Área: BIO **Nº de Inscrição: 81**

Are the illicit drugs 25H-NBOH and 25H-NBOMe toxic to zebrafish embryos?

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Keywords: *Recreational drugs, Zebrafish, Embryotoxicity, Teratogenicity.*

Highlights

●Toxic effects of 25H-NBOH and 25H-NBOMe on zebrafish embryos were evaluated. ●Both substances were teratogenic to zebrafish embryos and negatively modulated the activities of ChE, LDH and GST.

Abstract

Substances named as NBOH and NBOMe comprise a family of phenethylamines that act as serotonin receptor agonists (5-HT_2 family), causing hallucinogenic effects. These substances have been sold as recreational drugs and several deaths have been reported after ingestion of these phenethylamines; however, there are no studies evaluating their *in vivo* toxic effects.[1] Zebrafish (*Danio rerio*) is a tropical teleost fish which is a recognized animal model in biomedical research due to the low cost maintenance, high fecundity, short life cycle and high similarity of its genome to the human genome. These advantages confer *D. rerio* a useful model for application high performance techniques for screening new drugs and their potential toxic effects.[2,3] In this work, we have studied the effects of illicit drugs 25H-NBOH and 25H-NBOMe *in vivo* using a zebrafish embryos. The embryos with up to 3 hours post fertilization of age were exposed to five crescent concentrations of 25H-NBOH (5, 10, 20, 40 and 80 mg/L) and 25H-NBOMe (5, 20, 50, 70 and 100 mg/L) for 96 h and the apical endpoints were analyzed each 24 h post-incubation to the drugs. The number of deaths was used to calculate the LC_{50}. Additionally, sublethal effects were also recorded daily. Observations were performed in a stereomicroscope (x 80 magnification) and photographed (Zeiss). The activities of cholinesterase (ChE), lactase dehydrogenase (LDH) and glutathione S-transferase (GST) were determined for both substances in embryos exposed to three concentrations below the LC_{50}.[4] At the highest concentrations tested (80 and 100 mg/L of 25H-NBOH and 25H-NBOMe, respectively), both samples caused high embryo mortality and coagulation was the only endpoint for lethality observed. By decreasing the concentration of the tested-substances, lethality also decreased while non-lethal effects were predominant up to 10 and 50 mg/L of 25H-NBOH and 25H-NBOMe, respectively. The non-lethal effects observed were spine malformation, egg hatching delay and body malformation for both drugs, while otolith malformation, pericardial edema and blood clotting were found only for 25H-NBOMe. 25H-NBOH and 25H-NBOMe showed distinct toxicity profiles to zebrafish embryos, the LC_{50} values showed that 25H-NBOH was more lethal (LC_{50} 43.38 mg/L) than 25H-NBOMe (LC_{50} 82.96 mg/L). The activities of the enzymes ChE, LDH and GST were changed by 25H-NBOH and 25H-NBOMe, indicating that their toxic properties could be associated with the negative effects of these drugs on such enzymes. The quantification of the biomarker's activities showed that 25H-NBOH has significantly changed the activity of the three enzymes, but the ChE activity were the most affected. Our results showed that 25H-NBOH and/or 25H-NBOMe possess *in vivo* (neuro)toxic effects to zebrafish embryos and their sublethal effects, most accounting for teratogenicity, were quite relevant in lower concentrations.

References: [1]Forensic Sci. Int. v. 279, p. e1–e6, 2017; [2]Annals of the New York Academy of Sciences, v. 1374, n. 1, p. 68–77, 2016; [3]Nature, p. 498–503, 2013; [4]Toxicology & Pharmacology, v. 152, n. 3, p. 338–345, 2010.

Acknowledgments

The authors thanks to FAPEMIG, CAPES (Finance Code 001), CNPq, and FAPESQPB for the financial support.