CYTOTOXICITY AND GENOTOXICITY OF SOME POLYAROMATIC HYDROCARBONS (PAHS) AND THEIR OXIDATION PRODUCTS

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PAHs exposure is related to increased cancer risk. Their carcinogenicity depends on activation to electrophiles that damage biomolecules. Activation pathways include: diol-epoxide formation in bay/fjord regions, oxidation to radical cations, and formation of methylated derivatives, quinones, and ring opened metabolites. The role of oxidative stress in PAHs toxicity must be clarified. We investigated here the cytotoxicity and genotoxicity of indene[1,2,3-*cd*]pyrene, triphenylene, coronene, their quinones and hydroquinones. Quinones were obtained through PAHs oxidation with sodium dichromate. Quinones reduction with $NaBH_4$ generated hydroquinones, which were stabilized through acetylation with acetic anhydride/pyridine. Human hepatocarcinoma cell line (HepG2) and normal human liver cell line (THLE-2) were incubated with the PAHs, respective quinones or hydroquinones (16h, 20 to 200µM) for analysis of survival (MTT) and DNA oxidative damage (HepG2 8-oxodGuo). Dose dependent cytotoxicity was observed for the PAHs and oxidation products, with higher sensitivity of the THLE-2 cells. Oxidized triphenylene and indene[1,2,3-*cd*]pyrene were more cytotoxic and led to higher levels of 8-oxodGuo than the parent compounds. A 3-fold increase of 8-oxodGuo was observed in cells treated with the oxidized PAHs, compared to control cells. For coronene, the parent compound led to more damage than the oxidized one, but in general an induction of oxidative damage was observed. Acknowledgments: FAPESP, CNPq (Universal and Milênio-Redoxoma), CAPES, PRP/USP; Dr. Di Mascio, P., and Dr. Medeiros, M.H.G. for the mass spectrometer and HPLC systems.