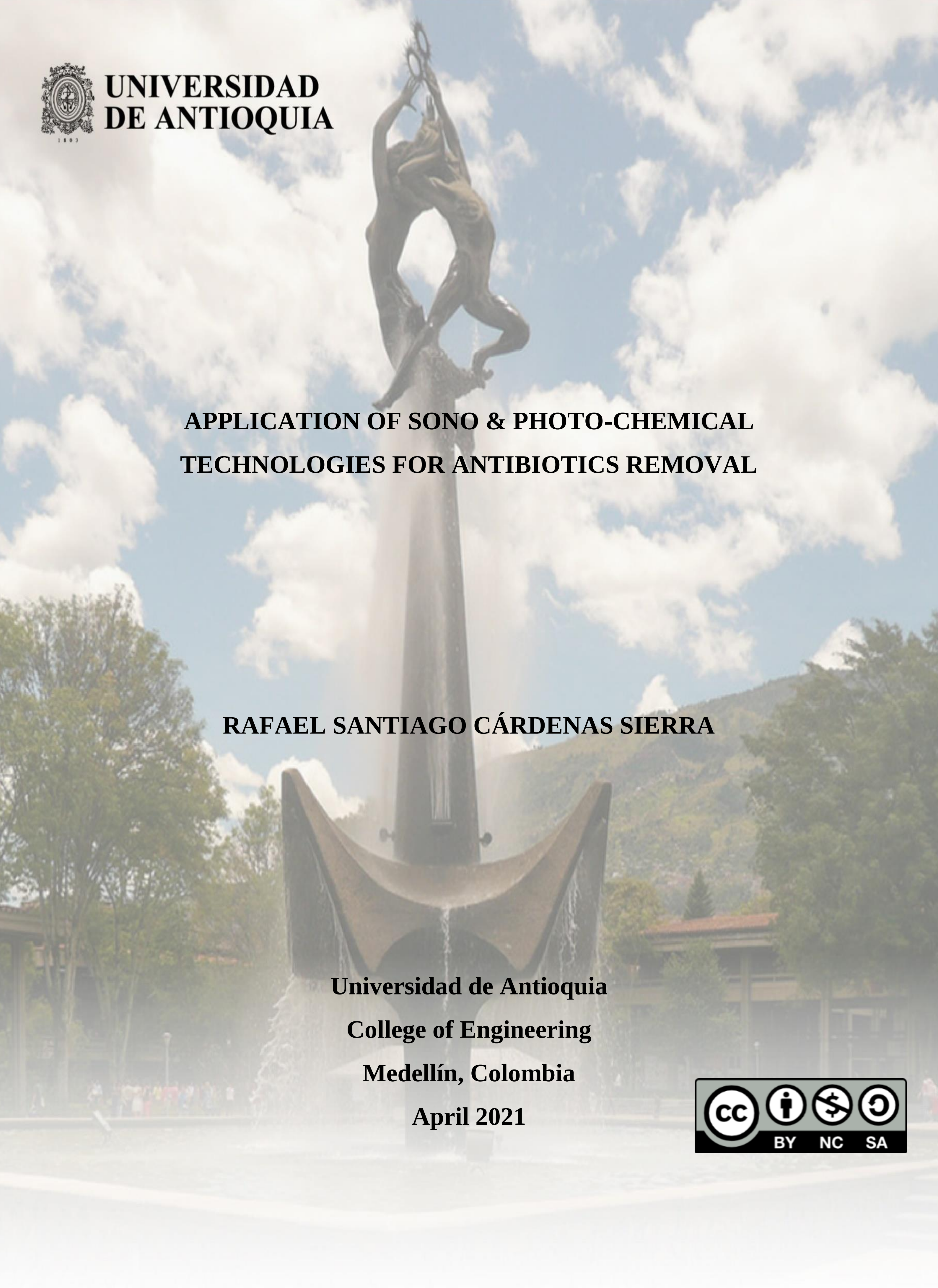


UNIVERSIDAD
DE ANTIOQUIA

# APPLICATION OF SONO & PHOTO-CHEMICAL TECHNOLOGIES FOR ANTIBIOTICS REMOVAL

**RAFAEL SANTIAGO CÁRDENAS SIERRA**

**Universidad de Antioquia**
**College of Engineering**
**Medellín, Colombia**
**April 2021**

# APPLICATION OF SONO & PHOTO-CHEMICAL TECHNOLOGIES FOR ANTIBIOTICS REMOVAL

**RAFAEL SANTIAGO CÁRDENAS SIERRA**

**Advisors:**
**Dr. Henry Nelson Zúñiga Benítez**
**Dr. Gustavo Antonio Peñuela Mesa**

**Research work submitted in partial fulfillment of the requirements for the degree of Master of Science in Chemical Engineering**

**Advanced Oxidation Technologies**
**Diagnóstico y Control de la Contaminación GDCON**

**Universidad de Antioquia**
**College of Engineering**
**Medellín, Colombia**
**April 2021**

CONTENT

## LIST OF FIGURES

## LIST OF TABLES

# APPLICATION OF SONO & PHOTO-CHEMICAL TECHNOLOGIES FOR ANTIBIOTICS REMOVAL

---

## ABSTRACT

Currently, there is a special concern about the presence and potential hazardous effects of antibiotics in the aquatic environment. These are part of the so-called emerging contaminants (EC), whose presence in aquatic ecosystems, even at low concentrations, represents a significant risk to environmental and human health. Cephalexin (CPX) and doxycycline (DOX) are two of the most used antibiotics to treat bacterial infections in human medicine, veterinary practices, animal husbandry, agriculture, aquaculture among others. Nevertheless, due to their excessive consumption and incomplete absorption during their metabolization, they have been detected in different environmental matrices and the effluents of wastewater treatment plants, which reflects that conventional methods are not enough to eliminate this type of compounds. In this sense, the need to develop new treatment alternatives that allow its total removal and minimize the eventual adverse effects has been evidenced.

UV/$H_2O_2$ and ultrasound (US) are advanced oxidation technologies (AOT), which have demonstrated to be suitable alternatives for the degradation of antibiotics residues in contaminated water. These technologies are based on pollutants removal by generating radical species, especially the hydroxyl radical (HO•), which has the potential to oxidize different organic molecules.

This research presents the main results about the removal of the antibiotics CPX and DOX using simulated sunlight radiation/$H_2O_2$ and low frequency US. The effects of operational parameters such as the solution initial pH, the concentration of $H_2O_2$ and the applied US power were assessed considering the response surface methodology and a face centered, central composite experimental design. In addition, in order to clarify the mechanisms of reaction, some control experiments, including photolysis, hydrolysis and the presence of a scavenger agent, were conducted. The effect of pollutants initial concentration, the total organic carbon variation and toxicity of the treated samples were also evaluated.

The results indicated that evaluated operational factors affect significantly each treatment performance and that this kind of technologies are able to remove completely the studied antibiotics. In addition, in terms of mineralization, experimental results showed a reduction of the organic carbon present in the solutions and a significant increase of ions (nitrates and sulfates) concentration, suggesting that part of the organic matter was transformed into $CO_2$, $H_2O$ and inorganic species. Likewise, toxicity assays demonstrated that both US and UV/$H_2O_2$ technologies are efficient not only to reduce pollutants presence but also, to inhibit samples toxicity, reducing the potential risk of hazardous effects on ecosystems and living beings.

Finally, it could be concluded that the HO• free radicals seem to be the main responsible specie to CPX and DOX removal using UV/$H_2O_2$ and US technologies under the evaluated experimental conditions.

**Keywords**: Advanced oxidation technologies; antibiotics; cephalexin; doxycycline; ultrasound and UV/$H_2O_2$.

## 1. PROBLEM STATEMENT

Water is an economic and ecological resource of vital importance, and the most important component of the Earth. Unfortunately, due to the rapid population growth its quality has been affected negatively. Some of the major sources of aquatic systems pollution are wastewater emissions that contain a considerable number of toxic substances. In this way, a high number of chemical and biological substances have been classified as potentially dangerous by different international organizations, including the European Commission and the United States Environmental Protection Agency (Geissen et al., 2015; Peña-Guzmán et al., 2019).

In recent decades, attention on water pollution research has been expanded from the conventional pollutants to the denominated emerging contaminants (EC), whose presence in the environmental matrices is not necessarily new, but the consequences of this fact have not been fully cleared. This kind of contaminants has been found in wastewater and surface water at concentrations that may be smaller than those of classical persistent and/or priority substances (Teodosiu et al., 2018). In addition, the development of analytical methods for its detection and quantification is limited (Gogoi et al., 2017; Rozman et al., 2017).

A wide variety of products for daily use with both domestic and industrial applications, such as pharmaceutical products, personal care products, antibiotics, surfactants, industrial additives, plasticizers, pesticides, and a large number of chemical compounds that could affect the endocrine functions of living beings have been catalogued as EC. Also, this substances could be bioaccumulated and difficult to remove through conventional water treatment processes (Cano-Carvajal et al., 2020; Geissen et al., 2015; Lado-Ribeiro et al., 2019).

Antibiotics are drugs used against pathogenic microorganisms in animals and humans. However, because of their incomplete absorption during their metabolization, and their extensive and continuous use, they have been largely released into the environment, resulting in their presence in environmental matrices such as surface waters, sediments, and soils. Reported data show that around 25–75 % of antibiotics administrated to animals are excreted and released into the environment via urine and feces, generating the contamination of soils and consequently surface and ground waters through leaching or run-off. In a similar way, the antibiotics that are excreted by humans enter the sewer network and could reach the wastewater treatment plants. In this sense, the presence of antibiotics in the different water bodies, together with the fact that they are resistant to biodegradation has received a great attention due to their potential contribution to the generation of bacterial resistance (Rodriguez-Mozaz et al., 2015; Sabri et al., 2020). When antibiotics reach bodies of natural water, they could provoke a selection of microorganisms and induce the production of resistant bacterial strains, which when in contact with living beings could cause diseases not treatable with conventional antibiotics and that, subsequently, can result in the spread of diseases (Du et al., 2017; Serna-Galvis, Silva-Agredo, Giraldo-Aguirre, et al., 2016; Voigt & Jaeger, 2017).

β-lactam and tetracyclines are worldwide highly consumed antibiotics, which has led to their introduction into different bodies of water, including the influents and effluents of wastewater treatment plants, surface waters and even drinking water (B. Huang et al., 2018; Miao et al., 2016; Saitoh et al., 2017; Saitoh & Shibayama, 2016; Xiong et al., 2018; Y. Zhou et al., 2018).

β-lactams are a group of antibiotics of natural or semi-synthetic origin that are characterized by having in its structure a beta-lactam ring. They constitute the largest family of antimicrobials and the most used in clinical practice. These antibiotics are compounds with slow bactericidal action, that present low toxicity and have a wide therapeutic margin of application. However, β-lactams presence in water bodies can harm the microbial community inducing the appearance of resistant bacteria (Miao et al., 2016; Saitoh & Shibayama, 2016).

**Cephalexin (CPX)** is a β-lactam antibiotic used to treat bacterial infections in the respiratory tract (pneumonia, pharyngitis), skin, bones and ear. In addition, it is used in cases of patients with hypersensitivity to penicillin. This antibiotic is discharged into wastewater, mainly through excretion after ingestion. Likewise, its accumulation in water bodies could interfere in the physiological functions of animals and humans due to the induction of mutagenic and carcinogenic effects (Khosravi et al., 2018).

The family of tetracycline antibiotics constitutes a group of natural and semi-synthetic products derived from different species of *Streptomyces spp*. They are agents basically bacteriostatic, with activity against a wide variety of microorganisms (Rodriguez-Mozaz et al., 2015; Saitoh et al., 2017; Vicente & Pérez-Trallero, 2010).

**Doxycycline (DOX)** is a well-known tetracycline antibiotic that can inhibit upper respiratory tract infections, tonsillitis, biliary tract infections and other diseases caused by gram-positive bacteria and gram-negative bacilli (Phaechamud et al., 2016). DOX has been detected in ground water and surface water, implying that its elimination by conventional wastewater treatment plants is not efficient (Naeimi & Faghihian, 2017; Vicente & Pérez-Trallero, 2010; Zaidi et al., 2019).

In addition, some studies have indicated that β-lactam (penicillins and cephalosporins) are the most used antibiotics in Colombia, being CPX the most prescribed. For its part, tetracyclines are the third most prescribed in the country, and DOX ranks first inside this group (López & Garay, 2016)**.**

Different techniques have been evaluated for the potential treatment of water containing antibiotics. Technologies such as chemical oxidation, ionic treatment, photodegradation, adsorption, and electrochemical process have been studied. However, in some cases these methods could present some limitations including low pollutants extent of elimination, and the potential production of more toxic intermediate substances (Bolobajev et al., 2016; Saitoh et al., 2017; W. L. Wang et al., 2018; Zaidi et al., 2019; Y. Zhou et al., 2018).

**Advanced oxidation technologies (AOT)** constitute one of the most used technological resources in the treatment of water contaminated with organic products that are not treatable by conventional techniques due to its high chemical stability and low biodegradability (Yan et al., 2019). AOT are designed to enhance the degradation and mineralization of micropollutants, or to transform them into less toxic compounds (Lado-Ribeiro et al., 2019). Likewise, AOT have also been used in processes of disinfection, discoloration and deodorization of effluents of treatment plants (Sievers, 2011; Suzuki et al., 2015). AOT mechanims of action include the production of the hydroxyl free radical (HO•), a powerful oxidant agent (E°=2.8 V) capable of oxidizing a wide range of organic compounds (Lou et al., 2017).

Among AOT, UV/$H_2O_2$ is one of the most used techniques for non-biodegradable organic compounds removal. Some of the advantages of this process are: (1) $H_2O_2$ has a higher oxidation potential than chlorine,

chlorine dioxide, and potassium permanganate, and may be produced by inexpensive, efficient, and environmentally friendly industrial processes; (2) there are no toxic byproducts generation, (3) UV is used for dissociation of $H_2O_2$ into two HO• (Xiao Tong et al., 2017; Zhou et al., 2012).

On the other hand, the use of ultrasound in advanced oxidation processes has lately received considerable attention due to the unique properties of ultrasound (US) for generating HO• and other oxygenated radicals. Besides, this technology could enhance the rate of mass transfer and its use does not imply the use of additional chemicals (Chiha et al., 2010; Wang et al., 2019). US is based on the acoustic cavitation phenomena occurring within a liquid medium by application of ultrasound frequencies. Cavitation bubbles, subjected to a series of compression and expansion cycles, before violently collapsing, are formed during ultrasonic waves propagation. During the collapse, very high temperature and pressure gradients are locally generated which can lead to the HO• radical formation via the dissociation of the water and/or $H_2O_2$ present in the solution (Papoutsakis et al., 2015). Due to its potential not only to promote the generation HO• radicals, but also by its ability to develop microscopic conditions of extreme temperature and pressure inside the solution, ultrasound would represent a viable option in the removal of antibiotics of interest (Torres-Palma & Serna-Galvis, 2018).

Some authors have evaluated the use of conventional and advanced processes like adsorption, heterogeneous photocatalysis and electrocoagulation on the removal of CPX and DOX from different aqueous matrices, reporting, in some cases, percentages of removal higher than 90% (Bolobajev et al., 2016; Lingzhi et al., 2018; Saitoh et al., 2017; Wang et al., 2018). However, there are not consolidated or deep results regarding the use of US and UV/$H_2O_2$ in the CPX and DOX elimination; and about the variation of samples toxicity and mineralization.

The above evidences the necessity of evaluating new alternatives for CPX and DOX removal in order to reduce the potential risk associated with the presence of these antibiotics in water bodies. In this sense, the main reason that promoted the development of this research project was **to evaluate the effectiveness of the advanced oxidation technologies UV/$H_2O_2$ and ultrasound in the removal of the antibiotics Cephalexin and Doxycycline in aqueous solutions.**

## 2. THEORETICAL FRAMEWORK AND BACKGROUND

### 2.1 Emerging contaminants:

Emerging contaminants are defined as compounds that are not currently covered by existing water-quality regulations and represent a potential threat to environmental ecosystems and the human health (Pereira et al., 2015; Salazar et al., 2020). They include a diverse group of synthetic and natural compounds, such as pesticides, cosmetics, pharmaceutical and personal care products (PPCPs), among others, whose use has been extended over time, becoming today indispensable for modern society (Gavrilescu et al., 2015; Peña-Guzmán et al., 2019).

The way that organic compounds enter the environment depends on their pattern of usage and mode of application (disposal of municipal, industrial and agricultural wastes, excretion of pharmaceuticals and accidental spills). Once in the environment, EC could be widely distributed at some time in different ecosystems (Chaukura et al., 2016), and depending on the compartment in which they are present (groundwater, surface water and sediment) could suffer different transformations, because of biodegradation and/or chemical and photochemical degradation. These transformations generate byproducts with a different toxicity than the initial compound, a situation that can also occur inside the treatment and purification plants, where processes used to purify the effluents involve the employ of substances that by reacting with organic pollutants could promote the generation of several metabolites (Bolobajev et al., 2016; Zhang et al., 2019; Zúñiga-Benítez et al., 2016).

The major source of emerging pollutants are the effluents of wastewater treatment plants, followed by runoff (from urban and rural areas, agricultural, livestock and mining areas, etc.) and atmospheric deposition (Camargo-Perea et al., 2020; Jiang et al., 2013; Pereira et al., 2015). In this way, it has been reported that EC could be present in natural, groundwater and wastewater at levels between 0.05 ng $L^{-1}$ and 42.0 μg $L^{-1}$ (Gogoi et al., 2017). Additionally, in most cases, conventional wastewater treatment plants do not have the appropriate design to remove EC since they were constructed especially with the intention to eliminate carbon, phosphorus, nitrogenous substances, and microorganisms (Rodriguez-Narvaez et al., 2017; Jianlong Wang & Zhuan, 2020).

## 2.2 Antibiotics:

Antibiotics are secondary metabolites or semi-synthetic/synthetic derivatives that can inhibit and kill pathogenic microorganisms. Some antibiotics also have anti-tumor, antiviral, immune suppression, and insecticide effects. According to their chemical structure antibiotics can be divided into β-lactam antibiotics, macrolides, aminoglycoside and tetracycline antibiotics (Du et al., 2017; Lingzhi et al., 2018).

### 2.2.1 β-lactam antibiotics:

β-lactams are the most successful chemical class of antibiotics used to treat infections in humans. They are characterized by the presence of a beta-lactam ring, which determines the mechanism of action (inhibition of cell wall synthesis), their wide spectrum of activity, excellent pharmacokinetics and lack of toxicity. β-lactam antibiotics include carbapenem, penicillin, monobactams, cephalosporins and inhibitors of beta-lactamases (B. Huang et al., 2018; Lingzhi et al., 2018).

Cephalexin (CPX) (Figure 1) belongs to the cephalosporins family, the second group of most consumed antibiotics worldwide. This pharmaceutical compound is used widely to treat infectious diseases caused by bacteria on skin, throat, tonsils, and the urinary tract. However, CPX is not totally metabolized during ingestion promoting its excretion and introduction into wastewater, and an eventual proliferation of organisms resistant to antibiotics. Besides, it has been reported that CPX could generate toxic effects, even at low concentrations, in aquatic compartments (López & Garay, 2016; Mirzaei et al., 2018).

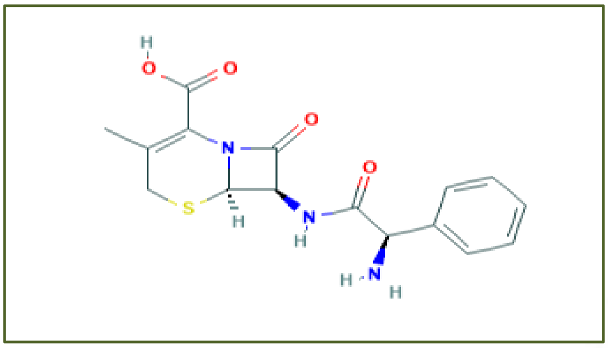


**Figure 1. Molecular structure of Cephalexin (U.S. National Library of Medicine and National Center for Biotechnology Information, 2019).**

### 2.2.2 Tetracyclines:

Tetracyclines or cyclins were the first family of broad-spectrum antibiotics in history. They are amphoteric crystalline substances with low solubility in water, available in the form of hydrochlorides, which are more soluble. In solution they are acidic and, except for chlortetracycline, quite stable (Peiris et al., 2017; Zaman et al., 2017).

Doxycycline (DOX) (Figure 2) is a tetracycline with potent antibacterial activity. It is used to treat infections caused by bacteria, including pneumonia and other respiratory tract infections; and some infections of the skin and eyes; infections of the lymphatic system, the digestive system, the reproductive system, and the urinary system. DOX might be released into surface waters and ground waters due to incomplete metabolism (in animals) and discharges from drug manufacturers, a situation that could lead to the development of antibiotic-resistant microorganisms, and eventual adverse impacts on human health through potential endocrine disruption and toxic by-products generation (Kong et al., 2019; Zeng et al., 2018).

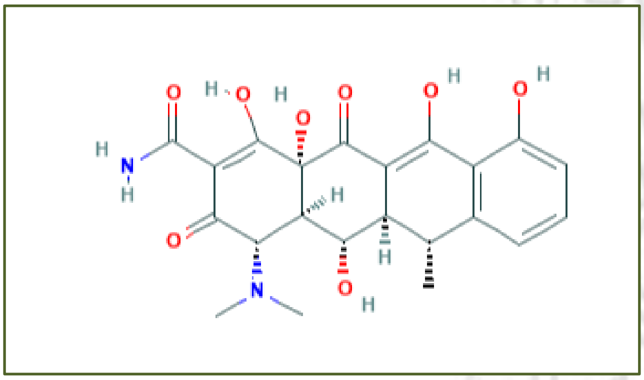


**Figure 2. Molecular structure of Doxycycline (U.S. National Library of Medicine and National Center for Biotechnology Information, 2019).**

## 2.3 Advanced oxidation technologies:

Advanced oxidation technologies (AOT) are a set of techniques that, under certain conditions, could transform organic contaminants into carbon dioxide, water and inorganic ions (Da Silva Brito et al., 2019). AOT involve the generation and use of powerful transient species as the hydroxyl free radical (HO•), which can be generated by photochemical processes (including sunlight), or by other forms of energy. HO• has high effectiveness for the oxidation of recalcitrant organic compounds, with reaction constants usually in the order of $10^6$-$10^{12}$ L mol$^{-1}$ s$^{-1}$ (Wols & Hofman-Caris, 2012). The efficiency of this type of processes is due to the fact that, in general, the involved reactions have a greater thermodynamic feasibility and high oxidation rates due to the participation of radicals (Doménech et al., 2003).

AOT can be classified according to different criteria. In this way, these technologies can be separated according to the reactive phase in homogeneous and heterogeneous, or according to the method used to generate the different radicals in chemical, electrochemical, sonochemical and photochemical processes. Specifically, depending on the use or not of light sources, AOT can be classified into photochemical or non-photochemical, as it is shown in Table 1 (Miklos et al., 2018; Oturan & Aaron, 2014).

**Table 1. Photochemical and non-photochemical AOT (Miklos et al., 2018; Oturan & Aaron, 2014).**

| Non-photochemical processes | Photochemical processes |
|---|---|
| Ozonation in alkaline medium ($O_3/OH^-$)<br>Ozonation with hydrogen peroxide ($O_3/H_2O_2$)<br>Fenton processes ($Fe^{2+}/H_2O_2$)<br>Electrochemical oxidation<br>Radiolysis and treatment with electron beams<br>Non-thermal plasma<br>Electrohydraulic discharge – Ultrasound | Photolysis of water in the vacuum ultraviolet (UVV)<br>$UV/H_2O_2$<br>$UV/O_3$<br>Photo-Fenton and related technologies<br>Heterogeneous photocatalysis |

The $UV/H_2O_2$ and US processes are AOT that have demonstrated its capacity to degrade different types of organic molecules such as pesticides, phenolic compounds, chlorophenols, drugs, and antibiotics. Figure 3 shows the number of scientific publications related to the use of US and $UV/H_2O_2$ in the removal of EC from water solutions. In this way, graph confirms that, in recent years, application of these techniques in water treatment has increased markedly.

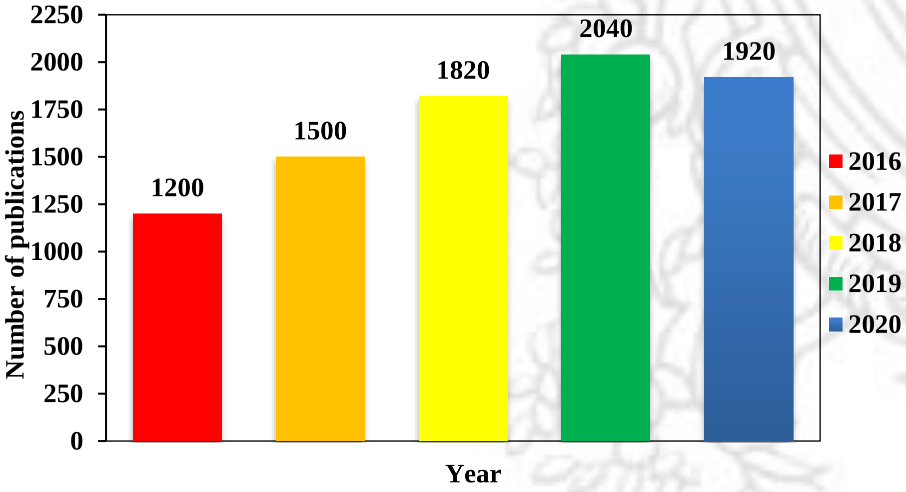


**Figure 3. Number of scientific publications on US and $UV/H_2O_2$ use in emerging pollutants removal from aqueous matrices. Period: January 2016-December 2020. Source: Scopus database. Search criteria: "Emerging pollutants removal from aqueous solution + ultrasound + $UV/H_2O_2$".**

In addition, Anjali & Shanthakumar (2019) and Kanakaraju et al. (2018) reported information regarding the use of different AOT on the removal of different antibiotics. Table 2 presents some of the most relevant aspects of these reports, which evidences that AOT are methods capable of degrading organic compounds of this nature efficiently.

**Table 2. Elimination of antibiotics using different advanced oxidation technologies (Anjali & Shanthakumar, 2019; Kanakaraju et al., 2018).**

| Applied technology | Antibiotic | Extent of pollutant(s) removal (%) | References |
|---|---|---|---|
| **Solar photo-Fenton** | Ciprofloxacin | >95.5 | Klamerth et al., 2013 |
| | Ofloxacin | >95.5 | Prieto-Rodríguez et al., 2013 |
| | Ofloxacin | 98.0 | Klamerth et al., 2012 |
| | Ofloxacin | 90.0 | Klamerth et al., 2013 |
| | Sulfamethoxazole | >95.5 | Klamerth et al., 2012 |
| | Sulfamethoxazole | 90.0 | Klamerth et al., 2013 |
| | Trimethoprim | >95.5 | Klamerth et al., 2013 |
| | Trimethoprim | 98.0 | Prieto-Rodríguez et al., 2013 |
| **$UV/H_2O_2$** | Azithromycin | 100.0 | De la Cruz et al., 2012 |
| | Clarithromycin | 100.0 | De la Cruz et al., 2012 |
| | Erythromycin | 100.0 | Kim et al., 2009 |
| | Norfloxacin | 100.0 | De la Cruz et al., 2012 |
| | Ofloxacin | 100.0 | De la Cruz et al., 2012 |
| | Ciprofloxacin | 100.0 | De la Cruz et al., 2012 |
| | Ciprofloxacin | >99.0 | Afonso-Olivares et al., 2016 |
| | Ciprofloxacin | 93 | Rodríguez-Chueca et al., 2019 |
| | Sulfamethoxazole | 100.0 | De la Cruz et al., 2012 |
| | Sulfapyridine | 100.0 | Kim et al., 2009 |
| | Sulfamethoxazole | >99.0 | Afonso-Olivares et al., 2016 |
| | Sulfapyridine | 97.3 | Pan et al., 2019 |
| | Sulfamethoxazole | 97.4 | Pan et al., 2019 |
| | Trimethoprim | 100.0 | Kim et al., 2009 |
| | Trimethoprim | 100.0 | De la Cruz et al., 2012 |
| | Metronidazole | 100.0 | De la Cruz et al., 2012 |
| | Metronidazole | 92.0 | Afonso-Olivares et al., 2016 |
| | Tetracycline | 99.0 | Kim et al., 2009 |
| | Tetracycline | 97.2 | Pan et al., 2019 |
| | Oxytetracycline | 97.3 | Pan et al., 2019 |
| **$UV/H_2O_2/Fe^{2+}$** | Ciprofloxacin | 100.0 | De la Cruz et al., 2012 |
| | Norfloxacin | 100.0 | De la Cruz et al., 2012 |
| | Ofloxacin | 100.0 | De la Cruz et al., 2012 |
| | Azithromycin | 100.0 | De la Cruz et al., 2012 |
| | Clarithromycin | 93.0 | De la Cruz et al., 2012 |
| | Sulfamethoxazole | 100.0 | De la Cruz et al., 2012 |
| | Sulfamethazine | 99.6 | Pan et al., 2019 |
| | Sulfadiazine | 99.7 | Pan et al., 2019 |
| | Metronidazole | 100 | De la Cruz et al., 2012 |

| | | | |
|---|---|---|---|
| | Tetracycline | 99.4 | Pan et al., 2019 |
| | Oxytetracycline | 99.5 | Pan et al., 2019 |
| **UVC/$H_2O_2$ and UVC/ $S_2O_8^{2-}$** | Azithromycin | >98.5 | Markic et al., 2018 |
| **Fenton process and ozone** | Ofloxacin | 100 | Michael et al., 2010 |
| | Ofloxacin | 100 | Carbajo et al., 2015 |
| | Ofloxacin | 98 | Prieto-Rodríguez et al., 2013 |
| | Trimethoprim | 98 | Prieto-Rodríguez et al., 2013 |
| | Sulfamethoxazole | >99.0 | Alharbi et al., 2016 |
| | Trimethoprim | >99.0 | Alharbi et al., 2016 |
| **Ultrasound** | Amoxicillin | >86.0 | Kıdak & Doğan, 2018 |
| | Ciprofloxacin | >90.0 | Seth et al., 2013 |
| | Colistin | >90.0 | Liu et al., 2016 |
| | Vancomycin | >90.0 | Liu et al., 2016 |

Based on the literature, the sonochemical degradation of CPX in aqueous solutions using a 24 kHz ultrasonic reactor was investigated by Guo et al. (2010). However, the effects of the pollutant initial concentration, the variations of samples total organic carbon (TOC), the presence of anions and toxicity were not evaluated. In addition, no previous studies have assessed the potential application of US in the elimination of DOX, and the use of the UV/$H_2O_2$ technology in the elimination of CPX and DOX has not been reported either.

### 2.3.1. UV/$H_2O_2$:

The sunlight that reaches the Earth surface has visible (400–700 nm), UVA (320–400 nm), and a portion of UVB (290–320 nm) component. This radiation is able to promote direct and/or indirect (mediated) transformations of organic pollutants such as antibiotics. Direct route (direct photolysis) is initiated by absorption of sunlight radiation, whereas indirect photolysis occurs throughout interaction of antibiotics with transient reactive intermediates such as singlet oxygen, hydroxyl radicals, or other reactive species formed from substances present in the water matrix (Periša et al., 2013). The UV/$H_2O_2$ technology consists in the $H_2O_2$ decomposition under UV light presence to generate hydroxyl radicals (equation 1). The main advantage of using UV/$H_2O_2$ for water and wastewater treatment is the fact that UV radiation can be, simultaneously, a disinfectant, and a promoter of $H_2O_2$ molecule breaking (Mierzwa et al., 2018; Rubio-Clemente et al., 2018).

$$H_2O_2 + hv \rightarrow 2\ HO\bullet \tag{1}$$

The reaction kinetics of the UV/$H_2O_2$ oxidation technology is a function of the solution pH, the peroxide initial concentration and the kind of organic pollutant to be removed (Mierzwa et al., 2018). Some of the advantages of this AOT are (Lopez-Alvarez et al., 2012):

- There is no sludge formation during the treatment.
- It can be carried out under environmental conditions (temperature and pressure).
- The costs associated with the production and handling of $H_2O_2$ are lower than, for example, the use of ozone or other oxidizing species.
- Hydrogen peroxide mixes easily with water, forming homogeneous solutions.

### 2.3.2. Ultrasound as AOT:

Due to its ability to produce radical species (mainly hydroxyl HO•) that promote the degradation of refractory substances in water, ultrasound is considered an AOT. Currently, this process is an alternative AOT with potential to eliminate chemical and microbiological pollutants in wastewaters as a tertiary treatment technology. Ultrasound has unique advantages compared to other AOT, such as no addition of chemicals, and differential or selective degradation according to the pollutant nature (Torres-Palma & Serna-Galvis, 2018).

Ultrasound refers to sound waves with frequencies above the detected by the human ear. It is ranged from 20 to 10000 kHz. Typically, ultrasound is divided into three regions according to frequency: (1) low, (2) high, and (3) very high. Low and high ultrasound frequencies are used in chemical processes, whereas very high frequency is applied in medical diagnostics. When high-intensity ultrasound waves interact with dissolved gases in liquid medium, acoustic cavitation (formation, growth, and implosive collapse of bubbles) it is promoted (Suslick, 1989). Ultrasound waves consist of compression and expansion cycles. During the expansion, waves having the sufficient intensity to exceed the molecular forces of liquid generate bubbles. These bubbles continually absorb energy from alternating compression and expansion ultrasound cycles. Thus, bubbles grow (by diffusion of vapor or gas from liquid medium) until they reach a critical size and then collapse (Figure 4) (Suslick, 1989). The bubble collapse acts as a localized "hot spot" with singular conditions of temperature (>5000 K) and pressure (>1000 atm), and short life (Torres-Palma & Serna-Galvis, 2018).

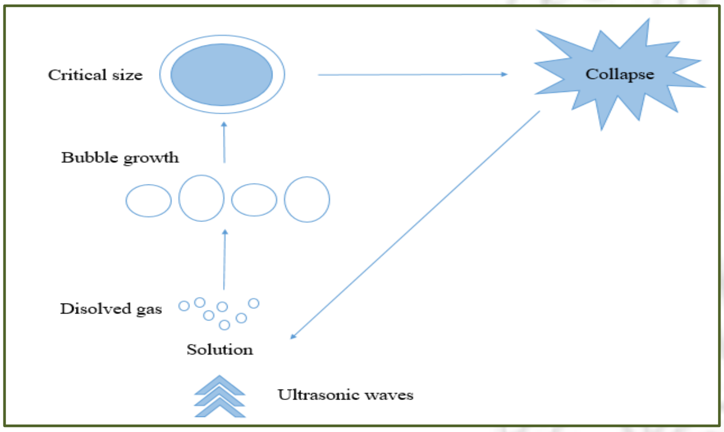


**Figure 4. Cavitation phenomenon induced by ultrasound (Torres-Palma & Serna-Galvis, 2018).**

In aqueous solutions, hydroxyl and hydrogen radicals are formed from the thermal dissociation of water vapor (equation 2), and the reaction with oxygen (equations 3-6) (Chiha, Hamdaoui, et al., 2010; Rao et al., 2016). Once generated, HO• radicals can migrate from the inside of the cavitation bubble to the rest of the solution and oxidize the organic matter (Chiha et al., 2011).

$$H_2O + ))) \rightarrow H\bullet + HO\bullet \qquad (2)$$

$$O_2 \rightarrow 2\,O \qquad (3)$$

$$H\bullet + O_2 \rightarrow HOO\bullet \qquad (4)$$

$$O + H_2O \rightarrow 2\,HO\bullet \qquad (5)$$

$$H\bullet + O_2 \rightarrow HO\bullet + O \qquad (6)$$

Sonochemical pollutants removal could take place at three different zones: (1) in the bulk solution, (2) in the interface cavitation bubble-solution, and (3) inside of the cavitation bubble (Figure 5). In this way, hydrophilic substances place in the bulk solution, hydrophobic nonvolatile compounds accumulate in the interfacial zone, while volatile substances would be inside the cavitation bubble (Chiha et al., 2011; Rubio-Clemente et al., 2014; Zúñiga-Benítez et al., 2014). According to this, the removal of hydrophilic compounds would be promoted by hydroxyl radicals that reach the bulk solution after the bubble collapse. Hydrophobic nonvolatile compounds are eliminated in the interfacial zone by radical attacks and/or thermal reactions, and volatile pollutants are pyrolyzed inside the bubbles (Torres-Palma & Serna-Galvis, 2018).

Additionally, the formed radicals that do not react with the substrate can also diffuse into the solution to produce hydrogen peroxide (equations 7 and 8) (Torres-Palma et al., 2010).

$$2\ HO\bullet \rightarrow H_2O_2 \tag{7}$$

$$2\ HOO\bullet \rightarrow H_2O_2 + O_2 \tag{8}$$

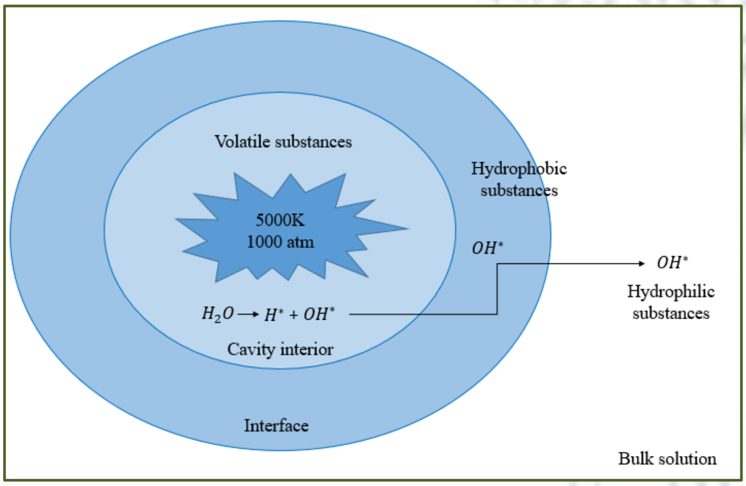


**Figure 5. Cavitation bubble (Torres-Palma & Serna-Galvis, 2018).**

Taking into account the above and the evidences of the effectiveness of the US and UV/$H_2O_2$ technologies on the removal of organic pollutants, they represent a potential option to remediate water polluted with CPX and DOX antibiotics.

On the other hand, researchers from GDCON group have conducted several projects in order to evaluate the employment of AOT on organic pollutants removal (some of them are listed in Table 3). This confirms the research group experience carrying out studies regarding the evaluation of AOT application in the remediation of environmental matrices.

**Table 3. Researches developed in GDCON group about the use of AOT.**

| Target pollutant(s) | Applied technology | Extent of pollutant(s) removal (%) | Reference |
|---|---|---|---|
| **Melatomil and Melation** | Photocatalysis with $TiO_2$ and $Fe^{3+}$ | >90.0 | Marín, 2002 |
| **Cyanide** | Heterogeneous photocatalysis with $TiO_2$ | >90.0 | Jaramillo, 2004 |
| **Chlorothalonil** | Fenton and solar photocatalysis | >90.0 | Bahamón, 2008 |
| **Oxolinic acid** | Heterogeneous photocatalysis with $TiO_2$ | >80.0 | Giraldo et al., 2010 |
| **Carbofuran and iprodione** | Solar photocatalysis | >90.0 | Lopez-Alvarez et al., 2012 |
| **Methylparaben, ethyl paraben, benzophenone-1, benzophenone-2 and benzophenone-3** | Photo-Fenton and Heterogeneous photocatalysis with $TiO_2$ | 100.0 | Zúñiga-Benítez, 2016 |
| **Benzophenone-3 and 1-H-Benzotriazole** | US | 100.0 | |
| **Triclosan, Benzophenone-1 and Benzophenone-3** | US, US/UV/ $H_2O_2$ and US/$Fe^{2+}$ | 100.0 | Vega-Garzon et al., 2018; Vega et al., 2019 |
| **Anthracene and benzopyrene** | UV/$H_2O_2$, photo-Fenton and Ultrasound | 100.0 | Rubio-Clemente, 2017 |
| **Azithromycin** | UV/$H_2O_2$ | 100.0 | Cano-Carvajal et al., 2020 |
| **Azithromycin** | Photo-Fenton | 100.0 | Jaramillo-Baquero et al., 2020 |
| **Azithromycin** | Sulfate radical | 70.0 | Ospino-Atehortúa et al., 2021 |
| **Azithromycin** | Ultrasound | 50.0 | Muñoz-Calderón et al., 2020 |

## 3. RESEARCH QUESTION AND OBJECTIVES

### 3.1 Research Question:

How efficient is the use of the advanced oxidation technologies UV/$H_2O_2$ and ultrasound in the removal, from aqueous solutions, of the antibiotics Cephalexin and Doxycycline?

### 3.2 General Objective:

To evaluate the potential application of UV/$H_2O_2$ and ultrasound technologies in the removal, from aqueous solutions, of CPX and DOX.

### 3.3 Specific objectives:

- To evaluate the effects of operational factors such as pH, pollutants concentration, US power and $H_2O_2$ presence on CPX and DOX removal using UV/$H_2O_2$ and US.
- To establish the optimized conditions, under the evaluated experimental range, that promote a higher antibiotics removal.
- To determine the reaction kinetics of CPX and DOX elimination using UV/$H_2O_2$ and US.
- To evaluate samples toxicity and extent of mineralization after the use of UV/$H_2O_2$ and US on CPX and DOX removal.

## 4. METHODOLOGY

### 4.1 Chemicals and reagents:

CPX ($C_{16}H_{17}N_3O_4S$, CAS 15686-71-2) and DOX ($C_{22}H_{24}N_2O_8$, CAS 564-25-0) chemical standards containing more than 98.0% of pure compounds were purchased from AK Scientific and used as received. All the aqueous solutions were prepared using ultra-pure water (Milli-Q water, 18.2 MΩ cm). Hydrogen peroxide ($H_2O_2$, 35.0% w/w, Merck) was used to carry out the UV/$H_2O_2$ experiments and sodium thiosulphate pentahydrate ($Na_2S_2O_3$•$5H_2O$, 99.9% w/w, Sigma Aldrich) was employed for quenching remaining $H_2O_2$ after the sampling stage.

Solutions pH adjustments were done with concentrated solutions of NaOH (0.1 N) and HCl (1.0 N) obtained from Alfa-Aesar. Role of HO• free radicals on pollutants removal was assessed using isopropyl alcohol ($C_3H_8O$, 99.8% w/w, Merck). HPLC-grade acetonitrile and methanol, acetic acid and formic acid were used for chromatographic analysis. Additionally, ammonium monovanadate ($NH_4VO_3$, 99.9% w/w, Merck) was employed for the determination of residual $H_2O_2$ after the UV/$H_2O_2$ experiments.

Microtox acute reagent, reconstitution solution, diluent and adjusting osmotic solution from Modern Water were employed for toxicity tests.

### 4.2 UV/$H_2O_2$ experiments using simulated sunlight and $H_2O_2$:

UV/$H_2O_2$ experiments were performed using a Suntest CPS+ photosimulator (Atlas, Figure 6) equipped with a xenon lamp filtered by a UV filter capable of emitting light in a spectrum similar to that of the sun (wavelength between 290 and 800 nm). Light irradiance was fixed at 500.0 W $m^{-2}$ considering reports about the average sunlight intensity in some regions of Colombia (Rubio-Clemente et al., 2018; Vanegas Chamorro et al., 2015). Pyrex flasks containing 50.0 mL of solution were used for light exposition. CPX and DOX initial concentration in most of the experiments was 2.0 mg $L^{-1}$ (condition that allowed to satisfy the requirements of the analytical methods in terms of precision, accuracy, detection and quantification limits). Solutions pH was adjusted after the addition of pollutants and $H_2O_2$. In addition, in order to ensure homogeneous conditions of reaction, system was stirred during experiments and the temperature was maintained at 35°C. Distance from the lamp to the liquid surface was ~20.0 cm, and the liquid depth inside the flasks was ~5.0 cm. Samples of 0.75 mL were withdrawn in different time intervals during the experiments, then 0.25 mL of $Na_2S_2O_3$•$5H_2O$ (100 mg $L^{-1}$) were added to inhibit the potential oxidative effect of remaining $H_2O_2$.

**Figure 6. Suntest CPS+ photosimulator.**

### 4.3 Sonochemical reactor:

Experiments were carried out using a 40 kHz ultrasonic transducer with a variable power generator (maximal power 50.0 W). The transducer was coupled to the bottom of a cylindrical glass reactor with a maximum capacity of 500 mL (Meinhardt Ultrasonics, Figure 7). Ultrasonic power density was calculated by the calorimetric method (Kimura et al., 1996). Solution temperature was maintained at 25°C using a water-cooling bath. CPX and DOX initial concentration in most of the experiments was 2.0 mg $L^{-1}$. A volume of 300 mL of reaction solution was used in each experiment and samples of 1.0 mL were withdrawn at different time intervals during the reaction.

**Figure 7. Sonochemical reactor (US generator-40 kHz ultrasonic transducer-glass reactor).**

### 4.4 Experimental design:

The response surface methodology (RSM) based on a face-centered, central composite design was employed to determine the conditions that favor pollutants higher degradation rates under the evaluated experimental conditions. RSM is a collection of mathematical and statistic tools useful for modelling and analyzing systems in which a response variable is influenced by different factors. This kind of experimental designs is used with the objective of optimizing the response variable and to determine the optimal conditions in an evaluated process (Pabari & Ramtoola, 2012; Prakash Maran et al., 2013).

Taking into account the above, the effects of operational factors such as solution pH, US power and $H_2O_2$ presence on CPX and DOX removal using UV/$H_2O_2$ and US were evaluated under three different levels (low, medium and high). A total of 11 experiments (three central points) were performed for each AOT. The response variable was the percentage of removal of each antibiotic after 30 minutes of treatment.

Some preliminary experiments, at natural pH (~6.0), were carried out in order to establish the experimental range of $H_2O_2$ initial concentration to be evaluated during the UV/$H_2O_2$ tests. In this way, according to equations

9 and 10, 9.2 mg $L^{-1}$ and 8.0 mg $L^{-1}$ of $H_2O_2$ are required to achieve a complete oxidation of 2.0 mg $L^{-1}$ of CPX and DOX, respectively. Experiments were done using an amount of $H_2O_2$ equivalent to the theoretical stoichiometric value, as well as conditions 0.25, 0.50, 0.75 and 1.25 times this condition. According to the obtained results (data not shown), it was decided to conduct the experimental design under the experimental levels presented by Table 4.

$$C_{16}H_{17}N_3O_4S + 47\ H_2O_2 \rightarrow 16\ CO_2 + 53\ H_2O + 3\ HNO_3 + H_2SO_4 \quad (9)$$

$$C_{22}H_{24}N_2O_8 + 53\ H_2O_2 \rightarrow 22\ CO_2 + 64\ H_2O + 2\ HNO_3 \quad (10)$$

**Table 4. Experimental levels evaluated in the removal of CPX and DOX using UV/$H_2O_2$.**

| Factor | CPX removal | | | DOX removal | | |
|---|---|---|---|---|---|---|
| | Level | | | Level | | |
| | Low | Medium | High | Low | Medium | High |
| **pH** | 3.0 | 6.0 | 9.0 | 3.0 | 6.0 | 9.0 |
| **$H_2O_2$ initial concentration (mg $L^{-1}$)** | 2.3 | 4.6 | 6.9 | 2.0 | 4.0 | 6.0 |

On the other hand, different authors have reported that the efficiency of the oxidation reactions in sonochemical treatments is associated with the effect of "chemically active cavitation" (Pétrier, 2014), which is related to the effectiveness of the formation, growing and imploding of the cavitation bubbles and with the ability of the pollutant molecules to diffuse into the exterior and interior of the bubble, where occurs of the organic pollutant degradation (Deojay et al., 2011; Guzman-Duque et al., 2011; Serna-Galvis, Silva-Agredo, Giraldo-Aguirre, et al., 2016; Vega-Garzón, 2014). The implementation of US process should consider the control and variation of different operating parameters such as the pH of the solution, the applied power and ultrasonic frequency since they can promote the production of HO• (Huang et al., 2017; Rao et al., 2016). In this sense, some preliminary tests were carried out to establish the experimental range of the solution initial pH and the applied US power that conduct to significant antibiotics eliminations (>50.0%). Tests were done varying the applied power between 10.0 and 50.0 W under natural solution pH (~6.0) during 30 min of reaction (data not shown). In this way, Table 5 shows the selected experimental levels to evaluate the effectiveness of the US technology in the removal of CPX and DOX antibiotics.

**Table 5. Experimental levels evaluated in the removal of CPX and DOX using US.**

| Factor | CPX removal | | | DOX removal | | |
|---|---|---|---|---|---|---|
| | Level | | | Level | | |
| | Low | Medium | High | Low | Medium | High |
| **pH** | 3.0 | 6.0 | 9.0 | 3.0 | 6.0 | 9.0 |
| **Applied power (Watts)** | 20.0 | 35.0 | 50.0 | 20.0 | 35.0 | 50.0 |

The RSM and the face-centered central composite experimental design allowed to evaluate the influence of each parameter and its interactions in the process. Furthermore, it allows to obtain a mathematical model that relates the significant factors and the response variable, and to establish the optimized conditions under which a higher removal of each substrate could be reached.

Statistical analysis of data was performed using the Statgraphics Centurion XVI software at a confidence level of 95%.

On the other hand, in order to investigate the effect of each pollutant initial concentration on reaction, experiments were carried out by varying this parameter in the range 1.0-5.0 mg $L^{-1}$.

Finally, to clarify the mechanism of reaction, some control experiments were conducted, in this way, experiments employing only light irradiation (photolysis), hydrolysis and the presence of a scavenger agent were performed.

All tests were conducted in triplicate and coefficients of variation of the data were below 5%.

## 4.5 Analytical methods:

### 4.5.1 Pollutants concentration determination

CPX and DOX concentrations in aqueous solutions were determined by reverse phase chromatography using an Agilent 1100-1200 series HPLC system. A Kinetex C18 column (silica 100 Å pore diameter, 2.5 µm, 4.6 × 150 mm), and a diode array detector (DAD) set to 261.4 nm were employed to quantify CPX. Likewise, a Phenomenex C18 column (120.0 Å pore diameter, 5.0 µm, 4.00 x 125.0 mm), and a DAD set to 325 nm were used for DOX determination. In addition, Table 6 presents the operating conditions and mobile phases employed for quantification of the studied antibiotics, and Figure 8 shows the obtained spectrums and chromatograms.

**Table 6. Operating conditions and mobile phases employed for the quantification of CPX and DOX using HPLC.**

| Analyte | Mobile phase | Flow type | Flow rate (mL $min^{-1}$) | Column average temperature (°C) | Injection volume (µL) | Mobile phase relation | Retention time (min) |
|---|---|---|---|---|---|---|---|
| **Cephalexin** | A: Water (0.1% v/v formic acid) | Gradient | 0.55 | 35.0 ± 1.0 | 50.0 | A:B 90:10 for 4 minutes, then A:B 30:70 for 1 minutes and finally, A:B 90:10 for 4 minutes. | ~5.45 |
| | B: Acetonitrile | | | | | | |
| **Doxycycline** | A: Acetonitrile | Isocratic | 0.80 | 25.0 ± 1.0 | 50.0 | A:B:C 25:55:20 for 5 minutes. | ~2.25 |
| | B: Water (0.5% v/v acetic acid) | | | | | | |
| | C: Methanol | | | | | | |

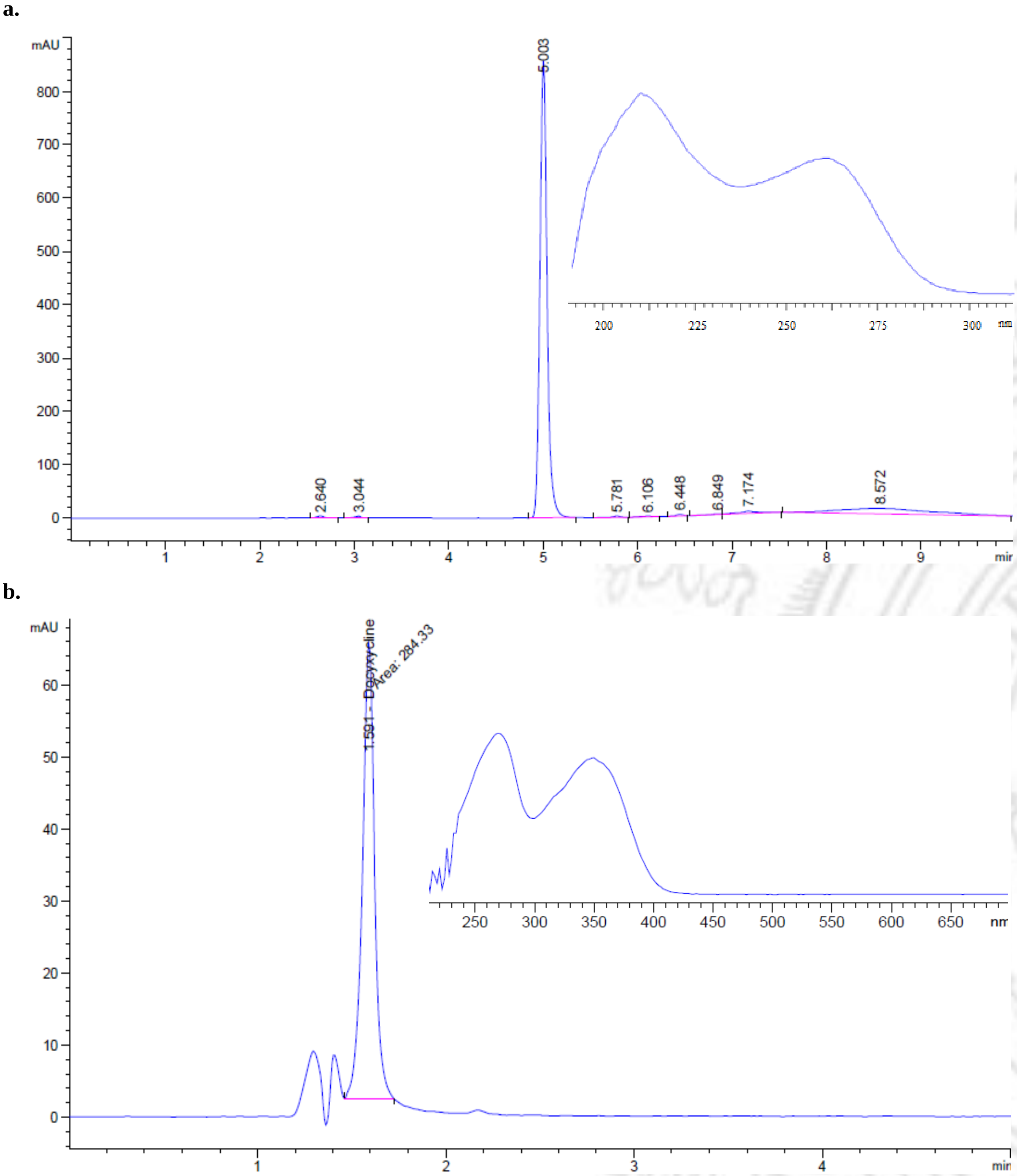


Figure 8. Spectrum and chromatogram for a. CPX and b. DOX.

### 4.5.2 Total organic carbon determination

Oxidation of the organic matter was evaluated measuring the total organic carbon (TOC) content in the treated samples using an APOLLO 9000 combustion TOC analyzer (Teledyne Tekmar). The methodology of analysis was the high combustion temperature method described in the *Standard Methods for the Examination of Water and Wastewater* (2017), method (5310B).

### 4.5.3 Anions analysis

Equations 9 and 10 indicate that total oxidation of CPX and DOX could conduct to an increase in the nitrates and sulfates presence in the solutions. In this way, $NO_3^{-1}$ and $SO_4^{2-}$ were evaluated using an a Dionex Integration HPLC system (Thermo Scientific). The methodology adopted was the Ion chromatography with chemical suppression of effluent conductivity, analytical method described in the *Standard Methods for the Examination of Water and Wastewater* (2017), method (4110B).

### 4.5.4 Toxicity analysis

Samples toxicity was evaluated using a Microtox model 500 analyzer (Modern Water), which is an *in vitro* testing system that uses bioluminescent bacteria (*Vibrio fischeri*) to detect toxic substances in different substrates such as water, air, soils and sediments. *Vibrio fischeri* are non-pathogenic, marine bacteria that luminesce as a natural part of their metabolism. When exposed to a toxic substance, the respiratory process of the bacteria is disrupted, reducing light output (Vega-Garzon et al., 2018).

Toxicity assays measure the decrease in the natural luminescence of bacteria in aqueous solutions. Diminishing bioluminescence indicates diminishing cellular respiration. Toxic substances change the percentage of protein and lipid synthesis, thus changing the light emission level. The toxicity is expressed as effective concentration $EC_{50}$ (pollutant concentration producing a 50% reduction in light emission) (Jouanneau et al., 2016).

### 4.5.5 Residual $H_2O_2$ analysis

Considering the fundamental role of $H_2O_2$ in the UV/$H_2O_2$ treatment, and that excess of $H_2O_2$ could be involved in HO• free radicals scavenging processes, and residual $H_2O_2$ could also imply a risk for living beings (Lan et al., 2015; Souza et al., 2014), its determination is of special interest in the evaluation of its potential application on water decontamination.

$H_2O_2$ was measured following the methodology proposed by Rubio Clemente et al. (2017), and using an Evolution 300 UV/Vis spectrophotometer (Thermo Scientific).

## 5. RESULTS AND DISCUSSION

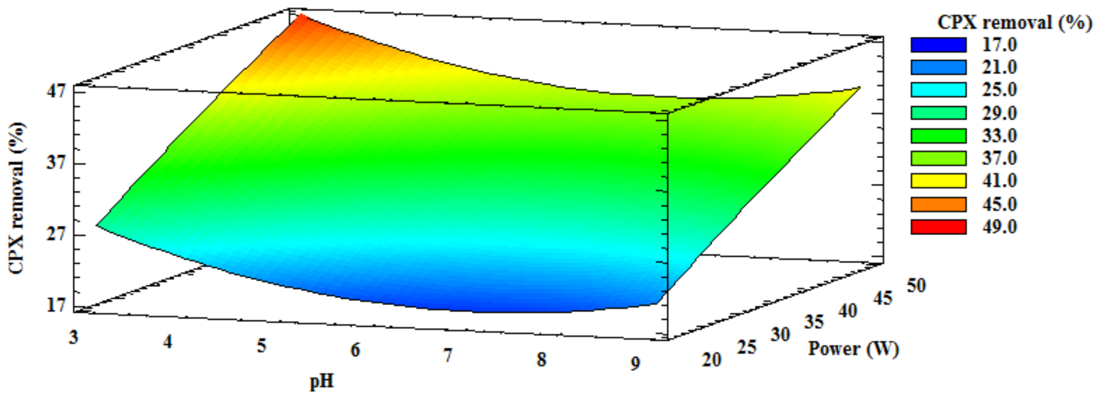
### 5.1 Antibiotics removal using low frequency ultrasound

The effects of the solution initial pH and the applied power on antibiotics removal using ultrasound were evaluated according to the levels indicated by Table 5. Likewise, Table 7 shows the matrix design and the response factor, corresponding to the substrates extent of degradation after 30 min of reaction; while Figure 9 shows the response surface obtained after carrying out the experiments. Both, Table 7 and Figure 9, indicate that the initial pH and the applied power affect the CPX and DOX removal, and allow to infer the conditions that could promote higher degradations.

**Table 7. Experimental design for CPX and DOX degradation (pollutants initial concentration: 2.0 mg L$^{-1}$, temperature: 25 ± 2 °C, frequency: 40 kHz, reaction time: 30 min).**

| Test | Solution pH | Applied power (W) | CPX removal (%) experimental | CPX removal (%) calculated by model | DOX removal (%) experimental | DOX removal (%) calculated by model |
|---|---|---|---|---|---|---|
| **1** | 3.0 | 50.0 | 47.0 | 47.4 | 65.8 | 65.8 |
| **2** | 9.0 | 20.0 | 21.2 | 20.9 | 32.6 | 32.9 |
| **3** | 6.0 | 35.0 | 31.3 | 29.5 | 32.4 | 32.5 |
| **4** | 3.0 | 20.0 | 29.6 | 28.0 | 34.5 | 36.4 |
| **5** | 9.0 | 35.0 | 32.7 | 31.4 | 36.4 | 37.5 |
| **6** | 3.0 | 35.0 | 37.1 | 38.3 | 45.9 | 44.0 |
| **7** | 6.0 | 35.0 | 28.7 | 29.5 | 31.8 | 32.5 |
| **8** | 6.0 | 20.0 | 17.2 | 19.1 | 28.6 | 26.4 |
| **9** | 6.0 | 35.0 | 28.3 | 29.5 | 32.5 | 32.5 |
| **10** | 9.0 | 50.0 | 39.3 | 40.9 | 57.9 | 56.4 |
| **11** | 6.0 | 50.0 | 40.8 | 38.8 | 51.4 | 52.8 |

**a.**



**b.**

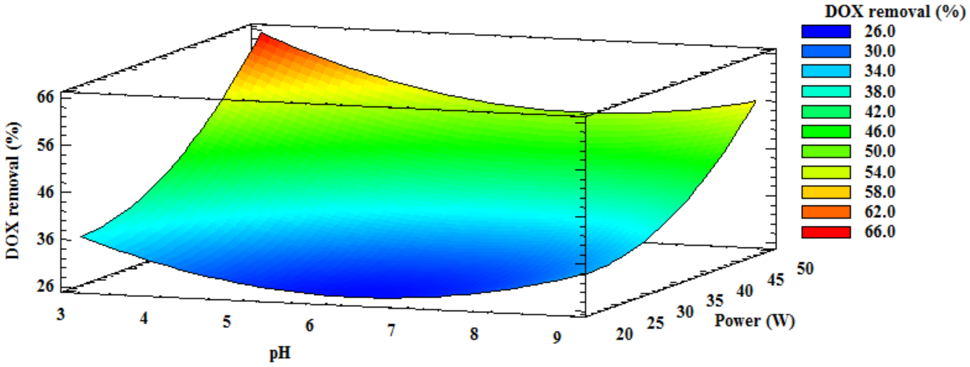
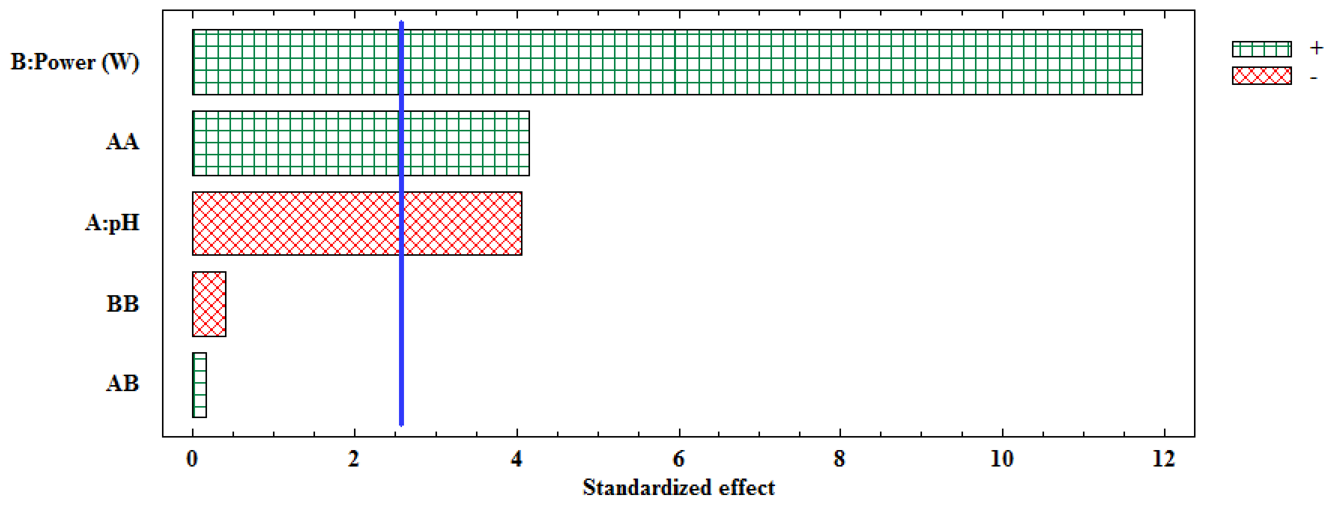


**Figure 9. Estimated response surface for a. CPX removal and b. DOX removal using ultrasound (pollutants initial concentration: 2.0 mg L$^{-1}$, temperature: 25 ± 2 °C, frequency: 40 kHz, reaction time: 30 min).**

### 5.1.1. Reaction conditions optimization

In order to optimize the reaction conditions on sonochemical treatments, it was necessary to evaluate which variables and interactions between them affect significantly each substrate elimination. Figure 10 corresponds to the Pareto chart, which shows the magnitude and the significance of the effects of the evaluated factors and its interactions (Giraldo et al., 2010). This chart contains a reference line (vertical line), and any effect or interaction that surpasses it has an important influence on the evaluated process. A positive effect (+) indicates that pollutant elimination increases under the presence of high levels of the respective factor or interaction; while a negative effect (-) indicates that degradation increases in the presence of low levels of the factor or interaction. In this way, according to the Figure 10a, the variables and interactions that can be considered significantly important for cephalexine removal are: pH (A), the square of the pH (AA) and power (B). In addition, this figure indicates that the applied power and the square of the pH have a positive effect on the CPX degradation, while the pH has a negative effect. Likewise, solution initial pH and power, together with its square interactions (AA y BB) were the factors with significant influence on DOX removal, and it can be observed from Figure 10b that the pH has a negative effect. These results could be associated with the interactions between the evaluated factors, the radical species generation, and the properties of the target contaminants.

**a.**



**b.**

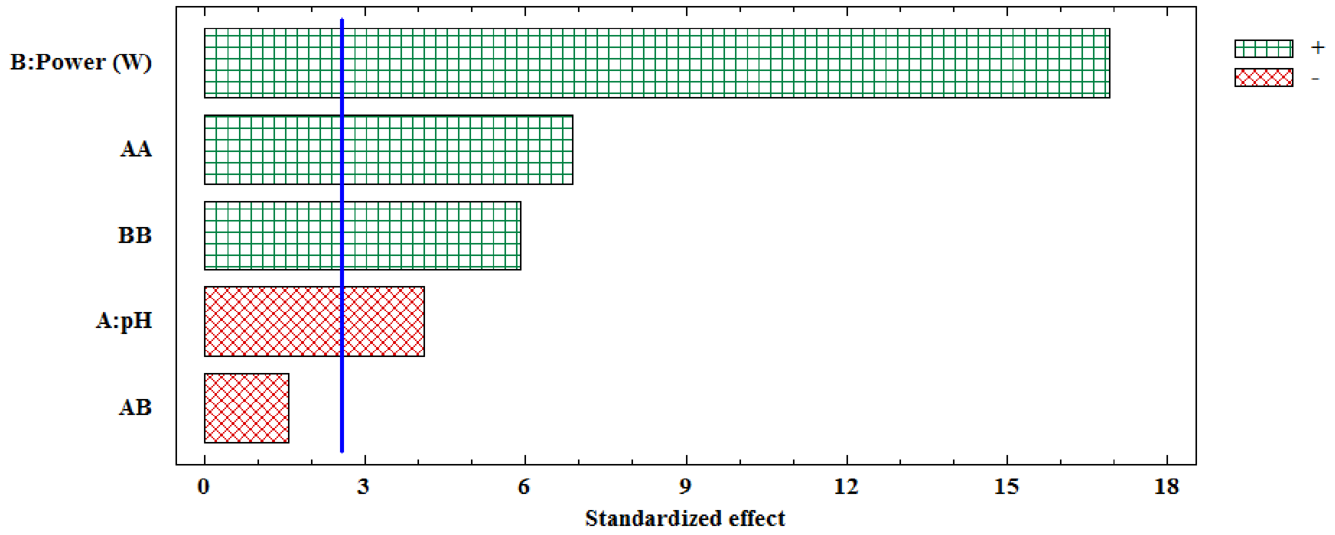
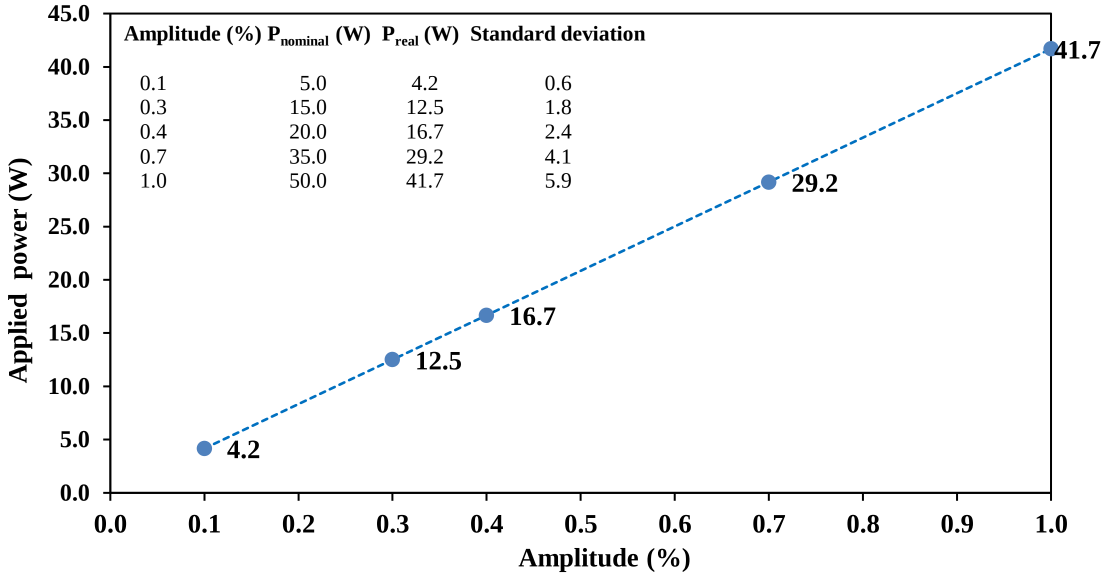


**Figure 10. Pareto charts for a. CPX removal and b. DOX removal using ultrasound (pollutants initial concentration: 2.0 mg L$^{-1}$, temperature: 25 ± 2 °C, frequency: 40 kHz, reaction time: 30 min).**

To clarify the role of each evaluated parameter, the individual effects of the applied US power and the solution initial pH on CPX and DOX removal were analyzed. The calorimetric method (Kimura et al., 1996) was conducted to determine the real power dissipated into the solution during the ultrasonic reaction. In this way, the experimental results (Figure 11) indicated that approximately 83.33% of the power is transmitted to the solution and the rest is lost mainly in form of heat. In addition, Figure 12 corresponds to the main effects plot for pollutants removal under the selected experimental conditions. From this figure, it can be seen that higher US power levels promote a higher elimination of CPX and DOX. These results could be associated to the fact that under higher US applied powers the amount of generated HO• radicals could be higher due to an increment in the number of formed cavitation bubbles and its eventual collapse. In addition, under higher US applied power, the radicals could be distributed uniformly in the solution (more movement of the fluid) (Braeutigam et al., 2012). However, some authors have reported that excessive increases in the applied power could provoke a negative effect on organic compounds elimination as a result of an oversaturation of bubbles in the solution, and less implosion. Furthermore, bubbles could not be able to expand during the rarefaction stage of the acoustic cycle, causing a potential decrease in the generation of hydroxyl radicals (Chiha et al., 2011; Deng et al., 2013; Deojay et al., 2011; Du et al., 2017; Torres-Palma & Serna-Galvis, 2018).



| Amplitude (%) | $P_{nominal}$ (W) | $P_{real}$ (W) | Standard deviation |
|---|---|---|---|
| 0.1 | 5.0 | 4.2 | 0.6 |
| 0.3 | 15.0 | 12.5 | 1.8 |
| 0.4 | 20.0 | 16.7 | 2.4 |
| 0.7 | 35.0 | 29.2 | 4.1 |
| 1.0 | 50.0 | 41.7 | 5.9 |

**Figure 11. Real applied power during CPX and DOX removal using US (based on the calorimetric method).**

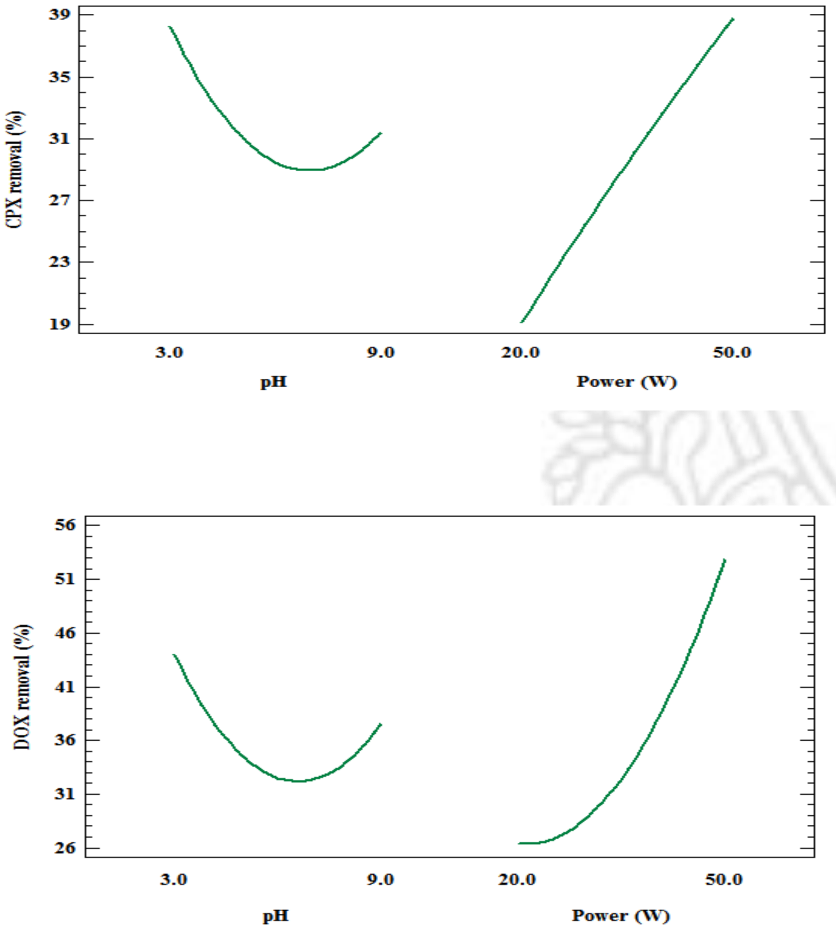


**Figure 12. Main effects plot for a. CPX removal and b. DOX removal (pollutants initial concentration: 2.0 mg $L^{-1}$, temperature: 25 ± 2 °C, frequency: 40 kHz, reaction time: 30 min).**

On the other hand, changes in the solution pH could lead to changes in the solubility of the substrates (Papoutsakis et al., 2015). The main effects plot (Figure 12) shows the effect of the initial pH of the solution on the removal of CPX and DOX. From this figure, it can be seen that CPX and DOX removals in aqueous solutions are strongly dependent on pH value. Table 8 shows some of the physicochemical properties of the studied antibiotics. CPX and DOX are non-volatile compounds and the region of sono-decomposition would be at the cavitation bubble interface and/or at the bulk solution. According to the Henry's law constants, CPX and DOX have low volatility and therefore cannot be degraded by pyrolysis inside the cavitation bubble. In contrast, these antibiotics have high solubility in water and relatively high octanol/water partition coefficient, indicating that these distribute at the interface and bulk solution regions. In this way, the HO• radicals generated by US would be the main species responsible for the pollutant degradation, which most probably occurs not only in the bulk solution but also on the bubble-liquid interfacial region where hydroxyl free radical concentration is higher (Méndez-Arriaga et al., 2008; Serna-Galvis et al., 2015; Vega et al., 2019;  Zúñiga-Benítez et al., 2014).

**Table 8. Physicochemical properties of CPX and DOX (NIST database, 2020).**

| Property | CPX | DOX |
|---|---|---|
| **Water solubility (mg $L^{-1}$), 25°C** | 1789.0 | 312.9 |
| **Henry's law constant (atm $m^3$ $mol^{-1}$), 25°C** | $2.77 \times 10^{-17}$ | $4.66 \times 10^{-24}$ |
| **Octanol/ water partition coefficient (Log $k_{ow}$)** | 0.65 | -0.02 |

CPX has two pKa values (logarithm of acid dissociation constant), one at 6.88 and other at 2.56 (Khosravi et al., 2018, Figure 13a), and exists in zwitterionic form in solution when the pH is between 2.56-6.88. In regards to the results presented by Figure 12a, ionic forms of CPX (at pH 3.0 and 9.0), favor its removal, while a more stable nature (zwitterionic form) could imply less reactivity and an eventual lower oxidation. Al-Musawi et al., 2019; Antonin et al., 2019; and Droguett et al., 2020 have reported that the primary attacks of HO• to CPX molecule could occur on three sites: 1) the β-lactam ring, which is a highly reactive site because the ring is very strained and the carbonyl-nitrogen bond is very labile (hydroxylation reaction); 2) the aromatic ring, which typically experiences electrophilic substitutions; 3) and in the secondary amide moiety, whose reactivity towards oxidants can be favored through the inductive and resonant effects generated by the substituents (oxidative reaction), besides, by the charge level in the medium.

On the other hand, DOX has three pKa values (3.50, 7.07 and 9.13, Figure 13b) (Bolobajev et al., 2016). In the range of 3.50-7.07, DOX exists in zwitterionic form which could imply less reactivity. At pH 3.0 and 9.0 the cationic and anionic form of DOX could promote its removal, as it is shown by Figure 12b, but high pH conditions may create more free radical scavengers leading to an eventual decrease of the available hydroxyl radicals, and a reduction of DOX removal at pH 9.0 in contrast with results obtained under pH 3.0 (this situation also applies for results regarding CPX removal under alkaline pH conditions). In addition, according to some researchers, the hydroxyl radical could promote either the loss of atoms and functional groups located at the doxycycline molecule periphery or the breakdown of its aromatic rings. In this way, substitution or addition reactions in this sites, where the antibiotic is less stable could occur (Borghi et al., 2015; Rivas et al., 2011).

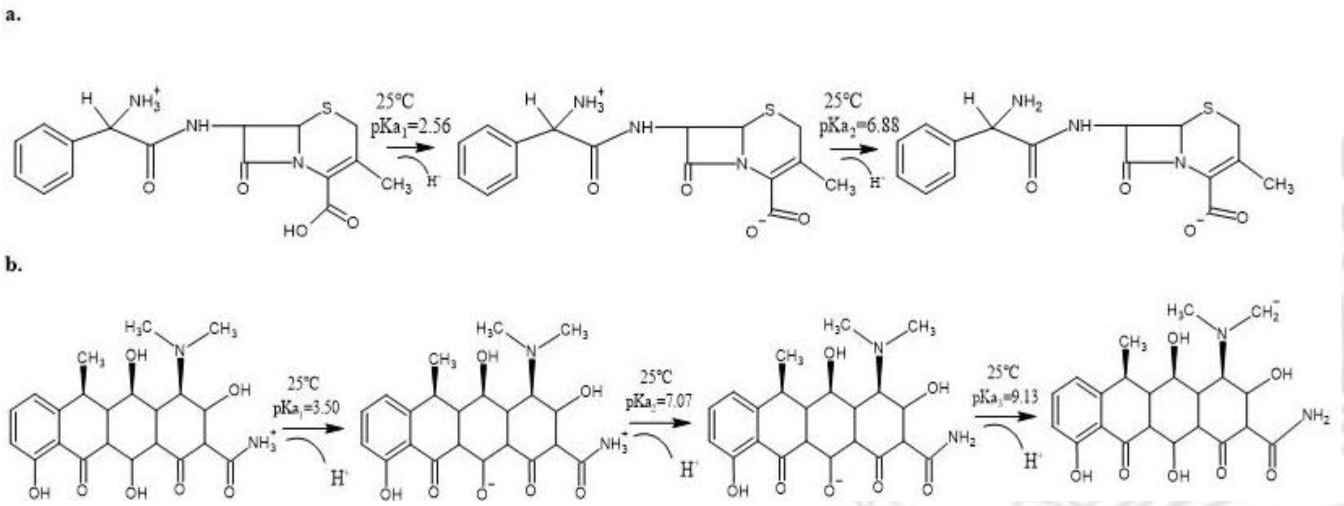


**Figure 13. Antibiotics ionization states a. CPX: pK$_1$: 2.56, pK$_2$: 6.88 (Legnoverde et al., 2014), b. DOX: pK$_1$: 3.50, pK$_2$: 7.07, pK$_3$: 9.13 (Bolobajev et al., 2016).**

Statistical analysis of results allowed to obtain a model that relates the dependent factor with the significant factors and interactions after 30 min of sonochemical treatment. In this way, after a nonlinear regression, using the statistical software Statgraphics Centurion XVI, were obtained the reduced models represented by equations 11 and 12. The coefficients of each term in the polynomial expressions indicate the weight of the variable/interaction under the processes.

$$\textbf{CPX removal (\%)} = 32.69 - 8.42[pH] + 0.79[power] + 0.59[pH]^2 + 0.003[pH][power] - 0.002[power]^2 \qquad (11)$$

$$\textbf{DOX removal (\%)} = 72.94 - 10.94[pH] - 1.14[power] + 0.91[pH]^2 - 0.03[pH][power] + 0.03[power]^2 \qquad (12)$$

[pH] is the solution initial pH and [power] is the applied US power.

Table 7 shows the comparison between experimental results and those predicted by the models. As it can be noted, the proposed polynomial expressions predict the experimental results adequately. Coefficients of determination ($R^2$), were 97.1% and 98.8% for CPX and DOX removal, respectively.

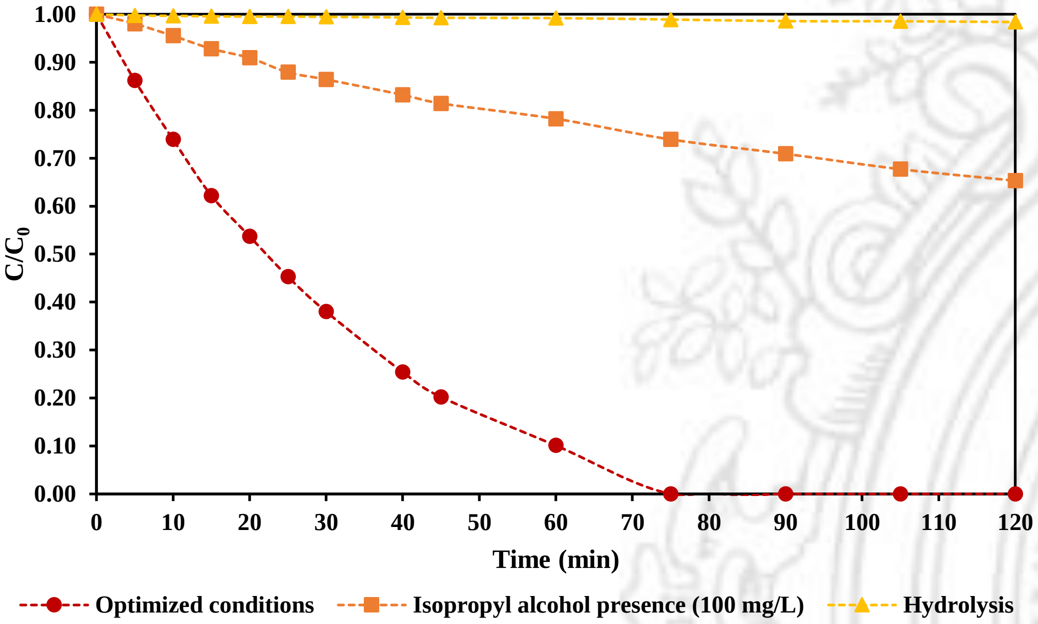
**Based on the exposed results, the conditions under the evaluated experimental range that lead to higher CPX and DOX removals are 50 W nominal power and solution pH 3.0.**

### 5.1.2. Pollutants removal using optimized conditions

CPX and DOX ultrasonic degradation was studied considering the established optimized conditions. Experimental results are shown in Figure 14. From this figure, it is possible to appreciate that in the case of CPX, pollutant was removed completely in 75 min of treatment, while the removal of DOX was reached after 90 min. In addition, hydrolysis experiments (at pH 3.0) indicated that after 120 min, substrates removal was just 1.6% and 3.8% for CPX and DOX respectively, indicating that antibiotics elimination is negligible in absence of US application.

In addition, in order to clarify the role of HO• radicals on CPX and DOX degradation, some tests were carried out under the presence of isopropanol (i-PrOH) that is known as a good HO• free radical scavenger (high rate constant of reaction between HO• and i-PrOH1.9 x $10^9$ mol $L^{-1}$ $s^{-1}$) (Dunia E. et al., 2013; Hu et al., 2008). Figure 14 shows that i-PrOH inhibits substrates removal markedly, suggesting that HO• radicals are the main oxidizing agent of CPX and DOX.

**a.**



**b.**

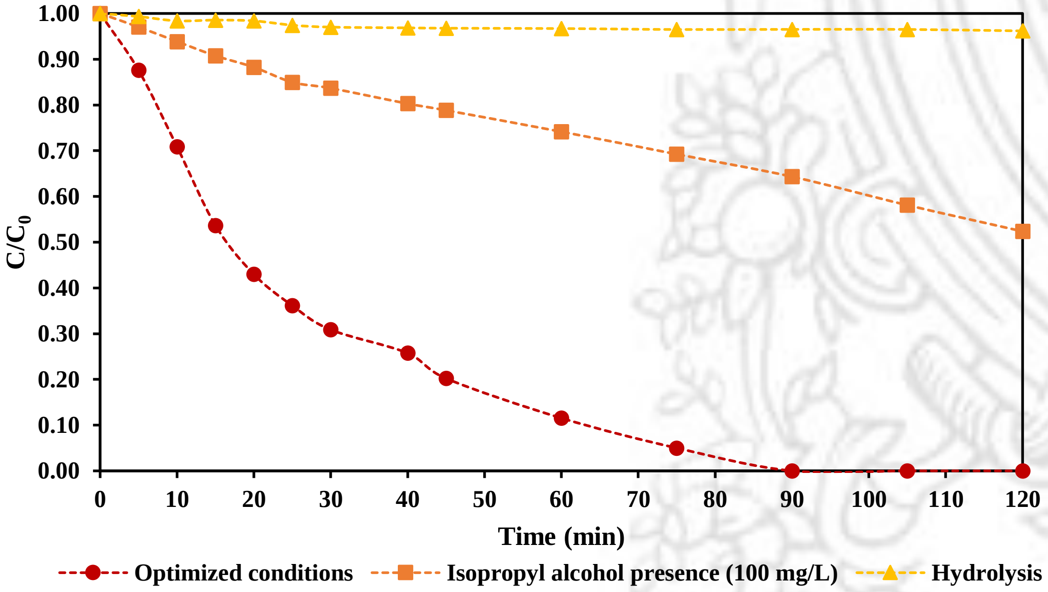


**Figure 14. Antibiotics elimination under optimized conditions a. CPX y b. DOX (pollutant initial concentration: 2.0 mg $L^{-1}$, pH: 3.0, US applied power: 50.0 W, frequency: 40 kHz, temperature: 25 ± 2 °C).**

### 5.1.3. Effect of pollutants initial concentration

In order to investigate the effect of CPX and DOX initial concentration on each reaction, experiments were performed by varying this parameter in the range 1.0-5.0 mg $L^{-1}$ (2.8-14.5 μmol $L^{-1}$ for CPX and 2.2-11.2 μmol $L^{-1}$ for DOX). The concentration variation profiles are shown by Figure 15. From figure, it can be seen that the extent of CPX and DOX degradation ($C/C_0$) is inversely proportional to the pollutant initial concentration. In this sense, organic pollutants removal using ultrasound irradiation can be described using a pseudo first-order reaction kinetic model (Equation 13, Al-Hamadani et al., 2016; Guo et al., 2010; Monteagudo et al., 2018; Villegas-Guzman et al., 2015). However, as it is shown by Figure 16, in both cases, a complete linear relationship was not observed for a first-order kinetic law and pollutants elimination could not be characterized by a single rate constant.

$$r = \frac{-dC}{dt} = k_0 C \tag{13}$$

where, $r$ is the initial degradation rate (μmol $L^{-1}$ $min^{-1}$), $k_0$ is the pseudo-rate constant (μmol $L^{-1}$ $min^{-1}$) and $C$ is the pollutant initial concentration (μmol $L^{-1}$).

On the other hand, some researches have studied different kinetic models for sonochemical degradation of non-volatile compounds (Chiha, Merouani, et al., 2010; Vega et al., 2019; Villegas-Guzman et al., 2015). These models based on a Langmuir type mechanism have suggested that substrates elimination is related to the amount of radicals and pollutants concentration (Lianou et al., 2018; Rao et al., 2016). In this way, the sonochemical degradation of some substrates have reported using the kinetic model proposed by Okitsu et al. (2005) (Chiha, Merouani, et al., 2010; Vega et al., 2019). This model indicates that organic molecules adsorb and desorb from the liquid interface layer surrounding of the cavitation bubble, reaching a pseudo-steady state. The degradation rate (r) can be represented by Equation (14):

$$r = \frac{k_0 K C}{1 + K C} \tag{14}$$

where, $r$ is the initial degradation rate (μmol $L^{-1}$ $min^{-1}$), $k_0$ is the pseudo-rate constant (μmol $L^{-1}$ $min^{-1}$), $C$ is the pollutant initial concentration (μmol $L^{-1}$) and and K is equilibrium constant of the target compound at the interfacial region, i.e., between the cavitation bubbles and the solution (μmol $L^{-1}$) (Chiha, Merouani, et al., 2010).

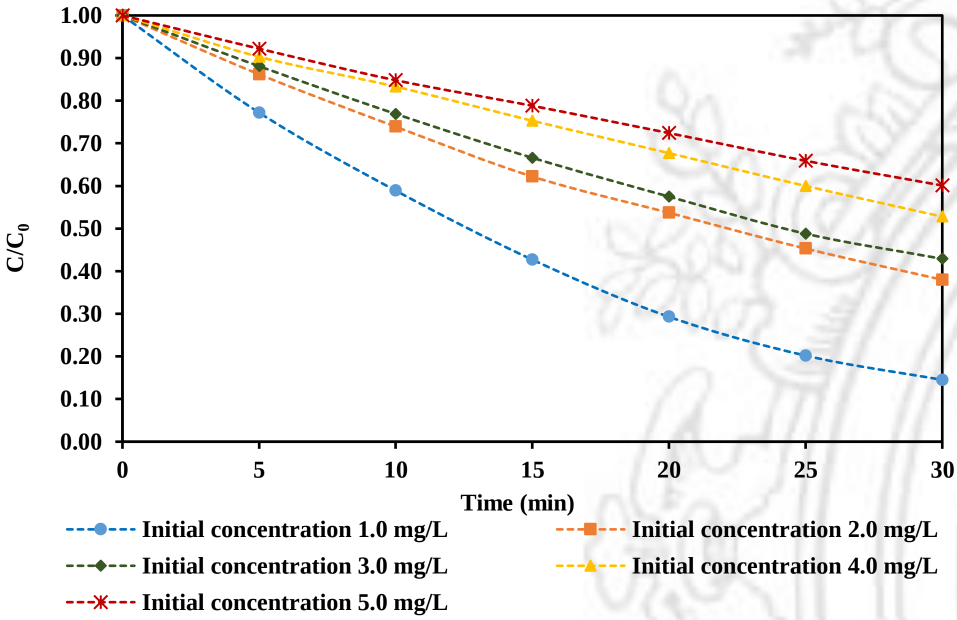
However, the most appropriate kinetic model for nonvolatile compounds was previously developed by Serpone et al. (1994). They described two regimes; one at the lower concentration in which the reaction occurs in the bulk solution, and other a regime at higher concentration in which the sonochemical reactivity occurs at the bubble-liquid interface and connects the sonochemical kinetic to a Langmuir-type mechanism. Thus, the degradation rate is the sum of the rates in the bulk and in the interface layer and can be expressed by Equation (15):

$$r = k_b + \frac{k_0 K C}{1 + K C} \tag{15}$$

where, $k_b$ is a constant representing the rate of decomposition in the bulk liquid (μmol $L^{-1}$ $min^{-1}$), $r$ is the initial degradation rate (μmol $L^{-1}$ $min^{-1}$), $k_0$ is the pseudo-rate constant (μmol $L^{-1}$ $min^{-1}$), $C$ is the pollutant initial concentration (μmol $L^{-1}$) and $K$ is equilibrium constant (μmol $L^{-1}$).

Having into account the above, the sonochemical degradation data of CPX and DOX were analyzed by nonlinear regression using the Solver complement of Microsoft Excel. The results of modeling are shown in Table 9 and Figure 16. Data indicates that the experimental results fit better (higher coefficient of determination $R^2$) with the model proposed by Serpone et al. (1994) in comparison with the Okitsu et al. model and the pseudo first-order kinetics model. In this way, it can be inferred that the pollutants degradation takes place at both the bubble-liquid interfacial region and in the bulk solution.

**a.**



**b.**

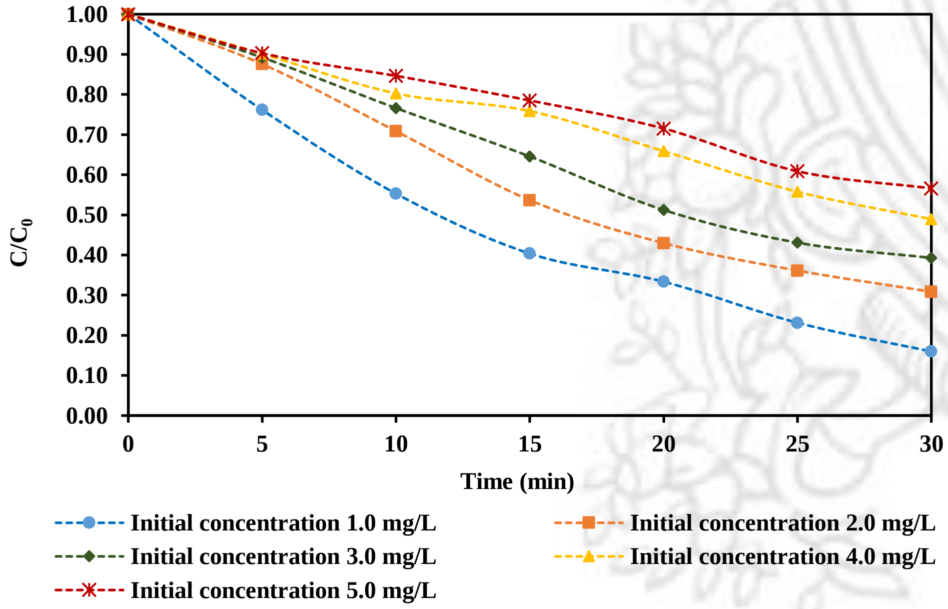
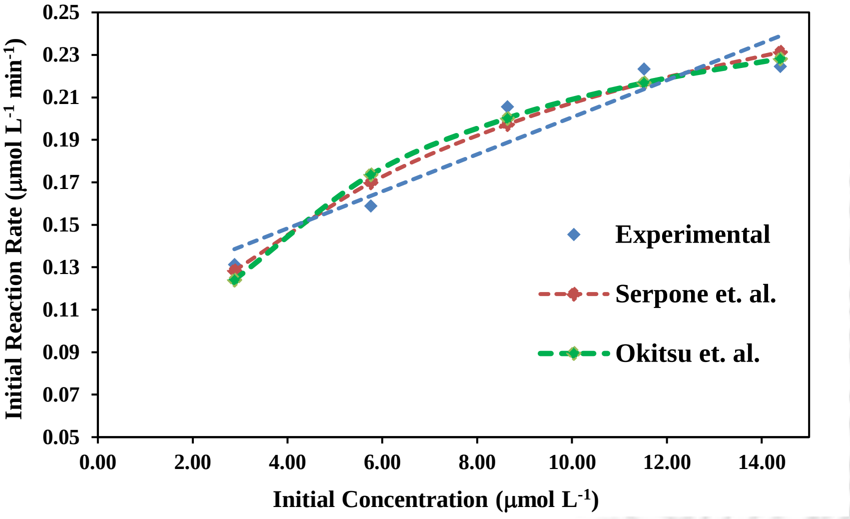


**Figure 15. Effect of initial concentration: a. CPX removal b. DOX removal using ultrasound (pH: 3.0, applied power 50.0 W, frequency: 40 kHz, temperature 25 ± 2 °C, reaction time 30 min).**

a.



b.

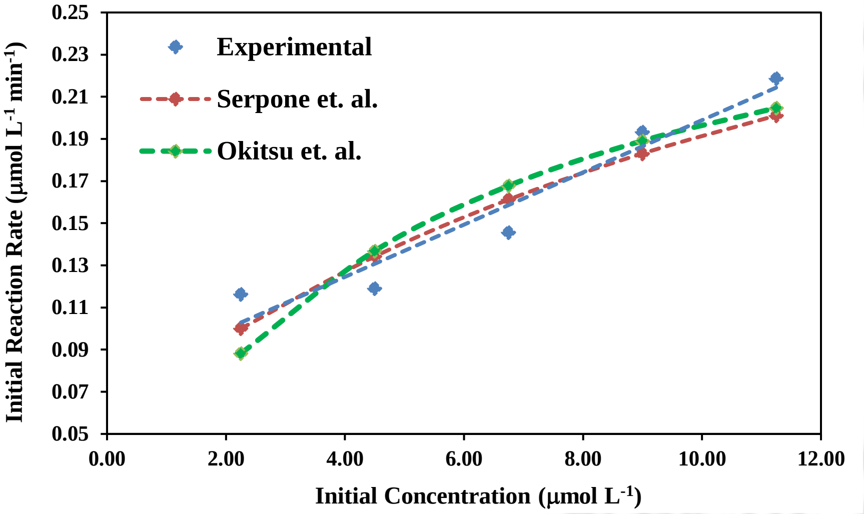


**Figure 16. Initial degradation rate as function of the initial concentration: a. CPX b. DOX and with predicted values (pH of the solution: 3.0, applied power: 50.0 W, frequency: 40 kHz, temperature: 25 ± 2 °C, reaction time: 30 min).**

**Table 9. Parameters of the models of pseudo first order, Okitsu et al. (2005) and Serpone et al. (1994) in the CPX and DOX ultrasonic treatment.**

| Model | Parameters | Cephalexin | Doxycycline |
|---|---|---|---|
| **Pseudo first-order model** | **$k_0$ (μmol L$^{-1}$ min$^{-1}$)** | 0.0087 | 0.0124 |
| | **$R^2$** | 0.9057 | 0.9339 |
| **Okitsu et al.** | **$k_0$ (μmol L$^{-1}$ min$^{-1}$)** | $0.28879 \pm 5.1819 \text{x} 10^{-5}$ | $0.30572 \pm 7.9139 \text{x} 10^{-5}$ |
| | **K (μmol L$^{-1}$)** | $0.26163 \pm 2.8499 \text{x} 10^{-5}$ | $0.18013 \pm 1.7899 \text{x} 10^{-5}$ |
| | **$R^2$** | 0.9182 | 0.9504 |
| **Serpone et al.** | **$k_0$ (μmol L$^{-1}$ min$^{-1}$)** | $0.27353 \pm 8.2243 \text{x} 10^{-6}$ | $0.33542 \pm 2.6701 \text{x} 10^{-4}$ |
| | **K (μmol L$^{-1}$)** | $0.11925 \pm 6.2241 \text{x} 10^{-5}$ | $0.06837 \pm 2.4167 \text{x} 10^{-4}$ |

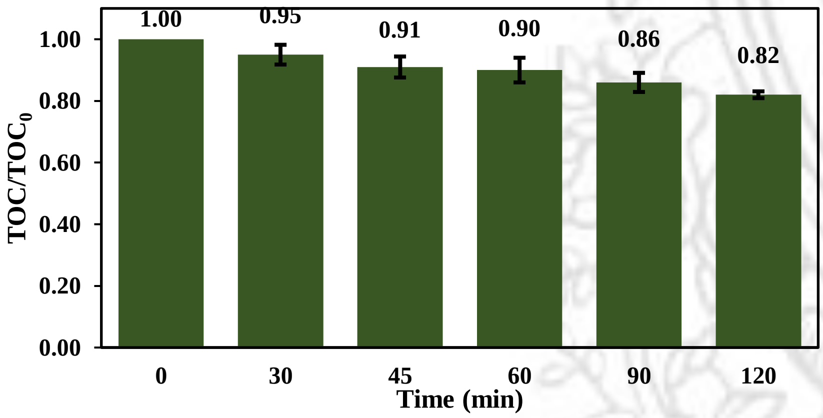
| | | | |
|---|---|---|---|
| | **$K_b$ (μmol $L^{-1}$ $min^{-1}$)** | 0.05849 ± 4.3764x$10^{-5}$ | 0.05528 ± 3.0756x$10^{-5}$ |
| | **$R^2$** | **0.9579** | **0.9841** |

### 5.1.4. Mineralization and toxicity analysis

Figure 17, 18 and 19 show the results regarding TOC, anions and toxicity variation after 120 min of ultrasonic irradiation under optimized conditions. According to the results, it can be inferred that part of the CPX and DOX molecules are being mineralized (reduction on the solutions organic carbon content was around ~18.0% for CPX and ~8.0% for DOX). This, together with an increase in the presence of ions on the solution (Figure 18) indicate that CPX and DOX are being transformed into organic compounds (byproducts) with probably low volatility and high hydrophilicity, which migrate to the bulk solution, where the concentration of radicals is much lower than in the interface (it implies that a total mineralization is not reached). A similar behavior has been found during the sonochemical degradation in water of various antibiotics such oxacillin (Serna-Galvis, Silva-Agredo, Giraldo, et al., 2016), tetracycline (Darvishi Cheshmeh Soltani et al., 2018), amoxicillin (Sepyani et al., 2018), ampicillin, cephradine cephadroxil, and cephadroxil (Estrada-Flórez et al., 2020).

The toxicity assessment has been achieved through Microtox toxicity test based on by monitoring light intensity of *Vibrio Fischeri* luminescent microorganisms during reaction. The results show that although the extent of degradation in both pollutants was 100.0% after 120 min, the toxicity reduction (Figure 19) was of 36.0% and 87.0 % for CPX and DOX respectively. This demonstrates that US technology is efficient not only to reduce pollutants presence but also, to inhibit samples toxicity and reduce the potential risk of hazardous effects on ecosystems and living beings.

**a.**



b.

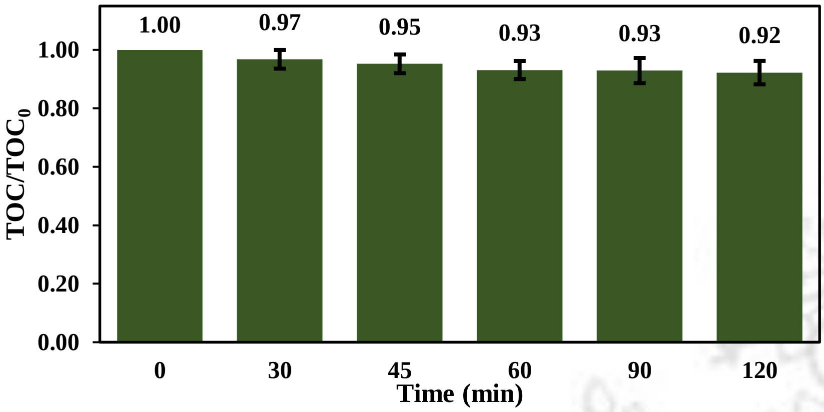
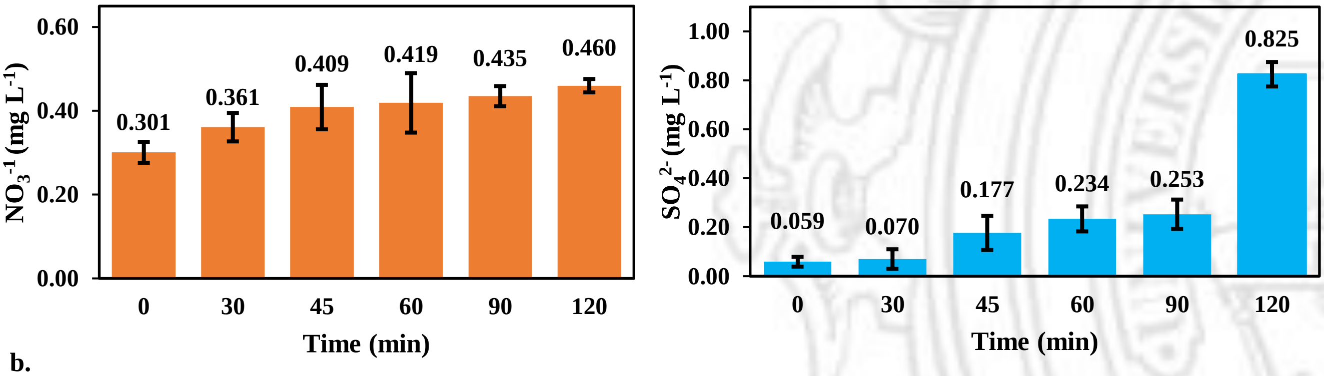


**Figure 17. Total organic carbon variation during a. CPX b. DOX removal under optimized conditions using US (pH of the solution: 3.0, applied power: 50.0 W, frequency: 40 kHz, temperature: 25 ± 2 °C, reaction time: 120 min).**

a.



b.

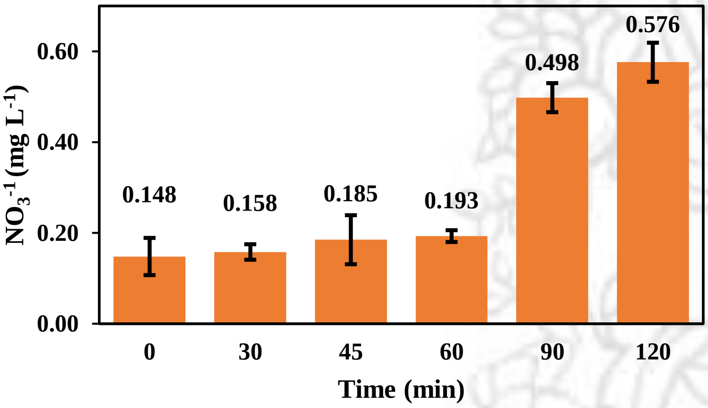
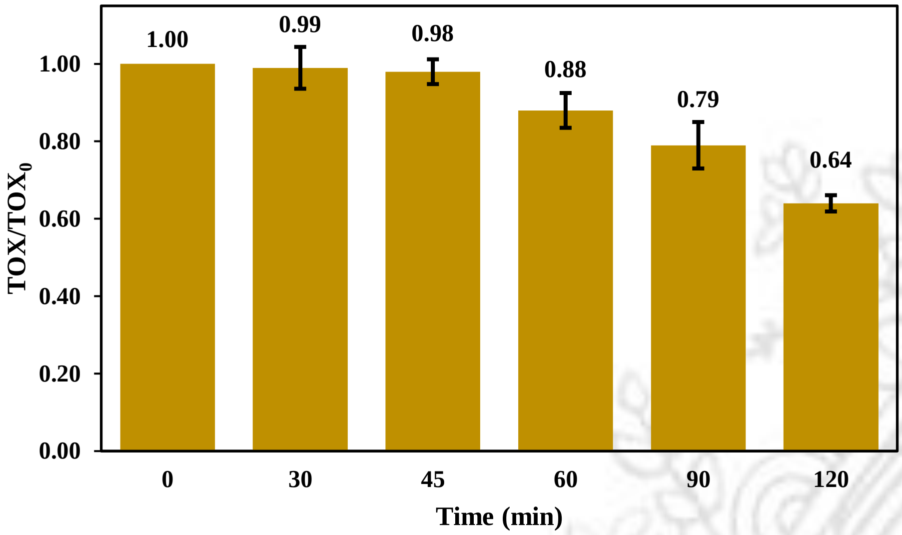


**Figure 18. a. Nitrate and sulfate ions concentration during CPX removal b. Nitrate ion concentration during DOX removal using US under optimized conditions (pH of the solution: 3.0, applied power: 50.0 W, frequency: 40 kHz, temperature: 25 ± 2 °C, reaction time: 120 min).**

**a.**



**b.**

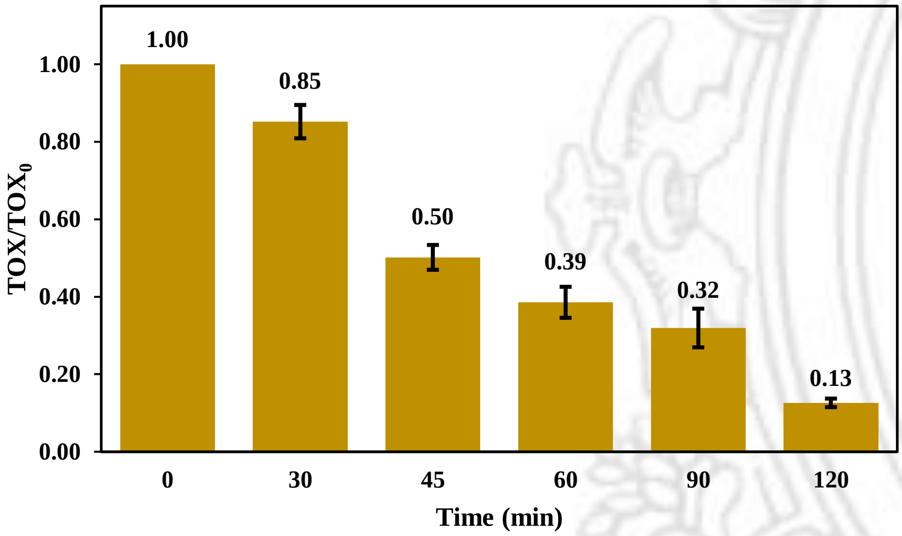


**Figure 19. Toxicity variation during a. CPX and b. DOX removal under optimized conditions using US (pH of the solution: 3.0, applied power: 50.0 W, frequency: 40 kHz, temperature: 25 ± 2 °C, reaction time: 120 min).**

## 5.2 Antibiotics removal using UV/$H_2O_2$

The reaction kinetics of the UV/$H_2O_2$ process is a function of the solution pH, the peroxide initial concentration and the physicochemical properties of the target pollutant (Ameta & Ameta, 2018; De Laat & Stefan, 2018). In addition, the fact that part of the solar radiation has a wavelength corresponding to the UV range, represents a possibility of implementing photo-treatment systems using solar light and $H_2O_2$ for water treatment.

The removal of CPX and DOX using simulated sunlight radiation and $H_2O_2$ was evaluated considering a face-centered central composite design, which together with the response surface methodology (response:

pollutants removal after 30 min of reaction) allowed to determine the conditions that conduct to a higher antibiotic's elimination. In this sense, the effect of the solution pH and the $H_2O_2$ initial concentration were assessed considering the experimental levels reported in Table 4. Tables 10 and 11 correspond to the experimental results obtained after carrying out the proposed experimental design, while Figure 20 depicts the associated response surfaces.

**Table 10. Experimental design for CPX removal using simulated sunlight radiation and $H_2O_2$ (pollutant initial concentration: 2.0 mg $L^{-1}$, irradiance: 500 W $m^{-2}$, temperature: 35 ± 2 °C, reaction time: 30 min).**

| Test | Solution pH | $H_2O_2$ initial concentration (mg $L^{-1}$) | CPX removal (%) experimental | CPX removal (%) calculated by model |
|---|---|---|---|---|
| **1** | 3.0 | 6.9 | 91.4 | 88.7 |
| **2** | 9.0 | 2.3 | 10.3 | 14.7 |
| **3** | 6.0 | 4.6 | 14.7 | 17.6 |
| **4** | 3.0 | 2.3 | 83.2 | 82.5 |
| **5** | 9.0 | 4.6 | 32.9 | 24.7 |
| **6** | 3.0 | 4.6 | 83.3 | 86.3 |
| **7** | 6.0 | 4.6 | 18.1 | 17.6 |
| **8** | 6.0 | 2.3 | 15.0 | 10.7 |
| **9** | 6.0 | 4.6 | 16.4 | 17.6 |
| **10** | 9.0 | 6.9 | 31.0 | 33.3 |
| **11** | 6.0 | 6.9 | 23.9 | 23.1 |

**Table 11. Experimental design for DOX removal using simulated sunlight radiation and $H_2O_2$ (pollutant initial concentration: 2.0 mg $L^{-1}$, irradiance: 500 W $m^{-2}$, temperature: 35 ± 2 °C, reaction time: 30 min).**

| Test | Solution pH | $H_2O_2$ initial concentration (mg $L^{-1}$) | DOX removal (%) experimental | DOX removal (%) calculated by model |
|---|---|---|---|---|
| **1** | 3.0 | 6.0 | 55.4 | 55.0 |
| **2** | 9.0 | 2.0 | 74.0 | 75.0 |
| **3** | 6.0 | 4.0 | 52.1 | 51.7 |
| **4** | 3.0 | 2.0 | 22.4 | 25.1 |
| **5** | 9.0 | 4.0 | 83.8 | 84.8 |
| **6** | 3.0 | 4.0 | 44.6 | 42.3 |
| **7** | 6.0 | 4.0 | 51.4 | 51.7 |
| **8** | 6.0 | 2.0 | 41.9 | 38.2 |
| **9** | 6.0 | 4.0 | 50.2 | 51.7 |
| **10** | 9.0 | 6.0 | 92.2 | 90.1 |
| **11** | 6.0 | 6.0 | 58.2 | 60.7 |

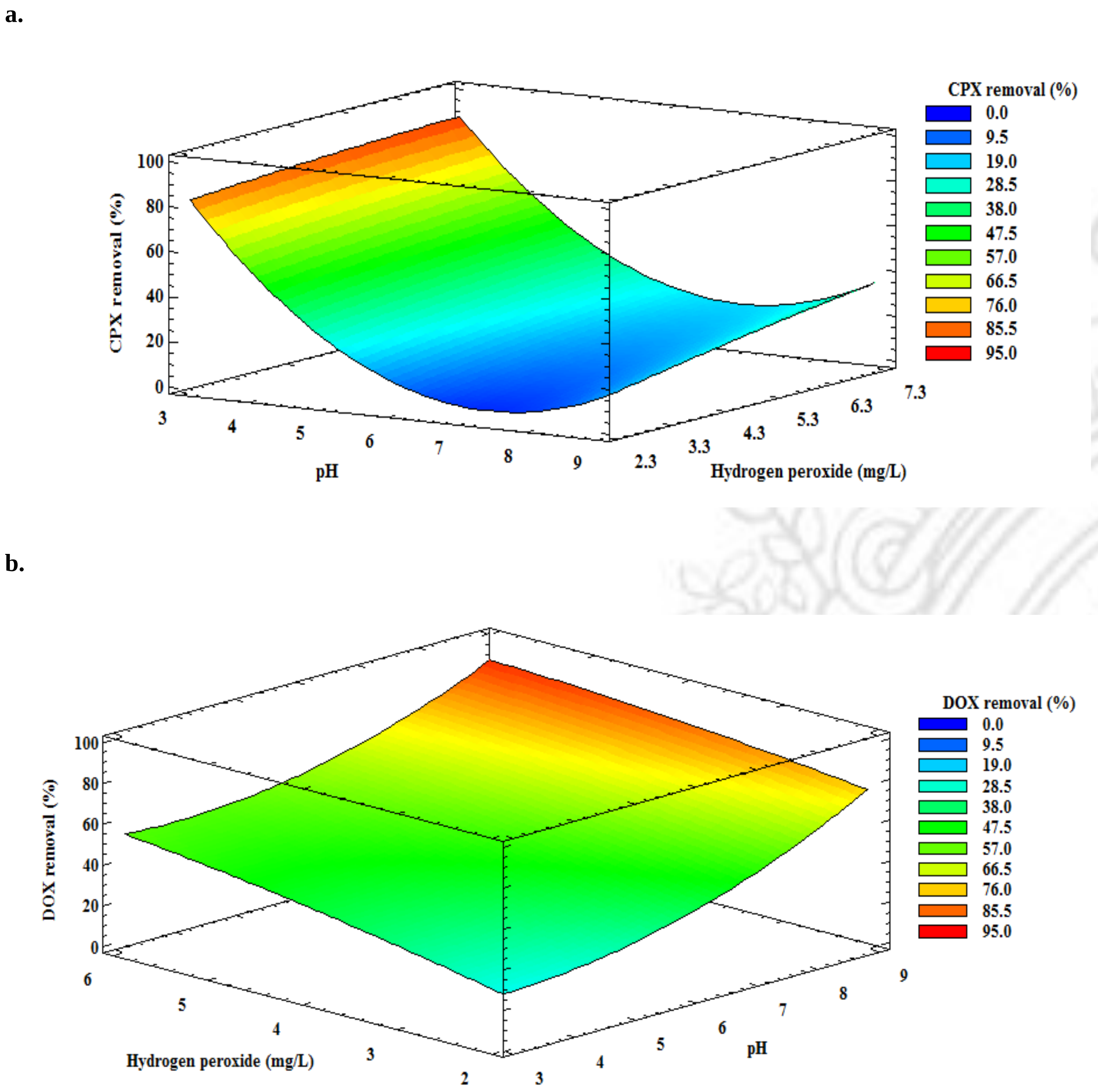


**Figure 20. Response surface for a. CPX removal and b. DOX removal using simulated sunlight radiation and $H_2O_2$ (pollutant initial concentration: 2.0 mg $L^{-1}$, temperature: 35 ± 2 °C, irradiance: 500.0W $m^{-2}$, reaction time: 30 min).**

### 5.2.1 Reaction conditions optimization

To optimize the reaction conditions, it is necessary to evaluate which variables and interactions between them affect the CPX and DOX elimination under the studied experimental conditions. Figure 21 corresponds to the Pareto chart for each substrate elimination. According to this figure, the parameters and interactions that can be considered significantly important for CPX and DOX elimination using simulated radiation and $H_2O_2$ are: the initial pH (A), its quadratic value (AA) and the initial dose of $H_2O_2$ (B). In addition, Figure 21a shows that the square value of pH, the pH-$H_2O_2$ interation (AB) and the initial $H_2O_2$ concentration (B) have a positive effect, while the quadratic value BB together with the initial pH have a negative influence on CPX removal. In the case of DOX experiments, Figure 21b indicates that with exception of the quadratic value of $H_2O_2$ initial concentration and the pH-$H_2O_2$ interation, the other factors/interactions have a positive effect on the reaction.

The response surface and the experimental results allowed to obtain the polynomial models represented by Equations 16 and 17, which show the relation between the response and the significant factors. In addition, Table 10 and 11 present the calculated values regarding the CPX and DOX removal using the proposed models. Results indicate that equations predict CPX and DOX elimination adequately, $R^2$ coefficient between experimental data and models were 0.986 and 0.989, respectively.

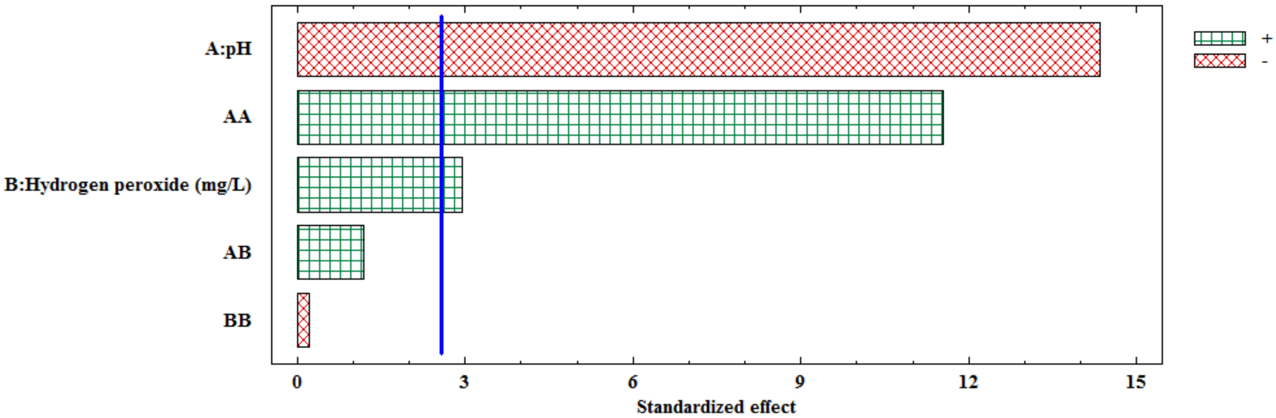
$$\textbf{CPX removal (\%)} = 227.83 - 62.85[pH] + 1.28[H_2O_2] + 4.21[pH]^2 + 0.45[pH][H_2O_2] - 0.14[H_2O_2]^2 \quad (16)$$

$$\textbf{DOX removal (\%)} = 10.47 - 6.32[pH] + 13.81[H_2O_2] + 1.32[pH]^2 - 0.61[pH][H_2O_2] - 0.56[H_2O_2]^2 \quad (17)$$

where [pH] is the initial solution pH and $[H_2O_2]$ is the initial dose of $H_2O_2$.

The positive quadratic factor of the hydrogen peroxide concentration in both polynomial expressions and analysis of Pareto charts, show that an increase in the concentrations of this reagent promotes an enhancement in the pollutants elimination using simulated sunlight and $H_2O_2$ since the formation of hydroxyl radicals is favored. Additionally, the negative quadratic factor of the solution initial pH regarding CPX experiments indicate that very high or very low values of this variable favors the pollutant extent of degradation, suggesting that the substrate removal could depend of molecule state (neutral or ionic). In the case of DOX experiments, its positive coefficient shows that an increase in the initial pH promotes an enhanced in the antibiotic elimination.

**a.**



**b.**

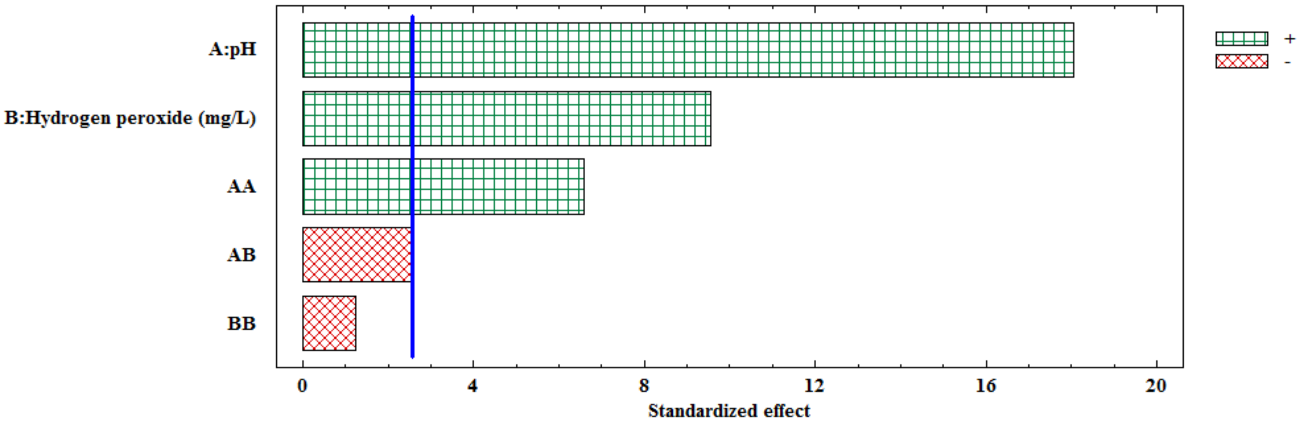
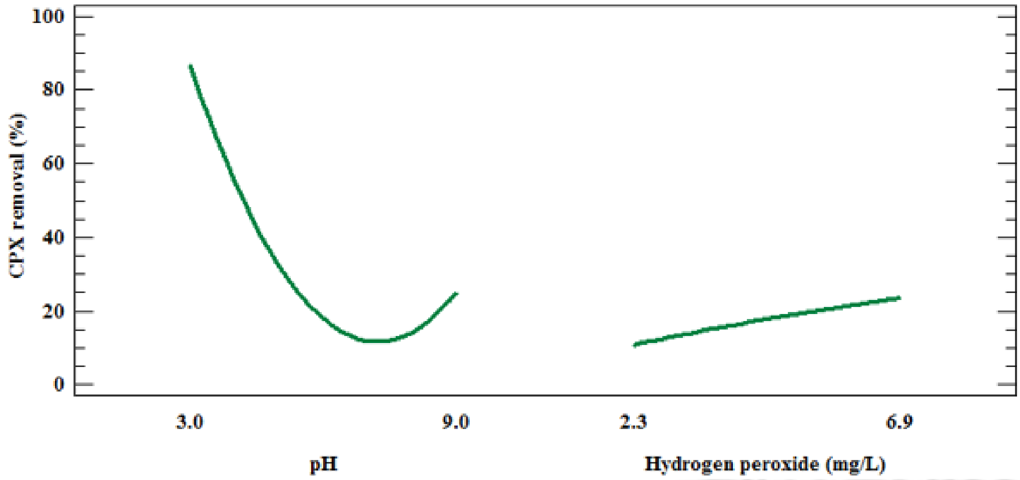


**Figure 21. Pareto charts for: a. CPX removal and b. DOX removal using simulated sunlight radiation and $H_2O_2$ (pollutants initial concentration: 2.0 mg $L^{-1}$, irradiance: 500 W $m^{-2}$, temperature: 35 ± 2 °C, reaction time: 30 min).**

Figure 22 corresponds to the main effects plot, and allows to determine the effect of each independent parameter on the response. From this figure, it can be appreciated that higher $H_2O_2$ concentrations lead to an enhancement in the substrates elimination, a fact that could be the result of a higher HO• radicals generation after the peroxide decomposition. However, it has been reported that excesses of $H_2O_2$ could generate an inhibitory effect on substrates removal due to the scavenging of HO• radicals. Likewise, the figure illustrates the effect of the solution initial pH on CPX and DOX removal during the experiments. The solution initial pH and molecule state under photolytic systems have been reported as factors that can lead to an increase in the rate of antibiotics degradation (Carlson et al., 2015). Figure 22a shows that the extent of CPX degradation increases in acid and alkaline conditions. However, at pH 9.0, the removal of CPX is lower in contrast with the results obtained under pH 3.0. In this way, some authors have reported that the rate of hydrogen peroxide decomposition increases in acidic medium leading to an increase in the rate of hydroxyl radicals formation (De Laat & Stefan, 2018). Additionally, according to CPX pKa values, the anionic and cationic form of the substrate at pH values of 3.0 and 9.0, would favor its removal, while a more stable nature (pH 6.0) could imply less reactivity with HO• and an eventual lower oxidation.

On the other hand, the effect of the pH on the degradation of DOX is illustrated in Figure 22b. From this figure, it can be seen that an increase in pH values promotes higher substrate removal. Giri et al., 2011 have reported that the efficiency of UV/$H_2O_2$ process at the alkaline pH region is attributed to hydroxyl radical formation generated under UV irradiation. The pKa values of DOX are 3.50, 7.07 and 9.13 (Bolobajev et al., 2016), which implies that at alkaline pH conditions; the substrate will be found primarily in anionic form, whereas at lower pH (3.5-7.03), a neutral form would be predominant. Considering this, at pH 9.0, the ionic form of DOX, favor its removal, while a more stable form could imply less reactivity with HO• and a reduction in the removal of pollutant.

**a.**



**b.**

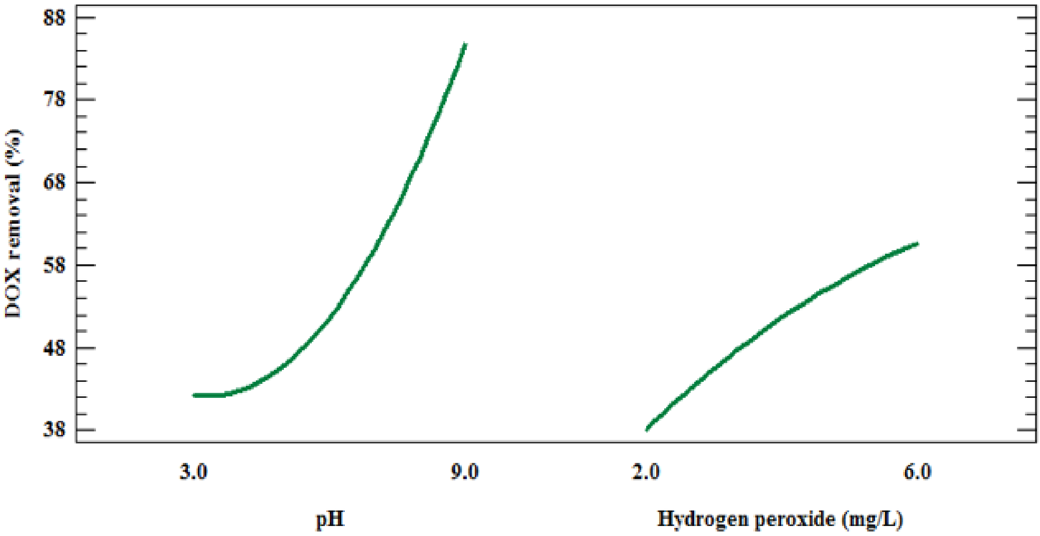


**Figure 22. Main effects plot for a. CPX removal and b. DOX removal using simulated sunlight radiation and $H_2O_2$ (pollutants initial concentration: 2.0 mg $L^{-1}$, irradiance: 500 W $m^{-2}$, temperature: 35 ± 2 °C, reaction time: 30 min).**

**Give the above, the conditions that conduct to a higher CPX removal are pH 3.0 and 6.9 mg $L^{-1}$ $H_2O_2$ initial concentration, and in the case of DOX the optimized conditions are pH 9.0 and 6.0 mg $L^{-1}$ $H_2O_2$ initial concentration.**

### 5.2.2 Pollutants removal using optimized conditions

Figure 23 shows the CPX and DOX removals under different experimental conditions including $H_2O_2$/sunlight radiation at optimized conditions, photolysis and hydrolysis tests, oxidation with $H_2O_2$ and the effect of the presence of a scavenger agent (isopropyl alcohol). From this figure, it can be observed that the UV/$H_2O_2$ treatment has the capacity to remove completely CPX and DOX in 50 and 40 min, respectively, which allows to infer that the xenon lamp used in the experiments is able to emit light at wavelengths below 300 nm, promoting the generation of hydroxyl radicals after the homolytic breakdown of hydrogen peroxide.

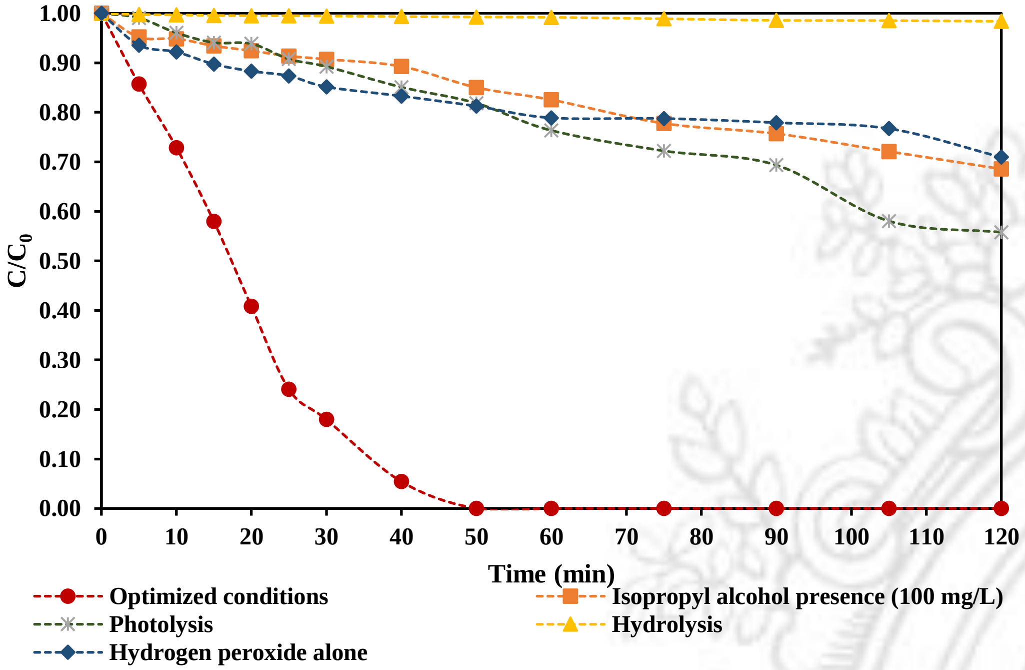
On the other hand, photolysis tests indicated that after 120 min of light irradiation ~44.2% of CPX and ~58.4% of DOX were removed, which is consistent with similar results about the photo-stability of these organic pollutants (Rivas et al., 2011; Seid-Mohammadi et al., 2019). In addition, hydrolysis experiments (under optimized pH) indicated that the removal of CPX without light presence is negligible, whereas for DOX, it was noticed that the removal under alkaline pH promotes its decomposition slightly (~15.0%), in this aspect, some literature reports have indicated that tetracyclines are less stable in alkaline than in acid conditions, which could promote its elimination in aqueous solutions (Kang et al., 2012; Pouliquen et al., 2007).

The role of the hydroxyl radicals was assessed by conducting experiments under the presence of isopropyl alcohol. The results presented in Figure 23 allow to observe that during the first 30 min of treatment, the presence of isopropanol decreased the extent of pollutants removal markedly (removal ~9.3% for CPX and ~49.4% for DOX), which would be a consequence of the reduction of the number of free hydroxyl radicals available to react with the organic matter, due to the scavenger effect caused by the presence of the alcohol. However, in the DOX experiments, a complete elimination of the antibiotic was observed after 120 min of photo-treatment, which could implied that initially the generated HO• radicals would react with isopropyl alcohol, but when the scavenger concentration is lower, the oxidation of the antibiotic is favored.

Hydroxylation and oxidation are the most common stages in the reaction mechanism of processes involving the generation of hydroxyl radicals under photochemical treatments (Serna-Galvis et al., 2017). In this sense, the reaction of HO• with cephalexin could lead to the hydroxylation of the aromatic ring and/or the β-lactam ring. This occur probably, due to the electrophilic character of HO• and the high electron density on the aromatic ring, which can experiment electrophilic substitutions (Clayden et al., 2001; Serna-Galvis et al., 2017). Also have reported that the presence of hydroxyl radicals could promote oxidation reactions after the breakdown of the secondary amide group of the antibiotic and the opening of the β-lactam ring. In the case of the DOX removal, the molecule aromatic rings could experience electrophilic substitutions generated by HO• (Misak et al., 2019). Some researchers have reported two pathways of degradation of doxycycline under alkaline conditions; the first is that, the anionic form of the molecule provokes that one methyl of the amino group is oxidized to an aldehyde group while, HO• would attack the aromatic ring and/or the molecule double bonds. Also can occur that, HO• could attack the amino group, producing a ketone (Cong & Bao, 2020; Sunaric et al., 2009).

On the other hand, hydrogen peroxide is a powerful oxidant agent (E°=1.76 V), widely used for the prevention of contamination, and disinfection of wastewater (Cuerda-Correa et al., 2020). Figure 24 shows the $H_2O_2$ evolution during the removal of CPX and DOX. From this figure, it can be observed that after 120 min of reaction under dark conditions, the degree of $H_2O_2$ consume was only ~10.0% for CPX and ~15.0% for DOX, while the removal of each substrate was 29.1% and 30.0%, respectively (Figure 23). This allows to infer that exists a synergistic effect between oxidation of antibiotics with $H_2O_2$ and hydrolysis, which would be favored the decomposition of substrates. In addition, Figure 24 allows to apreciate that under optimized conditions and under the isopropyl alcohol presence, $H_2O_2$ is consumed almost completely during the reaction, which would be related to its decomposition under the effect of the sunlight radiation and its reaction with CPX and DOX.

a.



b.

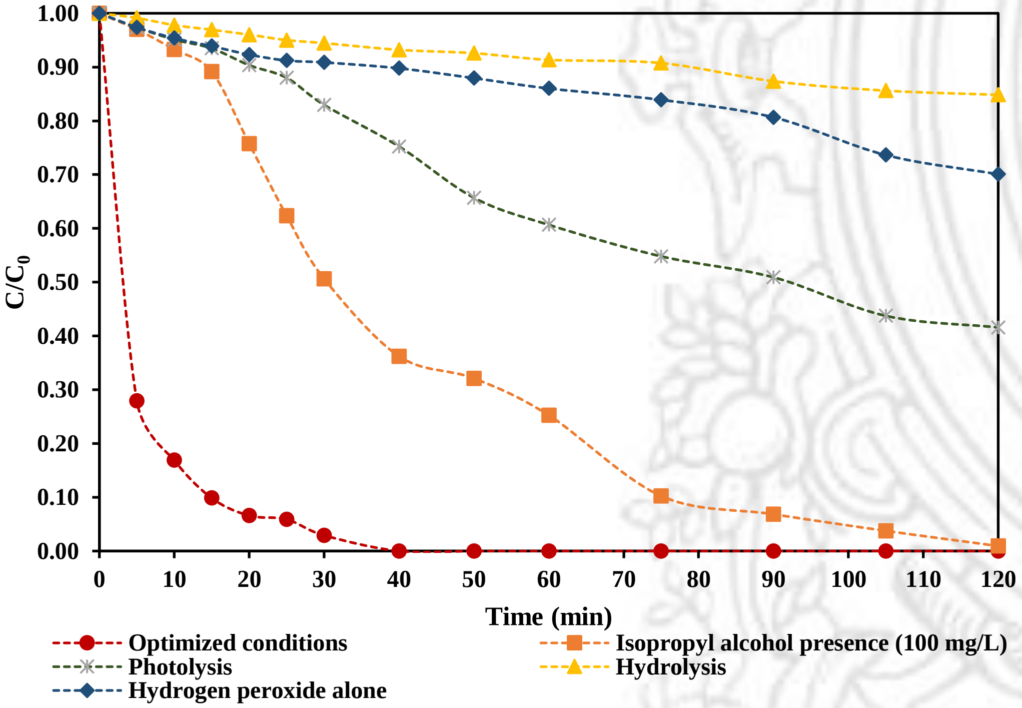
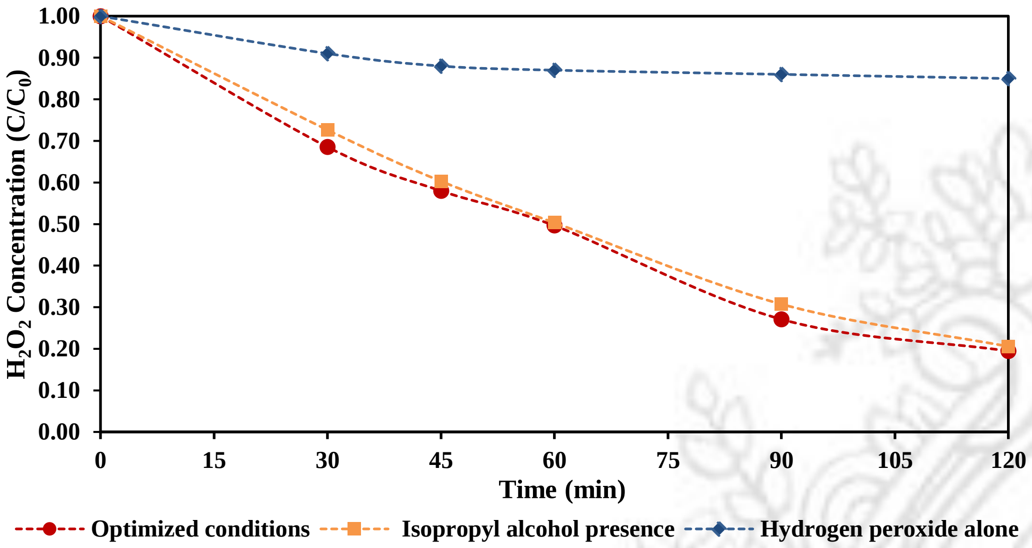


**Figure 23. a. CPX and b. DOX removal under optimized conditions of initial pH and initial dose of $H_2O_2$ using simulated sunlight radiation and $H_2O_2$ (pollutant initial concentration 2.0 mg $L^{-1}$, irradiance 500.0 $Wm^{-2}$, temperature: 35 ± 2 °C, reaction time: 120 min).**

a.



b.

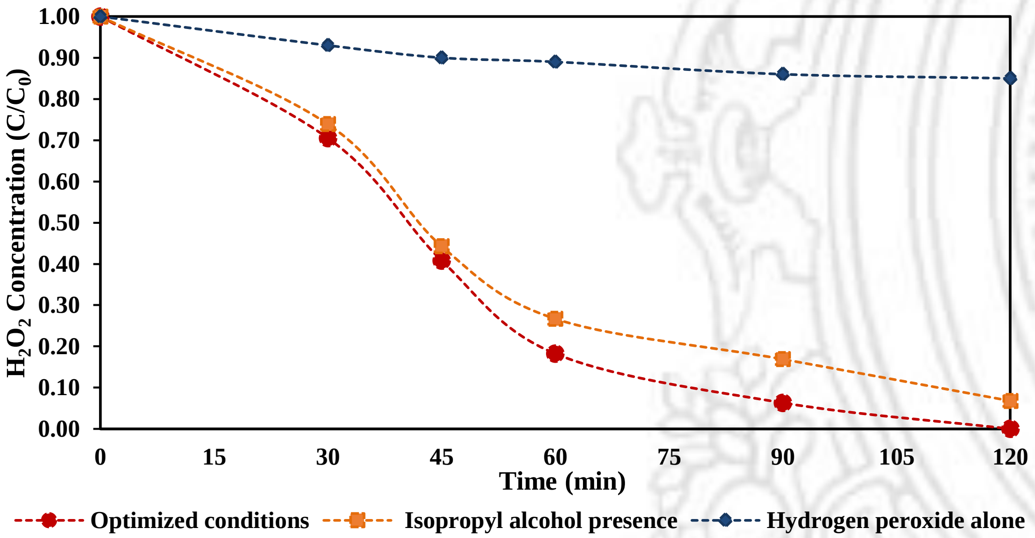


**Figure 24. $H_2O_2$ variation during a. CPX and b. DOX removal using simulated sunlight radiation and $H_2O_2$ (pollutant initial concentration 2.0 mg L$^{-1}$, irradiance 500.0 W m$^{-2}$, temperature: 35 ± 2 °C, reaction time: 120 min).**

### 5.2.3 Effect of pollutants initial concentration

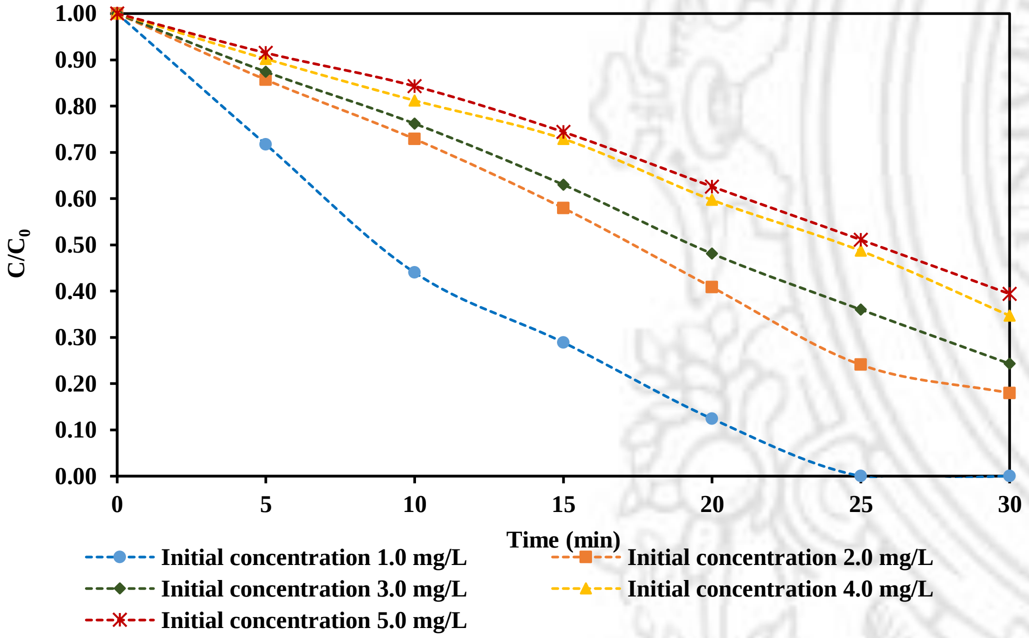
The effect of the initial concentration of the substrates in the UV/$H_2O_2$ technology was evaluated by varying this parameter in the range 1.0-5.0 mg L$^{-1}$. In general, authors have reported that reactions involving AOT, including UV/$H_2O_2$, satisfy a pseudo first-order reaction kinetics model (Equation 18, Ammar et al., 2016; Tan et al., 2013). In this sense, data depicted by Figure 25 indicate that after 30 min of UV/$H_2O_2$-treatment more than 60% of CPX and 80% of DOX were removed no matter the initial concentration. In addition, from this figure, it can be noted that under a higher pollutant initial concentration, extent of removal is lower, a situation that could be related to the fact that under higher pollutants concentrations, a higher amount of intermediates or byproducts is generated, which could mean a competition between CPX or DOX and byproducts for reacting with HO• radicals.

$$r = -\frac{dC}{dt} = kC \rightarrow -\ln\left(\frac{C}{C_0}\right) = kt \tag{18}$$

where $r$ is pollutant degradation/reaction rate, $C_0$ is the pollutant initial concentration and $k$ is the apparent pseudo first-order kinetic constant.

On the other hand, Figure 26 presents the relationship between pollutants initial concentration and the initial degradation rate (calculated as $\frac{\Delta C}{\Delta t}$ over the first five minutes of reaction). This figure indicates, that the experimental results fit adequately to a pseudo first-order reaction kinetics model ($R^2$> 0.910 for CPX and 0.998 for DOX) with associated apparent pseudo first-order kinetic constants 0.0078 $min^{-1}$ and 0.1275 $min^{-1}$. In this way, a pseudo first-order kinetic can be used to describe CPX and DOX using simulated sunlight radiation and $H_2O_2$, under the evaluated experimental conditions.

**a.**



**b.**

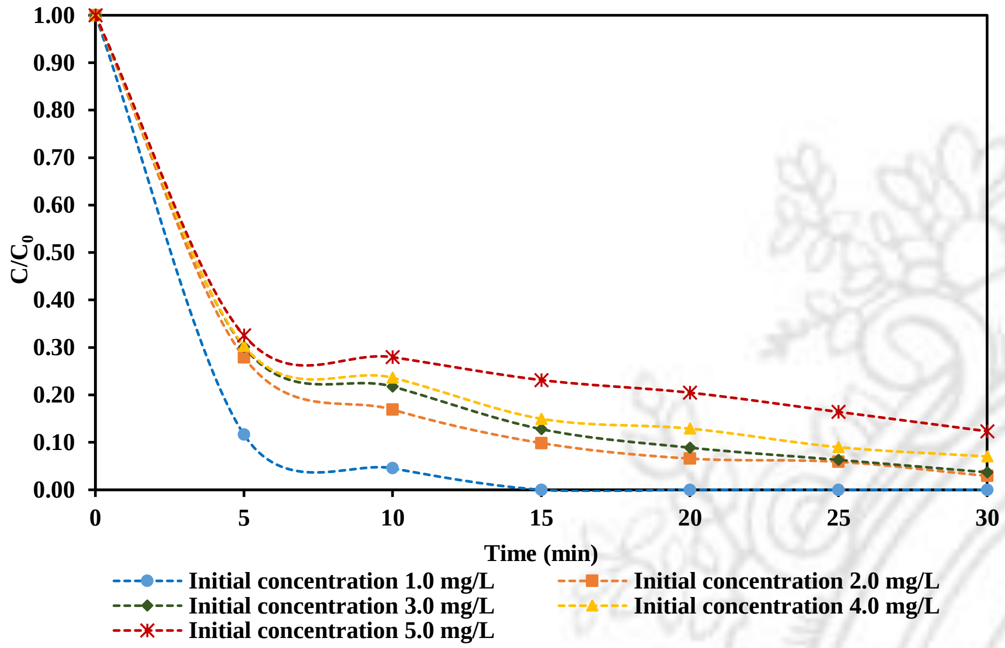
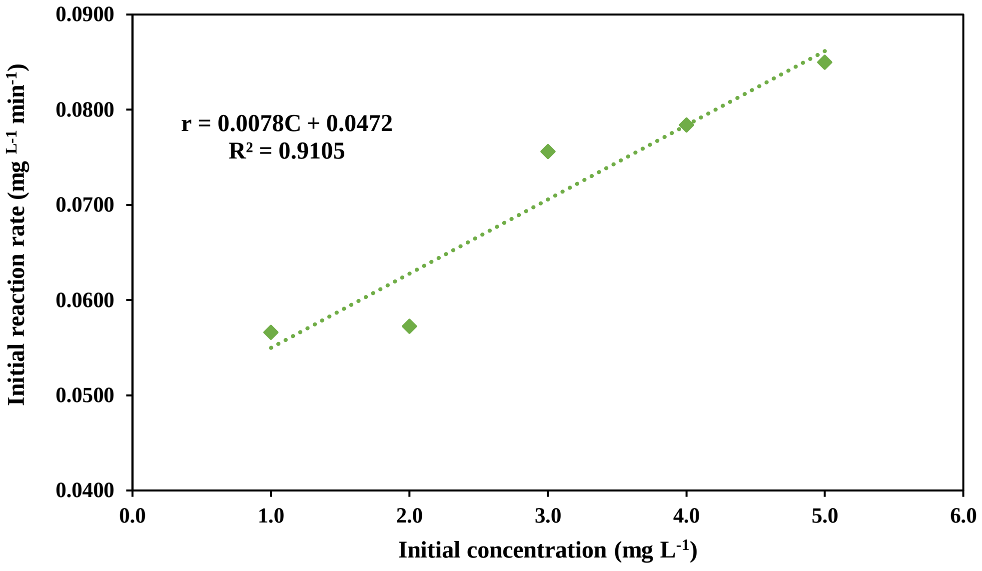


**Figure 25. Effect of initial concentration on a. CPX and b. DOX removal using simulated sunlight radiation and $H_2O_2$ under optimized conditions (irradiance 500.0 $Wm^{-2}$, temperature: 35 ± 2 °C, initial pH and $H_2O_2$ initial concentration optimal for each case, reaction time: 30 min).**

**a.**



**b.**

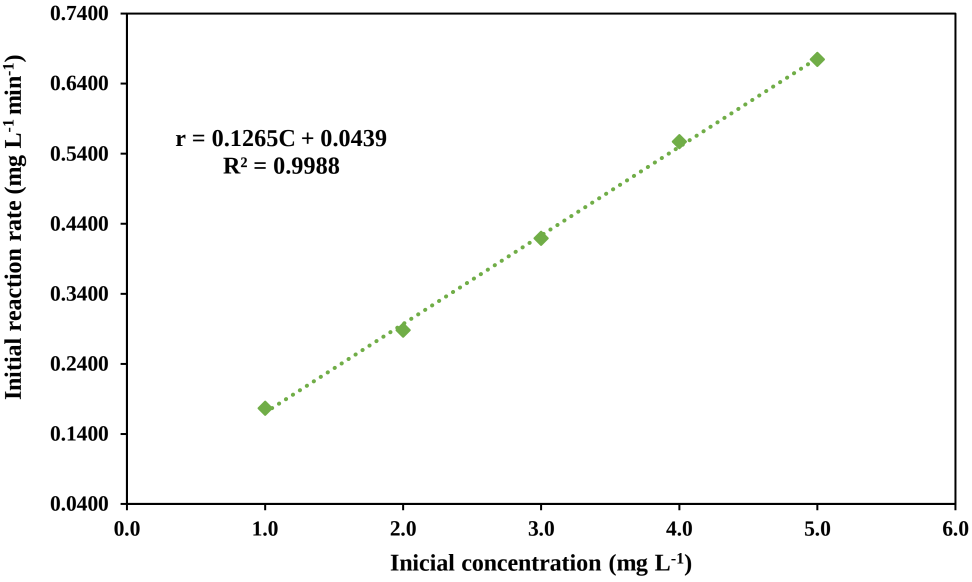


**Figure 26. Pollutants initial degradation rate as function of the initial concentration for a. CPX and b. DOX removal using simulated sunlight radiation and $H_2O_2$ under optimized conditions (irradiance 500.0 Wm$^{-2}$, temperature: 35 ± 2 °C, initial pH and $H_2O_2$ initial concentration optimal for each case, reaction time: 30 min).**

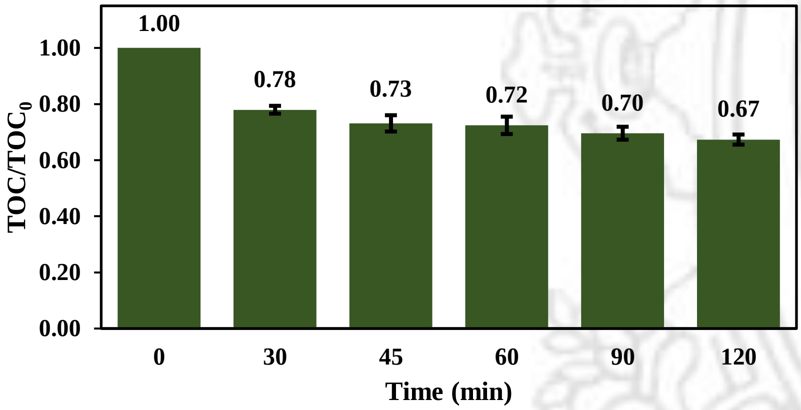
### 5.2.4 Mineralization and toxicity analysis

Complete oxidation of pollutants implies the reduction of the organic carbon content and an increase in the presence of ions (nitrates/sulfates) in the solution. Experiments were done using an initial dose of each substrate of 5.0 mg L-1 and under optimized conditions. In this way, Figures 27 and 28 indicate the results of the analysis of the variation of the total organic carbon and the ions concentration during CPX and DOX removal using simulated sunlight radiation and $H_2O_2$ under optimized conditions. From the figures, it can be observed that after 120 min of treatment, the degree of mineralization was ~33.0% for CPX and ~43.0% for DOX, whereas the presence of ions in the solution increased notably. These results suggest that the use of simulated sunlight radiation and $H_2O_2$ promoted the degradation of antibiotics but did not lead to its complete mineralization. According to equations 9 and 10, CPX and DOX could be subsequently converted into carbon dioxide, water and inorganic acids. Thus, 2.67 mg $NO_3^{-1}$ L$^{-1}$ and 1.38 mg $SO_4^{2-}$ L$^{-1}$ would be stoichiometrically obtained during CPX experiments, whereas for DOX 1.39 mg $NO_3^{-1}$ L$^{-1}$ will be obtained. Thus, Figure 38 shows that, after of 120 min of photo-treatment, the increase of $NO_3^{-1}$ and $SO_4^{2-}$ anions concentration for CPX experiments were 0.986 mg L$^{-1}$ and 1.299 mg L$^{-1}$, respectively, while the presence of $NO_3^{-1}$ was 0.383 mg L$^{-1}$ during DOX tests. In this sense, for CPX experiments, only 35.0% of $NO_3^{-1}$ and 36.0% of $SO_4^{2-}$ stoichiometrically possible were generated, whereas in DOX tests ~20.6% of the possible $NO_3^{-1}$ was obtained.

On the other hand, Figure 29a shows an increase in samples toxicity during the first 60 minutes of treatment, which it could imply that some of the formed by-products during the reaction are recalcitrant and it is necessary to use a post-treatment stage. In addition, some organic products generated could have more toxicity than CPX, which it could affect the water bodies quality. Al-Musawi et al., 2019; Antonin et al., 2019; Droguett et al., 2020 have identified some CPX by-products using photochemical advanced oxidation technologies, being HO• radical the main oxidant specie. Thus, 2-amino-N-[1- (5-methyl-3,6-dihydro-2H-[1,3]thiazin-2-yl)-2-oxo-ethyl]-2-phenylacetamide;2-amino-N-[1-hydroxy-2-(2-hydroxy-ethylamino)-2-mercaptoethyl]-2-phenyl-acetamide; 7-amino-3- hydroxy-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid; 3-methyl-8-oxo-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid); 3,8-dihydroxy-5-thia-1-aza-bicyclo[4.2.0]oct-2-ene-2-carboxylic acid and 2-amino-N-hydroxymethyl-2-phenyl-acetamide have been reported. In this way, the generation and accumulation of recalcitrant molecules of oxamic and oxalic carboxylic acids could lead to increase in the toxicity. According with Coledam et al., 2017, these CPX byproducts are due to hydroxylation reactions of the aromatic ring and/or the β-lactam ring, which have higher or same as toxic content as the parent compound.

Finally, Figure 29b indicates that toxicity reduction on DOX degradation was ~40. 0% after 120 min of UV/$H_2O_2$ treatment, which allows to infer that the use of sunlight simulated and $H_2O_2$ can also inhibit samples toxicity and reduce the potential risk of hazardous effects on ecosystems and human health.

**a.**



b.

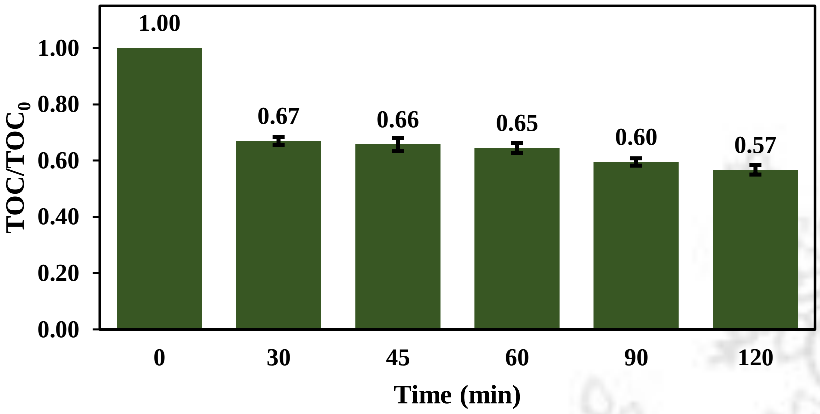
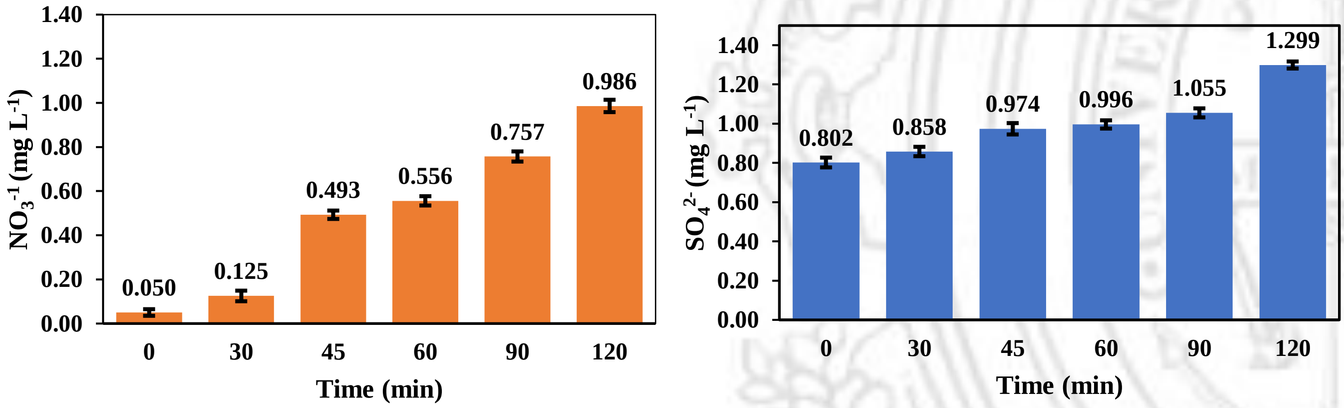


**Figure 27. Total organic carbon variation during a. CPX b. DOX removal under optimized conditions of initial pH and initial dose of $H_2O_2$ using simulated sunlight radiation and $H_2O_2$ (pollutant initial concentration 2.0 mg L$^{-1}$, irradiance 500.0 W m$^{-2}$, temperature: 35 ± 2 °C, reaction time: 120 min)**

a.



b.

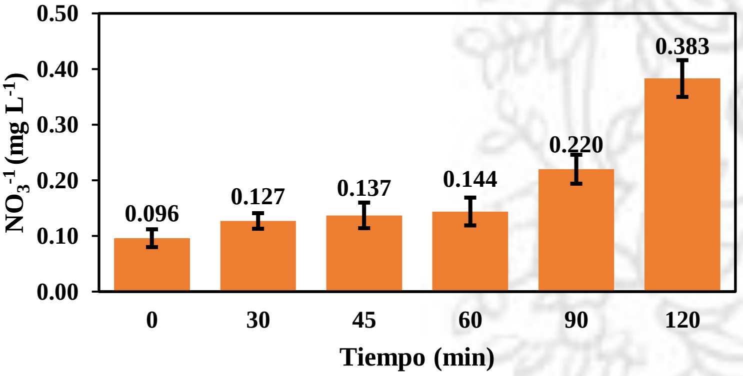


**Figure 28. a. Nitrate and sulfate ions concentration during CPX removal b. nitrate ion concentration during DOX removal under optimized conditions of initial pH and initial dose of $H_2O_2$ using simulated**

sunlight radiation and $H_2O_2$ (pollutant initial concentration 2.0 mg $L^{-1}$, irradiance 500.0 W $m^{-2}$, temperature: 35 ± 2 °C, reaction time: 120 min).**

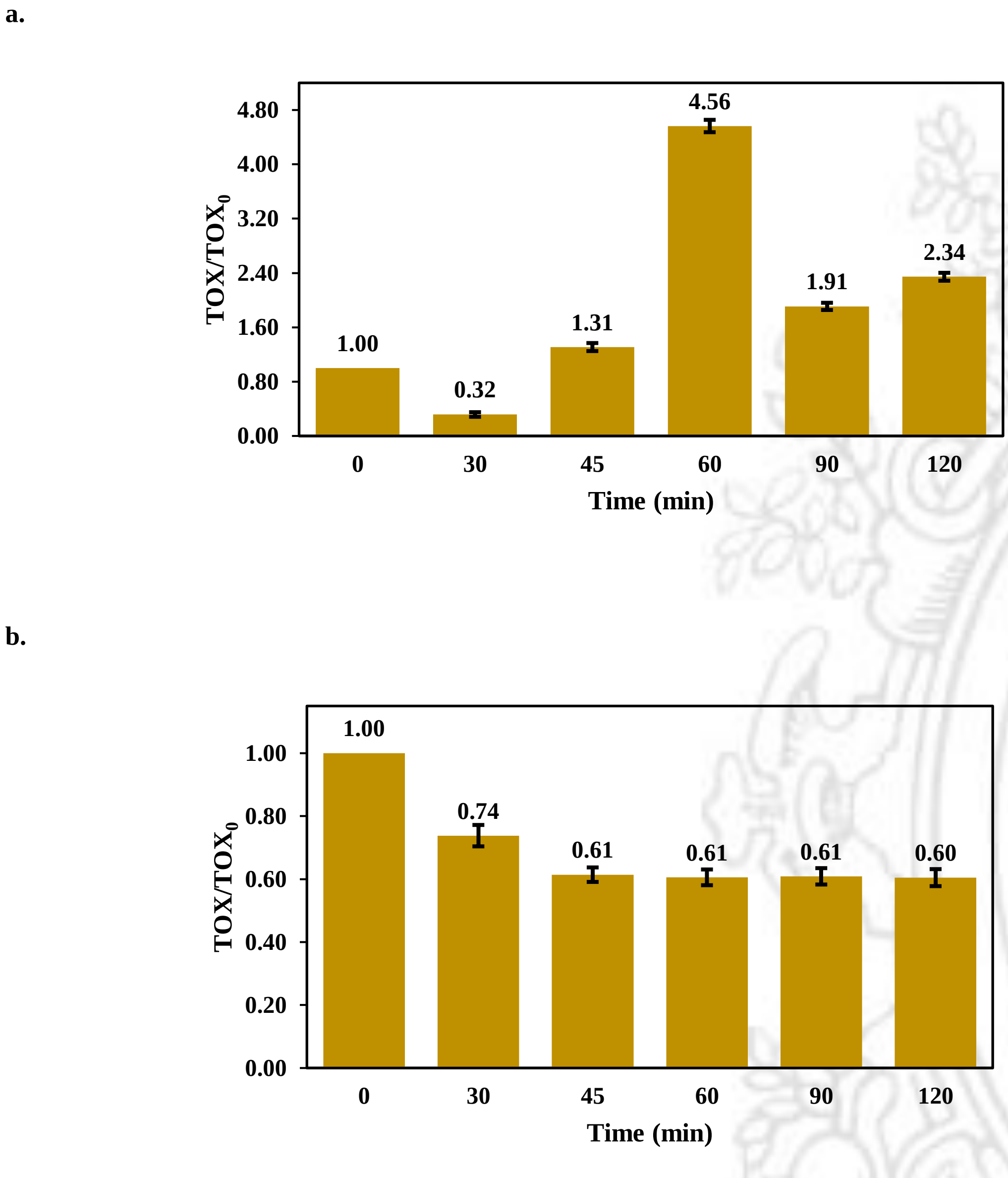


**Figure 29. Toxicity variation during a. CPX b. DOX removal under optimized conditions of initial pH and initial dose of $H_2O_2$ using simulated sunlight radiation and $H_2O_2$ (pollutant initial concentration 2.0 mg $L^{-1}$, irradiance 500.0 W $m^2$, temperature: 35 ± 2 °C, reaction time: 120 min).**

## 6. RECOMMENDATIONS AND FUTURE RESEARCHES

This document presents some relevant aspects related to the potential use of UV/$H_2O_2$ and US in the removal of CPX and DOX. However, it is important to highlight that some aspects need to be studied in future works in order to determine the reaction mechanisms and the potential application of the technologies at pilot or large scale, and in the treatment of real water (wastewater) samples. Some options that could be considered are:

- **To evaluate the effects of other operational factors such as frequency and temperature on CPX and DOX removal using US.**

- **To identify reaction byproducts.** According to obtained results, a complete mineralization of antibiotics using UV/$H_2O_2$ and US was not reached. This implies that part of the organic matter is being transformed into organic byproducts. The identification of these compounds would allow the design of post-treatment stages or the modification of the reaction conditions. In this way, the potential hazardous risk associated with this kind of pollutants would be minimized.
- **To evaluate the effect of water matrix.** Real wastewaters contain different types of organic and inorganic compounds that could inhibit or enhance CPX and DOX removal. In this sense, it is important to evaluate the effect of species like ions and natural organic matter on processes, and to stablish optimal conditions of reaction.
- **To combine technologies.** The results indicated that used AOT are able to remove target antibiotics completely. However, there are some limitations in terms of samples TOC and toxicity reduction. A combination of both technologies could help to increase the mineralization and the reduction of toxicity since peroxide could help US performance due to a potential higher radicals formation, and the action of UV radiation as disinfectant agent. In addition, US could help to reduce mass transfer problems inside the reaction media.

## 7. CONCLUSIONS

The removal of CPX and DOX antibiotics in aqueous samples was studied using UV/$H_2O_2$ and US. Experimental results demonstrated that the effect of operating parameters have a significant effect on antibiotics degradation. In US experiments, acid pH conditions and higher US power promote an increase on CPX and DOX removal, due mainly to the interaction between the ionic form of substrates and the amount of generated HO• radicals. Kinetic equations based on Langmuir-type mechanism and on pseudo-first order reaction kinetics were used to model the sonochemical degradation of studied antibiotics. The expression developed by Serpone et al. (1994) showed a better fit with the experimental data; in comparison with the Okitsu et al. (2005) and pseudo-first order models, indicating that pollutants degradation takes place at both the bubble-liquid interfacial region and in the bulk solution. In addition, mineralization and toxicity analysis showed that after 120 min of treatment CPX and DOX are being transformed into organic byproducts with less toxicity.

On the other hand, the use of simulated sunlight radiation and $H_2O_2$ was able to remove the antibiotics CPX and DOX from aqueous solutions, including considerable reductions of the organic matter content. Besides, the increase of some inorganic ions on the reaction could be associated to the formation of byproducts as $CO_2$, water, $HNO_3$ and $H_2SO_4$ (for CPX removal). In addition, it can be observed that a higher initial dose of $H_2O_2$ leads to an increase on the antibiotics removal. Antibiotics degradation rates increase with an increase in the substrate initial concentration, and under the evaluated experimental conditions, a pseudo-first-order kinetic model can be used to describe CPX and DOX removal.

Hydrolysis and photolysis (for CPX test) play a negligible role on substrates degradation. Experiments under the presence of isopropanol allowed to determine that HO• free radicals are the main specie responsible for each antibiotic elimination using UV/$H_2O_2$ and US. And, the evaluation of toxicity indicated that after 120 min of treatment, the solution toxicity was reduced in almost all processes.

Finally, the findings discussed throughout this document suggest that the UV/$H_2O_2$ and US technologies represent potential alternatives to remove CPX and DOX from aqueous solutions.

## 8. ASSOCIATED PRODUCTS

- **Scientific papers:**

  Rafael Santiago Cárdenas-Sierra, Henry Zúñiga-Benítez, Gustavo A. Peñuela (2020). **Experimental data on antibiotic cephalexin removal using hydrogen peroxide and simulated sunlight radiation at lab scale: Effects of pH and $H_2O_2$.** Data in Brief 30, 01-08. DOI: 10.1016/j.dib.2020.105437.

  Rafael Santiago Cárdenas-Sierra, Henry Zúñiga-Benítez, Gustavo A. Peñuela. **Elimination of cephalexin and doxycycline under low frequency ultrasound (In evaluation).**

- **Participation on academic events:**

  Rafael Santiago Cárdenas-Sierra, Henry Zúñiga-Benítez, Gustavo A. Peñuela (2019). **Remoción del antibiótico Cefalexina empleando $H_2O_2$ y luz solar simulada: Optimización de parámetros.** Memorias en libro: Diálogo intergeneracional de saberes ambientales. IV Congreso Nacional de Ciencias Ambientales, Universidad Autónoma de Occidente, Santiago de Calí. http://red.uao.edu.co//handle/10614/12407 **(Ponencia oral).**

### Acknowledgments

I want to thank the **Alcaldía de Medellín SAPIENCIA program** and the **Universidad de Antioquia Research Vice-Rectory** for their financial support of this research work. **Dr. Zúñiga-Benítez** for his interesting contributions that have helped me to improve this document substantially, and for his support during the development of the master’s program. I also want to thank **Dr. Gustavo A. Peñuela** for let me conduct this research in the GDCON research group. Finally, I want to thank **Dr. Carlos Fidel Granda Ramírez** and **Dra. Maria Isabel Mejía Correa** for their exhaustive revision and interesting contributions that have helped to substantially improve this manuscript.

## 9. REFERENCES

Afonso-Olivares, C., Fernández-Rodríguez, C., Ojeda-González, R. J., Sosa-Ferrera, Z., Santana-Rodríguez, J. J., & Rodríguez, J. M. D. (2016). Estimation of kinetic parameters and UV doses necessary to remove twenty-three pharmaceuticals from pre-treated urban wastewater by UV/$H_2O_2$. Journal of Photochemistry and Photobiology A: Chemistry, 329, 130–138.

Al-Hamadani, Y. A. J., Chu, K. H., Flora, J. R. V., Kim, D. H., Jang, M., Sohn, J., Joo, W., & Yoon, Y. (2016). Sonocatalytical degradation enhancement for ibuprofen and sulfamethoxazole in the presence of glass beads and single-walled carbon nanotubes. Ultrasonics Sonochemistry, 32, 440–448.

Al-Musawi, T. J., Kamani, H., Bazrafshan, E., Panahi, A. H., Silva, M. F., & Abi, G. (2019). Optimization the effects of physicochemical parameters on the degradation of cephalexin in sono-fenton reactor by using box-behnken response surface methodology. Catalysis Letters, 149(5), 1186–1196.

Alharbi, S. K., Price, W. E., Kang, J., Fujioka, T., & Nghiem, L. D. (2016). Ozonation of carbamazepine, diclofenac, sulfamethoxazole and trimethoprim and formation of major oxidation products. Desalination and Water Treatment, 57(60), 29340–29351.

Ameta, S. C., & Ameta, R. (2018). Advanced oxidation processes for wastewater treatment: Emerging green chemical technology. Advanced oxidation processes for wastewater treatment: Emerging Green Chemical Technology.

Ammar, H. B., Brahim, M. Ben, Abdelhédi, R., & Samet, Y. (2016). Enhanced degradation of metronidazole by sunlight via photo-Fenton process under gradual addition of hydrogen peroxide. Journal of Molecular Catalysis A: Chemical, 420, 222–227.

Anjali, R., & Shanthakumar, S. (2019). Insights on the current status of occurrence and removal of antibiotics in wastewater by advanced oxidation processes. Journal of Environmental Management, 246, 51–62.

Antonin, V. S., Aquino, J. M., Silva, B. F., Silva, A. J., & Rocha-Filho, R. C. (2019). Comparative study on the degradation of cephalexin by four electrochemical advanced oxidation processes: Evolution of oxidation intermediates and antimicrobial activity. Chemical Engineering Journal, 372, 1104–1112.

Bahamón, E. V. (2008). Estudio de la fotodegradación del clorotalonilo usando las técnicas de fenton y dióxido de titanio $TiO_2$ con radiación solar. Tesis para optar al título de Magíster en Ingeniería Ambiental. Universidad de Antioquia.

Bolobajev, J., Trapido, M., & Goi, A. (2016). Effect of iron ion on doxycycline photocatalytic and Fenton-based autocatatalytic decomposition. Chemosphere, 153, 220–226.

Borghi, A. A., Silva, M. F., Al Arni, S., Converti, A., & Palma, M. S. A. (2015). Doxycycline degradation by the oxidative fenton process.

Braeutigam, P., Franke, M., Schneider, R. J., Lehmann, A., Stolle, A., & Ondruschka, B. (2012). Degradation of carbamazepine in environmentally relevant concentrations in water by Hydrodynamic-Acoustic-Cavitation (HAC). Water Research, 46(7), 2469–2477.

Camargo-Perea, A. L., Rubio-Clemente, A., & Peñuela, G. A. (2020). Use of ultrasound as an advanced oxidation process for the degradation of emerging pollutants in water. Water, 12(4).

Cano-Carvajal, P. A., Jaramillo-Baquero, M., Zúñiga-Benítez, H., Londoño, Y. A., & Peñuela, G. A. (2020). Use of simulated sunlight radiation and hydrogen peroxide in azithromycin removal from aqueous solutions: Optimization & mineralization analysis. Emerging Contaminants, 6, 53–61.

Carbajo, J. B., Petre, A. L., Rosal, R., Herrera, S., Letón, P., García-Calvo, E., Fernández-Alba, A. R., & Perdigón-Melón, J. A. (2015). Continuous ozonation treatment of ofloxacin: Transformation products, water matrix effect and aquatic toxicity. Journal of Hazardous Materials, 292, 34–43.

Carlson, J. C., Stefan, M. I., Parnis, J. M., & Metcalfe, C. D. (2015). Direct UV photolysis of selected pharmaceuticals, personal care products and endocrine disruptors in aqueous solution. Water Research, 84, 350–361.

Chaukura, N., Gwenzi, W., Tavengwa, N., & Manyuchi, M. M. (2016). Biosorbents for the removal of synthetic organics and emerging pollutants: Opportunities and challenges for developing countries. Environmental Development, 19, 84–89.

Chiha, M., Hamdaoui, O., Baup, S., & Gondrexon, N. (2011). Sonolytic degradation of endocrine disrupting chemical 4-cumylphenol in water. Ultrasonics Sonochemistry, 18(5), 943–950.

Chiha, M., Hamdaoui, O., Baup, S., Gondrexon, N., & Pétrier, C. (2010). Effect of mineral and organic matrices on sonochemical degradation of 4-isopropylphenol at low concentrations. Separation Science and Technology, 45(11), 1587–1594.

Chiha, M., Merouani, S., Hamdaoui, O., Baup, S., Gondrexon, N., & Pétrier, C. (2010). Modeling of ultrasonic degradation of non-volatile organic compounds by Langmuir-type kinetics. Ultrasonics Sonochemistry, 17(5), 773–782.

Clayden, J., Greeves, N., Warren, S., & Wothers, P. (2001). Electrophilic aromatic substitution. Organic Chemestry, First, Oxford University Press, 547–579.

Coledam, D. A. C., Pupo, M. M. S., Silva, B. F., Silva, A. J., Eguiluz, K. I. B., Salazar-Banda, G. R., & Aquino, J. M. (2017). Electrochemical mineralization of cephalexin using a conductive diamond anode: A mechanistic and toxicity investigation. Chemosphere, 168, 638–647.

Cong, X., & Bao, J. (2020). Preparation of a $PbO_2$ Electrode with Graphene Interlayer and for Electrochemical Oxidation of Doxycycline. International Journal of Electrochemical Science, 15, 4352–4367.

Cuerda-Correa, E. M., Alexandre-Franco, M. F., & Fernández-González, C. (2020). Advanced oxidation processes for the removal of antibiotics from water. An overview. Water, 12(1), 102.

Da Silva Brito, G. F., Oliveira, R., Grisolia, C. K., Guirra, L. S., Weber, I. T., & de Almeida, F. V. (2019). Evaluation of advanced oxidative processes in biodiesel wastewater treatment. Journal of Photochemistry and Photobiology A: Chemistry, 375, 85–90.

Darvishi Cheshmeh Soltani, R., Mashayekhi, M., Jorfi, S., Khataee, A., Ghanadzadeh, M. J., & Sillanpää, M. (2018). Implementation of martite nanoparticles prepared through planetary ball milling as a heterogeneous activator of oxone for degradation of tetracycline antibiotic: Ultrasound and peroxy-enhancement. Chemosphere, 210, 699–708.

De la Cruz, N., Giménez, J., Esplugas, S., Grandjean, D., De Alencastro, L. F., & Pulgarín, C. (2012). Degradation of 32 emergent contaminants by UV and neutral photo-fenton in domestic wastewater effluent previously treated by activated sludge. Water Research, 46(6), 1947–1957.

De Laat, J., & Stefan, M. (2018). Chapter 9: UV/Chlorine process. Advanced oxidation processes for water treatment: Fundamentals and applications, 383–428.

Deng, J., Shao, Y., Gao, N., Xia, S., Tan, C., Zhou, S., & Hu, X. (2013). Degradation of the antiepileptic drug carbamazepine upon different UV-based advanced oxidation processes in water. Chemical Engineering Journal, 222, 150–158.

Deojay, D. M., Sostaric, J. Z., & Weavers, L. K. (2011). Exploring the effects of pulsed ultrasound at 205 and 616 kHz on the sonochemical degradation of octylbenzene sulfonate. Ultrasonics Sonochemistry, 18(3), 801–809.

Doménech, X., Jardim, W., & Litter, M. (2003). Procesos avanzados de oxidación para la eliminación de contaminantes. CYTED VIII-G.

Droguett, C., Salazar, R., Brillas, E., Sirés, I., Carlesi, C., Marco, J. F., & Thiam, A. (2020). Treatment of antibiotic cephalexin by heterogeneous electrochemical Fenton-based processes using chalcopyrite as sustainable catalyst. Science of the Total Environment, 740, 140154.

Du, J., Zhao, H., Liu, S., Xie, H., Wang, Y., & Chen, J. (2017). Antibiotics in the coastal water of the South Yellow Sea in China: Occurrence, distribution and ecological risks. Science of the Total Environment, 595, 521–527.

Dunia E., S., Doña-Rodríguez., J. M., Araña, J., Fernández-Rodríguez, C., González-Díaz, O., Pérez-Peña, J., & Silva, A. M. T. (2013). Optimization of the degradation of imazalil by photocatalysis: Comparison between commercial and lab-made photocatalysts. Applied Catalysis B: Environmental, 138–139, 391–400.

Estrada-Flórez, S. E., Serna-Galvis, E. A., & Torres-Palma, R. A. (2020). Photocatalytic vs. sonochemical removal of antibiotics in water: Structure-degradability relationship, mineralization, antimicrobial activity, and matrix effects. Journal of Environmental Chemical Engineering, 8(5), 104359.

Gavrilescu, M., Demnerová, K., Aamand, J., Agathos, S., & Fava, F. (2015). Emerging pollutants in the environment: Present and future challenges in biomonitoring, ecological risks and bioremediation. New Biotechnology, 32(1), 147–156.

Geissen, V., Mol, H., Klumpp, E., Umlauf, G., Nadal, M., Van der Ploeg, M., Van der, Z., Sjoerd, E., & Ritsema, C. J. (2015). Emerging pollutants in the environment: A challenge for water resource management. International Soil and Water Conservation Research, 3(1), 57–65.

Giraldo, A. L., Peñuela, G. A., Torres-Palma, R. A., Pino, N. J., Palominos, R. A., & Mansilla, H. D. (2010). Degradation of the antibiotic oxolinic acid by photocatalysis with $TiO_2$ in suspension. Water Research, 44(18), 5158–5167.

Giri, R. R., Ozaki, H., Takayanagi, Y., Taniguchi, S., & Takanami, R. (2011). Efficacy of ultraviolet radiation and hydrogen peroxide oxidation to eliminate large number of pharmaceutical compounds in mixed solution. International Journal of Environmental Science and Technology, 8(1), 19–30.

Gogoi, A., Mazumder, P., Tyagi, V. K., Tushara Chaminda, G. G., An, A. K., & Kumar, M. (2017). Occurrence and fate of emerging contaminants in water environment: A review. Groundwater for Sustainable Development, 6, 169–180.

Guo, W., Wang, H., Shi, Y., & Zhang, G. (2010). Sonochemical degradation of the antibiotic cephalexin in aqueous solution. Water Research Commission, 36(5), 651–654.

Guzman-Duque, F., Pétrier, C., Pulgarin, C., Peñuela, G., & Torres-Palma, R. A. (2011). Effects of sonochemical parameters and inorganic ions during the sonochemical degradation of crystal violet in water. Ultrasonics Sonochemistry, 18(1), 440–446.

Hu, Q., Zhang, C., Wang, Z., Chen, Y., Mao, K., Zhang, X., Xiong, Y., & Zhu, M. (2008). Photodegradation of methyl tert-butyl ether (MTBE) by UV/$H_2O_2$ and UV/$TiO_2$. Journal of Hazardous Materials, 154(1–3), 795–803.

Huang, B., Wang, H. C., Cui, D., Zhang, B., Chen, Z. B., & Wang, A. J. (2018). Treatment of pharmaceutical wastewater containing B-lactams antibiotics by a pilot-scale anaerobic membrane bioreactor (AnMBR). Chemical Engineering Journal, 341, 238–247.

Huang, T., Zhang, G., Chong, S., Liu, Y., Zhang, N., Fang, S., & Zhu, J. (2017). Effects and mechanism of diclofenac degradation in aqueous solution by US/$Zn^0$. Ultrasonics Sonochemistry, 37, 676–685.

Jaramillo-Baquero, M., Zúñiga-Benítez, H., & Peñuela, G. A. (2020). Use of photo-fenton for macrolide antibiotic azithromycin removal. Acta Periodica Technologica, 51, 1–206.

Jaramillo, N. A. (2004). Fotodegradación de cianuro mediante fotocatálisis heterogénea con $TiO_2$, utilizando colector solar y lámpara de luz ultravioleta. Tesis para optar al título de Magíster en Ingeniería Ambiental. Universidad de Antioquia.

Jiang, J. Q., Zhou, Z., & Sharma, V. K. (2013). Occurrence, transportation, monitoring and treatment of emerging micro-pollutants in waste water - A review from global views. Microchemical Journal, 110, 292–300.

Jouanneau, S., Durand-Thouand, M.-J., & Thouand, G. (2016). Design of a toxicity biosensor based on Aliivibrio fischeri entrapped in a disposable card. Environmental Science and Pollution Research, 23, 4340–4345.

Kanakaraju, D., Glass, B. D., & Oelgemöller, M. (2018). Advanced oxidation process-mediated removal of pharmaceuticals from water: A review. Journal of Environmental Management, 219, 189–207.

Kang, H. J., Lim, M. Y., & Kwon, J. H. (2012). Effects of adsorption onto silica sand particles on the hydrolysis of tetracycline antibiotics. Journal of Environmental Monitoring, 14(7), 1853–1859.

Khosravi, R., Zarei, A., Heidari, M., Ahmadfazeli, A., Vosughi, M., & Fazlzadeh, M. (2018). Application of ZnO and $TiO_2$ nanoparticles coated onto montmorillonite in the presence of $H_2O_2$ for efficient removal of cephalexin from aqueous solutions. Korean Journal of Chemical Engineering, 35(4), 1000–1008.

Kim, I., Yamashita, N., & Tanaka, H. (2009). Performance of UV and UV/$H_2O_2$ processes for the removal of pharmaceuticals detected in secondary effluent of a sewage treatment plant in Japan. Journal of Hazardous Materials, 166(2–3), 1134–1140.

Kimura, T., Sakamoto, T., Leveque, J. M., Sohmiya, H., Fujita, M., Ikeda, S., & Ando, T. (1996). Standardization of ultrasonic power for sonochemical reaction. Ultrasonics Sonochemistry, 3(3), 157–161.

Kıdak, R., & Doğan, Ş. (2018). Medium-high frequency ultrasound and ozone based advanced oxidation for amoxicillin removal in water. Ultrasonics Sonochemistry, 40, 131–139.

Klamerth, N., Malato, S., Agüera, A., & Fernández-Alba, A. (2013). Photo-Fenton and modified photo-Fenton at neutral pH for the treatment of emerging contaminants in wastewater treatment plant effluents: A comparison. Water Research, 47(2), 833–840.

Klamerth, N., Malato, S., Agüera, A., Fernández-Alba, A., & Mailhot, G. (2012). Treatment of municipal wastewater treatment plant effluents with modified photo-fenton as a tertiary treatment for the degradation of micro pollutants and disinfection. Environmental Science and Technology, 46(5), 2885–2892.

Kong, Y., Wang, L., Ge, Y., Su, H., & Li, Z. (2019). Lignin xanthate resin–bentonite clay composite as a highly effective and low-cost adsorbent for the removal of doxycycline hydrochloride antibiotic and mercury ions in water. Journal of Hazardous Materials, 368, 33–41.

Lado-Ribeiro, A. R., Moreira, N. F. F., Li Puma, G., & Silva, A. M. T. (2019). Impact of water matrix on the removal of micropollutants by advanced oxidation technologies. Chemical Engineering Journal, 363, 155–173.

Lan, M., Di, Y., Zhu, X., Ng, T. W., Xia, J., Liu, W., Meng, X., Wang, P., Lee, C. S., & Zhang, W. (2015). A carbon dot-based fluorescence turn-on sensor for hydrogen peroxide with a photo-induced electron transfer mechanism. Chemical Communications, 51(85), 15574–15577.

Legnoverde, M. S., Simonetti, S., & Basaldella, E. I. (2014). Influence of pH on cephalexin adsorption onto SBA-15 mesoporous silica: Theoretical and experimental study. Applied Surface Science, 300, 37–42.

Lianou, A., Frontistis, Z., Chatzisymeon, E., Antonopoulou, M., Konstantinou, I., & Mantzavinos, D. (2018). Sonochemical oxidation of piroxicam drug: effect of key operating parameters and degradation pathways. Journal of Chemical Technology and Biotechnology, 93(1), 28–34.

Lingzhi, L., Haojie, G., Dan, G., Hongmei, M., Yang, L., Mengdie, J., Chengkun, Z., & Xiaohui, Z. (2018). The role of two-component regulatory system in β-lactam antibiotics resistance. Microbiological Research, 215, 126–129.

Liu, X., Yin, H., Weng, C. X., & Cai, Y. (2016). Low-frequency ultrasound enhances antimicrobial activity of Colistin-Vancomycin ombination against pan-resistant biofilm of acinetobacter baumannii. Ultrasound in Medicine and Biology, 42(8), 1968–1975.

Lopez-Alvarez, B., Torres-Palma, R. A., Ferraro, F., & Peñuela, G. (2012). Solar photo-Fenton treatment of carbofuran: Analysis of mineralization, toxicity, and organic by-products. Journal of Environmental Science and Health - Part A Toxic/Hazardous Substances and Environmental Engineering, 47(13), 2141–2150.

López, J. J., & Garay, A. M. (2016). Estudio de utilización de antibióticos en el servicio de consulta externa de un hospital de tercer nivel de la ciudad de Bogotá. Revista Colombiana de Ciencias Químico-Farmaceuticas, 45(1), 35–47.

Lou, W., Kane, A., Wolbert, D., Rtimi, S., & Assadi, A. A. (2017). Study of a photocatalytic process for removal of antibiotics from wastewater in a falling film photoreactor: Scavenger study and process intensification feasibility. Chemical Engineering and Processing: Process Intensification, 122, 213–221.

Marín, J. M. (2002). Fotodegradación sensibilizada con $TiO_2$ y $Fe^{+3}$ de los pesticidas metomil y malatión en aguas. Tesis para optar por el título de Magister en Ingeniería Ambiental. Universidad de Antioquia.

Markic, M., Cvetnic, M., Ukic, S., Kusic, H., Bolanca, T., & Bozic, A. L. (2018). Influence of process parameters on the effectiveness of photooxidative treatment of pharmaceuticals. Journal of Environmental Science and Health - Part A Toxic/Hazardous Substances and Environmental Engineering, 53(4), 338–351.

Méndez-Arriaga, F., Torres-Palma, R. A., Pétrier, C., Esplugas, S., Gimenez, J., & Pulgarin, C. (2008). Ultrasonic treatment of water contaminated with ibuprofen. Water Research, 42(16), 4243–4248.

Miao, M. S., Liu, Q., Shu, L., Wang, Z., Liu, Y. Z., & Kong, Q. (2016). Removal of cephalexin from effluent by activated carbon prepared from alligator weed: Kinetics, isotherms, and thermodynamic analyses. Process Safety and Environmental Protection, 104, 481–489.

Michael, I., Hapeshi, E., Michael, C., & Fatta-Kassinos, D. (2010). Solar Fenton and solar $TiO_2$ catalytic treatment of ofloxacin in secondary treated effluents: Evaluation of operational and kinetic parameters. Water Research, 44(18), 5450–5462.

Mierzwa, J. C., Rodrigues, R., & Teixeira, A. C. S. C. (2018). UV-Hydrogen Peroxide Processes. Advanced Oxidation Processes for Wastewater Treatment: Emerging Green Chemical Technology, 13–48.

Miklos, D. B., Remy, C., Jekel, M., Linden, K. G., Drewes, J. E., & Hübner, U. (2018). Evaluation of advanced oxidation processes for water and wastewater treatment – A critical review. Water Research, 139, 118–131.

Mirzaei, R., Yunesian, M., Nasseri, S., Gholami, M., Jalilzadeh, E., Shoeibi, S., & Mesdaghinia, A. (2018). Occurrence and fate of most prescribed antibiotics in different water environments of Tehran, Iran. Science of the Total Environment, 619–620, 446–459.

Misak, A., Kurakova, L., Goffa, E., Brezova, V., Grman, M., Ondriasova, E., Chovanec, M., & Ondrias, K. (2019). Sulfide (Na2S) and Polysulfide (Na2S2) Interacting with Doxycycline Produce/Scavenge Superoxide and Hydroxyl Radicals and Induce/Inhibit DNA Cleavage. Molecules, 24(6), 1148.

Monteagudo, J. M., El-taliawy, H., Durán, A., Caro, G., & Bester, K. (2018). Sono-activated persulfate oxidation of diclofenac: Degradation, kinetics, pathway and contribution of the different radicals involved. Journal of Hazardous Materials, 357, 457–465.

Muñoz-Calderón, A., Zúñiga-Benítez, H., Valencia, S. H., Rubio-Clemente, A., Upegui, S. A., & Peñuela, G. A. (2020). Use of low frequency ultrasound for water treatment: Data on azithromycin removal. Data in Brief, 31, 105947.

Naeimi, S., & Faghihian, H. (2017). Application of novel metal organic framework, MIL-53(Fe) and its magnetic hybrid: For removal of pharmaceutical pollutant, doxycycline from aqueous solutions. Environmental Toxicology and Pharmacology, 53, 121–132.

Okitsu, K., Iwasaki, K., Yobiko, Y., Bandow, H., Nishimura, R., & Maeda, Y. (2005). Sonochemical degradation of azo dyes in aqueous solution: A new heterogeneous kinetics model taking into account the local concentration of OH radicals and azo dyes. Ultrasonics Sonochemistry, 12(4), 255–262.

Ospino-Atehortúa, B., Zúñiga-Benítez, H., & A. Peñuela, G. (2021). Potential application of persulfate and simulated sunlight radiation on azithromycin removal. Environmental Engineering Research, 26(3).

Oturan, M. A., & Aaron, J. J. (2014). Advanced oxidation processes in water/wastewater treatment: Principles and applications. A review. Critical Reviews in Environmental Science and Technology, 44(23), 2577–2641.

Pabari, R. M., & Ramtoola, Z. (2012). Application of face centred central composite design to optimise compression force and tablet diameter for the formulation of mechanically strong and fast disintegrating orodispersible tablets. International Journal of Pharmaceutics, 430(1–2), 18–25.

Pan, Y., Zhang, Y., Zhou, M., Cai, J., & Tian, Y. (2019). Enhanced removal of antibiotics from secondary wastewater effluents by novel UV/pre-magnetized $Fe^0/H_2O_2$ process. Water Research, 153, 144–159.

Papoutsakis, S., Afshari, Z., Malato, S., & Pulgarin, C. (2015). Elimination of the iodinated contrast agent iohexol in water, wastewater and urine matrices by application of photo-Fenton and ultrasound advanced oxidation processes. Journal of Environmental Chemical Engineering, 3(3), 2002–2009.

Peiris, C., Gunatilake, S. R., Mlsna, T. E., Mohan, D., & Vithanage, M. (2017). Biochar based removal of antibiotic sulfonamides and tetracyclines in aquatic environments: A critical review. Bioresource Technology, 246, 150–159.

Peña-Guzmán, C., Ulloa-Sánchez, S., Mora, K., Helena-Bustos, R., Lopez-Barrera, E., Alvarez, J., & Rodriguez-Pinzón, M. (2019). Emerging pollutants in the urban water cycle in Latin America: A review of the current literature. Journal of Environmental Management, 237, 408–423.

Pereira, L. C., de Souza, A. O., Bernardes, M. F. F., Pazin, M., Tasso, M. J., Pereira, P. H., & Dorta, D. J. (2015). A perspective on the potential risks of emerging contaminants to human and environmental health. Environmental Science and Pollution Research, 22(18), 13800–13823.

Pérez, M. H., Vega, L. P., Zúñiga-Benítez, H., & Peñuela, G. A. (2018). Comparative Degradation of Alachlor Using Photocatalysis and Photo-Fenton. Water, Air, and Soil Pollution, 229(11), 346.

Periša, M., Babić, S., Škorić, I., Frömel, T., & Knepper, T. P. (2013). Photodegradation of sulfonamides and their N4-acetylated metabolites in water by simulated sunlight irradiation: Kinetics and identification of photoproducts. Environmental Science and Pollution Research, 20(12), 8934–8946.

Pétrier, C. (2014). The use of power ultrasound for water treatment. Power Ultrasonics: Applications of High-Intensity Ultrasound, 940–972.

Phaechamud, T., Chanyaboonsub, N., & Setthajindalert, O. (2016). Doxycycline hyclate-loaded bleached shellac in situ forming microparticle for intraperiodontal pocket local delivery. European Journal of Pharmaceutical Sciences, 93, 360–370.

Pouliquen, H., Delépée, R., Larhantec-Verdier, M., Morvan, M. L., & Le Bris, H. (2007). Comparative hydrolysis and photolysis of four antibacterial agents (oxytetracycline oxolinic acid, flumequine and florfenicol) in deionised water, freshwater and seawater under abiotic conditions. Aquaculture, 262(1), 23–28.

Prakash Maran, J., Manikandan, S., Vigna Nivetha, C., & Dinesh, R. (2013). Ultrasound assisted extraction of bioactive compounds from Nephelium lappaceum L. fruit peel using central composite face centered response surface design. Arabian Journal of Chemistry, 10, S1145–S1157.

Prieto-Rodríguez, L., Oller, I., Klamerth, N., Agüera, A., Rodríguez, E. M., & Malato, S. (2013). Application of solar AOPs and ozonation for elimination of micropollutants in municipal wastewater treatment plant effluents. Water Research, 47(4), 1521–1528.

Rao, Y., Yang, H., Xue, D., Guo, Y., Qi, F., & Ma, J. (2016). Sonolytic and sonophotolytic degradation of Carbamazepine: Kinetic and mechanisms. Ultrasonics Sonochemistry, 32, 371–379.

Rivas, J., Gimeno, O., Borralho, T., & Sagasti, J. (2011). UV-C and UV-C/peroxide elimination of selected pharmaceuticals in secondary effluents. Desalination, 279(1–3), 115–120.

Rodríguez-Chueca, J., Varella della Giustina, S., Rocha, J., Fernandes, T., Pablos, C., Encinas, Á., Barceló, D., Rodríguez-Mozaz, S., Manaia, C. M., & Marugán, J. (2019). Assessment of full-scale tertiary wastewater treatment by UV-C based-AOPs: Removal or persistence of antibiotics and antibiotic resistance genes? Science of The Total Environment, 652, 1051–1061.

Rodriguez-Mozaz, S., Chamorro, S., Marti, E., Huerta, B., Gros, M., Sànchez-Melsió, A., Borrego, C. M., Barceló, D., & Balcázar, J. L. (2015). Occurrence of antibiotics and antibiotic resistance genes in hospital and urban wastewaters and their impact on the receiving river. Water Research, 69, 234–242.

Rodriguez-Narvaez, O. M., Peralta-Hernandez, J. M., Goonetilleke, A., & Bandala, E. R. (2017). Treatment technologies for emerging contaminants in water: A review. Chemical Engineering Journal, 323, 361–380.

Rozman, D., Hrkal, Z., Váňa, M., Vymazal, J., & Boukalová, Z. (2017). Occurrence of Pharmaceuticals in Wastewater and Their Interaction with Shallow Aquifers: A Case Study of Horní Beřkovice, Czech Republic. Water, 9(3), 218.

Rubio-Clemente, A. (2017). Application of advanced oxidation processes for the degradation of emerging pollutants from water. Tesis para optar al título de Doctor en Ingeniería Ambiental. Universidad de Antioquia.

Rubio-Clemente, A., Chica, E., & Peñuela, G. A. (2018). Photovoltaic array for powering advanced oxidation processes: Sizing, application and investment costs for the degradation of a mixture of anthracene and benzo[a]pyrene in natural water by the UV/$H_2O_2$ system. Journal of Environmental Chemical Engineering, 6(2), 2751–2761.

Rubio-Clemente, A., Torres-Palma, R. A., & Peñuela, G. A. (2014). Removal of polycyclic aromatic hydrocarbons in aqueous environment by chemical treatments: A review. Science of the Total Environment, 478, 201–225.

Rubio Clemente, A., Cardona, C. A., Chica, E., & Peñuerla, G. . (2017). Sensitive spectrophotometric determination of hydrogen peroxide in aqueous samples from advanced oxidation processes: Evaluation of possible interferences. Afinidad: Revista de Química Teórica y Aplicada, 74(579), 161–168.

Sabri, N. A., Schmitt, H., Van Der Zaan, B., Gerritsen, H. W., Zuidema, T., Rijnaarts, H. H. M., & Langenhoff, A. A. M. (2020). Prevalence of antibiotics and antibiotic resistance genes in a wastewater effluent-receiving river in the Netherlands. Journal of Environmental Chemical Engineering, 8(1), 102245.

Saitoh, T., Shibata, K., Fujimori, K., & Ohtani, Y. (2017). Rapid removal of tetracycline antibiotics from water by coagulation-flotation of sodium dodecyl sulfate and poly(allylamine hydrochloride) in the presence of Al(III) ions. Separation and Purification Technology, 187, 76–83.

Saitoh, T., & Shibayama, T. (2016). Removal and degradation of β-lactam antibiotics in water using didodecyldimethylammonium bromide-modified montmorillonite organoclay. Journal of Hazardous Materials, 317, 677–685.

Salazar, H., Martins, P. M., Santos, B., Fernandes, M. M., Reizabal, A., Sebastián, V., Botelho, G., Tavares, C. J., Vilas-Vilela, J. L., & Lanceros-Mendez, S. (2020). Photocatalytic and antimicrobial multifunctional nanocomposite membranes for emerging pollutants water treatment applications. Chemosphere, 250, 126299.

Seid-Mohammadi, A., Bahrami, M., Omari, S., & Asadi, F. (2019). Removal of Cephalexin From Aqueous Solutions Using Magnesium Oxide/Granular Activated Carbon Hybrid Photocatalytic Process. Avicenna Journal of Environmental Health Engineering, 6(1), 24–32.

Sepyani, F., Darvishi Cheshmeh Soltani, R., Jorfi, S., Godini, H., & Safari, M. (2018). Implementation of continuously electro-generated $Fe_3O_4$ nanoparticles for activation of persulfate to decompose amoxicillin antibiotic in aquatic media: UV254 and ultrasound intensification. Journal of Environmental Management, 224, 315–326.

Serna-Galvis, E., Giraldo-Aguirre, A. L., Silva-Agredo, J., Flórez-Acosta, O. A., & Torres-Palma, R. A. (2017). Removal of antibiotic cloxacillin by means of electrochemical oxidation, $TiO_2$ photocatalysis, and photo-Fenton processes: analysis of degradation pathways and effect of the water matrix on the elimination of antimicrobial activity. Environmental Science and Pollution Research, 24(7), 6339–6352.

Serna-Galvis, E., Silva-Agredo, J., Giraldo-Aguirre, A. L., Flórez-Acosta, O. A., & Torres-Palma, R. A. (2016). High frequency ultrasound as a selective advanced oxidation process to remove penicillinic antibiotics and eliminate its antimicrobial activity from water. Ultrasonics Sonochemistry, 31, 276–283.

Serna-Galvis, E., Silva-Agredo, J., Giraldo-Aguirre, A. L., & Torres-Palma, R. A. (2015). Sonochemical degradation of the pharmaceutical fluoxetine: Effect of parameters, organic and inorganic additives and combination with a biological system. Science of the Total Environment, 524–525, 354–360.

Serna-Galvis, E., Silva-Agredo, J., Giraldo, A. L., Flórez, O. A., & Torres-Palma, R. A. (2016). Comparison of route, mechanism and extent of treatment for the degradation of a β-lactam antibiotic by $TiO_2$ photocatalysis, sonochemistry, electrochemistry and the photo-Fenton system. Chemical Engineering Journal, 284, 953–962.

Serpone, N., Terzian, R., Hidaka, H., & Pelizzetti, E. (1994). Ultrasonic induced dehalogenation and oxidation of 2-, 3-, and 4-chlorophenol in air-equilibrated aqueous media. Similarities with irradiated semiconductor particulates. Journal of Physical Chemistry, 98(10), 2634–2640.

Seth, A. K., Nguyen, K. T., Geringer, M. R., Hong, S. J., Leung, K. P., Mustoe, T. A., & Galiano, R. D. (2013). Noncontact, low-frequency ultrasound as an effective therapy against Pseudomonas aeruginosa-infected biofilm wounds. Wound Repair and Regeneration, 21(2), 266–274.

Sievers, M. (2011). Advanced Oxidation Processes. Treatise on Water Science, 4, 377–408.

Souza, B. S., Dantas, R. F., Cruz, A., Sans, C., Esplugas, S., & Dezotti, M. (2014). Photochemical oxidation of municipal secondary effluents at low $H_2O_2$ dosage: Study of hydroxyl radical scavenging and process performance. Chemical Engineering Journal, 237, 268–276.

Sunaric, S. M., Mitic, S. S., Miletic, G. Z., Pavlovic, A. N., & Naskovic-Djokic, D. (2009). Determination of doxycycline in pharmaceuticals based on its degradation by Cu(II)/$H_2O_2$ reagent in aqueous solution. Journal of Analytical Chemistry, 64(3), 231–237.

Suslick, K. S. (1989). The Chemical Effects of Ultrasound. Scientific American, 260, 80–87.

Suzuki, H., Araki, S., & Yamamoto, H. (2015). Evaluation of advanced oxidation processes (AOP) using O3, UV, and $TiO_2$ for the degradation of phenol in water. Journal of Water Process Engineering, 7, 54–60.

Tan, C., Gao, N., Deng, Y., Zhang, Y., Sui, M., Deng, J., & Zhou, S. (2013). Degradation of antipyrine by UV, UV/$H_2O_2$ and UV/PS. Journal of Hazardous Materials, 260, 1008–1016.

Teodosiu, C., Gilca, A. F., Barjoveanu, G., & Fiore, S. (2018). Emerging pollutants removal through advanced drinking water treatment: A review on processes and environmental performances assessment. Journal of Cleaner Production, 197, 1210–1221.

Torres-Palma, R. A., Nieto, J. I., Combet, E., Pétrier, C., & Pulgarin, C. (2010). An innovative ultrasound, Fe2+ and $TiO_2$ photoassisted process for bisphenol a mineralization. Water Research, 44(7), 2245–2252.

Torres-Palma, R. A., & Serna-Galvis, E. A. (2018). Sonolysis. Advanced Oxidation Processes for Waste Water Treatment, 177–213.

U.S. National Library of Medicine and National Center for Biotechnology Information. (2019).

Vanegas Chamorro, M., Villicaña Ortíz, E., & Arrieta Viana, L. (2015). Cuantificación y caracterización de la radiación solar en el departamento de la guajira-colombia mediante el calculo de transmisibilidad atmosférica. Prospectiva, 13(2), 54.

Vega-Garzón, L. P. (2014). Sonochemical Degradation of Triclosan, Benzophenone-1 and Benzophenone -3. Tesis para optar al título de Doctor en Ingeniería Ambiental. Universidad de Antioquia.

Vega-Garzon, L. P., Gomez-Miranda, I. N., & Peñuela, G. A. (2018). Benzophenone-3 ultrasound degradation in a multifrequency reactor: Response surface methodology approach. Ultrasonics Sonochemistry, 43, 201–207.

Vega, L. P., Soltan, J., & Peñuela, G. A. (2019). Sonochemical degradation of triclosan in water in a multifrequency reactor. Environmental Science and Pollution Research, 26(5), 4450–4461.

Vicente, D., & Pérez-Trallero, E. (2010). Tetraciclinas, sulfamidas y metronidazol. Enfermedades Infecciosas y Microbiologia Clinica, 28(2), 122–130.

Villegas-Guzman, P., Silva-Agredo, J., Giraldo-Aguirre, A. L., Flórez-Acosta, O., Petrier, C., & Torres-Palma, R. A. (2015). Enhancement and inhibition effects of water matrices during the sonochemical degradation of the antibiotic dicloxacillin. Ultrasonics Sonochemistry, 22, 211–219.

Voigt, M., & Jaeger, M. (2017). On the photodegradation of azithromycin, erythromycin and tylosin and their transformation products – A kinetic study. Sustainable Chemistry and Pharmacy, 5, 131–140.

Wang, Jianlong, & Zhuan, R. (2020). Degradation of antibiotics by advanced oxidation processes: An overview. Science of the Total Environment, 701, 1–46.

Wang, Jing, Wang, Z., Vieira, C. L. Z., Wolfson, J. M., Pingtian, G., & Huang, S. (2019). Review on the treatment of organic pollutants in water by ultrasonic technology. Ultrasonics Sonochemistry, 55, 273–278.

Wang, Wu, Q. Y., Huang, N., Xu, Z. Bin, Lee, M. Y., & Hu, H. Y. (2018). Potential risks from UV/$H_2O_2$ oxidation and UV photocatalysis: A review of toxic, assimilable, and sensory-unpleasant transformation products. Water Research, 141, 109–125.

Wols, B. A., & Hofman-Caris, C. H. M. (2012). Review of photochemical reaction constants of organic micropollutants required for UV advanced oxidation processes in water. Water Research, 46(9), 2815–2827.

Xiao Tong, L., Zhang, X., Du, Y., Wu, Q. Y., Lu, Y., & Hu, H. Y. (2017). Solar light irradiation significantly reduced cytotoxicity and disinfection byproducts in chlorinated reclaimed water. Water Research, 125, 162–169.

Xiong, W., Zeng, G., Yang, Z., Zhou, Y., Zhang, C., Cheng, M., Liu, Y., Hu, L., Wan, J., Zhou, C., Xu, R., & Li, X. (2018). Adsorption of tetracycline antibiotics from aqueous solutions on nanocomposite multi-walled carbon nanotube functionalized MIL-53(Fe) as new adsorbent. Science of the Total Environment, 627, 235–244.

Yan, W., Xiao, Y., Yan, W., Ding, R., Wang, S., & Zhao, F. (2019). The effect of bioelectrochemical systems on antibiotics removal and antibiotic resistance genes: A review. Chemical Engineering Journal, 358, 1421–1437.

Zaidi, S., Chaabane, T., Sivasankar, V., Darchen, A., Maachi, R., & Msagati, T. A. M. (2019). Electro-coagulation coupled electro-flotation process: Feasible choice in doxycycline removal from pharmaceutical effluents. Arabian Journal of Chemistry, 12(8), 2798–2809.

Zaman, S. Bin, Hussain, M. A., Nye, R., Mehta, V., Mamun, K. T., & Hossain, N. (2017). A Review on Antibiotic Resistance: Alarm Bells are Ringing. Cureus, 9(6).

Zeng, Z. W., Tan, X. F., Liu, Y. G., Tian, S. R., Zeng, G. M., Jiang, L. H., Liu, S. B., Li, J., Liu, N., & Yin, Z. H. (2018). Comprehensive adsorption studies of doxycycline and ciprofloxacin antibiotics by biochars prepared at different temperatures. Frontiers in Chemistry, 6(MAR).

Zhang, Y., An, Y., Liu, C., Wang, Y., Song, Z., Li, Y., Meng, W., Qi, F., Xu, B., Croue, J. P., Yuan, D., & Ikhlaq, A. (2019). Catalytic ozonation of emerging pollutant and reduction of toxic by-products in secondary effluent matrix and effluent organic matter reaction activity. Water Research, 166, 115026.

Zhou, C., Gao, N., Deng, Y., Chu, W., Rong, W., & Zhou, S. (2012). Factors affecting ultraviolet irradiation/hydrogen peroxide (UV/$H_2O_2$) degradation of mixed N-nitrosamines in water. Journal of Hazardous Materials, 231–232, 43–48.

Zhou, Y., Yang, Q., Zhang, D., Gan, N., Li, Q., & Cuan, J. (2018). Detection and removal of antibiotic tetracycline in water with a highly stable luminescent MOF. Sensors and Actuators, B: Chemical, 262, 137–143.

Zúñiga-Benítez, H. (2016). Degradación de disruptores endocrinos tipo Alquil-Parabeno y Benzofenona mediante Procesos de Oxidación Avanzada. Tesis para optar al título de Doctor en Ingeniería Ambiental. Universidad de Antioquia.

Zúñiga-Benítez, H., Aristizábal-Ciro, C., & Peñuela, G. A. (2016). Heterogeneous photocatalytic degradation of the endocrine-disrupting chemical Benzophenone-3: Parameters optimization and by-products identification. Journal of Environmental Management, 167, 246–258.

Zúñiga-Benítez, H., Soltan, J., & Peñuela, G. (2014). Ultrasonic degradation of 1-H-benzotriazole in water. Water Science and Technology, 70(1), 152–159.