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# Combined chlorine dioxide oxidation and biological activated carbon processes for treatment of oxytetracycline wastewater

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**ABSTRACT**

Oxytetracycline (OTC) is a widely used antibiotic that has been frequently found in the aquatic environment. The potential reactions and kinetics of OTC degradation by chlorine dioxide ($ClO_2$) were studied in laboratory scale. The feasibility of a combined process of $ClO_2$ oxidation and biological activated carbon (BAC) treating real OTC wastewater from pharmaceutical wastewater treatment plant was also investigated. Experimental results show that OTC reacts stoichiometrically with $ClO_2$ and the highest OTC removal rate was 98.3% at pH 2 and $ClO_2$/OTC ratio 1.5:1. The reaction between OTC and $ClO_2$ was of second-order overall and the apparent second-order rate constants was 0.84 $M^{-1}$ $s^{-1}$ at pH 2 and room temperature (24°C–26°C). The combined process of $ClO_2$ pre-oxidation and BAC bio-treatment was proved to be a sustainable technology for pharmaceutical wastewater treatment. The $ClO_2$ pre-oxidation process could improve the biodegradability of OTC wastewater as the $BOD_5$/COD ratio increases from 0.04 to 0.23 at 0.2 mM $ClO_2$ oxidation of 30 min. Under the optimal conditions of $ClO_2$ 0.2 mM, hydraulic retention time 8 h and organic loading rate below 0.8 kg COD/$m^3$·d, the chemical oxygen demand (COD) removal efficiency was 68.1% and the effluent COD concentration was between 79.6 and 110.3 mg/L.

*Keywords:* Oxytetracycline; Chlorine dioxide; Biological activated carbon; Biodegradation treatment; Pharmaceutical wastewater

## 1. Introduction

Researches in the recent decade have shown that many pharmaceuticals are prevalent in the aquatic environment due to increasing use of these chemicals in daily lives. Among those, oxytetracycline (OTC), a member of tetracycline group antibiotics, is one of the extensively used antibiotics in human and farm animals for the purpose of therapeutical treatment and health protection [1], and as a growth promoter due to its broad spectrum of activity and low cost [2]. Conventional technologies used in wastewater treatment systems do not completely remove the antibiotic residues, which are then released, via treated effluent, to the environment [3]. Residues of OTC have been detected in surface water and soil in many countries, such as Italy [4], China [5,6], Iran [7] and Korea [8]. It was found that OTC would be more stable in soil and then could re-enter into the aqueous environment by surface runoff, leaching and desorption [6,9]. There is also concern by the occasional detection of OTC in underground water resources caused by urban wastewater infiltration [10]. Furthermore, the frequent detection of OTC residues in the environment may lead the development of antibiotic resistance genes in microorganisms, which can be transferred to animals and human beings [8]. Therefore, processes that can effectively remove or destroy OTC residues in water sources are desirable.

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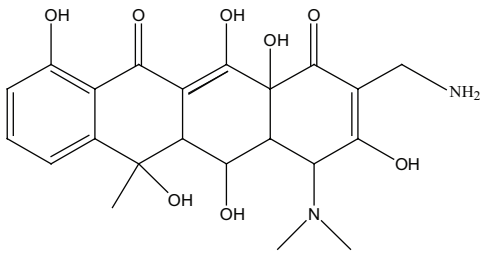
It was reported that significant removal of OTC in synthetic water was observed by photo-irradiation process. However, the toxicity of the by-products was increased [11]. OTC could also undergo solar photo-degradation and the presence of $Ca^{2+}$ accelerated its degradation [12]. Sponza et al. [13] reported that over 99% of OTC was removed by sequential anaerobic multichamber bed reactor/completely stirred tank reactor system when the initial OTC concentration was 0.65 mM. However, OTC was persistent to biodegradation and almost no elimination during conventional urban sewage treatment [3]. It was found that the effluent of the wastewater treatment plant still contains extremely high concentrations of OTC (0.04–1.74 mM) [14]. The removal efficiency of OTC from conventional wastewater treatment plant should be increased to prevent further pollution. In view of the extensive use of chlorine dioxide ($ClO_2$) in water treatment, it is of interest to determine the reactivity of $ClO_2$ with OTC with respect to the removal of OTC in aqueous or to improve the biocompatibility of OTC containing wastewater.

$ClO_2$ is a highly selective oxidant with respect to specific functional groups of organic compounds such as phenolic moieties or tertiary amino groups [15]. Many pharmaceuticals exhibit phenolic moieties and/or amino groups in their structure. Several pharmaceutical contaminants such as estrogenic 17$\alpha$-ethinylestradiol, analgesic diclofenac, antibiotic sulfamethoxazole, roxithromycin, β-lactams, fluoroquinolones and tetracycline antibiotics [16–19] have been reported to be oxidated by $ClO_2$. As shown in Fig. 1, OTC molecule contains several electron-rich moieties such as dimethylamino group, phenolic group and conjugated double bonds that are likely to be susceptible to attack by $ClO_2$.

One of the post-treatment technologies after the anaerobic treatment is the attached biomass processes such as biological activated carbon (BAC), which contains granular activated carbon (GAC) for attached growth of biomass and depth adsorption action [20]. BAC is a flexible and effective bioreactor that has been widely used for the advanced treatment in variety of wastewater treatments due to its economic advantages [20]. Furthermore, the GAC allows for higher concentration of active biomass than in a suspended growth activated sludge system so that the size of reactor can be reduced. The combination of pre-oxidation and biological treatment with BAC enhances the degradation of organic substances in many researches [21,22], and the question remains whether the combination of $ClO_2$ and BAC can reduce OTC or not to meet the discharge standard.




Oxytetracycline (OTC)
Molecular formula $C_{22}H_{24}N_2O_9$
Molecular weight 460.4g/mol

Fig. 1. Chemical structure of OTC.

The objectives of this study were to find a technical approach for the efficient removal of OTC by means of the combination of $ClO_2$ pre-oxidation and BAC adsorption and biological degradation. Specifically, the study was (1) to assess the potential of $ClO_2$ to oxidize OTC in synthetic aqueous solutions and to characterize the reaction kinetics; (2) to investigate the effects of $ClO_2$ on the biodegradability of real OTC wastewater from a pharmaceutical company under conditions relevant in water treatment by the assessment of biochemical oxygen demand ($BOD_5$)/dissolved chemical oxygen demand (COD) ratio; (3) to determine $ClO_2$ oxidation effects on the BAC biodegradability of OTC aqueous solutions under practical wastewater treatment conditions and (4) to explore the optimum technological parameters of BAC reactor for treating real OTC wastewater after $ClO_2$ pre-oxidation. The results derived from a lab-scale test would clarify the fate and behavior of OTC oxidation by $ClO_2$ and also provide significant information of pre-oxidation with biological treatment for industrial applications.

## 2. Experimental

### 2.1. Chemicals

Oxytetracycline (CAS no. 79-57-2) was purchased from North China Pharmaceutical Group Corporation (NCPC) (purity higher than 90%). The structure of OTC was shown in Fig. 1. $ClO_2$ was prepared by reacting reagent grade potassium chlorate and hydrogen peroxide in sulfuric acid. The gaseous $ClO_2$ was collected into Milli-Q water in a steady stream of $N_2$ and the impurities such as chlorine were removed from the gas stream by a sodium chlorite scrubber. The pure stock solution $ClO_2$ (10.2 mM) was stored in bottles covered by aluminum foil to block off light and placed in a refrigerator at 2°C for no longer than 1 month and standardized every time before use. Caution: $ClO_2$ present in the gas-phase equilibrated with an aqueous solution containing 8 g/L of $ClO_2$ (>20°C) is explosive. The other chemicals used were of reagent grade and were used without further purification. All aqueous solutions were prepared with Milli-Q water.

### 2.2. Experimental setup

#### 2.2.1. Single $ClO_2$ oxidation experiments

Using Milli-Q water, 0.1 mM concentration of OTC solution was prepared. The real OTC wastewater, which is helpful for practical applications, was taken from the effluent of biologically treated wastewater in NCPC (Shijiazhuang, China). In a typical experiment, 100 mL aqueous solution of OTC was placed in brown glass reactors to exclude potential light influence. A desired amount of $ClO_2$ stock solution was then added to initiate the reaction. The reactor was shaken sufficiently to mix the stock $ClO_2$ and OTC solution. At pre-selected time intervals, 10 mL of sample was rapidly transferred with a pipette to a small beaker containing 100 μL of $Na_2S_2O_3$ (0.1 M) to dechlorinate $ClO_2$ residues. The samples were filtrated with a membrane filter (pore size, 0.45 μm) before analyzed.

All runs were conducted in triplicate. The results shown correspond to the average of the individual runs and the relative standard deviations were below 6%.

#### 2.2.2. Combined processes experiments

The combined $ClO_2$ oxidation and BAC bio-treatment ($ClO_2$-BAC) experiments were investigated to compare the feasibility of them for real OTC wastewater. The BAC reactor was a plexiglass column with total effective volume 3 L, height 600 mm and inner diameter 100 mm. The column was filled with approximately 2.0 L of GAC (diameter 3 mm, drying in a 110°C oven for 24 h). The effluent of $ClO_2$ pre-oxidation OTC wastewater was pumped into BAC through BT100-2J peristaltic pump (Baoding Longer Pump Ltd., Baoding, Hebei, China). The activated sludge used for BAC start-up was obtained from a pharmaceutical wastewater treatment plant and the inoculation amount was 3 g VSS/L. The experimental tests were carried out at indoor room temperature which was in the range 24°C–26°C. In the start-up stage, the BAC was fed with the synthetic glucose wastewater and a certain amount of nutrient and trace elements (glucose substrate [COD 300-–400 mg/L], glucose: 350 mg/L, $KH_2PO_4$: 52.9 mg/L, $MgSO_4{\cdot}7H_2O$: 32.2 mg/L, $MnSO_4{\cdot}7H_2O$: 3.66 mg/L, $FeSO_4$: 0.3 mg/L, $CaCl_2$: 6 mg/L, $NaHCO_3$: 111 mg/L). Subsequently, the influent OTC concentration increased each day by adjusting to the proportion of actual wastewater, until the effluent water was stable, which indicated that the start-up had finished. The start-up stage was almost run for 40 d. Experiments with different $ClO_2$ dosages (0.2, 0.4, 0.6 mM) and hydraulic retention time (HRT: 4, 8, 12 and 24 h) were studied. The effects of organic loading rate (OLR, 0.32, 0.56, 0.8 and 1.35 kg COD/$m^3$·d) on BAC performance was also investigated.

### 2.3. Analytical methods

The concentration of OTC in samples were analyzed by high-pressure liquid chromatography (LC-20A Shimadzu, Japan) equipped with a hypersil BDS C18 column (250 mm × 4.6 mm× 5 μm, Agilent, USA) and UV detector at a wavelength of 353 nm. The mobile phase was $NaH_2PO_4$ aqueous (0.01 mol/L)/acetonitrile mixture (80/20, v/v) at a flow rate of 1.0 mL/min. Solution pH was measured using a digital pH meter (CHN868, Thermo Orion, USA). The COD was determined using the closed reflux colorimetric method (Standard Methods of Ministry of Health PRC [GB/T-5749.7–2006]). Aqueous $ClO_2$ solution was measured using Hach method 10126 at 530 nm on a DR5000 UV–Vis spectrophotometer. The $BOD_5$ analyses were performed in accordance with APHA (1998) standard method (5210B, 5-d BOD test) using 60-mL BOD bottles and a mixed bacterial culture adapted to municipal wastewater was used as inoculum.

To identify the degradation products of OTC, the solution with 0.1 mM OTC was subjected to $ClO_2$ oxidation for 2 h. The mass spectrometric measurement was performed by electrospray ionization at positive mode (ESI+) with fragmentor voltage of 120–220 V and mass scan range of m/z 100–600.The nebulizer pressure was at 25 Psi, the capillary voltage 4,000 V and ion-transfer capillary temperature of 220°C. Nitrogen was used as sheath gas at a flow rate of 20 arbitrary units.

## 3. Results and discussion

### 3.1. Single $ClO_2$ oxidation experiments

#### 3.1.1. Reaction of $ClO_2$ with OTC

Several $ClO_2$/OTC molar ratios were examined to determine the stoichiometry of the reaction for degradation of OTC. In addition, it was purposed to find out whether or not $ClO_2$ amounts can affect OTC degradation to a significant extent. Experiments were conducted with varying $ClO_2$ concentration from 0.025 to 0.2 mM. It is well established that $ClO_2$ reactions with pharmaceuticals were much dependent on pH and under acidic conditions (pH 2), the rate of reaction was the highest [23]. Therefore, the solution was adjusted to pH = 2 to maximize the impact of $ClO_2$ oxidation. The other experimental conditions were conducted at room temperature (24°C–26°C) and sufficient reaction time $t$ = 24 h. The results were presented in Fig. 2. As it can be seen there, OTC removal efficiency increased proportionally with the $ClO_2$ dose. The removal percentage was achieved 98.3% when the $ClO_2$ consumption was 0.15 mM ($ClO_2$/OTC = 1.5:1) and it slightly increased to 98.9% when the $ClO_2$/OTC ratio was 2:1. The reaction at this acidic pH value seems to exhibit an approximately 1.5:1 stoichiometric ratio between $ClO_2$ and OTC.

#### 3.1.2. Degradation kinetic of OTC with $ClO_2$

For the kinetic measurement, initial concentration of $ClO_2$ was chosen to be at least 10 times lower than the OTC concentration and thus the concentration of $ClO_2$ could be taken as invariable during the reaction. Therefore, OTC degradation kinetics was simulated using the simple pseudo-first-order model and it can be expressed as follows:

$$\frac{d[\mathrm{OTC}]}{dt} = -k[\mathrm{OTC}] \tag{1}$$

where [OTC] is the OTC concentration and $k$ is pseudo-first-order the rate constant.

For OTC degradation with different $ClO_2$ initial concentrations, a linear correlation was always obtained between $\ln([\mathrm{OTC}]_t/[\mathrm{OTC}]_0)$ and $t$ for each investigated initial concentration (Fig. 3(a)). The coefficient of determination was determined to be between 0.991 and 0.993. These results

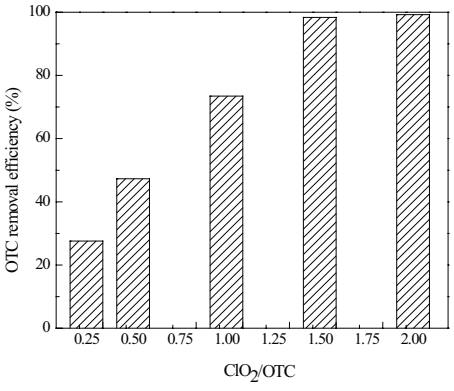



Fig. 2. OTC degradation by $ClO_2$ at pH 2 after 24 h of reaction.

revealed that the pseudo-first-order model gave a good fit within the time scales investigated. Furthermore, the pseudo-first-order rate constant ($k$, $s^{-1}$) increased linearly as increasing $ClO_2$ concentration (Fig. 3(b)), which implies that OTC degradation was also of pseudo-first-order with respect to $ClO_2$. In fact, pseudo-first-order kinetics with respect to $ClO_2$ and the target compound was generally observed in $ClO_2$ oxidation of target compounds [23]. Thus, the oxidation kinetics of OTC by $ClO_2$ could be expressed by second-order kinetics:

$$\frac{d[\mathrm{OTC}]}{dt} = -k''[\mathrm{OTC}][\mathrm{ClO_2}]_0 \quad (2)$$

where $k$" was the second-order reaction rate constant and $[ClO_2]_0$ is initial concentrations of the $ClO_2$. Based on Eqs. (1) and (2), it can be deduced that:

$$k'' = \frac{k}{[\mathrm{ClO_2}]_0} \quad (3)$$

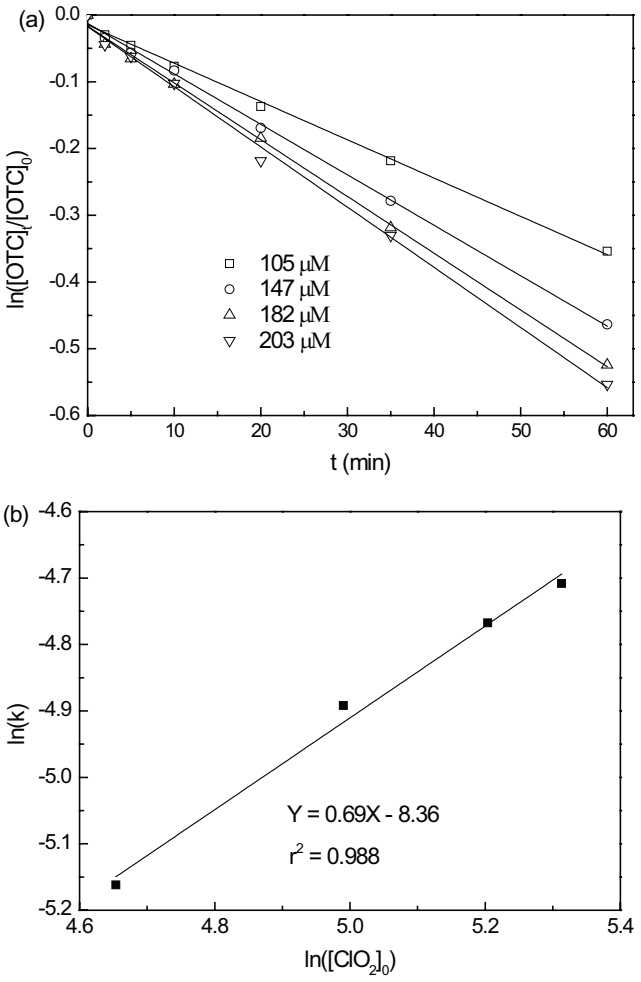



Fig. 3. Determination of reaction order for OTC degradation by $ClO_2$: (a) plot of $\ln([OTC]_t/[OTC]_0)$ vs. reaction time to get the pseudo-first-order rate constants (k, $s^{-1}$) at different initial $ClO_2$ concentrations and (b) plot of ln(k) vs. $\ln([ClO_2]_0)$ to determine reaction order (pH = 2.0, $T$ = 24°C).

The value of $k$" was determined to be 0.84 $M^{-1}$ $s^{-1}$ at pH 2 and room temperature (24°C–26°C). As the real wastewater has a pH 7, the kinetics was also calculated at pH 7 and the value $k$" slightly decreased to 0.81 $M^{-1}$ $s^{-1}$. The neutral and positively charged OTC molecules are dominant in a solution of pH 2–7 [23] and it is reported that the contribution from the cationic and neutral species to the overall $k$" is insignificant [19].

### 3.2. Changes in biodegradability

In order to checkout whether or not that $ClO_2$ oxidation improves the biodegradability of real OTC wastewater for raising OTC removal efficiency in wastewater treatment plant, experiments were conducted to study the $BOD_5$/COD ratio of OTC. The $BOD_5$/COD ratio is usually used as the criteria for evaluating the biodegradability of the wastewater and it has been generally accepted that a $BOD_5$/COD ratio higher than 0.3 represents a "readily biodegradable" wastewater. It is desired to carry out the $ClO_2$ oxidation at pH 7 in practical process, since the biological treatment is generally performed at pH 7 and further pH adjustment of OTC wastewater is not needed after $ClO_2$ oxidation. Consequently, the effect of $ClO_2$ oxidation on the biodegradability of OTC wastewater was all conducted at pH 7 in the followed experiments. The initial $BOD_5$ and COD were 18.9–23.7 and 472.7–523.4 mg/L for OTC wastewater with 0.89–0.11 mM OTC. It implies the non-biodegradable nature of OTC wastewater ($BOD_5$/COD: 0.03–0.06). After 30 min of $ClO_2$ oxidation, the $BOD_5$/COD ratio increases from 0.04 to 0.23 as shown in Fig. 4 and it is evident that the biodegradability increases with increasing $ClO_2$ oxidation time. However, there was a slight raise of biodegradability when $ClO_2$ oxidation time increased from 30 to 60min, suggesting oxidation time should be kept below 30 min based on the consideration of operating cost in the practical application. Moreover, the COD removal efficiency reached 34.1% when the oxidation time was 10 min and further prolonging oxidation time had little effects on the COD removal. The results indicate that $ClO_2$ could only be capable of partial oxidation other than complete oxidation of

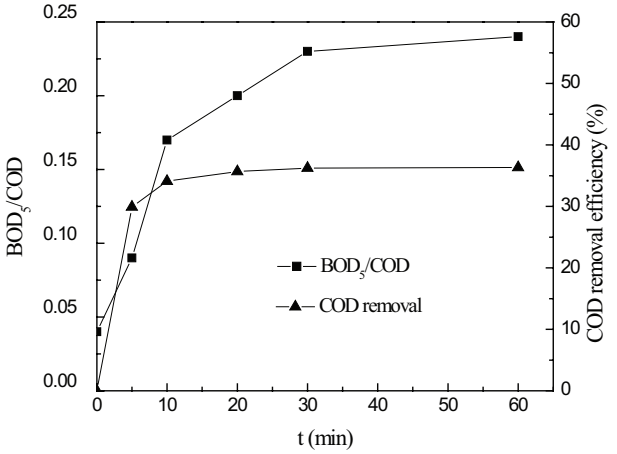



Fig. 4. Effect of $ClO_2$ oxidation time on the biodegradability and COD removal of OTC wastewater ($ClO_2$ 0.2 mM, pH 7.0, $BOD_5$ test at pH 7).

the soluble organic matter even at prolonged oxidation time, resulting in the formation of more biodegradable molecules but no significant decrease of COD.

For better understanding bio-available intermediates, the reaction products of OTC with $ClO_2$ at pH 7 were analyzed by liquid chromatography–mass spectrometry (LC/MS). Two main by-products were found as shown in Fig. 5. The molecular ion of OTC was m/z 461. The products were written as M+49 and M–228 in short, indicating the net mass gain or loss of the product from the parent compound. Due to the lack of authentic standards, a true quantification of the products is not possible. OTC is known to have degradation products, such as 4-epi-oxytetracycline, α-apo-oxytetracycline and β-apo-oxytetracycline, which were not found in this reaction. The possibility that some reaction products are not detectable by LC is likely. Identification of $ClO_2$ by-products and the biodegradability intermediates of OTC by LC/MS is a subject of further studies.

### 3.3. Combined $ClO_2$ and BAC processes experiments

#### 3.3.1. Effects of $ClO_2$ and HRT

$ClO_2$ oxidation provides a feasible means to enhance the biodegradability of OTC wastewater. The effects of $ClO_2$ pre-oxidation on biological treatment, therefore, became the main concern of this study. Fig. 6 presents the concentration changes of COD along the $ClO_2$-BAC processes under different $ClO_2$ dosages and HRT. The horizontal dotted lines were plotted to easily understand the local discharge standard (Discharge standards of water pollutants for pharmaceutical industry fermentation products category GB 21903-2008), which requires the effluent COD below 120 mg/L. During the experiments, the $ClO_2$ concentrations varied from 0.2 to 0.6 mM and oxidation time was all set at 30 min. Every experiment ran for 8 or 9 d and samples were taken every day for COD analyzing. The real OTC wastewater without $ClO_2$ pre-oxidation can hardly be biodegradated as the COD removal efficiencies were around 2%–6% after 9 d biodegradation in BAC reactor under conditions HRT 24 h, dissolved oxygen 3 mg/L and OLR 0.3 kg COD/$m^3$·d. The influent COD concentration (mean value) of BAC reactor was 363.4, 361.1 and 328.2 mg/L for 0.2, 0.4 and 0.6 mM $ClO_2$ pre-oxidation, respectively, indicating that COD removal efficiencies increased as the $ClO_2$ dosage increases. The highest COD removal rates of 31.2% were detected under $ClO_2$ dosage of 0.6 mM. The result was in agree with the single $ClO_2$ oxidation of synthetic OTC aqueous solution, where the COD removal increased as the $ClO_2$ dosage increases (Fig. 2). However, pre-oxidations with high $ClO_2$ dosages had little benefits on BAC operating. As shown in Fig. 6(c), the COD in effluent were 120–140 mg/L, exceeding the local standard

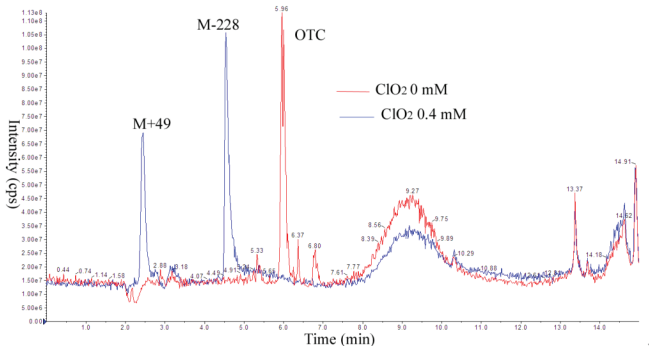



Fig. 5. LC chromatograms (data not smoothed) of OTC and its degradation byproducts (OTC 0.1 mM, $ClO_2$ 0.4 mM, reaction time 2 h, pH 7.0).

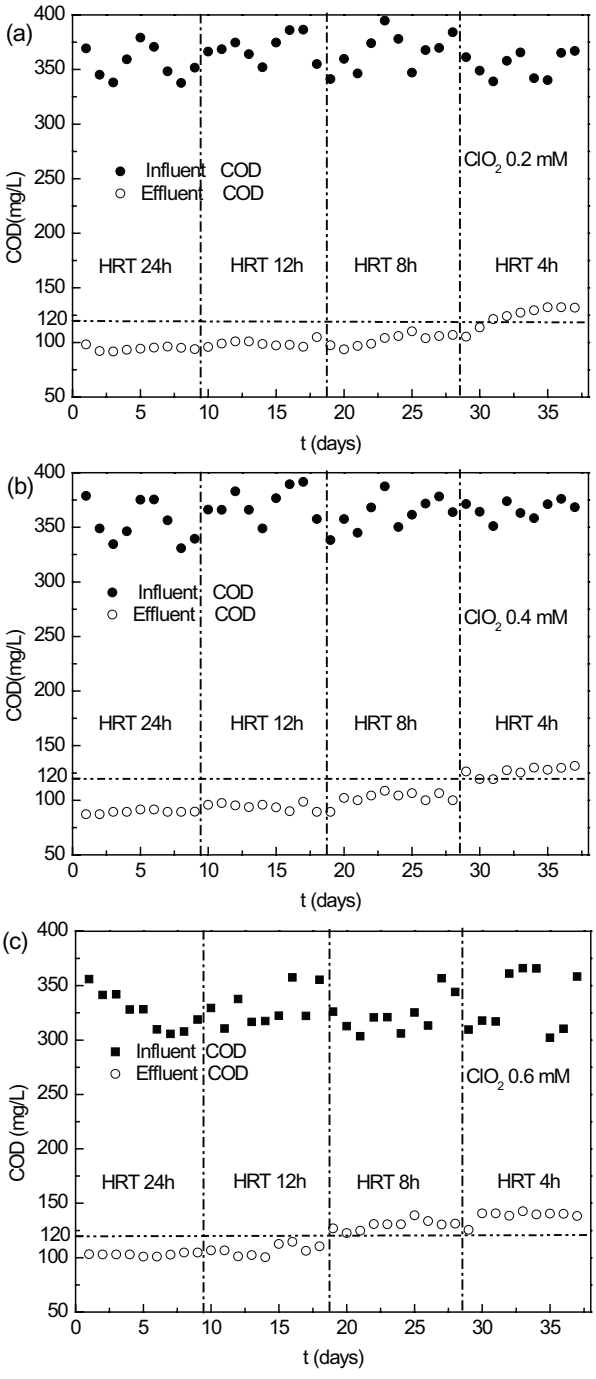



Fig. 6. COD removal by BAC reactor combined with (a) 0.2 mM $ClO_2$ pre-oxidation, (b) 0.4 mM $ClO_2$ pre-oxidation and (c) 0.6 mM $ClO_2$ pre-oxidation as a function of HRT under DO 3 mg/L and OLR 0.25 kg COD/$m^3$·d.

(COD < 120 mg/L), when the HRT was below 12 h. On the other hand, the COD in effluent could meet the standard and the average COD removal efficiencies were higher than 73% when the HRT exceeded 4 h under pre-oxidation with moderate $ClO_2$ dosages (Figs. 6(a) and (b)). It was deduced that at high $ClO_2$ dosage, the un-reacted $ClO_2$ was remained in water and is not conducive to microbial reproduction in BAC as $ClO_2$ was a widely disinfectant and antiseptic. It was detected negligible $ClO_2$ in the solution when the $ClO_2$ dosage was 0.2 and 0.4 mM, respectively, while the $ClO_2$ residual was 0.11 rmM when the $ClO_2$ dosage was 0.6 mM.

HRT is a crucial parameter in biological wastewater treatment and significantly affects microbial ecology and characteristics in BAC operational systems [24]. The average COD removal rates of 75.7%, 74.3% and 71.0% were detected under HRT of 24, 12 and 8 h and $ClO_2$ dosage of 0.4 mM, respectively, and the effluent COD concentrations of 89.4, 93.8 and 105.8 mg/L, respectively, satisfied the discharge standard for pharmaceutical wastewater (China). The same trends were found for $ClO_2$ dosage of 0.2 mM and HRT of 24, 12 and 8 h. Taking account of running cost, the optimal condition was found at $ClO_2$ dosage of 0.2 mM and HRT of 8 h.

### 3.3.2. Effects of OLR

The effects of OLR on the efficiency and performance of BAC were shown in Fig. 7. The experiments were done under HRT of 8 h and $ClO_2$ dosage of 0.2 mM. It is evident that COD removal efficiencies decreased with the increase of OLR. The average COD removal efficiency was 75.7%, 72.4%, 68.1% and 57.3%, respectively, under organic loading of 0.32, 0.56, 0.8 and 1.35 kg COD/$m^3$·d. The COD concentrations in influent of BAC were distributed in the range of 327.7–367.8 mg/L. The results suggest that the effluent of BAC was 327.7–367.8 mg/L and in accordance with local discharge limits of water pollutants (COD < 120 mg/L) under design running conditions as long as OLR not exceeding 0.8 kg COD/$m^3$·d. It was reported that when the influent COD was 10,000 mg/L and the OLR achieved 10 kg COD/$m^3$·d, the effluent from the BAC reactor could meet the discharge standard without further treatment [25]. The BAC provides enormous surface area for microbe inhabitance by filling with GAC media, and also it strengthened filtration of the suspended particles, where both effects improved COD removal. Furthermore, it has been reported that some microorganisms could produce extracellular exopolymers during organism growth, which could be used as biological flocculants to enhance the performance of water treatment [26].

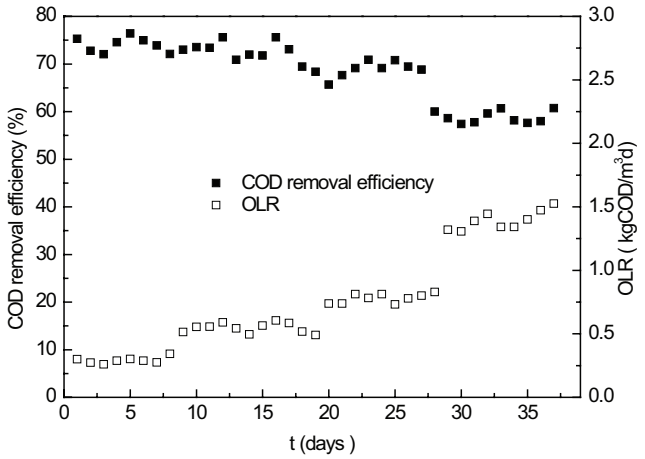



Fig. 7. Effects of OLR on BAC performance under HRT of 8 h and $ClO_2$ dosage of 78.9 mg/L.

## 4. Conclusions

The OTC reacts extremely rapidly with $ClO_2$ in synthetic water under conditions pH 2.0 and $ClO_2$/OTC ratio 1.5:1 and under this conditions, 98.3% OTC was removed. The kinetics between $ClO_2$ and OTC was of second-order overall, with first-order in OTC and $ClO_2$, respectively. $ClO_2$ can be used as a pre-process of biological treatment of pharmaceutical wastewater as the biodegradability of OTC wastewater was largely improved from 0.04 to 0.23 for real OTC wastewater. The real OTC wastewater could be well treated by the combined process of $ClO_2$ and BAC under the optimal condition of 0.2 mM $ClO_2$ pre-oxidation, BAC HRT 8 h and OLR < 0.8 kg COD/$m^3$·d. The COD in influent of BAC was 327.7–367.8 mg/L and the effluents with COD 79.6–110.3 mg/L were satisfied the discharge standard for pharmaceutical wastewater (China). It has been demonstrated the combined process of $ClO_2$ and BAC is a sustainable and environmentally attractive method for the removal of pharmaceuticals in small wastewater treatment plants where ozonation could be too expensive and complicated.

## Acknowledgments

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