Thesis Summary

Introduction: Previous studies have demonstrated that mitochondrial toxicity can lead to various cardiac toxicities. Isolated mitochondria, serving as highly efficient screening tools, have been utilized to assess mitochondrial toxicity, predict cardiac complications, and explore mechanical evaluations. IFO, an anticancer drug, is known to be associated with an elevated risk of cardiac toxicity. Given the limited information on the direct effects of IFO on mitochondrial function, the aim of this study was to thoroughly examine the direct effect of IFO on isolated heart mitochondria obtained from heart.

Material and method: Mitochondria were isolated with mechanical lysis and differential centrifugation form heart and treated with various concentrations of IFO (0, 5, 50, 100, 500, 1000 and 2000 μM) Using biochemical and flowcytometry assays we evaluated mitochondrial succinate dehydrogenases (SDH) activity, mitochondrial swelling, mitochondrial lipid peroxidation, reactive oxygen species (ROS) production and mitochondrial membrane potential (MMP) during 1 hour.

Results: Our experimental results demonstrated that the direct administration of IFO did not cause deleterious alterations in mitochondrial function, mitochondrial swelling, lipid peroxidation, ROS formation and MMP collapse in isolated heart mitochondria.

Discussion and conclusion: In summary, the data from this study suggest that IFO does not directly induce toxicity in isolated heart mitochondria, and other pathways and metabolisms may contribute to the compound's toxicity. Furthermore, this study confirmed that mitochondria alone do not play the main role in the cardiac toxicity resulting from IFO. It is recommended that additional research be conducted on other pathways that produce toxic metabolites to mitigate the toxicity of this drug.

Key words: Ifosfamide, Cardiotoxicity, Predictive Toxicology, mitochondria