

Beta-oxidation of fatty acids

Definition

- Beta-Oxidation may be defined as the oxidation of fatty acids on the β -carbon atom.
- This results in the sequential removal of a two carbon fragment.

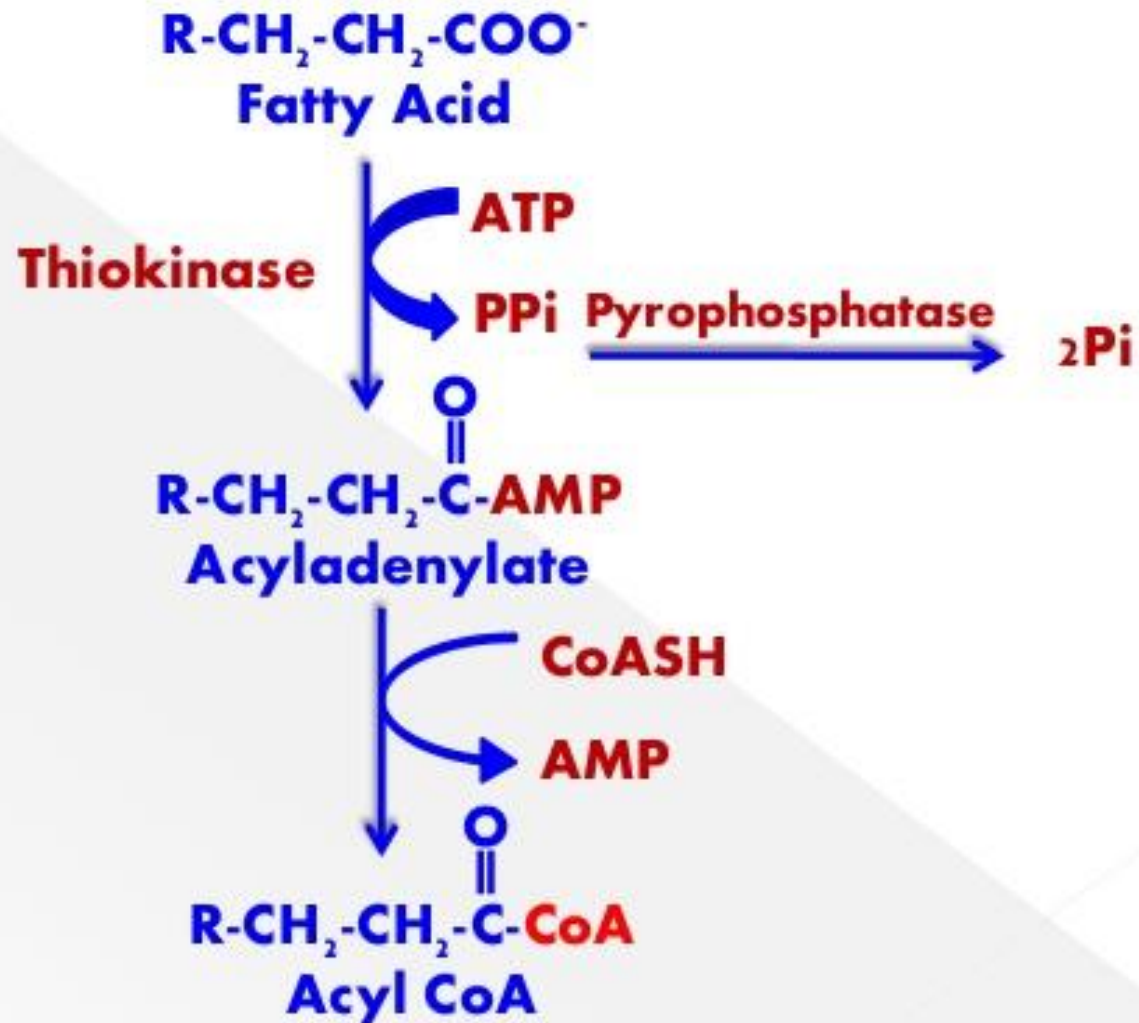
Stages and tissues

- Three stages
 1. Activation of fatty acids - in the cytosol
 2. Transport of fatty acids into mitochondria
 3. Beta-Oxidation proper in the mitochondrial matrix
- Fatty acids are oxidized by most of the tissues in the body.
- Brain, erythrocytes & adrenal medulla cannot utilize fatty acids for energy requirement.

Fatty acid Activation

- Fatty acid activation taking place in cytoplasm
- Fatty acids are converted in to Acyl adenylate
- Acyl adenylate converted in to Acyl CoA by thiokinases or acyl CoA synthetases.
- The reaction occurs in two steps & requires ATP, coenzyme A and Mg^{2+}
- Fatty acid reacts with ATP to form acyladenylate which then combines with coenzyme A to produce acyl CoA.
- Two high energy phosphates are utilized, since ATP is converted to pyrophosphate (PPi).
- The enzyme inorganic pyrophosphatase hydrolyses PPi to phosphate.

Activation of fatty acid to Acyl CoA



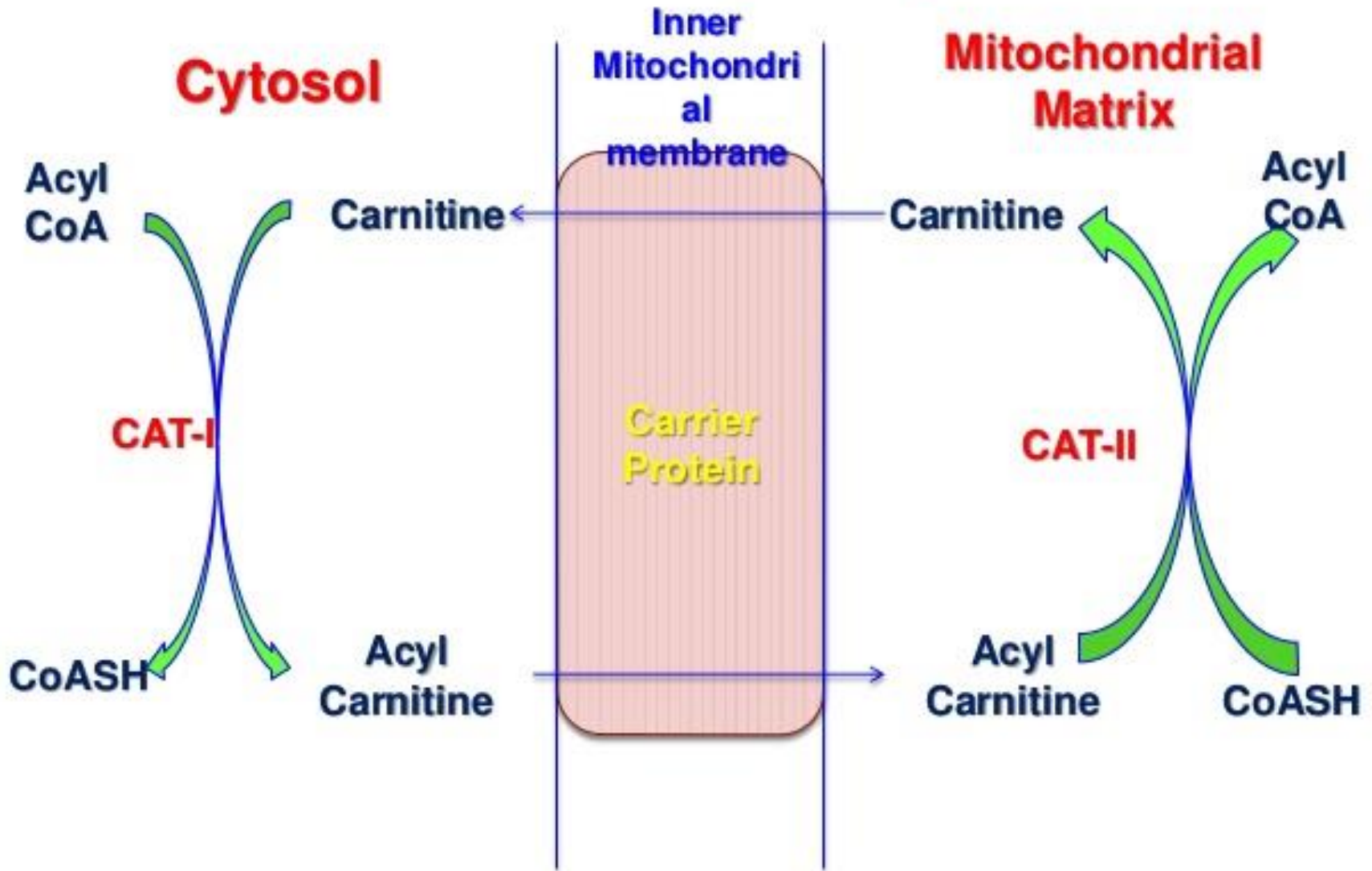
Transport of Acyl CoA in to mitochondria

- The inner mitochondrial membrane is impermeable to fatty acids.
- A specialized carnitine carrier system (carnitine shuttle) operates to transport activated fatty acids from cytosol to the mitochondria.
- Carnitine is β -hydroxy γ -trimethyl aminobutyrate, synthesized by lysine & methionine in liver & kidney.

Stages

- It occurs in four stages.
 1. Acyl group of acyl CoA is transferred to carnitine catalyzed by carnitine acyltransferase I (CAT-I) (present on the outer surface of inner mitochondrial membrane).
 2. The acyl-carnitine is transported across the membrane to mitochondrial matrix by a specific carrier protein (Translocase).
 3. Carnitine acyltransferase II (CAT-II) (found on the inner surface of inner mitochondrial membrane) converts acyl-carnitine to acyl CoA.
 4. The carnitine released returns to cytosol for reuse by translocase.

Carnitine transport system

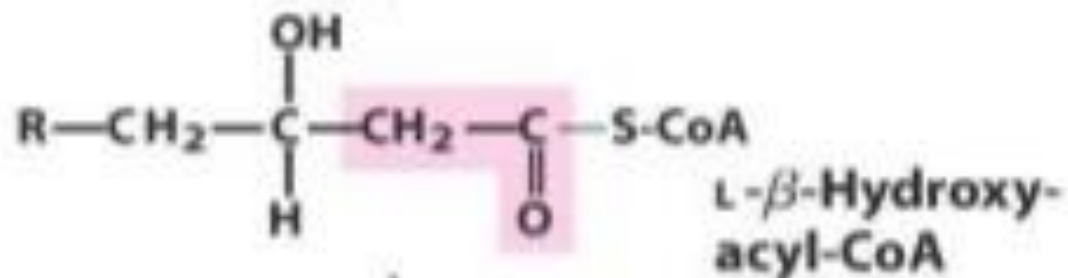
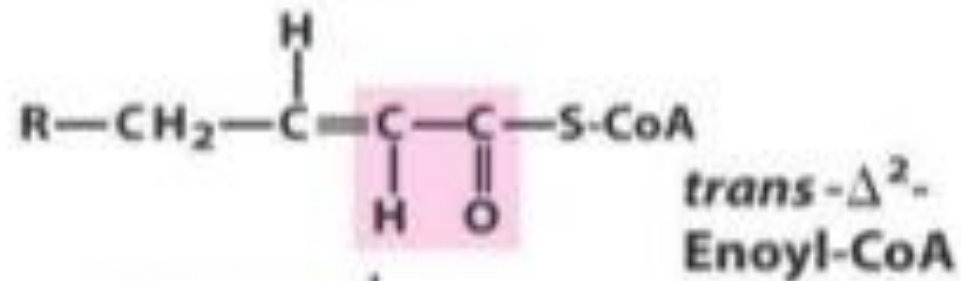
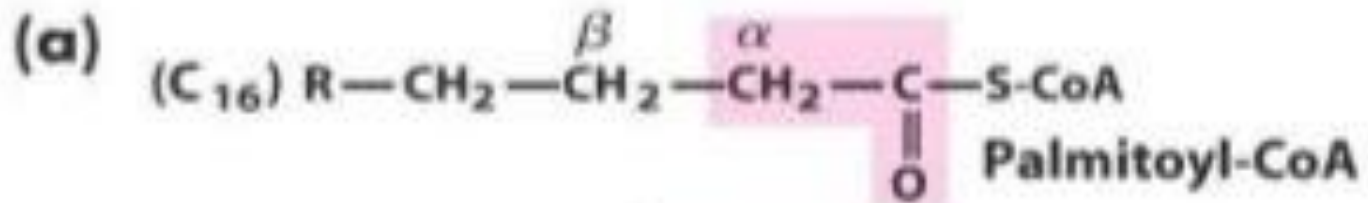


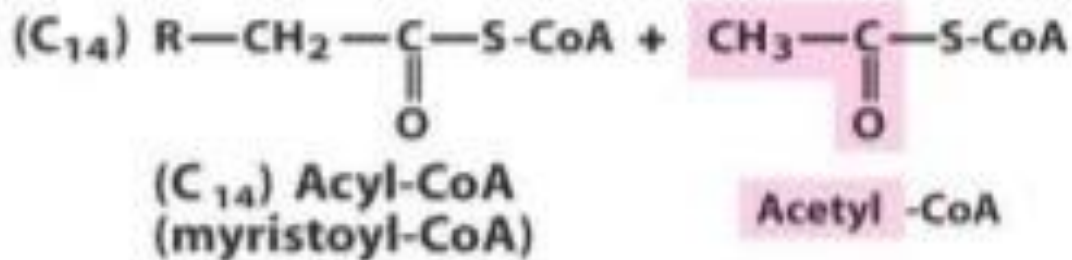
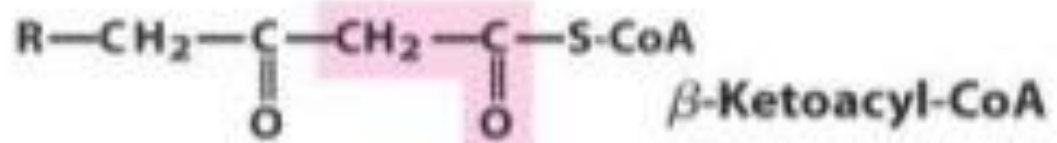
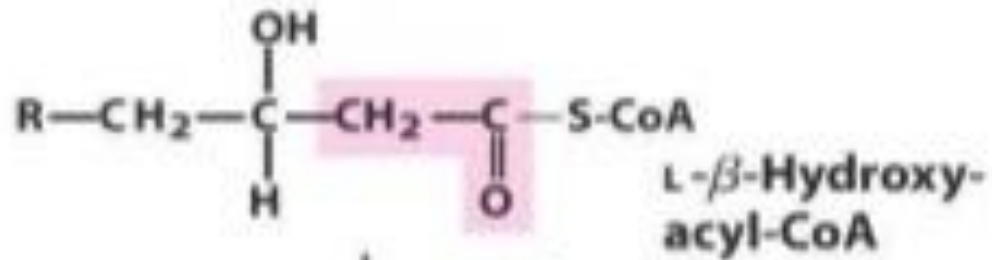
β -oxidation Proper

- Each cycle of β –oxidation, liberating a two carbon unit-acetyl CoA, occurs in a sequence of four reactions
 1. Dehydrogenation
 2. Hydration
 3. Dehydrogenation
 4. Cleavage

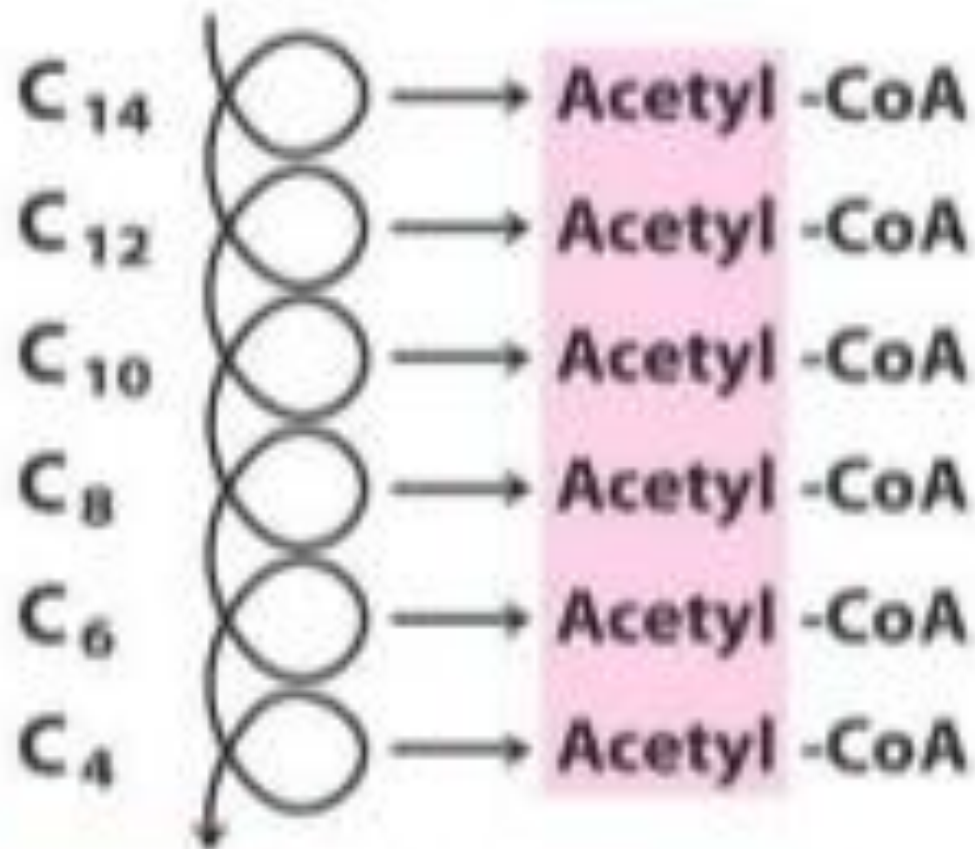
- **Dehydrogenation:**
- Acyl CoA undergoes dehydrogenation by an FAD-dependent flavoenzyme, acyl CoA dehydrogenase.
- A double bond is formed between α & β carbons (i.e., 2 & 3 carbons)
- **Hydration:**
- Enoyl CoA hydratase brings about the hydration of the double bond to form β -hydroxyacyl CoA.
- **Dehydrogenation**
- β -Hydroxyacyl CoA dehydrogenase catalyses the second oxidation & generates NADH.
- The product formed is β -ketoacyl CoA.

- 4. Cleavage
- The final reaction in β -oxidation is the liberation of a 2 carbon fragment, acetyl CoA from acyl CoA.
- This occurs by a thiolytic cleavage catalysed by β - ketoacyl CoA thiolase (or thiolase).
- The new acyl CoA, containing two carbons less than the original, reenters the β - oxidation cycle.
- The process continues till the fatty acid is completely oxidized.





(b)



Acetyl -CoA



β -Oxidation and ATP

Activation of a fatty acid requires:

- **2 ATP**

One cycle of oxidation of a fatty acid produces:

- **1 NADH \longrightarrow 3 ATP**
- **1 FADH₂ \longrightarrow 2 ATP**

Acetyl CoA entering the citric acid cycle produces:

- **1 Acetyl CoA \longrightarrow 12 ATP**

Mechanism	ATP Yield (New Concept)	ATP Yield (Old Concept)
1. β-oxidation 7 cycles 7 FADH_2 and 7 NADH are generated when oxidized by ETC	$7\text{FADH}_2 - 7 \times 1.5 = 10.5$ $7\text{NADH} - 7 \times 2.5 = 17.5$	$7 \times 2 = 14$ $7 \times 3 = 21$
2. From 8 acetyl CoA 1 acetyl CoA = 3 NADH + 1 FADH_2 + 1 GTP Oxidized by citric acid cycle, each acetyl CoA provides ATP	$10 \times 8 = 80$	$12 \times 8 = 96$
Total Energy from one mole of palmitoyl CoA	108	131
Energy utilized for activation (Formation of Palmitoyl CoA)	2	2
Net yield of oxidation of one mole of palmitate	$108 - 2 = 106$	$131 - 2 = 129$