

Molecular Mechanisms of Toxicology (MMD-997)

Credit Hours 3 (3-0)

Course Description

Molecular toxicology involves studying biophysics and biochemistry heavily as well as applying the knowledge in laboratory and environmental settings. It studies the effects of chemicals on living microscopic organisms. This form of toxicology examines both naturally occurring and synthetic chemicals. Also considered are the effects of genetic, physiologic and environmental factors on organisms.

Educational Objective

- To gain knowledge on experimental approaches to identify and quantify metabolites, reactive intermediates and their selective interaction with specific cellular target molecules (selective toxicity)
- To get acquainted with the procedures applied to assess the toxicity of drugs and chemicals
- To understand the role of bioactivation and bio-inactivation in the toxicity of drugs and other xenobiotics
- To be able to apply strategies used to predict toxicity
- To understand strategies to reduce or prevent toxicity
- To understand risk factors involved in inter-individual susceptibility to xenobiotics, including genetic polymorphisms, drug- drug and food-drug interactions

Course Outcomes

The students will be able to:

- Predict the metabolic fate of compounds from their chemical structure.
- Describe the molecular mechanisms behind the deleterious effects of selected chemicals on membranes, proteins and DNA.
- Discuss impact and timing of toxic manifestations in the cell.

Course Contents

1. Molecular and Biochemical Toxicology: Definition and Scope
 - Introduction
 - Principles of Toxicology

- Molecular, Cellular and Biochemical Toxicology
 - Risk Assessment
2. Disposition of Toxicants
- Absorption, Distribution, and Excretion of Toxicants
 - Cellular transport and selective accumulation of potentially toxic xenobiotics
 - Biotransformation of xenobiotics
 - Toxicokinetics
3. Non-Organ Directed Toxicity
- Xenobiotic-induced oxidative stress: cell injury, signaling, and gene regulation
 - Disruption of cellular calcium homeostasis
 - Mechanisms of necrotic and apoptotic cell death
 - Impairment of cell proliferation and tissue repair
 - Immune mechanisms
 - Cytokine-mediated toxicity
 - Nuclear receptor-mediated toxicity
 - Disruption of signal transduction by xenobiotics
 - Disruption of mitochondrial function
4. Organ Targeted Toxicity
- Toxic Responses of the Blood
 - Toxic Responses of the Immune System
 - Toxic Responses of the Liver
 - Toxic Responses of the Kidney
 - Toxic Responses of the Respiratory System
 - Toxic Responses of the Nervous System
 - Toxic Responses of the Ocular and Visual System
 - Toxic Responses of the Heart and Vascular System
 - Toxic Responses of the Skin
 - Toxic Responses of the Reproductive System
 - Toxic Responses of the Endocrine System
5. Emerging area in Toxicology: Nanotoxicology
- Introduction
 - Naturally Occurring and Unintentional Nanoparticles
 - Engineered Nanomaterials

- Exposure to Nanoparticles
 - Protein Corona Formation on Nanoparticles
 - Nanoparticle Interactions with Biological Barriers
 - Degradation and Clearance
 - Adverse Effects of Nanoparticles
 - Nanomedicine
6. Novel mechanisms derived from systems toxicology

Recommended Books

1. Smart, R. C., & Hodgson, E. (Eds.). (2018). *Molecular and biochemical toxicology*. John Wiley & Sons.
2. Klaassen, C. D., & Watkins, J. B. (2015). *Casarett & Doull's essentials of toxicology*. McGraw Hill Professional.
3. Boelsterli, U. A. (2007). *Mechanistic toxicology: the molecular basis of how chemicals disrupt biological targets*. CRC press.