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Oxidation of Mixed Active Pharmaceutical Ingredients in Biologically Treated Wastewater

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Abstract

Biologically treated wastewater containing a mixture of 53 active pharmaceutical ingredients (APIs) was treated with 0-20 mg/l chlorine dioxide (ClO_2) solution. Wastewater effluents were taken from two wastewater treatment plants in Sweden, one with (low COD) and one without (high COD) extended nitrogen removal. The removal of the APIs varied from no significant removal at the highest dose of ClO_2 (20 mg/l) to 90% removal at a dose of 0.5 mg/l of the oxidant. From the low COD effluent, only 4 APIs were removed by more than 90% at the lowest oxidant dose of 0.5 mg/l whereas most of the APIs were removed at 5 mg/l ClO_2 dose. Removal of the same APIs from the high COD effluent was observed when the ClO_2 dose was increased to 1.25 mg/l and an increase in API removal only after treatment with 8 mg/l ClO_2. This illustrates that treatment of wastewater effluents with chlorine dioxide has potential to remove pharmaceuticals traces from wastewater treatment plant effluents.

Keywords: Pharmaceuticals; Chlorine dioxide; Wastewater effluent

Introduction

One of the pressing problems in wastewater treatment plants (WWTPs) nowadays is the inability of conventional methods to quantitatively remove the large number of active pharmaceutical ingredients (APIs) due to their high resistance to biodegradation and/or limited biological activity especially in cold climates like Sweden. The heavy usage and hence the release of these complex mixture of untreated pharmaceuticals in the wastewater effluents may lead to significant surface and groundwater contamination compromising the health of the aquatic ecosystem and the environment [1, 2, 3].

Where biological treatment is not sufficient, an improvement in WWTPs can be achieved by chemical oxidation as an additional treatment technology to remove potential pollutants that cannot be degraded biologically [4, 5, 6]. Among the chemical oxidants applied in water treatment and reported in literature, chlorine dioxide is one that merits further investigation on its potential to remove APIs in wastewater. Comparable to ozonation, the application of chlorine dioxide on drinking water, surface water and wastewater effluents treatment has shown promising results on pharmaceuticals removal. The non-steroidal anti-inflammatory drug diclofenac was among the pharmaceuticals completely degraded during drinking and surface water treatment at the lowest ClO_2 dose applied [7]. In wastewater effluents, steroid estrogens were also removed fast at low doses of ClO_2. At the same time, removal of estrogenic potency was also observed [8]. The removal of several antibiotics in water also demonstrated the reactivity of ClO_2 [9, 10].

In this study, the removal of a mixture of 53 different active pharmaceutical ingredients (APIs) in biologically treated wastewater was investigated in both low and high COD (chemical oxygen demand) effluents using different doses of chlorine dioxide. Effectiveness of the treatment was evaluated by monitoring the oxidant consumption and the amount of APIs removed. The aim of the study was to evaluate the potential for implementation of treatment of chlorine dioxide as a tertiary treatment step in municipal and hospital WWTPs.

Materials and methods

All chemicals except chloride dioxide were of analytical grade and purchased from Sigma-Aldrich.

Preparation of chlorine dioxide stock solution: Chlorine dioxide was synthesized by mixing 400 ml demineralized water with equal volume of 25 ml each of 9% HCl and 7.5% $NaClO_2$ and diluted to 1000 ml with water. The solution was allowed to react by stirring in the dark for at least 1 hour. This resulted to approximately 1 g/l ClO_2 solution.

Oxidation experiment: Wastewater effluents were collected from two WWTPs in Sweden, one with extended nitrogen removal (Eff 1) and one without (Eff 2). To characterize the wastewater, the pH and COD (Chemical oxygen demand measured spectrophotometrically by standardized Dr. Lange DR 2800 COD LCK 114 cuvette test) of the effluents were determined. Based on its respective COD value, the wastewater effluent was classified as low (Eff 1) and high (Eff 2) COD. The initial COD values of Eff 1 and Eff 2 were 35 and 55 mg/l, respectively. Effluent samples of 150 ml each were prepared in Schott Duran® bottles and spiked with mixed APIs to a final concentration of approx. 1 μg/l. ClO_2 was added to duplicate samples in the range from 0-20 mg/l. All samples were stored in the dark and allowed to react overnight (approx. 18h), thereafter, the pH and oxidant concentration of the samples were measured. Residual oxidants were removed by addition of 50 mg/l sodium sulfite.

Chlorine dioxide analysis: The concentration of ClO_2 residual in all samples was quantified by reaction with DPD (N,N-diethyl-p-phenylenediamine) using the Allcon spectrophotometer (Alldos GmbH Germany) with a built-in calibration line for ClO_2. The analysis of ClO_2 with DPD was performed according to the photometer manufacturer (Alldos GmbH).

APIs analysis: Samples of 100 ml treated effluent were filtered using a 0.45 μm membrane filter (Millipore) then acidified to pH 3 using sulfuric acid. A 50 ng/l internal standard, a mixture of 13 ^{13}C labelled APIs, was added before solid-phase extraction (SPE). SPE columns (Oasis® HLB 3 cc/60 mg, Waters) were conditioned serially with 5 ml each of methanol, ethyl acetate and acidified water (pH 3). Samples were extracted at a maximum flow rate of 2 ml/min. SPE columns were dried completely by drawing air through the columns for at least 30 min. The dried cartridges were eluted with 5 ml methanol followed by 2 ml ethyl acetate. The collected extracts were evaporated to dryness to change solvent to 30 % methanol with 0.1 % formic acid prior to analysis. A triple stage quadrupole MS/MS TSQ Quantum Ultra EMR (Thermo Fisher Scientific, San Jose, CA, USA) coupled with an Accela LC pump (Thermo Fisher Scientific, San Jose, CA, USA) and a PAL HTC autosampler (CTC Analytics AG, Zwingen, Switzerland) were used as analytical system. A 20 µL sample was loaded onto a Hypersil GOLD aQ^{TM} column (50 mm x 2.1 mm ID x 5 µm particles, Thermo Fisher Scientific, San Jose, CA, USA) preceded by a guard column. For elution of the analytes, a gradient flow with methanol and acetonitrile in water (all solvents buffered by 0.1% formic acid) was used. Both heated electrospray (HESI) and atmospheric pressure photoionization (APPI) in positive and negative ion modes were used for ionization of target compounds. Both first and third quadrupoles were operated at resolution 0.7 FMWH, and two or three selected reaction monitoring (SRM) transitions were monitored for each analyte. With SRM, the ion monitored in the first step is required to form a given fragment through a selected reaction in order to be positively identified. Samples were quantified using the SRM method and several calibration standards covering all concentration ranges were measured before, in the middle and at the end of sample sequences. The maximum difference between results at quantification and qualification mass transition was set to 30% as criterion for positive identification. The names of the APIs are mentioned in Figure 2.

Results and discussion

The initial pH of the effluents was 6.8 and 7.2 for Eff 1 and Eff 2, respectively and no further pH adjustments were made during the entire experiment. The pH in all samples did not change significantly after treatment even with the highest oxidant dose of 20 mg/l where pH remained slightly acidic (~pH 6.2).

Figure 1 shows the concentration profile of ClO_2 in the 2 effluents spiked with APIs. It can be seen that high COD effluent consumed more oxidant than low COD effluent which is evident when the dose was increased from 8 up to 20 mg/l ClO_2. Table 1 summarizes the total number of APIs that can be removed by more than 90% at each ClO_2 dose applied in both effluents. It shows that ClO_2 oxidation of wastewater effluent Eff 1 was able to remove 33 out of 53 APIs with 8 mg/l ClO_2 and no further API removal was observed despite increasing the dose up to 20 mg/l. For Eff 2, most of the APIs were removed at 10 mg/l oxidant dose and increasing the dose two-fold only removed 1 more API.

The removal of the APIs in the 2 wastewater effluents varied from no significant removal with 20 mg/l ClO_2 to more than 90% removal with just 0.5 mg/l of the oxidant. As shown in Table 1 and Figure 2, only 4 APIs from the low COD effluent (Eff 1) namely promethazine, dipyridamole, clindamycine and buprenorphine were easily removed by more than 90% at the lowest dose of 0.5 mg/l ClO_2. With 1.25 mg/l ClO_2, another 5 APIs, including hormones, (see Figure 2) were removed and by increasing further the oxidant dose, most of the APIs were already removed at 5 mg/l ClO_2. For the high COD effluent (Eff 2), a dose of 0.5 mg/l ClO_2 is not enough to allow any API removal. Removal of the same type of APIs as in Eff 1 was only observed when ClO_2 dose was increased to 1.25 mg/l and further increase in the number of APIs removed was evident after treatment with 8 mg/l ClO_2 as shown in Table 1 and Figure 3. In this case, the higher the COD content, the more oxidant the effluent needs to be able to remove the same compound. And, as can be expected, the high COD effluent has more recalcitrant APIs than the low COD effluent. In addition, the presence of other components in the wastewater aside from the APIs also consumes the oxidant resulting to a decrease in the removal of the target compounds [6].

As shown in the results for the 2 effluents, some of the APIs including diclofenac, sulfonamide antibiotic sulfamethoxazole and the estrogens, estriol, EE2 and estrone, were significantly removed at fairly low oxidant dose (1.25 - 3.75 mg/l) which was also observed in previous study done on surface and drinking water [7] and in wastewater effluents for a range of estrogens [8]. Similarly, the fluoroquinolone antibiotic ciprofloxacin also showed high reactivity to ClO_2 when tested in both surface water and wastewater effluent [9]. No literature data on removal during treatment of wastewater with ClO_2 has been found for the rest of the APIs that showed high reactivity to ClO_2 (see Figures 2 and 3).

The mechanism of API removal by ClO_2 oxidation appears to be similar to ozonation as both are selective oxidants and capable of transforming organic contaminants based on reactivity of the structure and the presence of other constituents, mostly organics, in the wastewater. Certainly, these chemical oxidants react with electron-rich functional groups such as phenolic and amino groups and these can be found in the structures of most of the APIs removed in this study. For example in this study, the most reactive API promethazine contains an amine functional group and phenolic for the steroid estrogens which are believed to be highly reactive to chemical oxidation in a number of studies [6, 7, 12, 13, 14].

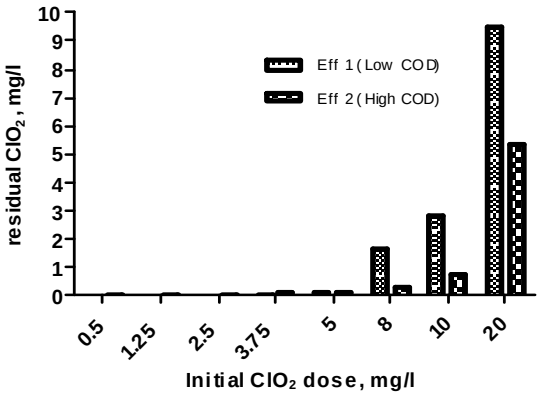

Figure 1. Residual concentration of ClO_2 in the 2 effluents after treatment with different initial oxidant doses.

ClO_2 dose, mg/l	No. of APIs removed by more than 90% Eff 1	Eff 2
0.5	4	0
1.25	9	4
2.5	15	8
3.75	24	12
5	30	18
8	33	29
10	33	32
20	33	33

Table 1. Summary of the number of APIs that can be removed for each oxidant dose

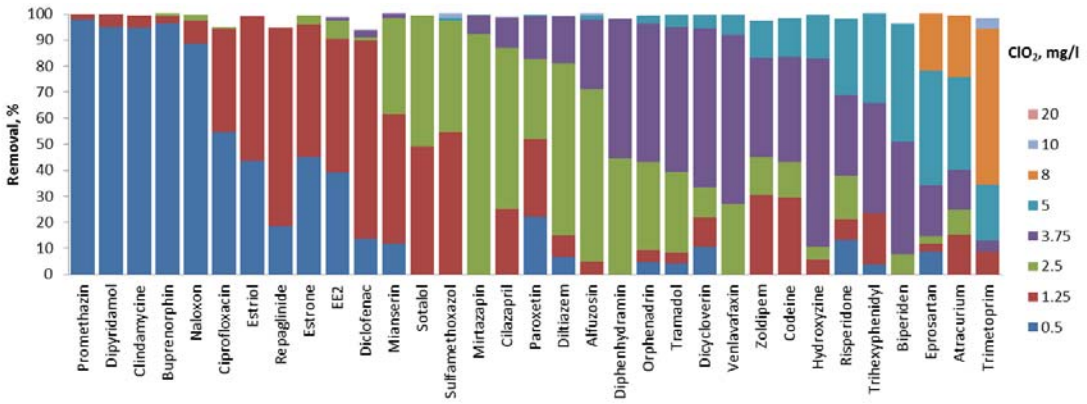

Figure 2. Percentage removal of APIs in Eff 1 at different ClO_2 doses.

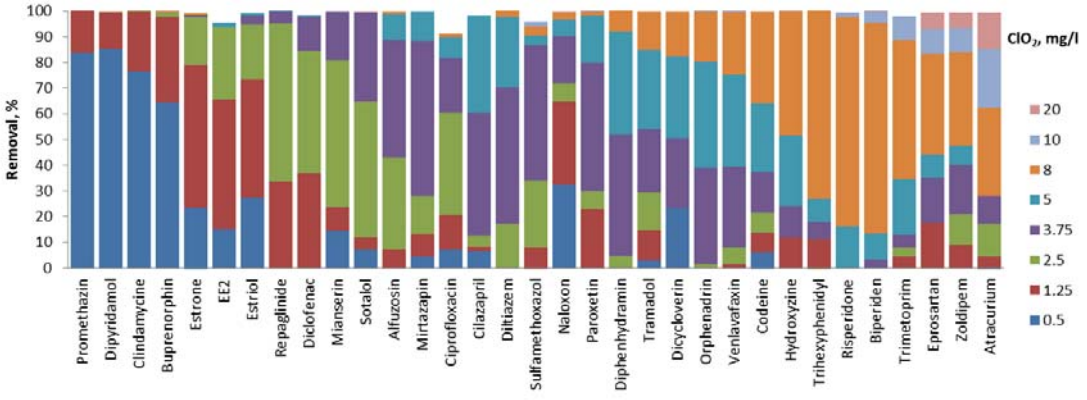

Figure 3. Percentage removal of APIs in Eff 2 at different ClO_2 doses.

The remaining 20 APIs (data not shown) were oxidized by less than 90% in both wastewater effluents even at 20 mg/l treatment dose suggesting the low reactivity of these APIs to ClO_2 oxidation. Among the APIs not degraded significantly at 20 mg/l oxidant dose are carbamazepine, alprazolam, beclomethason, budesonide, bupropion, clonazepam, finasteride, flutamid, ibersartan, and telmisartan. Carbamazepine has been shown in previous investigations to be recalcitrant to ClO_2 oxidation during drinking water [7] and wastewater treatment [6] except when treated in distilled water where around 50% removal of carbamazepine was reached [11]. Most of these APIs have not been investigated before and no data can show their reactivity towards oxidation by ClO_2. As shown in this study, some APIs are fast oxidizing and are readily removed at low oxidant dose (see Figures 2 and 3) while others need more ClO_2 or do not react at all [7]. This difference in API removal can be attributed to the reactivity of the respective functional group to ClO2 oxidation.

Compared to ozonation, ClO_2 was able to oxidise fewer APIs effectively in the concentration range for ClO_2 tested, but for a good part of the APIs that ClO_2 react well with the treatment dose required for removal was comparable to the ozone dose required for the same removal. Since ClO_2 is slightly more expensive than ozone to produce then the running costs are considered, but it is less expensive to build an installation. The treatment perspective is mainly to use ClO_2-treatment for small scale WWTP effluents or where treatment is required only for a limited time.

Conclusions

The removal of the APIs showed to be dependent on the type of wastewater, the one with extended nitrogen removal (low COD) has better API removal than the one without (high COD) for the same oxidant dose. In addition, the difference in API removal between the two wastewaters can be affected not only with its COD content but also the presence of other organic compounds in the wastewater that consumes ClO_2. As an alternative to ozone, ClO_2 can be applied during wastewater treatment in removing potentially toxic pharmaceuticals as long as the residual ClO_2 is minimized and does not exceed the standard, which requires a minimal reaction time before contact with the receiving waters. The use of ClO_2 oxidation for pharmaceutical wastewater treatment is especially beneficial in colder climates where biological treatment is not possible but taking into consideration the transformation products by carrying out toxicity evaluation of the treated effluent.

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