

Ubisol Q10 Protects Against Glutamate Toxicity in Neuronal Cells by Inhibiting Mitochondrial Dysfunction

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Background: Glutamate-induced toxicity is a specific type of neurotoxicity that occurs when there is an abrupt, rapid influx of glutamate in the brain as often occurs during cerebral ischemia/stroke. The results of this influx can be long lasting even after the initial ischemic event has resolved, conferring degenerative signals that increase neuron loss. Mitochondria play a key role in energy production, calcium homeostasis, cell survival, and death and are particularly effected by glutamate exposure. Adverse stimulations may result in mitochondrial dynamic imbalance, free radical production, calcium accumulation, intrinsic cell death pathway activation and eventually cell death. Therefore, preserving or promoting mitochondrial function is a potential therapeutic target for the treatment of glutamate excitotoxicity. Ubisol Coenzyme Q-10 (CoQ10) is a water soluble electron transporter with low bioavailability. **Aim:** The aim of this study was to determine if Coenzyme Q10 can protect neuronal cells against glutamate toxicity primarily through the improvement of mitochondrial function. **Methods:** Cell viability in the mouse hippocampal cell line, HT22, was examined using rezasurin fluorescence assays and light microscopy. Western blotting was used to determine activation status of pathways involved in mitochondrial biogenesis and survival. **Results:** Observation of HT22 cells under 10X magnification shows significant degeneration of cells after glutamate exposure and addition of CoQ10 protects against this. Cell viability decreases in a dose-dependent manner after glutamate exposure while pre-treatment with CoQ10 returns viability to that of control cells. Using a kit to measure mitochondrial biogenesis, we found that glutamate reduced mitochondrial biogenesis and this reduction was prevented by CoQ10 treatment. Western blot analysis shows regulators of mitochondrial biogenesis, PGC1alpha and NRF2, are both reduced by glutamate and restored with CoQ10 pre-treatment. An additional regulator, TFAM, was unaffected. The cell survival AKT pathway was also examined. While glutamate exposure significantly reduced AKT and pAKT expression, CoQ10 was only able to restore AKT while phosphorylated AKT remained low. **Conclusions:** In summary, we believe that Ubisol-Q10 protects cells from glutamate toxicity by preserving the structure and function of mitochondria. CoQ10 pre-treatment may prevent glutamate-induced loss of mitochondrial biogenesis and prevent dysfunction by restoring pathways involving AKT, PGC1-alpha and NRF2. Therefore, adequate CoQ10 supplementation may be beneficial in preventing mitochondrial damage that occurs during cerebral stroke and other neurodegenerative disorders in which excitotoxicity is known to play a role.