## Chronic embryonic exposure of arsenic trioxide induced alteration on motor functions and anxiety-like esponses in zebrafish (*Danio rerio*) larvae

## ABSTRACT

Arsenic trioxide  $(As_2O_3)$  is a heavy metal that is widely used for therapeutic purpose and is found ubiquitously in the environment. Currently, information about the adverse effects associated with exposure to low levels of inorganic arsenic on the developing organisms is limited. We examined the effects of embryonic exposure of As<sub>2</sub>O<sub>3</sub> on motor functions and anxiety-like behaviors in the developing zebrafish. The embryos were exposed to 4 different concentrations (20, 30, 40, 50 µM) starting from 5 hpf until hatching (72 hpf) in a semi-static condition. The control groups were maintained in the embryo media. The mortality rate increased in a dose dependent manner. We found that chronic embryonic exposure to 30 and 40 µM decreased the number of tail coiling, heartbeat, and swimming activity. Meanwhile, exposure 20 µM did not produce any significant alteration in these parameters. To further understand the effects of As<sub>2</sub>O<sub>3</sub> interferences on the development of anxiety-related behavior, we chose 30 µM As<sub>2</sub>O<sub>3</sub> exposed larvae since the 40 µM As<sub>2</sub>O<sub>3</sub> achieved 100% mortality before the behavioral recording was conducted on 6 dpf. However, we found no alterations on thigmotaxis, avoidance response, speed and percentage of resting of 6 dpf larvae. Since we found no alterations in all parameters measured for anxiety related behavior, we evaluated the apoptosis in the eye of the larvae using acridine orange. We found a significant increase in the apoptotic signal particularly in the eye region. These results showed that exposure to microconcentration of As<sub>2</sub>O<sub>3</sub> do not alter the anxiety related responses, yet, inducing apoptosis in the retina and lens, which may contribute to visual deficit. The potential underlying mechanisms and implication of As<sub>2</sub>O<sub>3</sub> on visual acuity, motor performance and anxiety-like responses need further investigation.

Keyword: Anxiety; Zebrafish; In vivo; Heavy metal; Behavioural assessment