Effect of Clavulanic Acid on Trimethyltin-Induced Cytotoxicity in PC12

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Abstract

Introduction: Trimethyltin (TMT) is a short-chain trialkyltin used as a stabilizer of plastics. It is also a known neurotoxic agent in both human and animals. Clavulanic acid is previously known as a non-competitive inhibitor of β-lactamase. Oral bioavailability, low antibiotic activity and good CNS penetration are important properties of CA which nominated this compound for evaluation neuroprotective effects. Materials and Methods: PC12 cells were exposed to different concentrations of CA for 24 h. Then, TMT at final concentration 20 µM was added. After 24 h exposure, cell viability was determined using MTT test. For evaluation reactive oxygen species production, 2,7-dichlorofluorescein diacetate (DCFH-DA) method was used. Additionally the levels of Bax, Bcl-2 and Caspase 3 proteins were evaluated using western blot analysis. Results: Exposure to TMT significantly increased ROS production, Bax/Bcl-2 and Caspase 3 protein levels while decreased cell viability. Pretreatment of cells with CA inhibited ROS production and increased viability. Also, CA could decrease apoptosis through modulation of proteins involved in apoptotic pathway. Conclusion: The oxidative stress and apoptosis pathway have important roles in toxicity of TMT in PC12 cells. Clavulanic acid exhibited protective effects through inhibition of oxidative stress and apoptosis pathway.

Keywords: Clavulanic acid, Trimethyltin, Apoptosis, Oxidative stress

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