

Photosensitized Oxidation of Hypoxanthine and Xanthine by Aluminum Phthalocyanine Tetrasulfonate. Role of the Alkylating Quinone 2,5-dichloro-diaziridiny-1,4-benzoquinone

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Background and Objective: Photodynamic therapy (PDT) is a cancer treatment that uses a combination of red laser light, a photosensitizing agent, and molecular oxygen to produce the therapeutic effect. Solid tumors are often hypoxic. Therefore, direct killing of the hypoxic cells by singlet oxygen is very limited. However, since red-light-absorbing dyes also photoreduce oxygen, these should also photoreduce molecules having nearly equal or more positive redox potentials than oxygen in anoxic/hypoxic cells. If the reducible substrate is a DNA alkylating quinone, which is activated by reduction, DNA alkylation should be expected, with the consequent cell death, if repair of the DNA damage is insufficient.

Methods: Nitrogen-saturated aqueous solutions containing aluminum phthalocyanine tetrasulfonate (AIPcS₄), 2,5-dichloro-diaziridiny-1,4-benzoquinone (AZDCIQ) and hypoxanthine (HX) were photoirradiated at 675 nm.

Results: The oxidized HX derivatives, xanthine (X) and uric acid (UA) were produced. Concentrations of the AZDCIQ semiquinone, X and UA increase at the expense of HX with an increase in irradiation time. Addition of calf-thymus DNA produces quinone-DNA covalent adducts after photolysis of anaerobic samples containing quinone, DNA and AIPcS₄, in the presence or absence of HX and at pH 5.5. Furthermore, larger amounts of quinone-DNA adducts are detected if HX is present.

Discussion and Conclusions: The results presented here should have applications in the photodynamic treatment of hypoxic tissues such as solid tumors, under conditions of high HX concentration, where type I pathways could be more important than singlet oxygen generation.

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