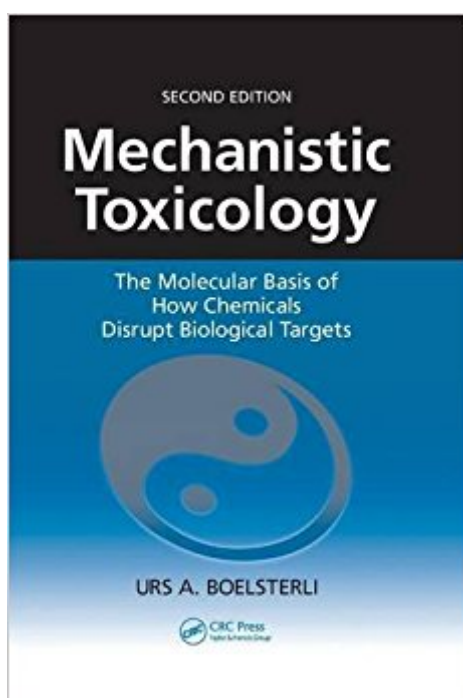


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# Mechanistic Toxicology: The Molecular Basis Of How Chemicals Disrupt Biological Targets, Second Edition



## Synopsis

A thorough understanding of cellular and molecular mechanisms involved in the individual expression of toxic effects provides an important tool for assessment of human health risk. New aspects, major advances, and new areas in molecular and cellular biology and toxicology demand updated sources of information to elucidate the functional mechanics of human toxicology.

**Mechanistic Toxicology: The Molecular Basis of How Chemicals Disrupt Biological Targets**, Second Edition retains the accessible format of the original to present the general principles that link xenobiotic-induced toxicity with the molecular pathways that underlie these toxic effects. Extensively illustrated, this book forms a conceptual bridge between multiple events at the molecular level and the determinants of toxicity at the physiological and cellular level. Specific examples of drugs, environmental pollutants, and other chemicals are carefully chosen to illustrate and highlight the fundamental mechanisms of toxicity at different toxicokinetic and toxicodynamic levels. The book includes references and review articles at the end of each chapter, as well as boxed text for relevant review information on biological, biochemical, molecular, and toxicological background. Linking molecular pathways to more general biomedical contexts, the author ensures that the reader is not lost in the details and instead receives a broad understanding of the processes underlying xenobiotic toxicity. New in the Second Edition Updated chapters Types of toxic responses Disruption of signal transduction by xenobiotics Disruption of mitochondrial function

## Book Information

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## Customer Reviews

'Students taking formal training in toxicology would definitely benefit from adding this book to their collection, since it covers many recent advances in the field.' - British Toxicology Society Newsletter

'This recently-published volume is a clear state-of-the-art explanation and description of how chemicals disrupt biological targets on a molecular basis. It is a beauty!'. - Toxicology Letters

University of Connecticut, Storrs, USA

My only complaint for this book is the lack of chemical equations but beyond that this book is absolutely wonderful. I discovered it accidentally while doing an assignment from the Google preview and knew I should have it to prepare for my qualifying exams. It has all the classic toxic agents, gives history of them, and the explanations for the mechanisms are simple, easy to understand and quite detailed. And when a toxicant has multi-system effects he references them for you, so it's easy to keep track. He also provides his sources for further reading at the end of the chapter. I love this book!

It is one of the best toxicology books with mechanistic approach, simple to understand, lots of information.

The book arrived quickly and was perfect. It was so much more reasonably priced than at school.

A highly technical textbook to the undergraduate student but a toxicological review informed by more relevant examples to the expert, Mechanistic Toxicology is a well-organized and well-researched synopsis of the fundamentals of Toxicology. Chapters are structured to present the topics first in the "Contents" section, dive deeper into each topic with helpful headings and examples, summarize and simplify what was presented in the "Learning Points" section, and lastly, to suggest further reading. Examples provided in the body of each chapter can get highly technical, though the main points of the chapter are never lost in even the most extended example. The abundance of examples and in-depth discussions on specific mechanisms makes this book optimal for someone who already has some background in biology and an understanding of toxicological concepts. The reader who hopes to develop a basic understanding of toxicology should look elsewhere, unless that reader is willing to commit substantial amounts of time pulling the basics out of the somewhat technical contents of this book. Finally, the review question and answer section in the back of the book and the index are useful tools that demonstrate the author's ability to make

technical concepts more understandable, considering that the reader has some background in related topics. The book is well equipped to explain concepts that may be beyond that reader's understanding.

**Chapter-By-Chapter Synopsis:** Below, the title and a summary sentence is given for each chapter.

**Ch1 Introduction** An overview of what toxicology investigates and the meaning/importance of both toxicokinetics and toxicodynamics.

**Ch. 2. Organ-selective Toxicity** Organ-selective toxicity is based on some of the toxicokinetic and toxicodynamic factors discussed in the previous chapter.

**Ch. 3 Cellular Transport and Selective Accumulation of Potentially Toxic Xenobiotics** Structures and the properties resulting from structure of substances, coupled with transport proteins and membrane composition, determine if a xenobiotic can enter a cell and remain there long enough to demonstrate toxic effects.

**Ch. 4 Bioactivation of Xenobiotics and Reactive Metabolites** Toxicity is often induced when a substance is metabolized from its original form.

**Ch. 5 Xenobiotic-induced Oxidative Stress: Cell Injury, Signaling, and Gene Regulation** Oxidative species are created all the time in equilibrium with antioxidants, but when the equilibrium favors oxidative species (ROS, RNS) cell damage occurs.

**Ch. 6 Disruption of Cellular Calcium Homeostasis** Calcium is critical in regulating cell metabolism, activating enzymes and other proteins, and acting as a second messenger, but different xenobiotics can interfere with calcium in all of these processes.

**Ch. 7 Mechanisms of Necrotic and Apoptotic Cell Death** Necrosis is relatively random and unorganized cell death, whereas apoptosis is organized cell death that involves signals received by death receptors, action by caspases and checkpoints along the way.

**Ch. 8 Impairment of Cell proliferation and Tissue Repair** Xenobiotics can induce or impair cell proliferation.

**Ch. 9 Covalent Binding of Reactive Metabolites to Cellular Macromolecules** Some Xenobiotics can be activated into an electrophile that reacts with protein or DNA nucleophiles, forming covalent bonds.

**Ch. 10 Immune Mechanisms** Xenobiotics can inhibit immune response, increasing chances of infection, or increase immune response, causing damage through autoimmune action.

**Ch. 11 Cytokine-mediated Toxicity** Proinflammatory cytokines and chemokines can enhance or mediate toxicity.

**Ch. 12 Specific Inactivation of Enzymes and Other Proteins** Some xenobiotics target very specific proteins, organophosphates being a good example of this in their tendency to target acetylcholine esterase.

**Ch. 13 Nuclear Receptor-Mediated Toxicity** Some xenobiotics can bind to nuclear receptors and disrupt normal processes.

**Ch. 14 Interactions of Xenobiotics With Ion Transporters** Some xenobiotics can bind to ion channels and ion pumps, disrupting critical functions, like the action of sodium-potassium pumps.

**Ch. 15 Disruption of Cellular Energy Production by Xenobiotics** Xenobiotics interference of mitochondrial activity results in a cellular energy crisis and can add to the production of ROS (addressed in Ch. 5).

**Ch. 16 Outlook: From Mechanisms to Individual**

Expression of Genes Major advances including DNA sequencing and advances in molecular technology is helping provide massive quantities of data still requiring interpretation. The author, Urs A. Boelsterli, currently serves at the Chair in Mechanistic Toxicology in the Department of Pharmaceutical Sciences at the University of Connecticut. He earned a M. Sc. And Ph. D. from the University of Zurich and did his postdoctoral work at the University of Toxicology in Zurich, Switzerland. His most recent publication, Pharmacologic targeting of bacterial  $\beta$ -glucuronidase alleviates nonsteroidal anti-inflammatory drug-induced enteropathy in mice, was published in 2012. He is also on the editorial board of Toxicology Mechanisms and Methods.

This book is specialized to one particular area of toxicology, the mechanisms by which toxic substances work. It focuses on the general principles that link xenobiotic-induced toxicity with molecular pathways underlying those toxic effects. It includes many examples using drugs, environmental pollutants and other chemicals. In the five years since the first edition was published there have been major advances in virtually every aspect of the field. As a result each chapter has been updated and new chapters added. Although an introductory book on the subject, this book is intended for the advanced undergraduate or beginning graduate level student. Of course it might also be used by specialists in other areas needing information about the subject. To further this usage, there is an extensive bibliography of papers at the end of each chapter.

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