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Mechanistic toxicology at Simmons College: A model course for teaching toxicology concepts to chemistry students

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The Green Chemistry Commitment
TRANSFORMING CHEMISTRY EDUCATION

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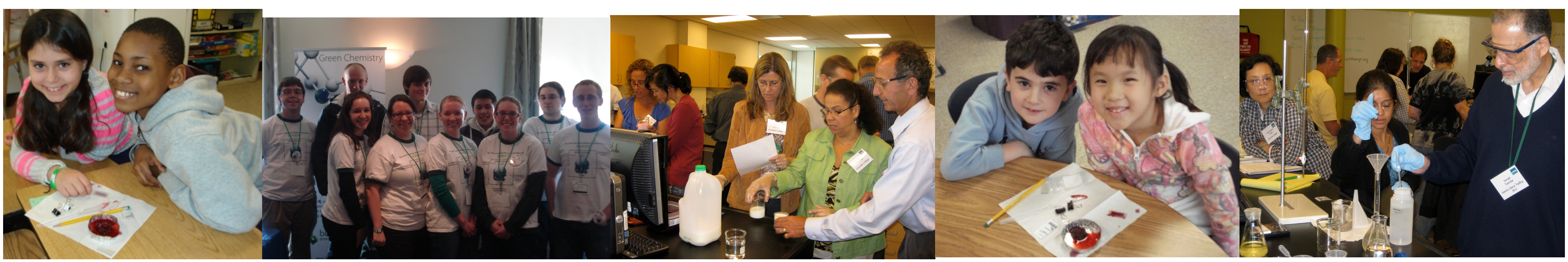
Non-profit organization founded in 2007 by Dr. John Warner and Dr. Amy Cannon, located north of Boston (Wilmington, MA).

<u>Mission:</u> Beyond Benign is dedicated to providing future and current scientists, educators and citizens with the tools to teach and learn about green chemistry in order to create a sustainable future.

<u>Vision:</u> Beyond Benign's vision is to revolutionize the way chemistry is taught to better prepare students to engage with their world while connecting chemistry, human health and the environment.



www.beyondbenign.org

BB Programs

K-12 Curriculum & Training

- Green Chemistry curriculum
- Professional development
  - Teacher training institutes/workshops
  - On-line courses
  - Lead Teacher program

Community Engagement

- College Student Fellows
- On-site field trips
- Outreach experiences and events

Green Chemistry Commitment

- Green Chemistry Education webinar series
- GC resources for higher education
- Toxicology in the chemistry curriculum

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The Green Chemistry Commitment

The Green Chemistry Student Learning Objectives

Signing institutions agree that upon graduation, all chemistry majors should have proficiency in the following essential **green chemistry competencies**:

- **Theory:** Have a working knowledge of the twelve principles of Green Chemistry
- **Toxicology**: Have an understanding of the principles of toxicology, the molecular mechanisms of how chemicals affect human health and the environment, and the resources to identify and assess molecular hazards
- **Laboratory Skills**: Possess the ability to assess chemical products and processes and design greener alternatives when appropriate
- **Application**: Be prepared to serve society in their professional capacity as scientists and professionals through the articulation, evaluation and employment of methods and chemicals that are benign for human health and the environment

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Toxicology is being "tested" in courses and programs

- Simmons College
  - Mechanistic Toxicology course for majors
- South Dakota State University
  - Toxicology course for majors
- University of California, Berkeley
  - Graduate course
- Grand Valley State University
  - Seminar series
- St. Catherine University
  - Seminar series for junior/senior seminar series
- Salem State University
  - Chemical Toxicology course in development
- SUNY Fredonia
  - Creating a course within the next two years
- Wittenberg University
  - Toxicology course and safety approach to integrating concepts

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The Twelve Principles of Green Chemistry

1. Prevention. It is better to prevent waste than to treat or clean up waste after it is formed.

2. Atom Economy. Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.

3. Less Hazardous Chemical Synthesis. Whenever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment.

4. Designing Safer Chemicals. Chemical products should be designed to preserve efficacy of the function while reducing toxicity.

5. Safer Solvents and Auxiliaries. The use of auxiliary substances (solvents, separation agents, etc.) should be made unnecessary whenever possible and, when used, innocuous.

6. Design for Energy Efficiency. Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure.

7. Use of Renewable Feedstocks. A raw material or feedstock should be renewable rather than depleting whenever technically and economically practical.

8. Reduce Derivatives. Unnecessary derivatization (blocking group, protection/deprotection, temporary modification of physical/chemical processes) should be avoided whenever possible .

9. Catalysis. Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.

10. Design for Degradation. Chemical products should be designed so that at the end of their function they do not persist in the environment and instead break down into innocuous degradation products.

11. Real-time Analysis for Pollution Prevention. Analytical methodologies need to be further developed to allow for real-time in-process monitoring and control prior to the formation of hazardous substances.

12. Inherently Safer Chemistry for Accident Prevention. Substance and the form of a substance used in a chemical process should be chosen so as to minimize the potential for chemical accidents, including releases, explosions, and fires.

Simmons College

- Department of Chemistry
- Chemistry 342: Mechanistic Toxicology and Environmental Health Sciences for Chemists
- Fall 2011, Spring 2014, Spring 2016
- Elective course for majors
- Pre-requisite: Organic chemistry, biochemistry (recommended)

Dr. Rich Gurney

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Chemistry 342: Mechanistic Toxicology

Learning Outcomes:

- Understanding the field of green chemistry.
- Understand how green chemistry can be applied to diverse set of disciplines and industry sectors.
- Learn about field of environmental health sciences and its overlap and differences from classical toxicology.
- Understand fundamental toxicological mechanisms and tools for reducing hazard through molecular design.
- Understand ecological toxicology and how chemicals impact ecosystems and the environment.

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Chemistry 342: Mechanistic Toxicology

Lecture Topics:

- Green Chemistry
- Biochemistry Review (optional)
- History and Introduction of Toxicology
- Principles of Toxicology
- Understanding hazard endpoints
- Toxicokinetics and Toxicodynamics
- Epidemiology
- Ozone Depletion, Climate Change and Energy
- Design for Biodegradability
  - Persistence and Bioaccumulation
- Predictive Tools for Reduced Molecular Hazard
- Understanding Structure Activity Relationships

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Guest Lectures

Mary Butow, UMass Lowell Toxic Use Reduction Institute

Environmental Health and Safety Library Guide

Beyond the MSDS: Finding Information to Inform Decision Making about Chemical Hazards

What does “hazardous” mean?

Where can I go to find credible data?

http://guides.turi.org/beyondmsds

QCAT: Quick Chemical Assessment Tool

QCAT:

- Developed by Washington State Dept. of Ecology
- Based on GreenScreen® methodology, data sources and hazard endpoints
- 9 hazard endpoints

Key:
C = Carcinogenicity
M = Mutagenicity
R = Reproductive toxicity
D = Developmental toxicity
E = Endocrine activity
AT = Acute Mammalian toxicity
AA = Acute Aquatic toxicity
P = Persistence
B = Bioaccumulation

Initial Grade	**F**
Final Grade (data gaps)	N/A*

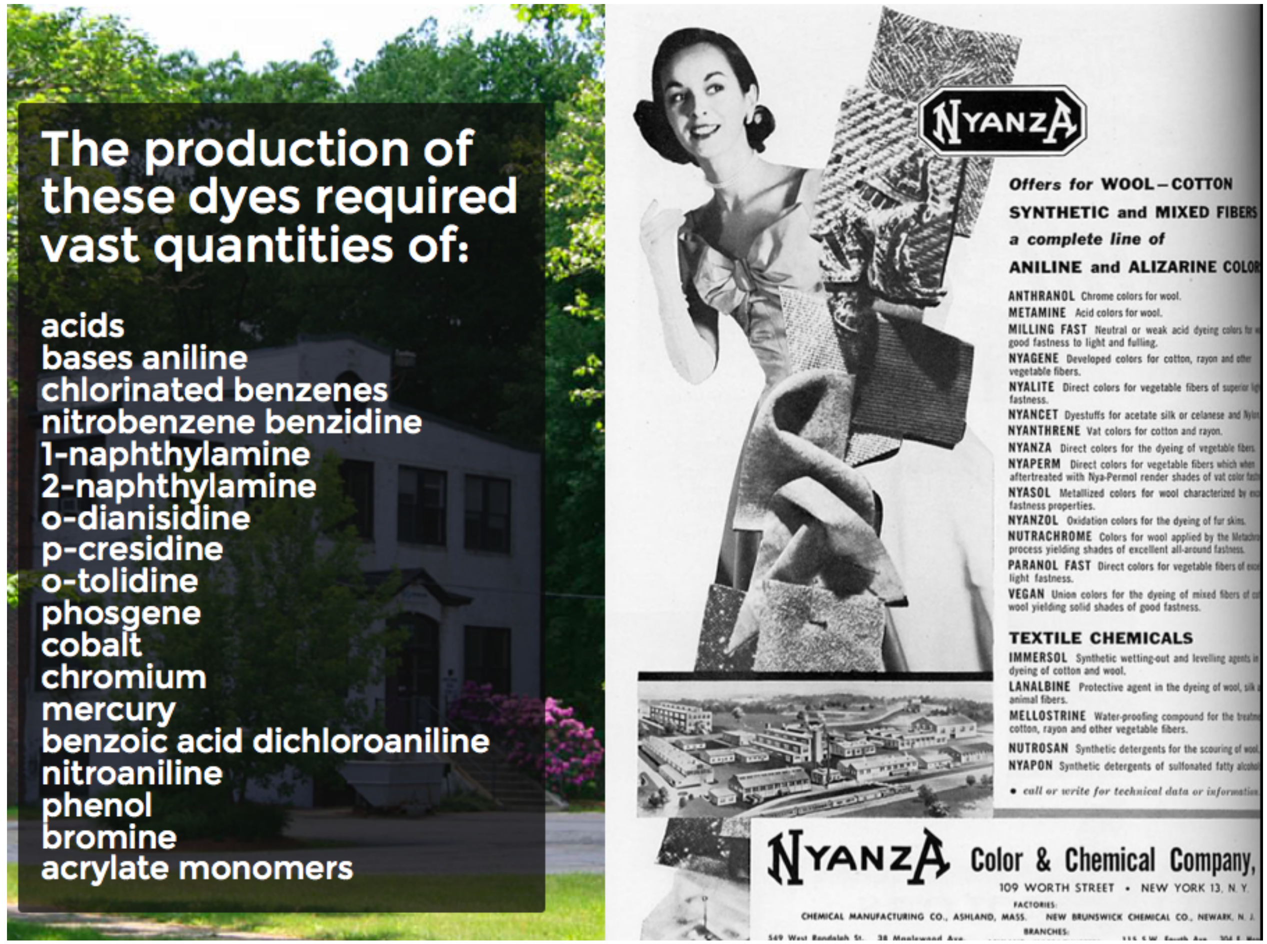
Human – Group 1 (chronic)					Human – Group 2 (acute)							Env. Health			Fate		Physical	
C	**M**	**R**	**D**	**E**	**AT**	**ST**	**N**	**SnS**	**SnR**	**Irs**	**IrE**	**AA**	**CA**	**Eo**	**P**	**B**	**Ex**	**F**
DG	DG	H	H	DG	M	X	X	X	X	X	X	L	X	X	H	L	X	X

Guest Lectures

Dr. Richard Clapp, BU School of Public Health
Molly Jacobs, University of Massachusetts Lowell

Understanding Epidemiology and how data can help us predict how chemicals impact human health

[**https://www.youtube.com/watch?v=C8jTVJyYwak**](https://www.youtube.com/watch?v=C8jTVJyYwak)

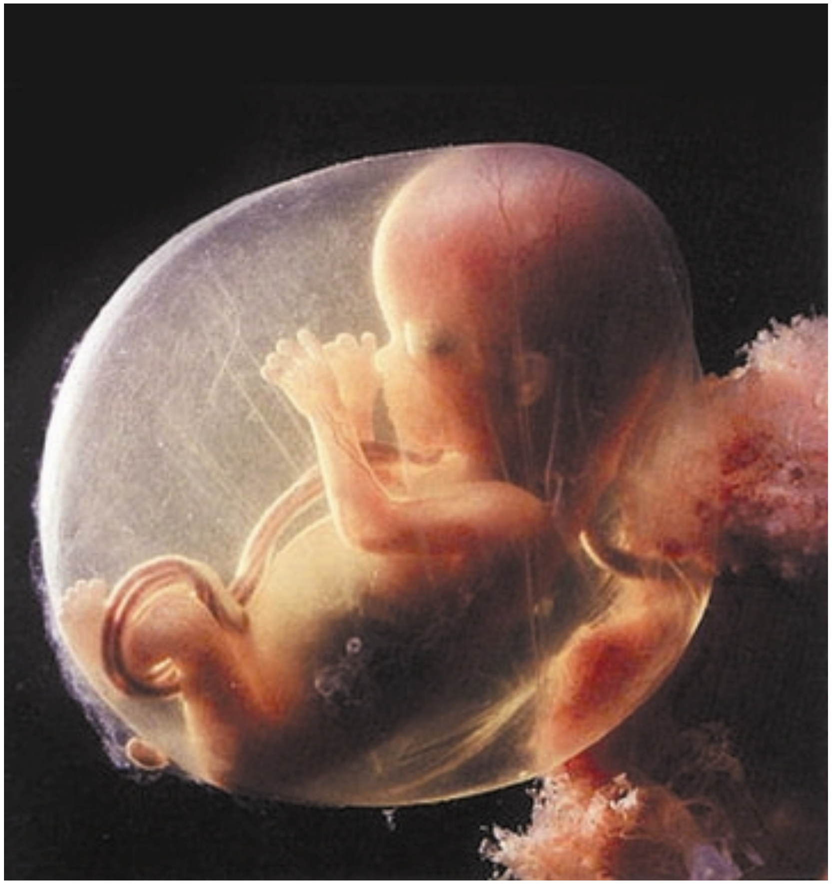


Nyanza Color & Chemical Company, Ashland, MA
Notice of high rates of a rare type of sarcoma: study on people who were exposed in the 1960's and 1970's (students walking to and from school)

Guest Lectures

Dr. Laura Vandenberg,
University of Mass Amherst

Endocrine System,
Endocrine Disruption and
Low Dose Effects



“From the day of conception until an individual is born or hatched, the development of each stage of life is fully under the control of hormones.

Changes that happen during development are far less reversible [than those occurring in an adult]; you can't go back and rewire the brain”.

-Theo Colborn, zoologist, writer

Assignments

1. Environmental and health hazards
2. Hazard Evaluation
3. Toxicokinetics
   – Toxicology Tutor II: **https://sis.nlm.nih.gov/enviro/toxtutor.html**
4. Ozone depletion and global warming
5. Final presentations
   – Disease or environmental issue
   – Chemical hazards
   – Green Chemistry solutions

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Toxicology Tutorials

- NIH NLM: Free tutorials available on-line
  - Basic Principles
  - Toxicokinetics
  - Cellular Toxicology
- Toxicokinetics tutorial
  - Connecting chemical and physical properties to absorption, distribution, metabolism, and excretion of chemicals in the body
  - i.e., pH, MW, lipophilicity, water solubility

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Rules of thumb for biodegradability

- Features that increase resistance to aerobic biodegradation:
  - Halogens (especially chlorine and fluorine and if more than 3 in a molecule) (Electron withdrawing groups on a phenyl ring makes the ring less susceptible to attack)
  - Chain branching if extensive (quaternary C's problematic)
  - Tertiary amine, nitro, nitroso, azo, and arylamino groups
  - Polycyclic residues (ex., PAHs) (especially with more than 3 rings)
  - Heterocyclic residues (ex., imidazole)
  - Aliphatic ether bonds (except in ethoxylates)

Chem. Reviews, 2007, Vol. 107, No. 6, 2207-2227

Rules of thumb for biodegradability

Molecular features that generally increase aerobic biodegradability

- Groups susceptible to enzymatic hydrolysis (esters, including phosphate esters) and amides
- Oxygen atoms in the form of hydroxyl, aldehyde, or carboxylic acid groups, ketones (not ether, with the exception of ethoxylate groups)
- Unsubstituted linear alkyl chains (especially ≥ 4 carbons) and phenyl rings

Chem. Reviews, 2007, Vol. 107, No. 6, 2207-2227

Biodegradability and toxicity

Advice	Toxicity endpoint/objective	Effect on biodegradability
Increase MW to >1000	Lower aquatic toxicity	Decrease
Reduce water solubility to <1 ug/L	Lower aquatic toxicity	Decreases availability to biodegradation enzymes
Increase steric hindrance at active site	Lower aquatic toxicity	Decreases availability to biodegradation enzymes
Add bulky groups to or ortho to amines	Reduce oncogenicity concern for aromatic amines	Decreases availability to biodegradation enzymes
Add hydrophilic groups, for example, sulfonate or COOH	Reduce oncogenicity concern (enhance excretion)	May increase or decrease depending on group

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Next steps

- Development of modules that can be placed on-line for faculty to access
- Recording lectures and posting materials

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Thank you!

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