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Formation of polychlorinated dibenzo-p-dioxins and furans (PCDD/Fs) in the electrochemical oxidation of polluted waters with pharmaceuticals used against COVID-19

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ABSTRACT

The COVID-19 pandemic has produced a huge impact on our lives, increasing the consumption of certain pharmaceuticals, and with this, contributing to the intensification of their presence in wastewater and in the environment. This situation demands the implementation of efficient remediation technologies, among them, electrochemical oxidation (ELOX) is one the most applied. This work studies the application of ELOX with the aim of eliminate pharmaceuticals used in the fight against COVID-19, assessing its degradation rate, as well as the risk of formation of toxic trace by-products, such as unintentional POPs like polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs). To this end, model solutions containing 10 mg L^{-1} of dexamethasone (DEX), paracetamol (PAR), amoxicillin (AMX), and sertraline (STR) with two different electrolytes (NaCl and Na_2SO_4) have been evaluated. However, electrochemical systems that contain chloride ions in solution together with PCDD/Fs precursor molecules may lead to the formation of these highly toxic by-products. So, PCDD/Fs were quantified under conditions of complete degradation of the drugs. Furthermore, the presence of PCDD/Fs precursors such as chlorophenols was determined, as well as the role of Cl^-, $Cl^\bullet$ and $SO_4^{\bullet-}$ radicals in the formation of the by-products and PCDD/Fs. The maximum measured concentration of PCDD/Fs was around 2700 pg L^{-1} for the amoxicillin case in NaCl medium. The obtained results emphasise the importance of not underestimating the potential formation of these highly toxic trace by-products, in addition to the correct selection of oxidation processes and operation variables, in order to avoid final higher toxicity in the medium.

1. Introduction

Water quality is an essential good for human health, in addition to being one of the factors that mostly affect the health of the ecosystems and the living organisms. Achieving the highest water quality represents a major challenge due to the increasing environmental threats appearing nowadays. Pharmaceutical and Personal Care Products (PPCPs), and within, pharmaceutical compounds, have acquired special attention during the last years due to their broad use in humans and animals, whose populations are constantly growing [1]. As a reference, in the United States around 100,000 over-the-counter (OTC) drugs and personal care products are sold in pharmacies and supermarkets; sales in 2021 reached 37.7 billion dollars, with 5.8 billion units sold [2,3]. Pharmaceutical compounds are conceived to be resistant to external conditions and in consequence, they are more persistent than other organic contaminants. They can reach the environment by their discharge intentionally or unintentionally into aquatic ecosystems from pharmaceutical industries, hospitals, households, aquaculture activities, or wastewater treatment plants (WWTPs), among others. In addition, they are ubiquitously present because of their continuous renovation from the mentioned origin sources [4,5]. Specifically, WWTPs effluents are great contributors to the discharge of pharmaceuticals, due to the ineffective elimination of these kinds of compounds in secondary treatments [6–10]. Therefore, these contaminants end up in surface waters, rivers and seawater [1,4,5,11]. In this situation, some regulatory organisms, such as UNESCO, have taken actions and have included pharmaceuticals in the 2030 Agenda for Sustainable Development-Goal 6: Water and sanitation [11,12].

Pharmaceuticals can be present in the environment in their initial form, as metabolites, or as degradation by-products, leading to chronic exposure to living beings. They can produce serious danger to humans due to bacterial resistance and with this, the suppression of immune

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response. Even at low concentrations (they are released from ng L^{-1} to mg L^{-1}) they can cause adverse effects to aquatic organisms like endocrine disruption or growth affections, because their mode of action and their properties are not designed to treat these organisms [6,9–11,13,14]. Among all the pharmaceuticals detected in water sources, the presence of analgesics and anti-inflammatories, (paracetamol, ibuprofen, ketoprofen or dexamethasone), antibiotics (amoxicillin, azithromycin, or sulfamethoxazole) or psychiatric drugs (sertraline, clonazepam or fluoxetine) is worth highlighting [15–20]. In this way, hospital wastewater (HWW) effluents can contain very high concentrations of some pharmaceuticals. Pariente et al. [21] in a review work reported high concentrations of several pharmaceutical compounds, for instance, in the case of paracetamol, amoxicillin and levofloxacin, values up to 1.3, 4 and 1.1 mg L^{-1} were found [21]. Added to this, it has been reported that the lack of legislation in some countries of southern Asia, such as India, Vietnam, Bangladesh or Taiwan among others, can increase this problem, because higher levels of pharmaceuticals are being disposed directly into the environment, without previous treatment [22,23]. On the other hand, pharmaceutical manufacturing is a point source of contamination due to the high discharge concentrations which can produce. This is more serious for developing countries, which lack proper industrial effluent treatments. For instance, In India, a 31 mg L^{-1} maximum ciprofloxacin (antibiotic, similar amoxicillin) concentration in these effluents has been reported. Analgesics such as acetaminophen (0.5 mg L^{-1}), ibuprofen (0.3 mg L^{-1}), antibiotics (penicillin 0.01 mg L^{-1}), antidepressants (sertraline 5.1 10–3 mg L^{-1}), blood pressure medications (diltiazem 1.16 mg L^{-1}), cardiovascular drugs (metoprolol 7.3 mg L^{-1}), among many other drugs, were discovered in water bodies receiving discharges from five manufacturing facilities in Ontario, Canada [24]. In general, manufacturing effluents contain 10−1000 times higher pharmaceuticals concentrations than other wastewaters. Finally, technologies such as reverse osmosis and ultrafiltration have been also used for pharmaceuticals compounds elimination. These technologies are able to successfully remove > 90 %, but generate a brine, which contains a high concentration of drugs, among other pollutants, generating major disposal concerns [25]. In the literature, these physical separations can increase their use combining to electrochemical advanced oxidation to effectively eliminate pharmaceuticals.

Specifically, among the drugs used in the fight against COVID-19 and its consequences stand up Dexamethasone (DEX), Amoxicillin (AMX), Paracetamol (PAR) and sertraline (STR). DEX is a glucocorticoid with anti-inflammatory and immunosuppressive activity, and is one of the most employed drugs to treat the COVID-19 symptoms [9,26–28]. Its occurrence in the environment has been widely detected, and unfortunately, it is expected to increase in the next few years [9]. Before the pandemic, concentrations ranging between 0.36 and 2.11 ng L^{-1} were determined in tap water and river water [19,29,30], 0.51–12 ng L^{-1} in river samples [31], 0.39–1.3 ng L^{-1} in surface waters [9], and in wastewater, higher concentrations were found (11–243 ng L^{-1}) [9]. AMX and PAR have been used to palliate the main symptoms caused by SARS-CoV-2, such as headache and fever [32,33]. Nason et al. [32] reported that amoxicillin and paracetamol consumption experienced a substantial rise during the full lockdown in 2020 in New Haven (USA), with data taken from 19 March 2020–30 June 2020. The World Health Organisation (WHO) recommended the use of paracetamol to treat the illness on March 17, 2020, and its utilisation increased by + 111 % [34]. In the case of amoxicillin, the most common antibiotic of choice, was administered as an antimicrobial treatment to a high percentage of hospitalised people, especially those who were suspected of bacterial infection pneumonia [35–37]. Both pharmaceuticals have been jointly detected over the years in different aqueous matrices. Recently, Sengar and Vijayanandan [18] published a review, collecting data from 35 published papers (up to 2020), where the human health and ecological risk of 98 PPCPs, which were detected in treated waters of India, finding concentrations of 11 μg L^{-1} and 0.062 μg L^{-1} for paracetamol and amoxicillin, respectively. The COVID-19 pandemic has also affected people's mental health, increasing anxiety or depression, due to the significant changes in work and living ways. In consequence, a rise in the use of antidepressants has been detected [11,38–41]. Specifically, STR, an antidepressant that belongs to the group of selective serotonin reuptake inhibitors (SSRIs), was the most frequently prescribed drug in 2019 in the United Kingdom, this drug accounted for additional sales of £ 113 million in 2020 compared to 2019 [38,40]. Its high demand during the pandemic in 2020 led to shortage in the United States between May 2020 and September 2021 [42]. Nason et al. [32] confirmed as well, an increase in its concentration in New Haven (USA) during the lockdown period. It has been detected in concentrations in the environment between 5.4 ng L^{-1} (Leça River, Portugal) to 1 μg L^{-1} (Niagara River, US) [6,11,18,43]. Meanwhile, in the influent and effluent of WWTPs, the concentrations ranged between 0.77 and 114 ng L^{-1} prior to COVID-19 (2015–2019); and 25–417 ng L^{-1} after COVID-19 (2020–2021) [38].

Advanced Oxidation Processes (AOPs) are successfully applied technologies to the degradation of recalcitrant pollutants [44–46]. In particular, electrochemical oxidation (ELOX) has been extensively investigated for the mineralisation of several organic compounds [47,48]. PAR or AMX were degraded, employing EOX using a boron-doped diamond (BDD) anode [14], achieving good elimination results (>90 %) when treating medium-high concentrations, 21–1000 mg L^{-1} for the paracetamol case [49–54] and 47.5–1455 mg L^{-1} for the case of amoxicillin [55–62]. Regarding dexamethasone and sertraline, very few studies reported their degradation with ELOX so far, or with different ELOX-combined treatments, even so achieving good results in terms of degradation, > 70 % [63–69]. However, previous studies have demonstrated that under the application of some AOPs, and using certain operating conditions [44,46,48,70–73], other compounds more harmful than the parent compounds can be formed, as in the case of polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs), causing, in the final sample, an increase in the toxicity with regard to the initial sample. Exist 210 PCDD/Fs (75 PCDDs and 135 PCDFs), and 17 deserve special attention due to their associated high toxicity, those with chlorine atoms in 2, 3, 7, 8 positions. PCDD/Fs can be formed from different precursors such as chlorinated organic compounds, or even from non-chlorinated organic compounds but in presence of chlorine. To our knowledge, to date, no studies of drugs have conducted the analysis of dioxins and furans after applying EOX. Scarce information exists in the literature about the toxicity associated with the treated samples by AOPs, underlining the necessity of understanding these processes and the influence of the operation variables, facing to avoid final higher toxicity in the medium.

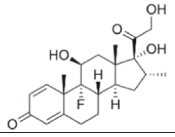
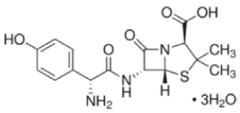
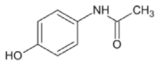
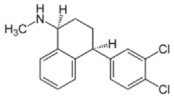
So, this study presents the successful degradation through electrochemical oxidation of four widely used pharmaceutical compounds to treat COVID-19 and its consequences, such as dexamethasone (DEX), amoxicillin (AMX), paracetamol (PAR), and sertraline (STR) employing two commonly used electrolytes, NaCl and Na_2SO_4. The advance in the knowledge proportioned in this research paper has allowed the demonstration of the PCDD/Fs formation from "non-classic" precursor compounds, organic compounds without chlorine atoms in the molecule, due to the influence of the medium, confirming the importance of carrying out a final evaluation of toxicity, as well as the selection of the optimal operating variables, when ELOX is used as a degradation treatment.

2. Materials and methods

2.1. Chemicals

Dexamethasone (≥98 %) (CAS: 50–02–2), amoxicillin trihydrate (≥95 %) (CAS: 61336–70–7) and paracetamol (acetaminophen) (≥99 %) (CAS: 103–90–2) were supplied from Sigma-Aldrich, and sertraline hydrochloride (≥98 %) (CAS: 79559–97–0) from TCI Chemicals. Phosphate buffer 0.05 M at pH 4.5 (prepared in laboratory) and acetonitrile

Table 1
Main characteristics of the pharmaceutical compound analysed in this work.

Compound	Molecular weight	Water solubility (mg L^{-1})	Structure
Dexamethasone $C_{22}H_{29}FO_5$	392.4	89	
Amoxicillin $C_{16}H_{19}N_3O_5S \cdot 3H_2O$	419.45	4150	
Paracetamol $C_8H_9NO_2$	151.1	14000	
Sertraline $C_8H_9NO_2 \cdot HCl$	342.7	3800	

LiChrosolv® (≥99.9 %) from Merck were employed for analysis by HPLC. EPA 1613 standard solutions were utilised (CS-1 to CS-5, LCS and ISS) to calibrate the equipment, the recovery and quantification of PCDD/Fs and quality control (Wellington Laboratories). Toluene Suprasolv®, dichloromethane UniSolv®, n-hexane UniSolv®, acetone Suprasolv®, sulphuric acid Normapur® and sodium sulphate Emsure® were supplied by Merck. Solid sorbents (silica, alumina and activated carbon chromatography columns) from Technospec were employed in the purification of PCDD/Fs samples through EPA 1613 method. 2.7 μm glass microfiber filter (Whatman) and two types of syringe filters, 1 μm APFB (Merck Millipore) and 0.45 μm Millex (Millipore), were employed. The solutions were prepared with deionized ultrapure Milli-Q-Water (resistivity=18.2 MΩ·cm) purified with a Milli-Q device (Millipore). Table 1 details the four compounds analysed in this work, and their main characteristics together with their molecular structure.

2.2. Electrochemical experiments

The electrochemical degradation of solutions (2 L) containing an initial concentration of 10 mg L^{-1} of the correspondent drug (DEX: 0.025 mM; AMX: 0.024 mM; PAR: 0.066 mM and STR: 0.029 mM) was carried out at laboratory scale in a medium/high power electrochemical plant (APRIA Systems S.L.). This plant possesses a jacketed mixing tank of 2 L and an electrochemical cell of two rectangular electrodes of 210 cm^2 of total anodic area (anode of Nb/BDD and cathode of AISI316 stainless steel) with an electrode gap of 2 mm. The operational flow rate was 300 L h^{-1} and the supporting electrolytes employed were NaCl (56 mM) and Na_2SO_4 plus NaCl (21 mM and 2.8 mM, respectively); these concentrations were selected in order to have approximately the same conductivity value, 7.5 mS cm^{-1}, in the electrolytic solution (value required to cell operation). The experiments were conducted in batch mode and replicated. Fig. 1 shows a representation of the experimental set-up. This is a polyvalent plant, which can also operate with UVA-LED, not used in this work.

2.3. Chemical analysis

The pharmaceutical compounds (dexamethasone, amoxicillin, paracetamol, and sertraline hydrochloride) were quantified in an Agilent Series 1100 HPLC chromatograph, equipped with an Agilent ZORBAX 80 Å Extend-C18 5 μm column (3.0 × 150 mm) and a photodiode array 1260 (PDA) detector. For each drug, ultra-pure water and acetonitrile were used as mobile phases in the proportions 60:40 (DEX), 95:5 (AMX) and 75:25 (PAR), the detection wavelengths 240 (DEX), 228 (AMX) and 248 (PAR) nm, the retention times 3.1 (DEX), 1.9 (AMX) and 1.2 (PAR) minutes, and the flowrates 0.5 mL min^{-1} (DEX), 0.5 mL min^{-1} (AMX) and 0.7 mL min^{-1} (PAR). For sertraline, phosphate buffer 0.05 M (pH = 4.5) and acetonitrile 50:50 were used as mobile phases, with a wavelength of 205 nm, a retention time of 1.5 min and a flowrate of 0.6 mL min^{-1}. In all cases, the column was kept at 30 °C and the injection volume was 50 μL. Compounds were confirmed by using authentic standards, matching their retention times and absorbance spectra.

The by-products present in the samples were determined in a Shimadzu QP2010 Ultra gas chromatography-mass spectrometry (GC-MS) equipped with auto-sampler. The separation occurred in an HP-5MS column (30 m × 0.25 mm × 0.1 mm). The mass spectrometer was operated in the electron impact ionisation mode (70 eV). The analytical method employed was different for the various chemical compounds studied and is detailed in Table S1 of the Supplementary material. The identification of the intermediates detected, formed during the electrochemical oxidation treatment, was carried out by the comparison of their mass spectra with those from the NIST08 spectra database. A match percentage was obtained by comparing the mass spectra and the characteristic ions of a peak with that of a known compound from the library. The compound was deemed identified and reported if the match percentage was higher than 70 %.

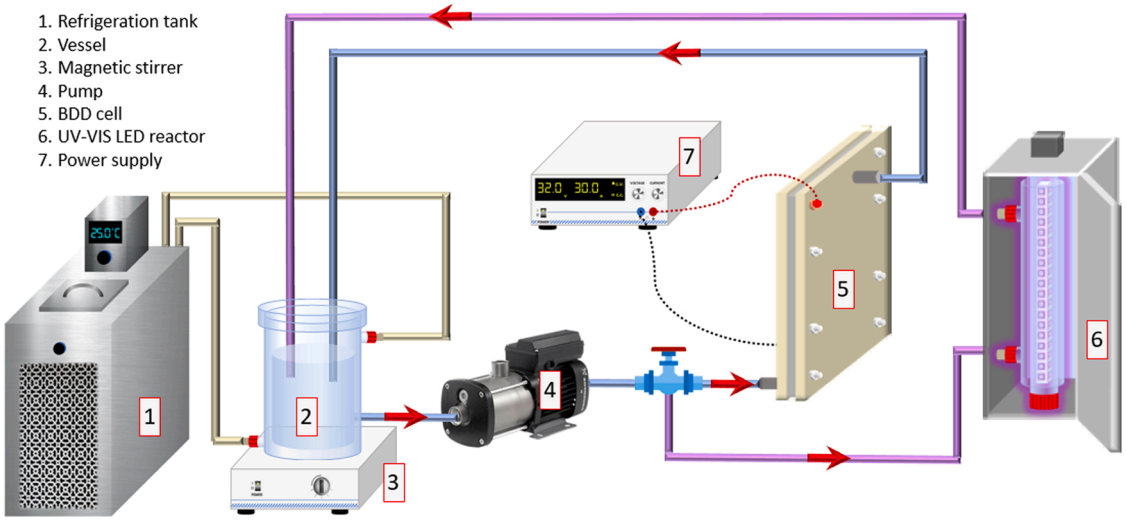


Fig. 1. Medium/high power laboratory-scale electrochemical plant supplied by APRIA Systems S.L.

2.4. PCDD/Fs analysis

PCDD/Fs were detected and quantified by carrying out the Standard Method US EPA 1613 by isotope dilution method and high-resolution gas chromatography/high-resolution mass spectrometry (HRGC-HRMS, Trace GC UltraTM, ThermoFisher Scientific) (US EPA, 1994) [74]. A volume of 10 μL of a ^{13}C-labelled PCDD/Fs solution (EPA 1613 LCS) was dissolved in 0.5 mL acetone Suprasolv® and added to the samples (500 mL). 60 mL of dichloromethane were used to extract the PCDD/Fs, stirring vigorously for 3 min (three times). Then, the organic phase goes through the following steps: concentration in a rotatory evaporator (Büchi R-210), attack with H_2SO_4 and filtration with sodium sulphate and glass-fibre filter to eliminate any possible rest of the water; then it was concentrated again in the rotatory evaporator, filtered through a 0.45 μm PTFE filter and a final purification step employing an automated system (Power-Prep™, Fluid Management Systems Inc.) employing three different columns of silica, alumina and activated carbon. The last concentration step is carried out in two stages, first in the rotatory evaporator and secondly, under a N_2 stream, till dryness. This whole purification process for each sample needs approximately five days. In Fig. 2 is shown the PCDD/Fs analytical method described above.

Finally, PCDD/Fs samples were analysed and quantified by the Chromatography Service of the University of Cantabria (SERCROM). Its quantification was performed through the isotopic dilution method. The exactitude of the PCDD/Fs analytical methodology can be guaranteed by two criteria: the analysis of blanks, which has undergone all the preparation steps, proves that PCDD/Fs concentration was either not detected or under the detection limit, which evidences the absence of contamination; and the mean recoveries obtained of the labelled PCDD/Fs after all sample preparation process, which are within the range established by EPA 1613 method (30–100 %). The average detection limits (LOD) were within the range 0.01–0.85 pg L^{-1} for all the analysis.

3. Results and discussion

3.1. Formation of radical species during the electrochemical oxidation

Electro-oxidation employing a BDD anode occurs by two mechanisms depending on the applied potential: direct oxidation, where the pollutant exchanges electrons with the anode surface and direct electron transfer is produced without other elements getting involved; or indirect oxidation, where presents species can exchange electrons with the anode generating species reactive oxygen species, ROS, such as the hydroxyl radicals (•OH) coming from water, be able to oxidation of the contaminants in the bulk [48,75]. These •OH radicals are generated in significant amounts and oxidise molecules in a non-selective manner, totally mineralising the organic contaminants (Eq. (1)):

$$BDD + H_2O \rightarrow BDD(^{\bullet}OH) + H^+ + e^- \quad (1)$$

The applied current density was established by referring to the limiting current density, which indicates the limit between the operating regimes controlled by the applied charge or by mass transfer. The limiting current density was estimated with Eq. 2 (Eq. (2)):

$$J_{lim} = 4 \cdot F \cdot k_m \cdot C \quad (2)$$

where F is the Faraday's constant (96,485 C mol^{-1}), k_m is the mass transport coefficient (1.48×10^{-5} m s^{-1}), which was calculated experimentally through the ferrocyanide/ferricyanide redox system [76], and C is expressed as mol of pollutant m^{-3}. In this work, the current density applied was 4.8 A m^{-2}; slightly higher, in all cases, than the limiting current density to ensure a mass-transfer controlled process; limiting current density: 3.2 A m^{-2} for DEX, 2.4 A m^{-2} for AMX, 3.2 A m^{-2} for PAR and 2.8 A m^{-2} for STR. The reaction between these drugs and •OH is favoured in the anode diffuse layer because of the high amount of electrogenerated •OH radicals, and due to this excess, it is expected that the further oxidation reactions follow first-order kinetic equations, according to the trends observed in the experimental data [75].

The electrochemical runs were conducted employing two different

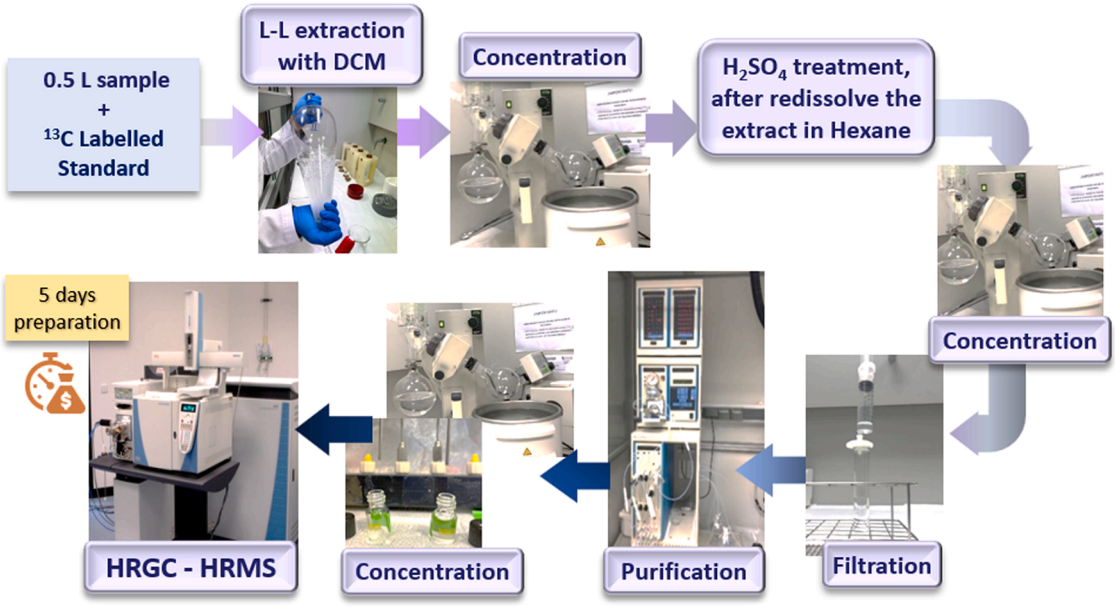


Fig. 2. Sample preparation and purification process for PCDD/Fs analysis.

electrolytes, NaCl (56 mM) and a solution containing the equivalent amount of the common chlorine (Cl^-) content in wastewater treatment plants effluents, around 100 mg L^{-1} (2.8 mM of NaCl), together with 21 mM of Na_2SO_4. Both electrolyte media gave the same initial conductivity (7.5 mS cm^{-1}). In all the runs, the pH range during the experiments varied between 5.5 and 6.8. In this sense, the analysis of the radicals formed was carried out at acid pH and taking into account the low current density applied, 4.8 A m^{-2}. The experimental pH is above the second pKa of sulphuric acid (pKa (HSO_4^-/SO_4^{2-}) = 1.92), and thus, SO_4^{2-} ions were the dominant species in the solution.

In chloride medium, electrochemically generated reactive chlorine species are produced regardless of electrode materials. A high amount of reactive chlorine species (RCSs) (Cl_2, HClO, and/or ClO^- which are prevalent at pH <3.0, 3.0–8.0 and >8.0, respectively) can be formed in the bulk solution through various reactions (Eqs. (3–5)) along with ROS [77–82] (standard electrode potentials under acidic conditions, E^0(HClO/0.5Cl_2)= 1.6 V, E^0(HClO/Cl^-)= 1.5 V and E^0(Cl_2/Cl^-)= 1.4 V [77,79,83–92]):

$$2Cl^- \rightarrow \ Cl_2 + 2e^- \quad (3)$$

$$Cl_2 + H_2O \rightarrow HClO + Cl^- + H^+ \qquad k_f = 11\ s^{-1};\ k_r = 1.8{\cdot}10^4\ M^{-2}\ s^{-1} \quad (4)$$

$$HClO \rightleftharpoons ClO^- + H^+ \qquad k_f = 1.6{\cdot}10^3\ M^{-1}s^{-1};\ k_r = 5{\cdot}10^{10}\ s^{-1} \quad (5)$$

Using a BDD anode and concentrations of 0.1–2.5 g L^{-1} of chloride, its direct oxidation produces stable oxidants such as $Cl^\bullet$ [81,82] (standard electrode potentials under acidic conditions, E^0($Cl^\bullet/Cl^-$)= 2.43 V [77,79,83–92]):

$$Cl^- \rightarrow \ Cl^\bullet + 1e^- \quad (6)$$

This radical can be combined with itself (Eq. (7)) or with other species (Eq. (8)), [79]; below pH 5.0–6.0, in an equilibrium process, may transform to dichloride radical anion, $Cl_2^{\bullet-}$ (Eq. (8)) [79,93], which explains the occurrence of different stable oxidants in the reaction medium [81,82] (standard electrode potentials under acidic conditions, E^0($Cl_2^{\bullet-}/2Cl^-$)= 2.13 V [77,79,83–92]):

$$Cl^\bullet + Cl^\bullet \rightarrow Cl_2 \qquad k_f = 1.0{\cdot}10^8\ M^{-1}s^{-1} \quad (7)$$

$$Cl^\bullet + Cl^- \rightleftharpoons \ Cl_2^{\bullet-}\ k_f = 6.5{\cdot}10^9 M^{-1}s^{-1};\qquad k_r = 1.1{\cdot}10^5\ M^{-1}s^{-1} \quad (8)$$

Finally, indirect oxidation of chloride by electrogenerated hydroxyl radicals ($^\bullet$OH), can take place, producing $ClOH^{\bullet-}$ radical, which is recombined generating different chloride radical species [81,82] (standard electrode potentials under acidic conditions, E^0($ClOH^{\bullet-}/Cl^-$)= 1.91 V, [77,79,83–92]):

$$^\bullet OH + Cl^- \rightleftharpoons ClOH^{\bullet-} \qquad k_f = 4.3{\cdot}10^9\ M^{-1}s^{-1};\ k_r = 6.1{\cdot}10^9\ s^{-1} \quad (9)$$

$$ClOH^{\bullet-} + H^+ \rightleftharpoons Cl^\bullet + H_2O \qquad k_f = 2.1{\cdot}10^{10}\ M^{-1}s^{-1};\ k_r = 2.5{\cdot}10^5\ M^{-1}s^{-1} \quad (10)$$

$$ClOH^{\bullet-} + Cl^- \rightleftharpoons \ Cl_2^{\bullet-} + OH^- \qquad k_f = 1.0{\cdot}10^5\ M^{-1}s^{-1};\quad k_r = 4.5{\cdot}10^7\ M^{-1}s^{-1} \quad (11)$$

Regarding the rest of the chlorine oxo-species such as ClO_2^-, ClO_3^-, and ClO_4^-, Sánchez-Carretero et al. [94], studied its formation during the electrooxidation of 0.1 M NaCl at different pHs and current densities with BDD anode. They concluded that these chlorine oxo-species are formed when the electrical charge is higher than 15 A h L^{-1} (J=300 A m^{-2}), assuming about 10 % of conversion of the total chloride.

In sulphate medium, the generation of reactive sulphate species ($S_2O_8^{2-}$, $SO_4^{\bullet-}$) at proper current density takes place. The $SO_4^{\bullet-}$, can be generated by the oxidation of SO_4^{2-} at the anode (Eq. (12)), however, there is no spectroscopic evidence that the oxidation of SO_4^{2-} by the generated $^\bullet$OH can produce $SO_4^{\bullet-}$ [95]. On the other hand, $S_2O_8^{2-}$is generated via oxidation of (i) SO_4^{2-} at the anode (Eq. (13)), (ii) by the reaction of SO_4^{2-} by electrogenerated and $^\bullet$OH (Eq. (14)), and (iii) by recombination of produced $SO_4^{\bullet-}$ (Eq. (15)) [81,82,91,95–98] (standard electrode potentials under acidic conditions, E^0($SO_4^{\bullet-}/SO_4^{2-}$)= 2.43 V and E^0($S_2O_8^{2-}/2SO_4^{2-}$, $2SO_4^{\bullet-}$)= 1.44 V [83,95,98–101]):

$$SO_4^{2-} + e^- \rightarrow \ SO_4^{\bullet-} \quad (12)$$

$$2SO_4^{2-} \rightarrow \ S_2O_8^{2-} + 2e^- \quad (13)$$

$$2SO_4^{2-} + 2HO^\bullet \rightarrow \ S_2O_8^{2-} + 2H_2O \quad (14)$$

$$SO_4^{\bullet-} + SO_4^{\bullet-} \rightarrow \ S_2O_8^{2-} \quad k_f = 7.6{\cdot}10^8\ M^{-1}s^{-1} \quad (15)$$

Finally, the joint presence of these two electrolytes, results in more inorganic oxidants that can be formed from the reaction between $Cl^\bullet$ and SO_4^{2-}, such as Cl^- and $SO_4^{\bullet-}$radicals (Eqs. 16–17). Vice versa, the reactions backward can also be produced [55,87,91,93,97,99,102–105].

$$Cl^\bullet + SO_4^{2-} \rightarrow SO_4^{\bullet-} + Cl^- + e^- \quad k = 2.5{\cdot}10^8 M^{-1}s^{-1} \quad (16)$$

$$SO_4^{\bullet-} + Cl^- \rightarrow Cl^\bullet + SO_4^{2-} \quad k = 3.8{\cdot}10^8 M^{-1}s^{-1} \quad (17)$$

3.2. Degradation of pharmaceutical compounds by electrochemical oxidation

Results of electrochemical oxidation expressed as a function of the specific electrical charge (Q) are presented in Fig. 3a (NaCl) and Fig. 3b (Na_2SO_4 and NaCl). In order to make a proper comparison, the degradation of the pharmaceuticals has been represented in mM. All experiments have been carried out in the same operating conditions (concentration of pharmaceutical compounds, 10 mg L^{-1}, electrolyte concentration (with a conductivity value of 7.5 mS cm^{-1}), current density, J = 4.8 A m^{-2} and volume, 2 L). In all cases, complete degradation has been achieved. The experimental data are represented with error bars, obtained after duplicating the experiments.

The specific electrical charge (Q) needed to achieve a complete degradation for AMX, PAR and STR was below 0.1 A h L^{-1}, when employing the NaCl electrolyte (Fig. 3a) and below 0.5 A h L^{-1}, when employing the Na_2SO_4 + NaCl electrolyte (Fig. 3b). On the contrary, the Q value for the complete DEX degradation was, for both electrolyte cases, around 0.6 A h L^{-1} (Fig. 3a and Fig. 3b). This behaviour can be explained by taking into account the pharmaceutical's molecular structure and the reactivity of radicals formed from chloride and sulphates. Even though PAR, AMX and STR are big molecules, they possess some weak bonds which can break easily, resulting in fast degradation. Conversely, DEX molecule has a very robust and stable complex structure (Table 1), being harder to decompose, regardless of the electrolyte used. To reach 50 % of de degradation, approximately 1, 7, 4, and 65 min were needed for STR, PAR, AMX and DEX respectively employing 56 mM of NaCl as electrolyte (Fig. 3a); and 5, 35, 15, and 45 min were needed for STR, PAR, AMX and DEX respectively, for the 21 mM Na_2SO_4 + 2.8 mM NaCl medium (Fig. 3b). Clearly, the process with the Na_2SO_4 electrolyte took more time to degrade the pharmaceutical compounds, except in the case of DEX, which was degraded slightly faster using the combined electrolyte. The fastest complete removal was for STR with the electrolyte NaCl, taking just 5 min, which can be explained by its hydrophobic nature [68]. The slowest complete degradation was for the DEX case with the electrolyte NaCl, taking 480 min.

In order to understand the degradation of each compound with each electrolyte (Fig. 3), an analysis of the oxidant species formed during the degradation process has been carried out. In the case of the radical species, regardless utilising NaCl or Na_2SO_4 + NaCl, $^\bullet$OH is the most reactive radical with a very high standard potential, E^0 ($^\bullet$OH/H_2O) = 2.73 V, despite its short lifetime, smaller than 1 μs [106,107]. $^\bullet$OH plays an important role in the degradation of organic compounds in natural waters owing to its high and non-specific reactivity, with second-order

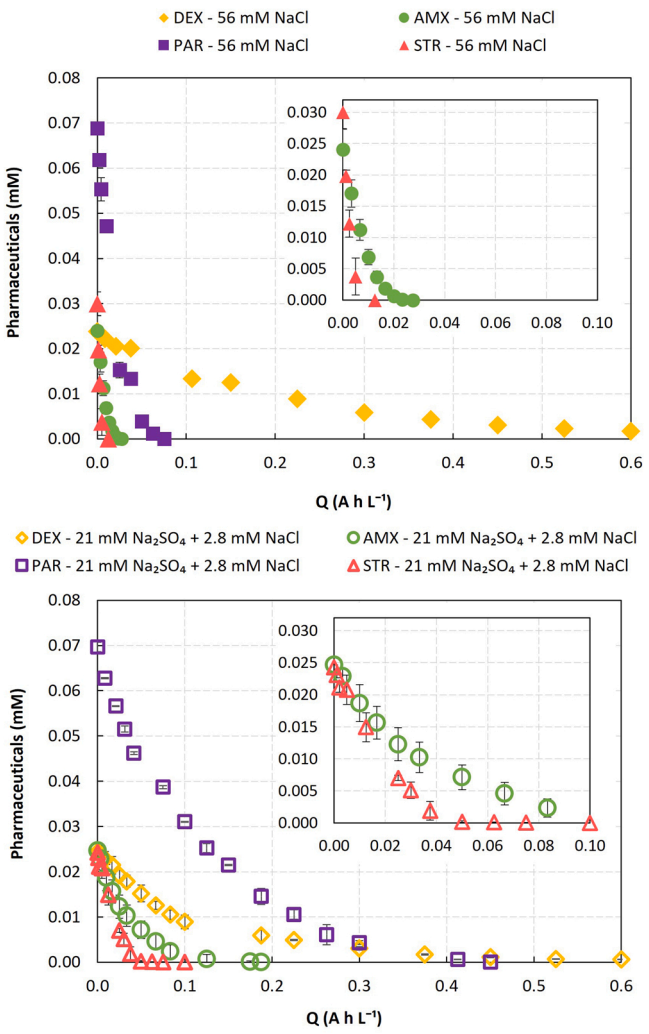


Fig. 3. Pharmaceuticals degradation in presence of different electrolytes: a) NaCl and b) Na_2SO_4 + NaCl. Experimental conditions (10 mg L^{-1}): [DEX]= 0.025 mM; [AMX]= 0.024 mM; [PAR]= 0.066 mM; [STR]= 0.029 mM; [NaCl]= 56 mM; [Na_2SO_4 + NaCl]= 21 mM + 2.8 mM; J= 4.8 A m^{-2}. The inset panels present an enlargement of the first quarter of the charts.

rate constants, in the range of 10^9–10^{11} M^{-1} s^{-1} [47,83,108]. When anodic treatment is applied in wastewaters and brines containing an abundance of halide species, such as Cl_2 and HOCl, among others, under acidic conditions, the rate of elimination of organic contaminants habitually increases owing to the additional formation of halogen-containing oxidants and radicals in the bulk solution, such as $Cl^{\bullet}$, $Cl_2^{\bullet-}$, $ClOH^{\bullet-}$, among others, which can indirectly oxidise the organic compounds (Eqs. (3), (4) and (5)). Brocenschi et al. [109] observed that the addition of Cl^- ions (0.36 mM) to the estrone solution (similar molecule to DEX) substantially enhanced the rate of degradation (regardless of pH), to the point that only 10 min (treating 0.5 L and 1.85 μmol L^{-1} at J = 10 mA cm^2) were employed to achieve a total degradation. Barazesh et al. [108] observed that the addition of 10 mM of chloride significantly increased the degradation rates of trace organic contaminants, like anticonvulsants, herbicides or antibiotics, among others, compared with those observed in the borate-buffered electrolyte, increasing between 4 and 20 times. Due to the electrochemical properties of BDD, chloride radical ($Cl^{\bullet}$) is the first-step product of the direct oxidation of chloride with BDD anode (Eq. (6)). In solution, $Cl^{\bullet}$ reacts with most organic pollutants at near diffusion-controlled rates (10^8–10^{10} M^{-1} s^{-1}). Nevertheless, other mechanisms of $Cl^{\bullet}$, e.g., in presence of an elevated chloride concentration, such as recombination with $Cl^{\bullet}$ to form Cl_2 (Eq. (7)), propagation with Cl^- to form $Cl_2^{\bullet-}$ (Eq. (8)), and reactions with other scavengers, may limit its role in pollutants transformation during the electrochemical treatment. $Cl_2^{\bullet-}$ reacts with organic compounds similar to $Cl^{\bullet}$ but typically at rates that are 2–4 orders of magnitude slower [110]. Additionally, assuming all reactions are diffusion-controlled, the $Cl^{\bullet}$ branching ratio depends on the Cl^- concentration with respect to the concentration of the organic compounds (S); at low $[Cl^-]/[S] < 1$, the reaction of $Cl^{\bullet}$ with substrates is prevalent, whereas at high $[Cl^-]/[S] > 1$, $Cl_2^{\bullet-}$ formation will preferentially occur. Park et al. [111] studied this behaviour concluding that a relatively high Cl^- concentration, 50 mM, in comparison to substrates, ~1 mM, such as chlorophenols and organic acids, forced $Cl^{\bullet}$ towards $Cl_2^{\bullet-}$ formation. In this work, the relation $[Cl^-]/[S]$ was between 0.2 and 0.5, so $Cl^{\bullet}$ was the main halide radical, which confirms the rapid degradation of AMX, PAR and STR in NaCl medium against the Na_2SO_4 + NaCl medium.

In conclusion, taking into consideration the formation rate of the oxidant species and radicals (Eqs. (4)-(11)), its redox potential, and the rate of degradation of organic compounds, the main species and radicals which take part in the degradation of DEX, AMX, PAR, STR -employing NaCl as electrolyte, with a pH between 5.5 and 6.8 and $J = 4.8$ A m^{-2}- can track the subsequent order according to its oxidation capacity and possible presence, $^{\bullet}OH \gg Cl^{\bullet} > Cl_2^{\bullet-} > ClOH^{\bullet} > HClO > Cl_2$, contributing all of these species to a higher degradation of these compounds against systems with non-oxidising electrolytes (Fig. 3a).

When Na_2SO_4 + NaCl electrolytes were used, it took more time to degrade the pharmaceutical compounds (except DEX) (Fig. 3b). This kind of behaviour can be explained considering that, although $SO_4^{\bullet-}$ (Eq. (12)) has a longer half-life (30–40 μs) than $^{\bullet}OH$ (<1 μs) [107,112], its standard electrode potential (2.43 V) is lower than the standard electrode potential of $^{\bullet}OH$ (2.73 V). Likewise, the second-order rate constants with the organic compounds usually show one to two orders of magnitude lower, between 10^5 to 10^9 M^{-1} s^{-1}, than that of $^{\bullet}OH$ radicals (10^6 to 10^{11} M^{-1} s^{-1}), regardless of the type of substrate dissolved in water. The reaction between $SO_4^{\bullet-}$ with the organic molecules is all diffusion-controlled [107,113]. Thermodynamically, $SO_4^{\bullet-}$ is a more powerful oxidant than $S_2O_8^{2-}$ (Eqs. (13)-(15)). $SO_4^{\bullet-}$ can selectively and rapidly attack the organic contaminants while $S_2O_8^{2-}$ react slowly [98]. In the present work, the concentration of chlorides is much lower than sulphates, besides, both, $Cl^{\bullet}$ and $SO_4^{\bullet-}$ act like scavengers between themselves (Eqs. (16) and (17)), consequently, its oxidation capacity in the medium is lower than using NaCl, as this is shown in the obtained results (Fig. 3b). As conclusion, the literature reports that processes with NaCl happen much faster than when using Na_2SO_4, due to the high amount of strong oxidising species present in the solution and its oxidant power ($Cl_2^{\bullet-}$, $Cl^{\bullet}$, $ClOH^{\bullet-}$, HClO and Cl_2 versus $S_2O_8^{2-}$ and $SO_4^{\bullet-}$); so, the degradation of the pollutants may occur in the bulk solution rivalling with the process which takes place at the surface of the anode. This result in mass transfer limitations and may explain the acceleration in the degradation when employing NaCl [114,115]; the kinetic data obtained in this work corroborated these results, with kinetic constants between (k) 0.011–0.999 min^{-1} for NaCl and 0.017–0.144 min^{-1} for

Table 2
Kinetic constants of the electrochemical degradation of the DEX, AMX, PAR and STR.

Compound	mM	Electrolyte			
		NaCl		Na_2SO_4 + NaCl	
		k (min^{-1})	R^2	k (min^{-1})	R^2
DEX	0.025	0.011	0.999	0.017	0.998
AMX	0.024	0.236	0.991	0.044	0.997
PAR	0.066	0.145	0.962	0.022	0.997
STR	0.029	0.999	0.996	0.144	0.973

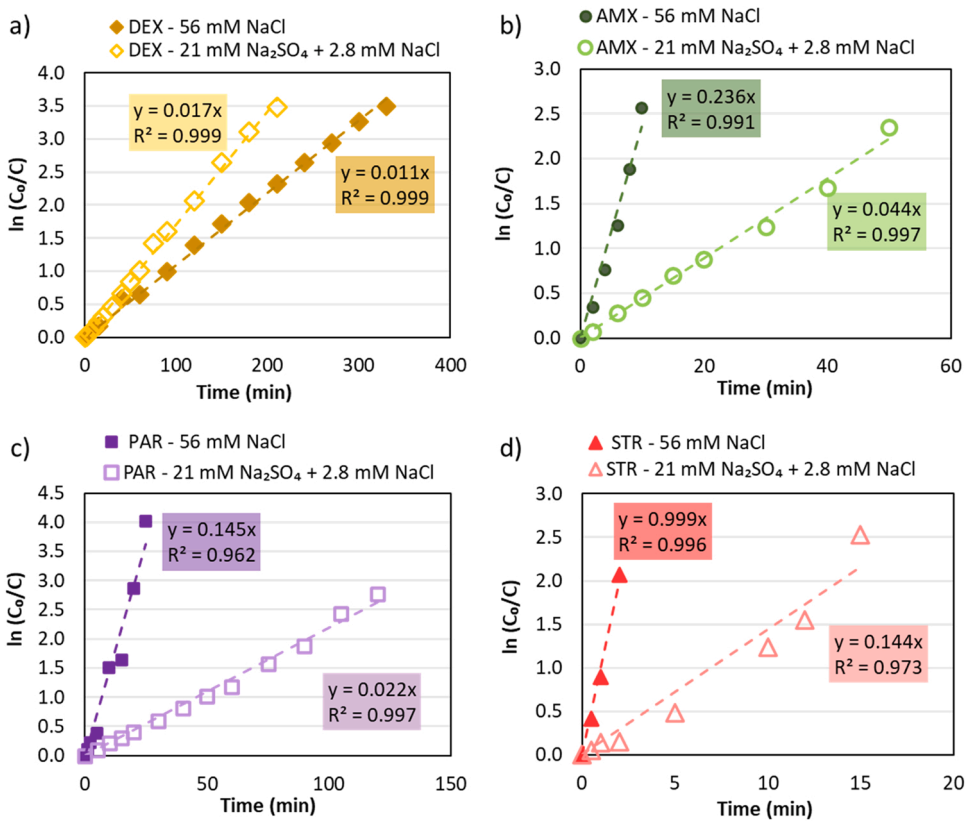


Fig. 4. Pseudo-first-order degradation kinetics: a) dexamethasone (DEX), b) amoxicillin (AMX), c) paracetamol (PAR) and sertraline (STR); for the two electrolytes employed, NaCl (solid dots) and Na_2SO_4 + NaCl (empty dots). Experimental conditions: [DEX] = 0.025 mM; [AMX] = 0.024 mM; [PAR] = 0.066 mM; [STR] = 0.029 mM; [NaCl] = 56 mM; [Na_2SO_4 + NaCl] = 21 mM + 2,8 mM; J = 4.8 A m^{-2}.

Na_2SO_4, as it can be seen in Table 2. Fig. 4 represents the kinetic data obtained after the linearization of the degradation experimental data for the four pharmaceuticals studied.

So far, there are not many studies the DEX degradation via electrochemical oxidation. Recently, Grilla et al. [65] reached a 90 % of DEX elimination by treating an initial concentration of 0.5 mg L^{-1} (0.001 mM), using an electrochemical cell with a BDD anode, a current density of 0.2 A m^{-2} and 0.1 M of Na_2SO_4 as electrolyte, obtaining a kinetic constant of 0.043 min^{-1}. Treating 2.0 mg L^{-1} (0.005 mM), employing a current density of 0.05 A m^{-2} and 0.1 M Na_2SO_4 of electrolyte, they obtained a kinetic constant of 0.01 min^{-1}. These kinetics constants are in the same order of magnitude as those obtained in the present study, 0.017 min^{-1} (Table 2), where 10 mg L^{-1} DEX (0.025 mM) were treated (90 % of degradation) using 4.8 A m^{-2} and 21 mM of Na_2SO_4 + 2.8 mM of NaCl as electrolyte. In regard to AMX, there are works which describe amoxicillin complete degradation, using 36.5 mg L^{-1} (0.1 mM), different current densities (0.41–20.83 mA cm^{-2}), a BDD anode and Na_2SO_4 (50 mM), obtaining k values between 0.020 and 6.5 min^{-1} [58,59,62]. Other authors working with slightly higher concentrations of amoxicillin, 47.5–100 mg L^{-1} (0.13–0.27 mM), using higher current densities, 15–44.4 mA cm^{-2} and 21.1–50 mM of Na_2SO_4 as electrolyte, achieved kinetic constants between 0.06 and 0.60 min^{-1} [61,116]. In the present work, using lower operation values, 10 mg L^{-1} (0.024 mM) of amoxicillin, J = 4.8 A m^{-2} (0.48 mA cm^{-2}) and Na_2SO_4 + NaCl as electrolyte (21 mM + 2.8 mM), a kinetic constant of 0.044 min^{-1} was obtained (Table 2), which is in the range of the values of literature reported previously, 0.020 min^{-1} and 0.06 min^{-1}, for comparable experimental conditions. With respect to paracetamol, its elimination was studied working with 151–190 mg L^{-1} (1.0–1.2 mM), 50 mM of Na_2SO_4 as electrolyte and current density of 100 mA cm^{-2}, reaching a degradation between 50 % and 91 % [49,53]; in one of these studies, Peralta-Hernández et al. [53] obtained a kinetic constant of 0.004 min^{-1}. Waterston et al. [54] reached 82 % of TOC reduction by treating 1 mM of paracetamol, using 25 mM of Na_2SO_4 and low current density, 54.4 mA cm^{-2}, obtaining a kinetic constant of k = 0.022 min^{-1}. In the present work, using lower operating values, 10 mg L^{-1} of paracetamol, J= 0.48 mA cm^{-2} and Na_2SO_4 (21 mM) + NaCl (2.8 mM), as electrolyte, a constant rate of 0.022 min^{-1} was obtained (Table 2), which is also in the range of the values of literature reported previously. Finally, for the sertraline case, various works employing AOPs have been found, but just two applied electrochemical oxidation. Radjenovic et al. [68] treated a reverse osmosis concentrate (ROC) from Brisbane, Australia, with several spiked pharmaceuticals and pesticides ($[STR]_0$ =17 μg L^{-1}), achieving at least 70 % degradation even for low current densities (1–10 A m^{-2}), but with no kinetic constants calculated. On the other hand, recently, Rachidi et al. [67] obtained similar results as those achieved in the current work, but applying electrofenton, reaching complete degradation when treating 0.1 mM of initial concentration (34.2 mg L^{-1}) with a current density of 80 mA cm^2 and adding 0.05 M of Na_2SO_4 as electrolyte, and 0.1 mM of Fe^{+2}. They obtained a kinetic constant of 0.90 min^{-1}, same as the obtained in the present work, 0.999 min^{-1} (Table 2). Again, this value is in the range of the literature values.

3.3. Assessment of formation of PCDD/Fs

It is necessary to take into consideration that the degradation of the starting pollutant can result in degradation products including more persistent chemicals such as unintentional POPs [117].

Especially if precursors such as chlorinated organic compounds are present, some degradation products more hazardous than the parent compounds such as PCDD/Fs can be formed, as a consequence of the presence of $^{\bullet}OH$ radicals present in the bulk solution facilitating coupling of aromatic compounds [73,117,118]. In the presence of elemental chlorine or another chlorinating agent even non-chlorinated organic compounds such as polyaromatic hydrocarbons or phenol can

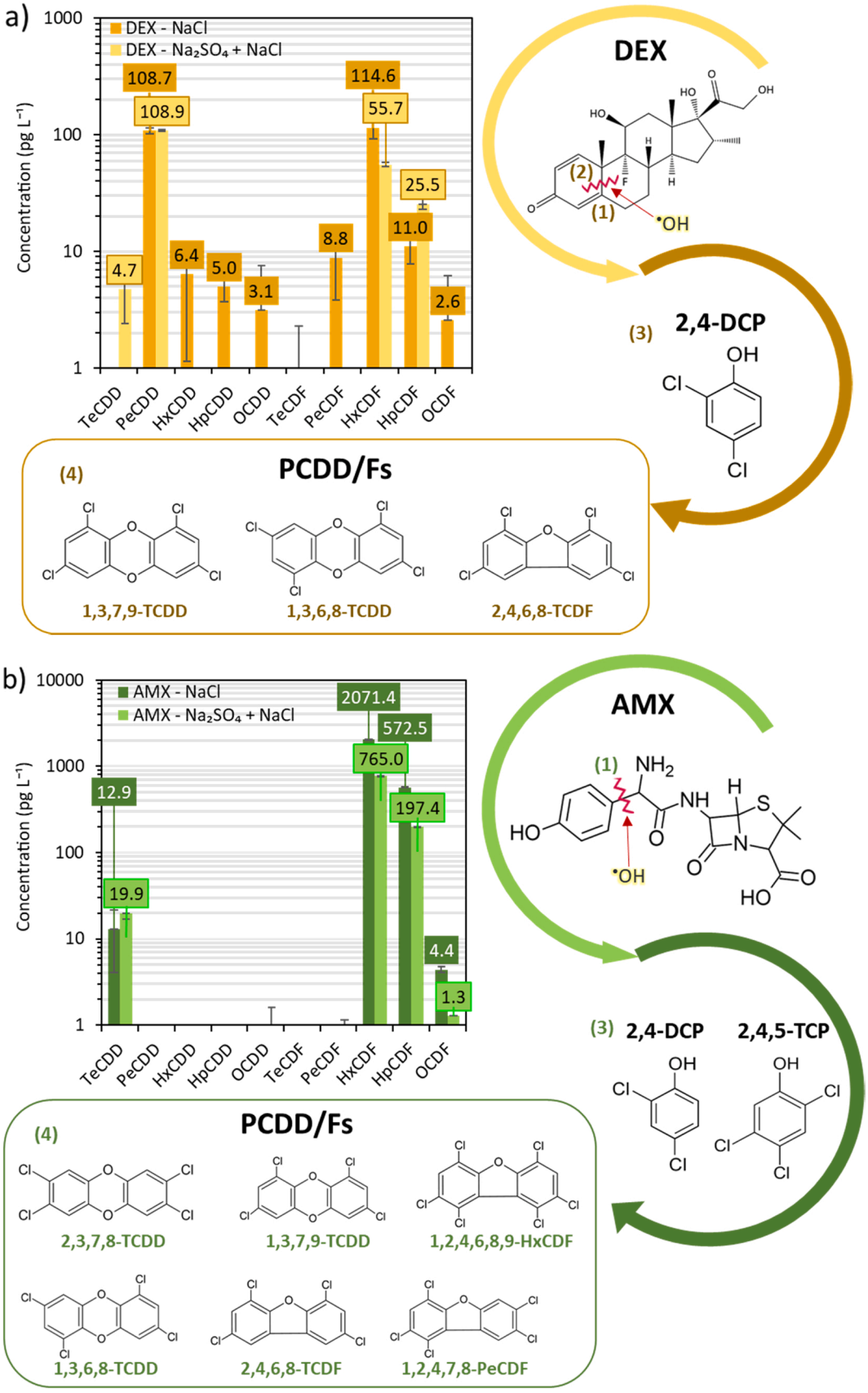


Fig. 5. PCDD/Fs formed during the electrochemical oxidation of: a) dexamethasone (DEX), b) amoxicillin (AMX), c) paracetamol (PAR) and sertraline (STR). Experimental conditions: [DEX]= 0.025 mM; [AMX]= 0.024 mM; [PAR]= 0.066 mM; [STR] = 0.029; NaCl= 56 mM; Na_2SO_4 + NaCl= 21 mM + 2,8 mM; J= 4.8 A m^{-2}.

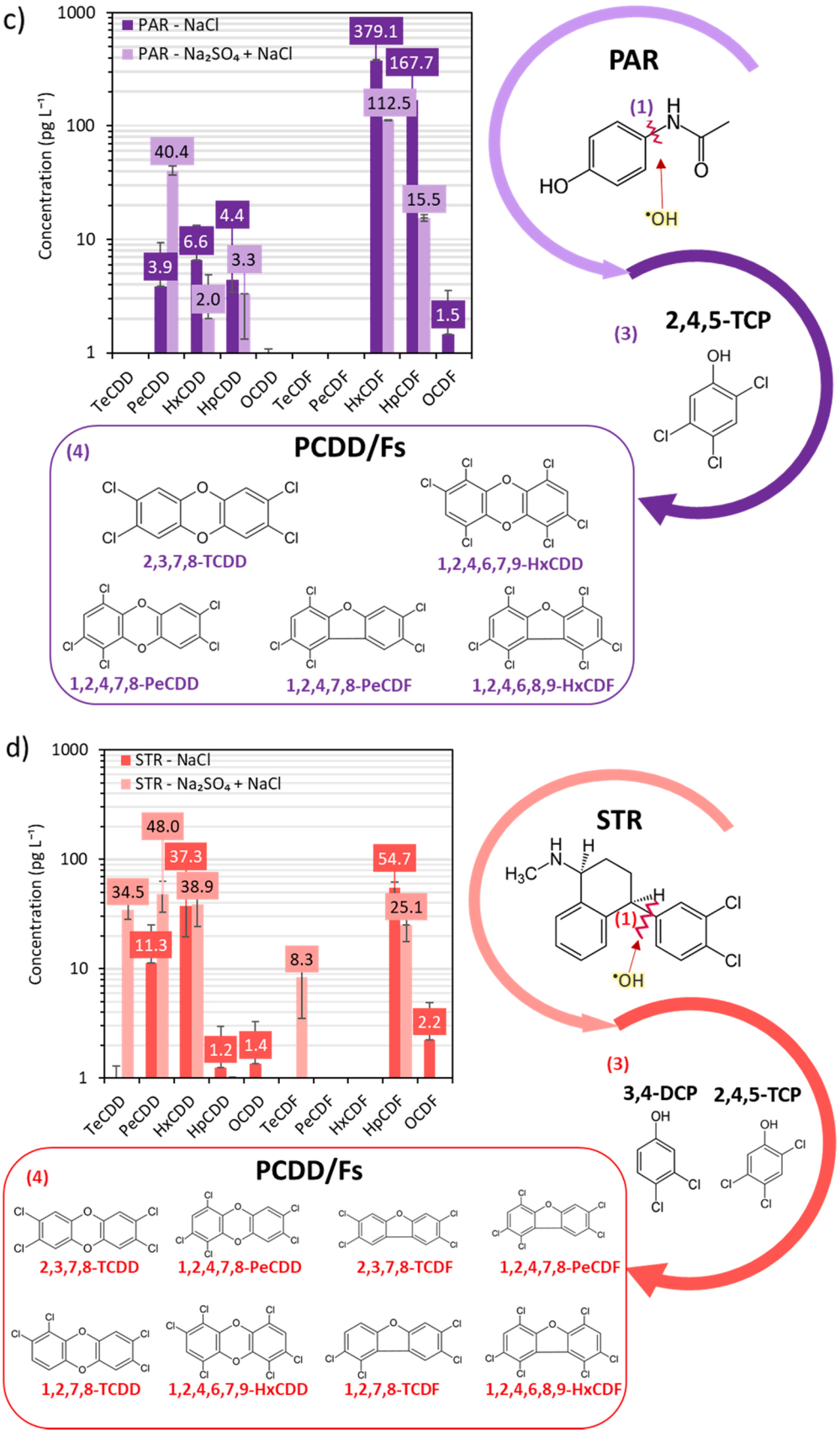


Fig. 5. (*continued*).

Table 3
Total amount (pg L^{-1}) of homologues generated during the electrochemical oxidation of DEX, AMX, PAR and STR.

Compound	Electrolyte	PCDDs (pg L^{-1}) (%)	PCDFs (pg L^{-1}) (%)	TOTAL Homologues (pg L^{-1}) (%)
DEX	56 mM NaCl	123.2 (47.1%)	137.9 (52.8%)	261.1 (100%)
	21 mM Na_2SO_4 + 2.8 mM NaCl	113.7 (58.4%)	81.1 (41.6%)	194.8 (100%)
AMX	56 mM NaCl	12.9 (0.5%)	2648.4 (99.5%)	2661.3 (100%)
	21 mM Na_2SO_4 + 2.8 mM NaCl	20.6 (2.1%)	964.1 (97.9%)	984.7 (100%)
PAR	56 mM NaCl	15.3 (2.7%)	548.2 (97.3%)	563.5 (100%)
	21 mM Na_2SO_4 + 2.8 mM NaCl	45.2 (26.3%)	127.9 (73.7%)	173.6 (100%)
STR	56 mM NaCl	51.7 (47.5%)	57.2 (52.5%)	108.9 (100%)
	21 mM Na_2SO_4 + 2.8 mM NaCl	122.2 (78.5%)	33.5 (21.5%)	155.7 (100%)

be chlorinated and form PCDD/Fs [119,120]. For this reason, the analysis of the PCDD/Fs's formation has been performed for all the degraded compounds in this study. In all cases, dioxins and furans samples were analysed at the final point of the oxidation process, when the pollutant has been completely degraded. Fig. 5 presents the PCDD/Fs homologues, the major PCDD/Fs congeners experimentally determined and also, proposed on the literature [121,122], and the major chlorophenols detected in each degradation experiment, along with the scheme of reaction proposed. Table 3 contains the concentration (and percentage) of the PCDDs, PCDFs and PCDD/Fs homologues formed during the electrochemical oxidation of DEX, AMX, PAR and STR, together with the experimental conditions applied.

According to the results depicted in Fig. 5 and Table 3, a clear tendency can be stated in a first approach: PCDFs are formed in higher concentrations than PCDDs in all cases where NaCl was employed. Also, the predominance of higher chlorinated PCDFs, such as HxCDF group was observed in all cases, reaching values near 2000 pg L^{-1} for the AMX degradation experiment (Fig. 5b). On the other hand, comparing the generated amounts of PCDDs, they were slightly higher for AMX, PAR, STR (Figs. 5b, 5c and 5d), or similar for DEX (Fig. 5a), in the experiments with Na_2SO_4 + NaCl as electrolyte, compared to the generated PCDDs using NaCl. PeCDD is the highest concentration homologue in the DEX case (Fig. 5a), HxCDF in AMX and PAR cases (Figs. 5b and 5c), and HpCDF in the STR case (Fig. 5d). Higher concentrations of the generated furans can reside in the affinity towards their formation versus dioxins.

In the current work, a qualitative screening of the intermediates produced during the electrochemical oxidation process, using NaCl as electrolyte has been carried out. Chlorophenols such as 2,4-dichlorophenol for DEX and AMX, 3,4-dichlorophenol for STR, and 2,4,5-trichlorophenol for AMX, PAR and STR (Fig. 5) were identified. Besides this, compounds like chlorohydroquinone and hydroquinone for AMX and PAR were also found (Figs. 5b and 5c). Chlorophenols are well-known precursors of PCDD/Fs; as it was reported in previous studies [44,73,118,121,123]. A recent investigation line reported PCDD/Fs formation when applying Fenton oxidation to remediate 2-chlorophenol solutions [44,46,72]. They studied their formation under several operating conditions, by changing temperature, H_2O_2 and iron dose, or the presence of chloride; Vallejo et al. [46,72] found that PCDD/Fs concentration experimented a high growth in comparison with the untreated samples; with a preferential formation of PCDFs over PCDDs. Furthermore, low-chlorinated congeners formation, like tetra/penta-PCDD/Fs were prevalent; Fernández-Castro et al. [44] focused on the analysis of non-chlorinated to very low-chlorinated DD/Fs (mono- to tri-), reporting a predominance of dichlorodibenzo dioxins and furans (DCDD/Fs) in the homologue profile of total PCDD/Fs. On the other hand, when 2-chlorophenol solutions were electrochemically oxidised, Vallejo et al. [73] found that total PCDD/Fs concentration increased by $2.68{\cdot}10^4$ and 200 times when employing NaCl and Na_2SO_4, respectively, emphasising the importance of the chloride concentration in the medium. Moreover, when using NaCl, PCDFs contributed 88% to the total PCDD/Fs concentration, with HxCDF was the main group of homologues. Likewise, when treating triclosan solutions by electrooxidation, Solá-Gutiérrez et al. [48] determined that the PCDD/Fs formation was also several times higher using NaCl, but on the contrary, PCDDs predominated over PCDFs. This can be explained due to the structure of the triclosan molecule, which is a diphenyl ether containing a further hydroxyl group and 3 chlorine atoms and therefore can form preferably PCDDs by HCl elimination.

In the present work, the formation of by-products from the electrochemical oxidation of pharmaceuticals is justified starting from $^{\bullet}OH$ radicals formed in the BDD anode, and the different chlorine and sulphate radicals produced from the electrolytes. $^{\bullet}OH$, a non-selective oxidant, is likely to react over to C═C bond, oxidising the benzene ring and provoking the breakage of the molecules [95,105]. This assumption is shown in Fig. 5, marked with the number (1), except to DEX (Fig. 5a), where the $^{\bullet}OH$ attack the saturated bond, marked with the number (2). The principal reaction in presence of Cl^- is the electrophilic addition of $^{\bullet}OH$ on the aromatic ring leading to the production of chlorophenol [85]. In the case of chlorine radicals, such $Cl^{\bullet}$ and $Cl_2^{\bullet-}$ (Eqs. (6) and (8)), they basically followed three reaction pathways: i) single electron transfer (SET), ii) H-abstraction and iii) addition pathways (chlorine addition) [87,111]. Chlorine addition is predictable as the most probable pathway, leading to the formation of chlorinated by-products, such as 2,4-dichlorophenol for DEX and AMX, 3,4-dichlorophenol for STR, and 2,4,5-trichlorophenol for AMX, PAR and STR (Fig. 5, number (3)). Actually, their formation has been observed from the reactions with some organic contaminants [124]. The reaction mechanism of $Cl^{\bullet}$ addition to an aromatic ring has been previously demonstrated by the detection of $Cl^{\bullet}$-adducts. Lei et al. [87] observed that when $Cl^{\bullet}$ reacted with various trace organic contaminants such as different β-lactams, macrolides or antipyretics analgesics, various chlorine by-products were formed. $Cl^{\bullet}$-adducts and phenoxyl radicals were observed, dominating the H-abstraction reaction for paracetamol and amoxicillin [87]. $Cl_2^{\bullet-}$, similar to $Cl^{\bullet}$, reacts via H-abstraction, electrophilic addition and direct electron transfer [111]. Moreover, it was proven that $Cl^{\bullet}$ was very reactive towards many trace organic contaminants, and $Cl_2^{\bullet-}$ was more selective [87]. Organic trace contaminants with a high fraction of electrons showed high reactivity towards $Cl_2^{\bullet-}$; and those results demonstrate that $Cl_2^{\bullet-}$ can play important roles in the degradation of these types of pollutants [87].

The results obtained in the present work regarding PCDD/Fs formation (Fig. 5) can be also explained in terms of the chlorine amount present in the solution. When NaCl is employed as electrolyte, large amounts of chlorine are present, forming the radicals and oxidants species such as $Cl_2^{\bullet-}$, $Cl^{\bullet}$, $ClOH^{\bullet-}$, HClO and Cl_2 (point 3.1) and with this, chlorophenols and clorohydroquinones. From the intermediates detected (several types of chlorophenols in the case of the four molecules), is well-known the direct formation of low-chlorination degree furans through the condensation of chlorophenols. Sidhu and Edwards [125] reported the preferential formation of furans over dioxins through the combination of two 2-clorophenoxy radicals (2-CPR) produced from 2-chlorophenol (2-CP) precursors, which are radical active species that possess enol and keto forms with the unpaired electron on the phenolic oxygen. Due to keto forms possess higher stability than enol forms, higher formation of DCDF it is expected [44]. Finally, the radicals and oxidant species attack low-chlorinated PCDD/Fs, increasing the chlorination degree and resulting in higher chlorination degree PCDD/Fs (HxCDF and HpCDF). Moreover, and supporting this, it is worth

highlighting that, all PCDD/Fs samples were taken at final time of the experiment, and it is probable that, at initial time, lower chlorination degree furans can be produced, reaching higher chlorination degree at final times, due to successive chlorination reactions (Fig. 5, number (4)).

On the other hand, when less chlorine amount is present in the medium (this is when using the combined electrolyte, Na_2SO_4 + NaCl), the same behaviour of NaCl medium of the oxidant species and radicals of chlorine is assumed. Furans are being formed in the same proportion but to a lesser extent, than when using just NaCl due to the less chlorine amount present in the medium, and also, due to the $SO_4^{\bullet-}$ is scavenged by the Cl^-, to produce $Cl^\bullet$ and continue reacting with Cl^- to generate less active radicals, as in the case of $Cl_2^{\bullet-}$ (Eqs. (8) and (17)) [105]. Moreover, a little bit higher amounts of lower chlorinated PCDDs are formed in a direct way from the condensation of 2-CPR, and they are also being chlorinated, thus, increasing the chlorination degree, as described above. In the case of $SO_4^{\bullet-}$, in order to degradation of the molecules, the three main pathways of reaction are more or less the same than those for chlorine radicals, being: i) H-abstraction from carbon atoms of the organics contaminants with saturated bonds, ii) additive reactions (electrophilic/radical additions) which take place when the unsaturated bonds are broken and iii) electron transfer with aromatic organic contaminants [107,126]. Frequently, $SO_4^{\bullet-}$, tends to react primarily via electron transfer mechanisms (is electrophilic, it is favoured to react with electron-donating groups such as amino, hydroxyl, alcoxy groups, π electrons present on aromatic molecules and other organic compounds that contain unsaturated bonds), and are predisposed to attack the conjugation bond in the molecules [105,107,112,113].

4. Conclusions

In this work, it is presented the electrochemical degradation of four pharmaceuticals (10 mg L^{-1}), three of them of very common use (amoxicillin, paracetamol, and sertraline) and the fourth one in crescent use over the past two years, dexamethasone, due to its application in COVID-19 treatment. Complete degradation of the parent compound was achieved in all cases. With both electrolytes NaCl and Na_2SO_4 + NaCl, sertraline (STR) achieved the fastest degradation rate, k = 1.0 min^{-1} and k = 0.14 min^{-1}, respectively, and oppositely, dexamethasone (DEX) had the lowest degradation rate, k = 0.011 min^{-1} and k = 0.017 min^{-1}, respectively. These tendencies are easily explained in relation to the complexity of their molecular structure, being DEX the most complex and robust one.

An extended analysis of the radicals produced during the electrooxidation of the pharmaceuticals has been performed. Taking into account the formation rate of the oxidants, their redox potential, and the degradation rate of organic compounds, the main species and radicals, which take part of the degradation of DEX, AMX, PAR, STR -pH between 5.5 and 6.8-, can track the subsequent order according to its oxidation capacity and possible presence, $^\bullet OH \gg Cl^\bullet > Cl_2^{\bullet-} > ClOH^\bullet > HClO > Cl_2$, in NaCl medium, versus $S_2O_8^{2-}$ and $SO_4^{\bullet-}$, in medium NaCl + Na_2SO_4, all of these species contributing to a higher degradation of these compounds against systems with non-oxidising electrolytes.

PCDD/Fs precursor compounds were determined, such as chlorophenols and quinones. When analysing the dioxins and furans produced during the process, medium NaCl gave rise to a higher total concentration (dioxins+furans). PCDFs are formed in higher concentration in NaCl medium, being the highest the HxCDF group, reaching a value around 2000 pg L^{-1} for AMX. In contrast, when using Na_2SO_4 +NaCl in combination, PCDDs are formed in higher concentrations in almost all cases; PeCDD for DEX, PAR and STR and TeCDD for AMX. In presence of NaCl, the formation of furans over dioxins is due to the combination of two 2-clorophenoxy radicals (2-CPR) produced from 2-chlorophenol (2-CP) precursor, which are radical active species that possess enol and keto forms with the unpaired electron on the phenolic oxygen. Due to keto forms possess higher stability than enol forms, higher formation of DCDF it was expected. Finally, the radicals and oxidant species attack low-chlorinated PCDD/Fs, increasing the chlorination degree and resulting in higher chlorination degree PCDD/Fs (HxCDF and HpCDF). In a further study the intermediates produced during the process, which are responsible of the PCDD/Fs formation will be analysed, together with the congeners and the proper measure of the toxicity in terms of TEQ.

CRediT authorship contribution statement

Sophie Schröder: Conceptualization, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing, **Inmaculada Ortiz**: Formal analysis, Review, **Ma-Fresnedo San-Román**: Conceptualization, Formal analysis, Funding acquisition, Investigation, Resources, Methodology, Project administration, Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data that has been used is confidential.

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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.2023.109305.

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