## ABSTRACT

**INTRODUCTION**: Drug-induced cardiotoxicity usually manifests as heart failure or left ventricular systolic dysfunction. Left ventricular dysfunction is a rarely reported side effect of bevacizumab (BEV) with an incidence of 1.2%, and this occurs irrespective of the route of administration. As we know there are many various ways for a drug to affecting body and make changes, finding out these ways will help prevent side effects of them or empowering their beneficial effects. Based on continuous working of the heart, one of main and necessary organelles in this organ is mitochondria because supply hearts ceaseless demands of energy.In this study, we focused on an analysis of bevacizumab effects on mitochondrial complexes activities. Rat heart mitochondria were isolated using differential centrifugation from wistar rats. Using biochemical and spectrophotometry assays we evaluated mitochondrial complexes activity, succinate dehydrogenases, mitochondrial swelling in isolated mitochondria. We observed only decreased activity of complexes II after exposure with bevacizumab (50 and 100 μg/ml). Together, for the first time, this preliminary study has demonstrated a significant decrease in activity of complexes II after exposure with bevacizumab.

**MATERIAL & METHODS** : Male wistar rats weighting 200-300g were purchased.Buffers and other needed material was prepared . Rats were anesthetized and the heart was surgically extracted. The isolated heart was chopped and destroyed with a glass homogenizer in a 10-fold volume of the medium containing isolation buffer. The homogenate was centrifuged at 1000× g for 10 min, and the pellet was removed. The mitochondria contained in the supernatant were sedimented at 10000× g for 10 min. The protein content in mitochondria was determined using the Bradford assay. Protein concentration in the suspension was 1 mg/mL. The enzymatic activities of oxidative phosphorylation (OXPHOS) complexes I, II, III, IV, I + III, II + III and citrate synthase were measured in isolated rat heart. For all assays, enzymatic activity was measured in the presence of 50 and 100 μg/ml bevacizumab. Experiments were performed at least three times for each treatment

**RESULT**: OXPHOS enzymatic activity in isolated mitochondria obtained from rat heart was measured.Complex II activity was significantly reduced by bevacizumab at 50 and 100 μg/ml compared with control group. Activities of complex I, complex III and complex IV were not affected by bevacizumab . Also complexes I/ III and II/ III activity were not significantly reduced to control activity by bevacizumab . In summary, these results confirm that complex II is the principal OXPHOS target for bevacizumab in rat heart mitochondria.



**KEY WORDS :** Bevacizumab, Cardiotoxicity, Mitochondria, Mitochondrial Complexes, mitochondrial toxicity