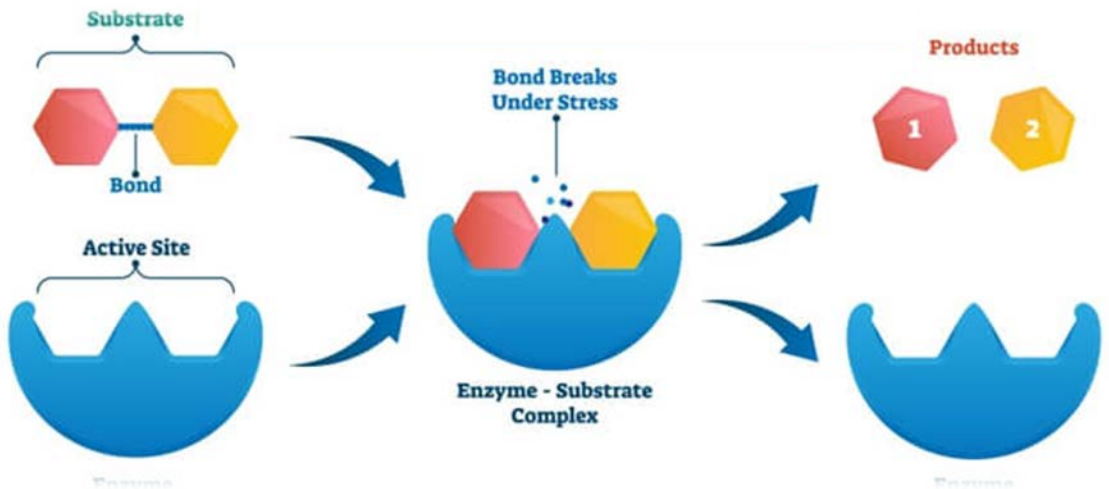
BIOCHEMISTRY - YEAR 2



Enzymes
Part 3
Lecture No: 16

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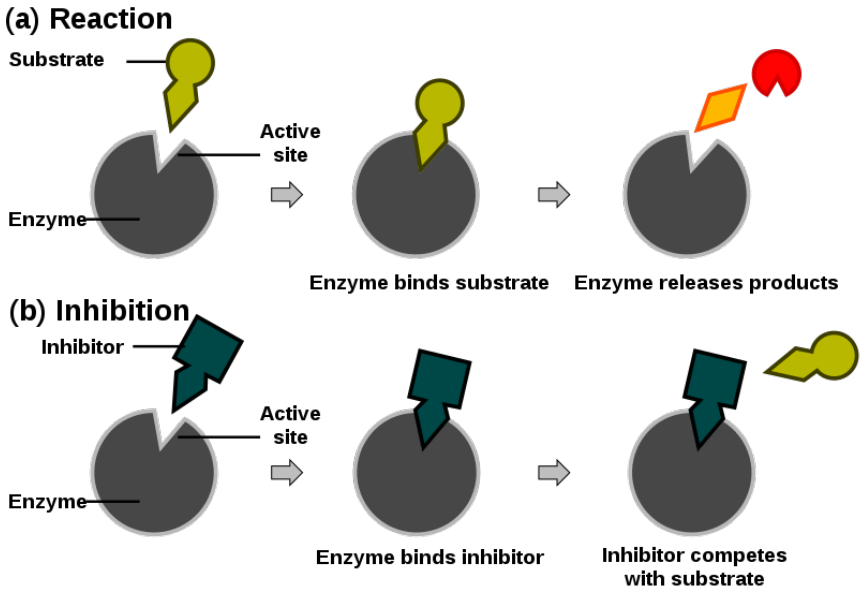
Enzyme Inhibition

- Many kinds of molecules called inhibitors cause enzymes to lose catalytic activity. Although inhibitors act differently, they all prevent the active site from binding with a substrate. Some inhibitors cause a reversible inhibition, which means that the enzyme regains activity when the inhibitor dissociates from the enzyme. In an irreversible inhibition, an inhibitor bonds covalently with an enzyme and cannot be removed, which makes the loss of enzyme irreversible.

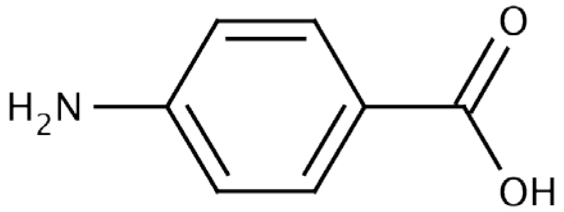
Reversible Competitive Inhibition

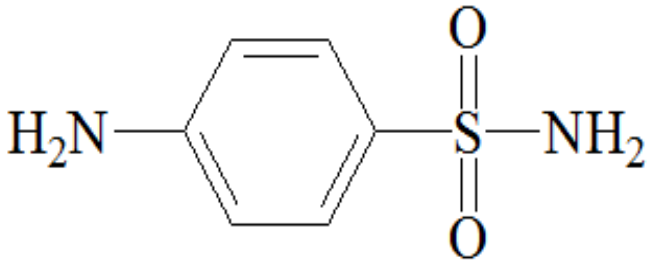
- Reversible inhibition can be competitive or noncompetitive. In competitive inhibition, an inhibitor competes for the active site, whereas in noncompetitive inhibition, the inhibitor acts on a site that is not the active site. A competitive inhibitor has a structure that is so similar to the substrate it can bond to the enzyme just like the substrate. Thus the competitive inhibitor competes with the substrate for the active site on the enzyme. As long as the inhibitor occupies the active site, the substrate cannot bind to the enzyme and no reaction takes place.



- Some bacterial infections are treated with competitive inhibitors called antimetabolites. Sulfanilamide, one of the first sulfa drugs, competes with PABA (p-aminobenzoic acid), which is an essential substance (metabolite) in the growth cycle of bacteria.
  - Substrate need to bacteria growth

Inhibitor





PABA (p-aminobenzoic acid)

Sulfanilamide

Reversible Noncompetitive Inhibition

The structure of a **noncompetitive inhibitor** does not resemble the substrate and dose not compete for the active site. Instead a noncompetitive inhibitor bind site on the enzyme that is not the active site. When the noncompetitive inhibitor bonded to the enzyme, the shape of the enzyme is distorted. Inhibition occurs because the substrate cannot fit in the active site, or it does not fit properly. Without the proper alignment of substrate with the amino acid side groups, no catalysis can take place.

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Because a noncompetitive inhibitor is not competing for the active site , the addition of more substrate does not reverse this type of inhibition . However , enzyme activity can be regained by lowering the concentration of the noncompetitive inhibitor making more enzyme molecules available . Examples of noncompetitive inhibitors are the heavy metal ions Pb^{2+} , Ag^{+}, and Hg^{2+} that bond with amino acid side groups such as – COO^{-} , or -OH . Catalytic activity is restored when chemical reagents remove the inhibitors .

Irreversible Inhibition

In irreversible inhibition, a molecule causes an enzyme to lose all enzymatic activity. Most irreversible inhibitors are toxic substances that destroy enzymes. Usually an irreversible inhibitor forms a covalent bond with an amino acid side group within the active site, which prevents the substrate from entering the active site or prevents catalytic activity. Insecticides and nerve gases act as irreversible inhibitors of acetylcholinesterase, an enzyme needed for nerve conduction. The compound DFP (diisopropyl fluorophosphate) forms a covalent bond with the side chain -CH, OH of serine in the active site. When acetylcholinesterase is inhibited, the transmission of nerve impulses is blocked, and paralysis occurs.

Antibiotics

Is produced by bacteria, mold, or yeast are irreversible inhibitors used to inhibit bacterial growth. For example, penicillin inhibits an enzyme needed for the formation of cell walls in bacteria, but not human cell membranes. With an incomplete cell wall, bacteria cannot survive, and the infection is stopped. However, some bacteria are resistant to penicillin because they produce penicillinase, an enzyme that breaks down penicillin. Over the years, derivatives of penicillin to which bacteria have not yet become resistant have been produced.

The End

Thank You All

Reference: General, organic,& biological chemistry structures of life.
Timberlake. Pearson Education. 2002