THE EFFECT OF MISONIDAZOLE ON RADIATION DAMAGE IN γ-IRRADIATED CALF THYMUS DNA

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In order to elucidate the mechanism responsible for radiosensitization by misonidazole (one of the effective radiosensitizers), a model system consisting of DNA-misonidazole complex was designed according to the theory by ADAMS & COOKE (1969), and the reliability of the theory was tested by biochemical and physicochemical methods after γ-irradiation of the complex. To make DNA-misonidazole complex, calf thymus DNA was mixed with misonidazole in aqueous solution at a molar ratio of 1 : 1 (Ntds/miso) and freeze-dried. The complex was irradiated under vacuum and subsequently dissolved in 10 mM NaCl solution at pH 7.0 in the presence or absence of oxygen using a specially designed glass tube. A part of the solution was examined by measuring the template activity of the DNA for RNA synthesis *in vitro*. Another part was subjected to measurement of the damage produced in the DNA (strand breaks, cross-links and alkali-labile sites). The yields of the damage were estimated by analytical ultracentrifugation, or by measuring the extent of occurrence of the insoluble gel formation. When the complexes were dissolved in a solution cantaining oxygen, no significant difference could be observed for the template activity and the yields of the damage. On the other hand, when the complexes were dissolved under an anaerobic condition, the protective effect of misonidazole was observed for the template activity, breaks and cross-links, and the sensitizing effect was observed for the yield of alkali-labile sites. Since it is known that the alkali-labile sites are non-repairable damaged areas in the cell, it is suggested that the increased production of these sites is responsible for radiosensitization by misonidazole.