Identifying Negative Control Chemicals for Use in Larval Zebrafish Behavior Assays

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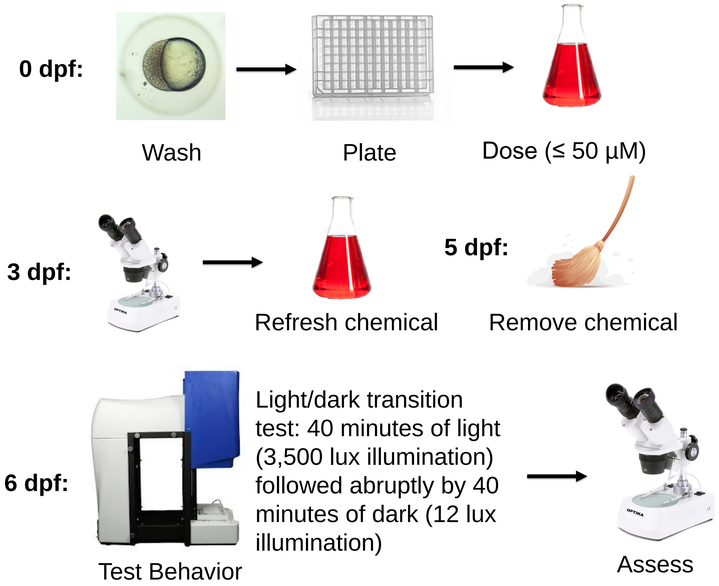
Background

- We assess the developmental neurotoxicity potential of chemicals using a medium-throughput, larval zebrafish screening assay which measures zebrafish locomotor behavior in response to visual stimuli.
- Sparse research has been done to identify chemicals that can serve as reliable negative controls in a larval zebrafish behavioral assay.
- Positive and negative control compounds allow researchers to measure the sensitivity and specificity of their assays.
- Martin and coworkers (PMID: 35908584) identified 9 candidate, negative control chemicals for developmental neurotoxicity testing based on literature reporting no developmental neurotoxicity in mammals[1].
- **Purpose:** Identify negative control chemicals for use in larval zebrafish locomotor assays.

Methods

Step 1: Assess the lethality and teratogenic potential of each chemical by performing a range-finding developmental toxicity study with a maximum exposure concentration of 100 µM.

Step 2: Using non-developmentally toxic exposure levels of each chemical, perform locomotor behavior assay at 6 days post fertilization (6 dpf).

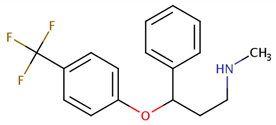


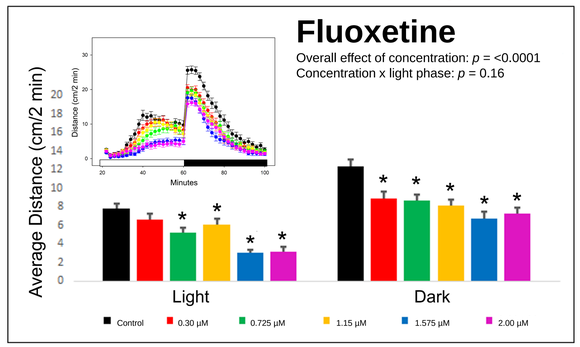
[1]Martin MM, Baker NC, Boyes WK, Carstens KE, Culbreth ME, Gilbert ME, Harrill JA, Nyffeler J, Padilla S, Friedman KP, Shafer TJ. An expert-driven literature review of "negative" chemicals for developmental neurotoxicity (DNT) *in vitro* assay evaluation. Neurotoxicol Teratol. 2022 Sep-Oct;93:107117. doi: 10.1016/j.ntt.2022.107117. Epub 2022 Jul 29. PMID: 35908584.

Results: All Chemicals Tested are Potential Negative Controls for Larval Zebrafish Behavioral Assays

Positive Control

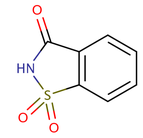
Antidepressant Drug

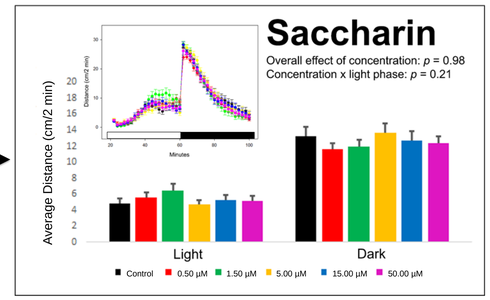




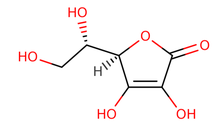
VS.

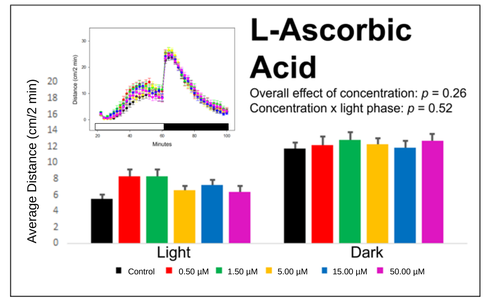
Sweetener





Vitamin C





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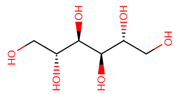
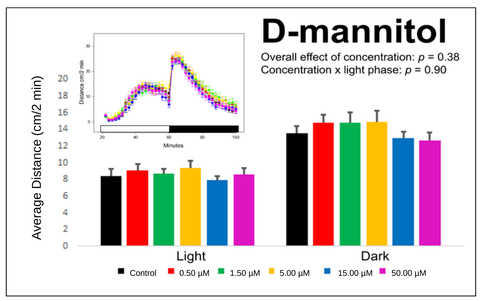
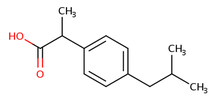
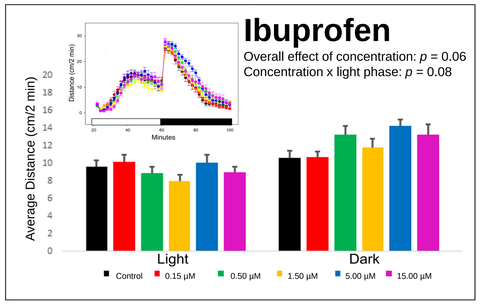


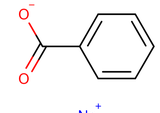


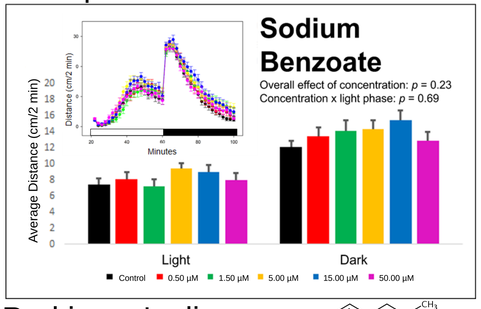
Nonsteroidal anti-inflammatory drug





Food preservative





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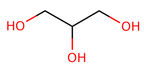
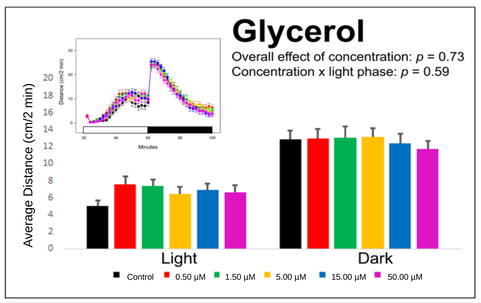
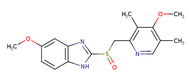
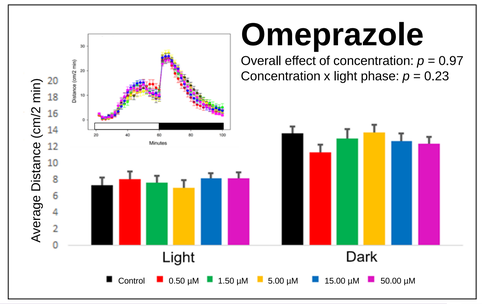


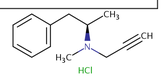


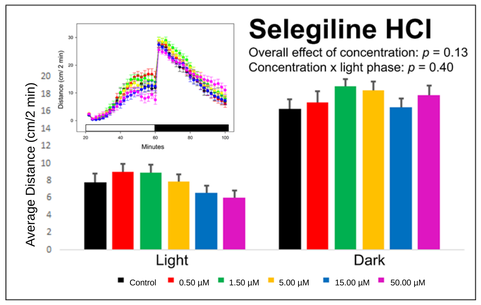
Heartburn treatment





Parkinson's disease treatment





Further Research

- Continue to identify more chemicals that could serve as negative controls for the larval zebrafish locomotor assay and potentially other behavioral assays.
- Incorporate these negative chemicals in chemical libraries to improve sensitivity and specificity of screening for developmental neurotoxicity.

Acknowledgements

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