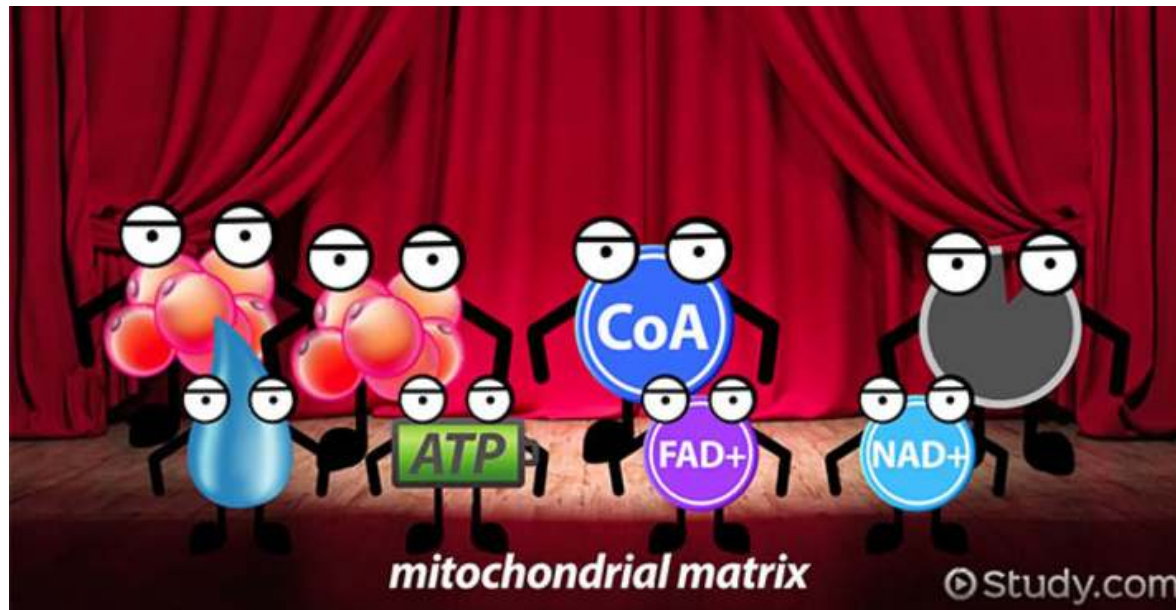


Beta oxidation of saturated fatty acid



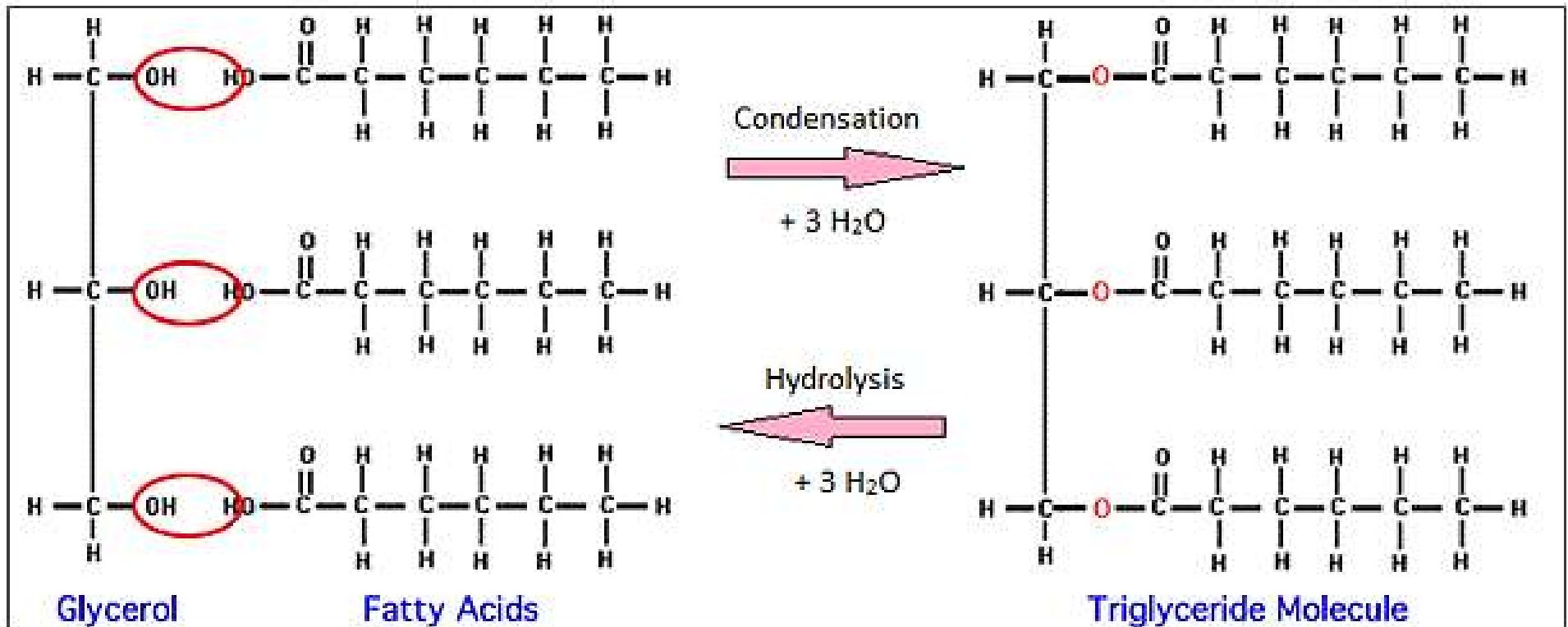
Necessity

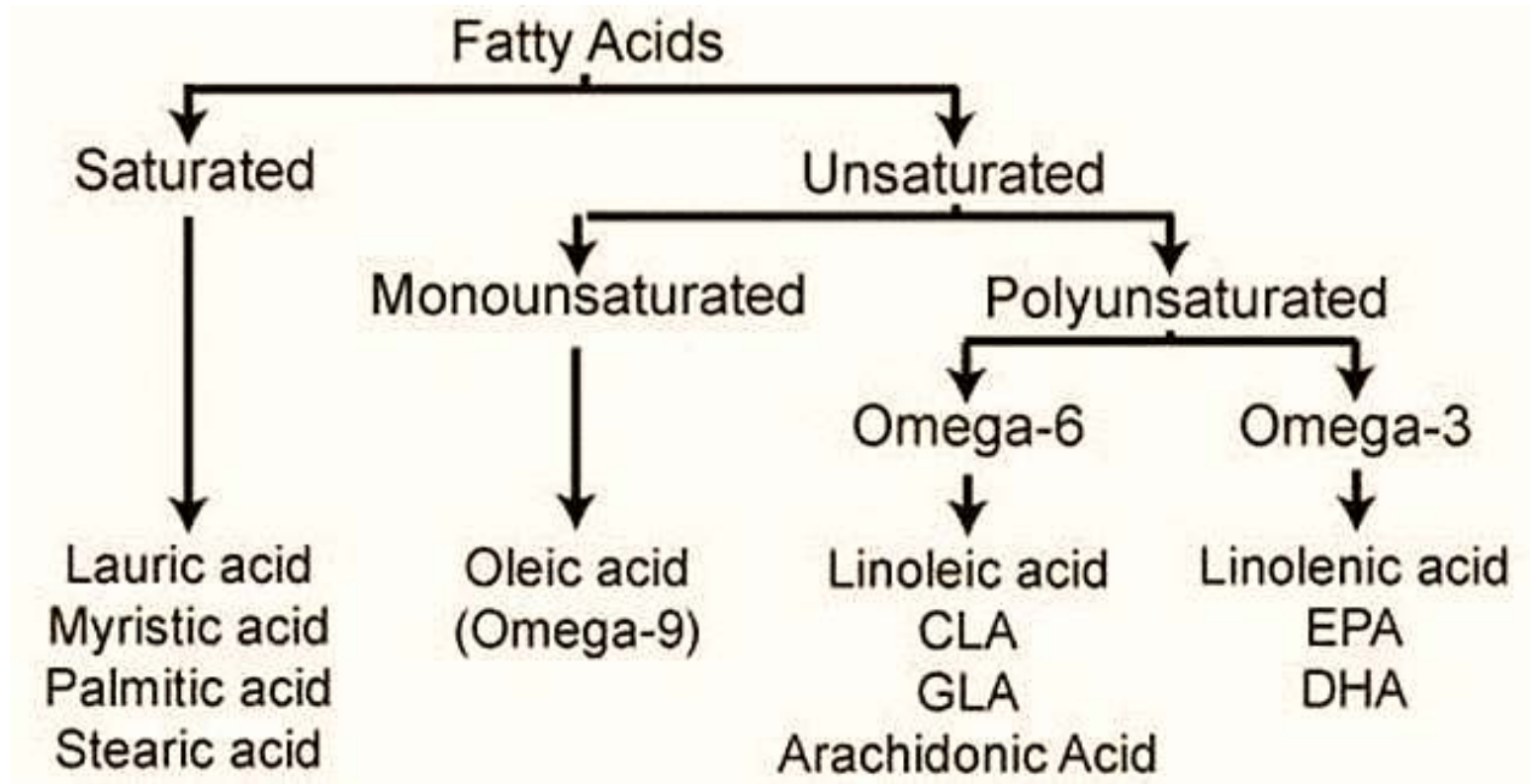
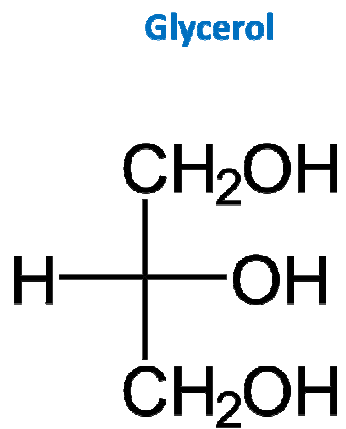
Fatty acid β -oxidation is a **multistep catabolic process** by which fatty acids are **broken down by various tissues to produce energy** in the cytosol in prokaryotes and in the mitochondria in eukaryotes to generate acetyl-CoA.



The rate of fatty acid oxidation changes in response to the nutritional and hormonal state of the animal. The rate of fatty acid oxidation is high during fasting but low in the fed animal.

Composition of lipid





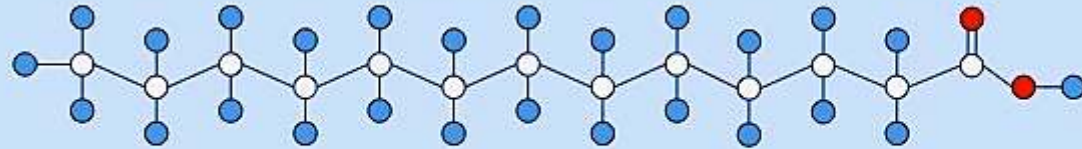
GLA (Gamma linoleic)

CLA (Conjugated linoleic acid)

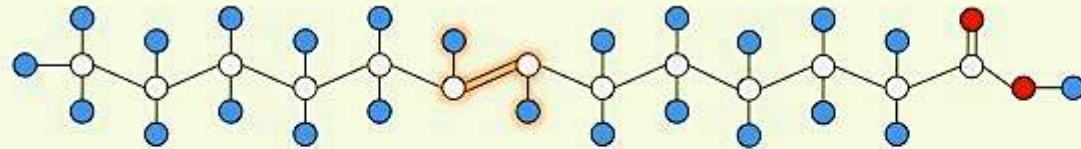
DHA (Docosahexanoic acid)

EPA (Eicosapentaenoic acid)

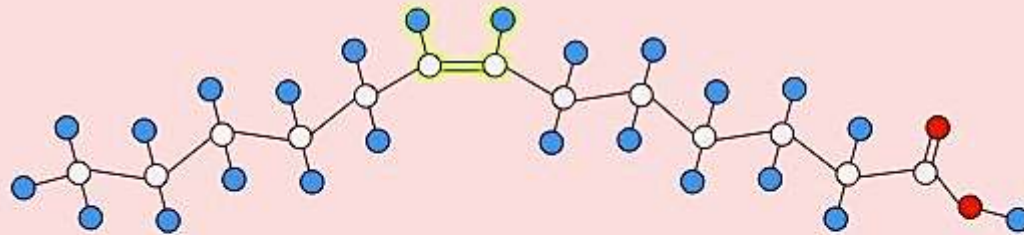
Saturated fatty acid
(*no* double bonds)



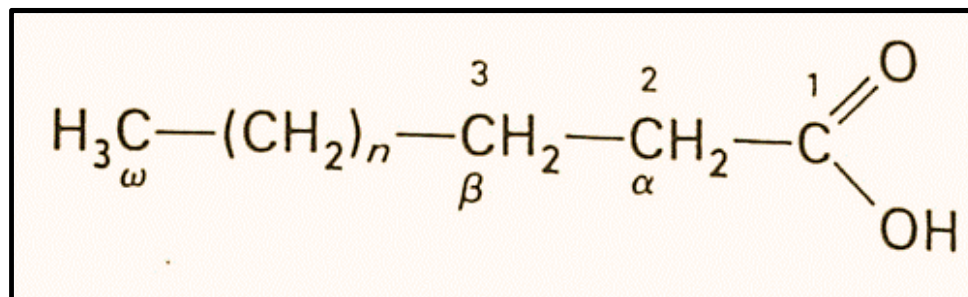
Unsaturated – *trans*
(H atoms opposite)



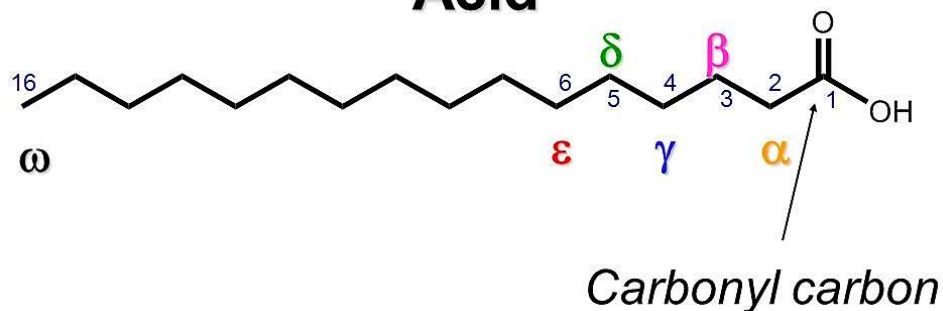
Unsaturated – *cis*
(H atoms same side)
⇒ *bent configuration*



Position of carbons in fatty acids



Naming Conventions: Palmitic Acid



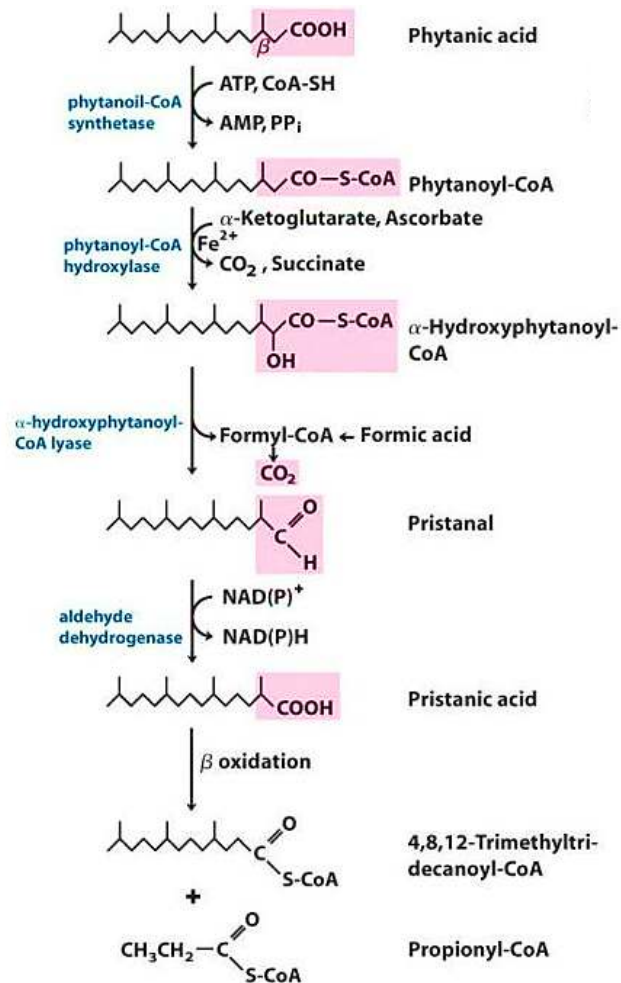
- ω omega, always the last alkyl carbon
- ϵ epsilon, fifth carbon after the carbonyl
- δ delta, fourth carbon after the carbonyl
- γ gamma, third carbon after the carbonyl
- β beta, second carbon after the carbonyl
- α alpha, first carbon after the carbonyl

Types of fatty acid oxidation

	Oxidation	Organelle	Fatty acids
Major	Beta oxidation	Mitochondria	Long, medium and short chain FA
	Beta oxidation	Peroxisomes	Very long chain FA
	Omega oxidation	Endoplasmic reticulum	Works only when mitochondria does not oxidize medium chain FA
	Alpha oxidation	Peroxisomes	Branched chain fatty acids

It is referred as “beta oxidation” because the beta carbon of the fatty acid undergoes oxidation to a carbonyl group.

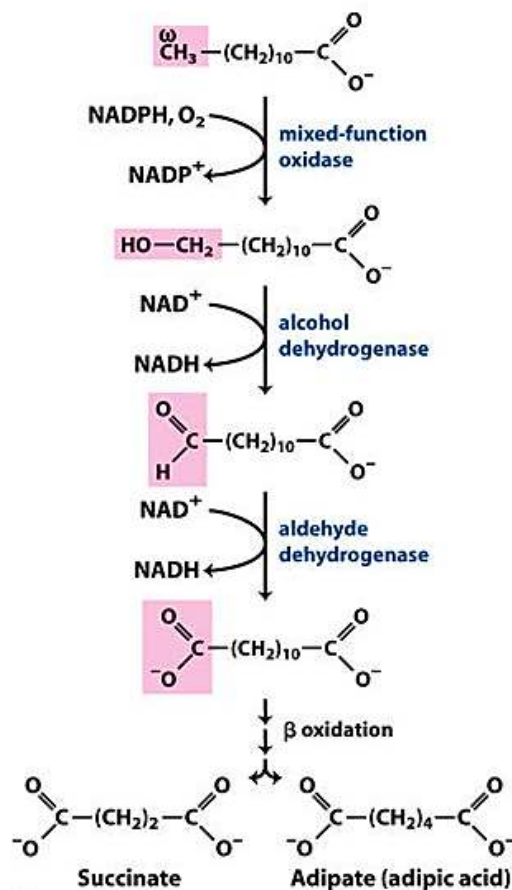
Alpha oxidation



- Stepwise decarboxylation.
- Peroxisome is the cellular site.
- Also occurs in brain and liver cells.
- No production of ATP.
- **Eg. Phytanic acid**

Omega oxidation

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1. There is another pathway in some species, including vertebrates, that involves oxidation of the omega carbon.
2. The enzymes unique to omega oxidation are located in the ER of liver and kidney.
3. The preferred substrates are fatty acids of 10 to 12 carbon.
4. The first step introduces a hydroxyl group on the omega carbon by mixed function oxidase involved in cytochrome p450 and NADPH.
5. This produces a carboxyl group at each end.
6. In each pass through the β -oxidation pathway, the double-ended fatty acid yields dicarboxylic acids such as succinic acid, which can enter the citric acid cycle.

Fatty acid beta oxidation

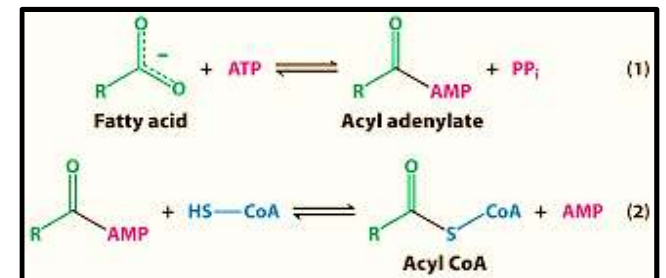
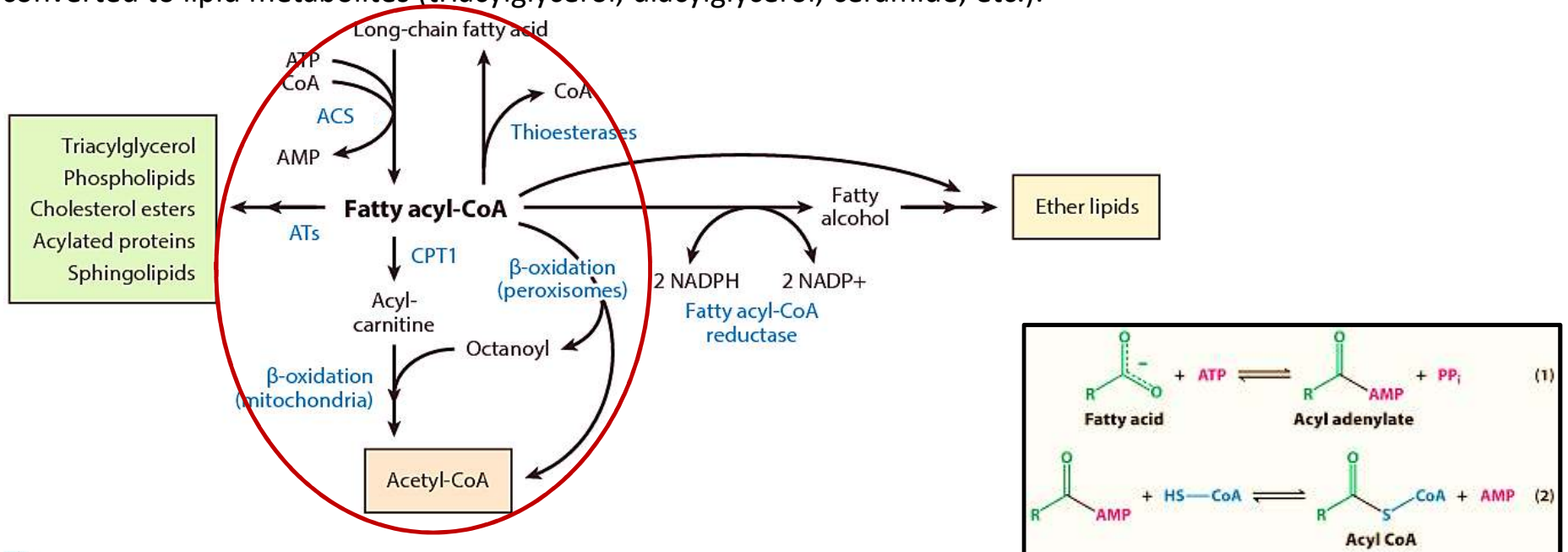
- Fatty acid oxidation is the **mitochondrial aerobic process** of breaking down a fatty acid **into acetyl-CoA units**. Fatty acids move in this pathway **as CoA derivatives utilizing NAD and FAD**.
- Fatty acids are **activated** before oxidation, utilizing ATP in the presence of CoA-SH and acyl-CoA synthetase.
- Long-chain acyl-CoA **enters mitochondria bound to carnitine**.
- Inside mitochondria beta oxidation of fatty acids takes place in which **two carbon atoms are removed in the form of acetyl-CoA from acyl-CoA at the carboxyl terminal**.
- The **bond is broken between the second carbon/beta carbon and the third carbon/gamma carbon**, hence the name beta oxidation.
- This process **provides energy** from fats.

Substrate: Free fatty acids

Products: One acetyl CoA, one NADH, and one FADH₂ for every removal of a two-carbon group from the fatty acid chain.

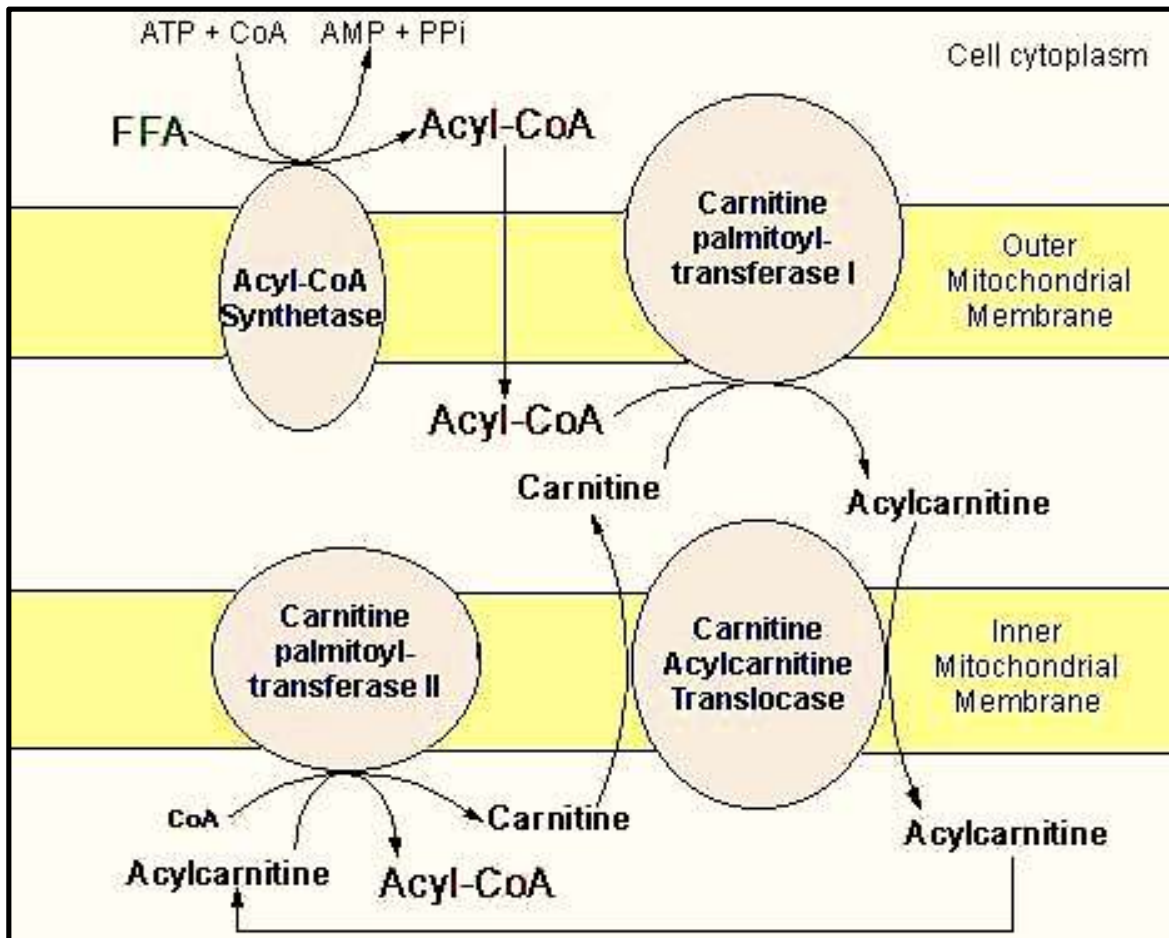
Step 1: Fatty acid esterification/activation to acyl-CoA

A fatty acid must be converted to fatty acyl-CoA in order for it to enter the mitochondria and be oxidized. The **enzyme responsible for esterification** of fatty acids to long-chain fatty acyl-CoA is **ACS (acyl-CoA synthase)**. For this reaction, FACS consumes the equivalent of **two ATP**. Another enzyme, **cytosolic thioesterase (CTE)**, **can remove the CoA** converting the fatty acyl-CoA back to a fatty acid. Fatty acyl-CoA can either be converted to acyl carnitine, allowing it to be transported into the mitochondria and enter fatty acid β -oxidation or be converted to lipid metabolites (triacylglycerol, diacylglycerol, ceramide, etc.).



Step 2: Carnitine shuttle

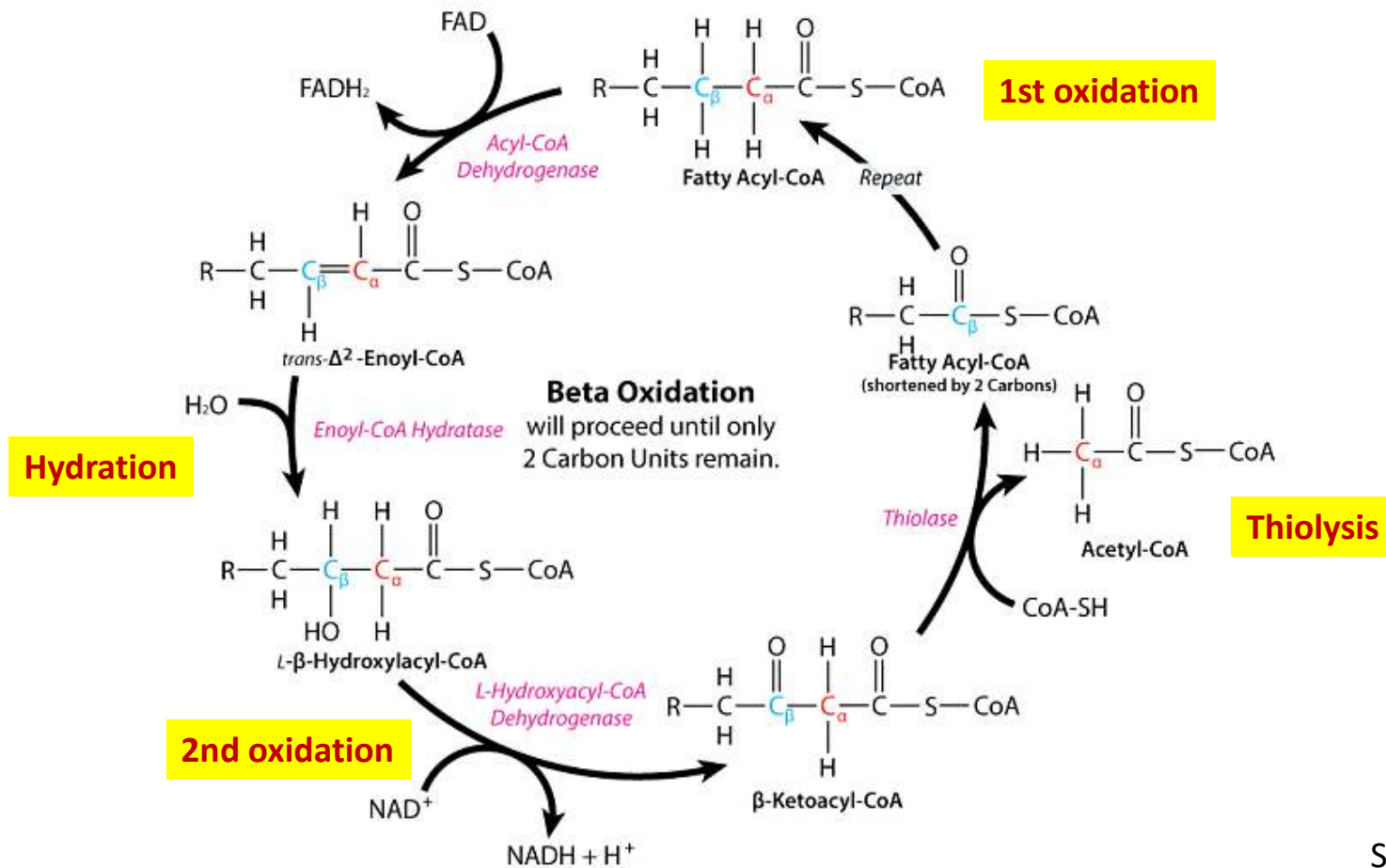
Subhadipa 2021



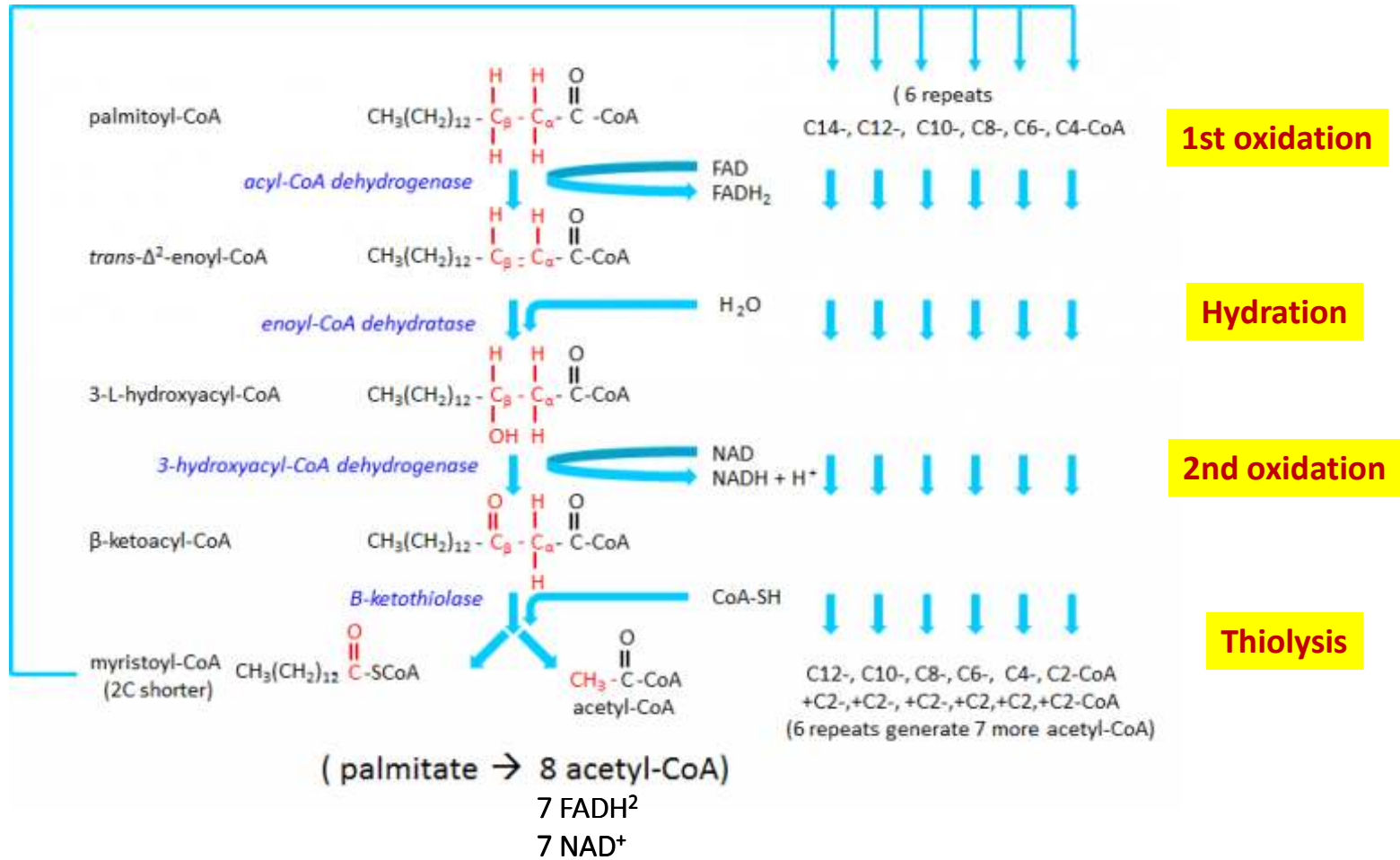
The carnitine shuttle represents a mechanism by which long-chain fatty acids, which are impermeable to the mitochondrial membranes, are transported into the mitochondrial matrix for the purpose β -oxidation and energy production.

Step 3: 1st oxidation, hydration, 2nd oxidation and thiolysis

During beta-oxidation, fatty acid molecules are broken down by removing two-carbon units from the carboxyl end of a fatty acid molecule to produce acetyl-CoA.



Beta oxidation (C16:0, Palmitic acid)



Energy production

The energetic yield of β -oxidation of Palmitic acid
– to eight acetyl coenzymes A

Palmitoyl CoA + 7 FAD + 7 NAD⁺ + 7 H₂O + 7 CoA → 8 acetyl CoA + 7 FADH₂ + 7 NADH + 7 H⁺

↓ ↓

14 ATP + 21 ATP – 2 ATP (activation of Palmitic acid)

– and eight acetyl CoA in the Citrate cycle

↓

8 X 12 ATP = 96 ATP

Net yield of complete Palmitic acid oxidation to CO₂

14 ATP + 21 ATP – 2 ATP + 96 ATP = 129 ATP

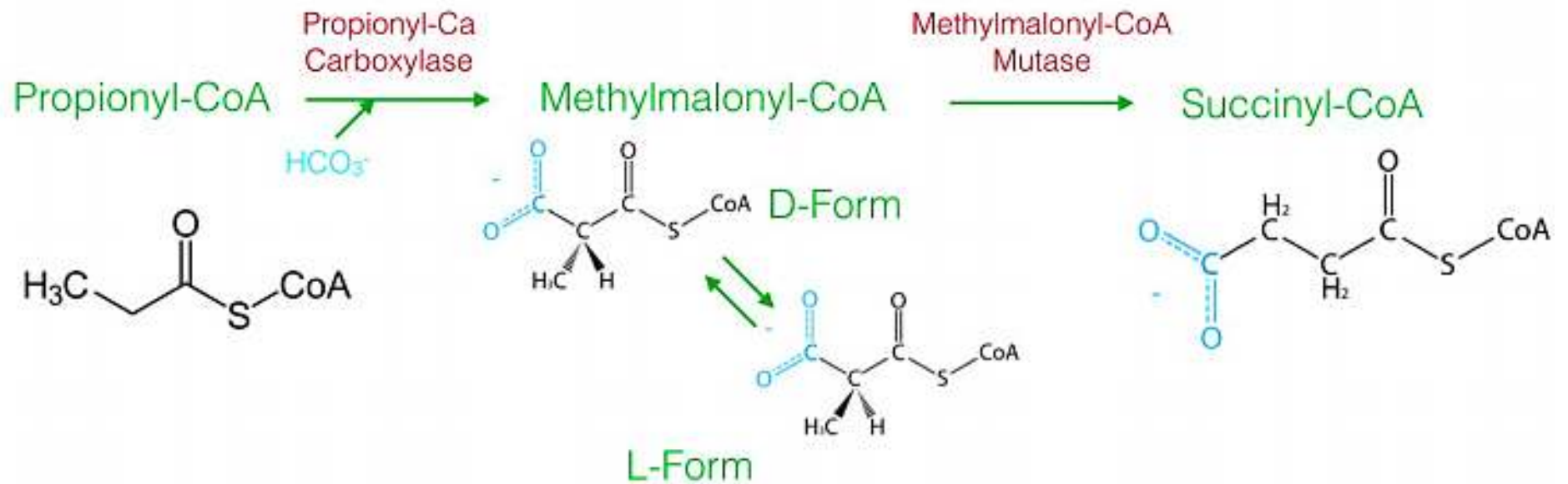
Standard free energy of Palmitic acid = 2340 Cal

Energy yield by its oxidation 129 ATP = 7.3 X 129 = 940 Cal

NET YEILD = 940/2340 X 100 = 40%

60% is used for HEAT GENERATION

Odd chain fatty acid oxidation



Purpose of beta oxidation

- Mitochondrial fatty acid β -oxidation is the major pathway for the degradation of fatty acids and is essential **for maintaining energy homeostasis** in the human body.
- Fatty acids are a crucial energy source in the post-absorptive and fasted states when glucose supply is limiting. But even when **glucose is abundantly available**, it is a **main energy source for the heart, skeletal muscle, and kidney**.
- It supplies energy during sustains **muscular work, cold thermogenesis, prolonged flight of birds, prolonged swims of migratory fishes and whales, also in case of carbohydrate deprivation stress and starvation**.
- Series of enzymes, transporters, and other facilitating proteins are involved in this process. **Recessively inherited defects** are known for most of the genes encoding these proteins. The clinical presentation of these disorders may include **hypoketotic hypoglycemia, (cardio)myopathy, arrhythmia, and rhabdomyolysis** and illustrates the importance beta oxidation during fasting and in hepatic and (cardio)muscular function.

Peroxisomal β -oxidation

- A secondary form of (oxidation occurs in microbodies that is peroxisomes) of the liver and kidney.
- It differs from its mitochondrial counterpart in several respects:
 - i. It is quantitatively less important.
 - ii. Entry of fatty acyl-CoA does not require the carnitine shuttle, for peroxisomes lack carnitine palmitoyltransferase I (CPT-I).
 - iii. Oxidation is catalyzed by different enzymes, such as oxidases that require a high oxygen tension, and produce H_2O_2 as a by-product.
 - iv. Catalase is a prevalent enzyme in peroxisomes.