DIPHENYL DISELENIDE PROTECTS HUMAN RETINAL PIGMENT EPITHELIAL CELLS FROM OXIDATIVE STRESS

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The damage caused by oxidative stress to retinal pigment epithelial (RPE) cells is known to be associated with age-related macular degeneration (AMD). The antioxidant properties of diphenyl diselenide [(PhSe)2] suggest a potential effect of this organoselenium compound on oxidative-stress-triggered apoptosis in RPE cells. Therefore, the purpose of the present study was to investigate the protective effect of (PhSe)2 against oxidative stress-induced cell death in a human RPE cell line (ARPE-19) and its underlying mechanism. The ARPE-19 cells were serum-starved for 8 hours and treated with (PhSe)2 (0.5, 1.0, 2.5, and 5.0 µM). Oxidative stress was induced 1 hour after (PhSe)2 exposure by treatment with TNF-α (10 ng/ml) and H2O2 (600 µM) for 14 hours to detect Hoechst-positive apoptotic cells or for 6 hours for Western blot and Immunocytochemistry analyses. (PhSe)2 at concentrations of 0.5 to 5 µM decreased the high amount of Hoechst-positive cells induced by TNF-α/H2O2. This antiapoptotic effect of (PhSe)2 lasted for 6 hours after oxidative stress induction. (PhSe)2 at a concentration of 2.5 µM attenuated oxidative stress-induced cyclooxygenase-2 (COX-2) expression. Nevertheless, (PhSe)2 did not protect against the interleukin-1 β-stimulated expression of COX-2 promoter transfected into ARPE-19 cells. Oxidative stress increased poly (ADP-ribose) polymerase (PARP) cleavage, which was completely abolished by 2.5 µM (PhSe)2. In addition, this compound at concentrations of 1 and 2.5 µM restored extracellular-signal-related kinase (ERK) phosphorylation inhibited by oxidative stress. c-Jun N-terminal kinase and p38 phosphorylation were not altered by oxidative stress and/or (PhSe)2. ERK pathway, inhibition of PARP cleavage, and anti-inflammatory properties of (PhSe)2 are, at least in part, mechanisms of action of this compound which contributed to cellular protection. In conclusion, (PhSe)2 offers a remarkable protective effect against oxidative injury in human retinal pigment epithelial cells, and may have a therapeutic effect on AMD and other oxidative stress-related retinal diseases.

Keywords: Selenium; Oxidative Stress; Age-Related Macular Degeneration.

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