Kinetic study of colored species formation during paracetamol removal from water in a semicontinuous ozonation contactor

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ABSTRACT

Paracetamol aqueous solutions, when ozonized, acquired a strong red coloration depending on the applied ozone dose and the initial pH of the aqueous solution. Then, this color loses intensity and turns to yellow. Color formation is favored when operating at initial pH_0=12.0 and ozone flow-rate 4.2 mg/min. A mechanism describing color formation was proposed, being the main pathway involved an initial paracetamol hydroxylation to yield 3-hydroxyacetaminophen followed by the formation of 2-amino-

5-hydroxyacetofenone. Then, these compounds are degraded to colored oxidation by-products. A model describing color evolution was also proposed, considering first-order kinetics for both color formation and degradation. The corresponding kinetic constant values were determined to be k_f=0.01 (1/min) and k_d=0.03 pH-0.055 (1/min), respectively. A relationship between aromaticity loss and color changes during the reaction has been estimated considering the parameter $\alpha=k_A/k_f$, being α=1.62 pH + 3.5 and the first-order rate constant for aromaticity loss given by k_A=0.0162 pH + 0.035 (1/min).

KEYWORDS

Chemical pathway; Color; Kinetic modelling; Ozone; Paracetamol; Initial pH

1. Introduction

Among the so called contaminants of emerging concern, pharmaceuticals stand out as one of the most detected families of compounds in wastewater effluents, but also in surface waters and drinking waters (Mompelat et al., 2009; Richardson, 2009; Seifrtová et al., 2009; Sun et al., 2014). These pollutants enter the water resources by means of industrial, agricultural and domestic residual effluents that are transported to wastewater treatment plants (WWTPs), where many of them –because of their chemical properties– cannot be effectively eliminated by the conventional treatment technologies typically implemented in those facilities (Blair et al., 2015; Baalbaki et al., 2016). Current research focus on the development of chemical processes able to degrade recalcitrant

chemicals from wastewater effluents and natural water compartments, in order to avoid their presence in urban water distribution networks (Ziylan-Yavaş and Hince, 2018). In this context, Advanced Oxidation Processes (AOPs) are considered a promising alternative (Hollender et al., 2009; Rosario-Ortiz et al., 2010; Oller et al., 2011; Margot et al., 2013; Lee et al., 2016).

This work focused on the study of paracetamol (4-hydroxyacetanilide, 4-acetamidephenol or acetaminophen) degradation by means of ozonation. This pharmaceutical is employed as anti-inflammatory and analgesic (Skoumal et al., 2006) and, despite human organism is capable of metabolizing up to a 90% of the consumed drug –excreting only a 3-5%– (Ellenhorn and Barceloux, 1988; McEvoy, 1992), the worldwide amount of this chemical reaching WWTPs have been estimated to be in the range of 292-585 ton/year (El Najjar et al., 2014). Moreover, this pollutant has been often found in municipal sewage effluents at concentrations up to 65 µg/L (Villaroel et al., 2014). Although the concentration of paracetamol detected in natural waters is generally below the µg/L range (Skoumal et al., 2006), its presence may potentially affect aquatic organisms (Santos et al., 2010) due to the ability of this chemical to bioaccumulate (Radjenović et al., 2009; Deblonde and Hartemann, 2013; Valdés et al., 2014; Zenker et al., 2014). Studies reported in the bibliography show that AOPs are usually effective treatments for degrading this kind of organic pollutants from water (Ay and Kargi, 2001). In addition, and due to the low concentrations of these substances in water matrices, membrane technology can be used to concentrate micropollutants prior to AOPs treatments reducing the volume of water to treat (Savchuk and Krizova, 2015).

Ozone is a powerful oxidant employed in drinking and wastewater treatment plants due to its ability for microorganisms inactivation and both inorganic and organic contaminants transformation (Paraskeva and Graham, 2002; Rodríguez et al., 2008; Gomes et al., 2017). However, the application of ozone presents some practical limitations related to operational pH: under acidic conditions, O_3 is relatively stable and directly reacts with pollutants, whereas for pH values corresponding to neutral and basic conditions this oxidizing species decomposes to highly oxidizing radicals (*i.e.*, hydroxyl radicals •OH) that enhance the process efficiency (Rodríguez et al., 2017). In addition, the physicochemical properties (*i.e.*, pKa and second-order rate constants with O_3 and OH•) of micropollutants determine their removal efficiencies according to the medium pH, which can be different depending on the wastewater origin. Therefore, it is interesting to perform a study that covers a wide range of operational pH. Furthermore, it is necessary to ensure a reduction in the toxicity of the ozonized effluents, which is normally attributed to the toxic character of the transformation products generated because of the treatment application (Wert et al., 2007; Lee and von Gunten, 2016; Maya et al., 2018). Thus, in order to ensure the treatment effectiveness, it is necessary to perform a complete study of the process assessing reaction kinetics, transformation products and toxicity of the treated water (Cruz-Alcalde et al., 2017).

During organic matter ozonation, a reduction in the relative amount of aromatic rings and conjugated bonds contained in the water matrix is produced. Also, the number of electron acceptors (*i.e.*, carboxyl, carbonyl, hydroxyl, alcoxy) increases (Swietlik and Sikorska, 2004). Ozone preferently degrades organic molecules with low oxidation state (low O/C ratio) and a high degree of insaturation (high H/C ratio), yielding more saturated and oxygenated (alcohols, aldehydes, carbonyls, ketones and carboxylic acids)

(Reemtsma and These, 2005; von Gunten, 2003). Among them, the relative amount of carboxylic acids generated during the process is generally much higher than that of aldehydes or ketones (Nawrocki and Kasprzyk-Hordern, 2003). They typically are compounds with short molecular chains (less than 5 C atoms), such as formic, acetic or oxalic acid (Can and Gurol, 2003).

During paracetamol ozonation, aqueous solutions of this chemical acquire a red tonality which gradually turns to yellow. In the present work, therefore, and since color is an important organoleptic parameter determining water quality (Villota et al., 2016), degradation intermediates causing this change of tone in water have been identified. According to the transformation products detected through LC-MS, the oxidation mechanism taking place simultaneously to the mentioned color changes in paracetamol solutions has been proposed. Moreover, the influence of main operational parameters of ozonation process (*i.e.*, initial pH and applied ozone flow-rate) on color formation, degree of mineralization and aromaticity, as well as on the mass transfer of ozone to the aqueous phase, has been studied including some toxicity studies (El Najjar et al., 2014). By this way, operational conditions leading to the formation of chromophoric intermediate (quinone compounds) increasing water toxicity have been characterized (Mijangos et al., 2006).

2. Materials and methods

2.1. Chemicals and reagents

Paracetamol solutions $[Pa]_0$=50.0 mg/L were prepared by dissolving pure paracetamol (Sigma-Aldrich 99.9%) in milli-Q water produced by a filtration system (Millipore, USA). Assays were performed operating under different initial pH conditions (pH_0 between 3.0 and 12.0) in order to assess the effect of this parameter on color formation during ozonation of paracetamol aqueous solutions. This range was selected to cover a wide range of water properties. The initial pH was adjusted by adding a few drops of concentrated HCl and NaOH solutions in order to avoid sample dilution. Although the operational pH has not been controlled during the reaction, its maximum variation has been less than 0.5 pH units (Mijangos et al., 2006). Pure oxygen (≥99.999%) for ozone production was supplied by Abelló Linde (Spain). The reproducibility of the ozonation assays was considered based on the mean of the colour of the values measured, obtaining standard deviations less than 5% in all cases.

2.2. Semicontinuous ozonation setup

For each ozonation experiment, 1.0 L of paracetamol solution was prepared and added into a jacketed reactor operating in semi-continuous mode. Experiments were performed at a constant temperature of 25.0 °C, maintained by means of a thermostatic bath. Ozone/oxygen gaseous mixtures were generated by means of a 301.19 Labor Ozonator (Sander, Germany) and injected at the bottom of the reactor employing a metallic difusser (pore size: 10 μm). The ozone flow rate applied was in the range 4.2 - 25.0 mg/min. The medium was under stirring conditions in order to ensure homogeneity. The inlet and outlet ozone concentration in the gas phase were meausured by means of two BMT 964 ozone analyzers (BMT Messtechnik GMBH, Germany), placed up and downstream the contactor, respectively. More information about the experimental setup

149 may be found elsewhere (Marcé et al., 2016). The dissolved ozone concentration was
150 measured by the Indigo colorimetric method (Bader and Hoigné, 1981; Greenberg et al.,
151 1999).

152

153 **2.4. Analytical procedures**

154

155 Paracetamol mineralization was estimated through total organic carbon (TOC, mgC/L)
156 measurements using a TOC-VCSN Shimadzu Analyzer. Color was determined using an
157 UV/Vis spectrophotometer (DR 6000-Hach Lange) by direct measurement of the
158 samples absorbance at λ=455 nm (Mijangos et al., 2006). For aromaticity loss
159 monitoring, UV absorbance measurements were performed at λ=254 nm. The samples
160 were analyzed by Liquid Chromatography-Mass Spectrometry (LC-MS) to elucidate the
161 paracetamol degradation pathways that induce high levels of color in the water during
162 the ozonation process. Samples were analyzed by HPLC coupled in series to a MS-TOF
163 (G3250AA by Agilent, USA) system and a UV detector (1100 Agilent). This
164 configuration allowed the comparison between chromatograms obtained through UV
165 and MS detectors, discarding this way interferences caused by artifacts.

166 MS data were collected in full scan mode (50–1500 m/z), employing negative
167 electrospray ionization. The column employed was a Teknokroma Mediterranea Sea 18
168 (250 mm × 4.6 mm and 5 μm size packing). The mobile phase consisted of a 65:35
169 volumetric mixture of methanol and Milli-Q water acidified at pH 3.0 by the addition of
170 H_3PO_4. The flow rate was maintained at 0.3 mL min^{-1} and the detection wavelength (for
171 the UV detector) was set to 200 nm and 243 nm. The spectrophotometer conditions
172 were voltage of capillary 3500 V and shredder 125 V, being the limit of detection
173 (LOD) 0.25 μM.

3. Results and discussion

3.1. Effect of applied ozone flow-rate on color formation

During the ozonation of aqueous solutions of paracetamol, a general aromaticity loss in the reaction medium is observed (Fig. 1). This fact confirms organic matter oxidation, leading to changes in molecular structures of species initially contained in the water matrix. During ozonation treatment, the highest absorption observed in the UV spectrum corresponds to the opening of aromatic rings causing the transformation of organic molecules (Xiong and Legube, 1991). This reaction is fast and it is characterized by the decrease of UV absorbance measured at 254 nm (von Gunten, 2003).

Results show a total loss of the aromaticity in the water produced when ozonation of 50.0 mg/L paracetamol solutions employing ozone flow rates higher than 7.5 mg O_3/min is applied. It is also observed that an increase of ozone flow-rate causes an increase in the rate of aromaticity reduction. However, this increase does not follow a linear tendency, which would indicate the existence of particular operation conditions leading to the activation of different degradation pathways through which the overall oxidation mechanism of paracetamol takes place.

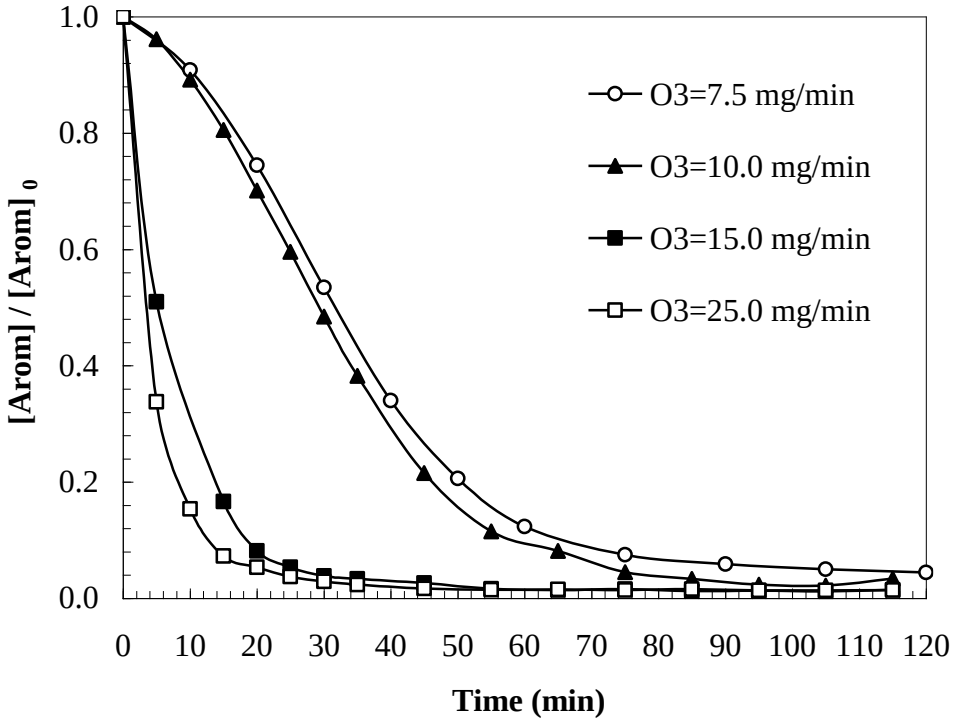


Fig. 1. Influence of the inlet ozone flow rate during paracetamol oxidation experiments on aromaticity loss. Experimental conditions: $[Pa]_0$=50.0 mg/L; pH_0=12.0; T=25.0ºC.

Simultaneously to aromaticity loss, color changes in oxidized waters also take place, indicating the kinetic evolution of a reaction intermediate (Fig. 2). Initially, colorless aqueous solutions containing paracetamol $Color_0$ (AU) gradually acquire a strong red tonality, until the maximum color intensity $Color_{max}$ (AU) is reached at a certain reaction time t_{max} (min). Then, color acquires a yellowish tone with time-decreasing intensity until a residual value of this parameter is reached ($Color_\infty$, AU). This fact would indicate the simultaneous cleavage of paracetamol molecules and subsequent formation of chromophoric groups –such as –C=O, -C=C y NO_2– in the respective structures of the degradation products.

Observed changes in color show an asymmetric bell-shaped tendency, with the decreasing part of this curve presenting a tail. This evolution can be explained by the

two stages taking place during ozonation of paracetamol (El Najjar et al., 2014). The first of these regimes, characterized by exhibiting fast oxidation kinetics, occurs during the first minutes of the process. During this period, in which a loss in water aromaticity is observed, paracetamol is oxidized to yield different reaction intermediates, some of them containing chromophoric terminations responsible for color appearance in the water matrix. Then, a slower ozonation stage starts to take place. At this point of the process, reaction intermediates –including colored species are slowly degraded to smaller molecules, ultimately leading to the formation of colorless carboxylic acids (i.e., oxalic, acetic and formic).

In order to analyze the effect of ozone flow-rate on color formation and degradation kinetics, the color signal (in color area units) as a function of the ozone flow-rate inlet has been represented (see Fig. 2). These results allow checking how, regardless of the employed operational conditions, paracetamol ozonation always leads to intermediates containing chromophoric groups in their molecular structures. However, colored species formation is better observed under low inlet ozone flow-rates ($[O_3]$=4.2 mg/min). When gradually increasing this dosing rate up to 25.0 mg/min, color curves with smaller areas are registered due to faster formation and degradation of chromophoric reaction intermediates.

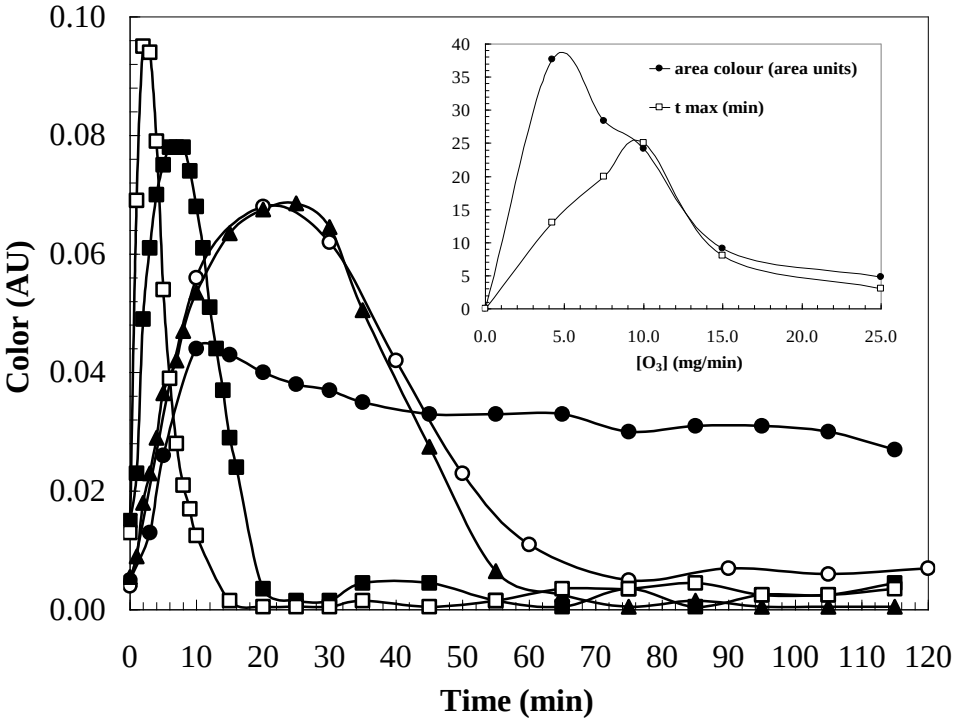


Fig. 2. Effect of flow rate of ozone applied during paracetamol oxidation on the color appearance in water matrices. Experimental conditions: $[Pa]_0$=50.0 mg/L; pH_0=12.0; T=25.0ºC. Legend: Inlet flow rate of ozone $[O_3]$= ● 4.2 mg/min, ○ 7.5 mg/min, ▲ 10.0 mg/min, ■ 15.0 mg/min, □ 25.0 mg/min.

To explain this phenomenon, it is necessary to analyze the reaction time –as a function of the volumetric ozone flow-rate– for which the maximum color intensity in water matrix is observed (t_{max}, min). This is shown in Fig. 2. This t_{max} parameter does not proportionally decrease with increasing ozone flow-rate. Instead, a maximum is observed for certain operational conditions, which would indicate that ozone does not exert a catalytic effect in oxidation but determines the degradation yield of paracetamol leading to colored species formation.

The ozone flow-rate employed during the process produces a selective paracetamol oxidation to yield colored species through different degradation routes. The overall degradation mechanism does not consist of a unique degradation via leading to the

generation of a single compound. On the contrary, a mix of chemical species coexists in the system. Therefore, the observed color kinetics would be caused by reaction intermediates presenting different molecular structures. The time for which the maximum color intensity is registered would indicate the generation of a group of predominant colored species, as well as the oxidative level in which these compounds are formed throughout the overall degradation mechanism.

3.2. Pathway of colored intermediates generation

Ozonized aqueous solutions of paracetamol ($[Pa]_0$=50.0 mg/L) corresponding to experiments with an ozone flow-rate of 4.2 mg/min and pH_0=12.0 as experimental conditions, have been analyzed by LC-MS to determine the nature of intermediates causing color in water. These are the operational conditions for which a higher color intensity remained in the residual water ozonized that makes possible to analyze the compounds contained in the colored water. In this situation, therefore, the formed chromophoric intermediates could be analyzed before their subsequent transformation to colorless acids. On the basis of the obtained results, and considering the degradation mechanisms of paracetamol reported in scientific literature, (He et al., 2018; Villota et al., 2018; Villota et al., 2016; Martignac et al., 2013; Moctezuma et al., 2012), an scheme of those reactions causing color generation in ozonized waters has been proposed (Fig. 3).

The nature of the detected ozonation by-products depends on the employed flow-rate of ozone. Previous works show that employing lower ozone dosages and high substrate concentrations leads to the detection of reaction intermediates containing from 4 to 6 C

atoms, whereas employing elevated ozone dosages favored the formation of smaller molecules generally containing 1-3 C atoms (Brunet et al., 1982). For the current case of study, therefore, the color observed during paracetamol ozonation operating at flow-rates lower than the stoichiometric value, may be induced by intermediate species exhibiting molecular structures with 4-6 carbon atoms.

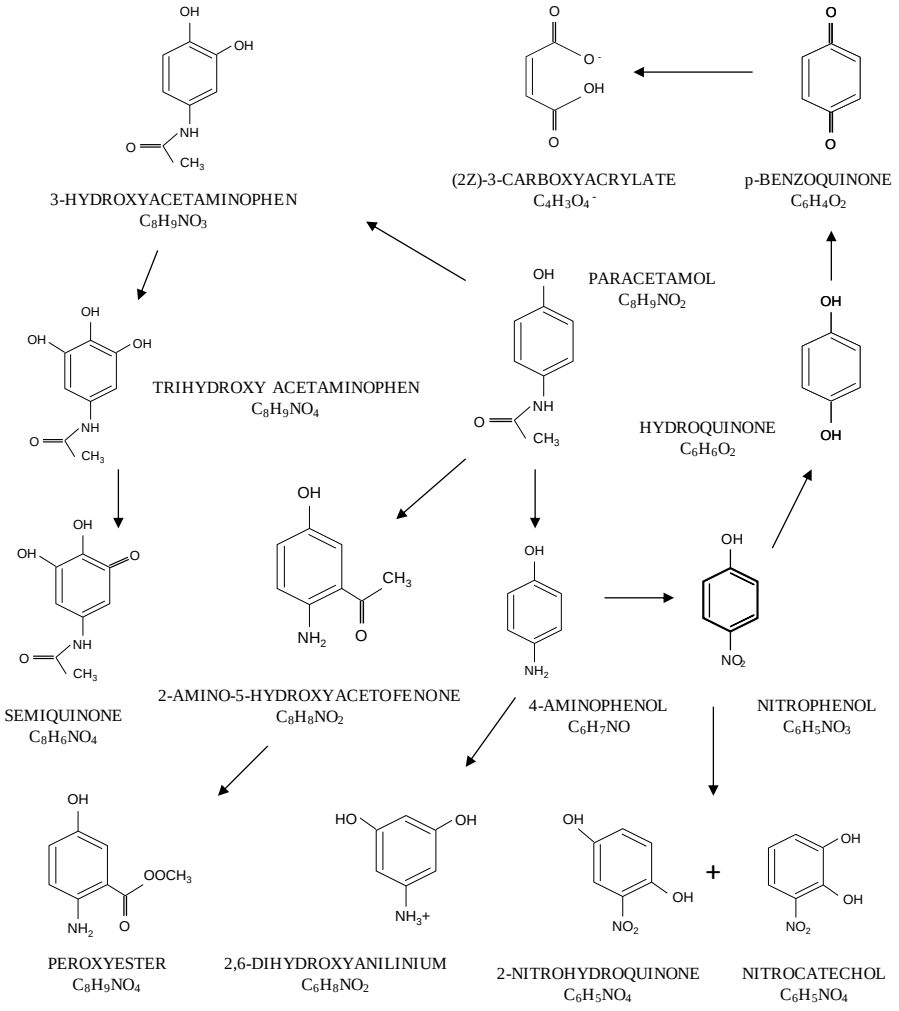


Fig. 3. Reaction intermediates generated during the ozonation of paracetamol aqueous solutions. Experimental conditions: $[Pa]_0$=50.0 mg/L; pH_0=12.0; $[O_3]$=4.2 mg/min; T=25.0ºC.

Analysis on the colored reaction mixture would indicate the formation of some transformation products such as hydroquinone, benzoquinone, p-aminophenol and p-nitrophenol. In accordance with the suggested mechanism, three reactions involving the initial attack of formed hydroxyl radicals ($HO^{\bullet}$) to finally yield ortho-meta- and para-hydroxylated compounds (with respect to the initial hydroxyl group of paracetamol) would compete to simultaneously take place in the system. Existent works dealing with this subject have reported that, during the initial stages of the oxidation process, hydroxyl and amino groups present a high reactivity towards ortho- and para- positions, due to the high electron-donating capacity exhibited by these moieties (Westerhoff et al., 1999). Contrarily, reactions occurring at meta- positions are less favored and, therefore, hydroxylation reactions at this point of the aromatic ring are considered to be of minor relevance (Vogna et al., 2002).

Oxidation could be initiated via hydroxyl radical addition to the ortho-position of paracetamol, leading to the formation of 3-hydroxyacetaminophen. The predominant pathway, however, is the one initiated by the generation of the paracetamol isomer 2-amino-5-hydroxyacetophenone. This reaction implies the migration of an acetyl group from the amino moiety of paracetamol in position para- (with respect to the hydroxyl group) to position ortho- (in the aromatic ring) with respect to the amino ($-NH_2$) group.

The presence of p-aminophenol and p-nitrophenol in the colored mixture has been also detected. This fact would indicate a deacylation mechanism, subsequently leading to the generation of an amide group bonded to the aromatic ring (Bahnemann et al., 2007). Due to the fact that hydroxyl radicals mainly react through addition to the aromatic ring, p-nitrophenol would be generated by oxidation of p-aminophenol. First, the addition of

311 $HO^{\bullet}$ to the aromatic ring would be produced, followed by the elimination of a hydroxyl
312 group. Then, a deprotonation of the formed radical cation would generate an easily
313 oxidizable anilinyl radical, to finally yield p-nitrophenol (Martignac et al., 2013).
314
315 During p-nitrophenol oxidation, two competitive chemical transformations could take
316 place: an hydroxylation in ortho- position to finally yield nitrocatechol, on one hand,
317 and a hydroxylation in para- position (with respect to the phenolic hydroxyl group) and
318 later elimination of the nitro group, obtaining by means of this way hydroquinone as
319 product (Moctezuma et al., 2007). Further hydroquinone oxidation would finally yield
320 benzoquinone.
321
322 **3.3. Influence of initial pH and oxidant dosage on ozonized water coloration**
323
324 Color formation in ozonized water has been analyzed, considering both the pH_0 (Fig. 4)
325 and ozone flow-rate ($[O_3]$ mg/min), (Fig. 5) employed during ozonation assays. The aim
326 of this study was to determine whether the degradation route causing color formation
327 consisted of a direct ozone oxidation of paracetamol or, on the contrary, could be
328 attributed to the unselective oxidation by hydroxyl radicals generated through ozone
329 decomposition (pH_0 values higher than 6.0). This part of the work was performed
330 operating within an initial pH range of 3.0-12.0 (see Fig. 4). Normalized TOC (mg/L)
331 and absorbance at 254 nm ([Arom], AU) values, together with the color ($Color_\infty$, AU)
332 and the ozone mass transfer coefficient (K_La, l/min) determined at the end of treatment
333 have been all represented. The maximum color generated during ozonation experiments
334 has been also included.
335

The determination of ozone transfer parameters may be done according to the equations of gas-liquid mass transfer (Rodriguez et al., 2017). Ozone consumption N_{O3} (mg/L min) can be expressed as the volumetric mass transfer coefficient K_La (1/min) multiplied by the mass transfer driving force, according to Eq. 1. The volumetric mass transfer coefficient has been estimated considering the mass transfer taking place from gas to liquid phase, being C_i (mol/L) the ozone concentration at the interphase, C_L (mg/L) in the liquid phase and C_L* in the liquid phase in equilibrium with the gas (mg/L). Note that in Eq. 1 K_La (1/min) is the global mass transfer coefficient, whereas k_Ga and k_La represent the individual coefficients for gas and liquid phases, respectively.

$$N_{O_3} = K_L a\,(C_L^* - C_L) = k_G a\,H\,(C_L^* - C_i) = k_L a\,(C_i - C_L) \quad (1)$$

Ozone mass transfer can be also expressed as a function of the ozone flow rate (Q_{O3}, L/min), the reaction volume (V, L) and the difference between the inlet and outlet ozone concentrations in the gas phase ($C_{G,in}$ and $C_{G,out}$ (mg/L), respectively) (see Eq. 2). It is worth to mention here that transferred ozone can be accumulated in the liquid phase or be consumed through two main mechanisms: direct oxidation reactions with the contaminant (R_{O3}, mg/L min), or O_3 self-decomposition leading to the generation of hydroxyl radicals (r_{O3}, mg/L min).

$$N_{O_3} = \frac{Q_{O_3}}{V}(C_{G,in} - C_{G,out}) = K_L a\,(C_L^* - C_L) = \frac{dC_L}{dt} + R_{O_3} + r_{O_3} \quad (2)$$

Ozone concentration in the liquid phase in equilibrium with gas phase can be estimated considering the Henry Law (Eq. 3), where H (atm/ozone molar fraction in the liquid) is the Henry constant and P_G (atm) is the partial pressure of ozone in the gas phase.

$$C_L^* = \frac{P_G}{H} \quad (3)$$

The Henry constant has been determined as a function of the liquid phase temperature (K) and pH, according to Eq. 4 (Roth and Sullivan, 1981).

$$H = 38 \cdot 10^6 \, C_{OH^-}^{0.035} \exp\left(\frac{-2428}{T}\right) \quad (4)$$

Obtained results allow checking how both aromaticity loss and residual color of ozonized waters do not experiment important variations with the medium pH_0. However, the maximum color generated in water shows a strong dependence from pH: when operating in the initial pH range comprised between 3.0 and 6.0, this intensity remains constant, whereas if this parameter is increased from 6.0 to 12.0, a potential rise in its value is observed. To explain these results, it is necessary to consider the Henderson-Hasselbach equation concerning the ionization curve of paracetamol. When water pH is increased, the concentration of hydroxide anions in the system also increases, and consequently does the ozone decomposition to hydroxyl radicals. This fact causes an enhancement in the oxidizing capacity of the system, leading to a higher degradation efficiency of the pharmaceutical to yield colored transformation products.

On the other hand, paracetamol is a weak acid, with a pKa value equal to 9.38 (Dastmalchi et al., 1995). This is going to determine the reactivity of this compound. When assays are performed within the operational pH interval comprised between 3.0 and 9.4, as the system is acidified, the number of non-dissociated or non-ionized molecules is relatively larger. On the contrary, for pH values higher than 9.4 (under basic conditions) the proportion of dissociated molecules increases. This fact could explain the strong color rise observed when operating at a pH value of 12.0, since paracetamol molecules under these conditions exhibit a high degree of dissociation. Because of this, this specie is degraded through oxidative routes conducting to the generation of chromophoric structures that provide color to the ozonized water.

As indicated in the relationship by Roth and Sullivan, 1981, if the system pH is increases this favors the ozone transfer to the reacting solution. However, obtained results in the current case of study suggest that the ozone transference to aqueous solutions of paracetamol is maximum when the process is performed at a pH value of 6.0. This phenomenon is accompanied by a decrease in the total organic carbon (TOC, mg/L). To explain this phenomenon, it is necessary to consider the nature of chemical species that are present in the reaction medium, since they can either accelerate the decomposition of ozone to hydroxyl radicals (radical chain reactions) or slowing it down. In this case, the pKa value for paracetamol (9.4) determines the process performance. The more acidic is the media the higher is the number of non-dissociated paracetamol molecules. On the contrary, at pH > pKa conditions, the number of unprotonated molecules becomes larger. This fact can considerably impact the ozone reactivity with this pharmaceutical. In addition, when operating within a pH range

between 6.0 and 12.0, the ozone concentration in water increasingly diminishes due a higher concentration of hydroxide (OH^-) ions.

This clearly affects the ozone transfer to the liquid phase, which is reflected in lower K_La values with increasing pH values. In addition to the effect exerted by the hydroxide ion, it is possible that, because of paracetamol mineralization, some inorganic species (mainly nitrogen anions) could be formed. These ions would act as ozone and radical scavengers, also affecting the ozone transfer to the liquid phase (Gottschalk et al., 2010; Sumegova et al., 2013).

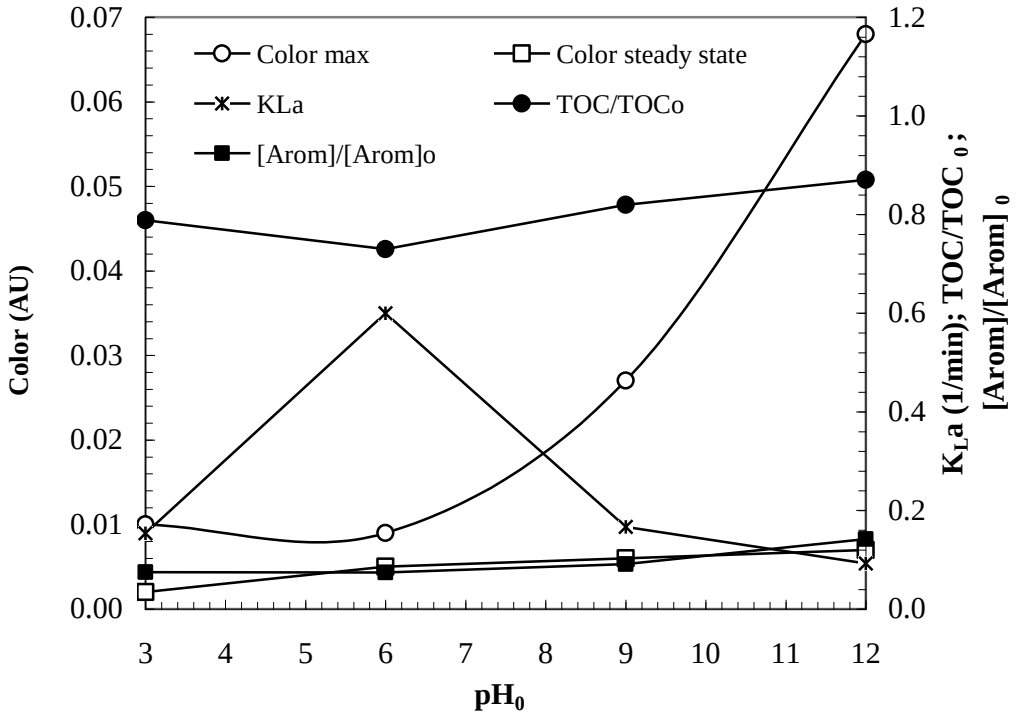
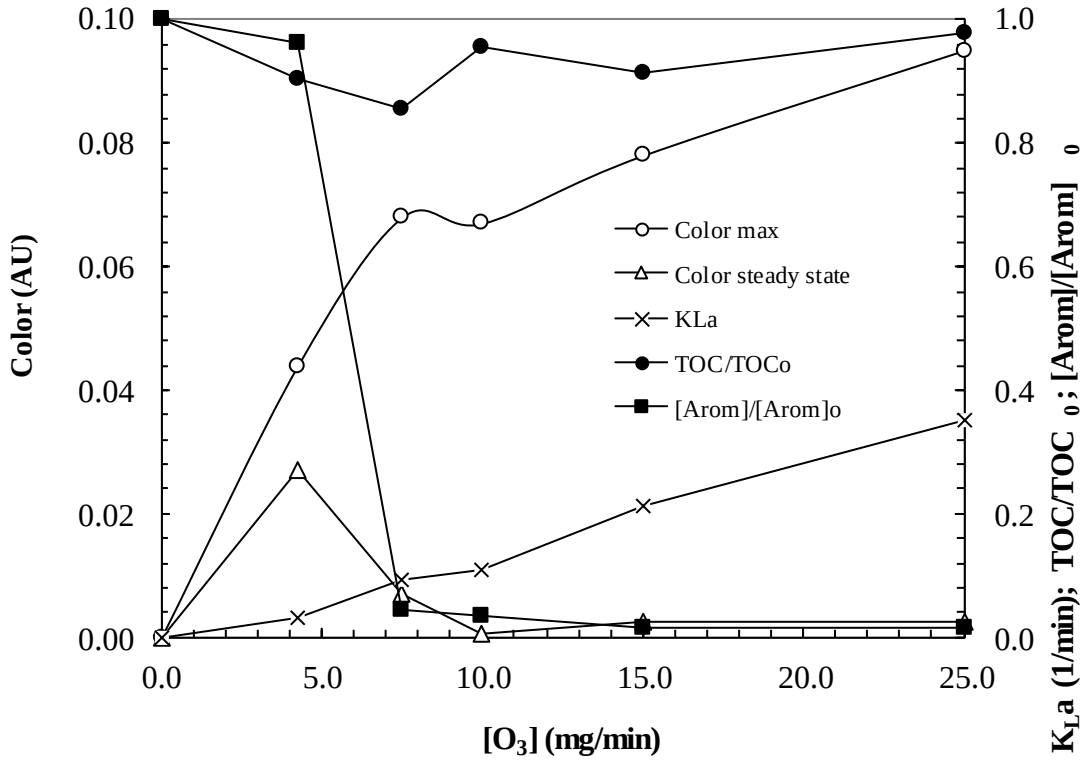


Fig. 4. Influence of initial pH on color (AU) formation, mass transfer coefficient K_La (l/min), organic matter mineralization TOC/TOC_0 and aromaticity loss ($[Arom]/[Arom]_0$) during paracetamol ozonation. Experimental conditions: $[Pa]_0$=50.0 mg/L; $[O_3]$=4.2 mg/min; T=25.0ºC; t=120 min.

421 The influence of the employed ozone dose was evaluated in ozonation assays carried
422 out at pH=12.0. As mentioned, these conditions potentiate the formation of colored
423 structures (Fig. 5). In this case, aromaticity loss exhibits a strong dependence with
424 ozone dose: when working at ozone flow rate below 4.2 mg/min for a total reaction time
425 of 2 h, the aromaticity reduction is less than 4%. If on the contrary, the oxidant flow rate
426 is increased up to 7.5 mg/min, an abrupt drop of this parameter (approximately a 95%)
427 is observed. The oxidant/substrate ratio corresponding to these experimental conditions,
428 57 mol O_3/mol $C_8H_9NO_2$, would therefore correspond to that stoichiometric relationship
429 required in order to produce a reduction in the aromaticity of the paracetamol
430 molecules. If ozone flow-rate is further increased, the observed final percentage of
431 aromatic species in solution is less than 5%. From this point, the depletion of this
432 residue follows a linear behavior with the ozone dose increment: for an ozone flow rate
433 of 1.0 L/min, for instance, water aromaticity reduction is 99%.
434



435
436

437 **Fig. 5.** Effect of ozone flow rate during paracetamol oxidation on color formation (AU),
438 mass transfer coefficient K_La (1/min), organic matter mineralization TOC/TOC_0 and
439 aromaticity loss ($[Arom]/[Arom]_0$). Experimental conditions: $[Pa]_0$=50.0 mg/L;
440 pH_0=12.0; T=25.0ºC; t=120 min.

441

442 Ozone transference to the aqueous solution increases with increasing inlet ozone flow-
443 rates, but only if operation pH is constant. This enhancement in the gas-liquid transfer
444 leads to an increase of the water-color formation. This phenomenon appears to indicate
445 that pH conditions define the selectivity ozonation mechanism, while the efficiency of
446 paracetamol degradation leading to colored species formation would be more influenced
447 by the applied ozone doses.

448

449 It has been verified that a residual coloration lasts in ozonized waters when the provided
450 ozone flow-rate is 4.2 mg/min. That color is less intense when the inlet flow of ozone is
451 7.5 mg/min. This maximum intensity value of the residual color would indicate that,

when operating at ozone doses below the stoichiometric relationship of 1/57 (mol paracetamol/mol ozone), the amount of oxidant provided to the system would not be enough to produce those significant alterations in the aromatic structures of paracetamol subsequently leading to a noticeable reduction in water aromaticity. Because of this, an aromatic chromophoric residue –conferring that characteristic color to the medium– persists in the treated waters.

3.4. Kinetic model for water coloration

The kinetic model suggested in the present study relates the aromaticity loss of ozonized paracetamol solutions with changes in color observed in the water matrix. In order to model aromaticity loss, in first place, a mathematical model based on the scheme shown in Fig. 1 has been considered. Thus, it is assumed that paracetamol ozonation process leads to the generation of transformation products exhibiting less aromaticity than the parent compound. The aromaticity reduction rate is given by the corresponding first-order kinetic constant k_A (1/min).

$$\text{Paracetamol} \xrightarrow{k_A} \text{degradation intermediates} \quad (5)$$

With,

k_A: first-order kinetic constant describing aromaticity loss in aqueous solutions of paracetamol during ozonation process (l/min)

In accordance with Eq. 5, a mass balance corresponding to aromaticity loss during paracetamol ozonation is considered (Eq. 6). It is also assumed that reduction of water aromaticity follows first-order kinetics.

$$\frac{d[Arom]}{dt} = -k_A \ [Arom] \quad (6)$$

being,

[Arom]: water aromaticity (AU)

t: time (min)

By integrating the mass balance (Eq. 7), the kinetic equation corresponding to aromaticity loss can be obtained (Eq. 8):

$$\int_{Arom_0}^{Arom} \frac{d[Arom]}{[Arom]} = -k_A \int_{t=0}^{t} dt \quad (7)$$

$$[Arom] = [Arom]_0 \exp(-k_A \ t) \quad (8)$$

In Fig. 6, both predicted and experimental results on aromaticity loss are shown, these allowing the estimation of the first-order kinetic constant describing aromaticity loss (k_A, 1/min) as a function of the pH (Eq. 9). On the other hand, it is verified that aromaticity of ozonized samples at the end of the treatment does not depend on initial pH, estimating a mean value for this parameter in the order of 0.06 AU (Eq. 10) that it

has been depreciated in the proposed model. Table 1 gathers the values of the estimated kinetic parameters.

$$k_A = 0.0162\,pH + 0.035 \quad (9)$$

r^2=0.9301

$$[\overline{Arom}]_\infty = 0.06\,(AU) \quad (10)$$

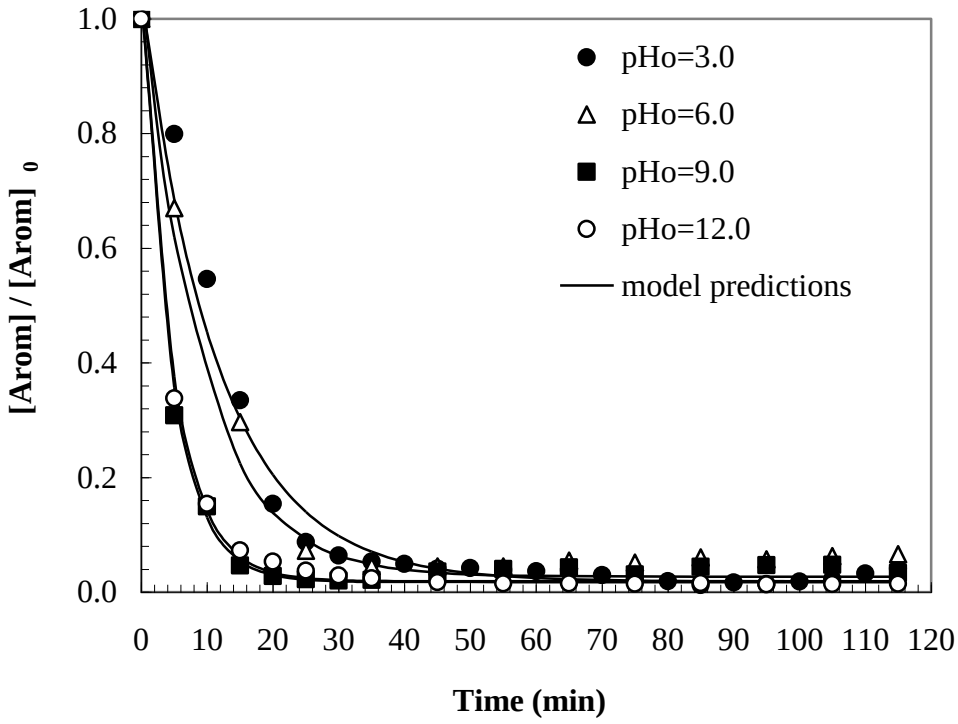


Fig. 6. Effect of initial pH on aromaticity loss for ozonized paracetamol solutions. Experimental conditions: Pa_0=50.0 mg/L; [O_3]=25.0 mg/min; T=25.0ºC.

Color changes taking place in water during paracetamol ozonation have been modelled based on studies reported in the bibliography about the changes of color observed in aqueous solutions of organic compounds oxidized by Fenton technologies (Villota et al., 2018), following the scheme shown in Eq. 11. As mentioned, colorless aqueous

514 solutions of this pharmaceutical acquire a strong reddish tonality that turns to yellow
515 when waters exhibit their maximum degree of coloration ($Color_{max}$). The rate of color
516 formation has been expressed as a function of the kinetic constant k_f (1/min). Then,
517 color is gradually degraded until a residual tonality is reached ($Color_{\infty}$). The velocity of
518 color degradation is given by the corresponding first-order kinetic constant, k_d (1/min).
519

520 $$Color_0 \xrightarrow{k_f} Color_{max} \xrightarrow{k_d} Color_{\infty} \quad (11)$$

521 Being,
522
523 $Color_0$: initial color of paracetamol aqueous solutions (AU)
524 $Color_{max}$: maximum intensity presented by oxidized paracetamol solutions (AU)
525 $Color_{\infty}$: color of oxidized paracetamol solutions at the end of treatment (AU)
526 k_f: first-order kinetic constant for color formation during paracetamol
527 ozonation (l/min).
528 k_d: first-order kinetic constant for color degradation during paracetamol
529 ozonation (l/min).
530 t_0: initial time (min)
531 t_{max}: time for which treated solutions show a maximum in color intensity (min).
532 t_{∞}: time corresponding to end of treatment (min)
533
534 According to the reaction scheme proposed in Eq. 11, the mass balances corresponding
535 to color formation-degradation processes have been applied (see Eqs. 12-13).
536

537 $$\frac{dColor}{dt} = k_f \left(Color + Color_0\right) \Big]_{Color_0}^{Color_{max}} \quad (12)$$

538

539 $$\frac{dColor}{dt} = -k_d \left(Color + Color_\infty\right) \Big]_{Color_{max}}^{Color_\infty} \quad (13)$$

540 Considering the fact that color evolves according to first-order kinetics, mass balances
541 above expressed have been both integrated to obtain explicit kinetic expressions for
542 color formation (Eq. 14) and degradation (Eq. 15).

543

544 $$Color = 2\,Color_0 \exp\left(k_f\ t\right) - Color_0 \Big]_{Color_0}^{Color_{max}} \quad (14)$$

545

546 $$Color = \left(Color_{max} - Color_\infty\right) \exp\left[-k_d \left(t - t_{max}\right)\right] + Color_\infty \Big]_{Color_{max}}^{Color_\infty} \quad (15)$$

547

548 In Fig. 7, predictions made according to the proposed model are shown. Table 1 also
549 gathers the values of the estimated kinetic parameters. Obtained results allow
550 concluding that the kinetic constant describing color formation (k_f, 1/min) does not
551 depend on pH. In fact, a mean value of k_f=0.01 1/min could be estimated (Eq. 16).
552 However, the kinetic constant for color degradation presents a linear dependency with
553 operation pH (Eq. 17). This fact could be explained as follows: despite the treatment
554 conditions appear to be powerful enough to degrade paracetamol molecules to colored
555 transformation species, further degrading these intermediates to colorless byproducts
556 could require a more severe oxidation. Because of this, in order to increase the rate of
557 color degradation it is necessary to favor –during ozonation process– the generation of
558 more oxidizing species (*i.e.*, hydroxyl radicals) by taking advantage of the pH effect.

559

$$\overline{k_f} = 0.01\,(1/\min) \quad (16)$$

$$k_d = 0.03\,pH_0 - 0.055 \quad (17)$$

r^2=0.9783

The influence of operational pH on the color of the treated water has been also assessed (Eqs. 18-20). As can be seen, this color intensity gets larger with increasing operation pH due to the fact that a higher concentration of oxidizing species is generated, causing the degradation of paracetamol to chromophoric reaction intermediates. In a similar way, the residual color at the end of the treatment is less intense when the reaction is carried out under basic medium conditions. This is explained by an enhancement in the oxidation efficiency of the process, leading to the generation of more hydroxyl radicals per consumed ozone, which allows a further oxidation of colored species to colorless degradation products. Therefore, the time for which the oxidized water reaches its peak color intensity diminishes with increasing operational pH.

$$Color_0 = 0.0006\,pH_0 + 0.006 \quad (18)$$

r^2=0.9818

$$Color_{max} = 0.0016\,pH_0^2 - 0.0139\,pH_0 + 0.0378 \quad (19)$$

r^2=0.9995

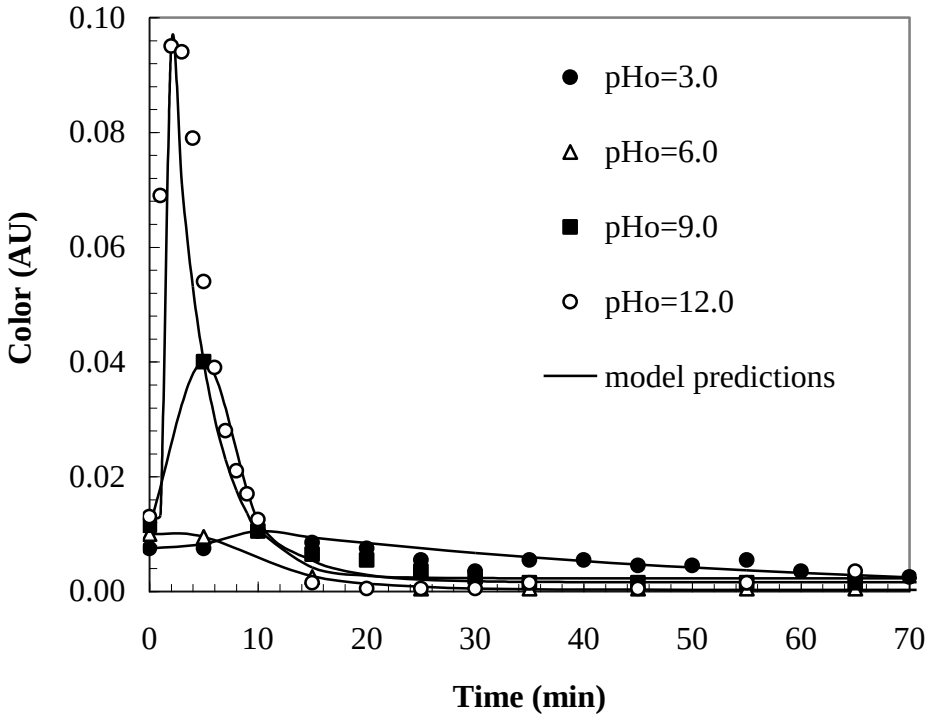
$$Color_\infty = 0.002 - 0.0004\,pH_0 \quad (20)$$

r^2=0.9831

585 $$t_{max} = 17.321 \exp\left(-0.1745\, pH_0\right) \quad (21)$$

586 r^2=0.9884

587



588

589 **Fig. 7.** Influence of initial pH on water color formation during ozonation of paracetamol
590 aqueous solutions. Experimental conditions: Pa_0=50.0 mg/L; [O_3]=25.0 mg/min;
591 T=25.0ºC.

592

593 According to the previous estimations, a parameter α (Eq. 23) expressing the
594 relationship between formed color and aromaticity loss as a function of pH has been
595 defined. To do so, the kinetic constants k_f (1/min) and k_A (1/min) have been both
596 considered, as expressed in Eq. 22.

597

598 $$k_A = \alpha\, k_f \quad (22)$$

599

600 $$\alpha = 1.62\, pH_0 + 3.5 \quad (23)$$

Table 1. Estimated kinetic parameters. Experimental conditions: $[Pa]_0$=50.0 mg/L; $[O_3]$=25.0 mg/min; T=25.0ºC.

pH_0	$Color_0$ (AU)	$Color_{max}$ (AU)	$Color_\infty$ (AU)	t_{max} (min)	k_f (1/min)	k_d (1/min)	$[Arom]_\infty$ (AU)	k_A (1/min)
3.0	0.0075	0.0105	0.0000	10	0.01	0.02	0.050	0.085
6.0	0.0100	0.0095	0.0003	6	0.01	0.15	0.070	0.110
9.0	0.0115	0.0400	0.0016	4	0.01	0.21	0.050	0.220
12.0	0.0130	0.0950	0.0023	2	0.01	0.30	0.060	0.210

4. Conclusions

The ozonation of paracetamol aqueous solutions produces in a first stage a strong red coloration at the same time that water aromaticity decreases. Then, a second stage takes place; color intensity diminishes until it reaches a residual yellow tonality. This color formation is favored when operating at pH_0=12.0 and ozone flow-rates applied in the range 4.2 mg/min. The ozonation of aqueous solutions of paracetamol leads to compounds such as p-aminophenol, p-nitrophenol, nitrocatechol, hydroquinone and benzoquinone.

The hydroxide ions activate ozone decomposition to hydroxyl radicals, as well as to the increasing degree of dissociation of paracetamol lead to the generation of chromophoric structures. Ozone transfer to water is maximum when operating at pH_0=6.0, being this explained by the presence, at higher pH values, of larger amounts of the hydroxide anion and a possible generation of inorganic salts acting as scavengers for ozone and hydroxyl radicals.

A first order kinetic for water color changes fits well the experimental results. The obtained kinetic constants for color formation and degradation were to be k_f=0.01 (1/min) and k_d=0.03 pH_0-0.055 (1/min), respectively. Finally, the aromaticity loss is related to color changes. The corresponding first-order kinetic constant for aromaticity is given by k_A=0.0162 pH_0+0.035 (1/min).

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