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**

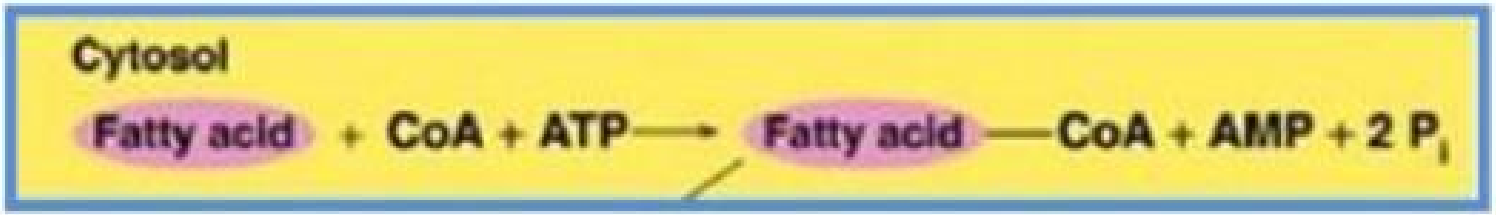
- The beta oxidation of fatty acids involve three stages:

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:

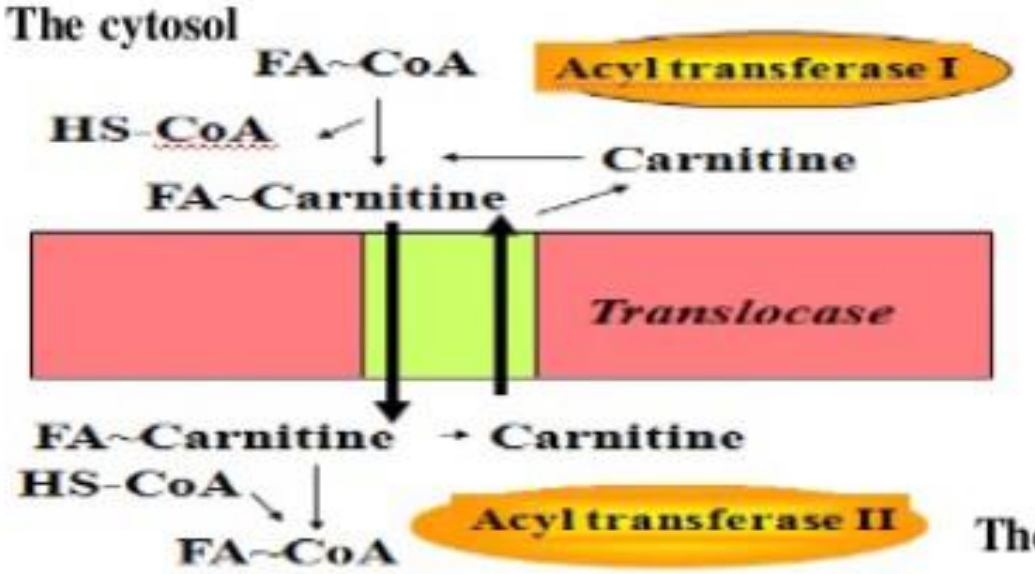
This proceeds by FA thiokinase (acyl COA synthetase) present in cytosol

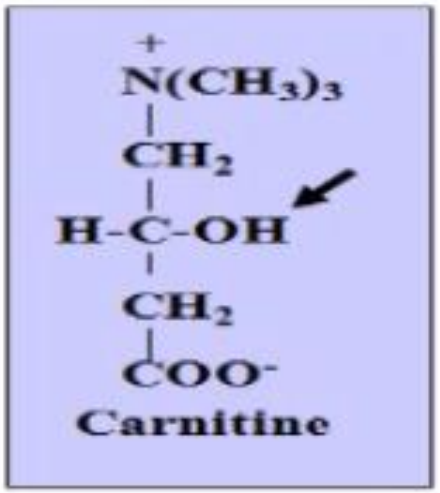
Thiokinase requires ATP, COA SH, Mg^{++}. The product of this reaction is FA acyl COA and water.



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

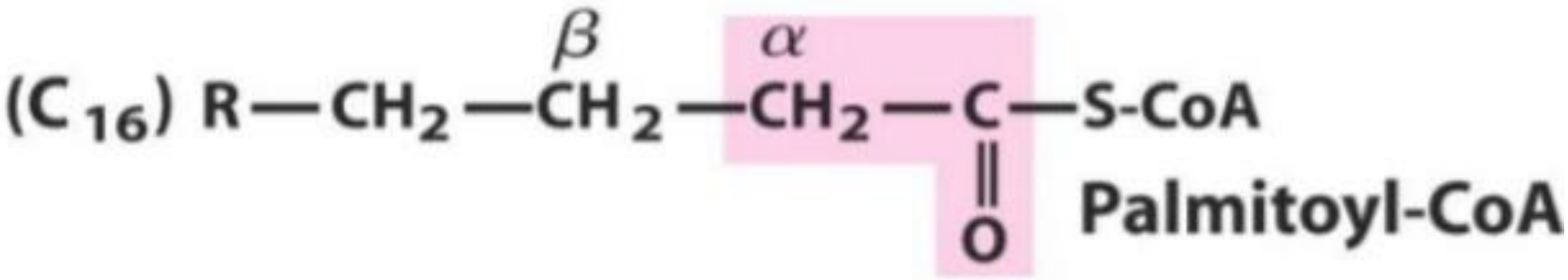
There are 4 steps in β – oxidation

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

Step II – Hydration by **Hydratase**

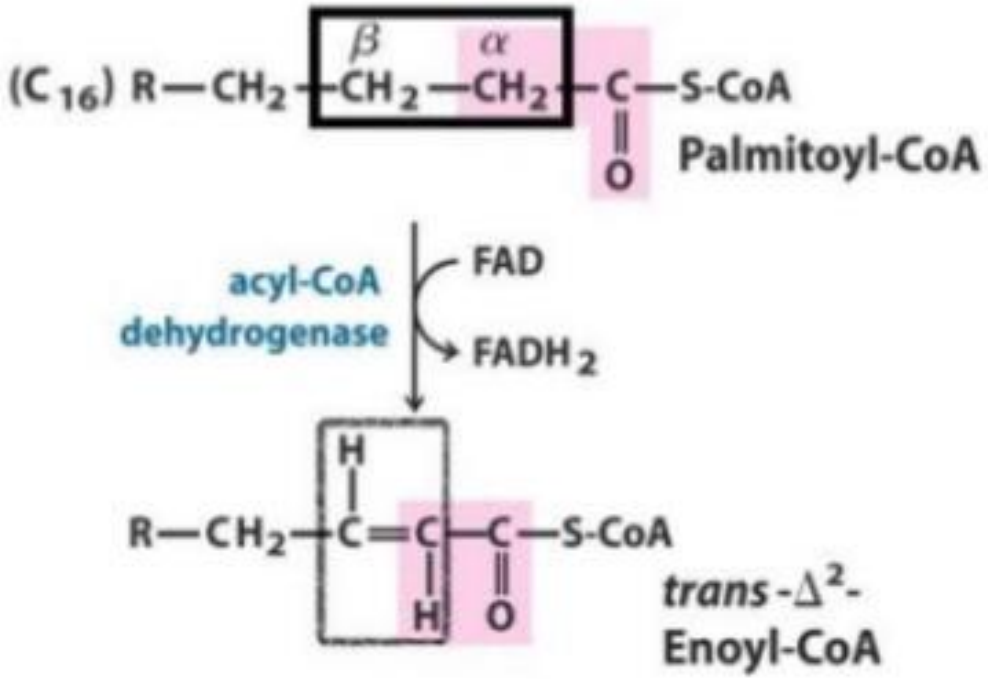
Step III – Oxidation by ***NAD linked dehydrogenase***

Step IV – Thiolytic clevage **Thiolase**

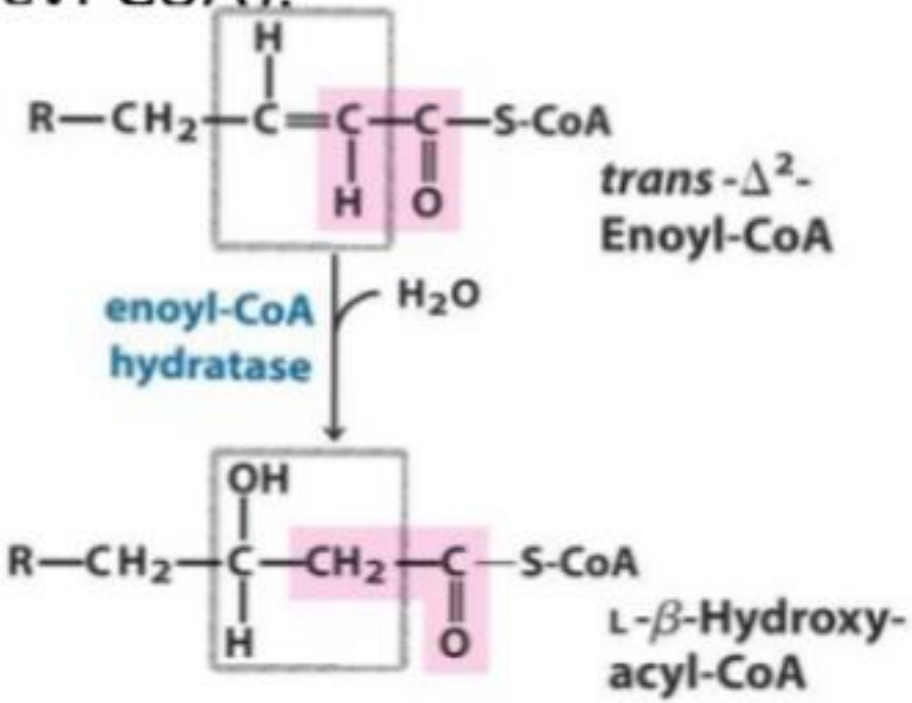


The first reaction is **the** **oxidation** of acyl CoA by an acyl CoA dehyrogenase to give α-β unsaturarted acyl CoA (enoyl CoA).

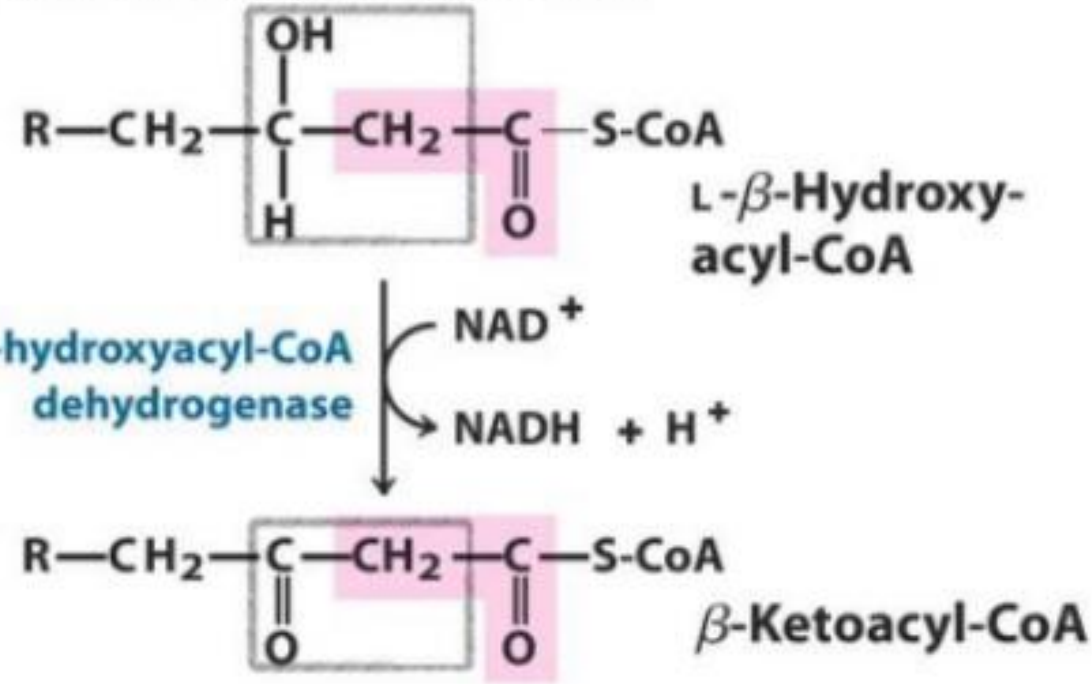
FAD is the hydrogen acceptor.



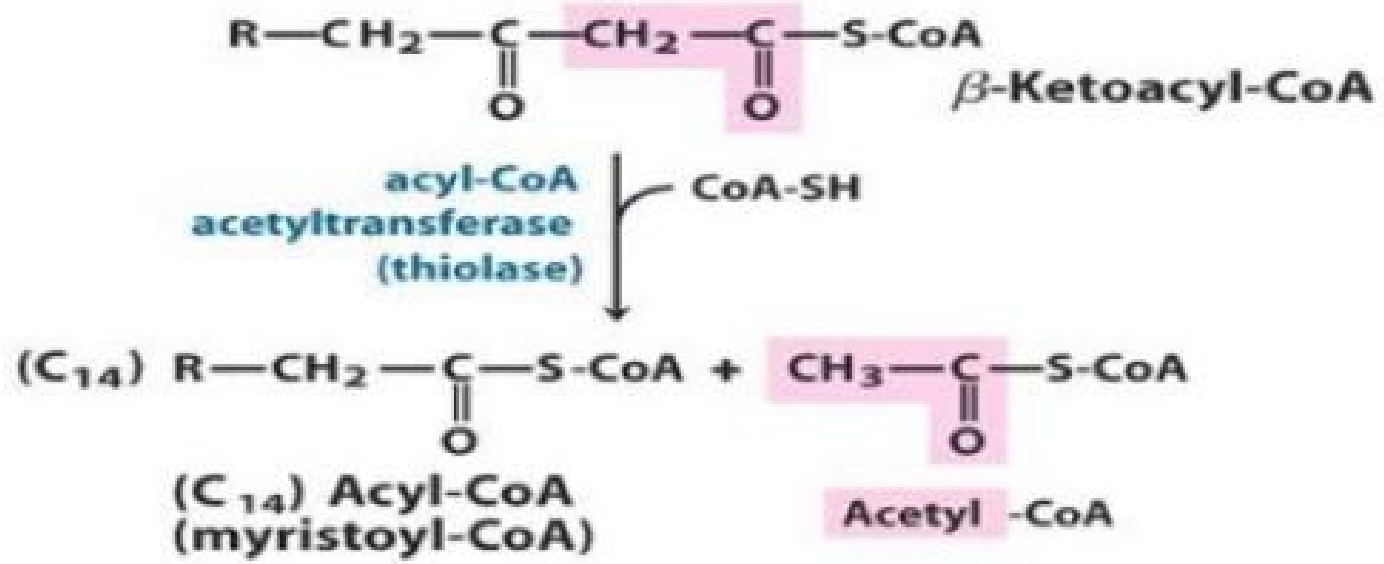
The second reaction is the **hydration** of the double bond to β-hydroxyacyl CoA (p-hydroxyacvl CoA).

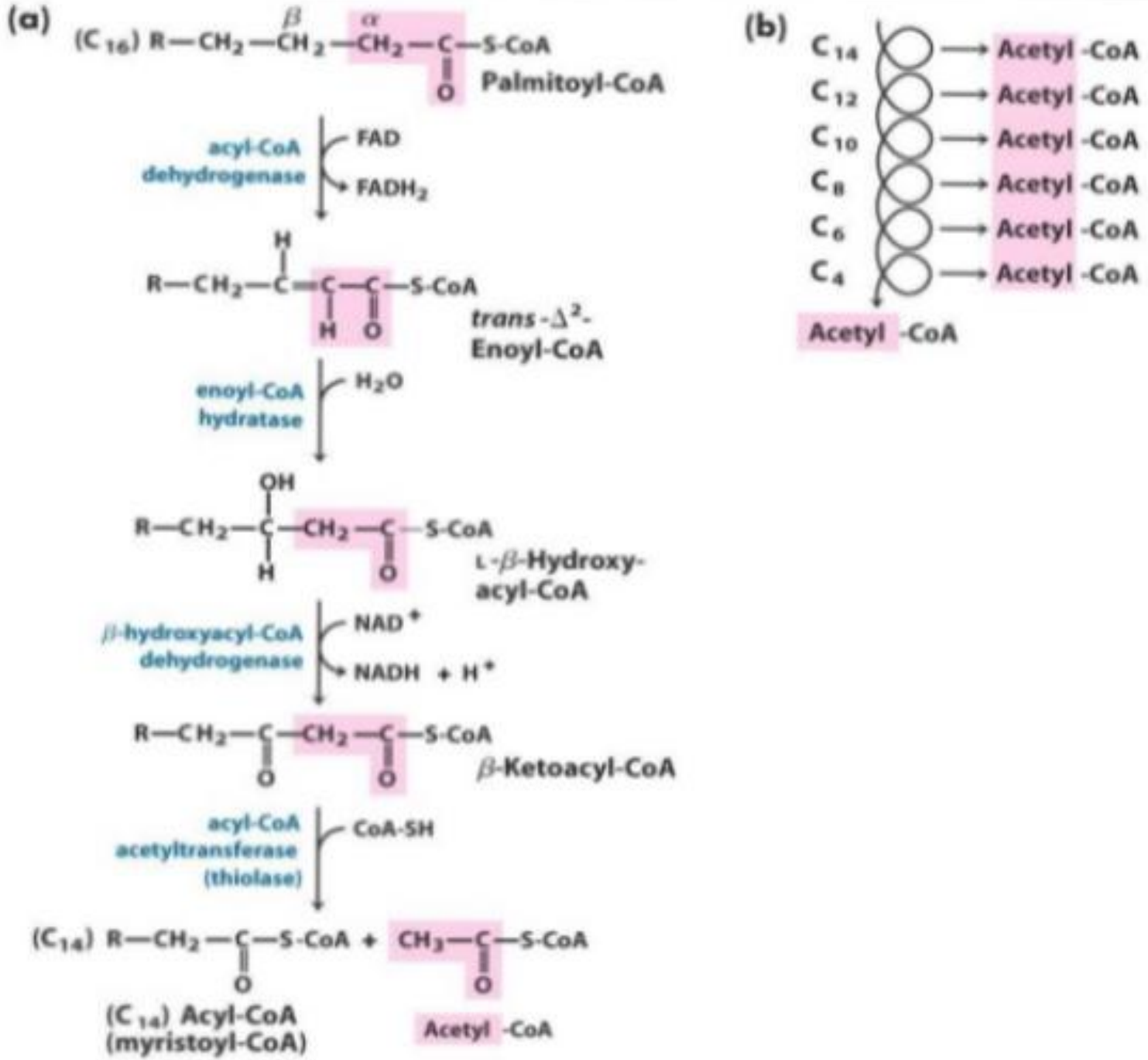


- **The third reaction** is the **oxidation** of β-hydroxyacyl CoA to produce β-Ketoacyl CoA a NAD-dependent reaction.



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




(a)
(C16) R—CH2—CH2—CH2—C—S-CoA
Palmitoyl-CoA
acyl-CoA dehydrogenase
FAD
FADH2
R—CH2—CH=CH—C—S-CoA
trans-Δ2-Enoyl-CoA
enoyl-CoA hydratase
H2O
R—CH2—CH(OH)—CH2—C—S-CoA
L-β-Hydroxy-acyl-CoA
β-hydroxyacyl-CoA dehydrogenase
NAD+
NADH + H+
R—CH2—C(=O)—CH2—C—S-CoA
β-Ketoacyl-CoA
acyl-CoA acetyltransferase (thiolase)
CoA-SH
(C14) R—CH2—C—S-CoA + CH3—C—S-CoA
(C14) Acyl-CoA (myristoyl-CoA)
Acetyl -CoA
(b)
C14 → Acetyl -CoA
C12 → Acetyl -CoA
C10 → Acetyl -CoA
C8 → Acetyl -CoA
C6 → Acetyl -CoA
C4 → Acetyl -CoA
Acetyl -CoA

- 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.