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SONOCHEMICAL DEGRADATION OF PHARMACEUTICALS IN NATURAL WATER

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SUMMARY

Pharmaceuticals pollutants are compounds of increased environmental importance and, nowadays there is interest among researchers in the evaluation of their presence, continuity, and elimination in different environmental matrices. Ultrasound, as an advanced oxidation process (AOP), is a process able to degrade persistent pollutants in aquatic environments which is subject to considerable interest.

This work compares the sonochemical degradation, in mineral water and distilled water, of seven high consumption pharmaceutical products: acetaminophen (ACE), cloxacillin (CXL), diclofenac (DCF), naproxen (NPX), piroxicam (PXC), sulfacetamide (SAM), and cefadroxyl (CDX), each with different chemical properties. To achieve this, first, the best frequency and power levels are established for the execution of the experiments (375 kHz and 24.4 W, respectively). The removal of the contaminant and the accumulation of hydrogen peroxide are taken as response variables throughout the work.

Obtained results indicated that mineral water matrix could induce an acceleration in the degradation of those compounds with hydrophilic characteristics, compared to removal obtained in distilled water. Some physico-chemical properties that determine the hydrophobicity of the molecules and their affinity for cavitation bubbles were used to explain these findings. Subsequently, it was determined that bicarbonate is the ionic constituent of mineral water that caused the acceleration in the degradation of the compounds through the formation of the carbonate radical.

Later, it was experimented with different initial concentrations (0.331, 0.662, 3.31, 16.55, 33.1, and 331 µM) of three pollutants that showed different behaviors in the previous results,

determining the influence of the concentration factor on the acceleration caused by bicarbonate, where it was evidenced that the lowest concentration experienced (0.331 µM) allowed an acceleration in the degradation of the three molecules in mineral water. Finally, the sonochemical process is combined with Fenton (Sono-Fenton) to accelerate the degradation of the contaminant with the lowest removal rate, managing to improve its degradation only in distilled water.

1. CHAPTER 1: STATEMENT

1.1. INTRODUCTION

Currently, there is a wide list of contaminants of emerging concern in the aqueous medium, requiring alternative processes to be degraded. Many of such pollutants are pharmacological-type, which are released through human and animal excretions to the sewage system (Martinez, 2009; Khetan & Collins, 2007; Serna-Galvis et al., 2016). Because the conventional municipal treatment plants are unable to eliminate the pharmaceuticals (Gogoi et al., 2018; Rozman et al., 2017; Hai et al., 2018), their effluents are contaminated with these recalcitrant substances, which subsequently enter the environment. Most pharmaceuticals also persist in the aquatic environment at the trace level and show acute toxicity against diverse life-forms (Gogoi et al., 2018; Emmanouil et al., 2019; Cleuvers, 2004; Jarvis et al., 2014; Guiloski et al., 2015). Hence, the continuous exposure to these compounds induces a negative impact on the ecosystems (Rao et al., 2016).

Pharmaceuticals have been found in diverse aqueous environments such as natural mineral water (which is highly consumed around the world as bottled mineral water) (Perret et al., 2006; Li et al., 2010; González Alonso et al., 2012; Lardy-Fontan et al., 2017; Akhbarizadeh et al., 2020). In fact, bicarbonate-rich water (as mineral water) has positive effects on human health (Keßler & Hesse, 2000; Schorr et al., 1996; Burckhardt, 2008). However, the presence of pharmaceuticals in these matrices represents a risk. Therefore, strategies to degrade these pollutants from mineral water are required.

Advanced oxidation processes (AOPs) have proven to be efficient for the degradation of persistent compounds in water. Specifically, AOPs based on ultrasound have been successfully utilized for degrading pharmacological compounds in diverse aqueous matrices (Mahamuni &

Adewuyi, 2010). The processes based on ultrasound (also called sonolysis or sonochemistry) involve waves (at specific frequency and power) that induce cycles of compression and expansion, that interact with dissolved gases in the liquid medium inducing the formation of cavitation bubbles. These bubbles grow until a critical size; which provokes their violent implosion, generating very high temperatures and pressures (5000 K and 1000 bar) in the medium (the so-called "hot spots") allowing the decomposition of water and oxygen molecule to generate radical species as HO• (Rao et al., 2016).

In the sonochemical system, three reaction zones are recognized: a) inside the cavitation bubble, b) the bubble-solution interface, and c) the bulk of the solution (Nie et al., 2014; Nasseri et al., 2017; Zúñiga-Benítez et al., 2016). The zone where degradation occurs is strongly dependent on pollutant nature. Hydrophobic, non-polar and/or volatile compounds react inside the cavitation bubbles and at the bubble/water interface, while hydrophilic and/or non-volatile pollutants react within the bulk solution (Nie et al., 2014; Jiang et al., 2002; Méndez-Arriaga et al., 2008; Chiha et al., 2010). Additionally, the matrix components may modify both the rate and routes of pollutants elimination by ultrasound (Nasseri et al., 2017; Al-Bsoul et al., 2020; Dalhatou et al., 2019).

It should be mentioned that the effect of organic and inorganic constituents in natural water on the degradation of some pharmaceuticals by ultrasound has been previously studied; e.g., dicloxacillin, fluoxetine, cefadroxyl, cloxacillin, losartan, and valsartan in mineral water by sonochemistry has been studied. Some researchers observed a beneficial effect, by the constituents of the water (Villegas-Guzman et al., 2015; Chiha et al., 2011), others found harmful effects (Serna-Galvis et al., 2015; Serna-Galvis et al., 2019), while others did not find contributions from the mineral content of water (Serna-Galvis et al., 2019). Therefore, a systematic study depicting

the effect of pharmaceuticals structure in a complex matrix as mineral water upon sonochemical action needs to be evaluated. Thus, the main objective of this work was to unravel the effect of the chemical properties of the compounds on their sonochemical degradation in mineral water.

In order to accomplish the main goal of this research, initially, primary sonochemical parameters (frequency and power) were varied, to established suitable conditions for the degradation of pharmaceuticals. Afterward, treatment of the pollutants in distilled and mineral water was performed and a correlation among the initial degradation rate of the pharmaceuticals (in both distilled and mineral water) and several physicochemical properties was established. It was found an accelerating effect on the removal of hydrophilic pharmaceuticals in mineral water. Then, the role of each mineral water component was evaluated, to determine the responsible for the enhancing effect. Subsequently, to better understand the interaction between nature (hydrophilic/hydrophobic) and the amount of pollutants, degradation of relevant pharmaceuticals in the mineral water at different concentrations of the pollutant was also tested. Finally, as a strategy to improve the removal rate, the effect of the mineral water constituents on the sonochemical process combined with Fenton was evaluated.

1.2. PROBLEM STATEMENT

Currently, there is a wide concern regarding the amount of emerging pollutants present in the water, since historically they had not been reported and which now represent a challenge in terms of its extensive consumption, its environmental impact, effects on human health, and its elimination from aquatic ecosystems (Gracia-Lor et al., 2012; Aristizabal-Ciro et al., 2017). Pharmaceutical and personal care products (PPCPs) are pollutants of greatest concern, which include human and veterinary drugs, food supplements, and other chemicals used in cosmetics, fragrances, and protective solar products. PPCPs are suspected to cause high rates of cancer,

impairment of the reproductive system in humans and other animals, and development and spread of antimicrobial resistance (Hao et al., 2007; Walters et al., 2010; Kosma et al., 2010).

PPCPs do not need to be recalcitrant to cause great concern regarding their presence in the environment, because their continuous introduction, given their high consumption, allows them to always be present in several ecosystems (Gracia-Lor et al., 2012; Hao et al., 2007). The PPCPs includes medicines anti-inflammatory, pain relievers, cholesterol-lowering drugs, antibiotics, anti-epileptics, anticonvulsants, hormones, beta-blockers, lipid regulators, hypnotics, X-ray contrast agents, caffeine, disinfectants, UV filters, preservatives, musk fragrances, insect repellents and, in general, ingredients or excipients used in cosmetics, food supplements, shampoos, toothpaste components, sunscreen agents and antiseptics (Hao et al., 2007; Gracia-Lor et al., 2012).

PPCPs enter the aquatic environment, mainly, through the effluents from wastewater treatment plants (WWTP) (Buchberger, 2011). Some compounds are retained in the sludge by conventional water treatment processes. Despite this, most of the compounds are persistent and polar, and go unnoticed through the WWTP, being released from the effluents to the receiving aquatic environments (Walters et al., 2010; Hao et al., 2007; Almeida et al., 2014). The presence of these pollutants in effluents from Potable Water Treatment Plants (PWTP) has also been reported (Ikehata et al., 2006).

Due to their resistance to being eliminated through conventional water treatment processes, different advanced oxidation processes (AOPs) have been investigated to remove PPCPs from water (Martínez et al., 2011; De la Cruz et al., 2013; Vogna et al., 2004; Güyer & Ince, 2011; Al-Hamadani et al., 2017). In this sense, because these contaminants are commonly present in wastewater or natural waters, the organic and/or inorganic composition of the matrix becomes an

important factor, since it can interfere positively or negatively with the efficiency of the process of oxidation.

Particularly, it is common to find ions of calcium (Ca^{2+}), magnesium (Mg^{2+}), sulfates (SO_4^{2-}), bicarbonates (HCO_3^-), chloride Cl^-, potassium (K^+), and fluorides (F^-), among others, in natural water, for this reason, the effect of these ions on the degradation of some organic compounds through AOPs, including the sonochemical process, has been studied (Tanaka et al., 2001; Neppolian et al., 2002; Serna-Galvis et al., 2019; Pétrier et al., 2010; Serna-Galvis et al., 2016; Chiha et al., 2011; Villegas-Guzman et al., 2015). Some works have shown that a positive or acceleration effect occurs in the sonochemical degradation rate of some pollutants when the water matrix has a significant ions content, also considering the effect of other relevant parameters in this process (Nasseri et al., 2017; Dalhatou et al., 2019; Zúñiga-Benítez et al., 2016). In the opposite case, others have shown an inhibitory effect due to the inorganic content of the water (Minero et al., 2008; Guzman-Duque et al., 2011; Serna-Galvis et al., 2019).

Considering that the real-scale sonochemical treatment of waters contaminated with pharmaceutical products is expected to be developed in complex matrices, it is of interest in this research work to estimate whether the positive or negative effect that the inorganic content of mineral water has on the degradation of pharmaceuticals, is directly related to the concentration of the contaminants and/or the chemical properties of each one of them.

1.3. HYPOTHESIS

There is a dependence between some chemical properties of pharmacological organic pollutants and the acceleration caused by their sonochemical degradation in mineral water with salts content.

The initial concentration of the pollutant to be degraded and the chemical species in mineral water are fundamental factors in achieving the desired acceleration in the sonochemical degradation of these pollutants.

1.4. OBJECTIVES

1.4.1. General

To evaluate the effect of the inorganic content of mineral water upon the sonochemical degradation of the pharmaceutical contaminants acetaminophen, sulfacetamide, cloxacillin, naproxen, piroxicam, cefadroxyl, and diclofenac, analyzing the influence of the chemical nature and the initial concentration of the compounds in the process.

1.4.2. Specific

- To define the suitable operation conditions of the ultrasound reactor to degrade the pharmaceuticals of interest, considering the frequency and power as determining factors in the efficiency of the sonochemical process.

- Determine the effect of the chemical structure of the pollutant upon its sonochemical degradation in mineral water, relating some of its chemical properties with its removal rate.

- Unraveling the role of the components of the mineral water matrix in the elimination of the pharmaceutical pollutants, considering their influence on the initial degradation rate.

- To evaluate the effect of the pharmaceutical concentration upon its sonochemical elimination in the mineral water matrix.

- To evaluate the sono-Fenton combination to improve the degradation efficiency of the pharmaceuticals, verifying the effect of the water matrix.

1.5. BACKGROUND

1.5.1. Environmental impacts produced by pharmaceuticals

Pharmaceutical compounds are a type of pollutants that reach the different environmental matrices, mainly through feces and urine, either as metabolites or as unaltered parent compounds (Naddeo et al., 2009). The disposal routes are effluents from sewage treatment plants, hospital effluents, through leachate from sanitary landfills, and incorrect dispositions in taps, among others (Gil et al., 2013; Naddeo et al., 2009). Fig. 1 shows a route for the disposal of pharmacological residues and how they are distributed in the environment.

The presence of pharmaceutical contaminants in the environment was not measured or controlled in the past because they did not cause concern and, in general terms, there were no studies demonstrating a health risk to humankind and living beings. Additionally, the use of pharmaceuticals was not as high as it is currently; and they were not detected in water, since advances in instrumental analytical chemistry have only recently permitted their quantification at ultra-trace and trace concentrations, ng L^{-1} to μg L^{-1} (Gogoi et al., 2018; Naddeo et al., 2009; Aristizabal-Ciro et al., 2017; Rozman et al., 2017). Indeed, in the last years, pharmaceutical contaminants have been identified and quantified in effluents from wastewater treatment plants, surface water, groundwater and even drinking water (Gogoi et al., 2018; Rozman et al., 2017; Hai et al., 2018; Emmanouil et al., 2019).

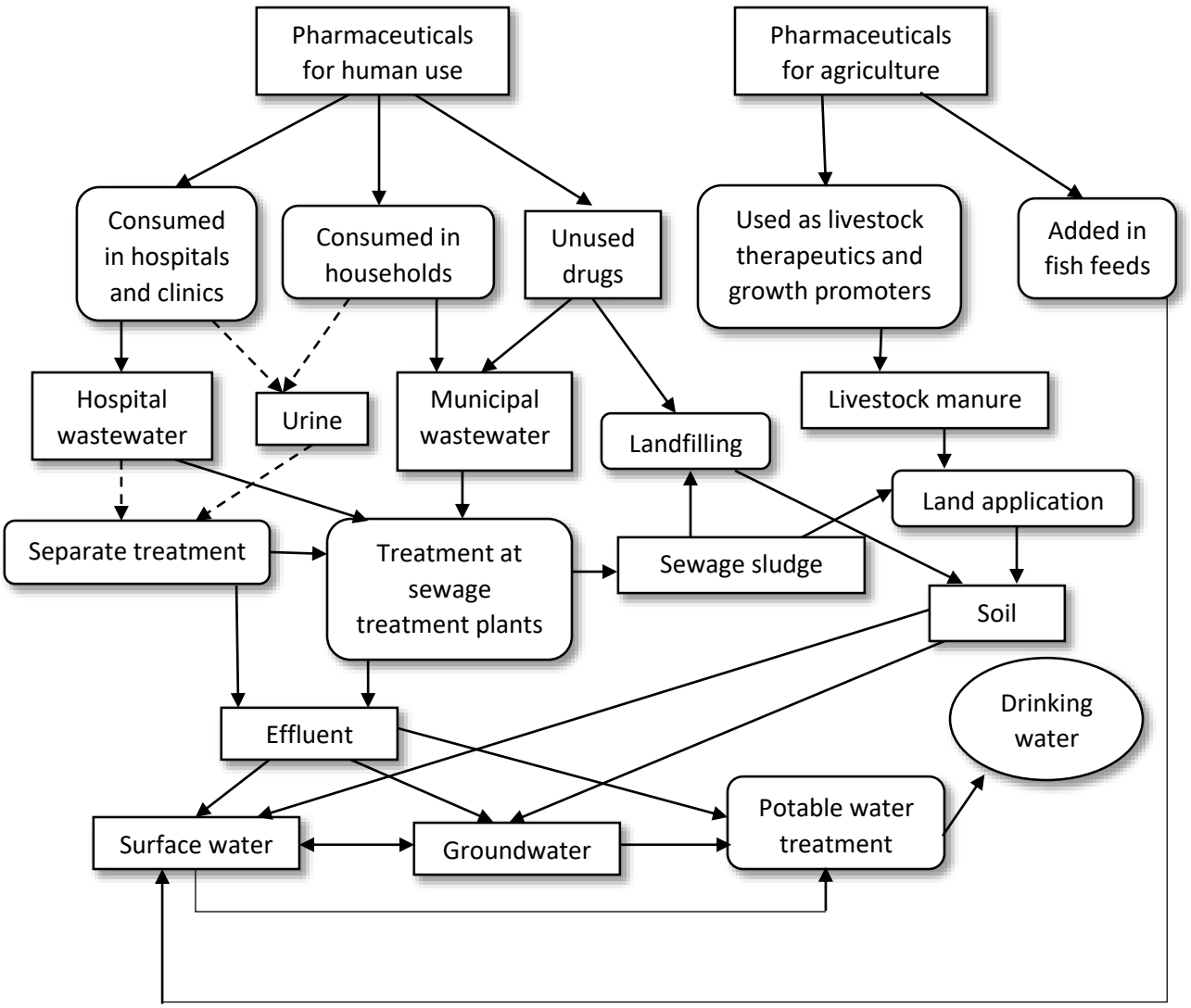

Fig. 1. Pharmaceutical contamination route in aquatic environments. Taken from Ikehata et al. (2006).

It is important to note that pharmaceuticals can have harmful effects on both the environment where they are located and human health. Nowadays, the toxicity ascribed to the presence of these pollutants on the environment has not been fully evaluated (Emmanouil et al., 2019); nevertheless, eco-toxicological studies are being conducted promising (Rao et al., 2016). In fact, direct or indirect exposure to pharmaceuticals has been reported to pose a serious risk (Gogoi et al., 2018; Cleuvers, 2004), since they can negatively influence algae, invertebrates, and

fish, as well as ecosystem dynamics and community structure (Jarvis et al., 2014; Almeida et al., 2014). Some of these pharmaceuticals have antimicrobial activity, leading to resistance of bacteria to commonly used antibiotics (Rozman et al., 2017) and subsequently to the global spread of diseases. Furthermore, pharmaceuticals can bio-accumulate (Emmanouil et al., 2019), changing cellular reactions in vital organs, such as the liver, kidneys, and gills (Schmidt et al., 2011).

1.5.2. Elimination of pharmaceuticals from water

It has been proven that pharmaceuticals are persistent pollutants that are hardly degraded by conventional processes (Emmanouil et al., 2019; Rubio-Clemente et al., 2014; Tran et al., 2013). For this reason, the implementation of new technologies to guarantee their removal is a need (Gogoi et al., 2018; Hai et al., 2018; Rubio-Clemente et al., 2014; González et al., 2010).

Advanced Oxidation Processes have been evaluated as an option for the degradation of a variety of organic pollutants in waters (Gil et al., 2013; Tran et al., 2015). Several works have been carried out assisted by AOPs to evaluate their efficiency in degrading pharmaceuticals. AOPs consist of the formation of the free hydroxyl radicals (HO•), which are capable of oxidizing toxic and/or recalcitrant organic compounds into more biodegradable and less dangerous products, such as oxidized species and short-chain hydrocarbons of low molecular weight (Torres-Palma & Serna-Galvis, 2018), among other innocuous products; thus, they provide an improvement to the treatability of AOP effluents (Rubio-Clemente et al., 2014). In fact, photocatalytic degradation has been conducted in the presence of UV radiation and photosensitizers including TiO_2, H_2O_2, and persulfate, among other chemical agents, obtaining very positive results (Güyer & Ince, 2011; Lin et al., 2017; Expósito et al., 2017). Likewise, photo-Fenton and ozonation at basic pH have been proven to be highly efficient in the degradation of this type of pollutants (Kakavandi & Ahmadi, 2019; Tran, et al., 2015). Therefore, these advanced systems offer a solution to the problem of

pharmaceuticals environmental accumulation and resistance to biological degradation, in contrast to other processes, such as conventional physical or chemical processes (Rubio-Clemente et al., 2014; Expósito et al., 2017).

1.5.3. Use of ultrasound as AOPs for the removal of pharmaceuticals

It should be noted that, among the different AOPs used in the treatment of pharmaceuticals present in water, the use of ultrasound (US) has been reported to be a highly efficient process, not only in the removal of this kind of contaminants but also in their degradation (Nie et al., 2014; Tran et al., 2017) and the conversion of other recalcitrant pollutants (Kakavandi & Ahmadi, 2019) and microbial load in water (Rubio-Clemente et al., 2019). Likewise, the use of ultrasound, as an advanced oxidation process, is environmentally "clean" since it does not require the addition of chemicals to the aqueous medium and it does not generate waste (Al-Hamadani et al., 2016). Consequently, the use of US waves is an alternative option for the conversion of recalcitrant pharmaceuticals.

It is noteworthy to mention that, by using the US process, mass transfer within the reaction medium is improved, as well as the pharmaceutic degradation reaction rates. Additionally, the consumption of chemicals, such as oxidizing and catalyzing agents, is reduced and no sludge is generated (Torres-Palma & Serna-Galvis, 2018; Ince et al., 2001).

Eqs. (1-4) show the decomposition of water and other molecules commonly dissolved in water by sonochemical waves (Rao et al., 2016; Mahamuni & Adewuyi, 2010), being the HO•, as well as the hydroperoxyl radicals (HO_2•) the main species that oxidize the organic compounds present in the aqueous medium.

$$H_2O \overset{)))}{\rightarrow} H^{\bullet} + HO^{\bullet} \quad \text{Eq. 1}$$

$$O_2 \overset{)))}{\rightarrow} 2O^{\bullet} \quad \text{Eq. 2}$$

$$N_2 \overset{)))}{\rightarrow} 2N^{\bullet} \quad \text{Eq. 3}$$

$$H^{\bullet} + O_2 \overset{)))}{\rightarrow} HO_2^{\bullet} \quad \text{Eq. 4}$$

When free radicals reach the aqueous solution, they can recombine, as expressed in Eq. (5-7), or react with hydroxyl ions (HO-) (Eq. 8), resulting in a decrease of the system oxidation potential.

$$HO_2^{\bullet} + HO_2^{\bullet} \rightarrow H_2O_2 + O_2 + O_2\,(a^1\,\Delta g) \qquad k = 8.3x10^5\ L\ mol^{-1}S^{-1} \qquad \text{Eq. 5}$$

$$HO^{\bullet} + HO^{\bullet} \rightarrow H_2O + 1/2\left(O_2 + O_2(a^1\,\Delta g)\right) \qquad k = 5.5x10^9\ L\ mol^{-1}S^{-1} \qquad \text{Eq. 6}$$

$$HO^{\bullet} + HO_2^{\bullet} \rightarrow H_2O + O_2 + O_2(a^1\,\Delta g) \qquad k = 7.1x10^9\ L\ mol^{-1}S^{-1} \qquad \text{Eq. 7}$$

$$HO_2^{\bullet} + HO^{-} \rightarrow O_2^{\bullet-} + H_2O \qquad k = 10^{10}\ L\ mol^{-1}S^{-1} \qquad \text{Eq. 8}$$

However, from Eq. (8), superoxide radicals ($O^{2\bullet-}$) are formed, as well as from the decomposition of $HO_2\bullet$, as described by Eq. (9), which also contribute to the degradation of emerging organic compounds, although in a smaller proportion than HO• (Litter & Quici, 2010). Additionally, in an acidic medium, $O_2\bullet$- can react with protons (H^+) to form $HO_2\bullet$ (Eq. 10). Both of the free radicals can recombine, as represented in Eq. (11), resulting in the production of HO_2^-, which in turn can be involved in HO• quenching (Eq. 12).

$$HO_2^{\bullet} \rightarrow H^+ + O_2^{\bullet-} \qquad k = 7.5x10^6\ L\ mol^{-1}S^{-1} \qquad \text{Eq. 9}$$

$$H^+ + O_2^{\bullet-} \rightarrow HO_2^{\bullet} \qquad k = 5.1x10^{10}\ L\ mol^{-1}S^{-1} \qquad \text{Eq. 10}$$

$$HO_2^{\bullet} + O_2^{\bullet-} \rightarrow HO_2^- + O_2 \qquad k = 9.7x10^7\ L\ mol^{-1}S^{-1} \qquad \text{Eq. 11}$$

$$HO^{\bullet} + HO_2^- \rightarrow HO_2^{\bullet} + HO^- \qquad k = 7.5x10^9\ L\ mol^{-1}S^{-1} \qquad \text{Eq. 12}$$

Hydrogen peroxide (H_2O_2) can also be formed in the ultrasound process, as described in Eq. 5. Although H_2O_2 can scavenge HO• or be decomposed (Eq. 13, 14, and 15, respectively), it can be involved in the oxidation of pollutants, as well as in the production of a higher amount of HO•, when the sonochemical process is combined with UV radiation.

$HO^{\bullet} + H_2O_2 \rightarrow H_2O + HO_2^{\bullet}$ $k = 3x10^{7}\ L\ mol^{-1}S^{-1}$ Eq. 13

$H_2O_2 \rightarrow HO_2^{-} + H^{+}$ $k = 2x10^{-2}\ L\ mol^{-1}S^{-1}$ Eq. 14

$HO_2^{-} + H^{+} \rightarrow H_2O_2$ $k = 10^{10}\ L\ mol^{-1}S^{-1}$ Eq. 15

The cavitation bubbles are produced in two ways, symmetrically and asymmetrically. The difference between these is the support provided by a rigid surface (for instance, the surface of the reactor) for the bubbles to be formed. This difference has a direct influence on the bubbles implosion, and thus on the release of pressure and temperature into the medium, resulting in the rupture of the water molecule and the formation of HO• (Rao et al., 2016). The symmetrical bubbles release energy in all directions around their surface, while the asymmetrical ones generate an eruption of the liquid, mainly on the parts of the bubbles that are far away from the surfaces, forming long-range "micro-jets" that go to the solid surfaces (Nie et al., 2014).

The reaction rate constants for the reactions expressed in Equations (5)–(15) were taken from Ivanova et al. (2012), demonstrating that, in general terms and according to the values of the reaction rate constants, the free radicals are easily formed through the US waves. As mentioned previously, these free radicals can react with the target pollutant; however, they can also recombine or be quenched by other compounds found in water such as the natural constituents of the matrix (Naddeo et al., 2010).

In the ultrasonic radiation process, as indicated above, three reaction zones are recognized for the degradation of compounds: the cavitation bubble, the bubble–water interface, and the bulk solution (Nie et al., 2014; Chiha et al., 2010; Song et al., 2005). The process by which degradation occurs differs from zone to zone. Hydrophilic substances are located within the solution, non-volatile hydrophobic compounds are mainly housed in the bubble–water interface, and volatile

substances are commonly located within the cavitation bubble (Torres-Palma & Serna-Galvis, 2018).

To evaluate the zone and the way in which a compound is degraded, Nie et al. (2014) have implemented the so-called "scavengers" of the HO•. In an experiment where the US process was used to degrade the pharmaceutical diclofenac (DCF), isopropyl alcohol and terephthalic acid were used to inhibit the reaction of the target compound with HO•, functioning as quenchers. The acid was considered to react with free radicals in the bulk solution, while the alcohol reacted both at the bubble–water interface and in the bulk solution. In this regard, the authors verified that when only the acid was added, the degradation of the compound was inhibited. However, when the alcohol was used exclusively as an inhibitor, the degradation of the target compound was considerably reduced. It was, therefore, concluded that oxidation of DCF occurred mainly by HO• in the supercritical interface, especially when water was saturated with air and oxygen (O_2). Nonetheless, under argon (Ar)- and nitrogen (N_2)- saturated conditions, DCF degradation occurred within the cavitation bubbles and/or the bulk solution.

In the case of acetaminophen (ACP), a polar compound with high solubility (12.5 mg mL^{-1}), Villaroel et al. (2014) reported that this contaminant was degraded in a greater proportion within the bulk, estimating that its behavior would be that of a hydrophilic substrate. Nonetheless, in this investigation, it was concluded that ACP can be housed both in the bulk solution and in the bubble–water interface, attributing its degradation to the HO• formed during the implosion of the cavitation bubbles. Based on the aforementioned author's estimations, the hydrophilic or hydrophobic behavior of the target compound was more related to the initial pH value of the solution at which the study was carried out.

On the other hand, ultrasonic frequency is a fundamental parameter in the performance of the US process, since the size and duration of the cavitation bubble, the violence of the implosion, and therefore, the production of HO• depend considerably on it Rao et al. (2016).

Rao et al. (2016) chose two frequency values (200 and 400 kHz) to determine the optimal one for the degradation of CBZ. The first of these values was more effective for the degradation of the target compound. This result was ascribed to the differences in calorimetric powers obtained for both frequencies under the same electrical power (100 W), resulting in a higher calorimetric power for the 200 kHz frequency.

On the other hand, in the research carried out by Güyer & Ince (2011), different levels of ultrasonic frequency were evaluated in the US process of the DCF. The results obtained allowed the conclusion that the maximal rates of DCF degradation were reached at a frequency of 861 kHz and the minimal ones at 1145 kHz (carrying out tests with values of 577, 861, and 1145 kHz). The improvement between the 577 and 861 kHz was due to the fact that the latter reduced the size of the bubbles, leading to a greater number of bubbles and active oscillations, which contributed to the generation of HO• improvement. However, for the highest frequency evaluated this efficiency was reduced because the “optimal” frequency related to the reactor configuration was surpassed.

For his part, the electrical power supplied to the ultrasonic transducer is a critical parameter that can largely determine the performance of the US process (Rao et al., 2016). It is important to note that the effect of ultrasonic power and oxidizing species can be influenced by bubble dynamics (Tran et al., 2013). The results reported by Gogate et al. (2011) indicated that the size, number, lifetime, and pressure of the bubbles were a complex function of the power dissipation rate.

For Jiang et al. (2002), the increase in ultrasonic power in the degradation of volatile compounds such as chlorobenzene, 1,4-dichlorobenzene, and 1-chloronaphthalene caused an increase in the cavitation energy, decreasing the cavitation limit and increasing the amount of bubbles produced. This resulted in a rise in the rate of degradation of this type of compound, considering that the bubbles formed had enough energy to pyrolyze the tested pollutants. This is justified by the fact that volatile compounds are pyrolyzed within the cavitation bubbles, so the more bubbles formed, the more spaces for these compounds to react.

On the other hand, Adityosulindro et al. (2017) evaluated the degradation of Ibuprofen (IBU) by the US process and the influence of the power density in the conversion of the target pharmaceutical. It was determined that increasing the power in a range between 25-100 W L^{-1}, over 180 min of treatment, contributed to a greater formation of HO•. However, the authors stated that above a critical or optimal power density value, a cloud of bubbles would be formed, dispersing the formation of sound waves, which would, in turn, decrease the efficiency of the process (Adityosulindro et al., 2017).

The pH of the solution is a fundamental parameter in oxidation-reduction reactions. In the US process, the pH would indicate the hydrophobic or hydrophilic nature of the target compound behavior, depending on whether the structure in which the pollutant is found is ionic or molecular. This property will allow the position to be determined in which the contaminant is housed in the US process, i.e., in the bulk solution (hydrophilic, non-volatile compounds), in the bubble–water interface (semi-volatile hydrophobic compounds), or within the cavitation bubble (hydrophobic, volatile compounds) (Rao et al., 2016). This position, in turn, will determine whether the degradation pathway of the contaminant is by pyrolysis or by reaction with the HO• formed by the implosion of the cavitation bubbles.

Al-Hamadani et al. (2016) evaluated the degradation of sulfamethoxazole (SFX) and IBU under three pH conditions: acid (3.5), below the pKa values of the target compounds; basic (7), above the pKa values; alkaline (9.5), well above these values. The results showed degradations near 100% of the compounds in 1 h of treatment for a pH below pKa, while degradation was significantly affected above these values. This is attributed to the molecular form of the compounds, i.e., when the pH of the solution was below pKa, the hydrophobicity of the drugs and, therefore, their position in the bubble–water interface is improved, favoring a rapid reaction with the HO• recently formed during the implosion of the cavitation bubbles.

In the case of the temperature of the solution, for some authors, the variation of this parameter in the US process directly influences cavitation intensity due to the changes in the physicochemical properties of the compound and the type of cavities formed, which can affect the kinetic velocity constant of the degradation reaction (Golash & Gogate, 2012).

1.5.4. Influence of the water matrix on the sonochemical process

Various investigations related to the degradation of pharmaceuticals in water through AOPs have been carried out in aqueous matrices with different constituents. On one hand, some researches have been developed with synthetic waters which, in general, involve the use of distilled water doped with the chemical components offering the specific characteristics with which the researcher wishes to work. On the other hand, there are works operating with real wastewater in which the efficiency of the process for natural surface and drinking water is evaluated.

For this research work, those works related to natural water matrices are of special interest. In the research conducted by Villaroel et al. (2014), the influence of ionic constituents of water on the degradation of ACP (82.69 μmol L^{-1} and 1.65 μmol L^{-1}), at a power of 60 W and ultrasonic

frequency of 600 kHz, was evaluated. The results obtained in distilled water and synthetic water containing calcium ions (Ca^{2+}), magnesium ions (Mg^{2+}), sulfates ions (SO_4^{2-}), bicarbonates ions (HCO_3^-), chloride ions (Cl^-), potassium ions (K^+), and fluorides ions (F^-) were compared. The results indicated that for the lowest concentration of ACP, a more pronounced acceleration of degradation was observed when this occurred in water with similar ion content than in distilled water. The authors attributed this to the high content of HCO_3^-, which was likely to be the protagonist in the formation of the carbonate radical (CO_3^{*-}) when reacting with HO• radicals, being HCO_3^-, an enhancer of the degradation of the target compound.

In the work reported by Adityosulindro et al. (2017) on the Fenton, US oxidation system and US-Fenton process, the efficiency of the degradation of IBU in distilled water and wastewater from a municipal treatment plant was compared. The results showed a negligible difference between the degradation capabilities of all the evaluated processes in both distilled water and wastewater. In this context, the authors stated that the organic and inorganic content of the sewage effluent did not compete with IBU for HO• and that the contaminant was able to react first with the oxidizing agent. It is important to highlight that the experimentation was carried out at acid pH, which could favor the location of IBU in the interface zone, making it more competitive when reacting with the HO• formed from the implosion of the cavitation bubbles.

Finally, Table 1 presents a summary of some important works carried out in recent years regarding the use of ultrasound as an advanced oxidation process to degrade PPCPs.

Table 1. Summary of works related to the removal of pharmaceuticals pollutants through the ultrasound process and its combination with other physical-chemical and advanced oxidation processes.

Process	Reference	Pollutant/ Type of Water	Operating Conditions	Found Results
US	(Nie et al., 2014)	DCF/Synthetic water	[DCF]: 0.05 mM. Frequency: 585 kHz. Power intensity 160 W L^{-1} pH: 7 Situations: air saturation, argon, oxygen, and nitrogen. Temperature: 4 °C Glass cylindrical reactor of 750 mL connected to a transducer Working volume: 500 mL. Treatment time: 60 min. HO• scavenger agents: Isopropyl alcohol and terephthalic acid. [H_2O_2]: 0.5 and 5 mM.	The elimination of DCF (without scavenger) and the formation of chloride ions were established as first-order reactions. Dichlorination rates, under all gas saturation conditions, were 1 to 2 times higher than DCF degradation rates. Dichlorination was a major reaction pathway during ultrasonic degradation of DCF; it developed within the solution by HO• attacks. There was only partial mineralization in the 4 gas saturation conditions. The lowest peroxide concentration allowed a higher rate of degradation of the DCF.
US	(Vega-Garzon et al., 2018)	Benzophenone-3 (BP-3)/ Synthetic water	Treatment time: 10 min Frequency: 574, 856 and 1134 kHz. Electrical Power: 100–200 W L^{-1}. [BP-3]: 1 ppm. Temperature: 25 ± 2 °C. Relationship of pulse time and silence time: PT/ST.	574 kHz or a lower frequency value is optimal for degradation of BP-3. The optimum power density level was 200 W L^{-1}. A maximum degradation level of 79.2% was obtained for EP = 200 W L^{-1}, a PT/ST ratio of 10, and frequency 574 kHz. The degradation was almost the same for all PT/ST ratios from 3 to 12.
US	(Vega et al., 2019)	Triclosan (TCS)/ Synthetic water	Treatment time: 60 min. Frequency: 215, 373, 574, 856 and 1134 kHz. Electrical Power: 40, 76, 140 and 200 W L^{-1} [TCS]: 1 mg L^{-1}. Temperature: 25 ± 2 °C. Treatment volume: 300 mL.	The 574 kHz frequency had the highest degradation rates. With 574 kHz, at 40 W L^{-1}, 88% of TCS degraded in 60 min, while at 140 W L^{-1}, TCS degraded completely in less than 25 min. The highest TCS degradation rate was obtained at the highest power density level of the equipment, 200 W L^{-1}. It was shown that the only variable that had statistical significance and an effect on degradation after 10 min was the power density.
US	(Pétrier et al., 2010)	Bisphenol-A/ Synthetic water	Frequency: 300 kHz. Electrical Power: 80 W. Treatment volume: 300 mL. [BPA]: 0.12 and 300 µM. pH: 8.3 [HCO_3^-]: 12–500 mg L^{-1} Temperature: 21 °C. Addition: Cl^-, SO_4^{2-} and HPO_4^{2-} [6 mM].	The addition of HCO_3^-, in the range of 12–500 mg L^{-1} did not have a significant effect on the BPA degradation rate. The bicarbonate concentration had a significant effect on the 0.12 BPA concentration: a higher bicarbonate concentration produced higher initial decomposition rates. Solutions containing ions other than bicarbonate showed significantly lower degradation rates. The bicarbonate/carbonate solution produced a significantly improved degradation rate of BPA.

US	(Villaroel et al., 2014)	Acetaminophen (ACP)/ Synthetic water and mineral water	Frequency: 600 kHz. Electrical Power: 20–60 W. Treatment volume: 300 mL. [ACP]: 82.69 µM. pH: 3–12. Temperature: 20 ± 1 °C. Addition: glucose, oxalic acid, propan-2-ol and hexan-1-ol.	The ultrasonic degradation in an acidic medium (pH 3.0–5.6) is greater than that obtained in basic aqueous solutions (pH 9.5–12.0). The degradation of ACP would increase if its hydrophobicity is favored. The degradation rate increases with increasing acoustic power. The substrate degradation rate increases with increasing initial substrate concentration to a plateau. The presence of organic compounds negatively affects the sonochemical degradation efficiency of ACP, except glucose. A positive effect of mineral water was observed when the ACP concentration decreased 50 times (1.65 µM).
US/Electro-oxidation (EO)	(Tran et al., 2015)	Ibuprofen (IBU)/ Synthetic water and sewage	[IBU] Synthetic: 10 mg L^{-1} Increase in conductivity Na_2SO_4 0.01 mol L^{-1}. [IBU] Municipal: 20, 100 µg L^{-1} and 10 mg L^{-1}. pH residual municipal: 6.6. Frequency: 520 kHz. Electric power: 10–40 W. Current densities: 3.6–35.7 mA cm^{-2}. Cylindrical reactor with a cathode and an anode immersed in the solution. Temperature: 5–40 °C. Working volume: 3 L. Treatment time: 30–180 min.	The best constant for speed and efficiency of degradation was obtained with the US/EO, process, followed by EO alone and then US alone. 84.74% elimination of the IBU was achieved with US/EO. In the EO process, HO• can be generated on the surface of the electrode, then the US increases the mass transfer between these and the contaminants. Between 10–40 °C, there were no significant differences in the degradation of IBU. The intensity of the current and treatment time are the most influential factors. Optimum conditions are 110 min treatment, 4.09 A, and 20 W. In municipal sewage, 90% of IBU was removed.
US O_3 O_3/US US/UV O_3/UV US/O_3/UV	(Nilsun H. Ince, 2018)	Azo dyes (AD), Endocrine Disrupting Compounds (EDC) and pharmaceuticals (PHAC)/ Synthetic water	Reactor 1: horn-type sonicator. Capacity of 100 mL. Frequency 20 kHz. Power: 0.46 W mL^{-1}. Reactor 2: plate-type sonicator. Frequency: 577, 866, 1100 kHz. Power intensity: 0.23 w mL^{-1}. Use US + O_3. Reactor 3: Ultrasonic bath. Frequency: 200 kHz. Power: 0.07 W mL^{-1}. Reactor 4: tailor-made hexagonal glass reactor coupled with 3 UV lamps (254 nm). Frequency: 520 kHz.	AD degradation is faster by O_3/US. The UV/US process was very effective in degrading AD. With the addition of H_2O_2 a better discoloration was obtained. The rate of AD decomposition is faster in the presence of solid particles. EDCs had better degradation at alkaline pH and low frequency. At acidic pH, degradation was improved by adding Fenton or O_3 processes. For PHAC, ultrasonic processes were more efficient at high frequencies and acid pH.

			Power: 0.19 W mL^{-1}.	
US/Zn^0	(Huang et al., 2017)	Diclofenac (DCF)/Synthetic water	[DCF]: 10 mg L^{-1}. Reactor: Beakers, ultrasound probe. Working volume: 100 mL. pH: 2–7. Frequency: 20 kHz Power: 30–300 W. Treatment time: 30 min. Addition of Zn^0	At acid pH, the US process accompanied by Zn^0 was more efficient, while adding Zn^0 alone and experimenting with the US alone did not result in further degradation of DCF. At pH higher than 2 the DCF was not eliminated. At pH 2, degradation of 80.92% was achieved in 15 min. Process of US/Zn^0. There were no significant differences in degradation at different Zn^0 concentrations and different power densities. Dichlorination was the degradation pathway. The main aspect of this reaction, together with the Zn^0 reduction, was the $O_2•^-$.
US Fenton/US	(Adityosulindro et al., 2017)	Ibuprofen (IBU)/Synthetic water and municipal sewage	[IBU]: 20 mg L^{-1}. pH: 2–8. Power density: 25–100 W L^{-1}. Frequency: 12–862 kHz. Addition of H_2O_2. Addition of Iron (Fe). HO scavenger agents: n-butanol and acetic acid. Reactor: 1 L glass. Ultrasound probe, cup horn type. Temperature: 25 °C.	At alkaline pH, the degradation rate decreased significantly. The addition of H_2O_2 did not contribute to the degradation of IBU by the US process. The sono-Fenton process was more efficient in eliminating the IBU than both processes separately. In the sono-Fenton process, no significant influence on the degradation of the IBU was achieved by varying the power density in the studied range. In the municipal sewage, the degradation was more effective with the combined processes, with results similar to those obtained with synthetic water. However, the efficiency of the individual US process decreased.
US US/UV	(Rao et al., 2016)	Carbamazepine (CBZ)/Synthetic water	[CBZ]: 0.00625–0.1 mM. Sonolytic Reactor: 500 mL Cylindrical glass beaker Frequency: 200 and 400 kHz. Power: 20–100 W. Temperature: 20 °C. pH: 2–11. Photolytic reactor: Camera with two low-pressure Hg lamps, 253.7 nm. Combined reactor: Assembly of the sonolytic reactor inside the photolytic reactor.	CBZ degradation follows a pseudo-first order kinetics. Faster degradation rate and greater removal with a frequency of 200 kHz. When methanol was applied as HO• sequestering agent, there was no significant drug removal. The HO• was the protagonist of the degradation. As electrical power increased, CBZ degradation increased. SO_4^{2-} and NO_3^- hindered the transfer of electrons during oxidation. The degradation of CBZ with UV radiation alone was negligible. The UV/US process achieved the highest CBZ removal. Twenty-one reaction intermediates were detected.
US/Single-walled carbon	(Al-Hamadani et al., 2016)	Sulfamethoxazole (SFX) and Ibuprofen	[SFX] and [IBU]: 10 µM. Single-walled carbon nanotubes (SCN). Stainless steel reactor.	As the temperature increased, the cavitation threshold decreased, bubble formation increased together with the amount of HO•.

nanotubes		(IBU)/ Synthetic water	Frequency: 1000 kHz Power: 180 W pH: 3.5–7–9.5. Temperature: 15 to 55 °C. Reaction time: 60 min. Working volume: 1 L.	At pH values below the pKa of the compounds, complete degradation was obtained within 50–60 minutes. At higher pH values, complete degradation was not achieved. In the presence of the SCN the degradation and the speed constant of the same was favored. The adsorption capacity of the SCN favored the removal of the compounds.
US/EO	(Tran et al., 2017)	Carbamazepine (CBZ) /Synthetic water	Working volume: Reactor 1: 1 L and Reactor 2: 100 L. Cathode and anode in the form of expanded metal plates. Anode: Ti/PbO_2 Cathode: Ti Electric current: 1–15 A. Type of water: Potable (from the tap). [CBZ]: 10 mg L^{-1}. Na_2SO_4: 0.01 mol L^{-1} Temperature: 20 °C. Ceramic transducer: diameter 4 cm. Frequency: 520 kHz. Power: between 10 and 40 W. Reaction time: between 90 and 180 min.	The combined US/EO process offered the best kinetic velocity constant. The degree of synergy, in the combination of the processes, rose with the increase in US power. As the current intensity increased, the depurative capacity rose. CBZ degradation was greater when the two processes (US and EO) were implemented simultaneously than separately. There was a 99.5% degradation of CBZ with the combined process.
US/Additives	(Serna-Galvis et al., 2016)	Oxacillin (OXA)/ Synthetic water	Working volume: 250 mL Electrical power: 60 W. Frequency: 275 kHz. Temperature: 20 °C. Mannitol and calcium carbonate were used as additives	In the presence of additives, OXA was efficiently removed. The sonochemical process was able to completely degrade the antibiotic, generating solutions without Antimicrobial Activity. The contaminant did not mineralize even after 360 min.
US/O_3	(Zúñiga-Benítez et al., 2016)	Benzophenone-3 (Bp3)/ Synthetic water	Frequency: 20 kHz. Electrical power: 55.9 W. Temperature: 25 °C. Working volume: 200 mL [Bp3]: 3.9 mg L^{-1}. pH: 2, 6.5, and 10. O_3: 0.5 mL min^{-1}. N_2 y O_2: 800 mL min^{-1}. Presence of nitrate, chloride, and bicarbonate ions [5 mmol L^{-1}].	Increasing electrical power also increases the degradation of Bp3. At a lower pH (2) a more effective degradation of Bp3 was observed. PKa Bp3: 8.06. The presence of O_2, O_3 and the combined process of US/O_3 improved the degradation of Bp3. Being faster US/O_3. Bicarbonate ions accelerated the degradation of Bp3.

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1.6. CONCEPTUAL FRAMEWORK

For a better understanding of the content of this document, it is important to be clear about the following concepts.

Acetaminophen (ACE)

Acetaminophen or paracetamol structure is shown in Fig, 2, it is a widely used nonprescription analgesic and antipyretic for mild-to-moderate pain and fever. It is a p-aminophenol derivative. The excellent tolerability of therapeutic doses of paracetamol (acetaminophen) is a major factor in the very wide use of the drug. The major problem in the use of paracetamol is its hepatotoxicity after an overdose. Hepatotoxicity has also been reported after therapeutic doses, but critical analysis indicates that most patients with alleged toxicity from therapeutic doses have taken overdoses. ACP is not completely removed in municipal wastewaters, and it is nowadays one of the most popular compounds found in natural and drinking waters. Detection of this pollutant is greater in highly populated areas such as urban areas where drug usage is expected to reach elevated proportions (de Luna et al., 2012).

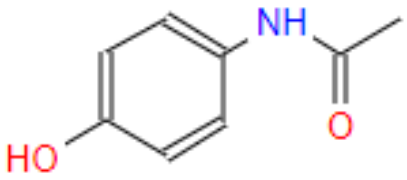
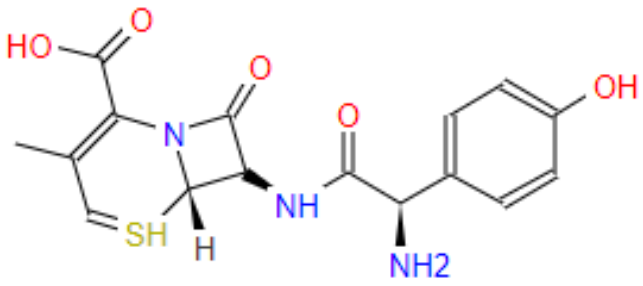


Fig. 2. Acetaminophen structure.

621 **Cefadroxil (CDX)**

622 Cefadroxil structure is shown in Fig. 3, it is a first-generation semi-synthetic β-lactam
623 antibiotic of the cephalosporins group. It is an orally active pharmaceutical for the treatment of
624 vulnerable infections of respiratory, genitor urinary, prostatitis, gynecologic, skin, central nervous
625 system, and urinary tracts (Makchit et al., 2006; Atif et al., 2020). It is a long-acting, broad-
626 spectrum, water-soluble, cephalexin derivative. Like all beta-lactam antibiotics, cefadroxil binds
627 to specific penicillin-binding proteins (PBPs) located inside the bacterial cell wall, causing the
628 inhibition of the third and last stage of bacterial cell wall synthesis.



629

630 **Fig. 3.** Cefadroxil structure.

631 **Cloxacillin (CXL)**

632 Cloxacillin structure is shown in Fig. 4, it is a semisynthetic beta-lactamase resistant
633 penicillin antibiotic with antibacterial activity, carrying a 3-(2-chlorophenyl)-5-methylisoxazole-
634 4-carboxamide group at position 6. Antibiotics, as the most commonly used group of
635 pharmaceuticals, are the most important therapeutic choice in human and veterinary medicine for
636 preventing/treating microbial infections, and as growth promoters in agriculture and fish farming
637 (Affam & Chaudhuri, 2014; Ojer-Usoz et al., 2014; Watkinson et al., 2007; Moussavi et al., 2018).
638 Therefore, although detected at low concentrations (μg L^{-1}) in water bodies, the continuous release

of these into receiving water bodies pose a serious risk to both human health and aquatic biota because of aquatic toxicity, development of resistance in pathogenic bacteria, genotoxicity, and endocrine disorders (Elmolla & Chaudhuri, 2010; Elmolla & Chaudhuri, 2012).

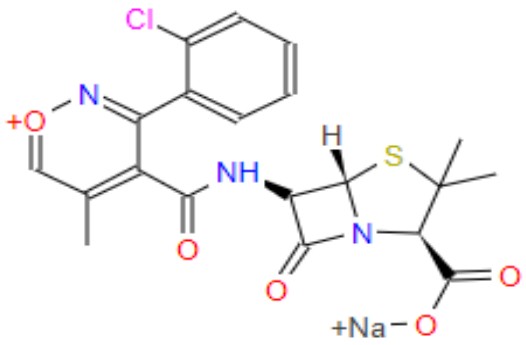


Fig. 4. Cloxacillin structure.

Diclofenac (DCF)

Diclofenac structure is shown in Fig 5, it is a non-steroidal anti-inflammatory pharmaceutic used to relieve post-traumatic and postoperative pain, inflammation, and swelling. It is also used as an adjuvant in painful inflammatory infections of the ear, nose, or throat; as well as in the treatment of inflammation and contractions caused by osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis. Immediate-release (short-acting) diclofenac is also used to treat painful periods (Santibáñez et al., 2014). This drug has been found in effluents from urban water treatment plants in concentrations of μg L^{-1} (Naddeo et al., 2009). Regarding the environmental impacts caused by this drug, Triebskorn et al. (2007) concluded that diclofenac showed negative effects on the liver, kidneys, and gills of larger fish compared to the effects caused by other drugs such as carbamazepine and metoprolol, observing the lowest effect concentration at 1 μg L^{-1}.

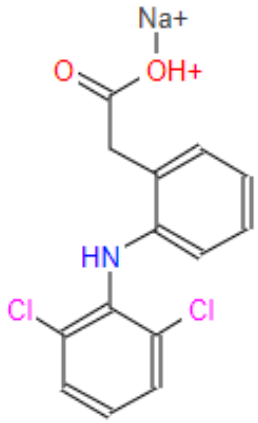


Fig. 5. Diclofenac structure.

Naproxen (NPX)

Naproxen structure is shown in Fig. 6, it is a non-steroidal anti-inflammatory drug (NSAID) commonly used for the reduction of mild to moderate pain, fever, inflammation, and stiffness caused by conditions such as osteoarthritis, rheumatoid arthritis, psoriatic arthritis, gout, ankylosing spondylitis, injury (like fractures), menstrual cramps, tendonitis, bursitis, and the treatment of primary dysmenorrhea. Naproxen and naproxen sodium are marketed under various trade names including Aleve, Anaprox, Naprogesic, Naprosyn, Naprelan. It is frequently detected in natural and anthropogenic aquatic environments (i.e. marine, drinking, riverine, tap and wastewater) and even sediments. This is because it is widely used worldwide to treat inflammation and pain. According to the study of naproxen toxicity for microorganisms, Górny et al. (2019) discovered that the presence of naproxen at high concentrations could cause some genotoxic effects (Tomul et al., 2020).

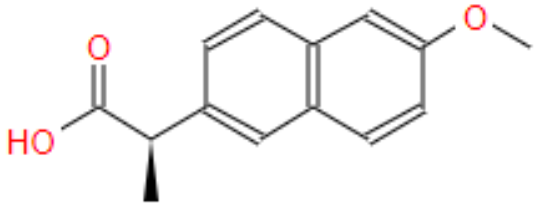


Fig. 6. Naproxen structure.

Piroxicam (PXC)

Piroxicam structure is shown in Fig 7, it is a commonly used NSAID that is available by prescription only and is used in the therapy of chronic arthritis. Piroxicam can cause mild serum aminotransferase elevations and, in rare instances, leads to clinically apparent acute liver injury that can be severe and even fatal. It is a monocarboxylic acid amide resulting from the formal condensation of the carboxy group of 4-hydroxy-2-methyl-2H-1,2-benzothiazine-3-carboxylic acid 1,1-dioxide with the exocyclic nitrogen of 2-aminopyridine. Piroxicam has been detected in average concentrations of 103 and 15 ng L^{-1} in effluent wastewaters and surface waters (Petre et al., 2016; Jiménez et al., 2018).

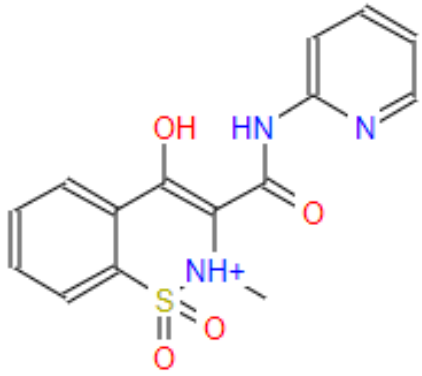


Fig. 7. Piroxicam structure.

Sulfacetamide (SAM)

Sulfacetamide is a sulfonamide, its structure is shown in Fig 8. It has a role as an antimicrobial agent and antiinfective agent and antibacterial drug. It is a sulfonamide drug widely used in current therapeutics, mainly to treat ophthalmic and skin infections. SAM is commonly available as eye-drop solutions alone or in combination with other drugs (Romdhani et al., 2019).

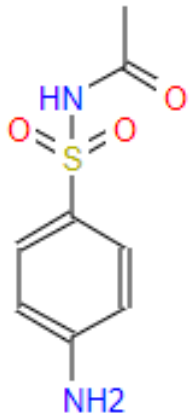


Fig. 8. Sulfacetamide structure.

Table 2 describes some chemical properties of the seven pharmaceuticals used in this research work:

Table 2. Chemical characteristics of the pharmaceuticals of interest. Information taken from ChemSpider,2020; PubChem, 2020; TOXNET, 2020; DrugBank, 2020

PHARMACEUTICALS	pK_a	Octanol/Water partition coefficient Log (P)	Water solubility (SW) (mg L^{-1})	Henry's Law constant (k_H) atm m^3 mol^{-1}	Reaction constant with HO• $M^{-1}s^{-1}$	Topological Polar Surface Area (TPSA) Å²
Acetaminophen (ACE)	9.38	0.46	14000	$6.42x10^{-13}$	$3.9 x10^{9}$	49.3
Cefadroxil monohydrate (CDX)	3.45 7.43	-0.4	1110	$7.84x10^{-21}$	Not reported	159

Cloxacillin sodium (CXL)	2.78	2.48	13.9	$1.89x10^{-17}$	$7.92x10^{9}$	141
Diclofenac sodium (DCF)	4.15	0.7	2430	$4.73x10^{-12}$	$9.29x10^{9}$	52.2
Naproxen (NPX)	4.15	3.18	15.9	$3.39x10^{-10}$	$2.5\ x10^{9}$	46.5
Piroxicam (PXC)	6.3	3.06	23	$2.9x10^{-19}$	$2.19x10^{9}$	108
Sulfacetamide (SAM)	4.3 2.14	-0.96	12500	$4.84x10^{-13}$	$5.3\ x10^{9}$	86.6

2. CHAPTER 2: METHODOLOGICAL DESIGN

2.1.Chemicals

Acetaminophen (ACE) was purchased from Bell Chem International S.A.S. Cefadroxil monohydrate (CDX) and sodium Cloxacillin (CXL) were obtained from Syntofarma S.A. Naproxen (NPX) and sodium diclofenac (DCF) were provided by Laproff. Piroxicam (PXC) was purchased from TCI. Sulfacetamide (SAM) was provided by Corpaul. Tetrahydrate ammonium hepta-molybdate ($(NH_4)_6Mo_7O_{24} * 4H_2O$), potassium bicarbonate ($KHCO_3$), magnesium sulfate heptahydrate ($MgSO_4 * 7H_2O$) and sodium nitrate ($NaNO_3$) were provided by Merck. Meanwhile, calcium chloride dehydrate ($CaCl_2$) and potassium iodide (KI) were purchased from PanReac. Iron sulfate heptahydrate ($FeSO_4 * 7H_2O$) was from Sigma-Aldrich. Acetonitrile (CH_3CN), formic acid ($H - COOH$), methanol (CH_3OH), sodium hydroxide ($NaOH$), and sulfuric acid (H_2SO_4) were purchased from Scharlau.

The mineral water was prepared in the laboratory, its chemical composition was based on the Evian water (Table 3, (Mascha, 2019)), by adding the reagents to distilled water.

Table 3. Chemical composition of synthetic mineral water used in sonochemical experiments.

Ca^{2+} (mg L^{-1})	Mg^{2+} (mg L^{-1})	Na^{+} (mg L^{-1})	K^{+} (mg L^{-1})	HCO_3^- (mg L^{-1})	SO_4^{2-} (mg L^{-1})	Cl^{-} (mg L^{-1})	NO_3^- (mg L^{-1})
5.7	2.5	1.4	228	357	10	5	3.8

2.2. Description of the execution of the experiments.

The sonochemical degradation experiments of the pharmaceuticals were carried out in a Meinhardt brand multi-frequency ultrasound laboratory reactor, with the capacity to work at

variable powers, with a volume of 500 mL, conditioned with a water-cooling jacket, which kept the temperature at 20±2°C through a Huber Minichiller, as it is shown by Fig. 9.

Fig. 9. Ultrasound reactor used for experiments.

The experiments of this investigation were carried out in distilled and mineral water matrices. The experimental solution was prepared in a 500 mL flat-bottom volumetric balloon. First, half the volume of the balloon was filled with water (mineral or distilled), then it was doped with the volume of the standard of the molecule required (7 pharmaceuticals, individually). Finally, the volumetric balloon was adjusted with the necessary water, and its pH was changed to 7.2±0.1. The working volume was 250 mL, therefore, the duplicate of each experiment was made with the same solution.

In all the sections of the experiments, an initial concentration of the pharmaceutical to be degraded of 3.31 µM was used, except section 3.4 where the initial concentrations of the compounds were modified to evaluate their effect. These values were chosen taking into account

752 that the literature reports the presence of pharmaceutical pollutants in bodies or water effluents
753 with values close to or similar to those presented in this research work.

754 The Minichiller turned on 10 minutes before starting the reaction. After this time, 250 mL
755 of the experimental solution were poured into the ultrasound reactor and covered; the reaction was
756 started and samples were taken, from time to time, for chromatographic and iodometric analyzes.

757 Sono-Fenton experiments were performed in the same way, by adding 250 μL (for [Fe^{2+}=
758 1 mg L^{-1}]) or 1250 μL (for [Fe^{2+}= 5 mg L^{-1}]) of $FeSO_4 7H_2O$ [1000 mg L^{-1}] to the reaction solution
759 (250 mL).

760 All experiments were performed in duplicate with a working volume of 250 mL and pH
761 7.2, adjusted with H_2SO_4 (0.1 M) and NaOH (0.1 M). The real acoustic power provided by the
762 reactor was quantified using the calorimetric method (Kimura et al., 1996).

763 **2.3. Independent or response variables**

764 **Pharmaceuticals concentration at sampling times: quantified by Chromatography**

765 In the current work, pharmaceuticals degradation was quantified using a Thermo Scientific
766 Dionex UltiMate 3000 UHPLC instrument (Fig. 10), equipped with an Acclaim™ 120 RP C18
767 column (5 μm, 4.6 × 150 mm) and a diode array detector. In the mobile phase, the formic acid
768 solution was used at 10 mM and pH 3.0. Table 4 summarizes the specific conditions for each
769 pharmaceutical.

770 **Table 4.** Chromatographic equipment used for pharmaceutical analysis.

Pharmaceuticals	Wavelengths of detection (nm)	Mobile phase Formic acid /Acetonitrile (% v/v)	Flow in isocratic mode (mL min^{-1})	Retention time (min)

ACE	243	85/15	0.45	7.0
DCF	260	30/70	0.5	7.5
NPX	227	65/35	1	5.2
PXC	340	40/60	0.6	7.4
CDX	254	80/20	0.5	4.2
SAM	280	60/40	0.5	4.2
CXL	225	50/50	0.7	6.1

Fig. 10. Sample reading chromatograph

H_2O_2 accumulation at sampling times: quantified by Spectrophotometry

Through iodometry, the accumulation of hydrogen peroxide in the reaction system was quantified. Iodometry is commonly used to analyze the concentration of oxidizing agents in water samples, such as oxygen saturation in ecological studies or active chlorine in the analysis of pool water. Indirect titration with iodine is performed in iodometry. In this case, a reading of the absorbance of the iodide reaction solution with hydrogen peroxide was carried out, where the reactions of the equations 16 and 17 take place:

$$H_2O_2 + 2KI \xrightarrow{AHM} 2KOH + I_2 \qquad \text{Eq. 16}$$

$$I_2 + I^- \rightarrow I_3^- \qquad \text{Eq. 17}$$

AHM: Ammonium hepta-molybdate (catalyst)

Subsequently, using Beer's law, the concentration of hydrogen peroxide will be determined, through Eq. 18.

$$C = \frac{A}{b*\varepsilon} \; x \; \frac{2000^*}{600} \qquad \text{Eq. 18}$$

A: Absorbance
b: optical path (1 cm)
ε: molar absorbance (26,400 $M^{-1}cm^{-1}$)
C: concentration of hydrogen peroxide
*: Dilution factor

For this, samples of the 600 µL experimental solution were taken, mixed in a quartz cell containing 1350 µL of potassium iodide (0.1 mL^{-1}) and 50 µL of ammonium hepta-molybdate (0.01 mL^{-1}), leaving react for 5 minutes. Subsequently, the absorbance at 350 nm was measured using a Mettler Toledo UV5 spectrophotometer.

A correlational experimental research work was carried, the global methodology of Fig. 11 was proposed and, carried out on a laboratory scale.

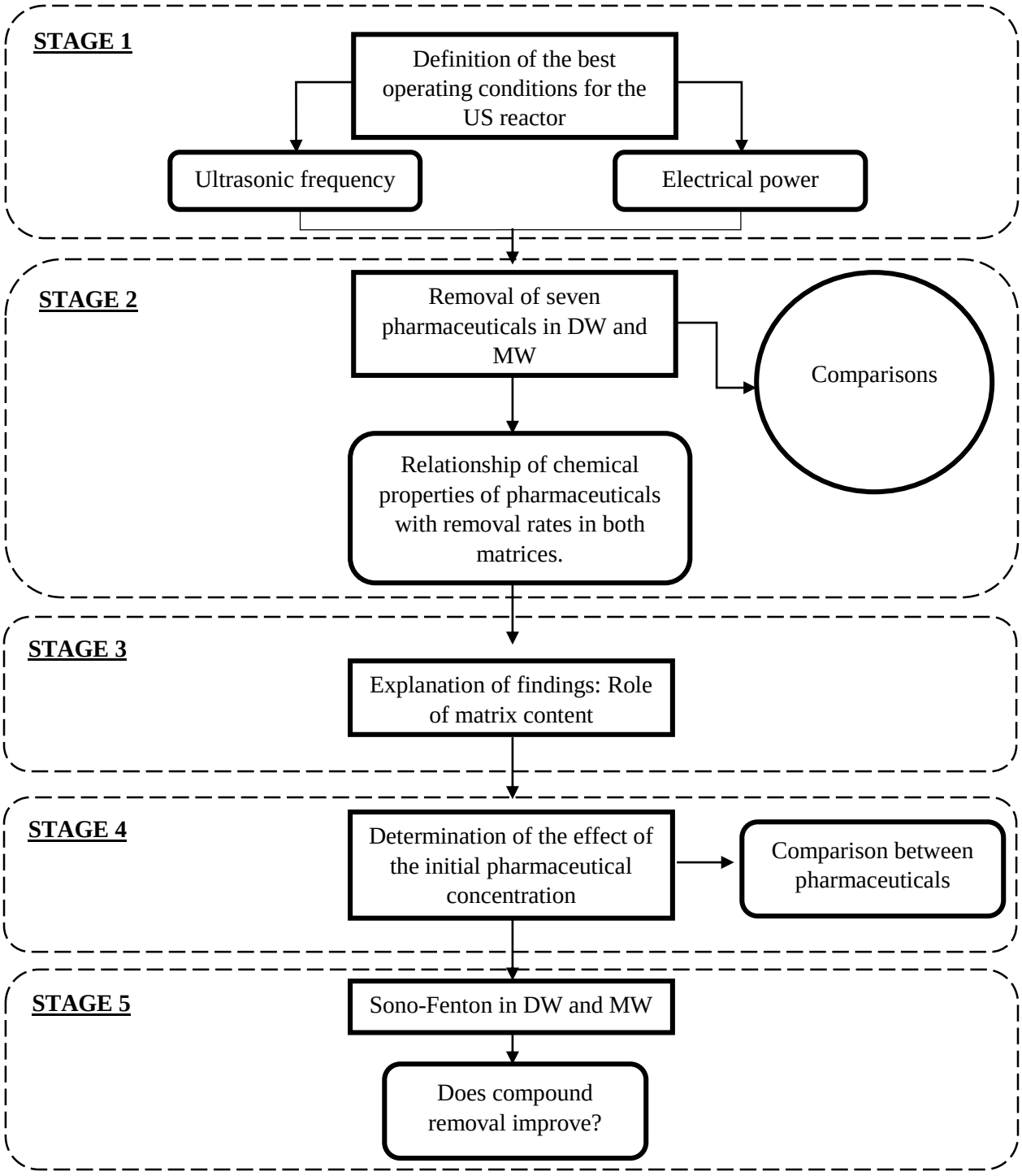


Fig. 11. Methodology flow diagram.

The first stage aimed to determine the proper operating conditions for the ultrasound reactor to degrade the pharmaceuticals of interest in our work. Here, the factors to be analyzed were the Frequency and Ultrasonic Power, testing both at different levels to determine in which the best percentages of compounds removal and hydrogen peroxide accumulation were obtained.

With the appropriate levels of frequency and power, in the second stage the degradation of the seven molecules or pharmaceuticals of interest was experienced, both in distilled water and in mineral water; analyzing the results obtained in both matrices based on the structure and chemical properties of the compounds.

The next stage defined the role of mineral water constituents on the degradation results obtained. Here we experimented with distilled water doped with each salt independently.

In the fourth stage, the initial concentrations of the pharmaceuticals to be degraded were modified, considering values below and above the initial concentration that has been used up to now. Comparisons of compounds with different chemical properties were made.

Finally, the last stage added the Fenton process to the sonochemical degradation that had been carried out. Here the molecule that had very low removal percentages in all the experiments developed previously was degraded. Sono-Fenton tests were performed on both distilled and mineral water.

3. CHAPTER 3: ANALYSIS OF RESULTS

3.1. Determination of suitable operation conditions for pharmaceuticals degradation

Frequency and acoustic power are recognized as primary operation parameters that determine the efficiency of the sonochemical system (Wood et al., 2017). Thus, experiments to establish the suitable settings of both parameters for the degradation of pollutants were initially performed using diclofenac (DCF) as a model compound. This substance was chosen because this is a pharmaceutical found frequently in diverse waters bodies and it has shown a good susceptibility to the sonochemical degradation (Güyer & Ince, 2011; Nie et al., 2014; Hartmann et al., 2008).

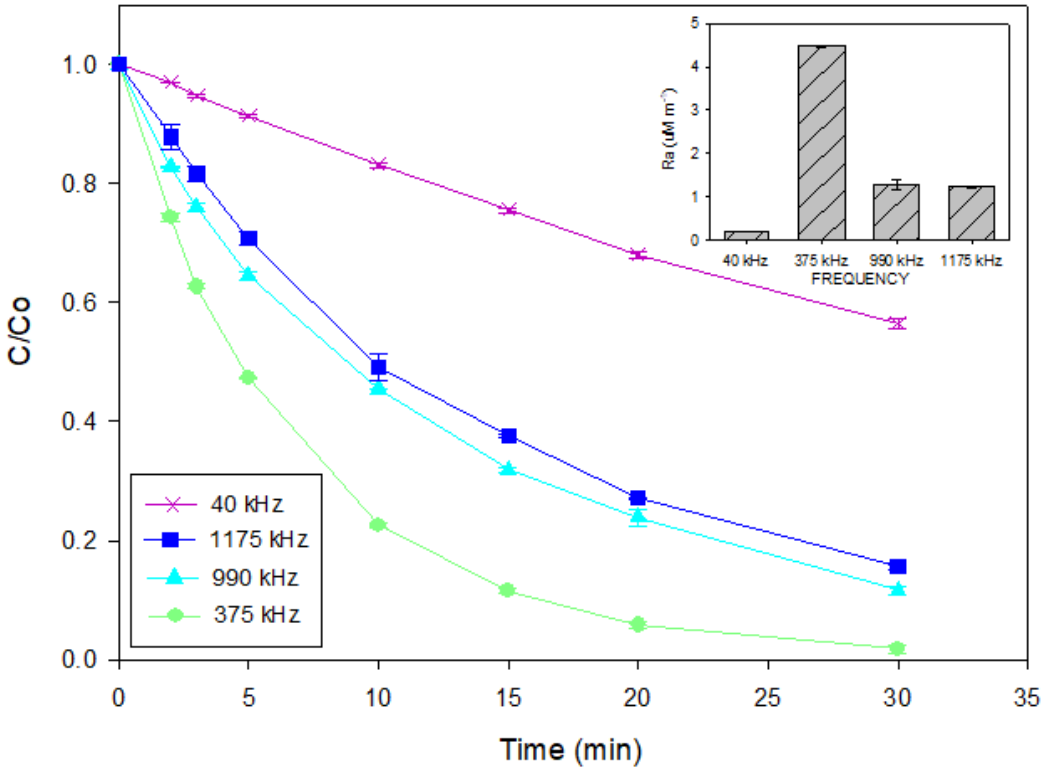


Fig. 12. Diclofenac (DCF) evolution under different sonolysis frequencies. Inset: H_2O_2 accumulation rate (Ra, µM min^{-1}) during DFC degradation. Conditions: initial DCF concentration: 3.31 µM, pH: 7.2±0.1, acoustic power: 24.4 W, temperature: 20 °C and volume: 250 mL.

The performance of the sonochemical system was followed in terms of the pollutant removal and accumulation of hydrogen peroxide. Two experimental sets, by modifying a single factor at a time, were developed. The first set had the frequency as a variable factor and the other operating conditions remained fixed. Fig. 12 shows the DCF removal under different frequency levels (i.e., 40, 375, 990, and 1175 kHz). Here, the lowest pollutant removal was obtained at 40 kHz (44% after 30 min of treatment). For 1175 and 990 kHz, close results of DCF removal were obtained (84% and 88% at 30 min, respectively). In turn, at 375 kHz of frequency, ~100% of the pharmaceutical was removed in the same treatment time.

The inset in Fig. 12 depicts the rate of H_2O_2 accumulation (Ra, in μM min^{-1}, see Annex A_1) at the different frequencies in the presence of DCF. For the frequency of 375 kHz was also obtained the greatest rate of H_2O_2 accumulation, which is attributed to the combination of sonogenerated radicals (Eqs. 5-7). It was also found that the frequencies of 990 kHz and 1175 kHz exhibit a similar Ra. Meanwhile, at 40 kHz there was a very low peroxide accumulation rate.

Ultrasonic frequency influences both cavitation collapse time and bubble size (Torres-Palma & Serna-Galvis, 2018; Lim et al., 2011). It is estimated that between 200 and 350 kHz occur the greatest formation of radicals (Kang et al., 1999). This explains the highest DCF degradation and Ra at 375 kHz under the tested conditions. Considering the above results, the following experiments were performed by using 375 kHz of frequency.

Fig. 13 presents the results for the DCF degradation under different levels of acoustic power (at 375 kHz). As this factor increased, the degradation of the pollutant also increased. Indeed, for ~1.0, 4.0, and 11.2 W of power, the removals were 1%, 32%, and 80%, respectively. The highest removal of DCF was obtained at 24.4 W (100% of degradation was achieved after 30 min of treatment). Similarly, the Ra was the highest at 24.4 W of power (see inset in Fig. 13). The rising

of the ultrasonic power increases the number of cavitation bubbles and consequently, the production of HO• is increased (Naddeo et al. 2009; Lifka et al., 2003; Tran et al., 2015). This is traduced in higher values of both removals of pollutants as DFC and sono-generation of H_2O_2. Considering that at 24.4 W of acoustic power was found greater production of HO• and higher degradation of the reference pollutant, this power was used for the development of the subsequent experiments.

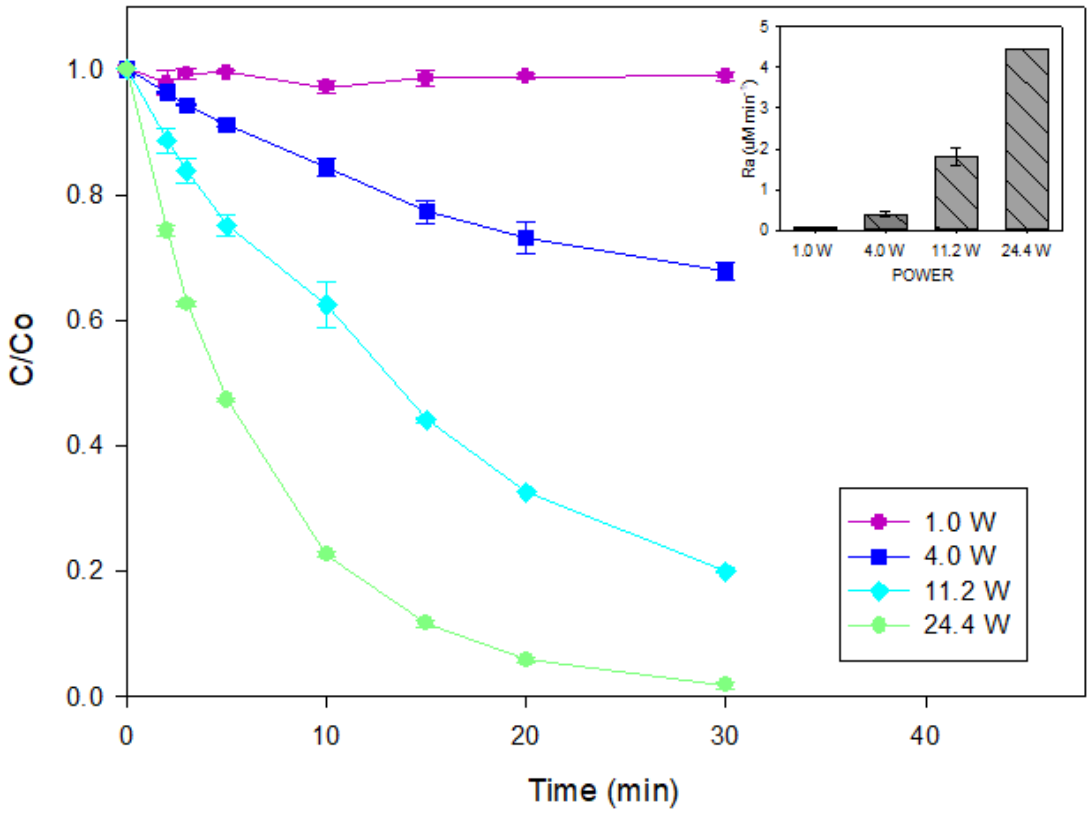


Fig. 13. DCF evolution under different acoustic powers. Inset: H_2O_2 accumulation rate (Ra, in µM min^{-1}) during DCF degradation. Experimental conditions: Initial DCF concentration: 3.31 µM, pH: 7.2±0.1, frequency: 375 kHz, temperature: 20 °C and volume: 250 mL.

3.2. Effect of the chemical structure of the contaminant on the sonochemical degradation in distilled and mineral water

After determination of the proper frequency and power for our sonochemical system, seven target pharmaceuticals (substances highly consumed and frequently found in diverse water matrices, Naddeo et al., 2009; Gil et al., 2013) were individually treated in distilled water and their evolutions were compared. Fig. 14 depicts the removal curves at 30 min of treatment. It can be observed significant differences among the pharmaceuticals. CXL, NPX, DCF, and PXC exhibited a fast degradation; in fact, after 10 min of treatment 62, 69, 69, and 83% of removal of them, respectively, were obtained. In contrast, CDX was the compound with the lowest removal, with percentages of 14 and 28% at 10 and 30 min, respectively. Meanwhile, SAM and ACE presented intermediate removals of 43 and 50% at 10 minutes and 71 and 80% at 30 minutes, respectively.

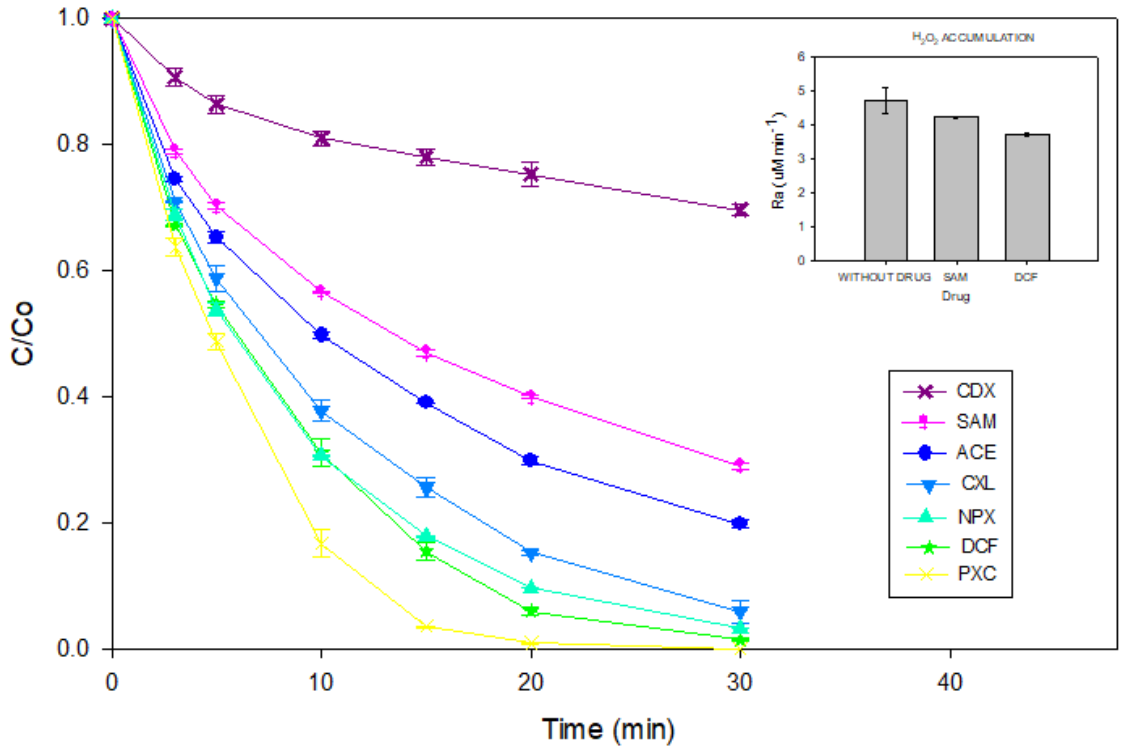


Fig. 14. Pharmaceuticals evolution during the sonochemical treatment in distilled water. Inset: H_2O_2 accumulation rate (Ra, µM min^{-1}). Experimental conditions: Initial pollutant concentration:

3.31 µM, initial pH: 7.2±0.1, Frequency: 375 kHz, Acoustic power: 24.4 W, Temperature: 20 °C and Volume: 250 mL.

The chemical nature of the compounds influences directly their removal through sonochemistry (Jiang at al., 2002; Dalhatou et al., 2015). Considering that none of the seven molecules is volatile, a pyrolysis route is not expected. Then, the degradation of the pharmaceutical can be associated with their reaction with the sonogenerated HO• (Méndez-Arriaga et al., 2008). To verify the degrading role of the hydroxyl radical, the accumulation rate of hydrogen peroxide (Ra) was measured during pharmaceuticals degradation and compared with a blank experiment (i.e., sonication of distilled water without pollutants).

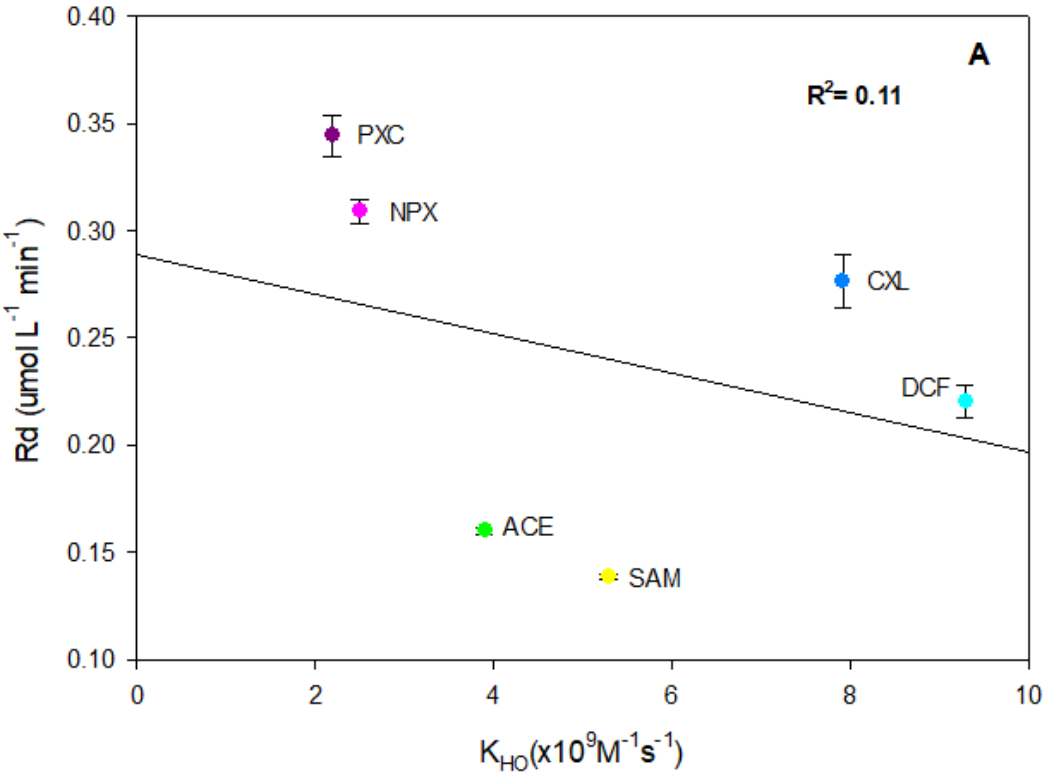
Inset in Fig. 14 contains values for the Ra in absence of pollutants and in presence of two illustrative pharmaceuticals SAM (which had a medium removal) and DCF (which presented a fast removal). As observed, when pollutants were no present, the accumulation rate of H_2O_2 was higher (4.72 µmol L^{-1} min^{-1}) than the obtained in the presence of SAM (4.22 µmol L^{-1} min^{-1}) or DCF (3.71 µmol L^{-1} min^{-1}). The lower accumulation of hydrogen peroxide under the presence of the pharmaceutical suggests the reaction of hydroxyl radical with these pollutants, which decreases the combination of sonogenerated HO• (Eq. 6) (Kask et al., 2019).

To understand the degradation order observed in Fig. 14, it was tested the relationship between the initial degradation rate of the pollutants (Rd, see Annex A_2) and their rate constant with the HO• ($k_{(HO)}$) (Fig. 15A). It can be noted that the order of degradation presented does not correlate well with the order exhibited by $k_{(HO)}$ of the pharmaceuticals (R^2: 0.11) (Cooper & Weihua, 2012; Feng et al., 2019; Jin et al., 2015; Szabó et al., 2016; Feng et al., 2015; Sági et al., 2015). This means that the degradation rate of the target molecules cannot be explained solely

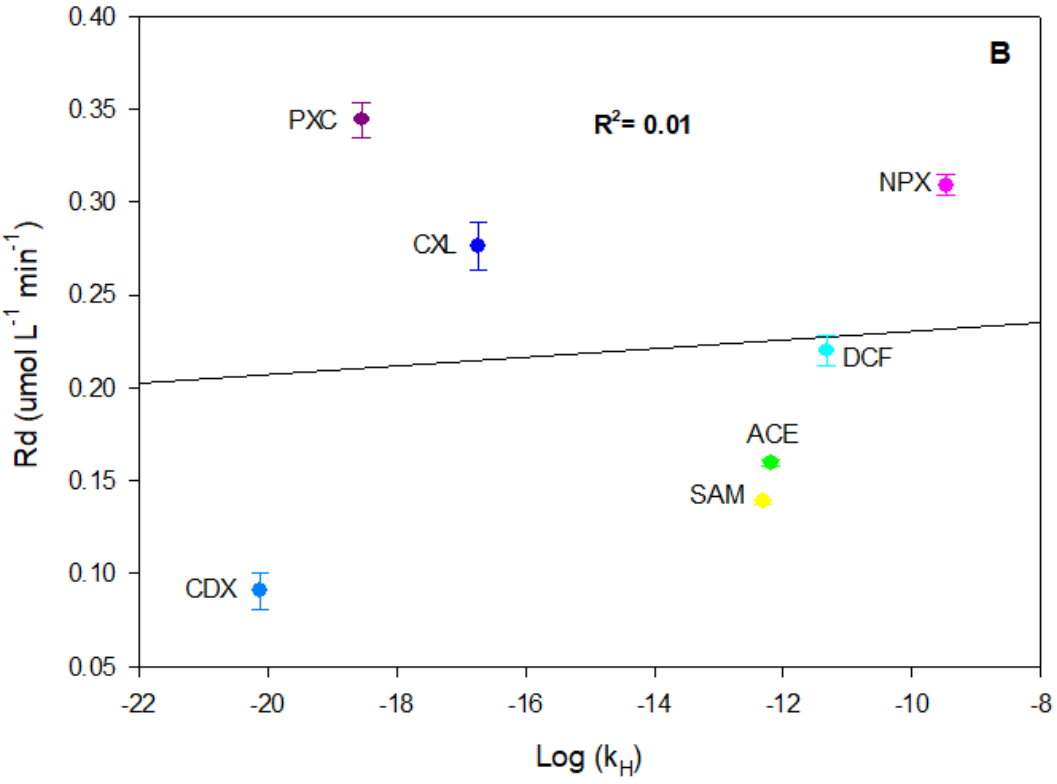
947 through the reaction with the HO•, and $k_{(HO)}$ did not determine which molecule is faster degraded
948 through ultrasound.

949 Therefore, to find a clearer explanation of the elimination order obtained in Fig. 14, it was
950 evaluated the correlation with the properties that offer information about
951 hydrophobicity/hydrophilicity of the pharmaceuticals. Such properties were: octanol/water
952 partition coefficient (Log (P)), solubility in water (Sw), Henry's Law constant (k_H), and topological
953 polar surface area (TPSA). The relationship between the initial degradation rate (Rd) and each one
954 of these parameters is presented in Fig. 15B-E.

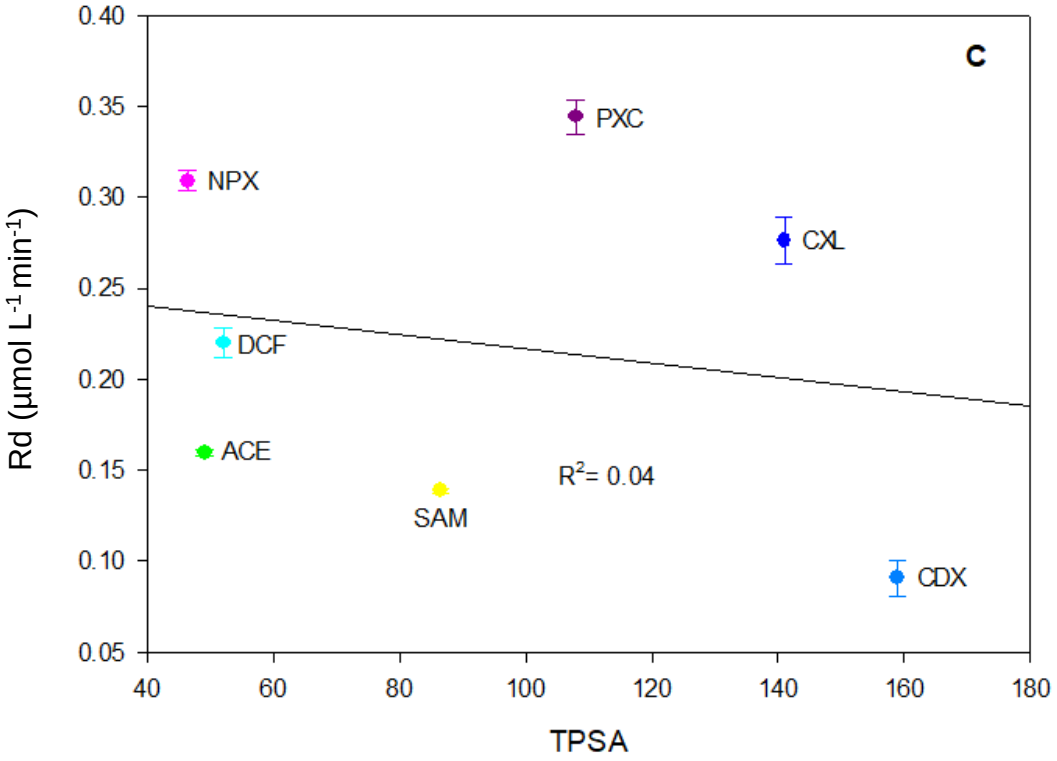
955 In the case of the Henry's law constant, it was no found a correlation with the initial
956 degradation rates (R^2= 0.01, Fig. 15B). The k_H represents the fugacity, which indicates the trend
957 of molecules to escape from aqueous media to the gas phase. Although this parameter has been
958 useful to rationalize sono-degradation of some phenolic compounds (Torres et al., 2008), for the
959 tested pharmaceuticals this is not the key parameter. Regarding the topological polar surface area
960 (TPSA), no correlation was observed either (R^2= 0.04, Fig. 15C). Despite TPSA denotes some
961 hydrophilicity of the substances, this parameter does not explain the behavior of the target
962 pollutants in the sonochemical process.


A
R^2= 0.11
PXC
NPX
CXL
DCF
ACE
SAM
Rd (umol L^{-1} min^{-1})
K_{HO}(x10^9 M^{-1} s^{-1})
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0
2
4
6
8
10

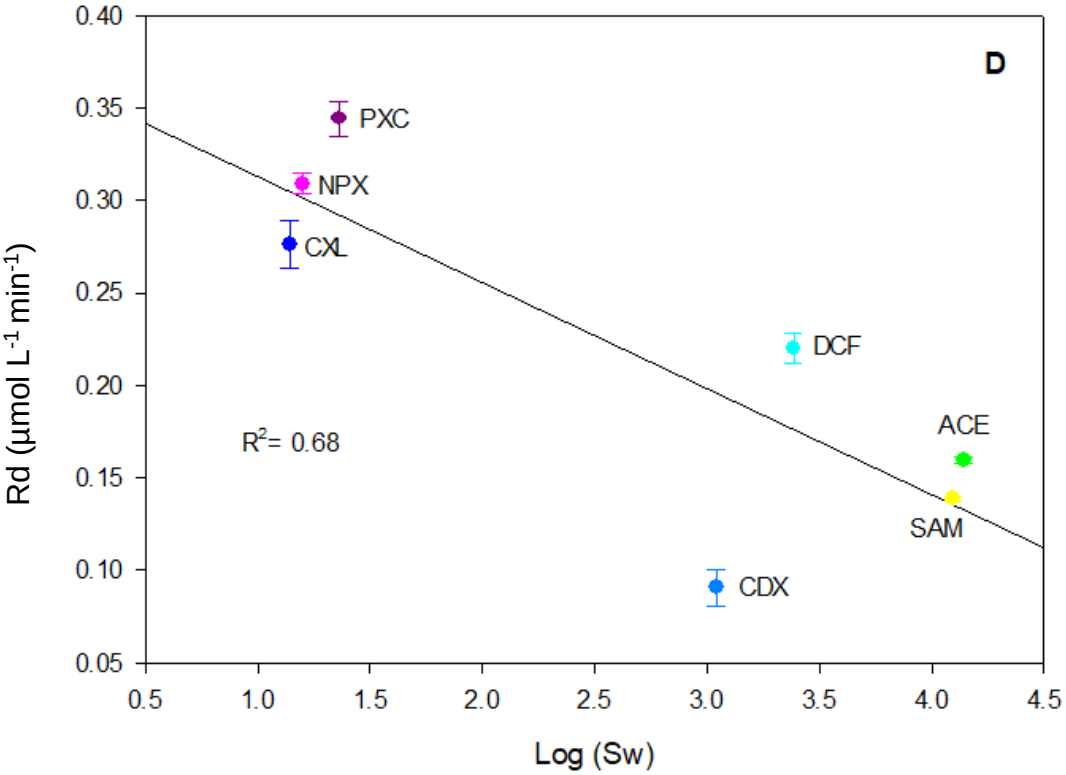
963


B
R^2= 0.01
PXC
NPX
CXL
DCF
ACE
SAM
CDX
Rd (umol L^{-1} min^{-1})
Log (k_H)
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
-22
-20
-18
-16
-14
-12
-10
-8

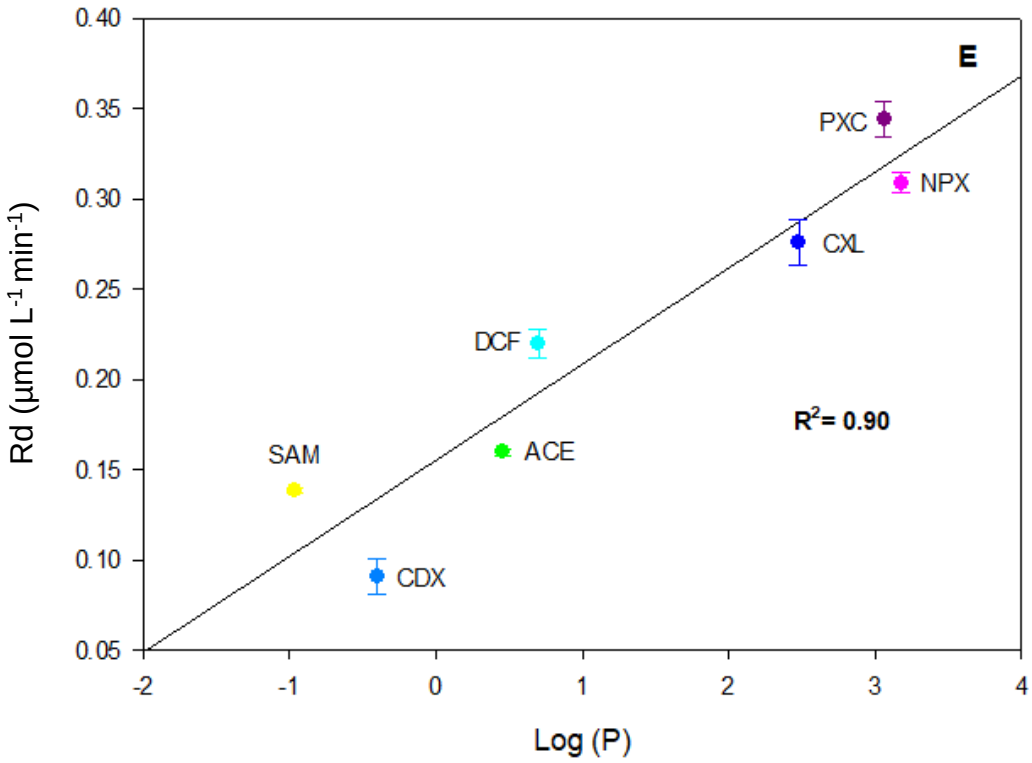
964


C
PXC
NPX
CXL
DCF
ACE
SAM
CDX
R^2= 0.04
Rd (µmol L^{-1} min^{-1})
TPSA
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
40
60
80
100
120
140
160
180

965


D
PXC
NPX
CXL
DCF
ACE
SAM
CDX
R^2= 0.68
Rd (µmol L^{-1} min^{-1})
Log (Sw)
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5

966
967



968
969
970 **Fig. 15.** Relationship between the initial degradation rate (Rd, µM min^{-1}) and different physico-
971 chemical parameters of pharmaceutical. **A.** Reaction rate constant with HO•, **B.** Henry's Law
972 constant, **C.** Topological Polar Surface Area (TPSA), **D.** Water solubility and **E.** Octanol/water
973 partition coefficient (Log (P)). Conditions: Initial pollutant concentration: 3.31 µM, initial pH:
974 7.2±0.1, Frequency: 375 kHz, Acoustic power: 24.4 W, Temperature: 20 °C and Volume: 250 mL.

975 In turn, a moderate correlation (R^2= 0.68) between the logarithm of water solubility (Log
976 Sw) and Rd is observed in Fig. 15D. In this figure it can be noted two groups of compounds, in
977 the first one are those pharmaceuticals that have low solubility and a high initial degradation rate
978 (i.e., CXL, NPX, and PXC), and the second group is formed by the compounds with greater
979 solubility in water and medium or low Rd (i.e., CDX, SAM, ACE, and DCF). Noting that CDX
980 has a low Rd and far from the trend line since despite being very soluble in water (Table 2) it
981 degrades slowly by ultrasound. For such reason, the Log Sw parameter had a moderate correlation

with Ra for the treatment of the pharmaceuticals. Solubility in water is a direct indicator of hydrophilicity, also it is recognized that high soluble substances are far from the cavitation bubbles and are slowly degraded by sonochemistry (Torres-Palma & Serna-Galvis, 2018).

Interestingly, a high correlation (R^2= 0.90) between the octanol/water partition coefficient (Log P) and the initial degradation rate (Rd) was observed (Fig. 15E). In fact, CXL, NPX, and PXC, which have a high Log P (2.48, 3.18, and 3.06, respectively) achieved a faster removal (Rd: 0.2762, 0.3089, and 0.3442 μmol L^{-1} min^{-1}, respectively). Meanwhile, CDX, SAM, ACE and DCF, the pharmaceuticals with low Log P (i.e., -0.4, -0.96, 0.46 and 0.70, respectively) had 0.0748, 0.1386, 0.1597 and 0.2201 μmol L^{-1} min^{-1} value for Rd, respectively. The octanol/water partition coefficient is a physicochemical property indicative of compounds hydrophobicity (Serna-Galvis et al., 2019; Ridder et al., 2009; Nanzai et al., 2008). Hydrophobicity of pharmaceuticals favors their proximity to the cavitation bubble, and therefore, a faster interaction with the sonogenerated HO•. Conversely, the hydrophilic compounds are impaired for their affinity with water and they are placed away from the cavitation bubble, which limits their reaction with the radicals (Torres-Palma & Serna-Galvis, 2018; Im et al., 2014; Adewuyi, 2005; Ince et al., 2001). This explains the good correlation between Log P and Rd for the considered pharmaceuticals.

Once considered the degradation of the pollutants in distilled water, it was studied the treatment of the pharmaceuticals in the mineral water (Fig. 16A). As seen, the degradations of CDX, SAM, ACE, and DCF were accelerated in the mineral water, achieving removal percentages of 23, 60, 73, and 82% at 10 minutes of treatment and 42, 99, 100, and 100% at 30 minutes, respectively. In turn, the most hydrophobic pharmaceuticals (e.g., CXL, NPX, and PXC) exhibited removal percentages very close to those obtained in the distilled water (Fig. 14), having values of 61, 68, and 81% at 10 minutes of treatment and 90, 96 and 100% at 30 minutes, respectively.

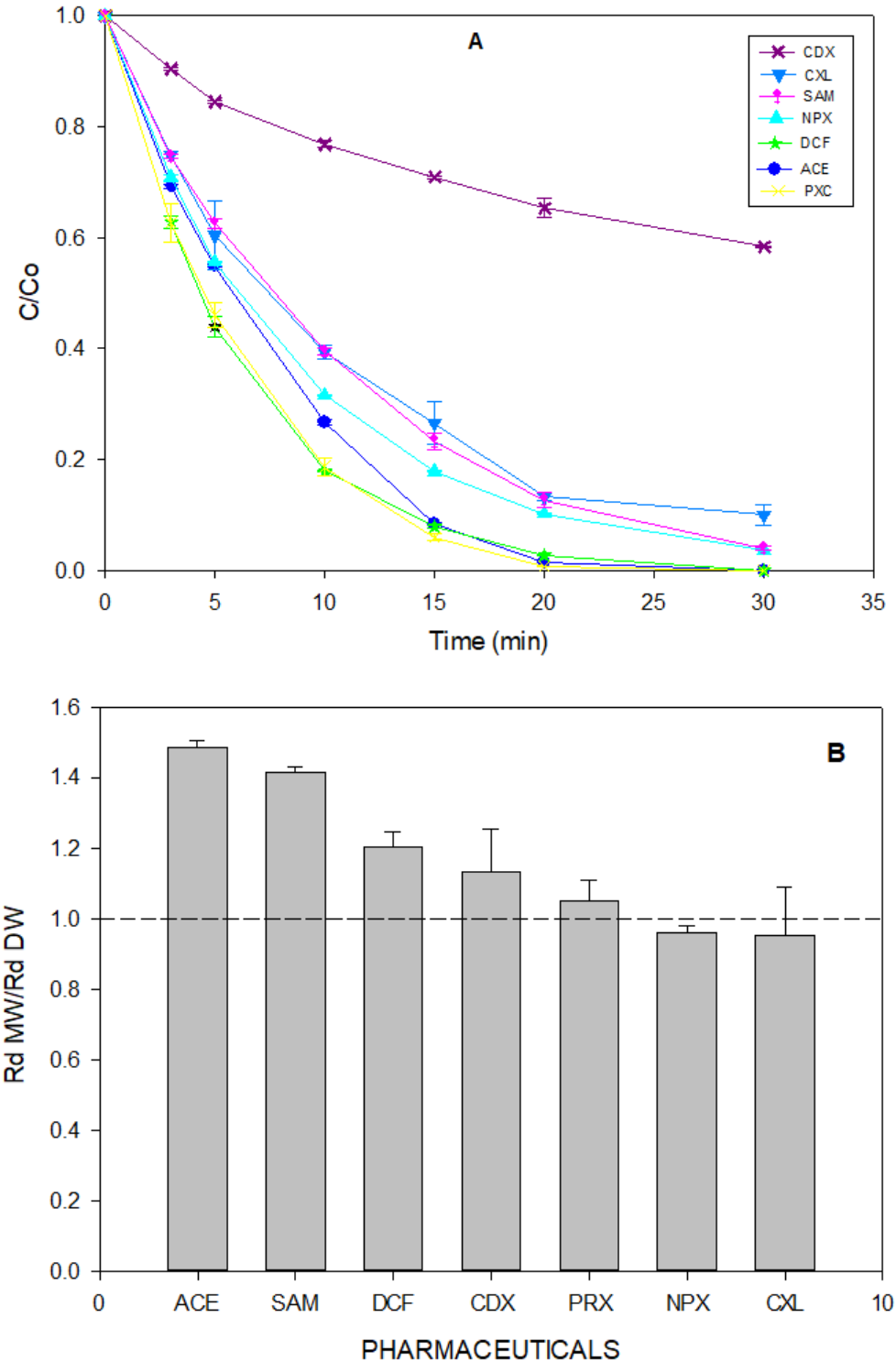


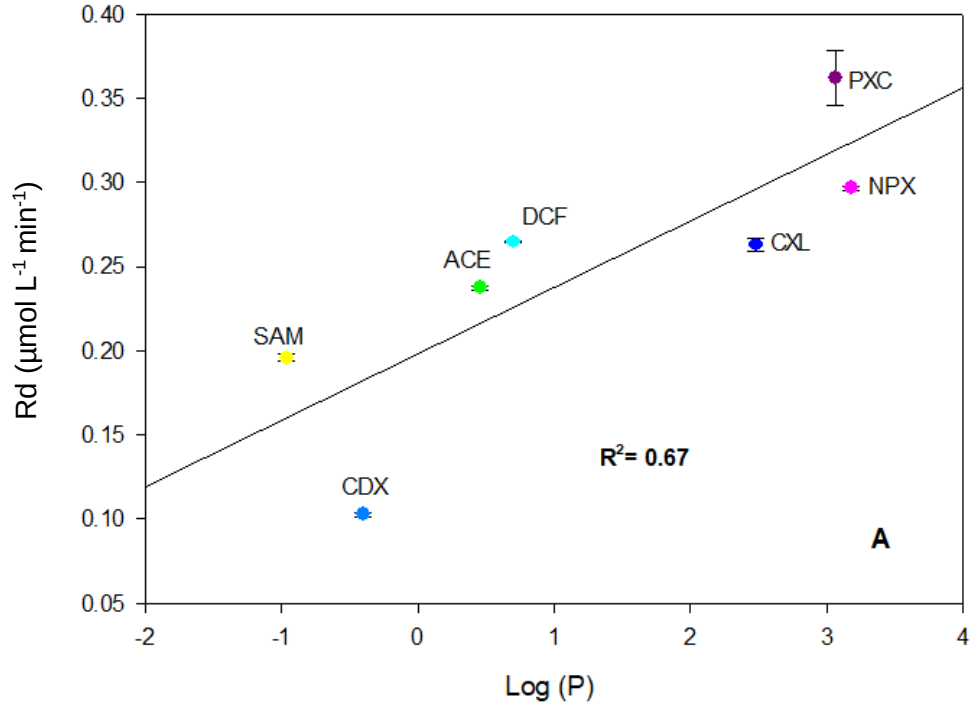
Fig. 16. Degradation of the target pollutants in mineral water. **A.** Pharmaceuticals evolution. **B.** Ratio between the initial degradation rate in mineral water and distilled water. Conditions: Initial

pollutant concentration: 3.31 µM, initial pH: 7.2±0.1, Frequency: 375 kHz, acoustic power: 24.4 W, Temperature: 20 °C and Volume: 250 mL.

To compare the results in mineral water and distilled water, the ratio between the initial degradation rates in mineral water and distilled water was calculated (i.e., R_dMW/R_dDW, Fig. 16B). If such ratio is lower than one indicates that the effect of mineral water matrix is inhibitory, whereas a ratio greater than one means that the pharmaceutical degradation was favored by the matrix. When the ratio is equal to one indicates that similar pollutant degradation in the mineral water and distilled water occur. ACE, SAM, DCF, and CDX showed a ratio higher than one (Fig. 16B), indicating that there was a positive effect of the mineral water matrix. On the other hand, PXC, NPX, and CXL present ratios close to one, which means that their initial degradation rates in both matrices were similar.

In an analogous way to developed for distilled water, it was evaluated the correlation of initial degradation rate (Rd) in mineral water (Fig. 17) with the two physico-chemical properties (Log (Sw) and Log P) that exhibited the best fits. It can be noted a difference between the slopes of the Log (P) graphs for distilled water and mineral water (Figs 15E and 17A). In mineral water, a more horizontal behavior of the slope is evidenced in comparison with that obtained in distilled water. This reaffirms that there was an increase in the initial degradation rate of some pollutants (those with the lower degradation rate: SAM, ACE, and CDX), when it was experimented in mineral water. However, unlike the observed for experiments in distilled water, in the mineral water matrix, the Log P and Log Sw parameters did not offer so good correlations with Rd (R^2: 0.67 and 0.32 were obtained for Log P and Log Sw, respectively). Consequently, these parameters cannot be used to explain the order of degradation of the pharmaceuticals in the mineral water. Hence, in addition to hydrophobicity, other criteria must be considered.

As ionic constituents (e.g., HCO_3^-, SO_4^{2-}, Cl^- y NO_3^-) are present in the mineral water, the acceleration of degradations of some compounds could also depend on these factors. Then, the role of matrix components was studied (this topic is detailed in the next section).



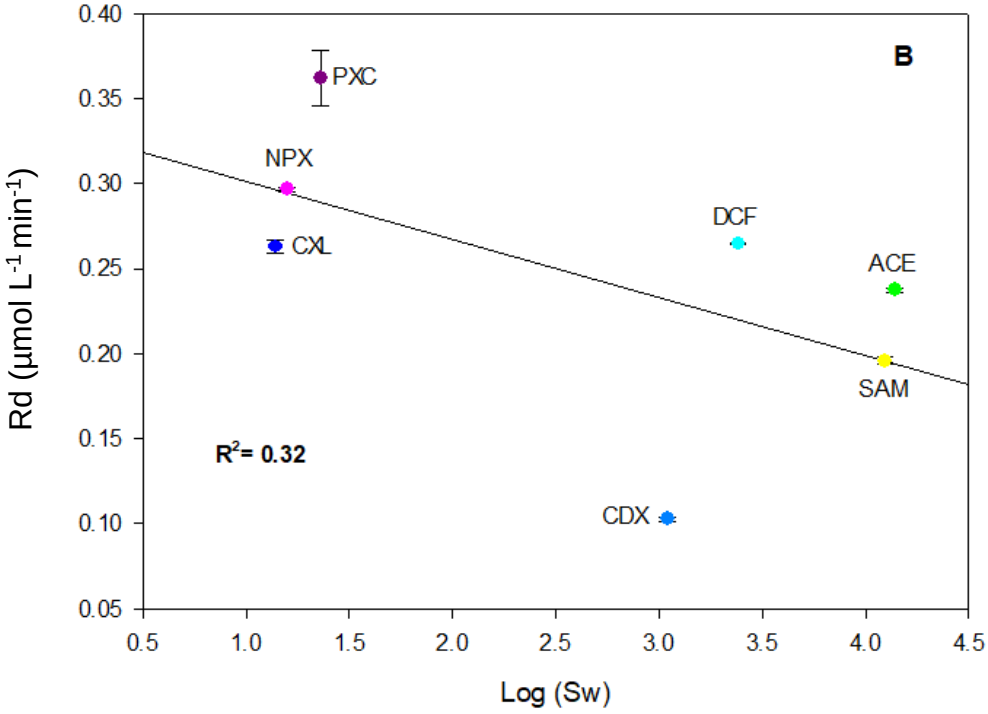


Fig. 17. Relationship between the initial degradation rate of the pharmaceuticals (Rd, μM min^{-1}) in mineral water and octanol/water partition coefficient **A**, water solubility **B**. Initial pollutant concentration: 3.31 μM, initial pH: 7.2±0.1, Frequency: 375 kHz, Acoustic power: 24.4 W, Temperature: 20 °C and Volume: 250 mL.

3.3. Understanding the role of the mineral water matrix components in pharmaceuticals degradation.

To determine the effect of the constituents of mineral water on the degradation of the pharmaceuticals, individual experiments in distilled water with each ion (at the same concentration that in mineral water, Table 3) were carried out. SAM was chosen as a probe molecule for this purpose, due to its high acceleration by the mineral water matrix in the previous experiments (see Fig. 16B).

The SAM removal curves in the presence of the different ions are shown in Fig 18. It can be noted that there were no significant differences in the degradation obtained in the presence of nitrate, sulfate, chloride, and distilled water alone, indicating that these ions did not contribute to the degradation of SAM. Interestingly, the removal of SAM in the presence of bicarbonate was greatly accelerated compared to that obtained in distilled water alone and with the other ions, achieving a degradation of 97% of the pollutant at 30 minutes of treatment. Indeed, the degradation evolution in the presence of only bicarbonate is very similar to the obtained in the mineral water (Fig. 18).

It is recognized that bicarbonate anion scavenges HO• (Eq. 19), and this substance is very concentrated in the water (5300 μM), which should affect the degradation of the pharmaceutical. However, as seen in Fig. 18, this ion favored the degradation of SAM, moving from an initial

degradation rate in distilled water of 0.1997 µM min^{-1} to one of 0.2495 µM min^{-1} in bicarbonate-containing water. Similar results were found by Pétrier et al., 2010, Villaroel et al., 2014 and Dalhatou et al., 2019, during the degradation of other organic pollutants in presence of bicarbonate. In addition to the SAM evolution, the Ra in the presence of the anions was also established and compared that in distilled water. Inset in Fig. 18 contains the ratio between the accumulation rates of H_2O_2 in water with the ions and distilled water. It was observed that for water with bicarbonate ions there was an inhibitory effect on the accumulation of H_2O_2, because that relationship is below one; while for the other ionic constituents this ratio was very close to one.

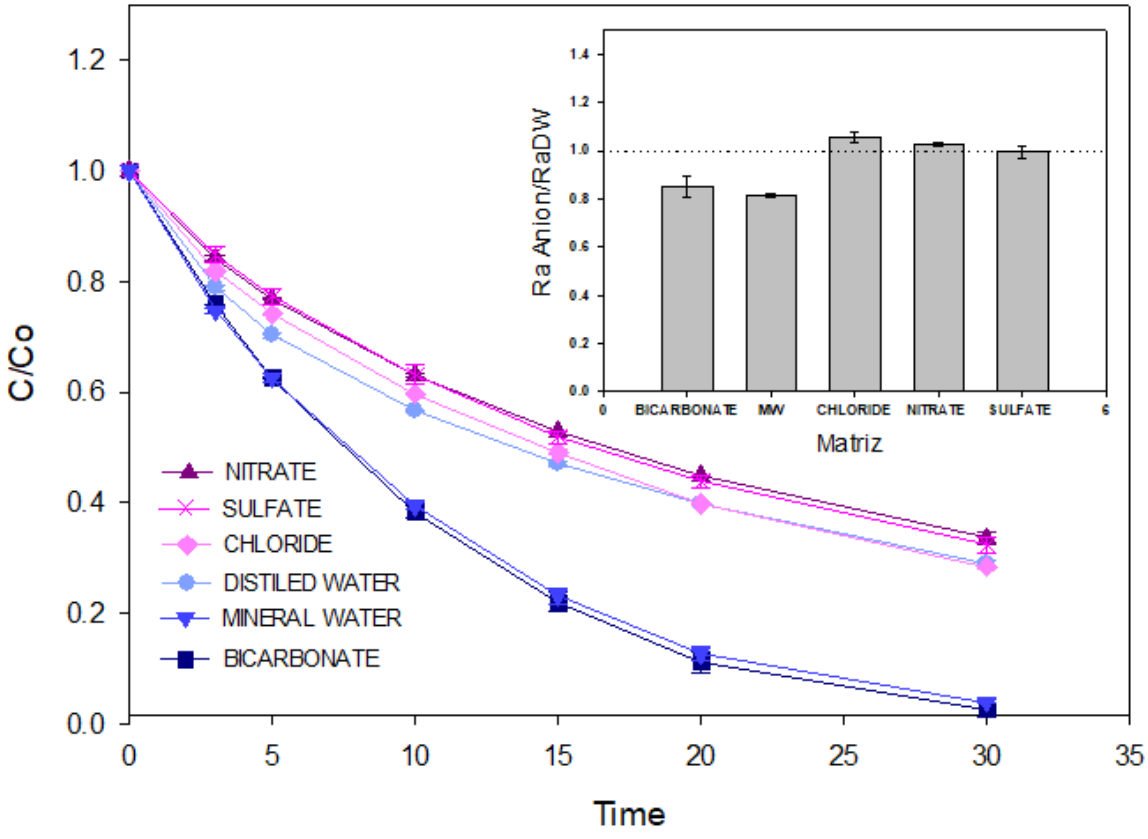


Fig. 18. Sulfacetamide (SAM) removal in the presence of individual components of mineral water constituents. Inset: Effect of ionic constituents on the H_2O_2 accumulation. Conditions: Initial

pharmaceutical concentration: 3.31 µM, initial pH: 7.2±0.1, Frequency: 375 kHz, Acoustic power: 24.4 W, Temperature: 20 °C and Volume: 250 mL.

The inhibition of H_2O_2 accumulation supports that HO• is captured by the bicarbonate (Eq. 19), decreasing the combination of radicals to form H_2O_2 (Eq. 6). The formed CO_3^{*-} is an oxidizing agent. Thereby, it is proposed that the formed carbonate radical attacks the compounds. Although the CO_3^{*-} (E°: 1.78 V) is less powerful than hydroxyl radical (E°: 2.8 V), it has a lower recombination rate ($1.2x10^7$ M^{-1} s^{-1}) than HO• ($5.5x10^9$ M^{-1} s^{-1}) and it can migrate to the solution bulk (Pétrier et al., 2010; Minero et al., 2008; Torres-Palma & Serna-Galvis, 2018; Xia et al., 2020) reaching hydrophilic substances as SAM, which are further away from the cavitation bubble. Consequently, this enhances the pollutant degradation with respect to water without bicarbonate ions (Fig. 18). In this way, it can be proposed that the presence of bicarbonate in mineral water promotes the formation of CO_3^{*-}, which improved the degradation of ACE, DCF, and CDX, just like SAM as observed in Fig. 16.

$$HCO_3^- + HO^* \rightarrow CO_3^{*-} + H_2O \qquad k = 8.5 \times 10^6 \text{ L mol}^{-1}\text{s}^{-1} \qquad \text{Eq. 19}$$

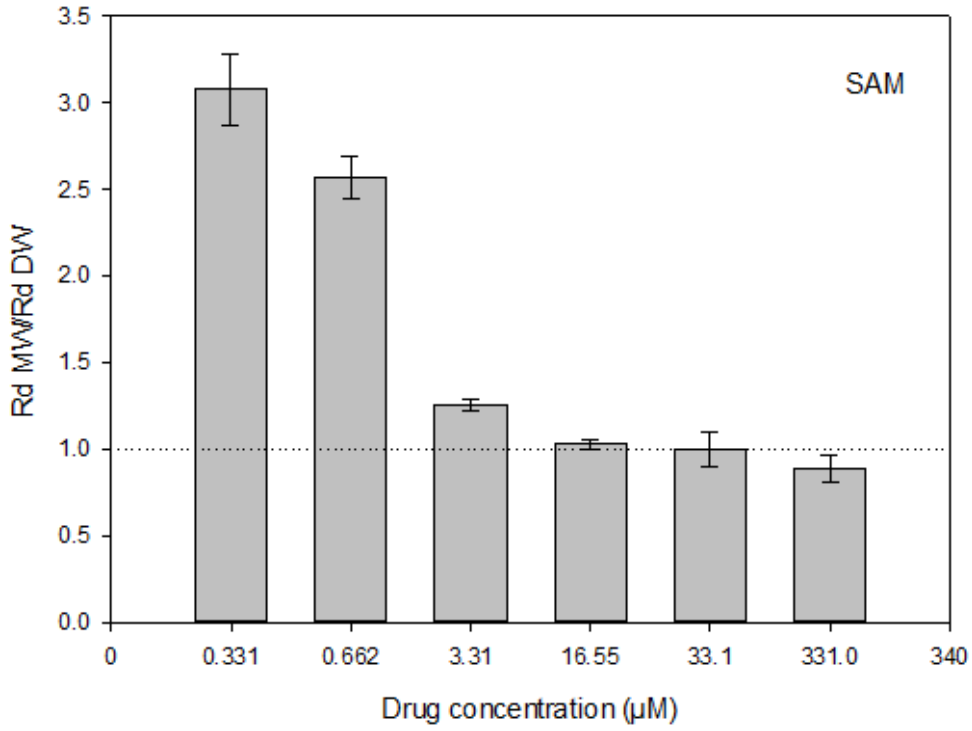
3.4. Effect of pharmaceutical concentration on its removal in mineral water

To study the enhancing effect exerted by the mineral water matrix as a function of the concentration of pollutants, three representative pharmaceuticals with different behavior were chosen. These substances were SAM (which has a pronounced acceleration of degradation in mineral water), CDX (pharmaceutical with a low acceleration in mineral water), and CXL (that experimented no acceleration in mineral water). Fig. 19 presents the ratio between the initial degradation rates in mineral water and distilled water, for diverse concentrations of the pharmaceuticals. Again, if the ratio is lower than one, the effect of the mineral water is inhibitory.

Meanwhile, if the ratio is greater than one indicates acceleration, and a ratio equal to one means that the matrix has no net effect on the degradation.

For SAM, it was found that the lowest concentrations of the pollutant (i.e., 0.331, 0.662, and 3.31 µM) had a ratio greater than one (Fig. 19A), indicating an acceleration of degradation in the mineral water. At the concentrations of 16.55 and 33.10 µM, it is observed that the ratio is very close to one, and for the highest concentration used in the experiments (331 µM) a negative effect on the degradation by the mineral water matrix is found. As SAM has a hydrophilic nature, this pharmaceutical is far away from the cavitation bubble, and a decrease of its concentration further limits the diffusion toward the interfacial zone. This allows to the majority of produced HO• react with the bicarbonate, leading to a high participation of CO_3^{*-} as a degrading agent of SAM (Eq. 20) in the bulk of the solution (where typically arrive low amounts of HO•). On the contrary, when the concentration of SAM in the mineral water is relatively high (e.g., 331 µM) the diffusion is favored, causing that more molecules of this pharmaceutical locate closer to the cavitation bubble. Then, a competition among the constituents of the matrix and the target compound for HO• occur, which decreases the SAM degradation as observed in the Fig. 19A.

$$CO_3^{*-} + \text{Pharmaceutical} \rightarrow \text{Oxidized products} \qquad \text{Eq. 20}$$



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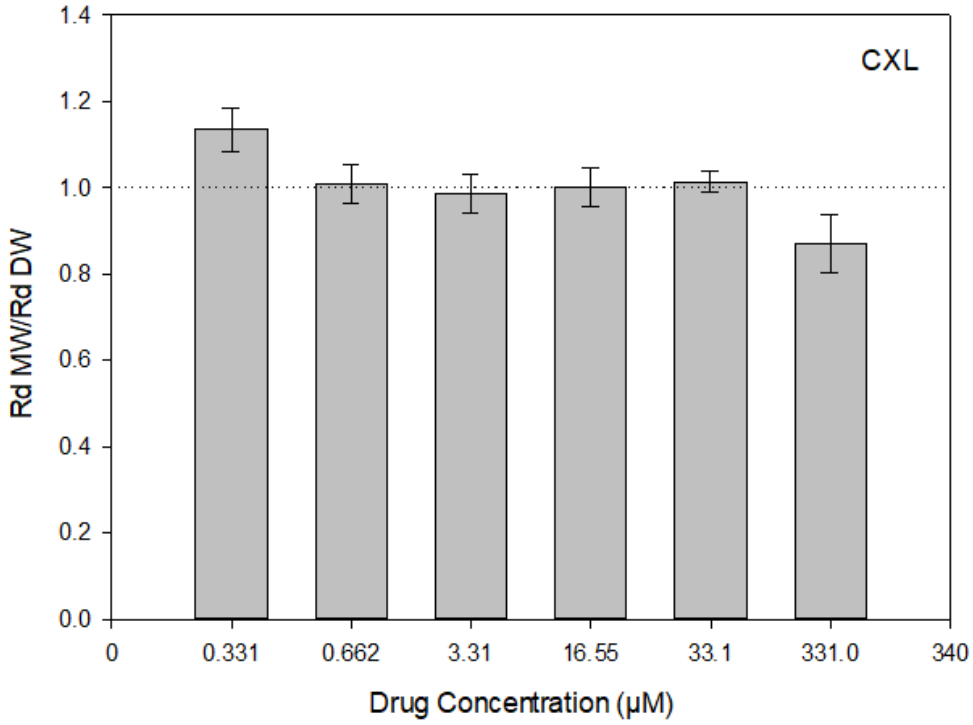

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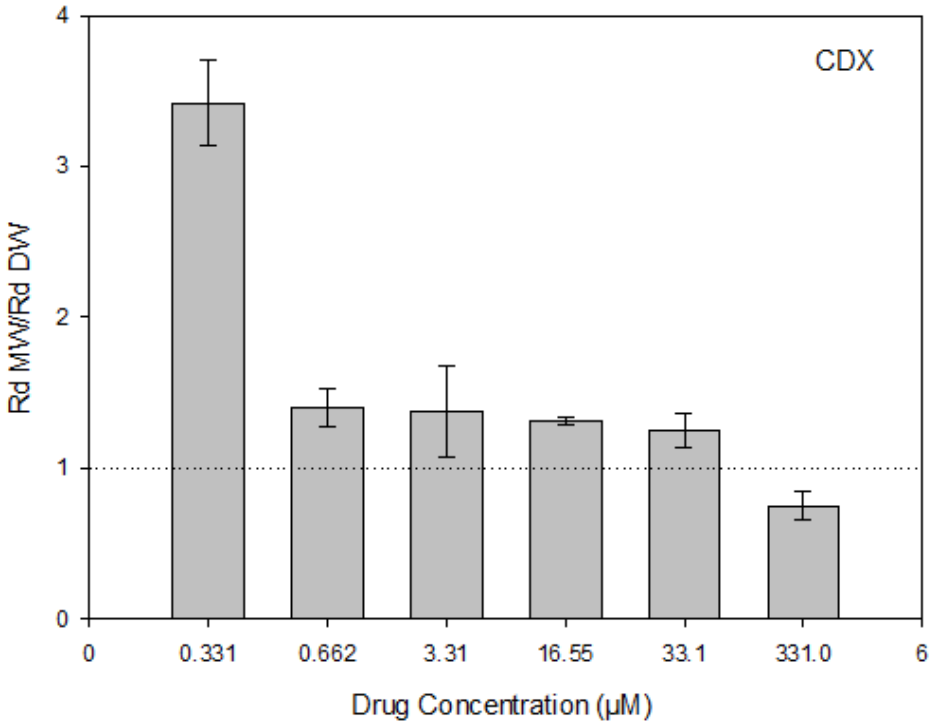


Fig. 19. Effect of pharmaceuticals concentration on the degradation in mineral water. RdMW/RdDW: Relationship between the initial degradation rate in mineral water and distilled water for different concentrations. **A**. SAM, **B.** CXL, and **C.** CDX. Conditions: initial pH: 7.2±0.1, Frequency: 375 kHz, Acoustic power: 24.4 W, Temperature: 20 °C and Volume: 250 mL.

The case of CXL (Fig. 19B) shows that a very small positive effect by the mineral water matrix only at the lowest concentration of CXL (0.331 µM). For the concentrations of 0.662, 3.31, 16.55, and 33.1 µM, the degradation rates in distilled water and mineral water were similar. On the contrary, at the highest concentration (331 µM) of CXL, a small inhibitory effect was observed. Unlike SAM, CXL has a hydrophobic behavior. Therefore, CXL is closer to the cavitation bubble, this allows it to react more quickly with hydroxyl radicals than the ionic constituents of mineral water (which are very hydrophilic). This justifies the non-competing effect for the concentrations of 0.662, 3.31, 16.55, and 33.1 µM, which allow to the compound to be mainly placed at the

interfacial reaction zone and available for the attack of sonogenerated hydroxyl radicals. However, at the lowest concentration of CXL, the result can be rationalized considering the greater dilution of the pollutant. In such condition, the pharmaceutical is far away from the cavitation bubble, so the bicarbonate radical may take an important role in the degradation (Eq. 20) as in the case of very hydrophilic pollutants. Regarding the highest concentration, it could be indicated that a competition between the CXL and the bicarbonate ions for the HO• occurs (Villegas-Guzman et al., 2015), leading to a ratio lower than one (Fig. 19B).

In the case of CDX (Fig. 19C), the ratios show that for almost all concentrations (0.331, 0662, 3.31, 16.55, and 33.1 µM) there was an accelerating effect by mineral water matrix. Taking into account that CDX is a compound of slow degradation by ultrasound (Fig. 12) because of its high hydrophilicity, this pharmaceutical is so far of the cavitation bubbles. Thus, in the mineral water, the carbonate radical improves the CDX degradation even in high CDX concentrations as 33.1 µM. Nevertheless, for a very high concentration (331 µM), an inhibitory effect is observed, which can be attributed to the competition of CDX with the matrix components (mainly bicarbonate, the most concentrated anion in the mineral water) for HO•.

On the other hand, the value of the ratio of the initial degradation rates for the lowest concentration of CDX was higher compared with that obtained for SAM and CXL. This can be explained considering that CDX is the most hydrophilic (Figs. 12 and 15E), such pharmaceutical is the farthest from the cavitation bubble. Thereby, in mineral water, the generated carbonate radical migrates more easily than the hydroxyl radical to the solution, and CO_3^{*-} has a greater opportunity to oxidize CDX (Eq. 20) compared with SAM and CXL.

From the above results, it is evident that the mineral water matrix (mainly the bicarbonate anion) plays a dual role (i.e., enhancer or inhibitor of degradation) with respect to a simpler

medium as distilled water. The specific role depends on two characteristics of the pollutants: the hydrophilic/hydrophobic nature and their concentration. At this point, it is also important to highlight that the predominance of the degradation enhancing effect by the mineral water occurs at very low concentrations (Fig. 19). This is an interesting result considering that the contaminants of emerging concern as pharmaceuticals are at trace levels in aqueous media (as real mineral water), which indicates the high potentiality/usefulness of the sonochemical process to successfully degrade pollutants in bicarbonate-rich waters.

3.4.1. Kinetic model

The sonochemical degradation of some pharmaceuticals can follows a Langmuir-like kinetics as proposed by Okitsu et al. (2005). Some researchers have evidenced the adjustment of the experimental results to this model (Villaroel et al., 2014; Villegas-Guzman et al., 2015; Serna-Galvis et al., 2015). In the Okitsu proposal, the ultrasonic degradation of non-volatile organic compounds is represented by the following equation:

$$r_d = \frac{k * K * C_0}{1 + K * C_0}$$

Where r_d is the initial degradation rate of the target pollutant determined at a given initial concentration (C_0); k is the pseudo constant rate and K is the equilibrium constant of the target compound in the interfacial region (Chiha et al., 2010). The Okitsu equation can be linearized as follows:

$$\frac{1}{r_d} = \frac{1}{k * K * C_0} + \frac{1}{k}$$

In this way, from the plot of $1/C_0$ Vs. $1/r_d$ the kinetic parameters of k and K can be obtained. Hence, the fitting of the experimental data, for the pharmaceuticals degradation in mineral water, to the Okitsu model was tested, and the kinetics parameters are summarized in Table 5. For the considered pharmaceuticals, the experimental data have a good correlation coefficient (R^2= 0.987, 0.998 and 0.992 for SAM, CXL y CDX, respectively); however, under the Average Percentage Errors (APE) criterion (6, 19 and 52% for SAM, CXL and CDX, respectively), only for SAM a good fit between the experimental value and the predicted value of the initial degradation rate was observed.

Table 5: Kinetics parameters from the application of the Okitsu Model.

PHARMACEUTIC	k ($\mu M\ min^{-1}$)	K (μM^{-1})
SAM	0.7138	0.2936
CXL	1.6778	0.0447
CDX	0.1717	0.0726

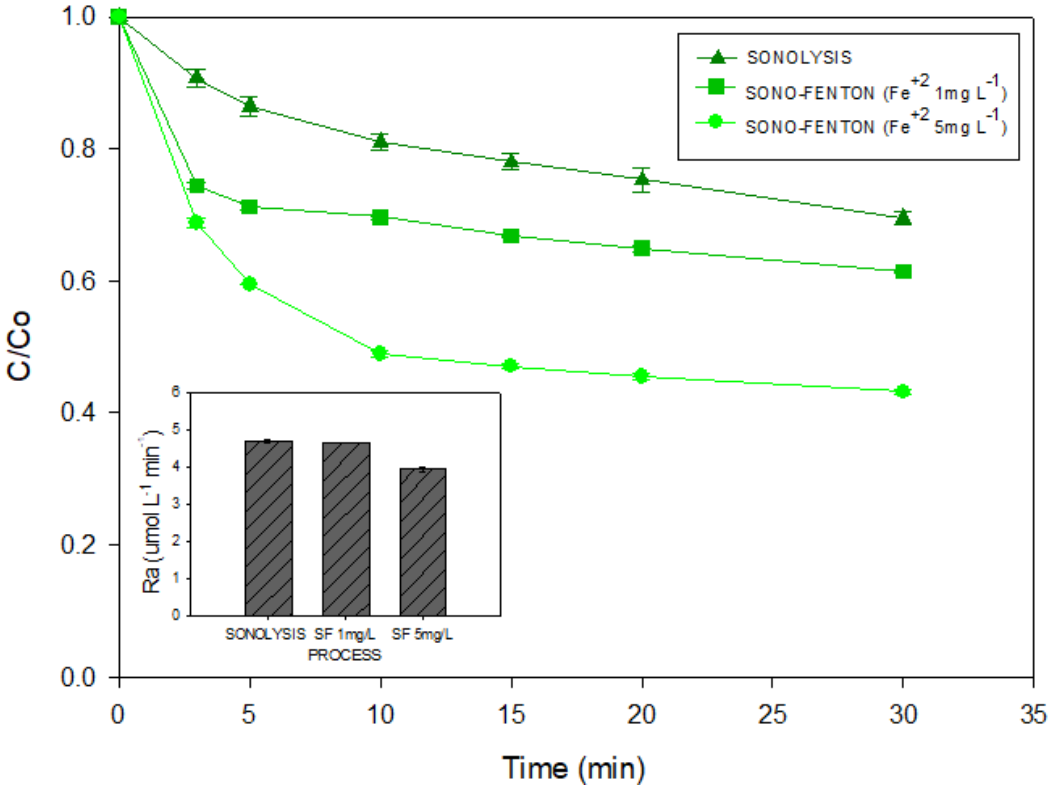
3.5. Effect of iron addition to the sonochemical system (Sono-Fenton process) to improve the degradation of hydrophilic substances.

The results in previous sections showed that the ultrasound process was more efficient for degrading hydrophobic contaminants in water. However, the removal of hydrophilic pollutants as CDX is limited either in distilled water or in mineral water (see Figs 12 and 16A). A possible solution for such limitation is the combination of ultrasound with other advanced oxidation processes (Mohapatra et al., 2013; Adityosulindro et al., 2017). In this work, the addition of ferrous ions to the sonochemical reactor, to produce a Sono-Fenton process, was performed. This system was chosen to take advantage of the H_2O_2 accumulated in the sonochemical system.

As an illustrative case of the hydrophilic pharmaceuticals, the treatment of CDX was considered. Initially, the effect of the concentration of iron was tested. Fig. 20 compares the CDX degradation in distilled water at different additions of iron (0, 1.0, and 5.0 mg L^{-1}). It can be noted the presence of ferrous ions at 1 mg L^{-1} leads to an increasing of in CDX degradation. Indeed, the Rd values for sonochemistry and sono-Fenton (1 mg L^{-1}) were calculated as 0.0908 and 0.1975 µM min^{-1}, respectively. Furthermore, when a higher dose of Fe^{2+} (5 mg L^{-1}) was considered, a removal of 57% after 30 min of treatment was achieved, indicating a stronger acceleration of the pharmaceutical removal (with a Ra of 0.2774 µM min^{-1}).

The presence of iron in the solution, induces the formation of extra hydroxyl radicals in the bulk of the solution, through reaction with the H_2O_2 accumulated (Eq. 21, Fenton reaction), thus increasing the rate of degradation of the contaminant. The interaction between iron and hydrogen peroxide is confirmed through the measurement of the accumulation rates of H_2O_2 (Ra). Inset in Fig. 20 shows that Ra in the presence of iron (4.6 and 3.9 µM min^{-1}, for 1.0 and 5.0 mg L^{-1}, respectively) are lower than in absence (4.7 µM min^{-1}).

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + HO^{\bullet} + HO^{-} \quad \text{Eq. 21}$$



1201

1202 **Fig. 20.** Removal of CDX through sono-Fenton process in distilled water. Inset: comparison of
1203 H_2O_2 accumulation rates (in µM min^{-1}) for individual sonolysis, sono-Fenton (Fe^{2+}= 1.0 mg L^{-1})
1204 and sono-Fenton (Fe^{2+}= 5.0 mg L^{-1}). Conditions: initial CDX concentration: 3.31 µM, pH: 7.2±0.1,
1205 frequency: 375 kHz, acoustic power: 24.4 W, temperature: 20 °C and volume: 250 mL.

1206 On the other hand, when CDX in the mineral water was treated by the sono-Fenton systems,
1207 it was no observed an improvement of the pollutant degradation with respect to the sonochemical
1208 system alone (Fig. 21).

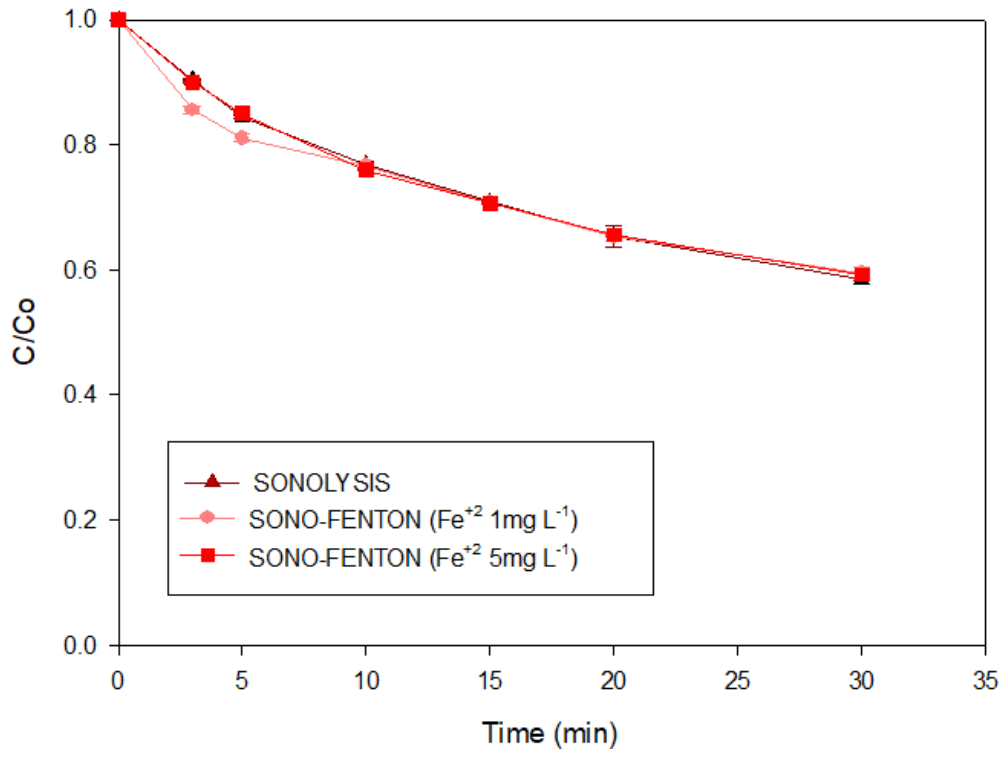


Fig. 21. Degradation of CDX in mineral water by the sono-Fenton process. Conditions: Initial pharmaceutical concentration: 3.31 µM, pH: 7.2±0.1, Frequency: 375 kHz, acoustic power: 24.4 W, Temperature: 20 °C and Volume: 250 mL.

Due to the high concentration of the bicarbonate anion, this scavenges the HO• sonogenerated, decreasing the accumulation of H_2O_2, and then limiting the Fenton reaction (Eq.21). Additionally, if hydroxyl radicals are produced by the interaction of ferrous ions with some of the accumulated hydrogen peroxide from the sonolysis, the bicarbonate anion may also induce trapping of such radicals in the bulk of solution (where is mainly placed the hydrophilic pollutants as CDX). Hence, there is no improvement of CDX removal in the mineral water by the addition of ferrous ions to the sonochemical system.

4. CHAPTER 4: CONCLUSIONS

After the study of the degradation of the target pollutants by the sonochemical process, the levels of 24.4 W and 375 kHz for frequency and acoustic power, respectively, were selected as the most appropriate conditions, since they demonstrated the highest DCF removal efficiency and greater accumulation of hydrogen peroxide, which allowed taking them as fixed factors for the other experiments.

The degradation of the seven representative pharmaceuticals in distilled water is highly dependent on their hydrophobic nature. Indeed, the most hydrophobic pharmaceuticals showed faster removals by the process. Additionally, the initial degradation rate correlated well with the Log P property of pollutants. For its part, in the mineral water, degradation of the hydrophilic substances is significantly accelerated in comparison to the removal in distilled water. This happens because the bicarbonate anion present in the mineral water reacts with the hydroxyl radical to form the carbonate radical, which can migrate to the solution, favoring/enhancing the degradation of the molecules placed far away from the cavitation bubble.

It is also concluded that when the concentration of the pharmaceutical is varied, the mineral water matrix (mainly the bicarbonate anion) exhibits a dual role (i.e., enhancer or inhibitor of degradation), which depends on the hydrophilic/hydrophobic nature of the pollutant (e.g., degradation of hydrophilic pharmaceuticals at a very low concentration is strongly accelerated, whereas the removal of a hydrophobic pollutant at high concentration is inhibited by the mineral water matrix). Thus, the predominance of the degradation enhancing effect by the mineral water occur at very low concentrations, which indicates the high potentiality/usefulness of the sonochemical process to treat bicarbonate-rich waters containing the contaminants of emerging concern (as pharmaceuticals) at trace levels.

Finally, the addition of ferrous ions to the sonochemical system (i.e., sono-Fenton process) accelerates the removal of the most hydrophilic pharmaceutical (CDX) in distilled water, thanks to extra production of hydroxyl radical by the Fenton reaction. However, such addition does not affect the removal of pollutants in mineral water because of the scavenger effect of bicarbonate ion.

5. CHAPTER 5: RECOMMENDATIONS OR PROPOSALS

Taking into account the conclusions given in the present work, certain questions could be solved by developing future research. Such questions are: What would be the effect of pH on the sonochemical degradation of pharmaceuticals in mineral water? The application of Sono-Fenton for the degradation of pharmaceuticals with hydrophobic or hydrophilic characteristics in mineral water would have a behavior similar to that observed in the individual sonochemical process? Would an economic evaluation of the process described in this work be competitive with current proposals on the matter? What would the behavior of HCO_3^- be in more complex matrices such as hospital wastewater, for example?

To answer each one of the previous questions, the development of experimental works that consider the variation of the pH levels in the presence of HCO_3^- is planned for the sonochemical degradation of the chosen indicator molecules. Likewise, it would be ideal to evaluate the Sono-Fenton process in various matrices such as hospital our municipal wastewater and mineral-drinking, fixing the presence of HCO_3^-, which would allow a broader vision of its leading role in the accelerated sonochemical degradation of hydrophilic compounds. Finally, it would be interesting to compare the costs associated with these processes, estimated on an industrial scale, with those found in the current literature.

6. ASSOCIATED PRODUCTS

6.5. Scientific Publications

- 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), 1068. https://doi.org/10.3390/w12041068

- Camargo-Perea, Ana L., Serna-Galvis, Efraim A. and Torres-Palma, Ricardo A. "Unraveling the enhancing or detrimental effects of mineral water matrix during sonochemical degradation of pharmaceuticals: Dependence on the chemical structure and concentration of the pollutant". Submitted to *Ultrasonics Sonochemistry*

7. REFERENCES

Adewuyi, Y. G. (2005). Sonochemistry in Environmental Remediation. 1. Combinative and Hybrid Sonophotochemical Oxidation Processes for the Treatment of Pollutants in Water. Environmental Science & Technology, 39(10), 3409-3420. https://doi.org/10.1021/es049138y

Adityosulindro, S., Barthe, L., González-Labrada, K., Jáuregui Haza, U. J., Delmas, H., & Julcour, C. (2017). Sonolysis and sono-Fenton oxidation for removal of ibuprofen in wastewater. Ultrasonics Sonochemistry, 39, 889-896. https://doi.org/10.1016/j.ultsonch.2017.06.008

Affam, A. C., & Chaudhuri, M. (2014). Optimization of Fenton treatment of amoxicillin and cloxacillin antibiotic aqueous solution. Desalination and Water Treatment, 52(10-12), 1878-1884. Scopus. https://doi.org/10.1080/19443994.2013.794015

Akhbarizadeh, R., Dobaradaran, S., Schmidt, T. C., Nabipour, I., & Spitz, J. (2020). Worldwide bottled water occurrence of emerging contaminants: A review of the recent scientific literature. Journal of Hazardous Materials, 392, 122271. https://doi.org/10.1016/j.jhazmat.2020.122271

Al-Bsoul, A., Al-Shannag, M., Tawalbeh, M., Al-Taani, A. A., Lafi, W. K., Al-Othman, A., & Alsheyab, M. (2020). Optimal conditions for olive mill wastewater treatment using ultrasound and advanced oxidation processes. Science of the Total Environment, 700, 134576. https://doi.org/10.1016/j.scitotenv.2019.134576

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. https://doi.org/10.1016/j.ultsonch.2016.03.030

Al-Hamadani, Y. A. J., Jung, C., Im, J.-K., Boateng, L. K., Flora, J. R. V., Jang, M., Heo, J., Park, C. M., & Yoon, Y. (2017). Sonocatalytic degradation coupled with single-walled carbon nanotubes for removal of ibuprofen and sulfamethoxazole. Chemical Engineering Science, 162, 300-308. https://doi.org/10.1016/j.ces.2017.01.011

Almeida, Â., Calisto, V., Esteves, V. I., Schneider, R. J., Soares, A. M. V. M., Figueira, E., & Freitas, R. (2014). Presence of the pharmaceutical drug carbamazepine in coastal systems: Effects on bivalves. Aquatic Toxicology, 156, 74-87. https://doi.org/10.1016/j.aquatox.2014.08.002

Aristizabal-Ciro, C., Botero-Coy, A. M., López, F. J., & Peñuela, G. A. (2017). Monitoring pharmaceuticals and personal care products in reservoir water used for drinking water supply. Environmental Science and Pollution Research, 24(8), 7335-7347. https://doi.org/10.1007/s11356-016-8253-1

Atif, S., Baig, J. A., Afridi, H. I., Kazi, T. G., & Waris, M. (2020). Novel nontoxic electrochemical method for the detection of cefadroxil in pharmaceutical formulations and biological samples. Microchemical Journal, 154, 104574. https://doi.org/10.1016/j.microc.2019.104574

Buchberger, W. W. (2011). Current approaches to trace analysis of pharmaceuticals and personal care products in the environment. Journal of Chromatography A, 1218(4), 603-618. https://doi.org/10.1016/j.chroma.2010.10.040

Burckhardt, P. (2008). The Effect of the Alkali Load of Mineral Water on Bone Metabolism: Interventional Studies. The Journal of Nutrition, 138(2), 435S-437S. https://doi.org/10.1093/jn/138.2.435S

Cefadroxil. (2020). Recuperado 5 de abril de 2020, de https://www.drugbank.ca/drugs/DB01140

ChemSpider | Search and share chemistry. (2019). Recuperado 31 de agosto de 2019, de http://www.chemspider.com/

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. https://doi.org/10.1016/j.ultsonch.2010.12.014

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. https://doi.org/10.1016/j.ultsonch.2010.03.007

Cleuvers, M. (2004). Mixture toxicity of the anti-inflammatory drugs diclofenac, ibuprofen, naproxen, and acetylsalicylic acid. Ecotoxicology and Environmental Safety, 59(3), 309-315. Scopus. https://doi.org/10.1016/S0147-6513(03)00141-6

Cooper, W. J., & Weihua, S. (2012). Advanced Oxidation Degradation of Diclofenac. http://inis.iaea.org/Search/search.aspx?orig_q=RN:46015381

Dalhatou, S., Laminsi, S., Pétrier, C., & Baup, S. (2019). Competition in sonochemical degradation of Naphthol Blue Black: Presence of an organic (nonylphenol) and a mineral (bicarbonate

ions) matrix. Journal of Environmental Chemical Engineering, 7(1), 102819. https://doi.org/10.1016/j.jece.2018.102819

Dalhatou, S., Pétrier, C., Laminsi, S., & Baup, S. (2015). Sonochemical removal of naphthol blue black azo dye: Influence of parameters and effect of mineral ions. International Journal of Environmental Science and Technology, 12(1), 35-44. https://doi.org/10.1007/s13762-013-0432-8

De la Cruz, N., Esquius, L., Grandjean, D., Magnet, A., Tungler, A., de Alencastro, L. F., & Pulgarín, C. (2013). Degradation of emergent contaminants by UV, UV/H2O2 and neutral photo-Fenton at pilot scale in a domestic wastewater treatment plant. Water Research, 47(15), 5836-5845. https://doi.org/10.1016/j.watres.2013.07.005

De Luna, M. D. G., Veciana, M. L., Su, C.-C., & Lu, M.-C. (2012). Acetaminophen degradation by electro-Fenton and photoelectro-Fenton using a double cathode electrochemical cell. Journal of Hazardous Materials, 217-218, 200-207. https://doi.org/10.1016/j.jhazmat.2012.03.018

Elmolla, E. S., & Chaudhuri, M. (2010). Photocatalytic degradation of amoxicillin, ampicillin and cloxacillin antibiotics in aqueous solution using UV/TiO2 and UV/H2O2/TiO2 photocatalysis. Desalination, 252(1), 46-52. https://doi.org/10.1016/j.desal.2009.11.003

Elmolla, E. S., & Chaudhuri, M. (2012). The feasibility of using combined Fenton-SBR for antibiotic wastewater treatment. Desalination, 285, 14-21. https://doi.org/10.1016/j.desal.2011.09.022

Emmanouil, C., Bekyrou, M., Psomopoulos, C., & Kungolos, A. (2019). An Insight into Ingredients of Toxicological Interest in Personal Care Products and a Small–Scale

Sampling Survey of the Greek Market: Delineating a Potential Contamination Source for Water Resources. Water, 11(12), 2501. https://doi.org/10.3390/w11122501

Expósito, A. J., Patterson, D. A., Monteagudo, J. M., & Durán, A. (2017). Sono-photo-degradation of carbamazepine in a thin falling film reactor: Operation costs in pilot plant. Ultrasonics Sonochemistry, 34(Supplement C), 496-503. https://doi.org/10.1016/j.ultsonch.2016.06.029

Feng, L., Serna-Galvis, E. A., Oturan, N., Giannakis, S., Torres-Palma, R. A., & Oturan, M. A. (2019). Evaluation of process influencing factors, degradation products, toxicity evolution and matrix-related effects during electro-Fenton removal of piroxicam from waters. Journal of Environmental Chemical Engineering, 7(5), 103400. https://doi.org/10.1016/j.jece.2019.103400

Feng, S., Zhang, X., & Liu, Y. (2015). New insights into the primary phototransformation of acetaminophen by UV/H2O2: Photo-Fries rearrangement versus hydroxyl radical induced hydroxylation. Water Research, 86, 35-45. https://doi.org/10.1016/j.watres.2015.05.008

Gil, M. J., Soto, A. M., Usma, J. I., & Gutiérrez, O. D. (2013). Contaminantes emergentes en aguas, efectos y posibles tratamientos. Producción + Limpia, 7(2). http://repository.lasallista.edu.co:8080/ojs/index.php/pl/article/view/265

Gogate, P. R., Sutkar, V. S., & Pandit, A. B. (2011). Sonochemical reactors: Important design and scale up considerations with a special emphasis on heterogeneous systems. Chemical Engineering Journal, 166(3), 1066-1082. https://doi.org/10.1016/j.cej.2010.11.069

Gogoi, A., Mazumder, P., Tyagi, V. K., Tushara Chaminda, G. G., An, A. K., & Kumar, M. (2018). Occurrence and fate of emerging contaminants in water environment: A review.

Groundwater for Sustainable Development, 6, 169-180. https://doi.org/10.1016/j.gsd.2017.12.009

Golash, N., & Gogate, P. R. (2012). Degradation of dichlorvos containing wastewaters using sonochemical reactors. Ultrasonics Sonochemistry, 19(5), 1051-1060. https://doi.org/10.1016/j.ultsonch.2012.02.011

González Alonso, S., Valcárcel, Y., Montero, J. C., & Catalá, M. (2012). Nicotine occurrence in bottled mineral water: Analysis of 10 brands of water in Spain. Science of the Total Environment, 416, 527-531. https://doi.org/10.1016/j.scitotenv.2011.11.046

González, K., Quesada, I., Julcour, C., Delmas, H., Cruz, G., & Jáuregui, U. J. (2010). El empleo del ultrasonido en el tratamiento de aguas residuales. Revista CENIC. Ciencias Químicas., 41, 1-11. http://www.redalyc.org/articulo.oa?id=181620500034

Górny, D., Guzik, U., Hupert-Kocurek, K., & Wojcieszyńska, D. (2019). Naproxen ecotoxicity and biodegradation by Bacillus thuringiensis strain. Ecotoxicology and Environmental Safety, 167, 505-512. https://doi.org/10.1016/j.ecoenv.2018.10.067

Gracia-Lor, E., Martínez, M., Sancho, J. V., Peñuela, G., & Hernández, F. (2012). Multi-class determination of personal care products and pharmaceuticals in environmental and wastewater samples by ultra-high performance liquid-chromatography-tandem mass spectrometry. Talanta, 99, 1011-1023. https://doi.org/10.1016/j.talanta.2012.07.091

Guiloski, I. C., Ribas, J. L. C., Pereira, L. da S., Neves, A. P. P., & Silva de Assis, H. C. (2015). Effects of trophic exposure to dexamethasone and diclofenac in freshwater fish. Ecotoxicology and Environmental Safety, 114, 204-211. https://doi.org/10.1016/j.ecoenv.2014.11.020

Güyer, G. T., & Ince, N. H. (2011). Degradation of diclofenac in water by homogeneous and heterogeneous sonolysis. Ultrasonics Sonochemistry, 18(1), 114-119. https://doi.org/10.1016/j.ultsonch.2010.03.008

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. https://doi.org/10.1016/j.ultsonch.2010.07.019

Hai, F. I., Yang, S., Asif, M. B., Sencadas, V., Shawkat, S., Sanderson-Smith, M., Gorman, J., Xu, Z.-Q., & Yamamoto, K. (2018). Carbamazepine as a Possible Anthropogenic Marker in Water: Occurrences, Toxicological Effects, Regulations and Removal by Wastewater Treatment Technologies. Water, 10(2), 107. https://doi.org/10.3390/w10020107

Hao, C., Zhao, X., & Yang, P. (2007). GC-MS and HPLC-MS analysis of bioactive pharmaceuticals and personal-care products in environmental matrices. TrAC Trends in Analytical Chemistry, 26(6), 569-580. https://doi.org/10.1016/j.trac.2007.02.011

Hartmann, J., Bartels, P., Mau, U., Witter, M., Tümpling, W. v., Hofmann, J., & Nietzschmann, E. (2008). Degradation of the drug diclofenac in water by sonolysis in presence of catalysts. Chemosphere, 70(3), 453-461. https://doi.org/10.1016/j.chemosphere.2007.06.063

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. https://doi.org/10.1016/j.ultsonch.2017.02.032

I. Litter, M., & Quici, N. (2010). Photochemical Advanced Oxidation Processes for Water and Wastewater Treatment [Text]. https://doi.org/info:doi/10.2174/187221210794578574

Ikehata, K., Naghashkar, N. J., & El-Din, M. G. (2006). Degradation of Aqueous Pharmaceuticals by Ozonation and Advanced Oxidation Processes: A Review. Ozone: Science & Engineering, 28(6), 353-414. https://doi.org/10.1080/01919510600985937

Im, J.-K., Boateng, L. K., Flora, J. R. V., Her, N., Zoh, K.-D., Son, A., & Yoon, Y. (2014). Enhanced ultrasonic degradation of acetaminophen and naproxen in the presence of powdered activated carbon and biochar adsorbents. Separation and Purification Technology, 123, 96-105. https://doi.org/10.1016/j.seppur.2013.12.021

Ince, N. H, Tezcanli, G., Belen, R. K., & Apikyan, İ. G. (2001). Ultrasound as a catalyzer of aqueous reaction systems: The state of the art and environmental applications. Applied Catalysis B: Environmental, 29(3), 167-176. https://doi.org/10.1016/S0926-3373(00)00224-1

Ince, Nilsun H. (2018). Ultrasound-assisted advanced oxidation processes for water decontamination. Ultrasonics Sonochemistry, 40, 97-103. https://doi.org/10.1016/j.ultsonch.2017.04.009

Ivanova, I. P., Trofimova, S. V., Piskarev, I. M., Aristova, N. A., Burhina, O. E., & Soshnikova, O. O. (2012). Mechanism of chemiluminescence in Fenton reaction. Journal of Biophysical Chemistry, Vol.03No.01, 4.

Jarvis, A. L., Bernot, M. J., & Bernot, R. J. (2014). The effects of the psychiatric drug carbamazepine on freshwater invertebrate communities and ecosystem dynamics. Science of the Total Environment, 496, 461-470. https://doi.org/10.1016/j.scitotenv.2014.07.084

Jiang, Y., Pétrier, C., & David Waite, T. (2002). Kinetics and mechanisms of ultrasonic degradation of volatile chlorinated aromatics in aqueous solutions. Ultrasonics Sonochemistry, 9(6), 317-323. https://doi.org/10.1016/S1350-4177(02)00085-8

Jiang, Y., Pétrier, C., & Waite, T. D. (2002). Effect of pH on the ultrasonic degradation of ionic aromatic compounds in aqueous solution. Ultrasonics Sonochemistry, 9(3), 163-168. https://doi.org/10.1016/S1350-4177(01)00114-6

Jiménez, J. J., Muñoz, B. E., Sánchez, M. I., & Pardo, R. (2018). Forced and long-term degradation assays of tenoxicam, piroxicam and meloxicam in river water. Degradation products and adsorption to sediment. Chemosphere, 191, 903-910. https://doi.org/10.1016/j.chemosphere.2017.10.056

Jin, X., Peldszus, S., & Huck, P. M. (2015). Predicting the reaction rate constants of micropollutants with hydroxyl radicals in water using QSPR modeling. Chemosphere, 138, 1-9. https://doi.org/10.1016/j.chemosphere.2015.05.034

Kakavandi, B., & Ahmadi, M. (2019). Efficient treatment of saline recalcitrant petrochemical wastewater using heterogeneous UV-assisted sono-Fenton process. Ultrasonics Sonochemistry, 56, 25-36. https://doi.org/10.1016/j.ultsonch.2019.03.005

Kang, J.-W., Hung, H.-M., Lin, A., & Hoffmann, M. R. (1999). Sonolytic destruction of methyl tert-butyl ether by ultrasonic irradiation: The role of O_3, H_2O_2, frequency, and power density. Environmental Science and Technology, 33(18), 3199-3205. Scopus. https://doi.org/10.1021/es9810383

Kask, M., Krichevskaya, M., & Bolobajev, J. (2019). Sonolytic degradation of pesticide metazachlor in water: The role of dissolved oxygen and ferric sludge in the process

intensification. Journal of Environmental Chemical Engineering, 7(3), 103095. https://doi.org/10.1016/j.jece.2019.103095

Keßler, T., & Hesse, A. (2000). Cross-over study of the influence of bicarbonate-rich mineral water on urinary composition in comparison with sodium potassium citrate in healthy male subjects. British Journal of Nutrition, 84(6), 865-871. https://doi.org/10.1017/S0007114500002488

Khetan, S. K., & Collins, T. J. (2007). Human pharmaceuticals in the aquatic environment: A challenge to green chemistry. Chemical Reviews, 107(6), 2319-2364. Scopus. https://doi.org/10.1021/cr020441w

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), S157-S161. https://doi.org/10.1016/S1350-4177(96)00021-1

Kosma, C. I., Lambropoulou, D. A., & Albanis, T. A. (2010). Occurrence and removal of PPCPs in municipal and hospital wastewaters in Greece. Journal of Hazardous Materials, 179(1), 804-817. https://doi.org/10.1016/j.jhazmat.2010.03.075

Lardy-Fontan, S., Le Diouron, V., Drouin, C., Lalere, B., Vaslin-Reimann, S., Dauchy, X., & Rosin, C. (2017). Validation of a method to monitor the occurrence of 20 relevant pharmaceuticals and personal care products in 167 bottled waters. Science of the Total Environment, 587-588, 118-127. https://doi.org/10.1016/j.scitotenv.2017.02.074

Li, X., Ying, G.-G., Su, H.-C., Yang, X.-B., & Wang, L. (2010). Simultaneous determination and assessment of 4-nonylphenol, bisphenol A and triclosan in tap water, bottled water and

baby bottles. Environment International, 36(6), 557-562. https://doi.org/10.1016/j.envint.2010.04.009

Lifka, J., Ondruschka, B., & Hofmann, J. (2003). The Use of Ultrasound for the Degradation of Pollutants in Water: Aquasonolysis – A Review. Engineering in Life Sciences, 3(6), 253-262. https://doi.org/10.1002/elsc.200390040

Lim, M., Son, Y., & Khim, J. (2011). Frequency effects on the sonochemical degradation of chlorinated compounds. Ultrasonics Sonochemistry, 18(1), 460-465. https://doi.org/10.1016/j.ultsonch.2010.07.021

Lin, L., Wang, H., & Xu, P. (2017). Immobilized TiO_2-reduced graphene oxide nanocomposites on optical fibers as high performance photocatalysts for degradation of pharmaceuticals. Chemical Engineering Journal, 310, Part 2, 389-398. https://doi.org/10.1016/j.cej.2016.04.024

Mahamuni, N. N., & Adewuyi, Y. G. (2010). Advanced oxidation processes (AOPs) involving ultrasound for waste water treatment: A review with emphasis on cost estimation. Ultrasonics Sonochemistry, 17(6), 990-1003. https://doi.org/10.1016/j.ultsonch.2009.09.005

Makchit, J., Upalee, S., Thongpoon, C., Liawruangrath, B., & Liawruangrath, S. (2006). Determination of cefadroxil by sequential injection with spectrophotometric detector. Analytical Sciences, 22(4), 591-597. Scopus. https://doi.org/10.2116/analsci.22.591

Martínez, C., Canle L., M., Fernández, M. I., Santaballa, J. A., & Faria, J. (2011). Kinetics and mechanism of aqueous degradation of carbamazepine by heterogeneous photocatalysis using nanocrystalline TiO_2, Zn^O and multi-walled carbon nanotubes–anatase composites.

Applied Catalysis B: Environmental, 102(3), 563-571. https://doi.org/10.1016/j.apcatb.2010.12.039

Martinez, J. L. (2009). Environmental pollution by antibiotics and by antibiotic resistance determinants. Environmental Pollution, 157(11), 2893-2902. https://doi.org/10.1016/j.envpol.2009.05.051

Mascha, E. (s. f.). Bottled Waters of the World. Recuperado 13 de mayo de 2020, de http://finewaters.com/bottled-waters-of-the-world

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. https://doi.org/10.1016/j.watres.2008.05.033

Minero, C., Pellizzari, P., Maurino, V., Pelizzetti, E., & Vione, D. (2008). Enhancement of dye sonochemical degradation by some inorganic anions present in natural waters. Applied Catalysis B: Environmental, 77(3), 308-316. https://doi.org/10.1016/j.apcatb.2007.08.001

Mohapatra, D. P., Brar, S. K., Tyagi, R. D., Picard, P., & Surampalli, R. Y. (2013). A comparative study of ultrasonication, Fenton's oxidation and ferro-sonication treatment for degradation of carbamazepine from wastewater and toxicity test by Yeast Estrogen Screen (YES) assay. Science of the Total Environment, 447(Supplement C), 280-285. https://doi.org/10.1016/j.scitotenv.2012.12.072

Moussavi, G., Rezaei, M., & Pourakbar, M. (2018). Comparing VUV and VUV/Fe2+ processes for decomposition of cloxacillin antibiotic: Degradation rate and pathways, mineralization and by-product analysis. Chemical Engineering Journal, 332, 140-149. https://doi.org/10.1016/j.cej.2017.09.057

Naddeo, V., Belgiorno, V., Kassinos, D., Mantzavinos, D., & Meric, S. (2010). Ultrasonic degradation, mineralization and detoxification of diclofenac in water: Optimization of operating parameters. Ultrasonics Sonochemistry, 17(1), 179-185. https://doi.org/10.1016/j.ultsonch.2009.04.003

Naddeo, Vincenzo, Belgiorno, V., Ricco, D., & Kassinos, D. (2009). Degradation of diclofenac during sonolysis, ozonation and their simultaneous application. Ultrasonics Sonochemistry, 16(6), 790-794. https://doi.org/10.1016/j.ultsonch.2009.03.003

Nanzai, B., Okitsu, K., Takenaka, N., Bandow, H., & Maeda, Y. (2008). Sonochemical degradation of various monocyclic aromatic compounds: Relation between hydrophobicities of organic compounds and the decomposition rates. Ultrasonics Sonochemistry, 15(4), 478-483. https://doi.org/10.1016/j.ultsonch.2007.06.010

Nasseri, S., Mahvi, A. H., Seyedsalehi, M., Yaghmaeian, K., Nabizadeh, R., Alimohammadi, M., & Safari, G. H. (2017). Degradation kinetics of tetracycline in aqueous solutions using peroxydisulfate activated by ultrasound irradiation: Effect of radical scavenger and water matrix. Journal of Molecular Liquids, 241, 704-714. https://doi.org/10.1016/j.molliq.2017.05.137

Neppolian, B., Choi, H. C., Sakthivel, S., Arabindoo, B., & Murugesan, V. (2002). Solar light induced and TiO2 assisted degradation of textile dye reactive blue 4. Chemosphere, 46(8), 1173-1181. https://doi.org/10.1016/S0045-6535(01)00284-3

Nie, E., Yang, M., Wang, D., Yang, X., Luo, X., & Zheng, Z. (2014). Degradation of diclofenac by ultrasonic irradiation: Kinetic studies and degradation pathways. Chemosphere, 113(Supplement C), 165-170. https://doi.org/10.1016/j.chemosphere.2014.05.031

Ojer-Usoz, E., González, D., García-Jalón, I., & Vitas, A. I. (2014). High dissemination of extended-spectrum β-lactamase-producing Enterobacteriaceae in effluents from wastewater treatment plants. Water Research, 56, 37-47. https://doi.org/10.1016/j.watres.2014.02.041

Perret, D., Gentili, A., Marchese, S., Greco, A., & Curini, R. (2006). Sulphonamide Residues in Italian Surface and Drinking Waters: A Small Scale Reconnaissance. Chromatographia, 63(5), 225-232. https://doi.org/10.1365/s10337-006-0737-6

Petre, J., Galaon, T., Iancu, V. I., Cruceru, L., & Niculescu, M. (2016). Simultaneous liquid chromatographytandem mass spectrometry determination of some pharmaceuticals and antimicrobial disinfectant agents in surface water and in urban wastewater. Journal of Environmental Protection and Ecology, 17(1), 119-126. Scopus.

Pétrier, C., Torres-Palma, R., Combet, E., Sarantakos, G., Baup, S., & Pulgarin, C. (2010). Enhanced sonochemical degradation of bisphenol-A by bicarbonate ions. Ultrasonics Sonochemistry, 17(1), 111-115. https://doi.org/10.1016/j.ultsonch.2009.05.010

PubChem. (2019). Recuperado 31 de agosto de 2019, de https://pubchem.ncbi.nlm.nih.gov/

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(Supplement C), 371-379. https://doi.org/10.1016/j.ultsonch.2016.04.005

Ridder, D. J. de, McConville, M., Verliefde, A. R. D., Aa, L. T. J. van der, Heijman, S. G. J., Verberk, J. Q. J. C., Rietveld, L. C., & Dijk, J. C. van. (2009). Development of a predictive model to determine micropollutant removal using granular activated carbon. Drinking Water Engineering and Science, 2(2), 57-62. https://doi.org/10.5194/dwes-2-57-2009

Romdhani, A., Martínez, F., Almanza, O. A., Peña, M. A., Jouyban, A., & Acree, W. E. (2019). Solubility of sulfacetamide in (ethanol + water) mixtures: Measurement, correlation, thermodynamics, preferential solvation and volumetric contribution at saturation. Journal of Molecular Liquids, 290, 111219. https://doi.org/10.1016/j.molliq.2019.111219

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. https://doi.org/10.3390/w9030218

Rubio-Clemente, A., Chica, E., & Peñuela, G. (2019). Total coliform inactivation in natural water by UV/H_2O_2, UV/US, and UV/US/H_2O_2 systems. Environmental Science and Pollution Research, 26(5), 4462-4473. https://doi.org/10.1007/s11356-018-3297-z

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. https://doi.org/10.1016/j.scitotenv.2013.12.126

Sági, G., Csay, T., Szabó, L., Pátzay, G., Csonka, E., Takács, E., & Wojnárovits, L. (2015). Analytical approaches to the OH radical induced degradation of sulfonamide antibiotics in dilute aqueous solutions. Journal of Pharmaceutical and Biomedical Analysis, 106, 52-60. https://doi.org/10.1016/j.jpba.2014.08.028

Santibáñez, S., García, J., & Gamboa, P. (2014). Determinación de la cinética de degradación de diclofenaco, ibuprofeno y su mezcla, a temperatura ambiente. Universidad Autónoma del Estado de México. http://ri.uaemex.mx/oca/bitstream/20.500.11799/14484/1/421048.pdf

Schmidt, W., O'Rourke, K., Hernan, R., & Quinn, B. (2011). Effects of the pharmaceuticals gemfibrozil and diclofenac on the marine mussel (Mytilus spp.) and their comparison with

standardized toxicity tests. Marine Pollution Bulletin, 62(7), 1389-1395. https://doi.org/10.1016/j.marpolbul.2011.04.043

Schorr, U., Distler, A., & Sharma, A. (1996). Effect of sodium chloride- and sodium bicarbonate-rich mineral water on blood pressure and metabolic parameters in elderly normotensive individuals: A randomized double-blind crossover trial. Journal of Hypertension, 14(1), 131-135.

Serna-Galvis, Efraim A., Isaza-Pineda, L., Moncayo-Lasso, A., Hernández, F., Ibáñez, M., & Torres-Palma, R. A. (2019). Comparative degradation of two highly consumed antihypertensives in water by sonochemical process. Determination of the reaction zone, primary degradation products and theoretical calculations on the oxidative process. Ultrasonics Sonochemistry, 58, 104635. https://doi.org/10.1016/j.ultsonch.2019.104635

Serna-Galvis, Efraím A., Montoya-Rodríguez, D., Isaza-Pineda, L., Ibáñez, M., Hernández, F., Moncayo-Lasso, A., & Torres-Palma, R. A. (2019). Sonochemical degradation of antibiotics from representative classes-Considerations on structural effects, initial transformation products, antimicrobial activity and matrix. Ultrasonics Sonochemistry, 50, 157-165. https://doi.org/10.1016/j.ultsonch.2018.09.012

Serna-Galvis, Efraim A., 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. https://doi.org/10.1016/j.ultsonch.2016.01.007

Serna-Galvis, Efraím A., 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. https://doi.org/10.1016/j.scitotenv.2015.04.053

Song, W., Teshiba, T., Rein, K., & O'Shea, K. E. (2005). Ultrasonically Induced Degradation and Detoxification of Microcystin-LR (Cyanobacterial Toxin). Environmental Science & Technology, 39(16), 6300-6305. https://doi.org/10.1021/es048350z

Szabó, L., Tóth, T., Takács, E., & Wojnárovits, L. (2016). One-electron oxidation of molecules with aromatic and thioether functions: Cl2−/Br2− and OH induced oxidation of penicillins studied by pulse radiolysis. Journal of Photochemistry and Photobiology A: Chemistry, 326, 50-59. https://doi.org/10.1016/j.jphotochem.2016.04.025

Tanaka, T., Tsuzuki, K., & Takagi, T. (2001). Chemical oxidation of organic matter in secondary-treated municipal wastewater by using methods involving ozone, ultraviolet radiation and TiO_2 catalyst. Water Science and Technology, 43(10), 295-302. https://doi.org/10.2166/wst.2001.0645

Tomul, F., Arslan, Y., Kabak, B., Trak, D., Kendüzler, E., Lima, E. C., & Tran, H. N. (2020). Peanut shells-derived biochars prepared from different carbonization processes: Comparison of characterization and mechanism of naproxen adsorption in water. Science of the Total Environment, 137828. https://doi.org/10.1016/j.scitotenv.2020.137828

Torres, R. A., Pétrier, C., Combet, E., Carrier, M., & Pulgarin, C. (2008). Ultrasonic cavitation applied to the treatment of bisphenol A. Effect of sonochemical parameters and analysis of BPA by-products. Ultrasonics Sonochemistry, 15(4), 605-611. https://doi.org/10.1016/j.ultsonch.2007.07.003

Torres-Palma, R. A., & Serna-Galvis, E. A. (2018). Chapter 7—Sonolysis. En S. C. Ameta & R. Ameta (Eds.), Advanced Oxidation Processes for Waste Water Treatment (pp. 177-213). Academic Press. https://doi.org/10.1016/B978-0-12-810499-6.00007-3

TOXNET. (2019). Recuperado 31 de agosto de 2019, de https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+hsdb:@term+@rn+@rel+103-90-2

Tran, N., Drogui, P., & Brar, S. K. (2015). Sonoelectrochemical oxidation of carbamazepine in waters: Optimization using response surface methodology. Journal of Chemical Technology & Biotechnology, 90(5), 921-929. https://doi.org/10.1002/jctb.4399

Tran, N., Drogui, P., Brar, S. K., & De Coninck, A. (2017). Synergistic effects of ultrasounds in the sonoelectrochemical oxidation of pharmaceutical carbamazepine pollutant. Ultrasonics Sonochemistry, 34(Supplement C), 380-388. https://doi.org/10.1016/j.ultsonch.2016.06.014

Tran, N., Drogui, P., Nguyen, L., & Brar, S. K. (2015). Optimization of sono-electrochemical oxidation of ibuprofen in wastewater. Journal of Environmental Chemical Engineering, 3(4, Part A), 2637-2646. https://doi.org/10.1016/j.jece.2015.05.001

Tran, N., Drogui, P., Zaviska, F., & Brar, S. K. (2013). Sonochemical degradation of the persistent pharmaceutical carbamazepine. Journal of Environmental Management, 131(Supplement C), 25-32. https://doi.org/10.1016/j.jenvman.2013.09.027

Triebskorn, R., Casper, H., Scheil, V., & Schwaiger, J. (2007). Ultrastructural effects of pharmaceuticals (carbamazepine, clofibric acid, metoprolol, diclofenac) in rainbow trout (Emphasis Type Italic Oncorhynchus mykiss Emphasis) and common carp (Emphasis Type

Italic Cyprinus carpio Emphasis). Analytical and Bioanalytical Chemistry, 387(4), 1405-1416. https://doi.org/10.1007/s00216-006-1033-x

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. https://doi.org/10.1007/s11356-018-1281-2

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. https://doi.org/10.1016/j.ultsonch.2017.10.014

Villaroel, E., Silva-Agredo, J., Petrier, C., Taborda, G., & Torres-Palma, R. A. (2014). Ultrasonic degradation of acetaminophen in water: Effect of sonochemical parameters and water matrix. Ultrasonics Sonochemistry, 21(5), 1763-1769. https://doi.org/10.1016/j.ultsonch.2014.04.002

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. https://doi.org/10.1016/j.ultsonch.2014.07.006

Vogna, D., Marotta, R., Andreozzi, R., Napolitano, A., & d'Ischia, M. (2004). Kinetic and chemical assessment of the UV/H2O2 treatment of antiepileptic drug carbamazepine. Chemosphere, 54(4), 497-505. https://doi.org/10.1016/S0045-6535(03)00757-4

Walters, E., McClellan, K., & Halden, R. U. (2010). Occurrence and loss over three years of 72 pharmaceuticals and personal care products from biosolids–soil mixtures in outdoor

mesocosms. Water Research, 44(20), 6011-6020. https://doi.org/10.1016/j.watres.2010.07.051

Watkinson, A. J., Murby, E. J., & Costanzo, S. D. (2007). Removal of antibiotics in conventional and advanced wastewater treatment: Implications for environmental discharge and wastewater recycling. Water Research, 41(18), 4164-4176. https://doi.org/10.1016/j.watres.2007.04.005

Wood, R. J., Lee, J., & Bussemaker, M. J. (2017). A parametric review of sonochemistry: Control and augmentation of sonochemical activity in aqueous solutions. Ultrasonics Sonochemistry, 38, 351-370. https://doi.org/10.1016/j.ultsonch.2017.03.030

Xia, L., Chen, F., Li, J., Chen, S., Bai, J., Zhou, T., Li, L., Xu, Q., & Zhou, B. (2020). Efficient organic pollutants conversion and electricity generation for carbonate-containing wastewater based on carbonate radical reactions initiated by BiVO4-Au/PVC system. Journal of Hazardous Materials, 389, 122140. https://doi.org/10.1016/j.jhazmat.2020.122140

Zúñiga-Benítez, H., Soltan, J., & Peñuela, G. A. (2016). Application of ultrasound for degradation of benzophenone-3 in aqueous solutions. International Journal of Environmental Science and Technology, 13(1), 77-86. https://doi.org/10.1007/s13762-015-0842-x

8. ANNEXES

A1: Calculation of Ra (Example)

The hydrogen peroxide is quantified by iodometry by measurement of the absorbance at 350 nm, which is based on the iodide reaction with hydrogen peroxide as presented below:

$$H_2O_2 + 2KI \xrightarrow{AHM} 2KOH + I_2$$

$$I_2 + I^- \rightarrow I_3^-$$

AHM: Ammonium heptamolybdate (catalyst).

Using Beer's Law, the concentration of hydrogen peroxide will be determined as:

$$C = \frac{A}{b*\varepsilon} \; x \; \frac{2000^*}{600}$$

A: Absorbance
b: optical path (1 cm)
ε: molar absorbance at 350 nm (26,400 M^{-1} cm^{-1})
C: concentration of hydrogen peroxide (M)
*: Dilution factor

In Table A1 is exemplified the calculations of hydrogen peroxide concentrations.

Table A1. Calculation of H_2O_2 concentrations in the samples.

CONDITIONS	TIME (min)	b (cm)	ε (M^{-1} cm^{-1})	A 1	A 2	C 1 (µM)	C 2 (µM)
3.31 uM DCF (375kHz – 24.4 W - 250 mL – pH 7.2)	0	1	26400	0.0000	0.0000	0.000	0.000
	3	1	26400	0.1115	0.1227	14.078	15.492
	5	1	26400	0.1845	0.2148	23.295	27.121
	10	1	26400	0.3791	0.3994	47.866	50.429
	15	1	26400	0.5632	0.5889	71.111	74.356
	20	1	26400	0.7242	0.7452	91.439	94.091
	30	1	26400	1.0538	1.0629	133.056	134.205

Fig. A1 exemplifies the determination of Ra (as the slope of $[H_2O_2]$ vs. time).

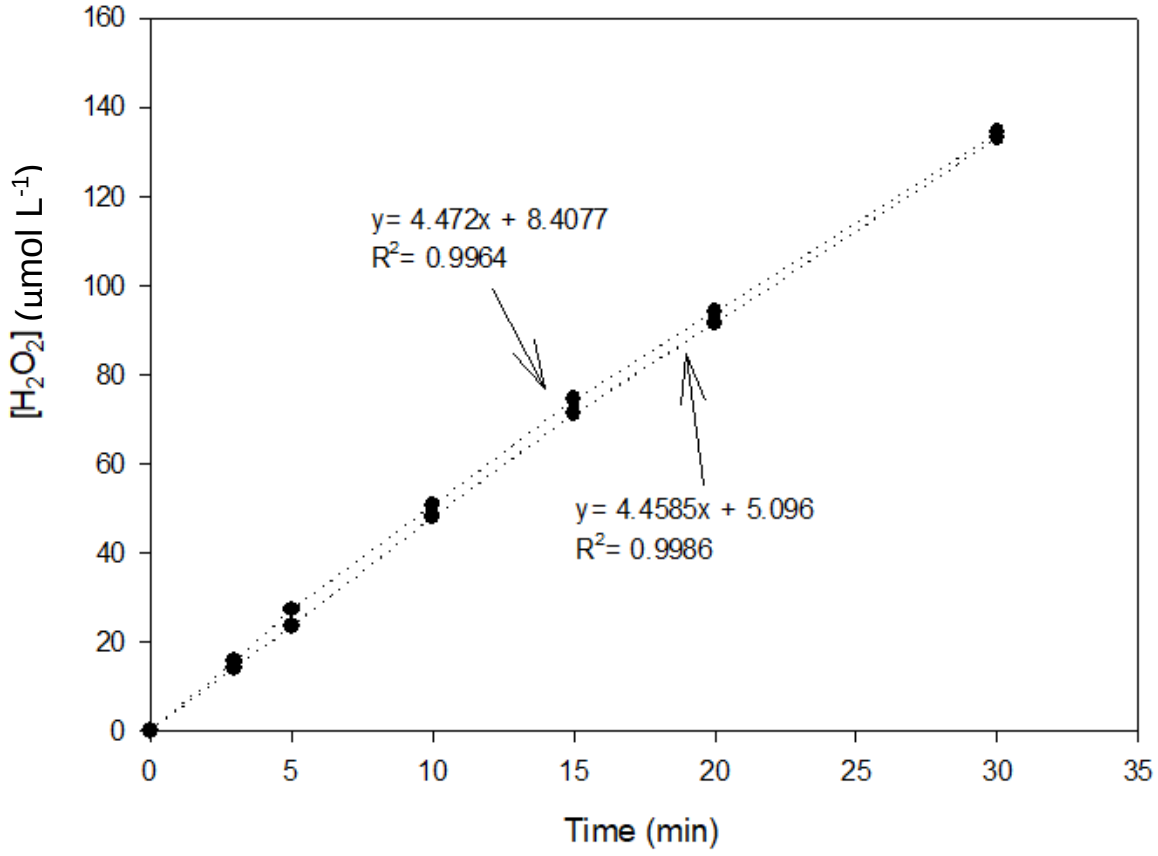


Fig. A1. Evolution of H_2O_2 concentration. Conditions: KI (0.1M)= 1350 µL, HMA (0.01 M)= 50 µL, absorbance measurement at 350 nm.

The slope of trend line is the accumulation rate of H_2O_2 (Ra, which is summarized in Table A2).

Table A2. Error and average value of the accumulation rate of H_2O_2.

Ra 1	Ra 2	Average Ra (µM min^{-1})	ERROR
4.472	4.4585	4.46525	0.00675

A_2: Calculation of R_d (Example)

For NPX degradation using ultrasound, the remaining concentrations (Cr, in µM) for each sampling time are shown in Table A3. This information is plotted in Fig. A2 was using the first three points in order to obtain the initial degradation rate (Rd).

Table A3. Remaining concentration for each sampling time.

TIME (min)	C_r (µM)	C_r (µM)
0	3.31	3.31
3	2.36	2.33
5	1.85	1.83
10	1.05	1.04
15	0.59	0.59
20	0.33	0.34
30	0.12	0.12

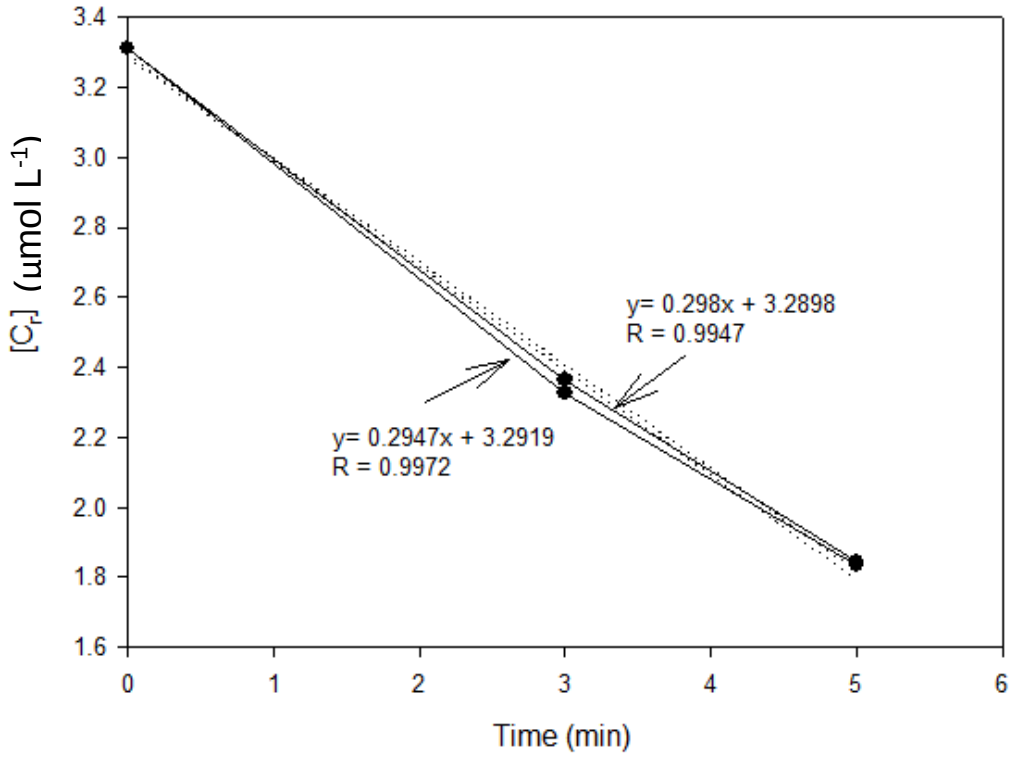


Fig. A2. Determination of Rd for NPX. Conditions: [NPX] = 3.31 µM, pH= 7.2, Frequency= 375 kHz, Power= 80%, volume= 250 mL.

The slope of the trend line denotes the initial degradation rate (Rd) for NPX. Table A4 presents establishes average and error values of the Rd data.

Table A4. Error and average value of the initial degradation rate.

R_d 1	R_d 2	Average R_d µmol L^{-1} min^{-1}	ERROR
0.2947	0.2980	0.2964	0.00165