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Cisplatin-induced DNA damage and neurotoxicity: Neuroprotection by coenzyme Q10

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Introduction: Coenzyme Q10 (ubiquinone) is a liposoluble provitamin that is endogenously synthesized and naturally found in various foods items. It is predominantly located in the inner mitochondrial membrane, where it is involved in reactions necessary to carry out oxidative phosphorylation via the electron transport chain. Coenzyme Q10 has attracted attention for being a mitochondrial antioxidant, decreasing DNA damage and maintaining genome stability. **Objective:** The study investigated the neuroprotective effects of water-soluble formulation of Coenzyme Q10 (WS-CoQ10) in cultured rat pheochromocytoma (PC12) cells exposed to cisplatin, a clinically relevant anticancer drug that has the neurotoxicity as a dose-limiting factor. PC12 cell line was used as a model of neuronal system. **Methods:** DNA damage was evaluated by the comet assay and cytokinesis-block micronucleus cytome assay; neuroprotection was performed by the neurite outgrowth assay, and quantitative real time PCR (RT-qPCR) used to determine *p53* gene expression. **Results:** In the CBMN Cyt, WS-CoQ10 (at a concentration of 0.1, 0.5 and 1.0 $\mu g.mL^{-1}$) protected PC12 cells from cisplatin-induced DNA damage (0.1 $\mu g.mL^{-1}$), reducing the micronuclei (MNi) and nuclear buds (NBUDs) frequencies. No evidence of genotoxic effect was observed in the PC12 cells after exposure to WS-CoQ10 (0.1, 0.5 and 1.0 $\mu g.mL^{-1}$) in comet assay. WS-CoQ10 (0.1 $\mu g.mL^{-1}$) showed neuroprotective activity by stimulating cisplatin-inhibited (10.0 $\mu g.mL^{-1}$) neurite outgrowth in nerve growth factor (NGF) differentiated PC12 cells and decreasing *p53* gene expression. **Conclusion:** In conclusion, WS-CoQ10 protected the PC12 cells from cisplatin-induced DNA damage and neurotoxicity. Moreover, the neuroprotective effects of WS-CoQ10 suggest its possible application in chemotherapeutic protocols.

Keywords: comet, PC12, cisplatin, neuronal cell model, DNA damage, neuroprotective agent

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