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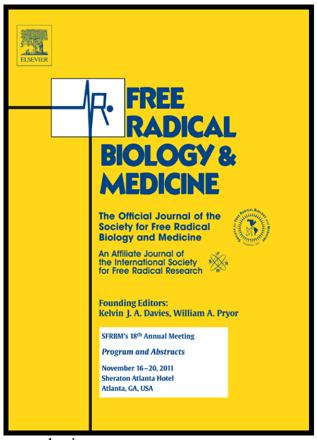

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Dimerization and oxidation of tryptophan in UV-A photolysis sensitized by kynurenic acid

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Abstract

Photoinduced generation of radicals in the eye lens may play an important role in the modification of proteins, leading to their coloration, aggregation, and insolubilization. The radicals can be formed via the reactions of photoexcited endogenous chromophores of the human lens with lens proteins, in particular with tryptophan residues. In the present work we studied the reactions induced by UV-A (315-400 nm) light between kynurenic acid (KNA), an effective photosensitizer present in the lens, and N-acetyl-L-tryptophan (NTrpH) under aerobic and anaerobic conditions. Our results show that the reaction mechanism strongly depends on the presence of oxygen in solution. Under aerobic conditions, the generation of singlet oxygen is the major channel of the effective NTrpH oxidation. In argon-bubbled solutions, the quenching of triplet KNA by NTrpH results in the formation of KNA•⁻ and NTrp• radicals. Under laser pulse irradiation, when the radical concentration is high, the main pathway of the radical decay is the back electron transfer with the restoration of initial reagents. Other reactions include (i) the radical combination yielding NTrp dimers and (ii) the oxygen atom transfer from KNA•⁻ to NTrp• with the formation of oxidized NTrp species and deoxygenated KNA products. In continuous-wave photolysis, even trace amounts of molecular oxygen are sufficient to oxidize the majority of KNA•⁻ radicals with the rate constant of $(2.0\pm0.2)\times10^{9}$ $M^{-1}s^{-1}$, leading to the restoration of KNA and the formation of superoxide radical O_2•⁻. The latter reacts with NTrp• via either the radical combination to form oxidized NTrp (minor pathway), or the electron transfer to restore NTrpH in the ground state (major pathway). As the result, the quantum yields of the starting compound decomposition under continuous-wave anaerobic photolysis are rather low: 1.6% for NTrpH and 0.02% for KNA. The photolysis of KNA with alpha-crystallin yields the same deoxygenated KNA products as the photolysis of KNA with NTrpH, indicating the similarity of the photolysis mechanisms. Thus, inside the eye lens KNA can sensitize both protein photooxidation and protein covalent cross-linking with the minor self-degradation. This may play an important role in the lens protein modifications during the normal aging and cataract development.

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