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# ENZYMES

- **Biological catalysts which speed up the rate of reaction without becoming part of the reaction but themselves cannot initiate any chemical reaction**
- **Enzymes : First name is of substrate second, ending in "ASE" indicating type of reaction catalyzed**
- **Clarify the reaction , e.g.**
- **L- Malate + NAD $\rightarrow$ Pyruvate + NADH-H + $CO_2$**
- **Malate NAD oxidoreductase (Decarboxylating)**
- **IUB Classification and Numbering**
- **Six major classes and 4-13 subclasses**
- **Numbering 1.2.3.4.5.6**

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# ENZYMES

**Nomenclature**

- Oxidoreductases
  - Enzymes acting on CH-OH group
  - Alcohol NAD oxidoreductase [Alcohol dehydrogenase]
  - Alcohol + NAD= Aldehyde or Ketone + NADH.H
  - Glucose+ ATP =Glucose-6 phosphate + ADP
  - ATP.D.Hexose – 6 Phosphotransferase (Hexokinase)

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# CO-FACTORS OF ENZYMES

| ENZYMES | CO FACTORS |
|---|---|
| Catalase<br>Peroxidase<br>Cytochrome oxidase | Iron<br>$Fe^{2+}$ or $Fe^{3+}$ |
| Cytochrome oxidase | Copper : $Cu^{+2}$ |
| Carbonic anhydrase alcohol dehydrogenase | Zinc : $Zn^{2+}$ |
| Hexokinase<br>Glucose-6-phosphatase<br>Pyruvate kinase | Magnesium<br>$Mg^{2+}$ |
| Arginase | Manganese $Mn^{2+}$ |
| Pyruvate kinase | Potassium $K^{+}$ |
| Urease | Nickel N $2^{+}$ |
| Glutathione Peroxidase | Selenium : Se |

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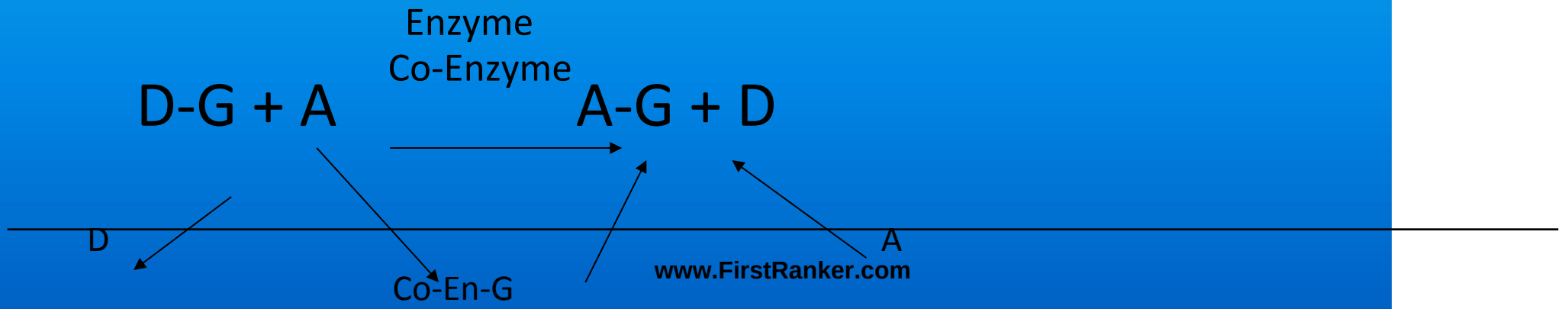
# COENZYMES

- Heat stable, low molecular weight organic compounds non-covalently linked with enzymes & can be separated. APO + CO = Holoenzyme
- If covalently linked to apoenzymes = prosthetic group
- Act as intermediate or ultimate acceptor in group transfer  enzyme catalyzed reactions

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# COENZYMES

| CO ENZYMES FOR TRANSFER OF $H^+$ | COENZYMES FOR TRANSFER OF OTHER GROUPS |
|---|---|
| NAD, NADP | SUGAR PHOSPHATES |
| FMN, FAD | THIAMINE PYROPHOSPHATE TPP, PYRIDOXAL PHOSPHATE |
| LIPOIC ACID | FOLATE AND COBAMIDE (VIT $B_{12}$), BIOTIN |
| COENZYME, Q | LIPOIC ACID |

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# CO-ENZYMES

## REDUCTION OF $NAD^+$ TO $NADH.H^+$

Lactic acid + NAD $\xrightarrow{\text{LDH}}$ Pyruvic acid + $NADH\text{-}H^+$

Malic acid + NAD $\xrightarrow{\text{Malic dehydrogenase}}$ Oxalo acetic acid + $NADH\ \text{-}H^+$

Glucose-6-phosphate + NADP $\xrightarrow{\text{G-6-P.D}}$ 6-Phosphoglucon-olactone +$NADPH\text{-}H^+$

## REDUCTION OF FAD OR FMN TO $FADH_2$ OR $FMNH_2$

FMN is co enzyme for Cytochrome C oxidase, L.Amino acid dehydrogenase

FAD is co-enzyme for xanthene oxidase, acyl-CoA dehydrogenase

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# CO-ENZYMES

Thiamine Pyrophosphate:

Co-enzyme for oxidative decarboxylation for ketoacids

Pyruvate —(CoA, NAD → NADH-H$^+$; Pyruvate dehydrogenase)→ Acetyl CoA

Pyruvate +TPP —(Pyruvate decarboxylase)→ Acetalaldehyde -TPP complex+$Co_2$

Alpha ketogluterate+6 CoA-SH —($\alpha$-ketogluteratedehydrogenase; NAD → NADH-H$^+$)→ Succinyl CoA + $Co_2$

Ribose-5 $Po_4$ + Xylulose-5-$Po_4$ —(Transketolase)→ Sedoheptulose 7-$Po_4$ + 3 phosphoglyceraldehyde

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# CO-ENZYMES

## Biotin

- Part of multiunit enzymes causing carboxylation reactions. Acts as carrier of $CO_2$

$$\text{Acetyl CoA} + HCo_3 + \text{ATP} \xrightarrow[\text{Enz-Biotin-COO}^- \rightarrow \text{Enz-Biotin}]{\text{Acetylcarboxylase}} \text{Malonyl-CoA}$$

$$\text{Pyruvate} + HCo_3 + \text{ATP} \xrightarrow{\text{Pyruvate carboxylase .Biotin}} \text{Oxaloacetate} + \text{ADP} + \text{Pi}$$

$$NH_4 + HCo_3 + 2\text{ATP} \xrightarrow{\text{Carbamoyl Po}_4\text{.Synthetase - Biotin}} \text{CarbamoylPO}_4 + 2\ \text{ADP} + 2\ \text{Pi}$$


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# CO-ENZYMES

## Ascorbic acid (Vitamin C)

- Strong reducing agent
  - Required for hydroxylation of proline into hydroxyproline for synthesis of collagen
  - Conversion of tyrosine into dopamine and into catecholamines (adrenaline and noradrenalin)
  - Bile acid formation
  - Conversion of cholesterol into 7-hydroxylcholesterol
  - Maintain metallic co-factors like $Cu^{+}$ in Monooxygenases and Fe in dioxygenases in reduced form
  - Conversion of cholesterol into steroid hormone in adrenal cortex
  - Absorption of iron by reducing into reduced form which is can be easily absorbed
  - Acts as antioxidant in GIT by preventing formation of nitrosamines during digestion

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# CO-ENZYMES

- **Folic acid**
  - Active form is tetrahydrofolate which acts as single carbon carrier for synthesis of various compounds like pyrimidines and purines e.g. conversion of dUMP (deoxyuridylate) into dTMP (deoxythymidylate)

- **Vitamin $B_{12}$**
  - Acts as co-enzyme in groups rearrangements in isomerases e.g. conversion of methyl malonyl CoA into succinyl-CoA by enzyme methylmalonyl-CoA mutase
  - Converts homocystein into methionine
  - Act as maturation factor for RBCs

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# CLASSIFICATION OF ENZYMES

- Formulated by the enzyme commission of I.U.B six major classes & 4-13 subclasses of each major class, based on the type of reactions catalyzed.

1. **Oxidoreductases**
   - Catalyzing oxidation reduction reactions
2. **Transferases**
   - Catalyzing group transfer
3. **Hydrolases**
   - Catalyzing hydrolytic breakdown

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# CLASSIFICATION OF ENZYMES

4. **Lyases**
   - Catalyzing removal of groups by mechanism other than hydrolysis and leaving behind double bonds or adding groups to already existing double bonds.
5. **Isomerases**
   - Catalyzing interconversion of isomers
6. **Ligases**
   - Catalyzing formation of bonds and new compounds

**1.Oxidoreductases**

– Catalyzing oxidation reduction reaction where one substrate is oxidized and other is reduced

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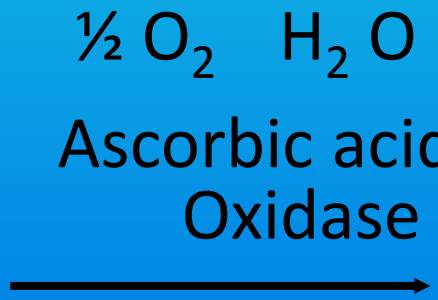
# CLASSIFICATION OF ENZYMES (OXIDOREDUCTASES)

**Oxidases.** Catalyzing oxidation of the substrate and atomic oxygen acts as recipient of hydrogen e.g. Ascorbic acid oxidase, Cytochrome oxidase, Tyrosinase




Ascorbic acid Dehydro ascorbic acid

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# CLASSIFICATION OF ENZYMES (OXIDOREDUCTASES)

**Aerobic Dehydrogenases.** Catalyzing oxidation of the substrate and molecular oxygen acts as recipients of hydrogen e.g. Glucose oxidase, L amino acid dehydrogenase, Xanthene dehydrogenase

$O_2$ $H_2O_2$

glucose Oxidase

Glucose ——— Gluconolactone

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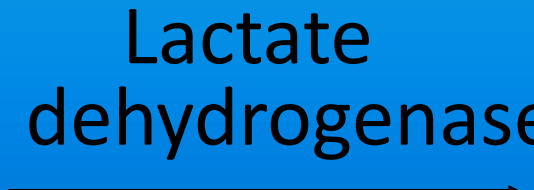
# CLASSIFICATION OF ENZYMES (OXIDOREDUCTASES)

**Anaerobic Dehydrogenases.** Catalyzing oxidation of the substrate and coenzymes act as recipients of hydrogen e.g. Lactate Dehydrogenase with NAD and Glucose 6 phosphate dehydrogenase with NADP




Lactic acid → Pyruvic acid

+ NAD → + NADH – $H^+$

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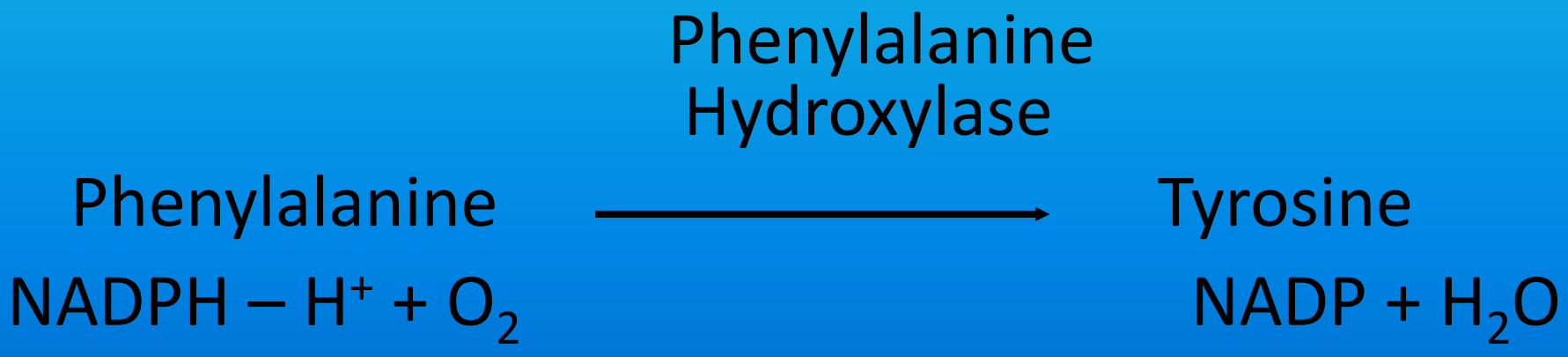
# CLASSIFICATION OF ENZYMES (OXIDOREDUCTASES)

**Oxygenases .** Catalyzing oxidation of the substrate and oxygen is added to the substrate eg are Homogentisate oxygenase, L Tryptophan dioxygenase

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# TRANSFERASES

**Transaminases.** Catalyzing transfer of amino group between an amino acid and a ketoacid e.g. Aspartate Transaminase (AST), Alanine Transaminase (ALT)

**Aspartate Transaminase (AST)**

**Glutamic acid +**
**+**
**Oxalo acetic acid** → **α Ketoglutaric acid**
**Aspartic acid**

**Alanine Transaminase (ALT)**

**Glutamic acid +**
**+**
**Pyruvic acid** → **α ketoglutaric acid**
**Alanine**

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# TRANSFERASES

**Transmethylases.** Catalyzing transfer of methyl group between to substrates e.g. COMT

**Catechol O Methyltransferase (COMT)**

Noradrenaline + $CH_3$ → Adrenaline

**Transpeptidases.** Catalyzing transfer of amino acids to substrates e.g. Benzyl-SCoA transpeptidase

Benzyl-SCoA Transpeptidase

Benzyl - SCoA + Glycine → Hippuric acid

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# TRANSFERASES

**Phosphotransferases.** Catalyzing transfer of phosphate group to substrates e.g. Hexokinase, Glucokinase

2.7.1.1 ATP D hexose- 6 Phosphotransferase [Hexokinase]

ATP + Glucose Hexokinase $\rightarrow$ADP + D-Glucose –6-P

**Acetyltransferase**. Catalyzing transfer of acetyl group to substrates e.g. Choline Acetyltransferase

Acetyl-CoA+ Choline $\rightarrow$ CoA + Acetyl- Choline

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# HYDROLASES

- **Catalyzing hydrolytic breakdown of different bonds. Most of the GIT enzymes belong to this class**

## Enzymes hydrolyzing Carbohydrates

### Polysaccharidases

**Starch** **Amylase** **Maltose, Maltotrios, Dextrins**

### Oligosaccharidases

**Dextrins** **Dextrinase** **Glucose**

### Disacharidases

**Maltose, Lactose, Sucrose Disacharidases (Maltase, Lactase, Sucrase)**

**Monosaccharides**

## Enzymes Hydrolysing Lipids

**Triacyl glycerol** **Lipase** **Monoacyl glycerol + 2 F.F.A**

**Cholesterol ester** Cholesterol **Esterase** Free Cholesterol + FFA

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# HYDROLASES

Phospholipids Phospholipase Lysophospholipids

Lecithin Lysolecithin

**Enzymes Acting on Peptide Bonds**

**Exopeptidases** Carboxypeptidase Amino acids

Aminopeptidase

**Endopeptidase** e.g. Pepsin Smaller Peptides

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# HYDROLASES

**Tripeptidase** : Tripeptide → A.A

**Dipeptidase** : Dipeptide → AA

**Phosphatases**

i. Phosphomonoesterases:

Glucose – 6.P. + $H_2O$ G 6. Phosphate $\xrightarrow[\text{Phosphatase}]{}$ Glucose +Pi

ii. Phosphodiesterases:

Removal of phosphate Group of diesters

~~breakdown of 3'-5' p linkages in cyclic AMP~~

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# LYASES

- Catalyzing reactions in which groups are removed without hydrolysis leaving a double bond or add groups to already existing double bonds

$CH_3.CO.COOH$ (Pyruvate) $\xrightarrow[\text{Decarboxylase T.P.P}]{\text{Pyruvate}}$ $CH_3.CHO + CO_2$ (Acetaldehyde)

$COOH.CH = CH.COOH$ (Fumaric acid) $\underset{\text{Fumerase}}{\rightleftharpoons}$ $COOH\text{-}CHOH.CH_2\text{-}COOH$ (Malic Acid)

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# ISOMERASES

- Involved in inter conversion of pair of isomeric compounds
- Glucose 6. P $\underset{\text{Mutase}}{\overset{\text{Phosphogluco}}{\rightleftharpoons}}$ glucose I.P
- Glucose 6.P $\underset{\text{Isomerase}}{\overset{\text{Phosphohexose}}{\rightleftharpoons}}$ Fructose 6.P
- All trans retinene $\xrightarrow[\text{Isomerase}]{\text{Retinene}}$ 11- CIS retinene
- UDP glucose $\xrightarrow[\text{Epimerase}]{\text{UDPG-4}}$ UDP – Galactose

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# LIGASES

- Catalyze reactions in which linking together of two molecules occur coupled with the breakdown of a high energy phosphate bonds like ATP, GTP

Acetate + CoA +ATP $\xrightarrow[\text{Synthetase}]{\text{Acetyl CoA}}$ Acetyl CoA+AMP+PP

Succinate + CoA + ATP $\xrightarrow[\text{Synthetase}]{\text{Succinyl CoA}}$ Succinyl CoA + ADP+ Pi

Pyruvate + $CO_2$ + ATP $\xrightarrow[\text{Carboxylase}]{\text{Pyruvate}}$ Oxaloacetate + ADP + Pi

Fatty acid + CoA + ATP $\xrightarrow[\text{Synthetase}]{\text{Acyl CoA}}$ Acyl CoA (Activated fatty acid) + AMP + PiPi

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# MECHANISM OF ACTION

- S+E ⟶ E-S ⟶ P
- D-G + A $\xrightarrow[ES]{\text{Enzyme (Enzyme}}$ – G) A-G + D

- **Factors affecting enzyme activity**
  - Enzyme concentration
  - Substrate concentration
  - Temperature
  - pH
  - Enzyme inhibitors

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# MICHEALIS – MENTON EQUATION

$$V_i = \frac{V_{max}[S]}{Km + \{S\}}$$

$V_i$ = Measured initial velocity

V max = Maximum velocity

S = Substrate

Km = Michaelis constant

Variations

A. **When (S) is much less than Km**

$$Vi = \frac{V_{max}[S]}{Km + \{S\}} \quad \text{OR} \quad \frac{V_{max}}{Km}[S] \; K\,[S]$$

So Vi depends upon substrate concentration

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# ENZYME KINETICS

**B. When substrate concentration is much greater than Km**

$$Vi = \frac{Vmax\,[S]}{Km + [S]} \quad \text{or} \quad Vi = \frac{Vmax\,[S]}{[S]}$$

Or $Vmax = Vi$

**C. When substrate concentration is equal to Km**

$$Vi = \frac{Vmax\,[S]}{Km + [S]} \quad \text{or} \quad Vi = \frac{Vmax\,[S]}{[S] + [S]}$$

Or $$Vi = \frac{Vmax\,[S]}{2\,[S]} \quad \text{or} \quad Vi = \frac{Vmax}{2}$$

So Vi = half of maximum velocity

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# Enzyme Catalysis

- Catalysis by Proximity : Higher conc of “S” will increase their proximity to each other thereby promoting enhanced binding to enzyme resulting in increased catalysis
- Acid-Base Catalysis : Ionizable functional gps of aminoacyl side chains & prosthetic gps can act as acids or bases. In “specific acid or base catalysis” rate of reaction is sensitive to changes in protons , but is independent of conc of other acids or bases present in the solution or at active site. In “general acid or base catalysis” reaction rates are sensitive to all acids & bases present .

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# Enzyme Catalysis

- Catalysis by Strain : Binding of Enzyme to substrates whose covalent bond are to be cleaved in an unfavorable configuration thereby exerting strain on the bonds ,stretching or distorting bonds.
- Covalent Catalysis: Formation of transient covalent bond between enzyme & substrate(s) makes it more reactant & introduces a new faster pathway of catalysis with much lowered energy of activation. On completion of reaction, enzyme returns to its original state. Cysteine, serine or histidine residues on enzyme participate in covalent catalysis

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