Effects of arsenic on ectonucleotidasic activities and behavior in zebrafish (Danio rerio)

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The zebrafish is a small teleost that has been considered an ideal model for studying many human diseases. The genome of this species is sequenced and studies have shown that many genes of this fish are similar to mammals, including humans. Evidence has indicated the important role played by ATP and adenosine in the central nervous system (CNS). The neurotransmitter ATP is stored in a vesicular manner and released into the synaptic cleft, where it can act on specific receptors located in the cell membrane. The inactivation of the signal mediated by extracellular ATP is performed by a family of enzymes called ectonucleotidases, including NTPDases (nucleoside triphosphate diphosphohydrolases) and ecto-5'-nucleotidase. These enzymes are responsible for the extracellular catabolism of the neurotransmitter ATP to adenosine. Studies from our laboratory showed the presence of ectonucleotidases, such as NTPDases and ecto-5'-nucleotidase in the CNS of zebrafish. The objective of this study was to investigate the in vivo effects of subchronic exposure (96 hours) to arsenic on NTPDases and ecto-5'-nucleotidase activities in zebrafish brain and to evaluate the behavioral changes induced by arsenic in this species. For the behavioral parameters, there was a decrease in locomotor activity of animals exposed to 5 mg/L arsenic (30.5%) when compared with the control group whereas there were no changes in the distance traveled during 5 minutes of analysis. During 5 minutes of behavioral assessment, no significant changes were observed in mean speed and in absolute turn for all arsenic concentrations tested. The time spent in the upper tank was not changed between the groups tested with different arsenic concentrations. The time spent in the middle of the tank significantly decreased at 0.05 mg/L (55%), 5 mg/L (62%) and 15 mg/L (62%) when compared to control group. Moreover, the time spent in the lower region is significantly higher (28%) only in the group treated with 5 mg/L arsenic when compared to control. There was a significant decrease in ATP hydrolysis in the presence of 0.05 mg/L (37.6%), 5 mg/L (34.8%), and 15 mg/L (30.6%) arsenic when compared to control. The inhibitory effect was also observed in ADP hydrolysis at 0.05 mg/L (25%), 5 mg/L (38%) and 15 mg/L (41%) when compared to control. Regarding to 5'-nucleotidase activity, a reduction in AMP was promoted by arsenic 0.05 mg/L (37.7%), 5 mg/L (26.7%), and 15 mg/L (35%). The results demonstrated that changes on ectonucleotidases after arsenic treatments can be one of the factors involved in behavioral and neurotoxic effects induced by this contaminant in the central nervous system.

**Keywords:** arsenic, ectonucleotidases, zebrafish, nucleoside triphosphate diphosphohydrolase, locomotor activity.