

## Molecular mechanism of metamphetamine toxicity in isolated rat liver mitochondria

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**Background and Aims:** The amphetamine synthetic derivatives such as methamphetamine, have been illegally used as recreational drugs and caused several life-threatening side effects like central nervous system (CNS) effects and cardiovascular disease. It was also reported that liver injury is one of the methamphetamine side effects. Despite several studies on amphetamines, the exact mechanism of methamphetamine toxicity is not well known. The goal of this study is to investigate mitochondrial toxicity by evaluating the effects of methamphetamine on rat liver mitochondrial swelling and complex II activity.

**Methods:** Liver was isolated from anesthetized male Sprague Dawley rats; then minced and homogenized in an ice bath. The mitochondria were isolated by two step centrifugation of homogenate. Mitochondrial protein concentration was normalized by Bradford protein assay. The activity of mitochondrial complex II (succinate dehydrogenase), was measured by methylthiazoletetrazolium (MTT) test using an Elisa Reader apparatus. In addition, analysis of mitochondrial swelling caused by methamphetamine, was estimated by changes in light scattering at 540 nm during 1 hour monitoring.

**Results:** The results showed that methamphetamine (1-100  $\mu\text{M}$ ) could inhibit mitochondrial electron transfer chain in complex II position. It was also found that mitochondrial swelling was increased in a concentration dependent manner in above mentioned concentrations.

**Conclusions:** Our results suggest that methamphetamine disrupts complex II of mitochondrial electron transfer chain. This toxic effect could initiate mitochondria dysfunction that finally causes mitochondrial swelling that is one of the final markers of mitochondrial toxicity.

**Keywords:** Isolated mitochondria; Metamphetamine; Rat liver