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### Mutagenic and genotoxic assessment of pure anatoxin-a

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In recent years, the proliferation of cyanobacterial blooms has significantly increased due to water eutrophication and climate change. The capacity of certain cyanobacterial strains to produce cyanotoxins is of public concern due to its toxic effects on humans, animals, and the environment. One of the most important cyanotoxins is anatoxin-a (ATX-a), a globally distributed freshwater neurotoxin that has been linked to human and animal poisonings. The main route of exposure of this cyanotoxin is oral, through the consumption of contaminated water and food. However, in spite of its importance, the toxicological database of ATX-a is limited.

For this reason, the aim of this study was to investigate the potential mutagenicity and genotoxicity of pure ATX-a, as they play a key role in the risk assessment of any food contaminant. Two different in vitro tests recommended by the European Food Safety Authority (EFSA) have been used. The mutagenicity of ATX-a was assessed by the bacterial reverse-mutation assay using the *Salmonella typhimurium* TA1537, TA98, TA100, TA102, TA1535 strains (Ames test, OECD 471) and its genotoxicity was investigated by the in vitro micronucleus (MN) assay (OCDE 487) in L5178Y Tk+/- cell line, both in absence and presence of metabolic fraction S9. The ranges of concentrations of ATX-a tested were from 0.125 to 20 µg/mL for 72 h in the Ames test and from 1.25 to 20 µg/mL for 4 h in the MN assay. The results showed no mutagenic effect in any of the tested strains in the range of concentrations tested. By contrast, in the MN assay, a significant increase of percentage of binucleated cells with micronuclei (BNMN) was observed after exposure to 10 µg/mL ATX-a in absence of the metabolic fraction S9. To our knowledge, these are the first results showing a potential genotoxicity of ATX-a in the in vitro MN assay. Nevertheless, further studies are needed to elucidate the toxicity profile of ATX-a.

**Acknowledgements:** This research was funded by the Spanish Ministerio de Ciencia e Innovación (PID2019-104890RB-I00/AEI/10.13039/501100011033). C. Plata-Calzado is grateful for the financial support of the Junta de Andalucía (PREDOC\_00447 contract). Leticia Diez-Quijada Jiménez thanks to the Junta de Andalucía for the award of a postdoctoral grant as Doctoral Researcher Junta de Andalucía, grant number POSTDOC\_21\_00130.

#### **Keywords:**

Anatoxin-a, genotoxicity, mutagenicity, Ames test, micronucleus assay.