Enzyme Inhibition

Enzymes

- Enzymes are the substance that increases the rate of a reaction.
- Reactants binds to enzyme and products are released.
- Enzymes can accelerate reactions as much as 10^{16} overall uncatalyzed reaction.

Enzymes

- Specificity of a enzyme towards its substrate scontrolled by its structure.

- This unique fit of substrate with enzyme controls the selectivity of substrate for its product formation.

Enzyme 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.

Enzyme Inhibition

E + S → ES COMPLEX → ENZYME + PRODUCT.

E + S+ I → ESI OR EI → NO PRODUCT FORMATION.

THERE CAN BE IRREVERSIBLE OR REVERSIBLE INHIBITORS.

Enzyme Inhibition

IRREVERSIBLE BIND TO ENZYME THROUGH COVALENT BOND.

REVERSIBLE BIND TO ENZYME THROUGH NON-COVALENT INTERACTIONS.

Enzyme 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

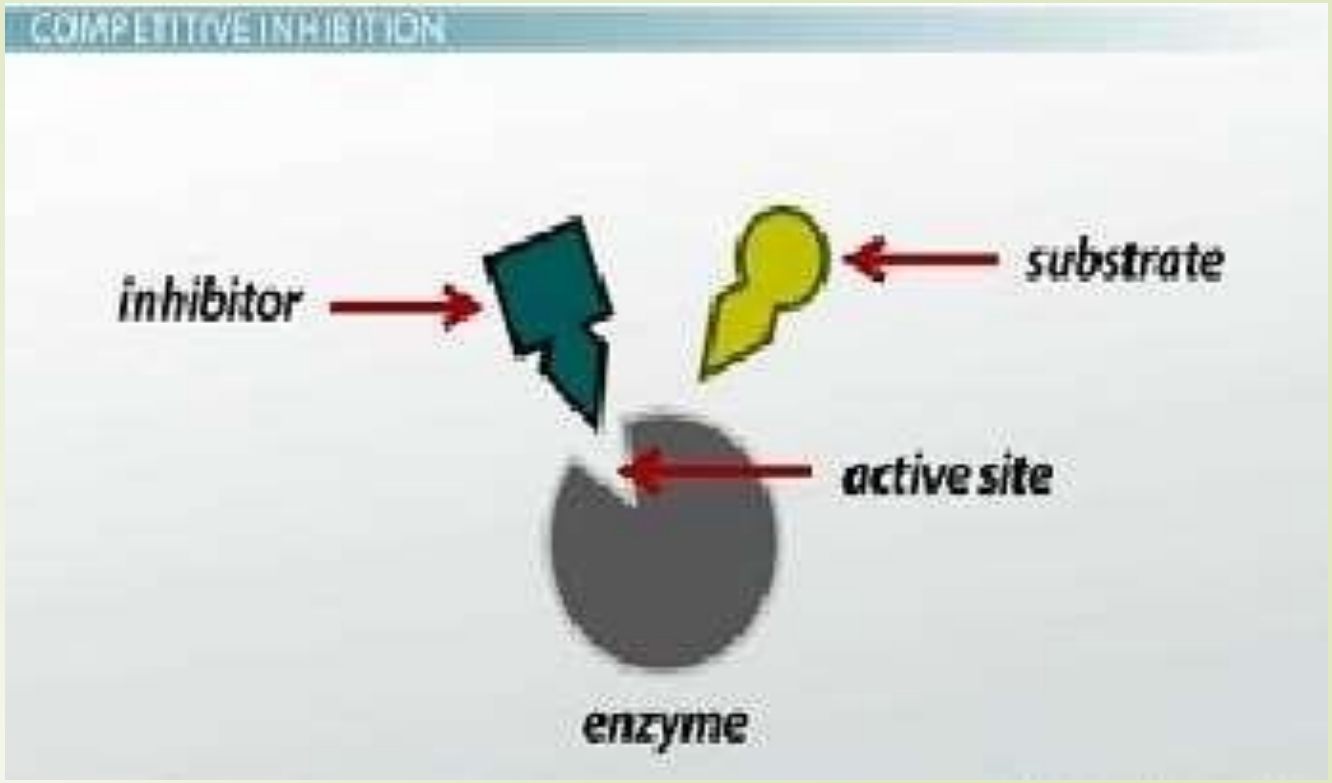
(2) UNCOMPETITIVE INHIBITION

(3) NON-COMPETITIVE INHIBITION

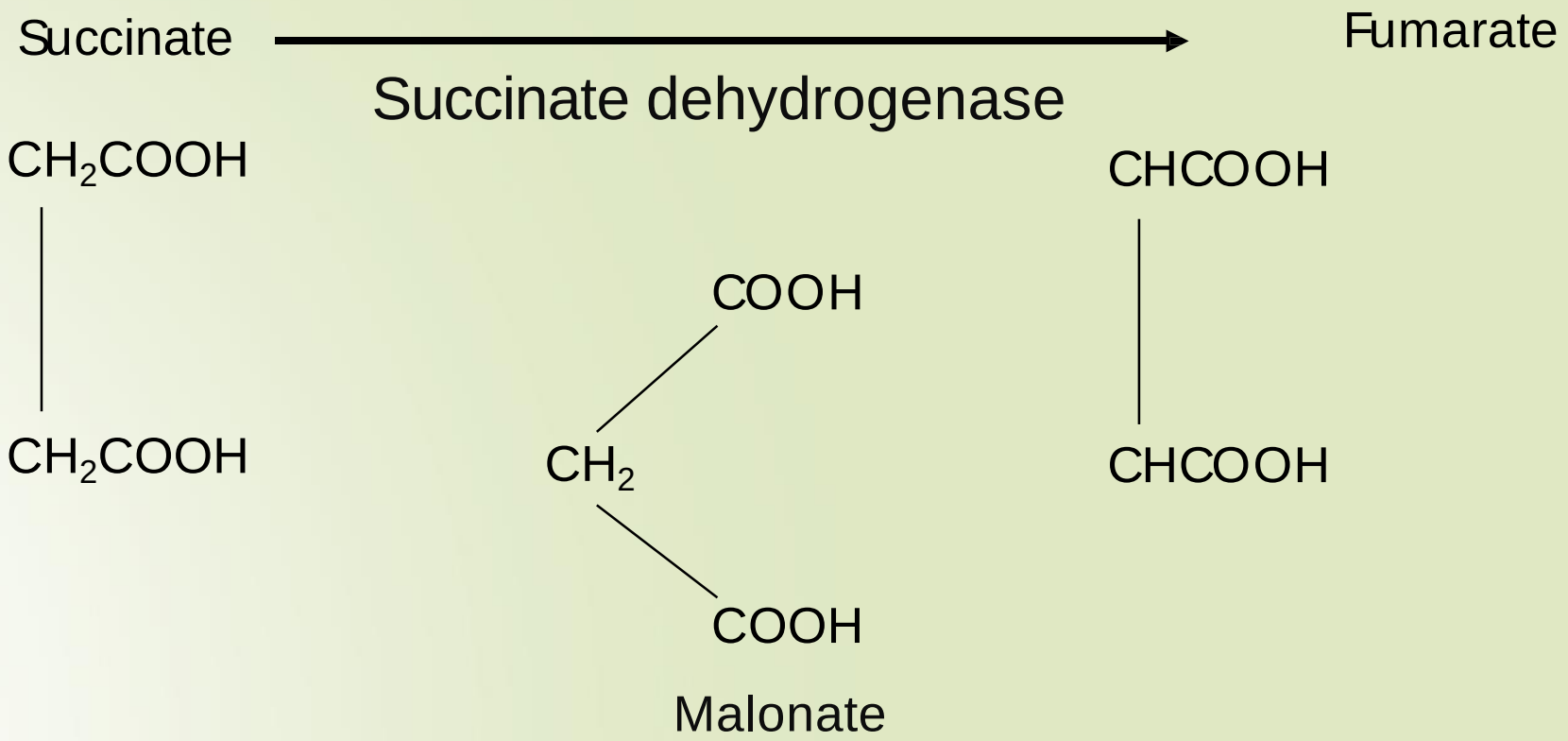
(1) COMPETITIVE INHIBITION

- 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.

COMPETITIVE INHIBITION



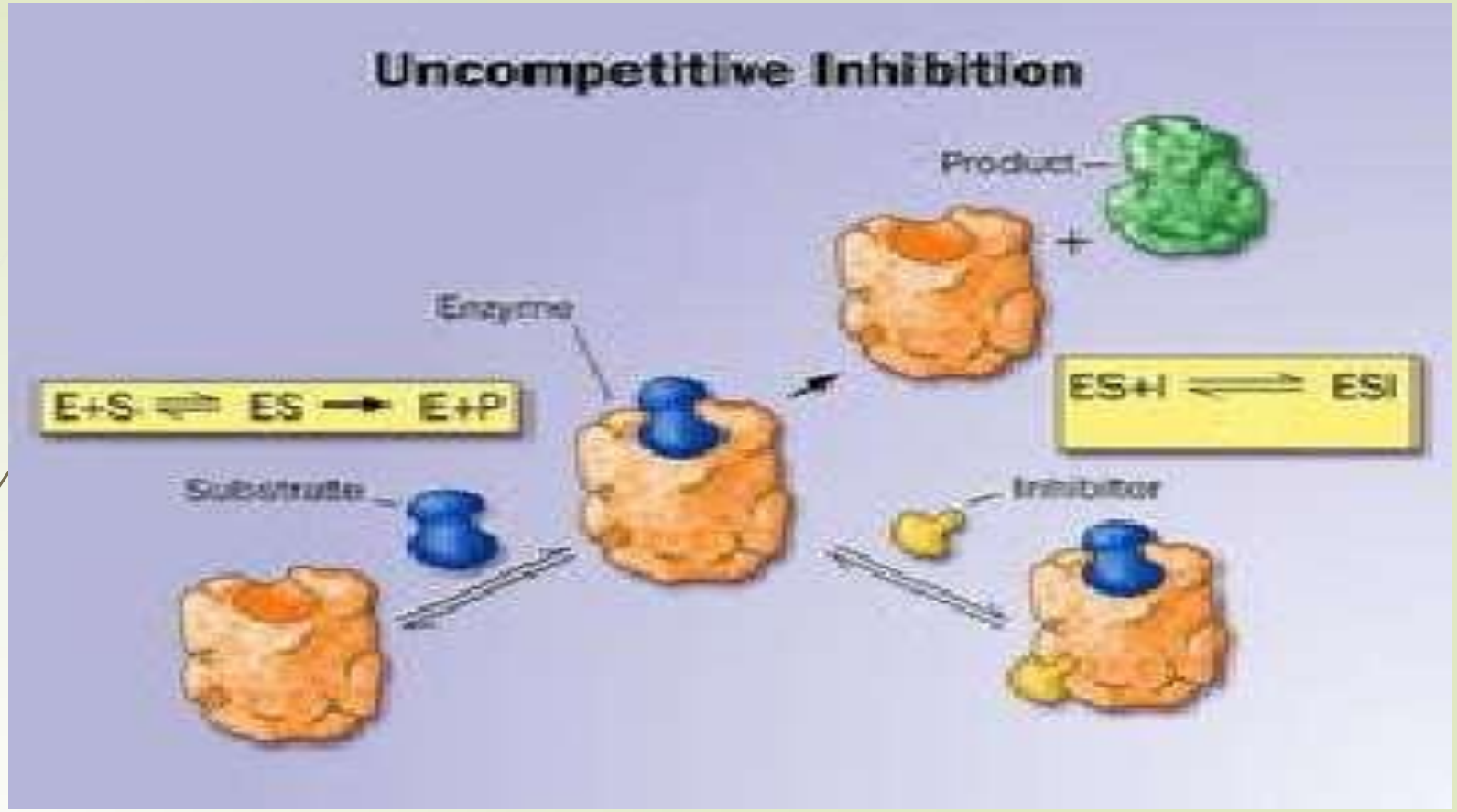
Example - Malonate is a competitive inhibitor for succinate dehydrogenase.



(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.
- EXAMPLE. – TETRAMETHYLENE SULFOXIDE & 3-BUTYLTHIOLENE-1-OXIDE ARE UNCOMPETITIVE INHIBITORS OF LIVER ALCOHALDEHYDROGENASE.

UNCOMPETITIVE INHIBITION

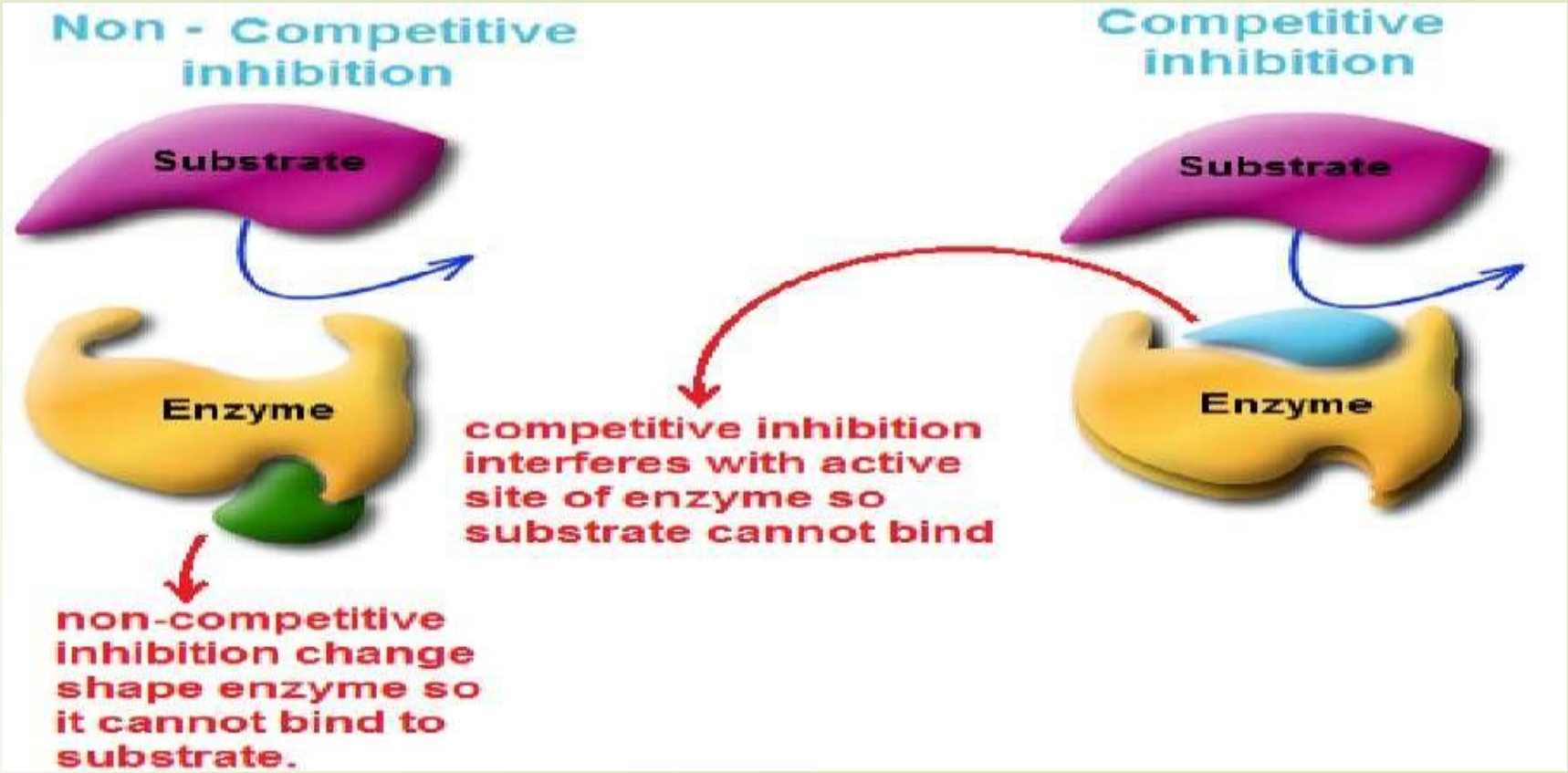


(3) Non-competitive inhibition

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

NON-COMPETITIVE INHIBITION

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



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.

IRREVERSIBLE ENZYME INHIBITORS

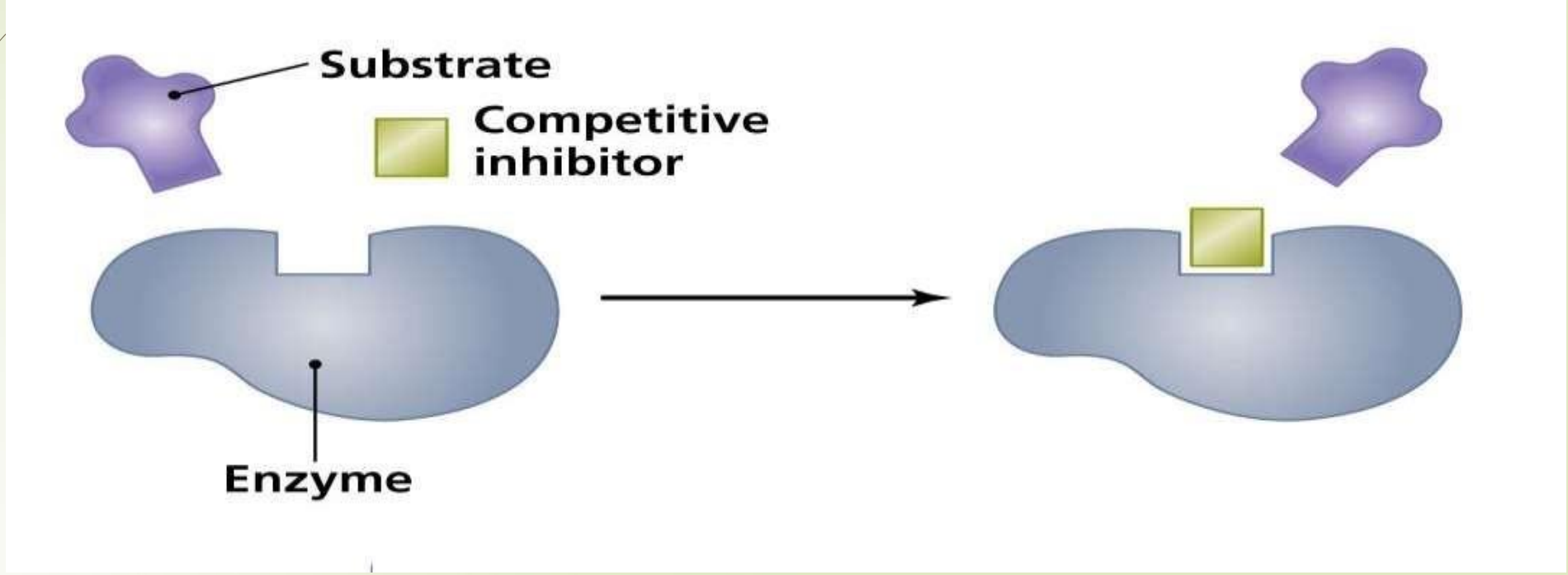
- THEY BIND COVALENTLY AND DESTROY THE FUNCTIONAL GROUP ON THE ENZYME THAT IS ESSENTIAL FOR ITS ACTIVITY.
- THEY COULD BE

(1) COMPETITIVE

(2) ALLOSTERIC

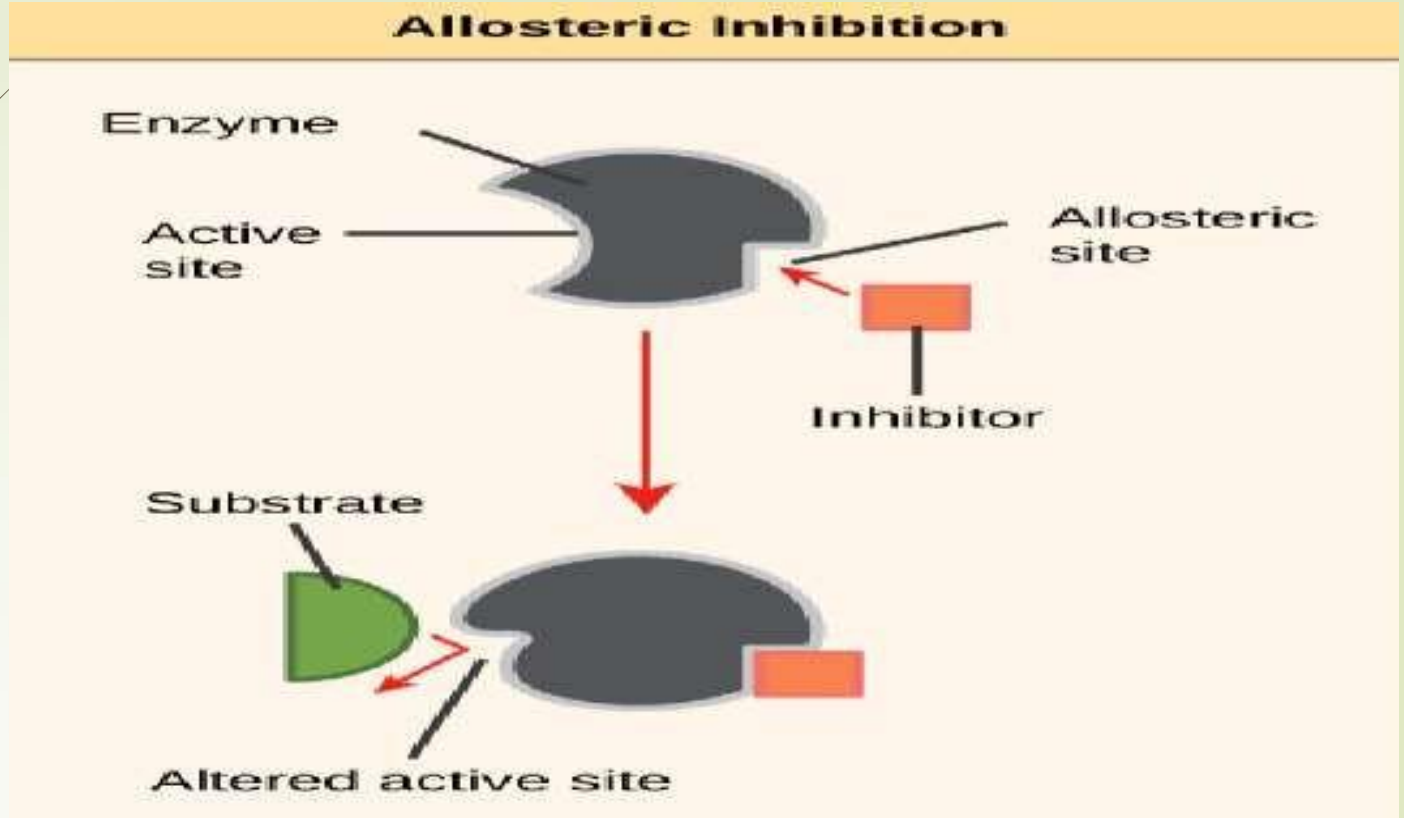
(1) COMPETITIVE

❖Permanent binding to enzyme active site.



(2) ALLOSTERIC

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



Example of irreversible inhibitors

- **Oxalic and citric acid** inhibit blood clotting by forming complexes with calcium ions necessary for the enzyme metal ion activator.
- **5- fluoro uracil**-used as anticancer drug

THANK YOU