PHARMACOLOGICAL ASSESSMENT OF SELENIUM COMPOUNDS AGAINST MERCURY CHLORIDE INDUCED CYTOTOXICITY IN PERIPHERAL BLOOD MONONUCLEAR CELLS

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ABSTRACT

INTRODUCTION: Mercury chloride (HgCl2) is a severely toxic inorganic form of Hg, and a foremost pollutant that poses significant threats to biodiversity and public health. Upon exposure in humans, mercury chloride ($HgCl_2$) exerts stress on the immune system and compromises mononuclear cells. OBJECTIVE: The objective of this study is to investigate and differentiate toxicological mechanisms of $HgCl_2$, its effects on human peripheral blood mononuclear cells (PBMCs) as well as to assess the pharmacological potential of organoselenium compounds such as ebselen (Ebs) and diphenyl diselenide $(PhSe)_2$ against $HgCl_2$-induced cytotoxicity. Ultimately, the goal is to determine in which ways the treatments' effects on PBMCs are mediated by mitochondrial dysfunction. MATERIAL AND METHODS: Peripheral blood was collected from healthy volunteers following protocol for isolating PBMCs. Approximately 4 x 10^6 cells/mL were isolated per group and exposed to 2.5µM $(PhSe)_2$ or ebselen, dissolved in 0.5% DMSO, and/or 5µM $HgCl_2$ in distilled water. The cells were cultured in RPMI medium supplemented with 10% fetal bovine serum (FBS) and 1% antibiotic-antimycotic at 37°C in 5% CO_2. After 3 hours of exposure, oxygen consumption rate was measured using High Resolution Respirometry (HRR), with titrations of 10mM Succinate, 2.5µM Oligomycin, 1-4µM FCCP, 0.5µM Rotenone and 2.5µM Antimycin. Once the HRR protocol was complete, basal electron flux values (Routine), oxidative phosphorylation (OXPHOS), maximum mitochondrial respiratory capacity (LEAK) and electron transport system (ETS CI/CII) were calculated and submitted to statistical analysis using one-way ANOVA followed by Tukey's post-hoc test. Differences were considered statistically significant for $p \leq 0.05$. RESULTS AND CONCLUSION: HRR assays indicate that the combination of 2.5µM $(PhSe)_2$ and 5µM $HgCl_2$ significantly reduced oxygen flux in Routine, LEAK, and ETS CI-linked states, while 5µM $HgCl_2$ alone decreased OXPHOS compared to Control. Similarly, 2.5µM Ebs and 5µM $HgCl_2$ inhibited OXPHOS, LEAK, and ETS CI-linked states. However, 2.5µM $(PhSe)_2$ and 2.5µM Ebs alone did not alter

mitochondrial parameters relative to Control. Further tests are required to determine other protective effects against mercury chloride-induced mitochondrial dysfunction.

Keywords: $HgCl_2$, Selenium, PBMCs.