Next Generation Morphological and Molecular Analysis of the Toxicity of Pharmaceutical-Derived Aquatic Contaminants (PPCPs)

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Pharmaceuticals and personal care products(PPCPs) are aquatic contaminants that have been detected in surface water globally. However, their aquatic toxicity, especially in complex mixtures, has not been well characterized. In order to understand PPCP toxicity, zebrafish embryos were exposed to single-chemical trials as well as mixtures of two cardiac-specific medications: triamterene(diuretic) and gemfibrozil(fibrate). Morphometric analysis revealed that GEM elicited a dose-dependent decrease in eye area and length(developmental delay), as well as an increase in yolk sac area, suggesting interference with lipid metabolism pathways; likewise, cardiotoxicity was observed. TRI induced a similar cardiotoxic phenotype. Mixture trials were compared to single-chemical trials using the response addition(RA) model; additive toxic effects were observed in all endpoints, with potential synergism evident in yolk sac. Thin layer chromatography coupled with flame ionization(TLC-FID) method was developed to quantify total lipid content and triglyceride/cholesterol levels in exposed embryos; results suggest that GEM blocks lipid metabolism. Further interpretation suggests that TRI+GEM may induce a distinct metabolic pathway than single-chemical exposure to produce toxicity during embryogenesis. These trends indicate that PPCPs are environmental stressors to non-target organisms and that PPCP mixtures could metabolically interact to produce greater than additive toxicity. Furthermore, novel TLC-FID method provides some of the first insight into the potential molecular mechanisms underlying PPCP toxicity. Overall, this study highlights the need for toxicity assays to incorporate PPCP mixtures to more accurately predict environmental effects and has implications for policy development.

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