Frontiers of Food Toxicology

Food Toxicology

Instructor: Gregory Möller, Ph.D.
University of Idaho

Course of Study

- Introduction to Food Toxicology
- History of US Food Regulation
- Concepts of Toxicology
- Pesticide Residues in Food
- Dose-Response Relationships
- Absorption of Toxicants
- Distribution and Storage of Toxicants
- Biotransformation and Elimination of Toxicants
- Target Organ Toxicity

Course of Study

- Teratogenesis, Mutagenesis, and Carcinogenesis
- Food Allergy
- Food Intolerance and Metabolic Disorders
- Food Additive Safety Assessment
- Toxicology of Selected Food Additives
- Genetically Modified Organisms in Food
- Food Irradiation
- Natural Toxins in Plants and Fungi: The Ecological Biochemistry of Food
- Toxic Mold and Mycotoxins

Course of Study

- Marine Toxins in Food
- Naturally Occurring Toxicants as Etiologic Agents of Foodborne Disease
- Bacterial Toxigenesis
- Animal Drug Residues in Food

- Toxicants Formed During Food Processing
- Dioxin and Related Compounds in the Human Food Chain
- Risk Assessment of Pb and As in the Human Food Chain
- Mercury in the Human Food Chain

The Frontiers

- The use of an integrated effects (response spectrum) vs. the use of single effect.
- New approaches for examination of combinations or mixtures of chemicals.
  - e.g. Natural flavor complexes.
- Development of new biomarkers of intoxication.
- Development of surrogate animal models.
  - Lower organisms with shorter life cycles.
    - Amphibian models.

The Frontiers

- *In Silico* approaches (computer modeling and visualization).
  - Iterative, systems approaches.
- Toxico-genomics: DNA/RNA targets.
- Toxico-proteomics: protein targets.
- Toxico-metabonomics: dynamic multiparametric metabolic response.
- Increased understanding of molecular biology of cellular processes such as apoptosis.
  - Chemical stimulation of programmed cell death.

The Frontiers

- Bench Mark Dose vs. NOAEL/LOAEL
  - NOAEL/LOAEL x Uncertainty $\longrightarrow$ RfD

Bench Mark Dose (BMD)

- An alternative to the NOAEL/LOAEL approach.
- More quantitative way of deriving regulatory levels for health effects assumed to have a nonlinear (threshold-like) low dose–response relationship.
  - NOAELs and LOAELs are discrete study doses.
- BMDs model the DR curve in the range of the observable data.
- Then interpolate an estimate of the dose that corresponds to a particular level of response.
- BMDL = lower CL of BMD.

Bench Mark Dose (BMD)

- The BMD approach can be used for dose–response modeling of all types of chemical and physical agents and associated endpoints.
  - Regardless of the assumptions about low-dose linearity or nonlinearity.
- This is because dose–response modeling is done in the observable range and the BMD is typically related to a response rate near the lower end of the observable dose range.

Computing a Benchmark Dose

- Bench Mark Response (BMR) selected.
- Dose–response model fit to the data.
- Best-fitting model used to calculate the BMD.
- Confidence limits computed for the estimate.
-

Human RA: Hormonally Active Substances

- The fungicide Vinclozolin and its two metabolites are androgen antagonists.
- Produces adverse effects when administered during sexual differentiation in the fetus or around the time of puberty.
  - Alters sexual fn in adult male rats.
- Study examined the effects of exposure to vinclozolin around puberty on the male reproductive tract and serum hormone levels.

Human Risk Assessment: Vinclozolin

- Rat study benchmark doses were calculated for age at preputial separation (separation of the prepuce from the glans penis), epididymal weight, seminal vesicle weight, ventral prostate weight, and serum concentrations of testosterone and luteinizing hormone (LH).
- LH is synthesized and secreted by the pituitary gland.
- In the female, an LH surge triggers ovulation; in the male, LH stimulates production of testosterone.

Mean Serum Luteinizing Hormone (ng/ml)

- The solid line is the fitted DR curve.
- For this example, the BMD is the dose at which the mean of the response variable is expected to change by an amount equal to the standard deviation of the control group.

BMDs and Lower 95 % CL for Endpoints

- Most endpoints form a cluster with similar BMDs and overlaping CLs.
- Serum LH has a substantially lower BMD.

The Frontiers

- Non-human antimicrobial usage and antimicrobial resistance.
- Safety evaluation of GM foods.
- Low level exposure effects.
- Biotoxins in Molluscan Bivalves.
  - Maximum levels, analysis methods, geographic distribution, biotoxin forming marine phytoplankton.
- Mycotoxin prevention and control.
- Probabilistic risk assessment of food allergy.
  - Enhanced immune system knowledge.

Course Goals

- To provide a broad foundation of knowledge about the sources, pathways, receptors, and controls of toxicants in the human food chain.
- To assist students in achieving a high-level of understanding and interpretative capacity in food toxicology.
- To help develop critical thinking skills about the risks of foodborne toxicants.