Denaturation:

It is a process in which proteins lose the quaternary structure, tertiary structure, and secondary structure which is present in their native state but not primary structure.

Denatured enzymes can exhibit a wide range of characteristics, such as conformational change , loss of its solubility and aggregation due to the exposure of hydrophobic groups. This means enzyme loses its shape which result in lose its function. Finally these changes may be results in disruption of cell activity and possibly cell death.

Denaturation is happened by application of some such as strong acids and bases, a concentrated inorganic salt, an organic solvent (e.g., alcohol or chloroform), freezing and thawing , radiation , heat , UV, X Ray, and hard moving .

Severity of denaturation depended on type and severity of factors that cause the denaturation as well as on exposure time.

Types of denaturation

Denaturation may be:

1-Reversible (the proteins can regain their native state when the denaturing influence is removed) e.g. Ribonuclease can be return to its native state by applied 7 pH and room temperature.

2- Irreversible denaturation (the proteins cannot regain their native state when the denaturing influence is removed).

Equilibrium Constant:

$V1 = K1\ [A][B]$

$v2 = k2\ [C][D]$

At equilibrium

V1=V2

$K1\ [A][B] = k2\ [C][D]$

$$\frac{K1}{K2} = \frac{[C][D]}{[A][B]} = K_{eq}$$ equilibrium constant

Where

K1 is the forward reaction rate constant.

V1 is velocity of forward reaction.

K2 is the rate constant for the reverse reaction.

V2 is velocity of reverse reaction.

Keq is equilibrium constant.

Enzymes

Definition:

Enzymes are macromolecular biological catalysts and were described in the late 1700s, there are more than 2000 different enzymes are currently known.

Enzymes are responsible for supporting almost all of the chemical reactions that maintain organisim homeostasis .Enzymes are known to catalyze more than 5,000 biochemical reaction types.

All enzymes are proteins (globular) with the exception of a small group of catalytic RNA molecules, the latter are called ribozymes. The term ribozyme is derived from ribonucleic acid. Most of the ribozymes catalyze reactions on one of their own phosphodiester bond or within other RNAs. In addition, these ribozymes may be catalyzing reactions on proteins, the best example being the peptidyltransferase of the large ribosomal subunit in protein synthesis pathway.

Substrates and products:

The molecules upon which enzymes may act are called **substrates** and the enzyme converts the substrates into different molecules known as products.

Enzymology:

It is a science deals with enzyme synthesis, enzyme kinetics, and enzyme purification, as well as applied this science in different fields such as medicine (diagnosis and therapeutics.), agriculture, pesticide, food industry ….etc.

Properties of enzymes:

1- Enzymes are not chemically altered in reaction i.e. they are not used up in reactions and can be used over and over again.

2-Enzymes do not change equilibrium constant (Keq) for reaction.

3- Enzymes increase rate of reaction by lower activation energy to get from reactants to products.

4- They operate under physiological conditions (moderate temperature, around neutral pH, and low concentration)

5- Very high specificity for both reaction catalyzed and Substrate used.

6– Very high efficiency commonly enhancing reaction rates by a factor of 10^6 or more. E.g. each *Catalase* enzyme molecule can break 40 million molecules of H_2O_2 per second .

7– They have ability for regulation.

Composition of enzyme:

Enzymes are classified into 2 types according to their composition:

1- Simple enzymes: They are formed of protein only.

2- Complex (conjugated) enzymes: They are formed of protein part and non protein part.

- Protein part is called apoenzyme.

- Non- protein part is called cofactor.

-The whole enzyme is called holoenzyme which is composed of apoenzyme and cofactor.

Holoenzyme = Apoenzyme + Cofactor

Cofactor:

Cofactor is a non –protein compound or substance is necessary to initiate the function of the enzyme. Cofactors can bind tightly or weakly to enzymes. Cofactors can be divided into two individual groups: Coenzymes and Metal.

1-Coenzymes: are small organic molecules that often derived from vitamins mainly vitamin B. e.g. flavin mononucleotide (FMN), flavin adenine dinucleotide (FAD), nicotinamide dinucleotide (NAD), nicotinamide dinucleotide phosphate (NADP).

Enzymes that use the same coenzymes often perform catalysis by the similar mechanisms.

2-metals ions: are inorganic monovalent and divalent such as K^{+}, Mn^{2+}, Mg^{2+},$Ca^{2+,}$ Cl^{-},Zn^{2+}, Co^{2+}, Fe^{2+} , Cu^{2+},Se^{2-}….etc.

These metals ions are important for enzymes (metalloenzymes) because they are molecular assistants that play a vital role in some of the enzymatic reactions in the body metabolism e.g.

- Thrombokinase, which converts prothrombin into thrombin during blood clotting, is activated by Calcium ions.
- Salivary amylase requires the presence of chloride ions before it converts starch into maltose.

Metals ions also act to stabilize the shapes of enzymes. For example, iron in hemoglobin which helps transport of oxygen to organs in the body and copper in superoxide dismutase which helps removing dangerous free radicals that accumulate inside the cells.

Remember that: Neither apoenzyme nor cofactor alone is catalytically active. Only when they are both combined together.

Prosthetic group:

When a coenzyme or metal ion that is very tightly or even covalently bound to the protein component of the enzyme, it is called a prosthetic group. e.g.

- Haem is an iron-containing prosthetic group. It may function as electron carrier and oxygen carrier in haemoglobin. It is also found in catalases and peroxidases, which catalyze the decomposition of hydrogen peroxide to water and oxygen.
- Succinate dehydrogenase is bound covalently to the flavin nucleotide.

A number of proteins contain more than one prosthetic group. e.g. Haemoglobin is a tetrameric protein containing four haem prosthetic groups,

• Weakly bound cofactor (which is NOT prosthetic groups) can associate and dissociate from enzymes between reactions cycles, behaving like substrates sometimes referred to as "cosubstrates"

Common Coenzymes and Reactions They Mediate

Coenzyme (precursor/vitamin)	Reaction Mediated (Group Transferred)
Biotin	Carboxylation (CO_2)
Cobalamin (B_{12})	Alkylation (methyl group), intramolecular rearrangements, and ribonucleotide reduction
Coenzyme A (pantothenate)	Acyl transfer (R–C=O group)
Flavin coenzymes (B_2)	Oxidation-reduction (hydrogen atoms) (1 or 2 e^- transfer)
Lipoic acid	Acyl group transfer
Nicotinamide coenzymes (niacin)	Oxidation reduction (hydride ions $H:^-$, 2 e^- transfers)
Pyridoxal phosphate (B_6)	Amino group transfer (and many other reactions)
Tetrahydrofolate (folic acid)	One-carbon transfer
Thiamine pyrophosphate (B_1)	Aldehyde transfer
Uridine diphosphate [UDP]	Sugar transfer (hexose units)