Unit - I

Enzymes

Introduction

→ Enzymes are biocatalyst.

→ They are catalyst of life

→ A Catalyst is defined as a substance that increases the velocity or the rate of a chemical reaction without itself undergoing any change in the overall process.

→ Life is possible due to the coordination of numerous metabolic reactions inside the cells

→ Almost all the functions of the body such as digestion, synthesis and breakdown of carbohydrates, fats and proteins are catalyzed and controlled by specific enzymes

→ A solution of lactose does not hydrolyse appreciably at body temperature, but on addition of a small quantity of the enzyme, lactase the lactose molecules are hydrolysed to corresponding monosaccharides

→ Usually 1 molecule of an enzyme can act upon about 1000 molecules of the substrate per minute

→ Lack of enzymes will lead to block in metabolic pathways causing inborn errors of metabolism

→ Detection of certain enzymes in body fluids or plasma will help in diagnosis

Definition:

Enzymes may be defined as biocatalysts synthesized by living cells, They are protein in nature, colloidal and thermolabile in character and specific in their action.

→ The substance upon which an enzyme acts is called the substrate,

→ The enzyme will convert the substrate into the product or products.

Nomenclature and Classification

→ Enzyme names give information about their function rather than the structure, focus on type of reaction catalyzed and the substrate

1. The suffix -ase identifies a ~~Substrate~~ substance as an enzyme

   Lipase acts on lipids

   Sucrase acts on sucrose, Lactase on lactose
   Nuclease on Nucleic acid,

2. Some enzymes have the suffix - in

   Trypsin, pepsin

2. The type of reaction catalyzed is often mixed with a prefix

   Oxidases catalyzes oxidation

3. The substrate is often noted

   Glucose oxidase
   Pyruvate Carboxylase

5) u Predicting enzyme function from an enzyme's name

a) Maltase - hydrolysis of maltose

b) Lactate dehydrogenase - dehydrogenation of Lactate

3) Fructose oxidase - oxidation of fructose

4) Maleate Isomerase - ~~Formation of~~ Isomerization of ~~maleate~~ ~~Isomer~~

→ these are known as trivial names of enzymes

→ Enzymes are sometimes considered under two broad categories

a) Intracellular enzymes : They are found within cells where they are

b) Extracellular enzymes - These (enzymes) are active outside the cell like the digestive enzymes belongs to this group.

IUB System of enzyme classification (International union of Biochemistry)

→ Enzymes are divided into six classes

→ Each class on its own represents the general type of reaction brought about by the enzymes of that class

1. Oxidoreductases - Enzymes involved in oxidation-reduction reactions

2. Transferases - Enzymes that catalyse the transfer of functional group

Hydrolases. Enzymes that bring about hydrolysis of various compounds

4 Lyases - Enzymes specialised in the addition of removal of water, ammonia, CO_2 etc

5) Isomerases: Enzymes involved in all the isomerization reactions

6 Ligases - Enzymes catalysing the synthetic reactions where two molecules are joined together and ATP is used

→ Each class in turn, is subdivided into many subclasses which are further divided

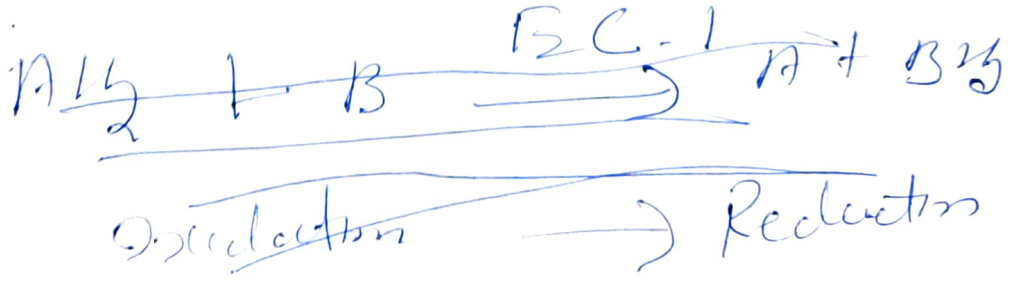
→ A four digit Enzyme Commission (EC) number is assigned to each enzyme

representing the Class (first digit)
Subclass (second digit)
Sub-subclass (Third digit) and
the individual name (Forth digit)

1. Oxidoreductases

→ This group of enzymes will Catalyze oxidation of one substrate with simultaneous reduction of another substrate

→ Responsible for oxidation and reduction
→ This reaction may be represented by



Eg. 1. Alcohol $\xrightarrow{\text{Alcohol dehydrogenase}}$ Aldehyde

NAD^+ $NADH$

IUB name : Alcohol - NAD - oxido reductase.

Code EC 1.1.1.1

primary alcohol

oxidoreductase

Acceptor NAD or NADP

Eg 2.

Glucose - 6 - phosphate → NADPH

NADP+

6 - phospho gluconolactone

→ The enzyme is Glucose - 6 - phosphate dehydrogenase

IUB systematic name is

Glucose - 6 - phosphate - NADP - oxidoreductase

Code number

1.1.1.49

1.1.1.27 - Lactate dehydrogenase

2) Transferases

→ This class of enzymes transfers one group (other than hydrogen) from the substrate to another substrate

→ This may be represented as

$$A-R + B \xrightleftharpoons{EC\ 2} A + B-R$$

Eg Hexose $\xrightarrow[ADP]{ATP}$ Hexose 6-phosphate

→ The name of enzyme is hexokinase

Systematic name: ATP-Hexose-6-phosphotransferase

Code number

EC 2.7.1.1

First Digit - Class

Second digit - group transferred

2.1 one carbon

2.2 - aldehyde or ketone

2.3 - acyl group

2.4 -

Hydrolases

This class of enzyme can hydrolyse ester, ether, peptide or glycosidic bonds by adding water and then breaking the bond

$A-B + H_2O \rightarrow AH + BOH$

Acetyl choline + H_2O → choline + acetate

— The enzyme is Acetyl choline esterase

Systematic name is Acetyl choline hydrolase

→ Code no: E.C. 3.1.1.7 — Ec 3.1 — esterase
3.2 — Glycosylase
3.1.1 — Carboxylic ester hydrolase

4) Lyases

These enzymes can remove group from substrate or break bonds by mechanisms other than hydrolysis,

Addition
$A-B + X-Y \rightarrow$ Elimination $AX-BY$

Eg

Malic acid ⟶ fumaric acid

Fumarate hydratase

Enzyme EC. 4. 2. 1. 2

Eg. 2 Aldolases

Substrate: ketose-1-phosphate

aldehyde + acid

Class: 4. 1. à 7

Second digit

4. 1 - Carbon-(oxygen) lyases

4. 2 - Carbon-oxygen lyases

Third digit

Acting on

Group removed

4. 1. 1 - CO_2

4. 2. 1 - H_2O

Isomerases

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

→ Racemases, epimerases, cis-trans isomerases are examples.

Intramolecular isomers

A ⟶ A

Glyceraldehyde 3-phosphate ⟷ Dihydroxy acetone-phosphate

Enzyme is Triose phosphate Isomerase

Systematic name: Glyceraldehyde-3-phosphate keto-Isomerase

Codes: EC. 5.3.1.1

6) Ligases

→ These enzymes link two substrates together, usually with the simultaneous hydrolysis of ATP

$$A + B \longrightarrow A - B$$

ATP → ADP + Pi

$$\text{Acetyl CoA} + CO_2 \xrightarrow{\text{Biotin}} \text{malonyl CoA}$$

ATP → ADP + Pi

Enzyme is Acetyl CoA Carboxyl

Systematic name: Acetyl CoA Carboxyl

Code no: E.C. 6.4.1.2.

Secondary bond forming

6.1 - C-O bond

6.2 - C-S bond

7) translocase (EC-7)

→ Translocase is a general term for a protein that assists in moving another molecule usually across a cell membrane

→ These enzyme catalyse the movement of ions or molecules across membranes or their separation within membrane

EC 7.1 - Catalyzing the translocation of electrons

EC 7.2 Catalyzing the translocation of inorganic cation

EC 7.3 Catalyzing the translocation of organic anions

EC 7.4 Catalyzing the translocation of amino acids and peptides

Examples

1) Ornithine translocases

2) Carnitine acyl Carnitine translocases

$$AX + B_{side\,1} \rightleftharpoons A + X + B_{side\,2}$$

Eg H^+ transporting two sector ATPase

$$ADP + H_2O + 4H^+_{side\,1} = ATP + \text{phosphate} + 4H^+_{side\,2}$$

Eg Na^+/K^+ ATPase pump - EC 7.2.2.13

7 - translocase class

2 - ~~translocating~~ Catalyzing the translocation of Inorganic Cations and their chelates

2. translocation of Inorganic cation (usually) by the hydrolysis of a nucleoside triphosphate

Summary of the Enzyme classes

Major Subclasses

1. Oxidoreductase
   - Dehydrogenase
   - Oxidases
   - Reductase
   - peroxidase
   - Catalase
   - oxygenases
   - Hydroxylases
2. Hydrolases
   - Esterases
   - Glycosidases
   - Peptidases
   - phosphatases
   - Thiolases
   - phospholipidases
   - Amidases
   - Deaminase
3. Transferases
   - Transaldolases
   - Transketolases
   - Acetyl transferase
   - Methyl transferase
   - glucosyl transferase
   - phosphoryl transferase
   - Kinases
   - phosphomutases
4. Lyases
   - Decarboxylases
   - Aldolases
   - Hydratases
   - Dehydratases
   - Synthases.

5) Isomerases

Racemases

Epimerases

Cis-trans Isomerases

mutases

6 Ligases

Synthetases

Carboxylases

1. Oxidoreductases.

→ These enzymes catalyze the oxidation and reduction reactions

→ Responsible ~~maybe for~~ transfer of electron or hydrogen ion

$$AH_2 + B \xrightarrow{EC-1} A + BH_2$$

Oxidation Reduction

Subclasses of oxidoreductases are

Eg
1. dehydrogenases
2. Oxidases
3. Reductases
4. Peroxidases
5. Catalase
6. oxygenase
7. Hydroxylases

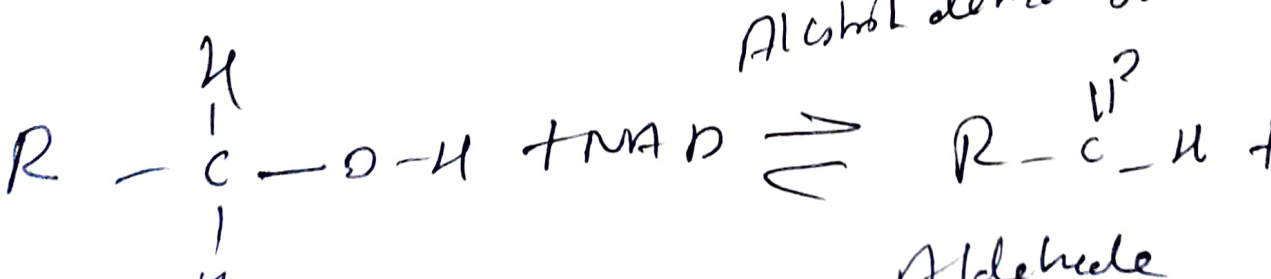
i Dehydrogenases - An enzyme that catalyse the removal of hydrogen atoms from a particular molecules

Eg Alcohol dehydrogenase oxidoreductase

Catalyse the oxidation of an alcohol to an aldehyde

→ The enzyme removes two electrons as two hydrogen from the alcohol to yield an aldehyde

→ The two electrons that are originally in the carbon - hydrogen bond of the alcohol are transferred to the NAD, which then become reduced



Nomenclature

Trivial Name: Alcohol dehydrogenase

Systema TUB Name: Alcohol - NAD - oxidoreductase

EC number:

Code EC 1.1.1.1

: Glucose - 6 - Phosphate → (Glucose-6-phosphate dehydrogenase) → 6-phosphogluconolactone

NADP$^+$ → NADPH + H$^+$

Trivial name: Glucose 6 phosphate

TUB name: Glucose-6-phosphate NADP+ oxidoreductase

Code: EC 1.1.1.49

other major classes Include

ii Oxidases - Transfer two electrons from the donor to oxygen
Eg Glucose oxidase

iii Reductases - An enzyme that catalyse the reduction. Eg 5-α-reductase

iv) peroxidases - To breakdown hydrogen peroxide (H_2O_2)
Eg Thyroid peroxidase

v) Catalase - Catalyzes the decomposition of hydrogen peroxide to water and oxygen

vi oxygenase - Oxygenase catalyze the incorporation of both atom of oxygen into a single substrate. Eg Catechol oxygenase

vii Hydroxylases - which add an hydroxyl group to organic compounds
Eg Tyrosine hydroxylase

Transferases

→ These enzymes are involved in transfer functional groups between donors and acceptors

$$A-R+B \xrightarrow{EC\text{-}2} A+B-R$$

→ The amino, acyl, phosphate, glucosyl, one carbon groups are the major moiety that are transferred

1. Aminotransferases (Transaminases)

→ Aminotransferases transfer the amino group from one ~~carbon~~ amino acid to a ketoacid acceptor resulting in the formation of a new amino acid and a new ketoacid

Eg. Alanine transaminase

Aspartate transaminase.

2. Kinases : Kinases

→ The are the phosphorylating enzymes that catalyzes the transfer of phosphoryl group from ATP or other nucleoside triphosphate to alcohol or amino group acceptors

Eg Hexokinase
glucokinase

3. glucosyl transferases — which catalyze the transfer of an activated glucosyl residue to a glycogen primer

Eg glycogen synthase
phosphorylase
glycogen phosphatase

4. Acyl transferases - that acts on acyl groups 

Eg. Glycerone phosphate O-acyltransferase
Lecithin-Cholesterol acyltransferase

5. Methyl transferases

→ Large group of enzymes that methylate their substrates

Eg. Histone methyl transferases
DNA/RNA methyl transferases

6. ~~Phosphoryl transferases~~

6. Transketolases and transaldolase

Transketolase transfers a two carbon unit where as transaldolase transfers a three Carbon unit

Eg. Erythrocyte transketolase

- Phosphomutases or phosphoglucomutase

An enzyme that catalyses the interconversion of isomers of glucose phosphates.

Eg ✱ glucose phosphomutase }

III Hydrolases

Hydrolase is a class of enzyme that commonly perform as biochemical catalyst that use water to break a chemical bond which typically results in dividing a large molecule to smaller molecules

→ They hydrolase ester, ether, peptide, or glycoside Common Examples of hydrolase include

Enzymes are

1. Esterases
2. Nucleases
3. Phosphodiesterases
4. Lipase
5. Phosphatase
6. DNA glycosylase
8) Protease
9) peptidase
10) GTPase

Phospholipases — Hydrolyses phosphoglycerides into fatty acids

By phospholipase A, B, C and D

Endothelial lipase

(2) Amidases - Catalyses the hydrolysis of amide

By Deaminase

(3) Ribonuclease - is a type of nuclease that catalyses the degradation of RNA into smaller components

By RNase A

RNase H,

Polynucleotide phosphorylase

(4) Thiolases - Converts two units of Acetyl CoA to acetoacetyl CoA in the mevalonate pathway

By acetoacetyl-CoA - thiolase.

) Proteases / peptidase / Proteinase

is an enzyme that catalyses proteolysis
i.e the breakdown of proteins into smaller
polypeptides or single amino acids.

Eg plasmin
thrombin
pepsin, trypsin,
Chymotrypsin
elastase.

) helicases — Class of enzyme, to
unpackage an organism's genes

Eg DNA helicase
RNA helicase

) Lipase — are a large group of hydrolase
Enzyme that bind to the CHO and hydrolyze

4. Lyases

⇒ These enzymes can remove groups from substrate or break bonds by mechanisms other than hydrolysis

→ These are the enzymes which add or remove the elements of water, ammonia or CO_2.

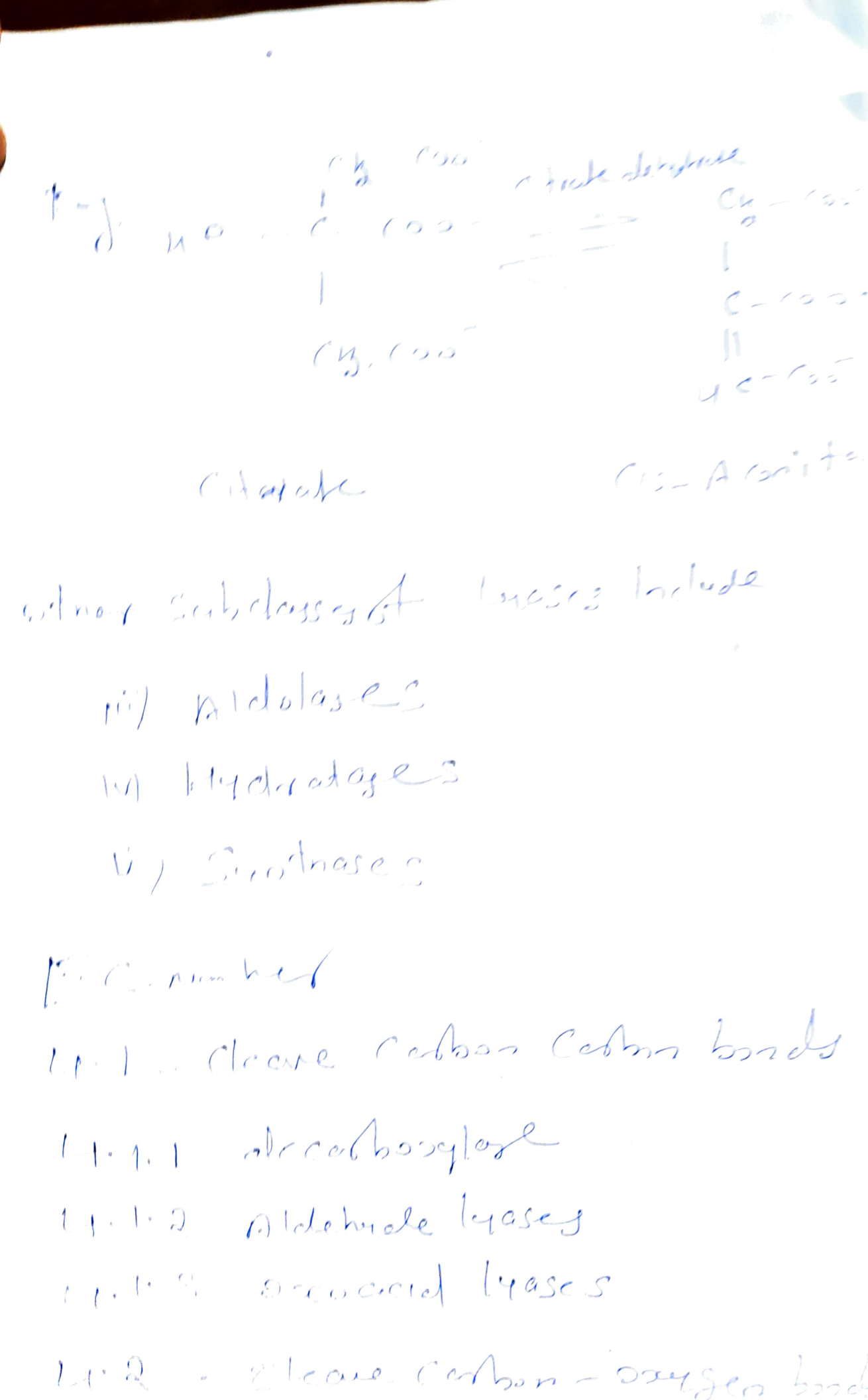
⇒ Sub classes include

i Decarboxylase – remove the element of ~~water~~ ammonia ~~or~~ CO_2 from α or β keto acids or amino acids

ii

(2) Dehydratases remove the elements

ii) of H_2O in a dehydration



7

→ Isomerases that catalyze inversion of asymmetric carbons are either epimerases or racemases

i) Epimerases → Target molecules with multiple chiral carbons by acting on one of them

ii) Racemases ⇒ may act on molecules containing one chiral carbon atom for stereochemical inversion

iii) Cis-trans Isomerase → Catalyze the isomerization of cis trans isomers

iv) Phosphomutases ⇒ Involves the intramolecular transfer of a group such as phosphoryl

4.5 - Cleave carbon-halide bonds

4.6 Cleaves phosphorus-oxygen

IEC-4.99.

Eg Aldolases

Systematic name: ketose-1-phosphate aldehyde lyase

Enzyme IEC 4.1.2.7

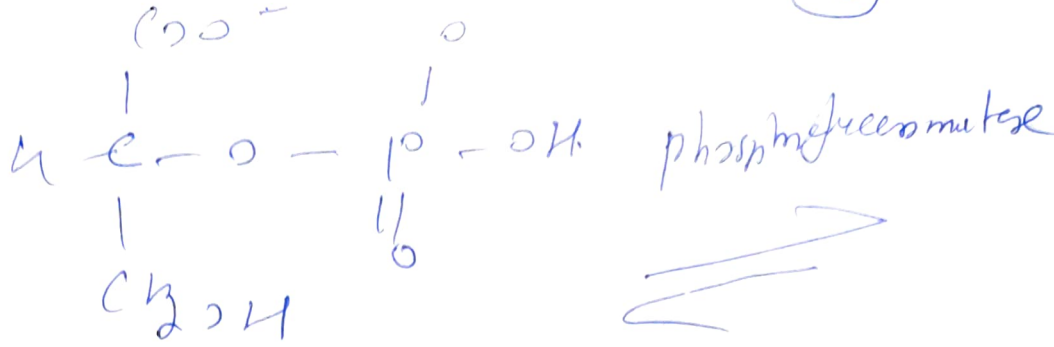
5) Isomerases

→ This is very heterogenous group of enzymes that catalyze isomerization of several types of intramolecular cis-trans, keto-enol, aldose-ketose

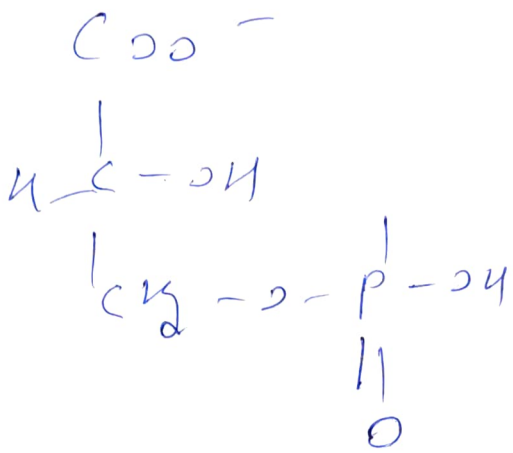
→ These enzymes can produce optical, geometric or positional isomers of substrates.

4.4 - Cleave co...

Fig-1.



2-phosphoglycerate



3-phosphoglycerate

EC number - 5

5-1- Racemases, Epimerases

5-1-1 - Act on amino acids derivative

5-1-2- " hydroxy acid and derivs

5-1-3 " Carbohydrate and derivs

5-1-99 " other Compounds

5.2 - Cis- trans Isomerase

5.3 - Intramolecular oxidoreductases

5.4 - Intramolecular transferases

5.5 - Intramolecular lyases

Glyceraldehyde phosphate $\underset{\text{Triose phosphate Isomerase}}{\rightleftharpoons}$ Dihydroxy acetone phosphate

Trivial Name - Triose phosphate Isomerase

Systematic name - Glyceraldehyde-3-phosphate ketol Isomerase

Code no. EC 5.3.1.1