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Toxicity of cylindrospermopsin in human lymphocytes: proliferation, viability and cell cycle studies

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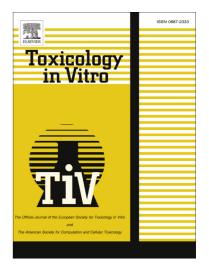
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ACCEPTED MANUSCRIPT

1	Toxicity of cylindrospermopsin in human lymphocytes: proliferation, viability and cell
2	cycle studies
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13	Abstract
14	The global expansion of cylindrospermopsin (CYN) producing cyanobacteria in surface
15	freshwater increases the risk of human exposure and poisoning. Following ingestion, CYN is
16	transported with blood in general circulation to the liver and kidneys, and can potentially
17	interact with immune system cells. In the present study, we investigated whether CYN (0.01 $-$
18	1.0 $\mu g \ ml^{1}$) can alter the function of human peripheral blood lymphocytes isolated from
19	healthy donors. It was found that CYN demonstrates significant antiproliferative activity in
20	lymphocytes during different phases of their activation. The most remarkable effects
21	(decrease by > 90%) were observed in lymphocytes exposed to 1 $\mu g \ ml^{-1}$ CYN at the
22	beginning of activation. Further analyses revealed a cell-cycle arrest at G0/G1 and prolonged
23	S phase in lymphocytes undergoing activation and significant apoptosis inducement in
24	activated cells. Reduced abilities to fight pathogenic microorganisms or malignant cells
25	should be taken into consideration in CYN exposure and risk assessments.
26	
27	Keywords: cylindrospermopsin; toxicity; lymphocyte; immune system
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