

BIOCHEMISTRY

UNIT 3 NOTES

LIPID METABOLISM

- BETA OXIDATION
- KETONE BODIES
- CHOLESTEROL
- DISORDERS OF LIPID METABOLISM

AMINO ACID METABOLISM

- TRANSAMINATION, DEAMINATION
- UREA CYCLE



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LIPID METABOLISM

- Lipids are generally the esters of Fatty Acids & Alcohols.
- Lipids constitutes about 15-20% of total body weight in humans
- They are present in our body in different forms like Triglycerides, Phospholipids, Fatty acids etc.
- About 85-90% part of lipids in our body is Triglycerides which is stored in the Adipose Tissue.
- The synthesis and breakdown of Lipid is known as Lipid Metabolism that involves Lipogenesis & Oxidation of fatty acids.

β - OXIDATION OF FATTY ACIDS

- Fatty Acids are obtained from breakdown of Lipids (Mainly Triglycerides)
- Oxidation of Fatty acid is the process that body uses to breakdown and use fatty acid as energy.
- The Fatty acids in the body are mostly oxidized by β -Oxidation.
- β Oxidation may be defined as oxidation of fatty acids on β -Carbon Atom.

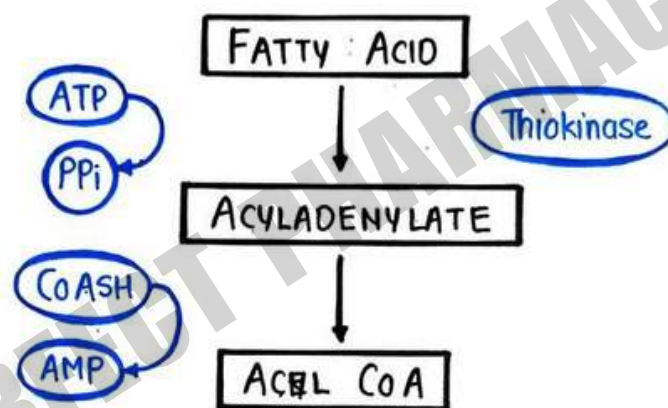
STAGES OF β - OXIDATION

β Oxidation of fatty acids occurs in three stages :

- Activation of Fatty Acids in cytosol
- Transport of Fatty Acid in Mitochondria.
- Proper β - Oxidation in Mitochondrial Matrix.

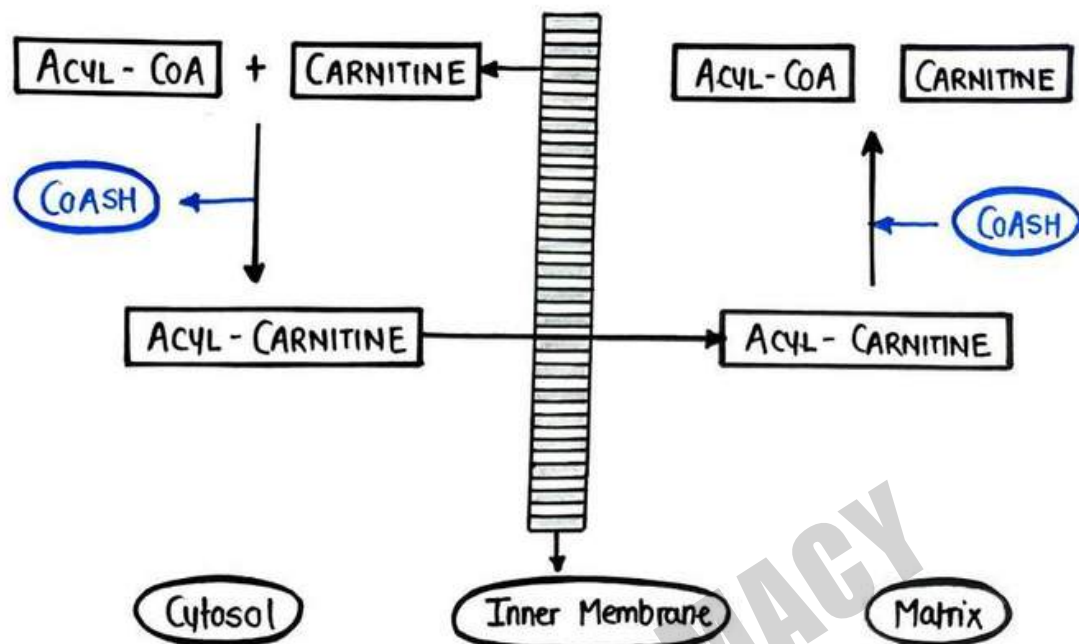
① ACTIVATION OF FATTY ACIDS

- Fatty acid activated into Acetyl Acyl CoA by Thiokinase.
- Reaction occurs in two steps & requires ATP, Mg^{2+} & CoA.
- In first step Fatty acids reacts with ATP & form Acyladenylate.
- In second step Acyladenylate combines with Coenzyme A & form Acyl CoA
- In activation 2 high energy phosphate utilized.



TRANSPORT OF ACTIVATED FATTY ACID IN MITOCHONDRIA

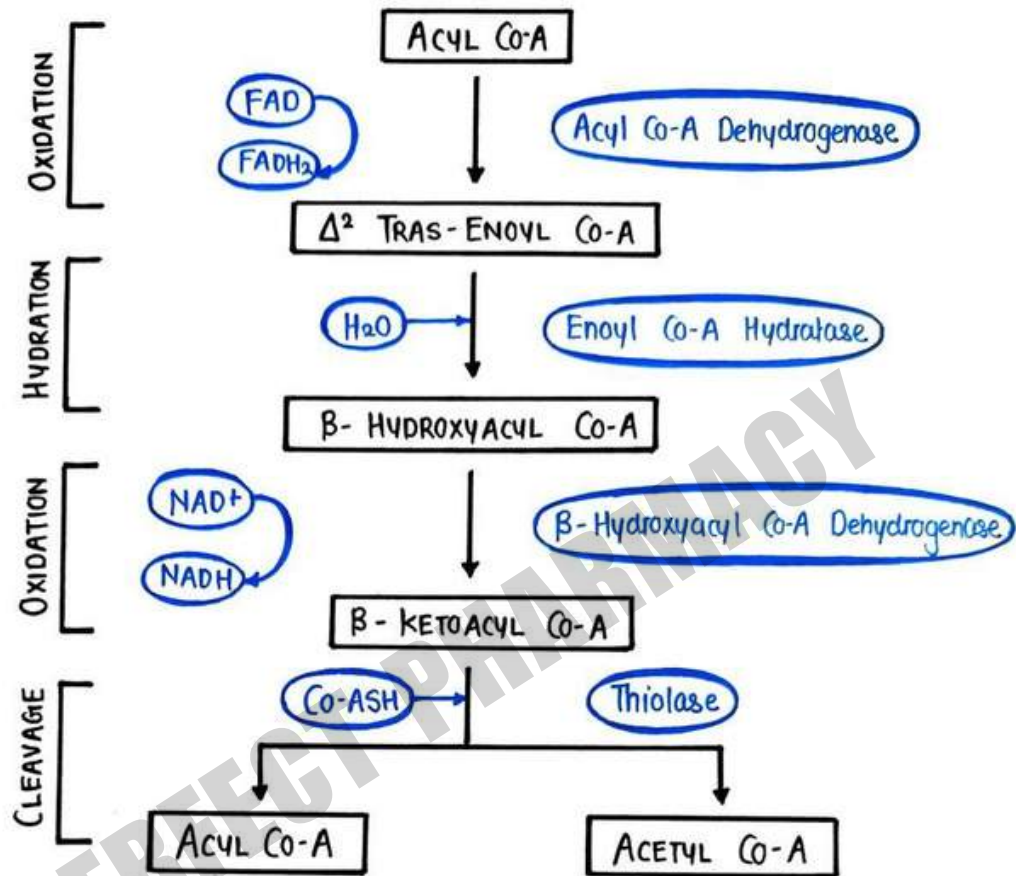
- Acyl group of Acyl CoA transferred to carnitine and the reaction is catalysed by Carnitine Acyl Transferase - I
- Acyl- carnitine is transported across the membrane to the mitochondrial matrix by specific carrier protein.
- Acyl carnitine again converted into Acyl Co-A inside the mitochondrial matrix by Carnitine Acyl Transferase - II.



PROPER β - OXIDATION OF FATTY ACIDS

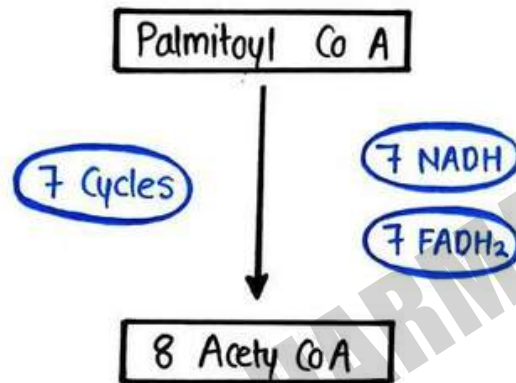
It occurs in following 4 steps :

- Oxidation : Acyl Co A undergoes Dehydrogenation by a flavoenzyme Acyl CoA Dehydrogenase.
- Hydration : Enoyl Co A cause the hydration of double bond to form β - hydroxyacyl Co-A
- Oxidation : In the second oxidation β - hydroxyacyl Co-A converted into β - ketoacyl Co-A & reaction is catalysed by β - hydroxyacyl CoA dehydrogenase.
- Cleavage : It is the final step of β -oxidation in which β - ketoacyl CoA cleaved into Acyl Co-A & Acetyl Co-A in the presence of thiolase enzyme.



ENERGETICS OF β - OXIDATION

- Generally Palmitic acid is used for the process of β -oxidation of fatty acid
- Now Palmitic acid is a 16 carbon compound that undergoes 7 cycle of β oxidation & form 8 Acetyl Co-A



- 1 Acetyl Co A = 10 ATP
- 1 NADH = 2.5 ATP
- 1 FADH₂ = 1.5 ATP

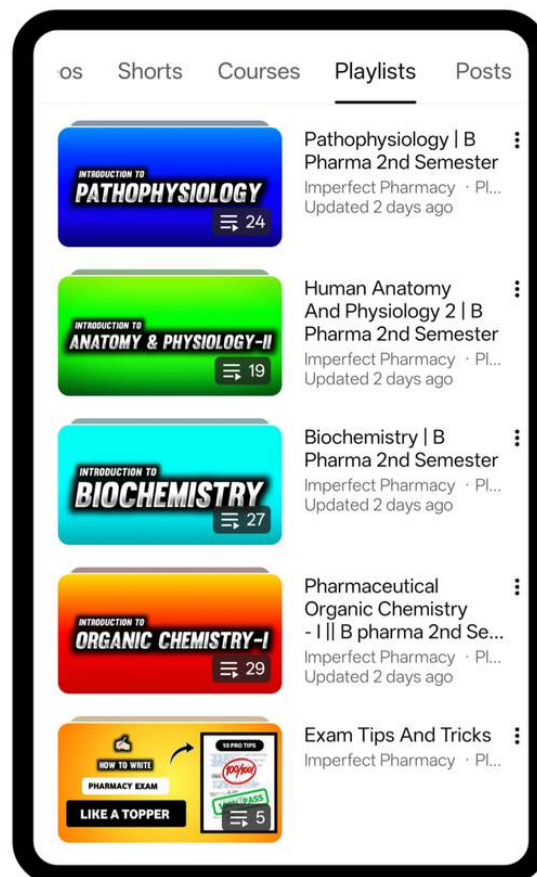
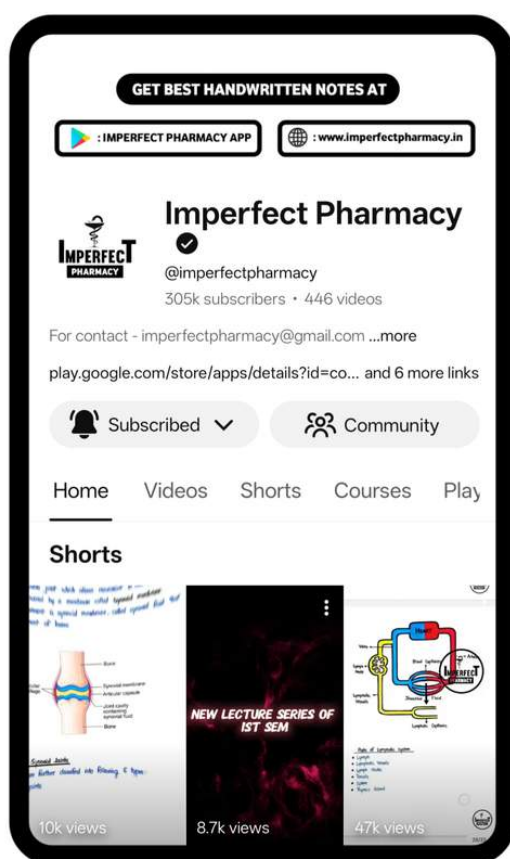
- Now in β - Oxidation of Palmitic acid , we have

- 8 Acetyl Co A = $10 \times 8 \rightarrow 80$ ATP
- 7 NADH = $2.5 \times 7 \rightarrow 17.5$ ATP
- 7 FADH₂ = $1.5 \times 7 \rightarrow 10.5$ ATP

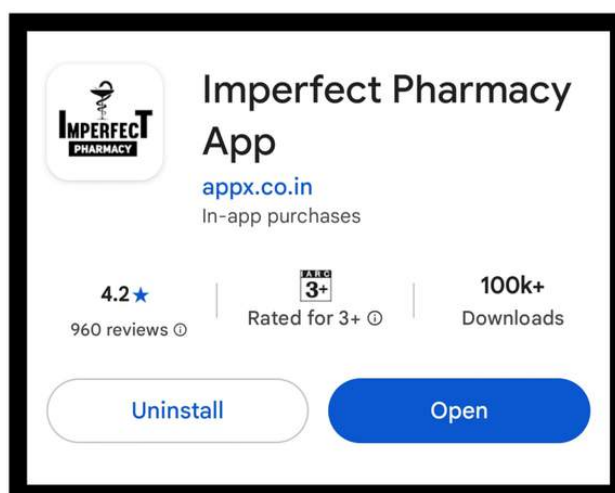
- Now Total ATP = $80 + 17.5 + 10.5 \rightarrow 108$ ATP
- But since 2 ATP is utilized in the activation , hence net ATP will be $108 - 2 = 106$

NET ATP $\rightarrow$ 106

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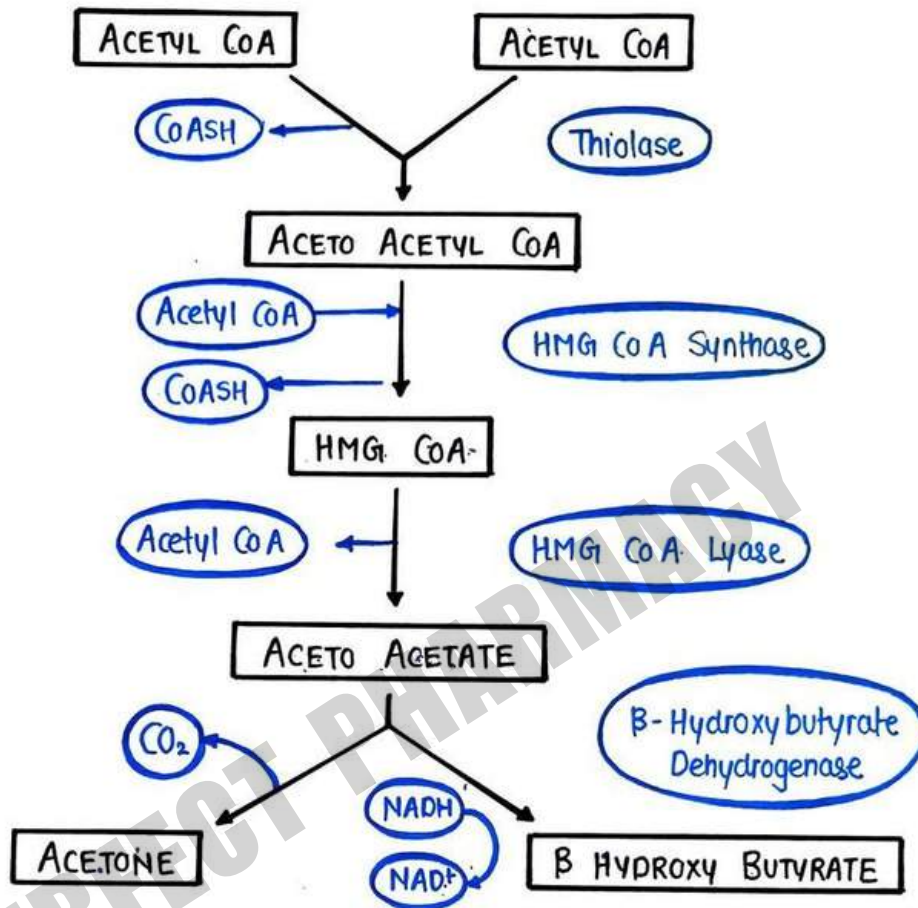
KETONE BODIES

- ketone bodies are metabolic products that produce energy during metabolism.
- They are produced by liver.
- ketone bodies are water soluble and energy yielding compounds that mainly produce energy during ~~metabolism~~ starvation and diabetes mellitus.
- There are mainly 3 types of ketone bodies:
 - ① Acetone
 - ② Aceto- acetate
 - ③ β - Hydroxybutyrate
- Now in the above 3 only first two are true ketone because β - Hydroxybutyrate doesn't possess a keto group.

FORMATION OF KETONE BODIES / KETOGENESIS

The formation of ketone bodies also known as ketogenesis occurs in the mitochondrial matrix of Liver. ketogenesis involves the following reactions :

- Acetoacetyl CoA formed by condensation of two moles of Acetyl CoA.
- Acetoacetyl CoA combines with 1 more molecule of Acetyl CoA & converted into HMG CoA (also known as β - Hydroxy- β - methyl glutaryl CoA) in the presence of HMG CoA synthase.
- HMG CoA cleaves into Aceto- acetate & Acetyl CoA.
- Now Acetoacetone can undergo spontaneous decarboxylation to form Acetone & it can be reduced to form β - hydroxybutyrate.

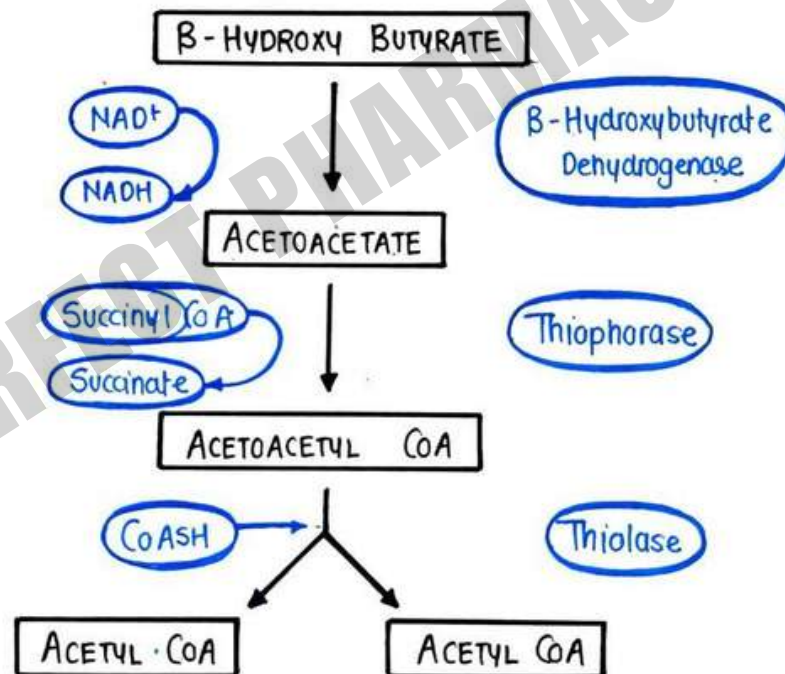


UTILIZATION OF KETONE BODIES

- The utilization of ketone bodies occurs through the process of ketolysis.
- ketolysis is the process of converting ketone bodies into Acetyl CoA to generate energy.
- ketone bodies are important source of energy for skeletal muscles, cardiac muscles, renal cortex etc.
- It is utilized during starvation & Diabetes Mellitus.
- ketolysis is just opposite to ketogenesis.

STEPS OF KETOLYSIS

- β -Hydroxybutyrate is first converted to Acetoacetate.
- Acetoacetate is activated to Acetoacetyl CoA by the thiophorase enzyme present in mitochondria.
- The CoA is denoted by Succinyl CoA
- Thiophorase is absent in liver, hence they are not utilized by liver cells.
- Acetyl CoA cleaves into two enzyme of moles of Acetyl CoA by Thiolase enzyme.



KETOACIDOSIS

- Both Acetoacetate & β -Hydroxybutyrate are strong acids.
- Now increase in their concentration in blood can cause ketoacidosis.
- ketoacidosis can be further divided into two types :
 - ① Alcoholic ketoacidosis
 - ② Diabetic ketoacidosis

ALCOHOLIC KETOACIDOSIS

- It occurs due to intake of alcohol for prolonged time.
- Excessive alcohol consumption can cause Malnourishment.
- Malnourished Alcoholic person has greater chances of developing Alcoholic ketoacidosis

DIABETIC KETOACIDOSIS

- Diabetic ketoacidosis occurs due to decrease in insulin level of body
- Diabetic ketoacidosis is a dangerous condition that may result in coma & even death, if not treated.
- Diabetic ketoacidosis required a rapid treatment.
- Insulin Therapy is the most useful treatment for diabetic ketoacidosis.

CHOLESTROL

- Cholestrol primarily belongs to a group of compounds known as sterols.
- It is the major component of cell membrane in human body.
- It is a type of lipid present in our body.
- It is naturally synthesized in our body in Liver and can also be obtained from external sources.
- It is present in the foods of animal origin and absent in the food of plant origin.

BIOLOGICAL SIGNIFICANCE OF CHOLESTROL

- It is the major structural component of cell membrane.
- It is the most essential ingredient in the structure of Lipoproteins
- It is the precursor of bile acid.
- It is the precursor of vitamin D.
- It is also the precursor of various steroidal hormones like progesteron , androgens , corticosteroids etc.
- Fatty acids are transported to liver as cholestrol esters .
- It insulates nerve fibres .
- Although cholestrol has various biological significance but its high concentration can leads to Atherosclerosis .

CHOLESTROL

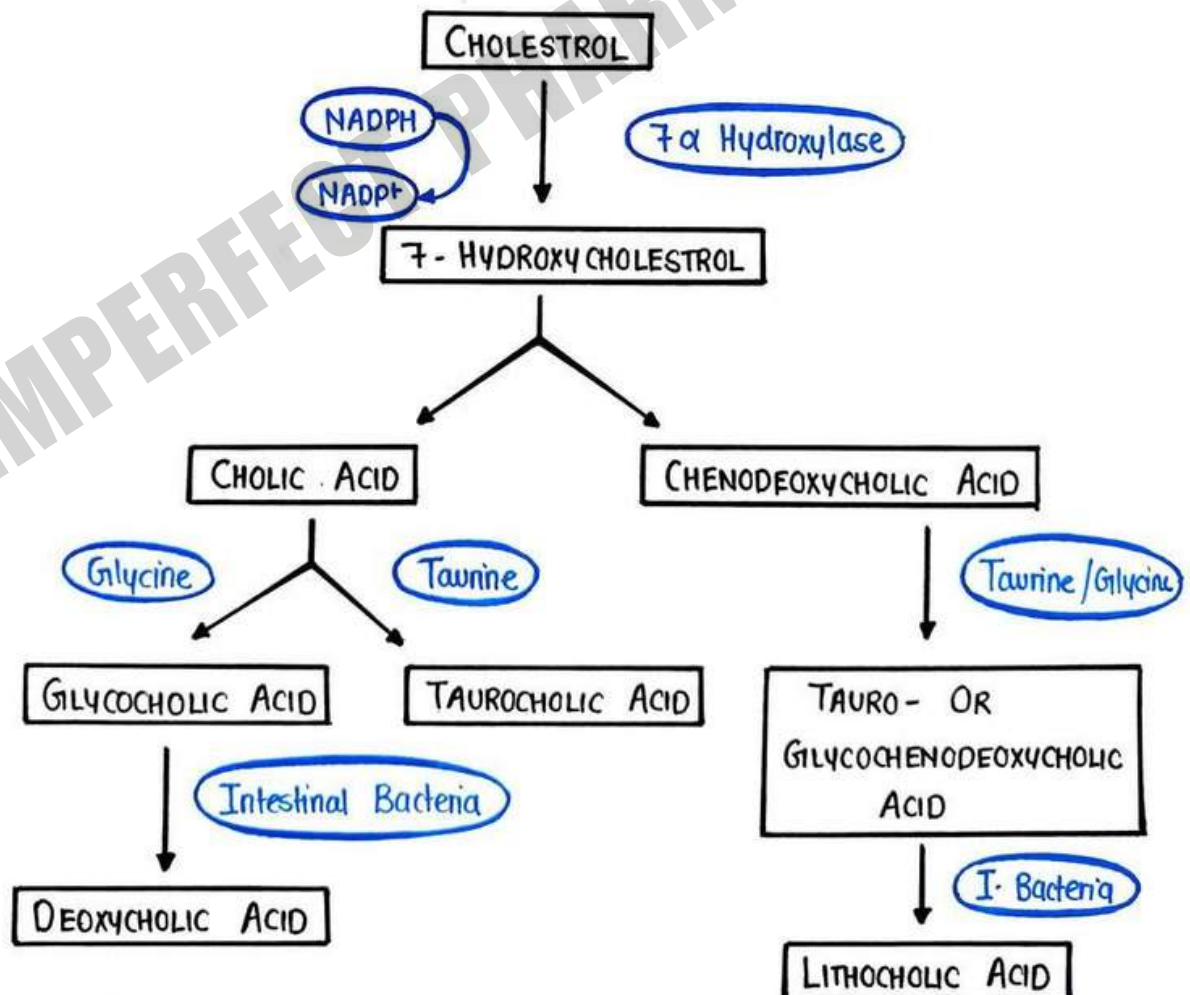
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CONVERSION OF CHOLESTROL INTO BILE ACID

- The synthesis of bile acid (bile juice) takes place in liver.
- bile acids promotes absorption of lipids & fat soluble vitamins.
- Cholestrol first converted into 7- Hydroxycholestrol in the presence of 7α Hydroxylase.
- 7- Hydroxycholestrol breaks into cholic acid & chenodeoxycholic acid & these are the primary bile acids.
- On conjugation with glycine or taurine ,conjugated bile acids (Glycocholic and Taurocholic acid) are formed.
- Finally in the presence of bacterial enzymes ,secondary bile acid forms.



AMINO ACID METABOLISM

- Amino Acids are building blocks of Proteins.
 - Amino Acid Metabolism can also be studied as Protein Metabolism.
 - There generally two types of Amino Acids.
- ① Essential Amino Acids.
 - ② Non - Essential Amino Acids.

General Reactions of Amino Acids

Amino Acids mainly undergoes following 3 types of general reactions :

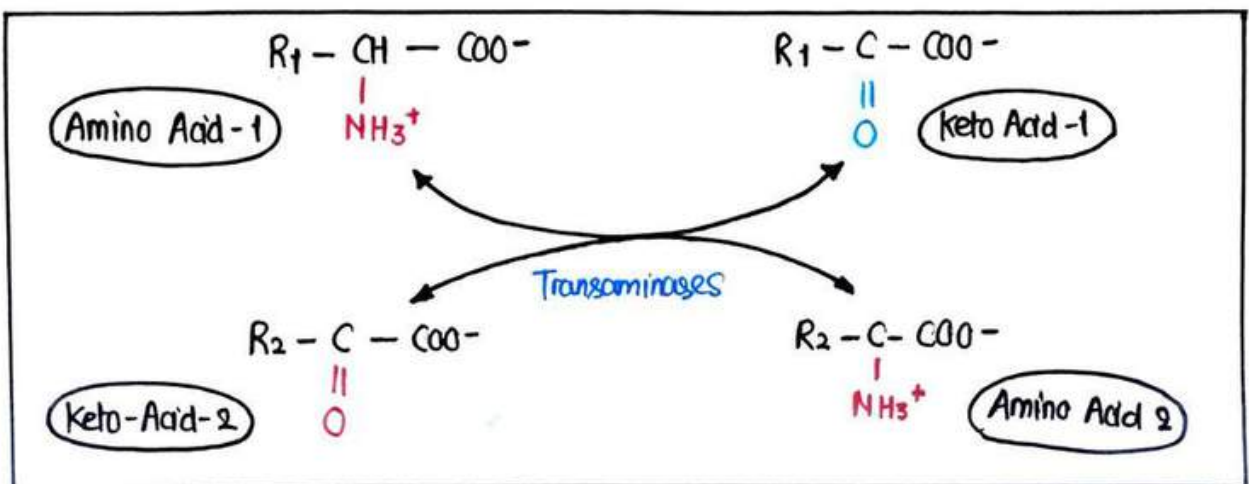
- ① Transamination
- ② Deamination
- ③ Decarboxylation

① TRANSAMINATION

The transfer of an amino group from an amino acid to a keto acid is known as Transamination.

This process involves interconversion of pair of amino acid to a pair of keto acids.

It is catalysed by group of enzymes called Transaminases.



Characteristics of Transamination

- All transaminases requires a coenzyme **Pyridoxal Phosphate (PLP)** a coenzyme, derived from Vitamin B₆.
- Specific transaminases exist for each pair of amino & keto acids.
- There is no free NH_3 liberated, only transfer of amino group occurs.
- Transamination is Reversible.
- The major tissues involves in transamination are Liver, kidney Heart & Brain.

Mechanism of Transamination

It occurs in two stages.

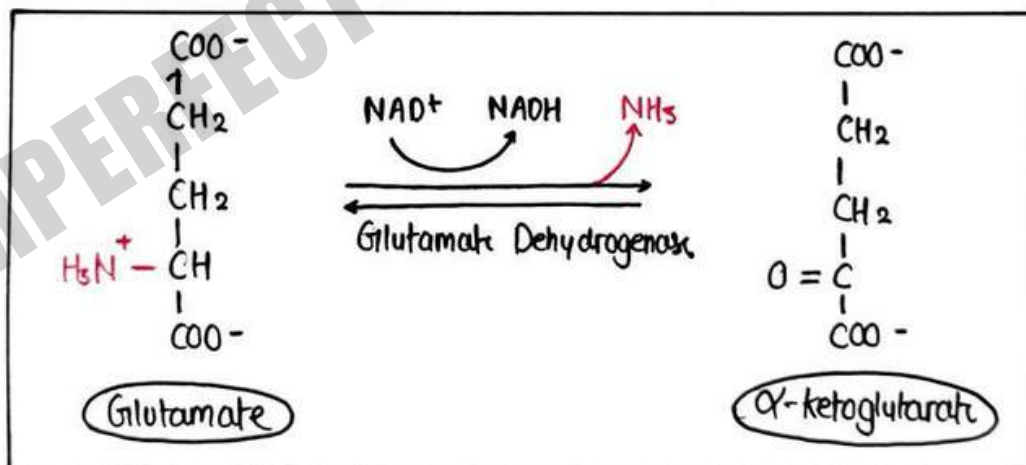
- Transfer of Amino Group to Pyridoxal Phosphate to form. Pyridoxamine Phosphate.
- Amino group from Pyridoxamine Phosphate transferred to keto Acid to produce new amino acid

② Deamination

- The removal of Amino Group from amino acids as NH_3 is known as deamination.
 - Deamination results in the liberation of Ammonia for Urea Synthesis.
 - It is of two types.
- (1) Oxidative Deamination
- (2) Non - Oxidative Deamination.

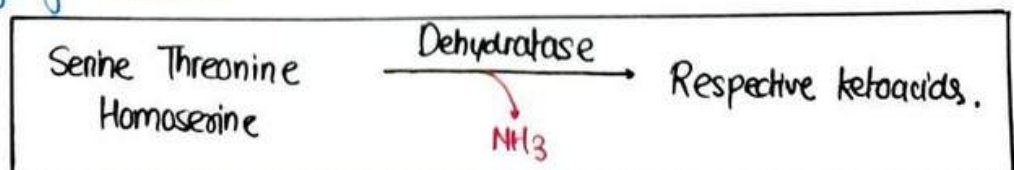
① Oxidative Deamination

- Oxidative Deamination is liberation of free ammonia from amino group of amino acids coupled with oxidation.
- It takes place mostly in Liver and kidneys.



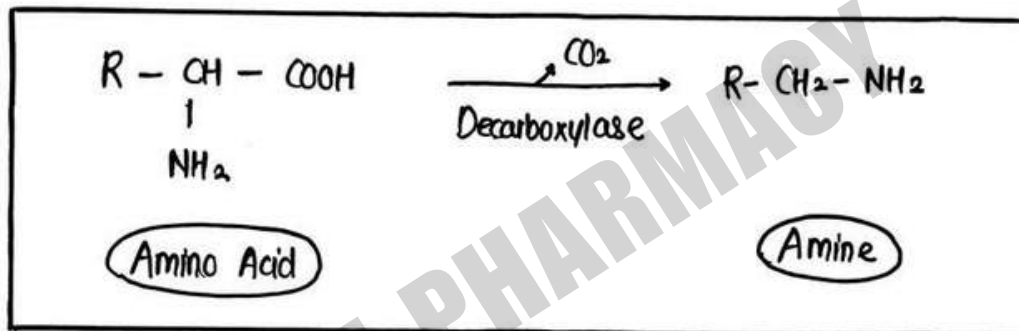
② Non - Oxidative Deamination

Some amino acids can be deaminated to liberate NH_3 without undergoing oxidation



③ DECARBOXYLATION

- Decarboxylation is the reaction by which CO_2 is removed from COOH group of an amino acid and as a result an amino acid is formed.
- Reaction is catalyzed by enzyme decarboxylase that requires pyridoxal P as coenzyme.



UREA CYCLE

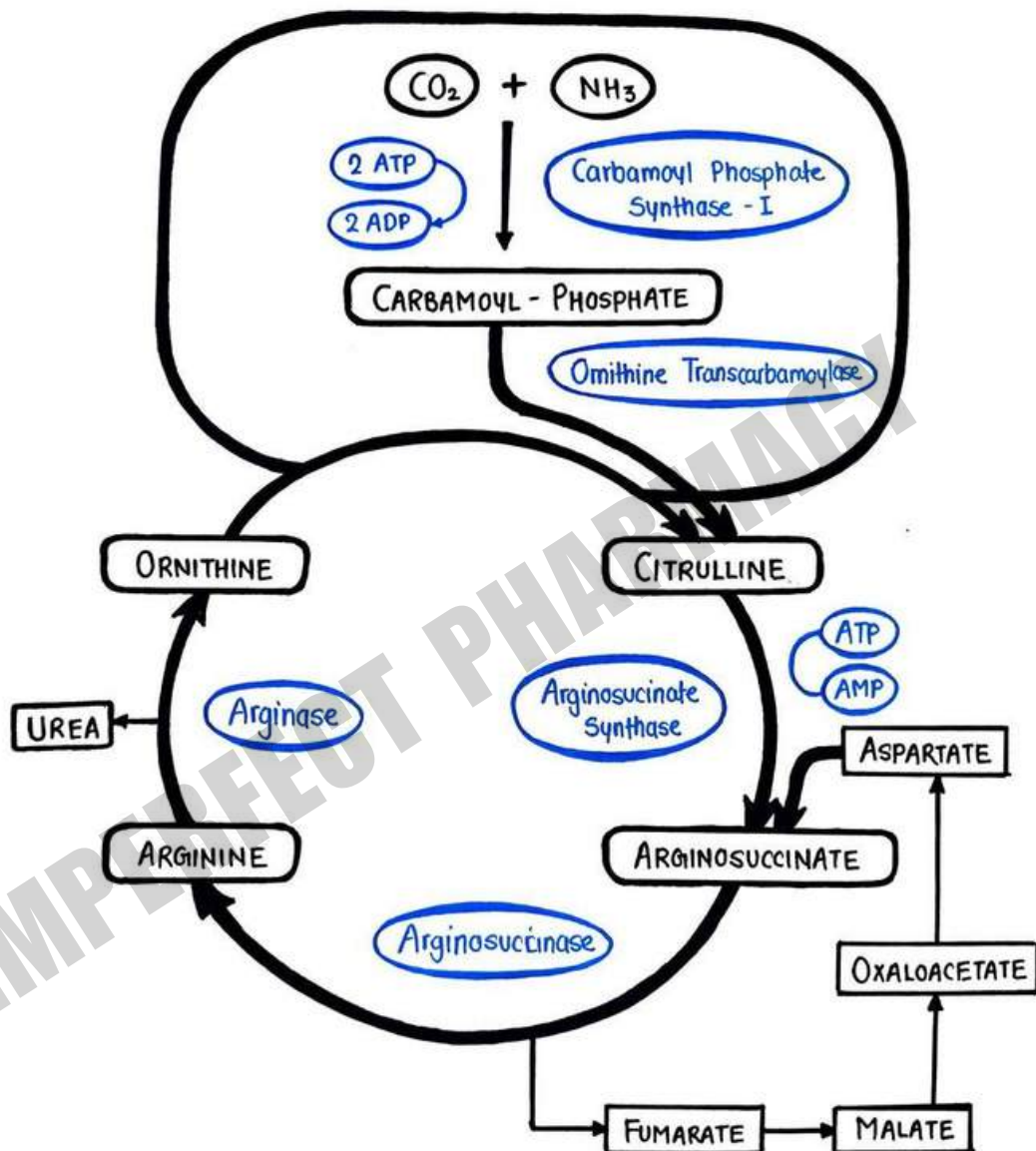
- Urea cycle is defined as the cyclic process in which Ammonia is converted into Urea.
- Urea cycle is also defined as the first cyclic process or first metabolism pathway discovered by Hans krebs and kurt Henseleit, hence also known as 'krebs Henseleit Cycle'. It is also called Ornithine Cycle.
- Urea synthesis occurs only in Liver and after that it is further transported to kidney through blood & excreted out from body.

Enzymes Involved In Urea Cycle

Urea cycle involves Five enzymes as follows

- ① Carbamoyl Phosphate Synthase I
- ② Ornithine Transcarbamoylase
- ③ Arginosuccinate Synthase
- ④ Arginosuccinase
- ⑤ Arginase

- Now in the above five enzymes, First 2 are found in mitochondria while rest 3 are found in cytosol of liver.
- Arginase is the enzyme only found in Liver, hence urea synthesis or Urea Cycle occurs only in liver.



STEPS OF UREA CYCLE

① Synthesis Of Carbamoyl Phosphate

- NH_3 condensed with CO_2 and activated in the presence of Carbamoyl Phosphate Synthase - I to form Carbamoyl Phosphate.
- This step consumes 2 ATP and is irreversible.

② Formation Of Citrulline

- Citrulline is synthesized from Carbamoyl Phosphate and Ornithine by Ornithine Transcarbamoylase.
- Ornithine is again regenerated & Urea cycle continues.

③ Synthesis Of Argininosuccinate

- Citrulline condenses with Aspartate to produce Argininosuccinate in the presence of Argininosuccinate Synthase.
- ATP is converted into AMP & Pyrophosphate (PPi).

④ Formation Of Arginine

- Argininosuccinate cleaves to produce Arginine & Fumarate in the presence of Argininosuccinase.
- Arginine is used as immediate precursor of Urea.

⑤ Formation Of Urea

- Arginine finally in the presence of Arginase converted into Urea and ornithine.
- Ornithine again used in Urea Cycle while Urea is excreted out from body through kidney.

ENERGETICS OF UREA CYCLE

- In Urea cycle 4 ATP molecules are consumed & it is irreversible process.
- Two ATP are utilized for synthesis of Carbamoyl Phosphate.
- One ATP is converted to AMP to produce Arginosuccinate which is equal to 2 ATP.

METABOLIC DISORDERS OF UREA CYCLE

- In healthy people, the normal blood Urea concentration is 10-40 mg/dl, now increase in blood-urea level can lead to various metabolic imbalances in our body.
- Urea cycle disorders are various genetic disorders that occur due to deficiency in enzymes involved in Urea Cycle.
- The five most common disorders are as follows:

① Hyper Ammonemia Type I	:	Carbamoyl Phosphate Synthase I
② Hyper Ammonemia Type II	:	Ornithine Transcarbamoylase
③ Citrullinemia	:	Arginosuccinate Synthase
④ Arginosuccinic Aciduria	:	Arginosuccinase
⑤ Hyperargininemia	:	Arginase

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