Bisphenol A-metabolites induces Oxidative DNA damage And reduced cell proliferation

K.H An, Bong-Hee Kim

College of Pharmacy, Chung Nam National University,

Xenoestrogens are chemicals with diverse structure that mimic estrogen. Bisphenol A, a monomer of polycarbonate and epoxy resins, has been detected in canned food and human saliva. BPA stimulate cell proliferation and induces expression of estrogen-response genes in vitro. BPA shares similarities in structure, metabolism and action with diethylstilbestrol, a known human teratogen and carcinogen. This report considers the hypothesis that BPA is converted in vivo to hydroxylated metabolites with reduced estrogenicity and cytotoxicity. The purpose of the this study was to evaluate the cytotoxicity and cell proliferation of bisphenol A in the presence of a rat liver S9 mix containing cytochrome P 450 enzymes and Cu(II). In the present study, we found that BPA in combination with Cu(II) exhibited a enhancement in cytotoxicity, which was inhibited by reacitve oxygen species scavenger. For cell proliferation assay MCF-7 cells were seeded on a 96-well multi-well-plate at 1.5 x 10(3) cells per well. After 24hr cultivation, the S9 mix and Cu(II) was added to the wells as an S9 mix group (+S9), and medium was added to the other wells as a none-S9 mix group (-S9), then 5 different concentrations of various BPA were added to each well. After 5 days, a sulforhodamine B (SRB) assay was conducted to measure cell proliferation. +S9 mix group enhanced the proliferation of MCF-7 cells at much lower concentrations than -S9 mix group which was inhibited by the ROS scavenger. These results suggest that reacitve oxygen species reacts with Cu(I) leading oxidative stress. Also the formation of reacitve oxygen species induced by BPA was dose-dependently by inhibited by tamoxifen, which suggests that the effect of BPA was estrogenic action via estrogen receptors.