ENZYMES

PRESENTED BY:

Dr Anita Joshi

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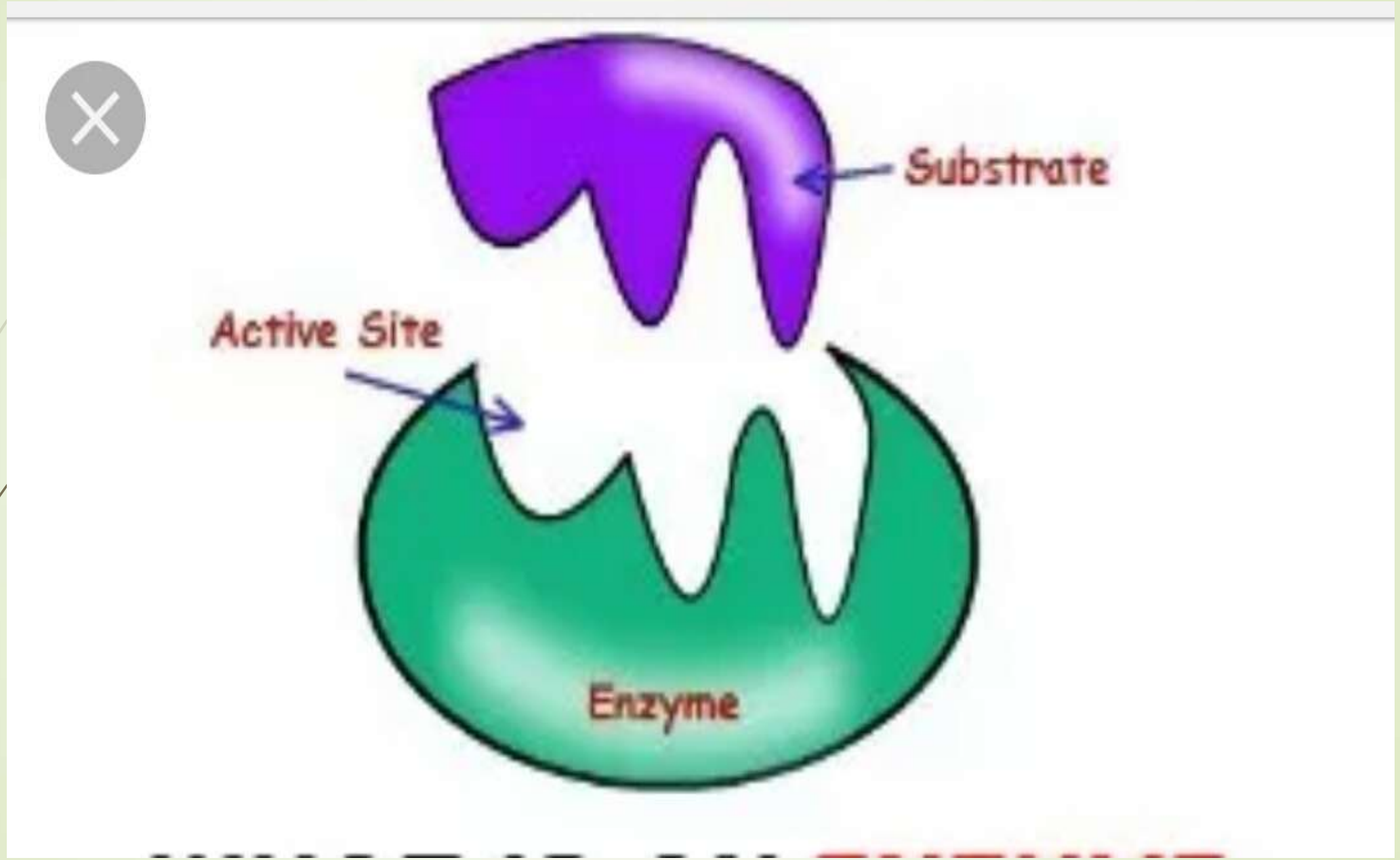
INTRODUCTION

1. Enzymes are biological catalysts that speed up the rate of the biochemical reaction.
2. Most enzymes are three dimensional globular proteins (tertiary and quaternary structure).
3. Some special RNA species also act as enzymes and are called Ribozymes e.g. hammerhead ribozyme


Substrate
Active Site
Enzyme

Nomenclature of enzymes

1) The first discovered enzymes were named according to their **source:** name of enzyme + suffix **-in**

Pepsin is found in the gastric juice (Greek *pepsis* = digestion).

2) Enzymes were named according to their **substrate**:

name of substrate + suffix **-ase**

Lipase catalyzes the hydrolysis of **lipids**.

Urease catalyzes the hydrolysis of **urea**.

3) In 1961 International Union of Biochemistry recommended that enzymes be systematically classified according to the **general type of reaction** they catalyze → **6 major classes**.

Each enzyme has a EC number (four-digit number)

Lactate dehydrogenase has the EC number 1.1.1.27

EXAMPLES:-

substrate	enzymes	products
lactose	lactase	Glucose + galactose
maltose	maltase	glucose
cellulose	Cellulase	glucose
lipid	lipase	Glycerol+ fatty acid
starch	amylase	maltose
protein	protease	Peptides + polypeptides

CLASSIFICATION OF ENZYMES

- A systematic classification of enzymes has been developed by International Enzyme Commission.
- This classification is based on the type of reactions catalyzed by enzymes.
- There are six major classes.
- Each class is further divided into sub classes, sub sub-classes and so on, to describe the huge number of different enzyme catalyzed reactions.

Classification of enzymes

ENZYME CLASS	REACTION TYPE	EXAMPLES
Oxidoreductases	Reduction-oxidation (redox)	Lactate dehydogenase
Transferases	Move chemical group	Hexokinase
Hydrolases	Hydrolysis; bond cleavage with transfer of functional group of water	lysozyme
Lysases	Non-hydrolytic bond cleavage	Fumarase
Isomerases	Intramolecular group transfer (isomerization)	Triose phosphate isomerase
Ligases	Synthesis of new covalent bond between substrates, using ATP hydrolysis	RNA polymerase

STRUCTURE OF ENZYMES

Enzyme structure

Proteins that work as a catalyst.

Speed up chemical reactions without being altered themselves.

Enzyme + Substrate

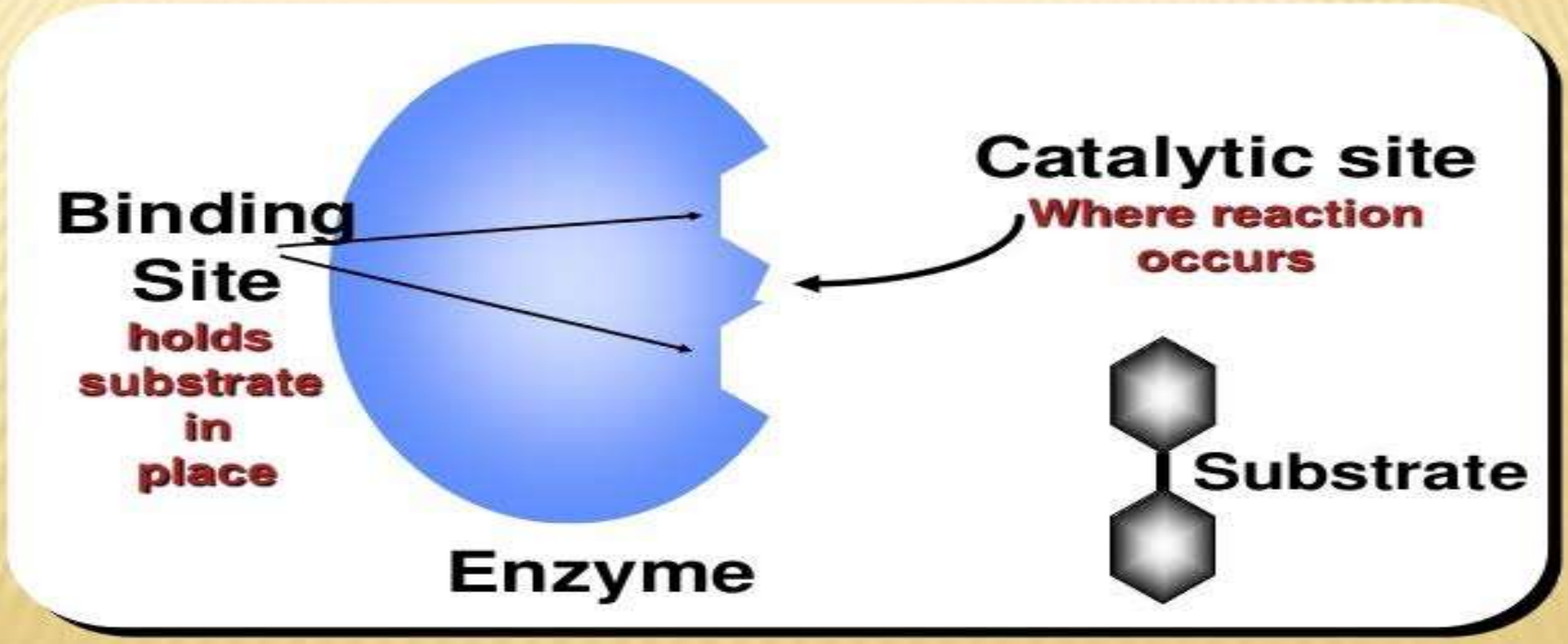
Enzyme-Substrate Complex

Enzyme + Products

STRUCTURE OF ENZYMES

- The active site of an enzyme is the region that binds substrates, co-factors and prosthetic groups and contains residue that helps to hold the substrate.
- Active sites generally occupy less than 5% of the total surface area of enzyme.
- Active site has a specific shape due to tertiary structure of protein.

THE ACTIVE SITE



ACTIVE SITE

- **Active site can be further divided into**

Binding site

- **It chooses the substrate and bind it to active site**

Catalytic site

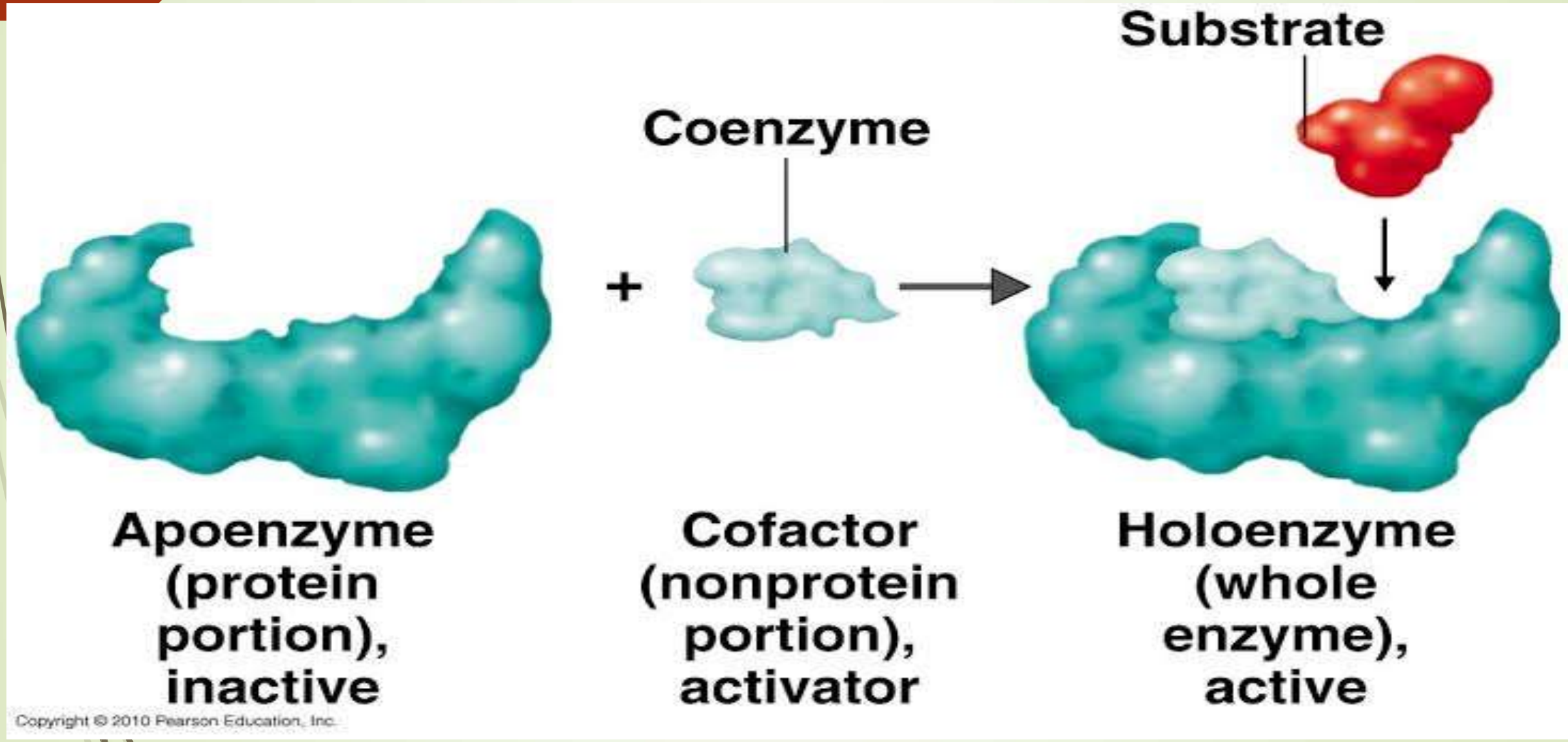
- **It performs the catalytic action of enzyme**

CO-FACTORS

- Co-factor is the non protein molecule which carries out chemical reactions that can not be performed by standard 20 amino acids.
- Co-factors are of two types:

1. Organic co-factors
2. Inorganic cofactors

CO-FACTORS


Substrate
Coenzyme
+
Apoenzyme (protein portion), inactive
Cofactor (nonprotein portion), activator
Holoenzyme (whole enzyme), active
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INORGANIC CO-FACTORS

- These are the inorganic molecules required for the proper activity of enzymes.
- Examples:

1. Enzyme carbonic anhydrase requires Zn for it‟s activity.
2. Hexokinase has co-factor Mg

ORGANIC CO-FACTORS

- o These are the organic molecules required for the proper activity of enzymes.
- Example:

 Glycogen phosphorylase requires the small organic molecule pyridoxal phosphate.

TYPES OF ORGANIC CO-FACTORS

Prosthetic group

- A prosthetic group is a tightly bound organic cofactor e.g. Flavins, heme groups and biotin.

coenzyme

- A coenzyme is loosely bound organic co-factor. E.g. NAD

Apoenzyme and Holoenzyme

- An enzyme with it‟s co-factor removed is designated as apoenzyme.
- The complete complex of a protein with all necessary small organic molecules, metal ions and other components is termed as holoenzyme of holoprotein.

CHARACTERISTICS OF ENZYMES

1. Enzymes speed up the reaction by lowering the activation energy of the reaction.
2. Their presence does not effect the nature and properties of end product.
3. They are highly specific in their action that is each enzyme can catalyze one kind of substrate.

4 Small amount of enzymes can accelerate chemical reactions.

5 Enzymes are sensitive to change in pH, temperature and substrate concentration.

6 Turnover number is defined as the number of substrate molecules transformed per minute by one enzyme molecule

Catalase turnover number = 6 x106/min

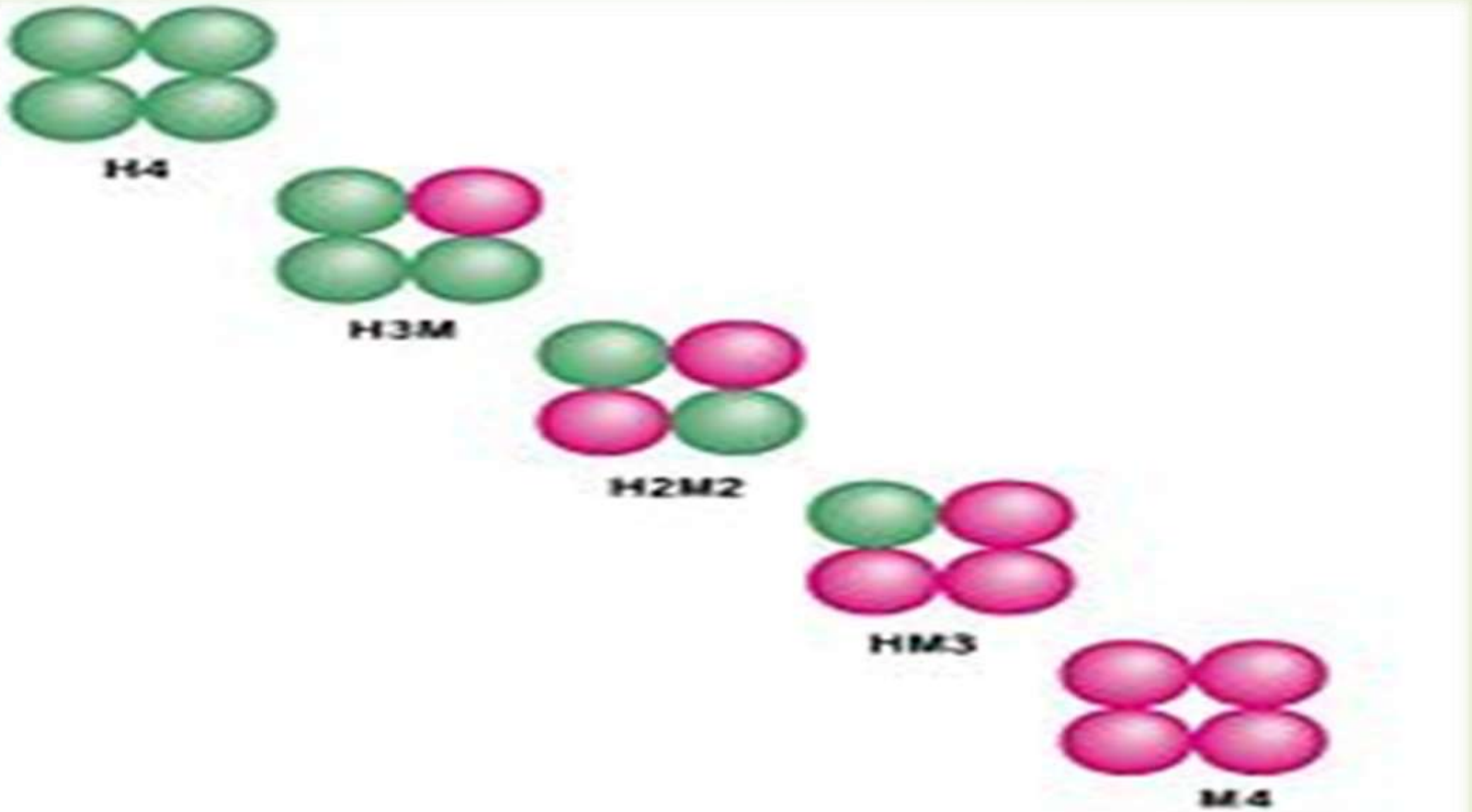
7 The enzyme activity can be controlled but the activity of catallysts can not be controlled

Isoenzymes

- They are physically distinct forms of the same enzyme activity. Multiple molecular form of an enzyme is described as **isoenzymes** or **isozymes**. They synthesized from various tissues
- Ex. **Lactate dehydrogenase** has 5 forms.
- The study of isoenzymes is useful to understand diseases of different organs.

Lactate Dehydrogenase(LDH)

- "Lactate dehydrogenase (LDH) is an enzyme present in a wide variety of organisms, including plants and animals".
- Its Enzyme Comission number is EC 1.1.1.27 where;
  - EC 1 = oxidoreductase.
  - EC 1.1 = acting on the CH-OH group of the donor.
  - EC 1.1.1 = With NAD or NADP as acceptor.
  - EC 1.1.1.27 = L-lactate dehydrogenase.
- Thus, it is an oxidoreductase enzyme that reversible reaction of lactate(LA) to pyruvate(PA) accompanied by the interconversion of NADH and NAD+.


H4
H3M
H2M2
HM3
M4

Lactate dehydrogenase isoenzymes

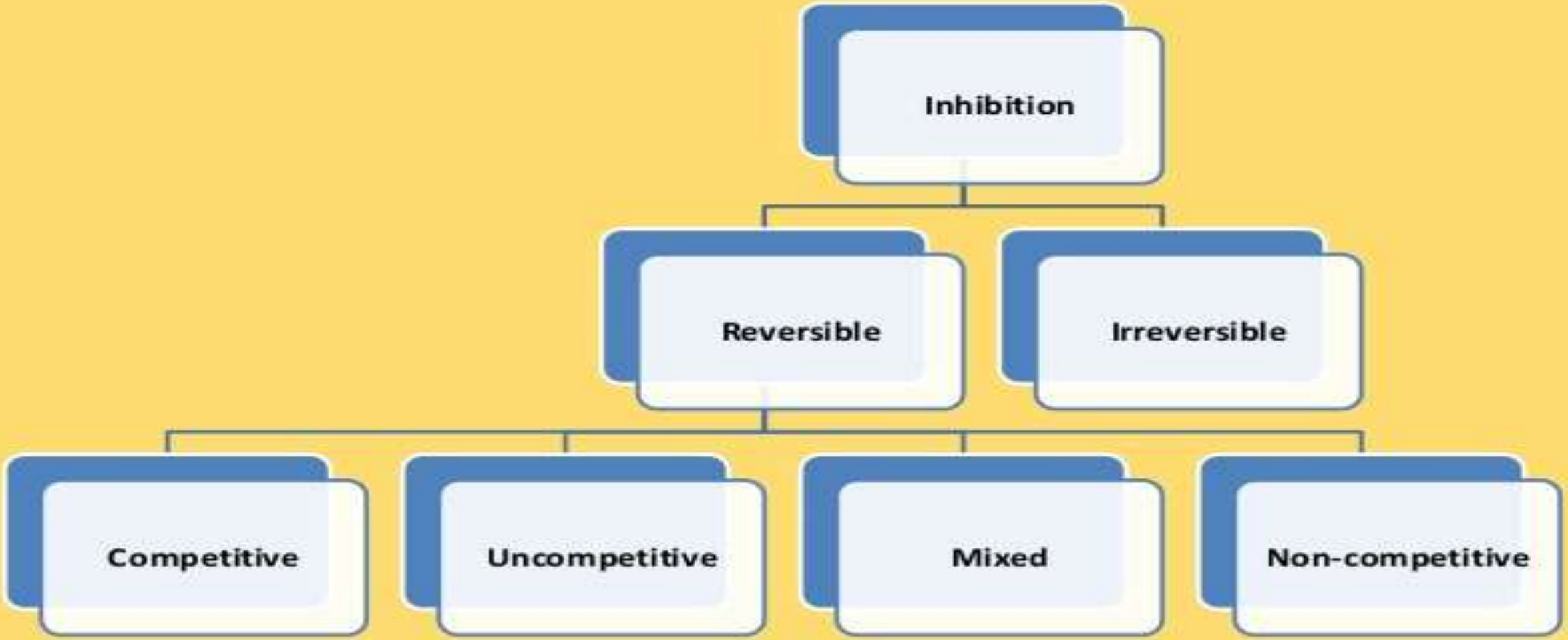
Isoenzyme name	Composition	Composition	Present in	Elevated in
LDH1	(H_4)	HHHH	Heart, RBC	myocardial infarction
LDH2	(H_3M_1)	HHHM	Heart, RBC	myocardial infarction
LDH3	(H_2M_2)	HHMM	lungs and spleen	leukemia
LDH4	(H_1M_3)	HMMM	lungs and spleen	viral hepatitis
LDH5	(M_4)	MMMM	Skeletal muscle, Liver	Skeletal muscle and liver diseases

INHIBITION

- The prevention of an enzyme process as a result of interaction of inhibitors with the enzyme.

- INHIBITORS: Any substance that can diminish the velocity of an enzyme catalyzed reaction is called an inhibitor.

TYPES OF INHIBITION



REVERSIBLE INHIBITION

- It is an inhibition of enzyme activity in which the inhibiting molecular entity can associate and dissociate from the protein's binding site.

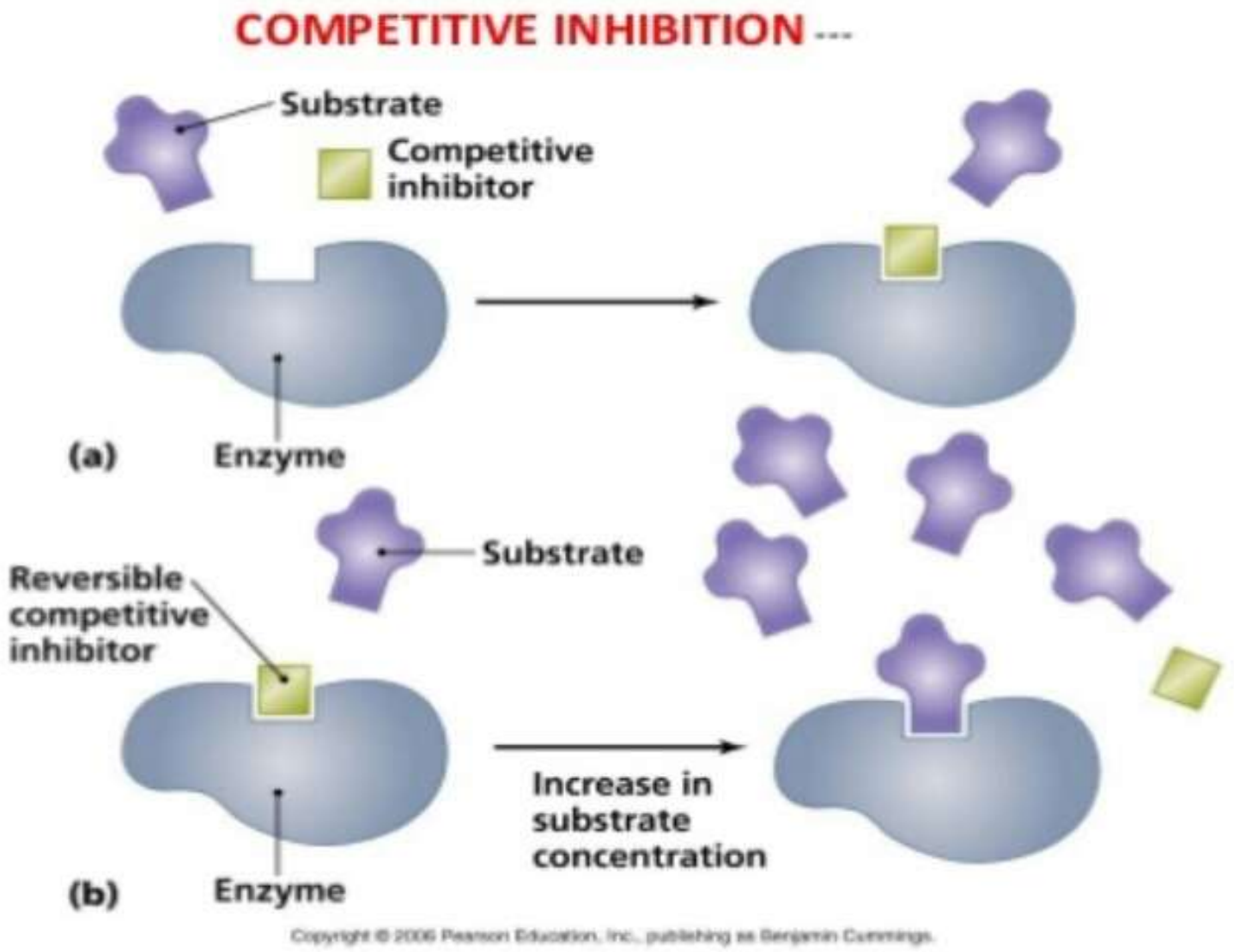
TYPES OF REVERSIBLE INHIBITION

There are four types:

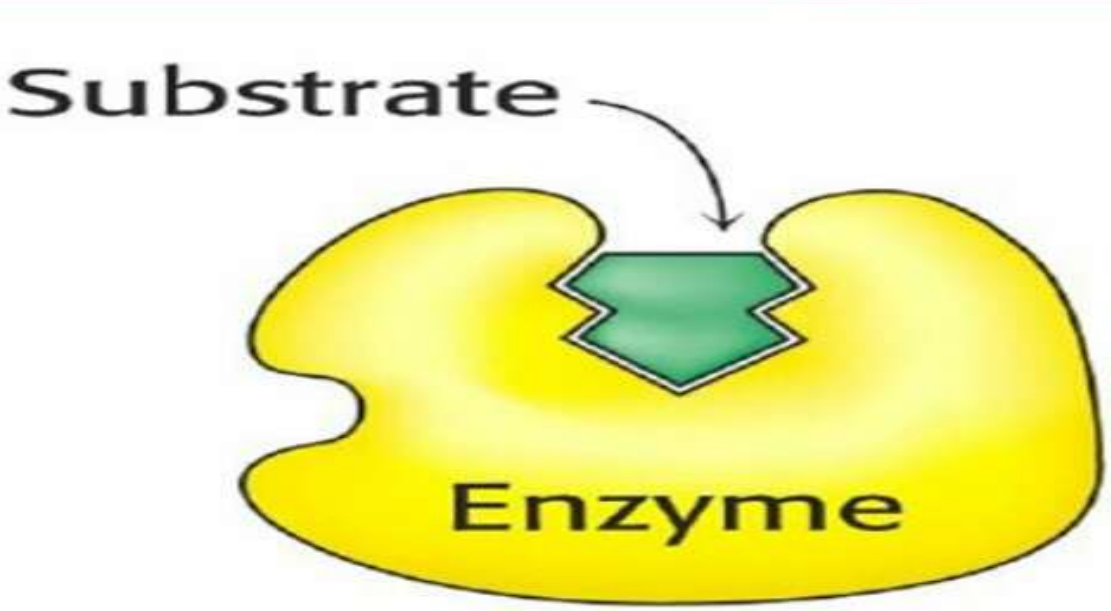
1. Competitive inhibition.
2. Uncompetitive inhibition.
3. Mixed inhibition.
4. Non-competitive inhibition.

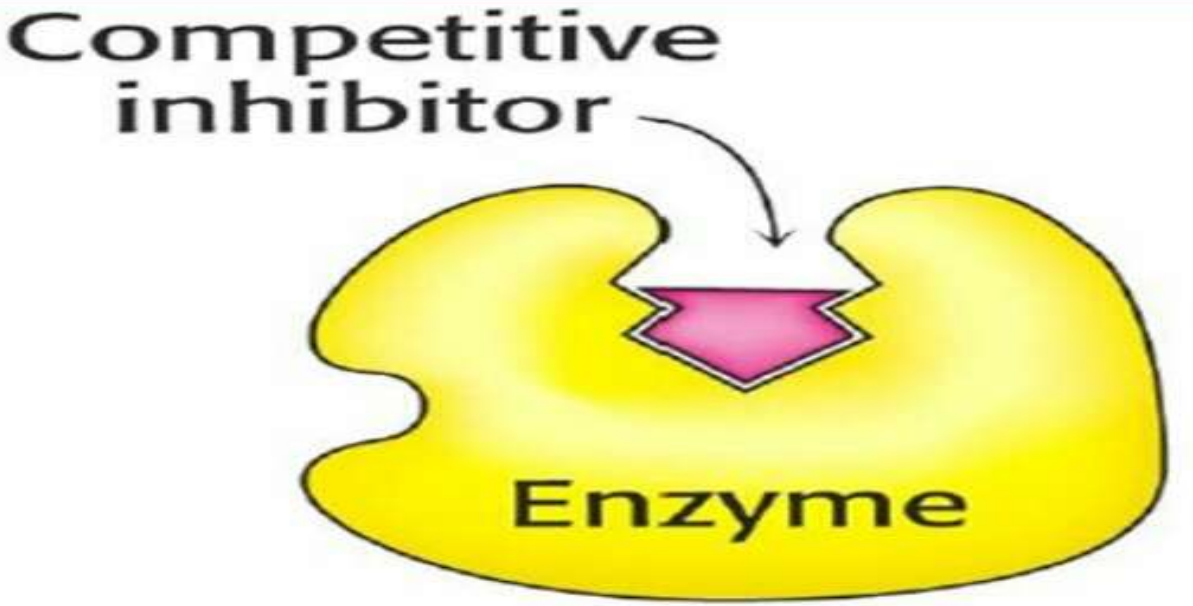
COMPETITIVE INHIBITION

Competitive inhibitors
1. competes with substrate for binding to active site but once bound substrate cannot be transformed into product by enzymes.
2.Inhibition by **Competitive inhibitors** can be reversed by simply increasing concentration of substrate



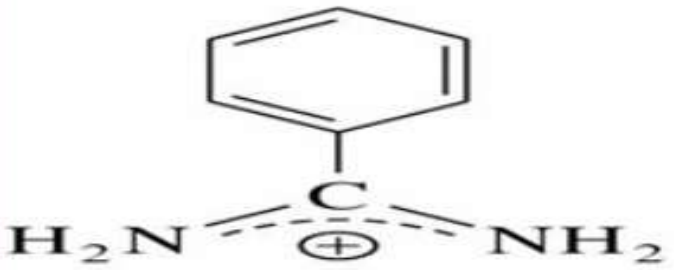
Competitive inhibition



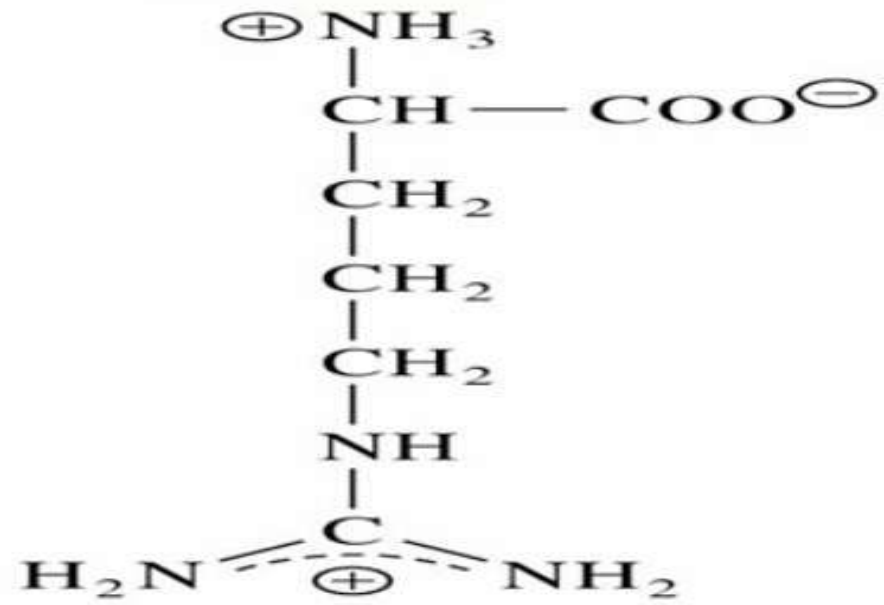


Example of competitive inhibition

Benzamidine competes with arginine for binding to trypsin



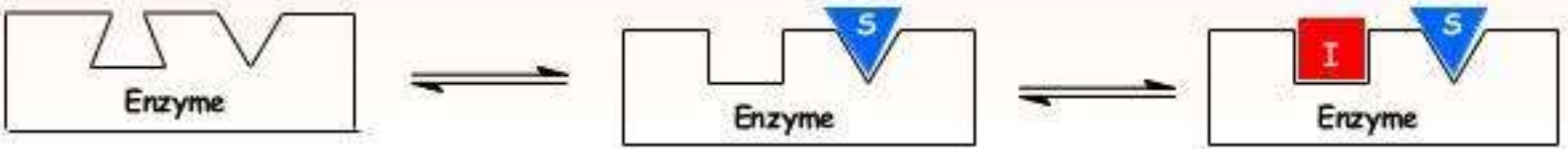
Benzamidine



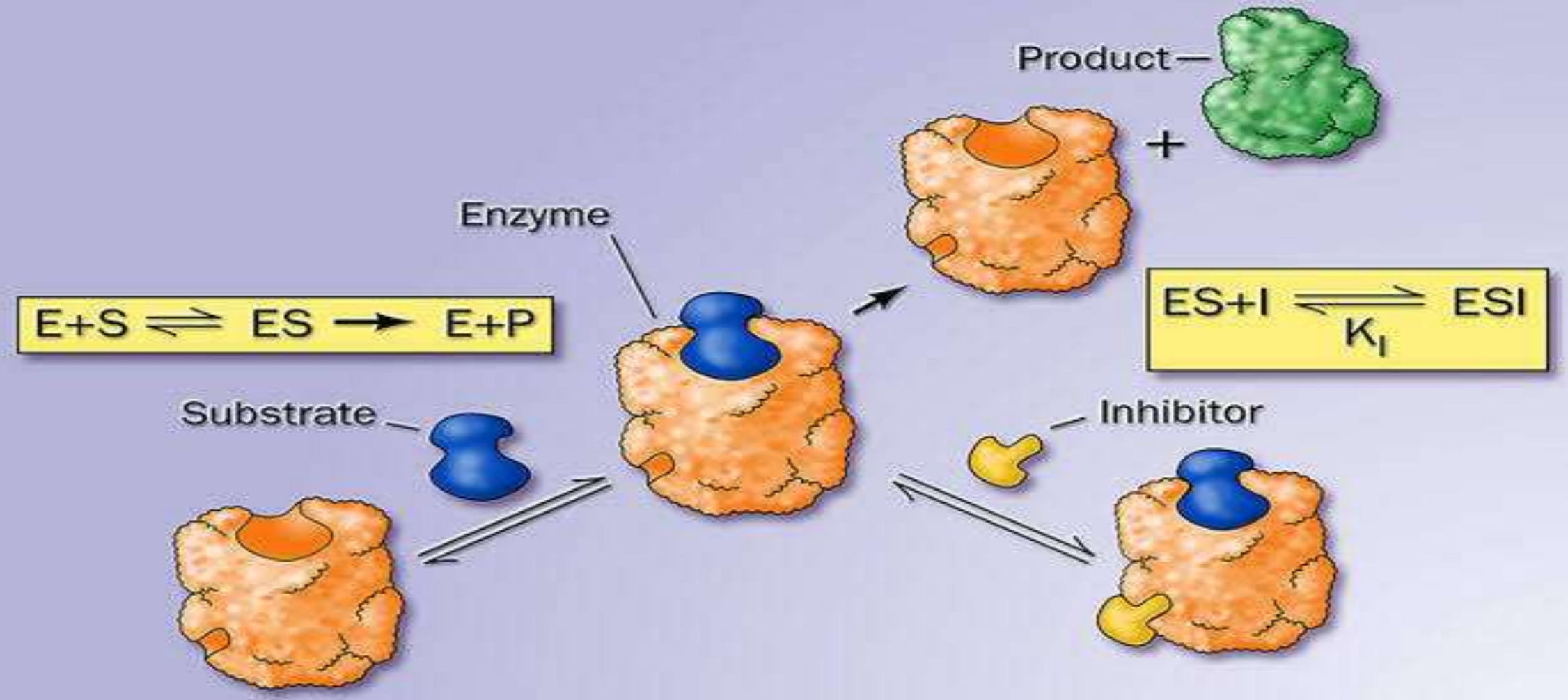
Arginine

Uncompetitive Inhibition

- I binds only to the ES complex , not to free E
- I - cause structural distortion of the active site - E catalytically inactive
- I can't be reversed by increasing the [S] since I doesn't compete with S for the same binding site
- Inhibition of placental alkaline phosphatase (Regan iso-enzyme) by phenylalanine .



Uncompetitive Inhibition



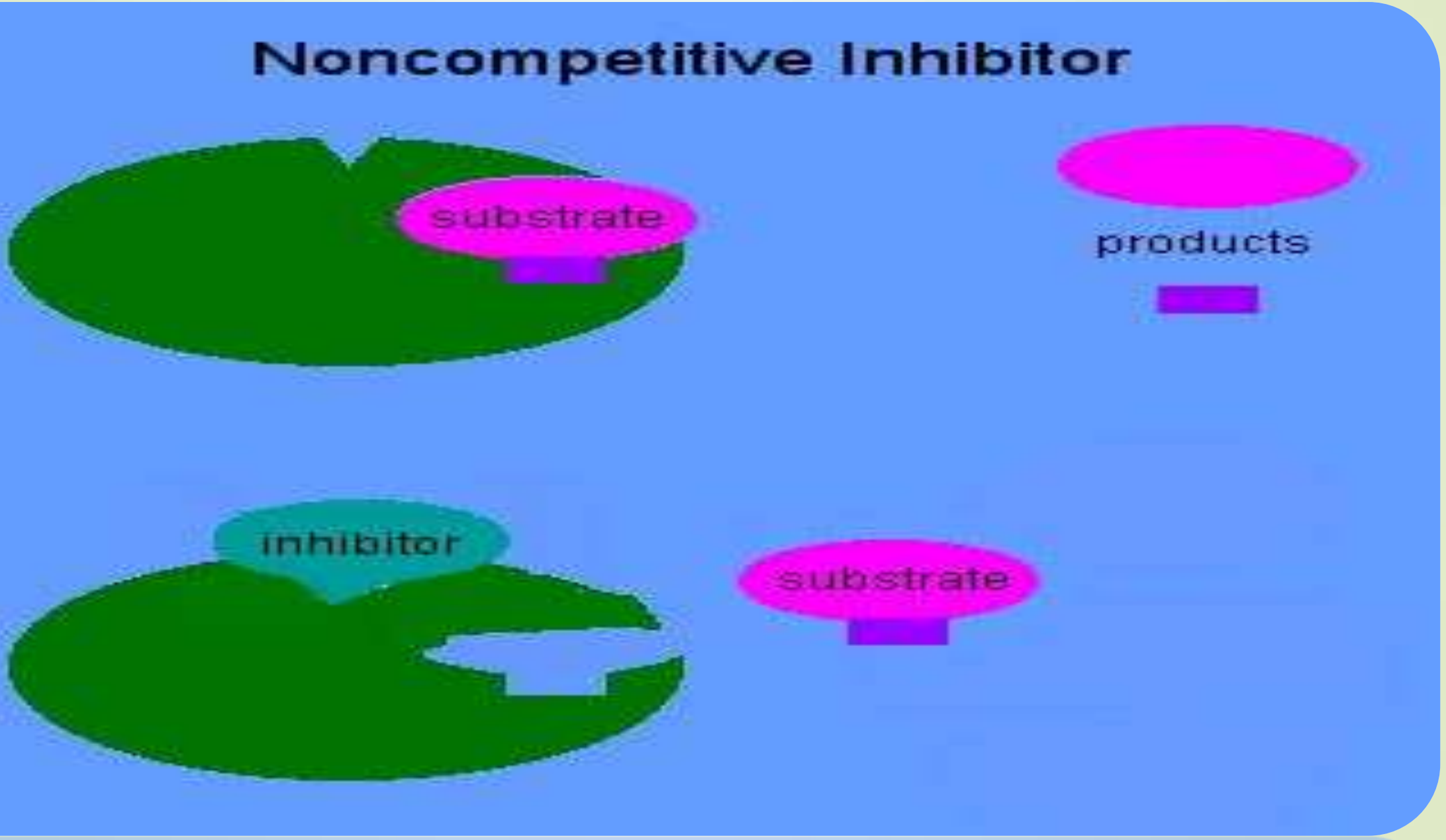
MIXED INHIBITION

- In this type of inhibition both E.I and E.S.I complexes are formed. o Both complexes are catalytically inactive.

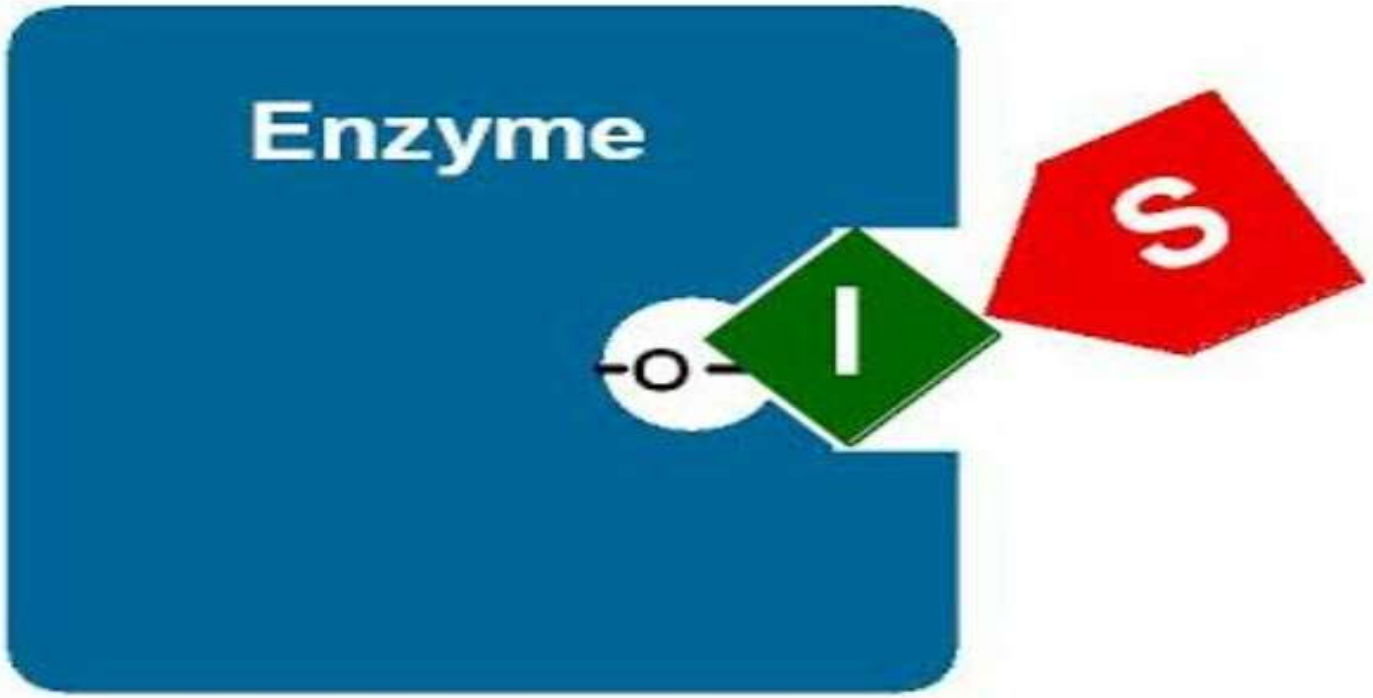
NON COMPETITIVE INHIBITION

- It is a special case of inhibition.
- oIn this inhibitor has the same affinity for either enzyme E or the E.S complex.

Noncompetitive Inhibitor



Irreversible Inhibition

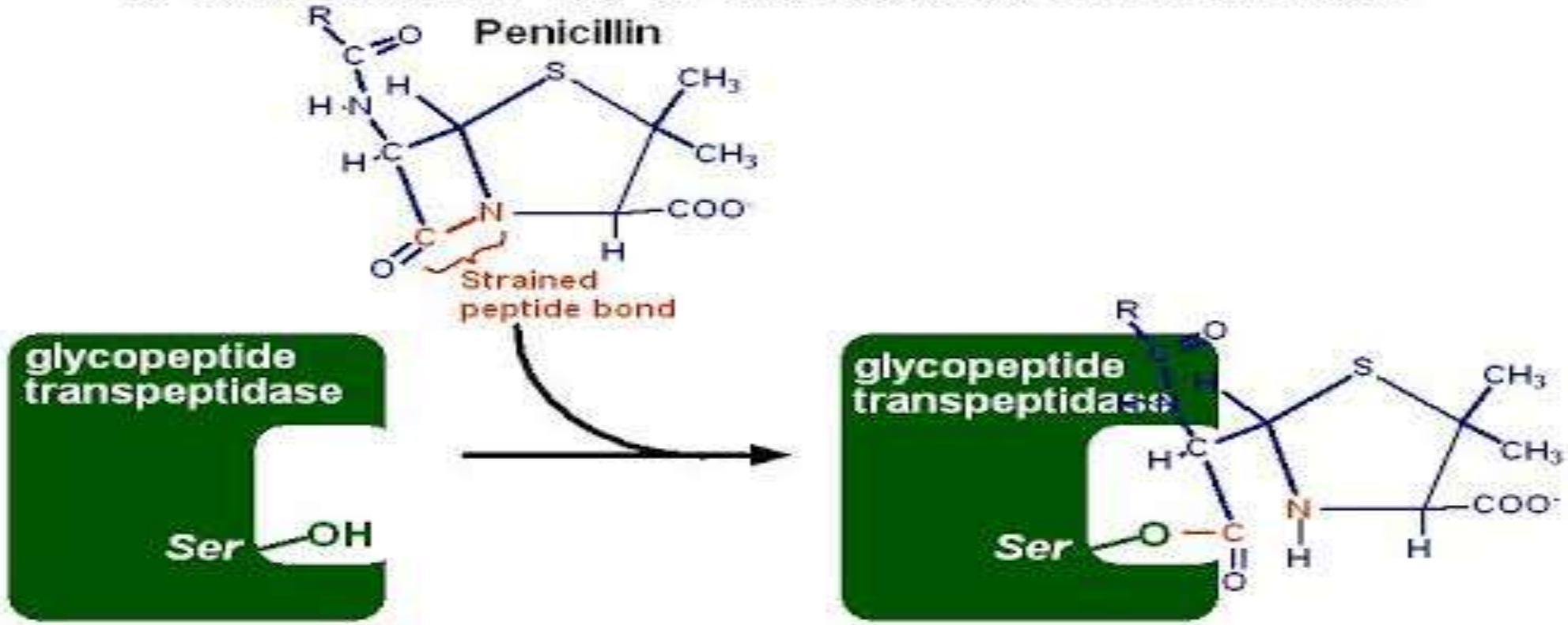


In irreversible inhibition, the inhibitor binds to the enzyme irreversibly through formation of a covalent bond with the enzyme , permanently inactivating the enzyme

EXAMPLES OF IRREVERSIBLE INHIBITION

1. Aspirin which targets and covalently modifies a key enzyme involved in inflammation is an irreversible inhibitor.
2. SUICIDE INHIBITION : It is an unusual type of irreversible inhibition where the enzyme converts the inhibitor into a reactive form in its active site.

Penicillin is a suicide inhibitor



Glycopeptide transpeptidase catalyzes the formation of cross-links between D-amino acids in the cell walls of bacteria. This enzyme also catalyzes the reverse reaction, the hydrolysis of peptide bonds. During the course of hydrolyzing the strained peptide bond in penicillin, the enzyme activates the inhibitor (penicillin), which then covalently modifies an active site serine in the enzyme. In effect, the enzyme "commits suicide" by hydrolyzing the strained peptide bond in penicillin.

THANK YOU