BORGES, J. M. P., LOUREIRO, A. P. M., **Investigation on Cytotoxicity and Genotoxicity of Aromatic Polycyclic Hydrocarbons Indene[1,2,3-*cd*]pyrene, triphenylene and coronene**. 2007. 97 f. Master´s Degree Dissertation – Faculty of Pharmaceutical Sciences, University of São Paulo, 2007.

Exposure to Polycyclic Aromatic Hydrocarbons (PAH) is related to the increase in the risk of cancer. These carcinogens depend on their activation by electrophilic intermediates to cause damage on biomolecules. The best understood activation pathways include (i) the formation of diol-epoxide in the bay and fjord regions of the PAH through epoxidations catalyzed by cytochrome P450 (CYP450), with an intermediate hydrolysis by epoxide hydrolase and (ii) oxidation (CYP450 or peroxidases) leading to the formation of a reactive cationic radical. Other pathways include the formation of methylated derivatives, quinones and open-ring metabolites whose contributions to carcinogenesis, as well as the role of oxidative stress on PAH toxicity, have not been extensively studied yet. This work investigated the cytotoxicity and genotoxicity of indene[1,2,3-*cd*]pyrene, triphenylene and coronene and their oxidation products (quinones and hydroquinones). Strains of human hepatocellular carcinoma (HepG2) and of normal human hepatocytes (THLE-2) were incubated with PAH and their respective quinones and acetylated hydroquinones and afterwards analyzed for cell viability (MTT) under different culture conditions (for 16 hours, 20 to 200μM). HepG2 cells were incubated for 16 hours with indene[1,2,3-*cd*]pyrene (50 μM), coronene (20 μM), triphenylene (10 μM) or their oxidation products (quinones and acetylated hydroquinones) and afterwards analyzed for oxidative damage on DNA and lipid peroxidation. In the mentioned concentrations, these structurally different PAHs and their oxidation products are cytotoxic and lead to an increase in the levels of 7,8-dihydro-8-oxo-2'-deoxyguanosine and malonaldehyde. Such damages may contribute to increase the risk of diseases like cancer in the exposed population.

Keywords: Cytotoxicity, Genotoxicity, Oxidative stress, DNA Adducts, Lipid peroxidation