



ENZYME INHIBITOR

Introduction

Inhibitors are the chemicals that reduce the rate of enzymatic reactions. They block the enzyme but they do not usually destroy it.

Types of enzyme inhibitors

Reversible

- a. Competitive
- b. Non competitive
- c. Uncompetitive

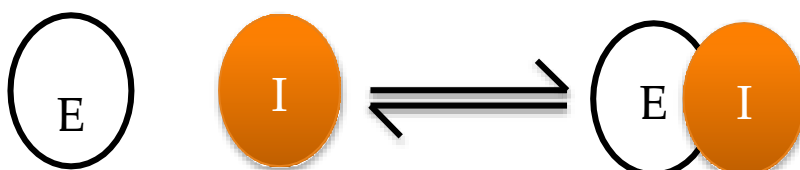
Irreversible

- a) Active site directed
- b) Suicide inhibitors

Reversible inhibitor:

Inhibitor binds to Enzyme reversibly through non covalent interactions.

An Equilibrium is established between the free inhibitor & EI Complex and is defined by an equilibrium constant (K_i)



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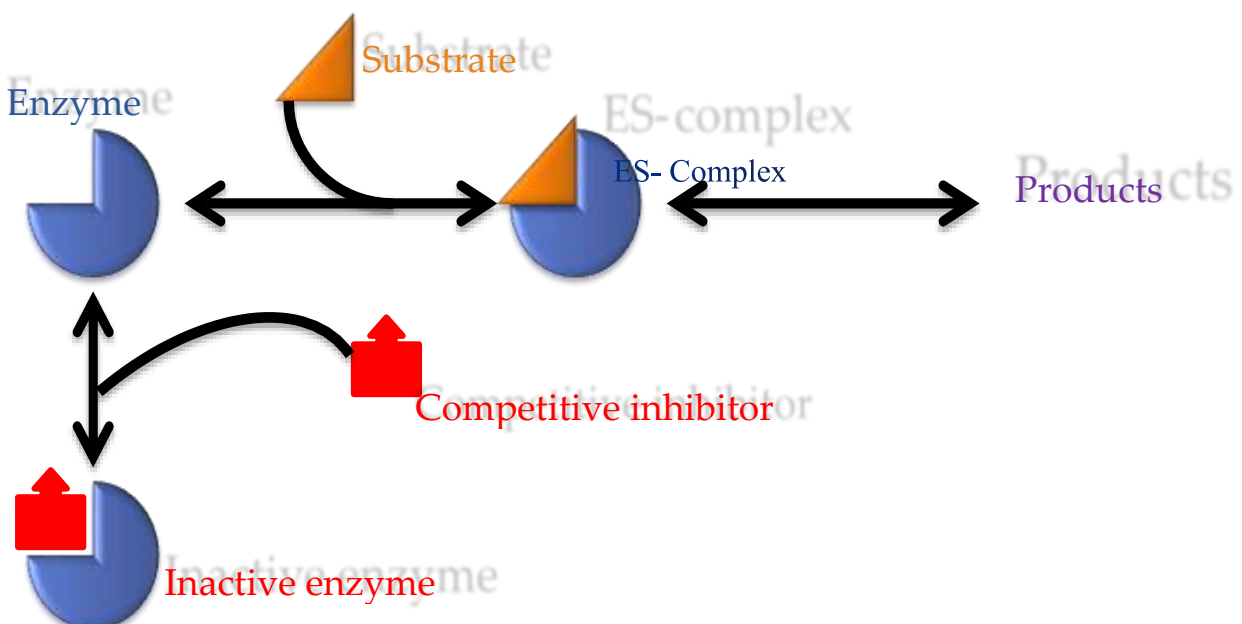
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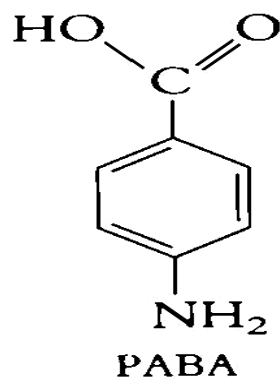
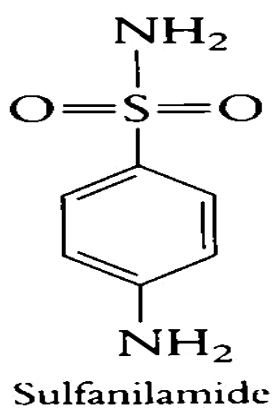
a) Competitive inhibitors :

A competitive inhibitor often has structural features similar to those of the substrate whose reactions they inhibit.

This means that a competitive inhibitor and enzyme's substrate are in direct competition for the same binding **active site** on the enzyme.



Example:



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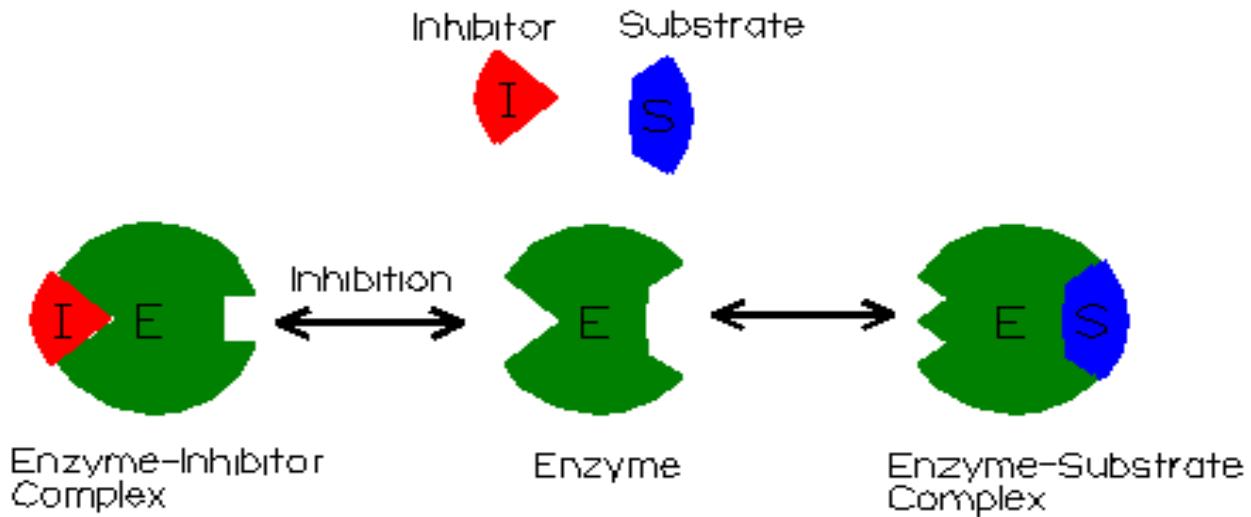
The antibiotic sulfanilamide is similar in structure to para- aminobenzoic acid (PABA), an intermediate in the biosynthetic pathway for folic acid. Sulfanilamide can competitively inhibit the enzyme that has PABA as its normal substrate by competitively occupying the active site of the enzyme.

b) Non competitive inhibitor

These are not influenced by the concentration of the substrate. It inhibits by binding irreversibly to the enzyme but not at the active site.

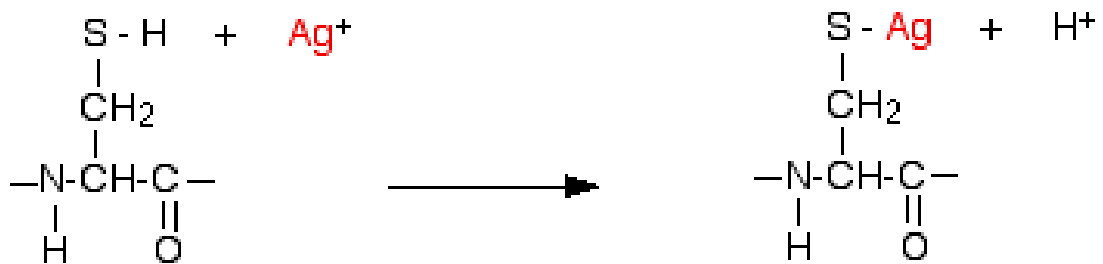
They also bind with the same affinity to the free enzyme and form the Enzyme-Substrate complex.

It change the shape of enzyme and active site.



Example:

Silver ions (heavy metal) react with -SH groups in the side groups of cysteine residues in the protein chain:



cysteine residue in protein chain



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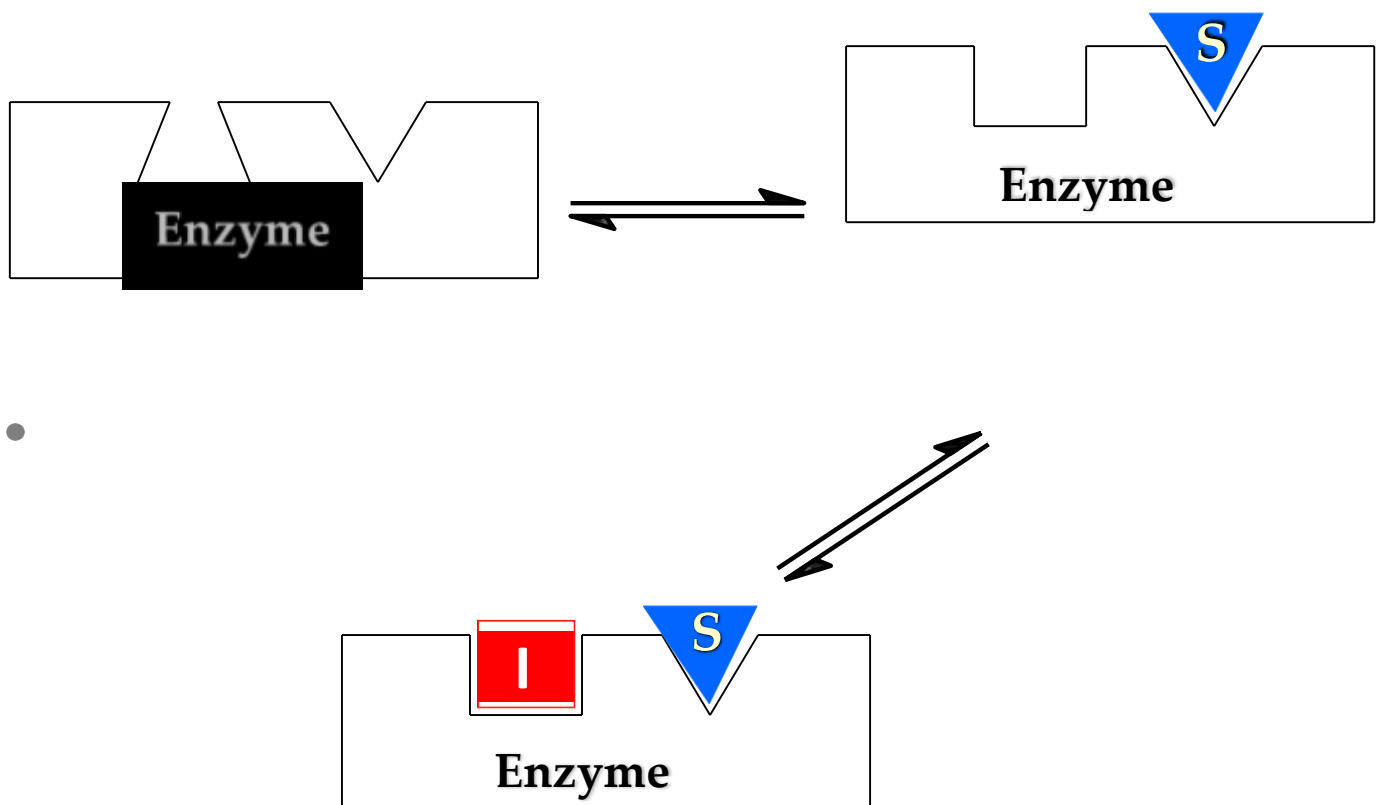
If the cysteine residue is somewhere on the protein chain which affects the way it folds into its tertiary structure, then altering this group could have an effect on the shape of the active site, and so stop the enzyme from working.

c) Uncompetitive inhibitor

Uncompetitive inhibitors do not bind to the free enzyme. They bind only to the enzyme-substrate complex to yield an inactive E. S. I complex.

Uncompetitive inhibitors frequently observed in multi substrate reaction.

Inhibition can't be reversed by increasing the [S] since (I) Inhibitor doesn't compete with S for the same binding site.



Irreversible inhibitor:

Inhibitor binds at or near the active site of the enzyme irreversibly, usually by covalent bonds, so it can't dissociate from the enzyme.

Irreversible inhibitors combine with the functional groups of the amino acids in the active site, irreversibly.

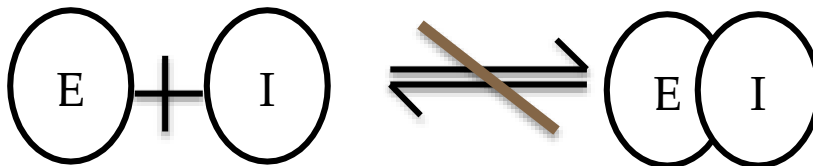
Irreversible inhibitors occupy or destroy the active sites of the enzyme permanently and decrease the reaction rate.

Enzyme activity is not regained on dialysis.



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a)Active site directed inhibitor

Active site directed inhibitor is also called as affinity label. It is a chemically reactive compound that is designed to resemble the substrate of an enzyme so that it binds at the active site and forms a stable covalent bond with a susceptible group of the nearby residue in the enzyme protein.

Affinity labels are very useful for identifying catalytically important residues.

b)Suicide inhibitor

A suicide inhibitor is a relatively inert molecule that is transformed by an enzyme at its active site into a reactive compound that irreversibly inactivates the enzyme.

They are substrate analogs designed so that via normal catalytic action of the enzyme, a very reactive group is generated.

The latter forms a covalent bond with a nearby functional group within the active site of the enzyme causing irreversible inhibition.

