

Molecular mechanisms of radiation damage in DNA: ESR and optical detection of oxidation reactions with 5-substituted uracil derivatives in frozen glasses.

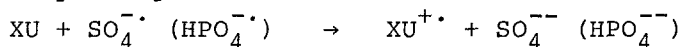
H. Riederer and J. Hüttermann

Institut für Biophysik und Physikalische Biochemie,
Universität Regensburg, Postfach 397, D-8400 Regensburg

Frozen glasses form a suitable system for the study of the reactions of the indirect effect of ionizing radiation on biological macromolecules. The primary radical intermediates of the water radiolysis H^\cdot , OH^\cdot and e^- are produced by X-irradiation at low temperatures (77 K) and can react with solute molecules upon annealing the samples at higher temperatures. With this procedure we have investigated the reactions of $SO_4^{\cdot-}$ and $HPO_4^{\cdot-}$ with several DNA constituents, especially 5-halogen-substituted uracil derivatives, in an acidic aqueous matrices ($6MH_2SO_4$, $14MH_3PO_4$). The radiation chemistry of this class of compounds deserves special attention because of its radiosensitizing properties when incorporated into native DNA instead of thymine.

The products of the attack of $SO_4^{\cdot-}$ ($HPO_4^{\cdot-}$) at ca. 150 K on thymine (T) and the range of 5-substituted bases (FU, ClU, BU, IU) and their nucleosides were identified by Electron Spin Resonance Spectroscopy (ESR) and by optical absorption.

Both species were found to oxidize the bases under formation of the corresponding base cations:

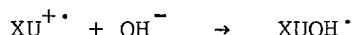


Both the ESR hyperfine parameters and the optical absorption bands of the cations $XU^{+\cdot}$ could be determined. They show a strong substituent dependence as expected from the spin density distribution.

The secondary reactions of $XU^{+\cdot}$ depend on the experimental conditions and the molecule under investigation. The radical cations of free bases may deprotonate at position N₁ thus forming a neutral radical



whereas in nucleosides in a water-rich environment the hydroxylate at C₆ is formed:



The importance of the above reactions for the radiation chemistry of in vivo DNA will be discussed.