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ABSTRACT 7

# A CHEMICAL STUDY OF RADIOBIOLOGICAL DAMAGE

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This work entails application of radiation chemistry to the analysis of radiobiological damage in order to determine which biochemical structures are most sensitive to the effects of irradiation and how these effects can be chemically modified to protect living systems. Damage-propagating effects of free radicals have long been postulated in irradiated tissue. In this work the relative rate constants for reactions between hydroxyl radicals and many biochemicals were measured. Wide variation was found in the susceptibilities of these compounds to radical attack, and long-range steric effects were quite evident. Polymeric chains and gels were found to have radical-capturing abilities, an order of magnitude less than values predicted from studies with the constituent monomers, suggesting that these more highly organized structures can exclude radicals from their interiors.

Many synthetic organic compounds were also examined in respect to their speed of reaction with hydroxyl radicals since fast reactants, which are also nontoxic, could be expected to protect living systems by sacrificial competition for the radicals. Of the compounds tested, erioglaucine, a relatively nontoxic food coloring, exhibits the most rapid reaction rate. This and other compounds were found to inhibit the radiation-induced hemolysis of human red blood cells in vitro, and the order of their protective abilities followed precisely the order of their reactivities with hydroxyl radicals.

Products of the reactions between organic compounds in aqueous solution and the radicals formed by radiolysis of water are themselves free radicals which can propagate damage in irradiated systems. Such organic radicals were studied by electron spin resonance spectrometry immediately after passage of the solutions through a gamma-radiation zone. In several cases, hyperfine splitting in the spectra allowed the chemical structures of the radicals to be determined, and from these structures, the vulnerable sites on the parent molecules as well as the



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nature of the attacking radicals could be inferred. Of particular interest are the long lifetimes of some organic radicals in water at room temperature, e.g., the half-life of the radical from irradiated solutions of p-nitrobenzoate ion was measured to be eight minutes. Formation of such long-lived intermediates in irradiated tissue might reduce the rate of chemical change until natural processes could repair the disturbance without permanent damage.



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