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Depleted uranium disrupted the bioenergetics of liver mitochondria: a potential mechanism of fatigue syndrome

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Background and Amis: The uranium that remains after processing, commonly referred as depleted uranium that although have 60% of the radioactivity of natural uranium but has same chemical and biological properties with U. The DU munitions were used in Gulf War for the first time. Gulf War Syndrome was reported after the war, with DU held as a possible causative agent which chronic fatigue syndrome-like illness was one of the most important symptoms. Previous studies showed that uranyl acetate significantly induced mitochondrial dysfunction that may contribute to chronic fatigue syndrome. However, the underlying mechanisms of DU toxicity in mitochondria have not yet been well understood.
Methods: Liver mitochondria were obtained using differential centrifugation and were incubated with different concentrations of uranyl acetate (a soluble salt of DU) (50,100 and 200µM). In this research, mitochondrial ROS production, collapse of mitochondrial membrane potential and mitochondrial swelling was examined by flow cytometry following addition of uranyl acetate (UA). Meanwhile, extent of mitochondrial lipid peroxidation and glutathione (GSH) oxidation were detected via spectroscopy. Furthermore, we investigated the concentration of ATP and ATP/ADP ratio using luciferase enzyme and release of cytochrome c from mitochondria which was detected by ELISA kit.
Results:UA caused concentration-dependent elevation of mitochondrial ROS production, lipid peroxidation, GSH oxidation. UA also induced mitochondrial permeability transition, ATP production decrease and increase in cytochrome c release.
Conclusions: This study concluded that impairment of oxidative phosphorylation in mitochondria may play a key role in DU toxicity.

Keywords: Depleted uranium; Isolated mitochondria; Oxidative phosphorylation; Oxidative stress