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HYBRID ELECTROCHEMICAL-PHOTOCHEMICAL SYSTEM FOR METFORMIN HYDROCHLORIDE DEGRADATION: OPERATIONAL OPTIMIZATION, KINETICS AND TOXICITY ASSESSMENT

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Abstract

The increased consumption of medications, intensified by the pandemic, has driven self-medication and the generation of pharmaceutical effluents. Such as the drug metformin hydrochloride, impact the environment and health. Thus, classical advanced oxidation processes (AOPs) and electrochemical processes (EAOPs) are applied as alternative treatments. The objective of this study was to develop a graphite electrode impregnated with magnetite to be used as an anode and to conduct a combined study of AOPs employing the electro-Fenton (EF) process followed by photo-Fenton (PF) to degrade the drug metformin hydrochloride. As a result, the highest degradation percentage (95.22%)

was achieved after 45 minutes of EF followed by an additional 30 minutes of PF. This outcome was obtained using the developed anode and pure graphite as the cathode, sodium chloride as the electrolyte ($0.1 \text{ mol}\cdot\text{L}^{-1}$), $30 \text{ A}\cdot\text{cm}^{-2}$, and a 3 cm distance between the electrodes. From the characterization of the catalyst on the electrode surface, the thermal stability of the graphite electrode, magnetite, and impregnated electrode was verified. Furthermore, the kinetic monitoring data showed a satisfactory fit to pseudo-first-order models. During the kinetic study, $2.3 \text{ mg}\cdot\text{L}^{-1}$ of H_2O_2 and $25.40 \text{ mg}\cdot\text{L}^{-1}$ of free chlorine were quantified in the system. Toxicity tests indicated that over the course of the treatment, the toxicity profile was classified as non-toxic for yellow onion but toxic for broccoli cabbage.

Keywords: AOPs; photo-Fenton; electro-Fenton; toxicity

1. Introduction

The treatment of industrial effluents has been extensively studied due to the increase in emerging contaminants in aquatic matrices, such as pharmaceuticals and hormones, which exhibit low biodegradability and high chemical stability. Conventional treatments such as filtration, decantation, and flocculation show low efficacy in removing these types of pollutants, which drives the search for more effective technologies to degrade recalcitrant contaminants (Faber and Oliveira 2025).

In this context, Advanced Oxidation Processes (AOPs) emerge as alternatives that use oxidizing agents, such as the hydroxyl radical ($\bullet\text{OH}$), capable of degrading persistent organic compounds. Among the different types of AOPs are heterogeneous photocatalysis, electrochemical processes, and photo-Fenton reactions, which stand out for their high efficiency. However, to improve effluent treatment especially in the presence of persistent organic compounds it is possible to combine different types of AOPs in order to achieve an even greater systemic efficiency (Guo et al., 2022).

Among the AOPs, electrochemical advanced oxidation processes (EAOPs) have gained prominence due to the continuous generation of oxidizing agent within the system. The electrogeneration of hydrogen peroxide (H_2O_2) occurs at the cathodic region, and through subsequent oxidative reactions, the hydroxyl radical ($\bullet\text{OH}$) is formed, thereby eliminating the need to add other sources of chemical reagents to the process (Ganiyu et al., 2021). Another AOP worth highlighting is photo-Fenton, which, through

photocatalytic reactions using ultraviolet irradiation and iron-based catalysts, is capable of degrading target contaminants due to its high oxidizing capacity, being widely employed for the treatment of water and effluents containing different types of organic contaminants, such as pharmaceuticals (Luo et al., 2021).

A. Alanís-Leal et al. (2025) evaluated the degradation of pharmaceuticals such as metformin hydrochloride (MET) and glibenclamide (GLI) in an aqueous matrix using the electro-Fenton system. To this end, the authors used a glassy carbon electrode as the anode and a carbon electrode as the cathode, applying a voltage of 227 mV for 45 min. They achieved a degradation of 60% for both contaminants.

Cavalcanti et al. (2025) evaluated the degradation of a mixture of the pharmaceuticals atenolol and propranolol ($10 \text{ mg}\cdot\text{L}^{-1}$) in an aqueous matrix using the heterogeneous photo-Fenton process. The experimental conditions selected were $100 \text{ mg}\cdot\text{L}^{-1}$ of H_2O_2 and 1 g of pyrite with zinc oxide. Under these conditions, the authors achieved a degradation of 89% of atenolol and 76% of propranolol after 240 min.

Brillas (2022) analyzed the degradation of the anti-inflammatory diclofenac (DCF) in distilled water using combined advanced oxidation processes (electro-Fenton/UV radiation). For the electro-Fenton process, a mixed titanium oxide/boron-doped diamond (TiO_2/BDD) composite was used as the anode, a graphite cathode, sodium sulfate ($0.05 \text{ mol}\cdot\text{L}^{-1}$) as the electrolyte, and a current density of $6.7 \text{ mA}\cdot\text{cm}^{-2}$. Subsequently, after the electrochemical reaction was completed, UV-C radiation was applied using a 25 W lamp for 300 min. This system achieved a degradation of 92% of the contaminant.

Considering that different classes of pharmaceuticals are found in aquatic matrices, the antidiabetic metformin hydrochloride stands out, as its presence has been associated with its high consumption by patients with Type II Diabetes Mellitus over the years. Because this, as high industrial production continues to meet the strong demand for this medication, a greater generation of effluents containing this type of contaminant occurs.

Given this question, this work aimed to employ a combined advanced oxidation process system, starting with the electro-Fenton system and finishing with the photo-Fenton system, to treat the pharmaceutical metformin hydrochloride. As specific objectives, the study sought to verify the efficiency of the combined EAOP and AOP system; monitor the generation of oxidizing agents, such as hydrogen peroxide (H_2O_2) and free chlorine (Cl^-); study the degradation kinetics of both the pharmaceutical and the

oxidizing agents; and evaluate the toxicity of the samples before and after the combined treatment, using seeds, bacteria, and microcrustaceans to determine possible toxicological impacts.

2. Materials and methods

2.1 Drug identification and quantification method

Initially, a stock solution of metformin hydrochloride (CMTF) ($C_4H_{11}N_5 \cdot HCl$) (Fórmula manipulation pharmacy, Batch: 19L09-B002-056467) was prepared at $1000\text{ mg}\cdot\text{L}^{-1}$, and identified and quantified in a quartz cuvette with a 1.0 cm optical path using an ultraviolet/visible (UV/vis) molecular absorption spectrophotometer (Metash brand, model UV-5100). Analyses were conducted at the drug's characteristic wavelength (λ) of 233 nm, using an analytical curve with a linear range of 1 to $15\text{ mg}\cdot\text{L}^{-1}$ to quantify the samples before and after treatment. The method was previously validated based on the following parameters: linear correlation coefficient ($r = 0.9998$), coefficient of variation ($CV < 5\%$), limit of quantification ($LOQ = 0.212\text{ mg}\cdot\text{L}^{-1}$), limit of detection ($LOD = 0.07\text{ mg}\cdot\text{L}^{-1}$), and accuracy (recovery percentages between 103.30 and 108.70%) (I. L. da S. Santana et al., 2025)

2.2 Electrode production and physicochemical properties

Two types of electrodes were used in the study: a commercial graphite electrode (C) and an identical electrode impregnated with magnetite (Fe_3O_4) on its surface, used as a heterogeneous catalyst for the process. Electrode production and physicochemical characterization followed the methodology previously described by Santana et al., (2025), who employed thermogravimetric analysis (TGA), Fourier-transform infrared spectroscopy (FT-IR), scanning electron microscopy coupled with energy-dispersive spectroscopy (SEM/EDS), and flame atomic absorption spectrometry (FAAS). Table 1 summarizes the characterization techniques employed.

Table 1 – Characterizations used on the modified electrode and the final solution.

Analytical technique	Equipment	Operating conditions	Analysis objective
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TGA	Netsch brand, model STA 449 F3 Júpiter	Inert atmosphere with flow of 100 mL·min ⁻¹ , heating rate of 20°C·min ⁻¹ over range of 25 to 800°C	To evaluate thermal stability across a given temperature range
FT-IR	Bruker brand, model Vertex 7.0	Attenuated total reflectance (ATR), spectral scan in the 4000 to 400 cm ⁻¹ region, resolution of 4 cm ⁻¹ over 64 scans	Identify the functional groups and chemical bonds present in the material
SEM/EDS	Tescan brand, model MIRA 3	Operated at 8 kV, in temperature of 21 ± 3°C	Conduct an analysis of the material's surface
FAAS	Varian brand, model AA 240MS	Operating at a wavelength of 327 nm, compressed air/acetylene was used as the gas, and a hollow- cathode lamp was used	Iron concentration in the catalyst and in the final solution

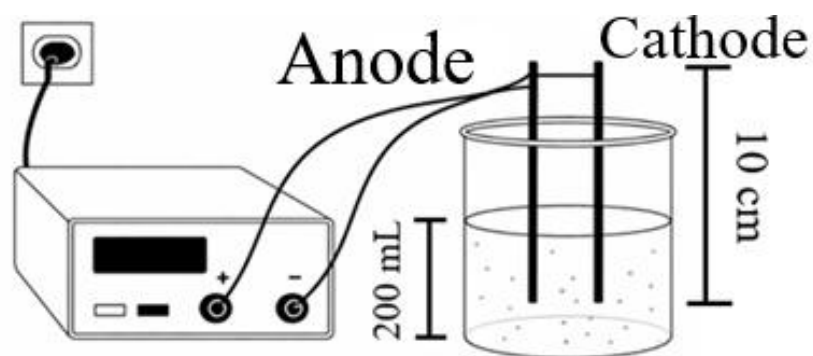
Source: Santana (2025)

2.3 Drug degradation studies using combined AOPs

For the drug degradation assays, a CMTF working solution was first prepared at a concentration of 10 mg·L⁻¹. Treatment of the contaminant was then initiated using a combined system, an electro-Fenton (EF) process followed by photo-Fenton (PF).

For the EF process, experimental parameters previously selected by the research group were used, such as: a distance of 3 cm between electrodes, a current density of 30 mA·cm⁻², and sodium chloride (NaCl) (0.05 mol·L⁻¹) as the electrolyte. The EAOP system was powered by an adjustable power supply (Minipa, Model OS-600), using the graphite electrode as the cathode and the magnetite (Fe₃O₄) impregnated graphite electrode as the anode. The aforementioned system is shown in Figure 1.

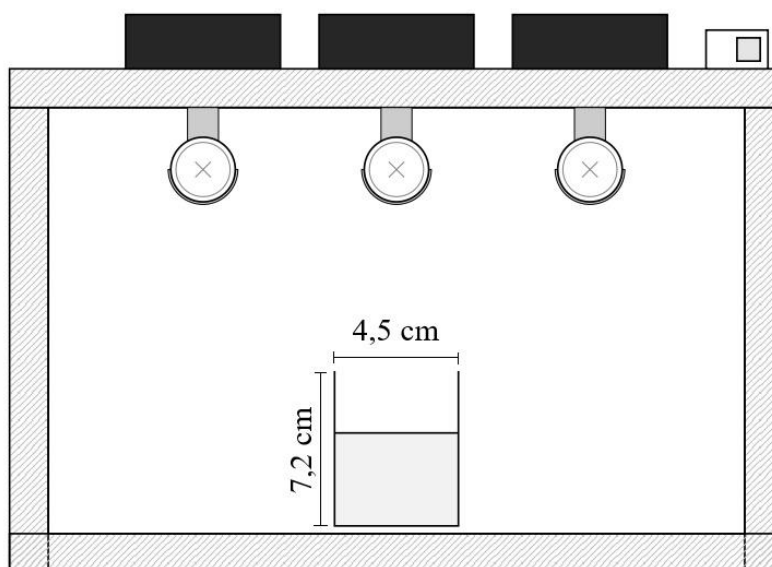
Figure 1 – Electrochemical system used to promote the degradation of drug under study



Source: the authors (2026).

Next, after treatment via the EF process, the working solution was exposed to the photo-Fenton (PF) system. For this evaluation, a bench-scale radiation chamber was used, composed of 3 UV-C lamps arranged in parallel with a power of 30 W each (totaling a photon emission of $3.7 \text{ mW} \cdot \text{cm}^{-2}$), as shown in the schematic diagram in Figure 2. To ensure even greater efficiency, the chamber was lined with aluminum foil.

Figure 2 – Layout of an irradiation chamber consisting of UV-C lamps arranged parallel



Source: the authors (2026).

Since the oxidizing agent is generated within the EF system, and one of the electrodes used had iron on its surface (initial concentration of $60.18 \text{ mg} \cdot \text{L}^{-1}$), no reagents were added beforehand when the sample was subjected to the PF process. To determine the amount of H_2O_2 generated, the methodology described by was used, employing ammonium metavanadate as the precursor agent.

The combined system was tested for different exposure times, as described in Table 2. The initial volume of treated sample was 200 mL, with 250 mL beakers (height = 5.5 cm and diameter = 7.7 cm) used as reactors. After selecting the experimental condition that resulted in the highest degradation percentage, the degradation kinetics of the drug were monitored.

Table 2 – Description of exposure times for each treatment system used for drug degradation

Trials	Time of exposure to the system (min)		Time total of treatment (min)
	Electro-Fenton	Photo-Fenton	
1	30	30	60
2	30	45	75
3	30	60	90
4	45	30	75
5	45	45	90
6	45	60	105
7	60	30	90
8	60	45	105
9	60	60	120

Source: the authors (2026).

2.4 Drug degradation kinetics

The degradation kinetics study was carried out by withdrawing 2 mL aliquots from the initial sample volume throughout the treatment, at sampling times of 0, 10, 20, 30, 40, 50, 60, 75, 90, and 120 min. For the data obtained in this experiment, the kinetic models of Chan and Chu (2003) and He et al. (2016) were tested, with the aim of evaluating the kinetic profile of contaminant degradation. Evaluation of the experimental data was carried out considering the linear regression coefficient (R^2) and residual plots, using Origin 8.0 software for data processing.

2.5 Kinetics of oxidizing agent generation in the electro-Fenton system

During the degradation kinetics study, the generation of oxidizing agents (H_2O_2 and Cl^-) in the EF process was also monitored. Throughout this treatment, the methodologies described by Santana et al. (2021) and Neves et al. (2022) were used to monitor the concentrations of hydrogen peroxide and free chlorine, respectively. Both determinations made use of a UV/Vis molecular absorption spectrophotometer at wavelengths of 543 and 515 nm, for H_2O_2 and Cl^- , respectively.

2.6 Toxicity

Three types of tests were chosen for the toxicity study: phytotoxicity, bacterial toxicity, and ecotoxicity. Some species of seeds, bacteria, and microcrustaceans, respectively, were used for these assays.

2.6.1 Phytotoxicity

For this study, yellow onion (*Allium cepa*) and Broccoli-cabbage (*Brassica oleracea var italica*) seeds were used, following the methodology of Santos et al., (2020). Initially, 4 mL aliquots of the samples were taken at different treatment times (0, 30, 60, 70, 90, and 120 min) and placed in Petri dishes lined internally with qualitative filter paper, containing 20 seeds. A negative control (distilled water) was also subjected to the assay, as well as a 3% boric acid solution as a positive control. The assays were carried out independently for each seed species, each in quintuplicate, and the samples were kept away from light for a period of 5 days. After this period, phytotoxicity was calculated based on the relative growth index (RGI) and germination index (GI), as described by Young et al. (2012)

2.6.2 Bacterial toxicity

Bacterial toxicity was evaluated using cell suspensions of *Escherichia coli* UFPEDA 224 and *Salmonella enteritidis* UFPEDA 414 ($16.6 \mu\text{L}$; 3×10^6 CFU/mL in 0.15 M NaCl solution) in Mueller-Hinton broth ($33.3 \mu\text{L}$). The assays were carried out with samples of the drug solution collected before and after each treatment time in the electro-

Fenton (EF) and photo-Fenton (PF) processes. For the evaluation, samples were used at their original concentration and after a 1:10 dilution (10⁻¹) in sterile ultrapure water (Milli-Q, Millipore).

Aliquots of 150 µL of each sample were incubated with the bacterial suspensions for 24 h at 37°C. The negative control consisted of bacterial cells incubated only in the presence of sterile ultrapure water. Before and after the incubation period, aliquots from each assay were transferred to 96-well microtiter plates, and optical density was determined at 600 nm (OD₆₀₀). The percentage of bacterial growth was calculated relative to the negative control, considered as 100% growth. Additionally, aliquots of the treatment samples were plated on Petri dishes containing Mueller-Hinton agar (MHA) to evaluate cell viability after 24 h of incubation at 37°C. The assays were performed in triplicate and repeated in three independent experiments.

2.6.3 Ecotoxicity in microcrustaceans

Ecotoxicity assays were carried out with the microcrustacean *Artemia salina*, following the methodology described by Aguiar et al. (2022). Initially, 500 mL of seawater was added to a beaker and kept under constant aeration. *Artemia salina* eggs were then introduced and incubated for 48 h at a temperature of 25 ± 3°C for nauplii hatching. After hatching, ten larvae were selected using a stereomicroscope (Wild M3B) and transferred to each experimental group. The ecotoxicity of the samples before and after treatment was then evaluated, considering seawater as the negative control and a 1.0 mg·L⁻¹ niclosamide solution as the positive control. The assays were performed in quadruplicate, and after 24 h of exposure of the organisms to the samples, the survival and mortality of the microcrustaceans were assessed.

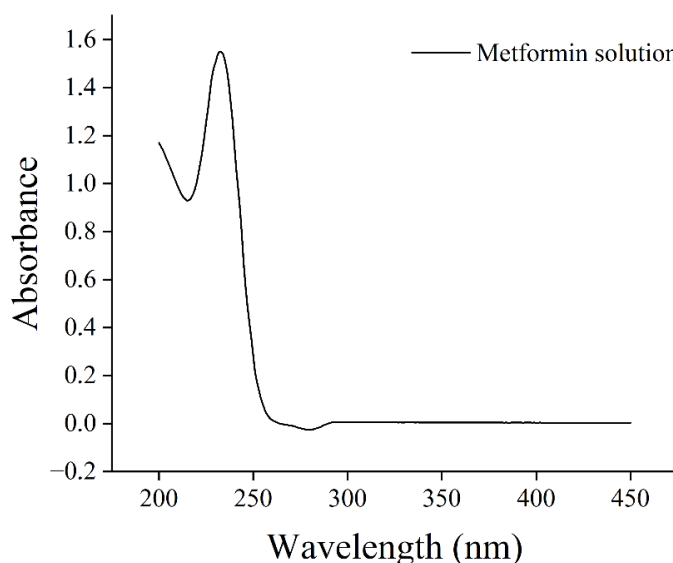
3. Results and Discussion

3.1 Drug identification and quantification

In order to confirm the behavior of metformin under the experimental conditions used, a spectral scan was performed between 200 and 450 nm. The spectrum obtained, shown in Figure 3, revealed a maximum absorption at 233 nm, in agreement with the

previously established value, this being the wavelength used for quantification of the drug.

Figure 3 – Spectrum of the metformin drug solution at $10 \text{ mg}\cdot\text{L}^{-1}$



Source: the authors (2026).

The result obtained in this work is close to that found in the study conducted by Kurdi et al. (2024), in which the authors used a UV-1800 model UV/Vis spectrophotometer (Shimadzu Corporation), equipped with a deuterium lamp + 20 W halogen lamp, performing a spectral scan between 200 and 400 nm. The authors determined a maximum absorption wavelength of 234 nm for metformin, showing agreement between the results.

Consequently, an analytical curve was constructed for the determination and quantification of the contaminant in the concentration range of $1 \text{ mg}\cdot\text{L}^{-1}$ to $15 \text{ mg}\cdot\text{L}^{-1}$. In order to statistically evaluate the dispersion of the determined values, the Grubbs test was applied at a 95% confidence level. The results showed that the values of the eight replicates met the criteria established by the Grubbs test, since the critical tabulated value for this number of samples is 2.023, while the calculated values ranged between 0.828 and 1.736 for $G<$ and between 1.219 and 1.902 for $G>$. Thus, no outliers were identified among the experimental data of the curve.

Regarding the precision of the method, the coefficients of variation (CV) obtained for the analyzed concentrations were below 5%, demonstrating adequate repeatability and compliance with the criteria established by ANVISA (2017). Accordingly, the analytical curve was constructed, whose linear regression resulted in the equation $y = 0.813x + 0.0064$ and a correlation coefficient (r) equal to 0.9998, indicating an excellent fit of the data to the linear model.

3.2 Study of metformin degradation using combined advanced oxidation processes

With the aim of using electrogenerated hydrogen peroxide and chlorine as oxidizing agents in the electrochemical system, the studies began with the EAOP process. The choice of this process is based on its ability to promote simultaneous in situ generation of these oxidants during the process, eliminating the need for prior addition of chemical reagents and contributing to operational simplification.

3.2.1 Electro-Fenton/Photo-Fenton system performance

The results obtained for the treatment using the combined advanced oxidation process are shown in Table 3.

Table 3 – Degradation and exposure times of the drug solution after being subjected to each treatment system

Trials	Electro-Fenton		Photo-Fenton		Total time (min)	Total degradation (%)
	Time (min)	Degradation (%)	Time (min)	Degradation (%)		
1	30	66.42	30	11.21	60	77.63
2	30	65.19	45	22.11	75	87.30
3	30	64.66	60	26.04	90	90.70
4	45	77.13	30	18.09	75	95.22
5	45	75.83	45	17.17	90	93.00
6	45	76.71	60	17.40	105	94.11
7	60	86.72	30	8.31	90	95.03
8	60	84.38	45	8.77	105	93.15

9	60	85.26	60	10.78	120	96.34
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Source: the authors (2026).

As can be seen in Table 4, the data show the direct influence of the EF system on metformin degradation, since increasing the exposure time to this process resulted in greater degradation efficiency. This behavior suggests greater *in situ* generation of oxidizing species throughout the electrochemical process, favoring oxidation of the contaminant. But, although the trials conducted with longer exposure times showed higher degradation efficiencies, the gains obtained became progressively less significant.

Also, it can be observed that the photo-Fenton treatment stage promoted an increase in metformin degradation under all conditions evaluated. This behavior can be attributed to the action of UV radiation in regenerating Fe^{2+} ions from the Fe^{3+} present, increasing the availability of catalytically active species for the decomposition of hydrogen peroxide and the consequent generation of hydroxyl radicals. Additionally, irradiation of ferric complexes and of hydrogen peroxide itself may contribute to the formation of additional oxidizing species, enhancing degradation of the contaminant.

When analyzing the combined system, the results show that the efficiency of the photo-Fenton stage was directly related to the condition previously established by the electro-Fenton process. For shorter EF times (30 min), the photochemical stage promoted gains of up to 26.04% in metformin degradation, indicating that significant amounts of the contaminant were still present in the sample. Regarding the oxidative species, it can be inferred that they required more EF process time to be generated and subsequently consumed. On the other hand, when longer electro-Fenton times were used (60 min), the observed gains were below 11%, suggesting that most of the degradation had already occurred in the electrochemical stage.

In this manner, a synergistic effect between the electro-Fenton and photo-Fenton processes is evident, since the electrochemical stage promotes the initial generation of oxidants and degradation of the contaminant, while the photochemical stage intensifies catalyst regeneration and the production/consumption of oxidizing radicals. As a result, degradation efficiencies above 95% were achieved without the need to excessively prolong the electrolysis time.

From an operational standpoint, prolonging the process would imply increased energy consumption, raising the costs associated with treatment. Therefore, when jointly considering degradation efficiency and the process's energy demand, the condition

corresponding to trial 4 (45 min of electro-Fenton followed by 30 min of photo-Fenton) was selected as the most suitable, since the conditions with longer total treatment time achieved additional efficiency gains of less than 2%, which did not justify increasing the operational time given the system's energy consumption.

3.2.2 Electrode characterization

The physicochemical characterization of the electrodes and the magnetite used in this study was previously carried out by Santana et al. (2025) using TGA, FT-IR, SEM/EDS, and FAAS techniques. The results obtained confirmed the incorporation of magnetite onto the graphite electrode surface, as well as its thermal stability, morphological characteristics, and chemical composition suitable for application as a heterogeneous catalyst.

Overall, the TGA analyses showed high thermal stability for the graphite, the synthesized magnetite, and the modified electrode, with mass losses of around 2% across the temperature range evaluated by Santana et al. (2025). According to the authors, this small variation is mainly associated with the elimination of residual water adsorbed during the material drying step. The low mass loss observed indicates that magnetite impregnation did not compromise the thermal stability of the graphite electrode, showing strong interaction between the two materials. This characteristic is relevant for applications in electrochemical processes, since thermally stable materials tend to show greater resistance to operating conditions and greater durability when used as heterogeneous catalysts (Martincic et al., 2024).

The FT-IR analyses showed the characteristic bands of magnetite, including the vibrations associated with hydroxyl groups (O–H) and Fe–O bonds, confirming the formation of the iron oxide. Additionally, the presence of these bands in the spectrum of the modified electrode confirmed the immobilization of magnetite on the graphite surface. Similar results were described by Manikandan et al. (2022).

The SEM/EDS analyses showed morphological changes on the electrode surface after the modification process. The graphite electrode showed a surface with irregular porosity, a characteristic also observed by Andersen et al. (2021). The deposition of particles on the material's surface was also observed, attributed to the synthesized magnetite, indicating the formation of a catalytic layer potentially capable of increasing the availability of active sites for the heterogeneous reactions involved in the electro-

Fenton process. The EDS results corroborated this observation, revealing the presence of iron (42.7%) and oxygen (31.5%) by mass on the surface of the modified electrode, a composition consistent with the presence of iron oxides. These results confirm the efficiency of the methodology used for the synthesis and impregnation of magnetite, showing the distribution of the catalyst on the graphite surface.

Additionally, flame atomic absorption spectrometry (FAAS) analysis allowed quantification of the iron content incorporated into the material, resulting in a concentration of $60.18 \pm 0.47 \mu\text{g}\cdot\text{mL}^{-1}$ in the modified electrode. Furthermore, iron concentrations of $0.08 \pm 0.02 \mu\text{g}\cdot\text{mL}^{-1}$ in the initial solution and $0.24 \pm 0.01 \mu\text{g}\cdot\text{mL}^{-1}$ after treatment were determined. These results indicate low leaching of the catalyst into the reaction medium, demonstrating that the immobilization strategy used was effective in retaining magnetite on the electrode surface. According to Santana et al., (2025), the iron concentration observed after treatment was approximately seven times lower than that found for electrodes impregnated with magnetite alone, showing greater stability of the material.

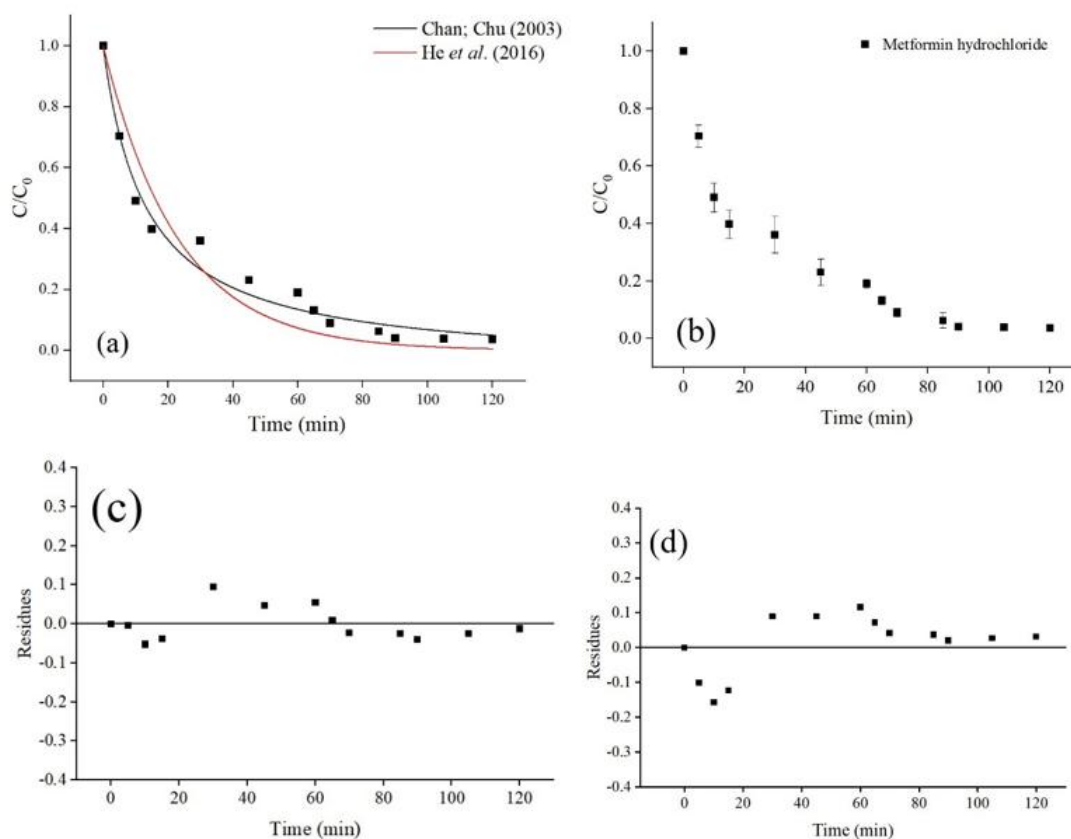
Similar results are reported in the literature, in which iron immobilization strategies seek to reduce its release into the reaction medium. In contrast, Song et al., (2024), when degrading diclofenac by electro-Fenton using graphite as the cathode and metallic iron as the anode, observed a leached iron concentration of 1.021 mg L^{-1} after 30 min of treatment. Comparatively, the modified electrode developed by Santana et al. (2025) showed lower iron release into the solution, indicating greater stability of the catalyst and lower potential for secondary contamination of the treated effluent. This characteristic is particularly relevant for integrated electro-Fenton/photo-Fenton systems, since it favors the maintenance of active catalytic sites throughout the treatment and reduces the need for subsequent catalyst separation steps, minimizing the introduction of residual iron into the treated effluent.

3.3 KINETIC STUDY OF THE ADVANCED OXIDATION PROCESS

The data obtained during monitoring of metformin degradation were fitted to the kinetic models proposed by Chan and Chu (2003) and He et al. (2016), as shown in Figure 4.

Figure 4 – (a) Fit of the kinetic models to the experimental metformin degradation data, (b) Deviations in the experimental data obtained during the treatment and distribution of waste from

the kinetic models fitted to the experimental data from the combined electro-Fenton and photo-Fenton process: (c) Chan and Chu (2003) and (d) He *et al.* (2016).



Source: the authors (2026).

It can be observed in Figure 4(a) that metformin degradation occurred more intensely during the first 20 min of treatment, followed by a slower degradation stage until the process stabilized at approximately 90 min, reaching a maximum degradation of 96.22%. As observed in Figures 4(c) and 4(d), the residuals are randomly distributed around the reference line, with no evident systematic trends present. This behavior indicates that both models are able to adequately represent the kinetics of metformin degradation, with the Chan and Chu (2003) model showing the best statistical performance.

Furthermore, it can be seen that both models evaluated were able to satisfactorily describe the experimental behavior of the system, a fact that can be confirmed by the statistical parameters presented in Table 3.

Table 4 – Kinetic parameters of the tested models

Model	Parameter	
Chan; Chu (2003)	R^2	0,97
	Sr^2	2.01×10^{-3}
	$1/\sigma$	1.053 ± 0.0292
	$1/\rho \text{ (min}^{-1}\text{)}$	0.080 ± 0.020
He <i>et al.</i> (2016)	R^2	0.91
	Sr^2	7.49×10^{-3}
	$K \text{ (min}^{-1}\text{)}$	0.04 ± 0.005

Source: the authors (2026).

According to the results presented in Table 4, it can be seen that both models showed high linear regression coefficients (R^2), with values of 0.97 obtained for the Chan and Chu (2003) model and 0.91 for the He et al. (2016) model. These results indicate a good representation of the experimental data by the models evaluated and suggest that metformin degradation can be adequately described by pseudo-first-order kinetics.

Analysis of the squared residuals (Sr^2) showed better performance for the Chan and Chu (2003) model, which presented the lowest value for this parameter (2.01×10^{-3}), compared to the He et al. (2016) model (7.49×10^{-3}). This result shows a smaller dispersion between the experimental values and the values predicted by the model, indicating a better fitting capacity.

For the Chan and Chu (2003) model, values of $1/\sigma$ and $1/\rho$ equal to 1.053 ± 0.029 and $0.080 \pm 0.070 \text{ min}^{-1}$, respectively, were obtained. The parameter $1/\sigma$ is related to the maximum oxidative capacity of the system, while $1/\rho$ is associated with the initial degradation rate of the contaminant (kinetic constant). The results corroborate the behavior observed experimentally, characterized by a rapid reduction in contaminant concentration during the first twenty minutes of treatment, followed by a gradual approach to equilibrium.

For the He et al. (2016) model, a kinetic constant of $0.040 \pm 0.005 \text{ min}^{-1}$ was determined. Comparing the kinetic parameters obtained by the two models, it can be observed that the Chan and Chu (2003) model showed a higher rate constant, reflecting a higher degradation rate and reinforcing its better suitability for describing the process studied.

Similar results were reported by Li et al. (2025), who evaluated the degradation of fluoroquinolone in an aquatic matrix through the photo-Fenton process using UV-C radiation (1.88 W lamps each) and an iron concentration of $30 \text{ mg}\cdot\text{L}^{-1}$. The authors obtained a degradation efficiency of 86% after 60 min of treatment, finding that the process followed pseudo-first-order kinetics.

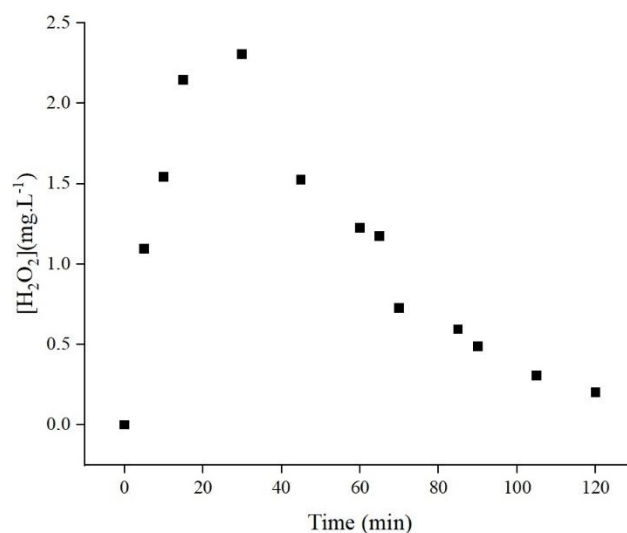
Similarly, Gonzaga et al. (2023) investigated the degradation of the drug levofloxacin by photoperoxidation using hydrogen peroxide at a concentration of $0.5 \text{ mol}\cdot\text{L}^{-1}$ and three UV-C lamps of 65 W each. After 120 min of treatment, a degradation efficiency of 96.40% was achieved, with the kinetic behavior also described by a pseudo-first-order model.

Thus, the results obtained in this study are in agreement with those reported in the literature for advanced oxidation processes applied to the removal of pharmaceuticals in aquatic matrices, showing the efficiency of the electro-Fenton process combined with photo-Fenton in the degradation of metformin. After evaluating the degradation kinetics, the generation of hydrogen peroxide was monitored throughout the treatment.

3.3.1 Evaluation of hydrogen peroxide generation and consumption

Throughout the electrochemical treatment, the concentration of hydrogen peroxide (H_2O_2) in the reaction medium was monitored, in order to evaluate its generation and consumption during application of the electro-Fenton and photo-Fenton processes. The results obtained are shown in Figure 6.

Figure 6 – Kinetics of H_2O_2 generation and consumption during metformin treatment in the electro-Fenton and photo-Fenton process



Source: the authors (2026).

As observed in Figure 6, the H₂O₂ concentration increased gradually during the initial moments of the process, reaching a maximum value of approximately 2.3 mg·L⁻¹ at 30 min of treatment. This behavior confirms the *in situ* generation of the oxidizing agent at the cathodic surface, a fundamental step for the occurrence of the reactions characteristic of the electro-Fenton process. After reaching the maximum concentration, a progressive reduction in H₂O₂ levels was observed in the reaction medium. Between 40 and 60 min of treatment, the decrease in oxidant concentration became more evident, indicating its consumption in the contaminant oxidation reactions. This can be attributed to the reaction of H₂O₂ with the Fe²⁺ ions present in the system, promoting the continuous formation of hydroxyl radicals (•OH), highly reactive species responsible for metformin degradation. Additionally, the incidence of UV-C radiation during the photo-Fenton stage may contribute to the consumption of hydrogen peroxide, generating additional oxidizing species and increasing process efficiency.

At the end of the treatment, a residual concentration of approximately 0.2 mg·L⁻¹ of H₂O₂ was observed, indicating that most of the oxidant generated was effectively consumed throughout the process. This result shows the balance between the generation and consumption stages of hydrogen peroxide, a characteristic frequently observed in electro-Fenton systems operating under adequate conditions of electron transfer and catalytic regeneration.

Furthermore, a direct relationship can be observed between the H₂O₂ generation profile and the metformin degradation kinetics presented earlier. The highest hydrogen peroxide concentration was observed at 30 min of treatment, a period that coincides with

the stage of greatest contaminant degradation, as shown in Figure 5. This may be due to the high availability of H_2O_2 in the initial moments of the process, which favored the formation of hydroxyl radicals ($\bullet\text{OH}$), increasing the rate of metformin degradation. As the H_2O_2 concentration decreases due to its consumption in the photo-Fenton process, a reduction in the contaminant's degradation rate is also observed, as evidenced by the kinetic profile obtained.

Similar results were reported by Cornejo et al. (2024), who evaluated hydrogen peroxide generation in electrochemical advanced oxidation processes using graphite as the cathode and boron-doped diamond (BDD) as the anode, under a current density of $30 \text{ mA}\cdot\text{cm}^{-2}$ for 120 min of treatment. The authors observed a residual H_2O_2 concentration of $0.36 \text{ mg}\cdot\text{L}^{-1}$ at the end of the experiment, demonstrating the progressive consumption of the oxidant throughout the process.

Similarly, Hu et al. (2022) investigated H_2O_2 generation in electrochemical systems using bismuth oxide-based electrodes and sodium bicarbonate electrolyte ($1.0 \text{ mol}\cdot\text{L}^{-1}$), with a current density of $1.0 \text{ A}\cdot\text{cm}^{-2}$ for 30 min. The authors found a residual concentration of approximately $0.5 \text{ mg}\cdot\text{L}^{-1}$ of H_2O_2 at the end of treatment, a result consistent with the behavior observed in the present study.

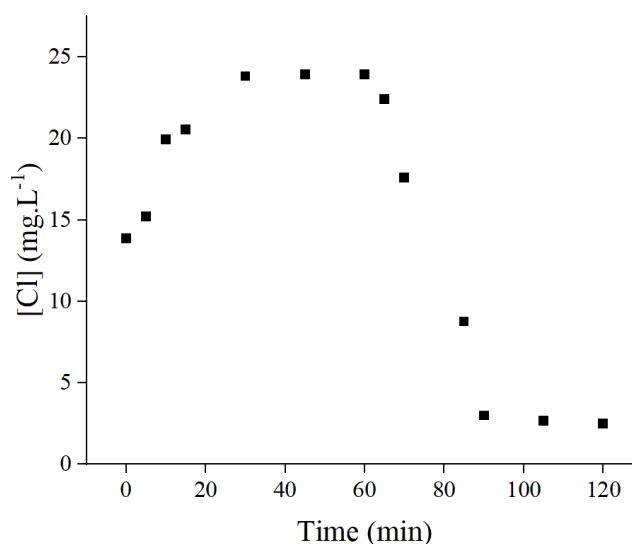
The results obtained demonstrate that the electrochemical system was able to efficiently generate hydrogen peroxide, favoring the continuous production of oxidizing species responsible for metformin degradation. Combined with the electrochemical generation of H_2O_2 , the application of UV-C radiation contributed to intensifying the photo-Fenton process, favoring both the catalytic regeneration of Fe^{2+} ions and the additional production of oxidizing species. Together, these mechanisms contributed to the high metformin degradation efficiency observed in this study.

After evaluating the H_2O_2 generation and consumption profile, the study proceeded to investigate the formation of free chlorine in the electrochemical system, resulting from the use of sodium chloride (NaCl) as the electrolyte.

3.3.2 Evaluation of free chlorine Generation

Just as with the monitoring carried out for hydrogen peroxide, the formation of free chlorine was evaluated throughout the treatment, due to the use of sodium chloride (NaCl) as the electrolyte of the electrochemical system. The results obtained are shown in Figure 7.

Figure 7 – Kinetics of free chlorine generation and consumption during the electro-Fenton and photo-Fenton process



Source: the authors (2026).

As observed in Figure 7, the presence of free chlorine was detected from the initial moments of treatment, showing the electrochemical oxidation of the chloride ions present in the electrolyte. During the first 30 min of operation, a gradual increase in the free chlorine concentration was observed, reaching values close to $25 \text{ mg}\cdot\text{L}^{-1}$. This result is associated with the anodic oxidation reactions of the chloride ion, which promote the formation of active chlorine oxidizing species, such as molecular chlorine (Cl_2), hypochlorous acid (HClO), and hypochlorite ion (OCl^-), a behavior similar to that observed by Luo et al. (2021).

Between 30 and 60 min of treatment, the free chlorine concentration stabilized, remaining around $25 \text{ mg}\cdot\text{L}^{-1}$, with a maximum value of $25.4 \text{ mg}\cdot\text{L}^{-1}$. This may be associated with the establishment of a dynamic equilibrium between the generation and consumption processes of the chlorinated species in the reaction medium.

After 60 min, a marked reduction in the free chlorine concentration was observed, indicating consumption of the oxidizing species formed during treatment, which may be related to the participation of these species in the oxidation reactions of metformin and its degradation intermediates. Furthermore, during the photo-Fenton stage, the incidence

of UV-C radiation may favor the decomposition of photoactive chlorinated species, contributing to the decrease in residual free chlorine concentration observed at the end of the experiment.

The generation of chlorine-based oxidizing species may act in a complementary way to the hydroxyl radicals produced in the photo-Fenton process, contributing to degradation of the contaminant. Thus, in addition to the reactions associated with the $\text{Fe}^{2+}/\text{H}_2\text{O}_2$ system, the presence of active chlorine may represent an additional oxidation route, enhancing the overall efficiency of the treatment.

Li et al. (2023) also found similar results when evaluating the degradation of norfloxacin by the electro-Fenton process using sodium chloride ($0.1 \text{ mol}\cdot\text{L}^{-1}$) as the electrolyte and a current density of $30 \text{ mA}\cdot\text{cm}^{-2}$. The authors obtained a maximum free chlorine concentration of $30 \text{ mg}\cdot\text{L}^{-1}$ over the 30 min of treatment, associated with a contaminant degradation efficiency of 76%.

Similarly, Ren et al. (2022) were able to determine the free chlorine concentration when degrading ofloxacin using titanium electrodes as the cathode and boron-doped diamond (BDD) as the anode, employing NaCl ($1.45 \text{ g}\cdot\text{L}^{-1}$) as the electrolyte and a current density of $25 \text{ mA}\cdot\text{cm}^{-2}$. Within a treatment time of 10 min, the authors obtained a drug degradation of 30.5%, and found a maximum free chlorine value generated equal to $50 \text{ mg}\cdot\text{L}^{-1}$, demonstrating the relevance of chlorinated species in electrochemical systems containing chloride-based electrolytes.

The results obtained indicate that the use of NaCl as the electrolyte favored the formation of active chlorine oxidizing species throughout the treatment. Together with the hydroxyl radicals generated by the photo-Fenton process, these species may have contributed to the high metformin degradation efficiency observed in this study.

3.4 Toxicity

Advanced oxidation processes can promote the formation of intermediate products during contaminant degradation, which may exhibit toxicity different from that observed for the original compound. Thus, in addition to degradation efficiency, it becomes essential to evaluate the possible toxicological effects of the treated samples on organisms representative of the biota.

3.4.1 Phytotoxicity test

The phytotoxicity assays were carried out as a function of metformin treatment time, using the same experimental conditions employed in the kinetic study (item 3.3). For this evaluation, the germination index (GI) and root growth index (RGI) were determined for broccoli and yellow onion seeds, as shown in Table 5.

Table 5 – Germination index (GI) and root growth index (RGI) for broccoli-cabbage and yellow onion seeds exposed to the treated samples

Samples	Broccoli-cabbage		Yellow onion	
	GI (%)	RGI	GI (%)	RGI
Negative control	100.0	1.00	100.00	1.00
Initial solution	79.86	0.79	48.97	0.55
30 min	56.90	0.56	28.86	0.51
60 min	63.92	0.61	53.36	0.70
70 min	48.07	0.52	63.31	0.78
90 min	31.49	0.29	76.84	0.82
120 min	57.06	0.55	93.76	0.88

Source: the authors (2026).

As observed in Table 5, the initial solution containing metformin showed a reduction in the germination index for both plant species compared to the negative control, showing the toxic potential of the drug. This result is in agreement with what was reported by Phadwal et al. (2022), who highlight the adverse effects of pharmaceutical residues on plant organisms.

For broccoli-cabbage seeds, a reduction in the root growth index was observed throughout treatment, with values ranging between 0.29 and 0.79. According to the criterion proposed by Young et al. (2012), RGI values below 0.80 indicate the presence of a toxic effect. Thus, the results suggest that the compounds present after treatment still exerted a negative influence on root development in this species. This may be related both to the formation of intermediate byproducts during metformin degradation and to the residual presence of chemical species generated during the treatment process. Additionally, the use of sodium chloride as the electrolyte may influence plant

development due to increased salinity of the medium, a condition that can affect water absorption by the seeds and impair their growth, as discussed by Seal et al. (2021).

In contrast, yellow onion seeds showed a different behavior, since the RGI progressively increased throughout treatment, rising from 0.55 in the initial solution to 0.88 after 120 min of treatment. This indicates a reduction in sample toxicity over the course of the process, reaching values above the minimum threshold of 0.80 established by Young et al. (2012), which suggests the absence of significant toxic effect at the end of treatment.

In the study by Pizzichetti et al. (2023), in which the authors evaluated diclofenac degradation by photoperoxidation ($20 \text{ mg} \cdot \text{L}^{-1} \text{ H}_2\text{O}_2$) using radish (*Raphanus sativus*) and tomato (*Solanum lycopersicum*) seeds as test organisms, an increase in germination percentages was observed, from 39% to 57% and from 23% to 36%, respectively, after 60 min of drug treatment, indicating the persistence of a certain degree of residual toxicity associated with the byproducts formed during the process. Similarly, Cardoso et al. (2024) evaluated phenacetin degradation by electro-Fenton using polytetrafluoroethylene (PTFE)-modified carbon as the cathode and platinum as the anode. After 120 min of treatment using sodium sulfate ($0.05 \text{ mol} \cdot \text{L}^{-1}$) as the electrolyte and a current density of $60 \text{ mA} \cdot \text{cm}^{-2}$, the authors observed a germination index of 76.2% for lettuce (*Lactuca sativa*) seeds, concluding that the treated sample showed low toxicity.

The results obtained in this study demonstrate that the toxicological response depends on the plant species evaluated. While yellow onion seeds showed a reduction in toxicity throughout treatment, broccoli seeds showed greater sensitivity to the compounds present in the treated samples. These results highlight the importance of using different test organisms for a more comprehensive assessment of the toxicological effects associated with advanced oxidation processes.

3.4.2 Microbial toxicity test

The toxicity of the solution before and after the electro-Fenton (EF) and electro-Fenton followed by photo-Fenton (EF+PF) treatments was evaluated by means of the growth inhibition of the bacteria *Escherichia coli* and *Salmonella enteritidis*. The results obtained are shown in Table 6.

Table 6 – Bacterial growth results

Samples	<i>Escherichia coli</i>		<i>Salmonella enteritidis</i>	
	OD ₆₀₀	Growth (%)	OD ₆₀₀	Growth (%)
Negative control	0.207±0.017	100.00	0.593±0.016	100.00
Initial solution	0.135±0.054	65.14	0.485±0.010	81.87
Final solution (EF)	0.094±0.009	45.19	0.694±0.053	117.11
Final solution (EF+PF)	0.061±0.002	29.56	0.604±0.041	101.93

OD₆₀₀ – Optical density measured turbidimetrically at 600 nm; EF = electro-Fenton and PF = photo-Fenton.

Source: the author (2026).

Analyzing Table 6, it can be observed that for *E. coli*, the initial solution showed a relative growth of 65.14%, indicating a toxic effect of the drug on this organism even before treatment. After the EF process, this value decreased to 45.19%, while after the combined treatment (EF+PF), it dropped to 29.56%, showing a progressive increase in toxicity for this bacterium. This behavior may be related to the formation of intermediate products from metformin degradation.

In contrast, *S. enteritidis* showed a different behavior. The initial solution promoted a slight reduction in growth (81.87%), while the treated samples showed growth rates higher than the negative control (117.11% for EF and 101.93% for EF+PF). These results indicate the absence of a significant toxic effect for this bacterial species after the treatments applied.

This difference in response shows that toxicity depends on the sensitivity of the organism, since different bacteria present distinct physiological and metabolic mechanisms in response to the compounds present. Thus, the results reinforce that evaluation of AOP efficiency should consider not only pollutant degradation, but also the toxicity of the products formed during the process, which may affect different organisms representative of the biota in different ways.

3.4.3 Ecotoxicity test in microcrustaceans

Artemia salina nauplii were used as the test organism due to their high sensitivity to environmental contaminants, rapid reproduction, and wide application in ecotoxicological studies (Checa-Fernández et al., 2024). According to Das Pramanik et al. (2023), the toxicity evaluated by *A. salina* occurs as a function of the duration and dosage of exposure. Therefore, intermediate products generated in the oxidative process may affect the organism's behavioral characteristics and mortality.

No mortality was observed in the initial solution or after the EF+PF treatments. Although the electro-Fenton process promoted high degradation, a mortality rate of 95% of the individuals was observed. The high mortality observed suggests that this treatment may have significant toxic effects due to the transformation products generated by the process. In addition to mortality, the surviving organisms exposed to the samples from the EF processes showed significant alterations, with behaviors characterized by low motility, uncoordinated movements, and episodes of paralysis. Behavioral changes of this type are frequently used as sublethal indicators of toxicity, and may precede the mortality of organisms. The results contribute to mitigating adverse effects of transformation products generated during treatment, highlighting that after a combined treatment (EF followed by PF), there was a significant reduction in toxicity due to the survival of the individuals.

The results indicate that, although the process reduced toxicity for certain organisms, toxic effects were still observed in others. This behavior suggests that drug degradation may not have been complete, favoring the formation of undesirable intermediate byproducts. The presence of these intermediates may lead to different toxicity profiles depending on the organism evaluated. To address this, it is important to understand how the degradation process may occur and which products may be formed, as can be seen in Equation 1.



Initially, the electrochemical process was used in the proposed treatment. Through this process, oxidizing species are formed at both the cathode and the anode, as described in Equations 2 and 3.

Cathode:



Anode:



Given that one of the electrodes consisted of graphite and iron the latter in the form of magnetite (Fe_3O_4) it can be concluded that hydroxyl radicals and ions were also generated via electro-Fenton reactions, as described in Equation 4.



Given the presence of the products formed in Equations 2, 3, and 4, it is clear that species such as hydroxyl radicals ($\bullet\text{OH}$) and chlorine derived species ($\text{Cl}^\bullet$; $\text{Cl}_2^\bullet$; HOCl ; and OCl^-) are simultaneously present in the system, allowing sequential reactions to occur, as shown in Equations 5 through 9.



Given the successive oxidation reactions, cleavage of the C–N bonds in the drug's central chain occurs, potentially leading to the formation of compounds such as guanylhurea, methylguanidine, guanidine, and urea (Hosseini et al., 2026). In addition to these compounds, the presence of chlorine can lead to nitrogenous intermediate reactions with HOCl and chlorine radicals, forming different chlorinated derivatives such as organic chloroamines (Ghani et al., 2022). These species may be responsible for the toxicity present in the solution after the EF process.

When the sample treated by the EF process was subjected to the photo-Fenton AOP, additional production of hydroxyl radical occurred, allowing continued degradation of both the initial compound and the possible intermediates present. After application of the photo-Fenton process, the formation of carboxylic acids such as formic, acetic, and

oxalic acid may have occurred Amado-Piña et al. (2025), and finally, partial mineralization forming carbon dioxide and water may also have taken place, in addition to the formation of NH_4^+ , NO_2^- , and NO_3^- ions (Castañeda-Sánchez et al., 2025). The presence of these compounds and ions may explain the presence of toxicity, reinforcing the need to monitor different organisms and carry out more detailed future assays.

4. Conclusion

The results obtained demonstrated that the combination of the electro-Fenton (EF) and photo-Fenton (PF) processes was effective for the degradation of metformin hydrochloride in an aqueous medium, providing a degradation efficiency of 96.34%. This result shows the synergistic effect promoted by the combination of electrochemical generation of oxidizing species and the incidence of UV-C radiation.

It was possible to observe that increasing the application time of the EF process favored degradation of the contaminant, and that the photo-Fenton treatment stage, in turn, contributed to the complementary degradation of the intermediate compounds possibly formed.

The kinetic study demonstrated that drug degradation showed behavior consistent with pseudo-first-order kinetics. Additionally, monitoring of the oxidizing species revealed a maximum hydrogen peroxide concentration of $2.3 \text{ mg}\cdot\text{L}^{-1}$ at 30 min of treatment and a maximum free chlorine concentration of $25.40 \text{ mg}\cdot\text{L}^{-1}$ at 60 min, indicating the formation of reactive species that contributed to drug degradation.

The ecotoxicological evaluation indicated that the toxicological response depends on the organism evaluated. While yellow onion seeds showed a reduction in toxicity throughout treatment, reaching values indicative of the absence of significant toxic effect at the end of the process, broccoli seeds maintained sensitivity to the compounds present in the treated samples. For the microcrustacean assays, it was shown that the photo-Fenton stage was essential for reducing the toxicity of intermediate products formed during the electro-Fenton process. These results reinforce the importance of using different test organisms to evaluate the possible environmental impacts associated with advanced oxidation processes. Therefore, the use of combined AOPs proved to be a promising alternative for the treatment of aqueous matrices contaminated with metformin hydrochloride, promoting high degradation efficiency and reducing toxic effects for

certain organisms. However, complementary studies are still needed to identify the byproducts formed during treatment and to evaluate their possible environmental impacts.

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Declarations

Ethical approval: This is not applicable.

Consent to participate: This is not applicable

Consent for publication: This is not applicable

Competing interests: The authors declare no competing interests.

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