

Zebrafish Embryonic Phenotypes as Indicators for Chemical's Modes of Action

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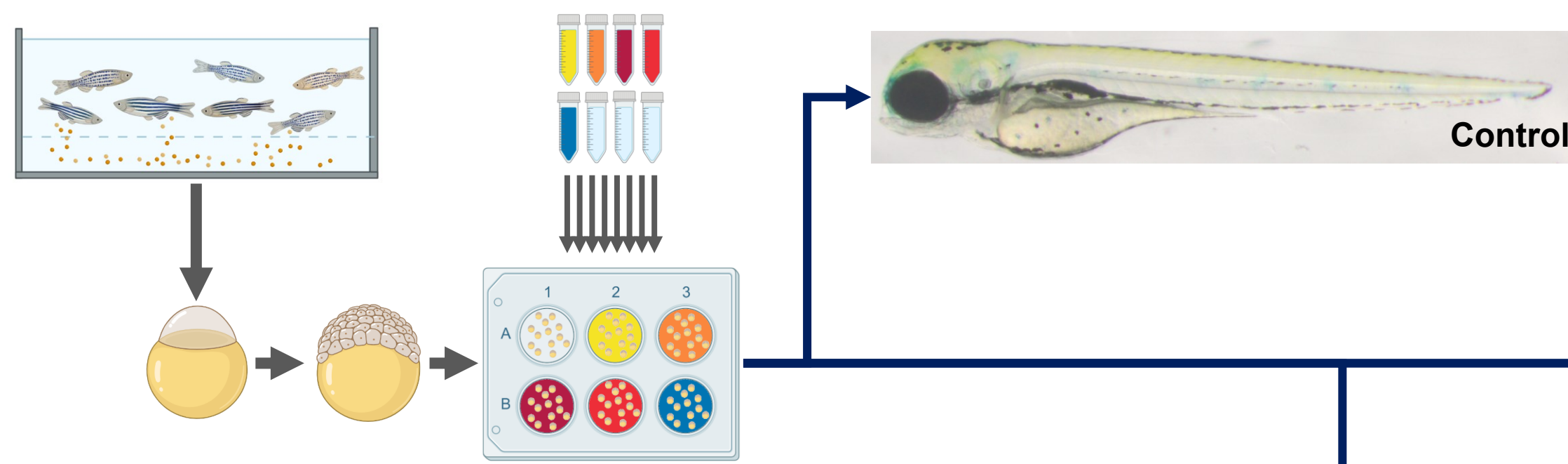
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INTRODUCTION

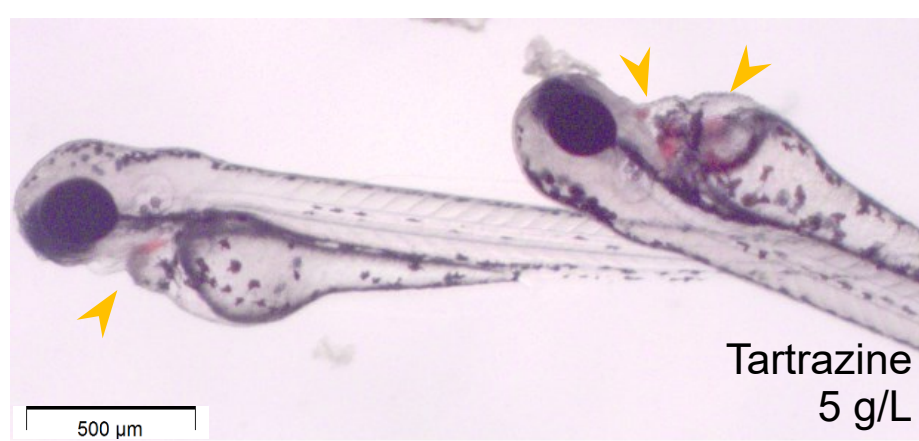
The zebrafish embryotoxicity test (ZET) has become increasingly prominent in evaluating the bioactivity and safety of chemicals and drugs, attracting scientists and legislators. Within the joint projects between the Laboratory for Organogenesis and Regeneration (ULiege) and the Faculty of Biology (VNU University of Science, Vietnam), we found that some chemicals may induce specific morphological effects on zebrafish embryos. Some of these phenotypic endpoints may indicate underlying mechanisms involved. Our studies have added several specific endpoints to the collection of bioactive indicators.

MAIN FINDINGS

Experimental scheme



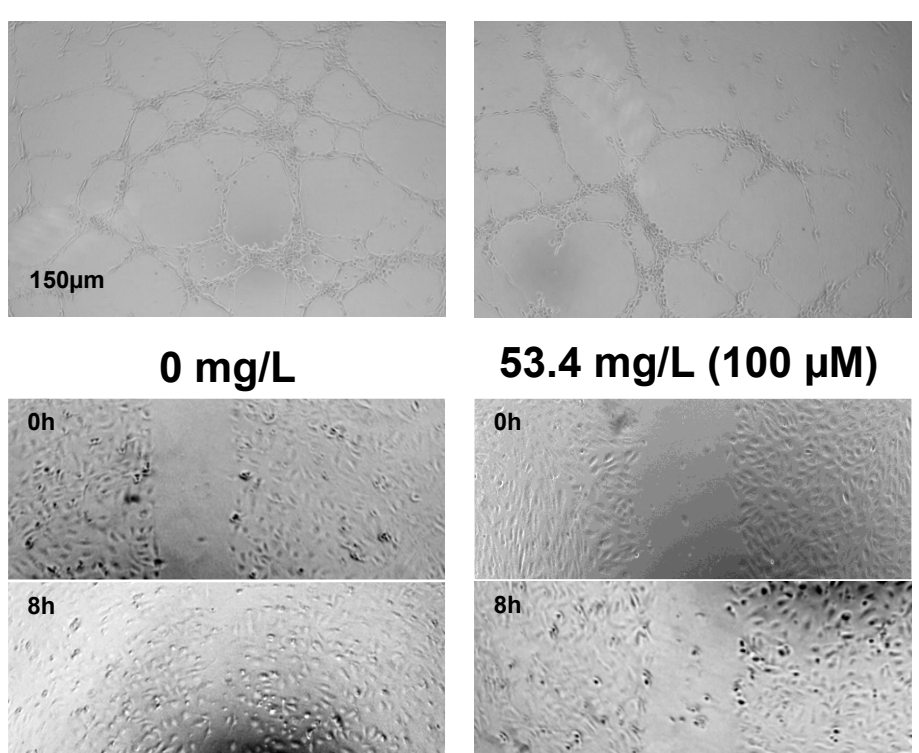
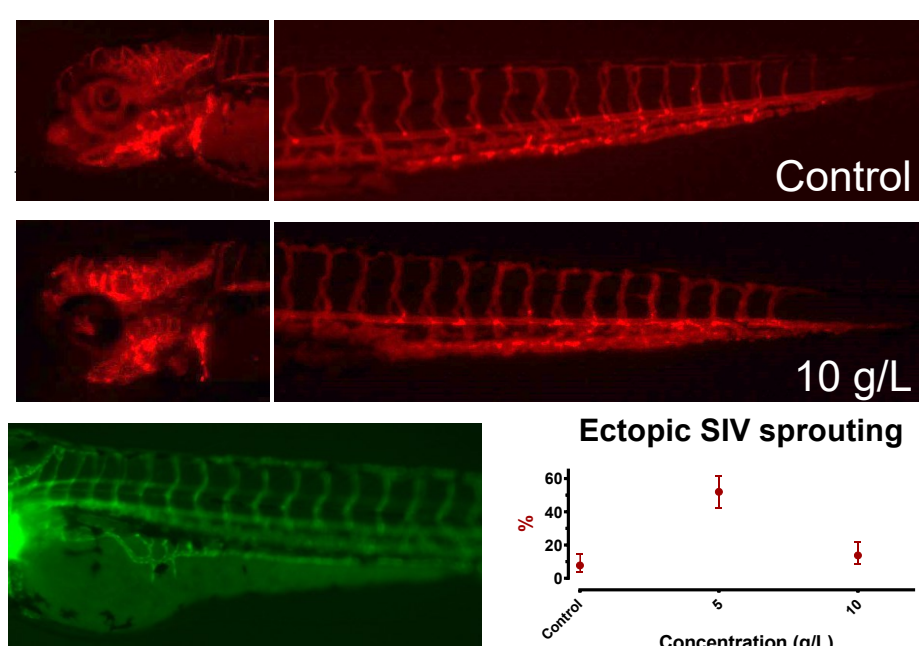
Hemorrhages hint at vasculogenic defects



Some chemicals, such as the food dye Tartrazine (TTZ), can induce hemorrhages in treated embryos.

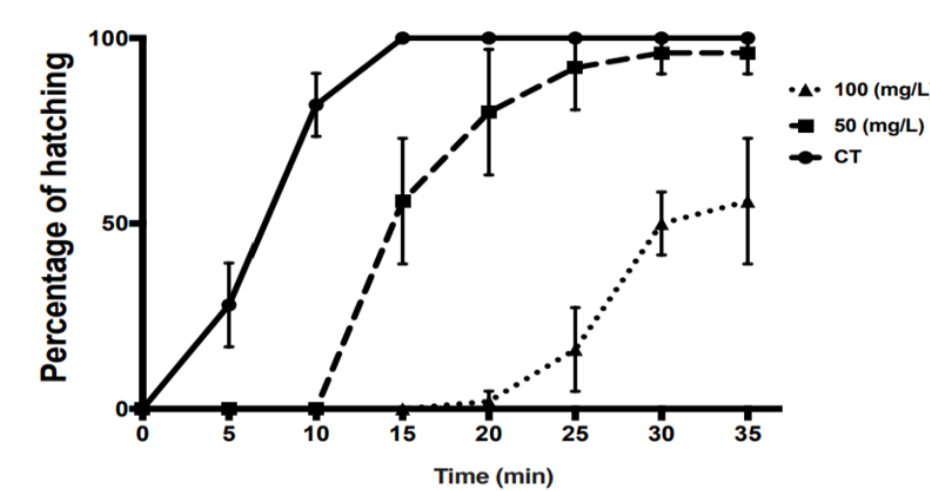
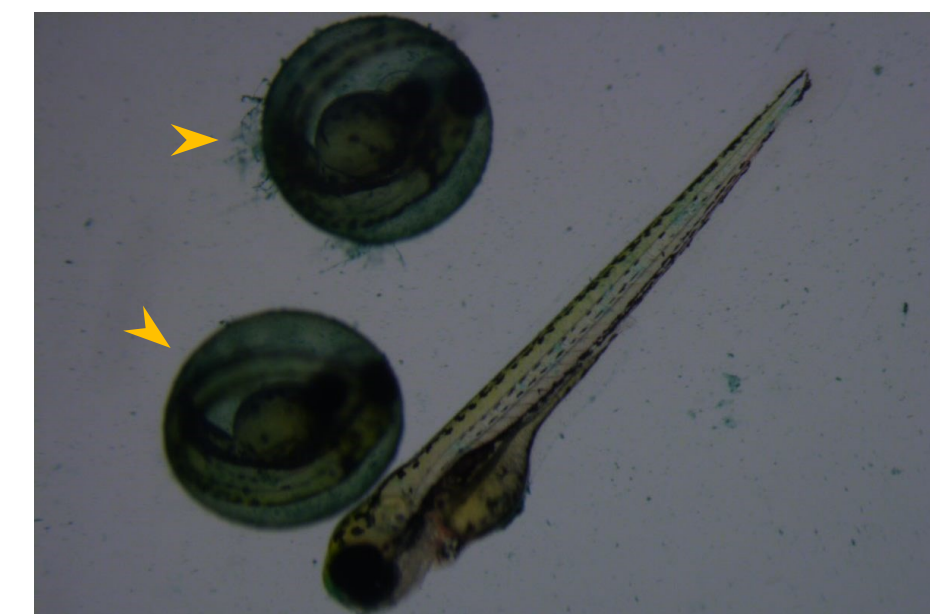
Further experiments on zebrafish transgenic reporter lines revealed disrupted vascular formations caused by TTZ - most prominently on the cephalic vessels, the caudal vein plexus, and the sub-intestinal vein (SIV) plexus.

In vitro assays using human endothelial cells also showed impaired tube formation and migration following TTZ treatments. These proved that food dye is an anti-vasculogenic agent [1]. Similar vasculogenic effects were found with *Caesalpinia sappan* plant extracts [2] and *Mallotus barbatus* [3].



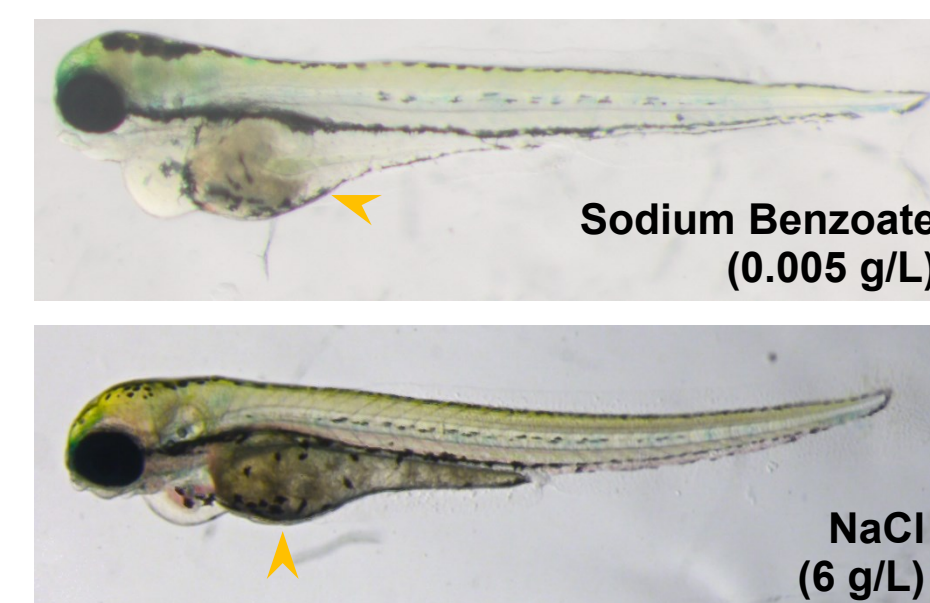
Hatching delay and protease activities

C. sappan extract can prevent hatching in multiple embryos, even inhibiting pronase (a protease mixture for dechoriation) activity [2]. Literature browsing shows several publications verifying *C. sappan* as a potent protease inhibitor, such as [4].



Darkened yolk suggests nephrotoxicity

The darkened yolk sac phenotype was found in several conditions, such as when exposed to sodium benzoate (SB) or at high salinity.



Interestingly, high salinity can damage kidney, and SB was recently found to be nephrotoxic. Other studies on renal damage also showed the darkened yolk phenotype – being previously unacknowledged [5].

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