A TOXICOKINETIC APPROACH TO ASSESS THE EFFECTS ON METABOLISM OF TRICLOSAN AND BENZOTRIAZOLES IN ZEBRAFISH (*DANIO RERIO*) EMBRYOS

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A significant number of environmental contaminants have been proven to enter the hydrosphere *via* wastewater treatment plants (WWTPs), due to their incomplete removal (Farrè et al. 2008). It is challenging to understand the adverse environmental and health impact of these xenobiotics and their biotransformation products, as they may bioaccumulated by aquatic biota, up to concentrations that exert adverse physiological effects. Various model organisms have been used over the last decade in order to assess the toxicity of such compounds.

Zebrafish (*Danio rerio*) emerges as a powerful model organism to study various aspect of developmental and cell biology as well as physiology. In addition, it provides an alternative model for toxicological studies, since mammalian and zebrafish toxicity profiles are strikingly similar (McGrath et al. 2012). One additional significant advantage is that zebrafish expresses genes similar to mammalian cytochrome P450 (CYP), UGT and sulfotransferases (SULTs) isoforms throughout early development.

In this work, we investigate the effects of triclosan and three benzotriazoles (BTRs) (1H-BTR, 4-Me-BTR, 5-Me-BTR) on zebrafish embryos. These analytes are present in the effluent wastewaters of Athens (Bletsou et al. 2015). We integrate toxicological information, kinetic information, as well as, a full characterization of zebrafish xenometabolome, which consists of the unmodified xenobiotics and their biotransformation products (Southam et al. 2014).

More specifically, we used the zebrafish embryo toxicity assay to calculate the LC50 of these compounds as well as a liver specific fluorescent transgenic line (*Tg:LFABP:GFP*) to evaluate their liver toxicity potential. In addition, we used 96-hours post fertilization (hpf) zebrafish for the kinetic experiment. Samples were collected in 5 different time intervals, from 30 sec up to 24 h post exposure (hpe), to examine the time profiles of both the parent xenobiotics and their biotransformation products.

Moreover, the thorough study of xenobiotics metabolism is of particular importance, as it affects the internal concentration measured, which is a better dose metric for describing toxicity to aquatic organisms (Escher et al. 2010). Extracts were analyzed with RPLC and HILIC methods, in both positive and negative ionization mode, using a LC-QTOF-HR-MS/MS instrument. Data was acquired not only with data independent, but also with data dependent acquisition. For the detection and identification of tentative biotransformation products, both suspect and non-target screening workflows have been applied (Gago-Ferrero et al. 2015). A total of 35 biotransformation products were tentatively identified for all the xenobiotics, 19 are reported for the first time for the benzotriazoles. Metabolic pathways for the detoxification of xenobiotics were proposed.

The overall results are expected to provide insights into understanding toxicological effects and xenobiotic metabolism in zebrafish and will be discussed during the meeting.

Keywords: zebrafish, toxicokinetics, xenobiotic metabolism, suspect – non target screening

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