8.0 Enzymes: Biological Catalysis

Objectives

1. Know the general properties of enzymes.
2. Know various catalytic mechanisms.
3. Know the transition state diagram.
4. Understand the transition state inhibitors and catalytic antibodies.
5. Understand the Philip's mechanism of lysozyme action.
6. Understand the catalytic triad mechanism of serine proteases.
7. Know Michaelis-Menten kinetics.
8. Understand how to analyze kinetic data.
9. Know three types of enzyme inhibition.
10. Understand regulation of enzyme activity

8.1 General Properties of Enzymes

Enzymes are biological catalysts used to increase the velocity of biochemical reactions. Unlike chemical catalysts, enzymes have different catalytic power, specificity, reaction conditions, and ability to be regulated. These properties give cells the ability to modify kinetic properties of reactions in the body.

Biochemists classify enzymes by the type reaction they catalyze. There are six major types of enzymes:

1. Oxidoreductases
2. Transferases
3. Hydrolases
4. Lyases
5. Ligases
6. Isomerases

8.2 Catalytic Mechanisms

Enzymes catalyze reactions using one or more mechanisms in the body. Some mechanisms facilitate acid/base reactions, such as peptide hydrolysis by chymotrypsin. Chymotrypsin also participates in covalent catalysis.

In electrostatic stabilization, enzymes serve to stabilize molecules in their transition states, which lowers the required activation energy for the reaction. Metal ion catalysis assist in several ways or can inhibit reactions. Other enzymes catalyze reactions by physically orienting molecules to initiate the reaction.

In general, enyzmes bind more tightly to transition states. On a reaction coordinate diagram, enzyme activity is often reflected by stabilization of the transition state. Steric strain, desolvation, and entropy loss can be used to destabilize the catalyzed energy state.

8.3 Transition State Inhibitors and Catalytic Antibodies

Enzymes are not used up during catalysis, so regulating enzymatic activity requires deactivation of the enzyme. In transition state inhibitors, a molecule that mimics the reactant enters the active site on an enzyme and binds to it. This causes the enzyme to change its shape and transition state, preventing its enzymatic activity.

8.5 Philip's Mechanism

The enzyme lysozyme is used to hydryolyze glycosidic bonds between N-acetylmuramic acid (NAM) and N-acetylglucosmine (NAG) in bacterical cell walls.

8.6 Catalytic Triad Mechanism

The body contains a number of enzymes known as serine proteases. These enzymes are used to cleave polypeptides at specific sites, depending on the enzyme structure. One of these proteases, chymotrypsin, a digestive enzyme used to break down proteins in food, uses a catalytic triad to perform its catalysis.

The catalytic triad mechanism requires three amino acids in a specific structure at the enzyme's binding site to work together. The serine residue is used to cleave peptide bonds, while histidine and aspartic acid work together to deprotanate serine, giving it the charge necessary to briefly form a covalent bond with the peptide bond. A water molecule is then activated by histidine, and the oxgygen of the water attacks the serine carbonyl, releasing the protein fragment and regenerating the serine hydroxyl group.

8.7 Michaelis-Menten Kinetics

Enzyme kinetics can be described using Michaelis-Menten kinetics, a system of relating reaction rate to substrate concentration. The model makes three key assumptions:

- Assumption of equilibrium - This assumption states that a reversible enzyme-substrate complex is formed, which then dissociates further.
- Steady state assumption - The steady state assumption states that the enzyme-substrate complex forms at the same rate that it disappears.
- Initial velocity assumption - The formation of products should be very energetically favored, implying that products do not readily reform the original reactants.

The Michaelis-Menten equation describes the relationship between reaction rate and substrate concentration:

$$v = \frac{V_{max}[S]}{K_M + [S]}$$

8.8 Analyzing Kinetic Data

Enzyme kinetics are described by several features that are used to relate reaction velocity to the concentrations of enzyme and substrate:

- Km - The Michaelis constant, derived from the rate constants $(k_{-1} + k_2)/k_1$
- Vmax - Theoretical maximum rate of the reaction, when the reactants and products are balanced under optimal conditions
- Kcat - Turnover rate, equal to the number of reactions per unit of time
- Catalytic Efficiency - K_{cat}/K_M, an estimate of how effective the enzyme is

8.9 Three Types of Enzyme Inhibition

Since enzymes are not consumed, they must be inhibited when their catalytic mechanisms are not necessary. There are two main types of enzymatic inhibition in the body, irreversible and reversible. There are also three subtypes of reversible inhibition in the body, competitive, uncompetitive, and noncompetitive.

Competitive

In competitive inhibition, the inhibitor I binds only to the enzyme E. This binding can prevent or reduce enzymatic activity by blocking the active site or by changing it to be less catalytic.

Uncompetitive

Uncompetitive inhibition is a hypothetical type of inhibition where the inhibitor I binds to the enzyme-subtrate complex.

Noncompetitive

Also called mixed inhibition, in noncompetitive inhibition the inhibitor I binds to either the enzyme E and/or to the enzyme-substrate complex.

8.10 Understand regulation of enzyme activity

Enzyme activity is regulated by a variety of factors in the body, some due to the reactions themselves, others due to intentional influence from the body or medications. For example, as product accumulates, the reaction rate slows. Other influences include substrate availability and genetic controls.

Effectors can alter enzyme activity through covalent modification or through allosteric effects, altering the enzymes shape and structure. Finally, other molecules such as zymogens, isozymes, and modulator proteins can change enzyme activity.