β OXIDATION OF FATTY ACID

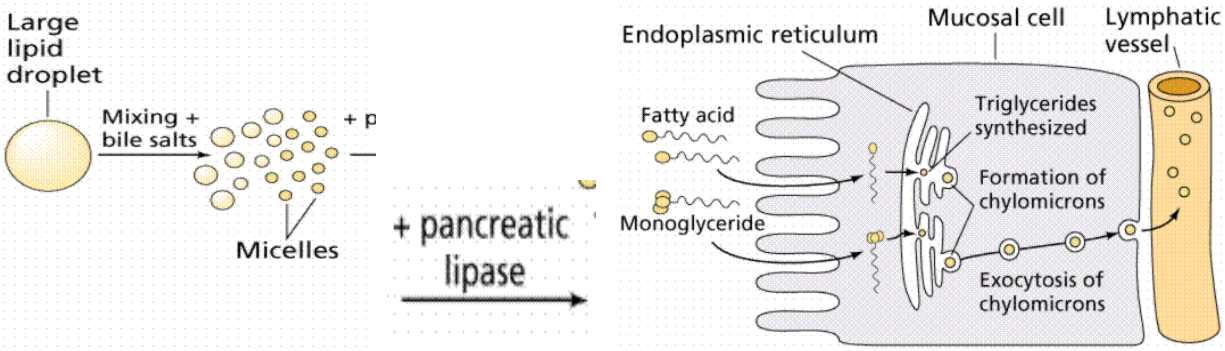
INTRODCUTION

Fat:

Fats are important source of energy as (1gm of fat gives 9 kcal energy). Mainly as triacylglycerols (triglycerides) in adipose cells.

Adipose tissue is found in various places in the body. Some of these locations include the subcutaneous layer under the skin; around the heart, kidneys, and nerve tissue; in yellow bone marrow and breast tissue; and within the buttocks, thighs, and abdominal cavity.

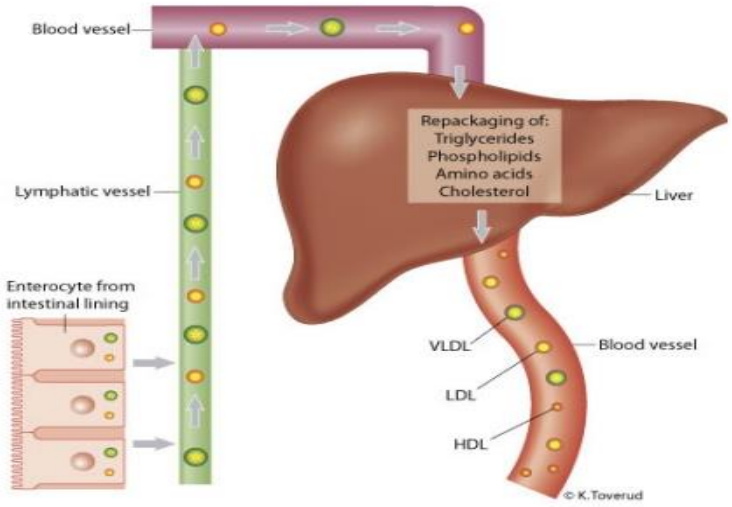
Digestion & Absorption of Lipids



Fats are digested by lipases that hydrolyze the glycerol fatty acid bonds. Of particular importance in fat digestion and absorption are the bile salts, which emulsify the **fats** to allow for their solution as micelles in the chyme, and increase the surface area for the pancreatic lipases to operate.

Absorption of fats occurs only in the small intestines. Once the triglycerides are broken down into individual fatty acids and glycerols, along with cholesterol, they will aggregate into structures called micelles.

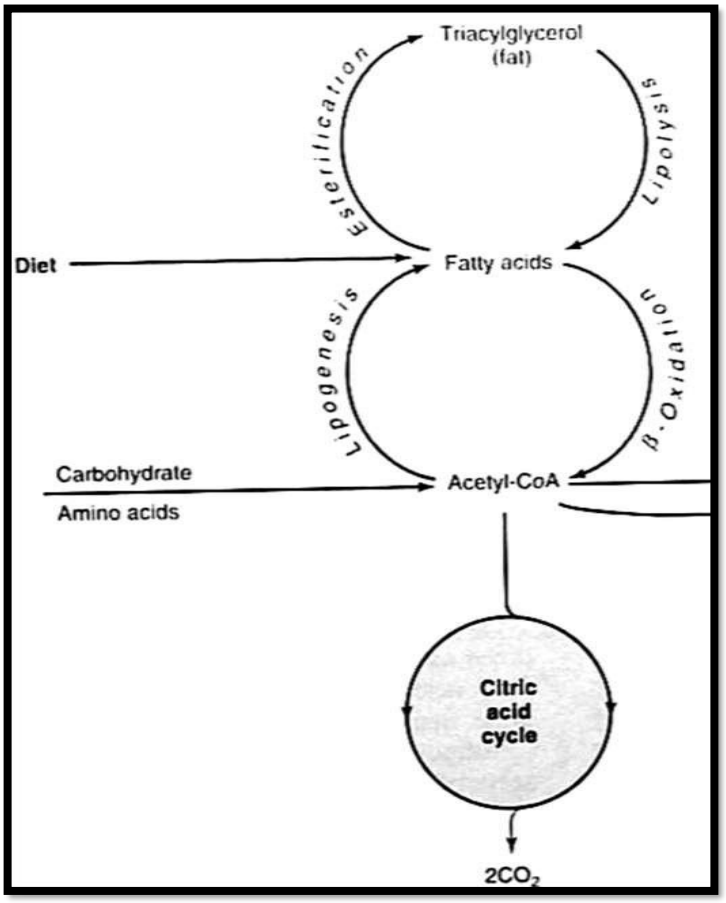
Transport & Storage



- Adipose tissue lacks Glycerol kinase, so phosphorylation can't be done hence glycerol produced in lipolysis is transported to liver
- The Fatty acids released by lipolysis in adipocytes enter circulation and are transported in a bound form with albumin.
- FFA enter various tissue and gives the energy
- 95% of energy obtained from Fat comes from oxidation of Fattyacids

β-oxidation of fatty acid :

The break down of a fatty acid to acetyl-CoA. . It occurs in the mitochondria. The 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 and RBC

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 involves three stages:

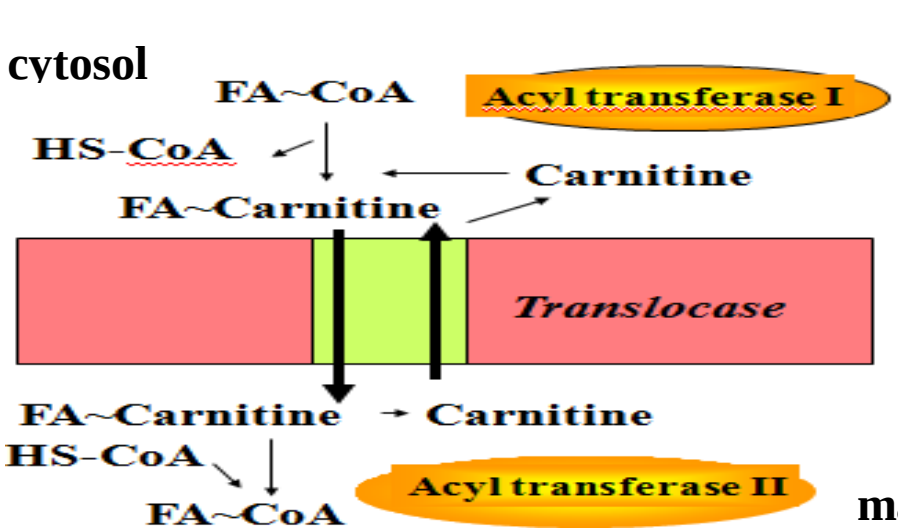
1. Activation of fatty acids in the cytosol
2. Transport of activated fatty acids into mitochondria (**carnitine shuttle**)
3. Beta oxidation proper in the mitochondrial matrix

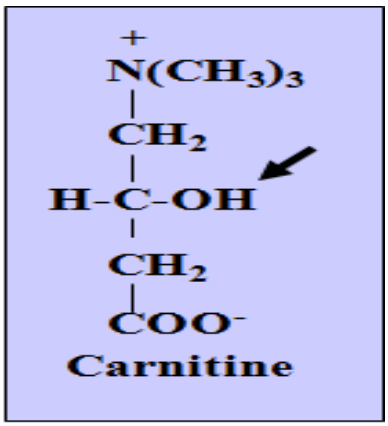
1) Activation of FA:

This proceeds by FA thiokinase (acyl COA synthetase) present in cytosol. Thiokinase requires ATP, COA SH, Mg^{++}. The product of this reaction is FAacyl 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



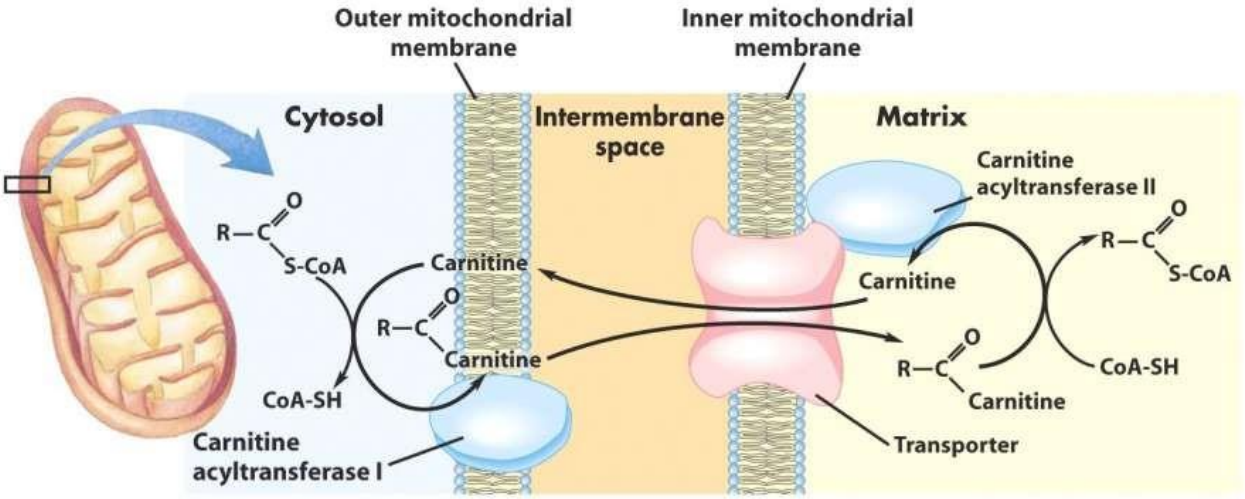


mechanism called **Carnitine shuttle**.

Transport of acyl CoA into themitochondria (rate-limiting step)

Acyl groups from acyl COA is transferred to carnitine to form acyl carnitine catalyzed by **carnitine acyltransferase I,** in the outer mitochondrial membrane..Acylcarnitine is then shuttled across the inner mitochondrial membrane by **a translocase** enzyme.The acyl group is transferred back to CoA in matrix by **carnitine acyl transferase II.**

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

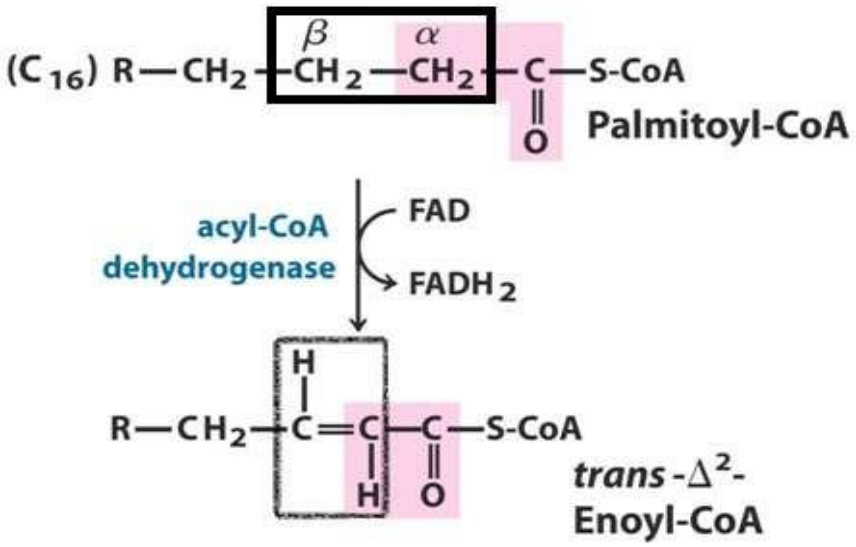
Step I – Oxidation by ***FAD linked dehydrogenase***

Step II – Hydration by **Hydratase**

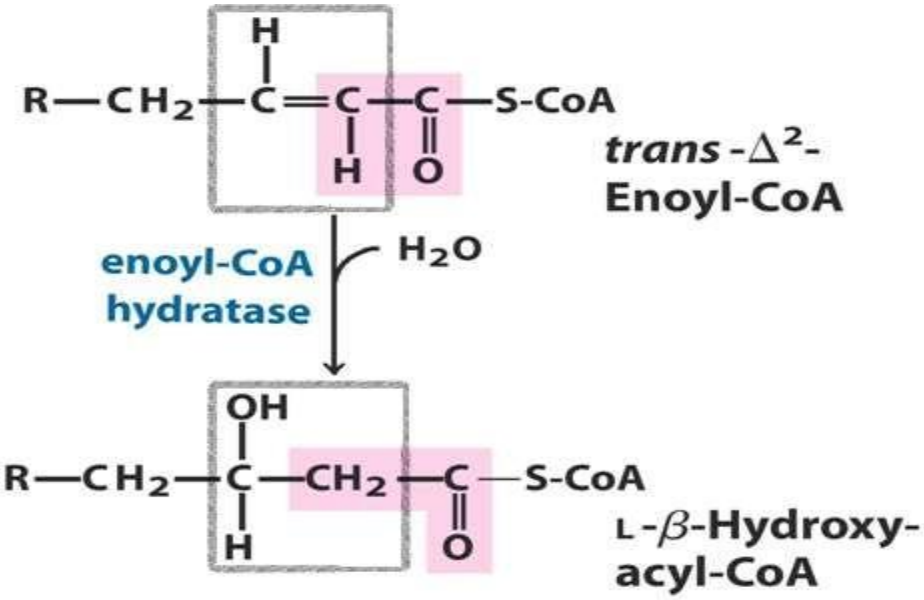
Step III – Oxidation by ***NAD linked dehydrogenase***

Step IV – Thiolytic clevage **Thiolase**

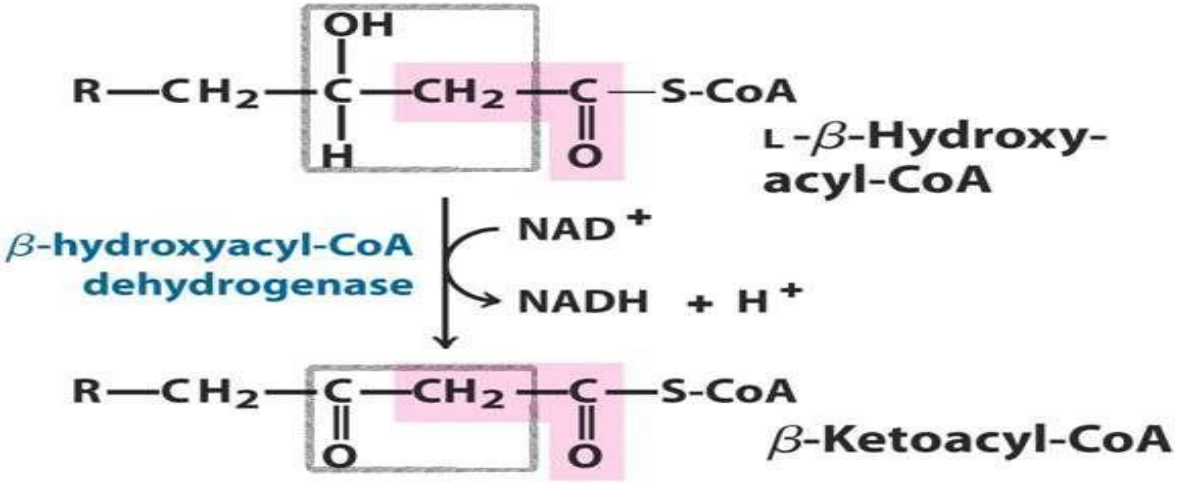
The first reaction is the oxidation of acyl CoA by an acyl CoA dehyrogenase to give α-β unsaturarted acyl CoA (enoyl CoA). FAD is the hydrogen acceptor.



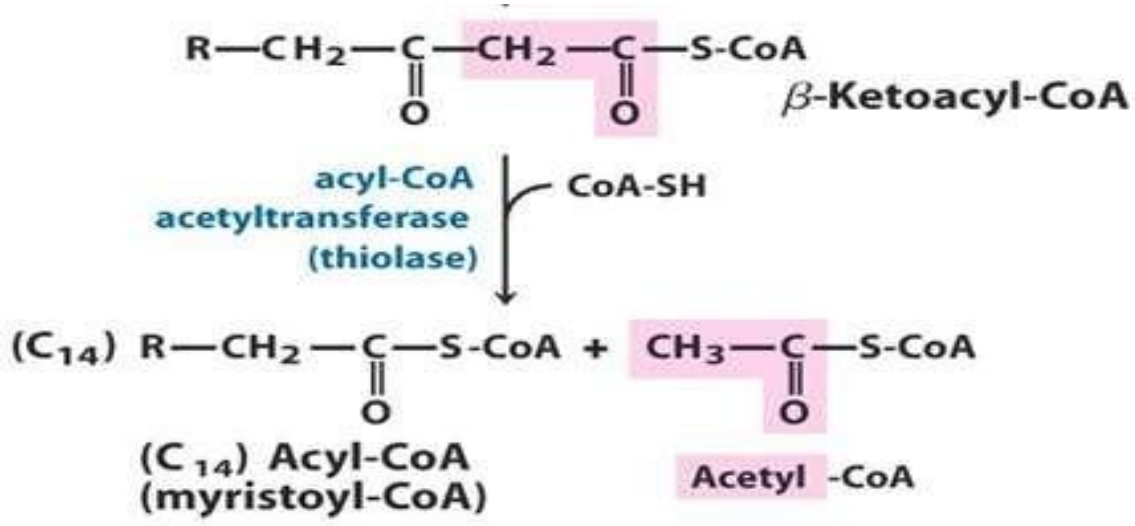
The second reaction is the **hydration** of the double bond to β-hydroxyacyl CoA (p- hydroxyacyl CoA).



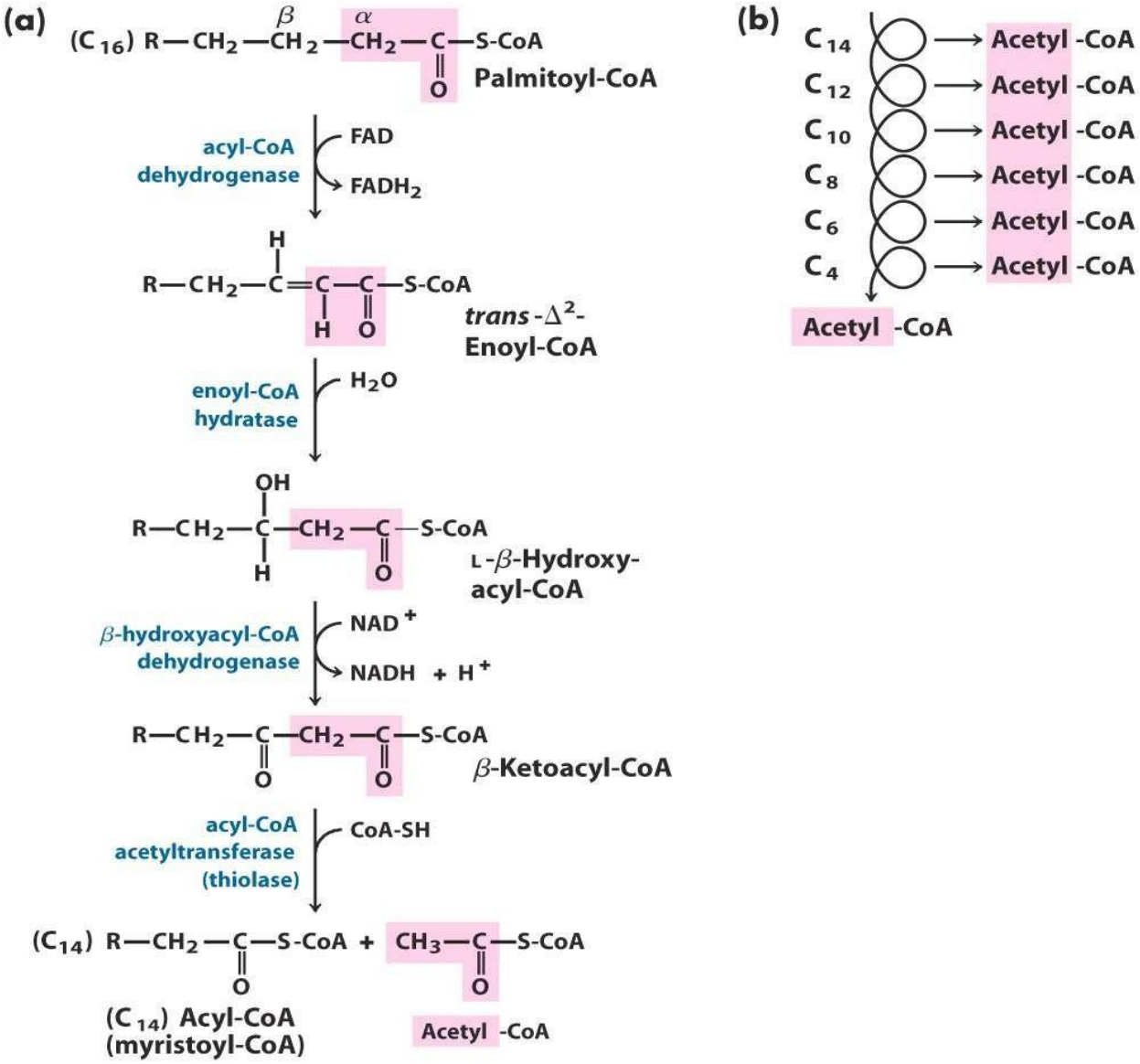
The third reaction is the **oxidation** of β- hydroxyacyl CoA to produce β-Ketoacyl CoA a NAD-dependent reaction.



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



BETA OXIDATION OF FATTY ACID:



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

Eg. Palmitic (16C):

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.

$$FADH_2 \longrightarrow 2\ ATP$$

$$NADH + H^+ \longrightarrow 3\ ATP$$

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. 2 ATP 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