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Superoxide mediated apoptosis in cell organelles by photosensitized 1,2:3,4-dibenzanthracene in HaCaT cells at ambient UV-B and natural sunlight

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Polycyclic aromatic hydrocarbons (PAHs) are recognized as environmental pollutants because of their intrinsic chemical stability, high resistance and toxic property worldwide. 1,2:3,4 dibenzanthracene (DBA) is a PAH, produced by incomplete combustion of fossil fuels, petroleum discharge. It gets adsorbed on atmospheric particles, mixed into soils, used in tattoo ink and remains for the longest time in the ecosystem. DBA showed strong absorption maxima (λmax) in UV-B (290-320 nm) with low absorption under UV-A (320-400 nm). DBA generates the significant amount of ROS such as O_2.-, .OH via type 1 mechanism. *In silico* study of DBA showed the interaction with aryl hydrocarbon receptor. DBA generates ROS photochemically and intracellularly which was confirmed by DCF/DHE fluorescence intensity while genotoxicity was assessed through comet assay, Hoechst staining, micronuclei formation. The generation of CPDs and 6-4 photoproduct formation, confirm the photo-genotoxic potential of DBA. Mitotracker/DAPI, Mitotracker/DHE, Mitotracker/DCF and JC-1 result showed the significant increase in mitochondrial permeability pore complex formation which leads to the release of cytochrome-c in cytosol showed strong evidence for apoptotic cell death by photoirradiation DBA. Cell cycle result showed G2/M phase arrest during cell division. DBA significantly showed over expression of Bax, Parp, Cyt-c, Bak, Caspase 3, Apaf-1, Cathepsin-B, Lamp-1, AhR, tBid, Calpain-7, γH2Ax, Keap-1, Caspase-12, Caspase-9 and lower expression of Bcl-2, Bid, Hmox and procaspase-3 protein expressions and up-regulation of Apaf-1, Cyt-C, Bax, Caspase-3, Calpain-7, Cathepsin-B, Nrf-2, Keap-1, AhR, Cdk-2, Cdk-4, Cycd1, Cycd2, Cycd3, Cdk6, Cyp1a2 and down regulation of Hmox, Bcl-2 genes. The exact mechanism behind DBA phototoxicity was involvement of ROS generation via type-1 mechanism, reduction of an antioxidant level and activation of the apoptotic pathway through mitochondria, nucleus as well as endoplasmic reticulum followed by AhR strongly promotes apoptotic cell death. The study suggests that after the DBA exposure, sunlight/UV-B exposure may avoid preventing from its harmful effects.

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Biography

Ajeet Kumar Srivastav has his research interest in the study of molecular mechanism involved in skin disease, phototoxicity/photogenotoxicity and molecular mechanism involved in skin disease by photosensitive drugs, cosmetics preservatives, hair dyes and PAHs under ambient UV-R/sunlight exposure. Presently, he is working as a Senior Research Fellow at Photobiology Division, Indian Institute of Toxicology Research, Lucknow, India.

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