Free-Radical-Induced Oxidative and Reductive Degradation of Fibrate Pharmaceuticals: Kinetic Studies and Degradation Mechanisms

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The presence of pharmaceutically active compounds (PhACs) in aquatic systems is an emerging environmental issue and poses a potential threat to ecosystems and human health. Unfortunately, current water treatment techniques do not efficiently remove all of the PhACs, which results in the occurrence of such compounds in surface and ground waters. Advanced oxidation/reduction processes (AO/RPs) which utilize free radical reactions to directly degrade chemical contaminants are alternatives to traditional water treatment methods. This study reports the absolute bimolecular reaction rate constants for three pharmaceutical compounds (fibrates), clofibric acid, bezafibrate, and gemfibrozil, with the hydroxyl radical (•OH) and hydrated electron (e^-_{aq}). The bimolecular reaction rate constants for •OH were $(6.98 \pm 0.12) \times 10^9$, $(8.00 \pm 0.22) \times 10^9$, and $(10.0 \pm 0.6) \times 10^9$, and for e^-_{aq} were $(6.59 \pm 0.43) \times 10^8$, $(112 \pm 3) \times 10^8$, and $(6.26 \pm 0.58) \times 10^8$, for clofibric acid, bezafibrate, and gemfibrozil, respectively. Transient spectra were obtained for the intermediate radicals produced by the hydroxyl radical reactions. In addition, preliminary degradation mechanisms and major products were elucidated using ^{137}Cs γ-irradiation and LC−MS. These data are required for evaluating the potential use of AO/RPs for the destruction of these compounds in treating water for various purposes.

Introduction

In recent years pharmaceutically active compounds (PhACs) have emerged as a novel class of water contaminants. Public interest is quickly increasing because of their potential impact on the environment and possibly human health, even at trace concentrations. Human and veterinary applications are the main sources of PhACs in the environment.[1] Human origin PhACs enter the environment either through excretion after use and subsequent transport to treatment systems[2] or by direct disposal "down the drain". Once these compounds are in the environment, it has been shown that they can adversely affect both aquatic and nonaquatic organisms and thus the ecosystem.[1,3,4]

Three fibrate pharmaceutical compounds, clofibric acid, bezafibrate, and gemfibrozil, were chosen as the focus of this study because of their large production volume and widespread use. They belong to a group of phenoxyalkanoic acids and are active blood lipid regulators.[5−10] Each of the three compounds in the current research has been found in the environment.

Clofibric acid, which is used as a fibrate pharmaceutical and is also a metabolite of two related fibrate lipid regulators, clofibrate and etofibrate, was first detected in domestic wastewater effluent nearly 30 years ago.[11,12] It is one of the most persistent drug residues known with an estimated environmental residence of 21 years.[4,13,14] Bezafibrate is extensively used throughout the world and has among the highest reported concentration of any drug in both effluents (13 nM)[15] and surface waters (9 nM).[15] The reported annual use of gemfibrozil is 289 000 kg[7] with concentrations of 3−6 nM being observed in surface waters in North America and Europe.[6,14]

Current wastewater treatment techniques, such as activated sludge or trickling filter, do not efficiently remove all of the PhACs.[16−20] Specifically, several research groups have indicated that biological treatment processes do not efficiently remove the fibrate family, whereas nanofiltration and reverse osmosis processes appear to be effective methods for the removal of these compounds from drinking water.[12,15,21,22] However, biofouling of membrane elements and energy consumption of the processes are of concern in both nanofiltration and reverse osmosis,[23] and, therefore, alternative water treatment technologies need to be developed, 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.

Recent studies have shown that advanced oxidation processes (AOPs) efficiently degrade PhACs in wastewater thus minimizing the risk of unpredictable long-term effects that these compounds may cause in the environment;[24,25] however, few studies have been focused on advanced reduction processes (ARPs). Although there are some reports of the degradation of fibrate compounds by AOPs,[26,27] there appears to be no reported kinetic data and only limited information on degradation mechanisms.[28] In order to evaluate the removal of PhACs in different natural waters, it is initially important to determine the bimolecular reaction rate constants of the PhACs in model conditions with oxidants and reductants including the hydroxyl radical (•OH), the solvated electron (e^-_{aq}), and the hydrogen atom (H•).[25]

In general, ARPs are not used extensively at the present; however, they may become more prevalent in the future as new processes are developed and older ones perfected. For example, the electron beam process is both an AOP and an ARP, and in a flowing system, such as would be deployed, irradiation doses over 4.17 kGy result in complete reaction of the solvated

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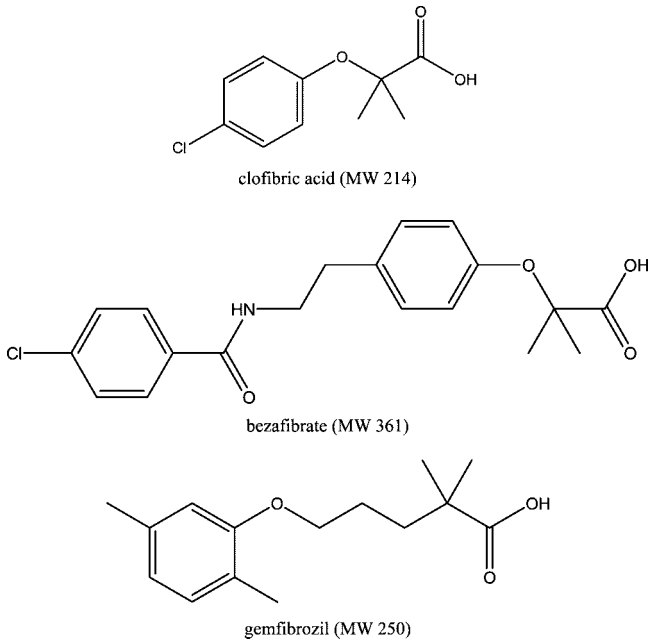


Figure 1. Chemical structures of the three fibrate pharmaceutical compounds investigated.

electron with oxygen (at saturation) and reduction proceeds more efficiently. However, it has been shown that even at lower doses, many chemicals compete with oxygen for the solvated electron and are removed at doses well below 4.17 kGy. For example carbon tetrachloride with a reaction rate constant of $(1.3-2.4) \times 10^{10}$ was removed in a flowing system at doses as low as 1 kGy.[29−32]

Therefore, the objective of this study was to determine the absolute bimolecular reaction rate constants for the hydroxyl radical (•OH) and hydrated electron (e^-_{aq}) with these three pharmaceutical compounds and to initiate a study to better understand the AO/RPs degradation mechanisms. The reaction efficiency of the initial reactions was also determined, and this information is useful in determining the placement of an AO/RP in a treatment system.

Methods and Materials

Materials. The pharmaceutical compounds clofibric acid, bezafibrate, and gemfibrozil were purchased from Sigma-Aldrich. All three compounds were shown to be ≥99% pure by high-performance liquid chromatography (see below). The chemical structures of these compounds are shown in Figure 1.

Pulse Radiolysis. Electron pulse radiolysis experiments were performed at the Notre Dame Radiation Laboratory with the 8 MeV Titan Beta model TBS-8/16-1S linear accelerator.[33] Upon generation of transient species, their absorption spectra and/or kinetics were measured. The light source was a pulsed Xe lamp, with the absorption changes being measured using a monochromator−photomultiplier tube arrangement. The photomultiplier output was collected with a digital oscilloscope and then stored on a computer for further analysis. Dosimetry[34] was performed using N_2O-saturated 1.00×10^{-2} M KSCN solutions at $\lambda =$ 472 nm ($G\epsilon = 5.2 \times 10^{-4}$ m^2 J^{-1}) with average doses of 3−5 Gy per 2−3 ns pulse. All experimental data were determined by averaging 8−12 replicate pulses using the continuous flow mode of the instrument.

The radiolysis of water is described in eq 1

$$H_2O \rightsquigarrow (0.28)\bullet OH + (0.06)H\bullet + (0.27)e^-_{aq} + (0.05)H_2 + (0.07)H_2O_2 + (0.27)H^+ \quad (1)$$

where the numbers in parentheses are the G values (yields)[35,36] and the units of G are μmol J^{-1}. To study only the reactions of the hydroxyl radical, solutions were presaturated with nitrous oxide (N_2O), which quantitatively converts the hydrated electrons and hydrogen atoms to hydroxyl radicals via the following reactions:[36]

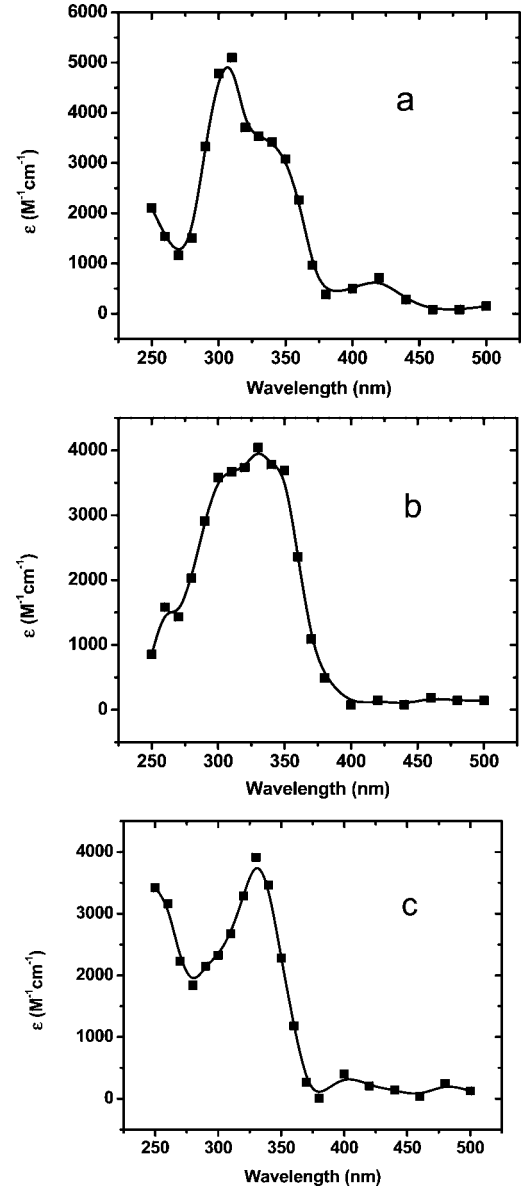


Figure 2. Transient absorption spectra from the reaction of the •OH with clofibric acid (a), bezafibrate (b), and gemfibrozil (c) in N_2O-saturated phosphate-buffered water (pH 7.0) at room temperature.

TABLE 1: Measured Rate Constants (M^{-1} s^{-1}) and Spectral Parameters for Hydroxyl Radical and Hydrated Electron Reaction with Fibrate Pharmaceuticals

compound	clofibric acid	bezafibrate	gemfibrozil
$\lambda_{max}{}^{\bullet OH}$/nm	310.0	330.0	330.0
$\epsilon_{max}{}^{\bullet OH}$/M^{-1} cm^{-1}	5099	4042	3913
$10^9 k_{\bullet OH}$/M^{-1} s^{-1}	(6.98 ± 0.12)	(8.00 ± 0.22)	(10.0 ± 0.6)
$10^8 k e^-_{aq}$/M^{-1} s^{-1}	(6.59 ± 0.43)	(112 ± 3)	(6.26 ± 0.58)

$$e^-_{aq} + N_2O + H_2O \rightarrow N_2 + HO^- + \bullet OH \qquad k_2 = 9.1\times10^9\ M^{-1}\ s^{-1} \quad (2)$$

$$H\bullet + N_2O \rightarrow \bullet OH + N_2 \qquad k_3 = 2.1\times10^6\ M^{-1}\ s^{-1} \quad (3)$$

To isolate hydrated electron reactions, solutions were presaturated with nitrogen in the presence of 0.10 M isopropanol to scavenge the hydroxyl radicals and hydrogen atoms, converting them into relatively inert isopropanol radicals:[36]

$$(CH_3)_2CHOH + \bullet OH \rightarrow (CH_3)_2C^{\bullet}OH + H_2O \qquad k_4 = 1.9\times10^9\ M^{-1}\ s^{-1} \quad (4)$$

$$(CH_3)_2CHOH + H\bullet \rightarrow (CH_3)_2C^{\bullet}OH + H_2 \qquad k_5 = 7.4\times10^7\ M^{-1}\ s^{-1} \quad (5)$$

Solutions were prepared immediately before use with water filtered through a Millipore Milli-Q™ system. This system was constantly illuminated by an UV lamp to keep organic contaminant concentrations below 13 μg L^{-1}. All solutions were buffered with 5.0 mM phosphate adjusted to pH 7.0 and were then stirred and continuously sparged with the appropriate gas (N_2 or N_2O) to keep them oxygen-free during the irradiation process.

γ-Radiolysis. Steady-state experiments were conducted using continuous γ-radiation where solutions were irradiated with a ^{137}Cs (662 keV γ-radiation) using a J. L. Shepherd Mark I Model A68 Irradiator. This instrument has a fixed central rod source in a 30 cm diameter, 33 cm high cavity. Samples in glass test tubes were placed reproducibly in a rack at varying distances from the source guide tube to provide dosage rates varying from 4.2×10^3 Gy h^{-1} (0.42 Mrad h^{-1}) to less than 5×10^2 Gy h^{-1} (0.05 Mrad h^{-1}).

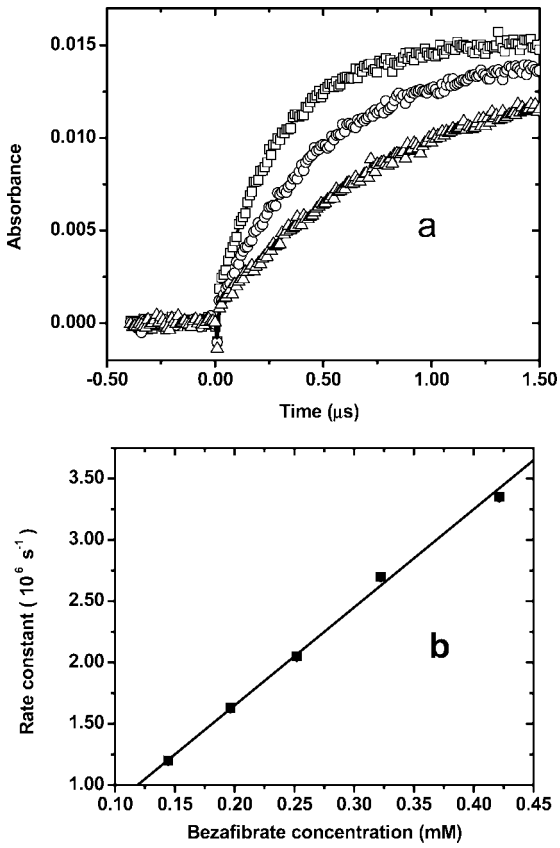


Figure 3. (a) Typical growth kinetics of the transient absorption of bezafibrate reaction products at 320 nm in phosphate-buffered aqueous solution (pH 7.0) at room temperature for 0.421 (□), 0.252 (O), and 0.144 (Δ) mM bezafibrate. (b) Second-order rate constants for the reaction of hydroxyl radicals with bezafibrate at 320 nm. Solid line corresponds to a value of $k = (8.00 \pm 0.22) \times 10^9$ M^{-1} s^{-1} for the overall rate constant of the reaction.

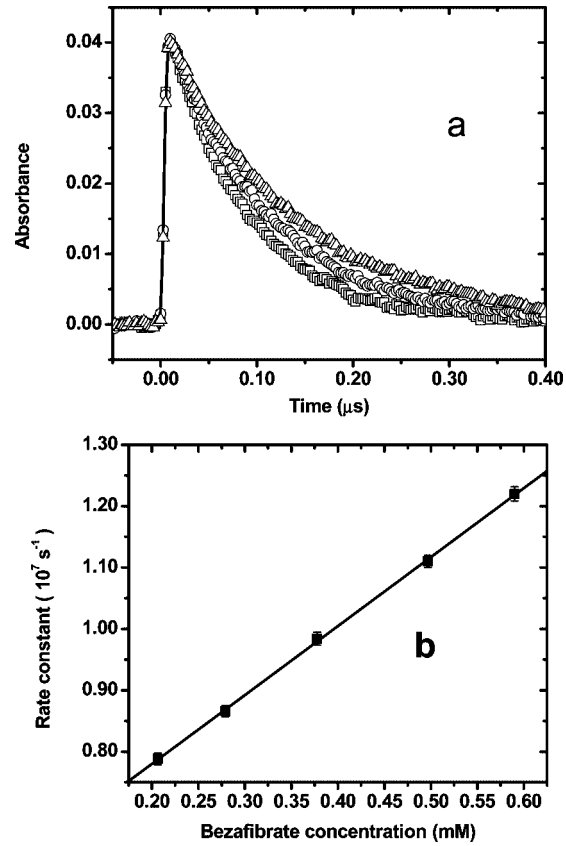


Figure 4. (a) Typical decay kinetics for hydrated electron reduction monitored at 700 nm for 0.590 (□), 0.378 (O), and 0.207 (Δ) mM bezafibrate at pH = 7.0 and room temperature. (b) Second-order rate constant determination for the reaction of the hydrated electron with bezafibrate. The straight line is the weighted linear plot, with a slope of $(112 \pm 3) \times 10^8$ M^{-1} s^{-1}.

HPLC and LC−MS Analysis. The pharmaceutical compounds and their reaction products were analyzed by HPLC under the following conditions: column, Phenomenex Gemini C_{18} 250 × 4.6 mm i.d.; the mobile phase consisted of isocratic mixtures varying between 40 and 70% CH_3OH and 60 and 30% 10 mM phosphate buffer solution (pH 3.0). The detector was operated at wavelengths of 227, 228, and 220 nm for clofibric acid, bezafibrate, and gemfibrozil, respectively. The LC−MS system used in the study consisted of an Agilent 1100 HPLC Pump and a Waters LCT Classic Mass Spectrometer with an electrospray ionization source. A sample volume of 10 μL was injected into a Phenomenex Luna C_{18} (2) HPLC column (2.0 × 150 mm). The mobile phase was A, 98% H_2O + 2% CH_3CN + 0.2% acetic acid, and B, CH_3CN + 0.2% acetic acid. Gradient elution was 2% B for 1 min followed by a linear increase to 95% B at 50 min, which was held constant for an additional 7 min before reestablishing the initial conditions. Mass spectra were collected in negative ion mode between *m*/*z* 80 and 350.

Results and Discussion

OH Transient Spectra. The reaction of the •OH with all three fibrate pharmaceutical compounds provided transient

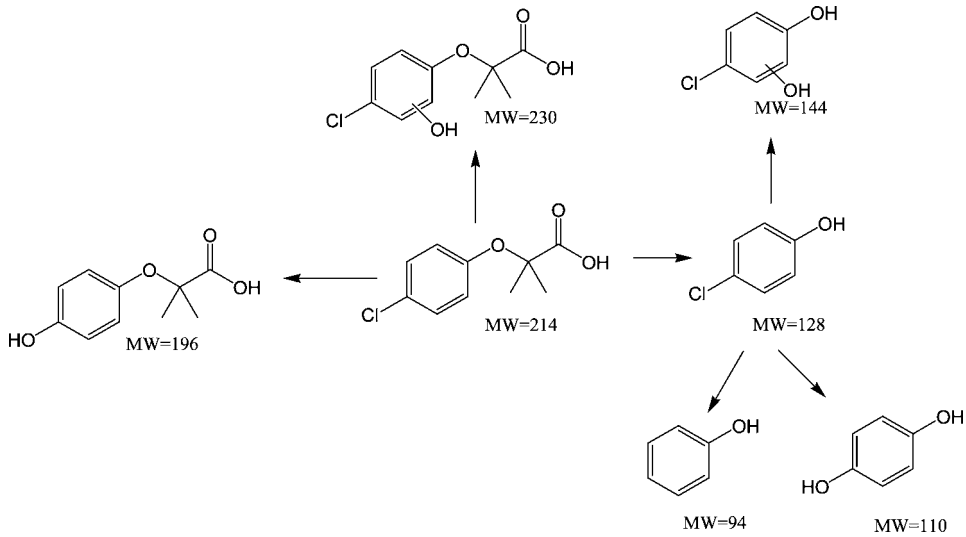


Figure 5. Degradation products and proposed reaction pathways for •OH oxidation of clofibric acid.

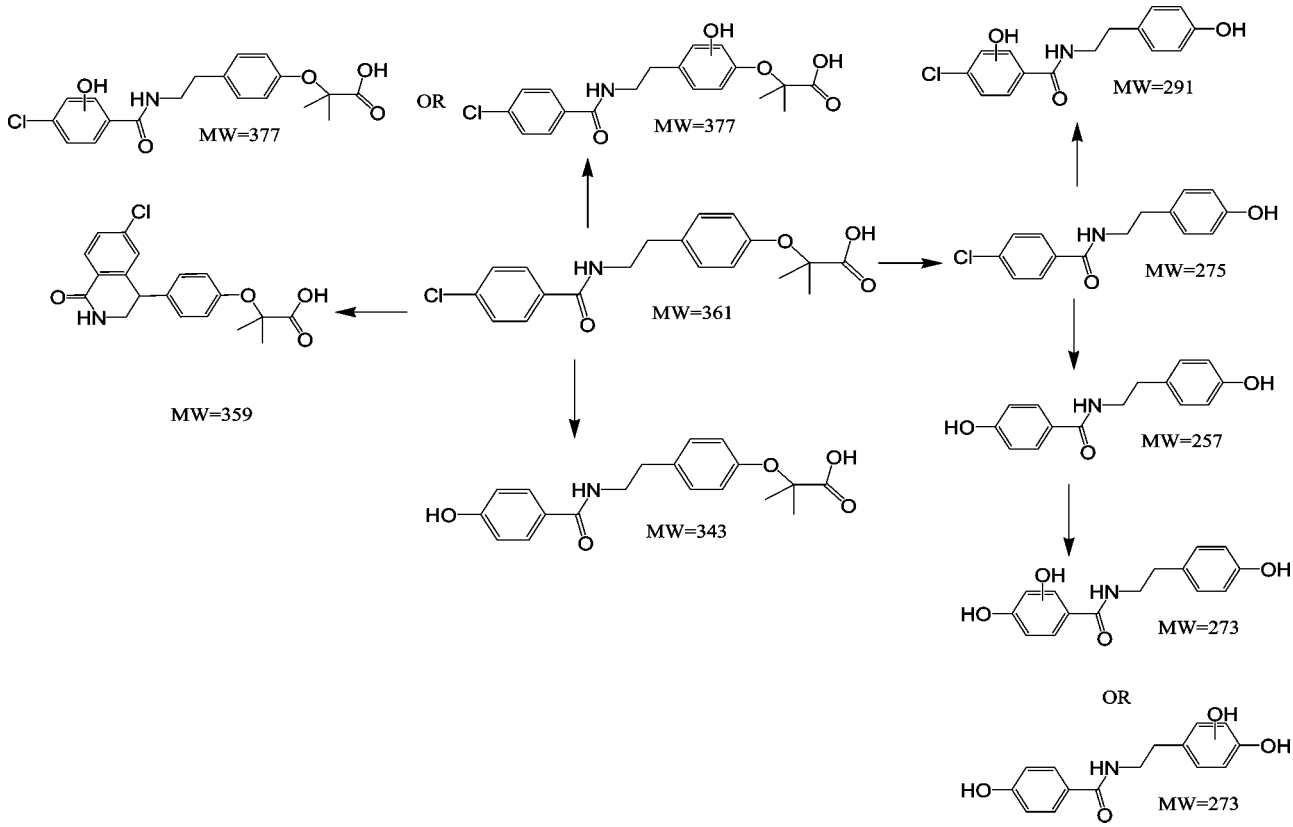


Figure 6. Degradation products and proposed reaction pathways for •OH oxidation of bezafibrate.

absorption spectra (Figure 2). A maximum absorbance in the range 300−350 nm was observed for all compounds, and this is characteristic of attack at the aromatic ring and formation of hydroxycyclohexadienyl radicals. Absorption coefficient values were calculated using a hydroxyl radical *G* value of 0.59 μmol J^{-1} under the reaction conditions used, based upon the intraspur scavenging model calculations of LaVerne and Pimblott.[37] The transient spectra obtained for the reaction of clofibric acid exhibited a peak at 310 nm with a shoulder at 330 nm. The spectrum for bezafibrate had a broad unresolved peak with maximum absorption at 330 nm and a shoulder at approximately 310 nm. Comparable results have also been observed for chlorophenol under similar reaction conditions.[38−40] The spectrum for gemfibrozil had no shoulder and a maximum absorption at 330 nm. The reactions of hydroxyl radicals with aromatic rings in fibrate compounds appear to be the major reaction pathway. H-abstractions, on the aliphatic chain, typically have rate constants on the order of 10^7-10^8 M^{-1} s^{-1}, which is slower than •OH addition to the aromatic ring. Therefore, such reaction pathways are likely to be of less importance to the overall reaction rate measurements of fibrate pharmaceuticals.

Kinetic Measurements. The bimolecular reaction rate constants for reaction of the fibrate pharmaceuticals with the hydroxyl radical were determined using the change in the rate of the appearance of the transient maximum wavelength at various concentrations of the starting material. Typical kinetic data for bezafibrate are given in Figure 3a. These data were processed using the procedures outlined by Mezyk et al.[41] The

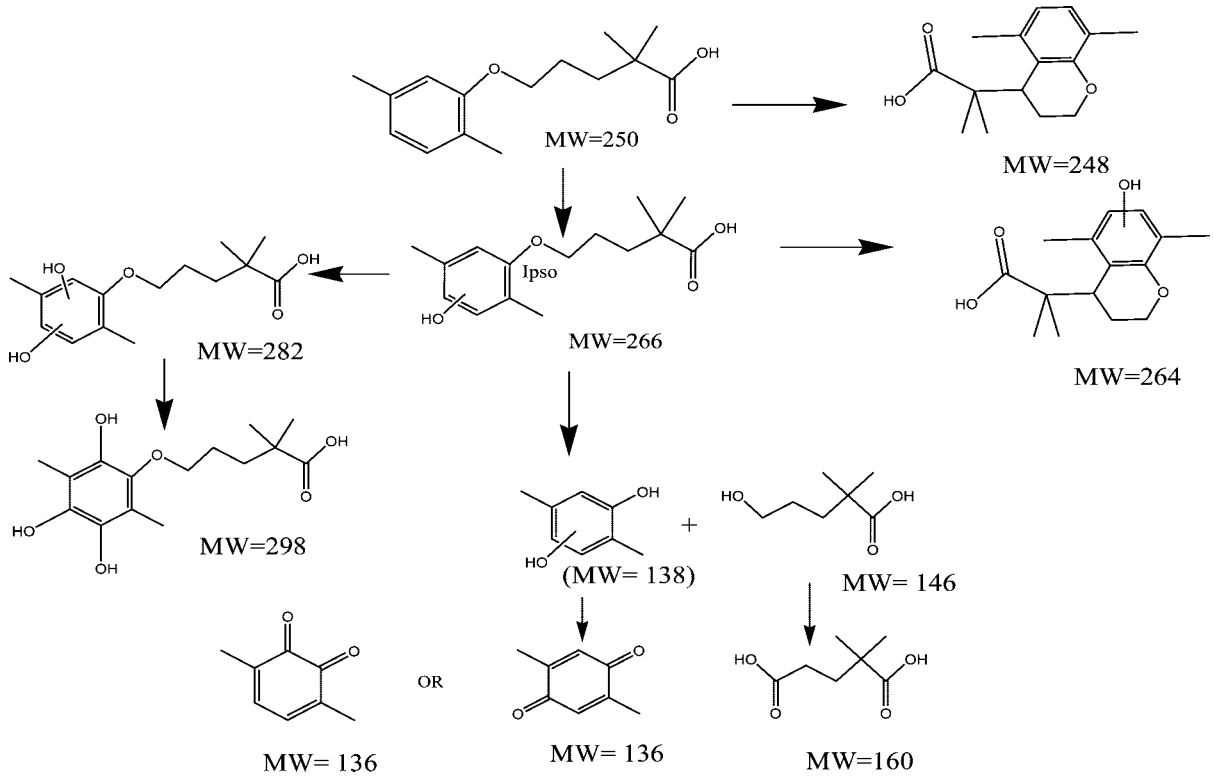
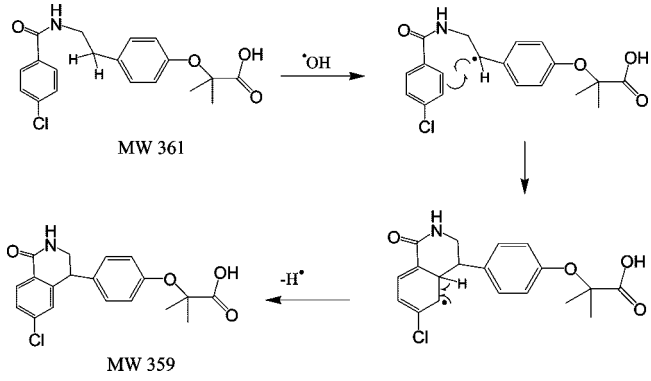


Figure 7. Degradation products and proposed reaction pathways for •OH oxidation of gemfibrozil.

SCHEME 1



absolute hydroxyl radical rate constants were measured by fitting exponential curves to the pseudo-first-order growth kinetics (Figure 3a) and then plotting these values as a function of the concentration of bezafibrate (Figure 3b). Data for all three compounds is summarized in Table 1.

The range ((6−10) × 10^9 M^{-1} s^{-1}) of the rate constants for hydroxyl radical reaction with the three fibrate compounds is comparable to previous rate constant measurements for aqueous hydroxyl radical reaction with benzene ((7.5−7.8) × 10^9 M^{-1} s^{-1})[36] further supporting our assignment that the initial product formation is of hydroxycyclohexadienyl radicals. The measured value for gemfibrozil ((10.0 ± 0.6) × 10^9 M^{-1} s^{-1}) was the fastest of the three rate constants in this group of PhACs, presumably because of the presence of the electron-donating methyl groups. Although the bezafibrate has two aromatic rings, its rate constant ((8.00 ± 0.22) × 10^9 M^{-1} s^{-1}) was slower presumably because of the presence of the chloro and amide-carbonyl groups, both of which are electron withdrawing. Clofibric acid which has a single chloro-substituted aromatic ring had the slowest rate constant (6.98 ± 0.12) × 10^9 M^{-1} s^{-1}). The slower rate constants of bezafibrate and clofibric acid are consistent with those measured for chlorobenzene, 5.6 × 10^9 M^{-1} s^{-1} at 20 °C,[42] and benzamide, 4.6 × 10^9 M^{-1} s^{-1},[43] both of which have substituent groups that withdraw electrons from the aromatic ring.

The rate constants for the reaction of hydrated electron with the three fibrates were measured by directly monitoring the change in the absorption of the e^-_{aq} at 700 nm in nitrogen-saturated solutions at pH 7.0.[41] Figure 4 shows the results obtained for bezafibrate. The decay curves (Figure 4a) were fitted to pseudo-first-order exponential kinetics, from which the second-order linear plot was obtained (Figure 4b); the slope is the second-order rate constant for e^-_{aq} reduction of bezafibrate.

Table 1 summarizes the measured e^-_{aq} reaction rate constants for the three pharmaceuticals. The e^-_{aq} rate constant for bezafibrate ((112 ± 3) × 10^8 M^{-1} s^{-1}) is about 17 times higher than those of clofibric acid ((6.59 ± 0.43) × 10^8 M^{-1} s^{-1}) and gemfibrozil ((6.26 ± 0.58) × 10^8 M^{-1} s^{-1}). The magnitude of the difference between bezafibrate and clofibric acid rate constants was surprising as both have chlorine-substituted benzene rings and the rate constant obtained for the reaction of clofibric acid with e^-_{aq} was consistent with that of 4-chlorophenol (2.9 × 10^8 M^{-1} s^{-1}).[44] The difference between clofibric acid and bezafibrate reaction rates may be that the chlorinated aromatic ring of bezafibrate has a benzyl carbonyl (as part of an amide linkage) that extends the conjugation. For example, it has been reported that the hydrated electron rate constants for benzamide (1.9 × 10^{10} M^{-1} s^{-1}) [45,46] and benzaldehyde (2.4 × 10^{10} M^{-1} s^{-1})[47] are significantly faster than the values for benzene (0.9 × 10^7 M^{-1} s^{-1})[48] and phenol (3.0 × 10^7 M^{-1} s^{-1}).[49] The result obtained for bezafibrate suggests that the two substituents that comprise the amide linkage may stabilize the transition state thus resulting in an increase in reaction rate. An alternative possibility might be the reaction of e^-_{aq} with a carbonyl-amide substituent, similar to that observed with acetone, which results in the formation of the 2-hydroxy-2-

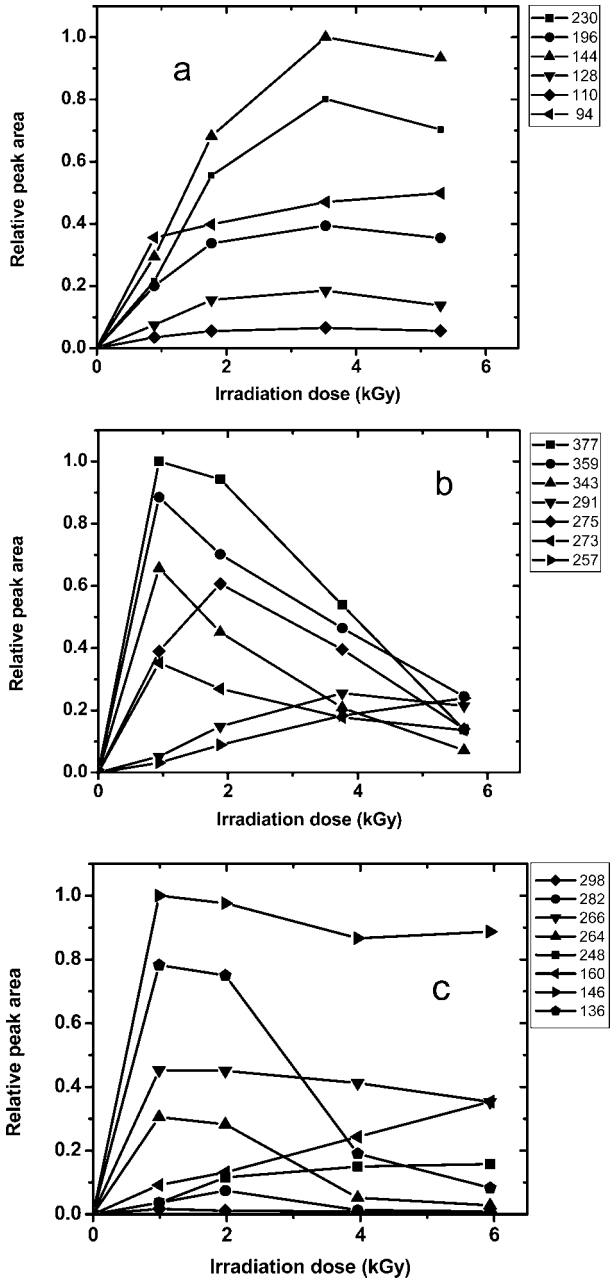


Figure 8. Reaction profiles of byproducts (listed by MW) by γ-irradiation of clofibric acid (a), bezafibrate (b), and gemfibrozil (c) using LC−MS.

propyl radical[50] However, the efficiency of the reaction of e^-_{aq} and bezafibrate (see below) suggests that the e^-_{aq} attack leads to dissociative electron attachment and that the amide moiety serves to stabilize the transition state thus accelerating the destruction of bezafibrate.

Reaction Efficiency. The absolute bimolecular reaction rate constants are not the only consideration when using AO/RPs for the destruction of compounds. It has been shown that the reaction efficiencies, defined as the loss of parent compound per number of reactive species, are also critical.[51,52] Steady-state experiments were performed using ^{137}Cs radiolysis to determine the efficiency of hydroxyl radical and hydrated electron degradation of the fibrate pharmaceuticals. Steady-state irradiation of these three compounds in aerated aqueous solution resulted in decreasing concentrations as the dose was increased. The results are shown in Figure 1S, Supporting Information.

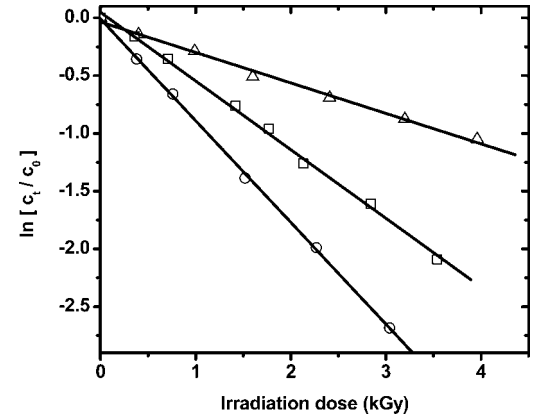


Figure 9. Measured loss of clofibric acid (□), bezafibrate (O), and gemfibrozil (Δ) in aerated aqueous solution during ^{137}Cs γ-irradiation.

To determine the overall removal efficiency, estimates of the initial slopes were determined for the individual compounds (Figure 1S). These lines correspond to the removal of each of these lipid regulator drugs, assuming no interference from stable reaction products occurred. Under the experimental conditions used, all the generated hydroxyl radicals will initially react with the target drugs, while the hydrated electrons will react with both the drugs and the dissolved oxygen present. Given the rate constant for the reaction of e^-_{aq} with oxygen is 1.9×10^{10} M^{-1} s^{-1}, and using the known concentrations of the drugs and O_2 (assumed 2.5×10^{-4} M), it was determined that 7.7%, 59%, and 7.3% of the e^-_{aq} would react with clofibric acid, bezafibrate, and gemfibrozil, respectively. From the •OH and e^-_{aq} yield G values (see eq 1), initial slopes of -2.95×10^{-4}, -4.29×10^{-4}, and -1.87×10^{-4} M kGy^{-1} were derived for clofibric acid, bezafibrate, and gemfibrozil, respectively. Using these slopes it was concluded that the combination of •OH and e^-_{aq} reactions with clofibric acid, bezafibrate, and gemfibrozil occurred with 95%, 98%, and 62% efficiency, respectively.

Degradation Mechanisms. The structural assignments for the decomposition of the pharmaceuticals during γ-irradiation were based on the analysis of the total ion chromatogram (TIC) and the corresponding mass spectra that were obtained by negative ion electrospray LC−MS. The masses of the different products were determined from the peaks corresponding to the deprotonated molecule, $[M - H]^-$. The product assignments arising from γ-irradiation of clofibric acid (MW 214) are shown in Figure 5. A product with MW 230 (addition of 16 mass units to the parent compound) was observed which is consistent with hydroxylation of the aromatic ring. The addition of an electrophilic hydroxyl radical to the aromatic ring forms a resonance-stabilized carbon-centered radical to which there is a subsequent addition of oxygen. This is followed by the elimination of a hydroperoxyl radical yielding a phenolic product.[51]

The product with MW 196 arises from addition of •OH at the chloro site, resulting in the substitution of the chlorine atom, again forming a phenolic derivative. The product with MW 128 (4-chlorophenol) results from the hydroxyl radical reaction at the ipso ether position of the parent compound. The 4-chlorophenol is then further oxidized by the addition of a second hydroxyl radical to the benzene ring forming dihydroxy chlorinated benzene with MW 144. Alternatively the 4-chlorophenol is reduced to phenol (MW 94) or oxidized to dihydroxybenzene (MW 110).

Irradiation of bezafibrate (MW 361) resulted in 10 detectable breakdown products as summarized in Figure 6. With two

benzene rings in the structure there are multiple sites for hydroxylation, and two separate products with a MW of 377 were observed, corresponding to the addition of oxygen to the parent peak. Oxidative dechlorination (hydroxyl attack at the ipso chloro position) also occurred giving a MW 343 species, similar to that in clofibric acid.

The reaction product with a MW 359 was surprising, as it is only two amu below the parent compound. It appeared early, that is at a low dose, and in relatively high concentration. The appearance of this compound implies that either we have the formation of a double bond or cyclization within the molecule. To our knowledge the formation of a double is unprecedented. One alternative mechanism that accounts for the compound at MW 359 is shown in Scheme 1. Another possibility is •OH attack at the aromatic ring, followed by cyclization and loss of HOH. To determine the details of this reaction will require further studies, including isolation of the intermediate compound and structural identification using NMR spectroscopy.

The product with MW 275 is due to hydroxyl radical reaction at the ipso position of bezafibrate that results in the removal of the fibrate chain as was seen for clofibric acid. Further reaction of this 275 product results in hydroxy-substituted products, with or without dechlorination, having MW of 291, 257, and 273.

γ-Irradiation of gemfibrozil (MW 250) resulted in the formation of nine major products that are shown in Figure 7. The product with a MW 266 arises from the addition of 16 mass units to the parent compound (•OH radical addition to the benzene ring). A second and third addition of •OH radicals to the benzene ring also occurred resulting in the formation of products with MW 282 and 298, respectively. Cyclization of the parent compound as well as the monohydroxylated species resulted in the formation of compounds with MW 248 and MW 264. The ipso-directed oxidation should result in products with MW 138 and 146. However, these are apparently further oxidized. The compound of MW 138 forms the quinone with MW 136, while the released fibrate (MW 146) becomes a diacid with MW 160.

The relative concentration of all of the degradation products described above showed an initial increase with irradiation dose and then a decrease. Figure 8 illustrates the relative concentration of all of the degradation products as a function of irradiation time. Since many of the products have similar structures, we assumed that their response factors (peak intensity/molecule) are similar; hence, the peak intensities are somewhat indicative of the relative yields. Compared to bezafibrate and gemfibrozil, the products of clofibric acid are the most persistent; therefore, these results indicate that it will be more challenging to mineralize clofibric acid.

Figure 9 shows the relative destruction of these three compounds in distilled water with increasing irradiation dose. Although bezafibrate is most rapidly removed, as would be expected, there is a substantial difference between clofibric acid and gemfibrozil despite the similar rate constants which is explained by their relative removal efficiencies (as discussed above). Therefore in assessing treatability not only are the absolute reaction rates necessary but the efficiency of the reaction must also be used to assess the destruction of PhACs. This is especially important given that the ultimate aim is to produce nontoxic effluents by facilitating the degradation of these compounds.

Conclusion

In this study, electron pulse radiolysis techniques were used to evaluate the absolute bimolecular reaction rate constants for the reaction of fibrate pharmaceuticals with hydroxyl radical and hydrated electron. γ-Radiolysis experiments were used to provide initial insights into destruction mechanisms and to determine the degradation efficiency of these compounds by both radicals. It was concluded that the combined •OH and e^-_{aq} reactions with clofibric acid, bezafibrate, and gemfibrozil were 95%, 98%, and 62% efficient, respectively. As a result of the stability of these compounds in the environment it is possible that they may be found in water used for drinking purposes. Therefore, technologies to treat and remove these compounds are important, and this study suggests that AO/RP technologies, such as the electron beam process, which produces both hydroxyl radicals and hydrated electrons, may have advantages over those methods that produce only the hydroxyl radical.

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Supporting Information Available: Figure S1 shows loss of clofibric acid, bezafibrate, and gemfibrozil in aerated aqueous solution using ^{137}Cs γ-irradiation. This information was used to assess the efficiency of the reactions of •OH and e^-_{aq} with the fibrate compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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