

# **Prediction of micropollutant elimination during ozonation of a hospital wastewater effluent**

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## 24 **Abstract**

25 Determining optimal ozone doses for organic micropollutant elimination during wastewater  
26 ozonation is challenged by the presence of a large number of structurally diverse micropollutants for  
27 varying wastewater matrices compositions. A chemical kinetics approach based on ozone and  
28 hydroxyl radical ( $\bullet\text{OH}$ ) rate constant and measurements of ozone and  $\bullet\text{OH}$  exposures is proposed to  
29 predict the micropollutant elimination efficiency. To further test and validate the chemical kinetics  
30 approach, the elimination efficiency of 25 micropollutants present in a hospital wastewater effluent  
31 from a pilot-scale membrane bioreactor (MBR) were determined at pH 7.0 and 8.5 in bench-scale  
32 experiments with ozone alone and ozone combined with  $\text{H}_2\text{O}_2$  as a function of DOC-normalized  
33 specific ozone dose ( $\text{gO}_3/\text{gDOC}$ ). Furthermore, ozone and  $\bullet\text{OH}$  exposures,  $\bullet\text{OH}$  yields, and  $\bullet\text{OH}$   
34 consumption rates were determined. Consistent eliminations as a function of  $\text{gO}_3/\text{gDOC}$  were  
35 observed for micropollutants with similar ozone and  $\bullet\text{OH}$  rate constants. They could be classified  
36 into five groups having characteristic elimination patterns. By increasing the pH from 7.0 to 8.5, the  
37 elimination levels increased for the amine-containing micropollutants due to the increased apparent  
38 second-order ozone rate constants while decreased for most micropollutants due to the diminished  
39 ozone or  $\bullet\text{OH}$  exposures. Increased  $\bullet\text{OH}$  quenching by effluent organic matter and carbonate with  
40 increasing pH was responsible for the lower  $\bullet\text{OH}$  exposures. Upon  $\text{H}_2\text{O}_2$  addition, the elimination  
41 levels of the micropollutants slightly increased at pH 7 (<8%) while decreased considerably at pH  
42 8.5 (up to 31%). The elimination efficiencies of the selected micropollutants could be predicted  
43 based on their ozone and  $\bullet\text{OH}$  rate constants (predicted or taken from literature) and the determined  
44 ozone and  $\bullet\text{OH}$  exposures. Reasonable agreements between the measured and predicted elimination  
45 levels were found, demonstrating that the proposed chemical kinetics method can be used for a  
46 generalized prediction of micropollutant elimination during wastewater ozonation. Out of 67

analyzed micropollutants, 56 were present in the tested hospital wastewater effluent. Two-thirds of the present micropollutants were found to be ozone-reactive and efficiently eliminated at low ozone doses (e.g., >80% for  $\text{gO}_3/\text{gDOC} = 0.5$ ).

**Keywords:** ozonation, advanced oxidation process, micropollutant, pharmaceutical, hospital wastewater, QSAR

## 1. Introduction

In recent years, ozonation has been intensively tested as an advanced wastewater treatment technology from laboratory- to full-scale studies and demonstrated to be a useful, economically feasible method to improve the quality of municipal wastewater effluents (Flyborg et al., 2010; Gerrity et al., 2011 & 2012; Hollender et al., 2009; Huber et al., 2005; Lee et al., 2013; Margot et al., 2013; Nakada et al., 2007; Reungoat et al., 2012; von Sonntag and von Gunten, 2012; Zimmermann et al., 2011). These studies have shown that ozonation of secondary wastewater effluents can achieve significant abatement of many organic micropollutants and inactivation of bacteria and viruses at reasonable specific ozone doses (e.g.,  $\text{gO}_3/\text{gDOC} = 0.5 - 1.0$  in which the mass-based ozone to dissolved organic carbon ratio is a common operating parameter for ozone applications). Significant reductions of *in vitro* and *in vivo* toxicities were also demonstrated after ozonation or ozonation followed by biological filtration (Escher et al., 2009; Macova et al., 2010; Reungoat et al., 2012; Stalter et al., 2010a & 2010b).

The presence of a large number of structurally diverse micropollutants in wastewater matrices from various sources has been found to be challenging for ozonation process design for

micropollutant elimination (Lee et al., 2013). The number of organic micropollutants in wastewaters is up to several hundred (Oulton et al., 2010), which makes it cost-prohibitive and impractical to measure their elimination efficiencies individually. Wastewater quality parameters such as effluent organic matter (EfOM) or pH can vary considerably depending on the wastewater sources or operating conditions of wastewater treatment plants. EfOM is the main sink for ozone and OH radicals ( $\bullet$ OH), thus it has been difficult to predict the micropollutant elimination efficiency in wastewater effluents containing EfOMs with different concentration and characteristics.

A previous study showed that these challenges can be solved using an approach based on chemical kinetics (Lee et al., 2013). The elimination of a micropollutant (P) during ozonation is achieved by its reaction with ozone and  $\bullet$ OH, the latter is produced from the ozone decomposition (von Sonntag and von Gunten, 2012). The elimination of P in terms of logarithmic relative residual concentration of P can be predicted if the ozone and  $\bullet$ OH rate constant (i.e.,  $k_{O_3}$  and  $k_{\bullet OH}$ ) and the ozone and  $\bullet$ OH exposures ( $\int [O_3]dt$  and  $\int [\bullet OH]dt$ ) are known (eq 1).

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

Ozone reacts selectively with compounds containing electron-rich moieties (ERMs), such as phenols, anilines, activated aromatics, amines, organic sulfurs, and olefins with  $k_{O_3}$ -values typically ranging from  $10^3 - 10^7 \text{ M}^{-1} \text{ s}^{-1}$  at pH 7 (Lee and von Gunten, 2010). Quantitative structure-activity relationships (QSARs) have been found between the logarithmic  $k_{O_3}$ -values for the ozone reactions with compounds having a common ERM vs. Hammett or Taft sigma constants as substituent descriptor variables. These QSARs were found to be able to predict the  $k_{O_3}$ -values for various organic compounds within a factor of 1/3 – 3 compared to measured values (Lee and von Gunten, 2012).  $\bullet$ OH is a less selective oxidant with  $k_{\bullet OH}$ -values generally differing within only a factor of 3 for most organic compounds ( $k_{\bullet OH} = 3 \times 10^9 - 10^{10} \text{ M}^{-1} \text{ s}^{-1}$ , Buxton et al., 1988; NDRL/NIST Solution

Kinetic Database, <http://kinetics.nist.gov/solution/>). A group contribution method has been developed and demonstrated to be able to predict the  $k_{\bullet\text{OH}}$ -values for various compounds within a factor of 1/2 – 2 compared to measured values (Minakata et al., 2009). Based on eq 1, ozone-reactive micropollutants with ERMs can be more efficiently eliminated than ozone-resistant ones without ERMs due to the combined reaction with ozone and  $\bullet\text{OH}$ .

It was shown previously that similar  $\bullet\text{OH}$  exposures were achieved at the same specific ozone dose (i.e.,  $\text{gO}_3/\text{gDOC}$ ) during ozonation of 10 municipal wastewater effluents from Australia, Switzerland, and the USA regardless of water qualities (Lee et al., 2013). Variations of the ozone exposures for the same  $\text{gO}_3/\text{gDOC}$  were within a factor of 4 and were larger than the variations of the  $\bullet\text{OH}$  exposures that were within a factor of 2. Nevertheless, the large variations of the ozone exposure affected only the elimination efficiency of ozone-reactive micropollutants with elimination levels already close to the quantification limits (e.g., >95% elimination) for low ozone doses (e.g.,  $\text{gO}_3/\text{gDOC} < 0.5$ ). Overall, it was concluded that the elimination of micropollutants having the same or similar  $k_{\text{O}_3}$ - and  $k_{\bullet\text{OH}}$ -values was comparable at the same specific ozone dose ( $\text{gO}_3/\text{gDOC}$ ) during ozonation of wastewater effluents (Lee et al., 2013). Therefore, the specific ozone dose, and the  $k_{\text{O}_3}$ - and  $k_{\bullet\text{OH}}$ -values were identified as the key parameters to predict and generalize the elimination efficiency of micropollutants during ozonation of municipal wastewater effluent. To further test, validate, and upgrade the afore-described chemical kinetics approach, more measurements of the ozone and  $\bullet\text{OH}$  exposures in wastewater effluents with a range of matrix characteristics are recommended considering the still limited information for these parameters. Studies for comparing the measured and predicted elimination of micropollutants covering a broader range of chemical structure are also needed.

•OH exposure during ozonation has been determined indirectly from the decrease of •OH-probe compounds (ozone-resistant,  $k_{O_3} < 1 \text{ M}^{-1} \text{ s}^{-1}$ ) and using eq 1. *Para*-chlorobenzoic acid (*p*CBA) has been widely used as an •OH-probe compound that has to be spiked to test samples before ozonation (von Gunten and von Sonntag, 2012). Any ozone-resistant micropollutants originally present in test samples can also be used as an •OH-probe compound. Direct measurements of the ozone exposure from the ozone decay curves are difficult in wastewater effluents due to the rapid ozone consumption especially for  $\text{gO}_3/\text{gDOC} < 0.5$  (Lee et al., 2013). The ozone exposure can also be indirectly determined from a decrease of ozone-probe (or ozone-reactive) compounds and using eq 1 after correcting the elimination of the ozone-probe compound by •OH. However, the prediction of the elimination for micropollutants based on the ozone exposures determined by the indirect method was not successful in laboratory- or pilot-scale wastewater ozonation experiments (Huber et al. 2005; Hübner et al., 2013).

Hospital wastewaters contain various pharmaceuticals and disinfectants in high concentrations (Kovalova et al., 2012; Kovalova et al., 2013; Ort et al., 2010; Weissbrodt et al, 2009). They also contain pathogens and antibiotic resistant bacteria, which are of considerable public health concern (Blanch et al., 2003; Reinthaler et al., 2003). Separate treatment of hospital wastewater at the source has been thus proposed and tested as it avoids dilution of such contaminants of concern due to mixing with the municipal wastewaters and minimize their losses into the environment via sewer leaks and overflows (Kovalova et al., 2012 & 2013; Verlicchi et al., 2010). Membrane bioreactors (MBRs) have been shown to be a promising technology for separate treatment of hospital wastewaters due to their high removal efficiency of microorganisms, efficient nutrient removal, and small system footprint (Beier et al., 2011; Kovalova et al., 2012; Mahnik et al., 2007). Nevertheless, to achieve sufficient micropollutant elimination, additional treatment steps beyond the biological

treatment process were required such as ozonation or powered activated carbon (PAC) addition (Kovalova et al., 2013; Oulton et al., 2010). EfOM characteristics of the MBR permeate can differ from those from conventional activated sludge because larger biopolymers (e.g., >10 kDa) can be removed by ultrafiltration in the MBR (see Supporting Information, Figure S1). Considering these characteristics of hospital wastewater effluents treated by MBR (i.e., larger number of structurally diverse micropollutants and smaller average size of EfOM), they are a good candidate to test the chemical kinetics approach for predicting micropollutant elimination during ozonation.

To test and validate the chemical kinetics approach for micropollutant elimination prediction, a hospital wastewater effluent from a pilot-scale MBR was selected and treated in a bench-scale with ozone alone and the  $O_3/H_2O_2$  advanced oxidation process (AOP) for various specific ozone doses ( $gO_3/gDOC$ ). The pH was set to 7.0 and 8.5 to test the pH-effect in a typical pH-range of municipal wastewater effluents. The elimination levels of 25 micropollutants originally present in the wastewater effluent at concentrations  $>0.1 \mu g/L$  were quantified after each treatment and compared with the model predictions. The  $k_{O_3}$ - and  $k_{\bullet OH}$ -values for the selected micropollutants were taken from literature or estimated using a QSAR approach (Lee et al., 2012) and the group contribution method (Minakata et al., 2009), respectively, when not available. In addition, the ozone and  $\bullet OH$  exposures as a function of  $gO_3/gDOC$  were measured based on the elimination of ozone- and  $\bullet OH$ -probe compounds. The  $\bullet OH$  yield and the  $\bullet OH$  reaction rate constant with EfOM were also determined. Elimination levels for 33 additional micropollutants detected in the tested hospital wastewater effluent were predicted using the same kinetic approach. Finally, the formation of bromate after ozonation was assessed.

## **2. Materials and Methods**

### **2.1. Standards and reagents**

All chemicals and solvents (95% purity or higher) were used as received from various commercial suppliers. Ozone stock solutions (1 – 1.5 mM) were produced by sparging ozone containing oxygen gas through deionized water that was cooled in an ice bath. An ozone generator from Innovatec, Rheinbach (model CMG 3-3, Germany) was used. Stock solutions of hydrogen peroxide (10 mM) were prepared by diluting a ~30% H<sub>2</sub>O<sub>2</sub> solution from Sigma-Aldrich. Ozone and H<sub>2</sub>O<sub>2</sub> stock solutions were standardized spectrophotometrically based on their molar absorption coefficients:  $\epsilon = 3000 \text{ M}^{-1} \text{ cm}^{-1}$  at 258 nm (Huber et al., 2003) and  $\epsilon = 40 \text{ M}^{-1} \text{ cm}^{-1}$  at 240 nm for H<sub>2</sub>O<sub>2</sub> (Bader et al., 1998).

### **2.2. Hospital wastewater effluents**

Hospital wastewater effluents were taken as composite samples (24 hrs) from a pilot membrane bioreactor (MBR) installed at the cantonal hospital in Baden, Switzerland. The MBR was operating continuously for one year from April 2009 to March 2010 to treat 0.5% of the hospital wastewater (1.2 m<sup>3</sup> per day) taken flow-proportionally from the hospital sewer collection system. Water quality parameters of the MBR permeate used for ozonation experiments were: DOC = 5.1 mgC/L, pH = 8.5, alkalinity = 7.7 mM as HCO<sub>3</sub><sup>-</sup>, NH<sub>4</sub><sup>+</sup> = <6 µgN/L, NO<sub>2</sub><sup>-</sup> = 1 µgN/L, NO<sub>3</sub><sup>-</sup> = 4.2 mgN/L, and Br<sup>-</sup> = 32 µg/L. The pH of the wastewater effluent during the MBR operation was 8.1 – 8.5. Further details of the MBR pilot plant can be found elsewhere (Kovalova et al., 2012).

### **2.3. Ozonation of wastewater effluent**



The sampled hospital wastewater effluent (i.e., MBR permeate) was analysed for the presence of 67 target micropollutants including pharmaceuticals, their metabolites, and corrosion inhibitors (SI, Tables S1 and S2). Among these target micropollutants, 25 compounds (Table 1) were selected for assessing their elimination efficiency during ozonation. The ambient concentration of the 25 compounds were  $>0.1 \mu\text{g/L}$  except bezafibrate (Figure S2). As the elimination behaviour of bezafibrate as an ozone-probe compound was important in this study, it was spiked to the wastewater effluent to achieve  $1.6 \mu\text{g/L}$ . Elimination of the remaining 42 compounds could not be determined because their concentrations were below the method quantification limit, or were too low to determine elimination levels  $>50\%$ , or the uncertainty of the analytical method was too high.

Ozonation was performed in bench-scale using the wastewater effluent at pH 8.5 (original) and at pH 7.0 (adjusted by adding  $\text{H}_2\text{SO}_4$ ) and at a range of specific ozone doses ( $\text{gO}_3/\text{gDOC} = 0.25, 0.5, 1.0, \text{ and } 1.5$ ) and hydrogen peroxide doses (molar ratio  $\text{H}_2\text{O}_2/\text{O}_3 = 0, 0.25, \text{ and } 0.5$ ) at room temperature ( $22 \pm 2^\circ\text{C}$ ). Aliquots of ozone stock solutions were added under vigorous stirring to a series of identical reaction solutions (500 mL). For ozone/hydrogen peroxide experiments, stock solutions of hydrogen peroxide were added before the ozone addition. In experiments for the elimination of the indicator compounds (i.e., carbamazepine, bezafibrate, and *para*-chlorobenzoic acid (*pCBA*)), these compounds were spiked at  $1 \mu\text{M}$  (a few hundreds  $\mu\text{g/L}$ ) and then ozonated in a 25 mL reaction flask. After several hours (note that ozone decay was completed within 0.5 h), all ozonated samples were stored at  $4^\circ\text{C}$  prior to analysis of residual micropollutant concentrations. Bromide and bromate were also analysed for these samples. All ozonation experiments were performed in duplicate and average values are used. Description of further details of the bench-scale ozone experiments can be found elsewhere (Lee et al., 2013).

## 2.4. Prediction of ozone and $\bullet$ OH rate constants

Among the 56 micropollutants detected in the hospital wastewater effluent, the  $k_{O_3^-}$  or  $k_{\bullet OH^-}$  values were not available for 39 micropollutants (see Table S2). These rate constants were predicted in this study using a QSAR approach (Lee and von Gunten, 2012) and the group contribution method (Minakata et al., 2009), respectively. The following QSARs were used to estimate  $k_{O_3^-}$ -values:  $\log(k_{amine}) = 6.13 - 1.00\sum\sigma^*$  for amines such as lidocaine, ranitidine, sotalol, atenolol-acid, venlafaxine, and gabapentin;  $\log(k_{BZD}) = -0.04 - 3.35\sum\sigma_p^+$  for benzene derivatives such as furosemide, lidocaine, and sotalol;  $\log(k_{ArNH_2}) = 7.15 - 1.54\sum\sigma_{o,m,p}^-$  for anilines such as furosemide and sulfapyridine. In these equations,  $\sigma^*$  are Taft sigma constants, and  $\sigma_p^+$  and  $\sigma_{o,m,p}^-$  are Hammett sigma constants (Lee and von Gunten, 2012). Further details for the estimation of  $k_{O_3^-}$  and  $k_{\bullet OH^-}$  values are described in Table S3.

## 2.5. Ozone and $\bullet$ OH exposure, $\bullet$ OH yield, and $\bullet$ OH consumption rate constant in a hospital wastewater effluent

Ozone exposures (i.e.,  $\int [O_3]dt$ ) were obtained from the area under the ozone decay curves or calculated indirectly from the elimination of carbamazepine (CMP) or bezafibrate (BZF) as ozone probe compounds (see results & discussion sections for further details).  $\bullet$ OH exposures (i.e.,  $\int [\bullet OH]$ ) were calculated from the elimination of *p*CBA (von Gunten, 2003a). The  $\bullet$ OH yield during wastewater effluent ozonation was determined by measuring formaldehyde formation in the presence of excess *tert*-butanol (Nöthe et al., 2009; Lee et al., 2013).  $\bullet$ OH reaction rate constant with wastewater matrix components were determined by a competition kinetic method using *tert*-butanol (Nöthe et al., 2009; Lee et al., 2013).

## 2.6. Analytical methods

A detailed description of the sample preparation and analysis for the 67 micropollutants can be found elsewhere (Kovalova et al., 2012). Briefly, samples were filtered with a 0.7 µm GF/F glass-fiber filter (Whatman, Dassel, Germany) and further with a 0.2 µm regenerated cellulose filter (Sartorius AG, Göttingen, Germany), spiked with isotope labelled internal standards and analysed in a single multi-compound method by online SPE-HPLC-MS/MS with a Triple Quadrupol mass spectrometer (TSQ Quantum Ultra, Thermo Fisher Scientific). Limits of quantification are listed in the Supporting Information (SI, Table S1). Concentrations of carbamazepine, bezafibrate, and *p*CBA in the 0.01 – 1 µM range were determined with an Agilent 1100 HPLC/UV system (Lee and von Gunten, 2010).

Ozone and hydrogen peroxide were determined by the indigo method (Bader and Hoigné, 1981) and the DPD/peroxidase method (Bader et al., 1988), respectively. Formaldehyde was determined by the pre-column derivatization into 2,4-dinitrophenyldrazone and subsequent HPLC/UV analysis (Lipari and Swarin, 1982). Dissolved organic carbon (DOC) was determined by a LC-OCD instrument (DOC-Labor, Karlsruhe, Germany) (Huber et al., 2011). Bromide was measured with ion chromatography (IC) with conductivity detection and bromate was measured with IC and UV detection after a post-column reaction (Salhi and von Gunten, 1999).

## 3. Results and Discussions

### 3.1. Grouping micropollutants based on ozone and •OH reaction rate constants

25 micropollutants were selected on the basis of their presence in the MBR permeate at concentrations of >0.1 µg/L (Table S1, Figure S2), which allows the determination of a wide range

of their elimination levels during ozonation (typically 0 – >90%). These compounds were then classified into five groups according to their  $k_{O_3}$ - and  $k_{\bullet OH}$ -values (Table 1). The  $k_{O_3}$ - and  $k_{\bullet OH}$ -values for these compounds were taken from literature (see footnotes in Table 1) or predicted using the QSAR and the group contribution method (Table S3). The criteria for grouping micropollutants based on  $k_{O_3}$ - and  $k_{\bullet OH}$ -values were proposed recently (Lee et al., 2013) and further adapted in this study.

Group I shows high reactivity to ozone and a criteria for  $k_{O_3, pH7}$  ( $k_{O_3}$ -value at pH 7)  $\geq 10^5 \text{ M}^{-1} \text{ s}^{-1}$  was applied previously. In this study, the criteria for  $k_{O_3}$  was lowered from previously  $10^5 \text{ M}^{-1} \text{ s}^{-1}$  to  $10^4 \text{ M}^{-1} \text{ s}^{-1}$ , because elimination patterns for the micropollutants having  $k_{O_3} \geq 10^4 \text{ M}^{-1} \text{ s}^{-1}$  were quite similar. In addition, two sub-groups in group I are proposed with the following criteria: group Ia =  $k_{O_3, pH7}$  and  $k_{O_3, pH8.5} \geq 10^4 \text{ M}^{-1} \text{ s}^{-1}$  and group Ib =  $k_{O_3, pH7} < 10^4 \text{ M}^{-1} \text{ s}^{-1}$  and  $k_{O_3, pH8.5} \geq 10^4 \text{ M}^{-1} \text{ s}^{-1}$ . These criteria were proposed to reflect the pH dependent  $k_{O_3}$ -values for amine-containing compounds which typically increase from  $<10^4 \text{ M}^{-1} \text{ s}^{-1}$  at pH 7 to  $>10^4 \text{ M}^{-1} \text{ s}^{-1}$  at pH 8.5 (a factor of 10 increase of the  $k_{O_3}$ -value per unit pH increase). Therefore, the elimination efficiency of group Ib can differ considerably within the pH range 7 – 8.5. Group Ia includes compounds with phenols, anilines (aromatic amine-N), olefins, thioethers, tertiary/secondary aliphatic amines with  $pK_a$  values of  $<9$ , and combinations thereof. Group Ib includes compounds with tertiary or secondary aliphatic amines with  $pK_a$  values of  $>9$ . Group Ia compounds include carbamazepine (olefin), clarithromycin (tertiary amine), diclofenac (aromatic amine-N), furosemide (aromatic amine-N), lidocaine (tertiary amine and activated benzene), mefenamic acid (aromatic amine-N or activated benzene), ranitidine (thioether and tertiary amine), sotalol (activated benzene and secondary amine), sulfamethoxazole (aromatic amine-N), and sulfapyridine (aromatic amine-N). The moieties in the parenthesis indicate the expected main reaction sites (for the chemical structures, see Table S2). Phenolic compounds

usually belong to group Ia (Lee et al., 2013) but in this study no phenolic micropollutants was quantified above 0.1 µg/L in the tested wastewater effluent. Group Ib includes atenolol-acid (secondary amine), 4-methylbenzotriazole (activated benzene), metoprolol (secondary amine), tramadol (tertiary amine), and venlafaxine (tertiary amine) (Table 1).

Group II compounds have intermediate reactivities with ozone ( $50 \leq k_{O_3, pH7}$  and  $k_{O_3, pH8.5} < 10^4$  M<sup>-1</sup> s<sup>-1</sup>) and include N(4)-acetyl-sulfamethoxazole, benzotriazole, and bezafibrate with activated benzenes and gabapentin with a primary amine as the ozone-reactive sites, respectively (Table 1). The  $k_{O_3}$ -values of benzotriazole and gabapentin increase by a factor of 10 and 30, respectively, with an increase of pH from 7 to 8.5 due to the presence of a dissociable triazole and primary amine moiety, respectively. Group III compounds have low reactivities with ozone ( $k_{O_3, pH7}$  and  $k_{O_3, pH8.5} < 50$  M<sup>-1</sup> s<sup>-1</sup>) while appreciable reactivities with •OH ( $k_{•OH} \geq 5 \times 10^9$  M<sup>-1</sup> s<sup>-1</sup>). Oxazepam, primidone, and valsartan were classified into group III. These compounds contain benzene with mono- or di-substitution(s) (e.g., alkyl or halogen) in which •OH shows still high reactivity due to its rapid benzene ring-addition mechanism (Minakata et al., 2009). In addition to weakly-activated benzenes, aliphatic hydrocarbons with electron-donating alkyl substituents and >5 C atoms can show high reactivity to •OH due to a rapid H-abstraction mechanism. Finally, fluconazole, iopromide, and levetiracetam were classified into group IV. Fluconazole and iopromide are composed of benzenes with multiple halogens, triazoles, or small hydrocarbon chains with electro-negative hydroxyl- and amide-moieties all of which show negligible reactivity to ozone and low reactivity to •OH. Similarly, levetiracetam is composed of short hydrocarbon chains with amide-moieties (Table S2).

### 3.2. Elimination pattern of each group of micropollutants

297 Duplicate ozonation experiments were performed for each treatment condition and each treated  
298 sample was analyzed twice. Figures 1 – 3 show the obtained percentage (%) elimination data for the  
299 selected 25 micropollutants (Table 1). Error bars represent standard deviations of the measurements  
300 at each treatment condition. The standard deviations were usually below 5% and increased up to 9%  
301 for only a few cases, indicating that the results were quite reproducible. Figure S3 or Table S4 shows  
302 the average % elimination data for each group of micropollutants.

303 Figure 1 shows the % elimination of the group Ia (carbamazepine, clarithromycin, diclofenac,  
304 furosemide, lidocaine, mefenamic acid, ranitidine, sotalol, sulfamethoxazole, and sulfapyridine) and  
305 group Ib (atenolol acid, 4-methylbenzotriazole, metoprolol, tramadol, and venlafaxine)  
306 micropollutants as a function of the specific ozone doses ( $\text{gO}_3/\text{gDOC} = 0.25, 0.5, 1.0, \text{ and } 1.5$ ) at pH  
307 7.0 and 8.5. The elimination of group Ia compounds was efficient: at  $\text{gO}_3/\text{gDOC} \geq 0.5$ , the  
308 elimination level approached the method quantification limit ( $>92\text{--}100\%$ ) at both pH conditions.  
309 Even at  $\text{gO}_3/\text{gDOC} = 0.25$ , the average elimination level was 80% (65–92%) which is still  
310 considerable (Figure S3). This elimination level is comparable to that observed in municipal  
311 wastewater effluents ( $\approx 91\%$ ) at the same specific ozone dose (i.e.,  $\text{gO}_3/\text{gDOC} = 0.25$ ) with a  
312 negligible of ozone demand exerted by nitrite (Lee et al., 2013). The high elimination efficiency for  
313 group Ia compounds can be attributed to their high apparent  $k_{\text{O}_3}$ -values ( $k_{\text{O}_3,\text{pH}7}$  and  $k_{\text{O}_3,\text{pH}8.5} > 10^4$   
314  $\text{M}^{-1} \text{ s}^{-1}$ , Table 1). Direct ozone reactions mainly contributed to the elimination of these compounds,  
315 i.e., 74% at pH 7.0 and 814% at pH 8.5 and the remaining  $\leq 26\%$  was due to the reaction with  $\bullet\text{OH}$   
316 (Figure S4). The elimination level at  $\text{gO}_3/\text{gDOC} = 0.25$  decreased slightly ( $<6\%$ ) with an increase of  
317 pH from 7.0 to 8.5 for carbamazepine, diclofenac, furosemide, mefenamic acid, ranitidine,  
318 sulfamethoxazole, and sulfapyridine. These compounds except sulfapyridine show near constant  
319  $k_{\text{O}_3,\text{pH}7}$ - and  $k_{\text{O}_3,\text{pH}8.5}$ -values as the corresponding ozone-reactive moieties do not change their

320 speciation with variations in pH (Table 1). The reduction in elimination efficiency can be explained  
321 by the slightly reduced ozone exposure in the tested wastewater effluent at the higher pH caused by a  
322 more rapid ozone decay (Hoigné, 1998). In contrast, the elimination level slightly increased for  
323 clarithromycin and lidocaine by 14% and 9%, respectively, whose  $k_{O_3,pH-8.5}$ -values are 24- and 5-fold  
324 larger than  $k_{O_3,pH-7}$ -values (Table 1). For these compounds, the enhancement in the elimination level  
325 by the larger  $k_{O_3}$ -value outcompeted the smaller ozone exposure at the higher pH.

326 The elimination efficiency of group Ib compounds was lower than for group Ia, especially for pH  
327 7, which is consistent with their lower  $k_{O_3}$ -values (Table 1). The average elimination levels of group  
328 Ib compounds at pH 7 were 36% and 77% at  $g_{O_3}/gDOC$  of 0.25 and 0.5, respectively, and >98% at  
329  $g_{O_3}/gDOC \geq 1.0$ . For pH 8.5, the average elimination levels were 53% and 96% at  $g_{O_3}/gDOC$  of  
330 0.25 and 0.5, respectively, which were about 20% larger compared to those for pH 7. Near complete  
331 elimination (>98%) was achieved at  $g_{O_3}/gDOC \geq 0.5$  with an elimination pattern similar to the group  
332 Ia compounds (Figure S3). This result is consistent with the larger ( $22 \pm 6$ -fold)  $k_{O_3,pH8.5}$ -values than  
333  $k_{O_3,pH7}$ -values for the group Ib compounds. The contribution of the direct ozone reaction to the  
334 overall elimination for the group Ib compounds was 26% and 67% at pH 7.0 and 8.5, respectively,  
335 which was lower than for group Ia (Figure S4). For pH 7,  $\bullet OH$  contributed more than ozone to the  
336 elimination of group Ib compounds due to relatively low  $k_{O_3,pH7}$ -values ( $<10^4 \text{ M}^{-1} \text{ s}^{-1}$ ).

337 The % eliminations of group II (N(4)-acetyl-sulfamethoxazole, benzotriazole, bezafibrate, and  
338 gabapentin), group III (oxazepam, primidone, and valsartan), and group IV compounds (fluconazole,  
339 iopromide, and levetiracetam) are shown in Figure 2. The elimination of *p*CBA as an  $\bullet OH$ -probe  
340 compound is also shown in Figure 2 for comparison. The elimination efficiency of the group II  
341 compounds is lower than that of groups Ia & Ib, which is consistent with their lower  $k_{O_3}$ -values  
342 (Table 1). The average elimination levels of the group II compounds at pH 7 were 28%, 55%, 92%,

343 and >95% at gO<sub>3</sub>/gDOC of 0.25, 0.5, 1.0, and 1.5, respectively. At pH 8.5, the average elimination  
344 levels were slightly lower: 19%, 46%, 88%, and >95% at the same specific ozone doses, respectively  
345 (Figure S3). For the group II compounds, reactions with •OH are estimated to be mainly responsible  
346 for their elimination and their contribution is 89% and 92% at pH 7 and 8.5, respectively (Figure S4).  
347 Therefore, the lower elimination level with the pH increase for the group II compounds is mainly  
348 attributed to a reduced diminished •OH exposure. It will be shown later that the •OH consumption  
349 rate increases by a factor of 2 with an increase of pH from 7.0 to 8.5, which is consistent with a  
350 reduced •OH exposure.

351 The average elimination levels of group III compounds at pH 7 were 29%, 55%, 91%, and >96%  
352 at gO<sub>3</sub>/gDOC of 0.25, 0.5, 1.0, and 1.5, respectively. At pH 8.5, the average elimination levels were  
353 slightly lower and were 21%, 45%, 79%, and >92% at the same specific ozone doses, respectively  
354 (Figure S3). This similar elimination efficiency for the group II and III compounds can be explained  
355 by the fact that •OH is mainly responsible for their elimination (Figure S4) and the  $k_{\bullet\text{OH}}$ -values for  
356 these compounds are quite similar ( $6.8 \times 10^9 < k_{\bullet\text{OH}} < 10^{10} \text{ M}^{-1} \text{ s}^{-1}$ , Table 1). The lower elimination  
357 levels at the higher pH observed for oxazepam and valsartan can again be explained by a lower •OH  
358 exposure (see below). The elimination levels of *p*CBA were slightly lower than that of group II and  
359 III compounds but the elimination behaviour was quite similar, which is consistent with the  
360 reactivity of *p*CBA with ozone and •OH ( $k_{\text{O}_3} < 1 \text{ M}^{-1} \text{ s}^{-1}$  and  $k_{\bullet\text{OH}} = 5 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ , von Gunten,  
361 2003a).

362 The elimination levels of group IV compounds (fluconazole, iopromide, and levetiracetam) were  
363 lower than for the other groups and were 17%, 31%, 64%, and >83% for pH 7 and 13%, 31%, 50%,  
364 and >69% for pH 8.5 at gO<sub>3</sub>/gDOC of 0.25, 0.5, 1.0, and 1.5, respectively (Figure S3). The lower  
365 elimination of group IV is attributed to the lower  $k_{\bullet\text{OH}}$ -values for these compounds,  $k_{\bullet\text{OH}} =$



(3.3–4.4)×10<sup>9</sup> M<sup>-1</sup> s<sup>-1</sup> (Table 1). The reaction of •OH was estimated to be 100% responsible for the elimination of fluconazole and levetiracetam. For iopromide, however, the reaction of •OH explained only 84% and 53% of its elimination at pH 7 and 8.5, respectively (Figure S4). As iopromide has negligible reactivity to ozone ( $k_{O_3} < 0.8 \text{ M}^{-1} \text{ s}^{-1}$ , Table 1), the reaction of ozone is not expected to contribute to the observed additional elimination of iopromide. Similar underestimation for the elimination of iopromide by •OH reaction was also observed previously during ozonation of river waters (Huber et al., 2003).

### 3.3. Effect of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>)

H<sub>2</sub>O<sub>2</sub> can be added to an ozonation process to accelerate ozone decay and thus the •OH formation rate (von Gunten, 2003a). However, it was previously shown that H<sub>2</sub>O<sub>2</sub> addition during wastewater ozonation had a marginal influence on the micropollutant elimination efficiency (Lee et al., 2013; Kovalova et al. 2013). This is caused by a rapid consumption of ozone by EfOM (within a few minutes) for relatively low specific ozone doses ( $\text{gO}_3/\text{gDOC} < 0.5$ ). This reaction outcompetes the relatively slow reaction of ozone with H<sub>2</sub>O<sub>2</sub>. Therefore, there is a limited effect on the elimination efficiency of the ozone-reactive micropollutants (i.e., group I), which is already high (>80% elimination). For ozone-resistant micropollutants (i.e., groups III and IV), the elimination efficiency increased only slightly (<10%) by addition of H<sub>2</sub>O<sub>2</sub> during ozonation of wastewater effluents at pH ~7 (Lee et al., 2013). This can be attributed to the slightly higher yield of •OH in the O<sub>3</sub>/H<sub>2</sub>O<sub>2</sub> process compared to conventional ozonation. For drinking waters with lower DOC and high carbonate in which ozone decay is slow, nevertheless, it was shown that H<sub>2</sub>O<sub>2</sub> had a larger effect on the elimination efficiency of ozone-resistant micropollutants (Acero and von Gunten, 2001).

Figure 3 shows the % elimination of the groups II, III, and IV compounds during ozonation of wastewater effluent at pH 7.0 and 8.5 with  $\text{gO}_3/\text{gDOC} = 1.0$  and molar ratios of  $\text{H}_2\text{O}_2/\text{O}_3$  of 0, 0.25, and 0.5. For pH 7, the elimination level for all compounds changed little or slightly increased ( $<8\%$ ) upon  $\text{H}_2\text{O}_2$  addition, which is consistent with the results from a previous study (Lee et al., 2013). For pH 8.5, however, the  $\text{H}_2\text{O}_2$  addition ( $\text{H}_2\text{O}_2/\text{O}_3$  (mol/mol) = 0.5) resulted in reductions of the elimination levels by 16 – 31% for the group II compounds. This might be explained by the decreased ozone exposure upon the  $\text{H}_2\text{O}_2$  addition at pH 8.5 and the still important contribution of ozone to the elimination of group II compounds. The reaction rate of ozone with  $\text{H}_2\text{O}_2$  increases by a factor of 32 by increasing the pH from 7 to 8.5 (Staehelin and Hoigné, 1982), which may increase the ozone decay rate and therefore reduce the ozone exposure significantly at pH 8.5. For the group III and IV compounds, the elimination level changed marginally ( $<5\%$  decreases) except for oxazepam, primidone, and iopromide. The elimination level of *p*CBA increased 7% upon  $\text{H}_2\text{O}_2$  addition. This is consistent with previous observations that the  $\bullet\text{OH}$  scavenging rate or  $\bullet\text{OH}$  exposure is not significantly affected by  $\text{H}_2\text{O}_2$  addition and  $\bullet\text{OH}$  is mainly responsible for the elimination of these compounds (Acero and von Gunten, 2001). However, the elimination level for oxazepam, primidone, and iopromide decreased by 17%, 13%, and 12%, respectively. Analytical uncertainty might be responsible for this unexpected behavior, but the reason is currently not entirely clear. Overall, it is concluded that  $\text{H}_2\text{O}_2$  addition has a marginally positive (pH 7) or even a negative effect (pH 8.5) on the micropollutant elimination efficiency during ozonation of the selected hospital wastewater effluent.

### 3.4. $\bullet\text{OH}$ and ozone exposures

Figure 4 shows the  $\bullet\text{OH}$  exposures determined in the tested wastewater effluents at pH 7.0 and 8.5 as a function of the specific ozone dose. The  $\bullet\text{OH}$  exposure increased linearly with increasing ozone doses and the data could be approximated by using two linear regressions with the specific ozone dose ranges of  $0 \leq \text{gO}_3/\text{gDOC} < \sim 0.6$  (phase I) and  $0.6 < \text{gO}_3/\text{gDOC} \leq 1.7$  (phase II). The slope of the linear lines in Figure 4 represents the increase of  $\bullet\text{OH}$  exposure per specific ozone dose (i.e.,  $\Delta[\bullet\text{OH exposure}]/(\text{gO}_3/\text{gDOC})$ ) and was  $2.4 \times 10^{-10} \text{ M s}$  (phase I) and  $4.5 \times 10^{-10} \text{ M s}$  (phase II) for pH 7 and  $1.9 \times 10^{-10} \text{ M s}$  (phase I) and  $3.2 \times 10^{-10} \text{ M s}$  (phase II) for pH 8.5. The lower slopes in phase I compared to phase II could be due to the ozone consumption by EfOM moieties with less  $\bullet\text{OH}$  formation (e.g., olefins or tertiary amines). Alternatively, a decreasing  $\bullet\text{OH}$  scavenging rate by EfOM with increasing ozone dose due to EfOM oxidation might explain the higher slopes in the phase II compared to the phase I. Nevertheless, it should be noted that this is just an empirical interpretation of the two-phasic behavior of the  $\bullet\text{OH}$  exposure. The observed slopes in the phase II are within the ranges reported previously for municipal wastewater effluents ( $3.0 \times 10^{-10} - 5.3 \times 10^{-10} \text{ M s}$ , Lee et al., 2013).

Ozone exposures determined at various specific ozone doses are shown in Figure 5. The ozone exposures for  $\text{gO}_3/\text{gDOC} = 1$  were measured directly from the area under the ozone decay curves (Figure S5). The ozone exposures for  $\text{gO}_3/\text{gDOC}$  of 0 to 1 were determined indirectly on the basis of the elimination of carbamazepine (CMP) and bezafibrate (BZF) in the following two different specific ozone dose range, i.e.,  $\text{gO}_3/\text{gDOC} = 0.05-0.3$  using CMP and  $0.3-0.7$  using BZF, respectively. Eq 2 can be derived from a rearrangement of the eq 1 and used to calculate the ozone exposure:

$$\int [\text{O}_3] dt = - \frac{(\ln(\frac{[P]}{[P]_0}) + k_{\bullet\text{OH-P}} \int \bullet\text{OH} dt)}{k_{\text{O}_3\text{-P}}} \quad (2)$$

in which  $\ln\left(\frac{[P]}{[P]_0}\right)$  is the logarithmic elimination of the ozone-probe compound (P = CMP or BZF),  $\int[\bullet\text{OH}]dt$  is the  $\bullet\text{OH}$  exposure and can be calculated as  $-\frac{\ln\left(\frac{[p\text{CBA}]}{[p\text{CBA}]_0}\right)}{k_{\bullet\text{OH}-p\text{CBA}}}$  with  $k_{\bullet\text{OH}-p\text{CBA}} = 5 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ , and  $k_{\text{O}_3\text{-CMP}} = 3 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$  or  $k_{\text{O}_3\text{-BZF}} = 5.9 \times 10^2 \text{ M}^{-1} \text{ s}^{-1}$  (Huber et al., 2003). CMP and BZF were selected in this study based on their reliable, pH-independent, and representative  $k_{\text{O}_3}$ -values (high  $k_{\text{O}_3}$  for CMP and intermediate  $k_{\text{O}_3}$  for BZF), and their frequent occurrence in municipal wastewater effluents (Oulton et al., 2010). This indirect method for ozone exposure determination can be applied especially for low ozone doses (e.g.,  $\text{gO}_3/\text{DOC} < 0.5$ ) in which ozone decay is usually too fast to be measured using conventional kinetic methods. Nevertheless, it should be noted that this method gives a rough estimate for ozone exposure due to cumulative uncertainty in  $\ln\left(\frac{[P]}{[P]_0}\right)$ ,  $\int[\bullet\text{OH}]dt$ , and  $k_{\text{O}_3\text{-P}}$  values. The indirect method can be further calibrated against real ozone exposure measurements using rapid kinetic systems such as quench-flow or stopped-flow (Buffle et al., 2006a; Buffle et al., 2006b; Nöthe et al., 2009; Lee et al., 2013).

Figure 5 shows the logarithm of the ozone exposures (linear scale in the inset) determined at various specific ozone doses for pHs 7.0 and 8.5. The ozone exposure increased exponentially with increasing ozone dose with almost four orders of magnitude variation. For pH 7, the ozone exposures were  $0.6 \times 10^{-5}$ ,  $0.5 \times 10^{-3}$ , and  $0.8 \times 10^{-2} \text{ M s}$  for  $\text{gO}_3/\text{gDOC}$  of 0.25, 0.5, and 1.0, respectively. For pH 8.5, the ozone exposures were lower than at pH 7 and were  $0.4 \times 10^{-5}$ ,  $0.3 \times 10^{-3}$ , and  $0.2 \times 10^{-2} \text{ M s}$ , respectively, for the same specific ozone doses. The determined ozone exposures in the tested wastewaters at pH 7 are comparable or within literature values measured for municipal wastewater effluents at pH 7.2( $\pm 0.2$ ):  $1.5 \times 10^{-5}$ ,  $(0.2\text{--}2.8) \times 10^{-3}$ , and  $(0.4\text{--}1.3) \times 10^{-2} \text{ M s}$  for  $\text{gO}_3/\text{gDOC}$  of 0.25, 0.5, and 1.0, respectively, which were determined directly from the areas under the ozone decay curves (Lee et al., 2013).

### 3.5. Prediction of micropollutant elimination

The determined ozone and  $\bullet\text{OH}$  exposures (Figures 4 and 5) were used to predict the elimination levels of 25 micropollutants (Table 1) as a function of specific ozone dose by eq 1. Figure 6 shows that for both pH conditions, the elimination prediction is reasonable: for pH 7,  $r^2 = 0.87$ , and the standard errors of estimate ( $S_{y,x}$ ) = 9.6; for pH 8.5,  $r^2 = 0.84$ , and  $S_{y,x} = 11.6$ . This result clearly shows the usefulness of the chemical kinetic approach based on the measurements of the ozone and  $\bullet\text{OH}$  exposure and the  $k_{\text{O}_3}$  and  $k_{\bullet\text{OH}}$ -values in predicting elimination levels of various micropollutants. In addition, the indirect method for estimating ozone exposures using CMP or BZF as the ozone-probe compound was found to be applicable. Figures S6 – S9 show the measured and predicted % elimination of each group of micropollutants (i.e., group I – IV). The predictions were less accurate (lower  $r^2$  and  $S_{y,x}$  values) for ozone-reactive (e.g., group I) than for ozone-resistant compounds (e.g., group III), which indicates the relative larger uncertainty of the ozone exposures than the OH exposures. The less accurate prediction for pH 8.5 than pH 7.0 could be attributed to the different elimination behaviors of the group II, III, and IV compounds compared to that of *p*CBA for pH 8.5, which was mentioned earlier.

### 3.6. $\bullet\text{OH}$ yield and $\bullet\text{OH}$ consumption kinetics

As  $\bullet\text{OH}$  plays an important role for the elimination of ozone-refractory compounds, (a) the  $\bullet\text{OH}$  formation, and (b) the  $\bullet\text{OH}$  yields (moles of  $\bullet\text{OH}$  produced per mole of ozone consumed) as a function of specific ozone dose were investigated in the tested hospital wastewater effluent (Figure 7). The  $\bullet\text{OH}$  yield generally increased with increasing ozone dose, which could be approximated by a linear regression where the values in the parenthesis represent the 95% confidence intervals:  $\bullet\text{OH}$

yield (%) =  $6.7(\pm 2.7) \times (\text{gO}_3/\text{gDOC}) + 20.7(\pm 3.0)$ ,  $r^2 = 0.71$  for pH 7 and  $11.2(\pm 3.2) \times (\text{gO}_3/\text{gDOC}) + 22.0(\pm 3.6)$ ,  $r^2 = 0.83$  for pH 8.5. The determined  $\bullet\text{OH}$  yields for pH 7 (= 20 – 34%) are comparable to the values reported previously for municipal wastewater effluents while the  $\bullet\text{OH}$  yields for pH 8.5 (= 19 – 41%) were on average 6% higher compared to pH 7, which is opposite to the trend observed for the  $\bullet\text{OH}$  exposure. This contradiction can be explained by a significantly higher  $\bullet\text{OH}$  consumption rate with increasing pH, resulting in a lower  $\bullet\text{OH}$  exposure.

The  $\bullet\text{OH}$  consumption rate was determined by a competition kinetics method using *tert*-butanol as a competitor for  $\text{gO}_3/\text{gDOC} = 1$ . As shown in Figure 8, the  $\bullet\text{OH}$  consumption rate was  $1.5 \times 10^5 \text{ s}^{-1}$  at pH 7 and  $2.9 \times 10^5 \text{ s}^{-1}$  at pH 8.5. Using the information for the concentration of carbonate species in the tested wastewater effluent ( $[\text{HCO}_3^-/\text{CO}_3^{2-}] = 7.7 \text{ mM}$ ) and the  $\bullet\text{OH}$  reaction rate constant with carbonate species ( $k_{\bullet\text{OH}/\text{HCO}_3^-} = 8.5 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$  and  $k_{\bullet\text{OH}/\text{CO}_3^{2-}} = 3.9 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ , Buxton et al., 1988), the  $\bullet\text{OH}$  consumption rates by carbonate species were calculated to be  $5.0 \times 10^4$  and  $9.9 \times 10^4 \text{ s}^{-1}$  for pH 7.0 and 8.5, respectively, which are about 35% of the overall  $\bullet\text{OH}$  consumption rate. This indicates a significant formation of  $\text{CO}_3^{\bullet-}$  in the tested wastewater effluent. The increase in the  $\text{CO}_3^{2-}$  fraction of the total carbonate with increasing pH is responsible for the two-fold increase of the  $\bullet\text{OH}$  consumption rate by carbonate species. The remaining  $\bullet\text{OH}$  consumption rate is attributed to the contribution by EfOM allowing determination of the second-order rate constants for the reaction of  $\bullet\text{OH}$  with EfOM ( $k_{\bullet\text{OH}/\text{EfOM}}$ ) as  $k_{\bullet\text{OH}/\text{EfOM}} = 2.0 \times 10^4$  and  $4.1 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$  at pH 7 and 8.5, respectively. The ~two-fold greater  $k_{\bullet\text{OH}/\text{EfOM}}$ -value at pH 8.5 than at pH 7 might be attributed to deprotonation of phenol- or amine-moieties in EfOM resulting in higher  $\bullet\text{OH}$  reaction rate constants (Buxton et al., 1988). Overall, the ~two-fold increase of the overall  $\bullet\text{OH}$  consumption rate for pH 8.5 compared to pH 7 is consistent with the diminished  $\bullet\text{OH}$  exposure.

The average  $k_{\bullet\text{OH}/\text{EfOM}}$ -value during ozonation of municipal wastewater effluents at pH 7.2( $\pm 0.2$ ) was reported to be  $(2.1 \pm 0.6) \times 10^4 \text{ (mgC/L)}^{-1} \text{ s}^{-1}$  (Lee et al., 2013) or  $\sim 2.5 \times 10^4 \text{ (mgC/L)}^{-1} \text{ s}^{-1}$  (Lee and von Gunten, 2010; von Sonntag and von Gunten, 2012), which is similar to the  $k_{\bullet\text{OH}/\text{EfOM}}$ -value determined in this study for pH 7. However, it was reported previously that  $k_{\bullet\text{OH}/\text{EfOM}}$ -values increased with decreasing average MW of the EfOM (Dong et al., 2010). Our data support previous observations that  $k_{\bullet\text{OH}/\text{EfOM}}$ -values do not depend strongly on size characteristics of EfOM (Lee et al., 2013). The EfOM in the tested wastewater effluent is taken from the MBR permeate that is mainly composed of molecular weight (MW) fractions of  $< 1 \text{ kDa}$  due to the removal of larger biopolymer fractions ( $\text{MW} > 10 \text{ kDa}$ ) by ultrafiltration (Figure S1).

### **3.7. Prediction of the elimination for other micropollutants detected in hospital wastewater effluent**

Among the 67 target analytes monitored during the pilot-scale MBR operation for the hospital wastewater treatment, 56 micropollutants were detected in the MBR permeates (Kovalova et al., 2012 & 2013). For 25 micropollutants (Table 1), the elimination efficiency could be well predicted using the kinetic information (i.e., ozone and  $\bullet\text{OH}$  rate constants and exposures). The same approach can be used to predict the elimination efficiency of the remaining 31 micropollutants based on  $k_{\text{O}_3}$  and  $k_{\bullet\text{OH}}$ . For this, unknown  $k_{\text{O}_3}$ - and  $k_{\bullet\text{OH}}$ -values were estimated for 22 micropollutants using a QSAR and the group contribution methods, respectively (Tables S2 & S3). For the other 9 micropollutants, the  $k_{\text{O}_3}$ - and  $k_{\bullet\text{OH}}$ -values were taken from literature (Table S2). As a next step, these 31 micropollutants were classified into the five groups based on their  $k_{\text{O}_3}$ - and  $k_{\bullet\text{OH}}$ -values (Table S2). Based on this assessment, 38 among the 56 micropollutants belong to groups Ia & Ib, indicating  $\sim$ two-thirds of the micropollutants found in the hospital wastewater effluent can be efficiently

eliminated (e.g., >80% at  $\text{gO}_3/\text{gDOC} = 0.5$ ). It is also noteworthy that all iodinated contrast media belong to group IV (iomeprol, iopamidol, iopromide, and ioxitalamic) or group V (diatrizoate) compounds (Table S2), which require high specific ozone doses for sufficient elimination (e.g., ~70% elimination levels for  $\text{gO}_3/\text{gDOC} = 1.0$ ). A previous study found that over 80% of the micropollutant load in effluents of a MBR-treated hospital wastewater was due to iodinated contrast media (Kovalova et al., 2012).

### 3.8. Bromate formation

Ozonation of bromide-containing waters can form bromate, a probable human carcinogen with a drinking water standard of 10  $\mu\text{g/L}$  (von Gunten, 2003b). Information is currently limited for bromate formation levels during ozonation of municipal wastewater effluents. Figure S10 (or Table S5) shows the bromate formation at (a) pH 7 and (b) pH 8.5 as a function of the specific ozone dose after treatment of the selected hospital wastewater effluent with ozone alone and ozone/hydrogen peroxide. Under both pH conditions, bromate formation was less than 10  $\mu\text{g/L}$  at  $\text{gO}_3/\text{gDOC} \leq 1.0$ , and smaller at pH 8.5 than pH 7.0 which is consistent with lower exposures for ozone and  $\bullet\text{OH}$ . The low bromate formation is mainly attributed to the low initial bromide level of 33  $\mu\text{g/L}$ . Overall, the formation of the potentially carcinogenic bromate was not an issue for ozonation of the selected hospital wastewater.

## 4. Conclusions

- Combined information of chemical kinetics (ozone and  $\bullet\text{OH}$  rate constants) and water specific information (characterization of ozone and  $\bullet\text{OH}$  exposures as a function of specific ozone dose)



allows the prediction and generalization of the elimination efficiency of a large number of structurally diverse micropollutants. This was successfully demonstrated in this study for a hospital wastewater effluent from a MBR treatment.

- QSARs and the group contribution method were demonstrated to be useful in predicting ozone and  $\bullet\text{OH}$  rate constants, respectively, for organic micropollutants without published rate constants.
- Measurements of  $\bullet\text{OH}$  exposure as a function of  $\text{gO}_3/\text{gDOC}$  are recommended in the planning stage of wastewater ozonation facilities for micropollutant elimination and can be conveniently performed using laboratory batch elimination experiments for samples spiked with  $\bullet\text{OH}$ -probe compounds (e.g., *para*-chlorobenzoic acid).
- Ozone exposure can be indirectly estimated using  $\text{O}_3$ -probe compounds (e.g., carbamazepine or bezafibrate) especially for low specific ozone doses. For more reliable measurements, direct measurements from ozone decay curves are recommended.
- With increasing pH from 7.0 to 8.5, the elimination levels increased for ozone-reactive compounds with amine-moieties due to the higher ozone rate constants while decreased for most ozone-resistant compounds due to the reduced  $\bullet\text{OH}$  exposure caused by increased  $\bullet\text{OH}$  quenching rate by effluent organic matter and carbonate with increasing pH.
- The effect of  $\text{H}_2\text{O}_2$  addition on micropollutant elimination efficiency during ozonation was slightly beneficial for pH 7 but led to a smaller removal at pH 8.5 especially for some ozone-reactive compounds due to a decreased ozone exposure.
- Two-thirds of the micropollutants (38 out of 56) present in the hospital wastewater effluent were compounds containing ozone-reactive moieties such as phenols, anilines, activated aromatics, amines and thioethers and could be efficiently eliminated at low specific ozone doses (e.g.,  $93\pm 9\%$  at  $\text{gO}_3/\text{gDOC} = 0.5$ ).

- Iodinated contrast media, which constituted  $\geq 80\%$  of the mass load in the selected hospital wastewater effluent, were eliminated relatively inefficiently, e.g.,  $\sim 70\%$  for  $\text{gO}_3/\text{gDOC} = 1.0$  for iopromide, due to low ozone and  $\bullet\text{OH}$  rate constant.

## Supporting Information

Tables S1–S5 and Figures S1–S10 are available for further additional supplementary material and data.

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1 Table 1. Selected micropollutants and their second-order reaction rate constant with ozone and •OH.

compounds	$k_{O_3,pH7}^a$ , $M^{-1} s^{-1}$	$k_{O_3,pH8.5}^b$ , $M^{-1} s^{-1}$	$k_{O_3,ss}^c$ , $M^{-1} s^{-1}$	$k_{\bullet OH}^d$ , $M^{-1} s^{-1}$
Group Ia: $k_{O_3,pH7} \geq 1 \times 10^4$ and $k_{O_3,pH8.5} \geq 1 \times 10^4 M^{-1} s^{-1}$				
Carbamazepine	$3 \times 10^5$	$3 \times 10^5$	$3 \times 10^5$ <sup>e</sup>	$8.8 \times 10^9$ <sup>e</sup>
Clarithromycin	$4.0 \times 10^4$	$9.6 \times 10^5$	$4 \times 10^6$ <sup>f</sup>	$\sim 5 \times 10^9$ <sup>g</sup>
Diclofenac	$1 \times 10^6$	$1 \times 10^6$	$1 \times 10^6$ <sup>e</sup>	$7.5 \times 10^9$ <sup>e</sup>
Furosemide	$6.8 \times 10^4$	$6.8 \times 10^4$	$6.8 \times 10^4$ <sup>f</sup>	$\sim 10^{10}$ <sup>g</sup>
Lidocaine	$7.3 \times 10^4$	$3.9 \times 10^5$	$1.1 \times 10^4$ <sup>g,h</sup> / $4.5 \times 10^5$ <sup>g,i</sup>	$\sim 10^{10}$ <sup>g</sup>
Mefenamic acid	$6.4 \times 10^6$	$6.4 \times 10^6$	$6.4 \times 10^6$ <sup>g</sup>	$\sim 10^{10}$ <sup>g</sup>
Ranitidine	$4.1 \times 10^6$	$5.1 \times 10^6$	$4.0 \times 10^6$ <sup>g,j</sup> / $1.7 \times 10^6$ <sup>g,i</sup>	$\sim 10^{10}$ <sup>g</sup>
Sotalol	$1.9 \times 10^4$	$1.3 \times 10^5$	$1.5 \times 10^4$ <sup>g,h</sup> / $1.0 \times 10^6$ <sup>g,i</sup>	$\sim 10^{10}$ <sup>g</sup>
Sulfamethoxazole	$5.5 \times 10^5$	$5.7 \times 10^5$	$4.7 \times 10^4$ <sup>k,l</sup> / $5.7 \times 10^5$ <sup>k,m</sup>	$8.5 \times 10^9$ <sup>n</sup>
Sulfapyridine	$2.0 \times 10^5$	$8.5 \times 10^5$	$1.6 \times 10^5$ <sup>g,l</sup> / $1.6 \times 10^6$ <sup>g,m</sup>	$8.2 \times 10^9$ <sup>g</sup>
Group Ib: $k_{O_3,pH7} < 1 \times 10^4$ and $k_{O_3,pH8.5} \geq 1 \times 10^4 M^{-1} s^{-1}$				
4-methyl-benzotriazole	$7.8 \times 10^2$	$1.1 \times 10^4$	$3.1 \times 10^2$ <sup>g,l</sup> / $3.8 \times 10^4$ <sup>g,m</sup>	$\sim 8.6 \times 10^9$ <sup>g</sup>
Atenolol acid	$2.5 \times 10^3$	$6.2 \times 10^4$	$1.0 \times 10^6$ <sup>g,i</sup>	$\sim 10^{10}$ <sup>g</sup>
Metoprolol	$2.0 \times 10^3$	$5.1 \times 10^4$	$8.6 \times 10^5$ <sup>o,i</sup>	$7.3 \times 10^9$ <sup>o</sup>
Tramadol	$4.0 \times 10^3$	$1.1 \times 10^5$	$1.0 \times 10^6$ <sup>p,i</sup>	$6.3 \times 10^9$ <sup>p</sup>
Venlafaxine	$8.5 \times 10^3$	$1.5 \times 10^5$	$3.2 \times 10^3$ <sup>g,h</sup> / $1.3 \times 10^6$ <sup>g,i</sup>	$\sim 10^{10}$ <sup>g</sup>
Group II: $50 \leq k_{O_3,pH7}$ and $k_{O_3,pH8.5} < 1 \times 10^4 M^{-1} s^{-1}$				
N(4)-acetyl sulfamethoxazole	$2.5 \times 10^2$	$2.6 \times 10^2$	$2.0 \times 10^1$ <sup>k,l</sup> / $2.6 \times 10^2$ <sup>k,m</sup>	$6.8 \times 10^9$ <sup>k</sup>
Benzotriazole	$2.4 \times 10^2$	$2.3 \times 10^3$	$3.5 \times 10^3$ <sup>q,m</sup>	$7.6 \times 10^9$ <sup>r</sup>
Bezafibrate	$5.9 \times 10^2$	$5.9 \times 10^2$	$5.9 \times 10^2$ <sup>e</sup>	$7.4 \times 10^9$ <sup>e</sup>
Gabapentin	$2.2 \times 10^2$	$6.8 \times 10^3$	$1.8 \times 10^5$ <sup>g,m</sup>	$9.1 \times 10^9$ <sup>g</sup>
Group III: $k_{O_3,pH7}$ and $k_{O_3,pH8.5} < 50 M^{-1} s^{-1}$ and $k_{\bullet OH} \geq 5 \times 10^9 M^{-1} s^{-1}$				

Oxazepam	~1	~1	~1 <sup>g</sup>	9.1×10 <sup>9g</sup>
Primidone	<10	<10	<10 <sup>g</sup>	6.7×10 <sup>9s</sup>
Valsartan	38	38	38 <sup>g</sup>	~10 <sup>10g</sup>

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Group IV:  $k_{O_3,pH7}$  and  $k_{O_3,pH8.5} < 50 \text{ M}^{-1} \text{ s}^{-1}$  and  $1 \times 10^9 < k_{\bullet OH} < 5 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$

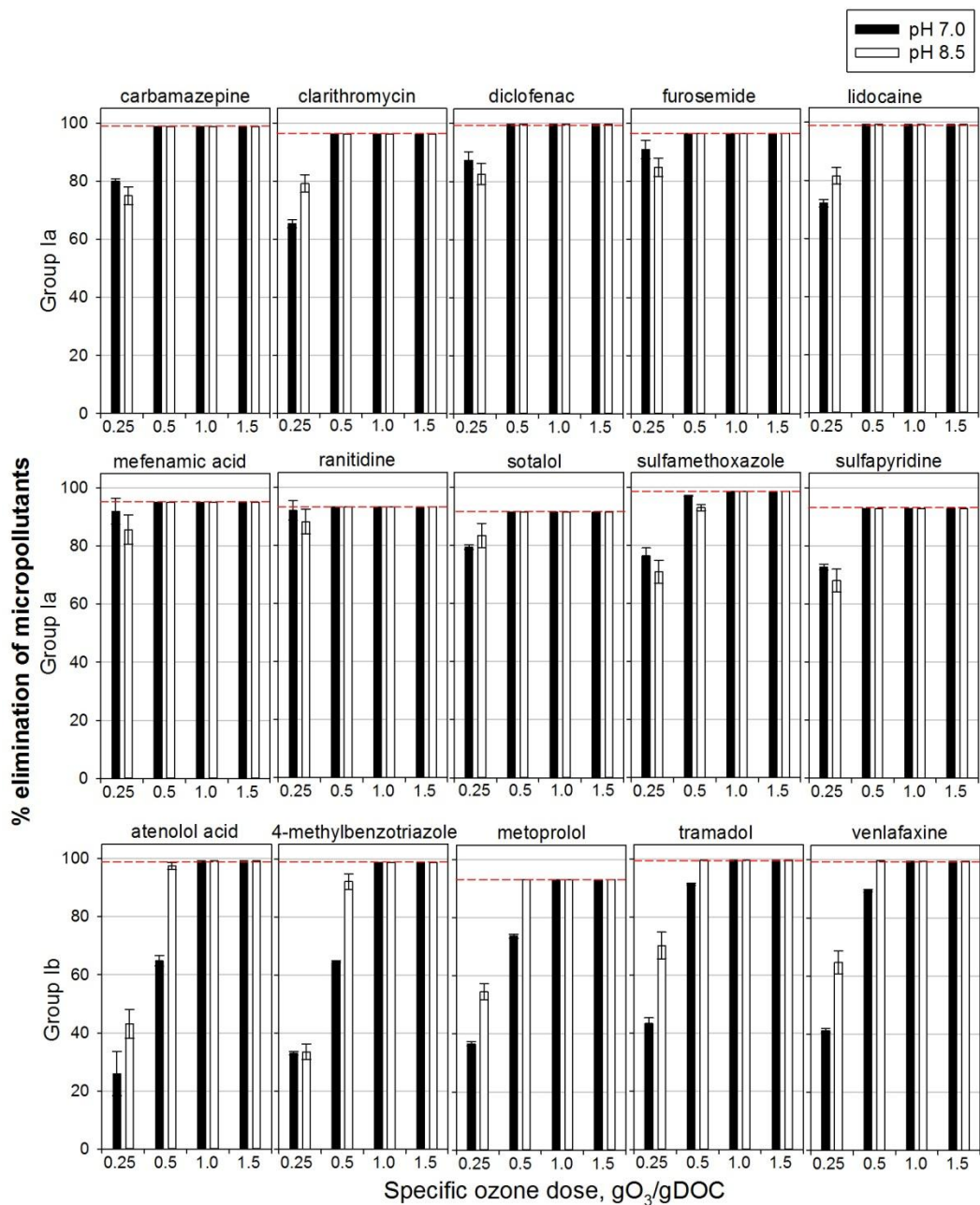
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Fluconazole	~2	~2	~2 <sup>g</sup>	4.4×10 <sup>9g</sup>
Iopromide	<0.8	<0.8	<0.8 <sup>e</sup>	3.3×10 <sup>9e</sup>
Levetiracetam	<1	<1	<1	3.8×10 <sup>9g</sup>

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<sup>a</sup>apparent  $k$ -value for the reaction of O<sub>3</sub> at pH 7, <sup>b</sup>apparent  $k$ -value for the reaction of O<sub>3</sub> at pH 8.5, <sup>c</sup>species-specific  $k$ -value for the reaction of O<sub>3</sub>, <sup>d</sup> $k$ -value for the reaction of •OH, <sup>e</sup>from Huber et al., 2003, <sup>f</sup>from Lange et al., 2006, <sup>g</sup>estimated in this study (SI, Table S3), <sup>h</sup> $k_{O_3}$ -value for the substituted benzene, <sup>i</sup> $k_{O_3}$ -value for the amine, <sup>j</sup> $k_{O_3}$ -value for the thioether, <sup>k</sup>from Dodd et al., 2006, <sup>l</sup> $k_{O_3}$ -value for the protonated species, <sup>m</sup> $k_{O_3}$ -value for the deprotonated species, <sup>n</sup>from Mezyk et al., 2007, <sup>o</sup>from Benner et al., 2008, <sup>p</sup>from Zimmermann et al., 2012, <sup>q</sup>from Lutze et al., 2005, <sup>r</sup>from Naik et al., 1995, <sup>s</sup>from Real et al., 2009.

Figure 1



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Figure 1. Elimination of group Ia (carbamazepine, clarithromycin, diclofenac, furosemide, lidocaine, mefenamic acid, ranitidine, sotalol, sulfamethoxazole, and sulfapyridine) and group Ib (atenolol acid, 4-methyl-benzotriazole, metoprolol, tramadol, and venlafaxine) micropollutants as a function of the specific ozone dose ( $\text{gO}_3/\text{gDOC}$ ) in a hospital wastewater effluent (DOC = 5.1 mgC/L). The dashed-lines indicate the method quantification limit (LOQ) for % elimination of micropollutants. Experimental conditions: pH = 7.0 (filled bars) and 8.5 (empty bars), specific ozone doses ( $\text{gO}_3/\text{gDOC}$ ) = 0.25, 0.5, 1.0, and 1.5), and  $T = 22 \pm 2^\circ\text{C}$ .

Figure 2

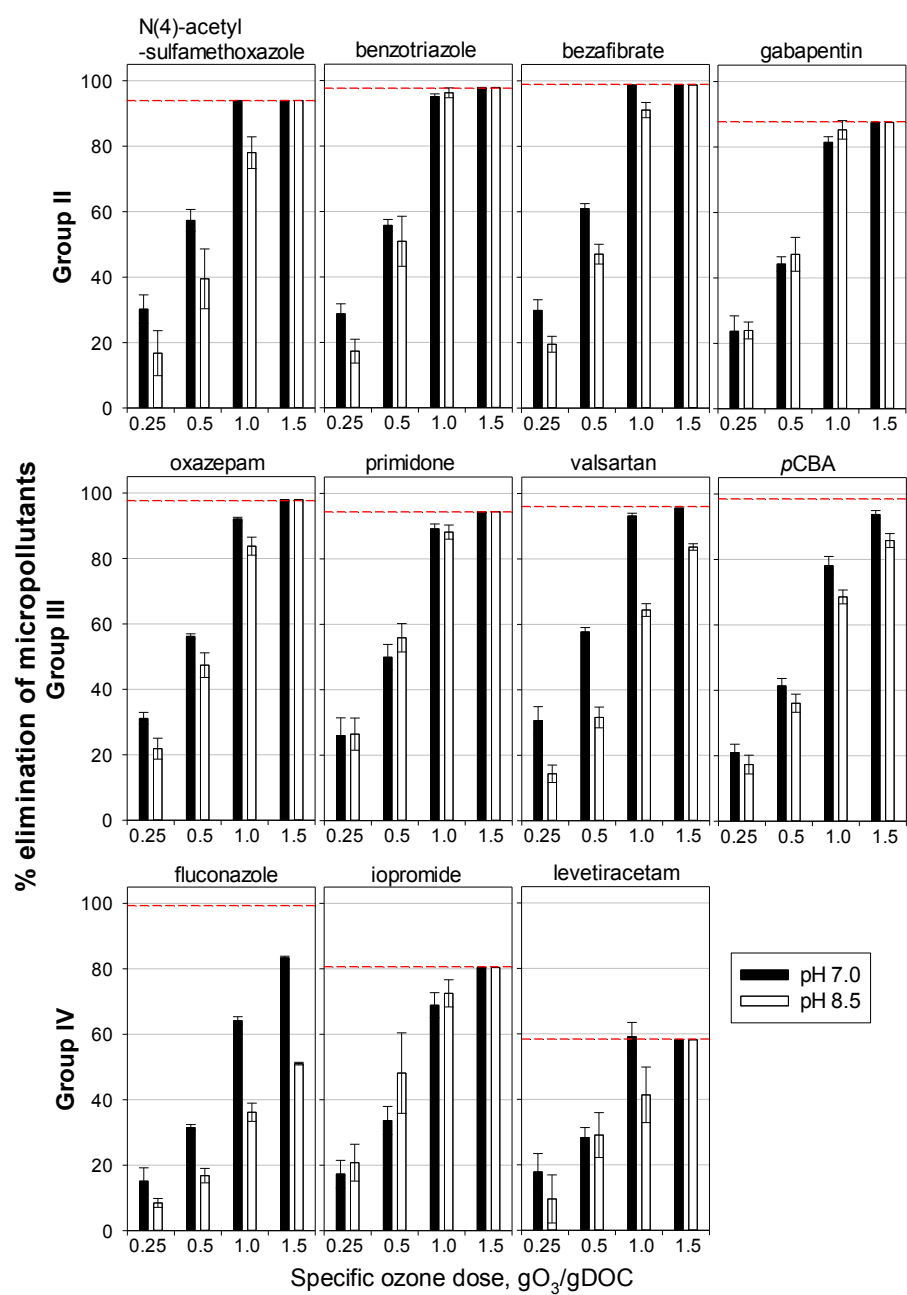


Figure 2. Elimination of group II (N(4)-acetylsulfamethoxazole, benzotriazole, bezafibrate, and gabapentin), Group III (oxazepam, primidone, and valsartan), and group IV (fluconazole, iopromide, and levetiracetam) micropollutants as a function of the specific ozone doses ( $\text{gO}_3/\text{gDOC}$ ) in a hospital wastewater effluent. The dashed-lines indicate the method quantification limit (LOQ) for % elimination of micropollutants. Experimental conditions are the same as in Figure 1: pH = 7.0 (filled bars) and 8.5 (empty bars).

Figure 3

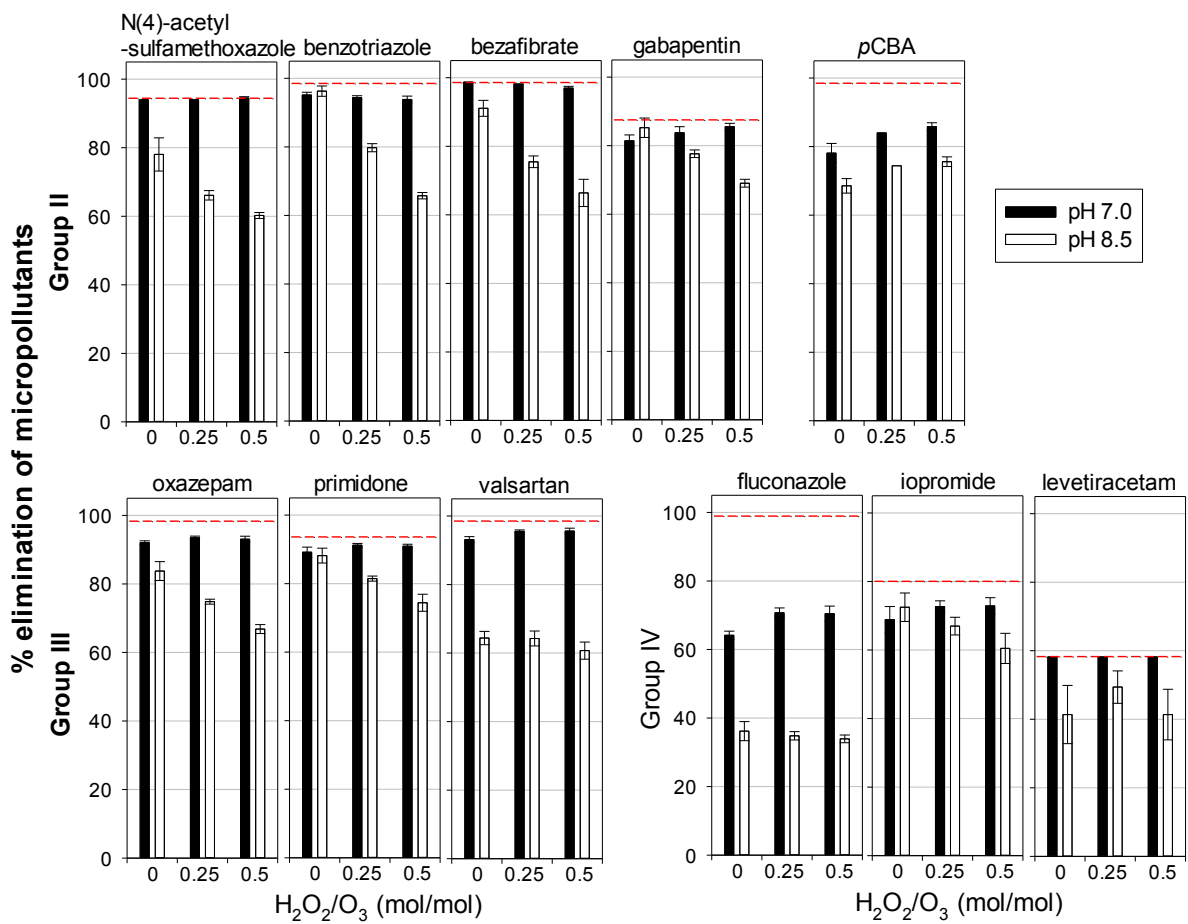


Figure 3. Effect of hydrogen peroxide addition on the elimination of group II, III, and IV during ozonation of the hospital wastewater effluent at pH 7.0 and 8.5. The applied specific ozone dose ( $gO_3/gDOC$ ) was 1.0 and the  $H_2O_2/O_3$  ratio (mol/mol) was 0, 0.25 and 0.5, respectively. The dashed-lines indicate the method quantification limit (LOQ) for % elimination of micropollutants. Experimental conditions are the same as in Figure 1: pH = 7.0 (filled bars) and 8.5 (empty bars)

Figure 4

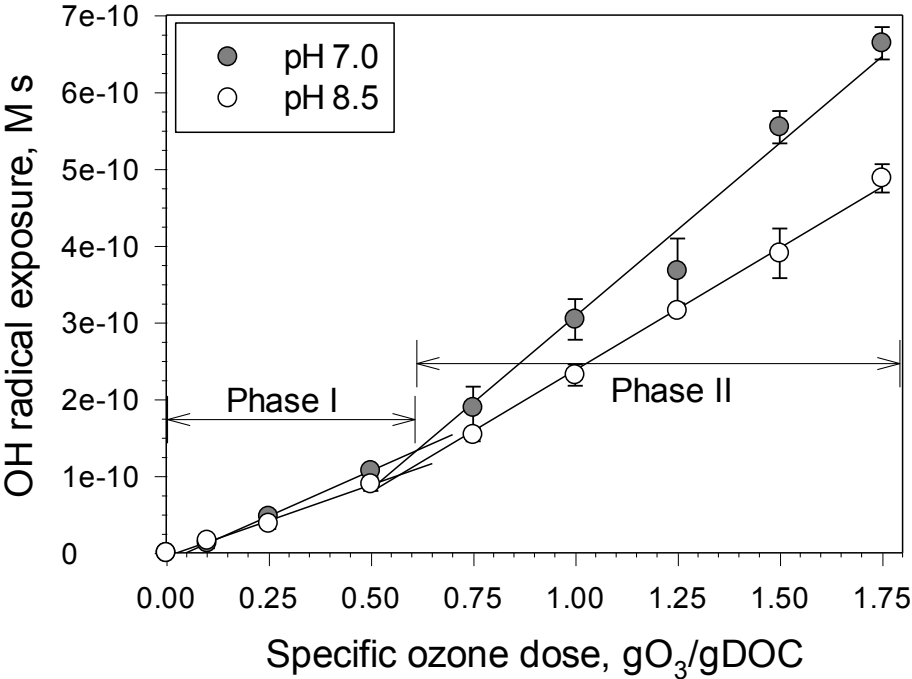


Figure 4.  $\bullet$ OH exposure determined for various specific ozone doses ( $\text{gO}_3/\text{gDOC}$ ) at pH 7 and 8.5 in a hospital wastewater effluent ( $\text{DOC} = 5.1 \text{ mgC/L}$  and  $T = 22 \pm 2^\circ\text{C}$ ).  $\bullet$ OH exposures were calculated from the decrease of *p*-chlorobenzoic acid (*p*CBA) as  $\bullet$ OH probe compound. The lines represent linear regressions of the experimental data for  $\bullet$ OH exposure vs.  $\text{gO}_3/\text{gDOC}$  (see text).

Figure 5

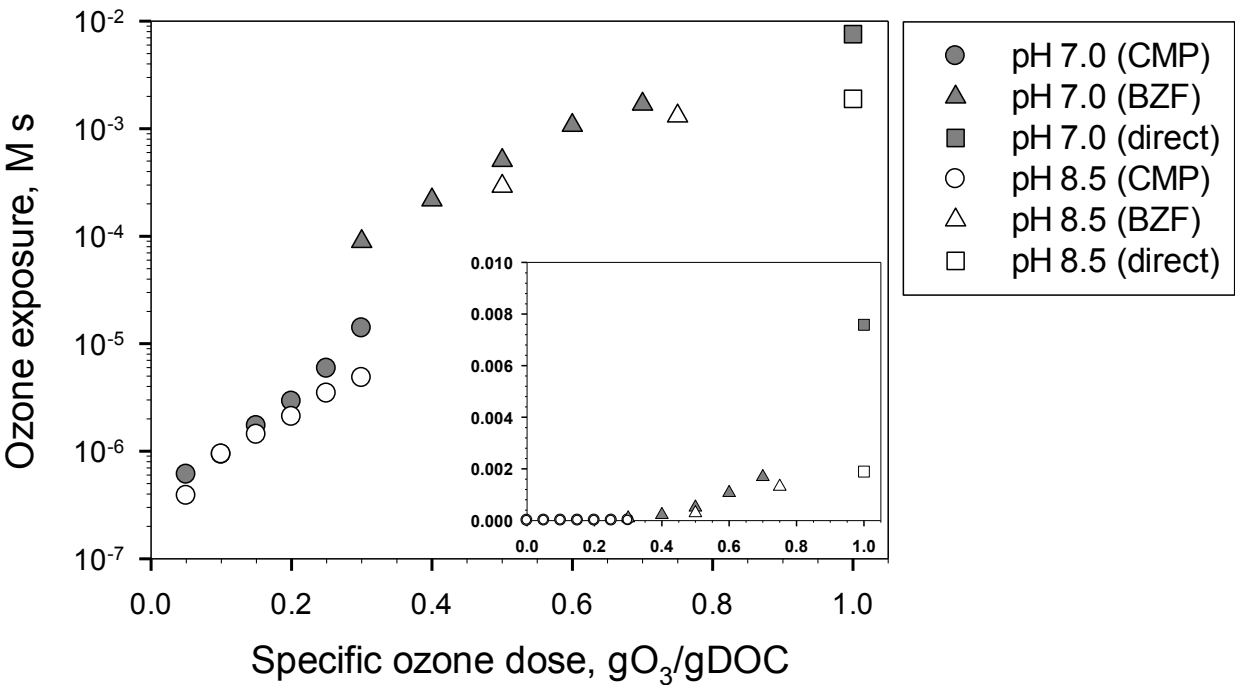


Figure 5. Ozone exposure determined for various specific ozone doses (gO<sub>3</sub>/gDOC) at pH 7 and 8.5 in a hospital wastewater effluents (DOC = 5.1 mgC/L and T = 22±2°C). Ozone exposures were calculated from the decrease of carbamazepine (CMP) for specific ozone doses of 0.05 – 0.3, from bezafibrate (BZF) for specific ozone doses of 0.3 – 0.7, and from the area under the ozone decay curves (direct). The main and inset figures show the ozone exposure in logarithmic and linear scales, respectively.



Figure 6

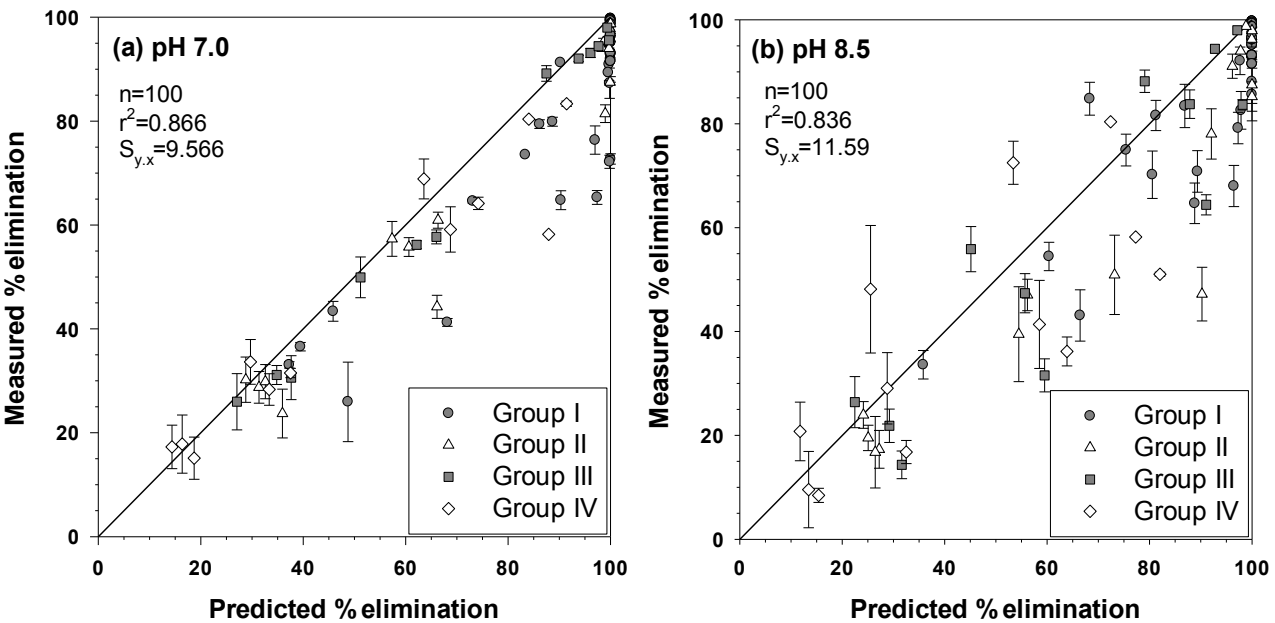


Figure 6. Measured and predicted % elimination of the 25 micropollutants (Table 1) during hospital wastewater effluent ozonation. (a) pH 7.0 and (b) pH 8.5. n is the number of data points (=100) and  $S_{y,x}$  represents the standard deviation (or standard errors of estimate) of the linear regression with an equation  $y=x$  and is calculated as  $(SS/df)^{1/2}$  where SS is the sum-of-squares of the distance of the linear regression from the data points ( $\sum(Y' - Y)^2$ ) and df is the degree of freedom of the fit (= n-2 = 98).

Figure 7

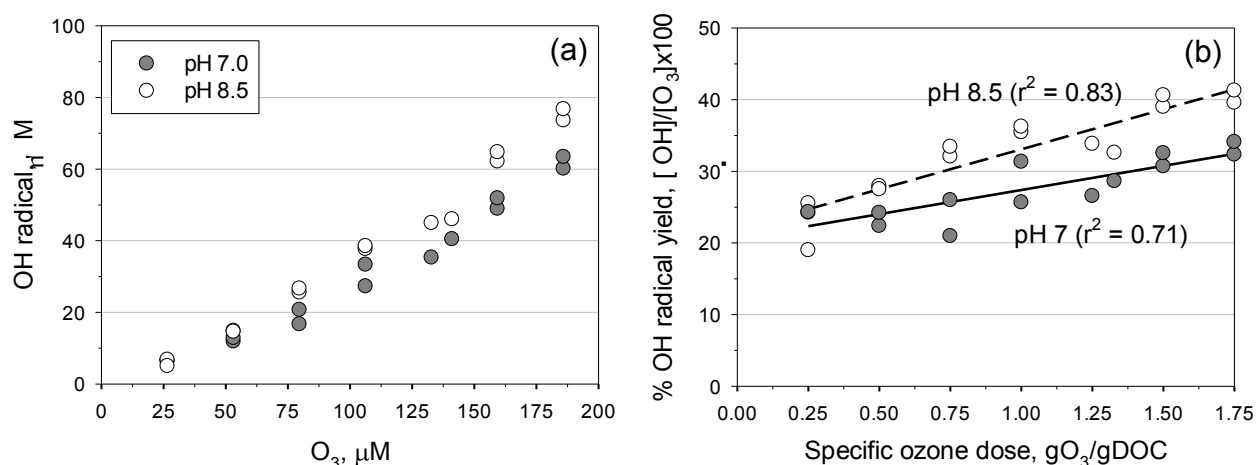


Figure 7.  $\bullet\text{OH}$  formation during ozonation of hospital wastewater effluent at pH 7 and 8.5. (a)  $\bullet\text{OH}$  concentration as a function of ozone dose, and (b) %  $\bullet\text{OH}$  yield as a function of the specific ozone dose ( $\text{gO}_3/\text{gDOC}$ ). The lines represent linear regressions of the data. The  $\bullet\text{OH}$  formation was estimated from the concentration of  $\text{CH}_2\text{O}$  formed in presence of excess *tert*-butanol (10 mM) as an  $\bullet\text{OH}$  scavenger (Nöthe et al., 2009).

Figure 8

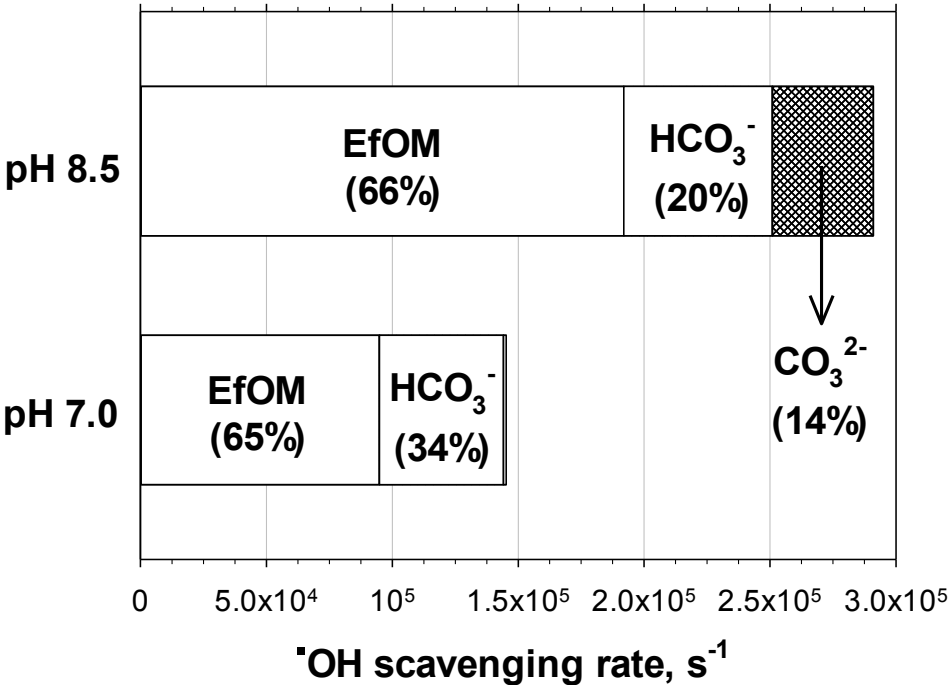
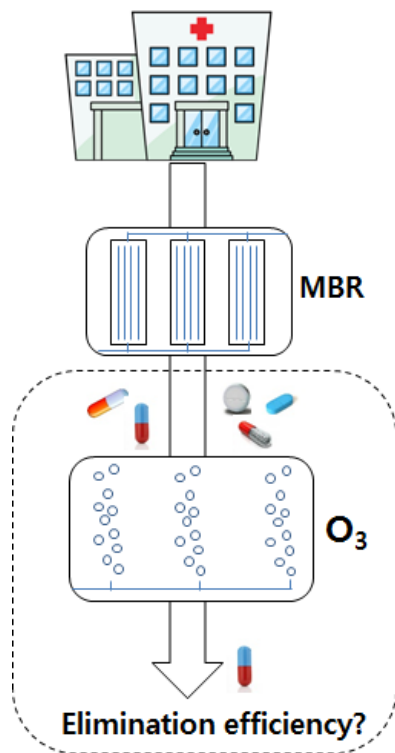


Figure 8.  $\bullet\text{OH}$  consumption rates during ozonation of a wastewater effluent at pH 7.0 and pH 8.5. The % areas in the bars represent the relative  $\bullet\text{OH}$  scavenging rate by EfOM and carbonate species ( $\text{HCO}_3^-$  and  $\text{CO}_3^{2-}$ ).  $\bullet\text{OH}$  scavenging rate was determined by using a competition kinetics method employing *tert*-butanol as a competitor.

- Elimination of micropollutants in hospital wastewater ozonation was well predicted.
- $O_3$  and  $\cdot OH$  rate constants could be predicted by QSARs and group contribution method.
- $O_3$  and  $\cdot OH$  exposures could be measured using proper  $O_3$ - and  $\cdot OH$ -probe compounds.
- Most micropollutants in hospital wastewater effluent could be efficiently eliminated.



Chemical kinetics + water specific information

