

Degradation of 17 α -ethinylestradiol in aqueous solution by ozonation

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Abstract

This study investigates the ozonation of 17 α -ethinylestradiol (EE₂) in aqueous solution. The affecting factors on the degradation of EE₂ were studied and described in details, such as initial EE₂ concentration, initial pH value and ozone concentration. In addition, some parameters such as pH, electrical conductivity, mineralization efficiency and degradation products were monitored during the process. The mineralization efficiency of EE₂ could reach 53.9%. During the ozonation process the rapid decrease of pH and the sharp increase of electrical conductivity indicated the formation of acidic by-products, small fragments and ions which were confirmed by high performance liquid chromatography (HPLC) and gas chromatography–mass spectrometry (GC/MS) analysis. Results showed that there were intermediate products of smaller molecule with higher polarity produced during the course of EE₂ degradation. Then a possible reaction pathway for EE₂ degradation involving all intermediates detected is proposed. During the ozonation process EE₂ was first oxidized into hydroxyl-semiquinone isomers which were subsequently degraded into low molecular weight compounds such as oxalic acid, malonate, glutarate, and so on. Furthermore, these organic acids are easily oxidized by ozone into carbon dioxide (CO₂). This work shows that ozonation process is promising for the removal of EE₂. The results can provide some useful information for the potential treatment of EE₂ by ozonation in aqueous solution.

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Keywords: 17 α -Ethinylestradiol (EE₂); Ozonation; Hydroxyl radical; Intermediate; Mechanism

1. Introduction

Recently, more chemical materials were released into the environment. Several types of these chemicals have been suggested to affect the health of human and wildlife and confirmed as the Environmental Endocrine Disruptors. Abnormal sexual development of animal and decrease in the average numbers of human spermatozoa are widely reported [1]. Thus, the environmental presence of compounds with estrogenic properties has become a major issue of worldwide concern [2]. The research on removal, transformation and degradation products of the environmental endocrine disruptors are necessary.

The synthetic estrogen 17 α -ethinylestradiol (EE₂), used in contraceptive pills, is known to enter the aquatic environment via sewage effluents, thereby posing a threat to aquatic wildlife [3].

EE₂ has been shown to induce the synthesis of the yolk-precursor protein vitellogenin in male rainbow trout at a concentration as low as 0.1 ng L⁻¹ [4], and it is difficult to remove EE₂ from wastewaters by primary and secondary treatment. New methods are needed for removing it from wastewater prior to their release into waters.

The degradation of this compound has not been extensively studied. There are few published articles studying the degradation of EE₂ in the environment or lab. Vader et al. [5] examined degradation of 50 μ g L⁻¹ EE₂ by nitrifying activated sludge and found that oxidation of EE₂ resulted in the formation of hydrophilic compounds with lower estrogenic activity. Segmuller et al. reported the photodegradation of EE₂ in solid state [6]. Furthermore, the Photodegradation of EE₂ in aqueous solution could be accelerated in the presence of Fe³⁺ or Anabaena cylindrical [7]. Rudder et al. [8] investigated the removal of EE₂ with the manganese oxide used as sorbent and catalyzer.

But generally the procedures time was long for these methods, so it is necessary to develop effective technology to remove EE₂.

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In the early 19th century, people knew that ozone was a strong oxidant. The standard electrode potential (E_0) is 2.07 V in acidity medium and 1.27 V in alkaline medium, respectively. Theoretically, it can provide sufficient energy in aqueous solution to degrade the persistent chemical substance. The treatments of various organics and inorganics with ozone are extensively discussed in the literature [9]. The main effects of ozonation are decolorization, elimination of taste and odors, degradation of organics and disinfection [10]. Bowers et al. [11] also showed that ozonation product could be finally converted to CO_2 and H_2O in special conditions. Moreover, excess ozone compared to other oxidants, could be decomposed to oxygen without harmful residue [12]. So, ozone becomes increasingly important as an effective and environmental friendly oxidation agent in many fields [13].

Huber et al. [14,15] investigated the removal of 17α -ethinylestradiol by ozonation, they studied the estrogenic activity of aqueous solution of EE_2 using Yeast Estrogen Screen (YES) and identified the oxidation products by LC/MS and GC/MS with the help of the model compounds. In this work, we selected 17α -ethinylestradiol as target compounds and aimed at investigating the affecting factors on EE_2 degradation, mineralization degree of EE_2 , and intermediate products during ozonation process.

2. Materials and methods

2.1. Chemicals

17α -Ethinylestradiol (EE_2) (>98%) was commercially obtained from the Sigma (USA) and used without further purification. The molecule structure of EE_2 is shown in Fig. 1.

Ozone was generated using a Proton Exchange Membrane (PEM) electrolysis ozone generator provided by Prof. Yuanquan, Zhou, Department of Chemistry, Wuhan University. Absolute acetonitrile was used as co-solvent of EE_2 . BSTFA + TMCS (99:1) were purchased from the Sigma (USA). HCl, NaOH, $\text{Ba}(\text{OH})_2$ were all analytical-grade, and doubly distilled water was used throughout.

2.2. Experimental procedures

For very low aqueous solubility of 17α -ethinylestradiol (EE_2), acetonitrile was used as the organic solvent. Stock solution was initially prepared at $337 \mu\text{mol L}^{-1}$ by dissolving EE_2 into acetonitrile:water mixture (40:60, v/v). Acetonitrile is miscible in water and has a low reactivity with ozone ($t_{1/2} > 18$ years,

at pH 7.0). Moreover, peroxides will not form during ozonation [16–18].

Various EE_2 concentrations could be made from stock solution by dilution. Ozone was bubbled into the EE_2 solution, which was continuously mixed using a magnetic stir bar at 80 rpm. The yield of O_3 was $11.6 \mu\text{mol min}^{-1}$, determined by means of iodometry [19]. The flow rate of O_3 gas could be controlled by a needle valve, through which different ozone dosage added into the system could be controlled. The superfluous ozone was adsorbed by activated carbon, and the reactions were terminated by flushing the reactor with nitrogen gas. A 2N $\text{Na}_2\text{S}_2\text{O}_3$ was added to the system to remove the residual O_3 and organic radical prior to analysis [17,18,20,21].

The pH of solution was adjusted to the desired values by HCl or NaOH. Ozonation experiments were carried out at initial EE_2 concentration 8.4 – $67.6 \mu\text{mol L}^{-1}$ under the condition of constant ozone amount $11.6 \mu\text{mol min}^{-1}$, another experiment were carried out at ozone amount 0.7 – $11.6 \mu\text{mol min}^{-1}$ under the condition of initial EE_2 concentration $33.7 \mu\text{mol L}^{-1}$. Without special elucidation, the initial concentration of EE_2 was $33.7 \mu\text{mol L}^{-1}$. In order to monitor the ozonation process, the pH value and electrical conductivity of a solution was measured before and after an experiment [22] by using AY120 pH-meter (SHIMADZU) and a conductivity meter DDS-11. All the experiments were conducted at $25 \pm 1^\circ\text{C}$.

2.3. Analysis

2.3.1. EE_2 determination

At different intervals, the EE_2 samples obtained under different conditions were taken out. Then the EE_2 concentration of the sample was analyzed with fluorescence spectrophotometer [7] using fluorescence spectrometer F-4500 (Hitachi, Japan). Its measurement type was wavelength scan, scan mode: emission. The main parameters of the Fluorescence photometer measurement were as follows: scan speed: 240 nm min^{-1} ; delay: 0 s; EX slit: 2.5 nm; EM slit: 10.0 nm; PMT voltage: 700 V s; response: 8.0 s. The fluorescence intensity of EE_2 was measured in a 1 cm quartz cell. Excitation and emission wavelengths used were set at 287 and 315 nm respectively. The detection limit of this fluorescence method was 0.6 mg L^{-1} , and the relative standard deviation was below 2%. In these measurements, others reagents (except EE_2) used in the aqueous solution had no fluorescence (or emission peak) at EX wavelength 287 nm and they have no effects on detection of EE_2 .

2.3.2. HPLC analysis

The results determined by fluorescence spectrophotometer also have been examined by reversed-phase HPLC equipped with UV detector. HPLC (with a $150 \text{ mm} \times 4.6 \text{ mm}$, Supelco C18 column) condition was: mobile phase was the mixture of acetonitrile-water (50:50, v/v) at a flow rate of 1 mL min^{-1} by the HPLC pump. The water sample was injected into the column and detected by an UV detector at 280 nm. The injection volume was $20 \mu\text{L}$. Both results are same. So, the results from determination using fluorescence spectrophotometer are reliable.

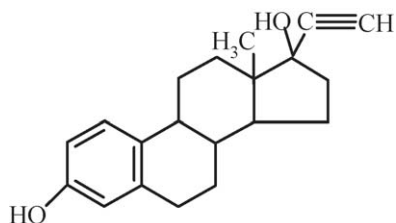


Fig. 1. The molecule structure of EE_2 .

2.3.3. CO₂ measurement

Carbon dioxide produced upon ozonation was determined as BaCO₃ [23] to inspect the mineralization degree of the EE₂ solution oxidized by ozonation. CO₂ was removed from solution by nitrogen gas and introduced into a concentrated Ba(OH)₂ solution to produce BaCO₃. The solution were collected, BaCO₃ was allowed to precipitate and excess of Ba(OH)₂ was titrated with 0.01677 mol L⁻¹ HCl solution with phenolphthalein as indicator. A blank experiment without EE₂ was performed under the same conditions.

2.3.4. GC/MS analysis

Ozonated samples were preconcentrated using solid-phase extraction (SPE) on small C₁₈ cartridges (Isolute Co., USA). The cartridges were first conditioned with 5 mL methanol, acetone and 5 mL water, and then 500 mL sample was passed through the SPE tube. Finally elute the organics by 5 mL methanol and acetone, respectively. Then the extractions were evaporated to dryness using Kuderna–Danish evaporation followed by N₂ gas bubbling. The completely dried sample was derived by silylation using BSTFA + TMCS (99:1) at 90 °C for 1h to convert all free –OH and –COOH groups into their volatile TMS-ether (–OSiMe₃) and TMS-ester (–CO₂SiMe₃) derivatives, respectively [18]. Then the samples were identified by GC/MS. A Varian 3400 chromatograph was used, equipped with a septum programmable injector Varian SPI 1093 and coupled with a thermostated transfer line with a mass spectrometric detector Varian Saturn II. The GC/MS column was a DB-5MS (J&W Scientific, Folsom, CA), 60 m × 0.25 mm i.d., thickness 0.25 μm. Helium (N60) was the carrier gas (flow rate 1.2 mL min⁻¹). The GC injection port temperature was 250 °C, and the column temperature was fixed at 80 °C for 8 min, and then programmed from 80 to 280 °C at 8 °C min⁻¹, the final temperature being maintained for 30 min. The transfer line and ion source were maintained at 170 °C and 180 °C, respectively. The MS detector was operated in the EI mode. Scanning in the range *m/z* 40–650 amu at 1.4 scan s⁻¹. The intermediate products were identified using an identification program of U.S. National Institute of Standards and Technology (NIST) Library.

2.3.5. Data analysis

The data are presented as means from triplicate experiments. The errors are below 5% and figures are presented without error bars.

3. Result and discussion

3.1. Effect of initial EE₂ concentration

To examine the effect of initial concentration of EE₂ on degradation of EE₂, five solution (8.4–67.6 μmol L⁻¹) of EE₂ were expose to ozone. The results are shown in Fig. 2.

As shown in Fig. 2, the higher the initial EE₂ concentration, the lower EE₂ degradation efficiency was obtained. The degradation efficiency reached 76.3% for 8.4 μmol L⁻¹ EE₂ after ozonation for 5 min, while the efficiency is only 12.0% for 67.6 μmol L⁻¹ EE₂.

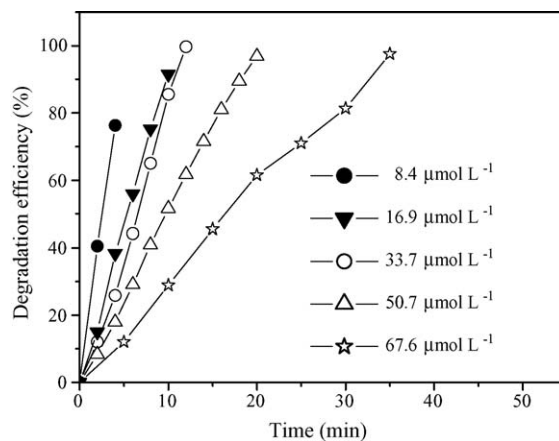


Fig. 2. Effect of initial EE₂ concentration on the degradation efficiency pH 6.5, gas flow rate was 48 mL min⁻¹, [O₃] = 11.6 μmol min⁻¹.

3.2. Effect of ozone concentration

The ozone dosage was controlled by means of altering the flow rate of ozone. The effect of different ozone concentrations on degradation efficiency is shown in Fig. 3.

With increasing of O₃ concentration, the degradation efficiency increased. The degradation efficiency is 84.6% for 11.6 μmol min⁻¹ ozone concentration at 10 min, while the efficiency is only 11.7% for 0.7 μmol min⁻¹ ozone concentration.

3.3. Effect of initial pH value

The degradation experiment was repeated over the range of 4.0–8.0, the result as a function of pH is shown in Fig. 4. There was an increase in the degradation efficiency with increasing pH value. Degradation efficiency varied from 33.7% to 95.4% when the pH values ranged from 4.0 to 8.0 after ozonation for 20 min. In general, ozone reacts with organic compounds in water and wastewater via two different pathways. Ozone may react directly with chemical molecules in aqueous solution; it may also generate secondary oxidants (mainly hydroxyl radical) to oxidize molecules [24–26]. •OH is a stronger and less-selective oxidant

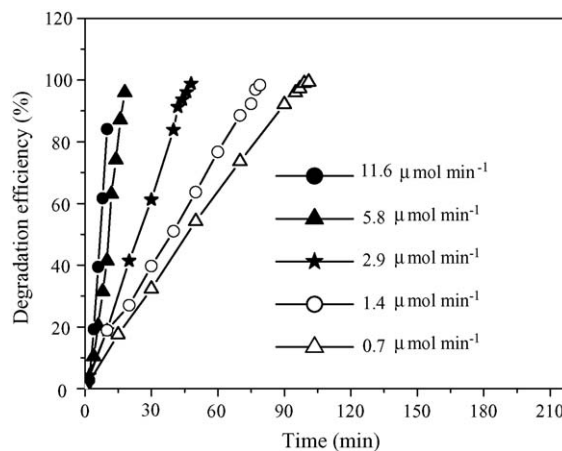


Fig. 3. Effect of ozone concentration on the degradation of EE₂ [EE₂]₀ = 33.7 μmol L⁻¹, pH 6.5, gas flow rate was 48 mL min⁻¹.

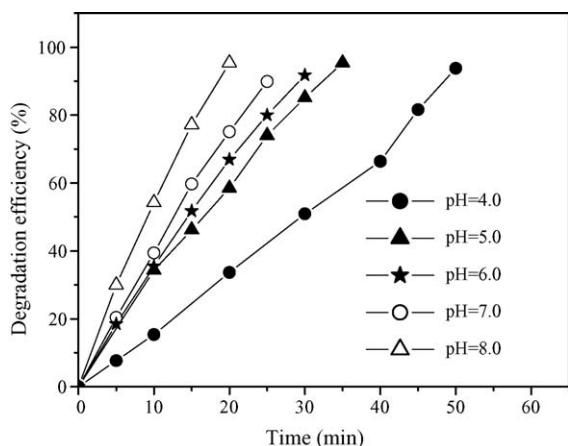
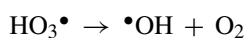
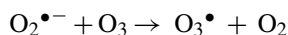
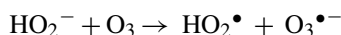
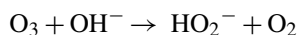
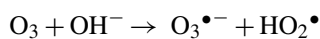


Fig. 4. Effect of pH value on the degradation efficiency of EE₂ [EE_2]₀ = 33.7 μmol L⁻¹, pH 6.5, [O₃] = 11.6 μmol min⁻¹.

than ozone, its reactions rate constants are about nine orders of magnitude greater than those of ozone for the same organic compound [27–29]. The pH values affect the reaction process by having impact on the rate of the ozone decomposition and the formation of hydroxyl radicals, which is favored at high pH values [12,31]. According to Yao et al. [17,19], ozone is autocatalytically decomposed to form hydroxyl radicals in aqueous solution at pH > 4.0. Formation of secondary free radicals is shown as follows [30,31]:



3.4. Varieties of the pH value and electrical conductivity of the solution

During the ozonation process, the pH values and electrical conductivity of the solution were measured. Results are shown in Fig. 5.

Fig. 5 shows that pH values dropped from 6.5 to 5.9, and the conductance varied from 13.7 to 50.3 μS after ozonation for 20 min. Concentration of H⁺ almost increased by four-fold which indicated the formation of acidic reaction intermediates. Besides, the ionization of these acids led to the increase of electrical conductivity and the decrease of pH value.

3.5. Result of HPLC chromatogram analysis

Products were detected by HPLC chromatogram after ozonation for different reaction time. The result is shown in Fig. 6.

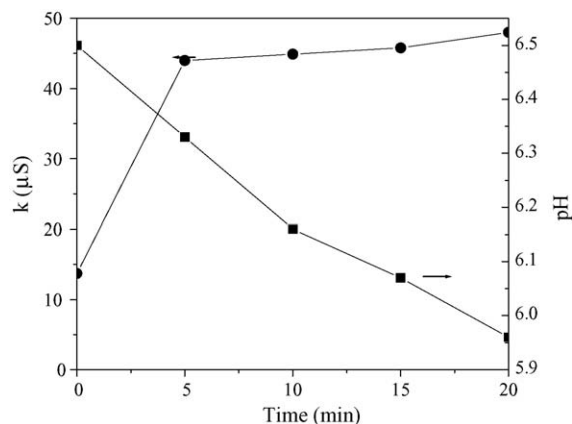


Fig. 5. Varieties of the pH and electrical conductivity of the solution [EE_2]₀ = 33.7 μmol L⁻¹, initial pH 6.5, [O₃] = 11.6 μmol min⁻¹.

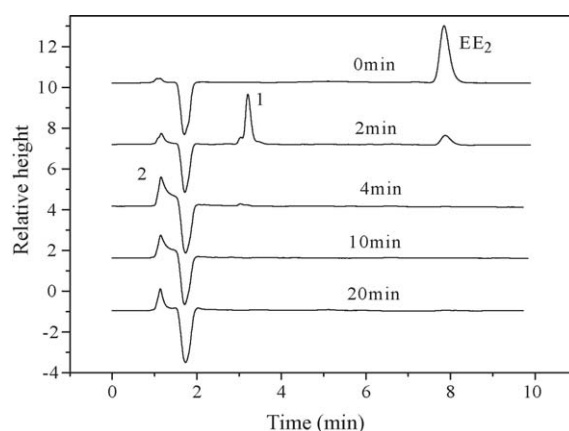


Fig. 6. HPLC chromatographs of EE₂ degradation by ozonation [EE_2]₀ = 33.7 μmol L⁻¹, pH 6.5, [O₃] = 11.6 μmol min⁻¹, λ = 280 nm.

In the HPLC chromatogram, the peaks corresponding to EE₂ decreased, and there were obvious product peaks at shorter retention time after ozonation for 2 min, indicating that some intermediate products of lower molecular weight and higher

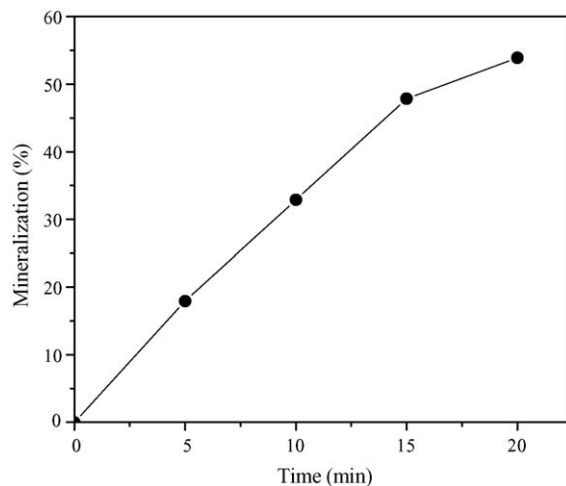


Fig. 7. Mineralization efficiency of EE₂ at different reaction time [EE_2]₀ = 33.7 μmol L⁻¹, temperature = 25 ± 1 °C, pH 6.5, [O₃] = 11.6 μmol min⁻¹.

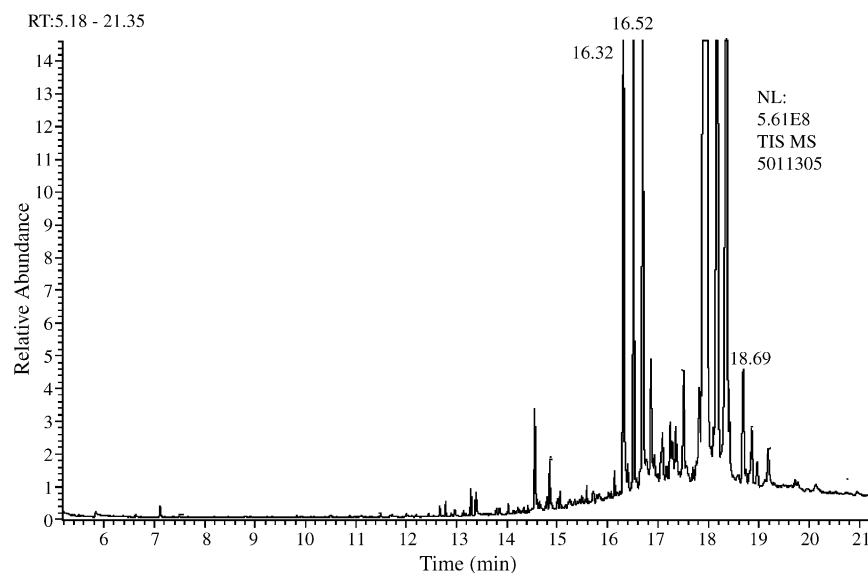


Fig. 8. Total ion chromatogram of sample oxidized for 2 min.

Table 1
Mass spectral data for EE₂ ozonation intermediates (2 min)

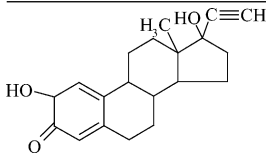
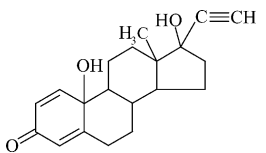
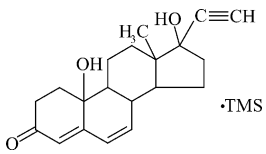
Products	GC retention time	Molecular weight of parent compound	Important ion peaks, <i>m/z</i>			
	16.32	312	124	91	79	
	16.52	312	171	123	91	
	18.69	312	353	196	160	133

Table 2
Mass spectral data for EE₂ ozonation intermediates (20 min)

Products	GC retention time (min)	Molecular weight of		Important ion peaks, <i>m/z</i>					
		Parent compound	TMS derivative ^a						
Bis(trimethylsilyl) oxalate	11.18	90	234	234(<i>M</i> ^{•+})	219	190	149	147	
Bis(trimethylsilyl) malonate	13.02	104	248	248(<i>M</i> ^{•+})	233	149	147		
Bis(trimethylsilyl) succinate	15.63	118	262	262(<i>M</i> ^{•+})	247	172	149	147	
Bis(trimethylsilyl) glutarate	17.33	132	276	276(<i>M</i> ^{•+})	261	233	158	149	147
Bis(trimethylsilyl) adipate	19.07	146	290	290(<i>M</i> ^{•+})	275	185	141	111	

^a Theoretical value based on the molecular weight of the proposed TMS derivative.

polarity were formed [32]. The peak 1 disappeared after ozonation for 4 min. Area of peak 2 increased and then decreased with reaction time. All of these phenomenons indicate that the parent compound and the intermediate products could be further oxidized by ozonation.

3.6. Mineralization of EE₂

To investigate the mineralization degree of EE₂ in ozone system, the experiment of EE₂ degradation by ozonation were conducted under the condition of O₃ concentration was 11.6 μmol min⁻¹, and the amount of CO₂ produced by the ozonation reaction was measured after ozonation for different reaction time. The result is shown in Fig. 7.

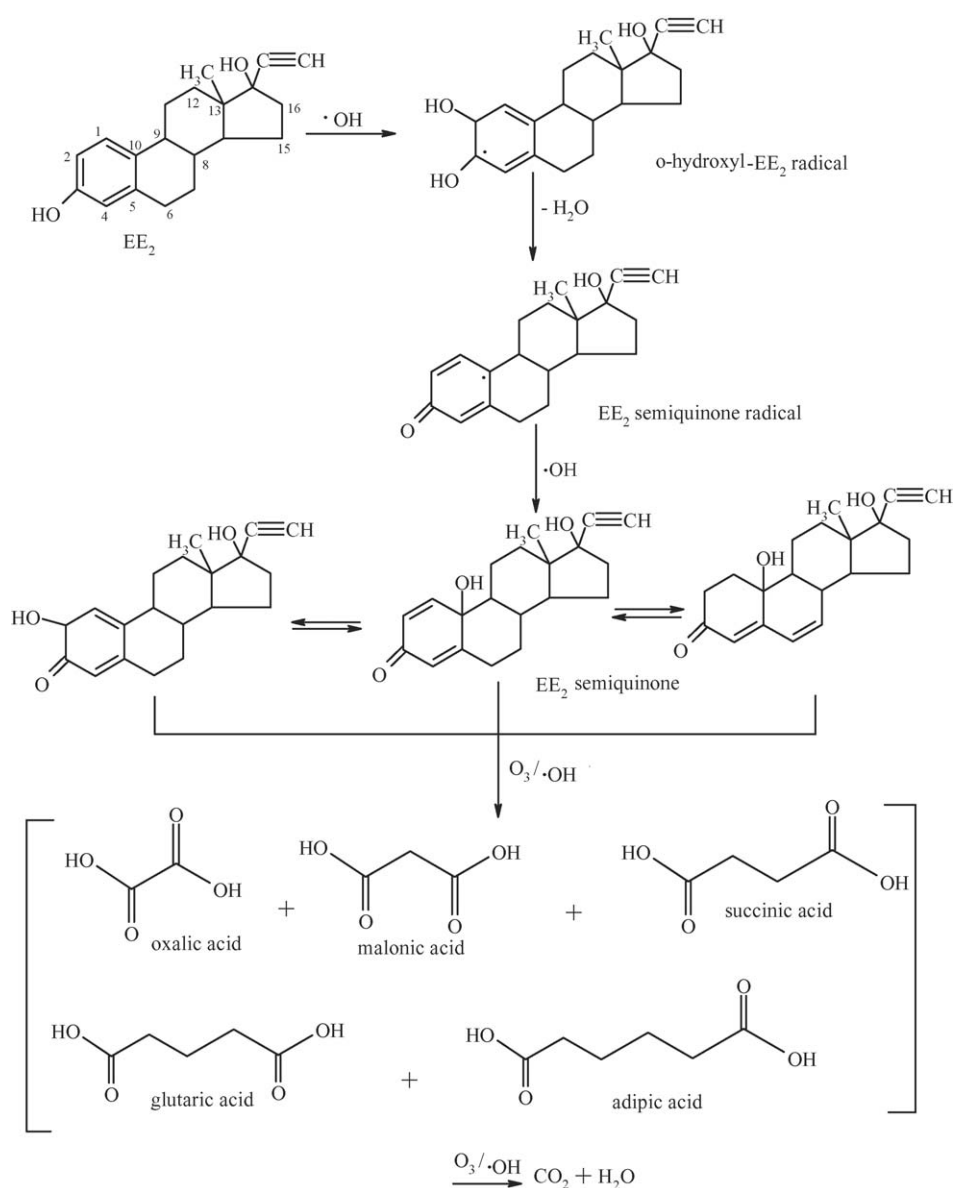
Fig. 7 showed that mineralization efficiency of EE₂ increased from 18.1% at 5 min to 53.9% at 20 min. Further oxidation

of parent compound and intermediate products induced the increase of mineralization of EE₂.

3.7. Results of GC/MS chromatogram analysis

To elucidate the structures of the intermediates, the sample oxidized by ozone for 2 min and 20 min were prepared as before and subjected to GC/MS analysis, respectively. Several peaks appeared in the chromatogram, total ion chromatograms of the samples were given in Figs. 8 and 9. Tables 1 and 2 reported the molecular weight of each detected by-products as well as the major ions in their ion spray mass spectra.

The results show that EE₂ was first oxidized by hydroxyl radical into semiquinone, which were finally degraded into organic acids and carbon dioxide. These could explain the decreasing of the solution pH and the increasing of the electrical conductivity



Scheme 1. Proposed pathways for EE₂ oxidation by ozone.

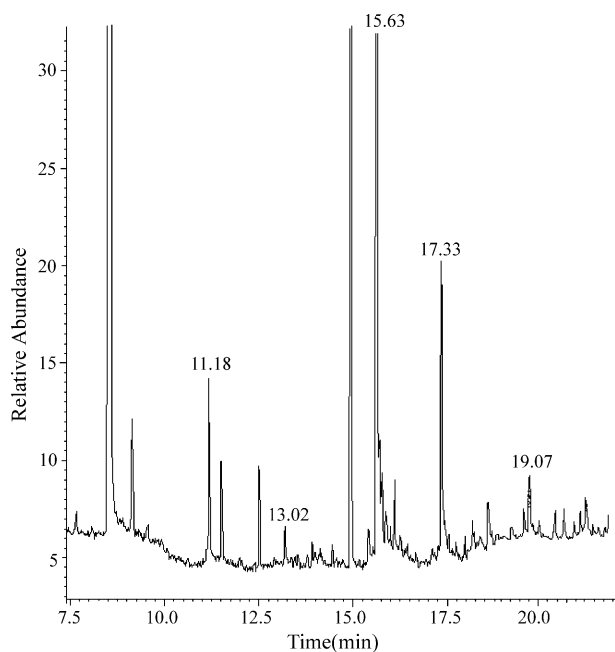


Fig. 9. Total ion chromatogram of sample oxidized for 20 min.

of the solution in ozonation process. Ohko et al. [1] evaluated the frontier electron densities (FEDs) for the E_2 molecule, indicating that the $2FED_{HOMO}^2$ was higher at phenol moiety, especially at the C_{10} and C_3 atoms (the values were 0.508 and 0.364, respectively). So, C_{10} or C_3 atoms should be the sites at which the first electron is extracted. The reaction may be initiated by addition of the $\bullet OH$ at the C_2 and C_5 atoms on the basis of $FED_{HOMO}^2 + FED_{LOMO}^2$ values. The EE_2 molecule structure is similar to E_2 , and the ethynyl will not affect the frontier electron densities much. So, EE_2 will be degraded in a similar manner. The mechanism of EE_2 decomposition by ozonation is proposed in Scheme 1.

The first addition of $\bullet OH$ radical occurs at the C_2 atom, and the corresponding *o*-hydroxyl- EE_2 radical could be produced. Then the $\bullet OH$ attack was followed by a dehydration reaction, and EE_2 semiquinone radical, a resonance structure, had been produced (but this intermediate had not been detected by GC/MS). Then EE_2 semiquinone would be produced by direct attack of $\bullet OH$ radical at the C_{10} and C_2 atoms of the resonance structure. Subsequently, further oxidation led to the breakdown of their aromatic structures, and then organic acids and carbon dioxide were formed.

4. Conclusion

The oxidation of EE_2 in aqueous solution has been studied by means of ozonation. Under the experimental condition ozone system demonstrated to be capable of removing EE_2 . The mineralization efficiency of EE_2 could reach 53.9% at pH 6.5 when ozone concentration was $11.6 \mu mol min^{-1}$. Initial EE_2 concentration and pH value had effects on degradation efficiency of EE_2 , which increased with increasing initial pH value of the solution, ozone concentration and decreased with increasing initial EE_2 concentration. During the course of EE_2 degradation,

the pH value decreased and the electrical conductivity of the solution increased with reaction time.

HPLC and GC/MS analysis allowed the identification of intermediates and products. The results showed that EE_2 could be degraded to products of lower molecular weight with greater polarity. The GC/MS chromatogram analysis indicated that the products were semiquinones, which were further oxidized to organic acid with smaller molecular weight (oxalic acid, malonate, glutarate, etc.). The results obtained indicated that ozonation is a highly effective way to remove EE_2 from wastewater and drinking water.

Acknowledgements

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