An educational expedition from the shores of Lake Superior to central Texas

Gavin Saari
PhD Candidate Baylor University
March 9, 2018
Bachelor of Science

Biology Major
Chemistry Minor
Core/Elective Classes

- Genetics
- Ecology
- Cell Biology
- Limnology
- Animal Physiology
- Ichthyology
- Fish Population Ecology and Management

- General Chemistry I
- General Chemistry II
- Organic Chemistry I and II
- Spectroscopy
- Water Chemistry
Core/Elective Classes

Genetics
Ecology
Cell Biology
Limnology
Animal Physiology
Ichthyology
Fish Population Ecology and Management

General Chemistry I
General Chemistry II
Organic Chemistry I and II
Spectroscopy
Water Chemistry

58-foot all-steel retired tug boat
Research equipment
Hydraulic sediment dredge and fish trawling
Lake Superior Research Institute

The Lake Superior Research Institute (LSRI) was created in 1967 and formally recognized by the University of Wisconsin’s Board of Regents in 1969. LSRI's mission is to conduct environmental research and provide services that directly benefit the people, industries, and natural resources of the Upper Midwest, the Great Lakes Region, and beyond; provide non-traditional learning and applied research opportunities for undergraduate students; and foster environmental education and outreach in the Twin Ports and surrounding communities.

Expertise

- Analytical chemistry
- Aquatic invasive species monitoring and outreach
- Benthic and zooplankton taxonomy
- Habitat restoration
- Microbiology
- Sediment and aquatic toxicology
- Quality assurance and data management
Lake Superior Research Institute (LSRI)

General lab procedures/techniques
Standard Operating Procedures (SOPs)
Culturing standard model organism
Reference toxicity tests (KCl)- healthy organisms?

STANDARD OPERATING PROCEDURE
CULTURING THE CLADOCERANS, Daphnia magna AND Ceriodaphnia dubia

SOP Written by Christine Polkinghorn
Title: Assistant Researcher
Date: 2 December 2010

Reviewed and Approved by Matthew TanEyck
Title: Associate Researcher
Date: 2 December 2010

Clearer For Issue by Kelsey Prihoda
Title: Quality Assurance/Quality Control Manager
Date: 2 December 2010

DISTRIBUTION LIST:
LSRI Hatchery staff and students, quality assurance staff, LSRI director, and any individual responsible for culturing Daphnia magna and/or Ceriodaphnia dubia.
Lake Superior Research Institute- model organisms

Green Algae- *Selenastrum capricornutum*

Zooplankton- *Brachionus calyciflorus*

https://www.youtube.com/watch?v=FRZ64_lZf_8
Lake Superior Research Institute- model organisms

- Waterflea- *Daphnia magna*
- Waterflea- *Ceriodaphnia dubia*
- Zooplankton- *Eucyclops sp*
- Freshwater shrimp- *Hyalella Azteca*
- Aquatic worm- *Lumbriculus variegatus*
- Bloodworm- *Chironomus dilutus*
Lake Superior Research Institute- Toxicity Testing

STANDARD OPERATING PROCEDURE
CONDUCTING A 28-DAY BIOACCUMULATION SEDIMENT TOXICITY TEST WITH THE OLIGOCHAETE, LUMBRICULUS VARIEGATUS

SOP Written by Christine Polkinghorne
Reviewed and Approved by Matthew TenEyck
Cleared For Issue by Kelsey Prihoda

Signature: Christine N. Polkinghorne
Title: Associate Researcher
Date: 30-Oct-2015

Signature: Matthew TenEyck
Title: Assistant Scientist
Date: 30-Oct-2015

Signature: Kelsey Prihoda
Title: Quality Assurance Manager
Date: 16-Nov-2015
Freshwater Ballast Testing Facility and Other Projects

Ballast Water Treatment
• Four 50,000 gl tanks
• Follow ships and sample ballast water at ports

Chemical monitoring in fish tissue, wild rice, and mussels

Effects of Pollutants to aquatic organisms

Survey of native and invasive plants
U.S. Environmental Protection Agency (EPA) Mission: to protect human health and the environment

Mid-Continent Ecology Division (MED)- National Health and Environmental Effects Research Laboratory (Duluth, MN)

- Forecast the effects of pollutants on the integrity of watersheds and freshwater ecosystems
- Characterize adverse outcome pathways of toxic exposure at multiple scales and levels of biological organization
- Link environmental condition to human health and well being
1990’s - scientists proposed that certain chemicals might be disrupting the endocrine systems of humans and wildlife


What should we do? Screen pesticide chemicals for potential produced effects similar to those by the female hormones (estrogen) in humans and screen other chemicals for all types of endocrine effects
ToxCast™ - 2007- High Throughput Assays (HTA) and Computational Tools

Expose cells and proteins to chemicals…changes in biological activity?
~1800 chemicals and ~700 HTAs

Toxicology Testing in the 21st Century (Tox21)

Collaboration between EPA, NIH, and FDA
10,000 chemicals; 50 quantitative HTAs

Effects of chemicals on cellular, molecular, and biochemical processes
Biologist - Student Contractor for the U.S. EPA

Use of Trout Liver Slices To Enhance Mechanistic Interpretation of Estrogen Receptor Binding for Cost-Effective Prioritization of Chemicals within Large Inventories

PATRICIA K. SCHMIEDER,†‡
MARK A. TAPPER,† JEFFREY S. DENNY,†
RICHARD C. KOLANCZYK,†
BARBARA R. SHEEDY,†
TALA R. HENRY,‡ AND
GILMAN D. VEITH§

Waterborne and sediment toxicity of fluoxetine to select organisms

Short communication

Aquatic ecotoxicology of fluoxetine

Fish on Prozac (and Zoloft): Ten years later

Bryan W. Brooks

Department of Environmental Science, Institute of Biomedical Studies, Center for Reservoir and Aquatic Systems Research, Baylor University, Waco, TX, USA
By 2050:

- World population reaches 9.6 bil (UN)
- 70% of all people will live in urban areas (UN)
- Consumer product and other chemical use is concentrated in cities…
The World's Megacities Are Set for Major Growth

Population growth of the world's top 15 megacities (millions, 2011-2025)

- Mexico City: 20m (25%), 25m (+25%)
- New York: 20m (20%), 24m (+20%)
- New Delhi: 23m (43%), 33m (+43%)
- Beijing: 16m (44%), 23m (+44%)
- Tokyo: 37m (5%), 39m (+5%)
- Shanghai: 20m (40%), 28m (+40%)
- Manila: 12m (33%), 16m (+33%)
- Sao Paulo: 20m (20%), 23m (+15%)
- Rio de Janeiro: 12m (17%), 14m (+17%)
- Buenos Aires: 14m (14%), 16m (+14%)
- Mumbai: 20m (35%), 27m (+35%)
- Dhaka: 15m (53%), 23m (+53%)

~ 20%
~ 40%

* Including metropolitan areas
Source: UN Population Division, World Economic Forum

Photo Credit: https://www.statista.com
The Urban Water Cycle is the New Normal

Dallas

John Bunker Sands Wetland

Wastewater--effluent-dominated streams as ecosystem-management tools in a drier climate

Richard G. Lothry, David L. Seilick, Megan H. Plumio, David Austin, and Vincent H. Rush
The Urban Water Cycle is the New Normal

River base flows are increasingly dominated/dependent upon wastewater treatment plant discharges
The Urban Water Cycle is the New Normal

River base flows are increasingly dominated/dependent upon wastewater treatment plant discharges
High Levels of endocrine pollutants in US streams during low flow due to insufficient wastewater dilution
Are they present in the environment?
Physiochemical characteristics - pharmaceuticals

\( K_{ow} \) - Octanol-water partition coefficient

Water solubility

\( t_{1/2} \) - Clearance and elimination

\( pKa \) – dissociation constant, 50:50% neutral and ionized)

Bioconcentration Factor (BCF) = \([\text{tissue}] / [\text{water}]\)
- Exposure via water across gills

Bioaccumulation Factor (BAF) = \([\text{tissue}] / [\text{diet}]\)
- Exposure via water and diet or all routes

Nichols et al. 2015
Physiochemical characteristics - pharmaceuticals

$K_{ow}$ - Octanol-water partition coefficient

Water solubility

$t_{\frac{1}{2}}$ - Clearance and elimination

$pK_a$ – dissociation constant, 50:50% neutral and ionized

Diphenhydramine

Bioconcentration Factor (BCF) = $\frac{\text{[tissue]}}{\text{[water]}}$
- Exposure via water across gills

Bioaccumulation Factor (BAF) = $\frac{\text{[tissue]}}{\text{[diet]}}$
- Exposure via water and diet or all routes

Nichols et al. 2015
Enantiospecific sublethal effects of the antidepressant fluoxetine to a model aquatic vertebrate and invertebrate

Jacob K. Stanley a,b,* , Alejandro J. Ramírez a,c , C. Kevin Chambliss a,c , Bryan W. Brooks a,d

* Center for Reservoir and Aquatic Systems Research, Baylor University, One Bear Place # 97266, Waco, TX 76798-7266, United States
b Department of Biology, Baylor University, One Bear Place # 97266, Waco, TX 76798-7266, United States
c Department of Chemistry and Biochemistry, Baylor University, One Bear Place # 97266, Waco, TX 76798-7266, United States
d Department of Environmental Studies, Baylor University, One Bear Place # 97266, Waco, TX 76798-7266, United States

Received 13 November 2006; received in revised form 19 April 2007; accepted 29 April 2007
Available online 19 June 2007

EFFECTS OF THE ANTIHISTAMINE DIPHENHYDRAMINE ON SELECTED AQUATIC ORGANISMS

JASON P. BERNINGER,†† BOWEN DUL ‡‡ KRISTIN A. CONNORS ‡‡ STEPHANIE A. EYCHESON ‡‡ MARK A. KOLMEN ‡‡ KRISTA N. PROSSER ‡‡ THEODORE W. VALENTI JR. ‡‡ C. KEVIN CHAMBLISS ‡‡§ and BRYAN W. BROOKS ‡‡§

† Institute of Biomedical Studies, Baylor University, Waco, Texas, USA
‡ Institute of Ecological, Earth, and Environmental Sciences, Baylor University, Waco, Texas, USA
§ Department of Environmental Science, Center for Reservoir and Aquatic Systems Research Baylor University, Waco, Texas, USA

(Submitted 2 February 2011; Returned for Revision 6 April 2011; Accepted 11 May 2011)
Effects in organisms?

Enantiospecific sublethal effects of the antidepressant fluoxetine to a model aquatic vertebrate and invertebrate

Jacob K. Stanley a,b,*, Alejandro J. Ramirez a,c, C. Kevin Chambliss a,c, Bryan W. Brooks a,d

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Jason P. Berninger,†‡ Bowen Du,§ Kristin A. Connors,‡ Stephanie A. Eytcheson,§ Mark A. Kolkmeier,§ Krista N. Prosser,§ Theodore W. Valenti Jr.,§ C. Kevin Chambliss,‡§ and Bryan W. Brooks‡¶

† Institute of Biomedical Studies, Baylor University, Waco, Texas, USA
‡ Institute of Ecological, Earth, and Environmental Sciences, Baylor University, Waco, Texas, USA
§ Department of Environmental Science, Center for Reservoir and Aquatic Systems Research, Baylor University, Waco, Texas, USA
¶ Department of Chemistry and Biochemistry, Baylor University, Waco, Texas, USA

(Submitted 2 February 2011; Returned for Revision 6 April 2011; Accepted 11 May 2011)
A Theoretical Model for Utilizing Mammalian Pharmacology and Safety Data to Prioritize Potential Impacts of Human Pharmaceuticals to Fish

2003

D. B. Huggett, J. C. Cook, J. F. Ericson, and R. T. Williams
Pfizer Global Research and Development, Groton, Connecticut, USA

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<td>Danio rerio</td>
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<tr>
<td>teleostei</td>
<td>Gobius morhua</td>
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<td>TRUE (68.6 %)</td>
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<tr>
<td>teleostei</td>
<td>Gasterosteus aculeatus</td>
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<tr>
<td>teleostei</td>
<td>Oreochromis niloticus</td>
<td>8128</td>
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<td>Oryzias latipes</td>
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<tr>
<td>teleostei</td>
<td>Poecilia formosa</td>
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<tr>
<td>teleostei</td>
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<td>Takifugu rubripes</td>
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<td>Xiphophorus maculatus</td>
<td>8083</td>
<td>inhibitor</td>
<td>TRUE (66 %)</td>
</tr>
</tbody>
</table>
# A Theoretical Model for Utilizing Mammalian Pharmacology and Safety Data to Prioritize Potential Impacts of Human Pharmaceuticals to Fish

2003

D. B. Huggett, J. C. Cook, J. F. Ericson, and R. T. Williams
Pfizer Global Research and Development, Groton, Connecticut, USA

## ECOdrug

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<tr>
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<td>13</td>
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<td>99883</td>
<td>TRUE (65.6 %)</td>
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<td>14</td>
<td>Xiphostomus maculatus</td>
<td></td>
<td>8083</td>
<td>TRUE (66 %)</td>
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</tbody>
</table>

Diagram:

- Homosapins
- Mammalia
- Amphibia
- Vertebrata
- Teleostei
- Hexapoda
- Crustacea
- Nematoda
- Mollusca
- Echinodermata
- Chordata
- Tunicata
- Bilateria
- Metazoa
- Chlorophyta
- Embryophyta
- Eukaryote
A Theoretical Model for Utilizing Mammalian Pharmacology and Safety Data to Prioritize Potential Impacts of Human Pharmaceuticals to Fish

D. B. Huggett, J. C. Cook, J. F. Ericson, and R. T. Williams
Pfizer Global Research and Development, Groton, Connecticut, USA
Fish plasma modeling

\[ C_{\text{min}} \text{ – minimum human therapeutic plasma dose} \]

\[ P_{BW} = \frac{\text{Blood:Water partition coefficient}}{} \]

\[ \text{THV} = \frac{C_{\text{max}}}{P_{BW}} \]

Diltiazem THV = 150 ng/l (pH: 8.3)

Based on adult rainbow trout experiments and uptake modeling.

**Therapeutic Hazard Value (THV)**

- Predicted water concentration expected to cause a human therapeutic level of a pharmaceutical in fish plasma

Physiochemical Properties:

- M.W. = 414.518
- \( \log K_{ow} = 2.73 - 4.73 \)
- \( pKa = 8.18-8.94 \)
- \( V_D = \sim 305 \text{ L (humans)} \)
- \( T_{1/2} = 3.0-4.5 \text{ hrs (humans)} \)
- \( C_{\text{min-max}} = 0.03 \) and \( 0.13 \text{ ng/ml} \)
Antidepressant uptake, CNS binding, anxiety behavior

Valenti et al. 2012
PREDICTED AND OBSERVED THERAPEUTIC DOSE EXCEEDANCES OF IONIZABLE PHARMACEUTICALS IN FISH PLASMA FROM URBAN COASTAL SYSTEMS

W. CASAN SCOTT, † BOWEN DU, † SAMUEL P. HADDAD, † CHRISTOPHER S. BREED, † GAVIN N. SAARI, † MARTIN KELLY, †
LINDA BROACH, † C. KEVIN CHAMBLISS, †§ and BRYAN W. BROOKS**†
†Department of Environmental Science, Center for Reservoir and Aquatic Systems Research, Baylor University, Waco, Texas, USA
‡Texas Commission on Environmental Quality, Houston, Texas, USA
§Department of Chemistry and Biochemistry, Baylor University, Waco, Texas, USA

(Submitted 26 June 2015; Returned for Revision 20 August 2015; Accepted 6 September 2015)
High blood pressure medication

Heart medication global occurrence?
Read across- mammals to fish?
Exposure across multiple life stages

Nichols et al, 2015; Incardona et al, 2004; 2011
U.S. EPA standard toxicity studies
Videomicroscopy

Contractility/Fractional Shortening
• \((\text{end-diastolic diameter} - \text{end-systolic diameter}) / \text{end diastolic diameter} \times 100\)

Chamber volume (prolate spheroid)
• \(\frac{4}{3}\pi \times a \times b^2\)

Stroke volume
• \(\text{end-diastolic volume} - \text{end-systolic volume}\)

Ejection fraction
• \(\frac{\text{stroke volume}}{\text{end-diastolic volume}}\)

Incardona et al, 2004; 2011
Control
Effects on swimming performance at human therapeutic levels?
Many people to thank…Questions?