

while the generally considered more radiosensitive organs, such as the spleen, pancreas and especially the leucocytes¹³, are among the lowest. A similar order holds for the relative cytochrome oxidase activity¹⁴.

Other consequences of the postulated role of copper in relation to radiobiological phenomena such as the effects of cyanide¹⁵ are to be published in greater detail elsewhere¹⁶.

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Possible Role of Copper Ions in Radiobiological Damage

THE mechanisms of the primary stage of radiobiological damage involve three major problems. First, the destructive effect of relatively small doses of radiation. This cannot be explained on a purely statistical basis, so long as most components in the living cell exhibit a comparable reactivity towards the primary radicals formed by radiation. Secondly, the oxygen effect which undoubtedly increases the radiosensitivity of the living system. This effect could possibly be explained by inhibiting the recombination of organic radicals by the formation of peroxides. Thirdly, the action of radiation protecting agents which can scarcely be explained quantitatively. These reagents are generally considered either as scavengers of the primary free radicals or as hydrogen atom donors in a repair mechanism. Recent experiments on the effect of metal ions on the radiolytic behaviour of organic solutes may throw some light on these problems.

It has been found that complexed metal ions, which undergo oxidation by the primary products of radiolysis, oxidize selectively their organic ligands^{1,2}. When alkyl diamines or amino-acids are radiolysed in dilute neutral aqueous solutions, the main radiolytic damage is induced by their interaction with OH radicals^{1,2}. The deamination of these compounds was taken as a measure of their radiolytic breakdown. In the presence of an efficient OH scavenger, for example isopropanol, the radiolytic damage to the amino-acid may be diminished to zero. When copper ions were added to the system, under oxygen, the yield of radiolytic deamination was increased and this increase was completely non-scavengable by isopropanol. This effect is most probably due to the oxidation of cupric ions, when in complexed form, by HO₂ or O₂ radicals to their trivalent state. The trivalent copper afterwards oxidizes its organic ligand. Electrons, which are known to reduce copper ions in radiolysed solutions to their monovalent state, did not induce any deamination. Thus it was shown that HO₂ radicals, which are generally mild reducing agents and which do not react at all with the given substrates, were made to produce oxidative

deamination by the presence of complexed copper ions². As HO₂ radicals are scarcely scavenged by any organic compound, the increase in the apparent radio-sensitivity of the organic ligand in this system may reach several orders of magnitude.

Other metal ions which were found to induce oxidative deamination of alkyldiamines include thallium^{1,2}, cobalt and vanadium³. Thallous ions which are extremely reactive towards OH radicals were shown to induce deamination in oxygen-free solutions even in the presence of OH scavengers².

It is felt that these findings have a strong bearing on the mechanisms of radiobiological damage. It has been shown that a certain molecule carrying a copper ion will undergo radiolytic decomposition preferentially to any other organic solute in the system. This effect of copper ions will increase with the oxygen tension over the radiolysed system, up to the point where all the hydrated electrons and hydrogen atoms are converted to HO₂ radicals. The selectivity of the induced damage may amount to several orders of magnitude above the statistical probability. Moreover, if macromolecule is affected, it will be the site of the metal ion which will undergo preferential radiolysis. This site may eventually be the active centre of an essential enzyme. The latter effect will amplify the induced damage to a particular site of an essential molecule by a factor of 10⁶ or more.

If the interaction of HO₂ or O₂ radicals with the copper ions is inhibited, or if the copper is removed from its original site by complexants of any kind, these will completely abolish the suggested mechanism of radiolytic damage. Now it is well known that most, if not all, protecting agents are excellent nucleophiles and complexing agents. By blocking complex formation with copper ions they may eliminate the possibility of radiolysing a particular site of a particular molecule, which would otherwise undergo preferential radiolysis. The protecting action, just as the radiosensitization, is thus amplified by many orders of magnitude over the statistical radical scavenging or hydrogen-donating abilities.

It should be emphasized that the given mechanism is only a suggested model which may presumably account quantitatively for certain radiobiological phenomena. Still, it does not exclude the existence of other mechanisms in the primary radiobiological damage.

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Thymidine-like Electron Spin Resonance Spectra in Gamma-irradiated Deoxyribonucleic Acid

SEVERAL investigations dealing with electron spin resonance on irradiated deoxyribonucleic acid (DNA) have been described during the past few years¹⁻⁶, documenting widely different results. It seems likely that these differences could to a large extent be due to the source and mode of preparation of the DNA investigated.

This communication summarizes the results obtained using a very pure sample of DNA from calf thymus, prepared according to Hammarsten⁷ and purified as described by Sevag et al.⁸. (The sample of DNA was kindly prepared by Mr. N. A. Eliasson, Department of Chemistry, Karolinska Institutet, Stockholm.) The samples were thoroughly evacuated and freed from oxygen by repeated flushing with pure nitrogen (from British Oxygen) and irradiated with cobalt-60 γ -rays at a dose rate of 0.4 Mrad/h. Electron spin resonance measurements were made with a Varian spectrometer having a 100 kc/s modulation unit⁹.