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Photoproduction of Superoxide Ion from Near Ultraviolet Light Plus Hydrogen Peroxide; their Synergistic Action on Phage T7

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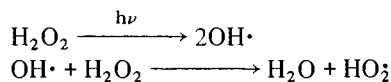
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The ultraviolet radiation of 300–400 nm, also known as near ultraviolet (NUV), can cause a variety of damage to viruses, bacteria and animal cells including DNA strand breaks, formation of pyrimidine dimers and interference in transport and repair systems [1]. The effect of NUV on the inactivation of phages and bacteria is significantly enhanced in the presence of hydrogen peroxide (H₂O₂). The synergistic action of the two agents can be observed at concentrations at which the individual agents may have little or no effect [2]. One reason for the phototoxicity by NUV is implicated with the photooxidation of endogenous tryptophan which, on photolysis, generates H₂O₂ and this agent in turn is photolysed to act synergistically on the biological systems.

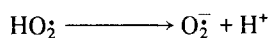
Ninety nine percent of a population of phage T7 is inactivated if exposed simultaneously to NUV (4.3 × 10⁴ J m⁻²) and H₂O₂ (0.3 mM). Addition of hydroxyl radical (OH•) scavengers, such as sodium benzoate, mannitol or isopropyl alcohol, to the system does not prevent the phage from being inactivated, suggesting that OH• is not the phototoxic agent. However, when the reaction mixture was supplemented with superoxide dismutase (SOD) phage inactivation was significantly reduced. This suggests that superoxide ion (O₂⁻) is possibly playing an important role in the synergistic killing of phage T7.

Production of O₂⁻ from the NUV photolysis of H₂O₂ was detected by the oxidation reaction of NADPH to NADP [3] and the reduction reaction of nitroblue tetrazolium (NBT) to formazan blue [4]. Furthermore, the reduction of NBT and the oxidation of NADPH were prevented in the presence of SOD. Presence of isopropyl alcohol or sodium benzoate in the reaction mixture did not prevent this diminution reaction.

An action spectrum of the reduction of NBT by H₂O₂ showed that the blue colour appeared maximally at 310 nm. Also it was noted that, within the range of pH 7 and 9, as the pH of the reaction mixture was increased the appearance of formazan blue increased proportionately. A sequence of reaction is described [5] to account for the production of O₂⁻ from the UV photolysis of H₂O₂:



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Is therefore superoxide ion, generated from the NUV photolysis of H₂O₂, responsible for the inactivation of T7 when exposed to these agents? To investigate this T7 was exposed to the agents in the presence of SOD. Phage inactivation was significantly reduced suggesting that O₂⁻ is the likely phototoxic agent. It is possible that O₂⁻ is directly reactive with the DNA causing strand breaks or that it is first reactive with a chromophore (perhaps a protein) which then reacts with the DNA. DNA to protein cross links in phage T7 in the presence of NUV plus H₂O₂ have been documented [6].

- 1 R. B. Webb, in 'Photochem. Photobiol. Review', Vol. II (K. C. Smith, ed.) Plenum Press, New York (1977).
- 2 H. N. Ananthaswamy and A. Eisenstark, *Photochem. Photobiol.*, **24**, 439 (1976).
- 3 A. M. Michelson, 'Superoxide & Superoxide Dismutase' (A. M. Michelson, J. M. McCord and I. Fridovich, eds.) pp. 87, Academic Press, New York (1971).
- 4 C. Beauchamp and I. Fridovich, *Anal. Biochem.*, **44**, 276 (1971).
- 5 J. H. Baxendale, *Radiat. Res.*, **17**, 312 (1962).
- 6 P. S. Hartman, A. Eisenstark and P. G. Pauw, *Proc. Natl. Acad. Sci. USA*, **76**, 3228 (1979).

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In vitro Cytostatic Activity of Palladium(II) and Platinum(II) Halide Complexes with Thiocarbamic Esters

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The thiuram disulfides and dithiocarbamates are widely used in industry, agriculture and medicine [1, 2]. Moreover disulfiram (tetraethylthiuram disulfide) has been used for over 20 years in the treatment of certain patients with chronic alcoholism and the reduced form of the compound, diethyldithiocarbamate anion (DDTC) has been used in the treatment of nickel carbonyl, arsenic and thallium poisoning [3].

Recently DDTC has been found to be an effective agent in attempts to reduce the dose-limiting nephrotoxicity of *cis*-platin [4]. This compound has been shown also to exert a protective effect against a variety of chemically-induced malignant tumors and a unique immunopotentiating activity [5].

Bearing in mind these findings, in recent years we have undertaken to study platinum(II) and palladium-