

Advanced Glycation Endproducts As Type I Photosensitizers In The Eye Lens

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Advanced glycation endproducts (AGEs) have been a subject of permanent interest through the last decade since they are related to many chronic diseases. Along with the multiple consequences of AGEs formation in vivo, is their photosensitizing activity, which is of special relevance in tissues that are exposed to light, particularly the eye lens, where they are thought to be related to cataract development. Within the lens, AGEs act as endogenous sensitizers generating reactive oxygen species upon irradiation with UVA light as it has been demonstrated in vitro. Nonetheless, the actual potential of damaging lens proteins has not been addressed properly. More over, the real conditions of the lens, which is a poorly oxygenated tissue, had not been considered. In the present work, we addressed the matter of protein photo-crosslinking and oxidation sensitized by AGEs, giving special emphasis to low oxygen conditions. The sensitizing mechanism of AGEs is further discussed. AGEs were prepared by incubating at 60°C a mixture of N α -acetylated lysine and arginine with glucose. Bovine lens proteins were irradiated with UVA-visible light in the presence of AGEs under 5, 20 and 100% oxygen pressure. Samples were analyzed by SDS-PAGE and quantified with Image Master software. At 5% O₂, the observed crosslinking was inhibited to a great extent by the presence of the electron-acceptor ferricyanide and only slightly increased by D₂O, which are consistent with the occurrence of type I photosensitizing mechanism. Nonetheless, at 20% and 100% O₂, type II mechanism begins to be important, with a consequent increase in the crosslinking degree. Trp decomposition quantum yields were also determined. In addition, oxidation was also examined at all oxygen concentrations, showing the same behavior than crosslinking. Finally, when the formation of peroxides was investigated, hydrogen peroxide was generated in a greater amount at 5% O₂. All of the results are consistent with AGEs acting as type I sensitizers at the low oxygen concentration found in the lens. A radical-mediated protein crosslinking mechanism is proposed.

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