

β - OXIDATION OF FATTY ACID

Definition:

β -Oxidation may be defined as the oxidation (break down) of fatty acids at the β -carbon atom with the sequential removal of a two carbon fragment, acetyl CoA, at a time from the carboxyl end of the molecule in the mitochondria in eukaryotic cell.

β -Oxidation of fatty acid is the process by which fatty acids are broken down to **produce energy**. The fatty acids in the body are mostly oxidized by β -oxidation.

Stages of β -oxidation of fatty acids

- I. Activation of fatty acids** to acyl CoA occurring in the cytosol
 - II. Transport of Activated fatty acid** (Acyl CoA) to mitochondria through Carnitine transport system.
 - III. β -Oxidation proper** in the mitochondrial matrix (Trick: **OHOC**) β -oxidation consists of four steps:
 - 1. Oxidation:** Dehydrogenation catalyzed by acyl-CoA dehydrogenase, which removes two hydrogens between carbons α and β which generate $FADH_2$.
 - 2. Hydration:** Hydration catalyzed by enoyl-CoA hydratase, which adds water across the double bond.
 - 3. Oxidation:** Dehydrogenation catalyzed by 3-hydroxyacyl-CoA dehydrogenase, which generates NADH.
 - 4. Cleavage:** Thiolytic cleavage catalyzed beta-ketothiolase, which cleaves the terminal acetyl-CoA group and forms a new acyl-CoA which is two carbons shorter than the previous one.
-

β-Oxidation of Fatty acid

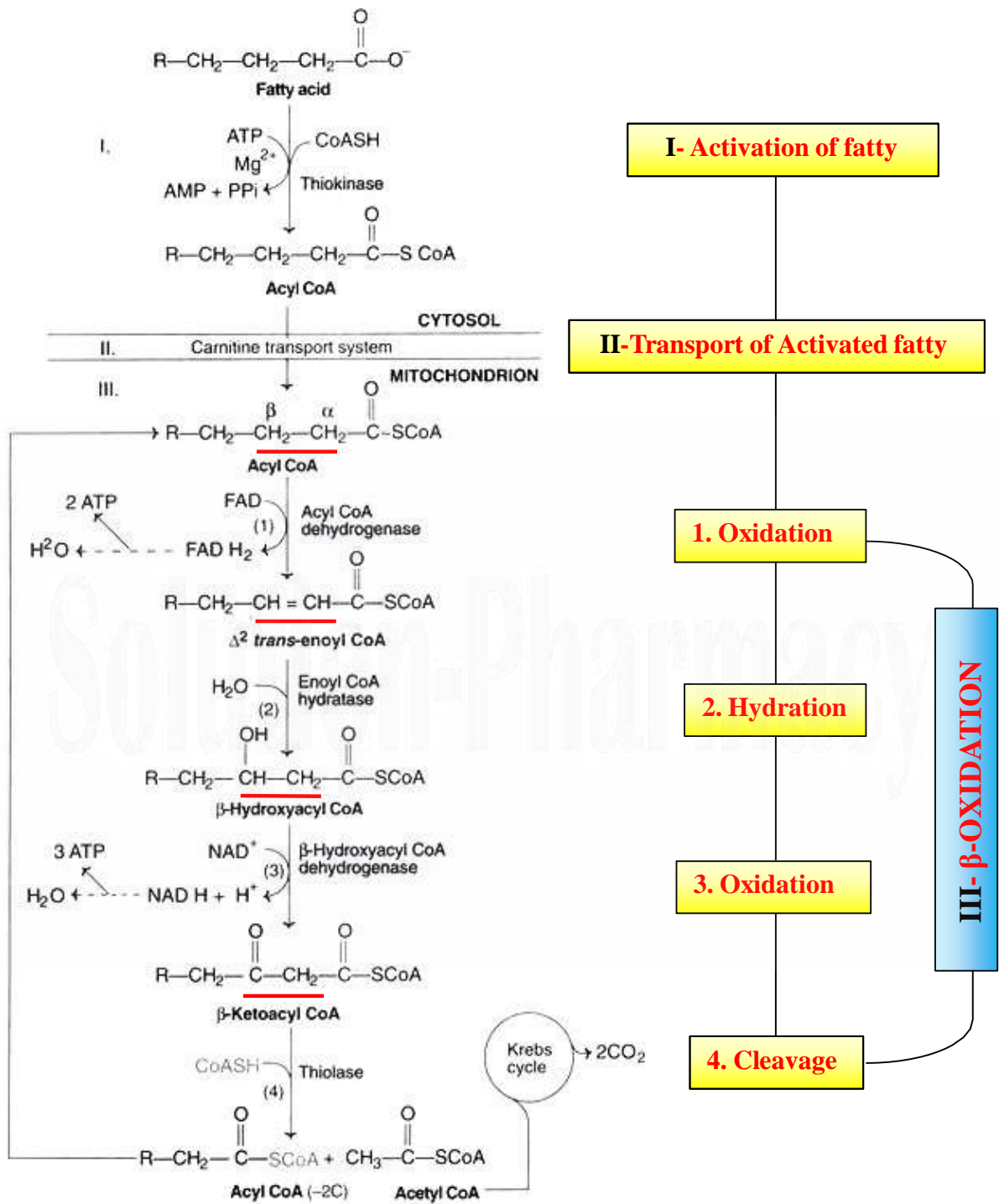
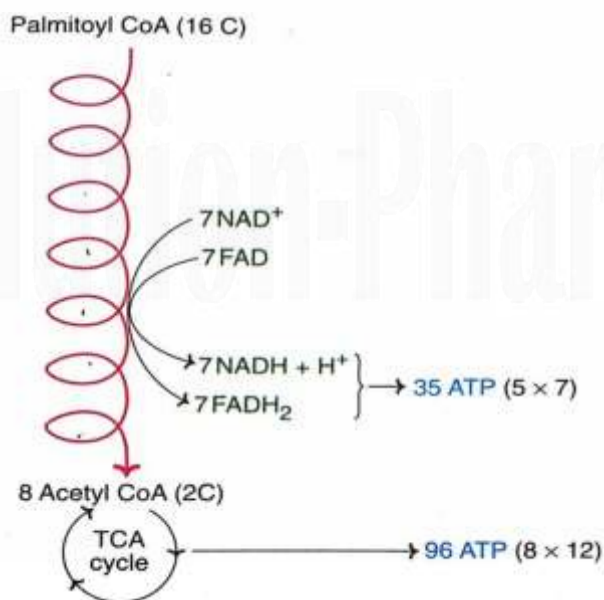


Fig. 67.10 : β-Oxidation of fatty acids : Palmitoyl CoA (16 carbon) undergoes seven cycles to yield 8 acetyl CoA [I-Activation; II-Transport; III-β Oxidation proper—(1) Oxidation, (2) Hydration, (3) Oxidation and (4) Cleavage]

Energetic of β -Oxidation of Palmitic acid

Beta oxidation of Palmitoyl CoA (16 C) undergoes seven cycle of to yield 8 Acetyl CoA. Acetyl CoA enters citric acid cycle and completely oxidized to CO_2 and H_2O



Mechanism	ATP Yield
1. β- oxidation 7 cycles	
Each NADH gives 3 ATP in electron transport chain	$7 \times 3 = 21$
Each FADH ₂ gives 2 ATP in electron transport chain	$7 \times 2 = 14$
2. From Acetyl CoA	
Each molecule of Acetyl CoA oxidized in TCA cycle provide 12 ATP	$8 \times 12 = 96$
Total energy from one molecule of Palmitoyl CoA	131
Energy Utilized for activation (Palmitoyl formation)	-2
Net yield of ATP	129

SYNTHESIS AND UTILIZATION OF KETONE BODIES

1. **Acetone, Acetoacetate and 3-β-Hydroxybutyrate** are known as ketone bodies.
Ketone bodies = Acetoacetate, D-β-Hydroxybutyrate and acetone.
2. Ketone bodies (except acetone) are synthesized and released by the liver and used as fuel for peripheral tissues.
3. Ketone bodies are water soluble molecules and energy yielding.

SYNTHESIS OF KETONE BODIES

1. The process of synthesis (formation) of ketone bodies is termed as **ketogenesis**.
2. Ketone bodies are **synthesized in the liver** from acetyl-CoA. Enzymes located in mitochondrial matrix.
3. Ketone bodies **used** as fuel in **muscle and brain**.
4. They are also formed when the body experienced starvation, carbohydrate restrictive diet, and prolonged intense exercises.

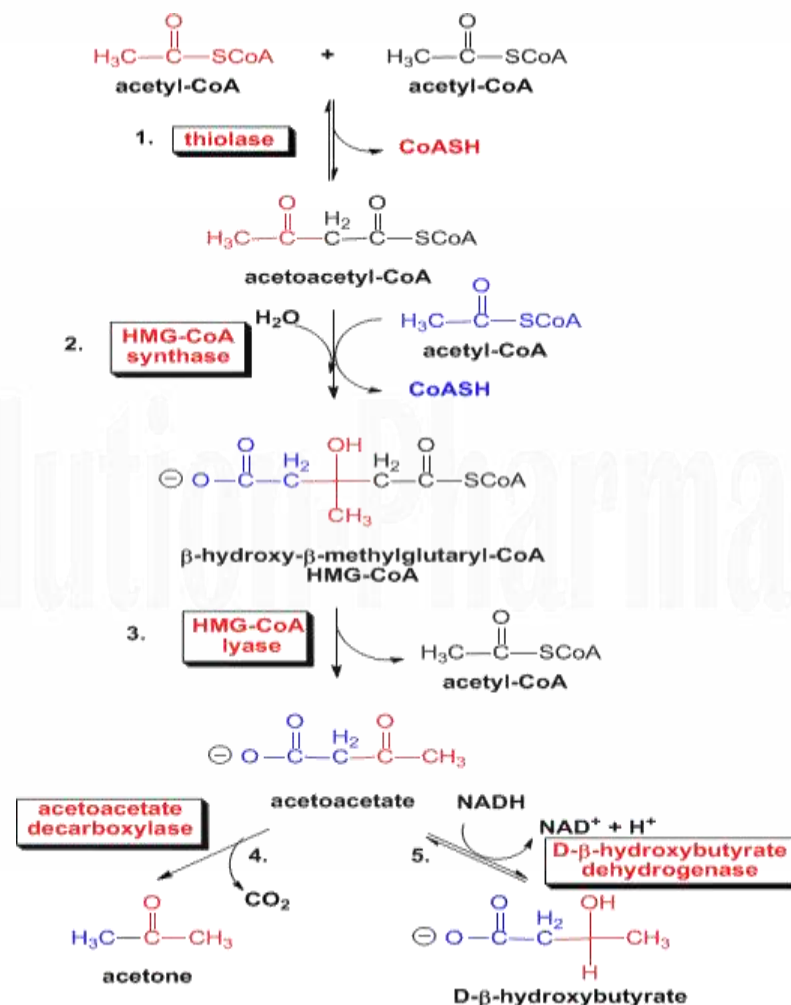


Fig.1: Ketone bodies Synthesis

UTILIZATION OF OF KETONE BODIES

1. The process of **breakdown of ketone bodies** occur in peripheral tissue is called **ketolysis**.
2. Ketone bodies utilized as fuels by the **extra hepatic tissues (brain, heart, and muscles)**.
3. Thiophorase is absent in liver hence ketone bodies are not utilized in liver.
4. The ketone bodies (Aceto acetate and β -Hydroxy butyrate) transported from liver to peripheral tissue, oxidized to acetyl-CoA for energy production. They will enter the citric acid cycle and oxidized in the mitochondria to be used as energy.
5. The synthesis and utilization of ketone bodies increases when glucose is in short supply as in:

- Individuals eating diets extremely high in fat and low in carbohydrates
- Starvation
Diabetes mellitus

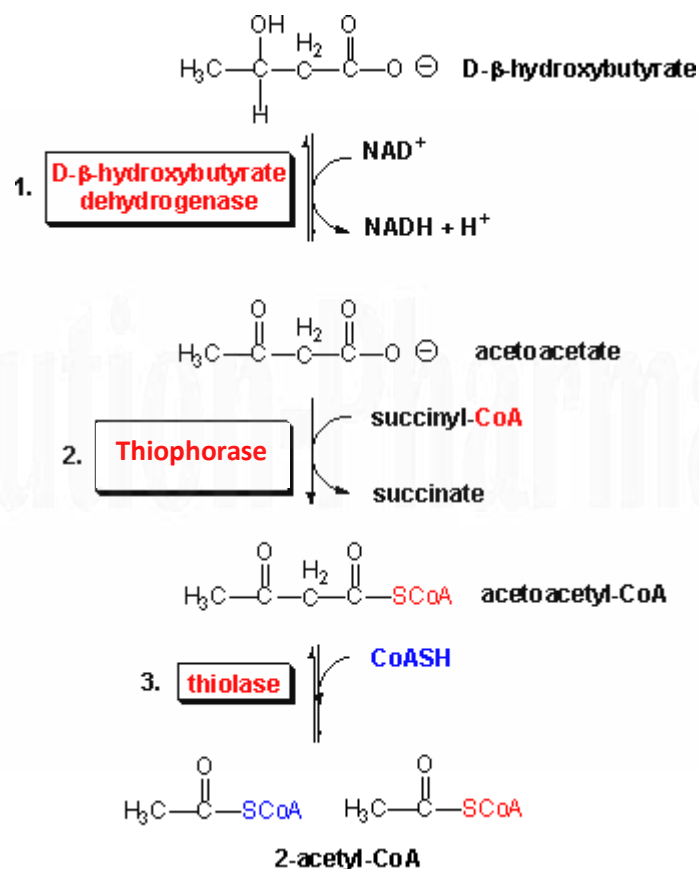


Fig.2: Ketone bodies Utilization

OVER PRODUCTION OF KETONE BODIES

1. In the normal individual there is constant production of ketone bodies by liver and utilization by extra hepatic tissue.
2. When the concentration of Ketone bodies increases in blood is known as ketonemia.
3. Excretion of ketone bodies in urine is known as Ketouria.
4. Ketonemia and Ketouria referred as ketosis. Commonly Associated with starvation and Severe uncontrolled Diabetes Mellitus

Ketonemia + Ketouria = Ketosis

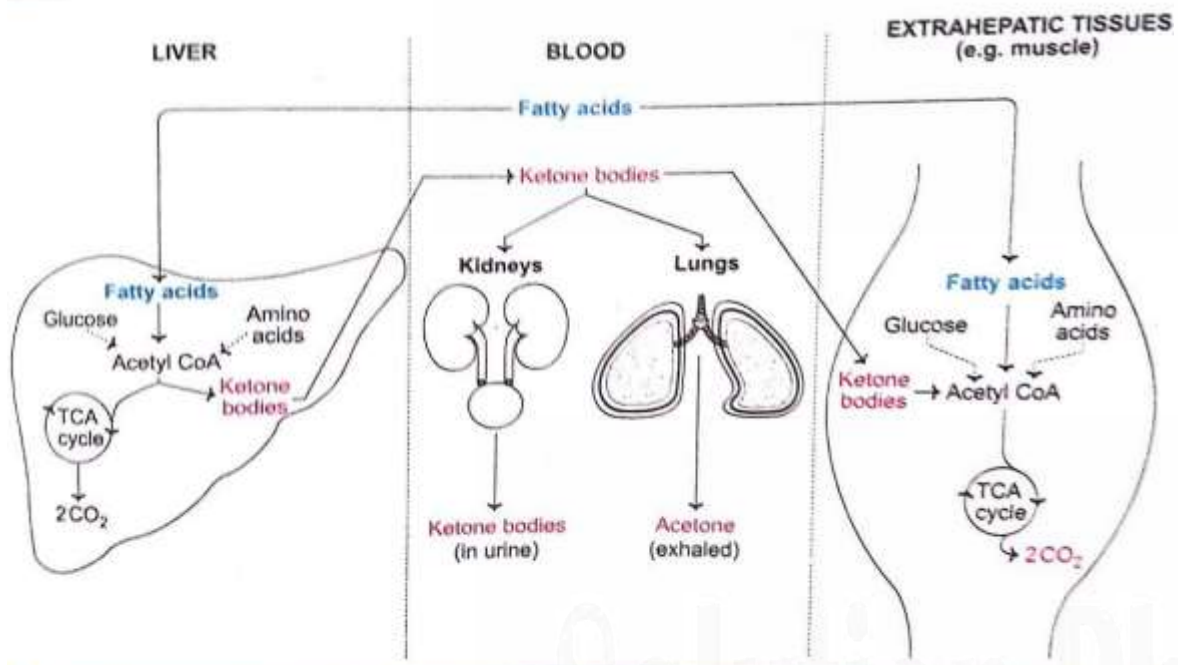


Fig. 3: Ketone bodies synthesis, utilization and excretion

REGULATION OF KETONE BODIES

1. Glucagon stimulates ketogenesis.
2. Insulin Inhibit ketogenesis.

KETOACIDOSIS

- Increased mobilization of fatty acid result in the over production of ketone bodies which often leads to ketoacidosis
- Both Acetoacetate and β -hydroxy butyrate are strong acid. Increase in their concentration in blood would cause ketoacidosis

- Ketone bodies in blood dissociate and release H^+ which lowers the pH.
- Their excretion in large quantities causes some loss of buffer action which depletes alkali reserve causing Ketoacidosis.
- Diabetic Ketoacidosis is dangerous, may result in Coma and even death if not treated.

Treatment of diabetic Ketoacidosis.

Administration of insulin is necessary to stimulate uptake of glucose by tissue and inhibition of ketogenesis.

Solution-Pharmacy