ENZYMES OF CLINICAL IMPORTANCE I

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Advanced Clinical Biochemistry II (MA 416)

Summer Semester

Lecture Five

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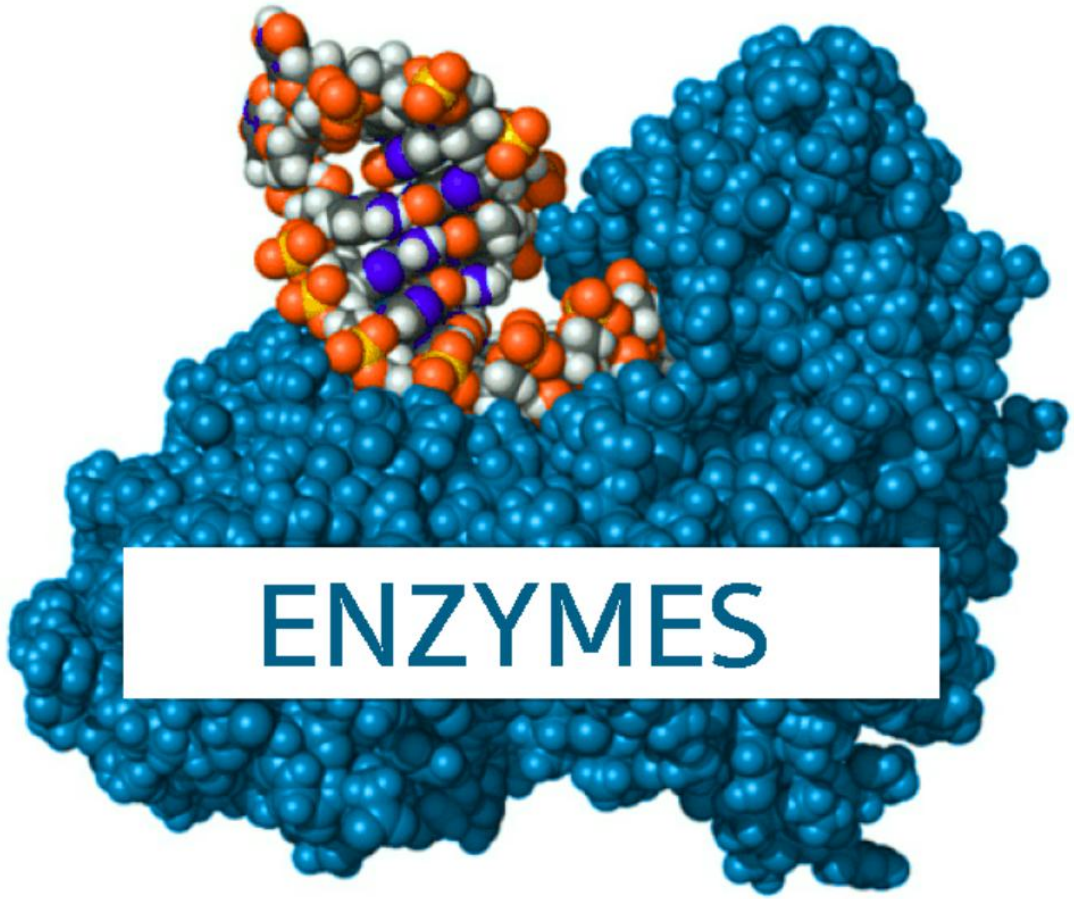
Outlines

- Introduction to enzymes
- Classification and properties
- Clinical enzyme assays and diagnostic relevance

Objectives

❑**At the end of this lesson, the students should be able to:**

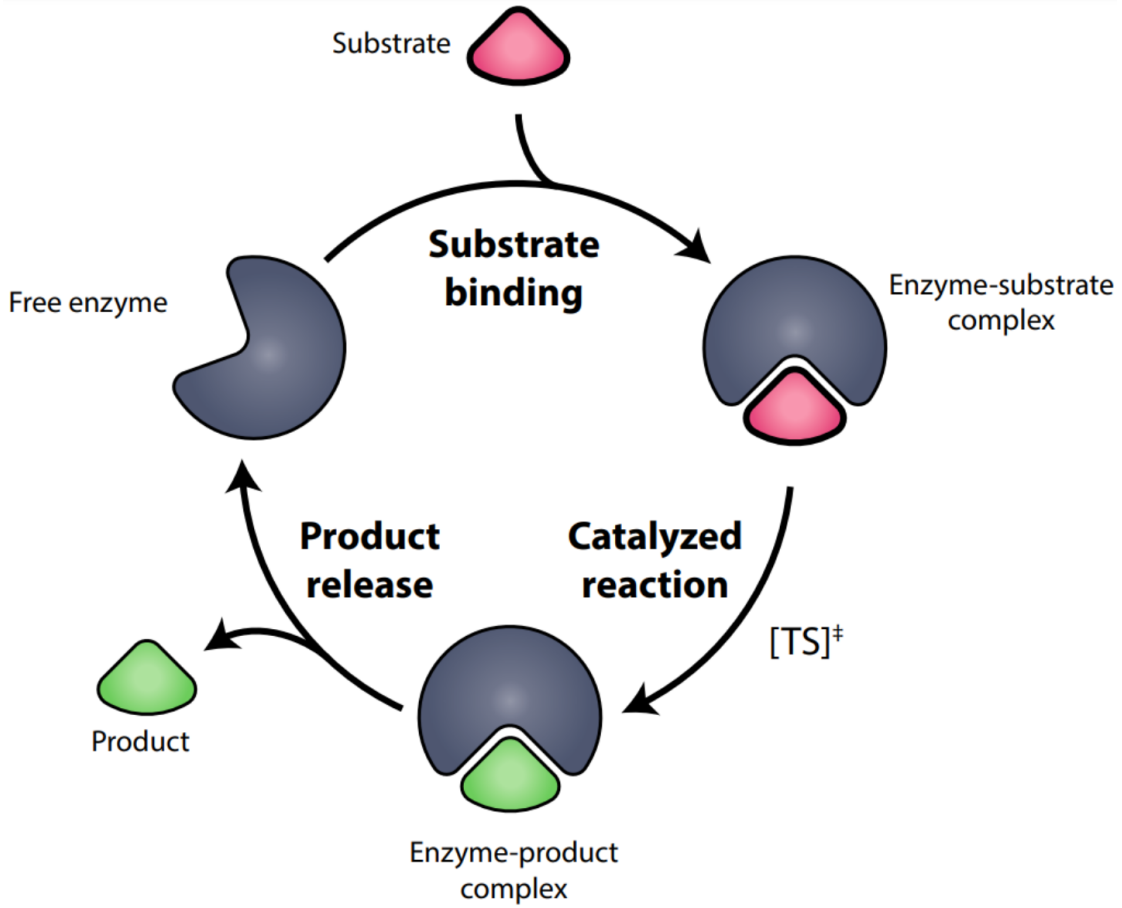
- Define enzymes and explain their biological role
- Describe enzyme structure and specificity
- Classify enzymes based on EC classification
- Discuss factors affecting enzyme activity
- Explain enzyme inhibition and regulation
- Describe clinical applications of enzymes in diagnosis



Introduction

- Enzymes are biological catalysts that speed up biochemical reactions.
- Mostly proteins (some are RNA called ribozymes).
- They increase reaction rate by lowering activation energy.
- Enzymes are not consumed in reactions.

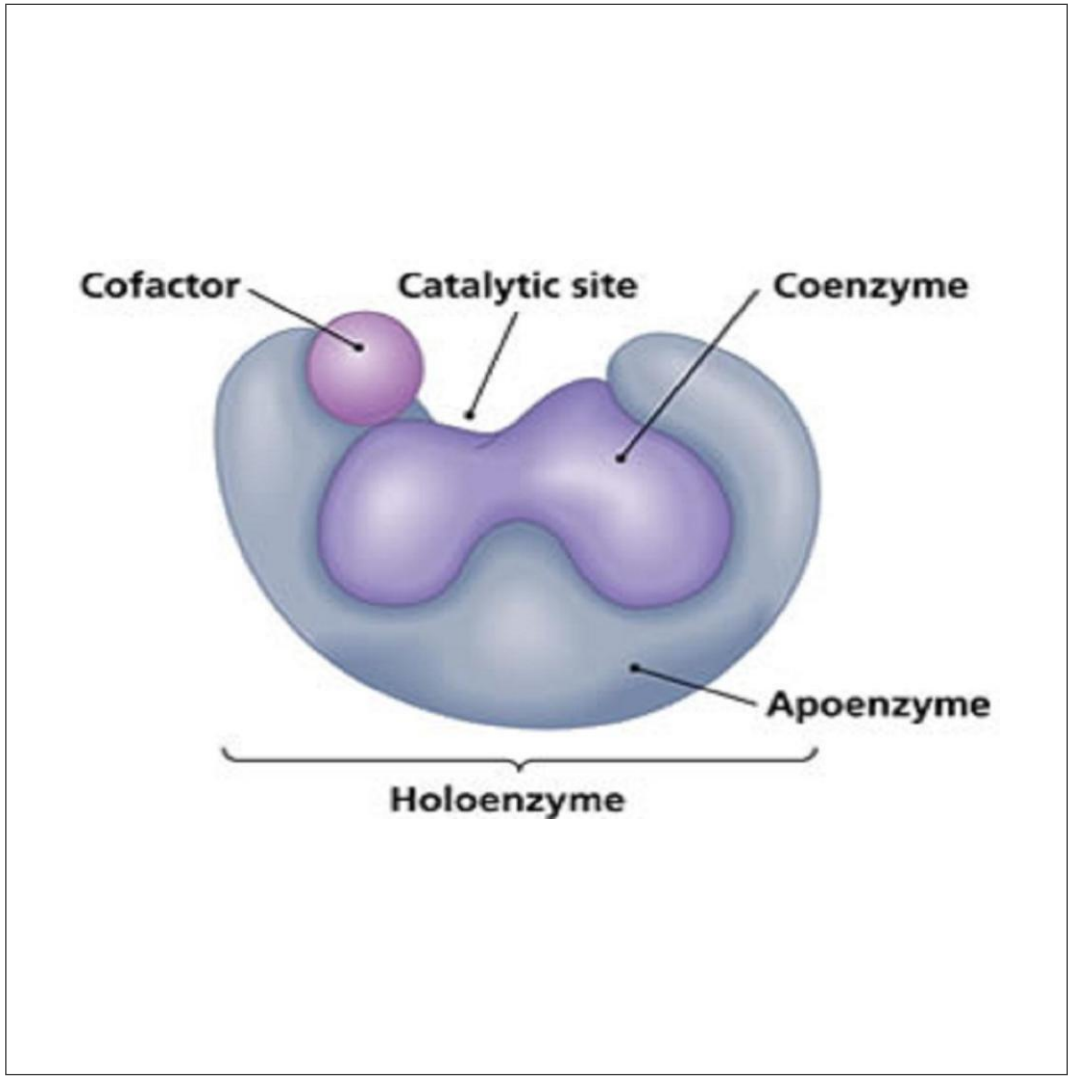
- **Example:**
- Catalase breaks down hydrogen peroxide: $2H_2O_2 \longrightarrow 2H_2O + O_2$



Importance of Enzymes in the Body

- **Functions**
  - Metabolism (glycolysis, Krebs cycle, lipid metabolism)
  - Digestion (amylase, lipase, protease)
  - DNA replication and repair (DNA polymerase)
  - Detoxification (cytochrome P450 enzymes)
  - Energy production (ATP synthase)
  - Signal transduction (protein kinases)

- **Clinical relevance:**
  - Enzyme abnormalities indicate tissue injury.



Enzyme Structure

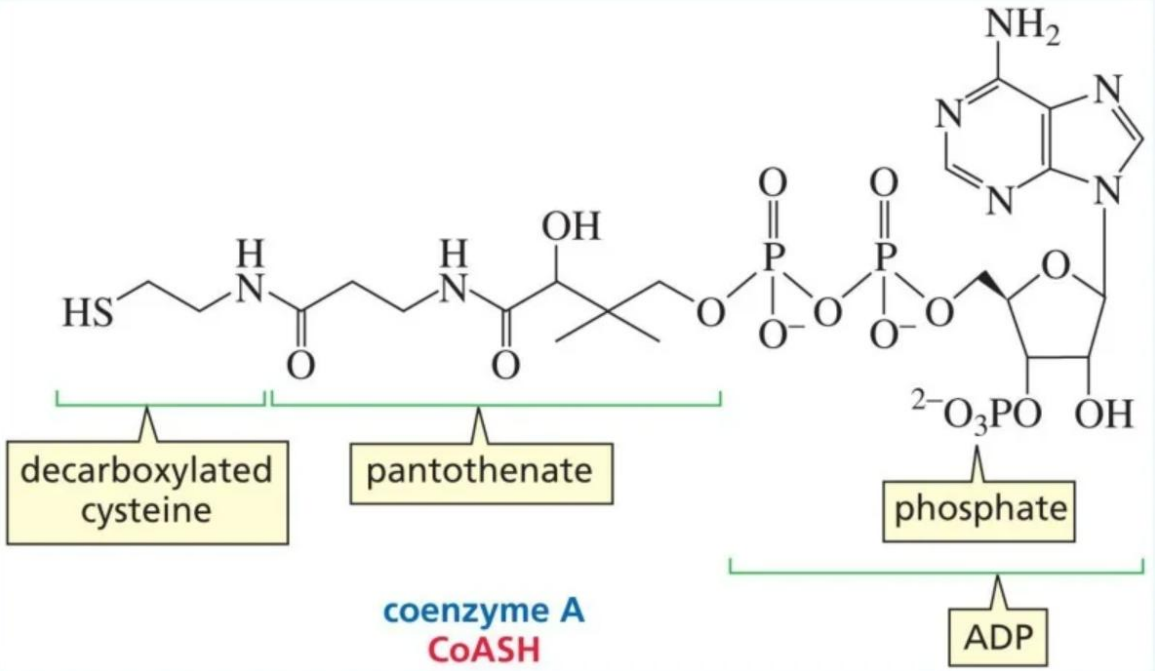
- **Structural Components**

- Apoenzyme: protein part of an enzyme.
- Cofactor: non-protein portion needed for activity
- Holoenzyme: apoenzyme + cofactor (active enzyme)

- Types of Cofactors

- Metal ions: Mg^{2+}, Zn^{2+}, Fe^{2+}
- Coenzymes: organic molecules (vitamin-derived)

- For Example: Zn^{2+} is required by carbonic anhydrase

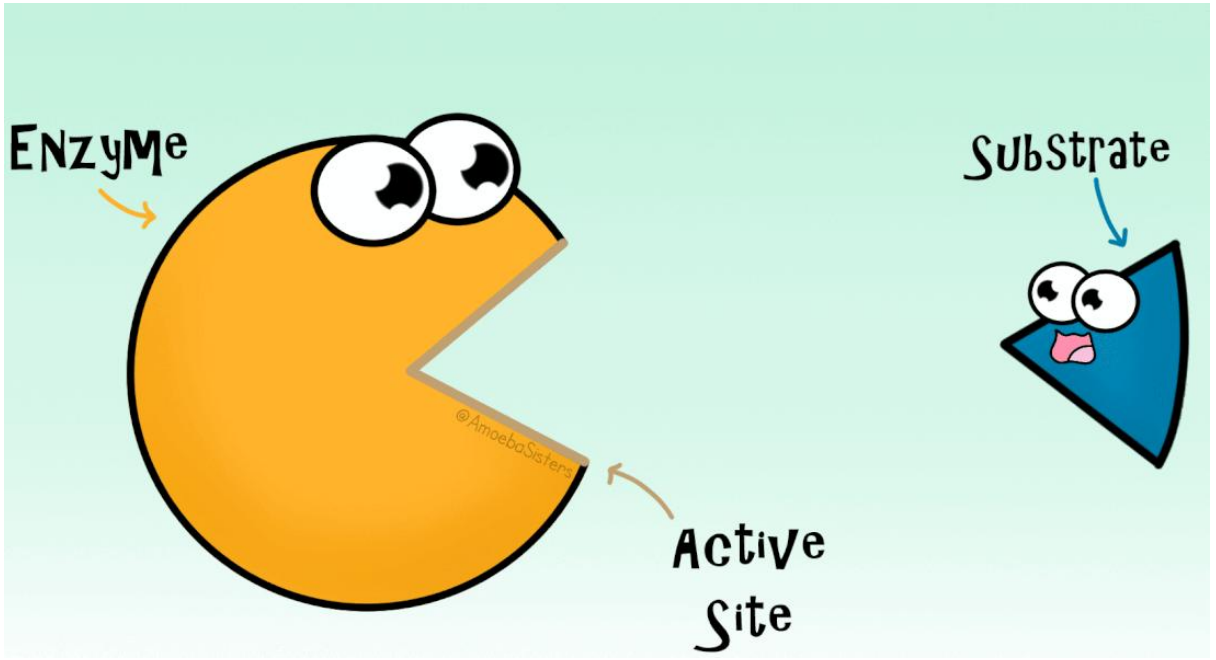


Coenzymes and Vitamins

- **Common Coenzymes**

- NAD^+ / $NADP^+$ (from niacin, Vitamin B3)
- FAD / FMN (from riboflavin, Vitamin B2)
- Coenzyme A (from pantothenic acid, Vitamin B5)
- TPP (from thiamine, Vitamin B1)
- Pyridoxal phosphate (Vitamin B6)

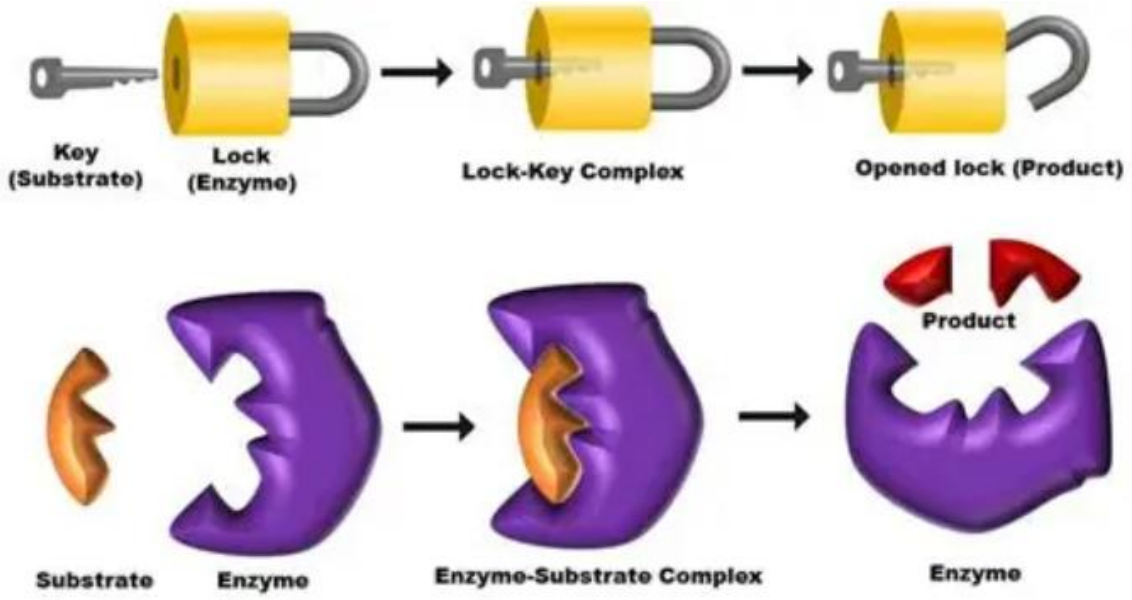
- Clinical note: Vitamin deficiency reduces enzyme function.



Active Site and Enzyme Specificity

- Active Site is a region where substrate binds and reaction occurs. It contains amino acid residues responsible for catalysis.

- Specificity Types
- Absolute specificity: acts on one substrate only
  (e.g., urease acts on urea)
- Group specificity: acts on related substrates
  (e.g., hexokinase acts on glucose, fructose)
- Bond specificity: acts on a specific bond type
- (e.g., lipase breaks ester bonds)
- Stereospecificity: acts on one stereoisomer
- (e.g., L-amino acid oxidase)

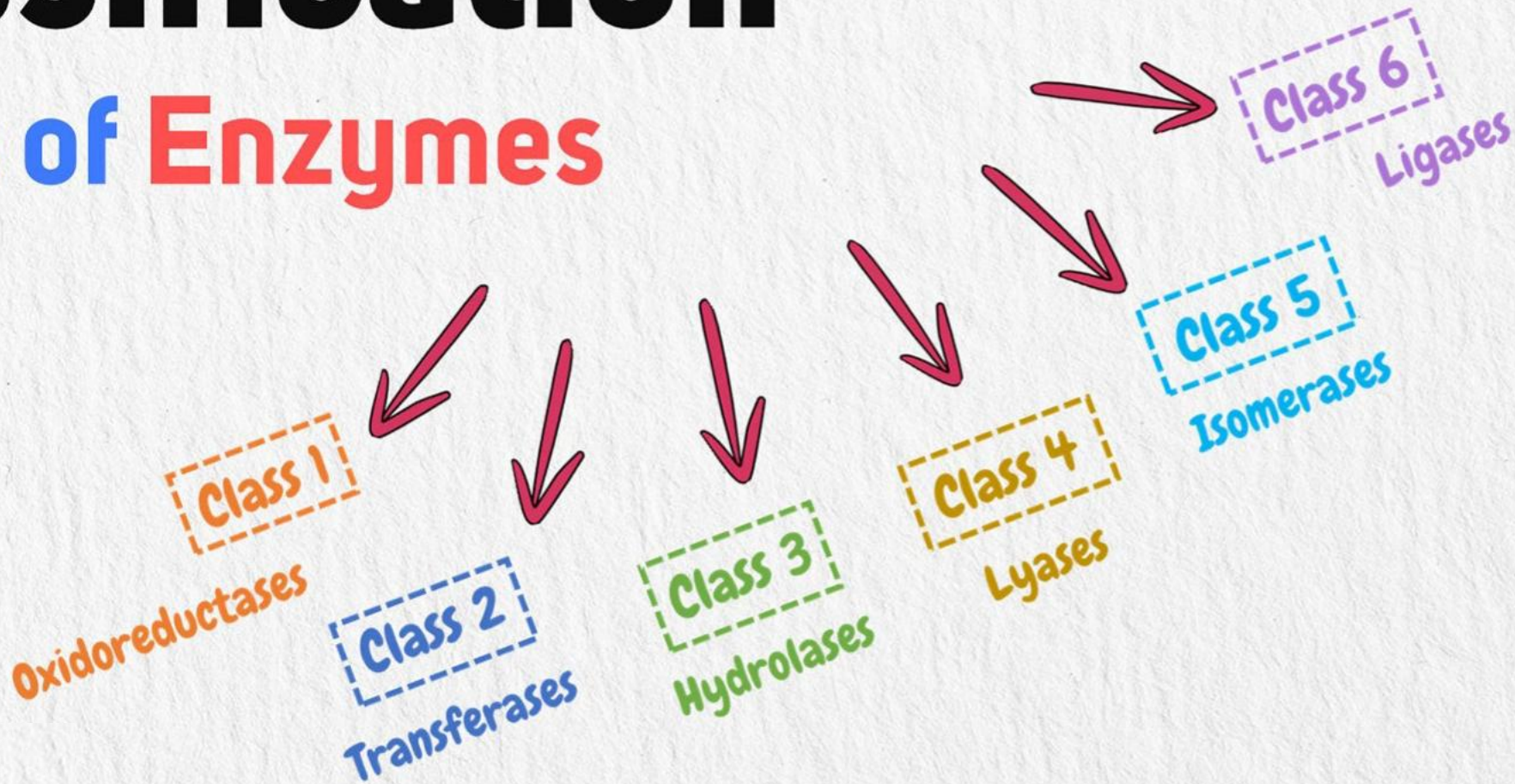


Lock-and-Key Model

- Active site is rigid and complementary to substrate.
- Induced Fit Model (More Accepted).
- Active site changes shape when substrate binds.
- Enhances catalytic efficiency.
- Clinical significance: Many drugs work by binding enzyme active sites.

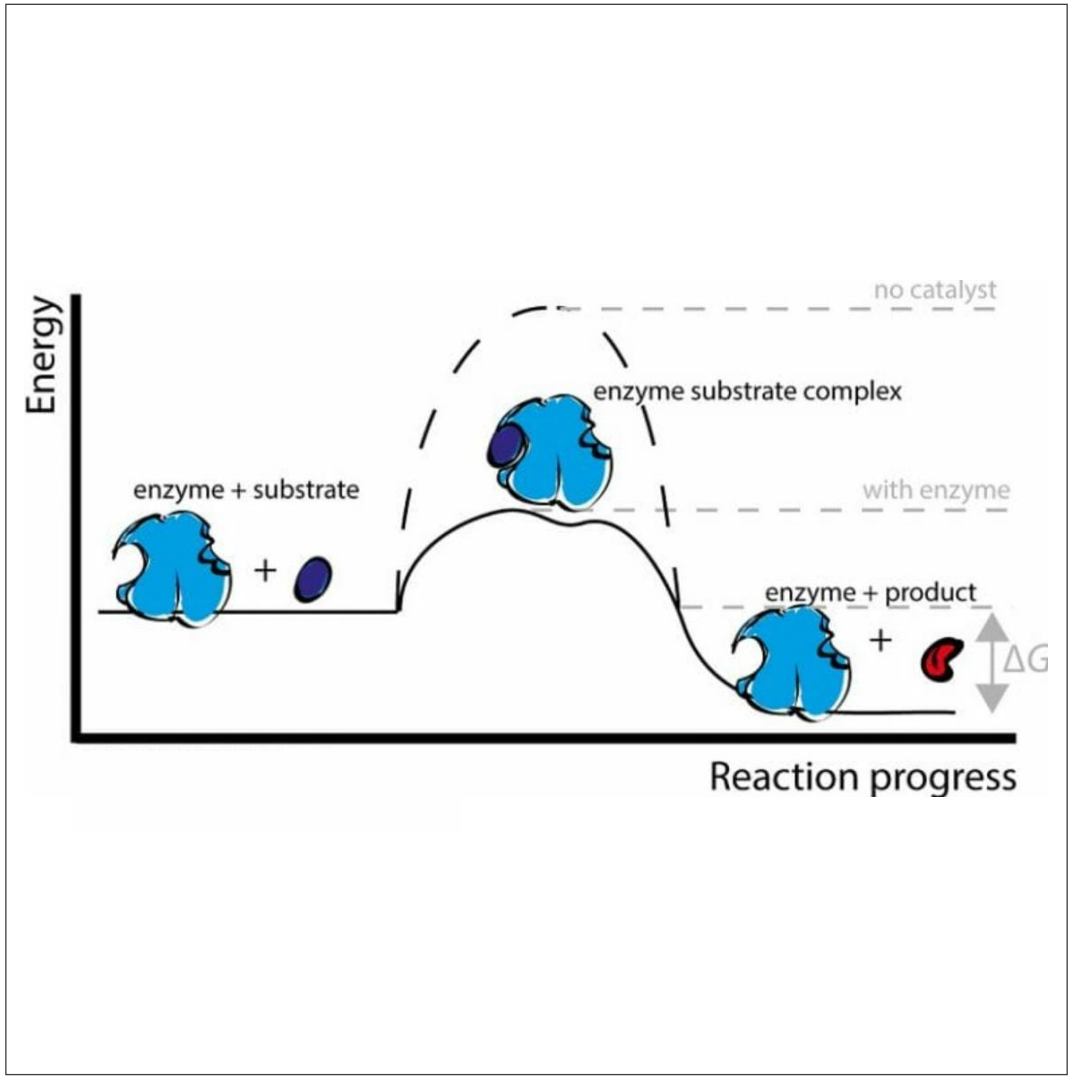
Classification

Basics of Enzymes



EC Classes with Examples

- Oxidoreductases catalyze oxidation-reduction reactions. Example: Lactate dehydrogenase (LDH)
- Transferases transfer functional groups. ALT and AST are the typical examples.
- Hydrolases break bonds using water. Eg. Amylase, lipase
- Lyases add or remove groups without hydrolysis, seen in Fumarase action.
- Isomerases convert one isomer to another, they include Phosphoglucose isomerase.
- Ligases join molecules using ATP such as DNA ligase

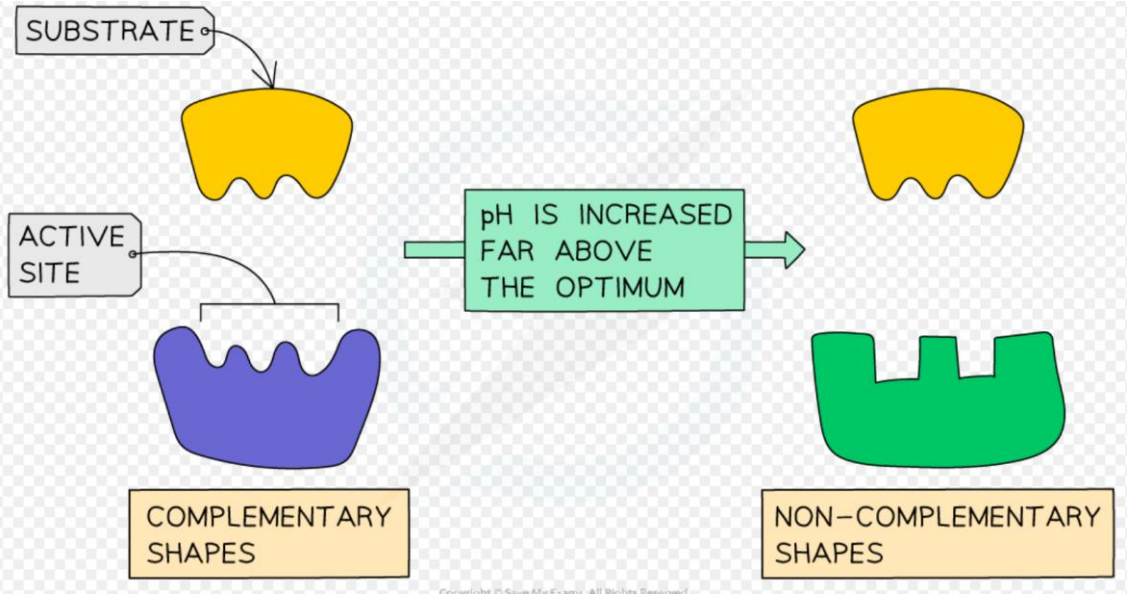


Mechanism of Enzyme Action

- Enzymes accelerate reactions by:
  - Lowering activation energy (Ea)
  - Stabilizing transition state
  - Proper orientation of substrates
  - Providing suitable microenvironment
  - Straining substrate bonds

- Enzymes do not change ΔG or equilibrium.

Factors Affecting Enzyme Activity



- **Temperature**

  - Activity increases with temperature up to optimum (~37°C in humans).
  - High temperature causes enzyme denaturation.

- **pH**

- Each enzyme has an optimum pH.
- Extreme pH disrupts ionic bonds.

  - Pepsin optimum pH = 2
  - Trypsin optimum pH = 8

Effect of Enzyme and Substrate Concentration

- **Enzyme Concentration:**

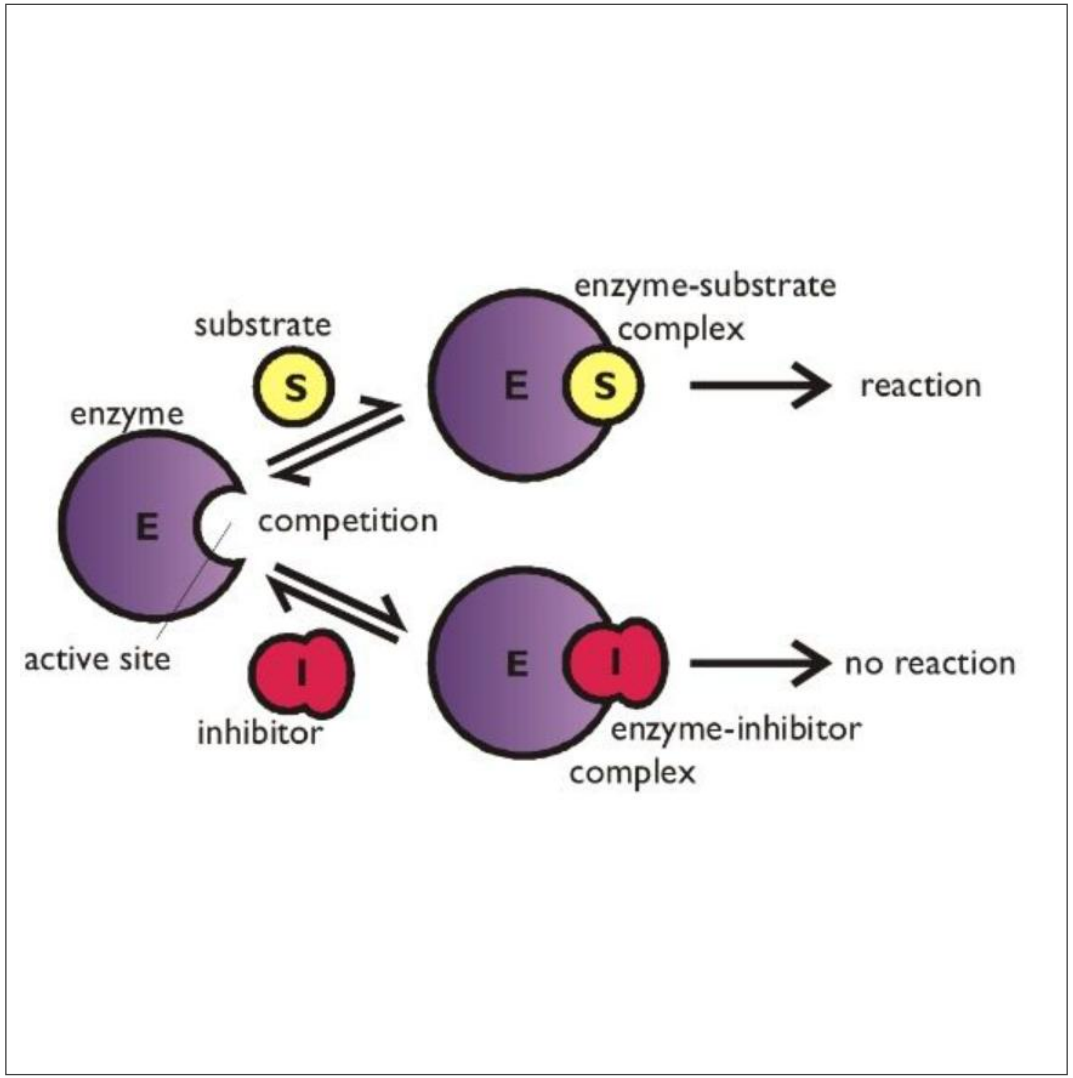
- Higher enzyme concentration increases the reaction rate if the substrate is sufficient.

- **Substrate Concentration:**

- Reaction rate increases until enzyme saturation.

- **Product Concentration:**

- Excess product may inhibit enzyme activity (feedback inhibition).

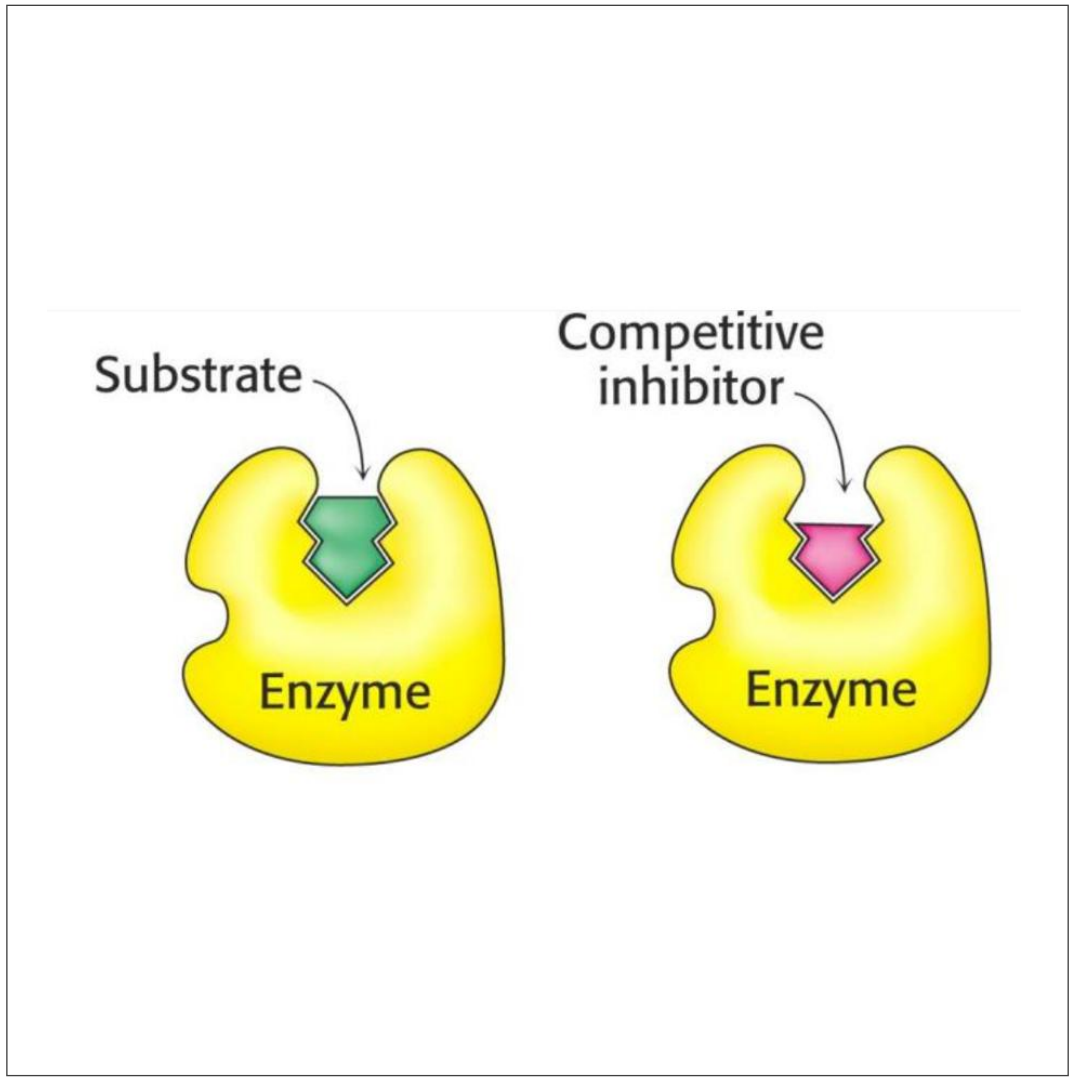


Enzyme Inhibition

- Types of Inhibition

  - Competitive inhibition
  - Non-competitive inhibition
  - Uncompetitive inhibition
  - Irreversible inhibition

- Enzyme inhibitors are clinically important in drug therapy.

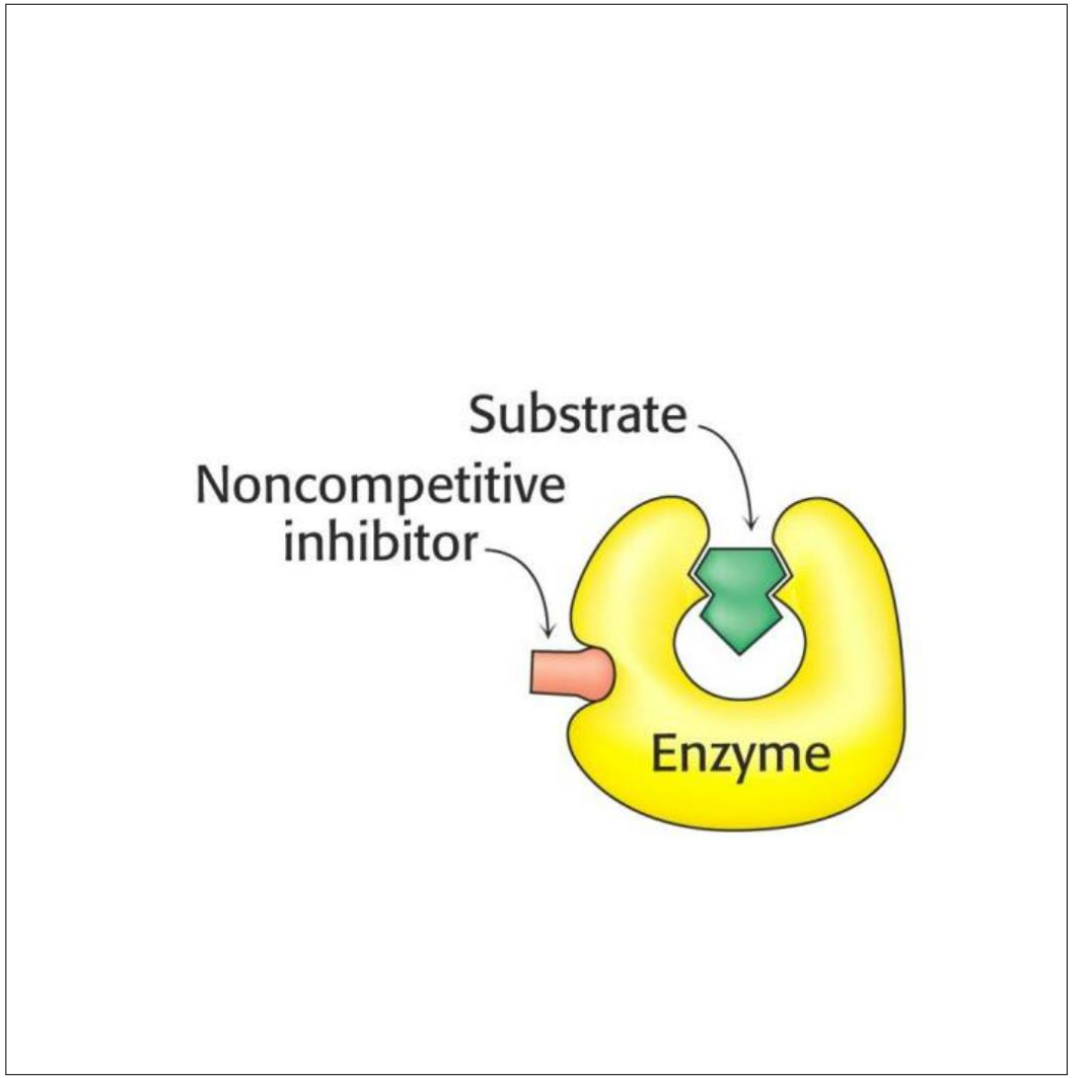


Competitive vs Non-Competitive Inhibition

- Competitive Inhibition

  - Inhibitor resembles substrate
  - Binds to active site
  - Km increases, Vmax unchanged
  - Can be overcome by increasing substrate

  - Example: Statins inhibit β-Hydroxy β-methylglutaryl-CoA (HMG-CoA) reductase.



Cont.

- Non-Competitive Inhibition

- Inhibitor binds to enzyme outside active site
- Changes enzyme shape
- Vmax decreases, Km unchanged
- Cannot be overcome by increasing substrate

- Heavy metals inhibiting enzymes.

Isoenzymes and Clinical Diagnosis

- Isoenzymes (Isozymes)
  - Different molecular forms of same enzyme
  - Catalyze same reaction
  - Found in different tissues

- Clinical LDH isoenzymes are found in heart, liver and muscle

  - CK isoenzymes:
  - CK-MM (skeletal muscle)
  - CK-MB (cardiac muscle)
  - CK-BB (brain)

- Isozymes helps identify source of damage in tissue.

Major Highlights

- Enzymes are biological catalysts that speed up a biochemical reactions without partaking into the reactions.
- They exist as halo or apo forms, which requires cofactors to perform their actions.
- Coenzymes is an organic non-proteneous moieties required by the apoenzymes to become halo enzymes.
- Active sites and allosteric sites are the key components of an enzyme.
- Enzymes are classified into 6 major classis according to their functions.
- Temperature, pH, substrate and Enzyme concentrations affects their function.
- Enzyme inhibition exist as competetive, uncompetitive and non-competitive.
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- Isozymes are the same enzymes with similar functions but exist in different compartments.

Interaction

- Why do organisms need enzymes to live?
- Enzymes exist as _____ and _____ forms
- Enzymes are highly specific in nature. What does that mean?.
- Differentiate between cofactor and coenzyme
- Mention at least 2 known coenzymes and their sources.
- What are the common electrolytes use by enzymes?
- Why is enzyme active site important?
- Highlight the factor that affect enzyme activities
- Explain how enzyme speed up a biochemical reaction.
- Differentiate between non-competitive and uncompetitive enzyme inhibition.


Questions
Comments
Feedback

Next Lecture

Enzymes of clinical importance II

References

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