قسم الكيمياء الحيوية
Biochemistry Department
College of Science - King Saud University

# Fatty Acid oxidation

# Fatty Acid oxidation

$$C^{\omega}H_3\text{-}(CH_2)n\text{-}C^{\beta}H_2\text{-}C^{\alpha}\ H_2\text{-}COOH$$

- Major Pathway
- β-oxidation

- Minor Pathway
- α-oxidation

 (branch-chain FA,e.g. Phytanic acid)
- ω-oxidation

# β-oxidation Pathway

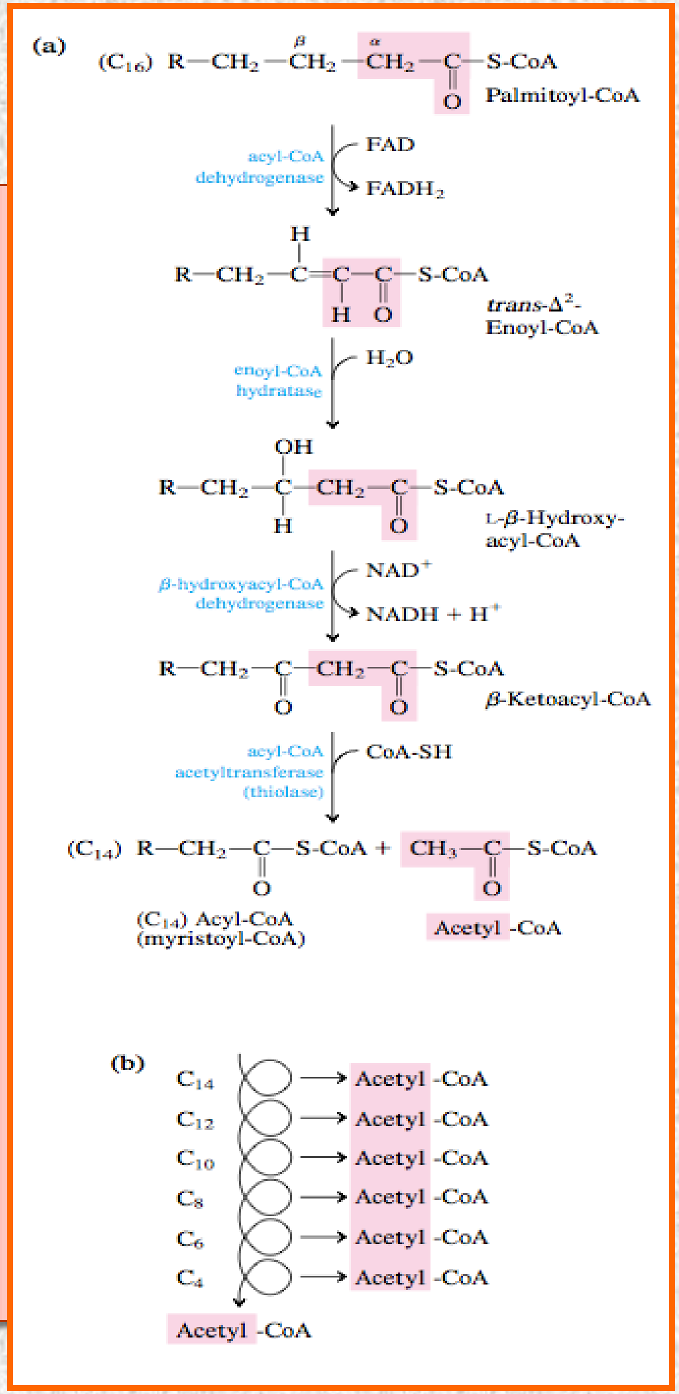
- Oxidation of fatty acids takes place in mitochondria where the various enzymes for fatty acid oxidation are present close to the enzymes of the electron transport chain.
- Fatty acid oxidation is a major source of cell ATP
- Oxidation of FAs occur at the β-carbon atom resulting in the elimination of the two terminal carbon atoms as acetyl CoA leaving fatty acyl CoA which has two carbon atoms less than the original fatty acid.
- **<u>β-oxidation has 4 steps:</u>**

1-Dehydrogenation (**FAD**-dependent)

2- Hydration

3-Dehydrogenation (**NAD**-dependent)

4-Cleavage (Remove 2C as acetyl CoA)



# Calculations

| Carbons in Fatty Acid | Acetyl CoA C/2 | β-oxidation cycles (C/2) -1 |
|---|---|---|
| 12 | 6 | 5 |
| 14 | 7 | 6 |
| 16 | 8 | 7 |
| 18 | 9 | 8 |

**Note:** In each round of β-oxidation *one molecule* of $FADH_2$ and *one molecule* of $NADH+H^+$ are produced which generates 2 and 3 ATP molecules, respectively

# *Example:* Energy of palmitoyl ~Co A (16 C) oxidation

- Number of cycles= n/2 -1 = 7 cycles
- Number of acetyl ~Co A = n/2 =8

→ So, 7 NADH, each provide 3 ATP when oxidized in the ETC 7X3=21 ATP

→ 7 $FADH_2$ each provide 2 ATP when oxidized in the ETC 7x 2=14 ATP

→ 8 acetyl ~Co A , each provides 12 ATP when converted to $CO_2$ & $H_2O$ by the TCA cycle 8x12= 96 ATP

So total energy yield of oxidation of palmitoyl ~Co A = 21 + 14 + 96 = 131 ATP

- As 2 molecules of ATP are used in the activation of a molecule of fatty acid →Therefore, there is a net yield of **129 molecules of ATP**

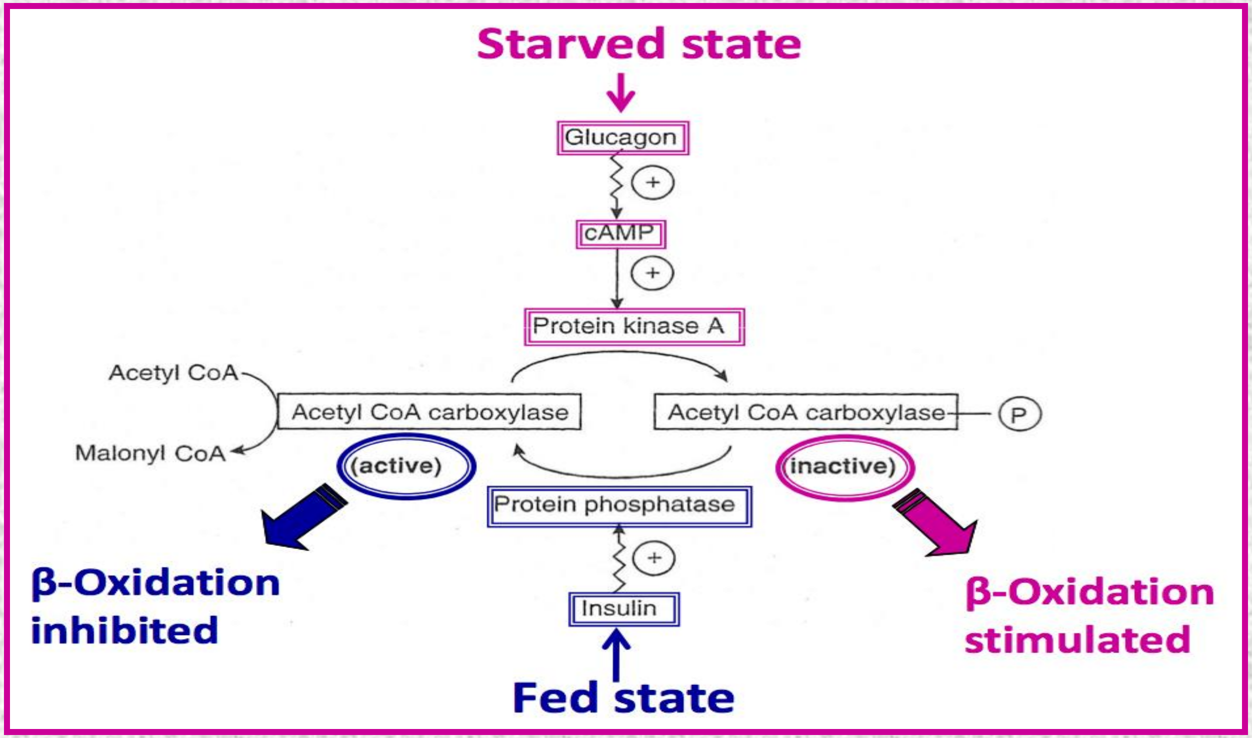
# Regulation of fatty acid β-oxidation

**1- The level of ATP in the cell :** If it is high in the cell, the rate of β- oxidation will decrease (Feed back inhibition)

**2- Malonyl-CoA**

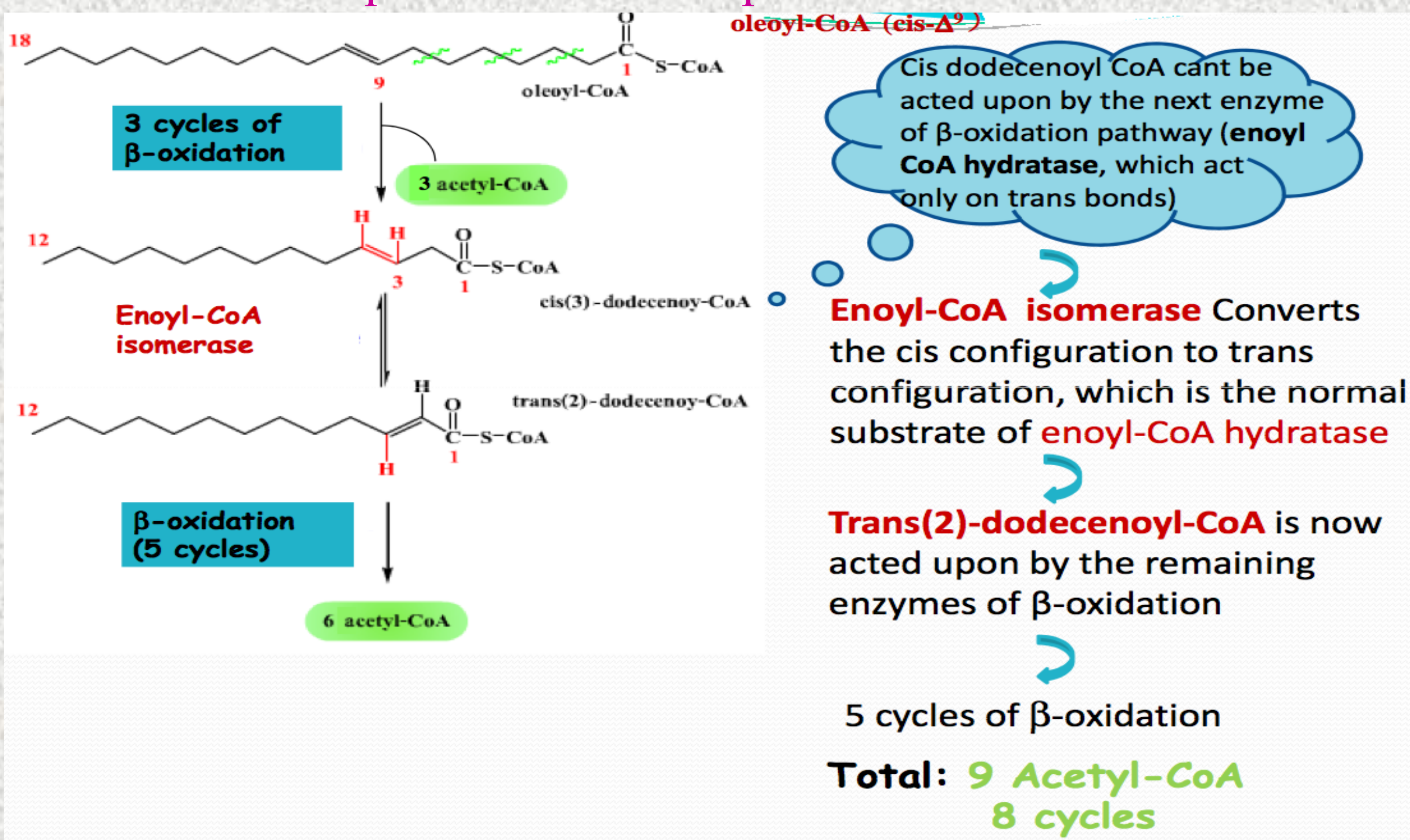
* (which is also a precursor for fatty acid synthesis) inhibits Carnitine Palmitoyl Transferase I and thus, inhibits β-oxidation

* Malonyl-CoA is produced from acetyl-CoA by the enzyme Acetyl-CoA Carboxylase



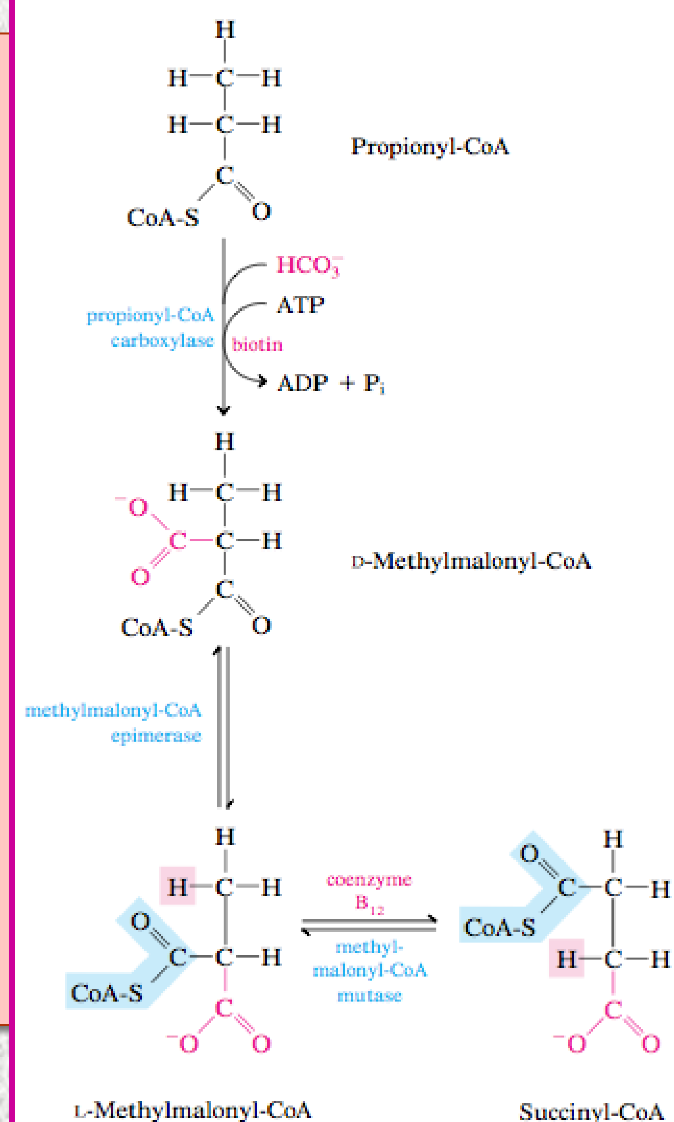
# Oxidation of Unsaturated Fatty Acid

- Slightly more complicated Requires additional enzymes
- Oxidation of unsaturated FAs produce *less energy* than that of saturated FAs (because they are less highly reduced, therefore, fewer reducing equivalents can be produced from these structures)



# Oxidation of Odd Numbered Fatty Acid

- Requires three additional extra reactions.
- Odd numbered lipids are present in plants and marine organisms
- Fatty acids with odd number of carbon atoms are also oxidized by the same process β-oxidation as even chain FAs, removing 2 carbons as acetyl CoA in each round of the oxidative process **BUT** the final round of β-oxidation of a fatty acid with an odd number of C atoms yields **acetyl-CoA** & **propionyl-CoA** (3C).



# Peroxisomes oxidize very long chain fatty acids

- Very long chain acyl-CoA synthetase facilitates the oxidation of very long chain fatty acids (e.g., C20, C22)
- These enzymes are induced by high-fat diets and by hypolipidemic drugs such as Clofibrate
- FAD is e- acceptor for peroxisomal acyl-CoA dehydrogenase, which catalyzes the 1st oxidative step of the pathway
- Within the peroxisome, $FADH_2$ generated by fatty acid oxidation is reoxidized producing hydrogen peroxide:

$$FADH_2 + O_2 \rightarrow FAD + H_2O_2$$

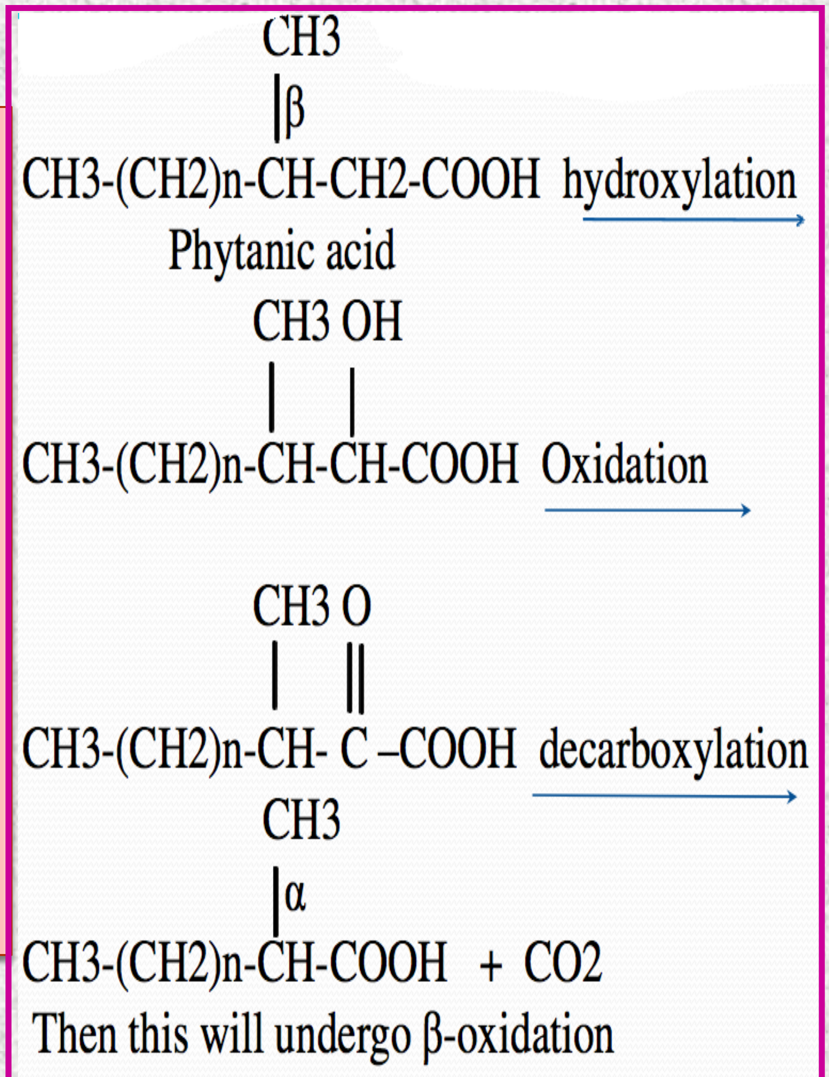
- The peroxisomal enzyme Catalase degrades $H_2O_2$:

$$2H_2O_2 \rightarrow 2H_2O + O_2$$

- These reactions produce no ATP
- ß-oxidation in the peroxisomes ends at octanoyl-CoA (C 8). It is subsequently removed from the peroxisomes in the form of octanoyl and acetylcarnitine and both are further oxidized in mitochondria.

# α-Oxidation Pathway

- α-oxidation occurs in brain tissue in order to oxidize short chain FAs
- Inα-oxidation,there is one carbon atom removed at time from α position
- It does not require CoA and does not generate high- energy phosphates
- This type of oxidation is significant in the metabolism of dietary FAs that are methylated on β-carbon e.g. phytanic acid (peroxisomes)



# ω-Oxidation Pathway

- ω-oxidation is a minor pathway and occurs in the endoplasmic reticulum of many tissues rather than the mitochondria, the site of β-oxidation.
- This process occurs primarily with medium chain FAs of adipose tissue which are mobilized to the liver under conditions of ketosis