Unit - I

Chapter - II :- ## Bioenergetics

→ The term bioenergetics means production of or consumption of Energy inside the living organism.

- In our body many biochemical reactions is always running and the study of energies involved during biochemical reactions is called bioenergetics.

$$C_6H_{12}O_6 + 6O_2 \longrightarrow 6CO_2 + 6H_2O + ATP$$

### Production of Energy :-

During biochemical reactions the production of energy is involve by two steps.

i) Oxidation Step :- Various Co-Enzyme like NADH, FADH, FMN are the $e^-$ excepters in the biochemical reactions. and after the oxidation of these $e^-$ excepters energy is produce

$$NADH + O_2 \longrightarrow NAD + H_2O$$

$$FADH_2 + O_2 \longrightarrow FAD + H_2O \longrightarrow ATP$$

ii) Phosphorylation Step :- After phosphorylation ATP is break into ADP and further into AMP and they produce energy.

$$ATP \longrightarrow ADP + EP + Energy$$

### Essentials of Bioenergetics :-

i) Energy is required for mechanical work

ii) Energy is required for chemical synthesis.

iii) growth

iv) Cleavage and breaking of bone

1) Laws of Bioenergetics

The concept of bioenergetics is based on three laws.

i) Law of Thermodynamics.
ii) Thermodynamics Concept.
iii) ATP & phosphagens.

i) Law of Thermodynamics:-

It is based on the first law of thermodynamics which states that energy is neither be created nor destroyed but it can change from one form into another.

$$\boxed{Q = \Delta E + W}$$

Q = Heat
$\Delta E$ = Internal Energy
W = Work.

ii) Thermodynamics Concept:-

The thermodynamics concept is the concept of enthalpy and entropy.

Enthalpy:-

The total internal energy at constant pressure and temp is called enthalpy..

During any biochemical reaction the change in enthalpy is considered.

$$\boxed{\Delta H = \Delta H_f - \Delta H_i}$$

$$\boxed{H = E + PV}$$

$\Delta H$ = Enthalpy
$\Delta H_f$ = Final Enthalpy
$\Delta H_i$ = Initial Enthalpy

Enbrofy

The Randomness or disorderness of system is called Enbrofy.

It can be calculated by using the formula -

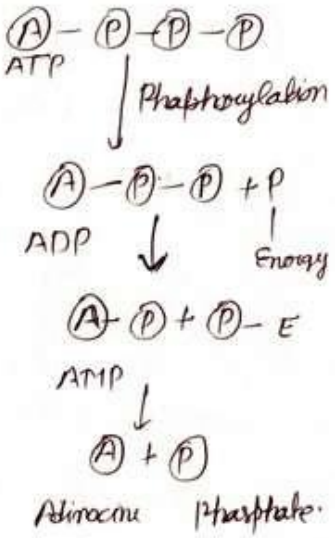
$$\Delta S = \Delta S_f - \Delta S_i$$

$\Delta S$ = Enbrofy

3) ATP & Phasphogens :-

The full name of TATP is Adinocine tri phasphate and it is the main saurce of energy.

After phasphorylation ATP breaks into ADP and ADP breaks into AMP and they produce energy.



## ÷ Concept of Free Energy or Gibbs free energy ÷

A) During any biochemical reaction some amount of energy is involve.

B) The concept of free energy was given by willard gibbs in 1875 so it is also known as gibbs free energy.

C) The gibbs free energy equation is –

$$\boxed{\Delta G = \Delta H - T\Delta S}$$

where ÷ $\Delta G$ = change in gibbs free energy.

$\Delta H$ = Enthalpy.

$T$ = Temprature

$\Delta S$ = change in enthrapy.

D) Acardeing to the value of $\Delta G$ biochemical reaction is of 2 types

if → $\Delta G$ = -Ve $\boxed{\Delta G < 0}$ = Exergonic [Spontenceaus]

$\Delta G$ = +Ve $\boxed{\Delta G > 0}$ = Endergonic [Non Spontenceaus]

### 1) Exergonic chemical Reaction ÷÷

In exergonic reaction the value of $\Delta G$ is always negative so it means it release the energy itself so it is called spontenaus reaction.

For Example ÷ In respiration process after the oxidation of glucose - 3012 Kcal energy is release

$$C_6H_{12}O_6 + 6O_2 \longrightarrow 6CO_2 + 6H_2O$$

-3012 Kcal energy.

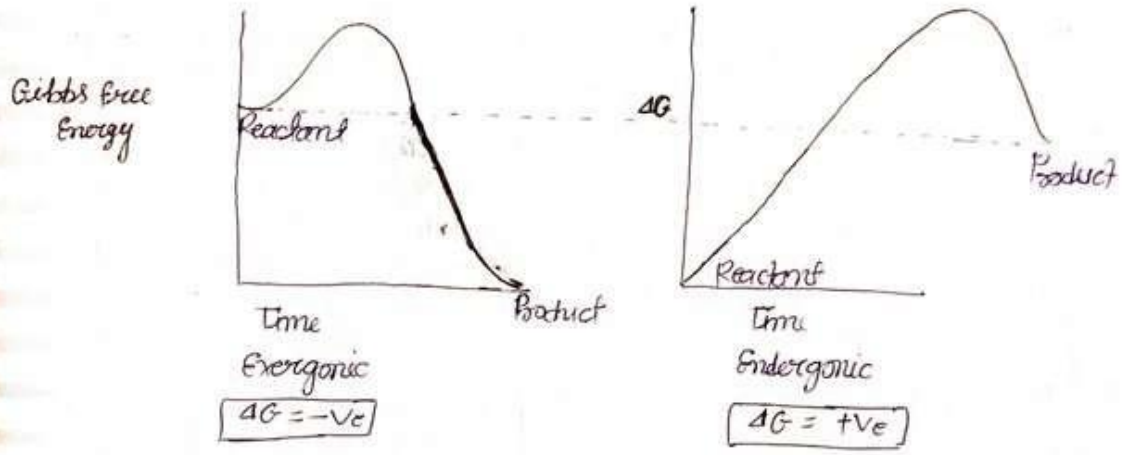
### 2) Endergonic chemical Reaction ÷

In this type of reaction the value of $\Delta G$ is positive it means it absorb the some amount of energy during the biochemical reaction so it is also called Non spontenaus reaction.

For Example :- The formation of protein and poly peptide chain after the condensation of amino acids is an endergonic reaction because is required 8 to 12 Kcal energy.

$NH_2-R-COOH + NH_2-R-COOH \longrightarrow NH_2-R-\overset{O}{\overset{\|}{C}}-NH-R-COOH + 9\text{-}12\ Kcal$

Amino Acid Amino Acid Protein




Relationship b/w free energy enthalpy & Entropy :-

$$\Delta G = \Delta H - T\Delta S$$

Case-1 :- Temp increase [↑] = $\Delta G$ = -Ve - Sponteneous

When the temp of reaction is increase then the value of $\Delta G$ becomes negative and reaction become sponteneous.

Case-ii :- Temprature decrease (↓) = $\Delta G$ = +Ve - Non sponteneous

When temprature of reaction is decrease then the value of $\Delta G$ is becomes positive and reaction become Non Sponteneous.

Case - iii :- If $\Delta H \uparrow$ & $\Delta S \downarrow \longrightarrow \Delta G$ = +Ve Non sponteneous

If the value of change in enthalpy is increase and the value of change in entropy is decrease then the value of $\Delta G$ will be positive and reaction become non sponten

4) If $\Delta H \downarrow$ & $\Delta S \uparrow \longrightarrow \Delta G$ = -ve Spontaneous.

If the value of change in enthalpy is decrease and the value of change in entropy is increase then the value of $\Delta G$ will be -ve and reaction becomes spontaneous

## ÷ Difference b/w exergonic and Endergonic Reaction ÷

| | Endergonic Reactions | Exergonic Reaction |
|---|---|---|
| 1. | It is also known as unfavorable reaction or non-spontaneous rxn which requires more energy. | It is also known as spontaneous rxn or a favourable rxn. |
| 2) | It absorbs energy from the surroundings | It release energy to the surroundings. |
| 3) | The reaction are non-spontaneous | The reaction are spontaneous. |

## Redox Potential :

Redox potential is the most imp for biochemical reaction which is used to characteries the free energy cost and direction of reaction invalue in nearst equation.

$$E = E^\circ + \frac{2.303RT}{nf} \log_{10} \frac{Oxi}{Red}$$

Where - E = Electrode potential
$E^\circ$ = Std. Electrode potential
R = Rudyard constent
T = Absalute temp
n = no of $e^-$ (malecule)
f = farade constent.

## Energyrich Compaernds :

Organism required high amaunt of energy for their metabolic and biological activity.

In our body there are many compaernds which release the energy after dissociation and after hydrolysis they are known as energy rich compaernd.

Those chemical compaernd. which contain Ester, Alkloid they releas less amaunt of energy after dissociation. 110-15 Kgfm

They are called energy poor compaernd.

But energy rich compaernds like phasphate and anhydride release high amaunt of energy after hydrolysis (30-60 Kfmol

Energy rich compound are formed in the cell in three diff method.

i) The main energy rich compound like Adenine, Ribose & phosphoric acid are always present in body

2) Intermediate compounds are formed with high energy phosphate group during high energy reactant

3) Some energy reach compound are produced in release of high energy phosphate with the help of kinase enzyme.

Reactant ⟶ Intermediate ⟶ Product.

$H_2CO_3$ — $H^+ + HCO_3^-$ ⟶ $2H^+ + CO_3^{--}$

Importance of Energy Reach Compound :-

i) They librate sufficient amount of energy.

→ They are not used from long term storage.

→ They carry the reaction from one reaction to another.

→ After hydrolysis these compound release energy.

→ High energy bond formed by oxidative phosphorylation.

Ex. - Phospho in all - Pyruvate — -62.2 kJ/mole.

- cAMP — -52.2 Kj/m

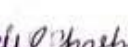
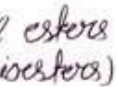
- Acetyl Phosphate — -43.3 Kj/m

- APP — -35.7 Kj/m

- ATP — -30.5 Kj/m

- Acetyl co-A — -31.5 Kj/m

## Classification of Energy rich compound

| Class | Bond | Example |
|---|---|---|
| Pyrophosphates | -C-P-P | ATP, Pyrophosphate |
| Acyl phosphates |  | 1,3-Biphosphoglycerate carboxyl phosphate, Acetyl Phosphate. |
| Enol Phosphates |  | Phosphoenol pyruvate |
| Thiol esters (Thioesters) |  | Acetyl CoA, Acyl Co-A |
| Guanido Phosphates (Phosphagens) |  | Phosphocreatine, Phosphoargin |

**Urea cycle**

1. Since ammonia is toxic to CNS even in traces liver rapidly removes ammonia from circulation and converts it to a non-toxic water soluble urea. Hence site of urea synthesis is liver.

2. The reactions leading to formation of urea from ammonia are proposed by Krebs and Henseleit. Hence, urea cycle is also called as Krebs-Henseleit cycle.

3. Formation of urea from ammonia in urea cycle occurs in five reactions. However the first reaction is not a part of the cycle but for the continuation of the cycle which consist of remaining four reactions product of the first reaction is essential..

4. Synthesis of urea from ammonia is a energy dependent process.

5. Enzymes of urea cycle are present in mitochondria and cytosol.

6. First two reactions of urea formation occurs in mitochondria and remaining reactions occur in cytosol.

**Reaction sequence of urea formation:** For the synthesis of urea only one ammonia molecule is used as such. Aspartate serves as donor of another molecule of ammonia. $HCO^{3-}$ serves as source of $CO_2$ required for urea formation.

1. **Formation of carbamoyl phosphate:** First reaction leading to urea formation is condensation of ammonia and HCO3– at the expense of two high-energy bonds to form carbamoyl phosphate. The reaction is catalyzed by mitochondrial carbamoyl phosphate synthetase-I.

**Reactions of urea cycle**

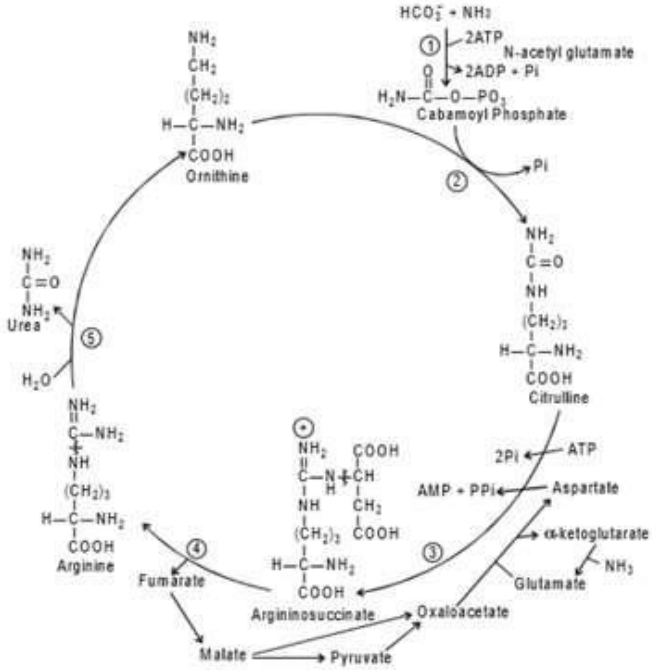
2. Now the first reaction of urea cycle is catalyzed by ornithine transcarbamoylase. It condenses carbamoyl phosphate and ornithine to form citrulline. This enzyme is present in mitochondria.

3. Arginino succinate synthetase present in cytosol catalyzes second reaction of urea cycle. It condenses citrulline and aspartate at the expense of two high energy bonds to form argininosuccinate.

4. In the third reaction of urea cycle argininosuccinate is cleaved by argininosuccinase to arginine and fumarate.

5. Regeneration of ornithine and formation of urea from arginine is the final reaction of urea cycle. This reaction is catalyzed by arginase.

The ornithine so formed enters mitochondria through specific transporter present in inner mitochondrial membrane to start reactions of urea cycle once again.




**Overall equation for urea formation**

$NH_3 + HCO^{-3}$ + Aspartate + 4ATP → Urea + Fumarate + 4ADP + 4Pi

**Fate of urea:** Urea has no physiological function. Hence it is transported to kidneys where it is excreted in urine. It is major end product of protein catabolism in humans. About 10-25 gm of urea is excreted in urine per day which makes up to 80-90% of total nitrogen excreted per day. However, blood also contains some urea.

**Blood urea** Normal blood urea level is 16-36 mg/100 ml.

**Medical Importance:** Urea formation is impaired in several inherited diseases. They are due to deficiency of enzymes of urea cycle. Since the urea cycle converts ammonia to urea these disorders of urea cycle cause ammonia intoxication. Some common clinical symptoms seen in these diseases are vomiting, irritability, lethargy, seizures, mental retardation, coma and early death. They are

1. **Hyper- ammonemia Type I :** It is due to deficiency of enzyme carbamoyl phosphate synthetase-I. Mental retardation is the main symptom of this condition.

2. **Hyper- ammonemia Type II:** It is most common among others. It is due to deficiency of enzyme ornithine trans carbamoylase. So, in this condition carbamoyl phosphate accumulates and diverted to pyrimidine formation. This results in excretion of oroticacid and uracil in urine. Glutamate also accumulates in this condition.

3. **Citrullinemia:** This condition is due to the absence of enzyme argininosuccinate synthetase. Hence citrulline accumulates in blood and excreted in urine.

4.**Argininosuccinicaciduria:** Argininosuccinase is absent in this condition. So, argininosuccinate accumulates in blood and excreted in urine.

5. **Hyper- argininemia:** This condition is due to low arginase activity. Hence, arginine accumulates and excreted in urine. However some urea may be excreted in urine due to kidney arginase.

6. **N-acetyl glutamate synthetase deficiency:** It is a rare disorder. N- acetyl glutamate synthetase is involved in formation of N- acetyl glutamate from acetyl- CoA and glutamate. Hyper ammonemia and aminoacid uria occurs in this condition.

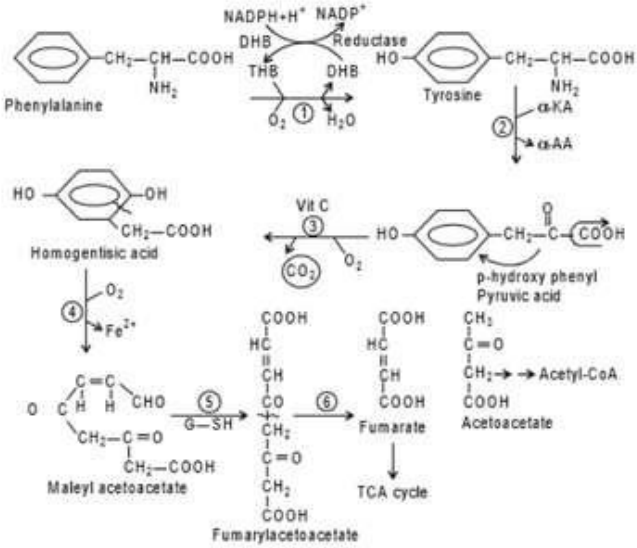
**Urea production may be decreased in liver diseases**

Treatment

Treatment of urea cycle disorders involves removal of excess ammonia from blood and reduction of dietary nitrogen load. Peritonial dialysis is employed to clear ammonia from blood. Administration of compounds which can increase nitrogen excretion is another line of treatment. Benzoic acid and phenyl acetate are two such compounds used in the treatment.

**Metabolism of phenyl alanine and Tyrosine:** Phenyl alanine is an essential amino acid. Since tyrosine is a hydroxylated phenyl alanine it is non- essential amino acid. In plants and bacteria, phenyl alanine and tyrosine are synthesized from erythrose- 4- phosphate and phosphoenolpyruvate.

**Degradation of phenyl alanine and tyrosine:** Phenyl alanine and tyrosine are degraded to fumarate and aceto- acetate. Since degradation of phenylalanine involves first its conversion to tyrosine, a single pathway is responsible for the degradation of both phenylalanine and tyrosine.




**Reaction sequence**

**1. Conversion of phenylalanine to tyrosine or tyrosine synthesis:** First reaction of phenylalanine catabolism is its hydroxylation to tyrosine, which requires a cofactor which is not encountered earlier. A tetra hydrobiopterin (THB) requiring phenylalanine hydroxylase catalyzes this hydroxylation. The enzyme is present in liver and it is a monooxygenase.

**2.** Now catabolism of tyrosine begins with transamination. p- hydroxy phenyl pyruvic acid is produced from tyrosine by the action of tyrosine transaminase in this reaction.

**3.** p-hydroxy phenyl pyruvate hydroxylase a copper containing dioxygenase converts phydroxy phenyl pyruvic acid to homogentisic acid in a complex reaction involving hydroxylation of benzene ring, decarboxylation and shifting of side chain.

**4.** In this reaction, benzene ring of homogentisic acid is cleaved by another dioxygenase called as homogentisic acid oxidase to form maleyl aceto acetate.

**5.** A glutathione dependent maleyl aceto acetate cis- trans isomerase isomerizes maleyl aceto acetate to fumaryl aceto acetate.

6. Finally fumarate and aceto acetate are formed from fumaryl aceto acetate by the action of an hydrolase.

Thus, four atoms of phenylalanine are released as fumarate, one carbon is released as $CO_2$ and remaining four atoms are released as aceto acetate. Fumarate may undergo further catabolism in TCA cycle.

**Biological importance**

1. Tyrosine is required for the synthesis of adrenal hormones like epinephrine, norepinephrine and dopamine.
2. Tyrosine is needed for the formation of melanin.
3. Thyroid hormones T3 and T4 are formed from tyrosine.
4. Tyrosine is a precursor of glucose and fatty acids or ketone bodies.
5. For the formation of proteins tyrosine and phenylalanine are required.
6. In the intestine tyrosine is decarboxylated by microorgnisms to tyramine.
7. Phosphorylation of tyrosine residues of proteins by kinases affects cell growth.

## Unit-3 :

## : Lipid Metabolism :

- Lipids and fats are the essential element of our body.
- Lipid and fat are synthesies in liver and observe in our body.
- Cholestrol and triglycarids are the main lipid which are synthesies and store in the liver.
- The cell membrane of cell of our body is made up of phospholipid which is also the derivative of lipid.
- Some other part and harmone are also made by lipid.
- Lipids are hydrophobic in nature. They are water insoluble and they transport in our blood in the form of lipoprotein.

### function of lipid :

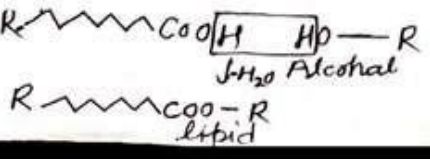
Lipids are imp source of metabolic energy. And they are rich in oils.

- lipids form the structural component of cell membrane.
- Lipids are works as biological carriers for the absorption of fat soluble vitamin (A, D, E, K)
- lipids are the source of essential fatty acid in our body.

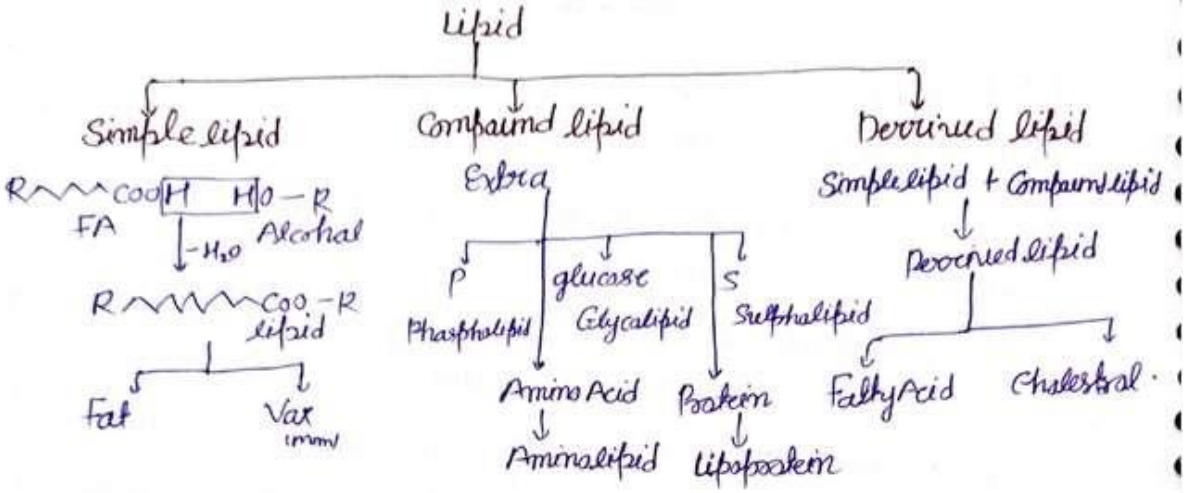
### Classification of fat ⇒ :

- Lipids are the easter of fatty acid and alcohal.
- Fatty acids are the long chain of hydrocarbon which contain one carboxylic acid group at the terminal.

when fatty acid and alcohal are condensed then lipid is form.



On the basis of structure of lipid it can be classified into three type




## Oxidation of Fatty Acid :-

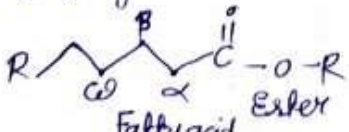
The addition of oxygene molecule in the carbon chain of fatty acids is called oxidation of fatty acid.

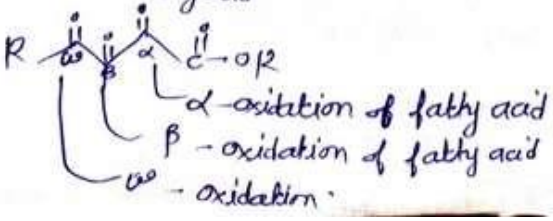
→ The oxidation of fatty acid was first discovered by Knoop in 1905.

→ After oxidation of fatty acid a large amount of energy is release.

→ On the basis of position of oxidation in fatty acid chain. it is of three type.

i) $\alpha$ - Oxidation of fatty acid
ii) $\beta$ - Oxidation of fatty acid
iii) $\omega$ - Oxidation of fatty acid



## β oxidation of fatty Acid

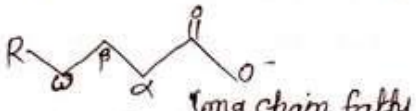
→ When the oxidation of fatty acid is takes place at β-position then it is called β-oxidation of fatty acid.

→ This is most common type of oxidation and it produce high amount of energy.

→ In this stage oxidation of fatty acid start by removal of two carbon unit from Acetyl Co-E-A.

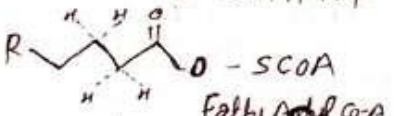
→ β oxidation of fatty acid involve following steps.

Where R = $C_{16}$




Long chain fatty

Thiokinase · Co-A SH (HS-Co) ATP → AMP + iP

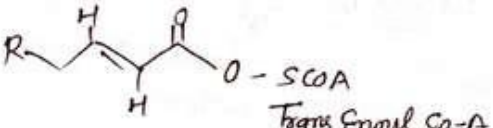



Fatty Acyl Co-A

Fatty Acyl CoA dehydrogenase · FAD → $FADH_2$

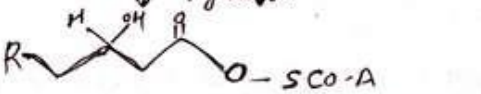
$FADH_2$ 2 ATP

NADH - 3 ATP



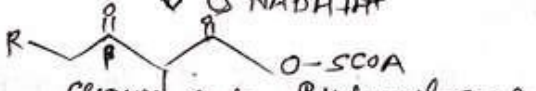

Trans Enoyl Co-A

$H_2O$ → Trans Enoyl CoA Hydratase

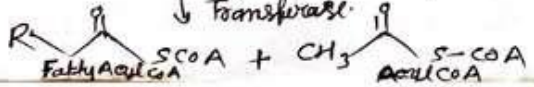



β Hydroxy Acyl Co A

dehydrogenase · $NAD^+$ → NADH + $H^+$




Cleavage · Acyl Co-A β Ketoacyl-Co-A Transferase ·




Fatty Acyl CoA  Acetyl CoA

## Energetics of β oxidation of Fatty Acid

Palmitic Acid $\frac{\text{full}}{\text{oxidation}}$ 7 Times.

1 Time — 1 FADH — 2 ATP

1 NADH — 3 ATP

in one cycle = 5 ATP

In complete oxidation = 7 × 5 = 35 ATP

Total 8 Acetyl co-A molecule Release

↳ goes in to krebs cycle

In krebs cycle — 1 Acetyl CoA = 12 ATP produce.

Total = 8 × 12 = 96 ATP

35 + 96 = 131 ATP

Total ATP consume = 2

Net gain - 131 - 2 = 129 ATP

## Cholesterol Biosynthesis & Its metabolism

Cholesterol is a type of Derived lipid which is waxy in nature.

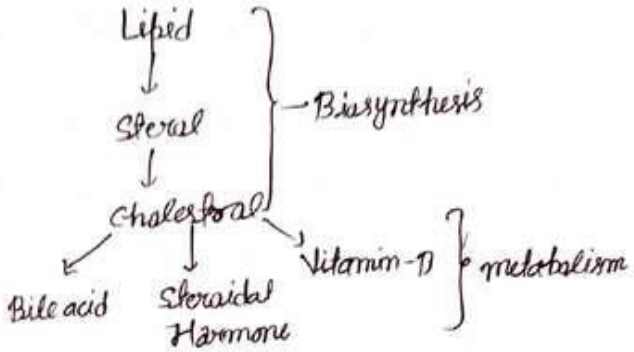
The formation of cholesterol is from steral molecule which is the derivative of fatty acid.

About 30% part of cell membrane is made by cholesterol.

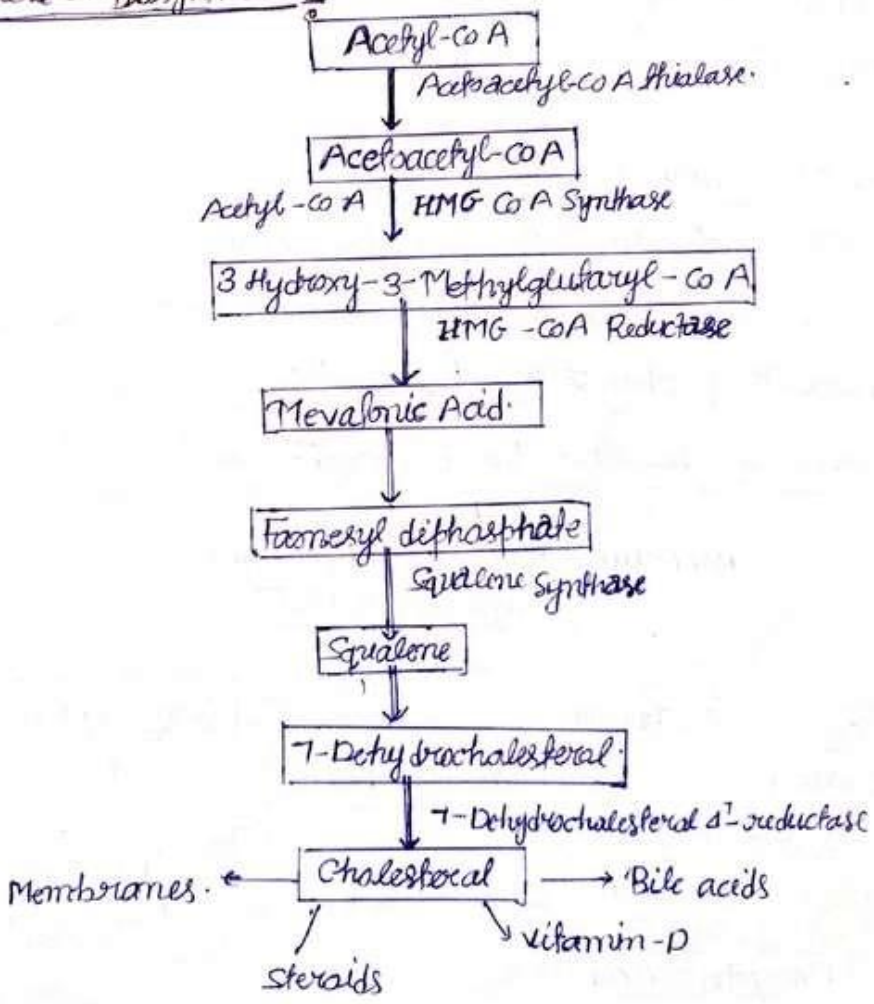
→ Cholesterol also take part in the biosynthesis of Bile acid, Steroidal hormone and vitamin-D

→ The dietry source of cholesterol is cheese, Egg yellow, Beef, Fish, Poultry.

Cholesterol is insoluble in water but it is soluble in organic solvent chloroform, Benzene, Acetone, Ethanol etc.




Cholesterol Biosynthesis :-



## Biological Significance of of cholesterol.

. Cholesterol is the structural component of cell membrane.

→ Cholesterol is an imp precursure for bile acid steroid and vit. D.

⇒ Cholesterol is an imp for lipoprotein structure.

→ It is imp in the metabolism of fat soluble vit. A, D, E, K.

## Side Effects of high cholesterol level :-

1) Atherosclerosis.
2) Coronary artery heart disease.
3) Heart Attack.
4) Angina pectaris.

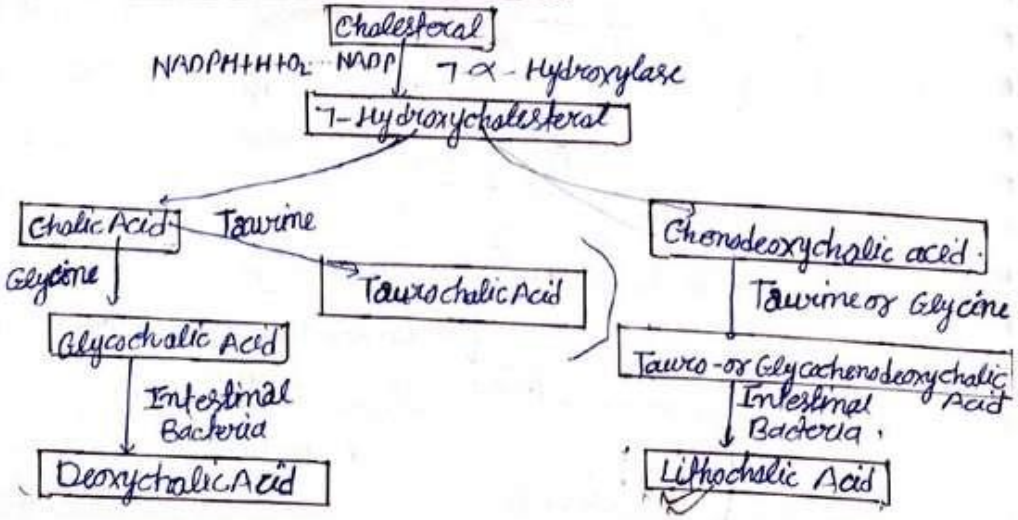
## Cholesterol Metabolism :-

i) Conversion of Cholesterol into bile Acid.

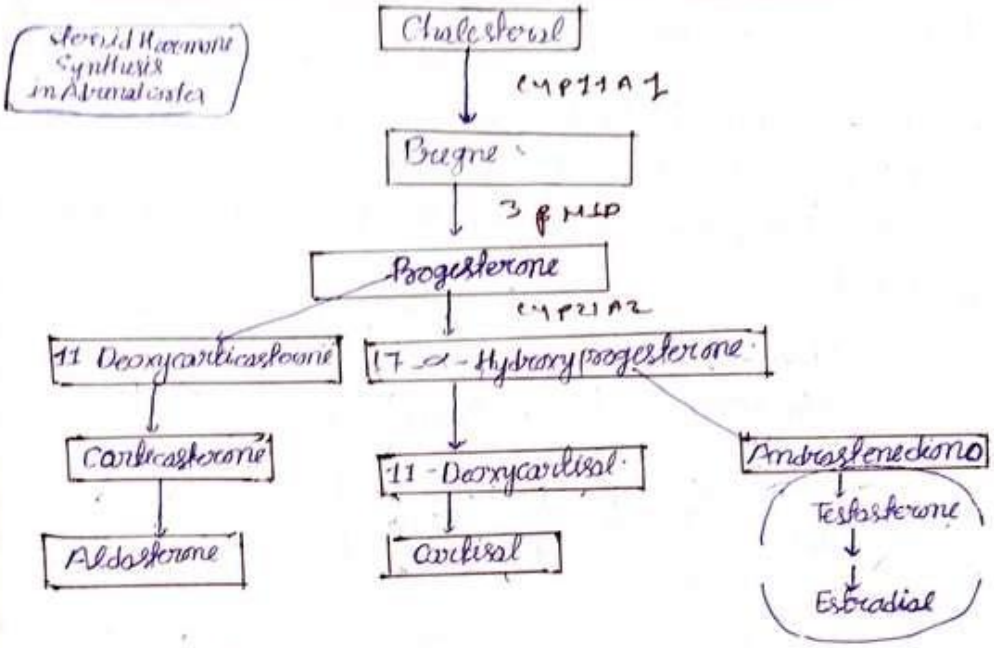
ii) Conversion of cholesterol into steroid harmone.

iii) Conversion of cholesterol into vit. D.

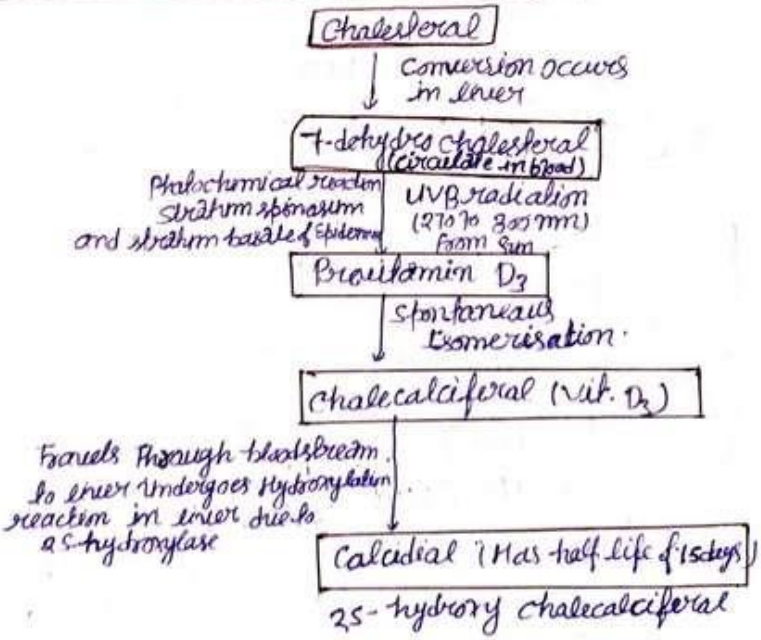
### i) :- Conversion of cholesterol into bile acid :-



ii) :- Conversion of Cholesterol into steroid Hormone :-




iii) Conversion of cholesterol into vitamin-D :-



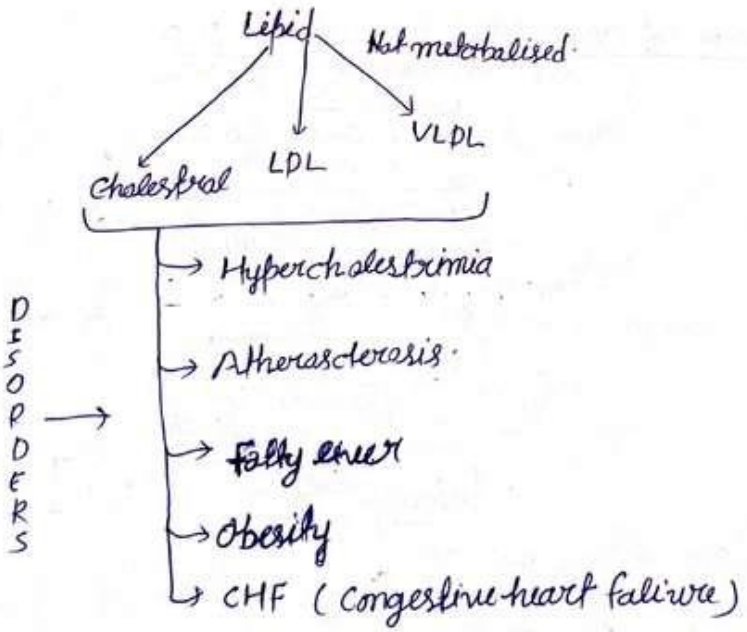
## Disorder of Lipid Metabolism:

→ Lipid is essential part of our body but when it is not metabolised completely then it converts into bad lipids.

→ LDL (Low density lipid), VLDL, and Cholesterol are sticky in nature so they are called bad lipid.

→ When the level of these bad lipid is increase then it causes diff. disorder.

| Cholesterol | Normal | Disease |
|---|---|---|
| Cholesterol | 200-239 mg/dl | ≥240 |
| LDL | 100 mg/dl | >100 |
| VLDL | 40 mg/dl | >40 |



Hypercholestrimia :-

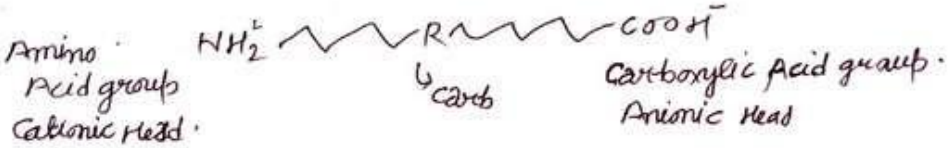
The normal level of cholesteral in side the body is 200 to 239 mg/dl if the level of cholesteral is high from its normal value then hypercholestrimia disease is occurs.

## Amino Acid

Amino Acid are the essential molecule of our body And it is building blocks of protein.

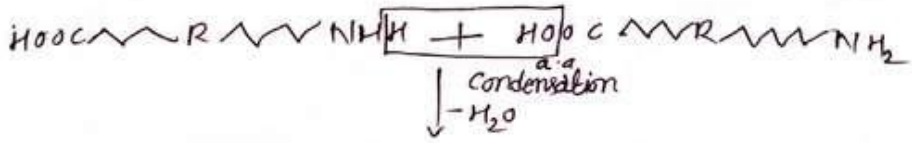
→ They provide diff structure of the body.

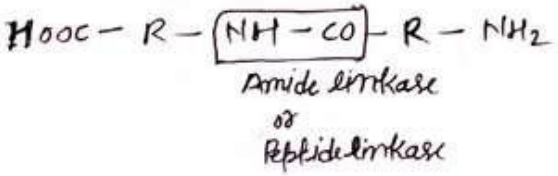
→ Chemicaly amino acid contain a long carbon chain and contain amine group at one end and carboxylic acid group another end.




→ Amino Acids are chemicaly zwitter ion in nature because it contains both cation and anion in the same compound.

→ Several amino acid are combine to each other and after condensation they produce protein in which poly peptide linkage is present.




## Classification of amino Acid :-

On the basis of need or Requirement

→ Some Amino Acids are synthesies in our body and some we have take from our diet.

On the basis of need it is of two type -

-i) Essential :-

These amino acid are not synthesies in our body. and we are depends on the fruits, vegetable and meat for these amino acids.

Ex Leucine, Isoleucine, Lysine, Threonine, Methionine, Phenyl Alanine, Valine & Tryptophan.

-ii) Non Essential Amino Acid

They are synthesies in our body -.

Ex Asparagine, Alanine, Arginine, Aspartic Acid, Cysteine, Glutamic Acid, Glutamine, Proline, Glycine, Tyrosine & Serine.

On the basis of structure :-

A) Containing Sulphur :- Cysteine, Methionine.

B) Neutral in nature :- Asparagine, Serine, Threonine, Glutamine

C) Acidic in Nature - Aspartic Acid, glutamic acid

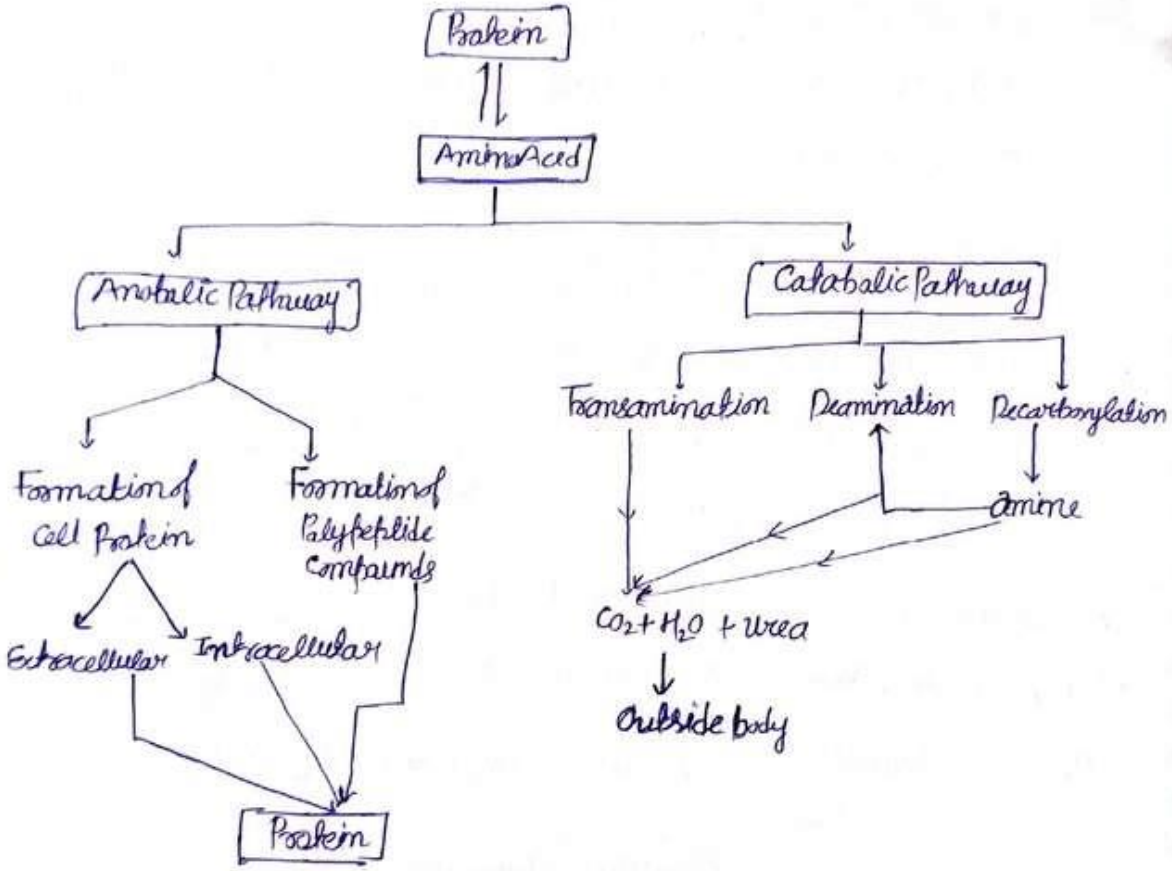
D) Basic in Nature - - Arginine, Lysine.

e) Aliphatic in nature :- Leucine, Isoleucine

4) Aromatic in Nature :- Phenyl Alanine, Tryptophan.

## Amino acid Metabolism :-

Amino acids form the protein after anabolic pathway, and they breakdown into $CO_2$ water, urea. after catabolic pathway this is called metabolism of amino acid.

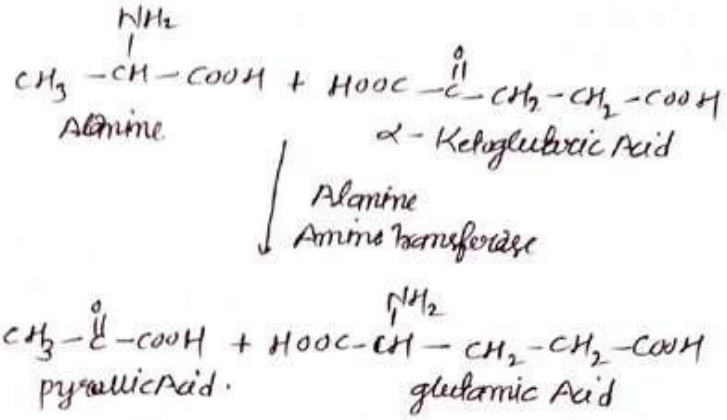



## Transamination :-

→ This is the transfer of amine group from Amino acid to α-Ketoglutaric Acid.

→ α-Ketoglutaric Acid is an intermediate compound of it Krebs cycle and it reacts with a.a in the presence of Amine transferase.

- After this process the amine group of a.a. this replaced by carbonil group and form pyruvic Acid.



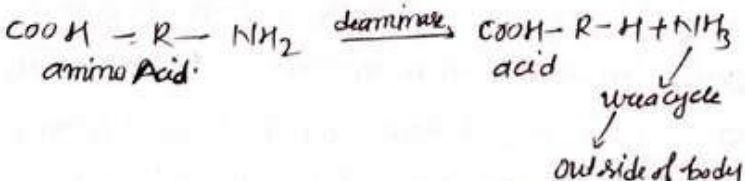

The amine transferase enzyme is specific for diff. diff amino acid. Ex. Alanine Amino Transferase, Sparkate Amino transfer, Methionine, A.T.

This enzyme is present in liver kidney and brain and this is are reversible reaction.

Deamination :-

The process of removal of amine group from any amino Acid and convert into acid is called Deamination.

- This process is controlled by enzyme deaminase.
- This enzyme is present in the liver so all deamination reaction is start in liver.




- After deamination process amonia is release which goes into urea cycle.
- The deamination reaction is may be of following type.

1) Reduction Reaction.
2) Oxidation Reaction.
3) Hydrolytic Rxn
4) Intramolecular Rxn.

## Decarboxylation :-

- The removal of carboxylic Acid group from amino acid by the presence of decarboxylase enzyme is called decarboxylation.

Pyridoxal phosphate (Vit $B_6$) is used as co-Enzyme for this rxn.
→ After decarboxylation process amino Acid is convert into amine which further go deamination process. and convert into ammonia.

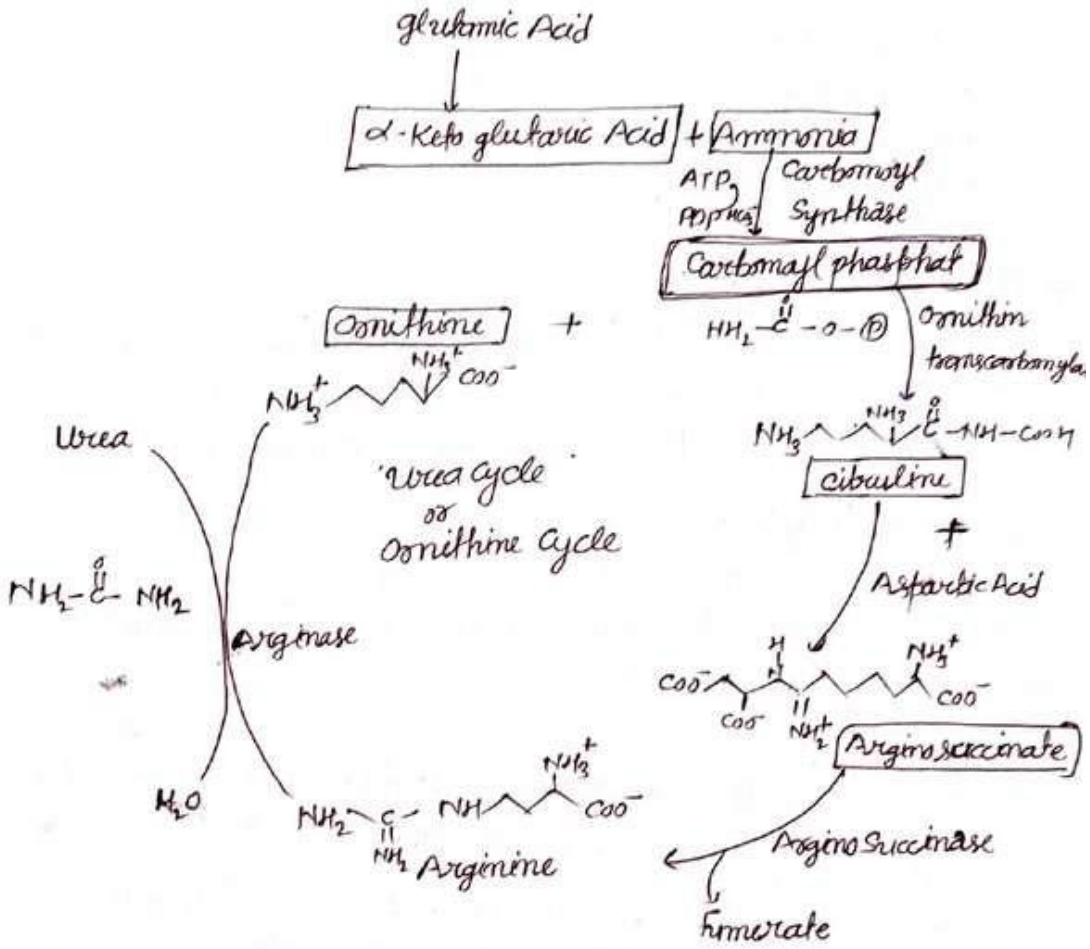
$NH_2-R-COOH \xrightarrow[\text{decarboxylase + Pyridoxal Phosphate}]{-CO_2} NH_2-R-H + CO_2$ (Amine)

$CO_2$ ↓ Excreation. out

Amine → Deamination → $NH_3$ → Urea cycle → out.

## Urea cycle :-

- Urea cycle is a biochemical process in which ammonia convert into urea.
- Ammonia is a nitrogenous waste which is form by the amino acid metabolism like. Transamination, Deamination, Decarboxylation.
- Ammonia is a toxic substance. which is very harmful for body.
- But ammonia cannot be excreted by our kidney.
- So Ammonia is convert into urea and excreate out from body.
→ Ornithin is the imp. Constituent for urea cycle so it is also k/a ornithin cycle..




-During Each urea cycle 2 moles of Ammonia is combined with 1 mole of $CO_2$ and it is convert into 1 mole of urea and 2 mole of water. and for each cycle three ATP is require.

$$2NH_3 + CO_2 + 3ATP \longrightarrow \text{urea} + ADP + H_2O$$

In urea cycle following steps are involve -

Metabolic disorder of urea cycle :-

If in any patient urea cycle is not properly operate then diff. diff disorder is start in our body -

→ Hyperammonia type -1
→ Hyperammonia type -2
→ Citrullinemia
→ Argininosuccinuria
→ Hyperarginemia

→ Hyperammonia type -1

This is caused by the difficiency of enzyme carbonyl phasphate synthase so the ammonia cannot be convert into carbonyl phasphat so the blood ammonia level is ↑es.

→ Hyperammonia type -2 :-

This if the caused by the difficiency of enzyme ornithin trans carbonylase in this disorder the level of blood glutamic acid is increase.

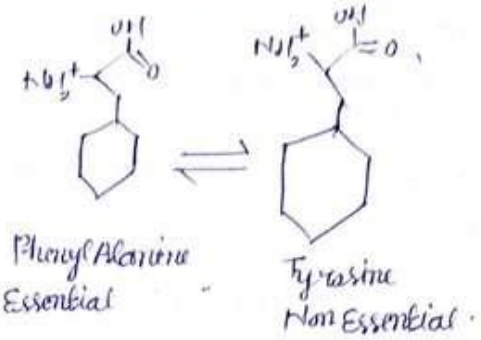
→ Citrullinemia :- It is a autosomal disorder this is caused by the difficiency of enzyme argino succinate synthase.
→ Citrulline is release by the urine 1 to 2 gm/day but if the level is increase then it is called citrullinemia.

- Argininosuccinic aciduria :-

This is a rare disease caused by the difficiency of enzyme argino succinase.
In this disorder the level of ammonia is increase in blood and the level of argininosuccinic acid is ↑es in plasma and CSF and blood become acidic.

Hyperarginemia :- This is a genetic disorder and caused by the difficiency of enzyme arginase first this is a mental disorder. in which the grouth is also affected by increase in the argintine level.

## Catabolism of Phenylalanine & Tyrosine



Phenyl Alanine
Essential

Tyrosine
Non Essential.

Phenyl alanine and Tyrosine are the aromatic amino acids Phenyl alanine is essential amino acid because it is not synthesies in our body, and phenyl alanine is convert into Tyrosine so tyrosine is non essential amino acid.

Phenyl alanine is source of energy for precursure of neuro-transmeters.

- The catabolism of phenyl alanine involve following steps.

Formation of Melanin :-

Melanin is a black pigment which is present in the skin of animal which decide the color of skin.

Phenyl alanine is converted in to tyrosine in the liver and tyrosine convert into melanin.

The conversion of tyrosine into melanin involve following step.

Metabolic disorder :-

Phenyl Ketonurea :-

Phenyl alanine is convert into tyrosine which with the help of enzyme phenyl alanine hydroxylase.

- If these enzyme is not work in then the level of phenyl alanine is increase in urine this condition is called Phenyle Keton urea.

Some general symptom of disorder is -

ii) Eczema - Infection of skin.

iii) Foul Smell -

iv) Discolaration of urin

2) Albinism :-

Albinism term is derived from term Albine which means white.

- Tyrosine is convert into melanin pigment by the help of enzyme Tyrosinase but when this enzyme is inhibit then the formation of melanin pigment is stop then skin become white.

- The condition of in which skin color becomes white and absence of Albine this is called albinism.
- It is also k/a Achromia and it is a genetic disorder.

Symptom :-

- White skin and red hair.
- Problem in vision.
- Eye color is blue, Red or Braun.
- They face the problem of photobia & Sunburn.

3) Alkaptonurea :- It is also k/a black urine disease. and it is the genetic disorder.

- When phenyl alanine and tyrosine is not completely convert into maleylacetoacetic Acid (MAA) Due to difficiency of enzyme HGD (Homogeristic dioxygenase)
- Due to this disorder urine color becomes black.

## Biosynthesis of purine nucleotides:

Many compounds contribute to the purinering of the nucleotides:

1. $N_1$ of purine is derived from amino groupof aspartate.
2. $C_2$ and Cs arise from formate of $N_{10}$formyl THF.
3. $N_3$ and $N_9$ are obtained from amide groupof glutamine.
4. $C_4$, $C_5$ and $N_7$ are contributed by glycine.
5. $C_6$ directly comes from $CO_2$.

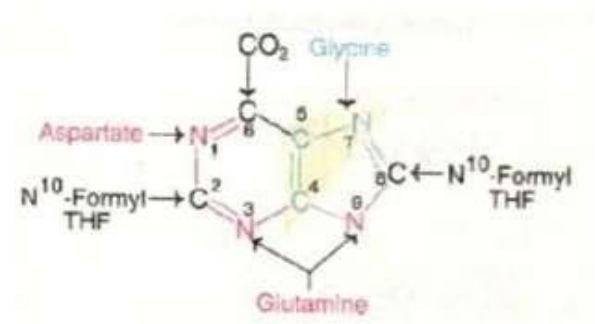
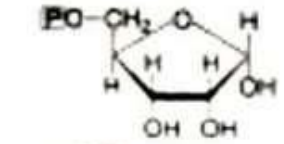
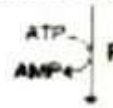


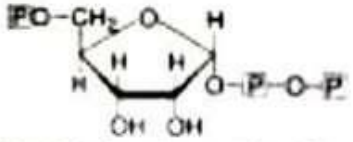

**Fig. 1 The sources of individual atoms in purine ring.**

Purine basesare not synthesized as such,but they are formedas ribonucleotides.The purines are built upon apre-existing ribose S-phosphate. Liver is themajor site for purine nucleotidesynthesis.Erythrocytespolymorphonuclearleukocytes andbrain cannot produce purines.

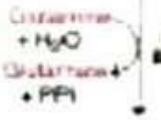


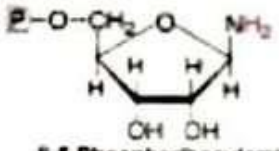
α-D-Ribose-5-phosphate



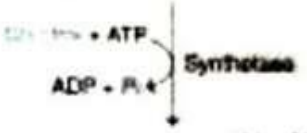



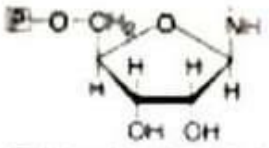
5-Phosphoribosyl α-pyrophosphate



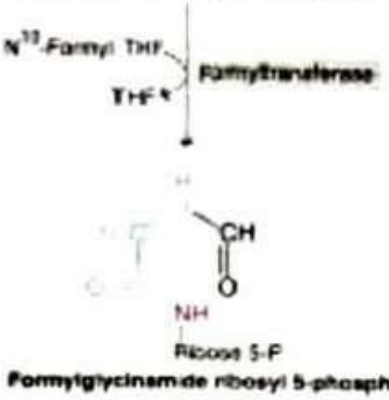



β-5-Phosphoribosylamine

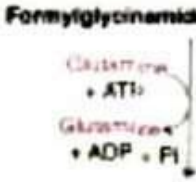


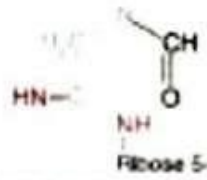



Glycinamide ribosyl 5-phosphate

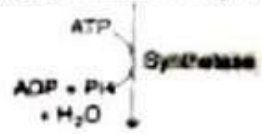


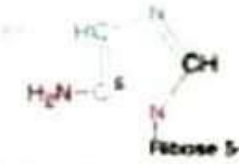

Formylglycinamide ribosyl 5-phosphate



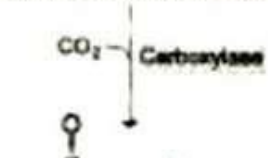



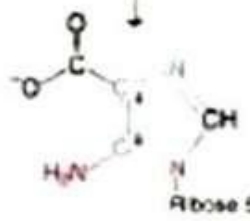

Formylglycinamidine ribosyl-5-phosphate



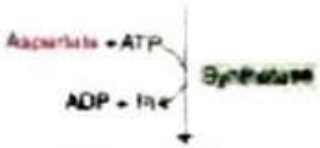



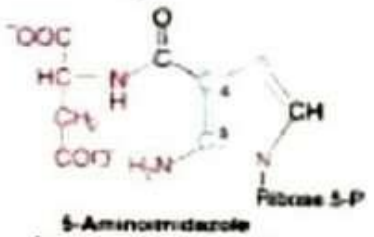

5-Aminoimidazole ribosyl-5-phosphate




5-Aminoimidazole carboxylate ribosyl 5-phosphate




5-Aminoimidazole 4-succinyl carboxamide ribosyl 5-phosphate

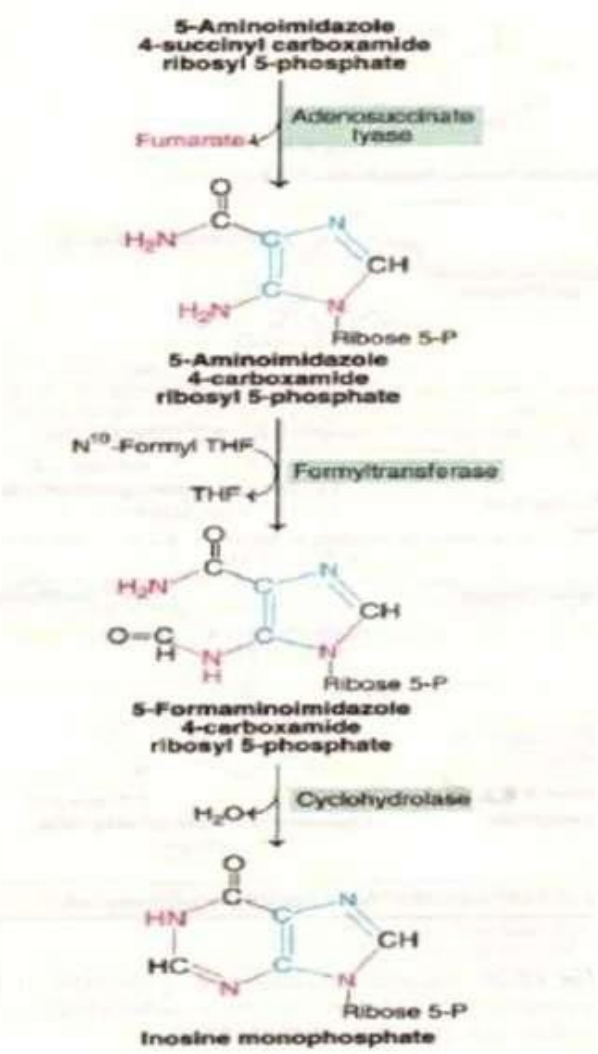



**Fig.2: The metabolic pathway for thesynthesis of inosine monophosphate, the parentpurinenucleotide (PRPP-Phosphoribosyl pyrophosphate;PPi-Pyrophosphate).**

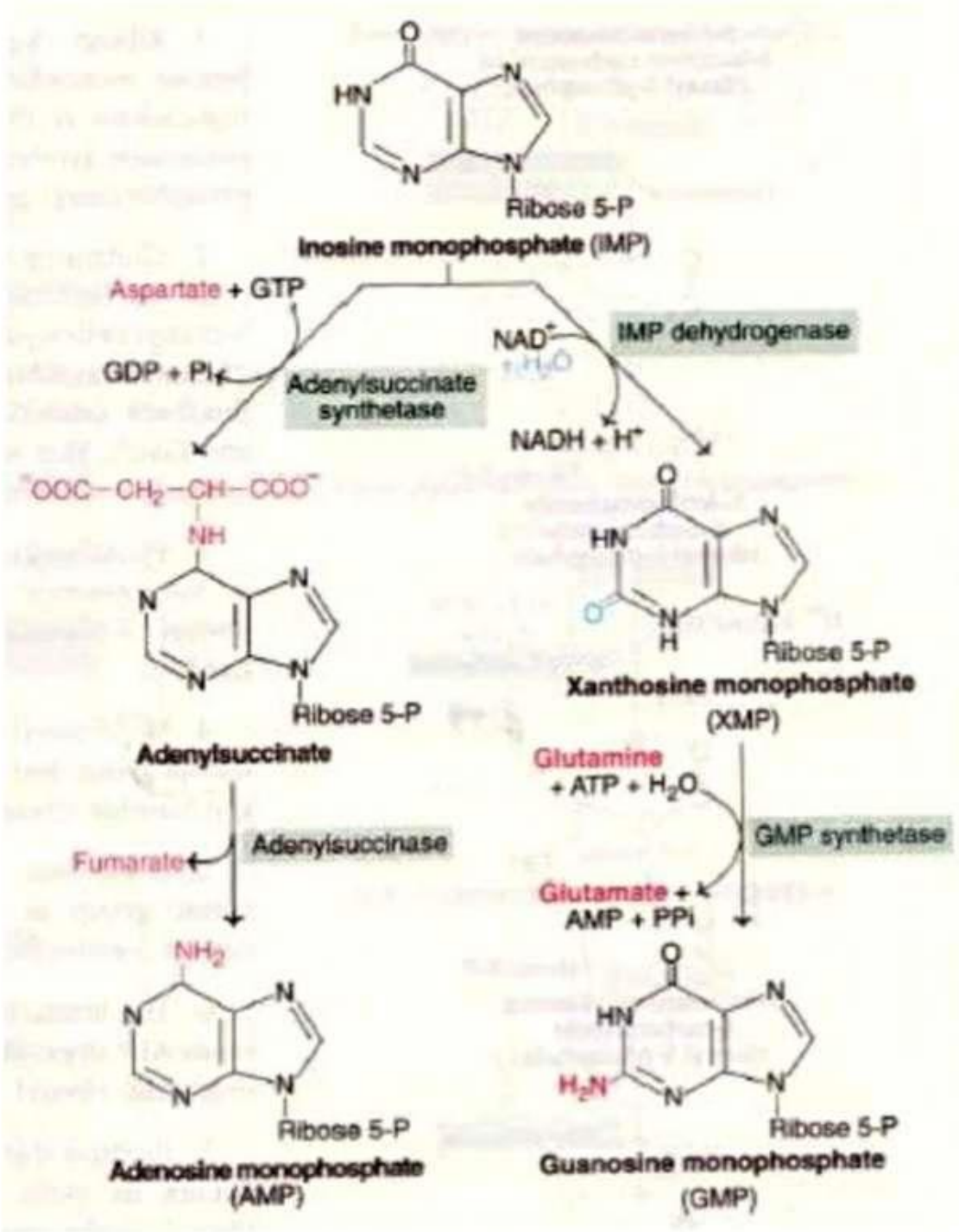



**Fig.3: Synthesis of AMP and GMP from inosine monophosphate.**

**Degradation of purine nucleotide:**

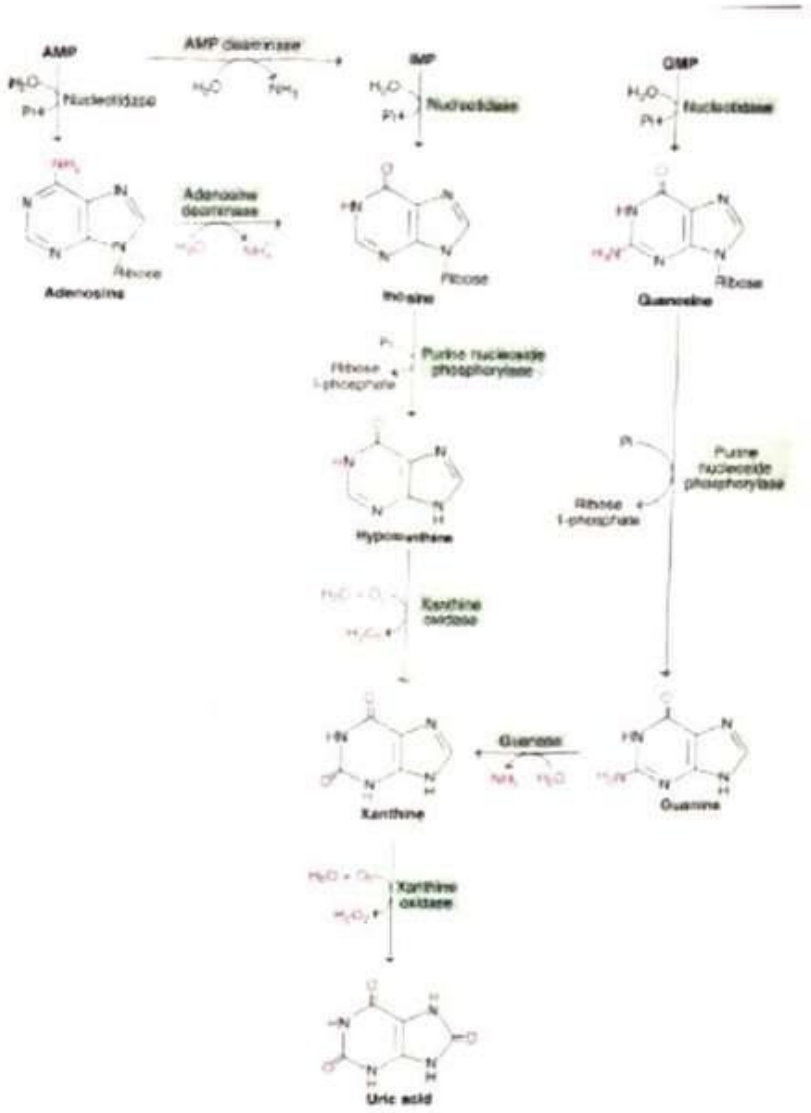



**Fig.7: Degradation of purine nucleotide to uricacid(AMP-Adenosine monophosphate IMP-Inosine monophosphate, GMP- Guanosinemonophosphate).**

## Disorder of purine metabolism:

Gout is of twotypes-primary and secondary.

1. Primary gout: It is an inborn error of metabolism due to over production of uric acid. This is mostly related to increased synthesis of purine nucleotides. The following are the important metabolic defects(enzymes) associated with primary gout(Fig. 9)

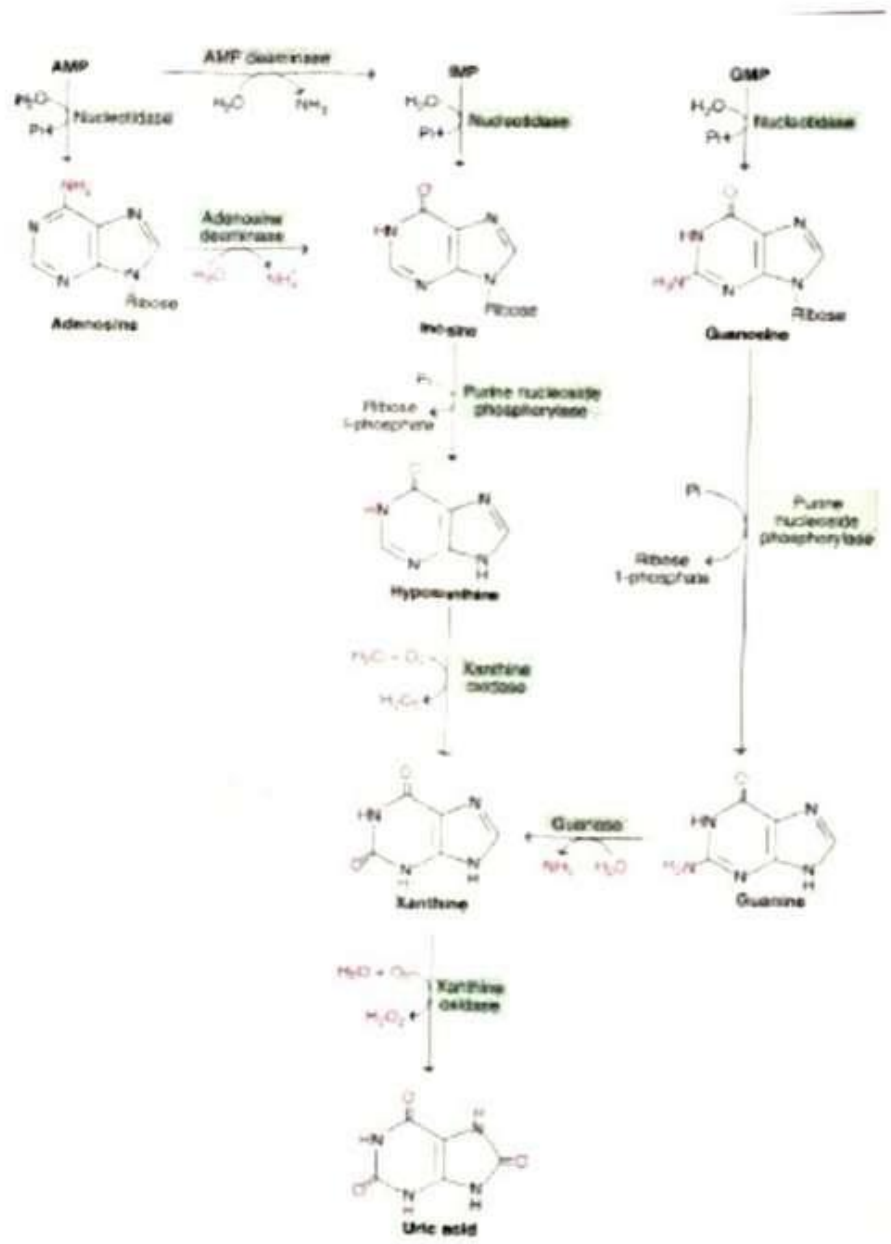
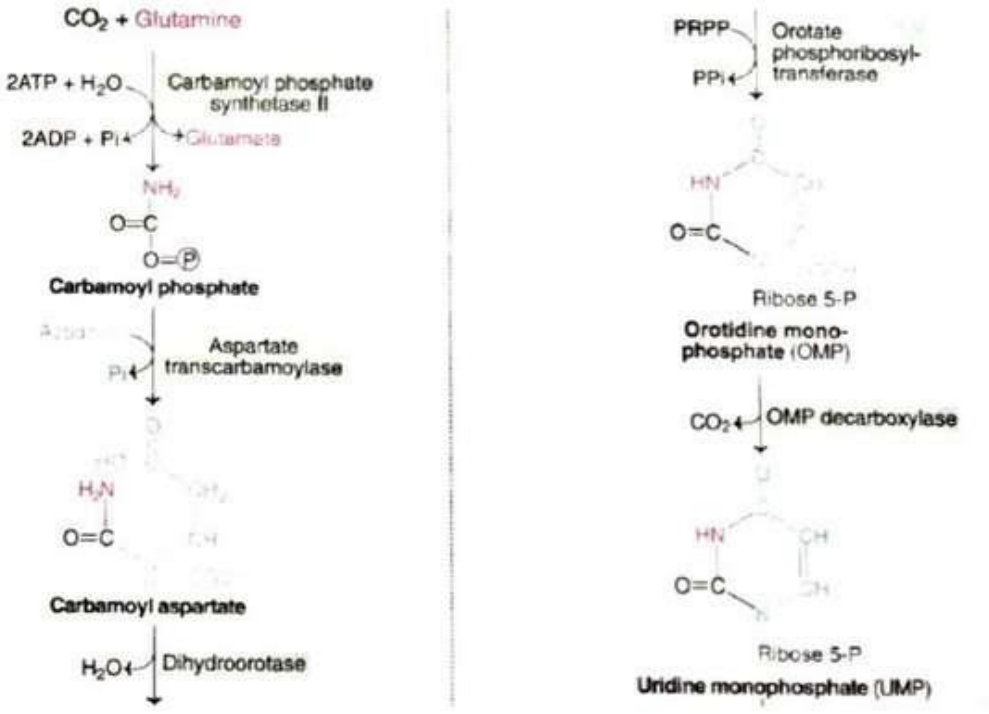



**Fig.7: Degradation of purine nucleotide to uricacid(AMP-Adenosine monophosphate IMP-Inosine monophosphate, GMP- Guanosinemonophosphate).**

## Biosynthesis of pyrimidine nucleotides:

Pyrimidine ring is first synthesized and then attached to ribose5-phosphate. This is in contrast to purine nucleotide synthesis where in purine ring is built upon a pre-existing ribose 5-phosphate. The pathway of pyrimidine synthesis is depicted in

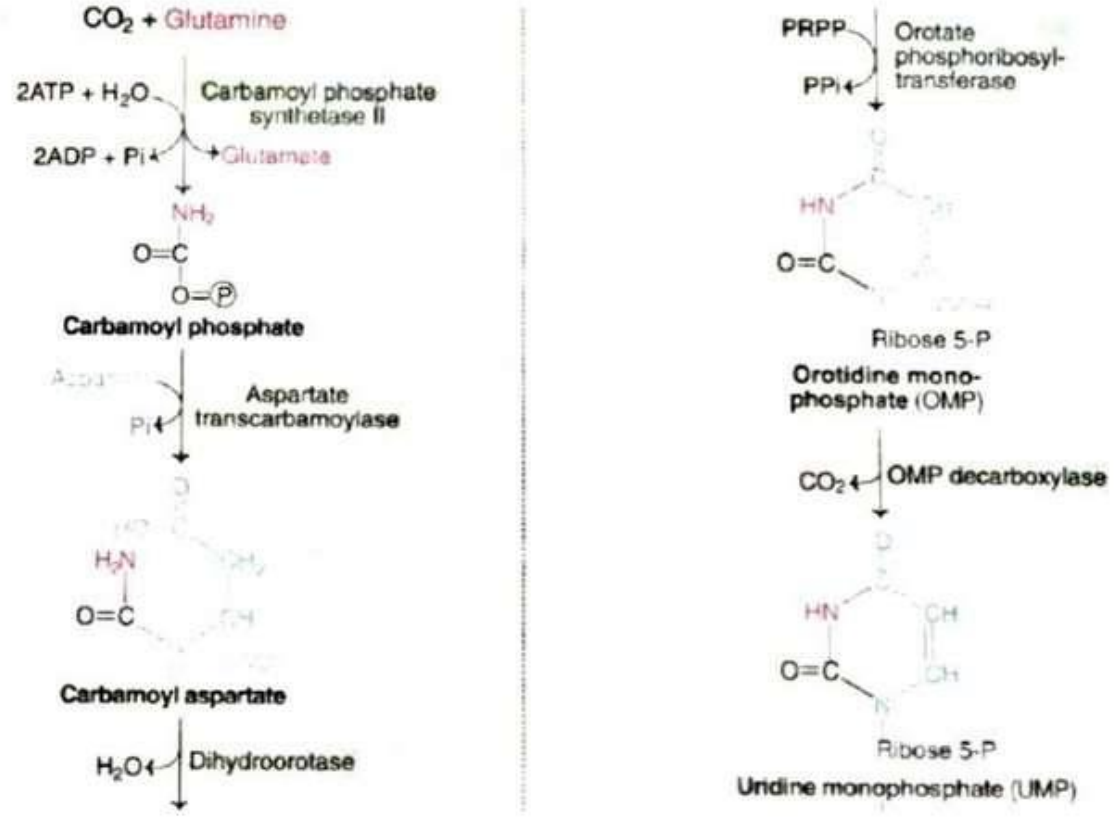
Fig.12, and the salient features are described below:



## Biosynthesis of pyrimidine nucleotides:

Pyrimidine ring is first synthesized and then attached to ribose5-phosphate. This is in contrast to purine nucleotide synthesis where in purine ring is built upon a pre-existing ribose 5-phosphate. The pathway of pyrimidine synthesis is depicted in

Fig.12, and the salient features are described below:



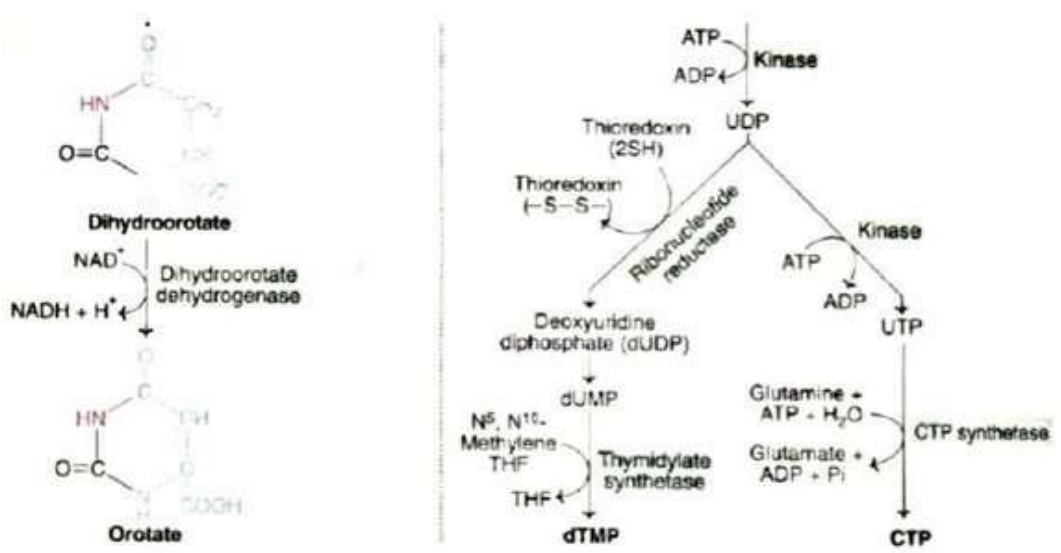



Fig.12 Metabolic pathway for the synthesis of pyrimidine nucleotides

## Structure of RNA:

RNA is a polymer of ribonucleotidesheld together by 3',5'-phosphodiester bridges. Although RNA has certain similarities with DNA structure, they have specific differences:

l. Pentose: The sugar in RNA is ribose in contrast to deoxyribose in DNA.

2. Pyrimidine: RNA contains the pyrimidine uracil in place of thymine (in DNA).

3. Single strand: RNA is usually a single stranded polynucleotide. However, this strand may fold at certain places to give a double stranded structure, if complementary base pairs are in close proximity.

4. Chargaff's rule-not obeyed: Due to thesingle-stranded nature, there is no specificrelation between purine and pyrimidine contents. Thus, the guanine content is not equal to cytosine (as is the case in DNA).

5. Susceptibility to alkali hydrolysis: Alkalican hydrolyse RNA to 2',3'-cyclic diesters.This is possible due to the presence of a hydroxyl group at 2' position. DNA cannot be subjected to alkali hydrolysis due to lack of this group.

6. Orcinol colour reaction: RNAs can be histologically identified by orcinol colour reaction due to the presence of ribose.

### Types of RNA:

The three major types of RNAs with theirrespectivecellularcompositionare given below:

1. Messenger RNA (mRNA): 5-10"/"
2. Transfer RNA (IRNA): 10-200/"
3. Ribosomal RNA (rRNA): 50-80%

### Messenger RNA (mRNA):

The mRNA is synthesized in the nucleus (in eukaryotes) as heterogeneous nuclear RNA (hnRNA). hnRNA,. mRNA has high molecular weight with a short half-life.

The eukaryotic mRNA is capped at the5'-terminal end by 7-methylguanosinetriphosphate. It is believed that this cap helps to prevent the hydrolysis of mRNA by 5'-exonucleases.

### Transfer RNA (tRNA):

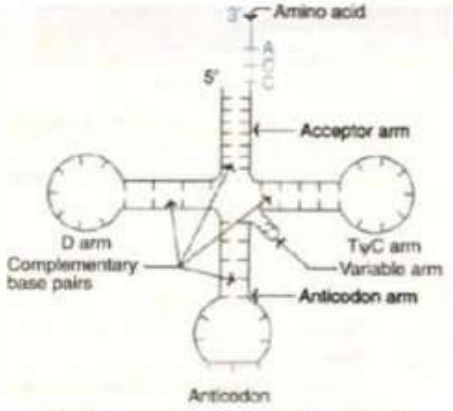



**Fig.Structure of transfer RNA**

1. The acceptor arm: This arm is capped with a sequenceCCA (5' to 3'). The amino acid is attached to the acceptor arm.

**Ribosomal RNA (rRNA):**

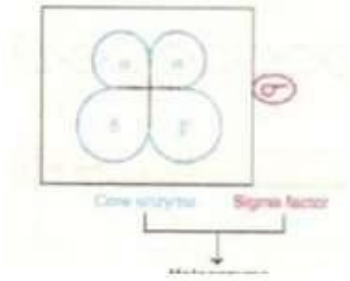
The ribosomes are the factories of protein synthesis. The eukaryotic ribosomes are composed of two major nucleoproteincomplexes-60S subunit and 40S subunit. The605 subunit contains 28S rRNA, 55 rRNA and5.8S rRNA while the 40S subunit contains 18SrRNA.The function of rRNAs in ribosomes is not clearly known. It is believed that they play a significant role in the binding of mRNA to ribosomes and protein synthesis.

# Transcription:

Transcriptionis a processin which ribonucleicacid (RNA) is synthesized from DNA. The word gene refers to the functional unit ofthe DNA that can be transcribed. Thus, the geneticinformationstoredin DNA is expressedthroughRNA.Forthis purpose,one of the twostrandsof DNA serveasa template(non-codingstrand or sense strand) and produces workingcopiesof RNAmoleculestheotherDNA strandwhich does not participatein transcriptionisreferredto as codingstrandor antisense strand(frequentlyreferredto as coding strandsincewith the exceptionof T for U, primarymRNAcontainscodonswith the samebasesequence.

**Transcription is selective:**

The entire molecule of DNA is not expressed in transcription RNAs are synthesized only for some selected regions of DNA. For certain other regions of DNA, there may not be any transcription at all.



# Nucleic acid metabolism & genetic information transfer

Unit = 1

## DNA Replication

1) Autocatalytic :- DNA direct the synthesis of DNA itself & from duplicate copy

   eg:- DNA ⟶ DNA

2) Heterocatalytic → DNA direct the formation of chemical other than itself

## Mechanism of DNA replication (Semi-conservative)

→ unwinding of double helix takes place
   ∴ Hydrogen bond b/w two strands are very weak.

→ when these two strands separate out each part of one strand constitute the complementary part of other strand

→ two parental strand do not separate completly, but are opened up at Replication fork

→ Due to this process exact nucleotide sequence would be automatically formed.

→ thus regeneration of DNA helix occur with one strand of orginal helix combining with freshly formed complement

## DNA replication (steps)

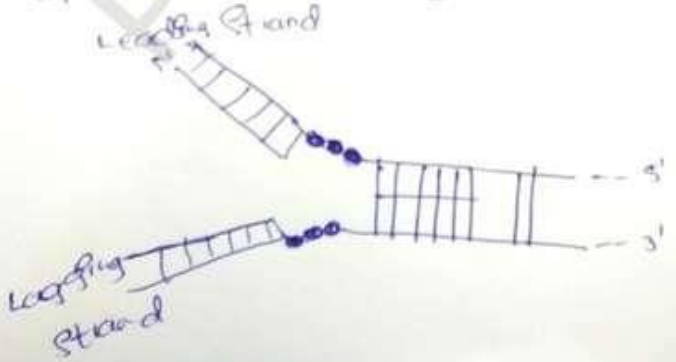
1) Activation of deoxyribonucleoside :-
4 nucleosides of DNA i.e AMP, GMP, CMP & TMP are activated by ATP to form ATP, GTP, CTP & TTP enzyme required at this step phosphorylase

2) Recognization Initiation point :-
from a particular point binding of DNA molecule starts, this specific point is called initiation point

3) Unwinding of DNA molecule :-
DNA double helix unwind & uncoil into single strand of DNA by breaking of weak hydrogen bond unwinding of helix is helped by enzyme enzyme Topoisomerase cut & rejoin strand of DNA helping the opening of DNA helix

4) formation of RNA Primer :-
DNA directed RNA polymerase form RNA primer

5) formation of new DNA chain :-
The enzyme DNA polymerase can polymerise the nucleotide only in 5' ⟶ 3' direction Because the two strands of DNA are in anti parallel direction the two strands synthesized by moving in opposite direction of DNA polymerase



6) Removal of RNA Primers:-

once the small pieces of okazaki fragments have been formed primers are removed from 5' end one by one by exonuclease activity of DNA polymerase

7) Proof reading & DNA repair:-

The specificity of base pairing ensures extract replication. wrong bases can be identified and collected by "Repair enzyme nuclease"

## Transcription

Transcription is process in which RNA is synthesized from DNA. the word gene refer functional unit of the DNA that can be transcribed.

→ During the process of transcription second strand of DNA with 5'- 3' formed

→ In RNA strand uracil is substituted for thymine

→ DNA strand which is not taking part in transcription is displaced this non-coding strand of DNA is called coding strand.

→ The promoter is present on 5' end of structural gene the promoter & terminator is exist on extreme sides of structural gene.

## Translation (Protein Synthesis)

The Protein have significant role in structural & functional Organisation of the cell.

DNA —Replication→ DNA —transcription / Reverse transcription→ RNA —translation→ Protein

### a) Activation of Amino acids

This reaction brought about by binding of Amino acid with ATP. the Step requires enzyme called Amino acyl RNA Synthetase

$$AA + ATP \xrightarrow{Enzyme} AA - AMP - Enzyme + PP$$

### b) transfer of aminoacid to t-RNA.

AA-AMP-enzyme Complex formed react with Specific t-RNA. thus amino acid is transferred to tRNA As a result the enzyme & AMP are liberated

$$tRNA \longrightarrow AA - tRNA + AMP + enzyme$$

### c) Initiation of polypeptide chains

Charged tRNA shift to Ribosome. Ribosome is the site where the protein Synthesis occur mRNA binds to 30s subunit Ribosome of 70s type. the information for sequence of AA present in sequence of nitrogen based of mRNA

## Important Questions

### 10 marks

1) Describe the biosynthesis of Purine nucleotides
2) Describe the biosynthesis of pyramidine nucleotides
3) Explain the biosynthesis of Protein the body

### 5 marks

1) Describe the double helical Structure of DNA
2) Explain different types of RNA
3) Define genetic code & give its salient features
4) Explain Protein Synthesis

### 2 marks

1) Define nucleoside & nucleotide
2) What is translation & transcription?
3) what is gout?
4) what are the functions of tRNA?
5) ~~what are~~ write the difference blw DNA & RNA

## ÷ Unit-5 ÷

## ÷ Enzyme ÷

Enzymes are the bio catalyst which control the biochemical reaction in the living body.

Those chemical reaction which perform in body is called biochemical reaction.

Enzyme can increase or decrease the rate of bio chemical reaction.

### Properties of Enzyme ÷

1. Enzymes are required in small amount.
2. They do not consume in biochemical reaction.
3. Enzymes are made up of protein.
4. They inactivated by heat and change in pH.

### Name of Enzyme ÷

During the nomenclature of enzyme suffix 'ase' is added in the name.

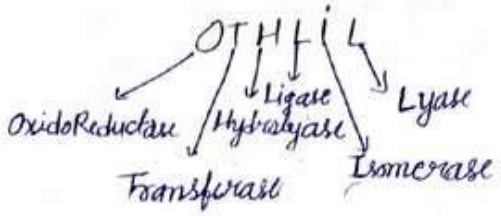
Suffix - "ase"

Maltose → Maltase
Protein → Protiase
Lactose → Lactase
Amylin → Amylase
Dehydration → Dehydrase
$Co_2$ Remove → DeCarboxylase
$H_2$ Remove → Dehydrogenate.

### Classification of Enzyme ÷

The Classification of Enzyme was given by IUBM (Agency) (International union of Bio molecule agency)
IUBM classify the enzymes into six category.

IUBM




**OxidoReductase** :- When oxidation and Reduction reaction takes place then oxido Reductase enzyme are used.

Ex Oxidation < O Add → Oxidase
$H_2$ Remove → Dehydrogenase.

Reduction < O Remove → de Oxidase
$H_2$ Add → Hydrogenase.

**Transferase** :- In chemical reaction when any group is transfer from one molecule to another then it is called transferase Enzyme.

| group | Enzyme. |
|---|---|
| Amine | → Transaminase |
| Peptide | → Transpeptidase. |

**Hydrolyase** :- when any molecule is hydrolyse in the presence of water then it is called hydrolyase enzyme.

Carbohydrase.
Esterase
Protease.

Ligase:-

When 2 molecule are link by enzyme.

DNA ligase
Acetyl Co-A- ligase.
Succinyl Co-A- ligase.

Isomerase

When any compound convert into their isomer.

Ex → Isomerase
⇒ Epimerase
→ Racemase

Lyase:-

When any complex molecule break into 2 molecule.

Ex. Carboxylase
Decarboxylase

Mechanism of Enzyme Action.

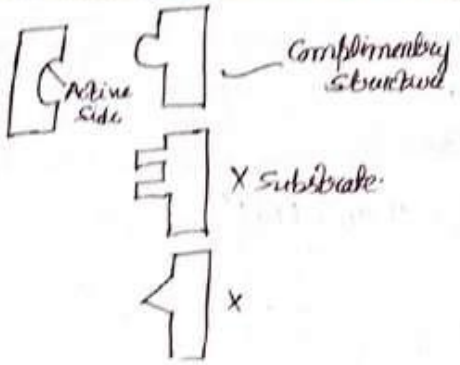
Enzyme binds with substrate and converd substrate into product.

Enzyme and substrate are ~~complimentary~~ the complimentory structure of each other.

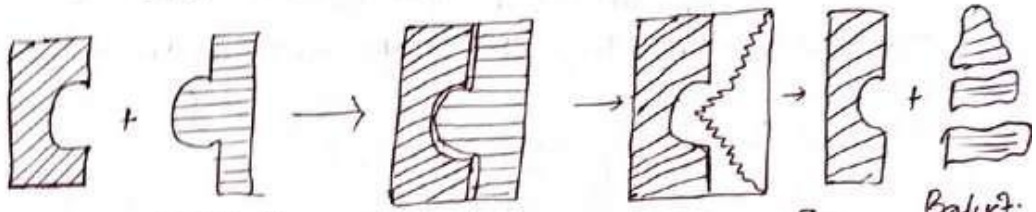
Enzyme have active side through which enzyme and substrate are bind like lock & Key.

After binding they form enzyme substrate complex.

After the complex formation the substrate is converd in to product. and enzyme becomes free so it will bind with another substance.




Mechanism of Enzyme action




**Proenzyme ∴ (Zymogen) :-**

Proenzyme are the enzymes which are inactive from but after releasing the pro group it becomes Active and perform the action.

Proenzyme (Inactive) → Pro + Enzyme (Active)

Ex. Trypsinogen → Trypsin
Pepsinogen → Pepsin
(Trypsin, Pepsin → Protein)

**Isoenzyme ∴**

These enzyme which have diff. physical & chemical properties but there mode of Action is same. They are called Isoenzyme.

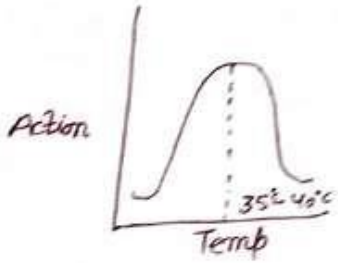
Ex. Lactate dehydrogenase (LDH) Exist in five form. All have diff. physical & chemical properties but all of them convert lactic acid into pyruvic Acid.

Lactic Acid
↓ LDH (Lactate dehydrogenase)
Pyruvic Acid

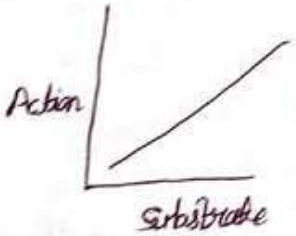
$LDH_1$, $LDH_2$, $LDH_3$, $LDH_4$, $LDH_5$

## Factors Affecting Enzyme Action :-

1. **Temprature :-**
Enzyme works at optimum temp 35°- 40°C
When temp are increase or decrease then Action is decrease.

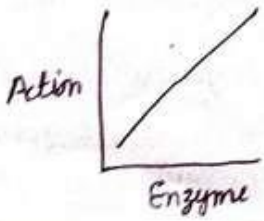



2. **Conc of Substrate :-** The conc of substrate is directly proportional to enzyme action.



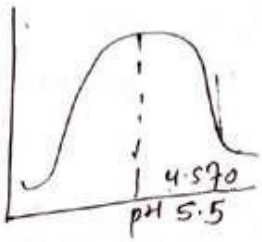

directly proportional.

(3) **Concentration of Enzyme :-** The conc of enzyme is also directly proportional to the enzyme Action.



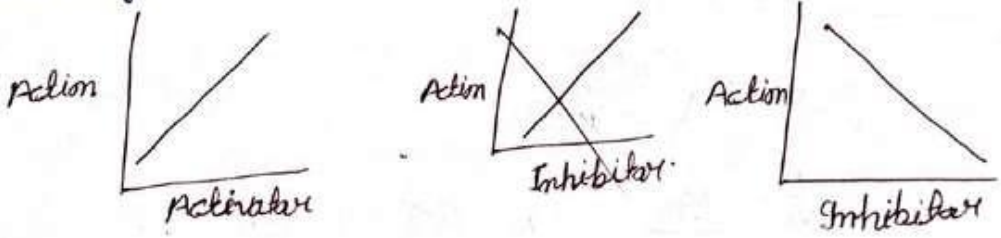
④ pH Range :- All enzyme works on optimum pH range 4.5 to 5.5 in pH range.

As well as we increase or decrease the pH the enzyme Action is decrease.




⑤ Activators and Inhibitors

The concentration of Activator is directly proportional and the conc. of inhibitors are ~~Inversely~~ proportional to enzyme Action.
Inversely.

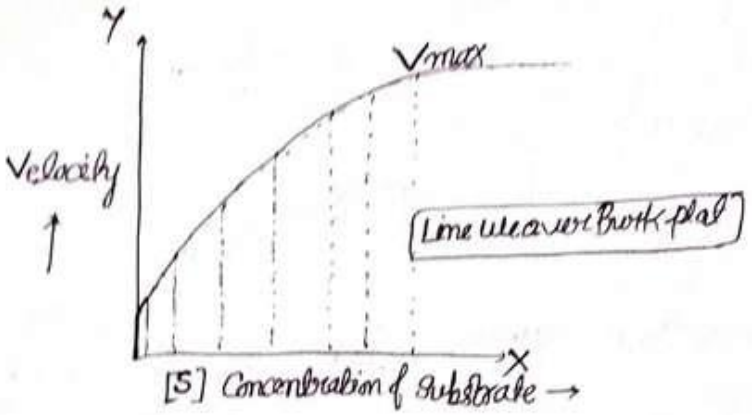



Michalis Menten Equation

Scientist Michalis and Menten give the relationship b/w velocity of reaction and conc. of substrate. Velocity is plotted on Y axis and conc of substrate is plotted on 'X' axis.

- At initial concentration the velocity is zero but as well as concentration is increase then the velocity is also increase.
- After reaching the Vmax the velocity of reaction is becomes constant.

This graph is called Line weaver burk plot.




$$V_0 = \frac{V_{max} \times [S]}{K_m + [S]}$$

Where - $V_0$ = initial Velocity
$V_{max}$ - Maximum Velocity
[S] - Conc of Substrate.
$K_m$ - Michalis menten Constant

Inverse the Equation

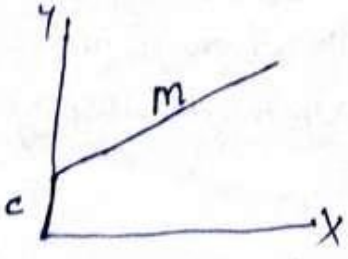
$$\frac{1}{V_0} = \frac{K_m + [S]}{V_{max} \times [S]}$$

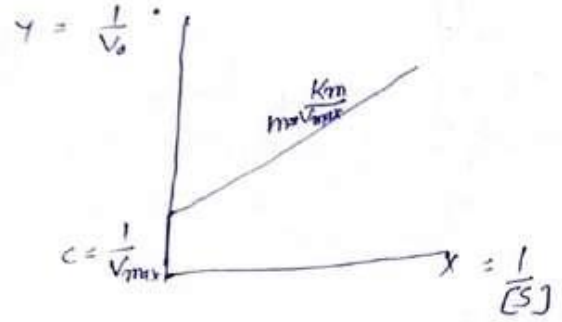
$$\frac{1}{V_0} = \frac{K_m}{V_{max} \times [S]} + \frac{[S]}{V_{max} \times [S]}$$

$$\frac{1}{V_0} = \frac{K_m}{V_{max}} \times \frac{1}{[S]} + \frac{1}{V_{max}}$$

Linear graph Equation :-

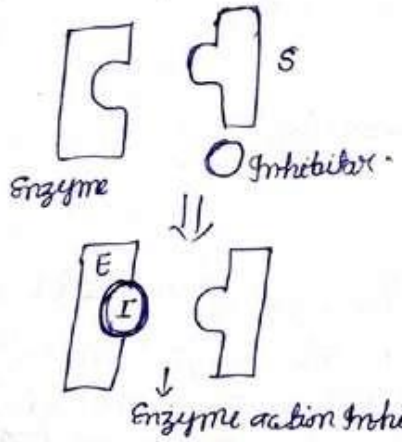
$$y = mx + c$$






Mechanism of Enzyme Inhibiton :-

When inhibitor molecule bind with the active side of enzyme then it block the active side of enzyme so the substrate cannot bind with the enzyme. So no action is produce this is called enzyme inhibition.



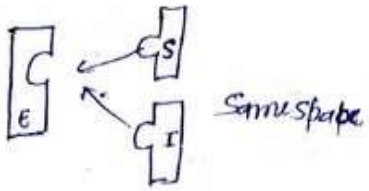

Types of Enzyme Inhibiton

It is of three type.

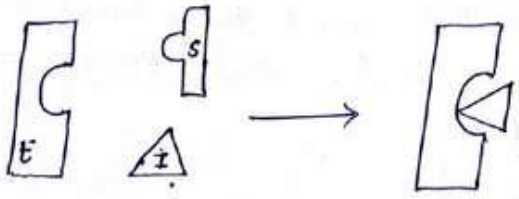
1. Competative Inhibiton
2. Non Competative Inhibiton.
3. Allosteric Inhibiton

1. Competitive Inhibiton

When the structure and shape of inhibitor is similar to the substrate then it is called competitive Inhibiton.




2. Non Competitive Inhibition :-
When the structure and shape of Inhibitor is not similar to the substrate then this is called Non competitive Inhibition.




No similar shape.

3. Allosteric Inhibition :-
In this type of inhibition when Inhibitor is bind with the enzyme then it change the shape of Active side so substrate cannot bind with enzyme and no action is produce this is called Allosteric Inhibition.


Change the shape of Active Side.

Isoenzyme :

These enzymes which have diff. Codon structure, diff. Function, Diff. Isoelectric point, diff. chemical property, but they Perform same function. They are called isoenzyme.

Amino Acid – ① → Codon → UGACUT
Amino Acid – ② – Codon → TCGUAT } Same function.

The isoenzyme where described by R.L Hunter and clement Markert in 1957.

Isoenzymes are made up of more diff paly peptide chain produce from diff gene.

→ During the duplication of gene the duplicate gene is certain and they leads to formation of isoenzyme.

& → LDH ( Lactase dehydrogenase
→ Alkaline Phosphetase.

* Therapeutic and dignostic Application of Enzyme and Isoenzyme

1) Enzymes are used in digestion
   Ex Amylase, Protease, Lipase
2) used as deworming agent.
   Ex Papaine
3) Used as anticlotting agent
   Ex Urokinase, Streptokinase.
4) Used in atherosclerosis.
   Ex Serratiopeptidase.

5) Used as disinfectant.
Ex Trypsin.
6) Used in stem Ulcer.
Ex Collagenase.
7) Used as Antiviral.
Ex Ribonuclase.
8) Used in Gaut.
Ex Uricase.

Diagnostic Application

1) Diagnosis of Acute pancreatitis -
Ex Amylase.
2) Diagnosis of viral Hepatitis.
Ex Alanine, SGPT.
3) Diagnosis of bone desorder.
Ex. Alkaline Phosphatase.

Co-Enzyme :-

Each and every enzyme is composed of two part.
i) Apoenzyme
ii) Co-Enzyme.

i) Apoenzyme
→ It is the proteinious part of the enzyme and it is also known as prosthatic group.
→ This part is responsible for the enzyme action.

ii) Coenzyme
→ It is the nonproteinious part of Co-Enzyme also known as co-factor.
→ This has no Enzyme action but influence the

Action of Enzyme.

Ex. 1) NAD / NADP
(Nicatinamide Adenine diphasphate.)

2) FMN / FAD
(Flavin mono Nucleatide) (Flavin Adenine di Nucleatide.

3) Co-Enzyme A (Co-A)

4) TPP
Thyamine pyro phasphate.

5) PAL
(Pridoxal Phasphate)