LEAD INDUCES OXIDATIVE STRESS AND APOPTOTIC RESPONSE IN *SACCHAROMYCES CEREVISIAE*

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Background: Heavy metals are found in the environment mainly due to anthropogenic activities. The presence of metals in surface waters and soils can create an environmental hazard and pose a serious risk to public health. Lead is a non essential metal for biological functions, displays a toxic effect and is classified as probable human carcinogen.

Objectives: In the present work, the mode of cell death induced by Pb in *Saccharomyces cerevisiae* was studied.

Methods: Cell proliferation capacity was evaluated by colony-forming units counting. Membrane integrity was assessed by the fluorescent probes bis(1,3-dibutylbarbituric acid trimethine oxonol) [$DiBAC_4(3)$] and propidium iodide. Reactive oxygen species (ROS) accumulation was examined by using 2′,7′-dichlorodihydrofluorescein diacetate (H_2DCFDA). Nuclear morphological modifications were revealed by diaminophenylindole (DAPI) staining.

Conclusions: Yeast cells, Pb-exposed, up to 6 hours, lost progressively the capacity to proliferate and maintained the membrane integrity. The exposition of yeast cells to Pb resulted in the intracellular accumulation of ROS. The addition of ascorbic acid (a ROS scavenger) strongly reduced the oxidative stress and impaired the loss of proliferation capacity in Pb-treated cells. Pb-induced death is an active process, which requires the participation of cellular metabolism, since the simultaneous addition of cycloheximide attenuated the loss of cell proliferation capacity. Pb-exposed cells displayed nuclear morphological alterations, like chromatin fragmentation. Together, the obtained data indicate that exposition of yeast cells to 1 mmol/l Pb results in a severe oxidative stress, which can be the trigger of programmed cell death by apoptosis.