Ozonation Treatment for Pharmaceuticals: Optimizing Mineralization Conditions and Assessing Eco-Toxicity

POSTER
Ph.D. Student: Y
Journal: NONE

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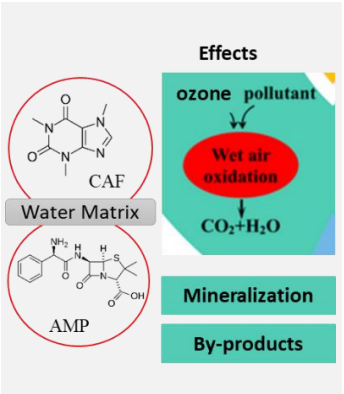

This study addresses the environmental risks posed by pharmaceuticals, emphasizing their low stability and persistence in water. Conventional treatment methods struggle with the complex structures of these compounds, necessitating advanced tertiary treatments. The ozonation process is explored as an effective method, aligning with stringent standards, yet concerns arise about potential toxicity from by-products. The research focuses on evaluating ozonation's impact on synthetic solutions containing the pharmaceuticals ampicillin and caffeine, optimizing operational conditions for mineralization. Results show a 34.04% mineralization efficiency influenced by alkaline conditions (pH 10) and a 15-minute process time. The study employs the QSAR-OECD tool to assess environmental toxicity, revealing concentrations post-ozonation below predicted toxic limits. However, the need for further research on by-products' environmental impact and potential additional treatments is emphasized.

Introduction

Pharmaceuticals, with their low stability and persistence, pose substantial health risks to humans and animals [1]. The complex structures create challenges for treatment in conventional water and effluent stations. Thus, advanced tertiary treatment methods are necessary to effectively remove these substances from water [2]. The ozonation process has been employed in treatment to align the treated matrix with stringent standards [3]. Despite numerous studies enabling the assessment of ozonation's effectiveness and its ability to remove various contaminants, certain by-products of the process may pose toxicity risks to organisms [4]. In this context, the work was conducted to evaluate the mineralization in solutions containing ampicillin (AMP) and caffeine (CAF). The QSAR-OECD tool was applied to asses the potential eco-toxicity of the by-products formed post-ozonation.

Material and Methods

Ozonation process

The ozonation system consisted of an oxygen air concentrator, an ozone generator, a liquid/gas contact ozone reactor, and a gas washer flask.

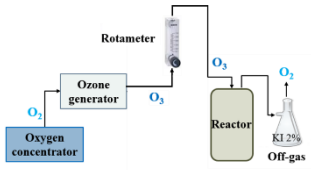

Figure 1. Representative diagram of the ozonation system.

For the experiments, a solution containing both pharmaceuticals was prepared at a concentration of 30 mg/L, chosen based on equipment detection limits. Ozone was continuously introduced into the reactor (1.5 g/h), and the excess of gas directed to a wash flask containing a 2% potassium iodide solution. A Central Composite Factorial Design (CCD) was employed to evaluate the mineralization capacity. Three factors were considered in 5 levels, in a randomized way. Table 1 outlines the coded values and variables in the experiment.

Table 1. Matrix of experimental design applied to the matrix.

		Level			
Independent variables	-α	-1	0	+1	+ α
x_1: pH	4	6	8	10	-
x_2: time (min)	1	5	10	15	30
x_3: gas flow (L/min)	0.2	0.4	0.6	0.8	1.0

Duplicates at the central point were included for assessing data reproducibility and experimental error. Mineralization capacity was calculated based on initial and final total organic carbon (TOC) values determined using a Shimadzu analyzer (TOC-VCSH).

Ecotoxicity in-silico QSAR

The in-silico QSAR analysis, conducted through the OECD Toolbox Version 4.3.1, integrated CAF and AMP chemical structures. Utilizing the Ecological Structure-Activity Relationship (ECOSAR) model, chemicals and their post degradation products were classified. The analysis included a thorough examination of parameters and endpoints, ranging from Bioaccumulation, Aquatic Toxicity, and Elimination to Carcinogenicity, Genetic Toxicity, Repeated Dose Toxicity, ToxCast, and others. Datasets from ECVAM, ECOTOX, and OASIS were utilized for this comprehensive evaluation.

Results and Discussion

Mineralization Capacity

Fig. 2 shows mineralization efficiencies in experiments with both pharmaceuticals, while Fig. 3 displays chromatograms before and after ozone degradation. The study determined optimal conditions for mineralization, achieving a significant rate of 34.04% at pH 10, 15 minutes, and a gas flow rate of 0.4 L/min, corresponding to an ozone concentration of 1.0 g/L.

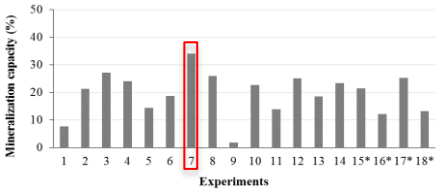

Figure 2. Experimental design response variables for the matrix.

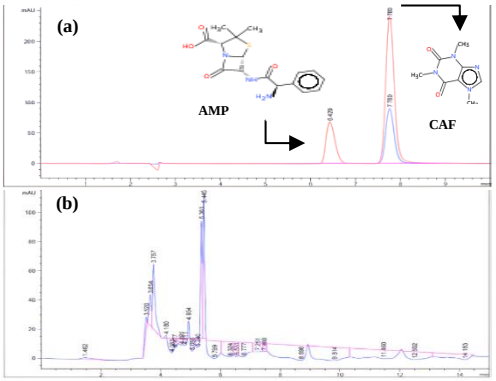

Figure 3. Chromatogram (a) before and (b) after ozone.

Chromatograms displayed initial retention times (6.5 and 8 min) for CAF and AMP before ozonation. Post-treatment, the disappearance of signals and emergence of three main signals representing degradation by-products suggest ozone's efficacy in pharmaceutical treatment [5]. Comparative analysis with previous studies [6] indicates comparable mineralization efficiencies for individually analyzed compounds, with minimal impact on increased by-product generation. However, toxicity analysis is crucial to identify potential formation of toxic intermediates [7].

Ecotoxicity in-silico QSAR

The final concentrations of 0.74 mg/L at 15 minutes and 0 mg/L at 30 minutes for the combined solution were compared with in-silico QSAR predictions to assess by-product toxicity and concentration limits. CAF bioaccumulation in *Schoenoplectus tabernaemontani* ranged from 2.36 to 3.41 log (L/kg) over 21 days, considering both respiratory and dietary exposure. *Xenopus laevis* exhibited toxicity at an EC50 of 0.0001 mg/L, while Pimephales promelas showed a tendency to die at an LC50 of 151 mg/L within 96 hours. CAF elimination studies reported a 4.9-hour half-life based on ADME reports. AMP demonstrated a low observed effect concentration (LOEC) of 0.015 mg/L in aquatic toxicity evaluation, indicating minimal adverse effects in environmental water. Additionally, a terrestrial toxicity range for AMP was determined to be 5–10 mg/L, with a half-life of 1.4 hours based on ADME reports.

The toxic hazard prediction indicates high potential toxicity for CAF and AMP, with seven and two degradation by-products respectively (biodegradation 0-10 days). Mutagenicity alerts for AMP, CAF and its second metabolite indicate positive effects due to hazardous functional groups. Elevated keratinocyte gene expression and specific functional group effects are observed in CAF and Metabolites 2 to 8. Skin irritation/corrosion assessments suggest log Kow values <-3.1 for CAF and <-0.5 for AMP and both metabolites.

Post-ozonation, pharmaceutical concentrations in aquatic environments significantly decrease, staying well below predicted toxic limits. Despite the usefulness of eco-toxicity QSAR, accurate predictions depend on high-quality and diverse training data.

Conclusions

The study focused on optimizing pharmaceutical mineralization using ozonation, analyzing degradation mechanisms and toxicity. It achieved efficient mineralization (34.04%) at pH 10 and a 15-minute process time. Ozone treatment demonstrated positive environmental safety implications, as post-treatment pharmaceutical concentrations were below toxic limits predicted by the QSAR-OECD tool. However, further research is needed to understand the environmental impact of by-products and assess the necessity of additional treatments to mitigate these effects.

Acknowledgments

Acknowledges to the Coordination for the Improvement of Higher Education Personnel (CAPES) and the Laboratory of Separation and Unitary Operations (LASOP) at the Federal University of Rio Grande do Sul (UFRGS), Porto Alegre, RS, Brazil.

References

[1] G. B. de Barros, L. T. Bezerra, D. M. Barbosa, A. F. V. da Silva, A. L. M. Romeiro, and E. S. de Araújo, "Mecanismos Causadores De Pressão E Impacto Ambiental Sobre Os Ecossistemas E Florestas Nativas," *Silvic. e Manejo Florest. Técnicas Util. e Conserv. da Nat. - Vol. 1*, pp. 233–252, 2021, doi: 10.37885/201102102.

[2] R. Anjali and S. Shanthakumar, "Simultaneous degradation of amoxicillin, ciprofloxacin and acetaminophen in a mixture by ozonation: Kinetics and mechanisms pathway," *J. Clean. Prod.*, vol. 378, no. August, p. 134509, 2022, doi: 10.1016/j.jclepro.2022.134509.

[3] L. R. de C. Costa and L. A. Féris, "Integration of ozonation with water treatment for pharmaceuticals removal from Arroio Diluvio in southern Brazil," *Water Sci. Technol.*, vol. 00, no. 0, pp. 1–16, 2023, doi: 10.2166/wst.2023.042.

[4] L. R. de C. Costa, J. T. De Oliveira, V. Jurado-Davila, and L. A. Féris, "Caffeine and ampicillin degradation by ozonation : Addressing pathways , performance and eco-toxicity," *Chem. Eng. Sci.*, vol. 288, p. 119817, 2024, doi: 10.1016/j.ces.2024.119817.

[5] L. R. de C. Costa, A. B. da L. Arsufi, J. T. de Oliveira, and L. A. Féris, "Ozonation for oxidation and transformation of pharmaceuticals in Arroio Diluvio River in Southern Brazil," *Ozone Sci. Eng.*, vol. 00, no. 00, pp. 1–12, 2023, doi: 10.1080/01919512.2023.2178383.

[6] S. Gokulakrishnan, K. Chandraraj, and S. N. Gummadi, "Microbial and enzymatic methods for the removal of caffeine," *Enzyme Microb. Technol.*, vol. 37, no. 2, pp. 225–232, 2005, doi: 10.1016/j.enzmictec.2005.03.004.

[7] Y. Lee *et al.*, "Prediction of micropollutant elimination during ozonation of municipal wastewater effluents: Use of kinetic and water specific information," *Environ. Sci. Technol.*, vol. 47, no. 11, pp. 5872–5881, 2013, doi: 10.1021/es400781r.