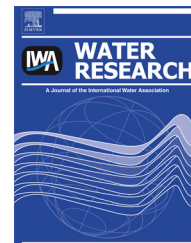


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# Photochemical transformation of terbutaline (pharmaceutical) in simulated natural waters: Degradation kinetics and mechanisms

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## ABSTRACT

In this study, varied nature organic matter isolates were employed to investigate the indirect photo transformation of terbutaline, which is a major feed additive medicine to increase the proportion of lean meat in the livestock. In the indirect photolysis of terbutaline under solar simulated irradiation, <sup>1</sup>O<sub>2</sub> plays an important role among the •OH and <sup>3</sup>DOM\*. The reaction rate constant of <sup>1</sup>O<sub>2</sub> was determined as  $(7.1 \pm 0.3) \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$  at pH 7.0, while the reaction rate constant of •OH was  $(6.87 \pm 0.43) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ . The contribution of singlet oxygen to the indirect photolysis of terbutaline (19–44%) was higher than that of the hydroxyl radical (1–7%). The pseudo first order rate constants for the photodegradation of terbutaline increase with increasing pH, which indicates that pH mainly affects the reaction rate of the singlet oxygen with the phenolic part of the terbutaline. The Quinone was identified as the main photosensitized product through LC–MS/MS analysis. It is also proposed that the degradation pathway of terbutaline involves reaction between the phenolic part of terbutaline and singlet oxygen. This finding strongly suggests that singlet oxygen was important factor for the photodegradation of terbutaline in natural waters.

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## 1. Introduction

Pharmaceuticals and personal care products (PPCPs) are emerging contaminants that have received extensive consideration due to their possible human health effects and ecological impacts, even at trace concentrations

(Schwarzenbach et al., 2006). The widespread therapeutic and preventative use of pharmaceuticals in both human and veterinary provides a continuous release of these substances or their metabolites to the aqueous environment (Fatta-Kassinos et al., 2011). In general, human used medicine can enter wastewater treatment plants via excretion, manufacturing

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facilities, or being dumped “down the drain” by consumers (Michael et al., 2013). Pharmaceuticals used in veterinary practices are quite different from human use. Veterinary medicines are widely used for prevention and treatment of infections and as a growth promoter. They mainly exist in animal wastes, may directly contaminate soils without any or minimal treatment when manure is applied to agricultural fields according to the rules of good agricultural practice (Boxall et al., 2003; Kemper, 2008). They further transport to ditches, streams and rivers via runoff and drain flow, to groundwater via leaching.

The degradation pathways of PPCPs in the surface waters include biodegradation, hydrolysis and photolysis. Biodegradation has been reported to be a likely removal pathway of PPCPs, but quantitative results were so far mainly focused on the wastewater treatment facilities and should be extrapolated to field conditions only with care (Ternes, 1998; Matamoros et al., 2009). Photodegradation is likely to play an important role in the environmental fate of PPCPs (Boreen et al., 2003; Ryan et al., 2011; Jasper and Sedlak, 2013). The direct photodegradation of PPCPs can occur when the absorption spectrum of the target compound overlaps with that of the sunlight. Otherwise, indirect photodegradation refers to reaction of the PPCPs with reactive oxygen species (ROS) generated by photosensitizers, in most cases dissolved organic matter (DOM). Photolysis of DOM leads to the formation of ROS, including  $\bullet\text{OH}$ ,  $^1\text{O}_2$ ,  $\text{O}_2^-$  and  $\text{H}_2\text{O}_2$ , as well as the reactive triplet state(s) of DOM ( $^3\text{DOM}^*$ ) (Burns et al., 2012; Luo et al., 2012; Whidbey et al., 2012). Previous studies have suggested that DOM may play a significant role in the photodegradation of organic pollutants (Wenk et al., 2011; Xu et al., 2011; Chen et al., 2012), however the underlying mechanism is still not fully understood.

Terbutaline is selected as the subject of this study because of its widely used in the livestock and considered as one of major feed additive medicines to increase the proportion of lean meat. For human used purpose, it belongs to  $\beta_2$ -adrenoceptor agonists to treat asthma and bronchitis, in addition, it is used in as many as 1 million pregnancies annually to arrest preterm labor despite the U.S. Food and Drug Administration has specifically warned against its use (Rhodes et al., 2004; Slotkin and Seidler, 2013).  $\beta_2$ -agonists possess a common  $\beta$ -phenyl- $\beta$ -ethanol amine group, in which the amine nitrogen and the phenyl ring can have different substituent (Hashem et al., 2011). The presence of two hydroxyl groups on the phenyl ring makes terbutaline hydrophilic (with  $\log K_{ow} = -1.07$ ) and not easily biodegradable (Howard and Muir, 2011). Hence, it can withstand conventional wastewater treatment or reach surface water bodies through runoff from animal wastes (Huerta-Fontela et al., 2011). Through drinking or irrigation, they ultimately have potential harmful effects on human health, and may also affect aquatic organisms in an unpredictable way.

Previous studies showed the photolysis of beta-blockers such as atenolol and metoprolol (Liu et al., 2009; Chen et al., 2012; Ji et al., 2012; Wang et al., 2012). Structurally,  $\beta$ -blockers and  $\beta$ -agonists share a common  $\text{CH}(\text{OH})\text{CH}_2\text{NH}$  side chain.  $\beta$ -agonists widely used just as  $\beta$ -blockers have potential risk to the environment (Lee et al., 2007). It is necessary to understand the photodegradation mechanism of  $\beta$ -agonists to

protect the human health. To our best knowledge, little is known about the photolysis of terbutaline in the aqueous environments, since most of existing studies of terbutaline are mainly focused on the developing of methods to its detection (Huerta-Fontela et al., 2010).

In this study, we investigated the photo-transformation of terbutaline in varied matrixes of DOM under solar simulated irradiation. The role of hydroxyl radical, singlet oxygen and triplet DOM has been evaluated. LC–MS/MS has been employed to identify the major degradation products. The phenolic ring in terbutaline structure could be the key point to understand the effect of pH on the photochemical fate. The reaction rate constants of hydroxyl radical and singlet oxygen have been determined. This information would be helpful in predicting the photochemical fate of  $\beta$ -agonists and may also be applicable to better understanding the environmental fate of other similar emerging contaminants.

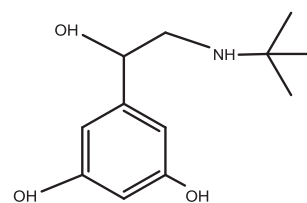
## 2. Materials and experimental details

### 2.1. Materials

Terbutaline hemisulfate ( $\geq 99\%$ ) (as shown in Scheme 1), furfuryl alcohol (FFA, 99%), terephthalic acid (TA, 98%), Rose Bengal (RB) were purchased from Sigma–Aldrich. Hydroxy-terephthalic acid (HOTA) was synthesized, the experimental details were shown in previous studies (Xu et al., 2011). Deuterium oxide ( $\text{D}_2\text{O}$ , 99.9%) was obtained from Cambridge Isotope Laboratories. Methanol, Trifluoroacetic acid (Fisher scientific) was of HPLC grade. Compressed nitrogen and oxygen were purchased from Wugang Inc, Shanghai. Dissolved organic matters, including Suwannee river humic acid (SRHA, 2S101H), Suwannee river fulvic acid (SRFA, 2S101F), Pahokee peat fulvic acid (PPFA, 1R107F), Nordic Reservoir DOM (DRDOM, 1R108N) and Suwannee River DOM (SRDOM, 1R101N) were obtained from the International Humic Substances Society (IHSS). Other two humic acids (Sigma HA, Aldrich HA) were obtained from Sigma–Aldrich. All experiments were conducted in  $20 \text{ mg L}^{-1}$  solutions of the seven DOM samples. For all of the experiments, solutions were prepared using water from an ultrapure system.

### 2.2. Photodegradation setup

To study the direct photolysis, terbutaline prepared in deionized Milli-Q® water and 0.56 mM phosphate buffer (pH = 7.0), were irradiated in a solar simulator (Suntest XLS<sup>+</sup>) equipped with a 1700 W Xenon lamp with 295 nm cut off filter.



Scheme 1 – Molecular structure of terbutaline.

The temperature control module (Sun cool) was set up as 30 °C.

To study the indirect photodegradation processes, terbutaline (22 μM) added in the solutions of DOM and exposed to simulated sunlight as above. Experiments were conducted in H<sub>2</sub>O or D<sub>2</sub>O to study the role of <sup>1</sup>O<sub>2</sub> and •OH with the addition of tert-Butanol (96 mM, •OH scavenger). The role of the triplet excited state of DOM was examined in deoxygenated solutions purged with nitrogen gas, and oxygen saturated solutions.

### 2.3. The steady-state concentration of <sup>1</sup>O<sub>2</sub> and bimolecular rate constants of <sup>1</sup>O<sub>2</sub>

To determine the steady-state concentration of <sup>1</sup>O<sub>2</sub>, solutions of DOM (20 mg L<sup>-1</sup>) and FFA (0.153 mM), as a <sup>1</sup>O<sub>2</sub> kinetic probe, were irradiated in the solar simulator. The steady-state concentration of <sup>1</sup>O<sub>2</sub> was determined using the following equations (Boreen et al., 2005):



$$d[\text{FFA}]/dt = -k_{1\text{O}_2, \text{FFA}}[\text{FFA}][{}^1\text{O}_2]_{\text{ss}} \quad (2)$$

where  $k_{1\text{O}_2, \text{FFA}} = 1.2 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$  (Haag and Hoigne, 1986)

To determine the rate constants of <sup>1</sup>O<sub>2</sub> with terbutaline, Rose Bengal (RB, 0.05mM) was used as the photosensitizer for producing <sup>1</sup>O<sub>2</sub>, and 0.1 mM FFA was added for competition kinetics, in the solar simulator. During the sunlight exposure, the loss of terbutaline was monitored along with the loss of FFA. The photodegradation rate constants for the terbutaline were determined by using plots of substrate degradation versus FFA degradation, shown in Equation (3).

$$\frac{k_{1\text{O}_2, \text{terbutaline}}}{k_{1\text{O}_2, \text{FFA}}} = \frac{\ln([\text{terbutaline}]_0/[\text{terbutaline}])}{\ln([\text{FFA}]_0/[\text{FFA}])} \quad (3)$$

### 2.4. •OH radical reaction rate measurement

Bimolecular reaction rate constant of •OH with terbutaline has been measured using electron pulse radiation. The experiments were conducted using an 8-MeV Titan Beta model TBS-8/16-1S linear accelerator and the details of pulse radiolysis have been discussed in detail elsewhere (Whitham et al., 1995; Mezyk et al., 2007). All pulse solutions were buffered with 5.0 mM phosphate adjusted to pH 7.0. Radiolysis of water generates three highly reactive species (•OH, e<sub>aq</sub><sup>-</sup>, and •H). To study the reaction of hydroxyl radicals, the solutions were pre-saturated with nitrous oxide (N<sub>2</sub>O), which quantitatively converts the hydrated electrons and hydrogen radicals to hydroxyl radicals.

### 2.5. Steady-state concentration of •OH under solar simulated irradiation

To determine the steady-state concentration of •OH, deionized water with 20 mg L<sup>-1</sup> SRDOM, TA (0.578 mM) was used. In air-saturated solutions, hydroxylation of TA forms hydroxyterephthalate (HOTA) with a reaction yield of 35% (Mark et al., 1998). The aliquots sampled from the solution were analyzed at various time points by a fluorescence detector in

HPLC ( $\lambda_{\text{excitation}} = 315 \text{ nm}$ ;  $\lambda_{\text{emission}} = 425 \text{ nm}$ ) (Fang et al., 1996; Page et al., 2010). The observed formation rate of HOTA was converted to the steady state •OH concentration by dividing the initial TA concentration (assumed to be constant during irradiation period), reaction yield and hydroxyl radical reaction rate constant, according to the following equations:



$$d[\text{HOTA}]/dt = 0.35 \cdot k_{\bullet\text{OH}, \text{TA}} \cdot [\text{TA}] \cdot [\bullet\text{OH}]_{\text{ss}} \quad (5)$$

where,  $k_{\bullet\text{OH}, \text{TA}} = 3.3 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ . (Mark et al., 1998)

### 2.6. HPLC and LC–MS/MS analytical procedures

The concentration of terbutaline was determined by HPLC (Agilent 1260), equipped with UV–visible and fluorescence detectors, and a Phenomenex Gemini C<sub>18</sub> column (5 μm, 250 × 4.60 mm). The isocratic mobile phase was a mixture of methanol and 0.05% trifluoroacetic acid buffer. The flow rate was 1.0 mL min<sup>-1</sup>. The UV detector was set at 230 nm. The experimental error in the HPLC analytical measurements is <2% on the basis of triplicate runs.

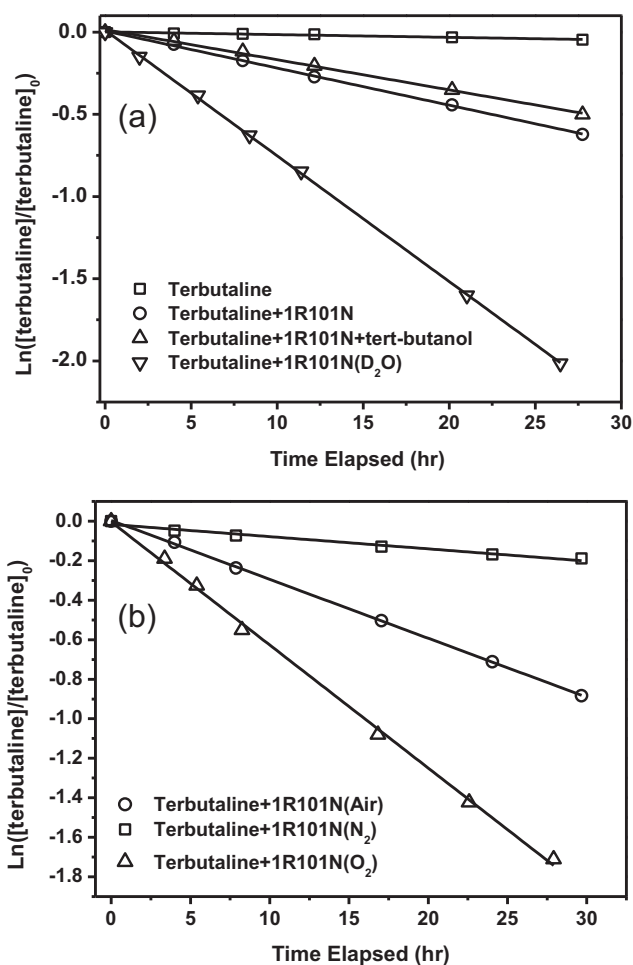
The photochemical product is analyzed by LC–MS/MS (ABI Qstar). The HPLC (Shimadzu 20AD) is equipped with ZORBAX 300SB-C18 column (3.5 μm, 300 Å, 0.1 × 150 mm). The mobile phase was a mixture of A (5% CH<sub>3</sub>OH, 0.1% HCOOH) and B (95% CH<sub>3</sub>OH, 0.1% HCOOH). The concentration of B is gradually increased from 5% at 5 min to 80% at 70 min, then decreased from 80% at 75 min to 5% at 80 min and stopped at 120 min. The flow rate is 300 nL min<sup>-1</sup>. MS data was acquired automatically using Analyst QS 1.0 software Service Pack 8 (ABI/MDS SCIEX, Concord, Canada). The analysis survey scans were acquired from 50 to 1000.

## 3. Results and discussion

### 3.1. Indirect photolysis and the role of ROS and <sup>3</sup>DOM\*

Direct photolysis of terbutaline in the phosphate buffered pH 7.0 Milli-Q water using a solar simulator suggested that at >295 nm direct photodegradation of terbutaline was very slow ( $k = (4.59 \pm 0.43) \times 10^{-7} \text{ s}^{-1}$ ). However, photosensitized degradation of terbutaline in the presence of SRDOM at pH 7.0 under simulated sunlight was significantly faster and gave a pseudo first order rate constant of  $(5.26 \pm 0.08) \times 10^{-6} \text{ s}^{-1}$ , as illustrated in the Fig. 1a. It suggests that indirect photodegradation is important in the photochemical fate of terbutaline in simulated natural waters, corroborating the low quantum efficiency of direct photolysis.

In general, indirect photodegradation passed through the reaction with •OH, <sup>1</sup>O<sub>2</sub> and <sup>3</sup>DOM\*. In the experiment with the addition of tert-butanol (96 mM), an •OH scavenger, there is merely a little decrease in the terbutaline loss rate compared to that with DOM only, indicating that •OH was play a minor role in the indirect photodegradation process (Fig. 1a). To explore the role of singlet oxygen, terbutaline solutions containing DOM were irradiated in D<sub>2</sub>O solutions. The disappear rate of terbutaline in D<sub>2</sub>O was  $(2.01 \pm 0.01) \times 10^{-5} \text{ s}^{-1}$ ,



**Fig. 1 – (a) Photolysis of terbutaline (22 μM) containing 20 mg L<sup>-1</sup> SRDOM irradiated in solar simulator at room temperature: control experiment without DOM (□), 20 mg L<sup>-1</sup> DOM in Milli-Q<sup>®</sup> water (○), with the addition of tert-butanol (Δ), in the D<sub>2</sub>O solution (∇). (b) 20 mg L<sup>-1</sup> SRDOM irradiated experiments under air saturated conditions (○), nitrogen saturated conditions (□) and oxygen saturated conditions (Δ). The experimental error in the analytical measurements is < 2% on the basis of triplicate runs.**

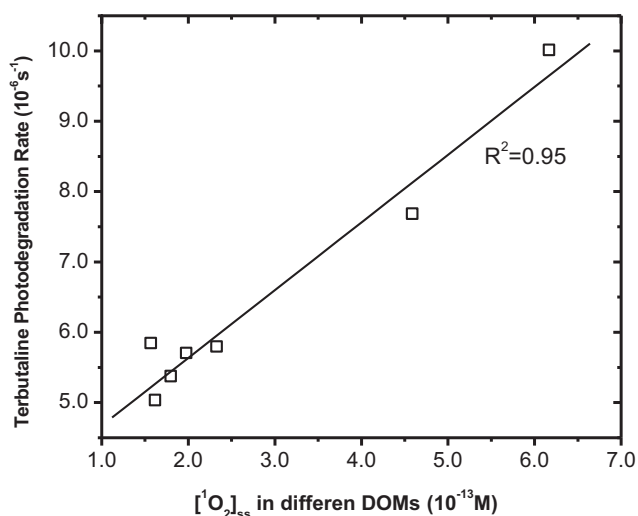
significantly faster than in H<sub>2</sub>O, suggesting that <sup>1</sup>O<sub>2</sub> was involved in the loss of the compound due to its increased lifetime in D<sub>2</sub>O as compared to that in H<sub>2</sub>O. To further understand the contribution of <sup>3</sup>DOM\*, nitrogen saturated experiments were conducted to eliminate oxygen effect, as shown in Fig. 1b. Because O<sub>2</sub> is known to be a triplet quencher, the absence of oxygen would lead to raise concentrations of <sup>3</sup>DOM\* (Chen et al., 2009) and reduce the concentration of <sup>1</sup>O<sub>2</sub>. The solution purged by nitrogen showed that the loss rate of terbutaline was slightly slower than the air saturated conditions, which indicated that oxygen involved processes are more essential than <sup>3</sup>DOM\* reaction. In comparison, the addition of O<sub>2</sub> resulted in a marked increase in the removal rate of terbutaline, likely as a result of an increase in <sup>1</sup>O<sub>2</sub>, while at the same time quenching the <sup>3</sup>DOM\*. On the other side, oxygen also could be involved in the type I photo-oxidation (Foot, 1999). This process could also be slow down upon removal of oxygen. These observations strongly suggested that the photodegradation of terbutaline proceeds mainly via reaction with <sup>1</sup>O<sub>2</sub> and/or oxygen involved type I photo-oxidation, the contribution of •OH and reaction of <sup>3</sup>DOM\* only, is of less importance.

### 3.2. The contribution of ROS in the different matrixes of DOM

The photodegradation of terbutaline in seven different DOM samples (SRDOM, NRDOM, PPFA, SRFA, SRHA, Sigma HA and Aldrich HA) was studied to explore the influence of the type of DOM on the photodegradation processes. The rate constants were determined from the slopes of the lines in Figure S1, Supplementary Material. It was reasoned that the observed differences in the loss rates of terbutaline among different DOM solutions were possibly due to the diverse photo reactivity of the DOM. The steady-state concentrations of ROS in seven different DOM solutions were then determined to describe the photo reactivity. The steady state concentration of <sup>1</sup>O<sub>2</sub> was determined using FFA (Figure S2, Supplementary Material) and the results are summarized in Table 1. The hydroxyl radical was determined using TA as a chemical probe. Similar method has also been employed to quantify steady state concentration of hydroxyl radical. (Page et al., 2010) Under our experimental conditions, around 90% of hydroxyl

**Table 1 – Measure steady-state concentrations (M) and pseudo first-order rate constants (s<sup>-1</sup>) of reactions of terbutaline (0.022 mM) with singlet oxygen and hydroxyl radical at presence of 20 mg L<sup>-1</sup> DOM (SRDOM, NRDOM, PPFA, SRFA, SRHA, Sigma HA and Aldrich HA) respectively.**

DOM	[ <sup>1</sup> O <sub>2</sub> ] <sub>ss</sub> (10 <sup>-13</sup> M)	k <sub>1O<sub>2</sub></sub> (10 <sup>-6</sup> s <sup>-1</sup> )	[•OH] <sub>ss</sub> (10 <sup>-17</sup> M)	k <sub>•OH</sub> (10 <sup>-7</sup> s <sup>-1</sup> )	K (10 <sup>-6</sup> s <sup>-1</sup> )
SRDOM	1.63 ± 0.03	1.16 ± 0.02	2.13 ± 0.06	1.46 ± 0.04	5.02 ± 0.12
NDDOM	1.58 ± 0.03	1.12 ± 0.02	6.06 ± 0.24	4.16 ± 0.16	5.83 ± 0.09
PDFFA	1.81 ± 0.06	1.29 ± 0.04	2.25 ± 0.16	1.55 ± 0.11	5.36 ± 0.44
SRFA	1.99 ± 0.06	1.41 ± 0.04	3.35 ± 0.23	2.30 ± 0.16	5.69 ± 0.20
SRHA	2.34 ± 0.07	1.66 ± 0.05	3.71 ± 0.28	2.55 ± 0.19	5.78 ± 0.28
Sigma HA	4.60 ± 0.07	3.27 ± 0.05	1.51 ± 0.02	1.03 ± 0.01	7.67 ± 0.25
Aldrich HA	6.18 ± 0.17	4.39 ± 0.12	1.54 ± 0.08	1.06 ± 0.05	10.00 ± 0.70



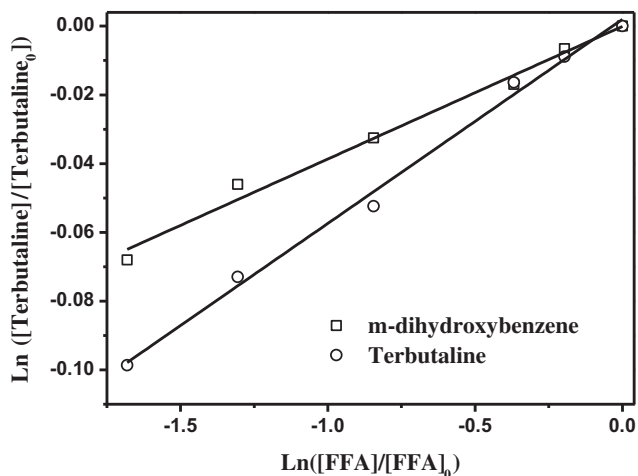
**Fig. 2** – The photodegradation rates of terbutaline (22  $\mu\text{M}$ ) in seven solutions of DOM (SRDOM, NRDOM, PFFA, SRFA, SRHA, Sigma HA, Aldrich HA 20  $\text{mg L}^{-1}$ ) as a function of the steady state concentrations of  $^1\text{O}_2$ .

radicals were trapped by TA. The steady state concentrations of hydroxyl radical could be slightly underestimated due to the inherent experimental error.

The pseudo first order degradation rates of terbutaline were linear related with the steady concentrations of  $^1\text{O}_2$ , as shown in Fig. 2; on the other hand, no relationship has been found with hydroxyl radical concentrations (data was not shown). These results demonstrated that singlet oxygen could be the key parameter for indirect photodegradation of terbutaline, even at diverse DOM matrix.

### 3.3. Kinetic studies for $^1\text{O}_2$ reaction with terbutaline

The bimolecular reaction rate constant of singlet oxygen with terbutaline was determined as  $(7.1 \pm 0.3) \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$  at pH



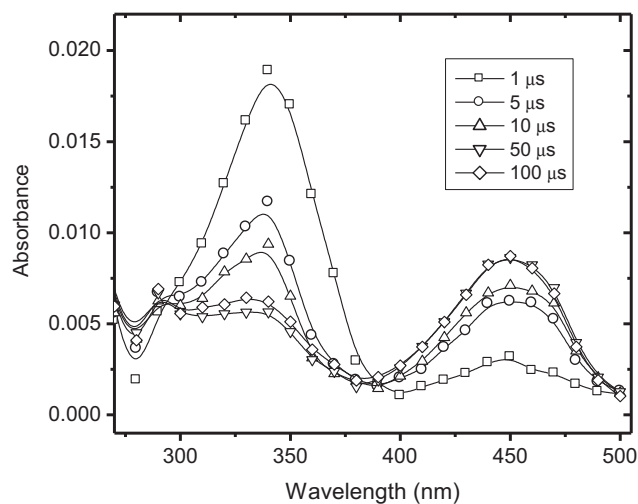
**Fig. 3** – Competitive  $^1\text{O}_2$  degradation of terbutaline and m-dihydroxybenzene in pH 7.0 buffered  $\text{H}_2\text{O}$  with RB using as sensitizer.  $k$  values were determined by multiplying the slope obtained from these plots by the  $k$  of FFA.

7.0 using Rose Bengal as photosensitizer, and FFA as the reference compound (as illustrated in Fig. 3). Based on both the steady state concentrations of singlet oxygen and reaction rate constant, it's possible to obtain the contribution of  $^1\text{O}_2$  in the photodegradation processes. The calculated results indicated that a part fraction of terbutaline loss (19–44%) was depleted via  $^1\text{O}_2$  degradation pathways. The unsolved photo-induced processes could be raised from the direct reaction of  $^3\text{DOM}^*$ , hydroxyl radical and oxygen depended type I photo-oxidation.

In view of the importance of  $^1\text{O}_2$  to the photodegradation of terbutaline, m-dihydroxybenzene was employed as the model compound to investigate the reactivity of phenolic moiety. Steady-state photolysis using RB as the sensitizer was also employed to determine the reaction rate constant of the sub-structural moiety (m-dihydroxybenzene) with  $^1\text{O}_2$ . The loss of substrate by the reaction with  $^1\text{O}_2$  was simultaneously monitored with that of the reference FFA. Fig. 3 shows the changes of concentration during the photodegradation of terbutaline and m-dihydroxybenzene versus that for FFA in the solar simulator. The reaction rate of terbutaline with  $^1\text{O}_2$  ( $(7.1 \pm 0.3) \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ ) was very similar to that for m-dihydroxybenzene ( $(4.6 \pm 0.2) \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ ). These results suggested that most of the reaction with  $^1\text{O}_2$  occurs at the phenol moiety of terbutaline. The difference were likely due to the fact that the side chain ( $\text{CH}(\text{OH})\text{CH}_2\text{NH}-$ ), as electron donating group, slightly increases the electron density of aromatic moiety, further enhanced the reactivity of  $^1\text{O}_2$  with terbutaline.

### 3.4. Kinetic studies of $\bullet\text{OH}$ reaction with terbutaline

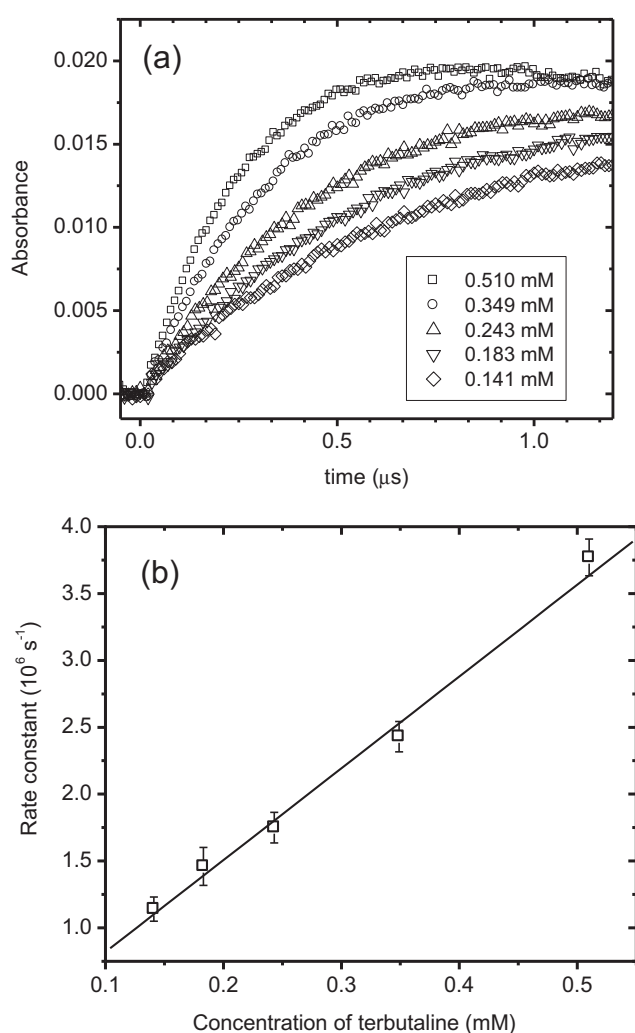
Although our scavenger experiments indicated the  $\bullet\text{OH}$  has a minor contribution to the photochemical fate of terbutaline in the aqueous environment, the detailed kinetic studies have been conducted using pulse radiation techniques. Firstly, the transient spectrum of  $\bullet\text{OH}$  with terbutaline has been recorded using scan mode, as shown in Fig. 4. The transient absorption



**Fig. 4** – Transient absorption spectra obtained from electron pulse radiolysis of  $\text{N}_2\text{O}$  saturated aqueous solutions of terbutaline at pH 7.0 and room temperature.

spectra of terbutaline exhibited a peak at 340 nm, which decayed within 50  $\mu\text{s}$ . The isosbestic point at 390 nm suggested that a second intermediate was produced with  $\lambda_{\text{max}}$  at 450 nm. It is possible that the initial formation of tri-hydroxyl benzene radical for terbutaline is not stable, followed eliminating  $\text{H}_2\text{O}$  to form oxygen radical. Similar results have been observed in the  $\bullet\text{OH}$  oxidation of phenolic compounds. (Kurata et al., 1988; Song et al., 2008a,b)

The bimolecular reaction rate constant for  $\bullet\text{OH}$  reaction with the terbutaline has been determined from the rates of absorption change with concentration at the  $\lambda_{\text{max}}$ . Typical kinetic data were given in Fig. 5a. These were processed using the previous procedures (Song et al., 2008a,b). In brief, the absolute hydroxyl radical rate constant was obtained by fitting exponential curves to the pseudo-first-order growth kinetics (Fig. 5a) and plotting these values as a function of the



**Fig. 5** – (a) Typical growth kinetics of transient absorption at 340 nm in a pulse irradiated solution at pH 7.00 and room temperature for 0.510 ( $\square$ ), 0.349 ( $\circ$ ), 0.243 ( $\triangle$ ), 0.183 ( $\nabla$ ) and 0.141 ( $\diamond$ ) mM terbutaline. (b) Second-order rate constant determination for the reaction of hydroxyl radicals with terbutaline at 340 nm. Solid line corresponds to the value of the overall rate constant  $(6.87 \pm 0.43) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ .

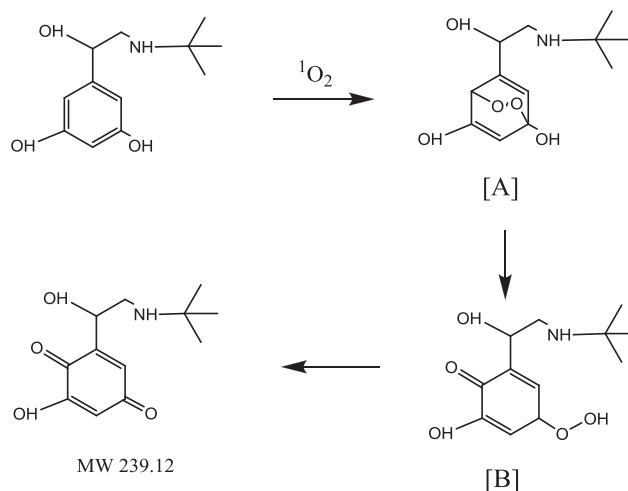
concentrations of terbutaline (Fig. 5b) to obtain the rate constant as  $(6.87 \pm 0.43) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ .

### 3.5. Effect of pH on photodegradation

In order to investigate the influence of pH in the photodegradation of terbutaline, studies were conducted over the pH range of 3.0–11.0. Under neutral and moderately alkaline conditions, noteworthy faster degradation of terbutaline was observed. The increase in the rate of degradation parallels the bimolecular reaction rates of  $^1\text{O}_2$  with terbutaline over the pH range, as shown in Figure S4, Supplementary Material. Three pKa values are given for terbutaline: 8.8, 10.1 and 11.2 (Karabey et al., 2003). With pH increased in our experimental range, the phenolic group of terbutaline was deprotonated and forming phenolate ion. Meanwhile  $^1\text{O}_2$  presented significant higher reaction rate constant with phenolate ion than phenolic group (Schwarzenbach et al., 2003). The influence of pH on the indirect degradation of terbutaline is similar to those observed phenolic compounds, further supports the hypothesis that  $^1\text{O}_2$  plays a key role in the photochemical fate of terbutaline (Tratnyek and Hoigne, 1991). The  $^1\text{O}_2$  reaction rates of terbutaline at varied pH have been also measured and presented in the Figure S5, Supplementary Material.

### 3.6. Identification of photoproducts and possible photodegradation pathways

In general,  $^1\text{O}_2$  reacts with nucleophilic organic compounds through four main mechanisms: the (2 + 2) Ene reaction, (2 + 4) Diels–Alder reaction with dienes, oxidation of sulfides and electron-transfer reaction (Scully Jr and Hoigné, 1987). As the phenol part of terbutaline plays a key role in the photodegradation of terbutaline, it is expected that the photodegradation products are mainly associated with the reaction between phenol portion and  $^1\text{O}_2$ . Previous studies show that  $^1\text{O}_2$  is the active agent in the aerobic dye sensitized photo oxygenation of phenols. Thus two plausible schemes had been proposed based on previous results. One is  $[\pi 2^s + \pi 4^s]$  of



**Fig. 6** – Proposed photodegradation pathway of terbutaline.

$^1\text{O}_2$  with the phenol and the unstable endoperoxide rearranged subsequently. The other is charge-transfer reaction between  $^1\text{O}_2$  and phenol (Thomas and Foote, 1978). The final product of reaction between phenol and  $^1\text{O}_2$  is 1, 4-benzoquinone. Hence, we assume that the mechanism of the reaction between terbutaline and  $^1\text{O}_2$  is similar to resveratrol. In order to understand the mechanism, photodegradation experiments were conducted using SRDOM as photosensitizer. One degradation product of terbutaline was identified through LC–ESI–QTOF–MS. The mass spectrum data was shown in Figure S6, Supplementary Material. The product (MW 239.12) was proposed as quinolinic compound. Firstly,  $^1\text{O}_2$  reacted with phenolic group forming peroxide bridged intermediate A, sequentially convert to intermediate B, through losing  $\text{H}_2\text{O}$  resulted in quinine. The pathway of indirect photodegradation of terbutaline was shown in Fig. 6.

#### 4. Conclusions

Terbutaline is a synthetic  $\beta_2$ -adrenoceptor agonist. It has been widely used in acute and chronic treatment of bronchial asthma and the boost of lean meat for swine in the livestock. In this study, a series of experiments were conducted to explore the role of  $\bullet\text{OH}$ ,  $^1\text{O}_2$  and  $^3\text{DOM}^*$  in the indirect photolysis of terbutaline. Our study results show that  $^1\text{O}_2$  can be attributed to 19–44% of loss of terbutaline, while 1–7% from  $\bullet\text{OH}$  in the varied DOM solutions. The indirect photodegradation rate of terbutaline is linearly related with steady state concentrations of  $^1\text{O}_2$  at varied DOM solutions. Therefore the concentration of  $^1\text{O}_2$  could be applied as a surrogate to predict the photochemical degradation rate of terbutaline. One major degradation product has been identified using LC–MS/MS and the degradation pathways further support the  $^1\text{O}_2$  mechanism. This fundamental information would be of considerable interest for predicting the environmental fate of  $\beta$ -agonists pharmaceuticals.

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#### Appendix A. Supplementary material

Supplementary material associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.watres.2013.08.029>.

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