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Influence of Benzodiazepine Delorazepam on *Xenopus laevis* Embryogenesis

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Extended Abstract

Benzodiazepines, psychotropic drugs used for the treatment of insomnia and anxiety, are worldwide one of the most prescribed treatments [1]. The massive use results in the release of their active principles and metabolites in the wastewater, where they persist since not eliminated by sewage treatments [2]. Consequently, they accumulate in effluent waters [3] reaching concentrations ranging from μg/L to ng/L. For these reasons, BZPs are being considered emerging contaminants [4] and represent, even at low concentrations, a potential environmental hazard, especially for aquatic species [5]. Bioaccumulation is already reported in marine invertebrates and vertebrates as significant effects on behavior, gene expression and enzymes activity [6,7]. The fate of BZDs in the aquatic environment is still not fully clear and so are the effects on non-target species which may come accidentally into contact with these drugs. In this study, we investigated the influence of the benzodiazepine delorazepam on *Xenopus laevis* embryogenesis. Embryos were exposed to an environmental concentration (1 μg/L) [8] and, to mimic the simultaneous exposure to multiple BZDs occurring in nature, to 5 and 10 times higher (5 and 10 μg/L) concentrations. Results demonstrated that delorazepam reduces vitality, with decreased heart rate and motility, induces marked cephalic and abdominal edema, and causes alterations in the gut. At the molecular level, the increase of ROS production is observed together with an altered expression of developmental genes and the production of pro-inflammatory cytokines. A significant increase in ATP-binding cassette activity is also observed, as an attempt to improve drug clearance. The resulting stressful condition significantly impairs embryos development and threatens their survival. Similar effects should be expected also in embryos belonging to other aquatic species that have not been yet considered targets for benzodiazepines.

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