

TOXICOGENETIC EVALUATION OF GLYPHOSATE-BASED FORMULATION AND ITS MAIN CONSTITUENTS ON THE ZEBRAFISH EARLY LIFE STAGES: CONTINUOUS AND REPEATED PULSE EXPOSURE

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Introduction: Glyphosate (GLY) is the active ingredient of several herbicide formulations used to control weeds in agricultural and non-agricultural areas. Due to intensive use of GLY-based formulations and the repeated applications once weed resistance, some of their components, including the active ingredient, may reach the aquatic environment through direct run-off and leaching. **Objectives:** The present study assessed the acute toxicity, after continuous and repeated exposures, and genotoxicity of the GLY-based formulation Atanor 48 (ATN) and its major constituents GLY, surfactant polyethoxylated tallow amine (POEA), as well as the main metabolite of GLY aminomethylphosphonic acid (AMPA) on zebrafish early life stages. Also, we evaluate larvae resilience after ATN, GLY and POEA pulsed-exposure. **Methodology:** The toxic effects of these chemicals were evaluated in the fish embryo acute toxicity test with zebrafish (*Danio rerio*), while genotoxic effects were investigated in the comet assay with cells from zebrafish larvae and rainbow trout gonad-2 (RTG-2). **Results and Discussion:** GLY and AMPA caused no acute toxic effect after continuous exposure, while ATN and POEA induced significant lethal effects in zebrafish (LC_{50-96 h} 76.50 mg/L and 5.49 mg/L, respectively). All compounds were genotoxic to zebrafish larvae (LOEC 1.7 mg/L for GLY, ATN, AMPA and 0.4 mg/L for POEA). Unlike *in vivo*, only POEA induced DNA damage in RTG-2 cells (LOEC 1.6 mg/L), suggesting that it is a direct acting genotoxic agent. GLY caused no acute toxic effect after repeated pulse exposure. However, ATN showed significant mortality (LC_{50-96 h} 148.80 mg/L) after 5 h pulse at 100 mg/L and POEA induced significant toxicity on zebrafish early life stages after 1, 2 and 5 h pulse with LC_{50-96 h} of 43.49 mg/L, 47.23 mg/L and 11.61 mg/L, respectively. Zebrafish was not able to reverse the sublethal effects induced by ATN, GLY and POEA during the recovery period. The toxic effects induced by ATN and POEA after pulsed-exposure were less than continuous exposure. **Conclusions:** Therefore, it's important to evaluate different toxicological endpoints with distinct exposure scenarios to predict the hazards of GLY-based formulations, their components and breakdown product to aquatic biota.

Keywords: surfactant, AMPA, FET, Comet assay, *Danio rerio*, resilience.

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