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O_3 and O_3/H_2O_2 treatment of sulfonamide and macrolide antibiotics in wastewater

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ABSTRACT

The ubiquitous presence of trace pharmaceutical compounds in the environment is a significant concern. While the implications of these compounds on ecosystems and human health are being determined, there has been increasing interest in their treatment such as by tertiary processes at sources and wastewater treatment facilities to arrest further release to the environment. We have examined the degradation of sulfonamide and macrolide antibiotics in a spiked water and a pharmaceutical wastewater by ozonation under varied conditions such as concentration, contact time, pH, and H_2O_2/O_3 mole ratio. The results show faster removal kinetics for sulfonamides containing the aromatic ring than for macrolides built of mostly saturated hydrocarbon structure, and that complete removal of all is achieved within 20 min of ozonation at the application rate of 0.17 g O_3/min. Degradation of contaminants containing unsaturated C–C bonds occurs faster at low pH, consistent with O_3 being the predominant oxidant and its aqueous concentration being higher at low pH. Degradation of erythromycin having a fully saturated structure is slower and more effective at higher pH or with added H_2O_2, both consistent with the enhanced production of OH radical under such conditions that contributes to removal of the saturated compound. Low pH favors degradation via molecular O_3 while high pH via OH radical; the optimal pH thus depends on target compounds being treated, and buffered pH at 7 facilitates removal of all tested compounds. The addition of H_2O_2 to ozonation abets contaminant removal, and at mole ratio of $H_2O_2/O_3 = 5$ it attains the highest degradation speed for all contaminants. However, a large excess of added H_2O_2 results in reduced or no benefits relative to O_3 alone. Thus, only a small dose of H_2O_2 is desirable when widely disparate compounds are treated by ozonation.

1. Introduction

Pharmaceutical chemicals are widely used for therapeutic and agricultural purposes today. A significant body of work has identified trace amounts of antibiotics in natural aquatic systems around the world, increasingly relating their occurrence to wastewaters and livestock operations. Issues such as acute and chronic effects of antibiotics on ecosystems, potential rise of antibiotic-resistant bacteria, and increasing tolerance of antibiotics by human and livestock are not well understood, and they are at the root of increasing public concern.

Numerous studies have reported the occurrence of trace antibiotics in aquatic environments worldwide [1–3]. Kolpin et al. [2] found 22 antibiotics in their survey of 139 rivers and streams in the US. In their investigation of eleven antibiotics in three rivers in Taiwan, Lin et al. [4] found consistent presence of erythromycin-H_2O and sulfamethoxazole with the former reaching 76 μg/L. The occurrence of veterinary antibiotics including macrolides, sulfonamides, and trimethoprim was observed at 7–360 ng/L in Vietnam's Mekong Delta [5]. Residential and agricultural waste streams have been identified as major contributors to contamination by antibiotics [6]. Modest removal of sulfonamides (43%) and little removal of macrolides (particularly erythromycin-H_2O) via secondary wastewater treatment processes were reported in Spain and Taiwan [7,8]. High concentrations of antibiotics (particularly sulfonamides, lincomycin, erythromycin-H_2O, and tylosin) were found in wastewater treatment plant effluents that impacted receiving water bodies [9,10].

Aside from conventional unit operations and processes in wastewater treatment facilities that often allow residual pharmaceuticals to pass through, oxidative treatments have been tested for removal of pharmaceutical compounds. Potential treatment agents include ferrate [11], chlorine dioxide [12], titanium dioxide as a photocatalyst [13,14], as well as UV photolysis [15]. Numerous studies found ozonation particularly effective, achieving over 90% degradation for a wide variety of compounds [16–22]. How-

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ever, pharmaceutical compounds are highly disparate chemicals varying in size, structure, polarity, solubility, and other electronic properties, which influence their susceptibility to a specific treatment approach. For example, ClO_2, while a strong oxidant, was only effective for sulfonamide and some macrolides and estrogens but was ineffective for many others [12]. Synder et al. [22] removed over 90% of some target compounds but less than 50% of others, and removal was improved only marginally when H_2O_2 was added to promote treatment via advanced oxidation processes (AOPs). In treating clofibric acid, ibuprofen, and diclofenac, Zwiener and Frimmel [23] found enhanced degradation efficiency when OH radical formation was promoted by adding H_2O_2 to ozonation. However, the addition of H_2O_2 to ozonation in a non-optimized manner did not result in higher removal of pharmaceuticals from wastewater [24]. As a large number of pharmaceuticals with very different properties are present in a waste stream, it would be desirable that a selected treatment method is effective for as many different compounds as possible.

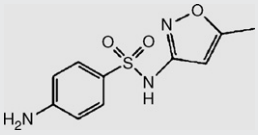
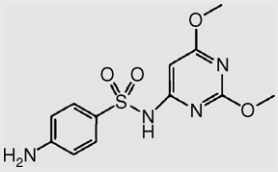
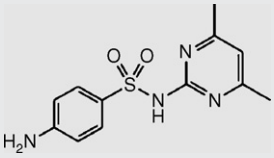
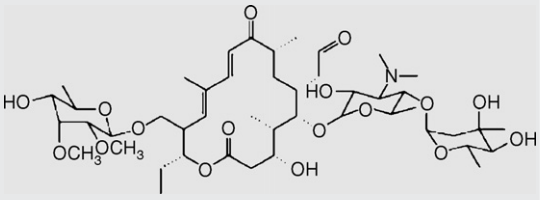
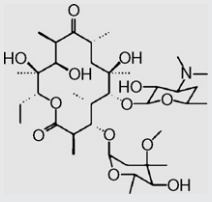
We hypothesize that varied degrees of treatment effectiveness via ozonation are due largely to the aromaticity within the compounds; therefore, we have tested in this work three sulfonamides that each contains an aromatic ring and two macrolides that one contains two and the other no unsaturated C–C bonds (see Table 1) as they are subjected to O_3 and O_3/H_2O_2 with varied amounts of added H_2O_2. This is to ascertain the usefulness of adding H_2O_2 during ozonation treatment of pharmaceutical compounds, and to identify the minimal dose of H_2O_2 that will enhance degradation for all chemicals, including saturated hydrocarbons that are benefited by increased $OH^{\bullet}$ production via H_2O_2 addition as well as aromatic compounds that are effectively treated by O_3 alone.

2. Experimental

2.1. Chemicals and standards

Sulfamethoxazole (SMX), sulfadimethoxine (SDM), sulfamethazine (SMT), erythromycin (ERM) and tylosin (TYL) tartrate, sodium thiosulphate, potassium indigo trisulfonate, sodium phosphate were purchased from Sigma–Aldrich (St. Louis, MO, USA). LC-grade methanol, ACS-grade disodium ethylenediaminetetraacetate (EDTA-2Na), and potassium iodide were purchased from Mallinckrodt Baker (Phillipsburg, PA, USA). ACS-grade formic acid and sodium persulfate were obtained from Riedel-de Haën (Seelze, Germany). Sulfuric acid was purchased from Fluka (Buchs, Switzerland), and phosphoric acid and sodium hydroxide were from Nacalai Tesque (Tokyo, Japan). Individual stock standard solutions were prepared in methanol on a weight basis. These solutions were stored in amber glass bottles at −20 °C for a maximum of 15 days. Standard mixtures at different concentrations were prepared by dilution of the stock solutions before each analytical run.

Table 1
Structures of study antibiotic compounds.

Compound name	Acronym	CAS number	Molecular weight	Molecular structure
Antibiotics-sulfonamides				
Sulfamethoxazole	SMX	723-46-6	253.3	
Sulfadimethoxine	SDM	122-11-2	310.3	
Sulfamethazine	SMT	57-68-1	278.3	
Antibiotics-macrolides				
Tylosin	TYL	1401-69-0	916.1	
Erythromycin	ERM	114-07-8	733.9	

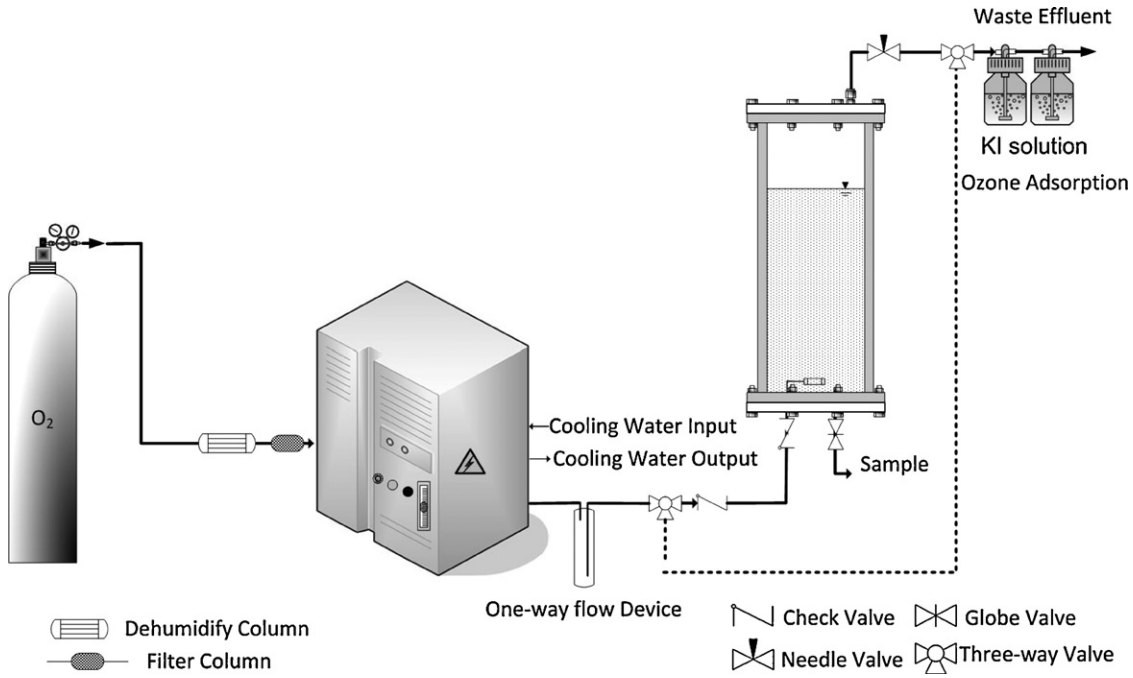


Fig. 1. Reactor setup

2.2. Reactor setup and procedures

The reactor was of stainless steel and formed by a cylinder with flanges secured by screws to a top plate and a bottom plate with an O-ring on each; the dimensions were of 13 cm in ID, 18.5 cm in OD, 40 cm in height, and 5 L in volume. The reactor system is as shown in Fig. 1. An O_3/O_2 mixture was supplied by an O_3 generator (OZONIA CFS-1 2G) at 5.3% O_3 (v/v) and 1.6 L/min. Gaseous and aqueous O_3 concentrations were determined by an iodide method (Method 2350 E) and Indigo method (Method 4500), respectively [25]; these results were used to compute the rate of O_3 application. In a typical experiment, the reactor was filled with three L of spiked water or wastewater and dosed with H_2O_2; O_3 influent was then introduced into the reactor through a diffuser near the bottom to start the reaction. The effluent gas was vented through an open port at the reactor top. Samples were obtained during reaction through opening of a sampling valve at the reactor bottom, with each sampling accomplished in 3 s. Experiments were performed with and without controlling the pH. Initial pH of the spike solution was 4.2–5.7 and it decreased to 2.4–3.4 without buffering agents. Experiments at constant pHs were performed with appropriate buffering agents consisting of salts of phosphate, H_2SO_4, and NaOH (I = 1 M). Parameters of study included contact time (0–1 h), pH (3–11), contaminant concentration (ppb–200 ppm) and kinds (five compounds), as well as H_2O_2/O_3 mole ratio (0–20). Experiments were conducted at room temperature of 24 ± 1 °C.

2.3. Analytical methods and equipment

Analytical methods based on solid phase extraction using Oasis HLB cartridges followed by liquid chromatography/tandem mass spectrometry (HPLC-MS/MS) had been widely used [26] and were adopted in this study. Samples before and after ozonation were filtered through a 0.2 μm filter (13 mm in diameter, PVDF) before injection, and chromatographic separation of analytes was performed using an Agilent 1200 module (Agilent, Palo Alto, CA, USA) equipped with a ZORBAX Eclipse XDB-C18 column (150 mm × 4.6 mm, 5 μm). Control experiments with air treatment in lieu of O_3 showed complete recovery (±3.7%) of all study compounds and no retention by the filter. A binary gradient was employed with mobile phase A containing 0.1% formic acid (v/v) in water and mobile phase B containing 0.1% formic acid (v/v) in methanol. Samples of 50 μL were injected for analysis. Quantification of the five target antibiotics was performed via liquid chromatography/tandem mass spectrometry (Agilent 1200 module, Agilent Technologies, Palo Alto, CA, USA; Sciex API 4000 quadrupole mass spectrometer, Applied Biosystems, Foster City, CA, USA) with multiple reaction monitoring (MRM), using the two highest characteristic precursor ion/product ion transition pairs. Compounds were identified using the LC retention time ±30% of retention time of a standard as well as the MRM ratio.

Direct injection of filtered, treated samples from spiked solutions was capable of detecting study compounds down to 0.1 μg/L. Solid phase extraction (SPE) technique was employed for wastewater samples from a drug manufacturer, which concentrated the samples by 1000 times and lowered the method detection limits to ng/L levels. Oasis HLB cartridges with 0.5 g of sorbent (6 mL, Waters, Milford, MA, USA) were used to extract the target pharmaceuticals. Cartridges were preconditioned sequentially with 6 mL of methanol and 6 mL of deionized (DI) water. Water samples were loaded and drawn through the cartridges at 3–6 mL/min. The cartridges were then washed with 6 mL of DI water to remove excess EDTA-2Na and dried with a stream of nitrogen gas. Analytes were then eluted with 4 mL of methanol followed by 4 mL of methanol–diethylether (50:50, v/v); analyte recoveries were ERM (108%), TYL (101%), SMX (69.1%), SDM (78.7%), and SMT (81.0%). The extracts were collected, concentrated by a N_2 stream, reconstituted with 25% of aqueous methanol and filtered (PVDF membrane of 0.45 μm) before HPLC-MS/MS analysis, using $^{13}C_6$-sulfamethazine as a surrogate standard and matrix matched external calibration (details reported previously [4]). It should be noted that erythromycin readily undergoes dehydration to become erythromycin-H_2O, which was monitored and reported as ERM in this study. Light absorption at 254 nm by the reaction medium was monitored with a UV-VIS spectrophotometer (GBC Cintra 20, Australia) throughout reaction.

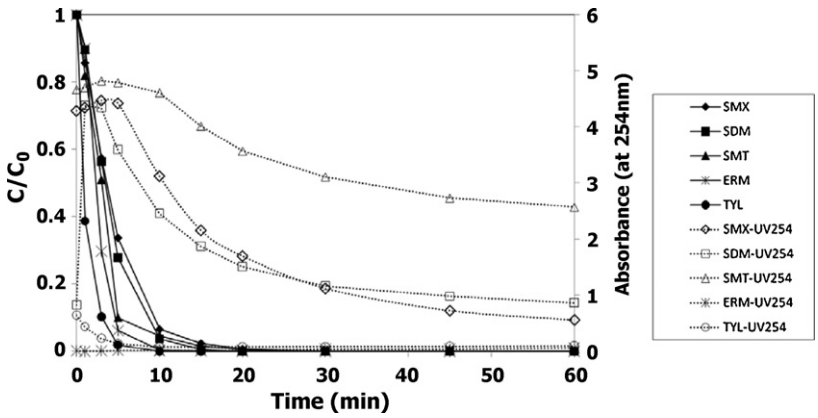


Fig. 2. Concentrations of antibiotic compounds vs. contact time as individual stock solution is subjected to ozonation or aeration; absorbance changes during ozonation are also shown (initial pHs were 4.2, 5.1, 5.2, 5.7, and 5.7 and pH after ozonation were 2.4, 2.8, 2.7, 3.4, and 3.3 for SMX, SDM, SMT, ERM, and TYL, respectively).

3. Results and discussion

3.1. Degradation of antibiotics by ozone

Fig. 2 shows concentrations vs. time profiles of antibiotic compounds as each spiked solution is individually subjected to ozonation. Concentrations of antibiotic compounds as shown in Fig. 2 (and all subsequent figures) were measured by HPLC-MS/MS with or without SPE as discussed in Section 2. The compounds disappeared rapidly upon ozonation. In Fig. 2 (and subsequent figures), UV absorbance ($\lambda = 254$ nm) of the solutions that correlated to the presence of organics was monitored throughout ozonation, which showed decreasing absorbance associated with disappearing antibiotic compounds through the course of reaction. The continual decrease in absorbance beyond 10 min when most target compounds were significantly removed was due to continued degradation of intermediates and organic fragments from the parent compounds. Reaction rate constants of O_3 with individual compounds were not determined because of the O_3-limiting reaction condition (i.e., expected [O_3] was <10 mg/L prior to full saturation and particularly so at the start of ozonation and it was less than the initial concentration of any of the target compounds at 200 mg/L) and because of concentration parameters changing concurrently throughout the reaction, e.g., dissolved O_3 concentration rising as ozonation started, target compound concentration continually decreasing as a result of degradation by O_3, and pH decreasing due to hydrolysis of O_3 which in turn determined the attainable steady-state concentration of O_3. At the O_3 application rate of 0.17 g O_3/min (i.e., 5.3% O_3 at flowrate of 1.6 L/min), the removal of SMX, SDM, SMT, ERM, and TYL was 93, 96, 95, >99, and >99%, respectively, within 10 min of ozonation and it was >99% removal of all compounds in 20 min. The absorbance (at 254 nm) vs. time profiles showed clear decreases in all solutions corresponding to degradation of parent and organic fragments throughout ozonation, except for the solution of ERM that absorbs little UV light for the absence of unsaturated C–C bonds in contrast to all others. The decreasing absorbance profiles were qualitative indications of parent compounds disappearing throughout the reaction.

Fig. 3 shows the concentration profiles of a mixed solution containing all five target compounds (each of 40 mg/L) as subjected to ozonation. The removal of all compounds exceeded 99% in 10 min of ozonation, except for ERM which showed only 58% removal in the first 10 min but eventually over 99% removal in 45 min. The degradation of ERM was slowest reflecting its fully saturated structure, which contains no electron-rich C–C bonds that electrophile O_3 preferentially attacks. Reactivities and degradative pathways are further discussed below. The absorbance at 254 nm indicative of organic contents in the water decreased rapidly initially that corresponded to the removal of the parent target compounds, and then it decreased gradually and flattened that corresponded to the disappearance of all residual organic compounds.

To address experimental reproducibility, degradation experiments for a mixed solution were performed in triplicates and the kinetic profiles were used to obtain pseudo first-order rate constants for each compound. The rate constants as obtained by regression analysis were 0.38 ± 0.012, 0.45 ± 0.017, 0.54 ± 0.035, 0.08 ± 0.003, and 0.37 ± 0.027 min^{-1} for SMX, SDM, SMT, ERM, and TYL, respectively, indicating reproducible kinetic results. However, it should be noted that these "pseudo first-order" rate constants pertain to the exact experimental configurations (e.g., influent O_3 gas concentration, gas transfer rate according to agitation, gas flow rate, liquid volume) that influence the transient, instantaneous O_3 concentration at the start of ozonation. For the reason of rapidly changing O_3 concentration and its low concentration at initial moments of reaction, intrinsic second-order rate constants of individual compounds with ozone were not determined.

3.2. Role of H_2O_2 in degradation of antibiotics

The H_2O_2-augmented ozonation treatment (i.e., O_3/H_2O_2) for the target antibiotics was explored by adding various amounts of H_2O_2 prior to the start of ozonation, as the results of Fig. 4 show. A mole ratio of 1× represents adding 2.8×10^{-5} M of H_2O_2 to the reactor (where the steady-state [O_3] was separately measured at 6.2×10^{-5} M); other shown mole ratios represent proportional amounts of added [H_2O_2] (e.g., 10× = 2.8×10^{-4} M). The results show accelerated removal of target compounds, with the maximum

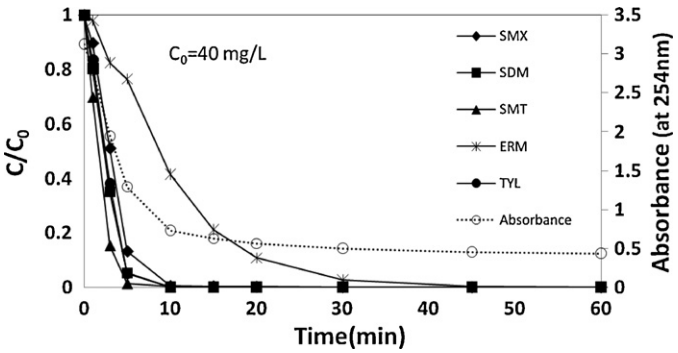


Fig. 3. Concentrations of antibiotic compounds in a mixed solution subject to ozonation (absorbance at 254 nm also shown).

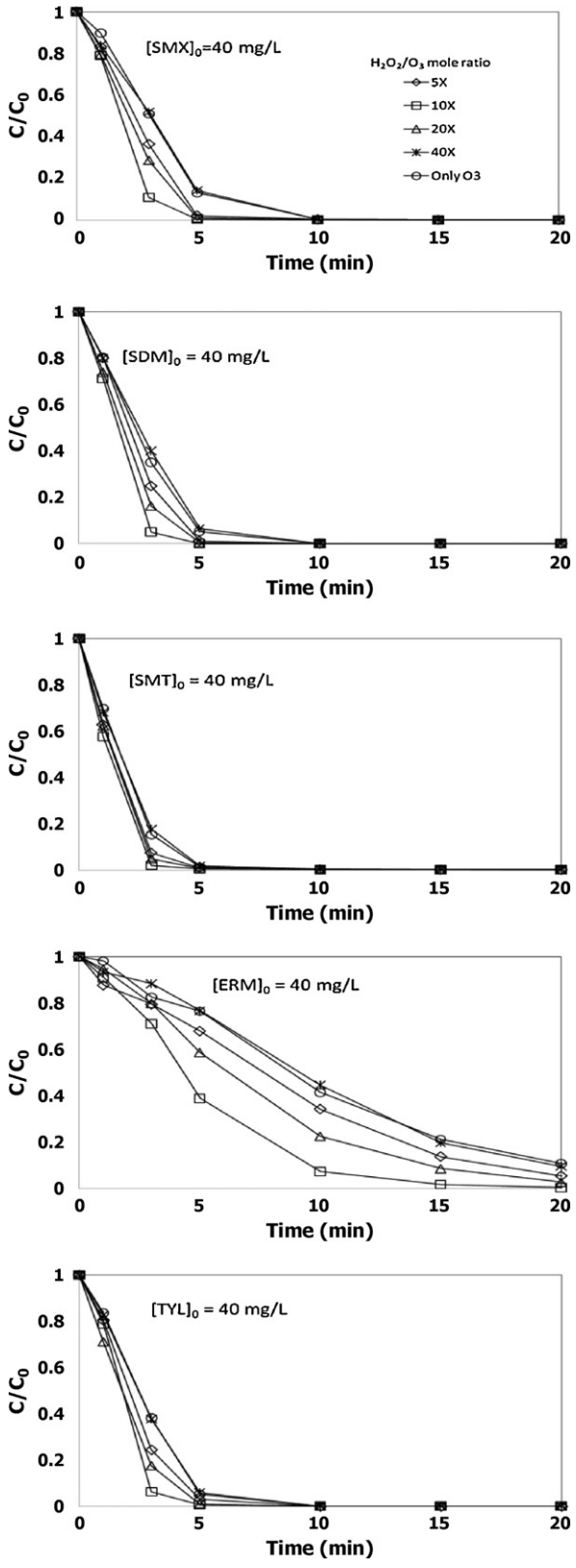


Fig. 4. Effects of added H_2O_2 amounts in ozonation treatment of a mixed solution of antibiotic compounds, where mole ratio of 1× is approximated by adding 10 μL of 30% H_2O_2 solution.

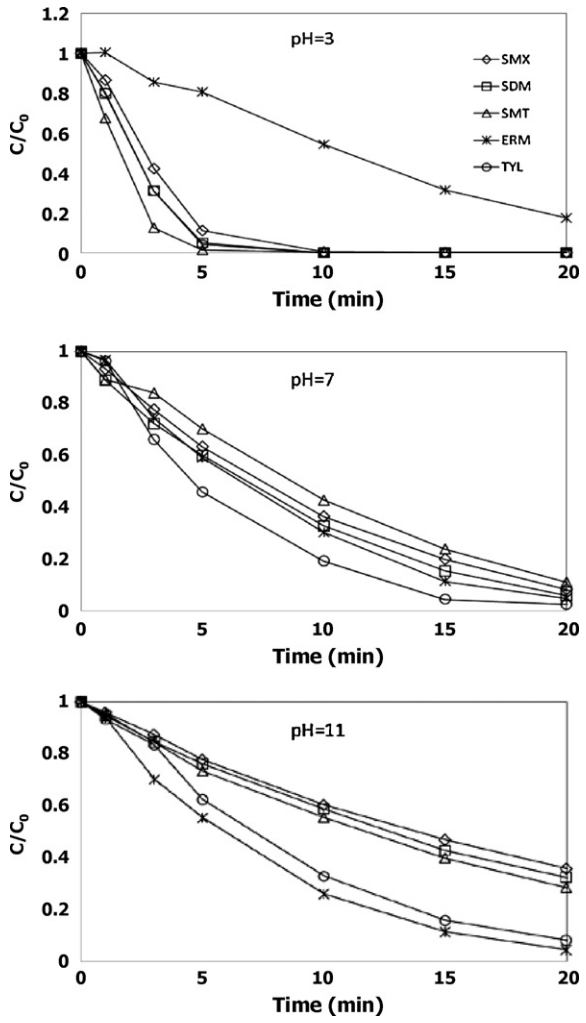


Fig. 5. Effects of buffered pH in ozonation treatment of a mixed solution of antibiotic compounds.

speed of removal at 10× of H_2O_2 addition (i.e., 2.8×10^{-4} M). The speed of removal of antibiotic compounds with O_3/H_2O_2 appeared to follow this decreasing order: 10× > 20× > 5× > 40× ~ 0×. While O_3 alone (i.e., 0×) appeared to be slowest and 10× addition of H_2O_2 fastest, increasing H_2O_2 addition to 40× reverted the removal speed to that of 0×. In studying the removal of a wide range of pharmaceuticals from water, Snyder et al. [22] observed little benefit in adding H_2O_2 for contaminant removal relative to O_3 alone; H_2O_2 addition marginally increased removal of certain pesticides at the expense of decreased removal for other hormone compounds. That O_3/H_2O_2 when applied without optimization in dosages offered little improvement of removal efficiency over O_3 alone were concluded by Ternes et al. [24]. It is important to recognize that OH radical and related free-radical degradation pathways occur readily even in treatment with O_3 alone. Where a wastewater containing contaminants that warrant enhanced treatment via degradation by OH radical, H_2O_2 should be applied sparingly as to promote generation of free radicals but not so high as to consume and deplete aqueous O_3 or even scavenge the resultant OH radical rapidly that would end up with no benefits in treatment. Among the tested doses of this work, the added amount of 2.8×10^{-4} M appeared to be beneficial. This means that the maximum degradation speed occurs at the mole ratio of $[H_2O_2]/[O_3] \sim 5$, where $[H_2O_2]$ is the initial dose of H_2O_2 and $[O_3]$ is the measured steady-state concentration during treatment.

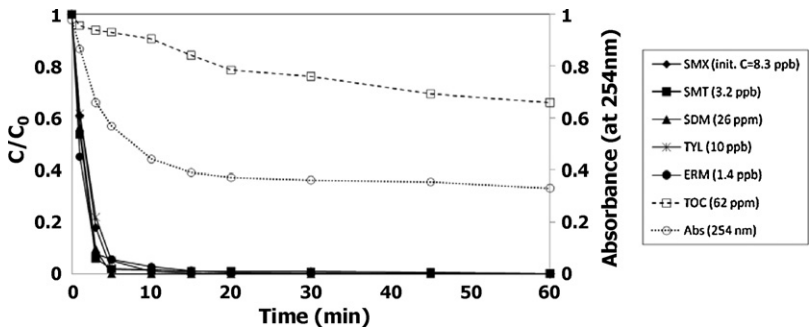


Fig. 6. Ozonation treatment of a pharmaceutical manufacturer wastewater containing the test compounds (initial and final pHs were 8.2 and 7.7, respectively; TOC and absorbance changes during treatment are also shown).

3.3. Effect of pH on treatment

The effect of pH on degradation of target antibiotics by ozonation is shown in Fig. 5. The rate of degradation occurring under buffered pH conditions followed this decreasing order: pH 3 > 7 > 11, except for ERM that showed pH 7 ~ 11 > 3. The former pattern would be consistent with that the principal, reactive oxidant for the test antibiotics being O_3, which would attain a higher concentration at low pH. The amount of dissolved O_3 in the aqueous phase is a result of two opposing processes—the supply of O_3 by gas-to-liquid transfer and the depletion of O_3 via reactions of O_3 with OH^- (>48 M^{-1} s^{-1}) and other reactions. When OH^- is scarce (i.e., low pH), the depletion reaction is slow allowing for accumulation of dissolved O_3 to a high level (e.g., typically 4–8 mg/L with air feed to an O_3 generator), whereas when OH^- is abundant (i.e., high pH), the depletion reaction is rapid thus prohibiting dissolved O_3 to accumulate (e.g., dissolved O_3 rarely exceeds 1 mg/L at pH 12 or higher). Thus, degradation of compounds (e.g., aromatic compounds) susceptible to electrophilic attack by O_3 is more rapid at low pH, where aqueous O_3 is higher. Contrarily, compounds resistant to O_3, e.g., saturated compounds such as ERM, undergo no faster degradation at low pH. The removal rates of ERM at pH 7 and 11 were similar and faster than at pH 3, which might have reflected OH radical being a viable alternate or more effective oxidant in comparison to O_3 for degradation of ERM. While the contribution of O_3 to ERM degradation is reduced at high pH due to reduced concentration, degradation rate is compensated by an increased concentration of OH radical resulting from increased hydrolysis of O_3. ERM indeed contains no unsaturated C–C bonds that O_3 would preferentially attack whereas other test compounds contain at least 2 unsaturated C–C bonds. Thus, removal of ERM was not hindered by reduced O_3 at high pH as that of other unsaturated compounds was, but was assisted by increased hydrolysis of O_3 and OH radical production at higher pH.

3.4. Degradation of antibiotics in a pharmaceutical wastewater

Fig. 6 shows the concentration profiles of the test compounds along with TOC and absorbance profiles for an authentic effluent wastewater sample from a pharmaceutical production facility subjected to ozonation. The sample contained the five target compounds in the ppb range except for SDM that reached 26 ppm. As with spiked water prior, all compounds in the wastewater including ERM were rapidly removed upon ozonation, with removals of 98, 98, >99, 97, and 97% for SMX, SMT, SDM, TYL, and ERM, respectively, in 10 min, and >99% for all compounds in 20 min of ozonation. At the end of 1 h, all compounds were reduced to below 1 ppb, albeit some reaching it sooner. The pharmaceutical wastewater contained far less target compounds (~10 times) than the spike solutions. In particular, ERM was found at 1.4 ppb in the wastewater compared to 40 ppm used in the spike. Unlike spike solutions, the pH of the wastewater decreased only slightly from 8.2 to 7.7 after 60 min of ozonation, suggesting significant alkalinity in the wastewater. Ozonation at this "buffered" pH appeared to have placed the degradation of ERM at similar rates to others; this is consistent with degradation results at buffered pH of Fig. 5 that show ERM degradation rate being closest to others at the medium pH of 7. The effect of pH on ERM degradation suggests maintaining pH at the neutral or alkaline range during ozonation is desirable. While TOC decreased gradually over the entire duration, UV absorbance decreased much faster initially corresponding to the removal of target compounds and then leveled off.

4. Conclusions

In treating pharmaceuticals in spiked and authentic wastewaters under varied operation parameters of contact time, contaminant concentration, H_2O_2 dose, and pH, ozonation proved to be effective for sulfonamide and macrolide compounds that included both aromatic and saturated compounds. Bubbling ozonation resulted in complete degradation (>99%) within 20 min for all test compounds at concentration as high as 200 ppm. In spiked water with mixed compounds of similar amounts, aromatic sulfonamide compounds were degraded more rapidly than saturated macrolides by O_3 alone, whereas judicious addition of H_2O_2 accelerated the degradation of all. An initial H_2O_2 dose at the low mole ratio of $[H_2O_2]_0/[O_3]_{ss} = 5$ appeared to heighten degradation for all compounds, in contrast to high excess ratios that showed no enhancement beyond O_3 alone. The rapid treatment by ozonation was affirmed by treatment of an authentic pharmaceutical wastewater that contained the test compounds at lower concentrations from ppb to 26 ppm, again demonstrating complete degradation in 20 min.

Acknowledgement

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