**SAXITOXIN INDUCES GENOTOXICITY AND APOPTOSIS IN NEURO-2A CELLS**

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**Abstract:** Saxitoxin (STX) is a potent neurotoxin of the PSP group, produced by some cyanobacteria in continental waters and less frequently in coastal marine waters and mitigated waters. In marine environment, this toxin can be also produced by eukaryotic microalgae. This toxin is increasingly involved in intoxication of aquatic animals and mammals including humans. Saxitoxin effects on ion channels are known, however its interferences with other cellular macromolecules and the consequences of such interferences are not fully documented. Therefore the evaluation of the toxic effects of STX and the determination of mechanisms triggering these effects are essential. The present experiments were designed to evaluate cytotoxic effects of STX (0.5 to 64 nM) to discriminate the pathways leading to cell death in a mouse neuroblastoma Neuro-2A, cells, using the end points measurement such as cell viability as determined by MTT test, DNA fragmentation assay and DNA methylation. The N2A cell line is found to be highly sensitive to STX as shown by the 50% inhibition concentration of 1.50nM in the MTT assay. STX induces genotoxic effects as shown by DNA fragmentation in agarose gel electrophoresis with some DNA ladders for all STX concentrations above 0.38nM. LDH and caspase-3 assessment suggests cell death by apoptosis mainly. The amounts of methylated cytosine residues (m5dC) in the DNA of treated cells are in accordance with the observed DNA fragmentation, however the lower concentration of STX (0.38nM) causes the highest rate of m5dC (68.54±0.26%) suggesting a significant disturbance of cellular regulation systems. The data obtained let us conclude that STX is an effective cytotoxic and genotoxic neurotoxin which may adversely affect important biological mechanisms at both genetic and epigenetic levels.

**Keywords:** Saxitoxin, Cytotoxicity Genotoxicity, Apoptosis, Neuroblastoma (Neuro-2A cells).