage of para-chlorophenol on anatase TiO₂ surface. *Surf. Sci.* 603, 664–669. <https://doi.org/10.1016/j.susc.2009.01.001>
- Wang, F., Wu, Y., Gao, Y., Li, H., Chen, Z., 2016. Effect of humic acid, oxalate and phosphate on Fenton-like oxidation of microcystin-LR by nanoscale zero-valent iron. *Sep. Purif. Technol.* 170, 337–343. <https://doi.org/10.1016/j.seppur.2016.06.046>
- Wang, W., Lu, Y., Luo, H., Liu, G., Zhang, R., Jin, S., 2018. A microbial electro-fenton cell for removing carbamazepine in wastewater with electricity output. *Water Res.* 139, 58–65. <https://doi.org/10.1016/j.watres.2018.03.066>
- Wilkinson, J.L., Hooda, P.S., Barker, J., Barton, S., Swinden, J., 2016. Ecotoxic pharmaceuticals, personal care products, and other emerging contaminants: A review of environmental, receptor-mediated, developmental, and epigenetic toxicity with discussion of proposed toxicity to humans. *Crit. Rev. Environ. Sci. Technol.* 46, 336–381. <https://doi.org/10.1080/10643389.2015.1096876>
- Xu, N., Zeng, Y., Li, J., Zhang, Y., Sun, W., 2015. Removal of 17 β -estrodial in a bio-electro-Fenton system: contribution of oxidation and generation of hydroxyl radicals with the Fenton reaction and carbon felt cathode. *RSC Adv.* 5, 56832–56840. <https://doi.org.proxy.findit.dtu.dk/10.1039/C5RA08053C>
- Xu, N., Zhang, Y., Tao, H., Zhou, S., Zeng, Y., 2013. Bio-electro-Fenton system for enhanced estrogens degradation. *Bioresour. Technol.* 138, 136–140. <https://doi.org/10.1016/j.biortech.2013.03.157>Get rights and content
- Yong, X.-Y., Gu, D.-Y., Wu, Y.-D., Yan, Z.-Y., Zhou, J., Wu, X.-Y., Wei, P., Jia, H.-H., Zheng, T., Yong, Y.-C., 2017. Bio-Electron-Fenton (BEF) process driven by microbial fuel cells for triphenyltin chloride (TPTC) degradation. *J. Hazard. Mater.* 324, 178–183. <https://doi.org/10.1016/j.jhazmat.2016.10.047>

- Zhang, H., Choi, H.J., Huang, C.-P., 2006. Treatment of landfill leachate by Fenton's reagent in a continuous stirred tank reactor. *J. Hazard. Mater.* 136, 618–623.
<https://doi.org/10.1016/j.jhazmat.2005.12.040>
- Zhang, H., Ran, X., Wu, X., 2012. Electro-Fenton treatment of mature landfill leachate in a continuous flow reactor. *J. Hazard. Mater.* 241, 259–266.
<https://doi.org/10.1016/j.jhazmat.2012.09.040>
- Zhang, L., Yin, X., Li, S.F.Y., 2015. Bio-electrochemical degradation of paracetamol in a microbial fuel cell-Fenton system. *Chem. Eng. J.* 276, 185–192.
<https://doi.org/10.1016/j.cej.2015.04.065>
- Zhang, X., Liu, Z., Kong, Q., Liu, G., Lv, W., Li, F., Lin, X., 2018. Aquatic photodegradation of clofibric acid under simulated sunlight irradiation: kinetics and mechanism analysis. *RSC Adv.* 8, 27796–27804. <https://doi.org/10.1039/C8RA03140A>
- Zhang, Y., Angelidaki, I., 2015. Recovery of ammonia and sulfate from waste streams and bioenergy production via bipolar bioelectrodialysis. *Water Res.* 85, 177–184.
<https://doi.org/10.1016/j.watres.2015.08.032>
- Zhang, Y., Wang, Y., Angelidaki, I., 2015. Alternate switching between microbial fuel cell and microbial electrolysis cell operation as a new method to control H₂O₂ level in Bioelectro-Fenton system. *J. Power Sources* 291, 108–116.
<https://doi.org/10.1016/j.jpowsour.2015.05.020>
- Zhao, X., Qu, J., Liu, H., Qiang, Z., Liu, R. and Hu, C. 2009. Photoelectrochemical degradation of anti-inflammatory pharmaceuticals at Bi₂MoO₆-boron-doped diamond hybrid electrode under visible light irradiation. *Appl. Catal. B Environ.* 91(1-2), 539-545
<https://doi.org/10.1016/j.apcatb.2009.06.025>
- Zhou, M., Oturan, M.A., Sires, I., 2018. *Electro-Fenton Process*. Springer.
<https://doi.org/10.1007/978-981-10-6406-7>

- Zhu, X., Ni, J., 2009. Simultaneous processes of electricity generation and p-nitrophenol degradation in a microbial fuel cell. *Electrochem. commun.* 11, 274–277.
<https://doi.org/10.1016/j.elecom.2008.11.023>
- Zupanc, M., Kosjek, T., Petkovšek, M., Dular, M., Kompare, B., Širok, B., Blažeka, Ž., Heath, E. 2013. Removal of pharmaceuticals from wastewater by biological processes, hydrodynamic cavitation and UV treatment. *Ultrason. sonochem.* 20 (4), 1104-1112.
<https://doi.org/10.1016/j.ultsonch.2012.12.003>

Figure captions

Fig. 1. Schematic of BEF system structure and operation. (a) Picture of 20-L BEF system. a, Synthetic nutrient medium feed in the anode chamber; b, Effluent from the anode chamber; c, Anode chamber; d, Cathode chamber; e, Synthetic pharmaceutical wastewater feed in the cathode chamber (Pharmaceuticals: carbamazepine, clofibric acid, ketoprofen, naproxen, diclofenac, ibuprofen); f, Effluent in the cathode chamber (treated pharmaceutical wastewater). (b) Graphical configuration of the electrode arrangement. (c) Flow chart of 20-L BEF system under operation condition.

Fig. 2. System performance on the degradation of six selected pharmaceuticals. Control 1, open circuit; Control 2, without air flow in the cathode; Control 3, without Fe^{2+} addition. BEF operational conditions: initial concentration of each pharmaceutical was $500 \mu\text{g L}^{-1}$, initial pH of 3, Fe^{2+} of 1 mM, Na_2SO_4 of 50 mM, applied voltage of 0.2 V (for the control experiment) and air flow rate of 350 mL min^{-1} .

Fig. 3. The effect of applied voltage on system performance. BEF operational conditions: initial concentration each pharmaceutical was $500 \mu\text{g L}^{-1}$, initial pH of 2.8, Fe^{2+} of 1 mM, Na_2SO_4 of 50 mM, HRT of 23 h, and air flow rate of 350 mL min^{-1} .

Fig. 4. The effect of the initial concentration of six selected pharmaceuticals on system performance. BEF operational conditions: initial pH of 2.8, Fe^{2+} of 1 mM, Na_2SO_4 of 50 mM, HRT of 23 h, and air flow rate of 350 mL min^{-1} .

Fig.5. The effect of HRT on system performance. BEF operational conditions: initial concentration each pharmaceutical was $500 \mu\text{g L}^{-1}$, initial pH of 2.8, Fe^{2+} of 1 mM, Na_2SO_4 of 50 mM, and air flow rate of 350 mL min^{-1} .

Fig.6. The effect of initial Fe^{2+} concentration on system performance. BEF operational conditions: initial concentration of each pharmaceutical was $500 \mu\text{g L}^{-1}$, initial pH of 2.8, applied voltage of 0.1 V, Na_2SO_4 of 50 mM, HRT of 26 h, and air flow rate of 350 mL min^{-1} .

Fig.7. Proposed clofibric acid transformation pathway during this 20-L BEF system.

Fig.8. The effect of the water matrix on the degradation of six selected pharmaceuticals by this 20-L BEF system. BEF operational conditions: initial concentration of each pharmaceutical was $500 \mu\text{g L}^{-1}$, initial pH of 2.8, applied voltage of 0.1 V and 0.2 V, HRT of 26 h and 36 h, and air flow rate of 350 mL min^{-1} .

Table 1. Summary of studies on the BEF process degradation of pharmaceuticals

Pollutants	Reactor design	BEF system volume	Optimized operational parameters	Removal rate	Operation mode	Reference
NSAIDs	Ketoprofen Diclofenac Ibuprofen Naproxen	Two chambers	The total volume of each chamber was 100 mL (80 mL of working volume)	Initial concentration of 40 $\mu\text{g L}^{-1}$ for each compound, Fe^{2+} of 7.5 mM, pH of 2, applied voltage of 0.3 V and air flow rate of 8 mL min^{-1}	59–61% removal of ketoprofen, 87–97% removal of diclofenac, 80–86% removal of ibuprofen and 75–81% removal of naproxen in 5 h	Batch (Nadaï et al., 2018)
Anticonvulsants	Carbamazepine	Single chamber	28 mL	Initial concentration of 10 mg L^{-1} , Na_2SO_4 of 5 g L^{-1} and 0.18 g L^{-1} of Fe-Mn binary oxide as a catalyst coated on the surface of the cathode	90% removal in 24 h.	Batch (Wang et al., 2018)
Prescription and OTC medication	Paracetamol	Two chambers	The working volume of cathode and anode chamber were 216 mL and 108 mL,	Initial concentration of 10 mg L^{-1} , Fe^{2+} of 5 mg L^{-1} , pH of 2, external resistance of 20 Ω	70% removal in 9 h	Batch (Zhang et al., 2015a)

Estrogen	17 α -ethynyl estradiol (EE2) 17 β -estradiol (E2)	Two chambers	respectively The working volume of each chamber was 75 mL	and air flow rate of 16.7 mL min ⁻¹ Initial concentration of 10 mg L ⁻¹ , Fe ²⁺ of 5 mg L ⁻¹ , pH of 2, external resistance of 20 Ω and air flow rate of 16.7 mL min ⁻¹	81% removal of E2 and 56% removal of EE2 in 10 h	Batch	(Xu et al., 2013)
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Table 1. (Continued)

Pollutants	Reactor design	BEF system volume	Optimized operational parameters	Removal rate	Operation mode	Reference
Estrogen	17 β -estradiol (E2)	Two chambers	The working volume of each chamber was 75 mL	Initial concentration of 0.12 mg L ⁻¹ , pH of 3, external resistance of 150 Ω and NaCl of 0.1 M	90% removal in 6 h	Batch (Xu et al., 2015)
Emerging contaminants	Bisphenol A (BPA) Estrone (E1) Sulfamethazine (SM2) Triclocarban (TCC)	Two chambers	The total volume of each chamber was 120 mL (64 mL of	Initial concentration of 1 mg L ⁻¹ for each compound, Fe ²⁺ of 1.25 mM, pH of 3, and Na ₂ SO ₄ of 0.1 M	100% of E1 and SM2, 99% of TCC, and 75% BPA in 24 h	Batch (Wang et al., 2017)

pharmaceutic als	Ketoprofen	Two chambe rs	The total volum e of each chamb er was 10 L (9 L of workin g volum e)	Initial concentrati on of 500 $\mu\text{g L}^{-1}$ for each compound, Fe^{2+} of 0.3 mM, Na_2SO_4 50 mM, Initial pH of 2.8, applied voltage of 0.1 V, HRT of 26 h	100% remova l in 26 h	Batch and contin ue	In this study
	Diclofenac						
	Ibuprofen						
	Naproxen						
	Carbamazepine						
	Clofibric acid						

CRedit authorship contribution statement

Rusen Zou: Methodology, Validation, Formal analysis, Writing - original draft. Irini Angelidaki: Resources, Supervision, Validation, Funding acquisition. Xiaoyong Yang: Investigation, Visualization. Kai Tang: Investigation, Visualization. Henrik Rasmus Andersen: Resources, Validation. Yifeng Zhang: Conceptualization, Resources, Supervision, Funding acquisition.

Declaration of competing interest

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

Journal Pre-proof

Graphical abstract

Highlights

- A 20-L BEF reactor was built for continuous pharmaceuticals wastewater treatment.
- Pharmaceuticals were completely removed with low energy consumption.
- The key operational parameters were investigated in 20-L BEF process.
- Two transformation pathways and six transformation products were identified.
- Successfully applied in continuous removal of pharmaceuticals in real wastewater.

Figure 1

Figure 2

Figure 3

Figure 4

Figure 5

Figure 6

Figure 7

Figure 8