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Original Article

Dicloxacillin and metformin degradation using a coupled activated sludge–peroxone system

Degradación de dicloxacilina y metformina mediante un sistema acoplado de lodos activados y peroxono

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Abstract

Introduction: Pharmaceuticals constitute a group of emerging pollutants of high environmental concern owing to their low removal rates in conventional treatment systems.
Objective: This study evaluated a system coupling activated sludge with peroxonation for the removal of organic matter, dicloxacillin (DXC), and metformin (MET) in a synthetic water matrix.
Methodology: As a preliminary step, the operating conditions of the O3/H2O2 process were optimized using a Box–Behnken experimental design with response surface analysis, defining %COD as the dependent variable. Subsequently, the conditions for assembling a batch activated sludge reactor (ASR) with a 24-hour hydraulic retention time, followed by treatment of the effluent with O3/H2O2, were evaluated.
Results: The overall COD removal efficiency increased from 65.3% (biological process alone) to 90.4%, with 100.0% removal of DXC and 72.1% of MET achieved under the optimal conditions: ozone = 6.0 g/h, [H2O2]0 = 0.5 mg/L, and pH = 6.0.
Conclusions: These findings provide empirical evidence of the synergy within a sequential hybrid system, demonstrating that the ASR–O3/H2O2 coupling is a technically promising alternative and highlighting the need to assess its subsequent transfer and scale-up for urban and hospital effluents.

Keywords: Advanced Oxidation, Coupling, Emerging Contaminants, Peroxonation, Pharmaceutical Removal.

Resumen

Introducción: Los productos farmacéuticos constituyen un grupo de contaminantes emergentes que suscitan gran preocupación medioambiental debido a sus bajas tasas de eliminación en los sistemas de tratamiento convencionales.
Objetivo: Este estudio evaluó un sistema que combina lodos activados con peroxonación para la eliminación de materia orgánica, dicloxacilina (DXC) y metformina (MET) en una matriz de agua sintética.
Metodología: Como paso preliminar, se optimizaron las condiciones de funcionamiento del proceso O□/H□O□ utilizando un diseño experimental de Box–Behnken con análisis de superficie de respuesta, definiendo el % de DQO como variable dependiente. Posteriormente, se evaluaron las condiciones para montar un reactor de lodos activados por lotes (ASR) con un tiempo de retención hidráulica de 24 horas, seguido del tratamiento del efluente con O□/H□O□.
Resultados: La eficiencia global de eliminación de la DQO aumentó del 65,3 % (solo proceso biológico) al 90,4 %, con una eliminación del 100,0 % de DXC y del 72,1 % de MET en condiciones óptimas: ozono = 6,0 g/h, [H□O□]□ = 0,5 mg/L y pH = 6,0.
Conclusiones: Estos resultados aportan evidencia empírica de la sinergia existente en un sistema híbrido secuencial, lo que demuestra que el acoplamiento ASR–O□/H□O□ es una alternativa técnicamente prometedora y pone de relieve la necesidad de evaluar su posterior transferencia y ampliación a efluentes urbanos y hospitalarios.

Palabras clave: Oxidación Avanzada, Acople, Contaminantes Emergentes, Peroxonación, Remoción de Fárma-

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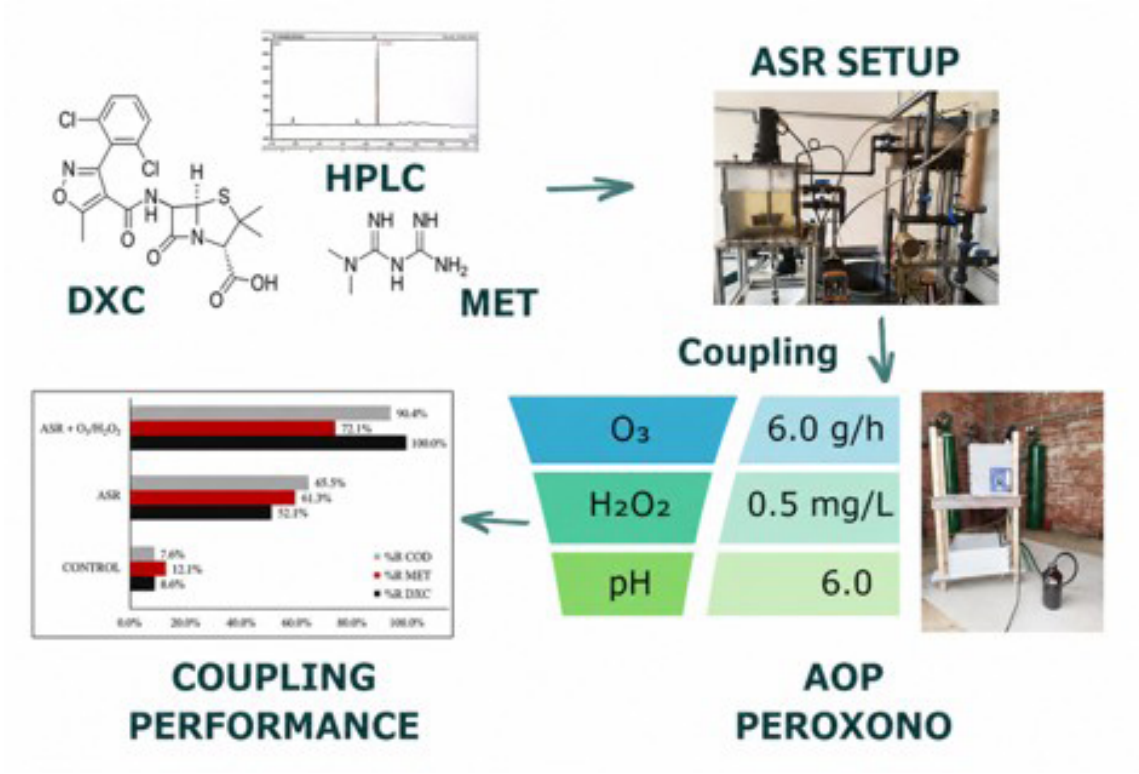
Spanish version

Why was this study conducted?
This study was carried out within the framework of a FINU research project aimed at applying technical and theoretical knowledge to address part of the problem associated with the discharge of pharmaceutically active compounds (PhACs) from hospital facilities. It seeks to generate relevant data and to establish a foundation for future research, enabling this work to be scaled up for application at the national and international levels.

What were the most relevant results?
The coupled ASR–peroxone system achieved removal efficiencies of 90.4% for COD, 72.1% for MET, and 100.0% for DXC, demonstrating its potential as an integrated alternative for the treatment of domestic and hospital wastewater.

What do they contribute?
A potential alternative for the treatment of domestic and hospital wastewater containing β-lactam antibiotics or metformin.

Graphical Abstract



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Introduction

Dicloxacillin (DXC) and metformin (MET) are emerging contaminants that are highly persistent in aqueous matrices as a result of their extensive clinical and household consumption (1–3). Between 38.0% and 50.0% of the administered DXC is excreted unchanged (4), which explains its frequent detection in sewer systems and hospital effluents (1,5,6). In Cali (Colombia), Madera-Parra et al. (7) reported traces of DXC in the effluent of the Cañaveralejo WWTP (190 ng/L) and in the Cauca River (23–150 ng/L), with a critical increase downstream of the discharge point. MET—a biguanide used to treat type 2 diabetes as well as oncological and neurodegenerative conditions—reaches average concentrations of 60 mg/L in WWTP effluents and of 1 to 8 mg/L in European surface waters (8–10). However, in developing countries such as Colombia these levels tend to be higher, owing to the deficit in sanitation infrastructure and the low efficiency of conventional systems for their removal (11). The accumulation of both pharmaceuticals alters the microbial dynamics of aquatic ecosystems (6,9).

In the treatment of wastewater containing pharmaceuticals, standalone biological processes exhibit low removal efficiencies (12). In this regard, Gámez and Rodríguez (13) reported removals of between 20.0% and 40.0% for certain antibiotics, associated with biodegradation and adsorption onto activated sludge. Nevertheless, because of their technical and economic capacity to remove high conventional organic loads, these systems remain central to municipal and hospital treatment plants (14). To address recalcitrant compounds, Advanced Oxidation Processes (AOPs) have emerged as an effective alternative, characterized by their high oxidizing power through the generation of hydroxyl radicals (HO·) (15,16). Within the range of AOPs, ozonation is one of the most widely studied techniques because of its high efficiencies, reaching removals of between 90.0% and 100.0% for β-lactam antibiotics (17,18). However, the exclusive action of these radicals is insufficient for the degradation of MET, owing to the complexity of its biguanide structure; efficiencies below 20.0% have been reported for peroxonation systems and biological processes operated separately (19,20).

The integration of ozone-based AOPs has intensified significantly in recent years, particularly in combinations with additional sources of free radicals. Notable among these are UV radiation, the use of heterogeneous catalysts—magnetite (O_3/Fe_3O_4) and titanium oxide (O_3/TiO_2)—and the addition of enhancing agents such as hydrogen peroxide (O_3/H_2O_2). The latter, known as peroxonation, is based on the accelerated decomposition of molecular ozone induced by the hydroperoxide ion, which triggers the massive formation of HO· radicals (21,22). Its mechanism of action begins with the dissociation of H_2O_2 in solution to form the hydroperoxide anion (HO_2^-) (Equation 1), which reacts rapidly with ozone and promotes the formation of intermediate species such as the hydroperoxyl radical ($HO_2\cdot$) and the superoxide radical ($O_2^{-}\cdot$) (Equations 2–3). These species act as reaction propagators, leading to a sustained production of HO· (Equations 4–6), considered the main oxidizing agents responsible for the non-selective degradation of complex organic compounds (23).

The radicals generated—particularly $O_2^{-}\cdot$—participate in recombination and electron-transfer reactions with ozone and other species present in the medium, amplifying the formation of HO· and other reactive oxygen species (ROS), which in turn recombine to produce additional $HO_2\cdot$

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radicals and other less reactive species (Equations 7–8).

$H_2O_2 \rightleftharpoons HO_2^- + H^+$ $K_a = 1.6 \times 10^{-12}$ (Equation 1)
$HO_2^- + O_3 \rightarrow O_3^- + HO_2\cdot$ $k = 2.8 \times 10^6\ M^{-1}s^{-1}$ (Equation 2)
$HO_2\cdot \rightleftharpoons O_2^{-}\cdot + H^+$ $K_a = 1.6 \times 10^{-5}$ (Equation 3)
$O_2^{-}\cdot + O_3 \rightarrow O_3^- + O_2$ $k = 1.6 \times 10^9\ M^{-1}s^{-1}$ (Equation 4)
$O_3^- + H^+ \rightarrow HO_3$ $k = 5.2 \times 10^{10}\ M^{-1}s^{-1}$ (Equation 5)
$HO_3 \rightarrow HO\cdot + O_2$ $k = 1.1 \times 10^5\ s^{-1}$ (Equation 6)
$O_3 + HO\cdot \rightarrow HO_2\cdot + O_2$ $k = 1.1 \times 10^5\ s^{-1}$ (Equation 7)
$O_3 + HO_2\cdot \rightarrow HO\cdot + 2O_2$ (Equation 8)

Nevertheless, AOPs present operational constraints—such as pH control and reagent dosing—that condition their economic viability and their integration with biological systems (24,25). Consequently, their coupling with biological reactors seeks functional complementarity in order to optimize costs and maximize efficiency in the treatment of complex effluents. Despite these advantages, the sequential integration of peroxonation with conventional activated sludge (ASR + O_3/H_2O_2) has not been reported in the literature. The scarce precedents involving peroxone are limited to membrane bioreactors, adsorption systems, or constructed wetlands applied to pesticides or other families of pharmaceuticals (20,22,26,27). In this context, the present study simultaneously addresses the optimization of the peroxonation process and the evaluation of its performance under batch conditions. In doing so, it seeks to help close the gaps related to treatment selectivity, the optimization of operating conditions, and the applicability of this type of hybrid system to matrices containing pharmaceuticals.

Materials and methods

Preparation of the water matrix

A synthetic water (SW) was standardized by adjusting the C:N:P ratio to 100:2:1. The matrix included, as carbon sources, whey (338.1 mg/L), sugar (90.5 mg/L), and starch (98.8 mg/L); nitrogen was supplied through urea (59.8 mg/L) and phosphorus through K_2HPO_4 (71.1 mg/L). The composition was complemented with mineral salts ($CaCl_2$: 9.1 mg/L; $MgSO_4$: 4.2 mg/L; $FeSO_4$: 2.0 mg/L; NaCl: 16.8 mg/L) and $NaHCO_3$ (591.0 mg/L) as a pH buffer. Finally, 18.7 mg/L of the pharmaceuticals under study, dissolved in ultrapure water, were added. DXC was obtained from a commercial formulation by LAFRANCOL S.A.S® (542.5 mg of dicloxacillin sodium with a purity of 92.2%) and MET from the commercial formulation by GENFAR® (850 mg of metformin hydrochloride with a purity of 77.3%). This composition made it possible to reproduce the organic load, nutrients, and pharmaceutical concentrations of hospital wastewater (28–31).

Optimization of the peroxonation parameters

A three-factor Box–Behnken experimental design was developed, with three replicates of the center point, for a total of 15 experiments, using Statgraphics Centurion 19 software. The assays were carried out in an effective volume of 500 mL under batch conditions, with sampling at 0.0, 10.0, 20.0, and 30.0 minutes of reaction. The levels selected for the design factors were defined on the basis of ranges reported in the literature, with the aim of evaluating the interaction among the variables and their effect on COD removal through response surface analysis.

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For ozone (2–6 g/h), these values correspond to doses commonly used in wastewater treatment, where increases in the ozonation rate favor mass transfer and the production of reactive species. Higher values may generate additional costs without improving removal efficiency, as has been reported in studies on the optimization of AOP processes (21,32). For hydrogen peroxide (0.5–1.5 mg/L), low to moderate concentrations were selected because of its dual effect as a promoter and, in excess, as a scavenger of HO· radicals, which influences process efficiency (33,34). Regarding pH, a wide range (3–9) was considered, in accordance with the optimal ranges established in the literature for the treatment of wastewater and leachates by ozone-based processes (32,35). The pH for the AOP was adjusted by adding NaOH or HCl (1 M).

Assembly of the ASR–peroxone coupling

The peroxonation setup was carried out in an amber borosilicate glass reactor with an effective volume of 0.5 L, fitted with a porous diffuser and connected to an ozone generator, model L23/24 (LABS–Pacific Ozone Technology®). Ozone was generated from industrial oxygen (99.5% v/v O_2) and regulated to a flow rate of 6.0 g/h, while H_2O_2 was dosed directly by means of a 0.1% v/v solution.

The ASR + O_3/H_2O_2 coupling was implemented with effective volumes of 1.0 L in the ASR and 0.5 L in the peroxone reactor, operating under batch conditions with retention times of 24 hours in the ASR and 20 minutes in the peroxonation reactor. Figure 1 presents the scheme of the coupled system in a sequential configuration. Sampling was performed at 0.0, 2.0, 5.0, 10.0, 20.0, 30.0, and 40.0 minutes of operation, and the variables %COD, %DXC, and %MET were evaluated.

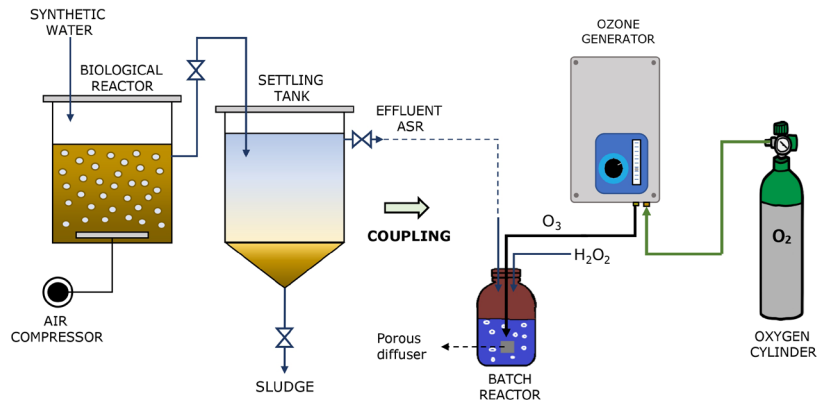

Figure 1. ASR–peroxone coupling.

Analytical methods

COD was quantified by the closed-reflux method SM 5220-D (36). The residual ozone concentration was determined with an HI83399 multiparameter photometer (HANNA Instruments®) following method 10.65, with a detection range of 0.0 to 2.0 mg/L. The residual H_2O_2 concentration was analyzed at a wavelength of 410 nm on a Thermo Scientific® Genesys 10S UV-VIS

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spectrophotometer, using the colorimetric method with titanium (IV) oxysulfate ($TiOSO_4$) described by Villamizar-Mosquera (37); for quantification, a calibration curve was constructed between 0.0 and 2.0 mg/L of H_2O_2, with an R^2 of 0.9969.

The degradation of DXC and MET was determined by reversed-phase ultra-high-performance liquid chromatography (UHPLC), using an Agilent® 1200 system equipped with a diode-array detector (DAD) and a 100-vial autosampler. The samples (10 µL) were injected onto an octadecylsilane (C18) column with dimensions of 150.0 mm × 3.0 mm internal diameter and a particle size of 2.7 µm.

A mobile phase composed of 0.5% phosphate buffer and acetonitrile was used, with gradient elution: 20.0% acetonitrile for 0.5 min, an increase to 100.0% over 10.0 min, a hold for 1.0 min, and a return to the initial conditions in 1.0 min. The chromatographic run was performed at room temperature, with a flow rate of 0.4 mL/min and detection at 225 nm. The calibration curve was constructed with concentrations of 0.0, 2.0, 5.0, 10.0, 15.0, 20.0, and 30.0 mg/L of DXC and MET. The removal efficiency for each variable was calculated using Equation 9.

%R=(C_o-C_f)/Co x100 (Equation 9)

Results and discussion

Standardization of the synthetic water

Table 1 presents the physicochemical characteristics of the standardized synthetic water. The COD and BOD values were adjusted with reference to reports for hospital wastewater (35,38).

Table 1. Characterization of the synthetic water.

Parameter	Units	Average value	Method
COD	mg/L O_2	630	SM 5220-C
BOD	mg/L O_2	395	SM 5210-B
Nitrates	mg/L $(NO_3)^-$	13	SM 4500-NO_3^-, B
Phosphates	mg/L $(PO_4)^{3-}$	8.2	SM 4500-P, C
DXC	mg/L	18.7	UHPLC
MET	mg/L	18.7	UHPLC

Optimization of the peroxonation parameters

The treatment of the synthetic water by ozonation with hydrogen peroxide yielded COD removal efficiencies above 60.0% in most of the assays, as shown in Figure 2. The maximum removal (80.9%) was achieved in experiment 11, with an O_3 flow of 6 g/h, $[H_2O_2]_0$ of 0.5 mg/L, and pH 6. The blanks illustrate the importance of the synergy between ozone and hydrogen peroxide (39), given that, on their own and at the optimal pH, they achieved removals lower than that of experiment 11.

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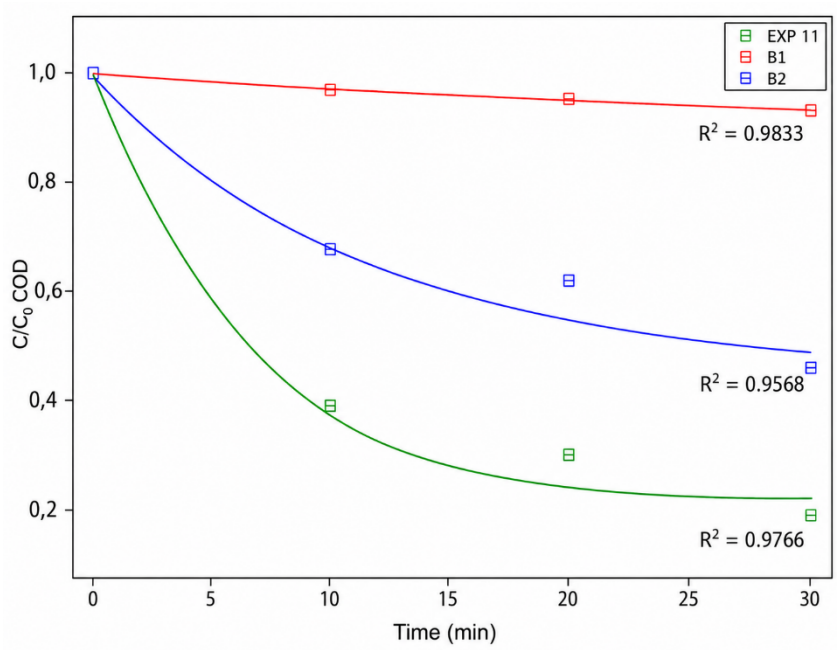

Figure 2. Removal efficiencies of the assays in terms of COD removal; EXP 11 (O_3 flow = 6 g/h, $[H_2O_2]_0$ = 0.5 mg/L, and pH = 6), B1 ($[H_2O_2]_0$ = 0.5 mg/L and pH = 6), B2 (O_3 flow = 6 g/h and pH = 6).

Table 2 presents the results of the analysis of variance (ANOVA) for COD removal based on the modeling data. It was found that the ozone flow and the H_2O_2 dose have a statistically significant effect on COD removal ($p < 0.05$), with ozone being the most influential variable in the peroxonation process ($p = 0.0076$). Likewise, the significance of the quadratic terms associated with the O_3 flow ($p = 0.0111$) and pH ($p = 0.0011$) indicates that these variables do not behave linearly but rather exhibit an optimal value within the range evaluated.

Table 2. Analysis of variance (ANOVA) for COD removal.

Source	Sum of Squares	df	Mean Square	F-Ratio	P-Value
A: O_3 flow	228.98	1	228.98	18.62	**0.0076**
B: $[H_2O_2]_0$	106.58	1	106.58	8.66	**0.0321**
C: pH	0.5	1	0.5	0.04	0.8482
AA	189.862	1	189.862	15.44	**0.0111**
AB	40.3225	1	40.3225	3.28	0.1300
AC	17.2225	1	17.2225	1.40	0.2899
BB	55.5616	1	55.5616	4.52	0.0869
BC	390.063	1	390.063	31.71	**0.0024**
CC	561.262	1	561.262	45.36	**0.0011**
Total error	61.5017	5	12.3003		
Total (corr.)	1697.3	14			

The Pareto chart (Figure 3) shows that the most relevant positive effects on COD removal correspond to the interaction between the peroxide dose and pH (BC) and, to a lesser extent, to the ozone flow (A and AA). This indicates that process efficiency is controlled mainly by the availability of oxidant and by conditions that favor the generation of reactive species.

The quadratic effect of pH (CC) presented a significant negative coefficient, indicating the constraint of an optimal pH value within the range evaluated. This behavior suggests that the relationship

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between pH and COD removal is not linear but follows a parabolic trend, in which both acidic and strongly alkaline values reduce process efficiency. From a chemical standpoint, at low pH the direct oxidation by molecular ozone predominates, characterized by a lower reaction rate, whereas at neutral to slightly acidic pH the decomposition of ozone and the formation of hydroxyl radicals—highly reactive and responsible for greater degradation of organic matter—are favored. This behavior has been widely reported in ozonation and peroxonation processes (23,40).

Second, the interaction between the H_2O_2 dose and pH (BC) shows a significant positive effect, evidencing a synergistic behavior between these variables. This interaction is key in peroxone-type processes, since pH regulates the stability of H_2O_2 and the rate of ozone decomposition. Under neutral to slightly acidic conditions, H_2O_2 promotes the generation of HO· radicals from ozone, whereas at lower pH this reaction is less favored (23). Therefore, an appropriate combination of pH and peroxide dose enhances the oxidative efficiency of the system.

Third, the effect of the ozone flow exerts an important positive influence, both linear and quadratic (AA), with the linear behavior predominating. This confirms that the oxidative capacity of the system increases with greater ozone availability up to a high threshold; however, the quadratic effect suggests that very high O_3 dosing rates may limit the removal of organic matter (21).

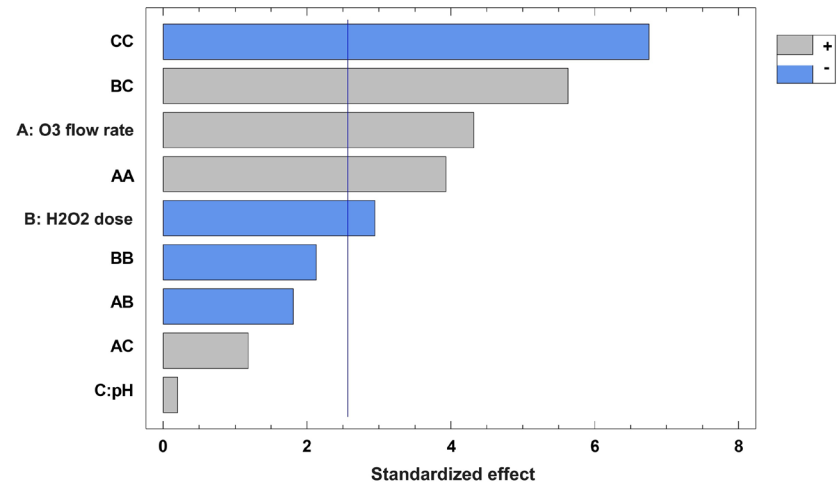

Figure 3. Pareto chart — factors affecting the peroxone process (O_3–H_2O_2).

Finally, the peroxide dose (B) exerts a slight negative effect on COD reduction; it is therefore advisable to work only with low reagent doses, since increasing H_2O_2 saturates the system and acts as a kinetic sink for free radicals. Operating at the lower dosing limit is recommended for matrices with an organic load (33). This negative behavior arises from two main competitive reactions: instead of the HO· radical oxidizing the organic matter, it is consumed by the peroxide itself or by its ionized form, giving rise to a greater number of hydroperoxyl radicals (HO_2·) with low oxidizing power (E° = 1.70 V).

The regression equation (Equation 10) indicates that COD removal is influenced by variables with an inverse relationship within the model. In particular, the negative coefficients associated with H_2O_2 show that increasing this factor does not produce a proportional improvement but may instead lead to the scavenging or consumption of reactive species. Similarly, the negative quadratic terms

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for H_2O_2 and pH confirm that both variables present an optimal operating point, and values outside it cause a decrease in removal efficiency.

COD Removal (Equation 10)

$$= 62.4833 - 10.5667 * O_3\text{flow} - 3.06667 * [H_2O_2]\text{o} + 8.5555 * pH + 1.79271 * (O_3\text{flow})^2 - 3.175 * O_3\text{flow} * [H_2O_2]\text{o} + 0.345833 * O_3\text{flow} * pH - 15.5167 * ([H_2O_2]\text{o})^2 + 6.5833 * [H_2O_2]\text{o} * pH - 1.36991 * pH^2$$

This equation was obtained with an adjusted R^2 of 0.96 and a coefficient of determination of 0.89, indicating that it can generate fairly precise values that agree with the experimental data.

The optimization of the peroxonation process and the identification of the critical operating points were analyzed using response surface methodology (RSM). Figure 4 presents the contour and three-dimensional surface plots, which allow visualization of the non-linear behavior and the curvature effects of the critical variables in the system. Plots 4a and 4b show an optimal effect at intermediate H_2O_2 concentrations (0.7–1.0 mg/L) combined with high ozone flows (> 5.5), exceeding 78.0% removal (red zone). If the H_2O_2 dose increases toward 1.5 mg/L, efficiency decreases markedly to around 63.0% (upper green zone), which visually validates the scavenging of HO· radicals by residual peroxide (34). Studies report that the positive effect of H_2O_2 on O_3 occurs at very low concentrations, conditioned by an ideal molar ratio (H_2O_2/O_3) that oscillates critically between 0.3 and 0.5. Increasing the H_2O_2 dose above a threshold of 1.0 mg/L may disrupt the optimal stoichiometric balance.

The interaction between the ozone flow and pH (Figures 4c–d) shows that COD removal improves at neutral to slightly acidic pH values (≈5.5–6.0), whereas at strongly alkaline pH values (> 8.0), even with high ozone flows, a drastic drop in removal—between 43.0% and 53.0%—is observed (blue/green zone). Although the general literature indicates that alkaline pH accelerates the decomposition of ozone to form HO· radicals, some authors attribute the negative effect of high pH values to the imbalance of inorganic carbon in the water, which shifts as dissolved CO_2 is transformed into bicarbonate (HCO_3^-) and carbonate (CO_3^{2-}) ions; these react with HO· radicals much more rapidly than COD does (34,41).

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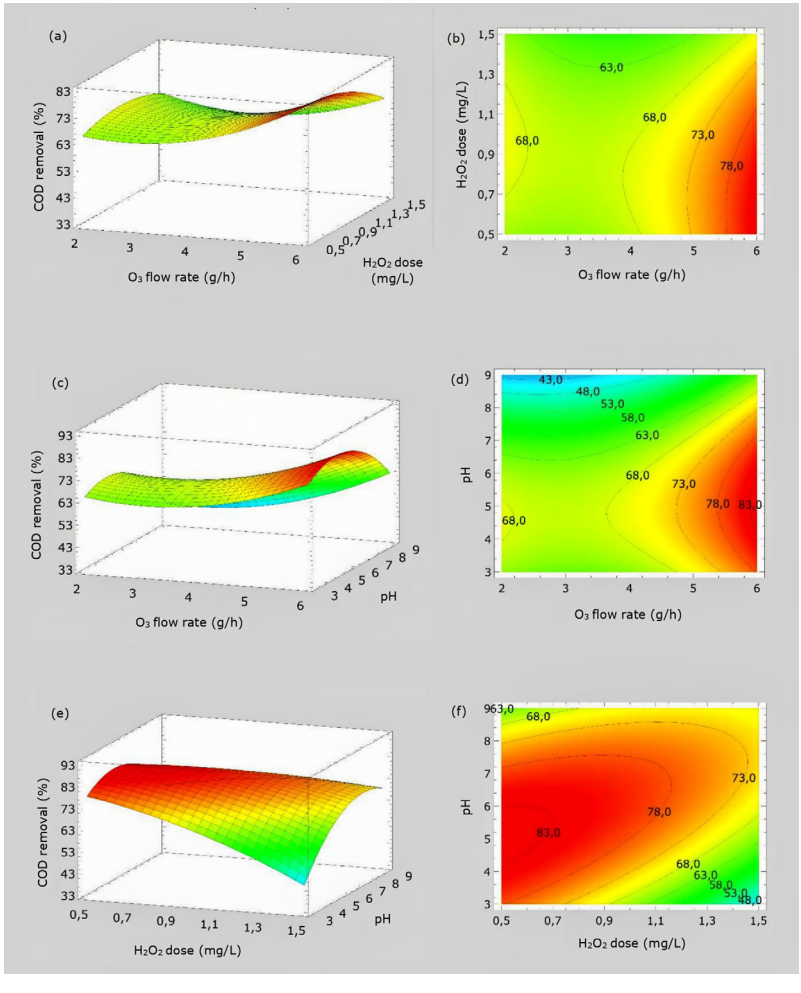

Figure 4. Estimated response surface plots of the effects; AB ((a)–(b)), AC ((c)–(d)), BC ((e)–(f)).

Likewise, Figures 4e and 4f show a marked decrease in efficiency, to values below 48.0% (green zone), when strongly acidic pH values (pH < 4.0) are combined with high H_2O_2 doses (> 1.3).

Degradation of DXC and MET under optimal peroxonation conditions

Under the optimal operating parameters defined by the RSM, the peroxonation process was replicated to evaluate the removal of the pharmaceuticals under study: dicloxacillin (DXC) and metformin (MET). Figure 5 shows that DXC was completely eliminated within the first 5 minutes of treatment. These results surpass, in terms of time, those obtained in other studies using simple ozone. Aleksić et al. (42) reported efficiencies of 90.0% for amoxicillin and ciprofloxacin after 30 minutes of treatment.

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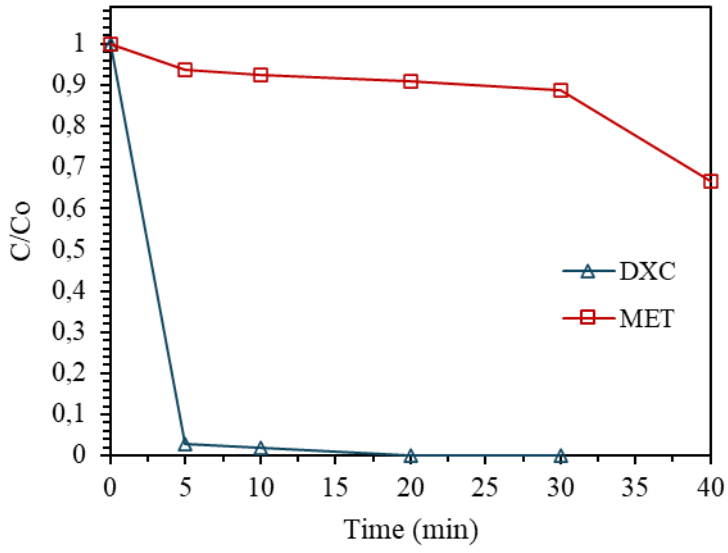

Figure 5. Removal of DXC and MET by peroxone under optimal conditions. Note. The initial concentration of the pharmaceuticals was C_0 = 18.69 mg/L.

In contrast, metformin exhibited resistance to peroxone oxidation, reaching only 12.3% removal and leaving a high residual at the end of the process (40 minutes). This low efficiency of MET is documented, with removals below 20.0% (19,20).

Removal efficiencies in the coupled system

Figure 6 shows a significant increase in the overall efficiencies of the ASR + H_2O_2/O_3 coupling compared with the standalone activated sludge process. This synergistic effect is validated by analyzing the individual behavior of the pharmaceuticals. With respect to metformin (MET), the ASR played a primary role in the first stage, accounting on its own for 61.2% of its removal, which allowed the overall hybrid system to increase its efficiency by close to 15.0%. Although MET usually shows a marked resistance to free radicals in chemical oxidation processes owing to the stability of its biguanide structure, its hydrophilic nature and the presence of amine groups make it a substrate susceptible to biodegradation or co-metabolism under the prolonged cell retention time conditions of the biological reactor (43). Thus, the ASR plays a fundamental role in relieving the COD and MET load prior to chemical treatment.

For its part, DXC exhibited a behavior that confirms the need for the chemical process. In the standalone biological treatment, the removal of this β-lactam antibiotic was limited, owing to its potential bactericidal effect and to the resistance of its chemical structure, which escapes conventional biodegradation. Nevertheless, when the ASR effluent was subjected to peroxonation, the complete elimination of DXC was achieved, representing a net increase of 48.0% in efficiency. The control sample consisted of the synthetic solution with the same concentrations of DXC and MET, without biomass and without being subjected to any chemical or biological process, in order to evaluate its structural stability over the experimental period. The values found for DXC and COD were lower than 10.0%, confirming that the observed removal is due strictly to the biological and chemical degradation mechanisms.

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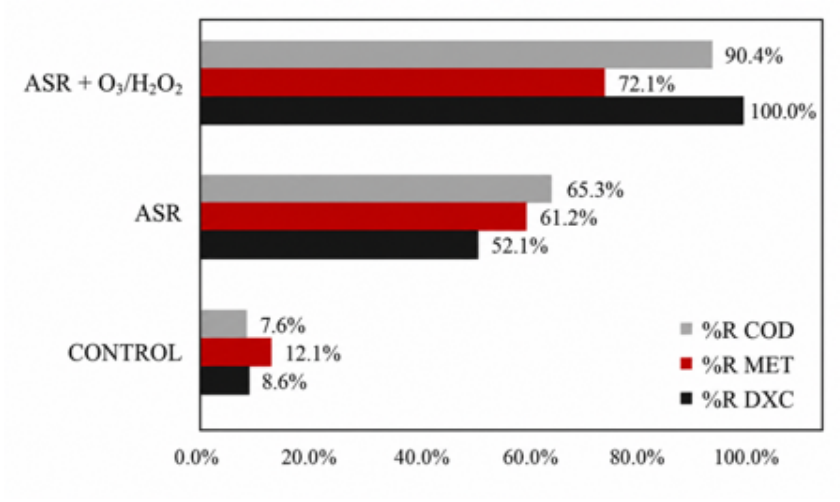

Figure 6. Removal efficiencies in the coupled system.

Conclusions

The O_3/H_2O_2 process was implemented for the initial treatment of the synthetic water simulating the characteristics of a hospital effluent. The response surface experimental design was successfully used to optimize the operating factors. The final efficiency in terms of COD, DXC, and MET removal under the optimal operating conditions (ozone flow of 6.0 g/h, H_2O_2 concentration of 0.5 mg/L, pH 6.0) was 80.9%, 100.0%, and 12.3%, respectively. The results demonstrated the reliability of the prediction model.

The ASR + O_3/H_2O_2 coupling showed high efficiency in the removal of DXC (100.0%) and MET (72.1%), supported by the capacity of the ASR to remove a large fraction of the organic matter, thereby reducing parasitic reactions and favoring the degradation of MET and DXC through advanced oxidation. This suggests the coupled system as a technically promising alternative for the treatment of wastewater containing β-lactam antibiotics and metformin.

The findings of this study provide empirical evidence of the synergy that exists in a sequential hybrid ASR + O_3/H_2O_2 system; nevertheless, it is necessary to evaluate its subsequent transfer and scale-up for urban and hospital effluents. This will contribute to reducing the pressure on wastewater treatment plants caused by pharmaceutically active compounds (PhACs) and to mitigating the ecotoxicological impacts on aquatic systems.

CrediT authorship contribution statement

Conceptualization - Ideas: Jenny Rosas-Vargas, Duvan Pedraza-Contreras. Data curation: Duvan Pedraza-Contreras. Formal analysis: Jenny Rosas-Vargas, Duvan Pedraza-Contreras. Adquisition Financiation: Jenny Rosas-Vargas, Dorance Becerra-Moreno Investigation: Duvan Pedraza-Contreras, Gina Hincapié-Mejía. Methodology: Jenny Rosas-Vargas, Doranca Becerra-Moreno, Duvan Pedraza-Contreras. Project Management: Jenny Rosas-Vargas, Dorance Becerra-Moreno. Resources: Jenny Rosas-Vargas, Dorance Becerra-Moreno, Duvan Pedraza-Contreras. Software: Duvan Pedraza-

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