

Removal efficiencies and kinetic rate constants of xenobiotics by ozonation in tertiary treatment

Baptiste Mathon, Marina Coquery, Cécile Miege, Ywann Penru and Jean-Marc Choubert

ABSTRACT

This study gives a full overview of the chemical oxidation by ozone of selected xenobiotics usually present in effluents of conventional wastewater treatment plants. A qualitative and quantitative overview of literature data was made, and describes the ozonation efficiency and processes for the elimination of 12 xenobiotics (pesticides and pharmaceuticals). A database was built, compiling literature results of experimental ozonation assays in laboratory and real-scale conditions. Special attention was paid to selecting the data and compiling reliable results on removal efficiencies and kinetic parameters. An original study was performed in a semi-batch reactor applying ozone on secondary effluent spiked beforehand with a cocktail of 12 xenobiotics. The results of this study were compared with the literature data to evaluate the influence of the kinetic competition of xenobiotics in spiked wastewater in the determination of kinetic rate constants. These 12 xenobiotics were classified into three groups (high-/medium-/low-oxidizable) according to the ranges of their direct kinetic rate constants (k_{O_3}). A best effective ozone dose between 0.2 and 0.4 gO₃ gDOC⁻¹ is proposed for the elimination of xenobiotics. The predominant elimination pathway between direct and indirect oxidation was identified for each xenobiotic.

Key words | direct and indirect ozonation, micropollutants, pesticides, pharmaceuticals, wastewater

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INTRODUCTION

Conventional wastewater treatment plants (WWTPs) partially eliminate xenobiotics present in domestic and industrial discharges (Choubert *et al.* 2011; Verlicchi *et al.* 2012). However, several xenobiotics are still present in the effluents of WWTPs at concentrations close to 0.1 µg L⁻¹ for some pesticides (e.g. diuron) and pharmaceuticals (e.g. carbamazepine, sotalol and diclofenac), and even more than 1 µg L⁻¹ for other xenobiotics, including aminomethylphosphonic acid, ibuprofen and gemfibrozil (Heberer 2002; Martin Ruel *et al.* 2011). The potential hazard of these xenobiotics calls for polishing treatment technologies that will remove xenobiotics and anticipate any future regulatory changes. One elimination pathway of proven effectiveness for the degradation of xenobiotics in drinking water is the use of one or more oxidants, such as UV radiation, ozone or hydrogen peroxide (Meunier *et al.* 2006; Martin Ruel *et al.* 2011).

This study focuses on the role of oxidation by ozone in the elimination of xenobiotics in polishing treatment. Ozone is a specific, efficient oxidant for the purification of drinking waters and some industrial wastewaters (Huber *et al.*, 2005; Snyder *et al.* 2006). For domestic secondary effluents, recent studies carried out in pilot or full-scale plants showed that chemical oxidation by ozone [0.25–0.5 gO₃/g dissolved organic carbon (DOC)] promoted the elimination of most of the pharmaceuticals studied (Hollender *et al.* 2009; Wert *et al.* 2009). Besnault *et al.* (2012) reported removal efficiencies higher than 90% for 24 out of 40 organic xenobiotics quantified in secondary effluents.

Each xenobiotic can be characterized by two second-order rate constants, one for exposure of the xenobiotic to ozone (k_{O_3}) and the other for its exposure to free hydroxyl (OH[•]) radicals (k_{OH}), also called direct and indirect oxidation pathways. The literature provides information on the direct and indirect oxidation of xenobiotics commonly

found in secondary effluents, for example, values for the herbicide diuron ($k_{O_3} = 16.4 \text{ M}^{-1} \text{ s}^{-1}$; Benitez *et al.* 2007) and for some pharmaceuticals: carbamazepine ($k_{O_3} = 3.0 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$; Gerrity *et al.* 2012) and atenolol ($k_{O_3} = 1.7 \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$; Hollender *et al.* 2009). However, predicting the elimination of a xenobiotic from these kinetic rate constants is difficult. Better knowledge of removal rates under various operating conditions could help stakeholders design polishing treatment processes using ozone.

We set out to make a thorough overview of the removal and kinetic degradation by ozonation of 12 pharmaceuticals and pesticides known to be refractory to conventional WWTPs. This overview aimed to improve our understanding of the behavior of xenobiotics in a tertiary treatment process using ozonation. Direct ozone oxidation and indirect free hydroxyl radical oxidation kinetic parameters were closely examined. Bibliographic data for xenobiotic removal efficiency obtained in wastewater were also reviewed. All this information was compiled in a database. We then set up an original study aiming at evaluating both removal efficiencies and kinetic constants for a cocktail of micropollutants in wastewaters. Finally, literature data and initial experimental data were compared to ensure the reliability of our method, and evaluate the influence of kinetic competition in the determination of kinetic rate constants.

MATERIALS AND METHODS

Selection of the xenobiotics studied

We focused on several xenobiotics known to be poorly biodegraded and poorly adsorbed. These xenobiotics can be considered as refractory to secondary treatment, and are frequently quantified in effluents of WWTPs (Ternes *et al.* 2004; Gabet-Giraud *et al.* 2010; Martin Ruel *et al.* 2010; Falås *et al.* 2012). A set of 12 substances were selected: erythromycin and clarithromycin (antibiotics), carbamazepine (antiepileptic), diazepam (benzodiazepine), diclofenac (anti-inflammatory drug), metoprolol, propranolol, atenolol and sotalol (betablockers), simazine, diuron and isoproturon (pesticides). They cover a broad range of physical and chemical properties (molecular weight, solubility, pK_a , $\log K_{ow}$), and are characterized by various functional groups and chemical bonds (Table 1). Robust accurate analytical methods were also available for all the xenobiotics selected (Gabet-Giraud *et al.* 2010).

Bibliographic study and compilation of information in a database

To estimate the efficiency of ozonation processes for the 12 xenobiotics studied, we selected scientific papers using the Scopus and Web of Science search engines, for the period 1991–2014. The keywords used were ‘ozone’, or ‘ozonation’, plus the names of the selected xenobiotics. A database was built in an MS Excel© spreadsheet to collect (i) descriptors of xenobiotic ozonation: xenobiotic removal efficiency, or/and direct kinetic rate constant (k_{O_3}) and indirect kinetic rate constant (k_{OH}), (ii) when reported, metadata on the experimental conditions such as information on xenobiotics (name, chemical structure, initial concentration, etc.), initial physical and chemical composition of the water (nitrate and nitrite concentrations, total organic carbon (TOC), DOC, etc.), ozone conditions (ozone dose, contact time, etc.), other experimental conditions (nature of exposure container, volume of reactor, etc.) and the analytical methods (method name, limit of quantification, etc.), and (iii) detected by-products when reported (see supplementary materials SPM1, available with the online version of this paper). The selection focused on studies that estimated xenobiotic removal efficiencies with treated wastewater; kinetic rate constants in wastewater are not reported in the literature, so the data measured in pure water were compiled.

Experimental study

Experimental strategy

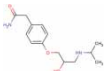
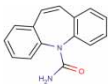
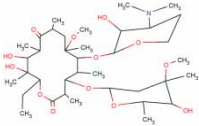
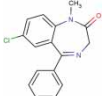

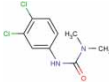
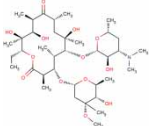
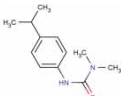
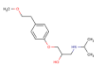

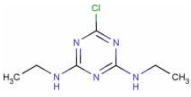

The experimental study was designed to determine direct (k_{O_3}) and indirect (k_{OH}) rate constants as defined in Equation (1):

$$-\ln\left(\frac{[MP]}{[MP]_0}\right) = k_{O_3} \cdot \int [O_3] dt + k_{OH} \int [\cdot OH] dt, \quad (1)$$

where [MP] is the concentration of xenobiotics in the aqueous (dissolved) phase (mg L^{-1}) during the study, $[MP]_0$ is the initial concentration, k_{O_3} is the kinetic rate constant of the reaction between the xenobiotic and ozone ($\text{M}^{-1} \text{ s}^{-1}$), k_{OH} is the kinetic rate constant of the reaction between the xenobiotic and OH radicals ($\text{M}^{-1} \text{ s}^{-1}$), and $\int [O_3] dt$ and $\int [\cdot OH] dt$ are the ozone and OH radical exposures.

Two batch experiments were conducted. In a first experiment we determined the direct kinetic rate constants (k_{O_3}) for the reactions between ozone and a cocktail of the 12 xenobiotics studied. It was performed at 17°C in the presence of tert-butanol (0.1 M) as OH radical scavenger (Staehelin & Hoigne 1985). In a second experiment we

Table 1 | Physical and chemical properties of the 12 xenobiotics studied and concentrations in secondary effluents

Substance (family)	Semi-developed formula	Chemical formula	Molecular weight (g mol ⁻¹)	Solubility in water at 25 °C (mg L ⁻¹)	pK _a	Log K _{OW}	Concentrations measured in secondary effluents (µg L ⁻¹)
Atenolol (Betablocker)		C ₁₄ H ₂₂ N ₂ O ₃	266	1.3 × 10 ⁴	9.6	0.16	0.01–7 ^a
Carbamazepine (Anti-epileptic)		C ₁₅ H ₁₂ N ₂ O	236	17.7	NIA	2.45	0.001–11 ^a
Clarithromycin (Antibiotic)		C ₃₈ H ₆₉ NO ₁₃	748	0.33	8.9	3.16	0.1–8 ^a
Diazepam (Anti-depressant)		C ₁₆ H ₁₃ ClN ₂ O	285	50	3.4	2.82	0.02–11 ^a
Diclofenac (Nonsteroidal anti-inflammatory agent)		C ₁₄ H ₁₁ Cl ₂ NO ₂	296	2.37	4.2	4.51	0.01–10 ^a
Diuron (Pesticide)		C ₉ H ₁₀ Cl ₂ N ₂ O	233	49	13.6	2.68	0.01–0.2 ^b
Erythromycin (Antibiotic)		C ₃₇ H ₆₇ NO ₁₃	734	2.0 × 10 ³	8.9	3.06	0.01–8 ^a
Isoproturon (Pesticide)		C ₁₂ H ₁₈ N ₂ O	206	70	NIA	2.87	0.01–0.1 ^b
Metoprolol (Betablocker)		C ₁₅ H ₂₅ NO ₃	267	1.7 × 10 ⁴	NIA	1.88	0.005–3 ^a
Propranolol (Betablocker)		C ₁₆ H ₂₁ NO ₂	259	61.7	9.4	3.48	0.01–0.8 ^a
Simazine (Pesticide)		C ₇ H ₁₂ ClN ₅	202	6.2	1.6	2.18	0.01–0.05 ^b
Sotalol (Betablocker)		C ₁₂ H ₂₀ N ₂ O ₃ S	272	5.5 × 10 ³	NIA	0.24	0.2–4 ^a

NIA = no information available.

^aAccording to the data available in Verlicchi *et al.* (2012).

^bAccording to the data available in Martin Ruel *et al.* (2010).

determined the indirect kinetic rate constants (k_{OH}) for the reactions between OH radicals and a cocktail of the 12 xenobiotics studied. It was performed at 17 °C in the presence of 4-chlorobenzoic acid (*p*-CBA).

No method yet exists for the direct measurement of OH radical concentrations. The approach proposed by Elovitz & von Gunten (1999) to measure the transient OH radical from the O₃ concentrations during ozonation experiments was

used. This method consists in measuring the decay of an ozone-resistant reference compound (*p*-CBA) that reacts rapidly with OH radicals (rate constant of reaction with OH radicals $5 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$; Buxton *et al.* 1988), and has a very low reactivity toward ozone (rate constant of reaction with ozone $0.15 \text{ M}^{-1} \text{ s}^{-1}$; Yao & Haag 1991).

For experiments 1 and 2, the effluent discharged by the Bouillides WWTP (GPS coordinates: $43^\circ 37' 5.892'' \text{ N}$; $4^\circ 3' 44.47'' \text{ E}$, France) was used. It used primary settling and two stages of submerged aerated filters for carbon and nitrogen removal (Penru *et al.* 2015). The specific ultraviolet absorbance at 254 nm (SUVA₂₅₄) of the effluent was $2.4 \text{ L m}^{-1} \text{ mg C}^{-1}$. TOC content was 8.25 mg L^{-1} , nitrite concentration was 0.08 mg L^{-1} in NO_2 , and alkalinity was 290 mg L^{-1} in HCO_3^- . The ratio R_{CT} , defined as the ratio of $\int [\text{O}_3] dt$ to $\int [\cdot\text{OH}] dt$ (Equation (2); Elovitz & von Gunten 1999), was determined experimentally from the decrease in the concentrations of the reference compound (*p*-CBA) and ozone, to 3.2×10^{-6} . The dissolved ozone concentration was monitored with an Orbisphere model 410 measurement probe (Hach Lange).

$$R_{\text{CT}} = \frac{\int [\cdot\text{OH}] dt}{\int [\text{O}_3] dt} \quad (2)$$

In both experiments, one glass container was filled with 30 L of secondary effluent from the Bouillides WWTP. The effluent was thoroughly mixed mechanically. Ozone gas was dispensed with ceramic porous diffusers set at the bottom of the container. The effluent was spiked with an aqueous solution containing a mixture of the 12 xenobiotics, to reach a final concentration of $1 \mu\text{g L}^{-1}$ (no organic solvent was used during this spiking step). Ozone was produced by an ozone generator (Mimaud Equipements, 60 L h^{-1}) applying a specific ozone dose of $1.6 \text{ g O}_3 \text{ g DOC}^{-1}$ in 15 minutes. Sampling was performed at 0, 3, 6, 10 and 15 minutes. The water samples were rapidly filtered at $0.7 \mu\text{m}$ (glass fiber filters) before analysis.

Target chemical analyses

The parent compounds (12 xenobiotics) were assayed by liquid chromatography coupled with API 4000 – AB Sciex tandem mass spectrometry (LC–MS/MS). The separation was performed on an ACQUITY UPLC HSS-T3 column (C18, $100 \times 2.1 \text{ mm}$, $1.7 \mu\text{m}$) after direct injection of an aliquot of $50 \mu\text{L}$ of each sample at a flow rate of 0.3 mL min^{-1} . The raw data acquired were processed quantitatively for parent compounds using TargetLynx for MassLynx 4.1 software (Waters Corp., Milford, USA). This validated analytical technique gives robust xenobiotic concentrations, obtained with low limits of quantification ($0.1\text{--}0.4 \text{ ng L}^{-1}$).

Calculation of constants k_{O_3} and k_{OH}

For all the xenobiotics studied, the direct kinetic rate constant with ozone (k_{O_3}) was determined using Equation (1) combined with the initial concentrations of micropollutants (MP_0), the concentrations after sampling at $t = 3 \text{ min}$ (MP) and the dissolved ozone concentration. When the concentrations of xenobiotics were below the limit of quantification after sampling at $t = 3 \text{ min}$, a minimal estimate of k_{O_3} was made. We then calculated the indirect kinetic rate constant with OH radicals (k_{OH}) for all the xenobiotics studied using the direct kinetic rate constant (k_{O_3}) and R_{CT} (see Equation (2)).

RESULTS AND DISCUSSION

General information from the bibliographic database

A total of 33 relevant scientific papers were published between 1991 and 2014 (see full references in supplementary materials SPM1). We compiled 416 data lines in the database, 61 on pesticides and 355 on pharmaceuticals. All these data, including the metadata on the experimental conditions applied, are fully presented in supplementary materials SPM2 (available with the online version of this paper). The database comprises 382 removal efficiency values obtained under various conditions, 23 direct kinetic rate constants (k_{O_3}) and 15 indirect kinetic rate constants for reaction with OH radicals (k_{OH}).

The percentage of data according to the nature of the xenobiotics is given in Figure 1. Most data concern removal efficiency on pharmaceuticals (83%), and much less data are available on pesticides. Of the data, 87% was for removal efficiencies measured in various types of wastewaters (sewage from hospitals, secondary treated effluent, reverse osmosis concentrate, etc.). The removal efficiencies were mostly measured in pilot scale plants, and at concentrations usually recorded in the environment (ng L^{-1} or $\mu\text{g L}^{-1}$ range). The other 13% of the data was for kinetic rate constants measured in pure water spiked with xenobiotics at a higher concentration range ($\sim \text{mg L}^{-1}$). For most of the xenobiotics, only one set of kinetic constants is available.

Information on the physical and chemical composition of the water used for the experiments was often lacking in the literature. The following parameters were only partially specified in some experiments: DOC (only 30% of the 416 data lines), nitrates (24%), alkalinity (21%), ammonium (21%) and TOC (21%).

When they were available, we also listed the by-products detected by the different studies (the full list is given in

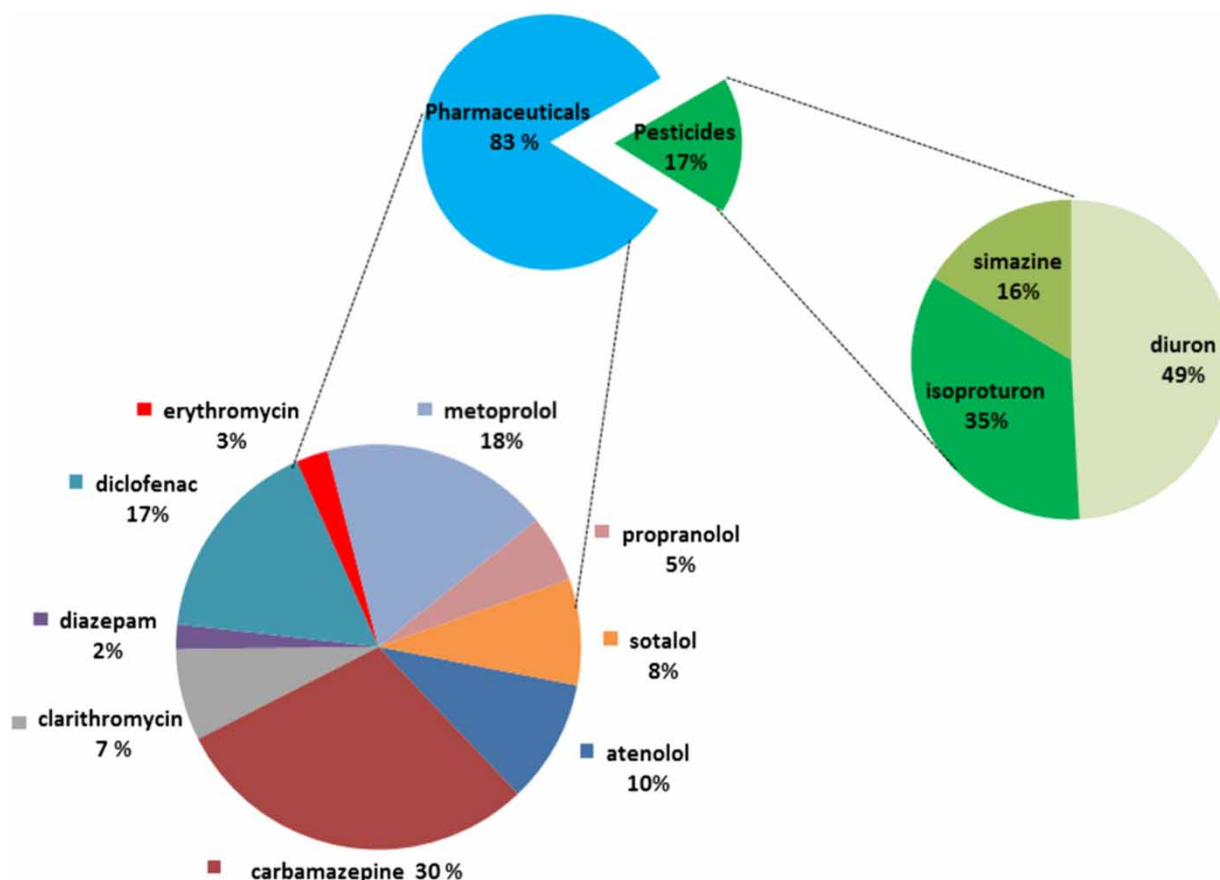


Figure 1 | Distribution (%) of data according to the 12 xenobiotics studied; $n = 61$ for pesticides and $n = 355$ for pharmaceuticals.

supplementary materials SPM3, available with the online version of this paper). Only six scientific papers reported the formation of by-products, along with removal efficiencies for parent compounds in the context of treated wastewater. In all, 67 by-products were listed for four xenobiotics (33 for atenolol, 11 for metoprolol, 10 for propranolol and 13 for carbamazepine). No information was reported for the other eight xenobiotics.

The formation and degradation of by-products can be usefully studied to find optimized operating conditions for the ozonation process (duration and ozone dose). It would be of interest to identify the by-products predominantly formed by the direct or indirect pathways, and adapt operating conditions accordingly. However, literature data are scant. Efforts are needed to investigate by-products, and assess their elimination during processing and their ecotoxicological impact.

Bibliographic information on the influence of ozone dose on removal efficiency

The database provided information on the range of effective ozone dose to apply to reach a high removal efficiency

(>70%) for the 12 xenobiotics studied. Figure 2 presents the example of five micropollutants, from which it could be deduced that the mean effective dose of ozone to obtain removal efficiency above 70% was at least $0.2 \text{ gO}_3 \text{ gDOC}^{-1}$. However, data variability was marked, as shown for instance for carbamazepine, with removal efficiency ranging between 40% and 100% for ozone doses between 0.2 and $0.3 \text{ gO}_3 \text{ gDOC}^{-1}$. The variability of ozonation efficiency (i.e. removal efficiency) is due to the varied nature of the water and experimental conditions (type of effluent, nitrite concentration, HCO_3^- concentration, contact time, etc.). Also, higher mean removal efficiencies were reached with higher ozone doses (e.g. 85% with $0.4 \text{ gO}_3 \text{ gDOC}^{-1}$, 90% with $0.6 \text{ gO}_3 \text{ gDOC}^{-1}$), but the data were also scattered around the mean values ($\pm 15\%$). The varied nature of the water and experimental conditions hinder any robust statistical comparison of removal efficiencies between xenobiotics; hence the utility of performing studies with several xenobiotics (e.g. by spiking) to compare their behavior in similar conditions.

As shown in Figure 2, information was obtainable for four other xenobiotics: clarithromycin, diclofenac, atenolol and metoprolol, with data for more than 10 removal efficiencies

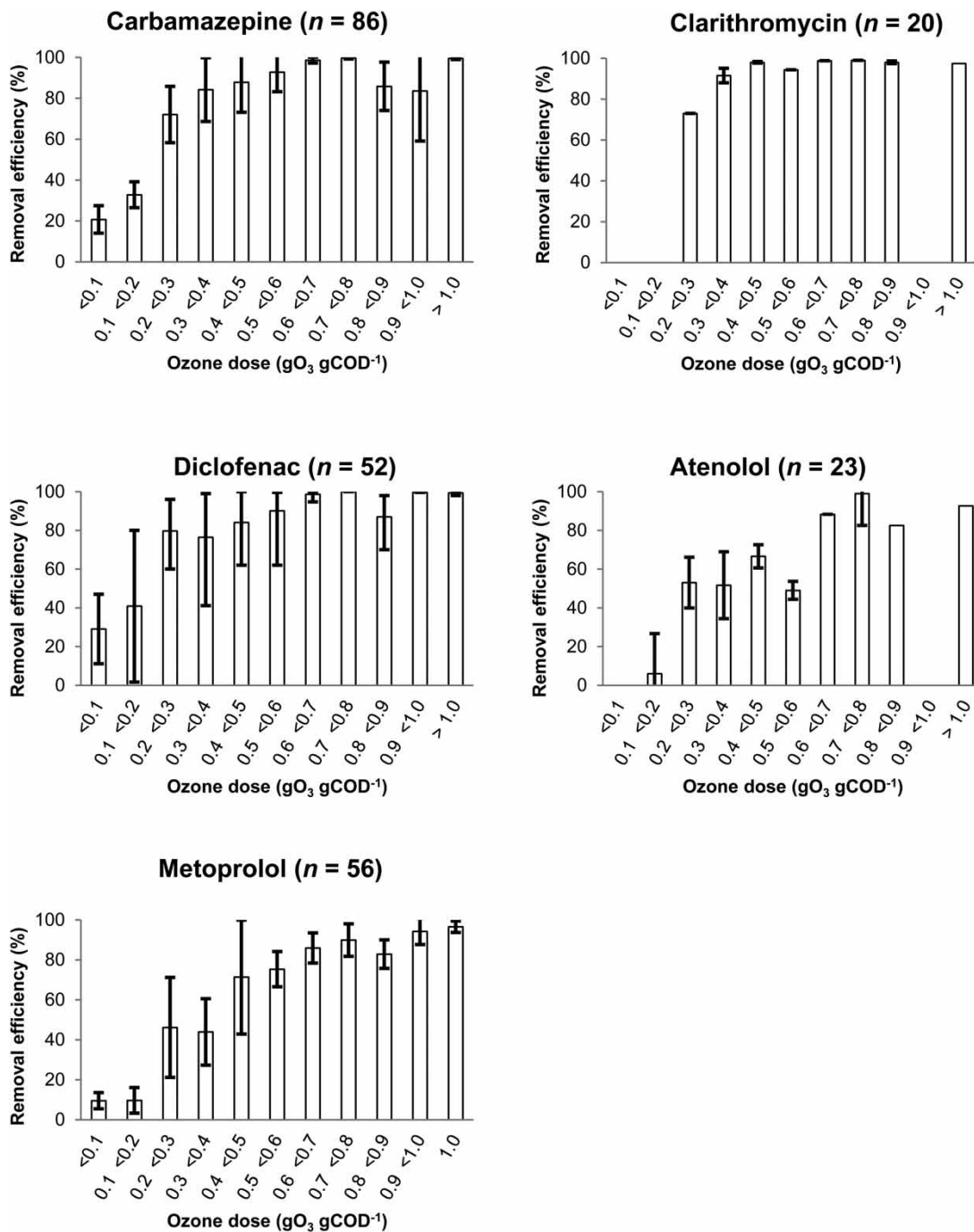


Figure 2 | Histograms showing the mean removal efficiency (%) for carbamazepine, clarithromycin, diclofenac, atenolol and metoprolol determined from the data in the database for different ranges of ozone dose (gO₃ gDOC⁻¹). The lines indicate the standard deviation of the mean data (n = total number of data; see full data in SPM2, available with the online version of this paper).

available. We deduced that the mean effective dose of ozone to obtain a removal efficiency above 70% was at least 0.2 gO₃ gDOC⁻¹ for clarithromycin and diclofenac and 0.4 gO₃ gDOC⁻¹ for atenolol and metoprolol. However, for the other xenobiotics, there was insufficient information (n <

10) to conclude on the best operating conditions. For diazepam, only three datapoints were available, and a mean removal efficiency of 70% was obtained for an ozone dose of 0.9 gO₃ gDOC⁻¹. For diuron, isoproturon and erythromycin, a mean removal efficiency of about 70% was achieved

with an ozone dose of $0.6 \text{ gO}_3 \text{ gDOC}^{-1}$, but only six, three and seven datapoints, respectively, were available. For propranolol and sotalol, an ozone dose of $0.3 \text{ gO}_3 \text{ gDOC}^{-1}$ led to a mean removal efficiency of 70%, but only nine datapoints were available. No data were found for simazine.

Comparison of kinetic rate constants for the 12 xenobiotics – experimental vs. bibliographic studies

The direct and indirect kinetic rate constants for 12 xenobiotics were determined experimentally (Table 2). Unlike those reported elsewhere, the values of these constants were determined in treated wastewater and in identical experimental conditions. These values were compared with those in the literature. No data were found from studies combining determination of removal efficiency and kinetic rate constant in wastewater.

To compare the efficiency of ozonation for each xenobiotic, we split the xenobiotics into three groups, according to the range of the direct kinetic rate constants (k_{O_3}) found in the literature:

- ‘low-oxidizable’ ($10^0 < k_{\text{O}_3} < 10^3 \text{ M}^{-1} \text{ s}^{-1}$) for diazepam, simazine and diuron (Beltrán et al. 2000; Huber et al. 2003; Benitez et al. 2007);
- ‘medium-oxidizable’ ($10^3 < k_{\text{O}_3} < 10^4 \text{ M}^{-1} \text{ s}^{-1}$) for atenolol, metoprolol and isoproturon (Benitez et al. 2007; Benner et al. 2008);
- ‘high-oxidizable’ ($k_{\text{O}_3} > 10^4 \text{ M}^{-1} \text{ s}^{-1}$) for sotalol, clarithromycin, erythromycin, propranolol, carbamazepine and diclofenac (Huber et al. 2003; Benner et al. 2008; Lee et al. 2014).

These studies confirmed that atenolol, metoprolol and isoproturon belonged to the group with intermediate oxidizability (medium-oxidizable), and diazepam, simazine and diuron to the one with low oxidizability (low-oxidizable). However, it was impossible to accurately determine a kinetic rate constant for xenobiotics classified as ‘high-oxidizable’ (i.e. clarithromycin, erythromycin, propranolol, sotalol, carbamazepine and diclofenac) because the concentrations of these xenobiotics were below the limit of quantification after sampling at $t = 3$ min. We accordingly made a minimal estimate for which the micropollutant had a removal efficiency of 100% with an exposure time of 3 minutes. A value of k_{O_3} higher than $10^4 \text{ M}^{-1} \text{ s}^{-1}$ was recorded.

For the ‘medium-oxidizable’ group (atenolol, metoprolol and isoproturon), kinetic rate constants with OH radicals (k_{OH}) were in the same range (1.2 to 2.8 times the value) as the literature values (between 7.3×10^9 and $8 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$; Benner et al. 2008). For the ‘low-oxidizable’ group

Table 2 | Direct kinetic rate constants (k_{O_3}) and kinetic rate constants for reaction with OH radicals (k_{OH}) determined for the 12 xenobiotics (literature and experimental results from this study)

Kinetic rate constants ($\text{M}^{-1} \text{ s}^{-1}$)		Diazepam	Simazine	Diuron	Atenolol	Metoprolol	Isoproturon	Clarithromycin	Erythromycin	Propranolol	Sotalol	Carbamazepine	Diclofenac
k_{O_3}	Literature ($t = 1$)	0.75 ^a	8.7 ^b	13.3 ^c	1.70×10^{3d}	2.00×10^{3e}	2.13×10^{3c}	4.00×10^{4f}	7.00×10^{4f}	1.00×10^{5e}	1.30×10^{5f}	3.00×10^{5g}	1.00×10^{6d}
	This experiment	11.4	7.8	14.9	2.12×10^3	2.97×10^3	5.89×10^3	$> 10^4$	$> 10^4$	$> 10^4$	$> 10^4$	$> 10^4$	$> 10^4$
k_{OH}	Literature ($t = 1$)	7.2×10^{9a}	2.0×10^{9b}	6.5×10^{9c}	8.0×10^{9d}	7.3×10^{9e}	7.9×10^{9c}	5.0×10^{9f}	5.0×10^{9f}	1.0×10^{10e}	1.0×10^{10f}	8.8×10^{9g}	7.5×10^{9d}
	This experiment	6.3×10^9	3.2×10^9	7.5×10^9	8.5×10^9	2.7×10^9	1.8×10^{10}	$> 10^9$	$> 10^9$	$> 10^9$	$> 10^9$	$> 10^9$	$> 10^9$

Experimental results are obtained with a specific ozone dose of $1.6 \text{ gO}_3 \text{ gDOC}^{-1}$ in 15 minutes, TOC content was 8.25 mgL^{-1} , R_{CT} was equal to 3.2×10^{-6} and temperature was 17°C . Boxes are white, light gray and dark gray for low, medium and high-oxidizable xenobiotics, respectively (see SPM1 for literature data references or SPM2 for full data, available with the online version of this paper).

^aAccording to the data available in Huber et al. (2000).

^bAccording to the data available in Beltrán et al. (2000).

^cAccording to the data available in Benitez et al. (2007).

^dAccording to the data available in Hollender et al. (2009).

^eAccording to the data available in Benner et al. (2008).

^fAccording to the data available in Lee et al. (2014).

^gAccording to the data available in Gerrity et al. (2012).

(diazepam, simazine and diuron), k_{OH} values were very close to the literature values (1.1 to 1.2 times the value), which were between 2.0×10^9 and $7.2 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ (Beltrán *et al.* 2000; Huber *et al.* 2003). Here again, it was impossible to determine a specific rate constant for xenobiotics classified as 'high-oxidizable' (clarithromycin, erythromycin, propranolol, sotalol, carbamazepine and diclofenac). We recorded these k_{OH} values as higher than $10^9 \text{ M}^{-1} \text{ s}^{-1}$.

The experimental data showed marked differences in the kinetic rate constants (k_{O_3}) of these 12 xenobiotics (from 7.8 up to $10^4 \text{ M}^{-1} \text{ s}^{-1}$), whereas the kinetic rate constants with OH radicals lay within one order of magnitude for xenobiotics in both the 'low' and 'medium-oxidizable' groups (from 2.7×10^9 to $1.8 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$).

Unlike the literature, where most studies were conducted on a single xenobiotic, our experimental data give deeper insight into the oxidation of a mixture of micropollutants. The comparison of the direct kinetic rate constants between xenobiotics is thus more robust, as they were determined under the same experimental conditions. These experimental values were very close to those of the literature within the same range, except for diazepam. This demonstrates that phenomena of kinetic competition between xenobiotics were insignificant.

From these kinetic rate constants and R_{CT} , we were able to estimate the contribution of the elimination of xenobiotics by the direct and indirect pathways with Equations (3) and (4) (Rosal *et al.* 2010).

$$f_{OH} = \frac{k_{OH} \cdot R_{CT}}{k_{OH} \cdot R_{CT} + k_{O_3}}, \quad (3)$$

$$f_{O_3} = 1 - f_{OH}. \quad (4)$$

The elimination of xenobiotics in the 'medium-oxidizable' and 'low-oxidizable' groups should be mainly driven by indirect ozonation, with f_{O_3} equal to 26% for metoprolol, 11% for isoproturon, 6% for atenolol and 1% for diazepam, simazine and diuron. By contrast, for molecules of the 'high-oxidizable' group, the direct ozone oxidation should predominate over indirect free hydroxyl radical oxidation. For the 'high-oxidizable' group, we could not determine exact k_{OH} and k_{O_3} values for the six studied xenobiotics, so the data from the literature were used. The values of f_{O_3} were: 71% for clarithromycin, 81% for erythromycin, 76% for propranolol, 80% for sotalol, 91% for carbamazepine and 98% for diclofenac. For the 'high-oxidizable' group, the direct ozone oxidation should predominate over indirect free hydroxyl radical oxidation.

Relation between xenobiotic removal efficiency and direct kinetic rate constants – experimental vs. bibliographic studies

Studying ozonation using only removal efficiencies is strongly influenced by the composition of the aqueous matrix, which contains various sinks for ozone and OH radicals (e.g. bromide, nitrite, and organic matter), and also by the chemical structure of the xenobiotics. Hence, a complementary approach based on chemical kinetics, independent of the composition of the aqueous matrix, is required to determine whether the differences observed for k_{O_3} can explain the variations in removal efficiencies.

To give a full overview of the role of k_{O_3} in determining the proneness of a xenobiotic to oxidation by ozone, we sorted literature data according to the applied ozone dose, and compared results with the experimental results of this study. The mean removal efficiencies for xenobiotics and the k_{O_3} values are plotted in Figure 3(a) for the bibliographic data (applied ozone doses between 0.2 and $0.4 \text{ gO}_3 \text{ gDOC}^{-1}$), and in Figure 3(b) for the data obtained in this study (ozone dose: $0.2 \text{ gO}_3 \text{ gDOC}^{-1}$). The experimental values of k_{O_3} for the three groups of xenobiotics previously defined were consistent with removal efficiencies obtained simultaneously for these xenobiotics (Figure 3(b)). For low-oxidizable xenobiotics ($k_{O_3} < 10^3 \text{ M}^{-1} \text{ s}^{-1}$) such as diazepam, simazine and diuron, the removal efficiency was low (<30%), whereas medium-oxidizable xenobiotics such as atenolol, metoprolol, and isoproturon had removal efficiencies between 50% and 90%, and high-oxidizable xenobiotics such as clarithromycin, erythromycin, propranolol, sotalol, carbamazepine and diclofenac ($k_{O_3} > 10^4 \text{ M}^{-1} \text{ s}^{-1}$) had removal efficiencies of >99%. Similar observations were made with literature data (Figure 3(a)), but this comparison using literature data was possible for only 9 of the 12 xenobiotics studied, because removal efficiencies were not found for diazepam, simazine and erythromycin at this ozone dose in batch conditions and with secondary treatment effluent. We report new information on removal efficiencies at this ozone dose for diazepam, simazine and erythromycin.

CONCLUSIONS

This study classifies 12 xenobiotics into high-oxidizable, medium-oxidizable and low-oxidizable categories. The effective dose of ozone needed to obtain a removal efficiency above 70% was found to be at least $0.2 \text{ gO}_3 \text{ gDOC}^{-1}$ for

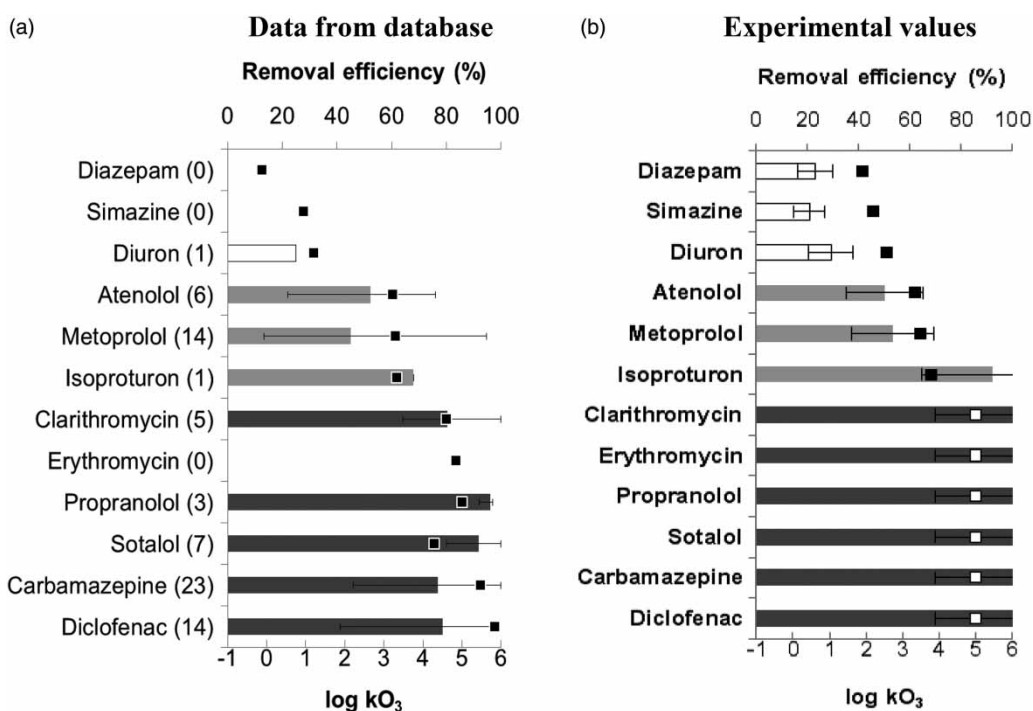


Figure 3 | Removal efficiencies (bar) and k_{O_3} (square) for 12 xenobiotics: (a) from the database (ozone dose between 0.2 and 0.4 $gO_3 gDOC^{-1}$), standard deviation with black line, number of data available in brackets; (b) from our experiments (one value measured with ozone dose: 0.2 $gO_3 gDOC^{-1}$), the error bars are determined as described in Choubert et al. (2012), full squares for accurately measured k_{O_3} , empty squares for the minimal estimate. The colors of the bars identify the three groups: low-oxidizable (white), medium-oxidizable (light gray) and high-oxidizable (dark gray) xenobiotics.

clarithromycin and diclofenac, 0.4 $gO_3 gDOC^{-1}$ for atenolol, metoprolol, propranolol and sotalol, and 0.6 $gO_3 gDOC^{-1}$ for diuron, isoproturon and erythromycin. The study also shows that the direct oxidation mechanism predominates for high-oxidizable xenobiotics, while the indirect oxidation mechanism predominates for medium-oxidizable and low-oxidizable xenobiotics. Future work will address the determination of oxidation rate constants for a broader range of xenobiotics, and the identification of generated by-products. It will also aim to develop a numerical model to optimize ozonation.

ASSOCIATED CONTENT

SPM1: all references used to complete the database; SPM1_reference_database.xlsx

SPM2: The database compiling information extracted from 33 publications on the ozonation of selected xenobiotics; SPM2_database.docx

SPM3: All by-products identified in the 33 publications for selected xenobiotics; SPM3_Byproducts.xlsx

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REFERENCES

- Beltrán, F. J., García-Araya, J. F., Rivas, J., Álvarez, P. M. & Rodriguez, E. 2000 Kinetics of simazine advanced oxidation in water. *Journal of Environmental Science and Health - Part B Pesticides. Food Contaminants and Agricultural Wastes* **35** (4), 439–454.
- Benitez, F. J., Real, F. J., Acero, J. L. & Garcia, C. 2007 Kinetics of the transformation of phenyl-urea herbicides during ozonation of natural waters: rate constants and model predictions. *Water Research* **41** (18), 4073–4084.
- Benner, J., Salhi, E., Ternes, T. & von Gunten, U. 2008 Ozonation of reverse osmosis concentrate: kinetics and efficiency of beta blocker oxidation. *Water Research* **42** (12), 3003–3012.

- Besnault, S., Martin Ruel, S., Baig, S., Heiniger, B., Esperanza, M., Budzinski, H., Le Menach, K., Miège, C. & Coquery, M. 2012 Reduction of refractory micropollutants in treated wastewater by advanced tertiary treatments. In: *IWA World Water Congress and Exhibition*, 16–21 September 2012, Busan, South Korea, p. 3.
- Buxton, G. V., Greenstock, C. L., Helman, W. P. & Ross, A. B. 1988 Critical review of rate constants for oxidation of hydrated electrons, hydrogen atoms and hydroxyl radicals (AOH/AO-) in aqueous solutions. *J. Phys. Chem. Ref. Data* **17**, 515–886.
- Choubert, J. M., Martin Ruel, S., Esperanza, M., Budzinski, H., Miège, C., Lagarrigue, C. & Coquery, M. 2011 Limiting the emissions of micropollutants: what efficiency can we expect from wastewater treatment plants? *Water Science and Technology* **63** (1), 57–65.
- Choubert, J. M., Martin-Ruel, S., Miège, C. & Coquery, M. 2012 Should rules for calculating removal rates of trace organic and inorganic compounds in wastewater plants be upgraded? In: *IWA World Water Congress*, 16–21 September 2012, Busan, South Korea, p. 12.
- Elovitz, M. S. & von Gunten, U. 1999 Hydroxyl radical/ozone ratios during ozonation processes. I. The R_{ct} concept. *Ozone Sci. Eng.* **21**, 239–260.
- Falás, P., Andersen, H. R., Ledin, A. & La Cour Jansen, J. 2012 Occurrence and reduction of pharmaceuticals in the water phase at Swedish wastewater treatment plants. *Water Science and Technology* **66**, 783–791.
- Gabet-Giraud, V., Miège, C., Choubert, J. M., Ruel, S. M. & Coquery, M. 2010 Occurrence and removal of estrogens and beta blockers by various processes in wastewater treatment plants. *Science of the Total Environment* **408**, 4257–4269.
- Gerrity, D., Gamage, S., Jones, D., Korshin, G. V., Lee, Y., Pisarenko, D., von Gunten, U., Wert, E. & Snyder, S. A. 2012 Development of surrogate correlation models to predict trace organic contaminant oxidation and microbial inactivation during ozonation. *Water Research* **46** (19), 6257–6272.
- Heberer, T. 2002 Occurrence, fate, and removal of pharmaceutical residues in the aquatic environment: a review of recent research data. *Toxicology Letters* **131** (1–2), 5–17.
- Hollender, J., Zimmermann, S. G., Koepke, S., Krauss, M., Mc Ardell, C. S., Ort, C., Singer, H., Von Gunten, U. & Siegrist, H. 2009 Elimination of organic micropollutants in a municipal wastewater treatment plant upgraded with a full-scale post-ozonation followed by sand filtration. *Environmental Science and Technology* **43** (20), 7862–7869.
- Huber, M. M., Canonica, S., Park, G.-Y. & von Gunten, U. 2003 Oxidation of pharmaceuticals during ozonation and advanced oxidation processes. *Environmental Science and Technology* **37** (5), 1016–1024.
- Huber, M. M., Göbel, A., Joss, A., Hermann, N., Löffler, D., Mc Ardell, C. S., Ried, A., Siegrist, H., Ternes, T. A. & von Gunten, U. 2005 Oxidation of pharmaceuticals during ozonation of municipal wastewater effluents: a pilot study. *Environmental Science and Technology* **39** (11), 4290–4299.
- Lee, Y., Kovalova, L., Mc Ardell, C. S. & von Gunten, U. 2014 Prediction of micropollutant elimination during ozonation of a hospital wastewater effluent. *Water Research* **64**, 134–148.
- Martin Ruel, S., Esperanza, M., Choubert, J. M., Valor, I., Budzinski, H. & Coquery, M. 2010 On-site evaluation of the efficiency of conventional and advanced secondary processes for the removal of 60 organic micropollutants. *Water Science and Technology* **62**, 2970–2978.
- Martin Ruel, S., Choubert, J. M., Esperanza, M., Miège, C., Navalón Madrigal, P., Budzinski, H., le Ménach, K., Lazarova, V. & Coquery, M. 2011 On-site evaluation of the removal of 100 micro-pollutants through advanced and conventional treatments for re-use applications. *Water Science and Technology* **63** (11), 2486–2497.
- Meunier, L., Canonica, S. & von Gunten, U. 2006 Implications of sequential use of UV and ozone for drinking water quality. *Water Research* **40** (9), 1864–1876.
- Penru, Y., Miège, C., Roussel-Galle, A., Dherret, L., Guillon, A., Esperanza, M., Martin Ruel, S., Coquery, M. & Choubert, J. M. 2015 Optimisation of full-scale ozonation tertiary treatment for micropollutants removal. In: *IWA World Water Congress and Exhibition*, 21–26 September 2014, Lisbon, Portugal, p. 6.
- Rosal, R., Rodríguez, A., Perdigón-Melón, J. A., Petre, A., García-Calvo, E., Gómez, M. J., Agüera, A. & Fernández-Alba, A. R. 2010 Occurrence of emerging pollutants in urban wastewater and their removal through biological treatment followed by ozonation. *Water Research* **44** (2), 578–588.
- Staelin, J. & Hoigne, J. 1985 Decomposition of ozone in water in the presence of organic solutes acting as promoters and inhibitors of radical chain reactions. *Environmental Science and Technology* **19**, 1206–1213.
- Snyder, S. A., Wert, E. C., Rexing, D. J., Zegers, R. E. & Drury, D. D. 2006 Ozone oxidation of endocrine disruptors and pharmaceuticals in surface water and wastewater. *Ozone: Science and Engineering* **28** (6), 445–460.
- Ternes, T., Janex-Habibi, T., Knaker, N., Kreuzinger, N. & Siegrist, H. 2004 Assessment of technologies for the removal of pharmaceuticals and personal care products in sewage and drinking water facilities to improve the indirect potable water reuse. Contract No. EVK1-CT-2000-00047.
- Verlicchi, P., Al Aukidy, M. & Zambello, E. 2012 Occurrence of pharmaceutical compounds in urban wastewater: removal, mass load and environmental risk after a secondary treatment – a review. *Science of the Total Environment* **429**, 123–155.
- Wert, E. C., Rosario-Ortiz, F. L. & Snyder, S. A. 2009 Effect of ozone exposure on the oxidation of trace organic contaminants in wastewater. *Water Research* **43** (4), 1005–1014.
- Yao, C. C. D. & Haag, W. R. 1991 Rate constants for direct reactions of ozone with several drinking water contaminants. *Water Research* **25** (7), 761–773.

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