

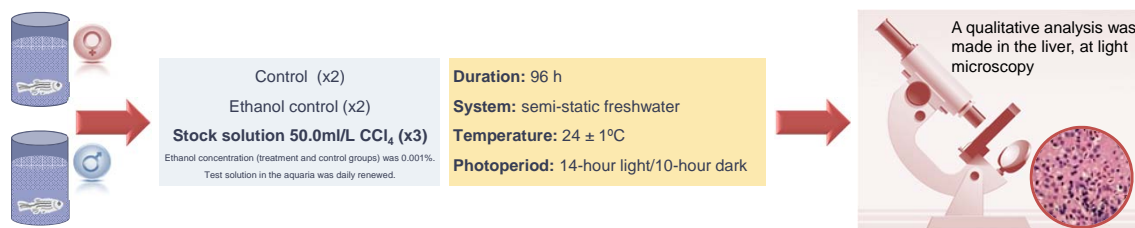
## NECROSIS INDUCED BY CARBON TETRACHLORIDE IN THE LIVER OF A MODEL ORGANISM: THE ZEBRAFISH (*DANIO RERIO*)

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### INTRODUCTION

Most acute and chronic liver diseases are characterized by an excessive rate of death of both hepatocytes and other types of liver cells. The generation of a fish model with a consistent pattern of hepatocellular necrosis is still lacking. The creation of such a model could contribute with new insights into the toxicological research. The aim of this study was, therefore, to analyze the liver histological changes in response to a high dose of CCl<sub>4</sub>.

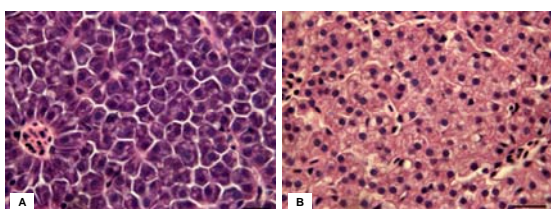
### MATERIAL AND METHODS



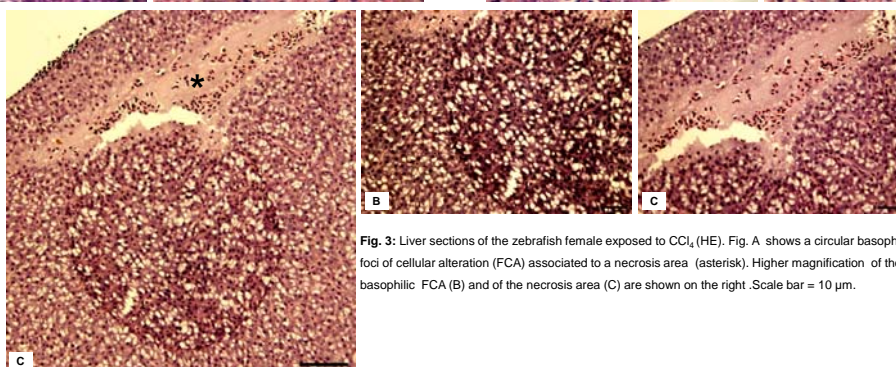
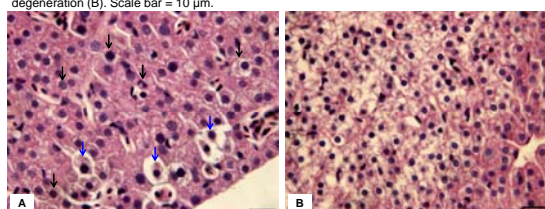
### RESULTS

Data point that the acute exposition to CCl<sub>4</sub> induced changes in hepatocytes of both male and female zebrafish when compared with the liver of the ones of the control group (Fig. 1A and 1B). Those morphologic changes do not appear to be specifically located within the liver and included: cell death, cellular and nuclear pleomorphism (Fig. 2A), hydropic vacuolation and ballooning degeneration (Fig. 2B). Those changes assumed higher expression in the female liver, where perfectly defined circular foci of basophilic hepatocytes (Fig. 3) were exclusively found and in some cases associated to a necrosis area (Fig. 3C).

**Fig. 1:** Female (A) and male (B) zebrafish liver sections of the control group (HE). The normal female hepatocytes are typically more basophilic than those of males. Scale bar = 10 µm.



**Fig. 2:** Male zebrafish liver sections of the experimental group (HE). CCl<sub>4</sub> induced single cell death (A – blue arrows) and cellular/nuclear pleomorphism (A – black arrows) and ballooning degeneration (B). Scale bar = 10 µm.



**Fig. 3:** Liver sections of the zebrafish female exposed to CCl<sub>4</sub> (HE). Fig. A shows a circular basophilic foci of cellular alteration (FCA) associated to a necrosis area (asterisk). Higher magnification of the basophilic FCA (B) and of the necrosis area (C) are shown on the right. Scale bar = 10 µm.

### CONCLUSION

Data showed that CCl<sub>4</sub> induced necrosis in the zebrafish liver in a random way. We now need to confirm the accuracy and reproducibility of this result, using both qualitative and quantitative approaches. We also intend to develop a liver dose-response regarding different CCl<sub>4</sub> concentrations. Herein, liver impacts of this toxicant varied with sex, therefore highlighting the importance of establishing different histopathologic endpoints for males and females in further toxicological studies. This is a very interesting result because of its biomedical and aquatic environmental implications, and consequently further investigation is warrant to understand the functional mechanisms behind the sex-related toxicity differences.

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