Chemical Engineering Journal 160 (2010) 72–78

Contents lists available at ScienceDirect

Chemical Engineering Journal

journal homepage: www.elsevier.com/locate/cej

Oxidation of hydrochlorothiazide by UV radiation, hydroxyl radicals and ozone: Kinetics and elimination from water systems

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ARTICLE INFO

Article history:
Received 25 November 2009
Received in revised form 1 March 2010
Accepted 2 March 2010

Keywords:
Pharmaceutical compounds
Hydrochlorothiazide
UV radiation
Hydroxyl radicals
Ozone
Rate constants
Quantum yields
Elimination in water matrices

ABSTRACT

Hydrochlorothiazide (6-chloro-1,1-dioxo-3,4-dihydro-2*H*-1,2,4-benzothiadiazine-7-sulfonamide), a thiazidic diuretic very frequently used in the treatment of hypertension, has been oxidized by means of UV radiation, Fenton's reagent and ozone. The influence of some operating variables was established, and the main kinetic parameters were determined. Specifically, for the photodegradation process, quantum yields ranging between 0.028 and 0.048 mol Eins^{-1} were obtained depending on the temperature and pH. At the same time, in the ozonation process and by using competition kinetics, the values deduced for the second-order rate constants varied from 91.3 M^{-1} s^{-1} at pH = 3 to 16 400 M^{-1} s^{-1} at pH = 9. Similarly, competition kinetics was also used in the Fenton's reagent process for the determination of the rate constants for the reaction of this pharmaceutical with hydroxyl radicals, and the value deduced at 20 °C was $(5.7 \pm 0.3) \times 10^9$ M^{-1} s^{-1}. The oxidation of this selected pharmaceutical was also followed in some water systems (a surface water from a reservoir SW, and a secondary effluent from a municipal wastewater treatment plant SE), by UV radiation and ozone. The influence of the operating conditions on the removal efficiency was established, and specifically for the ozonation process, a kinetic model was proposed for the prediction of the elimination of the selected pharmaceutical in these water systems, which could well reproduce experimental data.

1. Introduction

The occurrence of pharmaceutical and personal care products (PPCPs), and endocrine disrupting compounds (EDCs) has been routinely detected in aquatic environments worldwide, like surface waters [1,2] and drinking waters [3,4]. The release of these pollutants into the aquatic systems is attributed to their incomplete removal by conventional wastewater treatments [5,6]. The most representative pharmaceuticals detected in urban wastewaters are anti-inflammatory drugs, anticonvulsants, antibiotics and antihypertensives [7]. Despite their low concentrations, their occurrence has been linked to undesirable effects and toxicological impacts in fish species [8].

The presence of the antihypertensive hydrochlorothiazide (abbreviated HCTZ, 6-chloro-1,1-dioxo-3,4-dihydro-2*H*-1,2,4-benzothiadiazine-7-sulfonamide, molecular mass 297.74, chemical structure shown in Fig. 1), together with other numerous pharmaceuticals, has been detected in natural waters and wastewater secondary effluents [9]. However, the only study found in the literature on the chemical oxidation of this substance, reports the efficiency of two ozone-based treatments applied to the effluent from a secondary clarifier of a municipal wastewater treatment facility containing several different pharmaceuticals [10]. In that study, the results demonstrated that ozonation of those wastewaters degrades pharmaceuticals with a high efficiency, and removals higher than 90% were reached for most of target analytes, including HCTZ. However, no specific data has been found on the oxidation kinetics of HCTZ by general chemical oxidants, such as UV radiation, hydroxyl radicals or ozone. These mentioned oxidants have been recently used in technologies that promote an easier degradation of these micropollutants, due to the low removal levels of the current wastewater treatments towards some recalcitrant pharmaceuticals; and they have demonstrated high effectiveness in the degradation of pharmaceuticals in different water systems.

In this context, the present study was designed with the aim of evaluating quantum yields for photodegradation reactions of HCTZ, as well as rate constants for the reactions of this selected pharmaceutical with OH radicals and ozone. Later, some of these kinetic parameters are useful in the application of a proposed model that predicts the oxidation of this compound during ozonation processes in two water systems (a reservoir water and secondary effluent from a municipal wastewater treatment plant).

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doi:10.1016/j.cej.2010.03.009

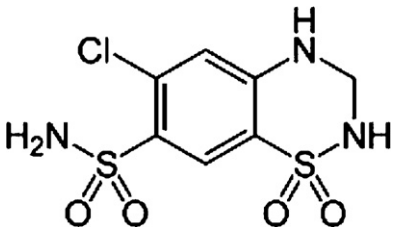

Fig. 1. Chemical structure of HCTZ.

2. Experimental

2.1. Standards, reagents and water systems

Hydrochlorothiazide was obtained from Sigma–Aldrich (Buchs SG, Schweiz) with the highest purity available. Other chemicals were of analytical grade or higher. Solutions of HCTZ, analytical reagents, ozone, and phosphate buffers were prepared with ultrapure water produced from a Milli-Q (Millipore, Bedford, USA) water purification system.

Two water systems were used to investigate the oxidation of the selected pharmaceutical under realistic water treatment conditions. The first one was a surface water (SW) from the public reservoir "Peña del Aguila" located near Badajoz (Extremadura region, South-West of Spain); and the second one was a secondary effluent (SE) generated in the municipal wastewater treatment plant of Badajoz. Samples were immediately processed or stored in a refrigerator (<4 °C) inside glass bottles. The values measured for pH, TOC content, absorbance at 254 nm, and alkalinity for these waters are listed in Table 1. Specifically, UV absorbance and TOC content constitute a significant indication of the total dissolved organic matter (DOM) present in these waters.

2.2. Experimental procedures

The reactor used in the photochemical experiments of hydrochlorothiazide consisted of a 500 mL cylindrical glass vessel with an external jacket surrounding the reactor, and a water stream was pumped from a thermostatic bath in order to maintain the temperature at the designed value within ±0.5 °C. For these photodegradation experiments, a low pressure vapor mercury lamp (TNN 15/32, nominal electrical power 15 W; Heraeus, Madrid, Spain) which emitted monochromatic radiation at 254 nm was used. This lamp was located inside the reactor in axial position and was protected by a quartz sleeve which housed the lamp. Several experiments were performed at different temperatures (10–40 °C) and pH values (3–9), and in the presence and absence of hydrogen peroxide. For every experiment conducted, the reactor was filled with 350 mL of HCTZ (10 μM) solutions (plus hydrogen peroxide in the combined UV/H_2O_2 experiments) at the selected pH (10 mM phosphate buffer). Samples were periodically withdrawn from the reactor to measure the residual HCTZ concentrations.

The oxidation experiments by Fenton's reagent were carried out in 250 mL Erlenmeyer flasks submerged in a thermostatic bath at 20 °C, and the solutions were homogenized by means of a magnetic stirrer. For every experiment conducted, each flask was filled with the aqueous solution containing the selected pharmaceutical, previously buffered at the selected pH (in the range 2–4) by adding a perchloric acid/perchlorate solution (10 mM). The required amounts of ferrous ion and hydrogen peroxide were also added to the reactor, thus starting the reaction. Sodium sulfite was used to quench the reaction in the samples withdrawn from the reactor at regular time intervals. Additional Fenton's reagent experiments were also performed for the determination of the rate constants of the reaction between HCTZ and hydroxyl radicals by competition kinetics. The selected reference compound was p-chlorobenzoic acid (p-CBA).

The ozonation experiments were carried out in heterogeneous conditions with respect to ozone (which was fed in a gas stream) in the same reactor used for the photochemical experiments, which was also provided with an additional outlet for the exit of the effluent gas. Ozone was produced from bottled synthetic air in a laboratory ozone generator (Sander, mod. 300.5; Ingetecsa, Barcelona, Spain). The ozone–air gas flow rate in every experiment was set at 40 L h^{-1}, and the ozone partial pressure was 0.049 kPa. This stream was introduced through a porous plate into the reactor, which contained a solution of 350 mL of HCTZ (10 μM) and tert-butylalcohol (t-BuOH, 0.01 M) as OH radical scavenger, and buffered at the selected pH (3–9) by adding phosphoric acid/phosphate solution (0.01 M). Competition kinetics was also applied to determine the second-order rate constant at 20 °C for the direct reaction between ozone and HCTZ, using metoprolol (10 μM) as the reference compound. At regular reaction times, samples were taken from the reactor for analysis.

Additional experiments were carried out with HCTZ dissolved in two water systems (SW and SE) at 20 °C and the natural pH of each water. Thus, photodegradation experiments were performed in the same reactor above described to investigate the elimination of HCTZ (1 μM) in the selected waters. Another set of homogeneous ozonation experiments was carried out in a 500 mL flask reactor. Ozone stock solutions were prepared by dissolving an ozone stream in ice-cold ultrapure water until the saturation was reached. Each run was initiated by injecting the volume of the ozone stock solution required to achieve the desired initial O_3 dose into the flask, which contained a solution of HCTZ and p-CBA (1 μM) in the selected water. The degradation of p-CBA throughout the ozonation process provided a measurement of OH radical exposure. At regular reaction times, two samples were withdrawn: one was directly introduced into an Indigo solution to determine the remaining ozone concentration; the second one was introduced into a vial containing potassium thiosulfate (0.1 M) to quench the residual ozone, and the pharmaceutical concentration was then measured. Finally, some ozonation experiments were performed in static dose mode by varying the initial ozone concentration (0–10 mg L^{-1}). These experiments were started by adding different amounts of the ozone stock solution to aliquots of 17 mL of HCTZ solutions (1 μM). The residual HCTZ concentration was analyzed after 2 h, time enough for complete ozone consumption.

Table 1
Water quality characteristics of the two real waters.

Parameter	Reservoir water (SW)	Secondary effluent (SE)
pH	7.3	8.0
TOC (mg L^{-1})	4.3	23.3
254 nm absorbance (cm^{-1})	0.118	0.191
Alkalinity (mg L^{-1} $CaCO_3$)	30	250

2.3. Analytical methods

The pharmaceutical HCTZ, as well as p-CBA and metoprolol (used as reference compounds), were analyzed by HPLC in a Waters Chromatograph equipped with a 2487 Dual λ Detector and a Waters Nova-Pak C18 Column (5 μm 150 mm × 3.9 mm). The detection was performed at 226 nm for HCTZ, 238 nm for p-CBA and 222 nm for metoprolol. The mobile phase was a mixture of methanol and 0.01 M aqueous phosphoric acid solution (10:90 in volume), the elution flow rate was 1 mL min^{-1} and the injection volume was 50 μL in all samples. The ozone concen-

Table 2
Experimental conditions and kinetics parameters obtained in the photodegradation of HCTZ in UP water. $[HCTZ]_0 = 10\ \mu M$.

Expt.	T (°C)	pH	$[H_2O_2]_0 \times 10^5$ (M)	X_{UV} (%) (5 min)	k_{UV} (min^{-1})	ϕ (mol $Eins^{-1}$)
UV-1	20	3		45.2	0.164	0.046
UV-2	20	5		43.2	0.149	0.040
UV-3	20	7		41.2	0.146	0.038
UV-4	20	9		43.8	0.151	0.038
UV-5	10	7		30.5	0.110	0.028
UV-6	30	7		53.1	0.164	0.046
UV-7	40	7		58.9	0.170	0.048
UVH-1	20	7	5	55.8	0.202	-
UVH-2	20	7	10	65.8	0.278	-

tration in the inlet gas ozone–oxygen stream was determined iodometrically, while the ozone concentration in the stock solutions was determined directly by measuring their UV absorbance at 258 nm ($\varepsilon = 3150\ L\ mol^{-1}\ cm^{-1}$). Remaining ozone concentration in the homogeneous ozonation experiments was analyzed by the Indigo method [11].

3. Results and discussion

3.1. Oxidation of hydrochlorothiazide in ultrapure water

In a first stage, the oxidation of the selected pharmaceutical HCTZ dissolved in ultrapure water was conducted by using different oxidizing systems: UV radiation, Fenton's reagent and ozone, with the aim of establishing the influence of some operating variables on the degradation process as well as of determining the main kinetic parameters. The initial concentration of HCTZ in these experiments was 10 μM.

Firstly, HCTZ photodegradation was studied out by means of the monochromatic radiation described in Section 2. These experiments were performed at different temperatures (10–40 °C) and pH values (3–9). Additionally, two experiments were also conducted in the presence of hydrogen peroxide at initial concentrations of 5×10^{-5} and 1×10^{-4} M. Table 2 compiles the runs performed and their experimental conditions. In order to examine the effect of these variables on the photodecomposition reaction, Table 2 also summarizes the HCTZ removal (X_{UV}) obtained after 5 min of reaction.

From these X_{UV} values, it is deduced that no significant effect was exerted by the pH, because similar removals were obtained at any pH, which suggests that only the direct photodecomposition contributes to the global elimination of HCTZ. On the other hand, the temperature of the reaction had a positive effect on the degradation rate as would be expected, with increasing removals when the temperature was increased.

In a first approach the kinetic study is conducted by considering that the photochemical process follows first-order kinetics. According to this, a plot of $\ln[HCTZ]_o/[HCTZ]$ vs. reaction time should result in a straight line, whose slope provides the first-order rate constant k_{UV}. Following this procedure and after regression analysis ($r^2 > 0.99$), the rate constants that are compiled in Table 2 were deduced. As observed for the variation of pH, the values are quite similar, with an average value of $0.152\ min^{-1}$. On the contrary, the rate constants increased with temperature, from 0.110 to $0.170\ min^{-1}$. Finally, the addition of hydrogen peroxide affected positively as was commented, and k_{UV} increased from $0.146\ min^{-1}$ (Expt. UV-2) to 0.202 and $0.278\ min^{-1}$ (Expts. UVH-1 and UVH-2).

A more rigorous kinetic study was based on the evaluation of the quantum yield (ϕ) for the photodegradation of the selected pharmaceutical compound. The reaction model described in detail in a previous work [12] was used, which provides a general equation for the rate of disappearance of a general micropollutant as a function of the absorbed radiation flux W_{abs}:

$$[HCTZ] = [HCTZ]_0 - \frac{\phi}{V}\int_0^t W_{abs}\ dt \quad (1)$$

The procedure for determining W_{abs}, was also described elsewhere [12], and the integral term $\int W_{abs}\,dt$ was calculated numerically, by fitting the experimental data (W_{abs}, t) to a polynomial expression by least squares regression, and integrating the resulting function. Previously, the radiation intensity emitted by the lamp into the reactor was evaluated by chemical actinometry experiments, using hydrogen peroxide as actinometer, being the obtained value of $2.0 \times 10^{-6}\ E\ s^{-1}$. At the same time, the molar extinction coefficient at 254 nm of HCTZ was determined at different pH values, with a value of $6650\ mol^{-1}\ L\ cm^{-1}$ valid in the pH range 3–9. A plot of the pharmaceutical concentration [HCTZ] vs. the corresponding integral $\int W_{abs}\,dt$ led to a straight line, whose slope provided the overall quantum yield ϕ of the photodegradation, values that are also listed in Table 2. It can be seen that the trend previously observed for k_{UV} is exactly reproduced in the quantum yields: almost no influence with the variation of the pH (an average value of 0.041 ± 0.004 mol $Eins^{-1}$ is proposed at any pH at 20 °C); while increasing ϕ values when the temperature was increased. Then, an Arrhenius-type expression can be proposed, and after linear regression analysis, 54 mol $Eins^{-1}$ and 2.14 kcal/mol were deduced for the ϕ_o and E_a parameters. It must be noted that this kinetic procedure cannot be applied to the oxidation experiments by the combination UV/H_2O_2 because its reaction mechanism is different than the single photoreaction mechanism, and additional reactions with different rate constants must be taken into account.

In a later stage, individual oxidation experiments of HCTZ with Fenton's reagent were performed at 20 °C as described in Section 2, by varying the initial concentrations of ferrous ions and hydrogen peroxide ($2.5–10 \times 10^{-5}$ for both reactants), as well as the pH (2–4).

As it is known, in the Fenton's reagent ferrous ion reacts with hydrogen peroxide to generate OH radicals. These radicals generated oxidize most organic compounds. From the experimental results obtained it can be concluded that both species, Fe^{2+} and H_2O_2, promote a direct effect on the pharmaceutical removal, which is consequent with the most important reaction of the Fenton's reagent, responsible of the generation of the oxidant OH radical [13].

In addition, decomposition experiments of HCTZ were performed by varying the pH from 2 to 4, which is proposed as the optimum range of pH by other authors [14,15]. The results confirm that the pH 3 is the optimum, being the obtained HCTZ removal highest; while at pH 2 and 4, the removals were lower. Thus, the decrease in the degradation at pH 4 can be attributed to a decrease of the free iron species in the solution, due to the precipitation of ferric oxyhydroxides. On the other hand, the decrease in the degradation at pH 2 is due to the inhibition of the formation Fe (III)-peroxy complexes, which are the precursors of iron (II) regeneration [16].

Table 3
Second-order rate constants for the reaction between ozone and HCTZ at different pH values. Experimental conditions: $[HCTZ]_0 = 10\,\mu M$; $T = 20\,^\circ C$; pO_3 in the gas inlet: 0.049 kPa.

Expt.	pH	X_{O_3} (%) (2 min)	k'_{O_3} (min^{-1})	k_{O_3-HCTZ}/k_{O_3-R}	$k_{O_3-HCTZ} \times 10^{-9}$ ($M^{-1}\,s^{-1}$)
O-1	3	19.2	0.083	0.38	91.3
O-2	5	21.2	0.102	0.29	80.3
O-3	7	60.8	0.533	3.62	5110
O-4	9	100[a]	2.56	1.29	16 400

[a] Total removal obtained before 2 min of reaction.

In general terms, the rate equation for the removal of an organic compound (here HCTZ) by means of hydroxyl radicals can be written in the form:

$$-\frac{d[HCTZ]}{dt} = k_{OH-HCTZ}[^\bullet OH][HCTZ] \quad (2)$$

where $k_{OH-HCTZ}$ is the second-order rate constant between OH radicals and the pharmaceutical compound. Generally, the radical rate constants present high values (in the range of 10^7–$10^{10}\,M^{-1}\,s^{-1}$) [17,18]. The determination of the unknown rate constant $k_{OH-HCTZ}$ cannot be made directly, and competition kinetics is frequently used, which is based in the simultaneous oxidation of the target compound (HCTZ in the present case) and a reference compound R whose rate constant for the reaction with OH radicals k_{OH-R} is previously known. The application of this model provides this relationship for the evaluation of the rate constant $k_{OH-HCTZ}$:

$$\ln\frac{[HCTZ]_0}{[HCTZ]} = \frac{k_{OH-HCTZ}}{k_{OH-R}}\ln\frac{[R]_0}{[R]} \quad (3)$$

In order to apply this model, two experiments of simultaneous oxidation of HCTZ and p-chlorobenzoic acid (p-CBA) by Fenton's reagent as oxidant were performed at 20 °C and similar experimental conditions than oxidation experiments of HCTZ alone. In this study, p-CBA was selected as reference compound because its k_{OH-R} value is $5 \times 10^9\,M^{-1}\,s^{-1}$ [17]. With the concentrations of HCTZ and p-CBA measured in the experiments performed, and according to Eq. (3), plots of the logarithmic terms led to straight lines whose slopes were $k_{OH-HCTZ}/k_{OH-R}$. As k_{OH-R} was known, a value of $(5.7 \pm 0.3) \times 10^9\,M^{-1}\,s^{-1}$ was deduced for the rate constant of the reaction between hydroxyl radicals and HCTZ. As can be seen, this is a very high rate constant, indicating that any AOP in which OH radicals are involved can be a plausible process for HCTZ elimination.

The oxidation of the selected pharmaceutical by ozone was studied in heterogeneous conditions experiments carried out at 20 °C, and by varying the pH from 3 to 9. As commented above, t-BuOH was used as a radical scavenger. Table 3 summarizes the experimental conditions applied and the removals (X_{O_3}) obtained in these experiments after 2 min of reaction. It is observed a significant increase in the oxidation rate when the pH was increased, which can be explained by considering that the ozone presents different reactivities with both species of HCTZ (protonated and neutral). Effectively, ozone is a highly selective electrophile that reacts mainly with specific moieties such as aromatic rings and amines. In the present case, ozone would react mainly with the secondary amine-moiety of HCTZ. In addition, the protonated amino group reacts with ozone much more slowly than neutral amines [19]. Therefore, the reactivity of amines depends strongly on the pK_a of the amine and the pH of the solution. By considering in a first approach that the reaction follows a global first-order kinetics, Table 3 also summarizes these first-order rate constants k_{O_3} for the ozonation of this pharmaceutical compound. The values obtained confirm this positive influence of the pH on the oxidation.

Competition kinetics described by Eq. (3) can be also applied for determining the apparent HCTZ ozonation rate constant (k_{O_3-HCTZ}) at 20 °C and different pH values. For this purpose, simultaneous ozonation experiments of HCTZ and metoprolol were conducted. In this case, metoprolol was selected as the reference compound because its reactivity towards ozone is in the same order of magnitude, and its apparent ozonation rate constants k_{O_3-R} were previously reported as a function of pH [20]. Following the procedure described and according to Eq. (3), the slopes k_{O_3-HCTZ}/k_{O_3-R} were obtained and are also reported in Table 3. By using the corresponding k_{O_3-R} values, the k_{O_3-HCTZ} values that are also given in Table 3 were deduced, which constitute the proposed apparent second-order rate constants for the direct reaction between ozone and HCTZ. According to these rate constants, ozone is a powerful oxidant to remove HCTZ from contaminated waters, especially at pH above 7.

It is again deduced from the rate constants that the reactivity of HCTZ with ozone increased with increasing the pH of the solution, which is a consequence of the acidic nature of the selected compound. Then, the study is now focused in the evaluation of the specific rate constants for the elementary reactions of ozone with the protonated and neutral species of the pharmaceutical, whose pK_a value is 7.9 [21]. The model initially proposed by Hoigne and Bader [22] and later successfully applied by other authors [23] can be used. This model establishes that:

$$k_{O_3-HCTZ} = \alpha_1 k_1 + \alpha_2 k_2 \quad (4)$$

where k_1 represents the specific rate constant for the protonated form; k_2 is the same rate constant for the neutral species; and α_1 and α_2 represent the respective fractions of the protonated and neutral forms, which can be calculated from the dissociation constant K_a at the specific pH of the solution. The determination of these specific rate constants k_1 and k_2 was carried out by applying a non-linear least squares regression analysis of Eq. (4) from the apparent rate constants k_{O_3-HCTZ} (summarized in Table 3) at different pH values, and with the corresponding values of α_1 and α_2 for each pH. After following this procedure, the deduced values for specific rate constant of the two species were: $k_1 = 75\,L\,mol^{-1}\,s^{-1}$ and $k_2 = 2.7 \times 10^4\,L\,mol^{-1}\,s^{-1}$ for the protonated and neutral species of HCTZ, respectively.

The evaluated specific rate constants must be validated, and for this purpose, Fig. 2 shows the plot of the apparent rate constants k_{O_3-HCTZ} in the range of pH from 3 to 9: symbols represent the experimentally deduced apparent rate constants depicted in Table 3, and lines represent the theoretical values obtained by the correlation given by Eq. (4), where the specific rate constants k_1 and k_2 previously determined were used. It is observed a quite satisfactory agreement between both, experimental and theoretical values, which confirms the goodness of the model used and the specific rate constants determined.

3.2. Oxidation of hydrochlorothiazide in water systems

In order to study the oxidation of HCTZ by UV radiation and ozone in real water systems, experiments were conducted dissolving this pharmaceutical in the two water matrices already described in Section 2: a reservoir water (SW) and a secondary effluent (SE). The experimental procedures for the photodegrada-

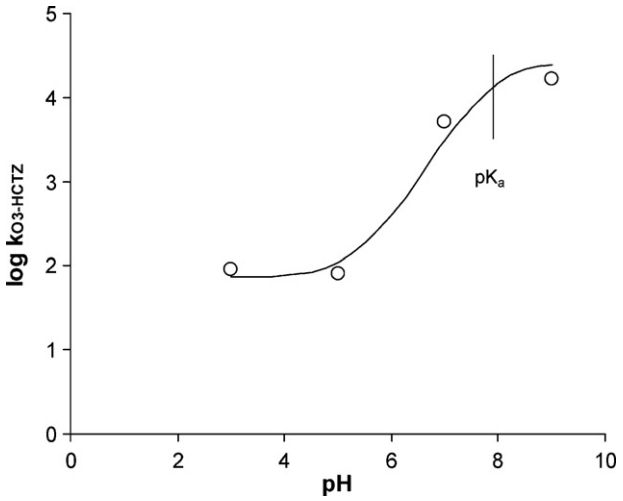

Fig. 2. Apparent rate constants for the oxidation of hydrochlorothiazide with ozone. Comparison of experimental (symbols) and calculated values from Eq. (4) (line). Experimental conditions: $[HCTZ]_0 = 10\ \mu M$; $T = 20\ ^\circ C$; pO_3 in the gas inlet: 0.049 kPa.

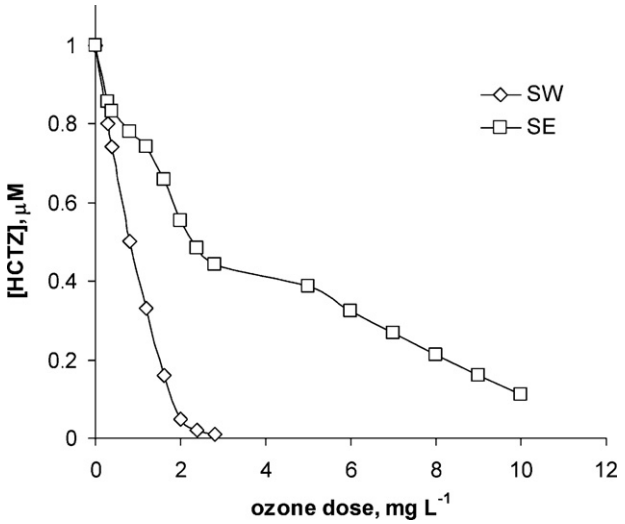

Fig. 3. Influence of the type of water matrix on the final removals of hydrochlorothiazide using different ozone doses. Experimental conditions: $T = 20\ ^\circ C$; pH = 7.3 for SW and pH = 8.0 for SE; $[HCTZ]_0 = 1.0\ \mu M$.

tion process were the same as for the UV degradation in ultrapure water. In the ozonation experiments, p-CBA was used as a probe compound to determine OH radical exposure. Several conditions were maintained constant in all these experiments: the temperature was 20 °C and the initial concentrations of HCTZ and p-CBA were 1 μM. These experiments were performed at the pH of each water, 7.3 and 8.0 for SW and SE, respectively.

Regarding to the photodegradation process, it is again considered that the process follows first-order kinetics, and therefore, the experimental terms $\ln([HCTZ]_0/[HCTZ])$ were plotted vs. reaction time. After regression analysis, the slopes were evaluated and provided the first-order rate constant k_{UV}. The values obtained are 0.117 and 0.094 min^{-1} for the SW and SE waters, respectively, below the value of 0.146 min^{-1} obtained in the experiment in UP water at the same operating conditions. From these rate constants, it can be observed a lower removal rate in the SE, intermediate in the SW, and higher rate in UP water. These results can be explained by the fact that the dissolved organic matter (DOM) present in the SW and the SE could absorb some amount of UV radiation, in a higher extent in the SE due to a higher content in DOM (see Table 1). On the contrary, UP water does not contain any amount of organic matter, and therefore, the radiation absorbed is totally consumed in the degradation of the pharmaceutical, providing a higher elimination rate ($k_{UV} = 0.146\ min^{-1}$). Nevertheless, HCTZ was almost completely eliminated after 30 min, even in the SE.

In the ozonation experiments performed in static dose mode, different ozone doses were added to both water matrices containing the pharmaceutical compound. Fig. 3 shows the remaining concentration of HCTZ obtained after complete ozone consumption. As it is seen, an increase in the ozone dose leads to a logical increase in the removal of HCTZ. It is also observed that the degradation extent was higher in the in the SW than in the SE, as a consequence of the DOM present which consumes part of the oxidant, being this DOM lower for SW and higher for the SE. Thus, while 3 $mg\,L^{-1}$ of ozone was enough to completely remove HCTZ from the SW, an ozone dose higher than 10 $mg\,L^{-1}$ was needed in the SE. In conclusion, in water systems with higher amount of dissolved organic matter, the amount of oxidant available to react with micropollutants is lower, requiring higher doses of oxidant to reach the desired degree of pollutant elimination.

Time-resolved experiments were run with an initial ozone dose of 4 $mg\,L^{-1}$ for SW water and 10 $mg\,L^{-1}$ for SE, as typically found in full-scale drinking water and secondary effluent treatments. Initial ozone decay (data not shown) was very fast due to fast reactions of ozone with organic and inorganic matter present in these waters (instantaneous ozone demand) in which hydroxyl radicals are generated. Then, ozone consumption became slower until complete depletion which was reached after 10 and 1 min in SW and SE, respectively. HCTZ elimination was very fast, being completely removed after 30 s in both water matrices. Therefore, HCTZ can be completely removed in water matrices of diverse quality when the ozone exposure is measurable (ozone residual after 30 s of reaction). These results confirm the high efficiency of ozone to remove the selected pharmaceutical in different waters.

In order to predict the ozonation process of HCTZ in different water matrices, a kinetic model is proposed, which is based on the previously calculated rate constants k_{O_3-HCTZ} and $k_{OH-HCTZ}$ as well as the ozone and OH radicals concentration decays. The ozone depletion in natural waters can be followed by measuring its concentration at regular reaction times. However the knowledge of the OH radical evolution presents more problems, since there is no method for the direct measurement of its concentration. Then, in order to measure the transient OH radical concentration during ozonation processes, Elovitz and von Gunten [24] introduced the R_{ct} parameter, defined as the ratio between the OH radicals and O_3 exposures:

$$R_{ct} = \frac{\int [^\bullet OH]\,dt}{\int [O_3]\,dt} \quad (5)$$

In this Eq. (5) the ozone exposure can be evaluated from the integration of the ozone concentration (directly measured) vs. time data; while the R_{ct} parameter must be determined by the measurement of the decay of an ozone-resistant probe compound, which reacts rapidly with OH radicals and presents a very low reactivity towards ozone. In this study, the probe compound selected was again p-CBA, whose rate constants with ozone and OH radicals are $k_{O_3-p\text{-}CBA} = 0.15\ M^{-1}\,s^{-1}$ and $k_{OH-p\text{-}CBA} = 5 \times 10^9\ M^{-1}\,s^{-1}$, respectively [25,17]. As the reaction between OH radicals and p-CBA follows second-order kinetics, the integration of its rate equation and the introduction of the defined R_{ct} parameter (Eq. (5)) leads to the following expression for the probe compound concentration profile:

$$\ln\left(\frac{[p\text{-}CBA]_0}{[p\text{-}CBA]_t}\right) = k_{OH-p\text{-}CBA}\int_0^t [OH]\,dt = k_{OH-p\text{-}CBA}\cdot R_{ct}\cdot\int_0^t [O_3]\,dt \quad (6)$$

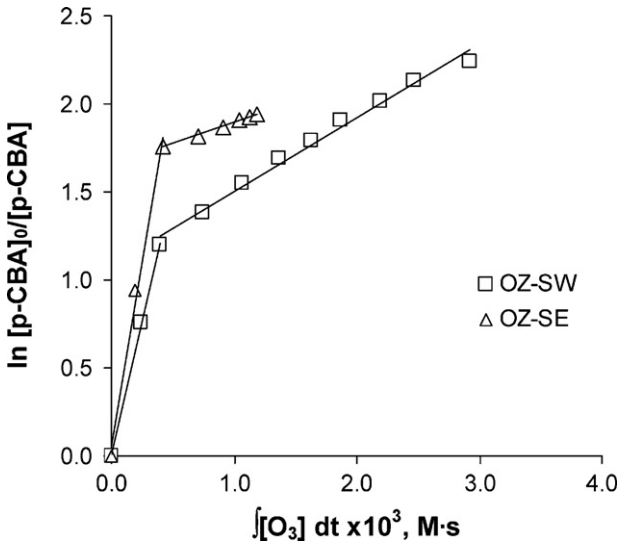

Fig. 4. Determination of the R_{ct} values in experiments performed with different water matrices. Experimental conditions: T = 20 °C, $[p\text{-CBA}]_0 = [HCTZ]_0 = 1.0\ \mu M$; $[O_3]_0 = 4\ mg\ L^{-1}$ in OZ-SW and $[O_3]_0 = 10\ mg\ L^{-1}$ in OZ-SE.

According to Eq. (6), the R_{ct} parameter can be experimentally calculated from the decreases in the concentrations of p-CBA and ozone, by plotting the term $\ln([p\text{-CBA}]_0/[p\text{-CBA}]_t)$ vs. the ozone exposure: after regression analysis, the slope can be determined; and from this slope and the known value of $k_{OH-p\text{-}CBA}$, the R_{ct} parameter is deduced. Once the R_{ct} value and the ozone exposure were obtained, the evaluation of the OH radicals exposure at any reaction time, and consequently, the knowledge of the OH radicals concentration profile in a ozonation process is obtained by using Eq. (5).

Following the described procedure, Fig. 4 presents the plots mentioned for both water matrices (Expts. OZ-SW and OZ-SE), and the R_{ct} values listed in Table 4 were determined. As can be observed, two R_{ct} values were deduced for each experiment: higher R_{ct} values in the initial period of the reaction indicate a higher amount of OH radicals formed from ozone decomposition, being this decomposition lower in the second period.

As was initially proposed, the final goal is the prediction and modeling of the oxidation of HCTZ in water systems by ozone and OH radicals as oxidant species. For this purpose, the R_{ct} values determined are useful. In effect, assuming second-order kinetics for the reaction between any micropollutant (HCTZ in this case) and both oxidants, the reaction rate for this compound when present in any type of water can be written in the form:

$$[HCTZ]_t = [HCTZ]_0 \exp\left\{-\left(\int_0^t [O_3]\,dt\right)\cdot(k_{OH-HCTZ}\cdot R_{ct} + k_{O_3-HCTZ})\right\} \quad (7)$$

As $k_{OH-HCTZ}$, k_{O_3-HCTZ} and the R_{ct} parameter have been previously determined, Eq. (7) can be applied for the determination of the theoretical concentrations of HCTZ in the experiments carried out, being these values compared with the experimental results obtained. The quite satisfactory agreement between values predicted by Eq. (7) and experimental values confirms the goodness of this kinetic approach.

Finally, the R_{ct} parameter is also useful for determining the relative importance of OH radicals and O_3 reaction pathways in the oxidation of a micropollutant present in water systems. Thus, the fraction of HCTZ degraded in the present study by OH radicals can be expressed in the form:

$$f_{OH} = \frac{k_{OH-HCTZ}[^{\bullet}OH][HCTZ]}{k_{OH-HCTZ}[^{\bullet}OH][HCTZ] + k_{O_3-HCTZ}[O_3][HCTZ]} = \frac{k_{OH-HCTZ}R_{ct}}{k_{OH-HCTZ}R_{ct} + k_{O_3-HCTZ}} \quad (8)$$

Eq. (8) was applied to the results obtained in the experiments carried out in the waters tested, being the percentages obtained for each compound also compiled in Table 4. From these values it is clearly deduced that the direct ozonation pathway predominates over the radical pathway, with almost no influence of the type of water; and this effect more especially in the second period, where the global degradation due to the radical pathway was 8.2 and 1.8%. These results coincide with those of previous authors, which showed that significant OH radical exposure can be experienced during the first seconds of reaction [26,27].

Table 4
Oxidation of HCTZ in real waters by ozone: R_{ct} values and fraction of HCTZ degraded by OH radicals.

Expt.	$R_{ct1} \times 10^8$	$R_{ct2} \times 10^8$	f_{OH1} (%)	f_{OH2} (%)
OZ-SW	61.7	8.4	39.7	8.2
OZ-SE	82.7	4.8	24.2	1.8

Acknowledgements

The authors wish to gratefully acknowledge financial support from the *Ministerio de Educacion y Ciencia of Spain* through the Project CTQ2007-60255 and the Project CONSOLIDER-INGENIO CSD2006-00044.

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