Enzymes

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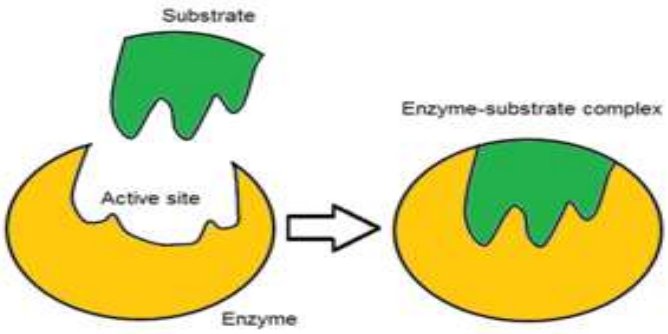
Enzymes are protein catalysts for chemical reaction in biological systems. They increase the rate of chemical reactions taking place within living cells without changing themselves. Enzymes are soluble in water, they are requiring in very small quantities.

Terminology

Some of the terms used in enzymology are defined below:

Substrate: The substance that the enzyme acts on it (the enzyme interact with it).



Product: The substrate formed as a result of the enzymatic action.

Active site or **catalytic site**: the site on the enzyme where in the substrate is bound and is converted into products.

Regulatory site: The site other than the active site on the enzyme wherein the effector or modulator is bound and controls the rate of enzyme catalyzed reaction.

Holoenzyme: A completely catalytically active enzyme.

Holoenzyme = Apoenzyme + Cofactor

(active) (inactive) (inactive)

Cofactor: The non-protein component of the enzyme molecule required for complete activity. Cofactors can be classified into three groups; coenzymes, prosthetic groups and metal ions.

Apoenzyme: The protein component of the enzyme.

Coenzyme: The non-protein organic molecule that is not covalently bound and can be readily dissociated from the protein component of the enzyme by dialysis.

Prosthetic group: The non-protein component that is covalently bound and not readily dissociated from the protein component of the enzyme by dialysis.

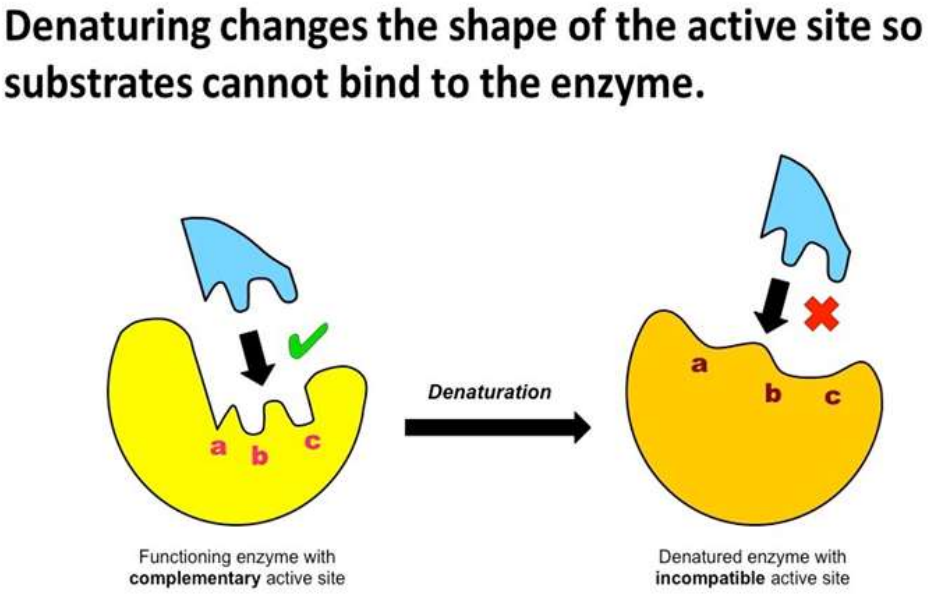
Zymogen or **Proenzyme**: The precursor form of the enzyme in an inactive form. .

Activator: Any substance that increases the rate of an enzyme catalyzed reaction.

Inhibitor: Any substance that reduces or inhibits the rate of an enzyme- catalyzed reaction.

General characteristics

All the enzymes as far as known are specialized proteins that catalyze biochemical reactions. Enzymes show all the properties of protein, i.e., like proteins, enzymes are chemically made up of amino acids as building-blocks linked by peptide bonds; can be hydrolyzed to yield a mixture of constituent amino acids; lose catalytic activity if subjected to temperature, strong acids or bases, organic solvents or other conditions which denature protein and give typical color tests like biuret reactions.



Nomenclature

Each enzyme is assigned two names:

- **Recommended name:** Most commonly used enzyme names have the suffix "-ase" attached to the substrate of the reaction, for example, glucosidase, urease, sucrase; or to a description of the action performed, for example, lactate dehydrogenase and adenylate cyclase.
- **Systematic name:** The International Union of Biochemistry and Molecular Biology (IUBMB) developed a system of nomenclature in which enzymes are divided into six major classes.

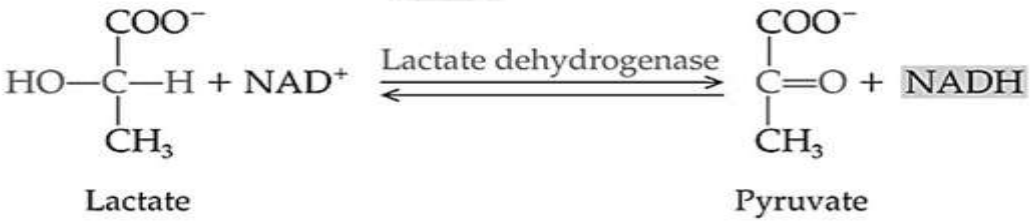
Classification of Enzymes

Class I. Oxido-reducatases:

These enzymes catalyze the oxidation-reduction reaction for substrates.

- Dehydrogenase (removal of hydrogen)
- Oxidase (add oxygen to hydrogen ,forming water)

Example: Lactate-dehydrogenase

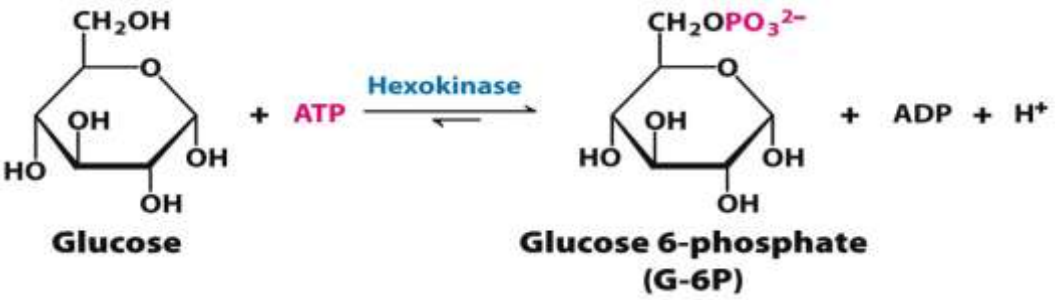


Class II. Transferases:

Enzymes catalyzing a transfer of functional group (other than hydrogen) from one molecule to the other (from the substrate to another substrate)

Example: Enzymes catalyzing transfer of phosphorus containing groups.

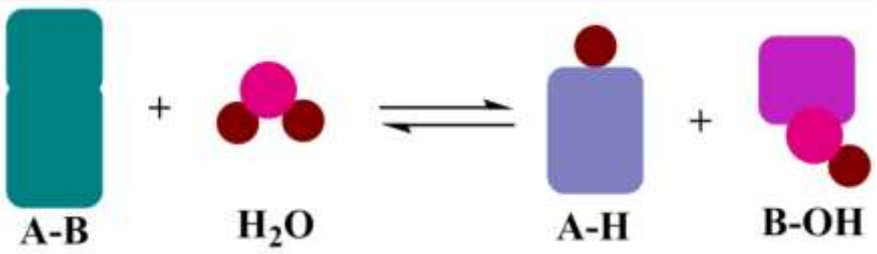
(E.g. Hexokinase).

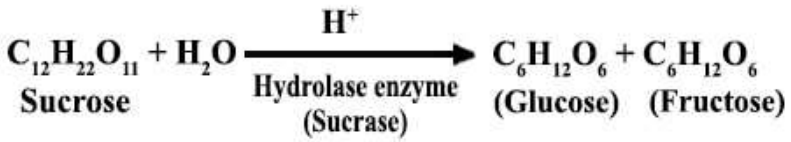


Class III. Hydrolases:

Enzymes catalyzing hydrolysis of ester, ether, peptido, C-C, C-halide, or P-N-bonds by utilizing water.

Example : Glucophosphatase, Trypsin, alkaline phosphatase

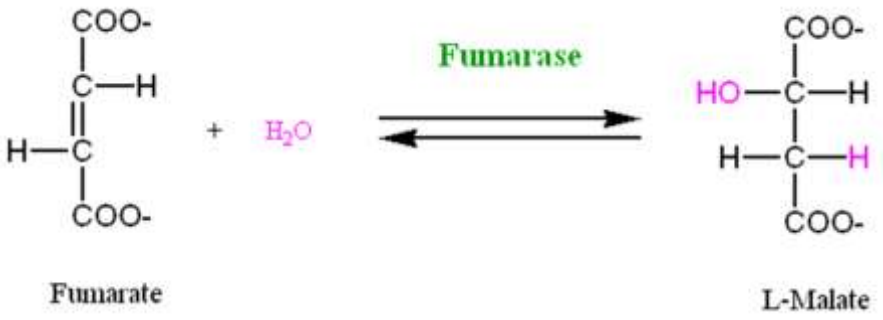




Class IV. Lyases:

Enzymes that catalyze removal of groups from substances by mechanisms other than hydrolysis and leaving double bonds, or addition a group to the double bond.

Example: Fumarase or Pyruvate decarboxylase

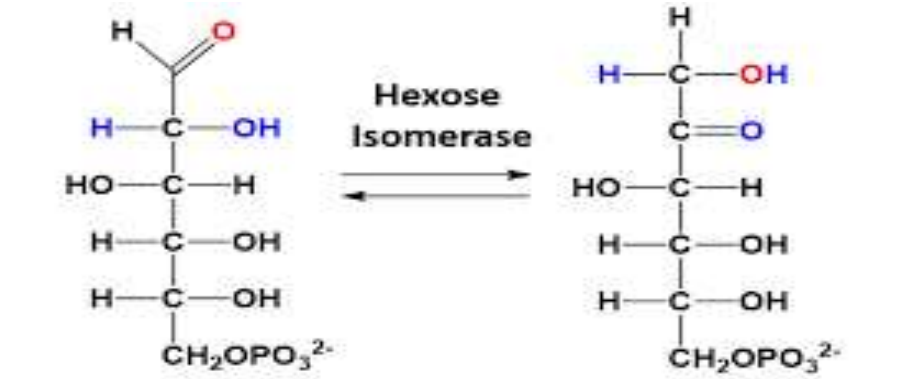


Fumarate L-Malate

Class V. Isomerases:

Includes all enzymes catalyzing interconversion and rearrangement of isomers.

Example: Enzymes catalyzing interconversion of aldose and ketoses (Phosphoglucose isomerase)

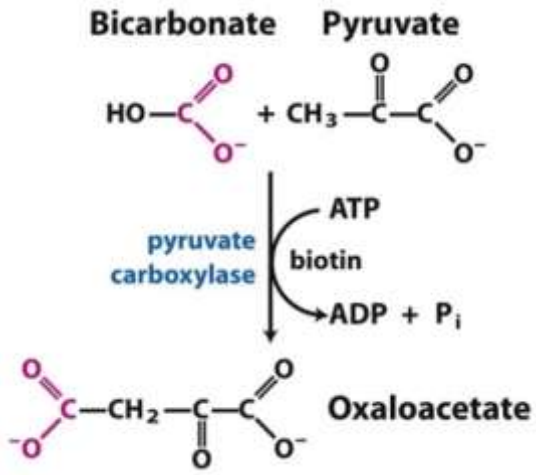


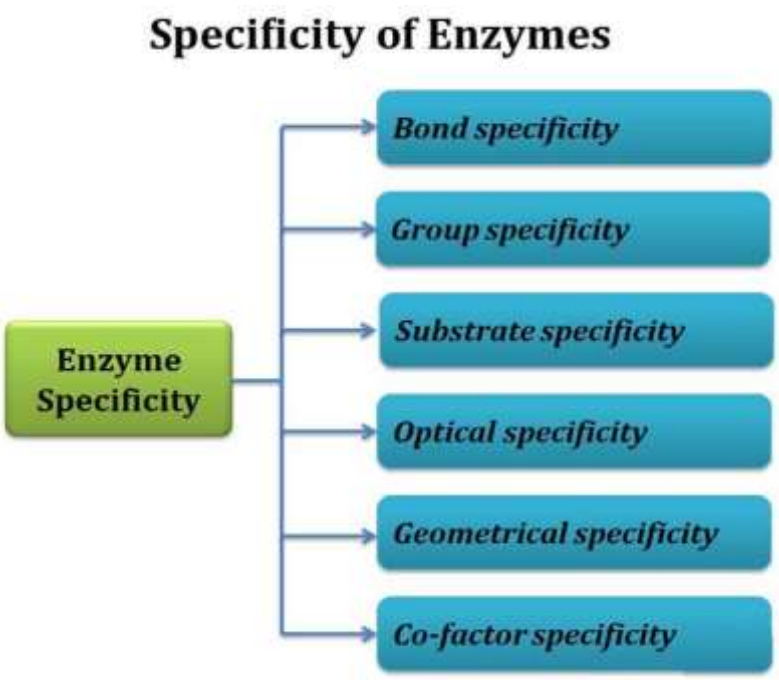
Glucose 6-phosphate Fructose 6-phosphate

Class VI. Ligases or synthetases:

Enzymes catalyzing the linking of two compounds by breaking of a pyrophosphate bond in ATP.

Example: Pyruvate carboxylase, RNA synthetase and DNA ligase



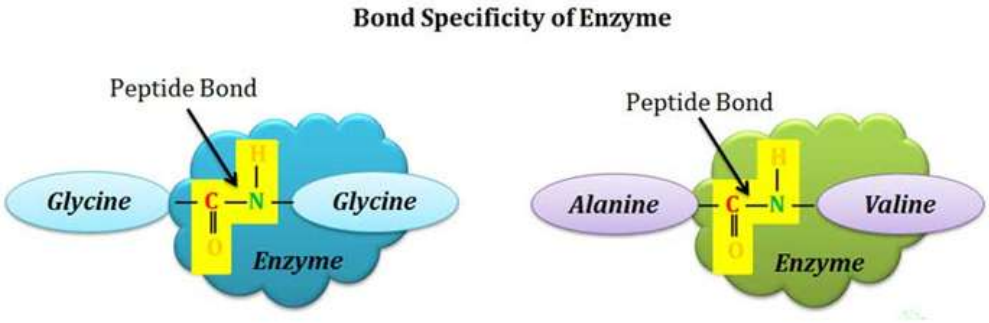


1. <u>Bond Specificity:</u>

- Specific to substrates having similar bonds and similar substrate.
- It is observed in case of:

Amylase: - can hydrolysis α -1-4 glycosidic bond in starch and glycogen.

Proteinases: - can hydrolysis all peptide bonds formed by any amino acids



2. **Group Specificity**

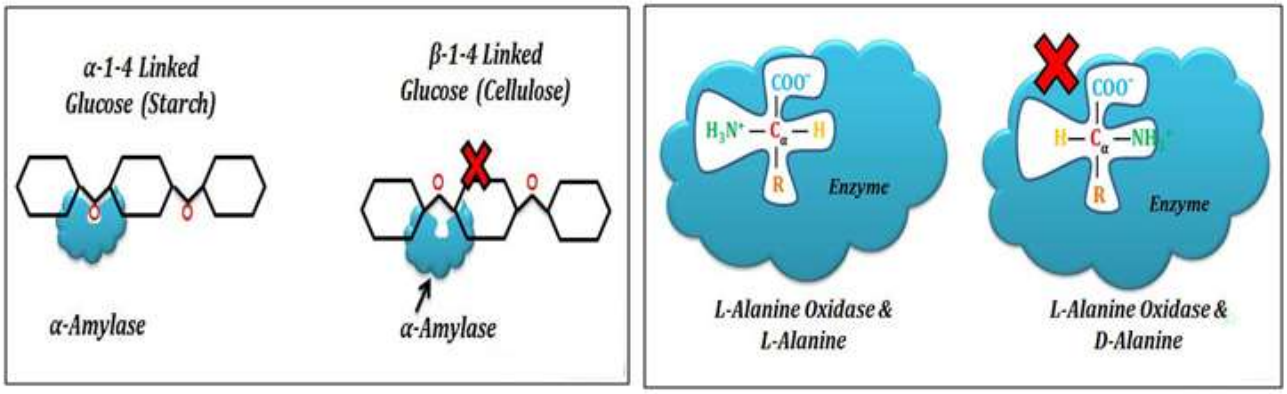
- Enzyme will act only on molecules that have specific functional groups, such as amino, phosphate, and methyl group specificity e.g. proteases split up proteins, phosphatases hydrolyse phosphate esters and Trypsin enzyme that act only on the basic amino acids (Lysine, arginine and histidine).
- More specificity than bond specificity.
- Also called structural specificity.

3. **Substrate specificity**

- Enzymes specific to only one substrate and one reaction.
- Specificity is high
- Also called Absolute specificity
- For examples:
  - ✓ Urease acts only on urea.
  - ✓ Sucrase act only on sucrose
  - ✓ Lactase act only on lactose
  - ✓ Maltase act only on maltose

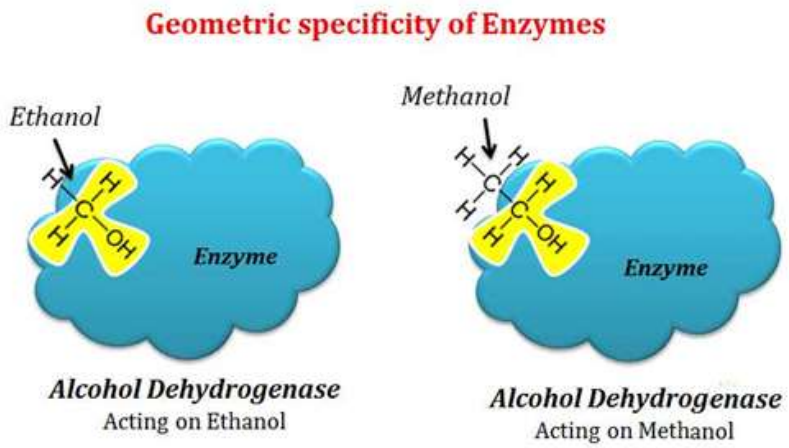
4. Optical specificity

- Also called Stereo chemical specificity
- Enzymes are specific not only to substrate but also specific to optical configuration (specific isomers)
- Specific is very high
- L- amino acid oxidase acts only on L-amino acid, α- glycosidase acts only on α- glycosidic linkage present in starch.



5. Geometric specificity

- Enzymes can act on different substrates having similar molecular geometric. but also specific to optical configuration (specific isomers)
- Specificity is less
- Alcohol dehydrogenase can oxidize ethanol and methanol



6. **Cofactor specificity**:

- Enzymes are specific to substrate and cofactor
- Specificity is high
- In the absence of specific cofactor, the enzyme will be inactive

Types of enzymes are present in human body:-

- **Intracellular enzymes** are produced by the cells of a particular tissues and function within that cell.

  Example: Enzymes of glycolysis, TCA cycle, and β oxidation of fatty acids.
- **Extracellular enzymes** which are produced by the cells of a particular tissues and function within the other tissues, example enzymes of digestive (trypsin).

Mechanism of enzyme action

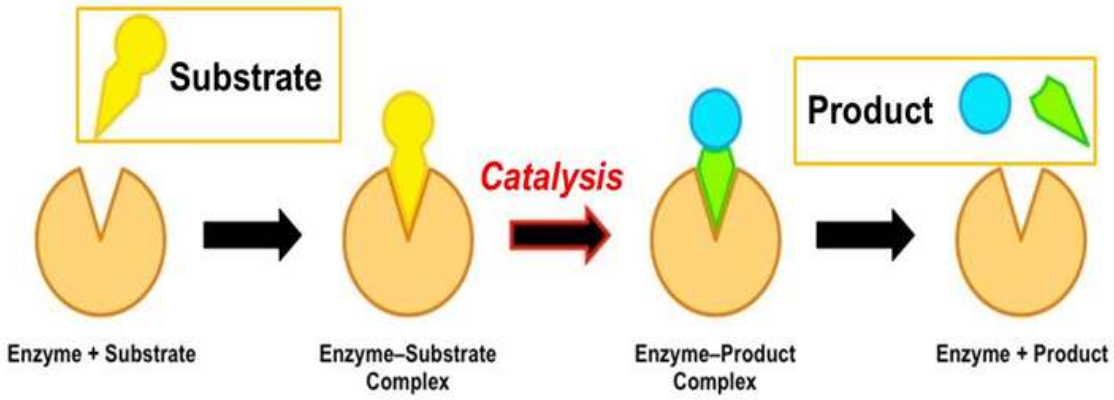
- An enzyme catalysed reaction can be written as:

$$S + E \rightarrow ES \rightarrow E + P$$

S: Substrate, E: Enzyme, ES: Enzyme-substrate complex, P: Product.

- Enzymes [E], at the first step react with substrate [S] produce complex [ES]

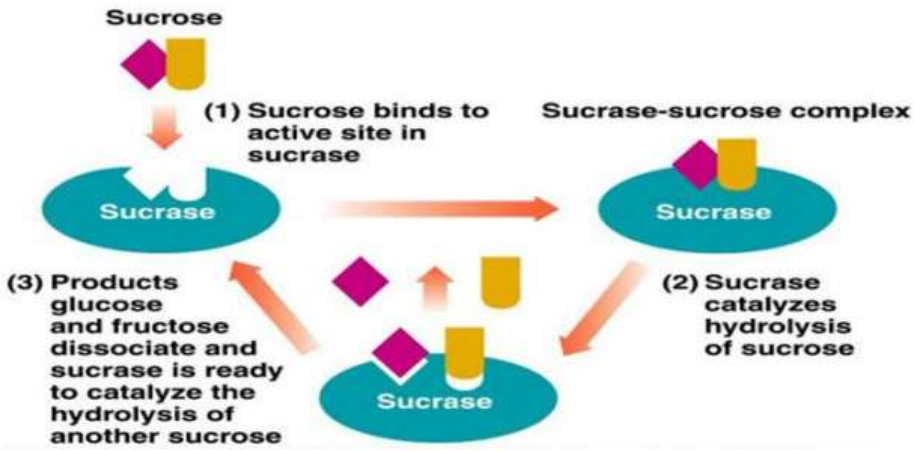
- The second step [ES] complex convert to product [P], and [E]. So the substrate convert to product, and the enzyme remain as the same without consume or any change in structure.
- The products are then released, allowing another substrate molecule to bind the enzyme.
- This cycle can be repeated millions times per minute.



- The reaction for sucrase catalysed hydrolysis of sucrose to glucose and fructose can be written as follows:

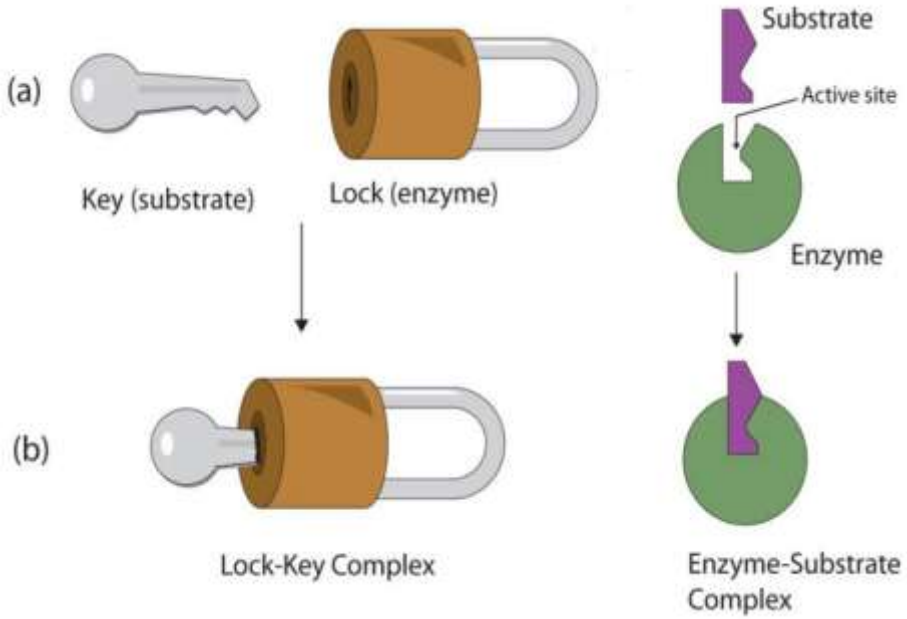
$$E + S \rightarrow ES \rightarrow E + P1 + P2$$

Where E= Sucrase, S= Sucrose, P1= Glucose and P2= Fructose.

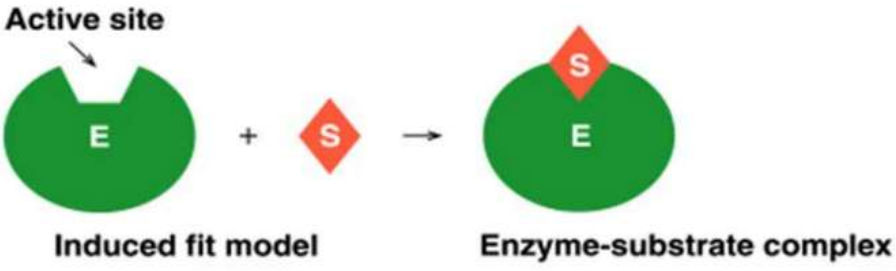


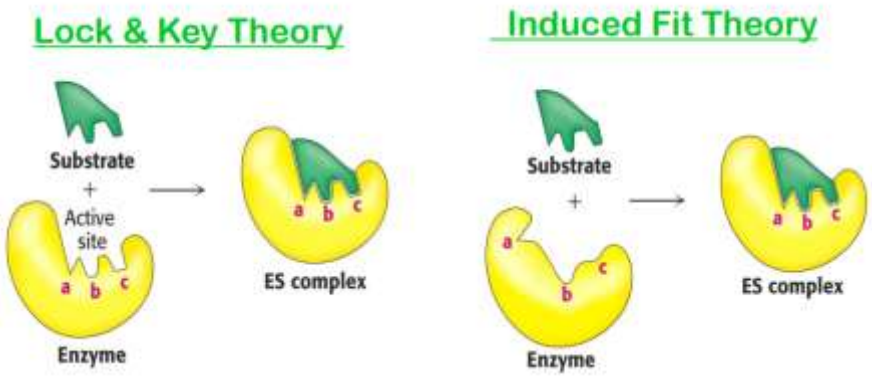
Models for enzyme / substrate

1. **Lock-and-key model**: substrate (key) fits into a perfectly shaped space in enzyme (lock) (The substrate and enzyme active site have complementary shapes).



2. **Induced fit model**: the substrate binds at the active site of the enzyme and then modifies the shape of the active site so that it becomes complementary for the substrate binding (the enzyme active site forms a complementary shape after binding).





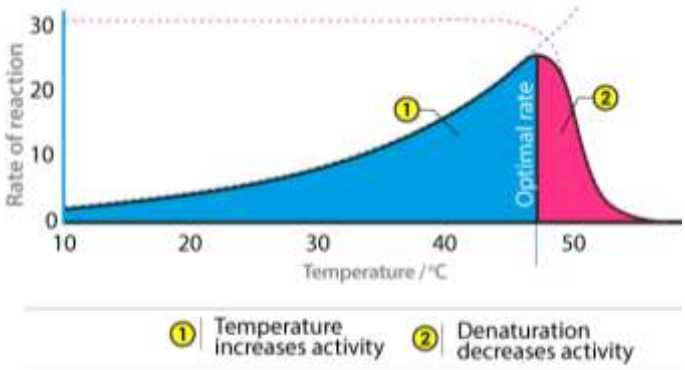
Factors Affecting Enzyme Activity

Physical and chemical factors are affecting the enzyme activity. These include

- Temperature
- pH
- Substrate concentration.
- Enzyme concentration
- Activators and inhibitor

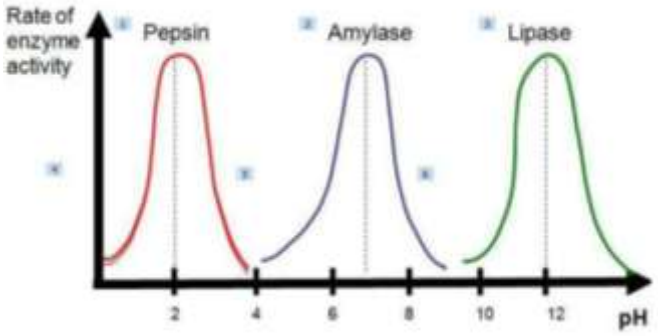
1. Effect of Temperature

The temperature increases the rate of enzyme activity and reaches maximum (optimum temperature). Enzymes are inactivated (loss of activity) at higher temperatures (over 40^{o} C) due to denaturation of the enzyme by heat. For most body enzymes the optimum temperature is around 37c, which is body temperature.



2. Effect of pH

Each enzyme has an optimum pH at which the activity of the enzyme has maximum speed or has the greatest activity, either increase or decrease pH causes a decrease in enzyme activity. Most enzymes in humans have optimal activity near the body's internal pH of 7.4. The pH at which maximum enzyme activity is achieved is different for different enzymes, for example, pepsin, a digestive enzyme in the stomach, has maximum action at pH 2, Whereas other enzymes designed to work at neutral pH, are denatured by such an acidic environment.

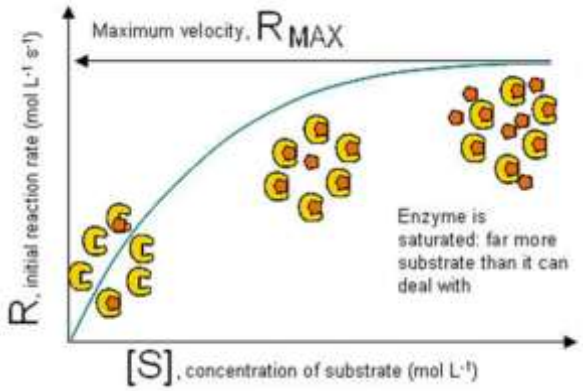


For example

- ✓ Optimum pH for pepsin is 2
- ✓ Optimum pH for amylase is 6.8
- ✓ Optimum pH for Lipase is 12
- ✓ Optimum pH for alkaline phosphatase (ALP) is 9

3. Substrate concentration

At fixed enzyme concentration, pH and temperature the activity of enzymes is influenced by increase in substrate concentration. An increase in the substrate concentration increases the enzyme activity until a maximum is reached. Further increase in substrate concentration does not increase rate of reaction. This condition shows that as concentration of substrate is increased, the substrate molecule combine with all available enzyme molecules at their active site and not more active sites are available (The active Sites become saturated).



4. Enzyme concentration

The velocity (rate) of enzyme reaction is directly proportional to the enzyme concentration when the substrate concentration is constant.