

ADVANCED OXIDATION DEGRADATION OF DICLOFENAC

William J. Cooper¹ and Weihua Song²

¹Urban Water Research Center, Department of Civil and Environmental Engineering, University of California, Irvine, CA 92697, United States

wcooper@uci.edu

²Department of Environmental Science & Engineering, Fudan University, Shanghai 200433, P. R. China

wsong@fudan.edu.cn

Abstract

Advanced oxidation/reduction processes (AO/RPs), utilize free radical reactions to directly degrade chemical contaminants as an alternative to traditional water treatment. This study reports the absolute rate constants for reaction of diclofenac sodium and the model compound (2, 6-dichloraniline) with the two major AO/RP radicals; the hydroxyl radical ($\bullet\text{OH}$) and hydrated electron (e^-_{aq}). The bimolecular reaction rate constants ($\text{M}^{-1} \text{s}^{-1}$) for diclofenac for $\bullet\text{OH}$ was $(9.29 \pm 0.11) \times 10^9$, and, for e^-_{aq} was $(1.53 \pm 0.03) \times 10^9$. Preliminary degradation mechanisms are suggested based on product analysis using ^{60}Co γ -irradiation and LC-MS for reaction by-product identification. The toxicity of products was evaluated using the *Vibrio fischeri* luminescent bacteria method.

Introduction

There is a rising concern about the occurrence and persistence of Pharmaceutical and Personal Care Products (PPCPs) in the aquatic environment, due to their potential impact on the aqueous ecosystems and human health (Schwarzenbach et al. 2006, Kumar and Xagorarakis 2010). The worldwide consumption of medicines provides a continuous release of the substances or their metabolites in the environment. Conventional wastewater treatment systems such as filtration and activated sludge do not efficiently remove many of these PPCPs and as a result they have been found in a wide range of environmental samples including surface water, groundwater and drinking water (Kolpin et al. 2002, Kim et al. 2007). Therefore, advanced treatments technologies need to be evaluated and eventually employed, that are capable of either the complete removal of these chemicals from wastewater or at the very least the destruction of their biological activity (Snyder et al. 2003).

Recently studies indicated that the nanofiltration and reverse osmosis processes guarantee the rejection of PPCPs (Radjenovic et al. 2008). However, biofouling of membrane elements and disposal of retentate are considered major problems in these processes (Snyder et al. 2007, Wintgens et al. 2006, Ben Abdelmelek et al. 2011). Ozonation can destroy some of PPCPs in raw and/or clarified water; unfortunately, the competition between the PPCPs and organic material in the raw water may lead to rapid depletion of ozone, resulting in incomplete oxidation of PPCPs (Ikehata et al. 2006).

Advanced oxidation/reduction processes (AO/RPs) are alternatives to traditional treatment and have recently received considerable attention for PPCPs removal. AO/RPs typically involve the formation of hydroxyl radicals ($\bullet\text{OH}$) as oxidizing species and either hydrated

electrons (e^-_{aq}) as reducing species, both can be utilized in the destruction of organic pollutants present in drinking or wastewater. AO/RPs are effective in the treatment of a variety of anthropogenic pollutants including PPCPs (Song et al. 2009, Song et al. 2008a, Song et al. 2008b). However, to provide a fundamental understanding of the applicability of these processes to degrade PPCPs, it is necessary to determine the bimolecular reaction rate constants and degradation mechanisms, more important, degradation products toxicities.

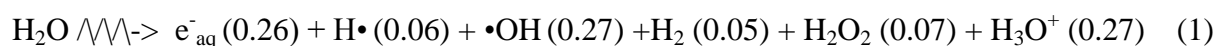
This study focused on the diclofenac, a common nonsteroidal anti-inflammatory drug (NSAID). It is often found as a persistent toxic waste and one of the most widely available drugs in the world. Average concentrations in the low $\mu\text{g L}^{-1}$ range were detected in influents and effluents of municipal sewage treatment plants and surface waters in Austria, Pakistan, Germany and United States (Kolpin et al. 2002, Stülten et al. 2008, Scheurell et al. 2009, Al-Rifai et al. 2007). Even at very low concentrations adverse effects have been observed in different organisms. In rainbow trout, livers, kidneys and gills, the lowest observed effect for cytopathology occurred at $1 \mu\text{g L}^{-1}$ (Triebkorn et al. 2004). For ecological effect, diclofenac residues have been reported to cause vulture population decline in Pakistan (Oaks et al. 2004). Therefore, it is critical to develop a fundamental understanding of the fate and oxidative and reductive degradation of diclofenac during water treatment processes.

Materials and Methods

Materials. Diclofenac and 2, 6-dichloraniline (DCA) were purchased from Sigma-Aldrich ($\geq 99\%$) and used without any further purification. Methanol, 2-propanol, and acetic acid (Fisher Science) were of HPLC grade. All solutions were prepared in 5.0 mM phosphate buffer and adjusted to pH 7.0 with NaOH or H_3PO_4 , as necessary.

Pulse radiolysis and γ -radiolysis. Pulse radiolysis experiments were performed at the US Department of Energy, Notre Dame Radiation Laboratory using an 8-MeV Titan Beta model TBS-8/16-1S linear accelerator that produces 2 ns electron pulses which generate radical concentrations of 1-3 μM per pulse. All experimental data were taken by averaging 8 to 15 replicate pulses using the continuous flow mode of the instrument. Dosimetry was performed with N_2O -saturated, $1.00 \times 10^{-2} \text{ M SCN}^-$ solutions monitored at $\lambda = 472 \text{ nm}$.

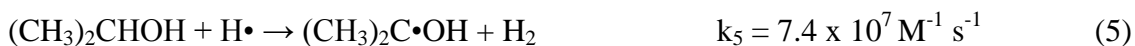
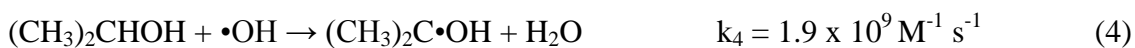
The radiolysis of water is described in Eq 1:



Where the numbers in parentheses are G values (yields) in $\mu\text{mol J}^{-1}$. To study the oxidative chemistry of the hydroxyl radical solutions were saturated with nitrous oxide (N_2O), which quantitatively converts the solvated electrons and hydrogen atoms ($\text{H}\cdot$) to the $\cdot\text{OH}$ radical.



Reactions between the solvated electron and diclofenac were studied in N_2 -saturated solutions buffered at pH 7.0. These solutions contained 0.10 M isopropanol to scavenge the hydroxyl radicals and hydrogen atoms, to convert them into relatively inert isopropanol radicals.



A Shepherd[®] 109-86 Cobalt-60 source was used for γ radiolysis with samples of 1.0 mM diclofenac saturated with air before irradiation. The dose rate was 8.14 krad min⁻¹ (0.0772 kGy min⁻¹), as measured by Fricke dosimetry.

HPLC and mass spectral analysis. The concentration of diclofenac was analyzed by an Agilent 1260 HPLC using the following conditions: column, Phenomenex Gemini C₁₈ 250 x 4.6 mm i.d.; mobile phase consisting of 15 % CH₃OH, 15 % CH₃CN and 70 % 10 mM phosphate buffer solution (pH 3.0). The LC-MS system was an Agilent 1100 HPLC Pump and Waters LCT Classic Mass Spectrometer with electrospray ionization source and a Phenomenex Luna C₁₈ (2) column (2.0 x 250 mm). The injection volume of the samples was 10 μ L. The mobile phase was A: 98 % H₂O + 2 % CH₃CN + 0.2 % formic acid and B: 50 % CH₃OH, 50 % CH₃CN and 0.2 % formic acid. Gradient elution was 0 % of B for 5 min followed by a linear increase to 100 % in 50 min, and then held constant for an additional 10 min. The mass spectra data were obtained in the positive ion mode by scanning from m/z 100 to 350.

Ion chromatography. Chloride ion released by the reaction of diclofenac with $\bullet\text{OH}$ and e^-_{aq} was quantified by ion chromatography (DX-120, Dionex) with conductivity detection. Separation was performed on an Ion-Pac AS16 anion column (4 250 mm, Dionex) using 35 mM NaOH eluent solution at a flow rate of 1.0 mL min

Results and Discussion

Kinetic Measurements. Pseudo-first-order growth rate constants for the reaction of hydroxyl radical with diclofenac were determined by fitting exponential growth curves to the time-dependent absorbance of the transient monitored at 330 nm and 370 nm, over a range of different diclofenac concentrations (Figure 1a). At both wavelengths, the initial growth in absorbance was followed by a second, smaller, concentration-independent growth, which was accounted for in the data fitting by using the sum of two exponential growths. The hydroxyl radical bimolecular rate constant for this reaction, $k = (9.29 \pm 0.11) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$, was then determined from a plot of these pseudo-first-order rate constants as a function of diclofenac concentration (see Figure 1b). This rate constant is slightly fast than the steady-state competition kinetic based value of $(7.5 \pm 1.5) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ recently reported by Huber (Huber et al. 2003) for $\bullet\text{OH}$ generated by γ -irradiation. To determine the site of reaction of $\bullet\text{OH}$ with diclofenac, the rate constant of $\bullet\text{OH}$ reaction with diclofenac was compared with that for several model compounds (Table 1). The rate constant of aniline was slightly higher than DCA, while both were similar with diclofenac. This suggests that $\bullet\text{OH}$ attacks both aromatic rings; however, when compared to DCA, the aniline ring is slightly more reactive due to the high electron density on the ring. The $\bullet\text{OH}$ radical reaction rate constant of acetic group was \sim 100 times slower, reflects the fact that $\bullet\text{OH}$ abstract hydrogen from alkyl group in the diclofenac plays a minor role.

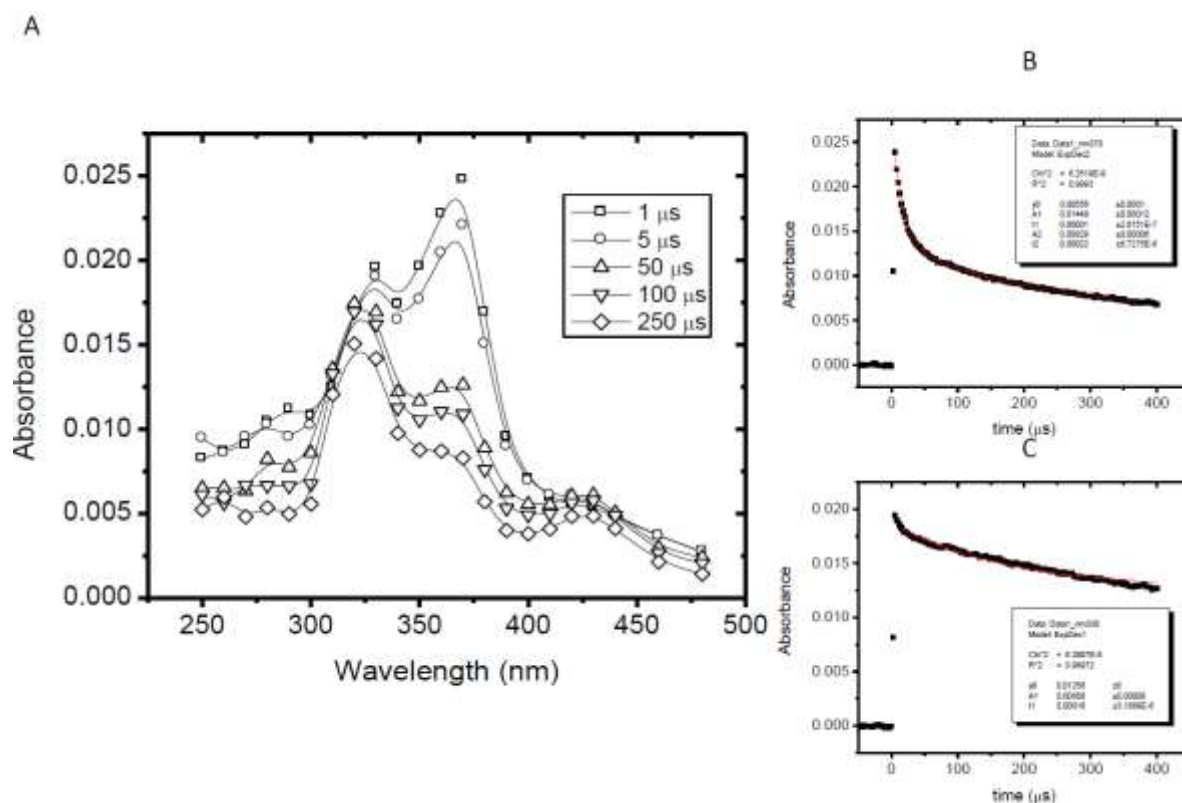


Fig. 1. (A) Transient absorption spectra obtained from electron pulse radiolysis of N_2O saturated aqueous solutions of diclofenac at room temperature and pH 7.0. Transient decay kinetics shown for at 310 nm (B) and 370 nm (C).

TABLE 1. SUMMARY OF SECOND-ORDER RATE CONSTANTS IN THIS STUDY (BOLD) IN COMPARISON TO VALUES FOR ANALOGOUS COMPOUNDS FROM LITERATURE.

Compound	$k_{OH}/M^{-1}s^{-1}$	$k_{e^{-}aq}/M^{-1}s^{-1}$
Diclofenac	$(9.29 \pm 0.11) \times 10^9$	$(1.53 \pm 0.03) \times 10^9$
2, 6-dichloroaniline	$(6.97 \pm 0.14) \times 10^9$	$(3.26 \pm 0.04) \times 10^9$
<i>m</i> -dichlorobenzene	5.7×10^9 (Kochany and Bolton 1992)	5.2×10^9 (Anbar and Hart 1964)
Aniline	1.0×10^{10} (Solar et al. 1986)	3.0×10^7 (Solar et al. 1986)
Acetic acid	8.5×10^7	1.1×10^6

The second order rate constant for the reaction of the solvated electron with diclofenac was determined by fitting single exponential decays to the absorbance of e^{-}_{aq} monitored at 700 nm. Plotting these pseudo-first-order values against diclofenac concentration, a second-order rate constant of $k = (1.53 \pm 0.03) \times 10^9 M^{-1} s^{-1}$ was obtained (Table 1) in comparison to values for

analogous compounds. Our diclofenac value is considerably faster than for the reduction of aniline ($3 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$) or acetic acid ($1.1 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$), nevertheless similar to rate constant for *m*-dichlorobenzene ($5.2 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$) or DCA. From these rate constants, it appears that the reduction occurs predominately via dissociative electron attachment at the chlorine moiety in diclofenac.

Degradation efficiency and dechlorination. Steady-state γ irradiation of diclofenac in N_2O saturated solutions ($\bullet\text{OH}$) and N_2 saturated aqueous isopropanol solutions (e^-_{aq}) showed decreasing concentration with increasing dose (see Figure 2a). The curvature of the plot is consistent with previously reported irradiation studies for other contaminants in water (Jeong et al. 2010a, Jeong et al. 2010b, Luo et al. 2012), suggesting competition for the reactive species ($\bullet\text{OH}$ and e^-_{aq}) between diclofenac and the reaction by-products at the higher applied doses.

These data allow estimation of the efficiencies of the initial $\bullet\text{OH}$ oxidation and e^-_{aq} reduction of diclofenac. From the lowest dose measurement, an estimate of the initial slope was $-3.23 \times 10^{-4} \text{ M kGy}^{-1}$ for the $\bullet\text{OH}$ radical, seen as the straight line in Figure 2a. This predicted line corresponds to the total removal of diclofenac, assuming no interference from stable products occurred. Under these experimental conditions all the produced hydroxyl radicals will initially react with diclofenac and the degradation efficiency was 60 %. The similar assumption has also been applied to estimate the solvated electron reaction efficiency and reported as 62 %.

The release of chloride ion from irradiated solutions of diclofenac was measured by ion chromatograph (Figure 2b). The dechlorination by $\bullet\text{OH}$ fit a straight line and the formation rate determined was $9.2 \times 10^{-5} \text{ M kGy}^{-1}$, which accounts for only 17% $\bullet\text{OH}$ radical attack. The of diclofenac by e^-_{aq} fit pseudo first order growth, and the initial formation rate is $2.7 \times 10^{-4} \text{ M kGy}^{-1}$. This rate was equal to the $G(\text{e}^-_{\text{aq}})$ value ($2.6 \times 10^{-4} \text{ M kGy}^{-1}$), and indicated an efficiency of 100 %.

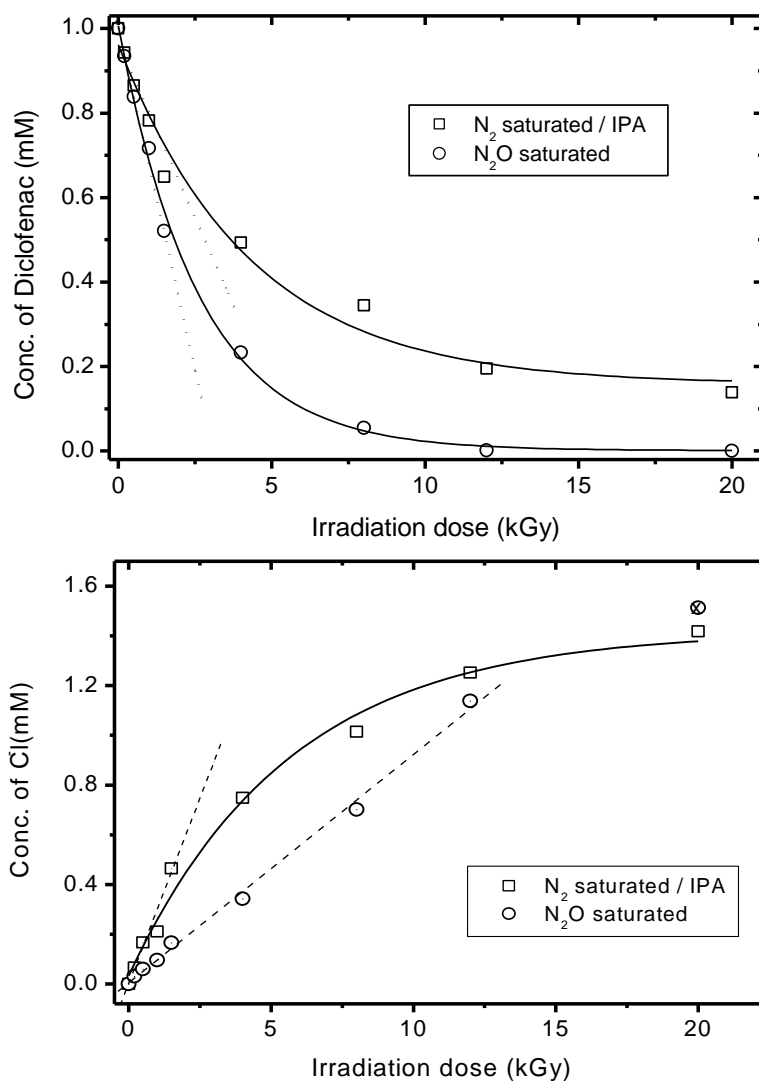


Fig. 2. Degradation curve of diclofenac at pH 7.0. Fast N_2O purging, medium air saturated, slowest N_2 purge and added isopropyl alcohol.

Degradation mechanism. Analyses by LC-MS at various doses revealed diclofenac decomposition products at N_2O saturated ($\bullet OH$ oxidation) or 0.1 M isopropanol N_2 saturated (solvated electron reduction) solutions. Our structural assignments of the breakdown products of diclofenac during γ -irradiation were based on the analysis of the Total Ion Chromatogram (TIC) and the corresponding mass spectra with consideration of isotopic abundance. The masses of the different products were determined from the peaks corresponding to the protonated molecule, $[M+H]^+$. For the purpose of this paper, we will refer to the products by molecular weight (MW).

The major degradation products produced in the steady-state γ irradiation of diclofenac in N_2O saturated solutions are summarized in Figure 3. Three separate products with MW of 311 were observed, corresponding to the addition of 16 mass units to the parent peak. This is

consistent with hydroxylation of the aromatic ring. The addition of the electrophilic hydroxyl radical to the aromatic ring forms a resonance-stabilized carbon-centered radical with subsequent addition of oxygen and elimination of a hydroperoxyl radical, yielding the phenolic products. Generally the specificity of electrophilic aromatic substitution is governed by the nature of the substituents, which may account for our observation of three different products with the same m/z ratio. Since the amino group is a strong electron donating group and acts as ortho-para directors, three main products are proposed in the Figure 3.

With further hydroxyl radical oxidation, multi di-hydroxylation products (MW 327) were formed, which verifies the assumption of hydroxyl substitution on the rings, since the hydroxyl group increases the electron density and the hydroxyl radical electrophilic adductions are favorable. It is proposed that the product with MW 309 is the result of further oxidation with the primary phenolic degradation product (a) to form quinine imine product, which is also observed in photo-Fenton degradation products (Pérez-Estrada et al. 2005). One minor product was observed with the MW 275, corresponding to the loss of HCl from the primary phenolic product (b). This suggests that the phenol group attacks the chlorine substituted carbon with subsequent cyclization to form a six-membered ring. The compound with a MW 177 could be formed, following hydroxyl radical ipso-adduction to the primary product MW 311 (c). Another mono-aromatic product of MW 151 was observed and isotope mass peak indicates there no chloric group present in this product. Therefore, the structure has also been proposed in Figure 3. It is suggested from hydroxyl radical ipso-adduction to the DCA ring. The associated product MW 162 is not detected under our experimental conditions, it may due to the low response for the positive ionization.

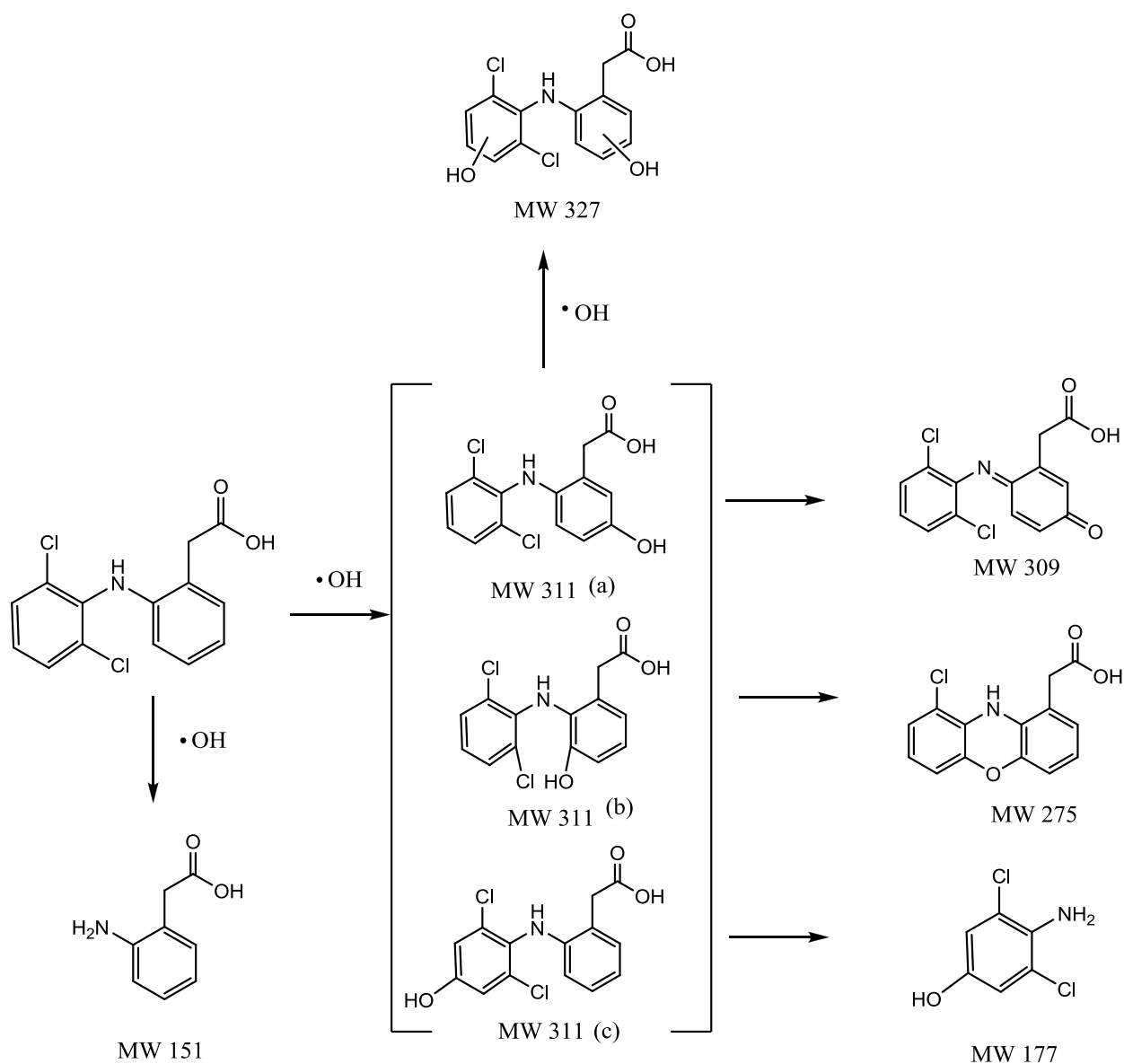


Fig. 3. Proposed oxidative ($\cdot\text{OH}$) degradation mechanism for diclofenac.

Diclofenac solution (with 0.1 M isopropanol) and N_2 saturated were used to study the solvated electron degradation mechanism. Dechlorination is the major degradation pathway, which is in agreement with chloride ion release. As carbon centered radical was the major intermediates after dechlorination, which either further abstract H atom from H_2O forming the product of MW 261, or with intra-molecular reaction forming the product of MW 259, as illustrated in Figure 4.

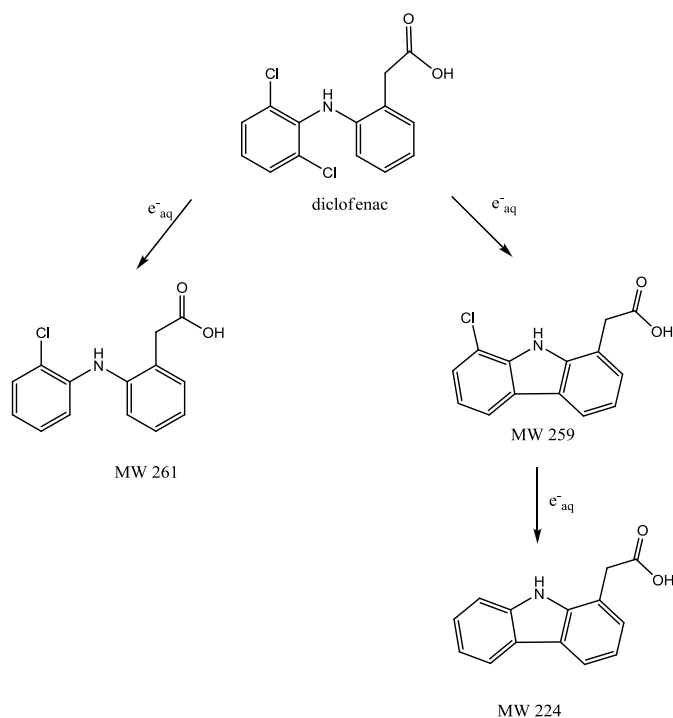


Fig. 4. Proposed reductive (e^-_{aq}) degradation mechanism for diclofenac.

Toxicity assessments. While our results demonstrate that $\bullet\text{OH}$ radical and e^-_{aq} effectively degrade diclofenac, it is critical to establish the biological activity of the resulting treated solution or the individual breakdown products. In general, $\bullet\text{OH}$ radical and e^-_{aq} lead to a complex mixture of products with low overall yields. As it is a daunting task to identify the individual reaction byproducts and assess their individual biological activities, we chose to use the *Vibrio fischeri* luminescent bacteria assay to assess the biological activity of the treated solutions at various doses. A calibration curve for the bacteria inhibition as a function of the concentration of diclofenac was used to evaluate the toxicity at increasing dose. With $\bullet\text{OH}$ radical oxidation in initial 4 kGy, 75 % of diclofenac had been destroyed. However, the biological activity of the treated samples was constant, implying that toxic breakdown products are formed to a significant extent. With further oxidation, the toxic products were eliminated and the toxicities of treated solution decrease slowly. While 100 % of diclofenac has been removed at 12 kGy, residue toxicity has been remained at 40 % inhibition.

Conclusion

The oxidative and reductive free radical reactions of diclofenac have been determined and their respective degradation mechanisms proposed. Not surprisingly the mechanisms are considerably different and result in different reaction by-products. The residual toxicity, as measured by the change in bioluminescence of *V. fischeri* showed that the by-products of the reductive processes were less toxic than those obtained by oxidative destruction of diclofenac. The reaction efficiency of both oxidation and reduction processes was approximately 60 % which confirms that diclofenac is relatively resistant to free AOP treatment.

Acknowledgments

Pulse radiation performed at the Radiation Laboratory, University of Notre Dame, which is supported by the Office of Basic Energy Sciences, U.S. Department of Energy. NSFC Grant 21107016, NSF Grant CBET-1034555, provided partial support of this work.

References

Schwarzenbach, R.P., Escher, B.I., Fenner, K., Hofstetter, T.B., Johnson, C.A., von Gunten, U. and Wehrli, B. (2006) The Challenge of Micropollutants in Aquatic Systems. *Science* 313(5790), 1072-1077.

Kumar, A. and Xagorarakis, I. (2010) Pharmaceuticals, personal care products and endocrine-disrupting chemicals in U.S. surface and finished drinking waters: A proposed ranking system. *Science of The Total Environment* 408(23), 5972-5989.

Kolpin, D.W., Furlong, E.T., Meyer, M.T., Thurman, E.M., Zaugg, S.D., Barber, L.B. and Buxton, H.T. (2002) Pharmaceuticals, Hormones, and Other Organic Wastewater Contaminants in U.S. Streams, 1999-2000: A National Reconnaissance. *Environ. Sci. Technol.* 36(6), 1202-1211.

Kim, S.D., Cho, J., Kim, I.S., Vanderford, B.J. and Snyder, S.A. (2007) Occurrence and removal of pharmaceuticals and endocrine disruptors in South Korean surface, drinking, and waste waters. *Water Res.* 41, 1013-1021.

Snyder, S.A., Westerhoff, P., Yoon, Y. and Sedlak, D.L. (2003) Pharmaceuticals, Personal Care Products, and Endocrine Disruptors in Water: Implications for the Water Industry. *Environ. Eng. Sci.* 20, 449-469.

Radjenovic, J., Petrovic, M., Ventura, F. and Barcelo, D. (2008) Rejection of pharmaceuticals in nanofiltration and reverse osmosis membrane drinking water treatment. *Water Res.* 42(14), 3601-3610.

Snyder, S.A., Adham, S., Redding, A.M., Cannon, F.S., DeCarolis, J., Oppenheimer, J., Wert, E.C. and Yoon, Y. (2007) Role of membranes and activated carbon in the removal of endocrine disruptors and pharmaceuticals. *Desalination* 202, 156-181.

Wintgens, T., Melin, T., Schafer, A., Khan, S., Muston, M., Bixio, D. and Thoeye, C. (2006) The role of membrane processes in municipal wastewater reclamation and reuse. *Desalination* 187, 271-282.

Ben Abdelmelek, S., Greaves, J., Ishida, K.P., Cooper, W.J. and Song, W. (2011) Removal of Pharmaceutical and Personal Care Products from Reverse Osmosis Retentate Using Advanced Oxidation Processes. *Environmental Science & Technology* 45(8), 3665-3671.

Ikehata, K., Naghashkar, N.J. and Gamal El-Din, M. (2006) Degradation of aqueous pharmaceuticals by ozonation and advanced oxidation processes: A review. *Ozone: Sci. Eng.* 28, 353-414.

Song, W., Cooper, W.J., Peake, B.M., Mezyk, S.P., Nickelsen, M.G. and O'Shea, K.E. (2009) Free-radical-induced oxidative and reductive degradation of N,N'-diethyl-m-toluamide (DEET): Kinetic studies and degradation pathway. *Water Res.* 43(3), 635-642.

Song, W., Cooper, W.J., Mezyk, S.P., Greaves, J. and Peake, B.M. (2008a) Free Radical Destruction of β -Blockers in Aqueous Solution. *Environ. Sci. Technol.* 42(4), 1256-1261.

Song, W., Chen, W., Cooper, W.J., Greaves, J. and Miller, G.E. (2008b) Free-Radical Destruction of β -Lactam Antibiotics in Aqueous Solution. *J. Phys. Chem. A* 112, 7411-7417.

Stülten, D., Zühlke, S., Lamshöft, M. and Spitteller, M. (2008) Occurrence of diclofenac and selected metabolites in sewage effluents. *Science of The Total Environment* 405(1-3), 310-316.

Scheurell, M., Franke, S., Shah, R.M. and Hühnerfuss, H. (2009) Occurrence of diclofenac and its metabolites in surface water and effluent samples from Karachi, Pakistan. *Chemosphere* 77(6), 870-876.

Al-Rifai, J.H., Gabelish, C.L. and Schäfer, A.I. (2007) Occurrence of pharmaceutically active and non-steroidal estrogenic compounds in three different wastewater recycling schemes in Australia. *Chemosphere* 69(5), 803-815.

Tribskorn, R., Casper, H., Heyd, A., Eikemper, R., Kohler, H.R. and Schwaiger, J. (2004) Toxic effects of the non-steroidal anti-inflammatory drug diclofenac Part II. Cytological effects in liver, kidney, gills and intestine of rainbow trout (*Oncorhynchus mykiss*). *Aquat. Toxicol.* 68(2), 151-166.

Oaks, L.J., Gilbert, M., Virani, M.Z., Watson, R.T., Meteyer, C.U., Rideout, B.A., Shivaprasad, H.L., Ahmed, S., Chaudhry, M., Arshad, M., Mahmood, S., Ali, A. and Khan, A.A. (2004) Diclofenac residues as the cause of vulture population decline in Pakistan. *Nature* 427, 630-633.

Merga, G., Schuchmann, H.P., Rao, B.S.M. and Von Conntag, C. (1996) OH radical-induced oxidation of chlorobenzene in aqueous solution in the absence and presence of oxygen. *J. Chem. Soc. Farad. T.* 2 6, 1097-1103.

Merga, G., Rao, B.S.M., Mohan, H. and Mittal, J.P. (1994) Reactions of OH and SO₄·⁻ with some halobenzenes and halotoluenes: A radiation chemical study. *J. Phy. Chem.* 98(37), 9158-9164.

Huber, M.M., Canonica, S., Park, G.-Y. and von Gunten, U. (2003) Oxidation of pharmaceuticals during ozonation and advanced oxidation processes. *Environ. Sci. Technol.* 37(5), 1016-1024.

Jeong, J., Jung, J., Cooper, W.J. and Song, W. (2010a) Degradation mechanisms and kinetic studies for the treatment of X-ray contrast media compounds by advanced oxidation/reduction processes. *Water Research* 44(15), 4391-4398.

Jeong, J., Song, W., Cooper, W.J., Jung, J. and Greaves, J. (2010b) Degradation of tetracycline antibiotics: Mechanisms and kinetic studies for advanced oxidation/reduction processes. *Chemosphere* 78(5), 533-540.

Luo, X., Zheng, Z., Greaves, J., Cooper, W.J. and Song, W. (2012) Trimethoprim: Kinetic and mechanistic considerations in photochemical environmental fate and AOP treatment. *Water Research* 46(4), 1327-1336.

Pérez-Estrada, L.A., Malato, S., Gernjak, W., Agüera, A., Thurman, E.M., Ferrer, I. and Fernández-Alba, A.R. (2005) Photo-Fenton Degradation of Diclofenac: Identification of Main Intermediates and Degradation Pathway. *Environmental Science & Technology* 39(21), 8300-8306.

Kochany, J. and Bolton, J.R. (1992) Mechanism of photodegradation of aqueous organic pollutants. 2. Measurement of the primary rate constants for reaction of $\cdot\text{OH}$ radicals with benzene and some halobenzenes using an EPR spin-trapping method following the photolysis of H_2O_2 . *Environ. Sci. & Technol.* 26, 262-265.

Anbar, M. and Hart, E.J. (1964) The reactivity of aromatic compounds toward hydrated electrons *J. Am. Chem. Soc.* 86, 5633-5637.

Solar, S., Solar, W. and Getoff, N. (1986) Resolved mutisite OH-attack on aqueous aniline studied by pulse radiolysis. *Radiat. Phys. Chem.* 28, 229-234.