Oxidation of Fatty Acids

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Fat

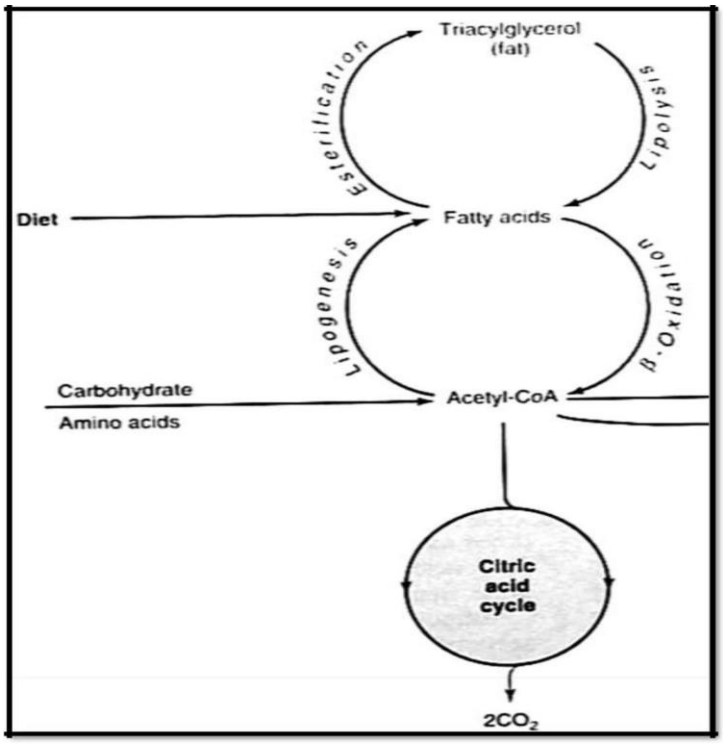
- Fats are **important source of energy** as (1gm of fat gives 9 kcal energy).
- **Mainly as triacylglycerols (triglycerides) in adipose cells**
- **Constitute 84% of stored energy**
    - **Protein - 15%**
    - **Carbohydrate (glucose or glycogen) - <1%**

β-oxidation of fatty acid

- **β-oxidation of fatty acid- The break down of a fatty acid to acetyl-CoA.**
- Occurs in the **mitochondria**
- Process is strictly **aerobic**
- After production **Acetyl-CoA is fed directly into the Krebs cycle**
- It occurs in many tissues including liver, kidney and heart.
- Fatty acids oxidation doesn't occur in the brain

○ There are several types of fatty acids oxidation.

(1) β- oxidation of fatty acid
(2) α- oxidation of fatty acids
(3) ω- oxidation of fatty acids



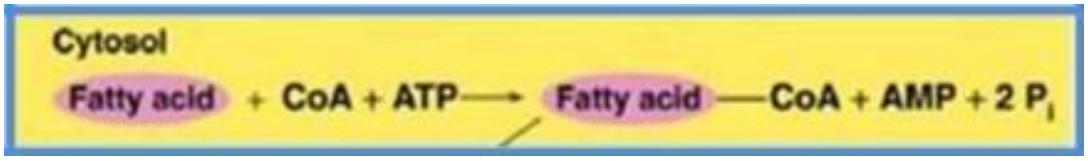
- The beta oxidation of fatty acids involve three stages:

1. Activation of fatty acids in the cytosol
2. Transport of activated fatty acids into mitochondria (**carnitine shuttle**)
3. Beta oxidation proper in the mitochondrial matrix

1) Activation of FA:

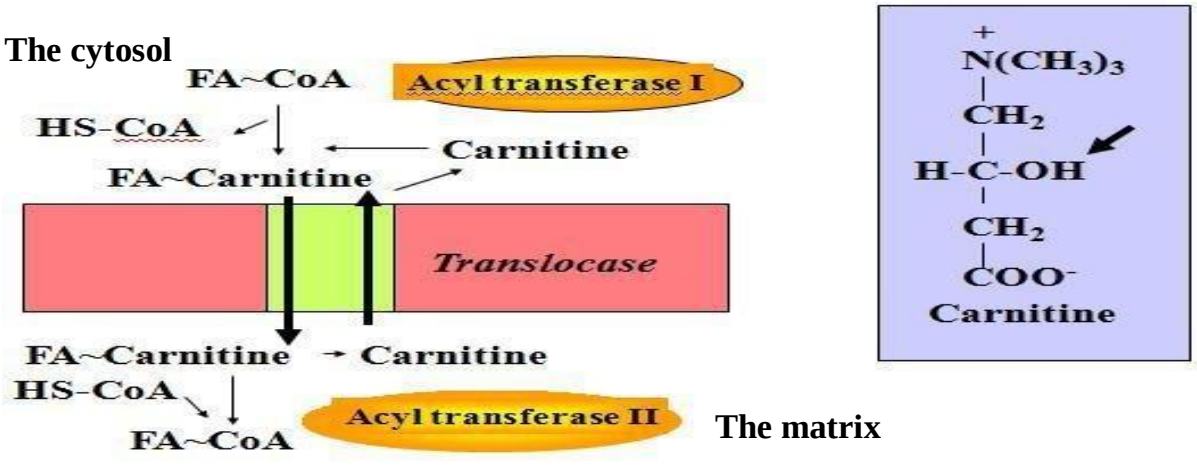
This proceeds by FA thiokinase (acyl COA synthetase) present in cytosol

Thiokinase requires ATP, COA SH, Mg^{++}. The product of this reaction is FA acyl COA and water.



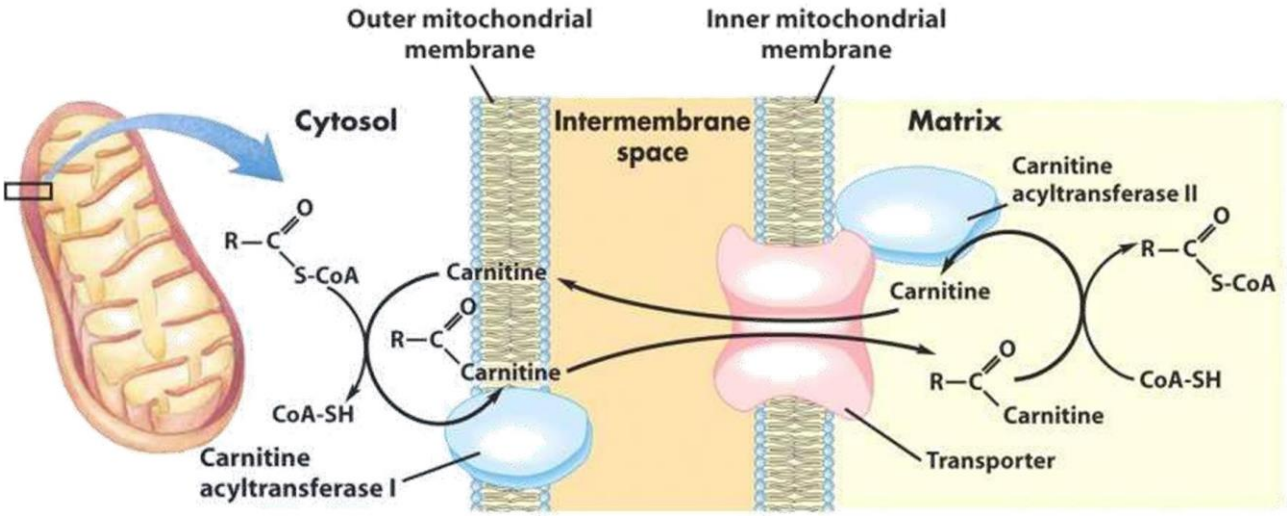
2- Transport of fatty acyl CoA from cytosol into mitochondria:

- **Long chain acyl CoA** traverses the inner mitochondria membrane with a special transport mechanism called **Carnitine shuttle**.



2-Transport of acyl CoA into the mitochondria (rate-limiting step)

1. Acyl groups from acyl COA is transferred to carnitine to form acyl carnitine catalyzed by **carnitine acyltransferase I,** in the outer mitochondrial membrane.
2. Acylcarnitine is then shuttled across the inner mitochondrial membrane by **a translocase** enzyme.
3. The acyl group is transferred back to CoA in matrix by **carnitine acyl transferase II.**
4. Finally, carnitine is returned to the cytosolic side by translocase, in exchange for an incoming acyl carnitine.



3. Proper of β – oxidation in the mitochondrial matrix

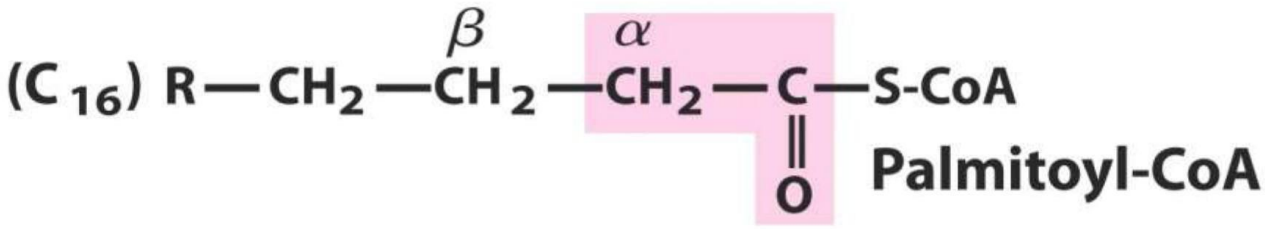
There are 4 steps in β – oxidation

Step I – Oxidation by ***FAD linked dehydrogenase***

Step II – Hydration by **Hydratase**

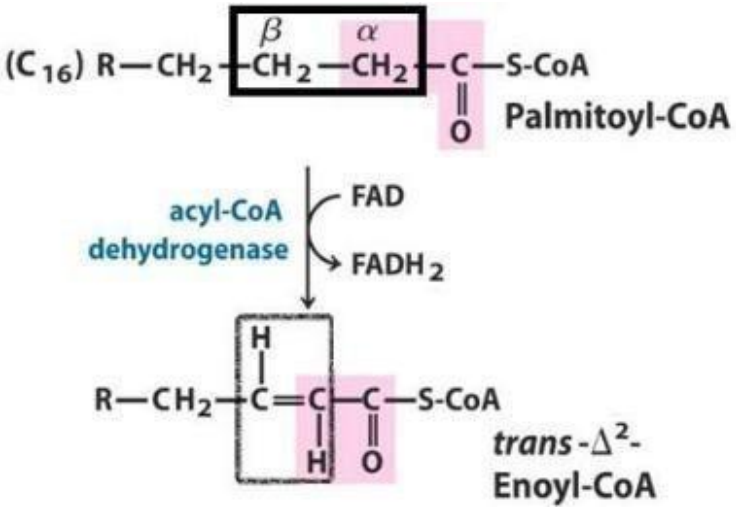
Step III – Oxidation by ***NAD linked dehydrogenase***

Step IV – Thiolytic clevage **Thiolase**

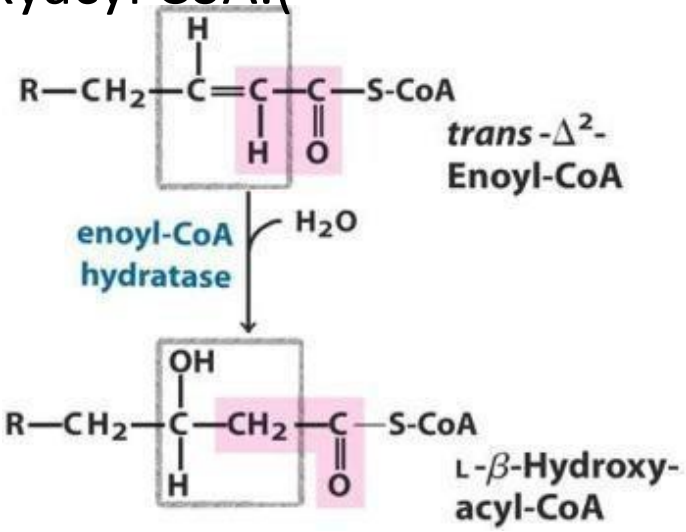


The first reaction is **the** **oxidation** of acyl CoA by an acyl CoA dehyrogenase to give α-β unsaturarted acyl CoA (enoyl CoA).

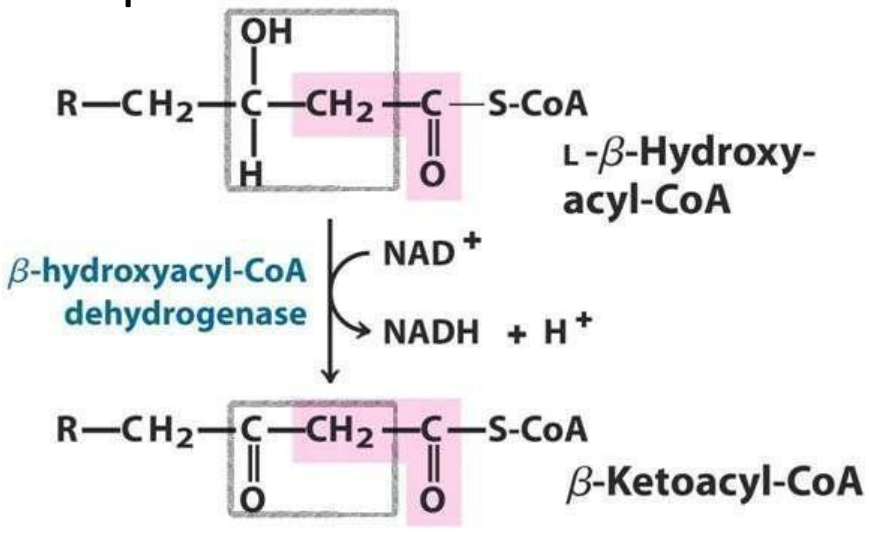
FAD is the hydrogen acceptor.



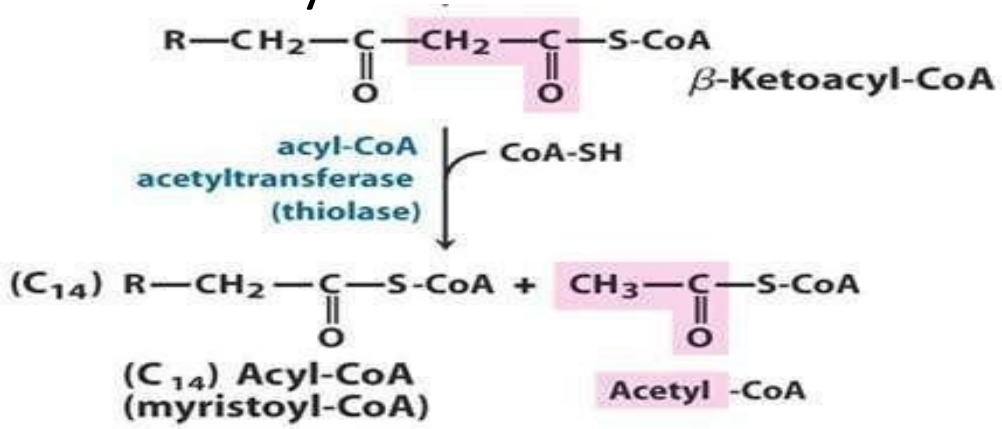
The second reaction is the **hydration** of the double bond to β-hydroxyacyl CoA (p-hydroxyacyl CoA.(

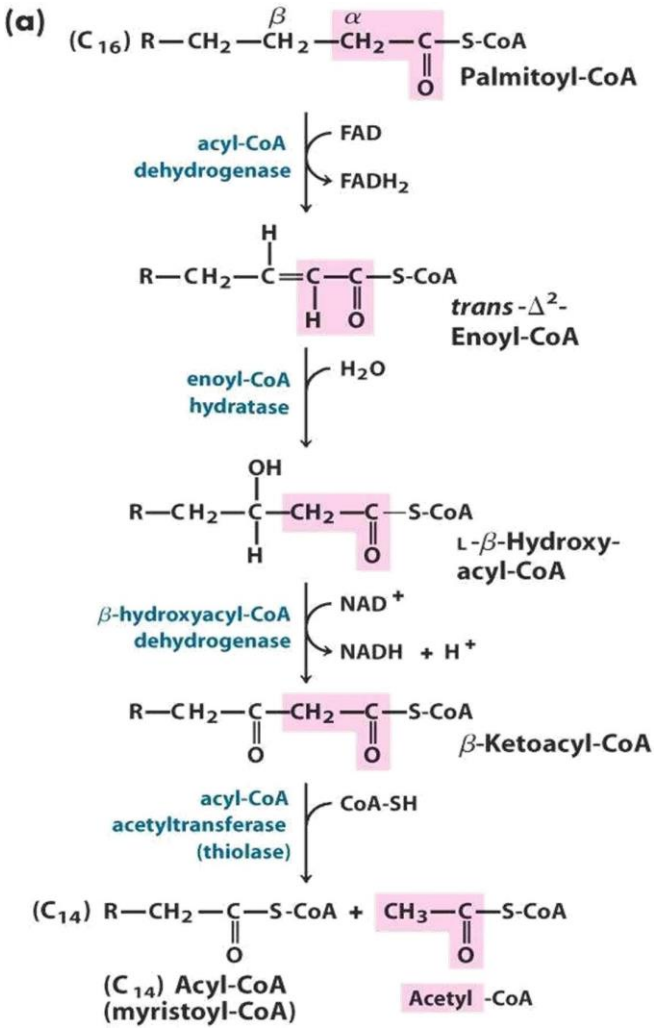


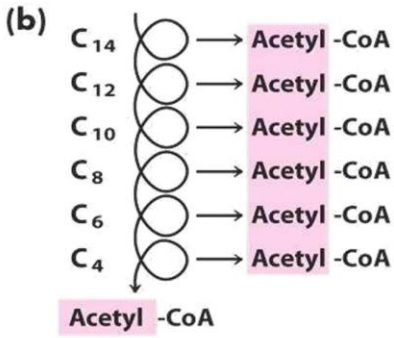
- **The third reaction** is the **oxidation** of β-hydroxyacyl CoA to produce β-Ketoacyl CoA a NAD-dependent reaction.



- The fourth reaction is cleavage of the two carbon fragment by splitting the bond between α and β carbons
- By thiolase enzyme.







- The release of acetyl CoA leaves an acyl CoA molecule shortened by 2 carbons.

- This acyl CoA molecule is the substrate for the next round of oxidation starting with acyl CoA dehydrogenase.

- Repetition continues until all the carbons of the original fatty acyl CoA are converted to acetyl CoA.

- In the last round a four carbon acyl CoA (butyryl CoA) is cleaved to 2 acetyl CoA.

- **Energetics of FA oxidation**
  e.g. Palmitic (16C):

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1. β-oxidation of palmitic acid will be repeated 7 cycles producing 8 molecules of acetyl COA.

2. In each cycle FADH2 and $NADH+H^+$ is produced and will be transported to the respiratory chain.

- $FADH_2$ ⟶ 2 ATP
- $NADH + H^+$ ⟶ 3 ATP
- So 7 cycles 5x7 = 35 ATP

3. Each acetyl COA which is oxidized in citric cycle gives 12 ATP (8 x 12 = 96 ATP(

4. 2ATP are utilized in the activation of fatty acid (It occurs once.(

- Energy gain = Energy produced - Energy utilized
- 35 =ATP + 96 ATP - 2 ATP = 129 ATP