[S-19]

In Vitro Mechanistic Studies of Photogenotoxicity of Polycyclic Aromatic Hydrocarbons

Jong-Hoon Choi, Ph.D.
Korea Institute of Toxicology

Many polycyclic aromatic hydrocarbons (PAH) are acutely toxic to fish and other aquatic organisms in the presence of environmentally realistic intensities of solar ultraviolet radiation (SUVR). The phototoxicity of polycyclic aromatic hydrocarbons (PAHs) occurs through photodynamic activation of PAH compounds. Oxygen molecules react as quenchers with excited triplet states of PAHs producing reactive oxygen species (ROS). ROS have a highly reactive chemical nature and their overproduction induces damage in biologically important macromolecules, such as proteins, DNA and lipids. Membrane damage through lipid peroxidation was suggested as a major mechanism of PAH phototoxicity and in this study, the production of lipid peroxidation product (malondialdehyde; MDA) upon PAH/simulated ultraviolet radiation (SUVR) was measured using fish liver microsomes and a fish hepatoma cell line (PLHC-1). The highest level of MDA production was found in the PAH/SUVR treatment. Neither PAH-only nor SUVR-only treatment produced significantly higher levels of MDA. MDA assay using the PLHC-1 cell line showed that increasing PAH concentration led to more MDA production. The role of the cytochrome (cyt) P450 enzyme system in PAH phototoxicity was assessed using a cyt P4501A1 inhibitor (clotrimazole) and HPLC analysis. HPLC analysis indicated that the cyt P450 system participated in PAH metabolism and the metabolism was significantly enhanced by the presence of SUVR. Reduced PLHC-1 cell mortality upon the clotrimazole treatment implied that cyt P450 metabolism in PAH phototoxicity functioned to lessen the toxicity probably by reducing the concentration of excited triplet states of phototoxic PAHs. Photoproducts of anthracene and other phototoxic PAHs had been reported to be toxic or phototoxic. But these studies were based on a plant model, so in this study toxicity/phototoxicity of major anthracene photolysis products (anthraquinone, 1,2-dihydroxyanthraquinone) was assessed based on PLHC-1 cell mortality assay. It was observed that, in PLHC-1 cells, photolysis reduced the phototoxicity of original anthracene compound and photoproducts were much less toxic/phototoxic. These results implied that the toxicity of anthracene photoproducts can be system (animal or plant) dependent.