



Application of Fenton-like oxidation as pre-treatment for carbamazepine biodegradation



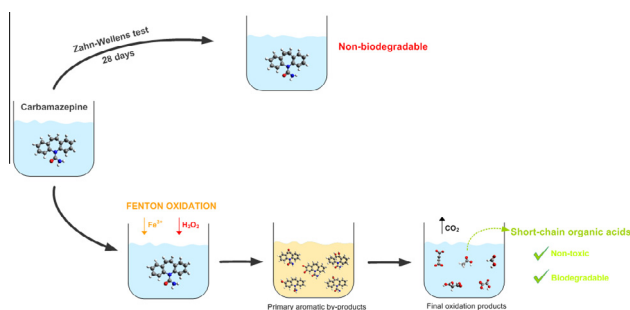
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HIGHLIGHTS

- CBZ inhibits the microbial activity being essentially non-biodegradable.
- Fenton oxidation allowed complete conversion of CBZ under mild operating conditions.
- The mineralization efficiency was increased by increasing the temperature.
- Aromatic intermediates were converted into non-toxic short-chain organic acids.
- Fenton oxidation of CBZ enhanced the biodegradability and reduced the toxicity.

GRAPHICAL ABSTRACT



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ABSTRACT

Degradation of carbamazepine (CBZ) upon Fenton-like oxidation has been investigated analyzing the effect of H_2O_2 dose and temperature at a very low catalyst concentration (2 mg L^{-1} of Fe^{3+}). Fenton-like oxidation allowed complete conversion of CBZ, the oxidation rate depending on the amount of H_2O_2 used. The addition of the theoretical stoichiometric amount of H_2O_2 led to the complete conversion of CBZ in 1 h reaction time. The reduction of the H_2O_2 initial concentration down to 10% of the stoichiometric led to a significant increase of that time up to 3 h. The mineralization efficiency of H_2O_2 was considerably increased by increasing the temperature (from 21 to 131 mg TOC/g H_2O_2 at 35 and 50 °C, respectively). Beyond 50 °C no significant effect was observed in the extension of reaction although it proceeded at significantly higher rate. The toxicity and biodegradability of the resulting effluents from Fenton-like oxidation were evaluated by respirometric tests using non-acclimated activated sludge. CBZ strongly inhibits the microbial activity ($\text{EC}_{50} = 1.8 \text{ mg L}^{-1}$) being essentially non-biodegradable. Fenton-like oxidation of CBZ (10 mg L^{-1}) at 50 °C with the theoretical stoichiometric H_2O_2 amount for complete mineralization ($5.6 \text{ mg H}_2\text{O}_2/\text{mg CBZ}$) allowed obtaining an easily biodegradable effluent.

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1. Introduction

There is an increasing concern on the presence of trace organic chemicals, such as pharmaceutically active species, personal care

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products, endocrine disruptors and pesticides, in water bodies. Approximately 3000 different pharmaceutical ingredients with different specific activity are used in Europe nowadays. Since these compounds commonly undergo transformations in the human body more or less complex combinations of them and their corresponding metabolites are excreted. Among the trace xenobiotics discharged into the aqueous media pharmaceuticals and personal care products are widely represented by a number of compounds largely consumed in modern societies, including drugs (antibiotics,

tranquillizers, anti-epileptics, etc.), hormones (natural and synthetic), X-ray contrast media, musk fragrances and phytosanitary products among others. These substances can cause different unique impacts on aquatic and terrestrial organisms [1,2]. Moreover, many of them are bioaccumulative since they have been specifically designed to cause biological effects even at trace levels.

Carbamazepine (CBZ), an anticonvulsant and mood-stabilizing drug mainly used for the treatment of epilepsy, bipolar disorder and trigeminal neuralgia, has been found in surface waters. This compound is discharged from private households and from hospitals and eventually reaches municipal wastewater treatment plants (WWTP) [3]. Low removal efficiencies of CBZ (below 10%) are achieved in conventional wastewater treatment plants due to its low biodegradability as well as the poor sorption capacity onto activated sludge [4,5]. Therefore, WWTP effluents are important gateways where carbamazepine can enter the water cycle. Ternes [6] reported the presence of CBZ in 30 WWTP effluents and in 24 of 26 samples from 20 rivers with a 90-percentile of 3.7 and $0.82 \mu\text{g L}^{-1}$, respectively. The maximum concentration of carbamazepine in WWTP effluents was $6.3 \mu\text{g L}^{-1}$, which was also the maximum concentration detected of all the 32 drugs analyzed in the survey.

Recently, different advanced oxidation processes (AOPs) have been evaluated to remove CBZ from wastewater [7]. Among the AOPs, Fenton oxidation combines some interesting features, like high performance, simplicity of design and both low cost and low toxicity of the reagents used. This process is based on the generation of hydroxyl radicals from hydrogen peroxide decomposition catalyzed by iron salts in acidic medium. Fenton and photo-Fenton processes are among the AOPs most widely studied for CBZ breakdown [8–11]. The potential application of heterogeneous Fenton oxidation for CBZ removal has been explored using nano-magnetite as catalyst. Sun et al. [12] used a modified Fenton process with ferric-nitritotriacetate complexes to prevent iron precipitation. Additionally, it has been proved that the estrogenic activity of CBZ and its degradation by-products can be effectively neutralized by Fenton oxidation and ferro-sonication, its combination with ultrasonication [13].

The ability of AOPs to reduce the toxicity and improve the biodegradability of recalcitrant compounds has been previously explored [14–16]. The main goal of those studies was to transform the persistent organic compounds into easily biodegradable intermediates, which would be then removed upon biological treatment. In many cases, these chemical oxidation pre-treatments can significantly reduce the toxicity of the starting pollutants but in some others, depending on the operating conditions, the resulting by-products can still be structurally similar to the original toxic and/or non-biodegradable compounds [17–19]. Thus, the effect of a preliminary chemical oxidation step can eventually be insignificant or even negative for further biological treatability of the effluent because of the formation of more toxic and/or less-biodegradable by-products. In the case of CBZ, it is known that when it is only partially mineralized it can be transformed into acride, a highly toxic by-product, under sunlight exposure [20]. Thereby, effective removal techniques need to be developed both in terms of yield and selectivity, while reducing the toxicity and enhancing the biodegradability of the resulting effluents so that can be effectively treated by conventional activated sludge systems.

The objective of the current study is learning on the potential application of Fenton-like ($\text{H}_2\text{O}_2/\text{Fe}^{3+}$) oxidation and its eventual combination with biological treatment (conventional activated sludge) for the abatement of CBZ. For this purpose, the effect of the H_2O_2 concentration and temperature will be analyzed as the main operating conditions in the Fenton-like oxidation step working always at very low iron concentration (2 mg L^{-1}). The toxicity

and biodegradability of the resulting effluents will be evaluated through respirometric tests.

2. Materials and methods

2.1. Fenton-like experiments

Fenton-like oxidation was carried out in stoppered glass batch flasks shaken in a constant-temperature bath at an equivalent stirring velocity around 200 rpm for 3 h. The reaction volume was 50 mL and the initial pH was adjusted to 3 with nitric acid, which is the well-known optimum for this process [21]. The starting concentration of CBZ was 10 mg L^{-1} in all the experiments. This is much higher than the trace concentrations commonly found in water bodies and wastewaters but allows better detection of the reaction by-products. The H_2O_2 concentration was tested within 10–100% of the theoretical stoichiometric amount for the complete mineralization of CBZ ($5.6 \text{ mg H}_2\text{O}_2/\text{mg CBZ}$) a fairly low concentration of catalyst ($2 \text{ mg L}^{-1} \text{ Fe}^{3+}$) was always used in order to prevent an uncontrolled generation of radicals and warrant an efficient consumption of H_2O_2 [22]. This reagent was added at the start of each experiment from 33% aqueous solution. The same for Fe^{3+} , which was fed as $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ 1.5 g L^{-1} aqueous solution. The effect of temperature was analyzed within the 35–65 °C range. Each experiment was carried out by triplicate being the standard deviation less than 5% in all cases. Blanks with CBZ in absence of H_2O_2 and Fe^{3+} were also performed at all the temperatures tested.

2.2. Biodegradability tests

The Zahn-Wellens test for the evaluation of inherent biodegradability was carried out according to the OECD guidelines [23]. In this test, a mixture containing the target substance and a certain amount of activated sludge in aqueous medium is agitated and aerated at 20–25 °C under diffuse light for 28 d. The ratio between the carbon content of the sample and the dry-weight of the inoculum must range between 1 and 4. Ethylene glycol was used as reference compound to check the degradation activity of the inoculum, which was removed up to 80% in 5 d. Samples were taken periodically for measuring the concentration of the target compound. In addition, the ready biodegradability of the Fenton-like effluents was evaluated in terms of the TOC reduction after 24 h. The biodegradability was tested in parallel in three different bottles to guarantee reproducibility.

2.3. Toxicity assessment

The toxicity of CBZ over the respiratory activity of a mixed liquor was evaluated following the procedure described by Polo et al. [24]. The toxicity assessment of the effluents from Fenton-like oxidation of CBZ was performed according to the method proposed by Ricco et al. [25], based on the OECD respiration inhibition test for activated sludge [26]. This method determines the inhibition from the ratio between the specific oxygen uptake rate value (SOUR) obtained with a reference substrate (sodium acetate) and the one for that substrate mixed with different concentrations of CBZ. EC_{50} is taken as the concentration of CBZ causing a 50% reduction of the reference SOUR. Experiments were carried out at 30 °C using a biomass concentration of $350 \text{ mg volatile suspended solids (VSS) L}^{-1}$.

2.4. Analytical methods

The progress of Fenton-like oxidation was followed periodically by withdrawing and analyzing liquid samples from the reactor.

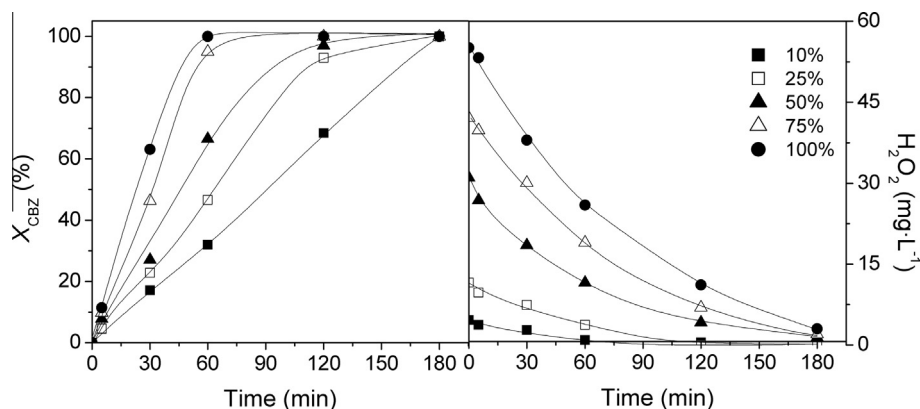


Fig. 1. Evolution of CBZ conversion upon Fenton oxidation at different H_2O_2 doses (in percentage of the stoichiometric): $T = 50^\circ C$; $[CBZ]_0 = 10 \text{ mg L}^{-1}$; $[Fe^{3+}]_0 = 2 \text{ mg L}^{-1}$; $pH_0 = 3$.

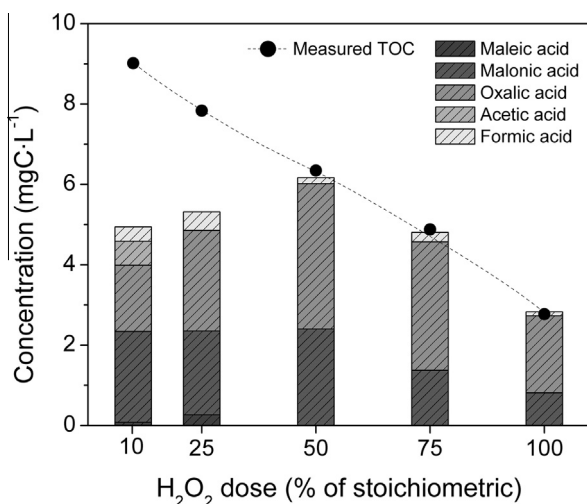


Fig. 2. Composition of the effluents of Fig. 1 at the end of the experiments (3 h).

CBZ was quantified by means of high-performance liquid chromatography (HPLC; Varian Pro-Start 325) equipped with a UV detector and a Microsorb C18 $5 \mu m$ column (MV 100, 15 cm length, 4.6 mm diameter) as the stationary phase. The analyses were carried out at 270 nm using a 55/45% (v/v) mixture of acetonitrile and acetic acid aqueous solution (75 mM) as the mobile phase. This method achieves detection limits at or below 0.1 mg L^{-1} . H_2O_2 concentration was determined by colorimetric titration following the titanium sulphate method [27] using an UV 1603 Shimadzu UV/vis spectrophotometer, being the detection limit 0.5 mg L^{-1} . Total organic carbon (TOC) was measured with an organic carbon analyzer (TOC-VCN, Shimadzu), with a detection limit of 0.2 mg L^{-1} . Short-chain organic acids were analyzed by ion chromatography with chemical suppression (Metrohm 790 IC) using a conductivity detector. A Metrosep A supp 5-250 column (25 cm length, 4 mm internal diameter) was used as stationary phase and 0.7 mL min^{-1} of an aqueous solution containing 3.2 mM Na_2CO_3 and 1 mM $NaHCO_3$ as the mobile phase. Detection limits of those analyses were within the range of $0.05\text{--}0.1 \text{ mg L}^{-1}$.

To learn on the oxidation by-products formed upon Fenton-like oxidation of CBZ, the effluents were analyzed by a Varian HPLC coupled to a 1200L quadrupole mass spectrometer. A Prontoil C8 (120-5, 50 cm length, 2.0 mm diameter) was used as the stationary phase. The mobile phase consisted of a solution containing 2 mM ammonium acetate in methanol (eluent A) and 2 mM

ammonium acetate in water (eluent B), which was pumped in a gradient mode from 10% to 100% A over 10 min and held at 100% A for 5 min.

3. Results and discussion

3.1. Fenton-like oxidation

Fig. 1 depicts the evolution of CBZ conversion and H_2O_2 decomposition in the Fenton-like oxidation experiments at different H_2O_2 concentrations. CBZ was completely converted in all the cases, although the concentration of H_2O_2 showed a significant effect on the reaction rate. CBZ disappeared completely in 1 h with the stoichiometric H_2O_2 concentration while 3 h were required at 10% of that amount.

The results obtained in this work improved significantly those previously reported in the literature where the degradation of CBZ by Fenton oxidation is commonly carried out at significantly higher H_2O_2 doses than those of Fig. 1 [12,28,29]. Sun et al. [13] studied the degradation of CBZ (15 mg L^{-1}) by Fenton-like oxidation using a high concentration of nano-magnetite as catalyst (2 g L^{-1}) and 20 g L^{-1} H_2O_2 (238 times the stoichiometric). The use of high amounts of oxidant and catalyst is also a common practice in other AOPs. Ghauch et al. [29] carried out the degradation of CBZ (10 mg L^{-1}) by a ultrasonic (40 kHz)/ Fe^0/H_2O_2 treatment with H_2O_2 concentrations in the range of $425\text{--}3400 \text{ mg L}^{-1}$ and Fe^0 concentrations from 24.6 to 200 mg L^{-1} . Miralles-Cuevas et al. [10] combined nanofiltration and photo-Fenton for the oxidation of different micropollutants including CBZ. They concluded that complete conversion of CBZ required a ratio of $24 \mu g H_2O_2/\mu g$ CBZ which represents 4 times the stoichiometric amount of H_2O_2 for mineralization.

It is well known that short-chain organic acids are formed from aromatic ring opening upon oxidation by HO^\bullet radicals. In this case, the organic acids identified and quantified were maleic, malonic, acetic, oxalic and formic. Fig. 2 shows the distribution of short-chain organic acids in terms of equivalent carbon at the end of the 3 h-experiments of Fig. 1. At H_2O_2 concentrations lower than 50% of the stoichiometric significant differences were observed between the TOC measured and the equivalent to the short-chain organic acids, due to the formation of aromatic by-products. Above 50% of the stoichiometric H_2O_2 concentration only short organic acids were remaining in the reaction media. It can be highlighted that more than 70% of the initial TOC was removed with the stoichiometric concentration of H_2O_2 .

The effluents from the experiments of Fig. 1 were analyzed by HPLC/MS to identify the reaction by-products. At H_2O_2

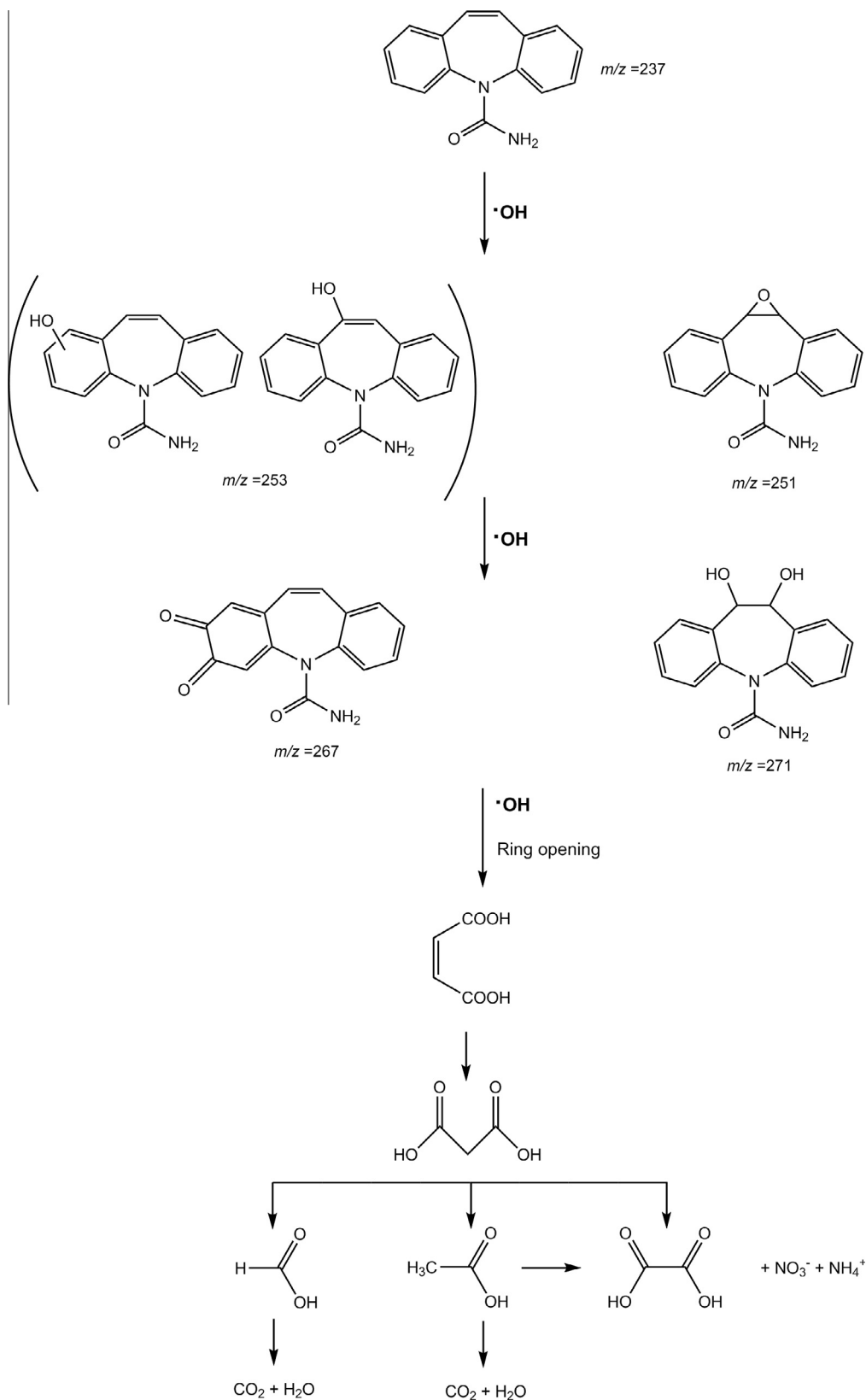


Fig. 3. Reaction pathway proposed for Fenton oxidation of CBZ.

concentrations below 50% of the stoichiometric the following aromatic intermediates were detected: hydroxycarbamazepine ($m/z = 253$), epoxycarbamazepine ($m/z = 251$), dihydroxycarbamazepine

($m/z = 271$) and carbamazepine-*o*-quinone ($m/z = 267$). Those aromatic by-products are consistent with the reported in the literature by previous authors [12,13,28]. From these results, the

reaction pathway depicted in Fig. 3 is proposed for Fenton-like oxidation of CBZ. Hydroxylation of CBZ leads to the formation of hydroxycarbamazepine and also epoxycarbamazepine. Further attack of HO[•] radicals would result in the formation of dihydroxycarbamazepine and carbamazepine-*o*-quinone. Ring-opening of those intermediates would give rise to short-chain organic acids, formerly maleic, then evolving into malonic, acetic, oxalic and formic. All the intermediates were finally oxidized to CO₂ and oxalic acid, this last was quite resistant to Fenton oxidation as reported in the literature [30–32].

3.2. Effect of temperature

Fig. 4 depicts the evolution of the CBZ concentration upon Fenton-like oxidation at different temperatures with the stoichiometric H₂O₂ concentration. As can be seen, increasing the temperature within a fairly narrow range (35–65 °C) increases dramatically the rate of CBZ disappearance. The time-course of CBZ can be usefully described by a simple pseudo-first order rate equation. The values obtained for the apparent rate constant were $(0.37 \pm 0.03) \cdot 10^{-2}$, $(4.09 \pm 0.23) \cdot 10^{-2}$ and $(32.99 \pm 1.33) \cdot 10^{-2} \text{ min}^{-1}$ at 35, 50 and 65 °C, respectively. From these values, an apparent activation energy of $129.6 \text{ kJ mol}^{-1}$ was calculated. Sun et al. [13] also found an important increase on the apparent rate constant with temperature (from 0.014 min^{-1} at 15 °C to 0.28 min^{-1} at 45 °C) in Fenton-like oxidation of CBZ (15 mg L⁻¹) with ferric-nitrilotriacetate complexes working at higher H₂O₂ concentration and catalyst loads (527 mg L⁻¹ of H₂O₂ and 5.56 mg L⁻¹ of Fe(III)). They reported a value of 76 kJ mol^{-1} for the apparent activation energy.

To learn more on the fate of CBZ upon Fenton-like oxidation at different temperatures, the evolution of TOC was followed and the results are shown in Fig. 5. A dramatic improvement of mineralization was observed by a temperature increase of only 15 °C. Moreover, the efficiency on the use of H₂O₂ (amount of TOC removed per unit of H₂O₂ decomposed) was considerably improved from 21 to 131 mg TOC/g H₂O₂ at 35 and 50 °C, respectively. Increasing the temperature above 50 °C led to a significant increase on the reaction rate but it did not enhance significantly the degree of mineralization. In fact, the efficiency in the consumption of H₂O₂ was not improved by increasing the temperature to 65 °C (124 mg TOC/g H₂O₂). Therefore, further experiments to evaluate

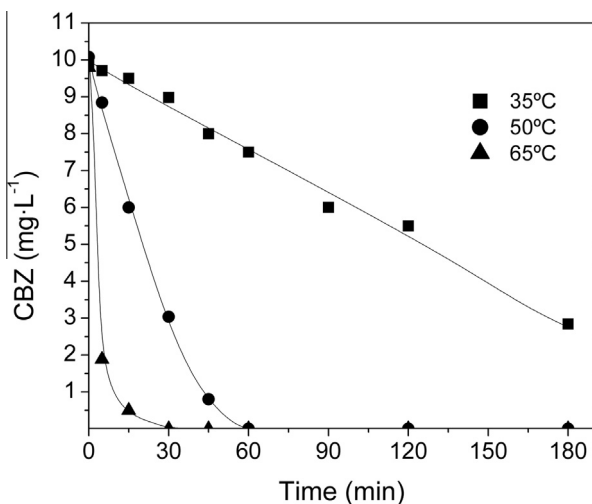


Fig. 4. Effect of temperature on the time-course of CBZ concentration upon Fenton oxidation ($[\text{CBZ}]_0 = 10 \text{ mg L}^{-1}$; $[\text{Fe}^{3+}]_0 = 2 \text{ mg L}^{-1}$; $[\text{H}_2\text{O}_2]_0 = 56 \text{ mg L}^{-1}$; $\text{pH}_0 = 3$).

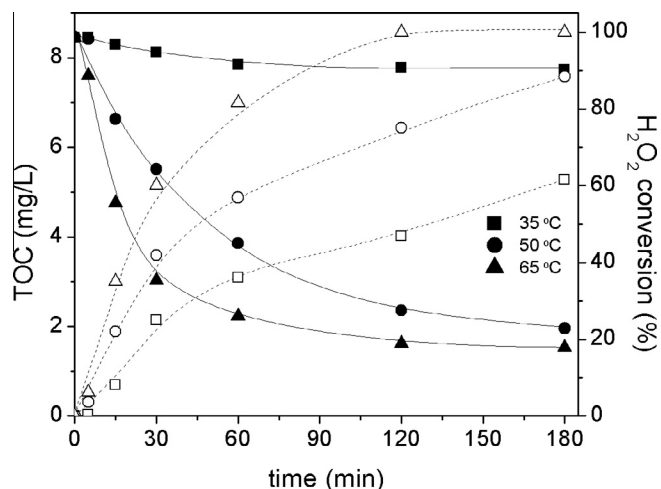


Fig. 5. Effect of temperature on the evolution of TOC and H₂O₂ conversion upon Fenton oxidation of CBZ ($[\text{CBZ}]_0 = 10 \text{ mg L}^{-1}$; $[\text{Fe}^{3+}]_0 = 2 \text{ mg L}^{-1}$; $[\text{H}_2\text{O}_2]_0 = 56 \text{ mg L}^{-1}$; $\text{pH}_0 = 3$).

the biological treatment of the effluents from Fenton-like oxidation were carried out at 50 °C.

The equivalent organic carbon from the short-chain organic acids remaining in the reaction media (oxalic, malonic and, to a lesser extent, formic acid) corresponds to the TOC measured at the end of the experiments carried out at different temperatures. Thus, the complete breakdown of CBZ was achieved under these operation conditions, forming CO₂ and short chain acids.

The high mineralization achieved contrasts with the results previously reported in the literature on the degradation of CBZ by different AOPs. Im et al. [33] reported 34% TOC reduction with O₃/UV/H₂O₂, although a higher value (72%) was reported by Deng et al. [34] with UV/H₂O₂ but using 1.2 times the stoichiometric concentration of H₂O₂.

3.3. Biodegradability of the Fenton-like effluents

First, the inherent biodegradability of CBZ was evaluated by the Zahn-Wellens test at 10 mg L^{-1} and at 1 and $5 \mu\text{g L}^{-1}$, these two last concentrations being within the range commonly found in the effluents from municipal wastewater treatment plants [35–37]. The abiotic tests showed negligible volatilization and sorption of CBZ. The biodegradability tests showed no changes of the concentration of CBZ after 28 d, which indicates that the non-acclimated activated sludge was not able to degrade this compound.

Fig. 6 shows the TOC reduction achieved upon the biodegradability tests (24 h) of the effluents from Fenton-like oxidation of CBZ at different H₂O₂ concentrations (Figs. 1 and 2). As can be seen, increasing the H₂O₂ concentration in the Fenton-like step leads to more biodegradable effluents, consistently with the progressive disappearance of the aromatic intermediates, which have been reported to be hardly biodegradable by unadapted biomass [38]. All the identified short-chain organic acids were degraded during the biodegradability test. Previous works have reported that acetic acid is the most readily biodegradable compound among the identified oxidation by-products. Malonic and maleic acids required a certain acclimation period (lag phase) of the sludge. Although formic and oxalic are hardly biodegradable, they were completely depleted at the low concentrations found in the Fenton-like effluents [19]. The TOC remaining at the end of the biodegradability tests must correspond to soluble microbial products (SMP). A prolonged exposure of the activated sludge to the resulting effluents from Fenton-like oxidation might lead to a further increase of the

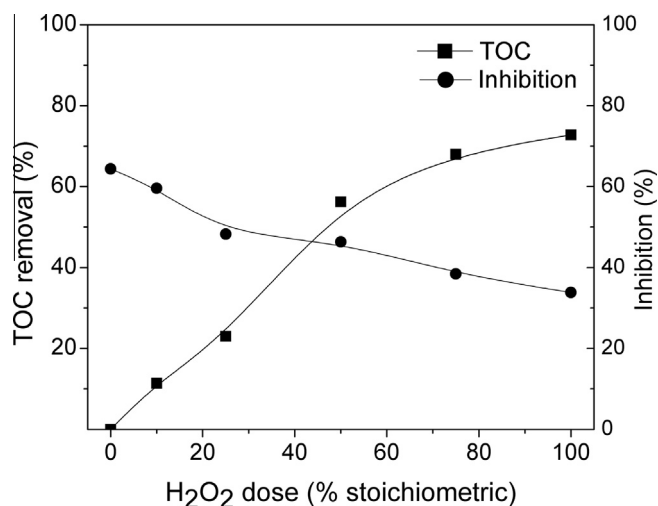


Fig. 6. TOC removal upon the biodegradability tests (24 h) and inhibition percentages of the effluents from Fenton oxidation.

biodegradability since the acclimation of the biomass has been claimed as an intensification strategy for the biological treatment of slowly biodegradable effluents [39].

Only limited data are available in the literature relative to the inhibitory effect of CBZ and, all of them correspond to standard ecotoxicity assays, like inhibition of bioluminescence with the marine bacterium *Vibrio fischeri* (ISO 11348-3), growth inhibition of the green algae *Pseudokirchneriella subcapitata* (ISO 8692), immobilization of the crustacean *Daphnia magna* Straus (ISO 6341), and *Oryzias latipes* (the medaka fish) [7,40,41]. The use of unadapted mixed culture allows predicting the toxic effect of CBZ in activated sludge-based biological systems in wastewater treatment plants. Thus, respirometric tests have been used to evaluate the inhibitory effect of CBZ and the effluents from Fenton-like oxidation at different H₂O₂ concentrations. An additional test was performed in presence and absence of H₂O₂ to evaluate the disturbances of the SOUR measurements induced by the oxygen formed by H₂O₂ decomposition, which resulted in a similar respirogram and TOC evolution. An EC₅₀ value of 1.8 mg L⁻¹ was obtained for CBZ, indicative of a fairly toxic effect of this compound on the activity of the activated sludge. The toxicity was reduced upon Fenton-like oxidation at increasing H₂O₂ concentrations as can be seen from the decreasing inhibition percentages showed in Fig. 6.

4. Conclusions

Complete CBZ conversion was achieved upon Fenton-like oxidation of a 10 mg L⁻¹ starting solution at very low iron concentration (2 mg L⁻¹) with the stoichiometric concentration of H₂O₂ at 50 °C in 1 h reaction time. Under those conditions, all the aromatic intermediates were completely converted into non-toxic short-chain organic acids and a high mineralization (75%) was achieved. The high value of the apparent activation energy for CBZ disappearance (129.6 kJ mol⁻¹) suggests a low reactivity of CBZ towards HO· radical attack. In this sense, a moderate increase on the operating temperature from 35 to 50 °C led to a dramatic increase of the oxidation rate. These results improved the previously reported in the literature regarding the application of AOPs to CBZ removal where large amounts of H₂O₂ (far from the stoichiometric concentration) and iron catalyst have been commonly used. The Fenton-like oxidation of CBZ reduced the toxic effect of CBZ, being effectively removed by activated sludge-based systems.

Acknowledgements

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