



# Optimization and application of a continuous flow photo-electro-Fenton system for the removal of pharmaceutical active compounds detected in irrigation water of Bogotá – Savanna (Colombia) Crops

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## ABSTRACT

In this study, a continuous flow photo-electro-Fenton (PEF) system was evaluated for its ability to remove pharmaceutically active compounds (PhACs) from irrigation water used in Bogotá-savanna crops. The PEF system consisted of dimensionally stable anode and graphite diffusion gas cathode, which were irradiated with LEDs. Firstly, the system was optimized using response surface methodology (RSM) in ultrapure water. The most favorable conditions for efficient generation of oxidants (the response variable) were found to be a flow rate of 210 mL/min, a current density of 15 mA/cm<sup>2</sup>, and an electrolyte concentration of 0.1 mol NaCl/L. Subsequently, model compounds of PhACs, including losartan (LOS), sulfamethoxazole (SMX), and diclofenac (DCF), were eliminated after only 10 min of treatment under the previously established conditions. After demonstrating the potential of the PEF system to eliminate PhACs, the system was applied to real irrigation water to evaluate the degradation of seven PhACs, namely carbamazepine (CBZ), sulfamethoxazole (SMX), ciprofloxacin (CIP), clarithromycin (CLR), diclofenac (DCF), valsartan (VAL), and trimethoprim (TMP). The results showed that after 30 min of treatment with the PEF system, the concentration of these compounds was drastically reduced remaining undetected. This demonstrates the high potential of the PEF system to reduce the presence of PhACs in irrigation water and associated environmental and food health risks.

## 1. Introduction

Irrigation water is of crucial importance in global agricultural production due to the strong relationship between water quality, crop nutritional needs, and production yields. However, climate change exerts great pressure on global agricultural production by causing prolonged periods of drought that prevent irrigation at the right times and places [1,2]. To combat water scarcity, farmers have implemented various mechanisms, including over-exploitation of nearby aquifers, reduced irrigation demand, and the use of alternative water resources of lower quality, e.g., reclaimed, brackish, or wastewater. These actions can significantly affect the quality of crops [3,4]. Recently, the presence of micropollutants known as contaminants of emerging concern (CECs) in water used for crop irrigation has been reported [5,6]. Among the CECs, pharmaceuticals have been frequently detected in water samples

and have demonstrated adverse effects on aquatic organisms, depending on the compound's exposure, bioavailability, susceptibility, and stability [7]. Pharmaceuticals can be directly discarded in the toilet, in the garbage, and depending on the pharmacology of the medical substance, they can be excreted as metabolites (substances not completely assimilated by the human body), as the unchanged compound, or conjugated with inactivating compounds attached to the molecule [8,9].

Particularly in Colombia, in the municipalities of the Bogotá-Savanna, such as Mosquera (see map in Fig. 1), untreated water from the Bogotá River is used to irrigate crops such as lettuce, tomato, spinach, coriander, and others due to its economic viability as a nearby water resource. However, the Bogotá River receives wastewater from neighboring cities, which contributes to the entry of pathogenic microorganisms, heavy metals, pharmaceutical active compounds (PhACs), and pesticides into crops [10–14]. The presence of contaminants such as

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PhACs in the irrigation water of the Bogotá River and its potential transfer towards various crops suggest that these compounds could be bioaccumulating in crops in the area. This has been reported in different vegetables, forage crops, and some fruit trees, compromising their quality and food safety, and representing a possible risk to the health of those who consume these foods [10,11,14–17].

The use of advanced oxidation processes (AOPs) is a highly effective alternative for removing a wide range of CECs from polluted water sources [18–22]. These processes share a common characteristic of generating extremely reactive oxidizing agents, such as hydroxyl ( $\bullet\text{OH}$ ) [23] or sulfate radicals [24], to facilitate the oxidation reactions. Among these AOPs, the electrochemical advanced oxidation processes (EAOPs) stands out as an environmentally friendly technology since it generates highly reactive species solely through the action of electric current in water [19,25,26]. Although no studies have reported the use of these systems for the treatment of irrigation water, their potential as an efficient alternative for the treatment of this type of water can be considered, since previous works have demonstrated their high efficiency in the elimination of pharmaceuticals, microorganisms, and genes associated with resistance to antibiotics in wastewater [18,19,25,26]. These treated waters can subsequently be reused in agro-industrial contexts for irrigation, thereby mitigating the potential negative effects of contaminated water on the environment, food safety, and human health [27–30].

In these EAOPs, parameter's optimization is an important process to determine the best conditions in terms of substance production or pollutant removal [31,32]. Different systems are now being optimized using multivariate statistical techniques. Among the most relevant is the response surface methodology (RSM), which is a set of techniques and statistics based on fitting a polynomial equation to experimental data, which must describe the behavior of a data set in order to make statistical predictions [6]. RSM is especially useful when multiple variables affect the response simultaneously [33,34].

Before applying RSM, it is necessary to choose an experimental design that defines which test should be performed within the region

under study. These designs for first-order models, such as factorial designs, can be used when the data set has no curvature [35]. However, when the experimental data cannot be described by linear functions, quadratic response surface designs such as three-level factorial, Box-Behnken, central composite (CCD), or Doehlert designs should be used [6,33,36,37].

The RSM approach can be implemented in (EAOPs), such as electro-Fenton (EF), photo-electro-Fenton (PEF) or persulfate based (PS) process, to identify the optimal combination of variables. Essential variables include flow rate, current density, electrolyte concentration, distance between electrodes, among others. These variables determine the adequate concentration of reagents present in the system such as iron ions, hydrogen peroxide, sulfate, persulfate, etc. and maximize the efficiency of the processes in removing contaminants [38–40]. By using this approach, treatment performance can be improved, energy consumption can be reduced, and costs associated with the use of reagents and energy consumption can be lowered, making the process more cost-effective.

In the PEF process, the Fenton reaction (Eq. 1) is promoted by an electrochemical cell and assisted by radiation. In this system the use of a gas diffusion cathode (GDE) ensures that hydrogen peroxide ( $\text{H}_2\text{O}_2$ ) is constantly electrogenerated (Eq. 2), eliminating the need for reagent addition during treatment [20,41].



During the electro-Fenton reaction, a transfer of electrons between electrogenerated  $\text{H}_2\text{O}_2$  and the ferrous ion added ( $\text{Fe}^{+2}$ ) yields the generation of a hydroxyl radical ( $\bullet\text{OH}$ ,  $E^\circ = 2.80 \text{ V vs. SHE}$  (standard hydrogen electrode)) (Eq. 1) [20]. This radical can oxidize organic contaminants and transform them into less harmful compounds (Eq. 3) or even mineralize them [21,42].

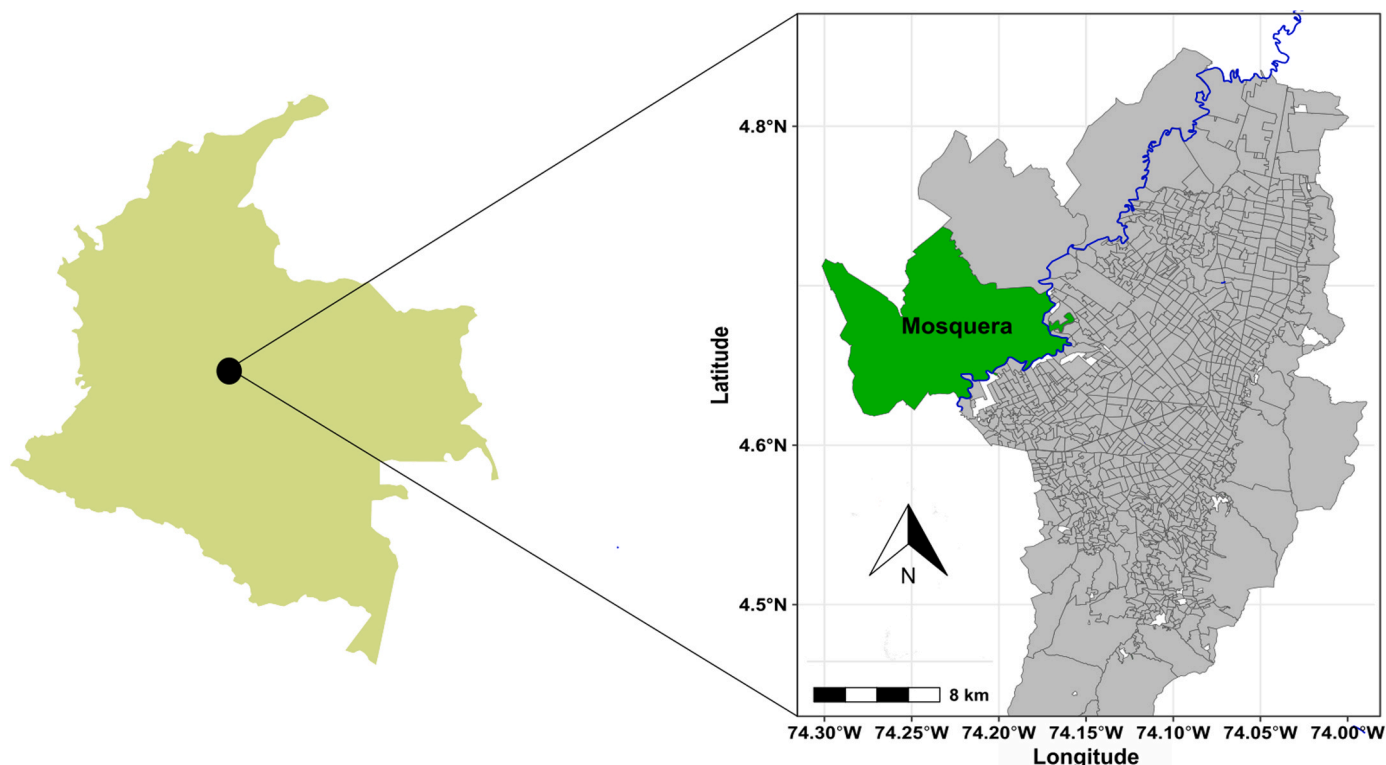
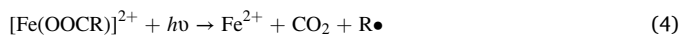


Fig. 1. Map of the location of municipalities bordering the middle basin of the Bogotá River. Zoom: Map of the Bogotá-Savanna where the municipality of Mosquera.

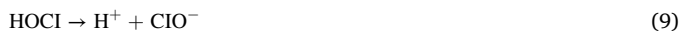
However, the major efficiency of the EF and PEF processes (like Fenton reaction) is observed at pH values close to 3.0, where the precipitation of the ferric ion limits the reaction. This issue can be resolved by adding organic acids as complexing agents for ferric iron [20,21,43], which undergo photolysis and reduce  $\text{Fe}^{+3}$  to  $\text{Fe}^{+2}$  (Eq. 4). This process facilitates the production of  $\bullet\text{OH}$  and organic radicals, which could contribute to the removal of contaminants [21,44].



Furthermore, the light source used in the PEF system also promotes the formation of  $\bullet\text{OH}$  from the homolytic cleavage of  $\text{H}_2\text{O}_2$  (Eq. 5). The direct photolysis of aqua-complexes that contain  $\text{Fe}^{2+}$  (Eq. 6) is promoted, keeping the  $\text{Fe}^{2+}$  available in the solution and increasing the efficiency in eliminating contaminants from water [45,46].



On the other hand, the use of dimensionally stable anodes (DSA) can improve the efficiency of the PEF system in removing contaminants from water by promoting the electro-generation of active chlorine species (ACS), such as  $\text{Cl}_2$ ,  $\text{HClO}$ , and  $\text{ClO}^-$  (Eqs. 7–9). These ACS can oxidize and degrade contaminants [47,48]. In this case, chloride ( $\text{Cl}^-$ ) serves as the supporting electrolyte.



This work focuses on implementing an experimental RSM to optimize three critical variables of the PEF system (flow, current density, and electrolyte concentration), with oxidant generation used as the response variable [38]. Next, the PEF system was implemented under the optimal conditions to eliminate seven pharmaceutically active compounds (PhACs) present in irrigation water from a farm in Mosquera, Colombia, and the efficiency of the PEF process was then evaluated in terms of PhACs removal (%).

## 2. Materials and methods

### 2.1. Chemicals

Losartan potassium (99.0 % purity), sulfamethoxazole (98.0 % purity), and diclofenac sodium salt (99.0 % purity) standard HPLC grade used in the laboratory experiments with HPLC-DAD measurement were purchased from Sigma-Aldrich. Reference standards of the six pharmaceuticals as well as their corresponding analyte isotopically labeled internal standards (ILIS) used for LC-MS/MS analysis were from LGC Standards and Dr. Ehrenstorfer. The HPLC grade acetonitrile ( $\text{CH}_3\text{CN} \geq 99.9\%$ ) was obtained from Panreac. Sodium chloride ( $\text{NaCl} \geq 99.5\%$ ), iron (II) sulfate heptahydrate ( $\text{FeSO}_4 \cdot 7\text{H}_2\text{O} \geq 99.5\%$ ), citric acid ( $\text{C}_6\text{H}_8\text{O}_7 \geq 99.5\%$ ), potassium hydrogen sulfite ( $\text{KHSO}_3 \geq 99.0\%$ ), potassium hydrogen phthalate ( $\text{C}_8\text{H}_5\text{KO}_4 \geq 99.0\%$ ), potassium bicarbonate ( $\text{KHCO}_3 \geq 99.9\%$ ), potassium carbonate ( $\text{K}_2\text{CO}_3 \geq 99.0\%$ ), orthophosphoric acid ( $\text{H}_3\text{PO}_4 \geq 85.0\%$ ) and potassium dihydrogen phosphate ( $\text{KH}_2\text{PO}_4 \geq 99.0\%$ ) were analytical quality obtained from Merck. All solutions were prepared with ultrapure water produced by a Stakpure GmbH system with a resistivity of  $> 18 \text{ M}\Omega \text{ cm}$  at  $25^\circ\text{C}$ .

### 2.2. Experimental procedure

#### 2.2.1. Electrochemical system

The PEF system was performed using a microflow cell (ElectroCell Multi-Purpose Serial No.1670), with a dimensionally stable anode (DSA) made of  $\text{RuO}_2$ -doped  $\text{TiO}_2$  and a gas diffusion cathode (GDE). The

electrodes had a reaction area of  $10 \text{ cm}^2$  each and were placed at  $0.5 \text{ cm}$  between them. The system operated on direct current from a PowerPRO-300 power supply (Cleaver Scientific). The flow microcell was connected to a glass reservoir where the solution to be treated was located. The solution was irradiated with white light from light-emitting diodes (LEDs) (United Kingdom, 3.8 W, 60 LEDs per meter) wrapped around the glass reservoir (Fig. 2).

In contrast, during the optimization phase, the electrochemical cell described above (GDE-DSA) was implemented without the addition of  $\text{Fe}^{2+}$  ions and without the use of LEDs. This approach promoted the generation of oxidants ( $\text{H}_2\text{O}_2$ -ACS) in an electro-peroxidation - electrochlorination (EP-EC) system, allowing for the quantification of total oxidants generated without interference from their consumption in other reactions.

A 500 mL glass reservoir was used as a container for the water to be treated in all the experiments (Fig. 1). In the optimization of operational conditions, the solution consisted of ultrapure water only, with a supporting electrolyte concentration (mol  $\text{NaCl}/\text{L}$ ) determined according to the experimental design (Table 2), without addition of  $\text{Fe}^{2+}$  ions or PhAC model. For the elimination of the PhAC used as a model, the solution contained losartan (LOS), sulfamethoxazole (SMX), and diclofenac (DCF) at a concentration of  $10 \text{ mg}/\text{L}$  each. Additionally, the solution contained  $\text{NaCl}/\text{L}$  (at different concentrations) as the supporting electrolyte,  $\text{Fe}^{2+}$  ions ( $3.6 \times 10^{-5} \text{ mol}/\text{L}$ ), and citric acid ( $3.6 \times 10^{-5} \text{ mol}/\text{L}$ ). The solution was aerated 15 min before treatment to saturate the system with oxygen and was continuously stirred throughout the process with a magnetic stir bar at 400 rpm on a VELP Scientifica ARECT magnetic stirrer to ensure proper mixing and transport of the reagents from the electrodes.

Additional experiments were carried out on irrigation water collected from a farm in the municipality of Mosquera, Colombia ( $4^\circ 39' 30.798'' \text{ N } 74^\circ 13' 48.559'' \text{ W}$ ), where untreated stagnant wastewater is used for irrigation of crops of commercial interest. The samples were collected by taking 3.8 L at a depth of 50 cm on three different days (July 13, July 15, and July 17, 2021), and storing them in high-density polyethylene bottles at  $4^\circ\text{C}$ . They were subsequently mixed to obtain a composite sample. They were then filtered through a disc filter (Qual, BOECO Germany) using a vacuum pump (BOECO R-430). The irrigation water presented the physicochemical characteristics described in Table 1. In total, 7 compounds commonly found in the urban wastewater (subsequently used as irrigation water in near-crops) of Bogotá [25] were evaluated in this study: 1 psychiatric drug (carbamazepine, CBZ), 4 antibiotics (sulfamethoxazole, SMX; ciprofloxacin, CIP; clarithromycin, CLR; and trimethoprim, TMP), 1 antihypertensive (valsartan, VAL), and 1 analgesic (diclofenac, DCF). The criteria used for their selection were the occurrence at relatively high concentration in the effluent wastewater release to the Bogotá – River, which is used in irrigation water, and data of population consumption. The chemical structure, therapeutic role, and the hydrophobicity of the target PhACs (measured as the  $\text{Log } K_{\text{ow}}$ ) as well as the concentrations found for the target pharmaceuticals in irrigation water after analysis by liquid chromatography-tandem mass spectrometry (LC-MS/MS) are shown in Table SM1.

#### 2.2.2. Physicochemical parameters

A pH-meter (HI 2212 from HANNA Instruments) was used to measure the pH values before and after each treatment. A Perkin Elmer UV/Vis Lambda 20 spectrophotometer was used to measure both the oxidants accumulation according to the iodometric method [20,25], and iron ( $\text{Fe}^{2+/3+}$ ) by the 1,10-phenanthroline method following ISO 6332 [49]. Total organic carbon (TOC) was measured by catalytic combustion at  $680^\circ\text{C}$  using highly pure  $\text{O}_2$  gas at a flow rate of  $190 \text{ mL}/\text{min}$ , using a Shimadzu LCSH TOC analyzer with a non-dispersive infrared detector. The calibration of the TOC analyzer was achieved with a standard solution of potassium phthalate at 99.5 %, and the injection volume was  $50 \mu\text{L}$  [20,21].

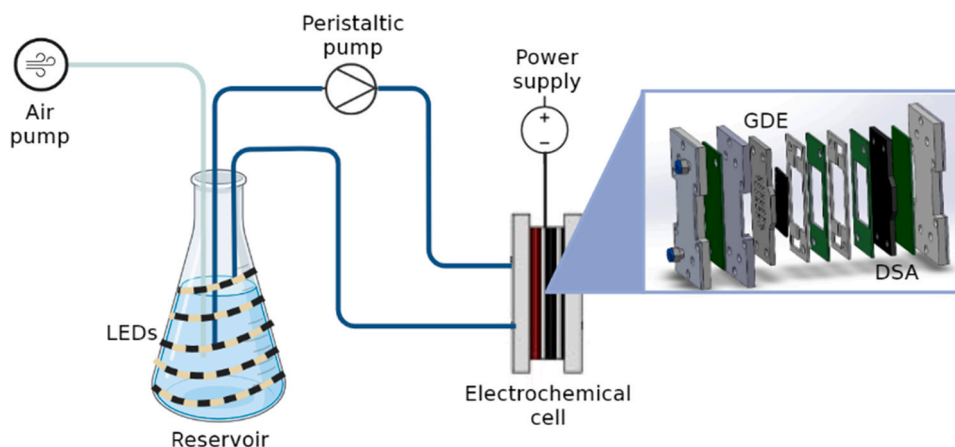


Fig. 2. Schematic diagram of recirculation PEF experimental system.

Table 1

Physicochemical characteristics of the irrigation water samples from the Mosquera farm, Colombia, treated and untreated using the PEF system.

| Parameters                          | Units                  | Value raw irrigation water | Value before treatment <sup>a,b</sup> | Value after 60 min of treatment <sup>a</sup> |
|-------------------------------------|------------------------|----------------------------|---------------------------------------|--|
| pH                                  | -                      | 6.8                        | 5.2                                   | 4.5  |
| Alkalinity                          | mg/L CaCO <sub>3</sub> | 243.0                      | 235.0                                 | 167.2  |
| Conductivity                        | µS/cm                  | 1461                       | 11500                                 | 11800  |
| Total suspended solids (TSS)        | mg/L                   | 196                        | 210                                   | 117  |
| Turbidity                           | UNT                    | 69                         | 72                                    | 32   |
| Dissolved oxygen (DO)               | %                      | 52.1                       | 93.5                                  | 84.3   |
| Oxidation-reduction potential (ORP) | mV                     | 252                        | 246                                   | 166  |
| Total organic carbon (TOC)          | mg/L C                 | 59.9                       | 66.1                                  | 38.1   |
| Fe <sup>2+</sup> / <sup>3+</sup>    | mg/L                   | 3.97                       | 4.08                                  | 4.53   |

<sup>a</sup> Each experiment was performed in triplicate with an RSD < 5.0 %.

<sup>b</sup> Irrigation water with the addition of [NaCl]: 0.1 mol/L, [citric acid]:  $3.6 \times 10^{-5}$  mol/L, and [Fe<sup>2+</sup>]:  $3.6 \times 10^{-5}$  mol/L.

## 2.3. Instrumentation and analytical measurements

### 2.3.1. HPLC-DAD instrumentation

A Shimadzu LC-20AT HPLC system equipped with a C18 column (Shim-pack GIST/GISS, 150 mm × 3.0 mm ID with particle sizes of 5 µm) and an SPD-M20A photodiode array detector was used. The detector was set at 220 nm for LOS, 270 nm for SMX, and 275 nm for DCF. The mobile phase was composed of a phosphate buffer (pH 3.5, 0.01 mol/L)/acetonitrile (50/50 v/v) at 25 °C under isocratic conditions. The mixture was pumped with a flow of 0.6 mL/min, resulting in a maximum system pressure of 78 bar. 20 microliters of sample were injected by full loop injection. Under these conditions, SMX, LOS and DCF were eluted at 2.01 min, 2.57 min and 7.87 min, respectively.

### 2.3.2. UHPLC-MS/MS

For the PhACs analysis, before and after the application of PEF treatment at lab scale, an ultra-performance liquid chromatography system (Waters, Milford, MA, USA) coupled to a triple quadrupole mass spectrometer Xevo TQS, with an orthogonal Z-spray electrospray interface, was employed. Aliquots of the effluent wastewater samples treated with PEF systems were taken at 5, 15, 30, and 60 min of treatment, together with an untreated sample, in centrifuge tubes and transported to the laboratory for sample treatment within 24 h. Once in the

laboratory, they were frozen at −20 °C and thawed at room temperature on the same day of the analysis. Sample aliquots were transferred to 2 mL eppendorf and centrifuged at 12,000 rpm for 3 min before analyses. The multiresidue LC-MS/MS procedure applied for sample analysis was based on our previous work, using direct injection of the samples without any pre-concentration step, with minor modifications [25]. To this aim, 950 µL sample aliquots were taken, and 50 µL of ILIS of 20 µg/L was added (final concentration of ILIS in the injected samples, 1 µg/L). Then, 50 µL were directly injected into the LC-MS/MS.

A set of quality control samples were prepared and analyzed together with the sample batch. Quality control samples consisted of irrigation and samples subjected to different treatments, all spiked with the target pharmaceuticals at three concentration levels 0.01, 0.1 and 1.0 µg/L. For their preparation, 900 µL of the sample was taken, and 50 µL of mix standard solution (0.2, 2.0 and 20 µg/L) and 50 µL of ILIS of 20 µg/L were added. The results obtained for QCs were in general satisfactory with recoveries between 60 % and 140 %. The only exception was for several QCs at the lowest spiked level (0.01 µg/L), whose recoveries were out of this range due to the presence of the compounds at high concentrations in the “blank” samples used for QCs preparation, according to methodology reported by Martínez-Pachón et al. [25].

## 2.4. Calculations and statistics

### 2.4.1. Response surface methodology (RSM)

Design Expert 6.0.7 software (Stat-Ease Inc., Minneapolis, USA) was employed for design, mathematical modeling, and optimization. The mathematical design centered on the use of RSM as an approximation of the response function  $y = f(x_1, x_2, \dots, x_k) + \epsilon$ , where  $\epsilon$  represented the error in the model,  $f$  represented the unknown response surface and the response variable (output variable), and  $x_1, x_2, \dots, x_k$  were the set of predictor variables (input variables). This model emerged to understand the underlying relationship between  $y$  and  $x$ ; for this, it was written as an empirical model  $y = f(x_1, x_2, \dots, x_k) + \epsilon$ , deriving a first or second-order polynomial to describe  $f$  [50].

The variables (independent factors) used in this study were: flow ( $X_1$ ), current density ( $X_2$ ), and electrolyte concentration ( $X_3$ ). The generation of oxidants ( $Y_1$ ) was considered a response variable (dependent factor). Iron concentration ( $3.6 \times 10^{-5}$  mol/L), citric acid concentration ( $3.6 \times 10^{-5}$  mol/L), temperature (18 °C), stirring speed (400 rpm), and distance between electrodes (0.5 cm) were kept constant to reduce the number of factors and simplify the experimental design [51].

Each variable's low, middle, and high levels are designated by the face-centered central composite design (CCD) as −1, −0.5, 0, 0.5, and +1, respectively. Table 2 shows the independent variables and their levels for the CCD used in the present study. The ranges of the flow (48–461 mL/min), current density (5–20 mA/cm<sup>2</sup>), and electrolyte



**Table 2**

Coded levels, factor values, and RSM analysis of oxidant generation in the EP-EC system. Operating conditions: pH<sub>initial</sub>: 6.7, volume: 500 mL, radiation source: Not applicable.

| Test | Level          |                |                | Factor values               |                             |                             | Experimental values<br>Y <sub>1</sub> <sup>d</sup> |
|------|----------------|----------------|----------------|-----------------------------|-----------------------------|-----------------------------|--|
|      | X <sub>1</sub> | X <sub>2</sub> | X <sub>3</sub> | X <sub>1</sub> <sup>a</sup> | X <sub>2</sub> <sup>b</sup> | X <sub>3</sub> <sup>c</sup> |  |
| 1    | -1             | -1             | -1             | 48.0                        | 5.0                         | 0.0125                      | 0.626  |
| 2    | +1             | -1             | -1             | 461.0                       | 5.0                         | 0.0125                      | 0.574  |
| 3    | -1             | +1             | -1             | 48.0                        | 20.0                        | 0.0125                      | 2.422  |
| 4    | +1             | +1             | -1             | 461.0                       | 20.0                        | 0.0125                      | 1.459  |
| 5    | -1             | -1             | +1             | 48.0                        | 5.0                         | 0.1000                      | 0.688  |
| 6    | +1             | -1             | +1             | 461.0                       | 5.0                         | 0.1000                      | 1.880  |
| 7    | -1             | +1             | +1             | 48.0                        | 20.0                        | 0.1000                      | 2.133  |
| 8    | +1             | +1             | +1             | 461.0                       | 20.0                        | 0.1000                      | 2.871  |
| 9    | -0.5           | 0              | 0              | 151.3                       | 12.5                        | 0.0563                      | 1.624  |
| 10   | +0.5           | 0              | 0              | 357.8                       | 12.5                        | 0.0563                      | 0.978  |
| 11   | 0              | -0.5           | 0              | 254.5                       | 8.8                         | 0.0563                      | 1.576  |
| 12   | 0              | +0.5           | 0              | 254.5                       | 16.3                        | 0.0563                      | 2.405  |
| 13   | 0              | 0              | -0.5           | 254.5                       | 12.5                        | 0.0344                      | 1.320  |
| 14   | 0              | 0              | +0.5           | 254.5                       | 12.5                        | 0.0781                      | 2.209  |
| 15   | 0              | 0              | 0              | 254.5                       | 12.5                        | 0.0563                      | 1.414  |

<sup>a</sup> Flow (mL/min) <sup>b</sup> Current density (mA/cm<sup>2</sup>) <sup>c</sup> Electrolyte concentration (mol NaCl/L) <sup>d</sup> Generation of oxidants at 60 min (mmol/L), each experiment was performed in triplicate with an RSD < 5.0 %.

concentration (0.0125–0.1000 mol/L) were determined by preliminary experiments based on the literature and equipment operational limits [52].

#### 2.4.2. Environmental risk assessment

Following the methodology reported by Martínez-Pachón et al. (2022) [25], this study delved into the environmental threat posed by specific PhACs in aquatic ecosystems, particularly when treated effluents are introduced into freshwater bodies. The assessment revolved around a risk parameter referred to as the "Risk Quotient" (RQ), which main focus is on the relationship between the anticipated concentration in the environment (PEC) and the anticipated no harmful effect concentration (PNEC), which represents the level at which no impacts on exposed organisms are expected. PEC is the ratio between the mean concentration (MC) and a dilution factor (DF). This DF is known as the "National Annual Mean Dilution Factor" and is related to the volume of fresh water available and the discharge of domestic wastewater in each country. In the case of Colombia, the value of the DF is 929.87 [53].

### 3. Results and discussion

#### 3.1. Experimental design and optimization of operation conditions (flow, current density, and supporting electrolyte) in the generation of oxidants

##### 3.1.1. Model and regression analysis

The PEF system has demonstrated significant potential for treating polluted water due to its relatively simple applicability and high efficiency in degrading PhACs. However, its application may face challenges, primarily due to the potential imbalance between energy consumption and pollutant removal efficiency. To address this issue, the RSM was employed to minimize energy consumption associated with the PEF system while maintaining efficient removal of target pollutants. This optimization was achieved through the follow-up of the generation of oxidants, which can significantly enhance pollutant degradation [54, 55]. To this end, an EP - EC system was implemented, which avoids the consumption of oxidants by Fe<sup>2+</sup> ions or radiation with the light-emitting diodes (LEDs) that typically occur in the complete PEF system (complete system).

Current density is among the most crucial variables in electrochemical systems, including PEF, due to its direct influence on the generation of oxidants, which involves electronic transfer on the electrodes to produce H<sub>2</sub>O<sub>2</sub> and ACS (Eqs. 3, 7–9) [38,56]. Moreover,

electrolyte concentration can affect the number of Cl<sup>-</sup> available for mass transfer to the anode surface, thus influencing the conductivity of the solution [57]. Additionally, when working with continuous or recirculating electrochemical systems, it is essential to consider the effect of flow, as it determines the time that the solution is in contact with the electrodes, thus affecting the mass transfer of the electrolyte on the electrode surface [38].

After considering the independent variables of flow, current density, and electrolyte concentration, a total of 15 experiments were conducted according to the experimental design presented in Table 2. The design was generated using Expert 11.0 design software. Subsequently, optimization conditions were obtained from the RSM statistical model, which was specified by the quadratic function (Eq. 10).

$$Y = 1.55 + 0.017X_1 - 0.38X_2 - 15.17X_3 - 1.13 \times 10^{-4}X_1X_2 + 0.04X_1X_3 - 0.082X_2X_3 - 3.39X_1^2 + 0.020X_2^2 + 120.2X_3^2 \quad (10)$$

An analysis of variance (ANOVA) was conducted using the same software to verify the significance of the prediction model employed. The *F*-value of the model was 5.84, indicating its significance, and the *p*-values were less than 0.0500, denoting the significance of the terms within the model. The coefficient of determination further confirmed the model's adequacy, with a value of 91.32 % of the total variability explained. Furthermore, the coefficient of determination was adjusted to 0.7569 to provide a significance of the model with *p*-values less than 0.05.

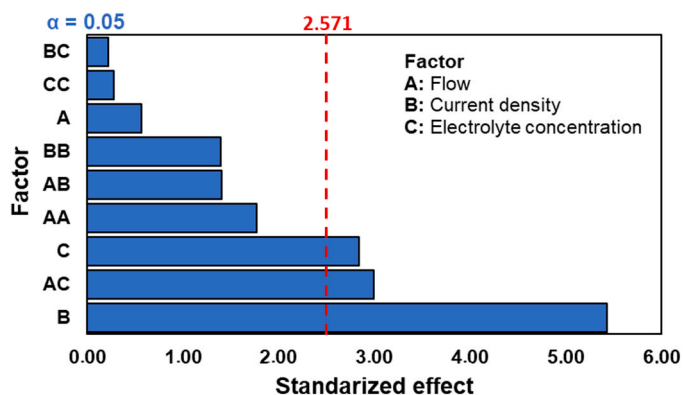
##### 3.1.2. Effect of independent variables on the generation of oxidants

The standardized effects of the first-order independent, quadratic, and interaction between variables were presented in the Pareto diagram (Fig. 2). The results demonstrated that factors B (current density), AC (flow in interaction with electrolyte concentration), and C (electrolyte concentration) exceeded the reference line set at 2.571 with an  $\alpha$  of 0.05, indicating their statistical significance and remarkable impact on oxidant generation. The reference line was established following an adaptation of the 70/30 proportion instead of the traditional Pareto principle of 80/20. This choice was based on the observation of a relatively uniform distribution of contributions across various factors, enabling the more effective capture of a broad and accurate proportion of influential and critical factors in the analysis [58,59].

Moreover, the most influential factor in the model was B, with a standardized effect of 5.437, due to the critical role of current density in the EP-EC system. The transfer of electrons, which is essential for oxidant generation (Eqs. 3, 7–9), is heavily influenced by current density, resulting in higher production rates of H<sub>2</sub>O<sub>2</sub> at the cathode and ACS at the anode [23,38,56,60]. However, the current density cannot be increased without limit, as electrode polarization may occur, resulting in the accumulation of charge at the electrode/solution interface, which enhances the cathodic decomposition of H<sub>2</sub>O<sub>2</sub> to H<sub>2</sub>O (Eq. 11) [61,62]. This phenomenon is illustrated in Fig. 3, where the factor BB (current density in quadratic effect) in the Pareto diagram is not statistically significant, implying that higher values of B do not necessarily lead to an increase in oxidant generation.



The second most crucial factor in the model is AC, with a standardized effect of 2.998. This factor demonstrates that the interaction between electrolyte concentration and flow can result in increased production of oxidizing species. This is because a more significant mass transfer of the electrolyte at the electrode surface is facilitated, primarily due to the possibility of increased contact with the electrodes due to the constant flow of the solution in the electrochemical cell [38,63]. On the contrary, factor A (flow) alone does not have a statistically significant effect on oxidant generation. It is not an influential variable in this system as it does not provide the "raw material" for oxidant generation, (Cl<sup>-</sup> or electrons) [63–65].



**Fig. 3.** Pareto chart showing the standardized effects of the variables (first order independent, quadratic, and interaction terms) in the generation of oxidants as output variable (dependent) in the EP-EC system. The red vertical line represents a reference (2.571) to determine statistically significant factors. Each experiment was carried out in triplicate with an RSD < 5.0 %.

The factor C (electrolyte) is the third most important factor in the model. Higher values of electrolyte concentrations lead to an increase in oxidant generation, primarily due to the greater number of  $\text{Cl}^-$  available for mass transfer to the anode surface (Eqs. 7–9) and higher conductivity of the solution, which facilitates the effective transfer of the electrons required for oxidant generation (Eqs. 3, 7–9) [38,66]. Additionally, as illustrated in Fig. 3 with the factor CC (concentration of electrolyte in quadratic effect), increasing C without a specific limit does not necessarily result in an increase in oxidant generation. The high  $\text{Cl}^-$  contents obtained with 0.100 mol NaCl/L in the experiments (Table 2) can produce sufficient  $\text{H}_2\text{O}_2$  and ACS, which saturate the solution. This indicates that the concentration of electrolyte can serve as a limiting factor [67,68]. Significant effects were observed with concentrations between 0.0781 and 0.100 mol NaCl/L.

### 3.1.3. Optimum values of operating conditions

After considering the importance and effect of factors B and C, corresponding to current density and electrolyte concentration, respectively (as shown in Fig. 3), the operational values of these factors were optimized to maximize oxidant generation, which is crucial for the future removal of the target PhACs. Fig. 4 represents the response surface for oxidant generation (mmol/L) in the EP-EC system, with varying flow rates in mL/min, current density in  $\text{mA}/\text{cm}^2$ , and electrolyte concentration in mol NaCl/L. The red area in the figure indicates the most suitable values of the factors for oxidant generation.

The results of the study revealed a significant relationship between current density and oxidant generation, as illustrated in Fig. 4A and 4C [27–29,31]. As discussed in the previous sections, values from 12.5 to 16.3  $\text{mA}/\text{cm}^2$  were considered, and 15  $\text{mA}/\text{cm}^2$  is suggested as the most suitable condition for removal of PhACs (Section 3.2). Under this condition a high energy efficiency in oxidants generation (~ 46.34 %) corresponding to 2.594 mmol/L [40,41,66,67]. This choice represents a positive correlation between oxidant generation and energy efficiency for the removal of PhACs.

Regarding electrolyte concentration, the results showed that the optimal range values are between 0.0781 and 0.100 mol NaCl/L (as seen in Fig. 4B and 4C), with a maximum production of oxidants of 2.594 mmol/L for 0.100 mol NaCl/L. This is due to the greater amount of  $\text{Cl}^-$  available, which leads to a higher mass transfer to the surface of the anode, and a higher conductivity of the solution, as discussed earlier in Section 3.1.2 [38,66]. Considering the generation of oxidants, the highest electrolyte concentration (0.100 mol NaCl/L) was chosen for the removal of PhACs (as discussed in Section 3.2) [54,55].

Finally, the flow rate, has the least effect on oxidant generation (as shown in Fig. 3), exhibiting optimal values between 200.0 and

300.0 mL/min (as seen in Fig. 4A and 4B). The difference in oxidant generation was observed between the lowest value (2.367 mmol/L of oxidants for 200.0 mL/min) and the highest value (2.583 mmol/L of oxidants for 300.0 mL/min), with the highest oxidant generation occurring at intermediate flow values. Specifically, a flow rate of 210.0 mL/min yielded the highest oxidant generation (2.594 mmol/L). Like the selection of 0.100 mol NaCl/L, the flow rate of 210.0 mL/min was chosen for the removal of PhACs (as discussed in Section 3.2), as it produced the highest generation of oxidants. Despite the low effect of flow, in combination with the concentration of the support electrolyte, it can lead to a higher efficiency in the PhAC removal process (see Fig. 4) [54,55].

## 3.2. Removal of PhACs using the PEF system under optimized operating conditions

### 3.2.1. Approach to the removal of model PhACs in ultrapure water

The removal of three model PhACs in ultrapure water was evaluated by HPLC-DAD analysis under operating conditions established through the RSM in previous sections (flow rate of 210.0 mL/min, current density of 15.0  $\text{mA}/\text{cm}^2$ , and electrolyte concentration of 0.100 mol NaCl/L) [69,70]. The PhACs were selected as representative compounds of different therapeutic groups, including one antihypertensive (LOS), one antibiotic (SMX), and one analgesic (DCF) drug. They are widely consumed, and are commonly present in different water sources, as a result of the incomplete removal by conventional wastewater treatments, which might lead to ecotoxicological effects [71–73]. The results were evaluated in terms of concentration ratios ( $C/C_0$ ) and degradation rates ( $k$ , mol/min).

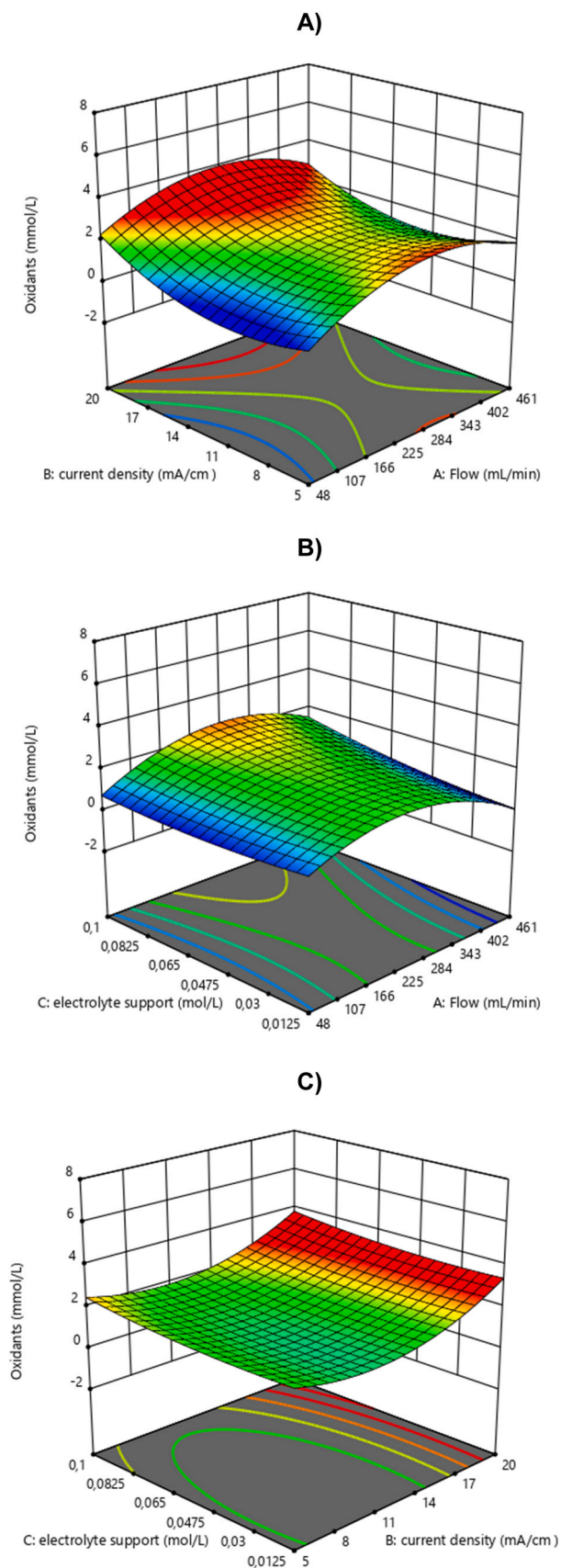
Fig. 5 shows that about 50 % of the PhACs were removed within 2 min of treatment, and complete removal was achieved after 10 min of treatment for all three compounds. Furthermore, the degradation rate constants ( $k$ ) were similar for all three PhACs, with values of 0.222, 0.246, and 0.234 mol/min for LOS, SMX, and DCF, respectively. This suggests that the chemical structures of these PhACs do not affect the degradation rate, but rather, it depends entirely on the oxidants generated in the system [38]. The PhACs analyzed present structural similarities with several amine groups susceptible to be attack by  $\bullet\text{OH}$  and electrochemically generated ACS [38].

In addition, the excess of oxidants produced is attributed to the high concentration of these during the treatment with the PEF system (Figure SM1), resulting that the reaction depends mainly on the concentration of the pollutant present in the solution.

During the initial minutes of treatment, total mineralization was not achieved (Figure SM1). However, at prolonged times (60 and 120 min), a significant reduction in TOC was observed (46 % and 76 % respectively). The remaining TOC could be attributed to the presence of degradation by-products (DPs), which are likely generated through the cleavage of the initial PhACs molecules due to attacks from  $\bullet\text{OH}$  and ACS on electrons-rich regions [7,20,61].

The formation of some DPs from molecules of LOS, SMX, and DCF has already been described by different authors (Table SM2) [7,20,74–76]. In the case of LOS degradation, it has been reported some DPs generated by the attack of  $\bullet\text{OH}$  to the  $-\text{C}=\text{C}-$  bonds of the imidazole ring (Table SM2: LDPs-1 and LDPs-2). In the presence of chloride in the solution ACS are generated (especially HClO) and can also attack the biphenyl-tetrazole group, producing LDPs-3 and LDPs-4 (Table SM2) [20]. In the degradation of SMX, it has been suggested that oxidation begins with the cleavage of the N-C bond of the oxazole-3-yl group or N-S bond, producing two DPs (Table SM2: SDPs-1 or SDPs-2, respectively) [74]. Finally, for the DCF, the hydroxylation in the benzene ring is one of the main degradation routes with the formation of three DPs (Table SM2: DDPs-1, DDPs-2, and DDPs-3) [75].

Despite the extensive identification and presence of DPs of the three model PhACs, it has not been reported the presence and accumulation of organochlorines in the treated solutions [20,75]. Some of the products



(caption on next column)

**Fig. 4.** Relationship between input variables (independent) in the generation of oxidants (mmol/L) as output variable (dependent) in the EP-EC system. **A.** Current density (mA/cm<sup>2</sup>) versus flow (mL/min). **B.** Electrolyte concentration (mol NaCl/L) versus flow (mL/min). **C.** Electrolyte concentration (mol NaCl/L) versus current density (mA/cm<sup>2</sup>). Operating conditions: Cathode: GDE, anode: DSA, pH<sub>initial</sub>: 6.8, [citric acid]: Not applicable, [Fe<sup>+2</sup>]: Not applicable, radiation source: Not applicable. Each experiment was performed in triplicate with an RSD < 5.0 %.

are easily biodegradable [7,21,74], while others are degraded in simpler molecules, such as short-chain organic acids, which also contribute to the remaining TOC as they are more resistant to oxidation [20].

### 3.2.2. Elimination of PhACs present in real irrigation waters

The efficiency of the PEF system was evaluated in a relevant environment using a real irrigation water sample contaminated with PhACs. The sample was obtained from a farming site in the municipality of Mosquera, located in the Bogotá-Savanna region of Colombia. This irrigation water was of particular interest because untreated stagnant wastewater was being used for commercial crops, such as lettuce. The physicochemical parameters of this sample before and after treatment with the PEF system are presented in Table 1. Samples were obtained from artificial channels of the 'La Ramada' irrigation district. This district captures water from the Bogotá River and untreated wastewater from Bogotá city, as well as municipalities surrounding it, such as Mosquera (Fig. 1) [12,19].

In irrigation water samples treated with the PEF system, after 60 min, the values of some physicochemical parameters were lower than the irrigation water not treated. Total Suspended Solids (TSS), turbidity, and TOC presented reductions in their values with percentages of 59.7 %, 46.4 %, and 63.6 %, respectively. These results demonstrate the potential of the PEF system to enhance the overall quality of the water treated in addition to the removal of micropollutants.

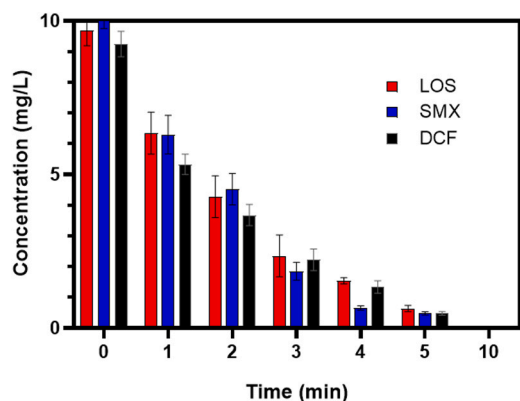
Furthermore, the irrigation water sample was analyzed using UHPLC-MS/MS to identify and quantify seven target PhACs selected in this study (CBZ, SMX, CIP, CLR, TMP, VAL, DCF), which are often considered markers of anthropogenic pollution, they are widely consumed globally, have been detected in different water sources in high concentrations, and are scarcely removed by wastewater treatment plant (WWTP) [73,77–79]. Fig. 6 shows the concentrations of the seven PhACs in the irrigation water sample before and after different treatment times using the PEF system under optimal conditions.

Two groups of PhACs were identified based on their initial concentrations: 1) those detected at concentrations between 100 and 1000 ng/L, which include CLR (at 800.0 ng/L), CIP (at 132.5 ng/L), TMP (at 119.3 ng/L), and DCF (at 140.2 ng/L); and 2) those detected at concentrations between 10 and 100 ng/L, which include SMX (at 72.3 ng/L), VAL (at 29.5 ng/L), and CBZ (at 18.2 ng/L).

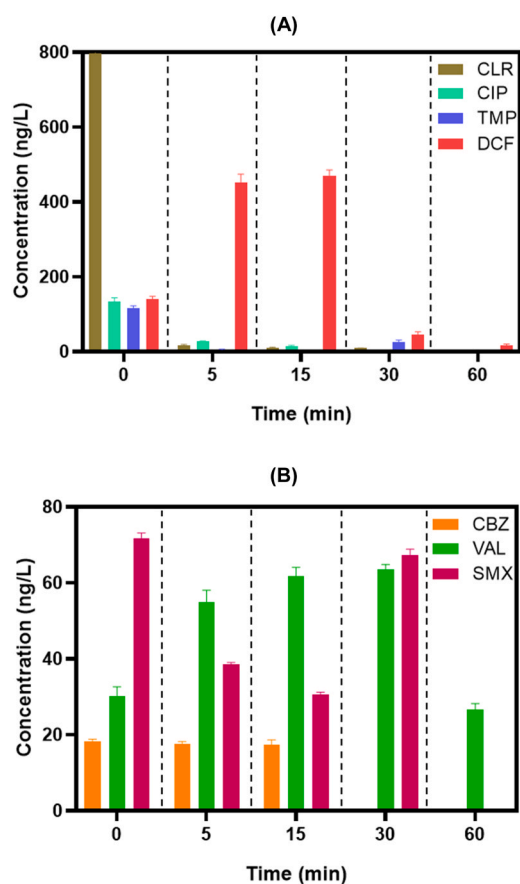
The high concentrations of antibiotics present in the group 1 may be associated with extensive livestock activity in the Bogotá-savanna, as drugs used for the prevention and treatment of cattle and swine diseases, such as spiramycin, enrofloxacin, and bovigram, mainly include CLR, CIP, or TMP [13,80,81]. Additionally, the extensive use of CLR, CIP, and TMP in human medicine has been documented, resulting in the emission of these antibiotics into the water of the Bogotá River by Bogotá D.C. and the municipalities in the Bogotá-savanna [19,25,79]. The highest concentration of DCF (Group 1) is associated with high and indiscriminate consumption in humans and animals. DCF is Colombia's third most consumed analgesic [82].

The presence of group 2 PhACs in irrigation water indicates their application in the treatment of psychiatric (CBZ), cardiac (VAL), and infectious (SMX) diseases mainly in humans. Unlike group 1, group 2 PhACs are not used in the livestock sector, so there is no major source of discharge to irrigation water. This may explain why group 2 PhACs are found in concentrations between 1.5 and 45 times lower than those detected for group 1 PhACs [78,83–85].





**Fig. 5.** Removal of model PhACs in ultrapure water (10 mg/L each one) by implementing the PEF system with optimized conditions. Continuous flow PEF system operating conditions: GDE cathode, DSA anode,  $\text{pH}_{\text{initial}}$ : 4.8 by adding citric acid (without modifying the pH), [citric acid]:  $3.6 \times 10^{-5}$  mol/L,  $[\text{Fe}^{+2}]$ :  $3.6 \times 10^{-5}$  mol/L, current density: 15.0 mA/cm<sup>2</sup>, [NaCl]: 0.100 mol/L, flow: 210.0 mL/min, radiation source: LEDs. Each experiment was performed in triplicate with an RSD < 5.0 %.



**Fig. 6.** PhACs concentration (detected in irrigation water samples) during PEF treatment. **A)** Group 1: PhACs detected at concentrations between 100 and 1000 ng/L, which include clarithromycin (CLR), ciprofloxacin (CIP), trimethoprim (TMP), and diclofenac (DCF). **B)** Group 2: PhACs detected at concentrations between 10 and 100 ng/L, which include carbamazepine (CBZ), sulfamethoxazole (SMX), and valsartan (VAL). Continuous flow PEF system operating conditions: GDE cathode, DSA anode,  $\text{pH}_{\text{initial}}$ : 4.8 by adding citric acid (without modifying the pH), [citric acid]:  $3.6 \times 10^{-5}$  mol/L,  $[\text{Fe}^{+2}]$ :  $3.6 \times 10^{-5}$  mol/L, current density: 15.0 mA/cm<sup>2</sup>, [NaCl]: 0.100 mol/L, flow: 210.0 mL/min, radiation source: LEDs. Each experiment was performed in triplicate with an RSD < 5.0 %.

After detecting the target PhACs in irrigation water, the efficiency of the PEF system was evaluated in terms of their removal. The results indicate that 100 % removal of CIP (Fig. 6A) and CBZ (Fig. 6B) was achieved after 30 min of treatment, while 100 % removal of CLR, TMP (Fig. 6A), and SMX (Fig. 6B), was achieved after 60 min of treatment. In the case of CBZ, high persistence was observed during the first fifteen min of treatment, possibly due to the molecule's two stable benzene rings, making it less susceptible to oxidation compared to the other PhACs [86]. However, with longer treatment times, the high concentration of oxidants in the PEF system would lead to complete and efficient removal of CBZ, as observed at 30 min. Once the rings have been broken, degradation can be favored by the oxidation of electron donor regions such as -OH or -NH<sub>2</sub> [87–89].

A particular behavior is observed with DCF, SMX, and VAL, as these compounds showed an increase in concentration during treatment with the PEF system, possibly due to the conjugation of the PhACs with sulfates or glucuronide present in the sample [79,90]. DCF can interact with carboxylic groups of other molecules present in the organic matter [91], forming conjugates that can be broken down and released back into the water due to physicochemical processes such as those that occur during treatment in the PEF system. This leads to an increase in DCF concentrations during the first min of treatment, resulting in negative removal percentages (Fig. 6A) [79]. However, after 30 min of treatment, the DCF concentration decreases, and total removal was observed after 60 min. Similarly, SMX can be conjugated with glucuronides to form Acetyl-SMX and SMX-glucuronide, which are excreted by humans [92, 93]. However, it is eliminated within 60 min using the PEF system.

To assess the environmental threat associated with the presence of PhACs in irrigation water and analyze the mitigation of this threat through removal using the PEF system, an evaluation of chemical risk assessment based on the Risk Quotient (RQ) approach was implemented. Pollutants with RQ values  $\leq 0.1$  are considered with low risk or low adverse effect, while those with  $0.1 < \text{RQ} < 1.0$  indicate a moderate risk and probable adverse effect. Pollutants with an RQ value  $\geq 1$  are deemed to pose a high risk to aquatic organisms [25,53]. The RQ values for each target pharmaceutical in irrigation water before and after treatment are summarized in Table SM3.

The initial RQs values for the compounds CIP, DCF, SMX, VAL, and CBZ were found to be below 0.01 (Table SM3), implying a minimal or non-existent level of ecological risk. However, even at extremely low concentrations, these PhACs could potentially exert toxicity through a synergistic combination due to cumulative effects on the total RQ, in addition to their high bioaccumulation potential. Therefore, determining the extent of risk that the PhACs present in this matrix could pose to the ecosystem becomes crucial [94–96].

It is worth noting that the highest RQ values were recorded for the antibiotics CLR and TMP, with 0.022 and 0.021, respectively. The presence of these antibiotics also underscores the risk associated with the spread of multiple antibiotic-resistance genes or resistant bacterial strains, which is a current concern due to potential implications for human health [97].

Despite the inherent risks associated with the ongoing presence of PhACs, a significant reduction in this risk is achieved through the application of the PEF system. Starting from a sample with a total RQ of 0.056 (Calculated from the sum of the RQs of each PhAC measured), indicating a low risk, a complete reduction of RQ is attained after 60 min of treatment. Previous research has also confirmed that the PEF system can effectively reduce the concentration of PhACs and their environmental threat in effluents from real WWTPs, with reductions in total RQ of up to three orders of magnitude observed after 60 min of treatment [25].

Considering the above, it is important to note that the concentrations of PhACs in irrigation water are constantly present and in contact with crops in the Bogotá-savanna. This may lead to the bioaccumulation of PhACs in plants, resulting in deficiencies in quality and agricultural production, which poses a risk to food and human health when



consuming these foods [10,79,98]. Therefore, it is necessary to expand research related to: *i*) the possible effects of irrigation water contaminated with PhACs on irrigated crops, and *ii*) the potential application of tertiary treatments such as the PEF system. This system has demonstrated high efficiencies for the elimination of different PhACs in real waters and may even allow for the elimination or mitigation of the negative effects, as proposed in this work.

#### 4. Conclusions

In this study, CCD and RSM were applied to optimize the PEF system, considering flow, current density, and electrolyte concentration in the generation of oxidants. A predictive quadratic model with high significance was established, allowing determination of the optimal experimental conditions for the proposed PEF system. Current density was found to be the main factor with the greatest impact on oxidant generation. Optimal conditions were a flow rate of 210.0 mL/min, a current density of 15.0 mA/cm<sup>2</sup>, and an electrolyte concentration of 0.100 mol NaCl/L, as these favored electron and mass transfer processes at the electrode surface, increasing the number of oxidants in the solution. When the PEF system with optimized conditions was applied to degrade SMX, DCF, and LOS in ultrapure water, total removal of PhACs was observed in 10 min of treatment with similar degradation kinetics ( $k = \sim 0.22$ ) among the three pollutants, due to the high concentration of oxidants in solution and their non-selective oxidation of PhACs. These results demonstrated the high efficiency of the PEF system under the applied operating conditions.

On the other hand, the application of PEF for removal antibiotics SMX, TMP, CIP, CLR, TMP, and the anticonvulsant CBZ, all of them detected in irrigation water, allowed their complete elimination after 60 min of treatment. A particular behavior was observed in the elimination of DCF and VAL, which increase their concentration during the first stage of treatment due to their conjugation with organic matter and other compounds present in the solution. However, additional time allows their total degradation.

According to the results obtained, the continuous flow PEF system proposed in this study can be a promising treatment for removing PhACs in real water. Its applicability in irrigation water allows for reducing the possible risks associated with the reuse of contaminated water in agriculture, maintaining the quality of the environment and crops.

#### CRedit authorship contribution statement

**Carlos A. Delgado-Vargas:** Conceptualization, Investigation, Methodology, Validation, Formal analysis, Writing-original draft, Writing-review & editing. **Johan S. Barreneche-Vasquez:** Conceptualization, Investigation, Formal analysis, Writing-review & editing. **Natalia González Cogua:** Conceptualization, Investigation and Writing-review & editing. **Félix Hernández:** Conceptualization, Methodology, Validation, Formal analysis, Writing-original draft. **Ana María Botero-Coy:** Conceptualization, Methodology, Validation, Formal analysis, Writing-original draft. **Diana Martínez-Pachón:** Conceptualization, Methodology, Writing-review & editing, Resources, Supervision, Project administration, Funding acquisition. **Alejandro Moncayo-Lasso:** Conceptualization, Methodology, Writing-review & editing, Resources, Supervision, Project administration, Funding acquisition.

#### Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Alejandro Moncayo-Lasso reports financial support was provided by Colombia Ministry of Science Technology and Innovation.

#### Data availability

No data was used for the research described in the article.

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#### Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jece.2023.111030.

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