12.1: Introduction to Biotransformation

Biotransformation is the process by which a substance changes from one chemical to another (transformed) by a chemical reaction within the body. **Metabolism** or **metabolic transformations** are terms frequently used for the biotransformation process. However, metabolism is sometimes not specific for the transformation process but may include other phases of toxicokinetics.

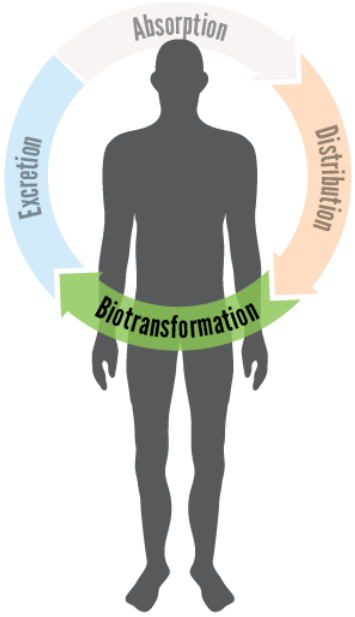

Figure 12.1.1. Processes of toxicokinetics (Image Source: Adapted from iStock Photos, ©)

Importance of Biotransformation

Biotransformation is vital to survival because it transforms absorbed nutrients (food, oxygen, etc.) into substances required for normal body functions. For some pharmaceuticals, it is a metabolite that is therapeutic and not the absorbed drug. For example, phenoxybenzamine, a drug given to relieve hypertension caused by pheochromocytoma, a kind of tumor, is biotransformed into a metabolite, which is the active agent. Biotransformation also serves as an important defense mechanism since toxic xenobiotics and body wastes are converted into less harmful substances and substances that can be excreted from the body.

Toxicants that are lipophilic, non-polar, and of low molecular weight are readily absorbed through the cell membranes of the skin, GI tract, and lung. These same chemical and physical properties control the distribution of a chemical throughout the body and its penetration into tissue cells. Lipophilic toxicants are hard for the body to eliminate and can accumulate to hazardous levels. However, most lipophilic toxicants can be transformed into hydrophilic metabolites that are less likely to pass through membranes of critical cells. Hydrophilic chemicals are easier for the body to eliminate than lipophilic substances. Biotransformation is thus a key body defense mechanism.

Fortunately, the human body has a well-developed capacity to biotransform most xenobiotics as well as body wastes.

Did you know?

Hemoglobin, the oxygen-carrying iron-protein complex in red blood cells, is an example of a body waste that must be eliminated. The normal destruction of aged red blood cells releases hemoglobin. Bilirubin is one of several hemoglobin metabolites. If the body cannot eliminate bilirubin via the liver because of disease, medicine, or infection, bilirubin builds up in the body and the whites of the eyes and the skin may look yellow. Bilirubin is toxic to the brain of newborns and, if present in high concentrations, may cause irreversible brain injury. Biotransformation of the lipophilic bilirubin molecule in the liver results in the production of water-soluble (hydrophilic) metabolites excreted into bile and eliminated via the feces.

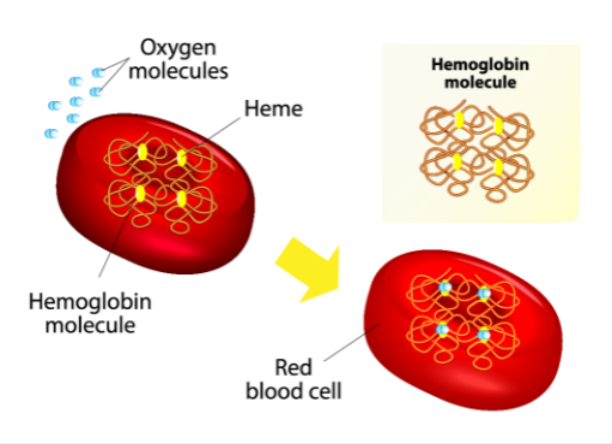

Figure 12.1.2 Human hemoglobin (Image Source: Adapted from iStock Photos, ©)

Potential Complications

The biotransformation process is not perfect. **Detoxification** occurs when biotransformation results in metabolites of lower toxicity. In many cases, however, the metabolites are more toxic than the parent substance, a process called **bioactivation**. Occasionally, biotransformation can produce an unusually reactive metabolite that may interact with cellular macromolecules like DNA. This can lead to very serious health effects such as cancer or birth defects.

An example is the biotransformation of vinyl chloride into vinyl chloride epoxide, which covalently binds to DNA and RNA, a step leading to cancer of the liver.

Knowledge Check

The term "biotransformation" refers to:

a. An increase in electrical charge in tissues produced by a biological transformer
b. Chemical reactions in the body that create a new chemical from another chemical
c. The transformation of one type of cell in a tissue to another type of cell

Answer

Chemical reactions in the body that create a new chemical from another chemical - **This is the correct answer.**
Biotransformation is the process whereby a substance is changed from one chemical to another (transformed) by a chemical reaction within the body.

Detoxification is a biotransformation process in which:

a. Metabolites of lower toxicity are produced
b. Metabolites of higher toxicity are produced

Answer

Metabolites of lower toxicity are produced - **This is the correct answer.**
When biotransformation results in metabolites of lower toxicity, the process is known as detoxification.

Bioactivation is a biotransformation process in which:

a. Metabolites of lower toxicity are produced
b. Metabolites of higher toxicity are produced

Answer

Metabolites of higher toxicity are produced - **This is the correct answer.**
When biotransformation results in metabolites of higher toxicity, this is known as bioactivation.
