# Pulse radiolysis of sparfloxacin in neutral aqueous solution postprint

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## Abstract

A pulse radiolysis study was carried out to investigate the radical anion and radical cation of sparfloxacin (SPAX). The reactions of SPAX with hydrate electron (eaq ), hydroxyl radical ( • OH) and azide radical ( • N3 ) were investigated in this study. The transient absorption spectra of SPAX radical anion and SPAX radical cation were obtained. Two transient rate constants 2.2\$$\times 1010 dm3 \cdot mol-1 \cdot s-1 and 1.7\times$\$1010 dm3 • mol 1 • s 1 for the reactions of SPAX with eaq and • OH were determined, respectively. Finally, based on the results obtained in this study, rational mechanisms of transient reactions were proposed.

## Full Text

## Preamble

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### Pulse Radiolysis of Sparfloxacin in Neutral Aqueous Solution

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### Abstract

A pulse radiolysis study was carried out to investigate the radical anion and radical cation of sparfloxacin (SPAX). The reactions of SPAX with hydrated electron ($eaq^-$), hydroxyl radical ( • OH) and azide radical ( • $N_3$) were investigated in this study. The transient absorption spectra of SPAX radical anion and SPAX radical cation were obtained. Two transient rate constants, 2.2$×10^{10}$ $dm^3 \cdot mol^{-1} \cdot s^{-1}$ and 1.7$×10^{10}$ $dm^3 \cdot mol^{-1} \cdot s^{-1}$, for the reactions of SPAX with $eaq^-$ and $\cdot OH$ were determined, respectively. Finally, based on the results obtained in this study, rational mechanisms of transient reactions were proposed.

**Key words:** Sparfloxacin, Pulse radiolysis, Radical cation, Radical anion

## Introduction

Fluoroquinolones (FQs) antibiotics are often used to treat various bacterial infections by inhibiting bacterial DNA synthesis. Sparfloxacin (SPAX) is an antibiotic drug from the fluoroquinolones family, which is often used to treat bacterial urinary tract infections, sexually transmitted diseases, prostatitis, selected pneumonias, and skin infections. SPAX is effective against a wide range of Gram-positive and Gram-negative organisms. However, SPAX has a drawback in usage: it frequently elicits photosensitive skin reactions.

Reports have suggested that SPAX is a phototoxic agent and can induce DNA strand breaks. The most important target for radiation-induced reproductive cell death is generally considered to be the DNA of the cell. Two components are believed to be responsible for DNA damage: the direct effect, where ionizing radiation is absorbed by the DNA itself, and the indirect effect, where DNA is attacked by active radicals, such as radical cations surrounding the DNA. As stated above, the drug SPAX can photo-induce DNA damage. Hence, it was reasonable to think that the SPAX oxidized radical may be an important factor inducing DNA damage.

Though sparfloxacin has been studied in terms of therapeutic activities, few reports about its transient products analysis are available in published literature. Especially, no studies of SPAX radical cation and radical anion were found in papers. However, results on SPAX radicals may be helpful to study the SPAX transient products and photo-induced DNA damage. To investigate the photochemical and photophysical properties of SPAX and the relationship between structure and effects, pulse radiolysis studies of transient radical cation and radical anion were carried out in this study.

## Materials and Methods

Sparfloxacin was purchased from Sigma Chemical Co. and sodium azide was purchased from J&K Scientific Co.; they were all used without further purification. Water was purified by a Millipore Milli-Q system.

The nanosecond pulse radiolysis experiments were performed utilizing a 10 MeV linear accelerator, which delivers an electron pulse with duration of 8 ns. The dosimetry of the electron pulse was determined by thiocyanate dosimeter using $G[(CNS)_2 \cdot^-] = 5.8$ in 0.1 mM KSCN saturated with $N_2O$, taking $_{480}$ = 7600 $dm^3 \cdot mol^{-1} \cdot s^{-1}$ for $(SCN)_2 \cdot^-$. The dose per electron pulse was 10 Gy. A

Xenon lamp was employed as detecting light source. The electron pulse and the analyzing light beam passed perpendicularly through a 10 mm$×10*mm*×$40 mm quartz cell. The transmitted light entered a monochromator equipped with an R955 photomultiplier. The output signal from the LeCroy wavemaster 8600A digital oscillograph was transferred to a personal computer for further analysis.

To create a reducing environment, tert-butanol (t-BuOH) was used to scavenge the ·OH radicals and the sample solutions were saturated with $N_2$, hence $eaq^-$ remained. To create an almost uniform ·OH radical oxidizing solution environment, the sample solution was saturated with $N_2O$ before pulse radiolysis, where $eaq^-$ is converted to ·OH, based on the reactions described below:

$H_2O \rightarrow eaq^-, H\cdot, \cdot OH, H_2, H_2O_2, H_3O^+$

$\cdot OH + \text{tert-BuOH} \rightarrow \text{tert-BuO}\cdot + H_2O$, k = 5.1$×10^{8}$ $dm^3 \cdot mol^{-1} \cdot s^{-1}$

$eaq^- + N_2O + H_2O \rightarrow \cdot OH + OH^- + N_2$, k = 8.7$×10^{9}$ $dm^3 \cdot mol^{-1} \cdot s^{-1}$

For the studies on ·OH with SPAX, the sample solutions were saturated with $N_2O$ to scavenge hydrated electrons $eaq^-$.

## Results and Discussion

### Reaction of SPAX with ·OH

Hydroxyl radical is a strong oxidizing agent and it is often used to study the radical cation or neutral radicals of a target. In this study, the reaction of SPAX with hydroxyl radical was investigated. The transient absorption spectra obtained after pulse radiolysis of 0.1 mM SPAX neutral aqueous solution are shown in Fig.1. After pulse radiolysis, a strong inverted absorption at about 370 nm was observed, which was assigned to bleaching as the UV-Vis experiment result showed that SPAX has a maximum absorption at about 370 nm. At the same time, a distinct transient absorption in the range of 400 550 nm with a maximum absorption at 420 nm appeared. As is well known, the reaction of hydroxyl radical with the target may proceed by three types: hydroxyl addition, hydrogen abstraction, and one-electron oxidation. Hence, it was reasonable to propose the following reactions:

$\text{SPAX} + \cdot OH \rightarrow [\text{SPAX-OH}]\cdot$

$\text{SPAX} + \cdot OH \rightarrow [\text{SPAX-H}]\cdot + H_2O$

$\text{SPAX} + \cdot OH \rightarrow \text{SPAX}^+\cdot + OH^-$

As discussed above, the transient absorption at 420 nm may be assigned to [SPAX-H]·, [SPAX-OH]· and/or $\text{SPAX}^+\cdot$. According to the dependence of the observed pseudo-first-order rate constants for the formation of absorption at 420 nm on the various concentrations of SPAX (see Fig.2), a rate constant of 1.73$×10^{10}$ $dm^3 \cdot mol^{-1} \cdot s^{-1}$ for the reaction of SPAX with ·OH was obtained.

[Figure 1: see original paper] Transient absorption spectra recorded at different times after the pulse radiolysis of $N_2O$-saturated 0.1 mM SPAX solution.

[Figure 2: see original paper] Dependence of the observed pseudo-first-order rate constants for the formation of absorption at 420 nm on the various concentrations of SPAX. Inset: the time profiles at 420 nm.

### One-Electron Oxidation Reaction

To investigate the transient absorption at 420 nm in depth, the one-electron oxidation experiment was carried out. As we know, azide radical ($\cdot N_3$) is a good electron acceptor in reactions. Hence, $\cdot N_3$ was chosen as an oxidant in the one-electron reaction of SPAX with $\cdot N_3$. In the reaction, the concentration of $NaN_3$ was chosen as 100 mM, which is much larger than the concentration of SPAX, for the purpose of ensuring hydroxyl radicals react with azide anion first. As shown in Fig.3, after the pulse, a negative absorption at about 370 nm and a positive absorption at about 420 nm were observed. As discussed above, the transient absorption at 370 nm was reasonably assigned to bleaching. According to the reaction of SPAX with $\cdot N_3$, the transient absorption at 420 nm was reasonably assigned to the SPAX radical cation ($SPAX^{+}\cdot$). The mechanism of one-electron reactions was proposed as below:

$\cdot OH + N_3{}^{-} \rightarrow OH^{-} + \cdot N_3$

$\cdot N_3 + SPAX \rightarrow N_3{}^{-} + SPAX^{+}\cdot$

[Figure 3: see original paper] Transient absorption spectra recorded at different times after the pulse radiolysis of $N_2O$-saturated 0.1 mM SPAX solution containing 0.1 M $NaN_3$ and 0.2 M t-BuOH. Inset: The time profile observed at 420 nm.

### Reaction of SPAX with $eaq^{-}$

To investigate the radical anion of SPAX, another pulse radiolysis experiment was carried out. In this study, the reaction of SPAX with hydrated electron ($eaq^{-}$) was studied. As shown in Fig.4, at the end of the pulse, the transient absorption of hydrated electron in the region of 500-700 nm was observed. Later, another transient absorption at 410 nm appeared with the decay of the hydrated electron. As we all know, hydrated electron is the main transient product at the end of the pulse. Hence, according to the reaction of one-electron reduction, the transient absorption at about 410 nm should be assigned to SPAX radical anion ($SPAX^{-}\cdot$). The transient one-electron reduction reaction of SPAX with hydrated electron was proposed as follows, and the rate constant of 2.2\$×10^{10}\$ $dm^3 \cdot mol^{-1} \cdot s^{-1}$ was obtained according to the dependence of the observed pseudo-first-order rate constants at 700 nm versus the various concentrations of SPAX (Fig.4, Inset).

$SPAX + eaq^{-} \rightarrow SPAX^{-}\cdot$

[Figure 4: see original paper] Transient absorption spectra recorded at different times after the pulse radiolysis of $N_2$-saturated 0.1 mM SPAX solution containing 0.2 M t-BuOH. Inset: The dependence of the observed pseudo-first-order rate constants at 700 nm vs the concentration of SPAX.

## Conclusion

The radical cation and radical anion of SPAX were investigated in this study. The transient spectra of SPAX radical cation and anion were obtained. According to the discussion, reactions of SPAX with $\cdot OH$, $\cdot N_3$ and $eaq^-$ were proposed. The rate constants for reactions of SPAX with $\cdot OH$ and $eaq^-$ were obtained as $1.7\times10^{10}$ $dm^3 \cdot mol^{-1} \cdot s^{-1}$ and $2.2\times10^{10}$ $dm^3 \cdot mol^{-1} \cdot s^{-1}$, respectively. The results obtained in this study may be helpful for exploring the phototoxicity and DNA damage induced by SPAX.

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