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DEGRADATION OF THE PHARMACEUTICAL CAPTOPRIL VIA FENTON PROCESS

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Abstract

Emerging contaminants (ECs) can be present at trace levels in different aquatic environments with potential adverse effects for human and environmental health. Alternative wastewater treatments, as advanced oxidative processes, are required to degrade ECs. Thus, the goal of this research was to estimate the degradation rates of the captopril (CAP) utilizing the homogeneous Fenton process in deionized water. The choice of operational conditions were: [CAP] = 250 mg L⁻¹, pH = 2.8, [H₂O₂] = 134 mg L⁻¹, [H₂O₂/Fe²⁺] = 5:1, time = 15 min, agitation = 150 rpm, temperature = 294 K. These could achieved 95% of CAP degradation. With these results, it is possible to conclude that the Fenton process is a promising technique for CAP degradation.

Key words: advanced oxidative process, captopril, emerging contaminants, Fenton process

Received: October, 2020; *Revised final:* March, 2021; *Accepted:* May, 2021; *Published in final edited form:* November, 2021

1. Introduction

The environmental contamination and pollution of water resources by emerging contaminants (ECs) have become widely studied by the scientific community. ECs can be considered persistent and refractory micropollutants, detrimental to the health of animals and humans (Gross-Sorokin et al., 2006). Some researches indicated that the presence of drug residues could lead to interferences in the ecosystem, e.g. the hormone 17- α -ethynylestradiol in the fish gender definition (Sumpter and Joblings, 1995). Species of vultures originating from southern Asia had serious risks of extinction by consuming carcasses of animals that had been treated with Diclofenac shortly before death (Oaks et al., 2004; Swan et al., 2006). Petrie et al. (2015) observed the spread of EC contamination in sanitary effluents and

the environment, pointing out the effects of degradation products on different environments, such as river and lake sediments.

Pharmacologically active compounds have been found in different water bodies, as well as in sanitary effluents, resulting from the incomplete metabolism of humans or animals, or by inadequate disposal in production centers or hospitals. Moreover, the process of removal of conventional sewage can be inefficient, making this a worrying issue of environmental chemistry (Boger et al., 2015; Mahmoud and Kümmerer, 2012).

The drug Captopril (CAP) is used in antihypertensive therapy because of its effectiveness and low human toxicity. It is also used in the treatment of patients with heart failure disease, myocardial infarction, or diabetic renal disorder acting as an inhibitor of the angiotensin-converting enzyme. This

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drug has been one of the most consumed active principles in Minas Gerais, distributed by the Unified Health System according to data from the Health Department of Minas Gerais (SES-MG, 2016). Due to its high intake, and as a consequence, of a high excretion rate without metabolizing, by the urinary system (40–50%) and its metabolite as disulfides, this EC can reach effluents and surface water. As low human toxicity, CAP may present low biodegradability and consequently aquatic biota toxicity (Cleuvers, 2003; Madden et al., 2009). These justifications show the importance to study the degradation of this active compound and the consequent treatment of wastewater (Marcatto et al., 2005; Mahmoud and Kummer, 2012).

Advanced oxidative processes (AOPs) have been used in EC treatments, in liquid effluents, as an alternative or complement to conventional biological processes that have lower efficiency for the degradation of this class of compounds (Zhang et al., 2019). AOP's such as Fenton process, are based on the production of highly reactive hydroxyl radicals (HO[•]), which can oxidize a wide range of substances (Comninellis et al., 2008; Li et al., 2012; Mirzaei et al., 2017; Tekin et al., 2006; Wilde et al., 2017). The use of Fenton process was observed to be efficient for the degradation of drugs such as diclofenac sodium (99.4%) (Rocha et al., 2009), oxytetracycline (90.8%) (Zouanti et al., 2020), ibuprofen (53.3%), propranolol (89%), paracetamol (66%) and dipyron (100%) (Odabasi and Buyukgungor, 2017).

Captopril, despite its wide use by population, is a drug very little studied in the environmental area. Considering the little information regarding CAP degradation by APOs, the objectives of this work are: (1) study the efficiency of Fenton process in CAP degradation. (2) optimize Fenton process to achieve maximum CAP degradation.

2. Materials and method

2.1. Laboratory glassware preparation

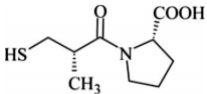
Seeking to minimize the contamination of the glassware used in the tests performed, the materials used underwent a cleaning process, by immersion in hydrochloric acid solution 2.5%, for 24 hours. After this period, the whole material was rinsed with ultrapure water for complete removal of hydrochloric acid. The glass vials used to store the samples to determine the dissolved organic carbon (DOC) were immersed in 20% nitric acid solution for 24 hours, followed by washing with ultrapure water.

2.2. Chemicals and sample

Captopril (Fiocruz/INCQS) was provided by the Fundação Ezequiel Dias (Minas Gerais), and used as received without further purification. Molecular structure of CAP in non-hydrolyzed form is illustrated in Table 1. The hydrogen peroxide (H₂O₂) was provided by Sulfal®; ferrous sulfate heptahydrate (FeSO₄·7H₂O), sulfuric acid (H₂SO₄) and sodium

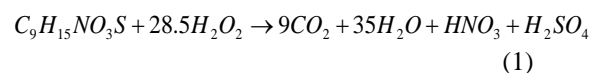
hydroxide (NaOH) were supplied by Emsure®. All chemicals used were of recognized analytical grade. Milli-Q water was utilized for the preparation of solutions (Q2:18.2 MΩ·cm, Millipore).

Table 1. Chemical structure, absorption maxima and molecular weight of CAP

Name	Chemical structure	λ_{max} (nm)	Molecular weight (g mol ⁻¹)
Captopril (C ₉ H ₁₅ NO ₃ S)		212	217.29

2.3. Experimental setup of Fenton process

Experiments carried out were performed in triplicate and with controlled experiments parameters: temperature, pH, hydrogen peroxide concentration, and CAP concentration. The reaction between CAP and H₂O₂ (Eq. 1) was considered to define the stoichiometric ratio of the H₂O₂ and Fe²⁺. This equation was elaborated by group, considering the stoichiometry among the reagents used. These H₂O₂/Fe ratios was studied before, setting 5:1 (mass units) as the optimum value.



The Fenton oxidation experiments were carried out on a laboratory scale, using borosilicate glass backers (600 mL) as reactors and continuously stirred using a Teflon coated magnetic bar, at room temperature. Aliquots were collected at different times, for analysis of H₂O₂ consumption and degradation of CAP. The degradation of the CAP was monitored by the reduction of the chromatographic peak area in HPLC at different treatment times. The peak areas were transformed in mass units (mg L⁻¹), by mean of a CAP calibration curve, and the decrease was calculated by (Eq. 2):

$$CAP(\%) = \frac{[CAP]_0 - [CAP]_t}{[CAP]_0} * 100 \quad (2)$$

where: [CAP]₀ and [CAP]_t is the concentration of CAP at initial and t times, and 100 is the percentage factor. All experiments were carried out in triplicate.

The optimization of the homogeneous Fenton process was performed in two steps:

1) application of different H₂O₂ concentration (44.2 – 134 mg L⁻¹) under the experimental conditions [CAP] = 250 mg L⁻¹, pH = 2.8, H₂O₂/Fe²⁺ ratio = 5:1, time 15 min, temperature = 294 K, agitation = 150 rpm;

2) variation of CAP concentration (200 mg L⁻¹) under the experimental condition's pH = 2.8, [H₂O₂] = 223 mg L⁻¹, [Fe²⁺] = 44.6 mg L⁻¹, time 40 min, temperature = 294 K, agitation = 150 rpm.

2.4. Analytical procedures

For hydrogen peroxide determination, it was added solutions of ammonium metavanadate (62 mmol L^{-1}) and sodium hydroxide (0.1 mmol L^{-1}) (Nogueira et al., 2005). The residual concentration of H_2O_2 was measured by a spectrophotometric method based on the formation of the red-orange peroxovanadium complex during the reaction of H_2O_2 with metavanadate, using an Agilent UV-Vis GII03A spectrophotometer with detection on $450 \text{ }\mu\text{m}$.

The samples were taken at established time intervals and an aliquot of NaOH and $\text{Na}_2\text{SO}_3 \text{ mol L}^{-1}$ were added to increase pH and to quench the H_2O_2 residual. Filtered samples ($0.22 \text{ }\mu\text{m}$ filter) taken from the reactor were analyzed for CAP and dissolved organic carbon (DOC). DOC was monitored to determine the degree of mineralization of Captopril.

High performance liquid chromatography (HPLC) was used to determine the concentrations of CAP and its degradation during the homogeneous Fenton process, using Agilent 1100 equipment with ultraviolet detector: column ODS ($4.6 \times 100 \text{ mm}$; $5 \mu\text{m}$) Merck; mobile phase mixture of water and methanol (20:80); flow 0.5 mL min^{-1} ; detection at 212 nm ; injection of $5 \text{ }\mu\text{L}$. Data were obtained in the equipment and converted into concentration, according to the linear regression model.

DOC was measured by using a TOC analyzer (TOC V_{CPH} , Shimadzu), with an operating principle based on the oxidation of carbon by catalytic combustion (680°C). After, these samples were analyzed at the NDIR analyzer. The value of total organic carbon was estimated by the non-purgeable organic carbon method in which the sample is acidified with hydrochloric acid and purged by high purity synthetic air in order to eliminate carbonates, and then oxidized by combustion in order to measure only organic carbon at NDIR analyzer.

All waste generated during the experiments was corrected discarded to avoid environmental contamination, according to the procedures in use at the institution where the study was carried out.

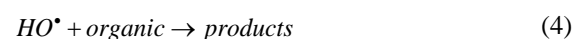
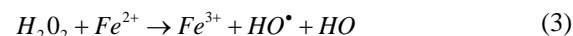
3. Results and discussion

3.1. Optimization of H_2O_2 concentration

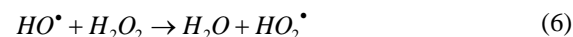
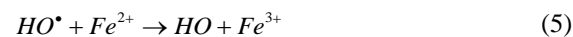
In order to degrade the CAP contaminant, a number of 4 trails (F1, F2, F3 e F4) were performed initially, in which Fenton process was applied in a solution containing a CAP concentration of 250 mg L^{-1} .

There were tested 4 different H_2O_2 concentrations (44.2 , 67.9 , 89.2 and 134 mg L^{-1}) under the experimental conditions: $\text{pH} = 2.8$, $\text{H}_2\text{O}_2/\text{Fe}^{2+}$ ratio = 5:1, time 15 min, temperature = 294 K , agitation = 150 rpm . The results are presented in Table 2.

The Fenton process generates hydroxyl radicals ($\text{HO}\cdot$) by the reaction between H_2O_2 and Fe^{2+} (Eq. 3), which degrade the organic contaminants (Eq. 4) by hydroxyl addition (unsaturated or aromatic), hydrogen abstraction (saturated aliphatic compound) or electron transfer (reduction of the hydroxyl radical into a hydroxyl anion) (Bello et al., 2019):



In Table 2, it was observed a CAP removal of 90.4% in F1. With increase of Fe^{2+} and H_2O_2 concentration in F2, F3 and F4, the CAP removal was not significantly increased (89.7, 93.9 and 95.4%, respectively). These results can be explained by scavenging reactions by excess of Fe^{2+} (Eq. 5) or H_2O_2 (Eq. 6). For this reason, iron concentration control can establish the efficiency of Fenton degradation (Lucas and Peres 2006):



CAP degradation was observed by the reduction of the chromatographic peak area over Fenton's reaction time (Fig. 1). The reduction in the CAP peak area is accompanied by the appearance of other chromatographic peaks (possible degradation products formed). It indicates that this process may be suitable for removal of CAP. Table 2 presents the area integrations for CAP peaks over the time and suggests the quantitative decrease of this area. The residual H_2O_2 concentration analysis was carried out for all samples taken at the end of the Fenton process (Fig. 3).

The residual concentrations were: 33.2%, 34.9%, 39.1% and 36.6% H_2O_2 , after the 15 min, respectively for F1, F2, F3 and F4 (Table 2). These results indicated that not all the reagent added into the solution was completely consumed during the monitored time, and H_2O_2 concentration decreases due to the degradation reaction of the compound of interest, as showed in Fig. 3 and Table 2.

Table 2. Performance of H_2O_2 optimization. Operational conditions: $[\text{CAP}] = 250 \text{ mg L}^{-1}$, $\text{pH} = 2.8$, $\text{H}_2\text{O}_2/\text{Fe}^{2+}$ ratio = 5:1, time 15 min, temperature = 294 K , agitation = 150 rpm

Assay	H_2O_2 (mg L^{-1})	Fe^{2+} (mg L^{-1})	[CAP] (residual)		H_2O_2 (residual)	
			mg L^{-1}	Removal (%)	mg L^{-1}	Removal (%)
F1	44.6	8.9	24.1	90.4	14.8	66.8
F2	67.9	13.4	25.7	89.7	23.7	65.1
F3	89.2	17.8	15.3	93.9	34.9	60.9
F4	134	26.8	11.1	95.4	49.1	63.4

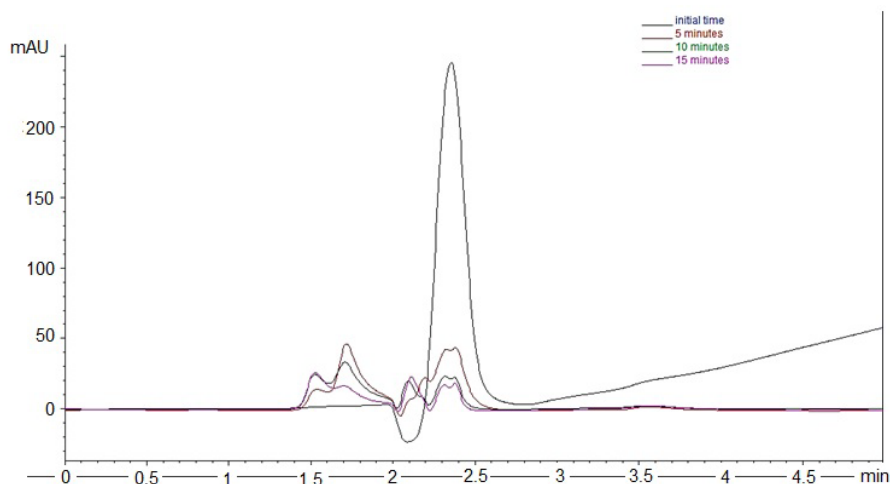


Fig. 1. Decrease in the CAP peak area was noted during Fenton process. Formation of co-products can be deduced by the appearance of the signals in a shorter retention time

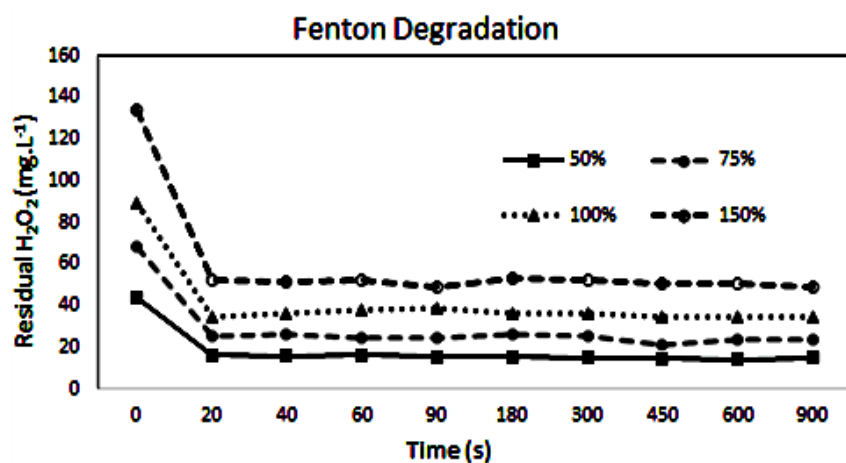


Fig. 3. Residual H_2O_2 concentration along the time in the different stoichiometric conditions

3.2. Optimization of the Fenton process

It was observed that Fenton process efficiency was affected by the H_2O_2 and Fe^{2+} concentrations. In this chapter it was tested the removal of CAP concentration pollutant (200 mg L^{-1}), under the operational conditions: $\text{pH} = 2.8$, $[\text{H}_2\text{O}_2] = 223 \text{ mg L}^{-1}$, $[\text{Fe}^{2+}] = 44.6 \text{ mg L}^{-1}$, time 15 min, temperature = 294 K, agitation = 150 rpm. In addition, H_2O_2 has been added gradually (Table 3), to decrease possible scavenging by H_2O_2 , as previously performed by Rodríguez-Chueca et al. (2017) for the treatment of winery wastewater. The effect of the gradually addition of peroxide could be observed in the level of DOC, which can be found at the level of 37.4% at the end of the experiment (Table 3).

The results showed a high CAP degradation capacity after 40 min of reaction; however, DOC degradation was considerably lower (37.3%). Similar results were observed by Lucas and Peres (2006) which observed that Reactive Black 5 (RB5) was rapidly degraded by Fenton process (96%), however achieved a TOC degradation of 21.6%. In Table 3, it is shown that, by adding of $223.0 \text{ mg L}^{-1} \text{ H}_2\text{O}_2$, a consumption of 98.3% H_2O_2 was found, which was

higher in comparison to the H_2O_2 consumption observed in chapter 3.1 (66.8%). These results suggested that a higher $\text{HO}\cdot$ radical production occurred, and the scavenging reactions were minimized.

Table 3. Optimization of Fenton process. Operational conditions: $[\text{CAP}] = 200 \text{ mg L}^{-1}$, $\text{pH} = 2.8$, $[\text{H}_2\text{O}_2] = 223 \text{ mg L}^{-1}$, $[\text{Fe}^{2+}] = 44.6 \text{ mg L}^{-1}$, time 40 min, temperature = 294 K, agitation = 150 rpm

Time (min)	$[\text{H}_2\text{O}_2]$ (mg L^{-1})	DOC		H_2O_2 consumption (%)
		mg C L^{-1}	Removal (%)	
0	8.9	32.08	-	-
5	17.9	27.03	15.7	93.4
10	26.8	26.12	18.6	95.7
15	35.9	24.11	24.8	96.7
20	44.8	24.85	22.5	96.5
25	66.8	24.21	24.5	96.3
30	133.6	22.73	29.2	97.2
35	179.0	21.73	32.3	98.2
40	223.0	20.12	37.3	98.3

Porous activated carbons (PAC) showed a 97.7% removal of CAP in simulated effluents. Although PAC leads to a phase transfer and does not

lead to a degradation of the drug under study (Kasperiski et al., 2018). Another study found a similar rapid initial degradation of EC, around 50 minutes, as presented by Elmolla and Chaudhuri (2009), when analyzing antibiotics degradation by Fenton process. The high efficiency is usually associated to hydroxyl radicals (Babuponnusami and Muthukumar, 2014).

4. Conclusions

This paper addresses the degradation of CAP by advanced oxidation processes, performed by a homogeneous Fenton process. Based on the experimental results, it can be concluded that:

1) When the operational conditions were: [CAP] = 250 mg L⁻¹, pH = 2.8, [H₂O₂] = 134 mg.L⁻¹, [Fe²⁺] = 26.8 mg.L⁻¹, time 15 min, temperature = 294 K, agitation = 150 rpm, a CAP removal of 95% was achieved;

2) When the operational conditions were: [CAP] = 200 mg L⁻¹, pH = 2.8, [H₂O₂] = 223 mg L⁻¹, [Fe²⁺] = 44.6 mg L⁻¹, time 40 min, temperature = 294 K, agitation = 150 rpm, a maximum DOC degradation of 37.3% was observed.

Therefore, the homogeneous Fenton is an efficient process for CAP degradation, with great potential of improvement and optimization.

Acknowledgements

We acknowledge the research incentives and financial support provided by the Fundação Ezequiel Dias (Funed), Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

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