OXIDATIVE STRESS PATHWAY: UNDERLYING MECHANISMS INDUCED BY FOUR CYTOTOXIC HEAVY METALS (As, Hg, Cd AND Pb) AND THEIR QUATERNARY MIXTURES ON MCF7 BREAST CANCER CELLS

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Abstract: Although the exact pathway of metal induced cytotoxicity is poorly understood, oxidative stress-induced cell death has been largely hypothesized to be the main mechanism by which heavy metals induce their toxic effects on cells. Oxidative stress has been largely linked to the activation of distinct apoptotic enzymes, but the direct mechanisms involved have remained largely elusive. This research studied the oxidative stress pathways by which four heavy metals and their quaternary mixtures induce their cytotoxic effects on breast cancer cells in the presence and absence of cellular antioxidant glutathione (GSH). Cellular levels of reactive oxygen species (ROS), mitochondria membrane potential (MMP), and glutathione (GSH) were assayed using the FACScalibur and cell quest pro software for data collection. The results showed that when cellular GSH was present, As induced cytotoxicity by collapsing the mitochondria membrane, Cd and the quaternary mixture by the production of superoxide anions and Hg by the production of ROS (nonspecific and superoxide anions). When the synthesis of cellular glutathione was inhibited, As and Cd were cytotoxic by the production of superoxide anion, Hg and the quaternary mixture by decreasing the mitochondria membrane potential and depleting the basal cellular GSH while Pb did not reveal any obvious cytotoxic effects on MCF7 in both in the presence and absence of GSH.