**Lesson Plan: Lecture 23**

**Molecular Toxicology**

**Description**

This lecture introduces Absorption, Distribution, Metabolism, and Excretion (ADME) concepts and how chemists can take advantage of physicochemical parameters like logP, molecular weight, and vapor pressure to redesign molecules that won’t absorb into the body, limit distribution, and facilitate metabolism and excretion. These concepts are reinforced by an in-class exercise that explores potential absorption routes by benzene. The lecture also explores new approaches to hazard minimization through molecular design.

**Prior to Lecture**

Required Readings:

* Zimmerman, J. B., & Anastas, P. T. “Toward designing safer chemicals”; *Science,* 2015a, *347*(6219), 215-215. doi: 10.1126/science.aaa6736

<http://science.sciencemag.org/content/347/6219/215.full>

* Zimmerman, J. B., & Anastas, P. T.; “Toward substitution with no regrets”; *Science*, 2015b, 347(6227), 1198-1199. doi: 10.1126/science.aaa0812

<http://science.sciencemag.org/content/347/6227/1198.full>

Videos

* [Toxicology - ADME](https://youtu.be/v6sFdawERRU)

**Topics to Cover in Lecture**

* Absorption, Distribution, Metabolism, Excretion
* Characteristics of an ideal chemical
* Approaches to hazard minimization through design

**Class Exercise**

Class Exercise - Electrophilic Reactions in Toxicity (Optional)

Advanced exercise for those who want to correlate reaction mechanisms with toxicity. Electrophilic-Nucleophilic reactions are one of the most common reactions in biological systems that can initiate a toxicological effect. The electrophilic-nucleophilic reactions result in the covalent binding between an electrophile (a xenobiotic molecule) and an endogenous nucleophile. These mechanisms can lead to many different endpoints such as skin sensitization, acute and cytotoxicity or mutagenicity. This exercise challenges students to determine which of the given molecules will undergo the reaction leading to a toxic effect.

Please see Electrophilic Reactions in Toxicity for details.

Class Exercise - Module 8 ADME and Rational Chemical Design (Optional)

Additional exercise to test ADME understanding using example of caffeine and dimethyl sulfoxide. Exercise uses the same assumptions as in-class benzene example.

Please see ADME and Rational Chemical Design for details.