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Oxidation of pharmaceutical compounds by ozonation and ozone/activated carbon coupling: a kinetic approach

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ABSTRACT

The aim of this work was to study the efficiency of ozone (O_3)/activated carbon (AC) coupling to remove metoprolol and fluoxetine. A kinetic study was performed at pH ranging from 3 to 9. Results were correctly modelled by a global first-order model ($r^2 > 0.99$) and were compared to those obtained with the ozonation process. It was shown that O_3/AC coupling was the most efficient process. At pH 9, the degradation kinetic constant reached 0.72 min^{-1} with O_3/AC coupling while its maximum value was 0.34 min^{-1} with ozonation. In each experimental condition and for the two target compounds, this coupling allowed a fast and total pollutant removal. Moreover, its performances were not significantly influenced by the experimental conditions, contrary to the ozonation process which is strongly influenced by the pH and the nature of the pollutant. O_3/AC coupling remained efficient even if the operational parameters disfavour pollutant oxidation.

Keywords: Pharmaceuticals; Wastewater treatment; Ozone; Activated carbon; Kinetics

1. Introduction

Several studies have revealed the presence of pharmaceutical compounds (PCs) and their metabolites in surface waters at concentrations ranging from ng L^{-1} to μg L^{-1} [1]. Even if the impact of these compounds on the environment and on human health is not clearly determined and remains controversial, they are considered as emerging pollutants [2,3]. According to several authors, pharmaceuticals could be toxic for humans and/or aquatic organisms (carcinogenic properties, endocrine disruptor properties) and could lead to the development of multi-resistant strains of bacteria [4–6]. Among these PCs, this study focuses on fluoxetine (FXT) and metoprolol (MTP). FXT is an antidepressant drug commercially named Prozac. Its principal metabolite is norfluoxetine. According to several studies on the PCs toxicity, the FXT has been classified among the most toxic compounds [7,8]. This product is suspected to induce disrupting effects on the endocrine systems of some aquatic organisms [9]. MTP is one of the most common β-blockers, used for the treatment of cardiovascular diseases. This compound has three main metabolites: α-hydroxy MTP, deaminated MTP and MTP acid. According to previous studies, low removals of this PC are obtained in

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wastewater treatment plants (from 0 to 31%) [10,11]. Nevertheless, some studies report that this compound shows high reactivity with O_3. For example, the reaction rate constant has been estimated at $2.0 \times 10^3\ M^{-1}\ s^{-1}$ [12,13].

It was also shown that some PCs are poorly removed by conventional wastewater treatments and are directly released into the environment [1,14]. Therefore, more specific methods of treatment need to be developed to remove these PCs from wastewater. Among the treatments used, advanced oxidation processes (AOP) appear to present the best efficiency [15–18]. According to several studies on micropollutant removal, AOP enable fast and total removal of the target pollutants. These results can be attributed to the generation of hydroxyl radicals ($HO^•$), one of the most reactive species in water. Ozone (O_3)/activated carbon (AC) coupling can be considered as an AOP since the interactions between O_3 and the AC surface groups lead to the formation of $HO^•$ [19,20]. This process also combines the effect of adsorption, and of direct and indirect ozonations. It has also been proved in recent studies that the AC is renewed *in situ* by the oxidative species, giving the material the role of reaction site. Moreover, the use of this process has proven its efficiency concerning the removal of micropollutants, even in natural (river water) or complex (wastewater) matrices [19].

The main objective of the current research was to study the degradation kinetics of two PCs by O_3/AC coupling. These compounds were MTP and FXT. According to the literature, these compounds are poorly removed by conventional wastewater treatments and present a potential risk for human health and the environment [21–24]. The results were compared to those obtained with the ozonation process and were modelled by a global pseudo-first-order kinetic model taking into account of all the effects occurring during the O_3/AC-coupling treatment. The influence of the pH, ranging from 3 to 9, was also studied.

2. Material and methods

2.1. Ozonation pilot

The experiments were performed in a 1-L cooling jacket reactor thermostated at 20°C and mechanically stirred (Fig. 1). The stirring mobile was chosen to limit granular AC attrition and to favour the O_3 mass transfer. O_3 was produced from pure oxygen in a BMT 803 N ozone generator supplied by the BMT company and analysed by a BMT 964 ozone analyser. It was introduced at the bottom of the reactor through a porous diffuser. The unconverted ozone in the outlet gas was removed by an O_3 catalytic destructor.

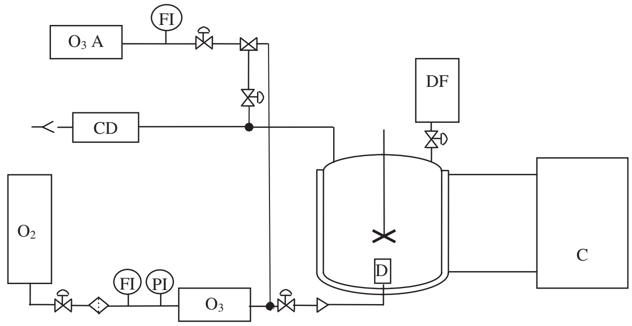

Fig. 1. Ozonation pilot. (C) cryothermostat, (DF) dropping funnel, (D) porous diffuser, (O_3) ozone generator, (O_2) oxygen bottle, (CD) catalytic destructor and (O_3A) ozone analyser.

2.2. Experimental procedure

To prepare the solutions of PC at the concentration of 1.10^{-3} mol L^{-1}, 0.3457 g of FXT or 0.3424 g of MTP was added to 1 L of phosphate buffer solution. The complete dissolution of the compound was verified through HPLC analysis. For the experiments performed with AC, $m_{AC} = 2$ g of AC was previously introduced into the reactor. The ozonated gas was fed at a flow rate $q = 0.06\ Nm^3\ h^{-1}$ and its O_3 concentration was $C_{O3} = 20\ g\ Nm^{-3}$. The ozone concentration in the outlet gas was also measured during the experiments. This compound being introduced in continuous flow, no significant modification of its concentration was measured during the experiments.

The experiments started when the solution was introduced by a dropping funnel into the reactor. Samples (5 mL) were withdrawn with a syringe at suitable time intervals and were filtered through a 0.45-μm membrane filter. O_3 was immediately removed by adding 100 μL of 0.1 mol L^{-1} sulphite solution to avoid further oxidation reaction. Moreover, the ozone concentration in liquid was measured by the carmin indigo method [25]. It was verified that this concentration remains constant during the experiments at about 4.2 mg L^{-1}.

2.3. AC properties

The AC used (L27) was supplied by Pica Jacobi. It was washed before each use to eliminate residual acidity due to the activation treatment and was then dried overnight at 100˚C. The characterization of the porosity was managed by conventional nitrogen adsorption–desorption isotherms at −196˚C (using a Micromeritics ASAP 2020) on samples of approximately 0.2 g after outgassing at 250˚C for 48 h and under a residual vacuum of less than 10^{-4} Pa. The adsorption isotherms were carried out with relative pressures ranging from 7.9×10^{-4} Pa to 0.99 and were analysed using the Dubinin–Radushkevich equation. This leads essentially to the micropore volume W_0 ($cm^3\ g^{-1}$) and the characteristic energy E_o, a quantity related to the average micropore width L_0 (nm). The sing α_S plot (using black carbon Vulcan 3 as a reference) was used to obtain values of the specific external surface S_{ext} ($m^2\ g^{-1}$), assuming that for slit-shaped micropores, the specific microporous surface S_{micro} ($m^2\ g^{-1}$) could be estimated using the specific microporous volume and the mean pore size. Boehm titration was used to determine the oxygen surface groups and FTIR measurements (FTIR Nicolet iS10 spectrophotometer) were also carried out. 0.2 g of AC dried overnight at 80˚C was introduced into 25 mL of the following 0.1 mol L^{-1} solutions: NaOH, Na_2CO_3, $NaHCO_3$ and HCl. The AC/solution mix was placed in a thermostated multi-agitation apparatus at 25˚C under mechanical stirring at 150 rpm for 48 h. The suspension was filtered through a 0.45-μm membrane filter and the excess of base or acid was titrated with 0.1 mol L^{-1} solutions of HCl or NaOH, respectively. Following the Boehm method, the carboxylic, phenolic and lactonic groups were quantified. The number of surface basic groups was calculated (but not identified) from the amount of HCl which reacts with the carbon. The determination of the pH_{PZC} was obtained by the method proposed by Rivera-Utrilla and Sanchez-Polo [26]. The micropore size distribution was determined by the DFT method included in the Micromeritic software. The L27 AC chemical and textural properties, reported in Table 1, show that this AC presents a balanced distribution of mesopores and micropores, a high total surface (S_{total}) and microporous volume (W_0) values. Moreover, it has a high amount of acidic surface groups and a low point of zero charge ($pH_{PZC} = 3$) [27].

2.4. Liquid chromatography

The HPLC system consisted of a Dionex Ultimate 3000 equipped with a PDA detector (DAD). Data were collected and processed with the Chromeleon version 6.8 software package. Chromatographic analyses were performed in reversed phase mode using a Hypersil GOLD column 100 mm × 2.1 mm with a particle size of 3 μm. The mobile phase was a mix of water (A) at pH 2.9 acidified by orthophosphoric acid 0.01% (v/v) and acetonitrile (B). The following multi-step linear gradient was applied from 10 B to 80% B in 25.45 min (slope of 2.75 mL min^{-1}), followed by a plateau for 2 min and then a decrease from 80 B to 10% B in 1 min and a final plateau of 3 min at the initial conditions. The flow rate was set at 0.25 mL min^{-1} and the injection volume at 50 μL. UV spectra of PCs were firstly recorded to select three detection wavelengths. (210, 225 and 355 nm). The detection temperature was 20˚C.

2.5. Reagents and PCs

The PCs chosen for this study, presented on Fig. 2, were of high purity grade (>98%). MTP tartrate was purchased from Alfa Aesar and FXT chlorhydrate from Tokyo Chemical Industry Co. The main properties of these compounds are reported in Table 2 [28–31]. The molar volume was calculated by the Chemsketch software.

The phosphate buffer was prepared with a mixture of different amounts of H_3PO_4 (purity up to 85%, obtained from Sigma Aldrich), KH_2PO_4 (purity up to 99%, obtained from Fluka) and Na_2HPO_4 (purity up to 99%, obtained from Fluka). HPLC grade acetonitrile, orthophosphoric acid 85% and water were purchased from VWR international.

2.6. Kinetic model

According to the literature, many effects occur during treatment by O_3/AC coupling. The target pollutants can be removed by direct or indirect reactions or adsorbed on the AC surface [32]. Moreover, interactions between O_3 and AC surface groups can favour $HO^{\bullet}$ generation. AC can act as reaction site, favouring

Table 1
Textural and chemical properties of AC L27

W_0 ($cm^3\ g^{-1}$)	L_0 (nm)	S_{ext} ($m^2\ g^{-1}$)	S_{micro} ($m^2\ g^{-1}$)	S_{total} ($m^2\ g^{-1}$)	Total acid (meq g^{-1})	Total basic (meq g^{-1})	pH_{PZC}
0.57	1.85	444	519	963	1.57	0.18	3.0

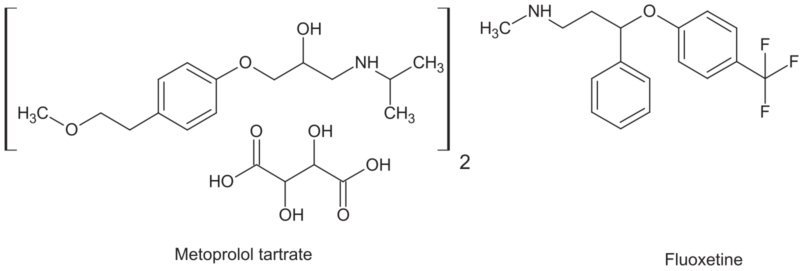

Fig. 2. Structure of PCs.

Table 2
PCs properties

Product	Pharmaceutical class	M (g mol^{-1})	pK_a	Solubility at 25°C (g L^{-1})
FLX	Antidepressant	345.79[a]	9.5	14[a]
MTP	Beta-blocker	684.82[b]	9.7	40.2[b]

[a] Fluoxetine hydrochloride.
[b] Metoprolol tartrate, [19–22].

the interaction between the pollutant and the oxidative species. It was also demonstrated in previous studies that a global pseudo-first-order model can be successfully used to describe the degradation kinetics of the pollutants [33,34],

$$-\frac{\mathrm{d[PC]}}{\mathrm{d}t} = k_1[\mathrm{PC}][\mathrm{O_3}] + k_2[\mathrm{PC}][\mathrm{HO^{\bullet}}] + k_3[\mathrm{PC}] + k_4[\mathrm{PC}][\mathrm{O_3}] + k_5[\mathrm{PC}][\mathrm{HO^{\bullet}}] \quad (1)$$

where [PC] is the concentration of PC (mol L^{-1}), [O$_3$] is the concentration of dissolved ozone (mol L^{-1}), [HO$^{\bullet}$] is the concentration of hydroxyl radicals (mol L^{-1}), and k_1 and k_2 are the kinetic constants of direct and indirect ozonations of PC in the bulk liquid, respectively, (L mol^{-1} min^{-1}), k_3 is the kinetic constant of PC adsorption (min^{-1}), k_4 is the kinetic constant of direct oxidation of PC on the AC surface (L mol^{-1} min^{-1}), k_5 is the kinetic constant of indirect ozonation of PC due to radical reactions initiated and promoted by interaction between O$_3$ and AC surface groups and t is the time (min). Assuming that the concentration of both O$_3$ and HO$^{\bullet}$ remains constant during experiments [35], Eq. (1) can be simplified as follows:

$$-\frac{\mathrm{d[PC]}}{\mathrm{d}t} = k_{\mathrm{global}}[\mathrm{PC}] \quad (2)$$

with

$$k_{\mathrm{global}} = k_{\mathrm{homo}} + k_{\mathrm{hetero}} \quad (3)$$

$$k_{\mathrm{homo}} = k_1[\mathrm{O_3}] + k_2[\mathrm{HO^{\bullet}}] \quad (4)$$

$$k_{\mathrm{hetero}} = k_3 + k_4[\mathrm{O_3}] + k_5[\mathrm{HO^{\bullet}}] \quad (5)$$

where k_{homo} represents the kinetic constant of reactions (direct or indirect) occurring in the bulk liquid in the absence of AC (min^{-1}). k_{hetero} represents the reactions occurring on the AC surface (k_5 includes radical reactions occurring in the bulk liquid but these reactions are initiated and promoted by heterogeneous reactions between O$_3$ and AC surface groups) (min^{-1}).

For experiments performed only with O$_3$, the PC degradation kinetics can be described by pseudo-first-order model:

$$-\frac{\mathrm{d[PC]}}{\mathrm{d}t} = k_{\mathrm{homo}}[\mathrm{PC}] \quad (6)$$

Having determined k_{global} and k_{homo} from Eqs. (2) and (6), the kinetic contribution of heterogeneous reactions to PC degradation (δ^{hetero}) can be estimated:

$$\delta^{\mathrm{hetero}} = \frac{k_{\mathrm{global}} - k_{\mathrm{homo}}}{k_{\mathrm{global}}} \times 100 \quad (7)$$

Some experiments were triplicated to determine the standard deviation of the kinetic parameters. The standard deviation of k_{global} and k_{homo} was estimated at 0.01 min^{-1}.

3. Results and discussion

3.1. Degradation of PCs by ozonation

The results presented in Fig. 3 show the evolution of MTP concentration during ozonation. Very few differences appeared between the results of the four experiments performed at pH ranging from 3 to 9. In all the experimental conditions, this compound was rapidly and totally removed in 40 min. It is generally admitted that in acidic conditions, oxidation mainly occurs by the molecular way, the HO$^{\bullet}$ species being generated by interaction between O_3 and hydroxide ions. This indicates that MTP is very reactive with molecular ozone and is mainly removed by the molecular way. The increase in HO$^{\bullet}$ concentration occurring with the rise in pH did not enhance the degradation kinetics of this compound. According to some previous studies, this phenomenon could be explained by two factors: the degradation of MET could lead to the formation of by-products competing with the parent products and quenching the HO$^{\bullet}$. Moreover, the counter ion (tartrate) could act as radical scavenger and then limit the effect of pH [13,36]. In a previous study, performed with MTP in its molecular form, Javier Benitez observed an evolution of the ozonation kinetic constant with the pH and showed that MTP was mainly removed by radical way [37]. It could confirm that tartrate acts as a radical scavenger during the experiments performed in this study.

On the contrary, the results presented in Fig. 4 show very significant differences in the degradation kinetics of FXT according to the pH value. In acidic conditions, total degradation of this pollutant was not obtained even after more than 45 min, whereas at pH 7 and 9, evolution was rapid and less than 20 min were needed to totally remove this compound. In a previous study concerning the removal of FXT by ozonation and catalytic ozonation processes, Mendez-Arriaga et al. showed the strong pH dependence in the FXT removal under all the experimental conditions tested [38]. The acceleration of the FXT degradation kinetics with an increase in pH shows that this compound is not very reactive with molecular ozone but highly reactive with HO$^{\bullet}$. FXT was mainly removed by indirect ozonation. In a study concerning the removal of FXT by AOPs, Mendez-Arriaga et al. observed that an AOP can enhance the removal efficiency [38]. The results obtained with the two PCs showed that the efficiency of ozonation to remove PCs depends on experimental parameters such as the pH and the nature of the pollutant. The total removal of PCs was obtained but can require a lengthy treatment time.

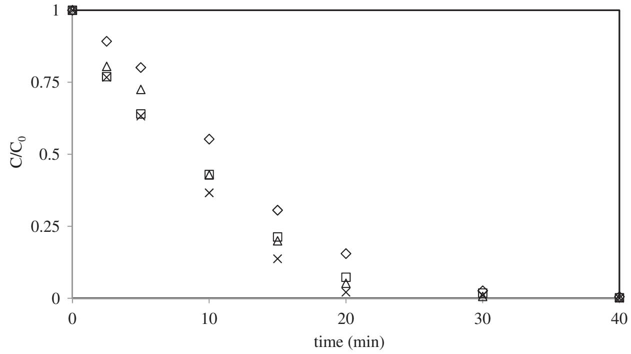

Fig. 3. MTP degradation kinetics at pH 3 (◊), pH 5 (□), pH 7 (Δ) and pH 9 (×) during the ozonation treatment with q = 0.06 Nm^3 h^{-1}, C_{O3} = 20 g Nm^{-3} and T = 20°C.

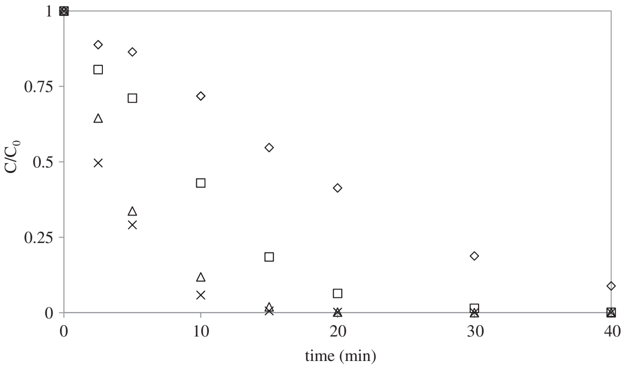

Fig. 4. FXT degradation kinetics at pH 3 (◊), pH 5 (□), pH 7 (Δ) and pH 9 (×) during the ozonation treatment with q = 0.06 Nm^3 h^{-1}, C_{O3} = 20 g Nm^{-3} and T = 20°C.

3.2. Degradation of PCs by O_3/AC coupling

The results of the degradation of MTP by O_3/AC coupling are presented on Fig. 5. These results were close to those obtained with ozonation. However, the comparison of results presented on Figs. 4 and 5 shows that the coupling slightly speeded up the pollutant degradation, especially in the first few minutes. For each pH value, the evolution of the pollutant concentration was very similar and about 30 min of treatment was needed to totally remove this compound. In this case, the use of O_3/AC coupling slightly enhanced the pollutant degradation. MTP is very reactive with molecular ozone and the effects and the coupling permit little increase in the removal efficiency.

On the contrary, the degradation of FXT by O_3/AC coupling was significantly enhanced compared to the ozonation process (Fig. 6). The total removal of this pollutant was obtained for treatment durations ranging

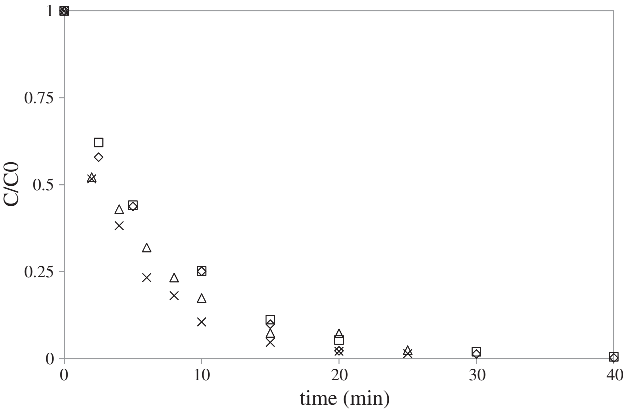

Fig. 5. MTP degradation kinetics at pH 3 (◇), pH 5 (□), pH 7 (Δ) and pH 9 (×) during the O_3/AC coupling treatment with $q = 0.06$ $Nm^3\ h^{-1}$, $C_{O3} = 20\ g\ Nm^{-3}$, $T = 20°C$ and $m_{AC} = 2.0$ g.

from 10 min (pH 9) to 30 min (pH 3). For FXT, which was shown to react slowly with molecular O_3, O_3/AC coupling leads to fast and total pollutant removal. It shows that this coupling is very useful and efficient when the experimental conditions disfavour the elimination of a pollutant (acidic conditions, refractory compound). O_3/AC coupling enables the fast and total removal of the pollutants whatever may be the experimental conditions and the nature of the pollutant.

3.3. Modelling the degradation kinetics

The global first-order model was applied to the experimental results. The values of r^2 reported in Tables 3 and 4 show that this model properly describes the degradation kinetics of MTP and FXT by both ozonation and O_3/AC coupling ($r^2 > 0.99$). For the ozonation process (Table 3), the kinetic constant values confirmed that the pH value does not influence the MTP degradation kinetics, k ranging from $0.13\ min^{-1}$ (pH 3) to $0.15\ min^{-1}$ (pH 9).

On the contrary, the rise in pH leads to a significant increase in the degradation kinetic constant of FXT, with k ranging from $0.06\ min^{-1}$ (pH 3) to $0.34\ min^{-1}$ (pH 9). It confirms that MTP was mainly removed by direct ozonation and FXT by the radical way.

Table 3
Modelling the PCs degradation kinetics by ozonation

	MTP		FXT	
pH	k_{homo} (min^{-1})	r^2	k_{homo} (min^{-1})	r^2
3	0.13	0.99	0.06	0.99
5	0.14	0.99	0.16	0.99
7	0.15	0.99	0.25	0.99
9	0.15	0.99	0.34	0.99

Table 4
Modelling the PCs degradation kinetics by O_3/AC coupling

	MTP		FXT	
pH	k_{global} (min^{-1})	r^2	k_{global} (min^{-1})	r^2
3	0.13	0.99	0.11	0.99
5	0.14	0.99	0.27	0.99
7	0.16	0.99	0.71	0.99
9	0.19	0.99	0.72	0.99

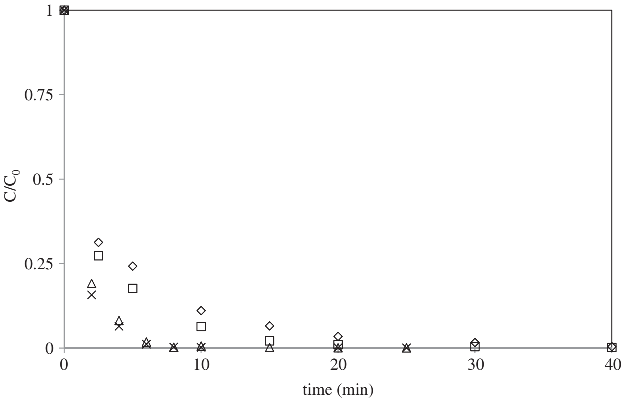

Fig. 6. FXT degradation kinetics at pH 3 (◇), pH 5 (□), pH 7 (Δ) and pH 9 (×) during the O_3/AC coupling treatment with $q = 0.06\ Nm^3\ h^{-1}$, $C_{O3} = 20\ g\ Nm^{-3}$, $T = 20°C$ and $m_{AC} = 2.0$ g.

For O_3/AC coupling (Table 4), the results obtained for MTP degradation show that this process showed no improvement over the results obtained with ozonation, whereas the degradation of FXT was significantly faster with the coupling, k ranging from $0.11\ min^{-1}$ (pH 3) to $0.72\ min^{-1}$ (pH 9). O_3/AC coupling is of great interest for the removal of this compound that is weakly reactive with molecular ozone.

These results also enable the value of k_{hetero} (Table 5) and of the kinetic contribution of heterogeneous degradation (Table 6) to be determined. It shows that the presence of AC weakly influences MTP degradation kinetics (δ^{hetero} varying from 0 to 21% and k_{hetero} from 0 to $0.04\ min^{-1}$) but strongly enhances that of FXT (δ^{hetero} varying from 41 to 65% and k_{hetero} from 0.05 to $0.46\ min^{-1}$). It confirms that the coupling is very useful when the operational parameters or the nature of the pollutant disfavours oxidation. In previous studies, it

Table 5
Values of k_{hetero}

	k_{hetero} (min^{-1})	
pH	MTP	FXT
3	0	0.05
5	0	0.11
7	0.01	0.46
9	0.04	0.38

Table 6
Kinetic contribution of heterogeneous reactions to PCs degradation

	δ^{hetero} (%)	
pH	MTP	FXT
3	0	45
5	0	41
7	6	65
9	21	53

was shown that this effect was mainly due to the generation of $HO^{\bullet}$ resulting from the interactions between O_3 and AC and to the heterogeneous catalyst role of the AC [34].

4. Conclusion

The degradation kinetics of two PCs by ozonation and O_3/AC coupling was studied. The results were very different for these compounds. MTP appeared to be efficiently degraded by ozonation. Even in acidic conditions (direct ozonation), its degradation kinetics was fast and was weakly enhanced by the use of O_3/AC coupling. The values of the kinetic contribution of heterogeneous degradation varied from 0 (pH 3) to 21% (pH 9), showing that this compound was mainly removed by oxidation in the bulk liquid. On the contrary, FXT was more slowly removed by ozonation. The use of an advanced oxidation process significantly increased the degradation kinetics of this pollutant. The values of the kinetic contribution of heterogeneous degradation varying between 41 and 65% show that the degradation of this pollutant was also due to interactions between O_3 and AC. This study has therefore shown that a process such as O_3/AC coupling is very efficient if the operational parameters disfavour pollutant oxidation. A high treatment efficiency (fast and complete degradation of the pollutants) was obtained whatever the operational conditions and the nature of the pollutant, contrary to ozonation which strongly depends on the pH and the pollutant. As O_3/AC coupling leads to the formation of by-products, a study of the evolution of the effluent toxicity should now be performed to validate this process for the removal of PCs in water.

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