

**A KINETIC APPROACH FOR PHARMACEUTICAL WASTEWATER ORGANIC
CARBON [DEGRADATION]**

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RESUMO

Este estudo teve como objetivo investigar a cinética de degradação do carbono orgânico total (COT) em efluentes farmacêuticos reais. Devido à complexidade das águas residuais reais e à falta de conhecimento sobre todas as reações envolvidas em sua degradação química, o uso de uma abordagem cinética torna-se difícil. Para contornar essa dificuldade, adotamos um modelo cinético baseado em equações químicas validadas para mecanismos de geração de radicais livres. As reações de foto-Fenton foram realizadas em um reator tubular de 1 L. O modelo desenvolvido descreveu satisfatoriamente a cinética de degradação do TOC em águas residuárias, com um R^2 de 0,9997. A constante da taxa de degradação TOC (k_d) foi estimada em $1 \times 10^{11} \text{ L}^2 \text{ mol}^{-2} \text{ s}^{-1}$, de acordo com os valores da literatura para a cinética de degradação de compostos orgânicos. A radiação UV teve um efeito positivo na degradação, contribuindo para a formação de HO^\bullet . A abordagem matemática adotada foi altamente sensível à constante de taxa de formação de HO^\bullet a partir de H_2O_2 (k_f). Nossos resultados sugerem, ainda que de forma incipiente, que a abordagem utilizada neste estudo pode ser estendida para o entendimento cinético de outras águas residuárias complexas.

PALAVRAS-CHAVE: Efluentes farmacêuticos, modelo cinético, degradação carbonácea, foto-Fenton

ABSTRACT

This study aimed to investigate the degradation kinetics of the total organic carbon (TOC) in real pharmaceutical wastewater. Because of the complexity of real wastewaters and the lack of knowledge on all reactions involved in their chemical degradation, the use of a kinetic approach becomes difficult. To overcome this difficulty, we adopted a kinetic model based on chemical equations validated for mechanisms of free radical generation. Photo-Fenton reactions were performed in a 1 L tubular reactor. The developed model satisfactorily described the degradation kinetics of TOC in wastewater, with an R^2 of 0.9997. The TOC degradation rate constant (k_d) was estimated at $1 \times 10^{11} \text{ L}^2 \text{ mol}^{-2} \text{ s}^{-1}$, in agreement with literature values for the degradation kinetics of organic compounds. UV radiation had a positive effect on degradation, contributing to HO^\bullet formation. The adopted mathematical approach was highly sensitive to the formation rate constant of HO^\bullet from H_2O_2 (k_f). Our results suggest, albeit in an incipient way, that the approach used in this study can be extended to the kinetic understanding of other complex wastewaters.

KEY WORDS: Pharmaceutical wastewater, Kinetic model, Carbonaceous degradation, Photo-Fenton.



INTRODUCTION

Veterinary and human pharmaceutical wastes are generated in various stages of drug production, from the weighing of raw materials to the packaging of the final product. Pharmaceutical wastewaters differ in composition (active ingredients, solvents, and excipients) and amount generated. In a survey conducted in 10 regions around the world, it was found that more than 90% of pharmaceutical wastewaters were discharged without prior treatment (UNEP 2010), a practice that is damaging to human health and the environment.

Pharmaceutical wastewater generated from chemical processes has been shown to have total organic carbon (TOC) values of 860–4940 mg L⁻¹, chemical oxygen demand (COD) of 375–32500 mg L⁻¹, biochemical oxygen demand (BOD₅) of 200–6000 mg L⁻¹, BOD₅/COD ratios of 0.1–0.6, pH 3.9–9.2, NH₄⁺-N 74–363 mg L⁻¹ and total phenol 95–125 mg L⁻¹ (Gadipelly et al. 2014; Rana et al. 2017). Another important aspect of wastewaters is that they are composed of rapidly biodegradable organic compounds and recalcitrant or refractory compounds, which are not removed by conventional biological treatments. Recalcitrance is mainly due to the biocidal action of drugs or the presence of complex chemical structures not amenable to biodegradation. Added to these characteristics is the resistance of active pharmaceutical ingredients (APIs) to metabolization.

Several alternatives for the treatment of wastewater containing APIs have been proposed. Because of the nondegradable nature of APIs and their pseudo-persistence, conventional biological and chemical treatments are often inefficient (Xiang et al. 2018). The most common alternative is the adoption of hybrid treatment systems, consisting of advanced oxidation processes (AOPs) as a first step to remove mainly recalcitrant/refractory toxins and some nonbiodegradable compounds, followed by biological treatments (Giannakis et al., 2021).

Fundamental aspects of the Fenton/photo-Fenton process are the reaction between [Fe²⁺], [Fe³⁺], and [H₂O₂] and the characteristics of the reaction medium (pH, temperature, and concentration of organic and inorganic constituents). These parameters determine the overall efficiency of reactions. One of the advantages of wastewater treatment by photocatalytic processes is the nonuse of chemical species that harm the environment. However, the use of Fenton processes may present some drawbacks, such as the dependence of pH control, generation of large amounts of iron-containing sludge and the generation of CO₂ from the oxidation of the organic carbon compounds.

OBJETIVE

This study aimed to investigate the decomposition of TOC in pharmaceutical wastewater using a kinetic approach based on chemical equations validated for mechanisms of free radical generation of the photo-Fenton process.

METHODOLOGY

The wastewater used in this study was provided by MSD Saúde Animal, a veterinary pharmaceutical industry located in Cruzeiro (latitude -22.580105°, longitude -44.951573°), Paraíba Valley, São Paulo State, Brazil. The anthelmintics found in a greater proportion in the effluent under study are Fenbendazole and Triclabendazole. The wastewater was stored at 4 °C.

Oxidation reactions were performed in a tubular reactor with a nominal volume of about 1 L. The source of UV irradiation (254 nm) was a set of low-pressure mercury lamps in quartz envelopes. Photochemical treatment was performed in batch mode using Fenton reagent (0.82 mol L⁻¹ FeSO₄·7H₂O and 30% w w⁻¹ H₂O₂) and solutions for pH adjustment (0.5 eq L⁻¹ NaOH or H₂SO₄).

TOC content was quantified on a TOC analyzer that provides results based on high-temperature catalytic oxidation and CO₂ determination by infrared spectroscopy. The analytical methods used for physicochemical characterization of wastewater are described in APHA (2012).

The following factors were investigated for their effects on TOC degradation: temperature (°C), pH, amount of H₂O₂, amount of Fe²⁺, and UV light power. Table 1 shows the factors and levels.

Table 1 Factors and levels used to assess the treatment of pharmaceutical wastewater by Fenton and photo-



Fenton

Factor	Level ^a	
	(1)	(2)
[T] (°C)	20	30
[pH]	2.0	3.0
[HP] ^b (g)	10.0	30.0
[Fe] ^c (g)	1.5	2.5
[UV] (W)	-	28

^a (1) and (2): low and high levels of the L₁₆ orthogonal array. ^b 30% (w w⁻¹) H₂O₂. ^c 0.82 mol FeSO₄·7H₂O L⁻¹.

These factors were studied using a Taguchi L₁₆ orthogonal array with two levels, (1) and (2). Factor levels were defined on the basis of previous experiments conducted as a three-level L₉ orthogonal array. Each run of the L₁₆ array was conducted in duplicate, totaling 32 experiments.

The response variable was the percentage reduction in TOC (TOC_{red}), calculated according to Eq. (1), where TOC_i and TOC_f are the initial and final TOC contents in pharmaceutical wastewater:

$$TOC_{red} = \frac{TOC_i - TOC_f}{TOC_i} \times 100 \quad (1)$$

The proposed model is based on a previous study (Izário Filho et al. 2018) and was developed using the molar balance equations of chemical species participating in the reaction (Table 2).

**Table 2** Reactions and rate constant equations considered in the kinetic model

Reaction	Rate constant equation	Parameter	Unit of measurement
$Fe^{2+} + H_2O_2 \xrightarrow{k_1} Fe^{3+} + HO^\bullet + OH^-$	$r_1 = k_1[Fe^{2+}][H_2O_2]$	$k_1 = 55$	$L \text{ mol}^{-1} \text{ s}^{-1}$
$Fe^{3+} + H_2O \xrightleftharpoons[k_{2f}]{k_{2r}} FeOH^{2+} + H^+$	$r_2 = k_{2f}[Fe^{3+}] - k_{2f}[FeOH^{2+}][H^+]$	$k_{2f} = 2.34 \times 10^7$ $k_{2r} = 1.00 \times 10^{10}$	s^{-1} $L \text{ mol}^{-1} \text{ s}^{-1}$
$FeOH^{2+} + h\nu \xrightarrow{k_3} Fe^{2+} + HO^\bullet$	$r_3 = k_3[FeOH^{2+}]$	$* k_3 = 6.2 \times 10^{-4}$ to 7.6×10^{-4}	s^{-1}
$H_2O_2 + h\nu \xrightarrow{k_4} 2HO^\bullet$	$r_4 = k_4[H_2O_2]^\beta$	$* k_4 = 0.12 \times 10^{-4}$ to 2.34×10^{-4} ; $\beta = 1$ to 2	s^{-1}
$Fe^{2+} + H_2O \xrightleftharpoons[k_{5f}]{k_{5r}} FeOH^+ + H^+$	$r_5 = k_{5f}[Fe^{2+}] - k_{5f}[FeOH^+][H^+]$	$k_{5f} = 1.9$ $k_{5r} = 1.00 \times 10^{10}$	s^{-1} $L \text{ mol}^{-1} \text{ s}^{-1}$
$Fe^{3+} + 2H_2O \xrightleftharpoons[k_{6f}]{k_{6r}} Fe(OH)_2^+ + 2H^+$	$r_{6f} = k_{6f}[Fe^{3+}] - k_{6r}[Fe(OH)_2^+][H^+]$	$k_{6f} = 1.12 \times 10^7$ $k_{6r} = 1.00 \times 10^{10}$	s^{-1} $L \text{ mol}^{-1} \text{ s}^{-1}$
$FeOH^+ + H_2O_2 \xrightarrow{k_7} Fe^{3+} + HO^\bullet + 2HO^-$	$r_7 = k_7[FeOH^+][H_2O_2]$	$k_7 = 5.90 \times 10^6$	$L \text{ mol}^{-1} \text{ s}^{-1}$
$Fe^{2+} + HO^\bullet \xrightarrow{k_8} Fe^{3+} + OH^-$	$r_8 = k_8[Fe^{2+}][HO^\bullet]$	$k_8 = 2.70 \times 10^8$	$L \text{ mol}^{-1} \text{ s}^{-1}$
$TOC + \alpha HO^\bullet \xrightarrow{k_d} Product$	$r_9 = k_d[TOC][HO^\bullet][H^+]$	$* k_d = 1 \times 10^{11}$ $* \alpha = 2$	$L^2 \text{ mol}^{-2} \text{ s}^{-1}$

Data collected from [Laat and Le \(2005\)](#), except those indicated by an asterisk (*), which were estimated in this study

RESULTS

TOC_{red} obtained in the Taguchi L₁₆ orthogonal array varied from 37.8 ± 4.9 to 73.6 ± 0.2 %.

The model developed to describe TOC degradation kinetics in pharmaceutical wastewater was fitted to experimental data. The degradation constant (k_d) and the stoichiometric coefficient (α) were fitted in the present study and their values agree with literature ([Andreozzi et al. 1999](#); [Izário Filho et al. 2018](#)). However, the fine tuning of the model was obtained by fitting the parameters k_3 and k_4 . These parameters refer to reactions that take into account the main factors of the experimental design (radiation, Fe and H₂O₂) and generates hydroxyl radicals, which are responsible by the TOC degradation. Predicted and experimental values are compared in [Figure 1](#).

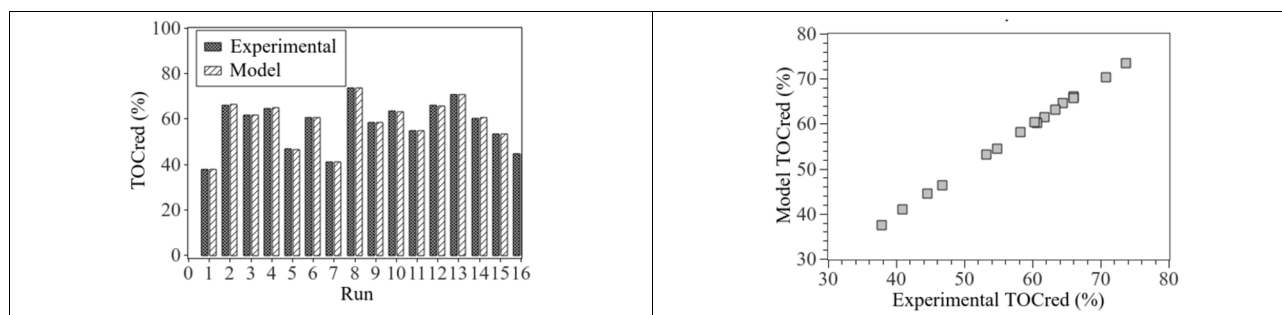


Figure 1 (a) Experimental and model-estimated reduction in total organic carbon (TOC_{red}). (b) Scatter plot of experimental versus model-estimated TOC_{red} values.

A coefficient of determination (R^2) of 0.9997 was obtained for the model developed assuming a TOC degradation rate constant (k_d) of $1 \times 10^{11} \text{ L}^2 \text{ mol}^{-2} \text{ s}^{-1}$, which was calculated from the third-order equation $r_9 = k_d [\text{TOC}] [\text{HO}^\bullet] [\text{H}^+]$.

As the pH was held constant throughout the reaction, it was possible to calculate the second-order degradation rate constant (k_d') by the equation $r_9' = k_d' [\text{TOC}] [\text{HO}^\bullet]$. The k_d' value was estimated to be 1×10^8 and $1 \times 10^9 \text{ L mol}^{-1} \text{ s}^{-1}$ for reactions conducted at pH 3 and 2, respectively. As expected, k_d values were within the range previously reported for the degradation of organic molecules (10^6 to $10^9 \text{ L mol}^{-1} \text{ s}^{-1}$) (Andreozzi et al. 1999; Hordern et al. 2003). It should be noted that these rate constants refer to chemical degradation, which represents a more suitable treatment in comparison to bioreactions, since the studied effluent is likely to contain recalcitrant compounds.

It was observed that variations in temperature from 20 to 30 °C did not have a clear effect on TOC_{red}. The stoichiometric coefficient of organic matter degradation (α) was found to be equal to 2; i.e., two HO^\bullet radicals are required, on average, for the degradation of one organic carbon atom. This finding suggests an abundance of tertiary and quaternary carbons in the organic matter fraction of the studied wastewater.

The decomposition rate constant (k_3) of FeOH^{2+} was estimated to be $6.2 \times 10^{-4} \text{ s}^{-1}$ in the absence of irradiation and $7.6 \times 10^{-4} \text{ s}^{-1}$ in the presence of UV light. These values are consistent with the fact that the decomposition of FeOH^{2+} is catalyzed by UV radiation.

As revealed by the simulation study, the model is highly sensitive to the parameter k_4 , which describes the rate of formation of HO^\bullet from H_2O_2 catalyzed by UV. Slight variations in k_4 were found to produce large variations in TOC_{red} results. On the other hand, TOC_{red} was not sensitive to k_d . These effects are illustrated in Figure 2.

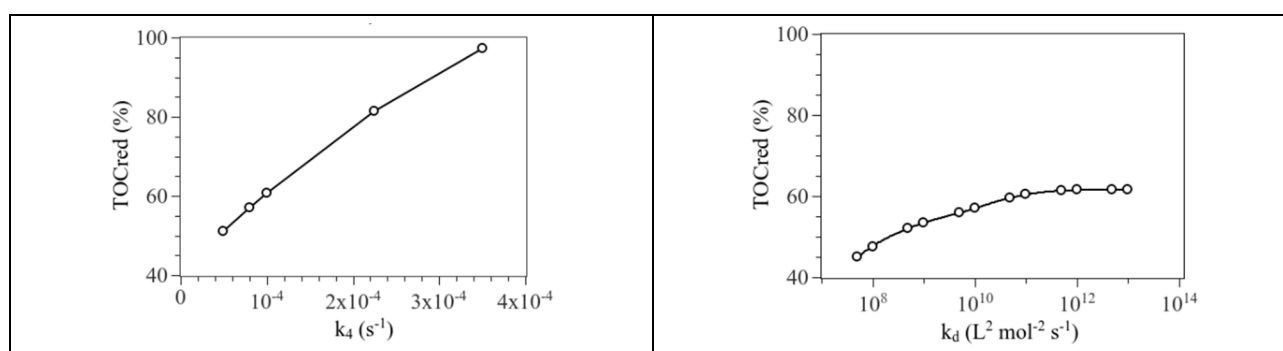


Figure 2. Simulations carried out using the conditions of Run 6 and varying (a) k_4 and (b) k_d . The other parameters were used as shown in Table 2

The strong influence of k_4 on TOC_{red}, evidenced by the pronounced differences in TOC_{red} values obtained within a narrow range of k_4 values, might have been caused by small discontinuities in the reaction medium. For this reason, this parameter was estimated separately for each run (Table 2).

It is important to point out that the proposed mechanism is an attempt to represent the oxidation system under study, however, it cannot be asserted that the correct mechanism was found. The comparison of different reaction orders for TOC degradation indicates that the best fit is achieved with the mechanism proposed herein.



CONCLUSION

A kinetic model based on molar balances for the species involved in the photo-Fenton process was developed and used to describe the treatment of real pharmaceutical wastewater. Simulations provided satisfactory results, with an R^2 of 0.9997. The TOC degradation rate constant (k_d) was estimated at $1 \times 10^{11} \text{ L}^2 \text{ mol}^2 \text{ s}^{-1}$, in agreement with literature values for the degradation kinetics of organic compounds. UV radiation had a positive effect on the degradation process, contributing to the formation of HO^\bullet , which was accounted for by the model through the parameter k_3 , which presented an average value of $6.9 \times 10^{-4} \text{ s}^{-1}$. The adopted mathematical approach was highly sensitive to the formation rate constant of HO^\bullet from H_2O_2 (k_4).

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