Photodegradation of diclofenac in aqueous solution by simulated sunlight irradiation: kinetics, thermodynamics and pathways

N. Zhang, J. M. Li, G. G. Liu, X. L. Chen and K. Jiang

ABSTRACT

Diclofenac (DCF) is one of the most frequently detected pharmaceuticals in various water samples. This paper studied the effects of aquatic environmental factors (pH, temperature and dissolved organic matter) on photodegradation of DCF under simulated sunlight. The results demonstrate that degradation pathways proceed via pseudo first-order kinetics in all cases and the photodegradation of DCF by simulated sunlight. Thermodynamic study indicated that the photodegradation course is spontaneous, exothermic and irreversible. The rate constant gradually increased when the pH increased from 3 to 5, then decreased when the pH increased from 5 to 8, and finally increased when the pH further increased from 8 to 12. Humic acid inhibited the photodegradation of DCF. Three kinds of main degradation products were observed by high performance liquid chromatography/mass spectrometry and the degradation pathways were suggested. A toxicity test using *Photobacterium phosphoreum* T_3 Sp indicated the generation of some more toxic products than DCF.

Key words | degradation pathway, diclofenac, reaction kinetics, thermodynamics, toxicity

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INTRODUCTION

Pharmaceutical and personal care products (PPCPs) have been found polluting a wide range of aquatic environments including groundwater, surface water and drinking water (Hofmann *et al.* 2007). Diclofenac (DCF) is a synthetic non-steroidal drug widely prescribed as an anti-inflammatory, mostly used as its sodium salt in medical care as an antiarthritic and analgesic, and found polluting a wide range of aquatic environments, including groundwater, surface water and drinking water (Lin *et al.* 2016). Accordingly, this emerging trend of environmental pollutants and their metabolites have the potential to have an adverse impact on aquatic environments (Gao *et al.* 2016). The behavior and fate of pharmaceuticals in aquatic environments remain poorly understood, and therefore studies of these phenomena would be valuable (Avetta *et al.* 2016; Jewell *et al.* 2016; Poirier-Larabie *et al.* 2016). However, several studies have demonstrated that the rate of degradation of DCF in communal sewage treatment plants is low. In the wastewater treatment plant, the level of DCF removal efficiency is still very uncertain, ranging from 21% to 40% (Zhang *et al.* 2008). DCF has been detected in maximum concentrations of 28.4 μg/L in surface water. It is also detected in groundwater in concentrations up to 0.59 μg/L. Nowadays, the harmful effects of DCF on different organisms in aquatic environments have been demonstrated (Czech & Oleszczuk 2016; De Oliveira *et al.* 2016; Lonappan *et al.* 2016). For example, DCF can cause renal failure in the Indian gyps vulture and alterations of the gills of rainbow trout, with effects observed with concentrations as low as 1 μg/L (Taggart *et al.* 2007; Wang *et al.* 2015a, 2015b) and it also can influence the biochemical functions of fish and lead to tissue damage (Mehinto *et al.* 2010). Recent studies have focused on examining the efficiency of various treatment processes on DCF removal. For example, Wang *et al.* (2015a) investigated DCF removal via potassium

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ferrate, Vogna *et al.* (2004) investigated DCF removal via UV-light irradiation in the presence of H_2O_2 and Wang *et al.* (2014) investigated oxidation of DCF in aqueous solution via aqueous chlorine dioxide. Hui *et al.* (Yu *et al.* 2013) investigated degradation of DCF by advanced oxidation and reduction processes. Ernest *et al.* (Marco-Urrea *et al.* 2010) investigated degradation of DCF by Trametes versicolor pellets. However, there have been few studies of the environmental behavior of DCF in natural water. For instance, Radke *et al.* (2010) analyzed the short-term dynamics of selected pharmaceuticals (bezafibrate, clofibric acid, DCF, naproxen) in the river downstream from a wastewater treatment plant. The factors affecting the environmental behavior of DCF and its photodegradation in the aquatic environment are clearly of interest, and the study of DCF degradation under simulated sunlight conditions would be of value.

Photodegradation is one of the principal abiotic degradation pathways of DCF in the aqueous environment. It occurs mainly at the water surface, and is affected by various environmental conditions. Therefore, aquatic environmental factors should be included when modeling the photodegradation of DCF under simulated sunlight irradiation. In natural waters, the main variables in the aquatic environment include pH, temperature and dissolved organic matter (DOM). DOM can influence photodegradation by acting as photosensitizers and/or HO· sinks (Koumaki *et al.* 2015; Poirier-Larabie *et al.* 2016). It has been proposed that humic acid (HA) in its photo-induced transient excited state (triplet state, 3HA*) reacts with pharmaceutical compounds by energy and/or electron transfer, and/or by hydrogen abstraction (Rigobello *et al.* 2013; Sadmani *et al.* 2014; Hu *et al.* 2016). However, in some cases, HA absorption spectra overlap with the absorption spectra of pharmaceuticals. Moreover, HA can scavenge reactive oxygen species (ROS), which can interfere with the direct photolysis of pharmaceuticals (Guerard *et al.* 2009).

Various aquatic environmental factors may affect the environmental fate and ecological risk of DCF. Therefore, the objectives of this study were to investigate both the reaction kinetics and the influences of temperature, pH and HA on DCF degradation under simulated sunlight irradiation. A further step was to identify the major transformation product, and the possible degradation pathway was proposed. To evaluate the phototoxicity risks, a toxicity assay by *Photobacterium phosphoreum* T_3 Sp was conducted to monitor the toxicity evolvement of reaction solutions.

MATERIALS AND METHODS

Chemicals

DCF, 2-[(2,6-dichlorophenyl) amino] benzeneacetic acid, sodium salt (98% purity), was purchased from J&K Chemical Co. Ltd (Beijing, China). HPLC-grade methanol was obtained from Suqian Guoda Chemical Reagent Co. Ltd (Jiangsu, China). All of the chemicals used were of analytical grade without further purification. Ultra-pure water from a Milli-Q water process (Millipore, USA) was used for preparing all aqueous solutions.

Fluka HA

Fluka HA was purchased from Saint-Quentin Fallavier Co. Ltd (France). The HA was used without any further purification. Stock solution of HA was prepared by weighing a given amount, dissolving it in 0.1 mL 0.1 mol/L NaOH, and diluting to a fixed volume using Milli-Q water; the concentration of HA stock solution was 2.5 g/L. The pH value of HA stock solution was approximately 7.6. This solution was stored at 4 °C in the dark.

Photodegradation experiments

A detailed description of the photodegradation processes has been reported elsewhere (Zhang *et al.* 2011), although the authors provided only a simple description of the experimental process.

Analytical methods

The concentrations of DCF solutions were determined via reversed-phase high-performance liquid chromatography (HPLC), which consisted of a Waters 1525 Binary HPLC pump and Waters 2998 Photodiode Array detector (Waters, Massachusetts, USA). Analytical column temperatures were controlled with a Model 1500 Column Heater (Waters, and Product of Singapore). The analytical column was a 150 mm × 4.6 mm Waters C18 column (particle size 5 μm). A Waters guard column (C18, 4.6 × 20 mm, particle size 5 μm) was used to protect the analytical column. The injection volume was 20 μL. The mobile phase was a mixture of 75% HPLC-grade methanol and 25% Milli-Q water (containing 1% acetic acid) at a constant flow rate of 1.0 mL/min, and the detection wavelength was set at 276 nm. The possible degradation products of DCF were

analyzed by an HPLC-mass spectrometry (MS) system (Waters Corporation) equipped with a C18 column (100 mm × 2.1 mm, 5 μm) and triple quadrupole detector. The mobile phase was a mixture of 65% HPLC-grade acetonitrile and 35% Milli-Q water (containing 1% acetic acid) at a constant flow rate of 0.3 mL/min. The injection volume was 3 μL. Single MS analysis was performed using an ion trap mass spectrometer equipped with an atmospheric pressure ionization interface and an electrospray ionization ion source. The flow rate of the high purity nitrogen (heater temperature, 350 °C) was maintained at 650 L·h^{-1}.

RESULTS AND DISCUSSION

Effect of temperature on the photodegradation of DCF

The linear plots of ln[DCF]/[DCF]$_0$) versus time under simulated sunlight at the temperature of 278, 288, 298 and 308 K are shown in Figure 1. The calculated apparent rate constants (k) were 0.174, 0.183, 0.205 and 0.216 min^{-1}, which revealed that the rate constant increased as the temperature increased. As can be seen from Figure 1, a positive linear correlation between the apparent rate constant and the reaction temperature was observed for the temperature range 278–308 K, according to the Arrhenius equation:

$$\ln k = \ln A - \frac{E}{RT} \quad (1)$$

where E is the apparent activation energy, R is the universal gas constant, and A is the Arrhenius pre-exponential constant. The apparent activation energy (E) and Arrhenius pre-exponential constant (A) were determined to be 5.302 and 1.707 kJ mol^{-1}, respectively, by fitting the temperature-dependent kinetic data with Equation (1). The active energy used to carry out the photochemical reaction is light energy, so the contribution of temperature to rate enhancement is limited. In addition, plotting ln(k/T) versus 1/T would show a linear relationship; the enthalpy (△H) and entropy (△S) were determined to be 3.13 kJ mol^{-1} and −247.67 J mol^{-1} K^{-1}, respectively, by fitting Equation (2) to the experimental data.

$$\ln\frac{k}{T} = -\frac{\Delta H}{R}\times\frac{1}{T} + \ln\frac{\Delta k_B}{h} + \frac{\Delta S}{R} \quad (2)$$

$$\Delta G = \Delta H + T\Delta S \quad (3)$$

Thermodynamic study indicated that the photodegradation course is spontaneous, exothermic and irreversible (△G < 0). It has been verified previously that the photodegradation of DCF can be predominantly attributed to direct photolysis and self sensitization (Zhang *et al.* 2011). The theoretical basis of self sensitization is provided through calculation of heat point temperature. In addition, at higher temperatures, the higher vibration energies of DCF molecules and inter-atomic forces promote chemical bond rupture.

Effect of initial DCF concentration on the photodegradation of DCF

The effect of different initial DCF concentrations on the photodegradation was investigated (Figure 2). Linear plots

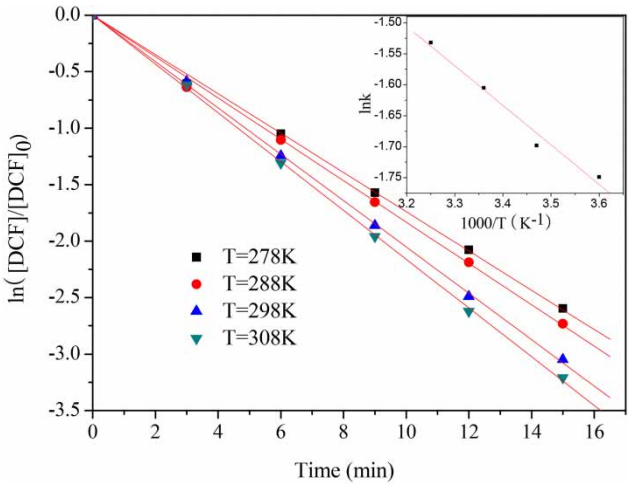

Figure 1 | Kinetics of DCF photodegradation at three temperatures, [DCF]$_0$ = 0.03 mmol/L. Error bars represent the 99% confidence interval.

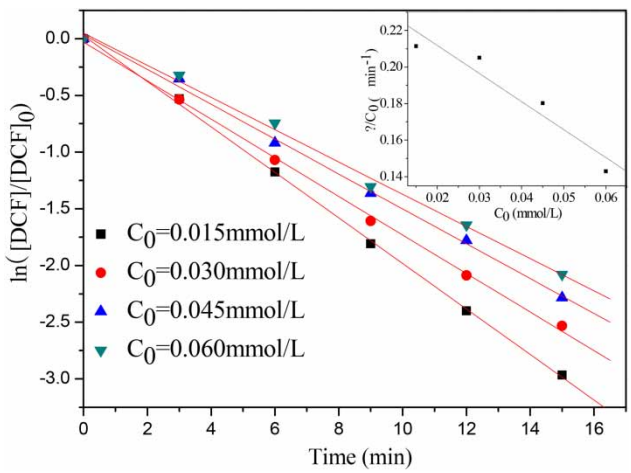

Figure 2 | The initial rate of DCF photodegradation versus various initial concentrations under simulated sunlight. Error bars represent the 99% confidence interval.

of $\ln([DCF]/[DCF]_0)$ versus time, obtained with the initial DCF concentrations of 0.015, 0.030, 0.045 and 0.060 mmol/L, gave correlation coefficients (R^2) of 0.9986, 0.9992, 0.9993 and 0.9988, respectively. The pseudo-first order rate constants (k) were 0.211, 0.205, 0.180 and 0.143 min^{-1} at DCF concentrations of 0.015, 0.030, 0.045 and 0.060 mmol/L, respectively. Linear plots of C0 versus υ/C0 obtained the y-intercepts as the rate constants of the direct photodegradation, which is consistent with the report by some literature (Werner *et al.* 2006; Chen *et al.* 2008). From Figure 2, the rate constants of the direct photodegradation resulting from extrapolation to $C0 = 0$, the rate constant of the direct photodegradation is 0.227 min^{-1}.

Effect of pH value on the photodegradation of DCF

The pH value of the reaction solution is an important parameter, which affects the degradation of pollutants (Li *et al.* 2009). The effect of different pH values on the degradation of DCF in the absence of simulated sunlight or the presence of any other illumination was investigated. The effect of pH on DCF degradation in the range 3–12 is shown in Figure 3 and demonstrates that the rate constant gradually increased when the pH increased from 3 to 5. At pH values greater than 4.35 ± 0.2, DCF predominantly exists in its ionic form, while at lower values it is principally found in its molecular form (Naddeo *et al.* 2010). Thus, it can be deduced that the ionic form of DCF photodegrades more quickly than the molecular form. Figure 3 also demonstrates that the degradation rate gradually decreased as the pH increased from 5 to 8 and gradually increased when the pH further increased from 8 to 12. DCF contains a nitrogen atom located between two aromatic rings, which is more likely to be protonated at lower pH values, and this facilitates the cleavage of the C-N-C bonds. The cleavage of the C-N-C bonds is important in the DCF degradation mechanism (Parker *et al.* 2003; Pérez-Estrada *et al.* 2005; Li *et al.* 2010). Furthermore, Supplementary Figure SI.1 (available with the online version of this paper) shows HPLC of the photoproduct at different pH values. At pH 12, the reaction liquid was colorless and transparent after 15 min of simulated sunlight irradiation, and at pH 8 the reaction liquid was yellow. It was also observed that a different degradation product was obtained at different pH values. This result can be explained by the fact that most photons are captured by colored product, which retards DCF combination with photons, hence inhibiting DCF degradation. This result demonstrates that blocking the generation of colored product can promote DCF degradation under alkaline conditions.

Effect of HA on the photodegradation of DCF

The effect of different concentrations of HA on the degradation of DCF under simulated sunlight is shown in Figure 4. It can be seen that the HA inhibits the DCF degradation whatever the concentration of HA, and the degradation rate of DCF changed little with increasing HA concentration. This can be explained by three competing mechanisms. HA absorbs photons in the emission spectrum of a xenon lamp, a wavelength region that overlaps with the absorbance of DCF, reducing the photodegradation of DCF. However, during UV irradiation HA can form a transient excited state (triplet state, $^3HA^*$) that may react with

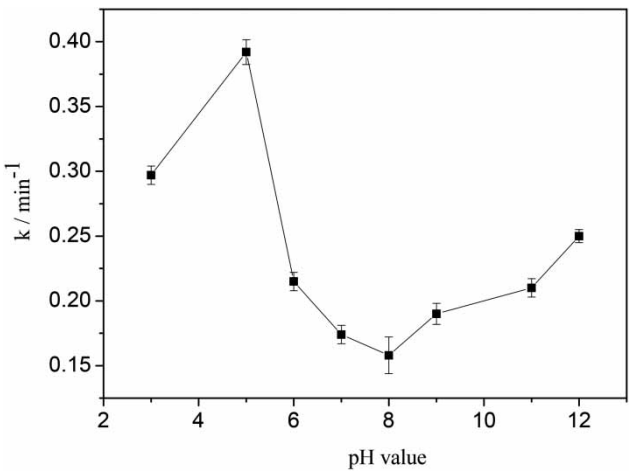

Figure 3 | Effect of pH value on the photodegradation of DCF, [DCF] 0 = 0.03 mmol/L. Error bars represent the 95% confidence interval.

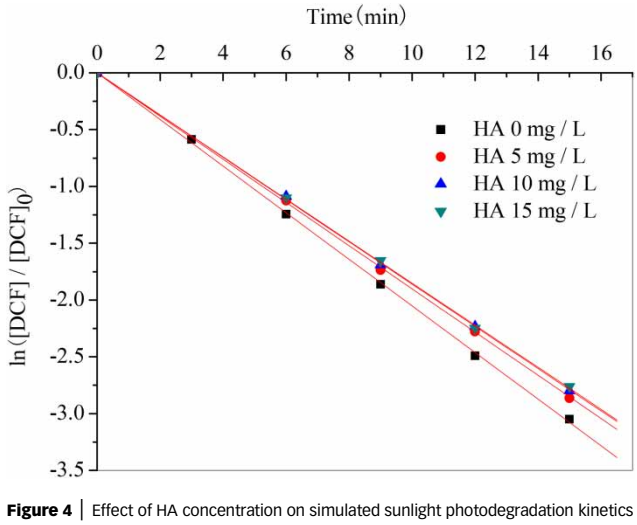

Figure 4 | Effect of HA concentration on simulated sunlight photodegradation kinetics of DCF ($[DCF]_0 = 0.03$ mmol/L) in water. Error bars represent the 95% confidence interval.

dissolved oxygen to form reactive species such as singlet oxygen, which would be expected to promote photodegradation. However, UV irradiation is very weak under simulated sunlight, and so the latter mechanism is likely to be less important under the experimental conditions (Haag & Hoigné 1986; Liu *et al.* 2010). Third, HA are likely to act as scavengers of ^{3}DCF*4 via the mechanism shown in the following reaction equations (Equations (4)–(7)).

$$DCF \xrightarrow{hv} {}^1DCF* \tag{4}$$

$${}^1DCF^* \rightarrow {}^3DCF^* \rightarrow Products \tag{5}$$

$${}^3DCF^* + HA \rightarrow DCF^{\bullet -} + HA^{\bullet +} \tag{6}$$

$$DCF^{\bullet -} + O_2 \rightarrow DCF + O_2^{\bullet -} \tag{7}$$

The overall effect of HA on the photodegradation of DCF depends on the balance between these mechanisms, and in this study HA was found to inhibit DCF degradation.

Photodegradation mechanisms and intermediates/products identification

Samples were analyzed for photoproducts by HPLC-MS. Total ion chromatogram of DCF solution after 3 h photodegradation in simulated sunlight is shown in Figure 5. This indicates that DCF was degraded into three products. As can be seen in Figure 5, it is confirmed that 5.61 min is the retention time of DCF, and three main peaks at 4.62, 5.00, and 5.32 min retention time were assigned to 2-(8-hydroxy-9H-carbazol-1-yl) acetic acid (m/z 240), 2-(8-hydroxy-9H-carbazol-1-yl)acetaldehyde (m/z 224) and 2-(8-chloro-9H-carbazol-1-yl)acetic acid (m/z 258), respectively. Three intermediates were detected by HPLC-MS (Figure 6), which were 2-(8-hydroxy-9H-carbazol-1-yl)acetic acid (m/z 240), 2-(8-hydroxy-9H-carbazol-1-yl)acetaldehyde (m/z 224) and 2-(8-chloro-9H-carbazol-1-yl)acetic acid (m/z 258). Thus, we speculated on the degradation pathway for pure DCF under simulated sunlight. Two different pathways of DCF photodegradation are shown in Figure 7. Pathway A: DCF (m/z 295) lost chlorine and hydrogen atoms to produce m/z 258, which was followed by subsequent loss of chloride ion and through an ·OH attack forming m/z 240. The product m/z 240 lost methyl and two hydroxyl to form a fragment ion with m/z 196, or m/z 240 lost hydroxyl to form m/z 224, which was followed by subsequent loss of hydroxyl and carbonyl to form fragment ion with m/z 180. Pathway B: DCF (m/z 295) lost carboxyl to form fragment ion with m/z 250; this was followed by subsequent loss of chloride ions, resulting in m/z 214. Moreover, product m/z 258 undergoes decarboxylation to yield m/z 214 (Martínez *et al.* 2011).

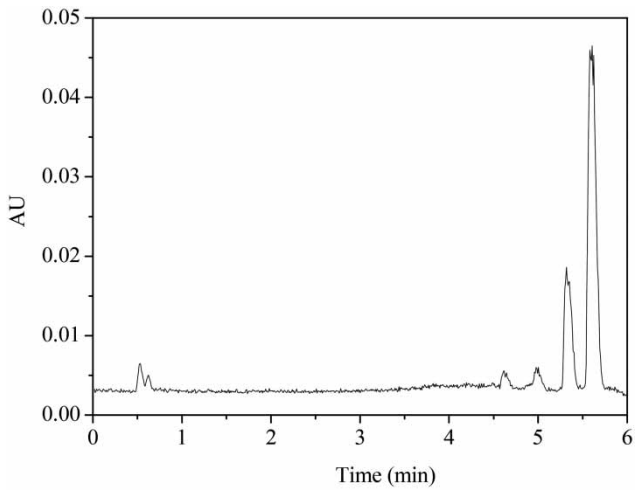

Figure 5 | Total ion chromatogram of DCF solution after 3 h photodegradation in simulated sunlight.

Toxicity of diclofenac to *Photobacterium phosphoreum* T3 Sp

The changes of luminescence inhibition rate (I%) to *Photobacterium phosphoreum* T_3 Sp during the photodegradation of DCF in aqueous solution are displayed in Figure 8. As can be seen from Figure 8, the inhibition rate of the photodegradation DCF solution decreased first, then increased, and finally decreased. The inhibition rate increased along with the irradiation time, which indicated the generation of some more toxic products of diclofenac than DCF. Therefore, the phototoxicities of the intermediates urge more concern over the ecological risk for the class of DCF.

CONCLUSIONS

This paper studied in detail the effects of temperature, pH and HA on the photodegradation of DCF under simulated sunlight conditions. The following conclusions can be drawn:

(1) Degradation pathways proceeded via pseudo first-order kinetics in all cases.
(2) The photodegradation course is spontaneous, exothermic and irreversible. The rate constant gradually

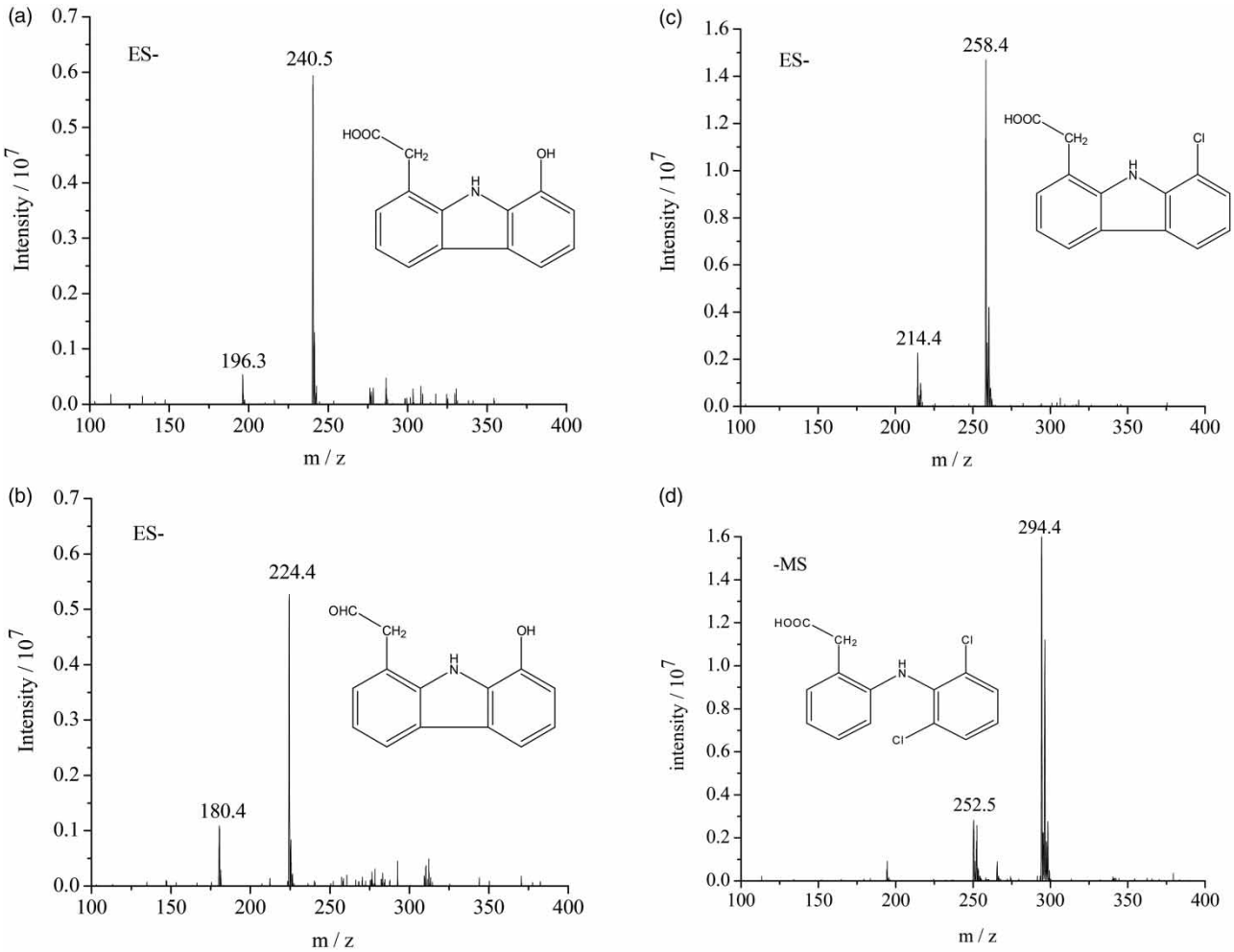

Figure 6 | Mass chromatogram: (a) mass chromatogram of P_1, (b) mass chromatogram of P_2, (c) mass chromatogram spectra of P_3 and (d) mass chromatogram of DCF.

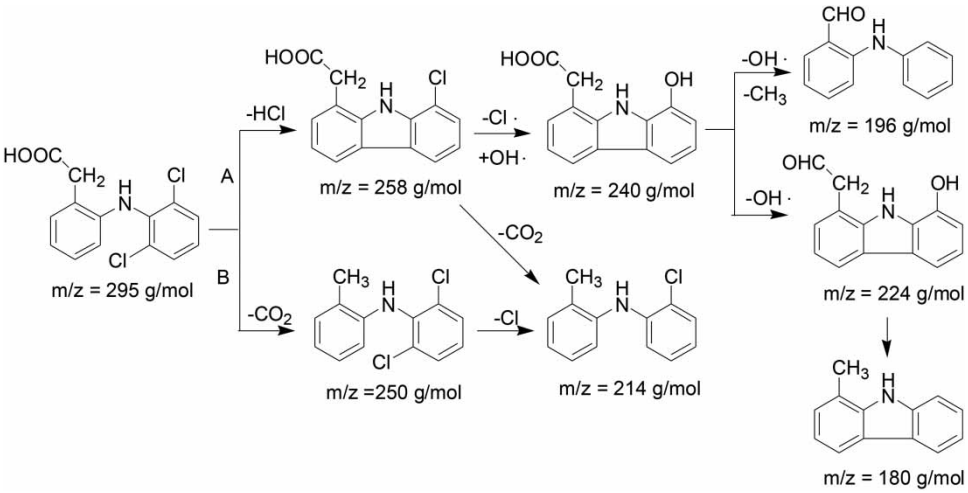

Figure 7 | Proposed transformation pathways of photodegradation of DCF.

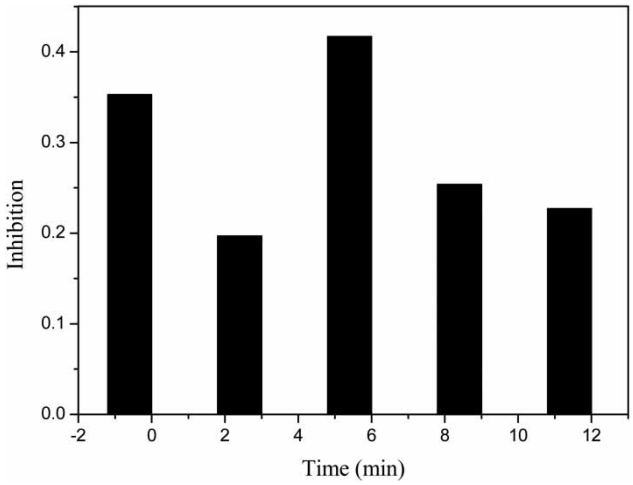

Figure 8 | Inhibition of the bioluminescence of *Photobacterium phosphoreum* T_3 Sp by the photodegradation products of DCF ($[DCF]_0 = 0.03$ mmol/L).

increased when the pH increased from 3 to 5 and decreased as the pH increased from 5 to 8, finally increasing when the pH further increased from 8 to 12.

(3) HA exerts inhibiting effects on the photodegradation of DCF.

(4) The transformation products of DCF were identified by HPLC/MS and the possible photoreaction pathways were proposed.

(5) A toxicity test using *Photobacterium phosphoreum* T3 Sp indicated the generation of some more toxic products than DCF.

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