



Removal of indomethacin using UV-vis/peroxydisulfate: Kinetics, toxicity, and transformation pathways

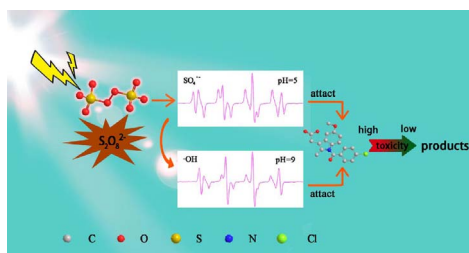


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GRAPHICAL ABSTRACT



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ABSTRACT

The extensive production and use of non-steroidal anti-inflammatory drugs (NSAIDs) has increased the volume of downstream residues that contaminate the environment, which pose great threats to ecosystems and human health. The decomposition of peroxydisulfate (PDS), which is activated by UV-vis to produce a potent oxidizing sulfate radical, comprises a new type of advanced oxidation technology. The degradation of indomethacin (IM) by the UV-vis activation of peroxydisulfate was investigated. The results demonstrated that IM degradation followed pseudo-first-order reaction kinetics. UV-vis irradiation led to the direct albeit slight photolysis of IM, whereas the addition of an oxidant significantly enhanced the removal efficiency. The IM degradation efficiency was increased when the pH was elevated from 5 to 7; however, the elimination of IM was reduced when the pH was elevated from 7 to 9 due to the conversion of $\text{SO}_4^{\cdot-}$ to $\text{HO}^{\cdot}$. A low concentration of Cl^- had a dual effect, while a high concentration led to a dramatic inhibitory effect. Fulvic acid (SRFA) inhibited the decomposition of IM through the light screening effect and the quenching of radicals. A quenching experiment revealed that $\text{SO}_4^{\cdot-}$ was the primary free radical, which is confirmed by electron spin resonance spectroscopy. The second-order rate constants of IM and $\text{SO}_4^{\cdot-}$ were also determined. The luminescent bacteria *Vibrio fischeri* was selected to assess the toxicity of the transformation products, which was further confirmed by quantitative structure-active relationship analysis. The cleavage of the bond between C on the benzene ring and N on the indole group, the hydroxylation of the benzene ring, and the decarboxylation of the aliphatic chain were the main pathways for the degradation of IM in the UV-vis/peroxydisulfate system.

1. Introduction

As an emerging class of environmental pollutants, pharmaceutical

and personal care products (PPCPs) have attracted increasing attention due to their adverse effects on human health and ambient ecosystems [1]. Non-steroidal anti-inflammatory drugs (NSAIDs), as an important

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class of PPCPs, are widely used as an antipyretic and analgesic. NSAIDs are often detected in the effluent of sewage treatment plants, and their concentrations in surface water can attain even ng L^{-1} to $\mu\text{g L}^{-1}$ levels [2]. This means that NSAIDs in sewage treatment plants are likely not completely removed, and are ultimately discharged into the ambient environment, which poses a significant threat to ecosystems. Therefore, the development of new technologies to avoid the permeation of NSAIDs into the environment is critical.

Advanced oxidation processes (AOPs) have shown to be promising and competitive technologies for the destruction of recalcitrant biodegradable organic compounds. AOPs are derived from a combination of technologies that generate highly oxidative species such as $\text{UV}/\text{H}_2\text{O}_2$, UV/O_3 , UV/TiO_2 , Fenton and electrochemical oxidation technologies [3–8]. Advanced oxidation based on sulfate radicals may be an alternative to traditional advanced oxidation techniques. Sulfate radicals can be readily generated through the thermal [9], transition metal (i.e., Fe^{2+} , Co^{2+}) [10–12], ultrasound irradiation [13], electrochemical process [14] and UV-light mediated decomposition of Peroxydisulfate (PDS) and peroxymonosulfate (PMS) [15,16]. The combination of persulfate with photocatalysis and metal-free catalysis for the generation of reactive radicals has also been reported [17–20]. The sulfate radicals ($\text{SO}_4^{\cdot-}$) can rapidly react with most organic and inorganic substances due to its high redox potential of ($E^\circ(\text{SO}_4^{\cdot-}/\text{SO}_4^{2-}) = 2.5\text{--}3.1\text{ V}$), which is comparable to $\text{HO}^\cdot$ ($E^\circ(\text{HO}^\cdot/\text{H}_2\text{O}) = 1.9\text{--}2.7\text{ V}$). The second-order reaction rate constant is in the range of from 10^7 to $10^{10}\text{ M}^{-1}\text{ s}^{-1}$ [21]. Similar to $\text{HO}^\cdot$, $\text{SO}_4^{\cdot-}$ may participate in reactions by three different routes: electron transfer, the addition of unsaturated double bonds, and hydrogen evolution reactions [22,23]. However, $\text{SO}_4^{\cdot-}$ is believed to be more selective than $\text{HO}^\cdot$ through single electron transfer [24]. Although $\text{SO}_4^{\cdot-}$ oxidation is more selective, most of the intermediates formed by the aromatic compounds that react with sulfate radicals are hydroxylated products, which are akin in performance to hydroxyl radicals [25,26].

Recent studies on PDS or PMS activation have focused on transition metal ion-mediated processes. Transition metal iron such as Co^{2+} or Cu^{2+} were found to be effective in activating $\text{SO}_4^{\cdot-}$ generation from PDS for contaminant degradation. Although heterogeneous oxide-mediated activators may reduce the population of harmful metal ions that reside in treated water [27,28], concerns arise from release of toxic metal ions. The adverse effects of residual metal ions on human health are supposed to be properly assessed. In UV-vis/PDS processes, sulfate radicals are generated via the cleavage of peroxidic bonds without the involvement of metal ions (Eq. (1)). The combination of UV-vis and PDS or PMS to form an active oxidizing species is considered to be an environmentally compatible and feasible way [29]. Product identification combined with determination such as toxicity and total organic carbon (TOC) can be a complement to evaluate the overall efficiency of the treatment processes.



Considering that IM is frequently detected in the aquatic environment, the core objectives of this paper are as follows: (1) Investigate the kinetics of IM degradation in the UV-vis/PDS system under different operating conditions; (2) Determine the second-order rate constant of IM with $\text{SO}_4^{\cdot-}$ through competitive kinetics; (3) Detect the radical species at different pH values through ESR; (4) Identify the reaction intermediates using mass spectrometry to investigate the IM conversion pathway by $\text{SO}_4^{\cdot-}$ oxidation.

2. Materials and methods

2.1. Chemicals

Indomethacin (IM, > 98%), benzoic acid (BA, ≥ 99%), and fulvic acid (SRFA, ≥ 90%) were purchased from Aladdin Industrial

Corporation (Shanghai), potassium peroxydisulfate (PDS > 99%) was obtained from the reagent company, Sinopharm Chemical Reagent (Shanghai, China); dimethyl pyridine N-oxide (DMPO) was purchased from Sigma-Aldrich; sodium chloride, sodium thiosulfate, sodium hydroxide, ethanol, and tert-butyl alcohol, were purchased from Chengdu Kelon Reagent Co., Ltd.. All of the reagents listed above were of analytical grade and required no further purification. The acetonitrile purchased from Analaqua Chemicals Supply Co. Ltd. (USA) was of HPLC grade. Ultrapure water of 18.25 MΩ/cm from a Milli-Q apparatus (Smart2 Pure ultrapure water system integration, TKA, Germany) was employed in the preparation of all aqueous solutions.

2.2. Experimental procedures

A 600 mL sealed cylindrical borosilicate glass reactor equipped with a 350W Xenon lamp was used to conduct the photochemical experiments (Fig. S1). A 500 mL solution of IM (0.02 mM) was added to the reactor. The photo-reactor was water cooled such that the reaction temperature was maintained at $25 \pm 2^\circ\text{C}$. The pH of solution was adjusted with 0.01 mM H_2SO_4 and NaOH. The effects of Cl^- (0–10 mM) and SRFA (0–10 mg C L^{-1}) were investigated to evaluate the effects of typical natural water constituents on the oxidation of IM. The Xenon lamp was turned on and the reaction was initiated, once an appropriate quantity of peroxydisulfate was added. Most of the experiments were performed in triplicate to assure accurate data acquisition and the error bars in the figures represent standard deviations.

2.3. Analytical methods

2.3.1. HPLC and TOC analysis

Liquid samples were periodically extracted and analyzed. The IM was quantified by an Agilent 1100 series HPLC (Agilent, USA) system equipped with a diode array detector (SPD-M20A). The column was a Chromolith Performance XDB-C18 column ($150 \times 2.1\text{ mm}$, $5\text{ }\mu\text{m}$), and the injection volume was 4 μL . The mobile phase was a mixture of acetonitrile and 5 mM ammonium acetate in water (65:35, v/v) at a flow rate of 0.2 mL/min. under isocratic conditions, and the UV wavelength for detection was 228 nm. Total organic carbon (TOC) was measured using a TOC-VCPH analyzer (Shimadzu, Japan).

2.3.2. Identification of transformation products

The identification of the intermediate products was carried out using liquid chromatography with tandem mass spectrometry (HPLC-MS/MS), equipped with a Hypersil ODS column ($250 \times 4.6\text{ mm}$, $5\text{ }\mu\text{m}$). Full scans and product ion scans were conducted in order to determine the quasi-molecular ions, and elucidate the structures of major transformation products. Detailed operational conditions are presented in the [Supplementary data, Text S1](#).

2.3.3. Toxicity analysis

The acute toxicity assay was carried out against *Vibrio fischeri* (*V. fischeri*) according to the Water Quality-Determination of the Acute Toxicity-Luminescent Bacteria Test (GB/T15441-1995). The QSAR analysis calculated by the Ecological Structure-Activity Relationship Model-ECOSAR program (ECOSAR, 2013) was conducted in order to predict the acute and chronic toxicities of IM and its transformation by-products to fish, Daphnia, and green algae [30]. Detailed information is provided in [Text S2](#).

2.3.4. ESR measurements

The electron spin resonance (ESR) signals of DMPO spin-trapped radicals were measured to detect $\text{SO}_4^{\cdot-}$ and $\text{HO}^\cdot$ using a Bruker model ESR JES-FA200 spectrometer.

2.3.5. Determination of the light screening factor (S_λ)

The light screening factor (S_λ) of SRFA was calculated according to

Eqs. (2) and (3) [31,32]:

$$S_{\lambda} = \frac{1 - 10^{-[\alpha_{\lambda} + \varepsilon_{\lambda}][\text{IM}]]l}}{2.303[\alpha_{\lambda} + \varepsilon_{\lambda}][\text{IM}]]l} \quad (2)$$

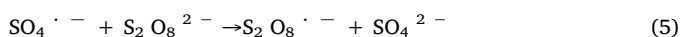
$$\sum S_{\lambda} = \frac{\sum L_{\lambda} S_{\lambda} \varepsilon_{\lambda}}{\sum L_{\lambda} \varepsilon_{\lambda}} \quad (3)$$

where α_{λ} is the light attenuation coefficient of SRFA (cm^{-1}), ε_{λ} is the molar absorption coefficient of IM (cm L mol^{-1}), $[\text{IM}]$ is the concentration of IM (mol L^{-1}), l is the light path (cm), S_{λ} refers to the light screening factor of SRFA, $\sum S_{\lambda}$ refers to the total light screening factor of SRFA under experimental conditions, and L_{λ} is the relative light intensity.

3. Results and discussion

3.1. Effect of PDS concentration in UV-vis/PDS system

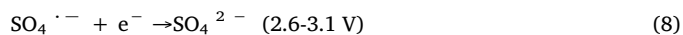
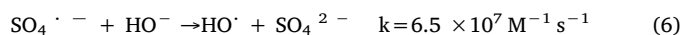
The effects of different concentrations of PDS on the degradation rate of IM are depicted in Fig. 1(a). These results indicate that the IM degradation rate was in line with first-order kinetics, and the degradation rate of IM was increased with higher PDS concentrations. Fig. 1(b) shows the variation of k as a function of PDS concentration. It can be seen that k increased gradually with increasing concentration of PDS within the range investigated. If the concentration of PDS continued to increase, the degradation rate of IM enhanced slightly. Otherwise, an increasing amount of PDS reacted with $\text{SO}_4^{\cdot-}$, thus affecting the degradation rate of IM, as shown in Eqs. (4) and (5) [21,33]. This is similar to the case where excess H_2O_2 in the Fenton system acts a $\text{HO}^{\cdot}$ quencher.



3.2. Effect of initial pH

Fig. 2(a) reveals the effects of different initial pH levels on the degradation of IM in UV-vis/PDS system. The k value presented in Fig. 2(b) first increased and then decreased. It may be seen that the degradation rate of IM was increased with elevated pH, from 5 to 7. Studies have shown that at a pH of from between 2 to 7, the UV-vis/PDS system is dominated by sulfate radicals as the active species. At pH 7, the IM is virtually 100% dissociated ($\text{pK}_a = 4.5$) [34], and the electron cloud density of IM is larger in the dissociated state, which facilitates its electron transfer and accelerates the reaction. The degradation rate of IM was decreased when the pH was raised to 9, due to

the conversion of $\text{SO}_4^{\cdot-}$ to $\text{HO}^{\cdot}$. Therefore, $\text{HO}^{\cdot}$ plays a considerable role as an oxidizing species under alkaline conditions, shown as Eq. (6) [21]. According to the oxidation-reduction potential of $\text{SO}_4^{\cdot-}$ and $\text{HO}^{\cdot}$, shown as Eqs. (7) and (8) [23,35,36], the redox potential of $\text{HO}^{\cdot}$ at alkaline condition is remarkably reduced (1.8 V); Hence, the degradation of IM is unfavorable under alkaline conditions.



3.3. Effects of natural water constituents

A number of commonly resident water constituents may react with radical species such as $\text{SO}_4^{\cdot-}$ and $\text{HO}^{\cdot}$ in competition with target contaminants [37–40]. Thus, the effects of Cl^- and SRFA (as a model aquatic NOM) on the degradation of IM at pH 5 was investigated.

The effect of Cl^- on the degradation of IM in the UV-vis/PDS system was illustrated in Fig. 3a. It seemed that a low concentration of Cl^- (0.01–0.1 mM) had no significant effect on the degradation of IM. In fact, a low level of Cl^- had dual effects. On the one hand, $\text{SO}_4^{\cdot-}$ generated would react with Cl^- to produce $\text{Cl}^{\cdot}$ according to Eq. (10), which has a redox potential ($E^{\circ}(\text{Cl}^{\cdot}/\text{Cl}^-) = 2.4 \text{ V}$) relatively lower than $\text{SO}_4^{\cdot-}$. On the other hand, chloride ions accelerated the generation of $^1\text{O}_2$, which can increase the degradation rate of IM [41]. When the Cl^- concentration was elevated to 10 mM, Cl^- acted primarily as a $\text{SO}_4^{\cdot-}$ scavenger, as Cl^- may react with $\text{SO}_4^{\cdot-}$ to produce relatively weaker species, such as $\text{Cl}^{\cdot}$, $\text{Cl}_2^{\cdot-}$, Cl_2 , and $\text{ClHO}^{\cdot-}$ according to Eqs. (10)–(15) [42,43,44], inhibited the degradation efficiency of IM significantly. According to Fig. 3c, k decreased drastically with increasing concentration of Cl^- to 10 mM. Fig. 3b shows the effect of SRFA on the degradation of IM, where it can be seen that IM degradation was dramatically inhibited with increased SRFA concentrations (from 1 mg/L to 10 mg/L). The UV-vis absorption spectra of different SRFA concentrations overlapped with IM (Fig. S2), indicating that the light attenuation effect may play a critical role in the decreased IM degradation rate. Therefore, we integrated a screening factor, shown in Eqs. (2) and (3), to further investigate the effects of SRFA in the degradation of IM in the UV-vis/PDS system [32]. The total screening factor $\sum S_{\lambda}$ of different concentrations of SRFA was calculated. The results indicated that the screening effect became stronger with increased SRFA concentrations, whereupon the degradation of IM was dramatically decreased (Table 1). Based on the total screening factor, the theoretical rate constant $k_0 \sum S_{\lambda}$ was greater than the actual rate constant k_a . This led to the conclusion that, besides the screening effect, SRFA may serve as a quencher with $\text{SO}_4^{\cdot-}$ and $\text{HO}^{\cdot}$.

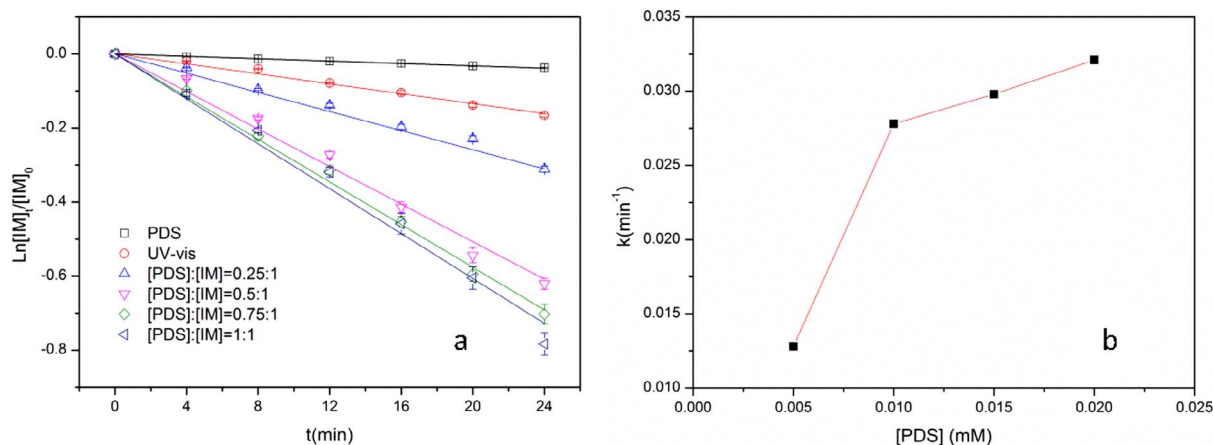


Fig. 1. (a) Effect of PDS initial concentration on the degradation of IM by UV-vis/PDS; (b) plot of k versus [PDS]. ($[\text{IM}] = 20 \mu\text{M}$, $\text{pH} = 5$).

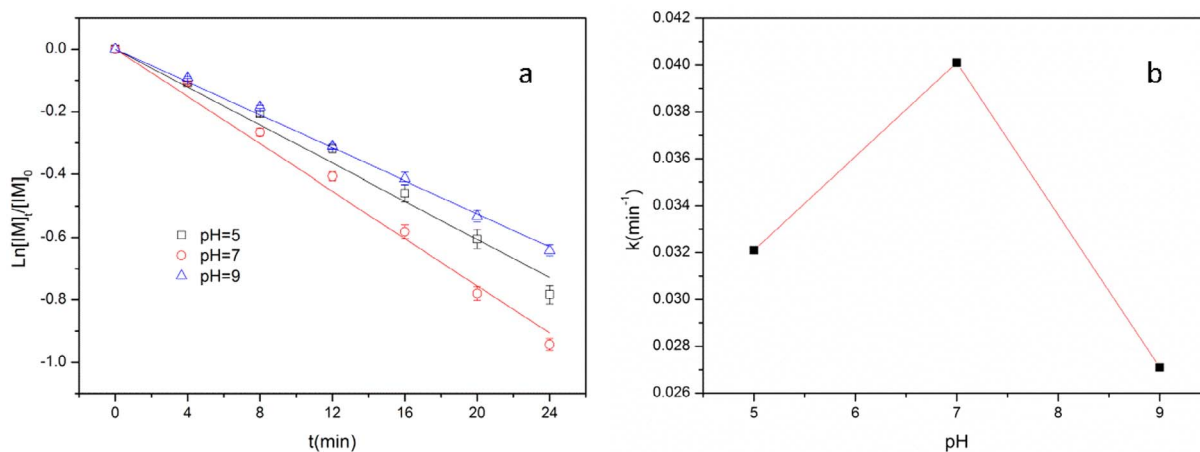


Fig. 2. (a) Effect of initial pH on the degradation of IM by UV-vis/PDS; (b) plot of k versus $[pH]$. ($[IM] = 20 \mu M$, $[PDS] = 20 \mu M$).

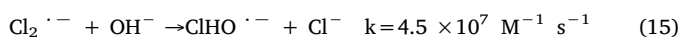
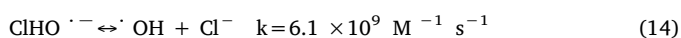
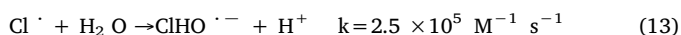
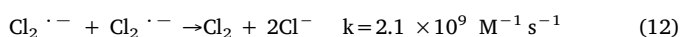
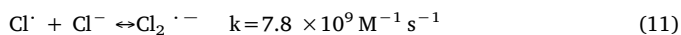
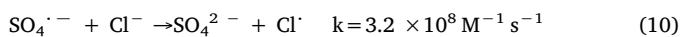


Table 1

Kinetics parameters of the influence of DOM on the photolysis of IM.

SRFA/mg C L ⁻¹	k_0/min	ΣS_{λ}	$k_0 \Sigma S_{\lambda}/\text{min}$	k_a/min
1	0.0321	0.8689	0.0279	0.0201
5	0.0321	0.6039	0.0194	0.0119
10	0.0321	0.4260	0.0137	0.0053

k_0 : the degradation rate constant of IM without SRFA; k_a : the degradation rate constant of IM without SRFA.

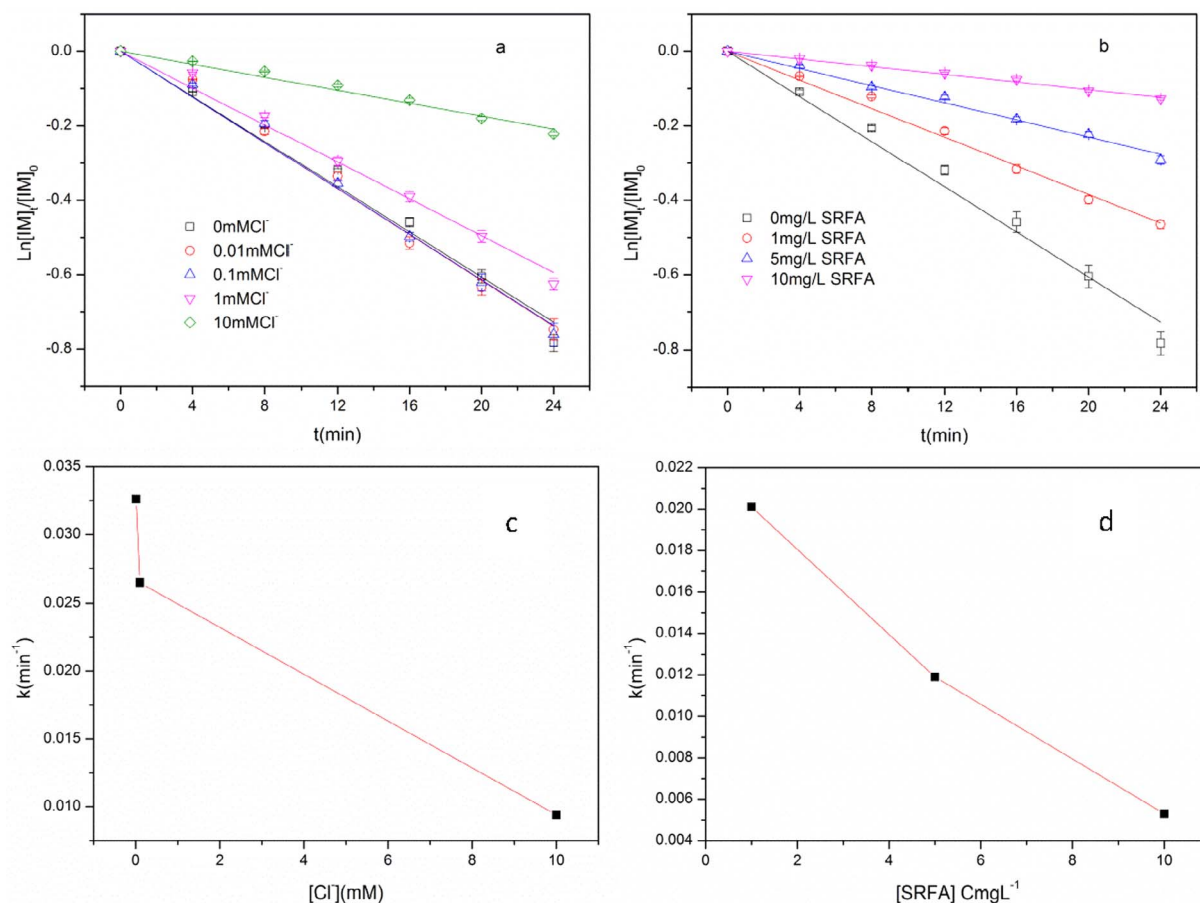


Fig. 3. Effects of natural water constituents on the degradation of IM by UV-vis/PDS: (a) Cl^- (b) SRFA (c) plot of k versus $[Cl^-]$ (d) plot of k versus $[SRFA]$ ($[IM] = 20 \mu M$, $pH = 5$).

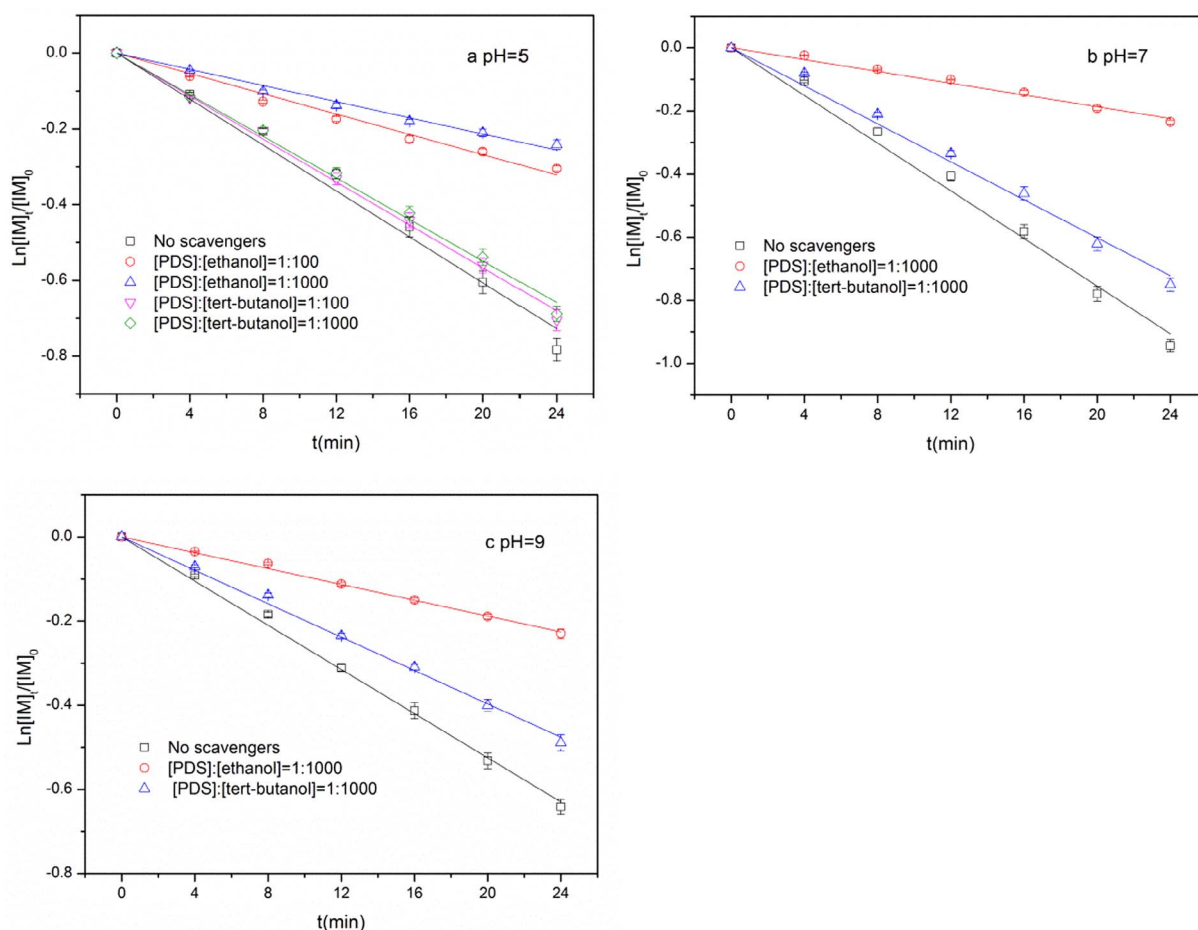


Fig. 4. Influence of tert-butanol and ethanol addition on IM degradation at different pH levels (a) pH = 5, (b) pH = 7, (c) pH = 9, (d) addition of 20 mM alcohol ([IM] = 20 μ M, [PDS] = 20 μ M).

3.4. Predominant oxidizing species

TBA and ethanol were added to the UV-vis/PDS system in order to identify the predominant oxidizing radical species. Ethanol acts as a scavenger of both $\text{SO}_4^{\cdot-}$ and $\text{HO}^{\cdot}$, at rate constants of 1.6×10^7 – $7.7 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$ and 1.2×10^9 – $2.8 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$. TBA without alpha hydrogen is used as an effective quenching agent for $\text{HO}^{\cdot}$. The reaction rate of TBA with $\text{SO}_4^{\cdot-}$ and $\text{HO}^{\cdot}$ was 4.0×10^5 – $9.1 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$ and 3.8×10^8 – $7.6 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ [22]. TBA reacts with $\text{HO}^{\cdot}$ at 1000 times faster rate than $\text{SO}_4^{\cdot-}$ while ethanol reacts quickly with both of them. Therefore, an excess of ethanol and tert-butanol were added to evaluate the reaction mechanism in the UV-vis/PDS system. Fig. 4 shows the effects of ethanol and tert-butanol on the degradation of IM under different pH values. At pH 5, the degradation of IM was only slightly inhibited with the addition of tert-butanol. The enhanced decrease of IM removal by ethanol over TBA suggested that the dominant radical species was $\text{SO}_4^{\cdot-}$. Moreover, the contribution of $\text{HO}^{\cdot}$ was elevated with the increasing pH, while the $\text{SO}_4^{\cdot-}$ could transfer to $\text{HO}^{\cdot}$ by a chain reaction under alkaline conditions, shown as Eq. (7).

3.5. ESR radical detection

The ESR technique was employed to identify radical species generated in the UV-vis/peroxydisulfate system under different pH levels. DMPO was used as a spin trap in ESR measurements, and no signal was observed in the persulfate solution without DMPO. As shown in Fig. 5a, the characteristics of the ESR spectra at pH 5 were identified to be those corresponding to DMPO-SO_4 , which indicated that $\text{SO}_4^{\cdot-}$ was

predominant under this condition. Further, the characteristics of the ESR spectra at pH 7.0, 9.0 were identified to be those corresponding to DMPO-SO_4 and DMPO-OH , which meant that both sulfate and hydroxyl radicals existed. The EPR spectra at pH 5.0, 7.0, and 9.0 were also determined at 4, 8, and 16 min., respectively. According to Fig. 5b, it may be seen that the intensity of DMPO-SO_4 and DMPO-OH were increased with longer reaction times. It is indicated in Fig. 5c that large amounts of $\text{HO}^{\cdot}$ and small portion of $\text{SO}_4^{\cdot-}$ were generated at pH=9. And it is worthy to note that the intensity of DMPO-SO_4 were stronger at pH 7.0 than at pH 9.0, which attributes to the conversion of $\text{SO}_4^{\cdot-}$ to $\text{HO}^{\cdot}$. These results were consistent with the degradation of IM being faster at pH 7.0 than at pH 9.0. As shown in Fig. 5d, there were no sulfate or hydroxyl radicals generated with the addition of ethanol, which accounted for the dramatic decrease of the first-order reaction rate constant of IM in the presence of ethanol.

3.6. Determination of second-order reaction rate constant

In order to determine the second-order rate constants for the reaction between IM and sulfate radicals, benzoic acid was used as a probe compound, and the constant reaction rate between sulfate radical and benzoic acid was $1.2 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ [45]. Due to the presence of two major active species ($\text{SO}_4^{\cdot-}$ and $\text{HO}^{\cdot}$) in the UV-vis/PDS system, the IM degradation kinetics may be expressed by the following Eq. (16):

$$-\frac{d[\text{IM}]}{dt} = k_{\text{SO}_4^{\cdot-}\text{-IM}}[\text{IM}][\text{SO}_4^{\cdot-}] + k_{\text{HO}^{\cdot}\text{-IM}}[\text{IM}][\text{HO}^{\cdot}] \quad (16)$$

When 20 mM of TBA was added, the attack on IM (20 μ M) by $\text{HO}^{\cdot}$ was negligible, which according to the reaction rate constant for TBA

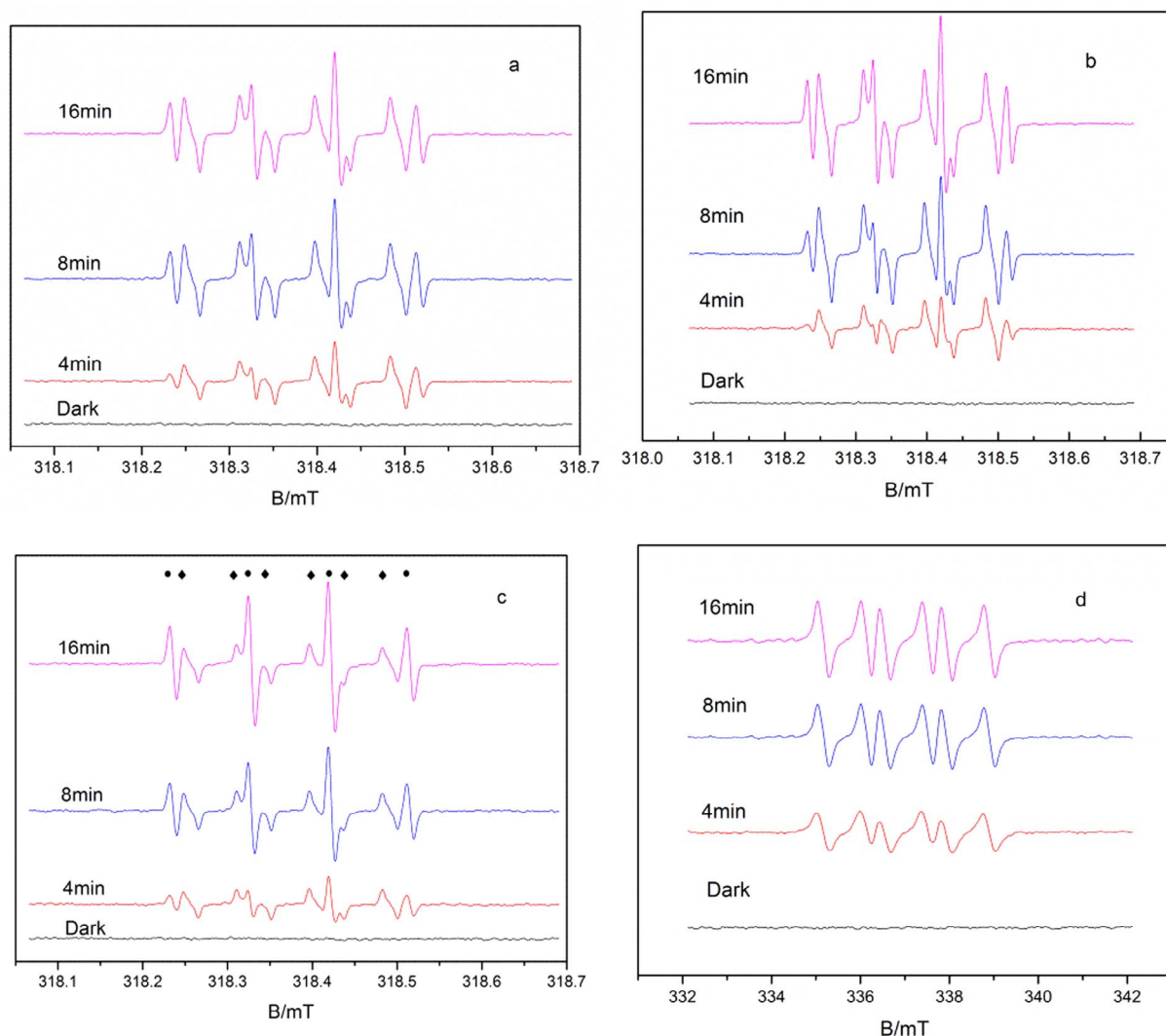


Fig. 5. ESR spectra of the radicals generated in the UV-vis/PDS system: (a) pH = 5, (b) pH = 7, (c) pH = 9, (d) addition of 20 mM alcohol (●: DMPO-OH, ◆: DMPO-SO₄) ([IM] = 20 μM, [PDS] = 20 μM, [DMPO] = 20 mM).

and $\cdot\text{OH}$ was 3.8×10^8 – $7.6 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$. The degradation of IM can be simplified to Eq. (17).

$$-\frac{d[\text{IM}]}{dt} = k_{\text{SO}_4^{\cdot-}\text{-IM}}[\text{IM}][\text{SO}_4^{\cdot-}] \quad (17)$$

Applying Eq. (17) to probe compound (BA) when coexisting with IM in system, Eq. (18) is obtained:

$$-\frac{d[\text{BA}]}{dt} = k_{\text{SO}_4^{\cdot-}\text{-BA}}[\text{BA}][\text{SO}_4^{\cdot-}] \quad (18)$$

After dividing Eqs. (17) with (18), the following Eq. (19) is obtained:

$$\frac{\ln([\text{IM}]_0/[\text{IM}]_t)}{\ln([\text{BA}]_0/[\text{BA}]_t)} = \frac{k_{\text{SO}_4^{\cdot-}\text{-IM}}}{k_{\text{SO}_4^{\cdot-}\text{-BA}}} \quad (19)$$

The plot of $\ln([\text{IM}]_0/[\text{IM}]_t)$ vs. $\ln([\text{BA}]_0/[\text{BA}]_t)$ yielded a straight line with a slope of 0.522, as depicted in Fig. 6. The calculated second-order rate constant of IM with $\text{SO}_4^{\cdot-}$ was $6.26 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$.

3.7. Reaction mechanism and pathway

When $\text{SO}_4^{\cdot-}$ participates in the reaction, electron transfer occurs to form a C-centered radical cation, which can react with H_2O via hydrogenation and an additional reaction to produce hydroxylated IM. When $\text{HO}^{\cdot}$ attacks IM molecules, hydroxylated IM tend to form through

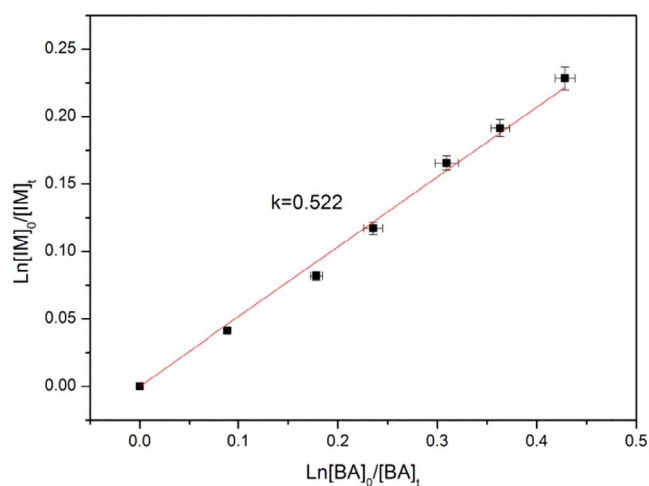


Fig. 6. $\ln([\text{IM}]_0/[\text{IM}]_t)$ vs. $\ln([\text{BA}]_0/[\text{BA}]_t)$ for UV-vis/PDS system. ([IM]₀ = 20 μM, [BA]₀ = 20 μM, [PDS]₀ = 20 μM, [TBA]₀ = 20 mM, pH 7.0).

hydrogen abstraction and addition reactions. $\text{SO}_4^{\cdot-}$ and $\text{HO}^{\cdot}$ participation in the reaction tend to generate the same intermediate product as Eqs. (16)–(18) [46,47]



Eight intermediates were detected and tentatively identified through LC-MS/MS. The retention time, m/z ratios, possible structural composition and product ions, as shown in Table S1; Fig. S3 represents the total ion chromatogram (TIC) of the degradation of IM in the UV-vis/peroxydisulfate system after 24 min. Transformation product structures were elucidated on the basis of their accurate mass measurement. Based on the principles of sulfate radical oxidation and experimental results of degradation of IM in other reaction systems, we have proposed the IM degradation pathway of attack by $\text{SO}_4^{\cdot-}$ in the UV-vis/PDS system. A comprehensive overview of IM degradation pathways under UV-vis/PDS is provided in Scheme 1. The cleavage of carbonyl carbon on the benzene ring and nitrogen on the indole group produces 4-chlorobenzaldehyde, which is further oxidized to form 4-chloro-benzoic acid (IM-PI). The first oxidations on C1 take place on the less hindered indole double bond to produce m/z 372 (IM-PII); the single electron transfer of IM attacked by sulfate radicals produced IM cationic radicals, and IM^+ reacted with H_2O to rapidly produce hydroxylated IM. In addition, the chlorinated ring was not conducive to $\text{SO}_4^{\cdot-}$ attack due to the electron-withdrawing effect of chlorine. In fact, the reaction with another electrophilic disinfectant (free chlorine) does not take place on the chlorinated ring for the same reason [48].

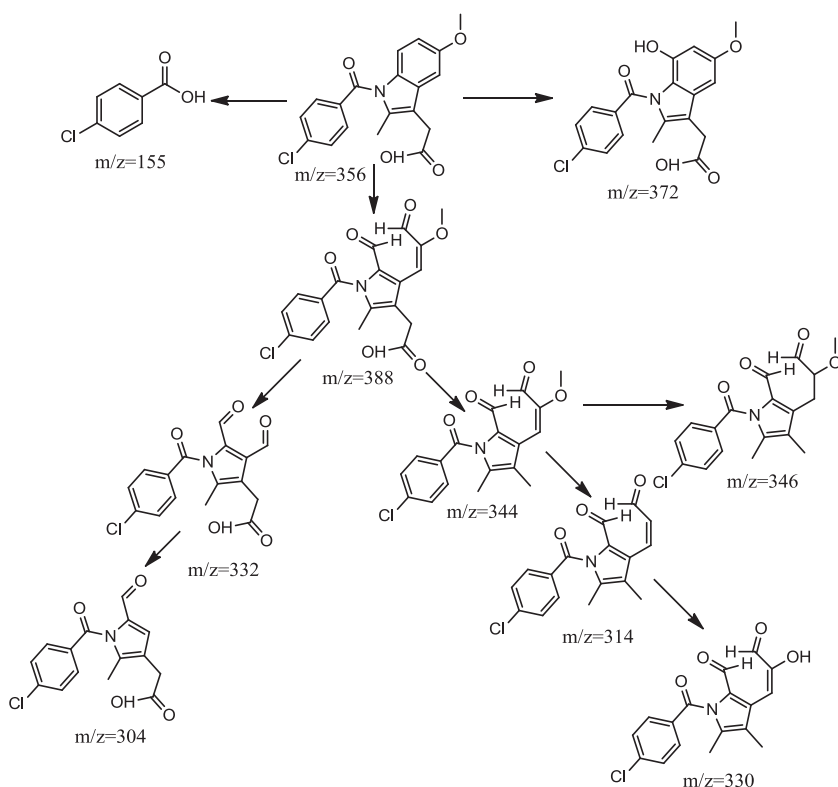
Hydroxylation may activate the aromatic ring due to the elevated electron density derived from the electron donating group ($-\text{OH}$), which favors further attack by electrophilic species to generate a multiple hydroxylation of intermediates [49,50]. A subsequent oxidations on C6 tend to produce a diol, which was reported for the degradation of IM by potassium permanganate. This is regarded as one of the typical first steps during the oxidation of aromatic compounds [51]. Unfortunately it could not be detected in this study due to its rapid oxidation through the open-ring conversion to dialdehyde m/z 388. On the

one hand, m/z 388 was further oxidized to form m/z 332 (IM-PIII) and m/z 304 (IM-PIV) by elimination of a part of an open cycle, on the other hand, m/z 388 was transformed to m/z 344 (IM-PV) through decarboxylation, whose spectra was without the loss of CO_2 . Similarly, this product may further react in two directions; Firstly, m/z 344 can be transformed to m/z 314 (IM-PVII) through the loss of OCH_3 . Instead, m/z 316 was further hydroxylated to form m/z 330 (IM-PVIII). Moreover, m/z 346 (IM-PVI) was produced by m/z 344 through double bond addition reactions.

3.8. Toxicity evaluation

The Microtox test has been most frequently employed to measure the acute toxicity of toxic substances [52,53]. Since the by-products of IM may be more toxic than IM is in its original form, it was necessary to assess the toxicity of the IM-contaminated water treated by UV-vis/PDS. The toxicity of the water samples was evaluated by monitoring changes in the natural emission of the luminescent bacteria *V. fischeri* when challenged with toxic compounds. Because the PDS residues in the samples had already been quenched with $\text{Na}_2\text{S}_2\text{O}_3$ prior to the Microtox test, the toxicity of PDS had no interference on the toxicity of the IM degradation samples [54]. The end products apparently exhibited less toxic effect towards *V. fischeri*.

The response of *V. fischeri* to IM following oxidation in the UV-vis/PDS system is shown in Fig. 7. The initial inhibition rate of IM by *V. fischeri* was 48% at 15 min. of exposure time. The inhibition rate increased with the destruction of IM and the accumulation of transformation products. As revealed in Fig. 1, from 0 to 12 min., a higher inhibition toward *V. fischeri* was obtained, which indicated the formation of degradation by-products that were more toxic than IM. Subsequently, the inhibition rate by *V. fischeri* attained the maximum values observed in the treated solution at 12 min. (70.3%). The toxicity to *V. fischeri* decreased from 12 min. with the increased TOC removal rate, indicating the elimination of highly toxic intermediates. The changes in toxicity were primarily attributed to the variation in concentrations of the intermediates.



Scheme 1. Proposed degradation pathway of IM in the system of UV-vis/PDS.

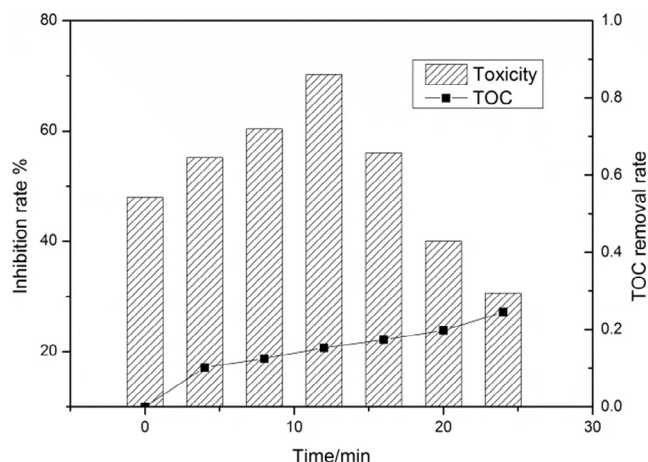


Fig. 7. Variation of toxicity to *V. fischeri* for 24 min and TOC removal rate of IM by UV-vis/PDS system. [IM] = 20 μ M, [PDS] = 20 μ M, pH = 7.

To further demonstrate the different responses toward IM and its transformation products from various species, QSAR analysis calculated by the ECOSAR program was used to estimate acute toxicity to fish, daphnids, and green algae [30,55]. The predicted values of IM and its transformation products are given in Table S4. As can be seen, the LC50, LC50, and EC50 values obtained for IM for fish, daphnids, and green algae were ~15.861, 4.028, and 4.395 mg/L, respectively. When these values were ranked, the LC50 values for fish showed that half of the transformation products exhibited higher toxicity than IM, and a similar trend was obtained for the daphnids and green algae. It should also be noted that a decrease in molecular weight will lead to an increase in molarity, which accounts for the toxicity increase in the system of UV-vis/PDS.

4. Conclusion

UV-vis/PDS may effectively eliminate IM with much higher efficacy than direct UV-vis photolysis. Increased dosages of persulfate were observed to enhance the degradation of IM. pH affected both and the contribution of reactive radicals and dissociation species of IM in solution and hence this significantly affects the degradation efficiency of IM. Cl^- and SRFA were believed to be the inhibitor for the degradation of IM through the light screening effect and the quenching of radicals in the UV-vis/PDS system. Quenching experiments and ESR detection revealed $\text{SO}_4^{\cdot-}$ was the predominant radicals and the contribution of $\text{HO}^\cdot$ enhanced with the increasing pH. The major degradation pathways of IM included the hydroxylation of the aromatic ring, cleavage of C-N bond on the indol, and the decarboxylation of the aliphatic chain. During the degradation of IM, several by-products more toxic than the initial IM compound were generated with the TOC removal rate increased. The present study provided important information as relates to the potential practical application of UV-vis/PDS. The transformation pathways of IM initially involved one electron transfer oxidation process, followed by hydroxylation processes, which allowing for the elimination of IM. The results from his study can contribute to the treatment and risk management of IM in wastewater aquatic environment. It's desirable to evaluate the ecotoxicological effects of IM transformation products in further studies.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.cej.2017.09.025>.

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