

Enzymes

There are multiple reactions that take place inside our body (such as digestion of food, secretion of hormones, production of energy, etc. require enzymes.)

These bio-reactions that occur in our body during various life processes also require catalysts; the substances that act as biocatalysts for the reactions inside our body are called enzymes.

Catalysts are those substances that **enhance the rate** of a chemical reaction **without themselves getting chemically modified.**

They **increase the rate of reaction** by **lowering** the **activation energy** of the reaction.

Enzymes are often referred to as the **biological catalysts.**

The catalysts of biochemical reactions are enzymes and are responsible for bringing about almost all of the chemical reactions in living organisms. **Without enzymes, these reactions take place at a rate far too slow for the pace of metabolism.**

All known enzymes are proteins. They are high molecular weight compounds made up principally of chains of amino acids linked together by **peptide bonds.**

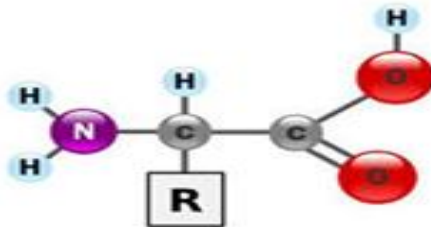
Enzymes are **bio-active organic molecules** found in the cells of both prokaryotes and eukaryotes, they are biomolecules that are **highly specific, it is a macromolecule that catalyses a biochemical reaction, interacts with a substrate, converting it into a new product. The substance upon which enzyme acts, is called the substrate.** The enzyme will convert the substrate into the product

All metabolic processes in the body need enzymes to catalyse reaction **at a faster rate.** The majority of enzymes are **globular proteins.**

Lack of enzyme will lead to block in metabolic pathways causing inborn errors of metabolism.

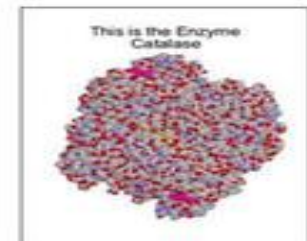
Enzymes are globular proteins

Proteins are made up of single units called **amino acids** linked together to form a **polypeptide chain**



One amino acid. The R group is a variable group that differs in different amino acids

Globular proteins are Compact, Spherical, Soluble molecules



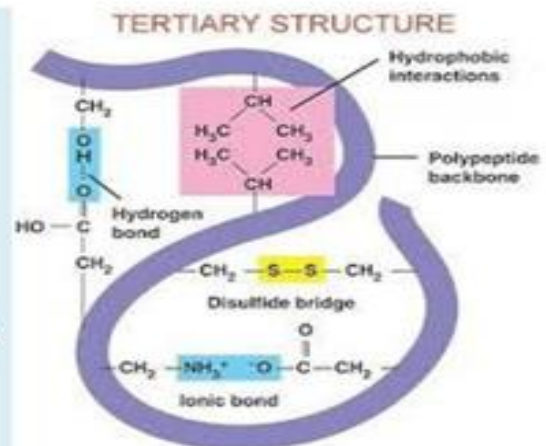
Enzymes are tertiary structure proteins

These have a **specific 3D shape**. *Why is this important in enzymes?*

Tertiary Structure is dependent on the bonds that form between **R groups** of an amino acid as the polypeptide chain folds.

These bonds are **disulphide bridges, hydrogen bonds, ionic bonds, hydrophobic interactions**.

These bonds give the enzyme a **very precise 3D shape**



Enzymes are catalysts

- They act as a catalyst to a chemical or biochemical reaction, with a defined mechanism.
- They **increase the speed** of that reaction, typically by 10^6 - 10^{14} times faster than the rate of the un-catalysed reaction.
- They are **selective** for a single substrate.
- They speed up rate of reaction by lowering the activation energy They are **stereospecific**, meaning the reaction produces a single product.

All the reactions require the biomolecule as definite controlling system.

The control should be for the **direction, speed and specificity of the undergoing reaction.**

The enzymes are always produced in the **proper amounts, at the proper time and the proper place** where they are needed and they are different factors that affect enzyme activity i.e., **PH, Temperature, Enzyme and Substrate Concentration.**

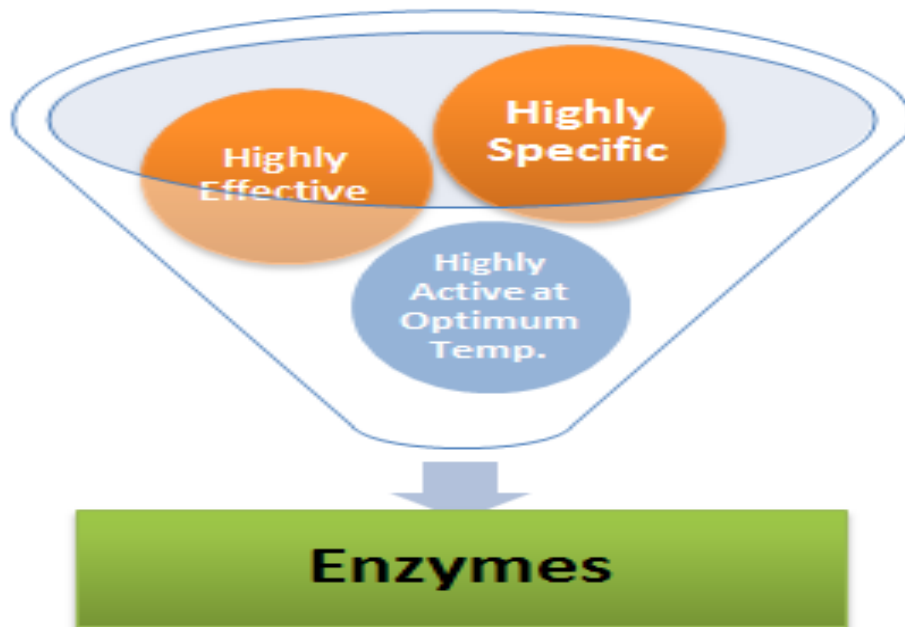
Properties of an Enzyme:

- Biological Catalyst
- Lowers the energy input/activation energy required for a chemical reaction to proceed.
- Speeds up rate of reaction
- Enzymes are proteins
- Enzymes remain unchanged after a reaction and therefore can work again.
- Enzymes are specific to a substrate of a reaction (Lock and Key).
- Enzymes are reversible and can catalyse a reaction going both ways (Synthesis/Lysis)
- Enzymes are denatured by:
 - Change in Temperature
 - Change in pH

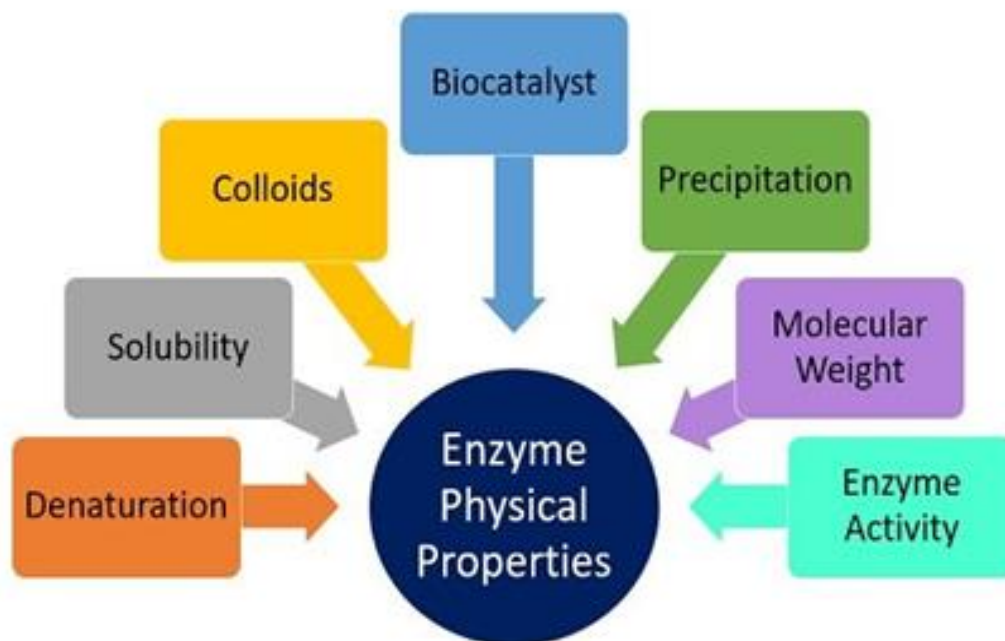
Therefore have an optimum Temperature and pH, where it works most effectively. In Humans that is usually around 37°C and a pH of 7.

The Most Important Properties Of An Enzyme Are:

1. Catalytic Property
2. Specificity
3. Reversibility
4. Sensitiveness to heat and temperature and pH



Physical Properties of Enzyme



Colloidal Nature

Enzymes behave as colloids due to their **large size** or high molecular weight.

Enzyme Precipitation

Acidic and alkaline solution can cause enzyme precipitation, as the enzymes are amphoteric (possess amino and carboxylic acid group towards the end of the chain).

Molecular Weight

Enzymes are large protein biomolecules possessing a polypeptide chain of various amino acid sequence. Nearly 200 to 300 peptide bonds hold the amino acids together. Therefore, enzymes have a high molecular weight.

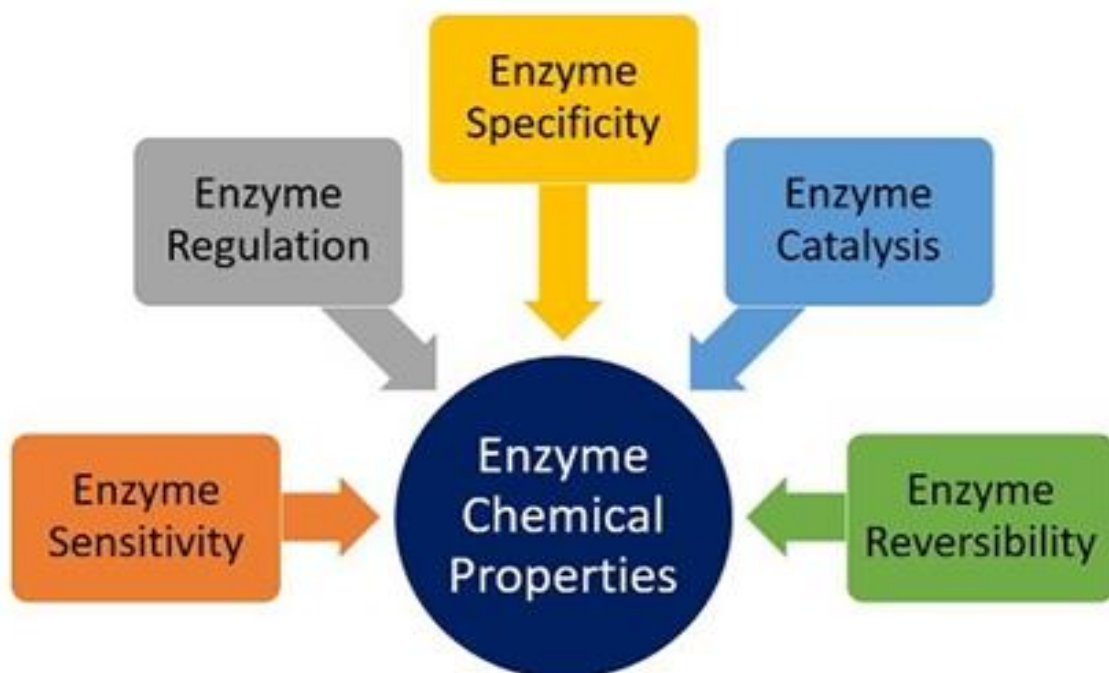
Enzyme Solubility

Enzymes are soluble in water, NaCl, diluted glycerol and alcohol.

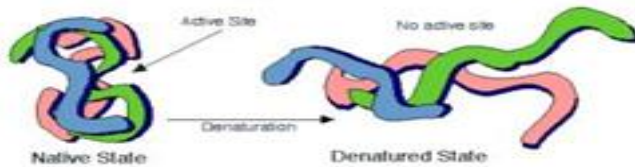
Enzyme Denaturation

High heat (above 40 degrees Celsius) and alternations in the pH (too low and too high), heavy metals, and high salt concentration etc., **denatures the enzyme by breaking the intra and inter-molecular noncovalent bonds. It distorts the enzyme's shape and active site and finally results in the loss of enzyme activity.**

Chemical Properties of Enzyme



Denaturation: Enzymes Unravel and Stop Functioning

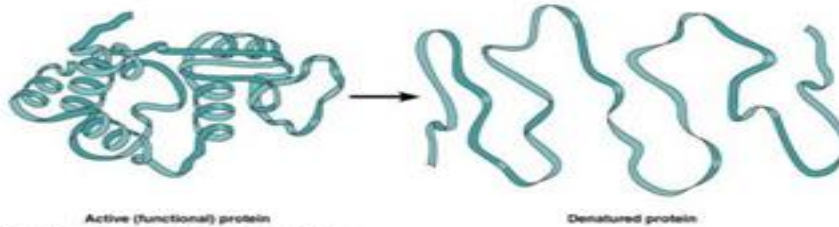


Enzyme shape can be affected by:

- Temperature
- pH

By interfering with bonds, changes in temp. and pH can change enzyme shape.

Substrate does not fit in active site.



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• The catalytic cycle of an enzyme

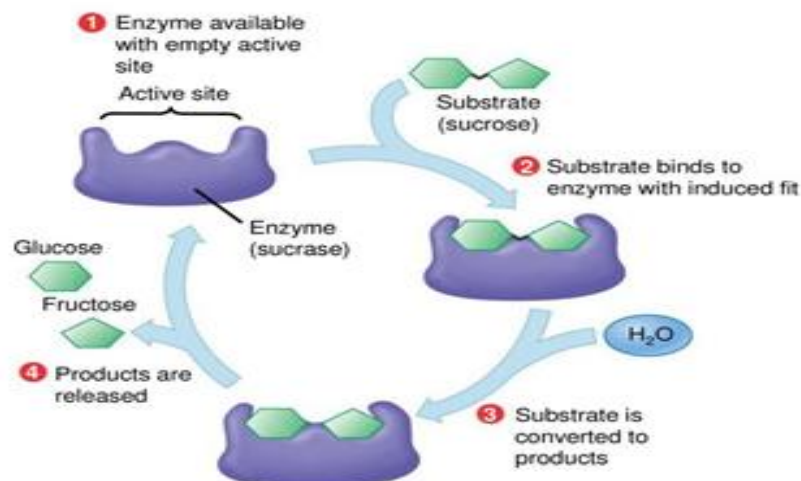
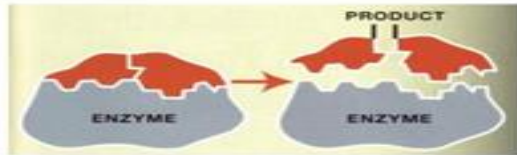


Figure 5.6

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Enzyme-Substrate Complex



Substrate = Reactant molecules; fit into enzymes.

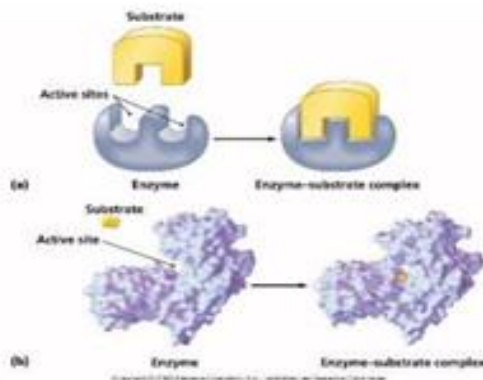
ACTIVE SITE: Location where substrate binds.

Enzyme will only bind to specific substrates based on SHAPE!

(Lock & Key fit)



Enzyme shape is important to fxn

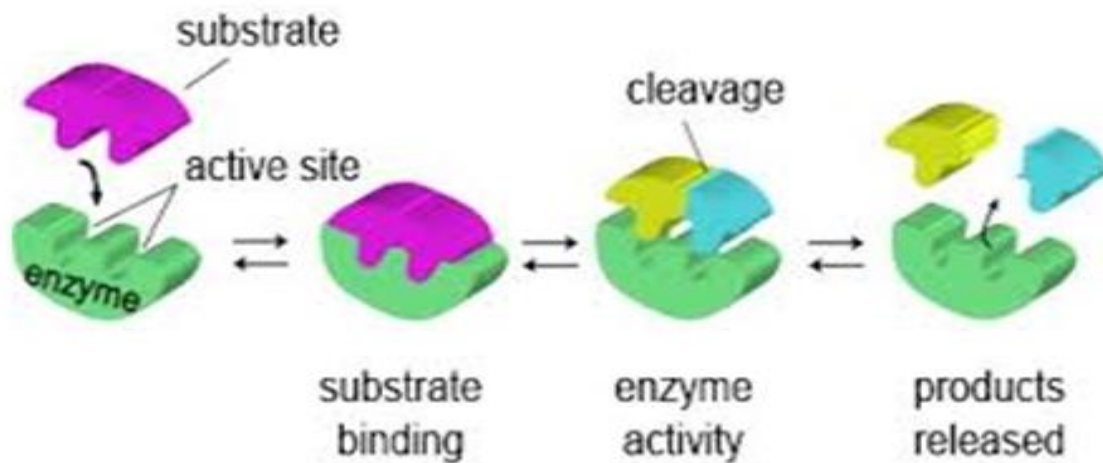


Enzyme fxn depends on shape of active site.

Shape of enzyme can be affected by ...

- **Temperature?**
- **pH?**
- **Presence of other binding molecules (inhibitors or "helpers")**





Specific shape: Enzymes have a specific shape which they maintain even after a reaction.

Reuse: Enzymes can be reused again and again because no reaction can mortalize them.

The specificity of reaction: Every enzyme is specific for a specific reaction. For Example, A. Maltase enzyme is used to break down Maltose into Glucose+Glucose. While Lactase enzyme is used to break down Lactose into Glucose+Galactose.

Sensitivity: Enzymes are much more sensitive to the change of temperature and PH because they work better at a moderate temp and PH, lower and higher values of both may cause disturbance or can stop enzyme activity.

Used in small amounts: Enzymes are used in a small amount because they are powerful and can easily provide basic necessities for a reaction.

Active Site/Centre: Enzymes have a specific active site where the entire reaction takes place. Active sites need a substrate to attach itself with it. The substrate can be protein or lipid etc.

Enzyme specificity

Enzymes show different levels of specificity which are:

1- Absolute specificity: In this condition, the enzyme reacts only on a specific substrate for example hydrolysis of urea to ammonia and carbon dioxide is catalyzed by urease. Urea is the only substrate for urease. Thiourea, though structurally similar to urea, will not act as the substrate for urease.

2- Group specificity (Structural specificity): In this condition, the enzyme acts on a special type of bond at a specific site and attached to specific groups e.g.:

Pepsin: acts on peptide bond between the amino group of aromatic amino acid and the carboxylic group of another amino acid.

Trypsin: acts on peptide bonds between the carboxylic group of basic amino acid and the amino group of another amino acid.

3- Relative specificity: In this condition, the enzyme acts at different rates on one type of bond in compounds chemically related e.g. pancreatic lipase hydrolyses the alpha ester bonds at positions 1 & 3 in Triglycerides.

4- Stereochemical specificity: enzymes act on D or L isomers e.g.

D-Amino acid oxidase acts only on D-amino acids

L- Amino acid oxidase acts only on L- amino acid

Enzymes act on a specific type of linkages according to the type of linkage (α or β) of the compounds attached to it e.g. Amylase hydrolyses α -1.4 glycosidic linkage of starch.

Terminology of enzymes

Enzymes that were discovered early were given general names which they are still used as ptyalin, pepsin, trypsin,, etc... Now a suffix (ase) is added to indicate enzyme.

The prefix may be:

1-Name indicating general nature of substrate e.g.: protease, lipase etc...

2-The real name of the substrate: urease, lactase, sucrase.

3-Type of reaction catalysed e.g.: Aldolase, mutase, 4-Combination of the above e.g.: Name of substrate + type of reactions.g.:

lactic acid Dehydrogenase ,Glycogen Synthetase.

Distribution of Enzymes

Cytoplasmic Enzymes: Those enzymes which are found dissolved in the fluid part of the cell.

Mitochondrial Enzymes: These enzymes are found mainly in Mitochondria the powerhouse of the cell where major process respiration takes place.

Plastid Enzyme: Enzymes which are found in the process of Photosynthesis ,plastid is a part of Chloroplast.

Ribosomal Enzymes: Enzymes which are found in the process of Protein Synthesis

Holo Enzymes: Enzymes which are composed of Protein part and non-Protein

Apo Enzymes: The protein part of the enzyme is the named the apoenzyme . It is heat labile.

Nomenclature

-The **Nomenclature Committee** of the "International Union of Biochemistry and Molecular Biology" (IUBMB) adopted rules in 1992 for the systematic **classification and designation** of enzymes based on **reaction specificity**.

-All enzymes are classified into **six major classes** according to the **nature of the chemical reaction catalyzed**:

1.Oxidoreductases.

2.Transferases.

3. Hydrolases.

4.Lyases (cleave C-C, C-O, C-N, and other groups by elimination, leaving double bonds, or conversely adding groups to double bonds).

5.Isomerases (involved in the catalysis of isomerizations within one molecule).

6.Ligases (involved in the biosynthesis of a compound with the simultaneous hydrolysis of a pyrophosphate bond in **ATP** or a similar triphosphate).

Classes of Enzymes

1. Oxidoreductases Enzymes involved in oxidation and reduction of their substrates.

2. Transferases Enzymes that catalyze transfer of a particular group from one substrate to another.

3. Hydrolases Enzymes that bring about hydrolysis

4. Lyases Enzymes that facilitate removal of small molecule from a large substrate

5. Isomerases Enzymes involved in isomerization of substrate.

6. Ligases (synthetases) Enzymes involved in joining together two substrate

Enzyme Classification Based on Reaction Types

Class	Type of Reaction Catalyzed	Example
Hydrolase	Hydrolysis (catabolic)	Lipase—breaks down lipid molecules
Isomerase	Rearrangement of atoms within a molecule (neither catabolic nor anabolic)	Phosphoglucisomerase—converts glucose 6-phosphate into fructose 6-phosphate during glycolysis
Ligase or polymerase	Joining two or more chemicals together (anabolic)	Acetyl-CoA synthetase—combines acetate and coenzyme A to form acetyl-CoA for the Krebs cycle
Lyase	Splitting a chemical into smaller parts without using water (catabolic)	Fructose 1,6-bisphosphate aldolase—splits fructose 1,6-bisphosphate into G3P and DHAP
Oxidoreductase	Transfer of electrons or hydrogen atoms from one molecule to another	Lactic acid dehydrogenase—oxidizes lactic acid to form pyruvic acid during fermentation
Transferase	Moving a functional group from one molecule to another (may be anabolic)	Hexokinase—transfers phosphate from ATP to glucose in the first step of glycolysis

Oxido-reductases are further classified into five subgroups:

A- Oxidases

These are enzymes that catalyse direct transfer of hydrogen to oxygen and form water e.g. cytochrome

B- Aerobic Dehydrogenases

These are enzymes that catalyse direct transfer of hydrogen to oxygen and form hydrogen peroxide (H₂O₂) e.g. L-amino and D-amino acid oxidase.

C- Anaerobic dehydrogenases

These are enzymes cannot transfer hydrogen directly to oxygen but hydrogen is indirectly transferred to oxygen through many hydrogen carriers e.g. glucose-6-phosphate dehydrogenase .phenylalanine hydroxylase.

D- Hydroperoxidase

These enzymes use hydrogen peroxide (H₂O₂) as substrate changing it into water (H₂O) e.g. peroxidases and catalases

E- Oxygenases

These enzymes catalyze direct incorporation of oxygen into substrate. e.g.

i- **Dioxygenases (True oxygenases): These enzymes catalyze incorporation of two oxygen atoms into substrate** e.g. tryptophan pyrrolase enzyme.

ii- **Monooxygenases (pseudo-oxygenases or hydroxylases): These enzymes incorporate one oxygen atom into substrate** e.g. cytochrome P450 omega hydroxylases, is used by cells to metabolize arachidonic acid .

Transferases

These are enzymes that catalyze transfer of a chemical group from one compound to another. They include:

A- Transaminases

These are enzymes that catalyze transfer of amino group (-NH₂) from amino acid to α-keto acid producing new amino acid and new keto acid e.g.

i- Alanine transaminase (ALT): It is also called serum glutamic pyruvic transaminase (SGPT).

ii- Aspartate transaminase (AST): It is also called serum glutamic oxalacetic transaminase (SGOT).

B- Acyl transferases

These enzymes catalyze the transfer of acyl (fatty acid) group to compounds. They need Coenzyme-A that acts as a carrier for acyl group e.g. choline acetylase.

C- Methyl transferases

These enzymes transfer methyl group (-CH₃) from methyl donor usually active methionine (S-adenosyl methionine) to the substrate e.g. formation of epinephrine (adrenaline) from norepinephrine(noradrenaline).

D- Phosphotransferases

These enzymes catalyse transfer of phosphate group e.g. hexokinase and glucokinase both catalyse transfer of phosphate group from ATP to glucose.

Hydrolases

These enzymes catalyze cleavage of their substrates by addition of water. All the digestive enzymes are hydrolases. Hydrolases include:

A- Enzymes hydrolyzing glycosidic link in carbohydrates

These enzymes catalyze hydrolysis of carbohydrates e.g. maltase, lactase, sucrase and amylase.

B- Lipase: Enzyme that hydrolyzes triglyceride into glycerol and three fatty acids.

C- Proteases: Enzymes that catalyze hydrolysis of proteins (proteolytic enzymes). e.g. pepsin and Trypsin

D- Phosphatases:

These enzymes catalyze hydrolysis of phosphoric acid esters e.g..

i- Phosphomonoesterases that catalyze hydrolysis of phosphoric acid monoesters as glucose-6-phosphatase

ii- Phosphodiesterases that catalyze hydrolysis of phosphoric acid diesters e.g. the enzyme that catalyzes the hydrolysis of cAMP (cyclic adenosine monophosphate) to AMP.

Lyases

These enzymes can remove groups from substrate or break bonds by mechanism other than hydrolysis .

They include:

A. Aldolase: It is an enzyme that splits aldehyde from alcohol e.g. fructose-1-6-diphosphate aldolase.

B. Dehydratases: These enzymes catalyze removal of water from their substrates e.g. fumarase and carbonic anhydrase.

C. Decarboxylases:

These enzymes catalyze the removal of CO₂ from their substrates. They need pyridoxal phosphate (PLP) as coenzyme e.g. amino acids decarboxylases as histidine decarboxylase, which removes CO₂ from histidine changing it to histamine

D. Phosphorylases: These enzymes catalyze cleavage of their substrates by addition of phosphoric acid e.g. glycogen phosphorylase.

Isomerases:

These enzymes can produce optical , geometric or positional isomers of substrates.

They include:

A. Aldose-ketose isomerases: These enzymes catalyse interconversion between aldoses and ketoses e.g. aldose reductase.

B. Epimerases: These enzymes catalyze interconversion between epimers e.g. methyl malonyl Co A epimerase.

C. Mutases: These enzymes catalyze transfer of chemical group from one position to another in the same compound e.g. biphosphoglycerate mutase.

D. Racemases: These enzymes catalyze interconversion between D & L enantiomers e.g. serine racemase.

E. Cis-Trans isomerases: These enzymes catalyze interconversion between cis and trans geometric isomers.

Trans retinol → Cis retinol

Ligases

Also known as **synthetases**, These enzymes link two substrates together , usually with simultaneous ATP e.g (glutamine synthetase , DNA ligase).

Synthetases and synthases are different . Synthases are ATP-dependent enzymes catalysing biosynthetic reaction ; they belong to ligases , While

Synthases are enzymes catalysing biosynthetic reaction ; but they do not require ATP directly ; the belong to classes other than ligase.

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