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REACTION OF RADIOLYTICALLY FORMED HYDROPEROXIDES ON DNA AND PRECURSOR COMPOUNDS WITH REDOX-ACTIVE METAL IONS AND COMPLEXES

The exposure of oxygenated aqueous solutions of nucleic acids and related compounds to ionising radiation leads to the formation of peroxidic products (H_2O_2 and organic hydroperoxides). Analytical techniques [1] previously developed for determination of peroxides at concentrations of 10^{-6} – 10^{-5} mol dm^{-3} have allowed study of the post-radiolytic decay of such species in systems ranging in complexity from the pyrimidine bases to RNA and DNA.

The metal ion-catalysed decomposition of peroxides is a well documented phenomenon, and the possible involvement of contaminating metal ions in the decay processes was considered. The influence of both chelating agents and a variety of redox-active metal ions on peroxide stability has therefore been examined.

Preliminary data concerning the interaction of the glycopeptide antibiotic, bleomycin, with DNA hydroperoxide have been obtained. The results may have important implications with regard to synergism in the DNA-cleaving activities of bleomycin combined with ionising radiation.

REFERENCE

- [1] J.E. FREW, P. JONES, G. SCHOLLES, *Anal. Chim. Acta*, **155**, 139 (1983).



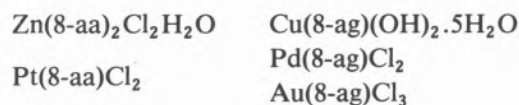
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TRANSITION METAL COMPLEXES WITH 8-AZAADENINE AND 8-AZAGUANINE

The biological properties of the azaderivatives of nucleic acid bases and nucleosides have been extensively studied and a number of them were found to be active chemotherapeutic agents. However very few reports have been published on complexes of metal ions with azapurines.

We have prepared and characterized a number of complexes of transition metal ions with 8-azaadenine and 8-azaguanine. These complexes were prepared by mixing equimolar aqueous solutions of the azapurines with the metal chloride or nitrate solution at an appropriate pH. On standing precipitated the complexes which were of the following composition:



These complexes were characterized by elemental analyses, conductivity and magnetic measurements, diffuse reflectance spectra and infrared spectroscopy. In the complexes prepared the 8-azapurines are acting as monodentate or bridging ligands, binding through the nitrogen of the imidazole ring.



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POLAROGRAPHIC AND SPECTROSCOPIC STUDY ON Pb^{+2} ION INTERACTION WITH DNA

The toxic effects of lead pollution seem to be already well established especially in the industrial countries [1]. The complexity of lead poisoning [2,3] was recently completed by the discovery of its carcinogenic actions in animals (for a review article, see ref. [4]). From the isotopic studies authors were not able, however, to establish whether metal ions are directly involved in DNA binding and if so which is the mode of lead binding to nucleic acid [5].

In this communication we present the polarographic and spectroscopic studies on the possible modes of interaction in the Pb^{+2} —DNA system.

RESULTS AND DISCUSSION

The lead-free DNA during a polarographic process in acetate buffer undergoes a reduction around -1.39 V. This process is usually assigned as a reduction of the adenine and cytosine residues of a double-stranded DNA molecule [6]. The relative height of a polarographic wave (h_{DNA}) is suggested to be a measure of a double-helical structure of nucleic acid [7,8].

Pb^{+2} —DNA solutions in 0.15 M acetate buffer

In the 0.15 M sodium acetate h_{DNA} reaches a value close to the maximum, which could indicate that

most of the studied DNA is in a double-helical structure. The increase of Pb^{+2} to phosphate molar ratio (P) changes distinctly the reduction potential of DNA from -1.398 V ($P=0.05$) to -1.443 V ($P=10$). The fact that the presence of Pb^{+2} ions causes a slight increase of h_{DNA} with time of solution storage and variation of the reduction potential of DNA may indicate that lead ions compete with sodium ions in the interaction with DNA and that the main interaction site is the phosphate site.

Pb^{+2} —DNA solutions in 0.05 M acetate buffer

Addition of Pb^{+2} ions to 0.05 M acetate buffer causes a distinct increase of h_{DNA} which depends on the Pb^{+2} ion concentration as well as on the time of DNA exposition on metal ions (Fig. 1). These results could clearly indicate the direct involvement of lead ions in the stabilization of a double-helical structure of DNA (increase of h_{DNA}).

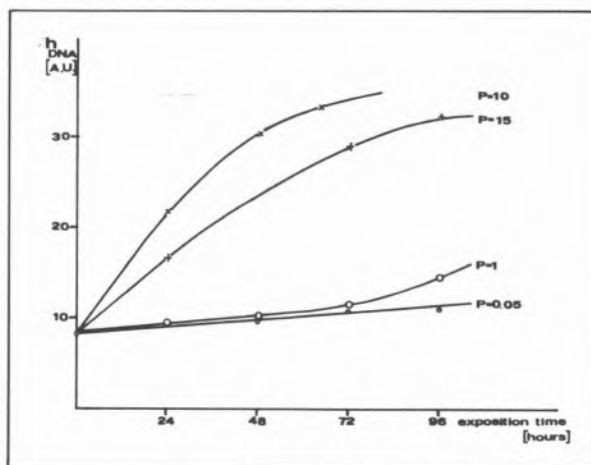


Fig. 1
Dependence of h_{DNA} on Pb^{+2} concentration and on exposition time (solution storage) ($c_{DNA}=25$ μ g/ml, 0.05 M acetate buffer)

The kinetics of this interaction is rather slow. The stabilizing effects of Pb^{+2} ions are supported by CD spectra. The results of CD spectra for $P > 10$ suggest the destabilizing effect of Pb^{+2} ions *i.e.* interaction with the base donors of DNA [9,10]. These results are supported also by the melting profiles for Pb^{+2} —DNA solutions (Table I). The data presented in Table I clearly show the stabilizing effects of lead ion of DNA for $P < 10$ and