CHAPTER OVERVIEW

Section 12: Biotransformation

Learning Objectives

After completing this lesson, you will be able to:

- Explain biotransformation, including its importance to survival and the body sites it involves.
- Define enzymes and the three types of enzyme specificity.
- Explain the two phases of biotransformation.
- Identify factors that influence the effectiveness of biotransformation.

In this section...

Topics include:

12.1: Introduction to Biotransformation
12.2: Chemical Reactions
12.3: Biotransformation Sites
12.4: Modifiers of Biotransformation

Section 12: Key Points

What We've Covered

This section made the following main points:

- Biotransformation is the process by which a substance changes from one chemical to another (transformed) by a chemical reaction within the body.
- Biotransformation is vital to survival because it transforms absorbed nutrients into substances required for normal body functions.
- Potential complications of biotransformation include:
  - Detoxification — biotransformation results in metabolites of lower toxicity than the parent substance.
  - Bioactivation — biotransformation results in metabolites of greater toxicity than the parent substance.
- Chemical reactions continually occur in the body to build up new tissue, tear down old tissue, convert food to energy, dispose of waste materials, and eliminate toxic xenobiotics.
- Enzymes are catalysts for nearly all biochemical reactions in the body; essential biotransformation reactions would be slowed or prevented without these enzymes, causing major health problems.
- There are generally three types of enzyme specificity:
  1. Enzymes with absolute specificity catalyze only one reaction.
  2. Enzymes with group specificity act only on molecules that have specific functional groups.
  3. Enzymes with linkage specificity act on a particular type of chemical bond regardless of the rest of the molecular structure.
- There are two biotransformation reaction phases:
  1. Phase I reactions modify the chemical by adding a functional structure, allowing the substance to "fit" into a second (Phase II) enzyme:
     - Oxidation — the substrate loses electrons.
     - Reduction — the substrate gains electrons.
     - Hydrolysis — the addition of water splits the toxicant into two fragments or smaller molecules.

2. Phase II reactions conjugate (join together) the modified xenobiotic with another substance. The most important Phase II reactions are:
    - Glucuronide conjugation, a high-capacity pathway — glucuronic acid is added directly to the toxicant or its Phase I metabolite, generally resulting in hydrophilic conjugates excreted by the kidney or bile.
    - Sulfate conjugation, a low-capacity pathway — decreases the toxicity of xenobiotics, resulting in highly polar sulfate conjugates readily secreted in the urine.

- Biotransformation sites are the:
    - Liver (primary site, which also makes it the most susceptible to damage by ingested toxicants).
    - Kidneys (about 10-30% of the liver's capacity).
    - Skin, intestines, testes, and placenta (low capacity).
- Biotransformation effectiveness depends on factors that can inhibit or induce enzymes and dose levels, including species, age, gender, genetic variability, nutrition, disease, exposure to other chemicals, and the dose level.
