Research in Pharmaceutical Sciences, 2012;7(5)
School of Pharmacy and Pharmaceutical Sciences
Isfahan University of Medical Sciences

Toxicity of depleted Uranium on isolated rat kidney mitochondria

F. Shaki[1,*], J. Pourahmad[2], M. Hosseini[3], M. Ghazi-Khansari[4]

[1]Faculty of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Department of Pharmacology and Toxicology, School of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran., Faculty of Pharmacy, Students Research Committee, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
[2]Faculty of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[3]Faculty of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran., Department of Pharmacology and Toxicology, Faculty of Pharmacy ,Zanjan University of Medical Sciences, Zanjan, Iran
[4]Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Background and Amis: Depleted uranium (DU), a waste product of uranium enrichment, has the same chemical toxicity as the natural uranium and has applications in several civilian and military fields. Kidney is known as the most sensitive target organ for U toxicity. Although the oxidative stress and mitochondrial damage induced by DU has been well investigated, the precise mechanism of DU-induced nephrotoxicity has not thoroughly beenrecognized yet.
Methods: Mitochondria were isolated from the rat kidney and incubated with a different concentration of uranyl acetate (UA) (50, 100 and 200µM). Our results manifested that UA can disrupt the electron transfer chain at complex II and III that leads to the generation of reactive oxygen species (ROS), lipid peroxidation and glutathione oxidation. Disturbances in oxidative phosphorylation were also demonstrated through decreased ATP concentration and ATP/ADP ratio in UA-induced mitochondria. In addition, UA induced a significant damage in mitochondrial outer membrane. Moreover, mitochondrial membrane potential (MMP) collapsing, mitochondrial swelling and cytochrome C releasing were observed following the UA treatment in isolated mitochondria. All these toxic effects were well inhibited via pretreatment of cyclosporine A (CsA), an inhibitor of mitochondrial permeability transition (MTP) pore and butylatedhydroxyltoluene (BHT), an antioxidant.
Conclusions: The present study concluded that DU-induced nephrotoxicity is linked to the impairment of electron transfer chain especially at complex II and III which leads to subsequent oxidative stress.

Keywords: Depleted Uranium; Mitochondria; Nephrotoxicity; Respiratory chain; Mitochondrial permeability transition; Cytochrome C