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Mutagenic and genotoxic potential produced by a mixture of the cyanotoxins Anatoxin-a and Cylindrospermopsin

C. Plata-Calzado, L. Diez-Quijada*, C. Medrano-Padial,
A. I. Prieto, A. Jos, & A. M. Cameán

Area of Toxicology, Faculty of Pharmacy, Universidad de Sevilla, Seville, Spain
**ldiezquijada@us.es*

The simultaneous occurrence of various cyanobacterial toxins can potentially induce toxic effects different than those observed for single cyanotoxins, as interactions may occur. This is a more common scenario in nature, where multiple toxins are frequently found in cyanobacterial blooms. Furthermore, the need for further studies based on the toxicity of cyanotoxins mixtures has been stated by the European Food Safety Authority (EFSA). Nevertheless, toxicological information on the topic is still scarce.

The aim of this study was to assess the mutagenic and genotoxic potential of mixtures of two of the most relevant cyanotoxins, Anatoxin-a (ATX-a) and Cylindrospermopsin (CYN), using a basic battery of in vitro test consisting of the bacterial reverse mutation test (Ames test, OECD 471) and the micronucleus (MN) assay (OCDE 487). Mixtures of 1:1 ATX-a/CYN were used to perform both assays. The Ames test were tested in five *Salmonella typhimurium* strains (TA98, TA100, TA102, TA1535, TA1537) in a concentration range from 0.125 to 2 µg/mL of toxins in presence and absence of S9 fraction from rat livers as metabolic activation system. The MN assays were performed on L5178YTk± cells in absence (0.084-1.35 µg/mL ATX-a/CYN) and in presence (0.125-2 µg/mL ATX-a/CYN) of S9 fraction. The exposure periods ranged between 4 and 72 h depending on the assay. There were no mutagenic effects after bacteria exposure to ATX-a/CYN mixture with or without metabolic activation in the concentrations range assayed. Significant changes were observed in the MN test of the mixture with or without S9 metabolic fraction, whereas previous studies only showed toxic effects in the presence of the S9 fraction after individual exposure to CYN. These results highlight the need for a specific evaluation of the genotoxicity of cyanotoxin mixtures, as their effects cannot be extrapolated from those of the individual cyanotoxins.

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Anatoxin-a, cylindrospermopsin, genotoxicity, mutagenicity, mixture.