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Free-Radical-Induced Oxidative and Reductive Degradation of Sulfa Drugs in Water: Absolute Kinetics and Efficiencies of Hydroxyl Radical and Hydrated Electron Reactions

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Absolute rate constants and degradation efficiencies for hydroxyl radical and hydrated electron reactions with four different sulfa drugs in water have been evaluated using a combination of electron pulse radiolysis/absorption spectroscopy and steady-state radiolysis/high-performance liquid chromatography measurements. For sulfamethazine, sulfamethizole, sulfamethoxazole, and sulfamerazine, absolute rate constants for hydroxyl radical oxidation were determined as $(8.3 \pm 0.8) \times 10^9$, $(7.9 \pm 0.4) \times 10^9$, $(8.5 \pm 0.3) \times 10^9$, and $(7.8 \pm 0.3) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$, respectively, with corresponding degradation efficiencies of $36\% \pm 6\%$, $46\% \pm 8\%$, $53\% \pm 8\%$, and $35\% \pm 5\%$. The reduction of these four compounds by their reaction with the hydrated electron occurred with rate constants of $(2.4 \pm 0.1) \times 10^{10}$, $(2.0 \pm 0.1) \times 10^{10}$, $(1.0 \pm 0.03) \times 10^{10}$, and $(2.0 \pm 0.1) \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$, respectively, with efficiencies of $0.5\% \pm 4\%$, $61\% \pm 9\%$, $71\% \pm 10\%$, and $19\% \pm 5\%$. We propose that hydroxyl radical adds predominantly to the sulfanilic acid ring of the different sulfa drugs based on similar hydroxyl radical rate constants and transient absorption spectra. In contrast, the variation in the rate constants for hydrated electrons with the sulfa drugs suggests the reaction occurs at different reaction sites, likely the different heterocyclic rings. The results of this study provide fundamental mechanistic parameters, hydroxyl radical and hydrated electron rate constants, and degradation efficiencies that are critical for the evaluation and implementation of advanced oxidation processes (AOPs).

Introduction

The removal of trace amounts of pharmaceutical drugs from aquatic environments has received increased attention in recent years. Of the many groups of these chemicals that have been identified, one of most prevalent is the sulfa-based antibiotics (sulfonamides), with concentrations up to $1.9 \mu\text{g/L}$ ^{1,2} found in waters in the United States^{3,4} and Europe.^{5,6} Sulfa drugs are used for the treatment of infections in humans,⁷ for veterinary purposes,^{1,2} as herbicides,⁸ and are prevalent in aquaculture,⁹ mainly from the disposal of drugs into sewage waters.^{10–13} Although no formal water restriction exists for these drugs, their presence, even at trace levels, may adversely affect aquatic ecosystems. While photochemical degradation of these compounds has been demonstrated,¹⁴ their residence lifetimes may be many hundreds of hours depending upon the ambient environmental conditions. Therefore, removal of these species, as well as other pharmaceuticals,¹⁵ may be necessary under some water use, or reuse, applications.

Radical-based treatment processes continue to gain interest as the technology of choice for the removal of trace amounts of contaminant chemicals in different quality waters. These technologies include ozone, UV/ozone, and UV/H₂O₂, which use oxidation via the hydroxyl radical ($\cdot\text{OH}$), and heterogeneous

catalysis by TiO₂, sonolysis, or the electron beam process, which produce a mixture of oxidizing $\cdot\text{OH}$ radicals and reducing hydrated electrons (e_{aq}^-) and hydrogen atoms ($\cdot\text{H}$). However, to ensure that any advanced oxidation processes (AOPs) treatment process occurs efficiently and quantitatively, a full understanding of the kinetics and mechanisms of all the chemical reactions involved under the conditions of use is necessary. Kinetic computer models enhance the understanding of experimental data by providing the best test against actual engineering data, as all the chemistry in the system is considered.¹⁶

In this study, we report on the oxidative and reductive behavior of four representative sulfa drugs in aqueous solution. Specifically, we have determined absolute reaction rate constants for oxidizing hydroxyl radicals and reducing hydrated electrons with four sulfonamides that contain various heterocyclic ring substituents. An important aspect of this work involves careful analyses of these free-radical reactions to determine absolute individual degradation efficiencies. The results of this study provide fundamental mechanistic parameters, hydroxyl radical and hydrated electron rate constants, and degradation efficiencies that are critical for the evaluation and implementation of radical-based AOPs.

Experimental Section

The chemicals used in this study were obtained from the Aldrich Chemical Co., of the highest purity available, and used as received. Solutions were made using water filtered by a Millipore Milli-Q system, which was constantly illuminated by a Xe arc lamp (172 nm) to keep organic contaminant concentrations below $13 \mu\text{g L}^{-1}$. All solutions were extensively sparged

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with high-purity N₂O (for hydroxyl radical experiments) or N₂ (hydrated electron experiments) to remove dissolved oxygen.

Electron Pulse Radiolysis. The linear accelerator (LINAC) electron pulse radiolysis system at the Radiation Laboratory, University of Notre Dame, was used for the reaction rate constant determinations of this study. This irradiation and transient absorption detection system has been described in detail previously.¹⁷

During rate constant measurements the solution vessels were sparged with only the minimum amount of gas necessary to prevent air ingress. Solution flow rates in these experiments were adjusted so that each irradiation was performed on a fresh sample. Dosimetry¹⁸ was performed using N₂O-saturated, 1.00 × 10⁻² M KSCN solutions at λ = 475 nm, (Gε = 5.2 × 10⁻⁴ m² J⁻¹) with average doses of 3–5 Gy per 2–3 ns pulse. Throughout this paper, *G* is defined in μmol J⁻¹, and ε is in units of M⁻¹ cm⁻¹.

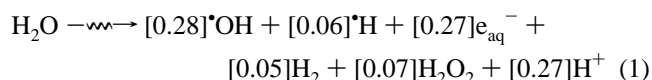
All kinetics experiments were performed at ambient temperature (21 ± 1 °C) and in natural pH (5.4–6.0) solution. Each kinetic trace was the average of 15 pulses.

Steady-State Experiments. The cobalt-60 γ irradiator was a Shepherd 109, with a dose rate of 0.101 kGy min⁻¹. For only oxidative conditions, aqueous solutions were presaturated with N₂O(g) before γ-irradiation. To assess the reactivity of the reductive aqueous electron, nitrogen gas-saturated or aerated solutions were used. High-performance liquid chromatography (HPLC) analyses were performed on the solutions at different treatment times/doses.

The loss of the sulfur drugs and the formation of intermediates were followed using a Waters HPLC system (Millennium 2010, Waters 717 plus autosampler, Waters 600 controller solvent pump) equipped with a Supelco Discovery C18 column, 5 μm (250 mm × 4.6 mm). A gradient solvent flow (1.0 mL/min) utilized water, aqueous acetic acid solution (1%), and methanol, where the initial solvent mixture was 1% acetic acid solution, 59% water, and 40% methanol. By the 10 min mark, the solvent flow changed to 3% aqueous acetic acid solution, 82% water, and 15% methanol. The solvent switched back to the original composition at 13 min. A photodiode array detector monitored the 200–400 nm range. Intermediates were identified by comparison to the retention times and spectra of authentic samples.

Results and Discussion

Hydroxyl Radical Reactions. The radiolysis of pure water produces free radicals according to the stoichiometry^{19,20}



where the numbers in brackets are the *G*-values (yields) for species production. The total radical concentrations typically used in our kinetics radiolysis experiments were ~2–4 μM per pulse.

The reaction of only hydroxyl radicals was achieved by presaturating the solutions with N₂O, which quantitatively converts the hydrated electrons, e_{aq}⁻, and hydrogen atoms, ·H, to this radical,¹⁹

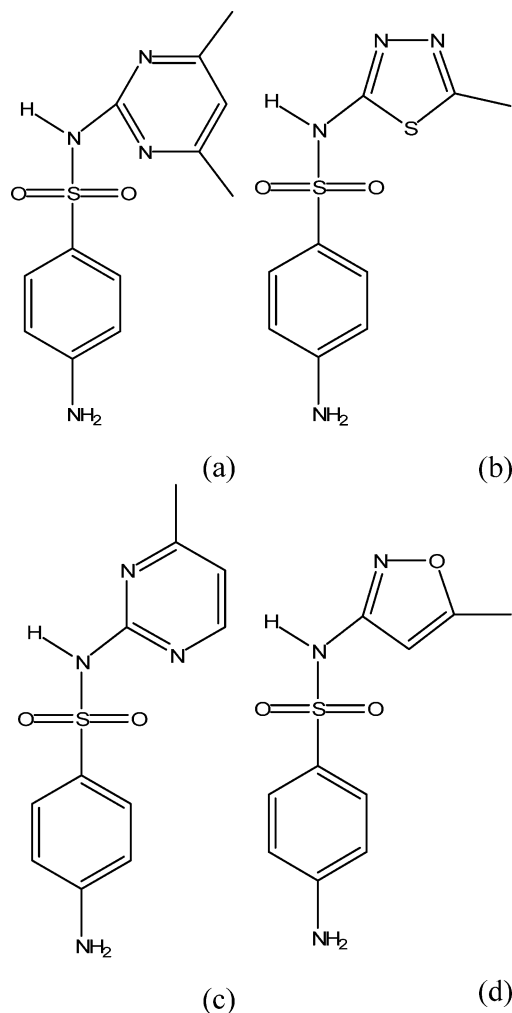
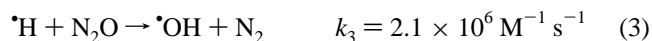
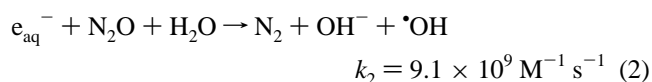


Figure 1. Structures of sulfa drugs of this study: (a) sulfamethazine, (b) sulfamethizole, (c) sulfamerazine, and (d) sulfamethoxazole.

The sulfa drugs employed in this study (Figure 1) react with hydroxyl radicals yielding similar transient absorption spectra, as shown for sulfamerazine in Figure 2a. This spectrum has a maximum absorption at 410 nm, with an absorption coefficient maximum of ε₄₁₀ = 4200 M⁻¹ cm⁻¹. The absorption coefficients were calculated using a *G*-value of 0.59 μmol J⁻¹ for the hydroxyl radical, based upon the intraspur scavenging model calculations of LaVerne and Pimblott.²¹ The absorption maxima and corresponding absorption coefficients for the transients for all the sulfa drugs used in this study are summarized in Table 1.

The hydroxyl radical will react with these sulfa drugs typically by either addition or hydrogen atom abstraction. A previous study²² on the reaction of hydroxyl radicals with sulfanilic acid (NH₂–C₆H₄–SO₃⁻), the common moiety of these sulfa drugs, yielded a very similar transient absorption spectrum with λ_{max} = 385 nm and ε₃₈₅ = 4900 M⁻¹ cm⁻¹. This similarity suggests that the hydroxyl radical reactions follow similar pathways and thus occur predominantly by addition to the benzene ring in the sulfanilic acid portion of the compounds.

Further evidence for a consistent site of oxidation is obtained from the measured kinetics of the hydroxyl radical reactions. The absolute hydroxyl radical rate constants were obtained by fitting exponential curves to the pseudo-first-order growth kinetics observed (see Figure 2a, inset) and plotting these values as a function of the sulfa drug concentrations (Figure 2b). The second-order plots for sulfamethoxazole, sulfamerazine, and

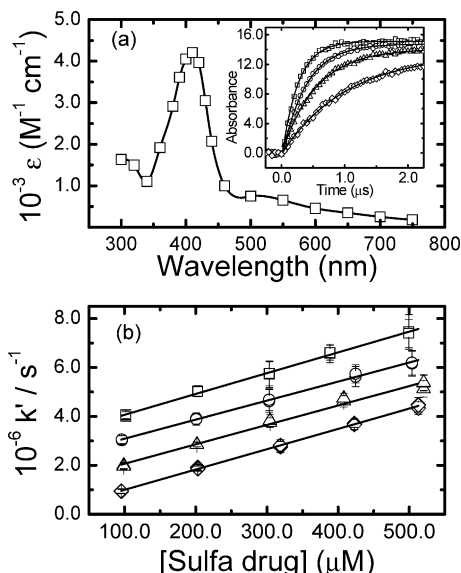


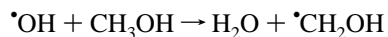
Figure 2. (a) Transient spectrum obtained upon the hydroxyl radical oxidation of 504 μM sulfamerazine in N_2O -saturated water at room temperature. Absolute absorption coefficients were calculated using an intraspur scavenged yield of 0.59 $\mu\text{mol J}^{-1}$ (see text). Inset: Growth kinetics observed at 410 nm for 503.4 (\square), 303.2 (\circ), 200.7 (Δ), and 96.4 μM (\diamond). Fitted lines are pseudo-first-order growth rate constants values of $(4.2 \pm 0.5) \times 10^6$, $(2.7 \pm 0.4) \times 10^6$, $(1.9 \pm 0.2) \times 10^6$, and $(1.0 \pm 0.2) \times 10^6 \text{ s}^{-1}$, respectively. (b) Second-order rate constant determinations for hydroxyl radical reaction with sulfamethoxazole (\square), sulfamerazine (\circ), sulfamethazole (Δ), and sulfamethazine (\diamond). Error bars are one standard deviation for precision only, as calculated from the pseudo-first-order growth fits of (a). Specific values for sulfamethoxazole, sulfamerazine, and sulfamethazole have been adjusted by $+3.0 \times 10^6$, $+2.0 \times 10^6$, and $+1.0 \times 10^6 \text{ s}^{-1}$ to aid the differentiation of these curves. Solid lines correspond to weighted linear fits, giving second-order rate constants for these sulfa drugs as $(8.5 \pm 0.3) \times 10^9$, $(7.8 \pm 0.3) \times 10^9$, $(7.9 \pm 0.4) \times 10^9$, and $(8.3 \pm 0.8) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$, respectively.

sulfathiazole have been offset to aid comparison in Figure 2b. The obtained rate constants, summarized in Table 1, are the same within experimental error. The average value of $8.1 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ is also in excellent agreement with the previous measurement of $8.2 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ for sulfanilic acid²² and considerably faster than the hydroxyl radical reaction with a free pyrimidine ring ($1.6 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$,²³) or with isoxazole ($3.5 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$,²⁴) in water. The rate constant for the thiadiazole ring of sulfamethizole was not available in the literature.

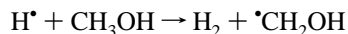
Hydroxyl radical reaction rate constants with sulfa drugs have recently been determined, using Fenton's reagent and competition kinetics at pH 3.0.¹⁴ Under the acidic conditions employed for these studies the drugs were predominantly in their protonated, positively charged, forms ($\text{pK}_{\text{a}2}$ values range from 5.0 to 7.4), whereas in our experiments the neutral species would predominate. As the oxidation occurs mainly with the sulfanilic acid ring, the state of protonation is not expected to significantly affect this rate constant. However, the previously determined rate constants for sulfamethizole, $(4.9 \pm 0.1) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$, and sulfamethoxazole, $(5.8 \pm 0.2) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$,¹⁴ measured at the more acidic pHs are considerably slower than the direct, absolute, values of this study. We suspect that the differences between the values of our study and those obtained previously may be due to complications of the Fenton's reagent methodology when using acetophenone as a standard.¹⁴

Hydrated Electron Reactions. No significant transient is observed from 250 to 800 nm following reaction of the hydrated

electron with the sulfa drugs employed in this study. Therefore, the rate constants for hydrated electron reaction were measured by directly monitoring the change in its absorption at 700 nm, in nitrogen-saturated solutions at natural pH. These solutions also contained 0.10 M methanol to scavenge the hydroxyl radicals and hydrogen atoms,¹⁹ converting them into relatively inert $\cdot\text{CH}_2\text{OH}$ radicals:



$$k_4 = 9.7 \times 10^8 \text{ M}^{-1} \text{ s}^{-1} \quad (4)$$



$$k_5 = 2.6 \times 10^6 \text{ M}^{-1} \text{ s}^{-1} \quad (5)$$

Typical kinetic data are shown in Figure 3a for sulfamethoxazole. The decays were fitted to pseudo-first-order exponential kinetics, from which the second-order linear plots shown in Figure 3b were obtained. The slopes of these plots are the second-order rate constants for hydrated electron reductions; these values are summarized in Table 1.

In contrast to the hydroxyl radical reaction, the hydrated electron rate constants show modest variation, ranging from 1.03 to $2.45 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$. No reduction rate constants for sulfa drugs in aqueous solution were found in the literature; however, the previously measured hydrated electron reaction rate constant for sulfanilic acid²⁵ of $4.6 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ is over a factor of 50 slower than observed in this study. The analogous reduction rate constant for pyrimidine²⁶ has been measured as $2.0 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$, in reasonable agreement with our values for sulfamethazine ($2.45 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$) and sulfamerazine ($1.99 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$). Unfortunately, no other kinetic data were found in the literature for reduction of the other heterocyclic ring systems present in our sulfa drugs. However, these data imply that the reduction does not occur to a major extent at the common sulfanilic acid moiety in these drugs; rather, it predominantly occurs at the heterocyclic rings.

Steady-State Irradiations. In addition to the absolute rate constants determined in this study, steady-state experiments were also performed to determine the efficiency of these radicals to degrade the sulfa drugs. Individual solutions of each compound were irradiated under aerated, N_2 -saturated, or N_2O -saturated conditions. In aerated and N_2 -saturated solutions, both hydrated electrons and hydroxyl radicals are present, as the dissolved oxygen concentration ($2.5 \times 10^{-4} \text{ M}$) in the aerated solutions is only able to scavenge a fraction of the electrons.

An authentic sample of sulfanilic acid was run on the HPLC to establish its importance as an intermediate in the degradation radical reactions of these four drugs. Consistent with previous free-radical-based degradation experiments reported for sulfamerazine and sulfamethazine,²⁷ and our pulse radiolysis data that suggests that the hydroxyl radical reacts with the sulfanilic acid moiety of these sulfa drugs, no sulfanilic acid was identified in our N_2O -saturated degradation experiments. The hydroxyl radical reaction is expected to lead to hydroxylation of the benzene ring and eventual ring opening, which would preclude the formation of sulfanilic acid under these conditions. In contrast, the radiolysis experiments in the aerated and N_2 -saturated sulfa drug solutions did result in the formation of sulfanilic acid, again in agreement with previous experiments under these conditions.²⁷ These results further support our proposed mechanism of reduction occurring predominantly at the heterocyclic ring structures of these drugs, with some elimination of the sulfanilic acid moiety.

TABLE 1: Summary of the Kinetic, Transient Spectral, and Degradation Efficiency Parameters for the Four Sulfa Drugs of This Study

name/parameter	sulfamethazine	sulfamethizole	sulfamethoxazole	sulfamerazine
$\cdot\text{OH}$				
$\lambda_{\text{max}}/\text{nm}$	400	420	415	410
$\epsilon_{\text{max}}/\text{M}^{-1}\text{cm}^{-1}$	3850	5050	4500	4200
$10^{-9} k_{\cdot\text{OH}}/\text{M}^{-1}\text{s}^{-1}$	8.3 ± 0.8	7.9 ± 0.4	8.5 ± 0.3	7.8 ± 0.3
$10^{-10} k_{\text{e}_{\text{aq}}^-}/\text{M}^{-1}\text{s}^{-1}$	2.4 ± 0.1	2.0 ± 0.1	1.0 ± 0.03	2.0 ± 0.1
removal constant/ kGy^{-1} (aerated)	0.100 ± 0.001	0.244 ± 0.009	0.249 ± 0.009	0.135 ± 0.003
removal constant/ kGy^{-1} (N_2O -saturated)	0.190 ± 0.004 (0.486) ^a	0.257 ± 0.012	0.292 ± 0.005	0.192 ± 0.009 (0.405) ^a
removal constant/ kGy^{-1} (N_2 -saturated)	0.093 ± 0.001 (0.324) ^a	0.280 ± 0.001	0.336 ± 0.001	0.17 ± 0.03 (0.294) ^a
$\cdot\text{OH}$ degradation efficiency/%	36 ± 6	46 ± 8	53 ± 8	35 ± 5
e_{aq}^- degradation efficiency/%	0.5 ± 4	61 ± 9	71 ± 10	19 ± 5

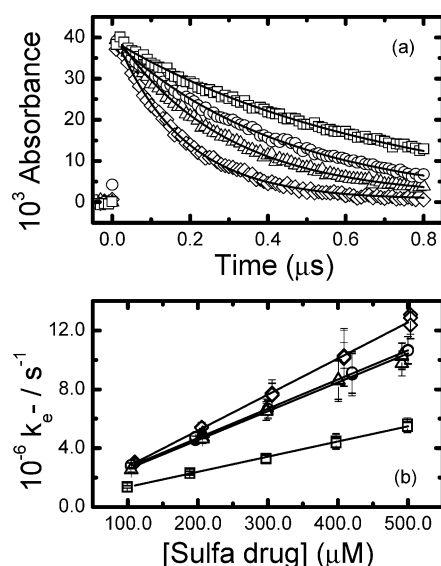
^a Literature value taken from ref 27.

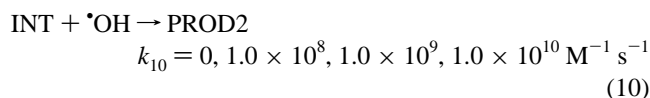
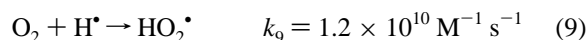
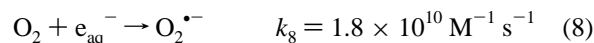
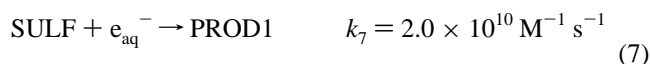
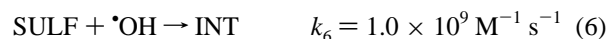
Figure 3. (a) Decay kinetics of the hydrated electron absorption at 700 nm for 499 (\diamond), 297.3 (Δ), 188.3 (\circ), and 99.0 μM (\square) sulfamethoxazole. Solid lines are pseudo-first-order decay rate constant values of $(5.5 \pm 0.4) \times 10^6$, $(3.3 \pm 0.2) \times 10^6$, $(2.3 \pm 0.1) \times 10^6$, and $(1.4 \pm 0.1) \times 10^6 \text{ s}^{-1}$, respectively. (b) Second-order rate constant determinations for hydroxyl radical reaction with sulfamethoxazole (\square), sulfamerazine (\circ), sulfamethizole (Δ), and sulfamethazine (\diamond). Solid lines are second-order rate constants for these sulfa drugs of $(1.0 \pm 0.03) \times 10^{10}$, $(2.0 \pm 0.1) \times 10^{10}$, $(2.0 \pm 0.1) \times 10^{10}$, and $(2.4 \pm 0.1) \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$, respectively.

For aerated sulfamerazine the change in concentration at several doses was followed using HPLC. These results are shown in Figure 4a, plotted as the natural log of the ratio of the remaining concentration divided by the original concentration against dose. The slopes from these plots give so-called “dose constant” values. For sulfamerazine, a straight line fit gave a calculated dose constant value of $0.18 \pm 0.01 \text{ kGy}^{-1}$. The same pattern of reactivity was noted for the other three sulfa drugs.

However, a closer examination of these data shows that the observed degradation is not truly exponential; in fact, a slight curvature in the log plot is evident. Similar curvature was observed for all of the compounds of this study. In addition, the slopes of these dose constant plots were found to be dependent upon the initial sulfa drug concentration, with the highest initial concentrations giving the lowest dose constant

values. These differences are attributed to competitive scavenging of the hydroxyl radicals and hydrated electrons by the stable products of the initial oxidation and reduction.

To further investigate the importance of this competition, computer modeling studies were conducted of these steady-state irradiation data, as summarized in Figure 4. The kinetic modeling was performed using the MAKSIMA-CHEMIST²⁸ differential equation solving code, with input of the standard set²⁹ of pure water radiolysis reactions (~ 60 specific equations), as well as the following specific reactions for the sulfa drug in our aerated water:



The k_6 and k_7 rate constants above were taken as “typical” values for the four different sulfa drugs measured in this study. In this computer modeling the reaction of the hydrated electron with the sulfur drug (SULF) was assumed to immediately result in a different stable product (called PROD1). Similar modeling predictions were found if a reduced intermediate was first formed, which could then react with both hydroxyl radicals and hydrated electrons. However, the amount of dissolved oxygen in these solutions dominated this radical chemistry, except at the highest sulfa drug concentration. Therefore, for simplicity of presentation, we assumed that only the initial reduction reaction was important. The values for k_8 and k_9 were from the literature.¹⁹ The dose rate was that of our experimental determinations, 0.101 kGy/min . The rate constant for k_{10} was varied from zero to $1.0 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$ to specifically determine the influence of oxidized intermediates on the removal of the parent sulfa drug.

With the value of $k_{10} = 0$, all interferences from hydroxyl radical reactions with the products of the initial radical reactions are discounted. These data are shown as the separate symbols

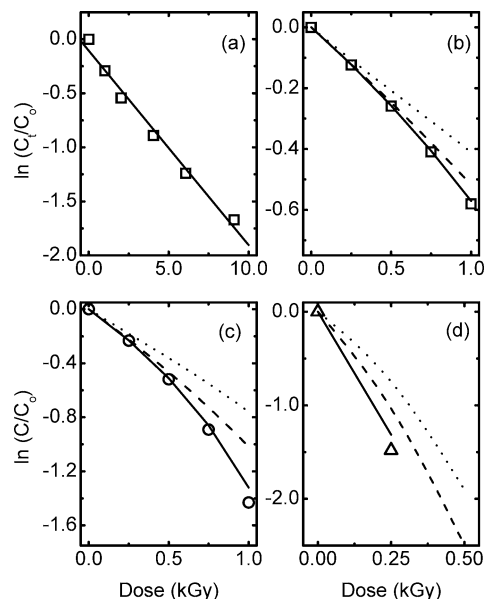


Figure 4. (a) Free-radical-induced sulfamerazine degradation in aerated solution at room temperature and 0.50 mM initial concentration. The slope corresponds to a dose constant value of 0.18 ± 0.01 . (b) Modeled degradation kinetics for an initial sulfa drug concentration of 1.0 mM (squares) without any stable product interference. Solid line, dashed line, and dotted line are concomitant model results for interfering stable product hydroxyl radical reactions with rate constants of $k_{10} = 1.0 \times 10^8$, 1.0×10^9 , and $1.0 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$, respectively. (c) Same as for (b) but with an initial sulfa drug concentration of 0.50 mM (circles). (d) Same as for (b) but with an initial sulfa drug concentration of 0.10 mM (triangles).

in Figures 4b–d for the three initial sulfa drug concentrations: 1.0 mM (squares, Figure 4b), 0.50 mM (circles, Figure 4c), and 0.10 mM (triangles, Figure 4d) modeled. It can be seen that at the highest concentration a relatively straight line is obtained. In contrast, at the middle concentration this plot is definitely curved, although the initial slope is not appreciably different from that of the 1.0 mM data. The initial slope for the lowest concentration modeled is considerably different to the other two concentrations. Unfortunately, for the lowest concentration, only the first two data points could be shown, as complete destruction of the sulfa drug at this concentration occurred after a dose of 0.40 kGy.

To investigate the importance of the reactions of the primary oxidized intermediate (INT), the kinetics for $k_{10} = 1.0 \times 10^8$, 1.0×10^9 , and $1.0 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$ were also modeled. The data obtained are shown as solid, dashed, and dotted lines, respectively, for each concentration. At the 1.0 mM sulfa drug concentration (Figure 4b) little change is seen in the loss profile, except at the very largest k_{10} value where the removal is slightly slower. However, at the 0.50 mM concentration (Figure 4c), and especially at the 0.10 mM concentration (Figure 4d), significant differences were found for the removal profiles, dependent upon the rate constant magnitude and the amount of delivered dose. These interference effects were the most evident at the lowest initial drug concentration and higher doses, as expected.

From this computer kinetic modeling, we conclude that the “dose constant” values obtained from fitting straight lines to removal data plotted as $\ln(C_i/C_0)$ against dose are dependent upon the initial solute concentration. This is consistent with our experimental observations. Therefore, comparing the slopes of these lines (if they are sufficiently linear) is only useful if the initial concentrations are the same. Furthermore, the modeling

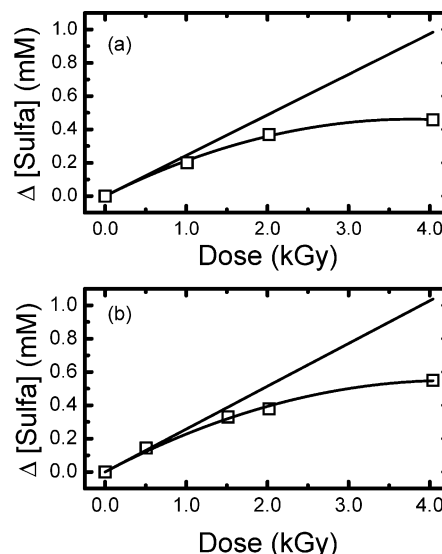


Figure 5. (a) Absolute sulfamethizole concentration change with dose in ^{60}Co -irradiated aerated aqueous solution. The curved line is a fitted quadratic function, and the straight line corresponds to the initial slope with a value of $(0.244 \pm 0.009) \text{ mM/kGy}$. (b) Analogous sulfamethizole removal in irradiated N_2O -saturated solution, with an initial slope value of $(0.257 \pm 0.012) \text{ mM/kGy}$.

confirmed that the measured removal efficiencies are significantly influenced by the products/intermediates formed, especially when the products/intermediates reactions are much faster than those of the parent compound. To obtain useful quantitative data for *only* the radical-induced removal reactions with these sulfa drugs, *high* solute concentrations must be used, even if this does not correspond to real-world conditions. Last, these interferences are magnified at larger doses, and thus only the *initial slopes* should be used for quantitative evaluations and comparisons.

On the basis of the computer modeling, the free-radical-induced degradation of the compounds employed in this study were carefully evaluated at only the highest concentration available, ca. 500 μM . Figure 5 shows the absolute change in sulfamethizole concentration with absorbed dose for aerated and N_2O -saturated solutions. To obtain initial slope values (removal constants), these data have been fitted to quadratic equations, where the linear coefficient of this fit corresponds to the best-fit initial slope. The intercepts of the quadratic fits were fixed to zero, all quadratic fits had $R^2 > 0.99$, and the removal constants were consistent with the approximate linear fits based only on the lowest irradiation dose value.

Our calculated removal constants can be directly compared to previous G -values for sulfamerazine and sulfamethazine,²⁷ measured using ^{60}Co irradiation and quantified by thin layer chromatography (TLC) techniques. Our values are significantly lower than those previously reported (see Table 1). We do not know the reason for this factor of 3–4 discrepancy. As the degradation source and solution conditions were the same, we can only attribute this difference to the lesser accuracy of the TLC methodology.

The removal constants obtained correspond to the absolute degradative loss of these compounds due to radical reactions. These values can be readily converted into *percentage efficiencies* of degradation for each radical,

$$\text{percentage efficiency} = 100 \times \frac{(\text{number of solute molecules degraded})}{(\text{number of specific radical reactions})}$$

in their reaction with these four sulfa drugs using eq 1, which gives the total number of radicals produced in these irradiations, and our measured kinetic rate constants for hydroxyl radical and hydrated electron reaction. Under N_2O -saturated conditions, almost all (>90%) of the produced hydrated electrons and hydrogen atoms are converted to hydroxyl radicals, by reactions 2 and 3. However, under aerated conditions the hydrated electron reaction is partitioned between the sulfa drug and the dissolved oxygen present. One can calculate the relative reaction pathway partitioning based upon the product of the rate constants and concentrations. Assuming that the reaction efficiencies for the hydroxyl radical and hydrated electron with the sulfa drugs are the same in N_2O -saturated and aerated solutions, we can then directly calculate the *efficiency* of each radical's reaction from our initial slope measurements under these two conditions. A typical detailed example of this calculation is given in the Supporting Information.

These calculated radical degradation efficiency values, along with their estimated errors, are summarized in Table 1. These efficiencies were also confirmed using the initial slopes determined from the N_2 -saturated solutions. The efficiency of the hydroxyl radical reaction with the four sulfa drugs is reasonably constant, ranging from 35% to 53%. This is consistent with the pulse radiolysis data, which showed similar kinetics and transient spectra for all four sulfa drugs. In contrast, the efficiencies for hydrated electron reaction vary considerably, from almost zero to over 70%. This variation is consistent with this reduction occurring at different reaction sites, predominantly at the varying heterocyclic ring in these chemicals. The reduced degradation of sulfamethazine and sulfamerazine may be related to the presence of methyl substituted pyrimidine rings. For sulfamethazine and sulfamerazine the reduction of the six-membered pyrimidine ring gives a relatively stable radical anion, which could subsequently transfer its excess electron to dissolved oxygen. For the other two drugs, reduction of their five-membered rings might instead result in immediate ring opening. We are presently further investigating these differences.

Conclusions

The reactions of the hydroxyl radical and hydrated electron with sulfamethazine, sulfamethizole, sulfamethoxazole, and sulfamerazine in aqueous solution are very rapid. The similarity of the transient absorption spectra and oxidation kinetics for these four compounds indicate that the hydroxyl radical reaction occurs predominantly by addition to the benzene ring in the common sulfanilic acid moiety. In contrast, the varying reactivity of the reductive process suggests that the hydrated electron reaction occurs mostly at the other heterocyclic rings. The γ radiolysis experiments and computer modeling results were also used to determine absolute removal constants and degradation efficiencies for the reactions of both radicals with these compounds. From high initial solute concentration and low dose experiments, reaction efficiencies for both radical reactions were determined to be considerably less than 100%. The results of this study offer a means for determining hydroxyl radical and aqueous electron degradation efficiencies and indicate that for removing these species from waters, AOP technologies such as the electron beam that generate both the hydroxyl radicals and hydrated electrons may have an advantage over those that only use hydroxyl radicals.

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Supporting Information Available: Sample calculation for the determination of hydroxyl radical and aqueous electron efficiencies using sulfamethoxazole (S) as the substrate. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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