Metformin as a Novel Method for Polychlorinated Biphenyl Induced Non-alcoholic Fatty Liver Disease Remediation in Danio rerio as a Model for Human Livers

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Non-alcoholic fatty liver disease has become a prevalent issue and today, over 80 million people in the U.S. are affected. NAFLD starts with the accumulation of lipids droplets in the liver contributing to hepatic steatosis which can progress to nonalcoholic steatohepatitis or hepatocellular carcinoma. Persistent organic pollutants like polychlorinated biphenyls may induce and/or progress the disease. In hepatocytes, PCB126 decreases ß-oxidation in the peroxisomes which can lead to lipid accumulation. Metformin, a type-II diabetes drug, is able to suppress de novo lipogenesis and increase fatty acid oxidation, leading to decreased lipid accumulation. This study investigated the ability of Metformin to suppress lipid accumulation induced by PCBs. This study used Danio rerio, zebrafish, as a model due to lipid metabolism pathway conservation between mammals and fish. The zebrafish were fed with lipid-rich egg yolk diets in order to induce lipid accumulation in the liver. There were four treatment groups including control, Metformin treated at 10 uM, PCB A1254 treated at .1 ppm, and a group treated with both. There were two rounds of testing to mimic how exposure to the pollutant occurs in the environment. In the first, the zebrafish were exposed to the treatments as embryos and then exposed again to PCBs through their diets. In the second, the PCBs were added solely to the food and were exposed to Metformin after the embryonic stage. The diet was given twice daily for 11 days starting at 6 days post fertilization. The zebrafish were then fixed in 4% paraformaldehyde and stained with Oil-Red-O lipophilic dye. The zebrafish were imaged using a confocal microscope and volume of lipid droplet accumulation was analyzed using Image J software.

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