

The Role of Enzymes in Biotransformation

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ABOUT THE STUDY

Biotransformation, also known as biotransformational metabolism or drug metabolism, is a complex and essential process that occurs in living organisms, primarily in the liver. It involves the conversion of various chemical compounds, including drugs, toxins, and other foreign substances, into more easily excretable forms. Biotransformation plays a crucial role in the body's ability to eliminate these substances and maintain homeostasis.

Biotransformation is a process by which the body modifies chemical compounds to make them more hydrophilic (water-soluble) and easier to eliminate. Lipophilic (fat-soluble) compounds tend to accumulate in fatty tissues and are difficult to excrete. Therefore, the transformation of lipophilic substances into hydrophilic forms is necessary for efficient elimination through urine or bile. The primary function of biotransformation is to facilitate the elimination of foreign compounds, including drugs, toxins, and environmental pollutants. Additionally, biotransformation can also convert prodrugs, which are inactive or less active compounds, into their active forms. This conversion is crucial for the therapeutic efficacy of many medications. Biotransformation ensures that substances entering the body undergo chemical modifications that render them less harmful or more useful. Although biotransformation occurs in various organs, the liver is the primary site for this process. The liver is equipped with a diverse array of enzymes, including Cytochrome P450 (CYP) enzymes, which play a central role in metabolizing a wide range of substances. However, other organs, such as the kidneys, lungs, intestines, and skin, also contribute to biotransformation to varying extents.

Enzymes involved in biotransformation

- CYP enzymes are a superfamily of heme-containing enzymes that catalyze the oxidation of lipophilic compounds. These enzymes are involved in the metabolism of approximately 75% of all known drugs. The human liver expresses several CYP enzymes, including CYP1A2, CYP2C9, CYP2D6, CYP2E1, and CYP3A4, each with distinct substrate specificities.

- Phase I enzymes are responsible for the initial modifications of foreign compounds. Apart from CYP enzymes, other phase I enzymes include Flavin-containing Monooxygenases (FMOs) and Monoamine Oxidases (MAOs). These enzymes catalyze various reactions, such as oxidation, reduction, and hydrolysis, to introduce or unmask functional groups on the parent compound.
- Phase II enzymes, also known as conjugation enzymes, facilitate the attachment of hydrophilic molecules (such as glucuronic acid, sulfate, glutathione, or amino acids) to the functional groups introduced in phase I reactions. This conjugation reaction increases the water solubility of the compound, making it more easily excretable. Common phase II enzymes include UDP-Glucuronosyltransferases (UGTs), Sulfotransferases (SULTs), and Glutathione S-Transferases (GSTs).

Phases of biotransformation

- Biotransformation is often classified into two phases: phase I and phase II reactions. While this classification provides a useful framework, it should be noted that the process is highly interconnected, and some compounds may undergo both phase I and phase II reactions simultaneously or in a sequential manner.
- Phase I reactions involve the introduction or unmasking of functional groups on the parent compound. The primary purpose of phase I reactions is to increase the polarity of lipophilic compounds and create sites for conjugation in phase II reactions. The most common phase I reaction is oxidation, mediated primarily by cytochrome P450 enzymes. Other phase I reactions include reduction and hydrolysis.
- Phase II reactions involve the conjugation of the functional groups introduced or unmasked in phase I reactions with hydrophilic molecules. The conjugation process increases the water solubility of the compounds, making them more easily excretable. Phase II reactions are typically catalyzed by specific enzymes, such as UDP-Glucuronosyltransferases (UGTs), Sulfotransferases (SULTs), and Glutathione S-Transferases (GSTs).

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