Test Bank for Understanding Toxicology 1st Edition by Mercurio

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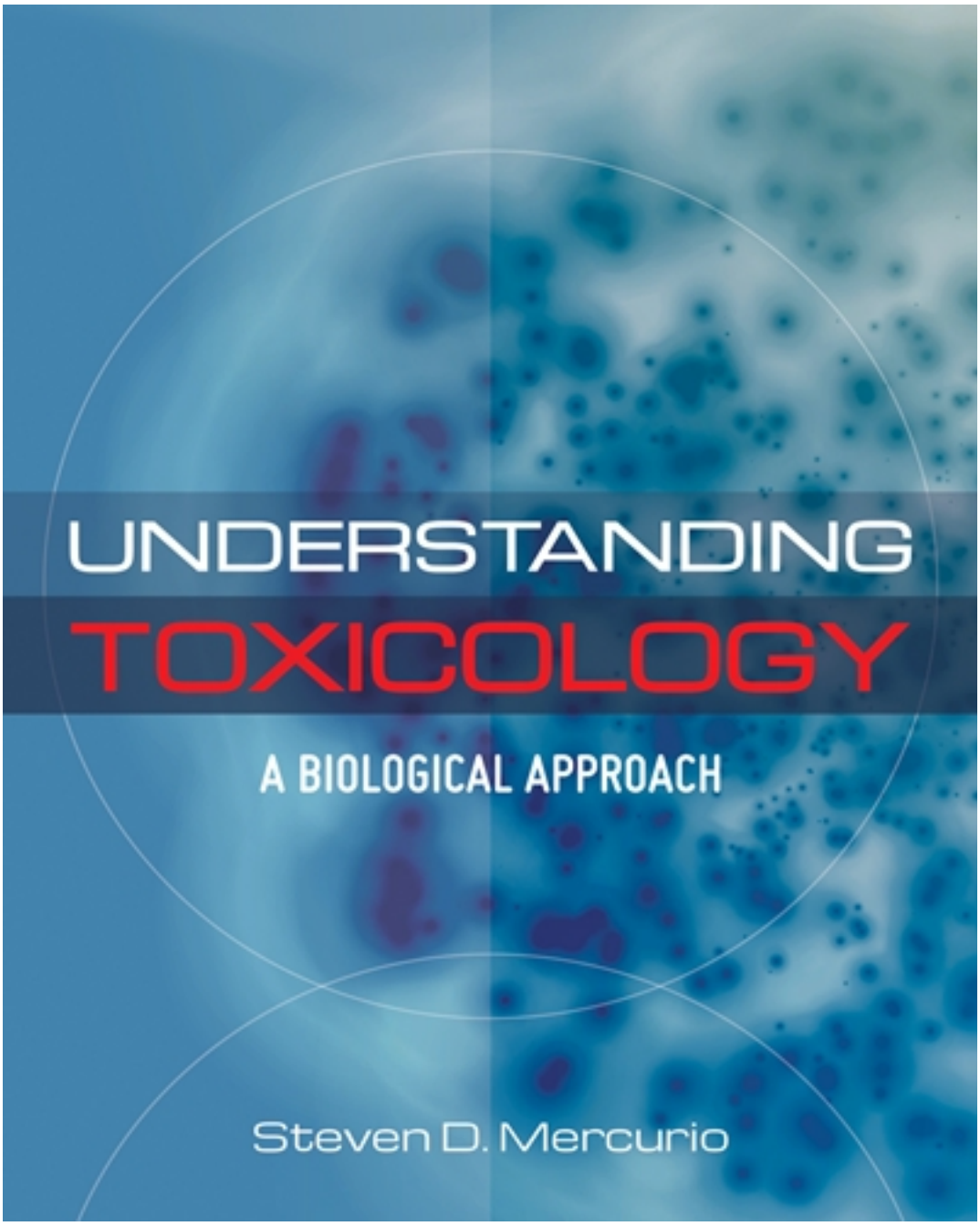

Test Bank

Understanding Toxicology: A Biological Approach
Steven Mercurio, PhD
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Chapter 1

1. Why are malformations of amphibians insufficient evidence for chemical toxicity?

   Answer: Malformations may come from parasites and other influences that are not necessarily related to pollutants. Also a one low concentration effect of a compound like atrazine does not mean that malformations found in the wild are due to that agent.

2. How is toxicogenomics a form of cellular toxicology?

   Answer: Toxicogenomics involves changes in DNA structure, expression and translation into protein (via mRNA transcription and tRNA/ribosomal protein synthesis) that are cellular functions of the nucleus (for eukaryotic organisms) and the cytoplasm/endoplasmic reticulum. A cancer cell may indeed by one aberrant cell whose genomics has been sufficiently altered to be a grave danger to the entire organism but started as a focus.

3. What toxicological information does the whole organism give toxicologists as exemplified by the injection of ^{14}C –labeled esophageal carcinogen N-nitrosomethylbenzylamine?

   Answer: The distribution and activation by biotransformation was highest in the target organ which cannot be determined by exposing just one cell fraction from one tissue.

Chapter 2

1. Why did Paracelsus believe that everything was poisonous?

   Answer: He discerned that anything given in excess in poisonous. It is the dosage that determines what effect a chemical will have on an organisms.

2. How did the Pure Food and Drug Act open the way for the field of toxicology in the U.S.?

   Answer: The isolation of the substances that had pharmacological and toxicological properties were investigated as adulteration of foods, medicines and cosmetics had led to many untoward effects (morbidity and mortality).

3. What did the book *Silent Spring* precede?

   Answer: The book indicated the carcinogenicity and toxicity of environmental chemicals such as the pesticide DDT. The U.S. EPA and OSHA came into being in 1970 as there was a growing awareness that environmental exposure to pesticides and occupational exposure to substances like asbestos led to human disease.

Chapter 3

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1. What is a probit and why is it important in toxicology measurements?

   Answer: A probit is a standard deviation unit. Populations of living creatures with diverse genetic backgrounds respond based on probits rather than increase toxicity linearly by percent of the population. This means that most animals of a species die at the LD_{50} and trail off on either side of this value based on standard deviation units from this value.

2. What is an IC_{50}? Is it the same as an EC_{50} or an LC_{50}?

   Answer: The concentration that causes 50% inhibition of an enzyme or function may be higher or lower that the toxic concentration that may cause illness (EC_{50}) or lethal concentration (LC_{50}) that causes half of cells or half of animals in an ecosystem to die depending on the enzyme and its link to vital functions of that cell or animal. In bacteriology the I_{50} can refer to a concentration that effects the growth curve of bacteria by half of untreated bacteria.

3. What is an agonist and antagonist and how can both be toxic?

   Answer: An agonist has the true physiological function of a substance at a receptor such as amphetamine has similar effects of dopamine. Both affect neurological and cardiovascular functions and can cause organ damage or death based on dose or doses over time. An antagonist blocks the action of a substance at a receptor such as a beta-blocker blocks the action of norepinephrine or epinephrine on the heart and thereby slows the heartbeat. At high doses, the heart can slow to create hypotension and cardiac arrest/death.

4. Which common medication that can be bought over-the-counter at a drug store are therapeutic as a dose and toxic as a dosage and which are therapeutic as a dosage but toxic as a dose?

   Answer: An example of the former are topical antibiotics or other dermal medications or eye drops that are meant to be used on the skin and not taken orally or absorbed in high quantities through the skin. Aspirin and other NSAIDS are acids (and inhibit COX enzymes that make prostaglandins that protect the stomach lining via mucus production) and irritate the G.I. tract as intact pills (dose) and therapeutic when they distribute an lower concentrations through the blood. Of course if an overdose of NSAIDS will disturb acid/base balances of the blood and be toxic as a dosage.

5. Why is the log P or log K_{OW} an important factor in determining the bioavailability or toxicity of a compound?

   Answer: This value determines the hydrophobicity of a compound. As cells or organisms have cell membranes or cell walls that contain significant amounts of lipid, more hydrophobic compounds are likely to be absorbed no matter the route of exposure, find their way to fat to accumulate and resist excretion until metabolized to more water soluble forms.

6. Why is the MTD a controversial way of dosing an animal to assess toxicity?