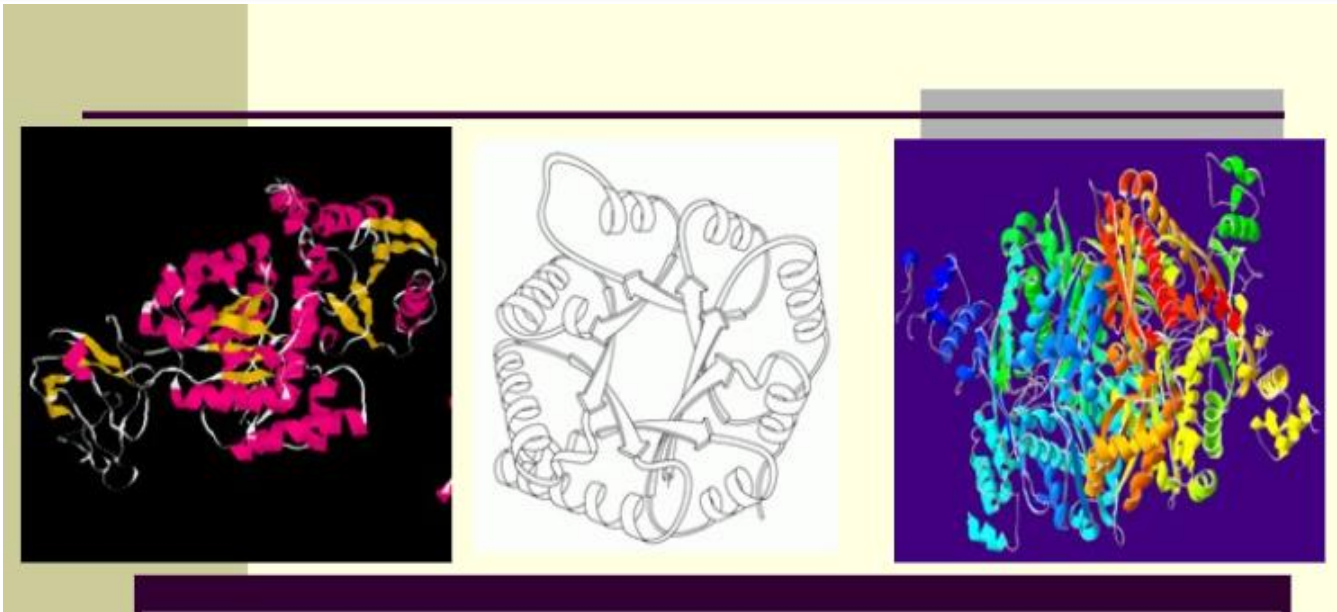


# ENZYMES INHIBITION



**Dr. Zarish Noreen**

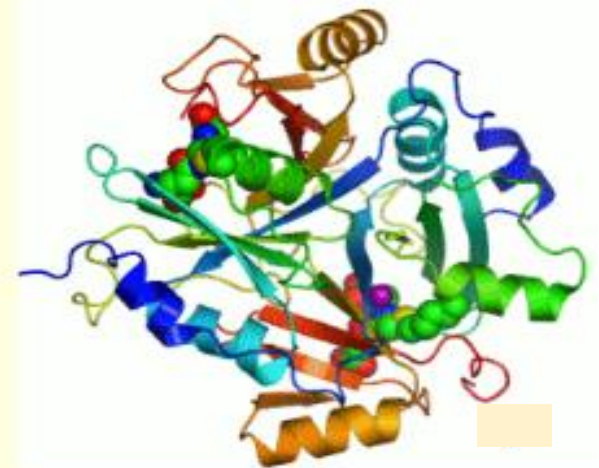
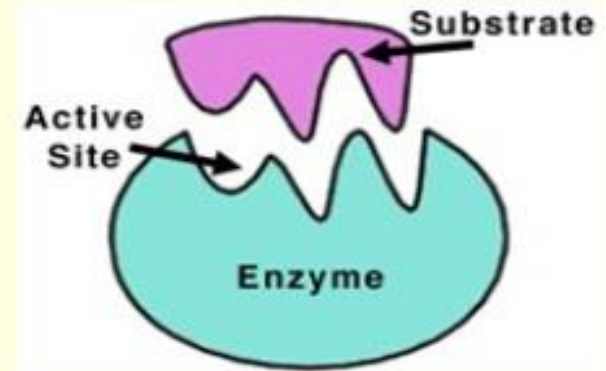
**Atta-ur-Rahman School of Applied Biosciences (ASAB)  
National University of Sciences and Technology (NUST), Islamabad**

# Enzymes

■ **Enzymes** are biomolecules that catalyze, increase the rates of chemical reactions without being altered during the reaction.

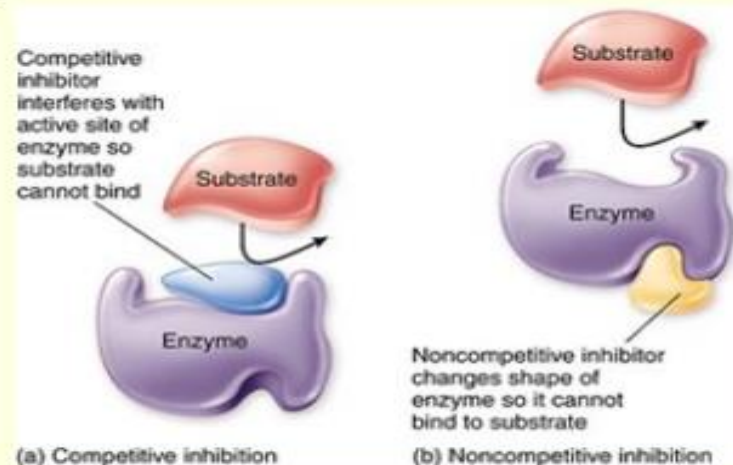
- Almost all enzymes are proteins;
- Enzymes are essential to life.

■ In enzymatic reactions, the molecules at the beginning of the process are called **substrates** , and the enzyme converts them into different molecules, the **products** .

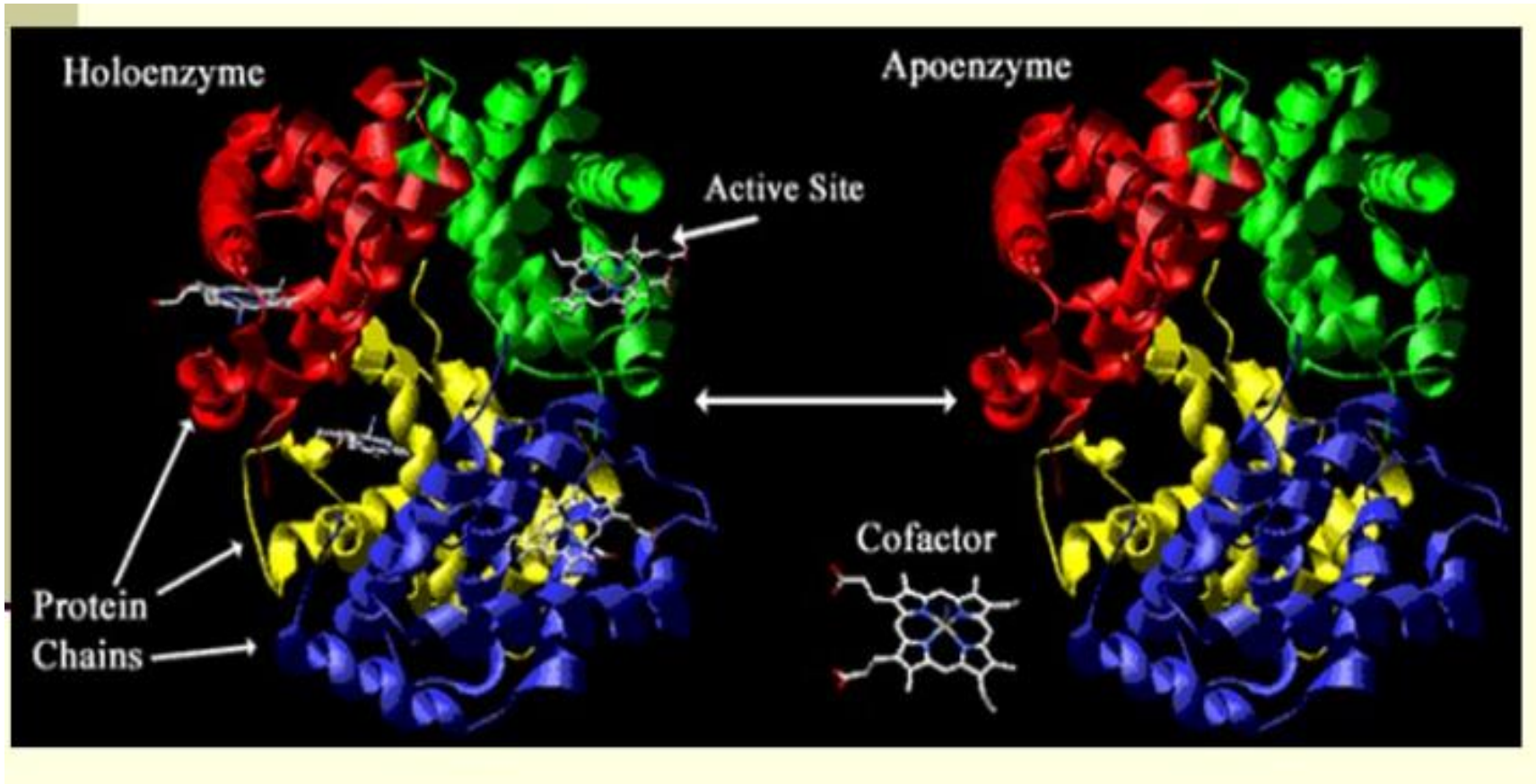


# Enzymes activity

- Enzyme activity can be affected by other molecules.
  - **Inhibitors** are molecules that decrease enzyme activity.
  - **Inducers** are molecules that increase activity. Many drugs and poisons are enzyme inhibitors.
- Activity is also affected by temperature, chemical environment (e.g. pH),



# Three-Dimensional Structure of Enzyme





# Enzyme Structure

- Most enzymes are **proteins**
- Enzymes may require a *non-peptide component as a cofactor*. The peptide component is called the **apoenzyme**, the cofactor is called as the **coenzyme** and the combined functional unit is the **holoenzyme**
- Cofactors that are tightly bound to the polypeptide are called **prosthetic groups**. Such proteins are called as *complex or conjugated proteins*. Proteins without prosthetic groups are simple proteins

# Enzymes Inhibitors and Inducers

Enzyme Inhibitor	Enzyme Inducer
Cimetidine	Rifampicin
Ketoconazole	Carbamazepine
Fluconazole	Phenobarbital
Miconazole	Phenytoin
Macrolides(except Azithromycin)	Griseofulvin
Fluoroquinolones(except Levofloxacin)	Smoking
	Chronic alcoholism

# Enzymes Inhibition

- Inhibitors are substances that binds to an enzyme and interfere in its activity.
- It can prevent formation of Enzyme-Substrate complex or can prevent ES breakdown to enzyme + product.
- Inhibitors are chemicals that reduce the rate of enzymic reactions.

# Enzymes Inhibition

➤  $E + S \rightarrow \text{ES Complex} \rightarrow \text{Enzyme} + \text{Product}$ .

➤  $E + S + I \rightarrow \text{ESI or EI} \rightarrow \text{No product formation}$ .

➤ There can be irreversible or reversible inhibitors.

➤ Irreversible bind to enzyme through covalent bond.

➤ Reversible bind to enzyme through non-covalent interactions.



# Enzymes Inhibition

- Reversible enzyme inhibitors
- Inhibition of enzyme activity in which the inhibiting molecular entity can associate and dissociate from the protein's binding site.
- There are 3 types of reversible inhibitors
- (1) Competitive inhibition
- (2) Uncompetitive inhibition
- (3) Non-competitive inhibition

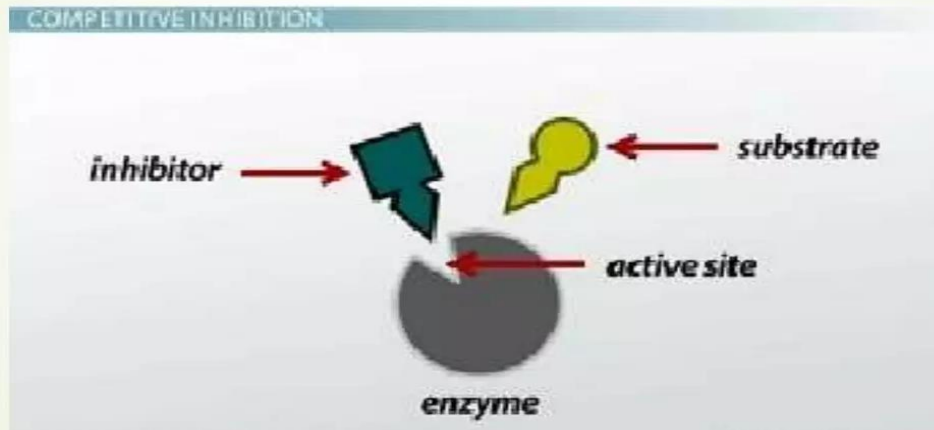
# Enzymes Inhibition

## (1) Competitive inhibition

- These compete with the substrate molecules for the active site.
- The inhibitors action is proportional to its concentration.
- It can reverse inhibition by adding more substrate.

# Enzymes Inhibition

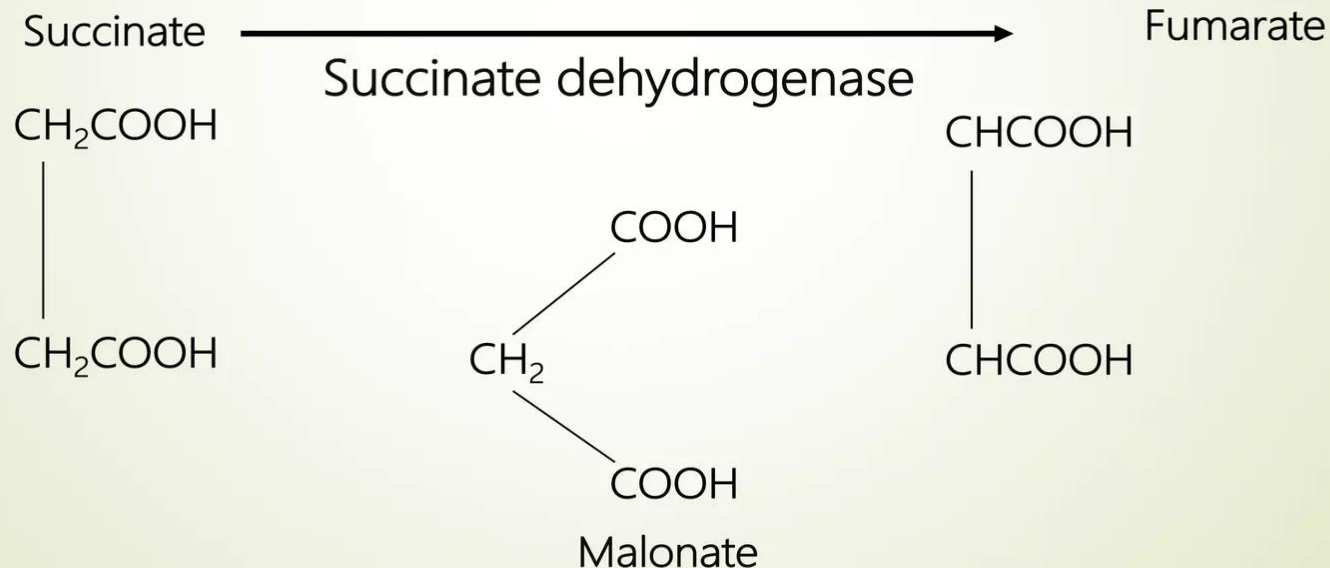
## (1) Competitive inhibition



# Enzymes Inhibition

## (1) Competitive inhibition

➡ E.g. - Malonate is a competitive inhibitor for succinate dehydrogenase.



# Enzymes Inhibition

## (2) Uncompetitive inhibition

- Inhibitor binds only to Enzyme-Substrate complex.
- Binding site for inhibitor is created only upon substrate binding.
- There's no EI complex, only E, ES, and ESI, but ESI can't make product.
- E.g. – Tetramethylene sulfoxide & 3-butylthiolene-1-oxide are uncompetitive inhibitors of liver alcoholdehydrogenase.



# Enzymes Inhibition

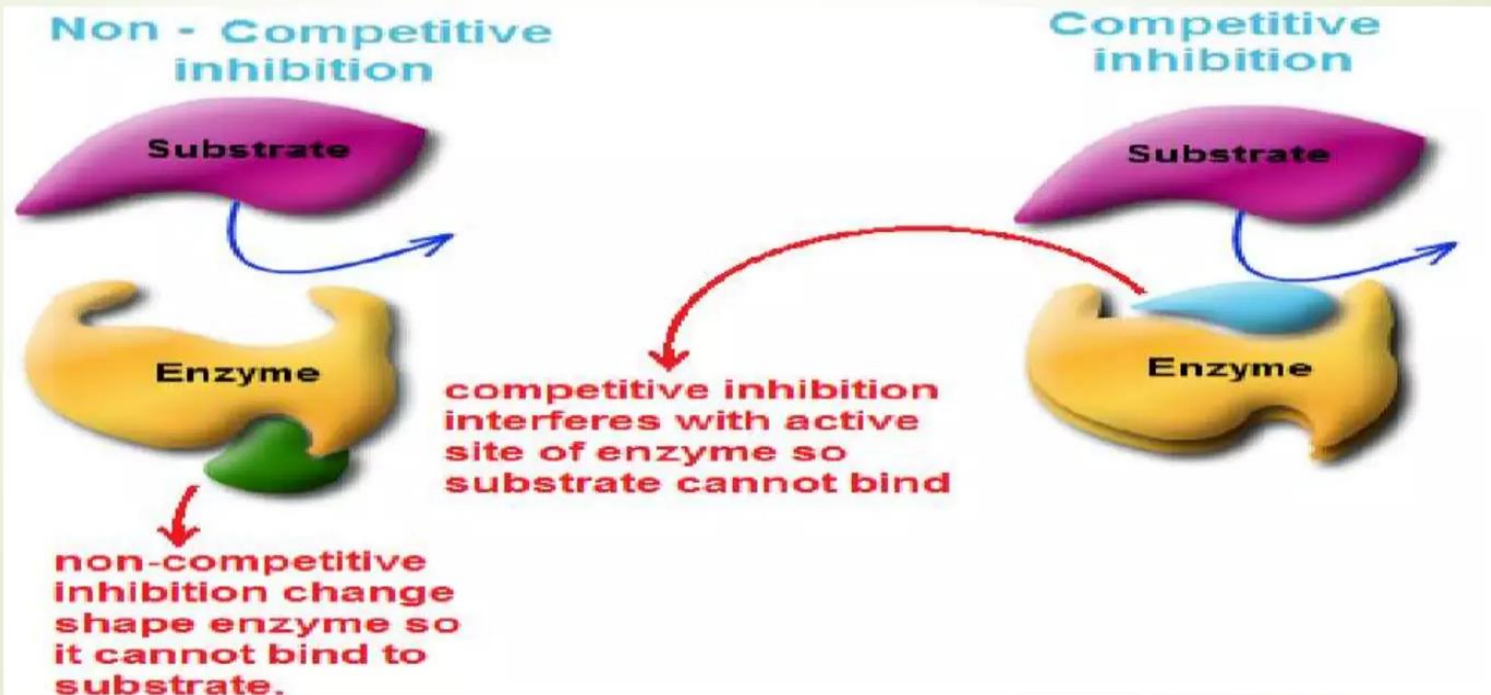
## (3) Non-competitive inhibition

- These can bind to enzyme or enzyme-substrate complex.
- Enzyme can bind both substrate and inhibitor , but ESI complex can't make product.
- Inhibits by binding irreversibly to the enzyme but not at the active site.

# Enzymes Inhibition

## (3) Non-competitive inhibition

- E.g.- Cyanide combines with the iron in the enzymes cytochrome oxidase.



# Enzymes Inhibition

## Enzyme Inhibition

- Irreversible enzyme inhibitors
- The binding of an inhibitor can stop a substrate from entering the enzyme's active site from catalyzing its reaction.
- Irreversible inhibitors usually react with the enzyme and change it chemically.

# Enzymes Inhibition

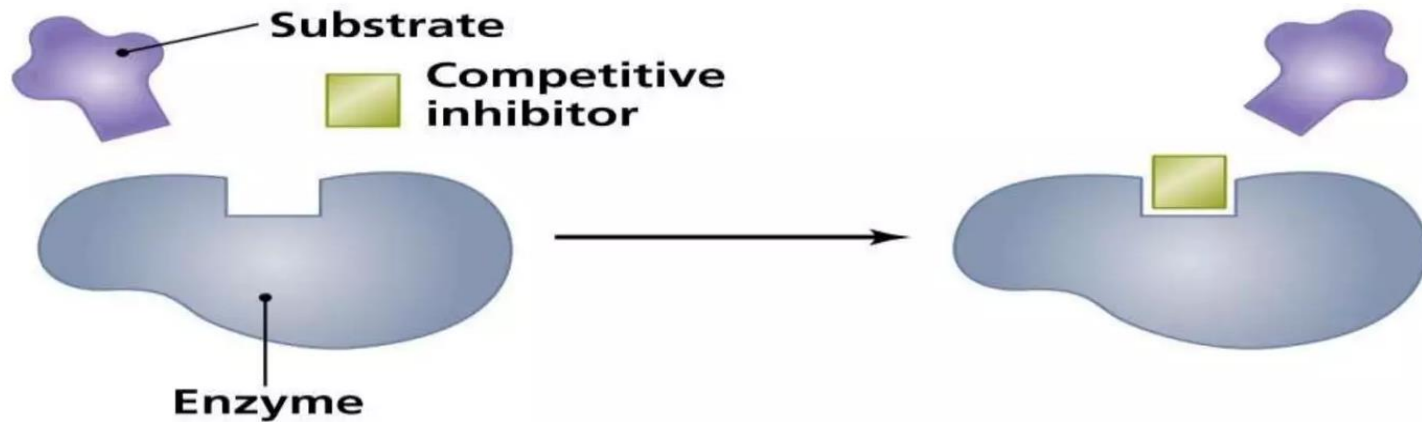
## Irreversible enzyme inhibitors

- They bind covalently and destroy the functional group on the enzyme that is essential for its activity.
- They could be
  - (1) Competitive
  - (2) Allosteric

# Enzymes Inhibition

## (1) Competitive

- Permanent binding to enzyme active site.

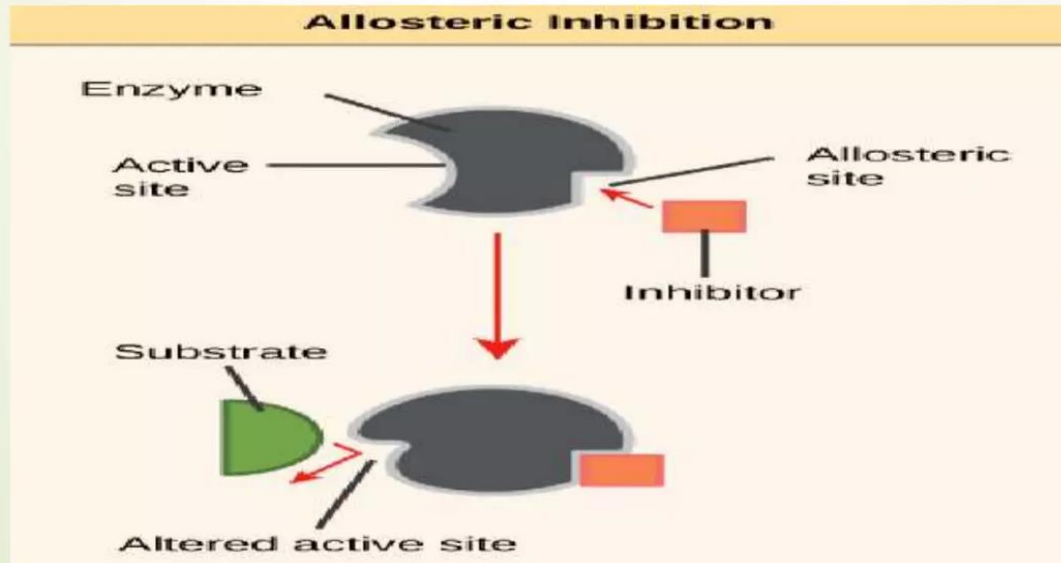




# Enzymes Inhibition

## (2) Allosteric

- Permanent binding to enzyme allosteric site.
- They changes the shape of the enzyme.



# Enzymes Inhibition

## Example of irreversible inhibitors

- Oxalic and citric acid inhibit blood clotting by forming complexes with calcium ions necessary for the enzyme metal ion activator.

