Lipids and lipid metabolism

Lipids are the fraction of animal and vegetable tissues which can be extracted with organic solvents such as chloroform, benzene, and petroleum ether. A wide variety of lipids occurs in animals and plant tissues. Lipids are classified as follow:

1. Fatty acids
2. Triglycerols
3. Phospholipids
4. Sphingomyeliens
5. Glycosphingolipids
6. Steroids

1. Fatty acids :

The naturally occurring fatty acids are monocarboxylic acids with unbranched hydrocarbon chains. Most of fatty acids have even no. of carbon atoms, although some contain odd number of carbon atoms. Some are saturated and others are saturated having one or more double bonds.

a. *Saturate Fatty Acids*: properties of saturated fatty acids depend upon the polar carboxylic group and partly on the non-polar hydrocarbon chain.

For example:

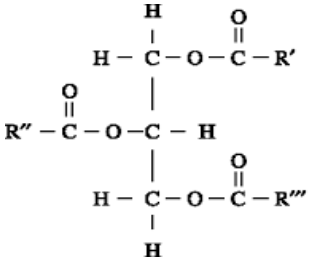
- Acetic acid and Propionic acid are miscible with water
- Butyric acid and Caproic acid have limited solubility with water
- Higher members are insoluble in water but soluble in organic solvent
- Boiling points and melting points of fatty acids rise with increase in chain length
- Saturated fatty acids with less than 10 carbons are liquid at room temperature

S No	Common Name	IUPAC Name	Chemical Formula
1	Acetic acid	Ethanoic acid	CH3COOH
2	Propionic acid	Propanoic acid	CH3CH2COOH
3	Butyric acid	Butanoic acid	CH3(CH2)2COOH
4	Caproic acid	n-Hexanoic acid	CH3(CH2)4COOH
5	Caprylic acid	n-Octanoic caid	CH3(CH2)6COOH
6	Capric acid	n-Decanoic caid	CH3(CH2)8COOH
7	Lauric acid	n-Dodecanoic acid	CH3(CH2)10COOH
8	Myristic acid	n-Tetradecanoic acid	CH3(CH2)12COOH
9	Palmitic acid	n-Hexadecanoic acid	CH3(CH2)14COOH
10	stearic acid	n-Octadecanoic acid	CH3(CH2)16COOH

b. ***Unsaturated Fatty Acid:*** Unsaturated fatty acids are characterized by presence of one or more double bonds. Unsaturated fatty acids are classified as *Monoenoic*, *Dienoic*, *Trienoic* and *Polyenoic acids.* Those unsaturated fatty acids with two or more double bond are known as polyunsaturated fatty acids.
For example:

S No	Common Name	Melting point	Chemical Formula
1	Oleic acid	4 °C	$CH_3(CH_2)_7CH=CH(CH_2)_7COOH$
2	Linoleic acid	-5 °C	$C_{18}H_{32}O_2$
3	Linolenic acid		$C_{18}H_{30}O_2$
4	Arachidonic acid	-49.5 °C	$C_{20}H_{32}O_2$

2. Triacylglycerol: Triglycerols are the most abundant group of lipids. Triacylglycerol included in group are lard, tallo, butter fate, olive oil, cotton seed oil, corn oil, peanut oil, coconut oil and soya been oil (vegetable oils). There molecule consist of ester between glycerol and long chain fatty acids.



3. Phospholipids: Phospholipids are ester of either Glycerol or of Sphygnosine (long chain dihydric amino alcohol one double bond).

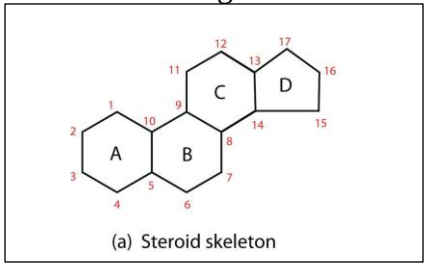
Glycerol + Two fatty acyl units + Phosphate	Phosphatidic acid + an alcohol
Components of Phosphatidic acid	Components of Phosphoglycerides

I. Phospatidylcholine (Lecithin)
II. Phosphotidylethanolamine
III. Phosphotidylserine

4. Steroids: steroids are usually insoluble in water but soluble in organic solvents and fates. Steroids possess the characteristics steroidal nucleus three rings 6-membered and one ring 5-membered. Steroids are physiologically very active.

Example of steroids:

I. Bile acids (Cholic acid)
II. Vit. D2 precursor (Ergosterol)
III. Sex hormones (Estrogen, Progesterone, Testosterone, Andosterone)



(a) Steroid skeleton

LIPID METABOLISM

Lipid metabolism states the degradation of lipids within the animal body which involve breakdown and storage of energy within human body. Lipids generally obtained from food and other fatty supplements like butter, milk, cheese oils and animal food. This substance generally converted into simpler structure fatty acid within liver. Synthesis of fat is termed as lipogenesis. Commonly found lipids within human body are triglycerides, cholesterol, fatty acids and membrane lipids. Lipid metabolism is considered as the digestion and absorption path for dietary fat. There are two ways in which organism can use fatty substance to obtain energy: utilize dietary fat and stored fat.

All living organism use both method of fate usage as a source of energy for various organs like as heart. Lipids are hydrophobic molecule, which need to be solubilized before metabolism start. Lipid metabolism generally started with hydrolysis which occurs with the help of various digestive enzymes.

I. **Need for Lipid Metabolism:** Lipid metabolism are important in following aspects:
   - Oxidation of lipids provides heat and energy.
   - Lipids are stored for further utilization.
   - Lipids are used for the synthesis of phospholipids and glycolipids.
   - Lipids are also required for the synthesis of Vit. D, bile salt and steroid hormones.

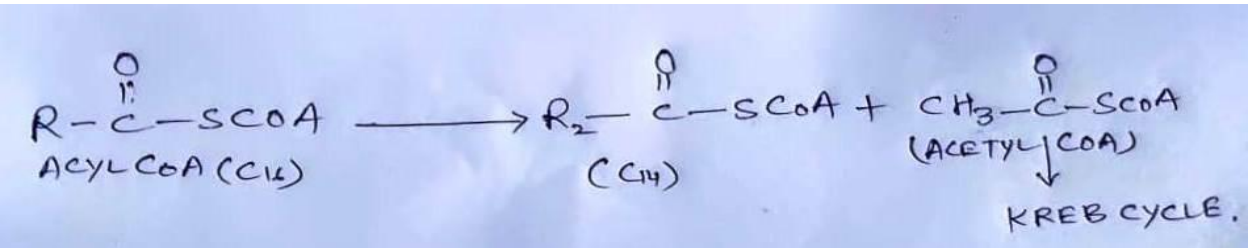
1. **Lipid metabolism:** lipid metabolism includes following reaction:
   a) Oxidation of fatty acids
   b) Biosynthesis of fatty acids
   c) Cholesterol synthesis

Lipids/fats are hydrolyzed and yield fatty acids and glycerol in the presence of enzyme lipase. Glycerol utilized by glycolytic pathway of carbohydrates. Fatty acids can be used for the synthesis of phospholipids, glycolipids, lipoproteins and energy production.

a) Oxidation of fatty acids:

Fatty acids can be oxidized by α, β and γ-oxidation. Among three most important pathway is β–oxidation.

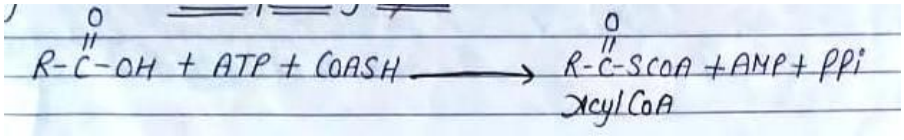
β ***–Oxidation:*** It is the catabolic process by which fatty acids molecule is broken down to generate Acetyl CoA enzyme which enter the citric acid cycle.



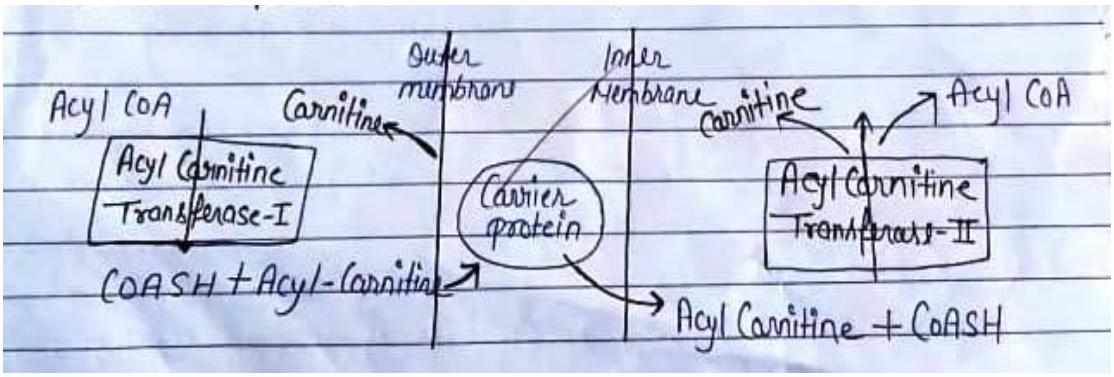
β –Oxidation involve following steps:

I. Activation of fatty acid
II. Transport of fatty acid to mitochondrial matrix
III. β –Oxidation proper

Activation of fatty acid:



Transport of Acyl CoA to mitochondrial matrix

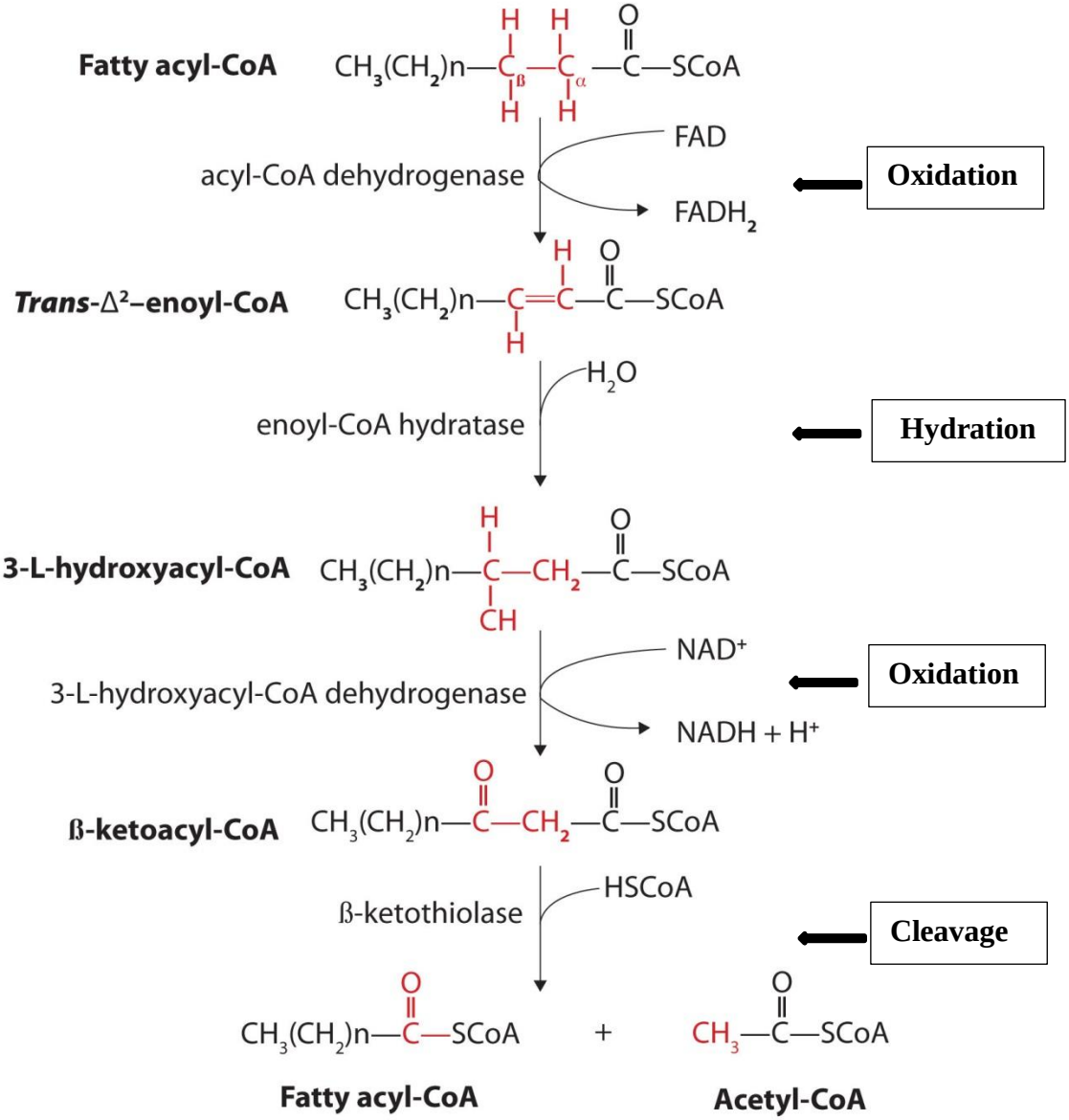


- Acyl CoA bind with Carnitine and form acyl Carnitine shuffle with the help of enzyme Acyl Carnitine Transferase-I.
- Carnitine shuffle transfer the acyl moiety from cytosol to mitochondria matrix via carrier protein.
- Acyl Carnitine Transferase-II present in inner membrane of mitochondria and release the acyl moiety to bind with CoASH and from Acyl CoA.
- Carnitine becomes free and comes to outer membrane for further process.

β –Oxidation proper:

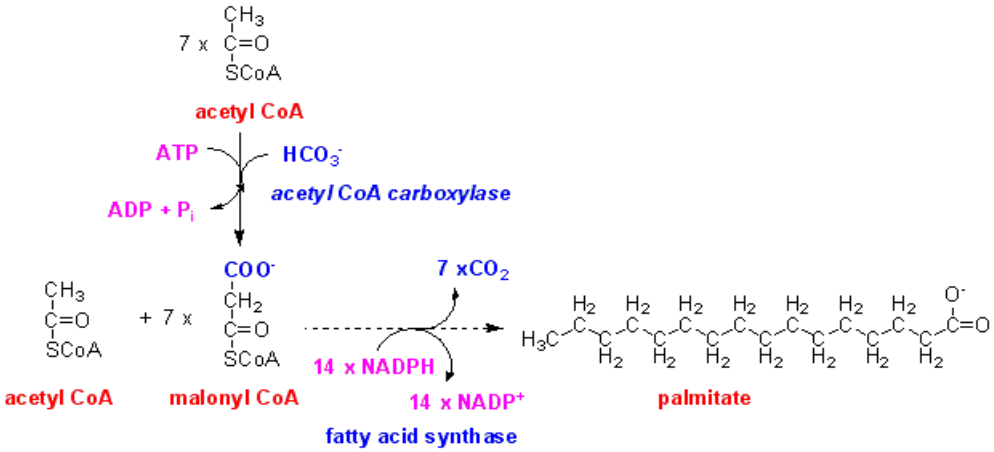
Occurs in mitochondrial matrix & involve four steps:

a) oxidation
b) hydration
c) oxidation
d) cleavage


Fatty acyl-CoA
CH3(CH2)n—Cβ—Cα—C—SCoA
acyl-CoA dehydrogenase
FAD
FADH2
Oxidation
Trans-Δ²–enoyl-CoA
CH3(CH2)n—C=C—C—SCoA
enoyl-CoA hydratase
H2O
Hydration
3-L-hydroxyacyl-CoA
CH3(CH2)n—C—CH2—C—SCoA
3-L-hydroxyacyl-CoA dehydrogenase
NAD+
NADH + H+
Oxidation
ß-ketoacyl-CoA
CH3(CH2)n—C—CH2—C—SCoA
ß-ketothiolase
HSCoA
Cleavage
CH3(CH2)n—C—SCoA
+
CH3—C—SCoA
Fatty acyl-CoA
Acetyl-CoA

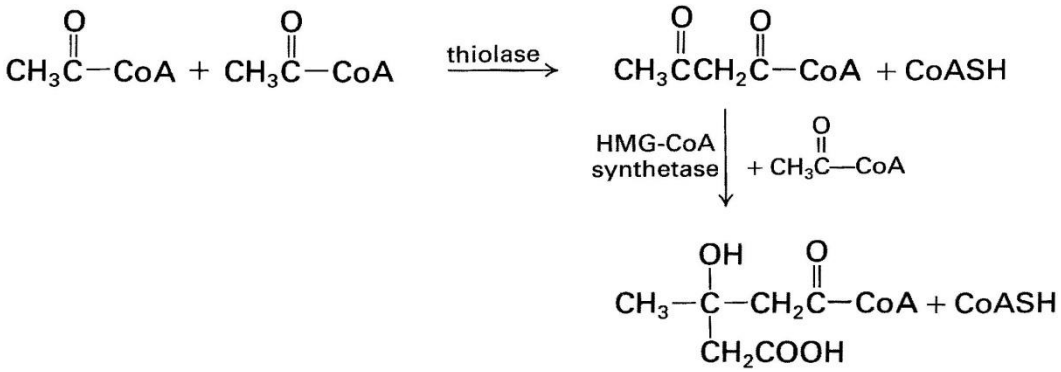
b) Biosynthesis of fatty acids

Fatty acid synthesis is the formation of fatty acids from acetyl-coA and NADPH through the action of enzymes called fatty acid synthases. This process occurs in the cytoplasm of the most cells. Most of the acetyl-CoA which is converted into fatty acids is obtained from carbohydrates via the glycolytic pathway. The glycolytic pathway also produce glycerol with which three fatty acids can combine to form triglycerides also known as "triacylglycerols" the final product of the lipogenic process. When only two fatty acids combine with glycerol and the third alcohol group is phosphorylated with a group such as phosphatidylcholine, a phospholipid is formed. Phospholipids constitute the bulk of the lipid bilayers that make up cell membranes within the cells (e.g. the cell nucleus, mitochondria, endoplasmic reticulum, Golgi apparatus etc.



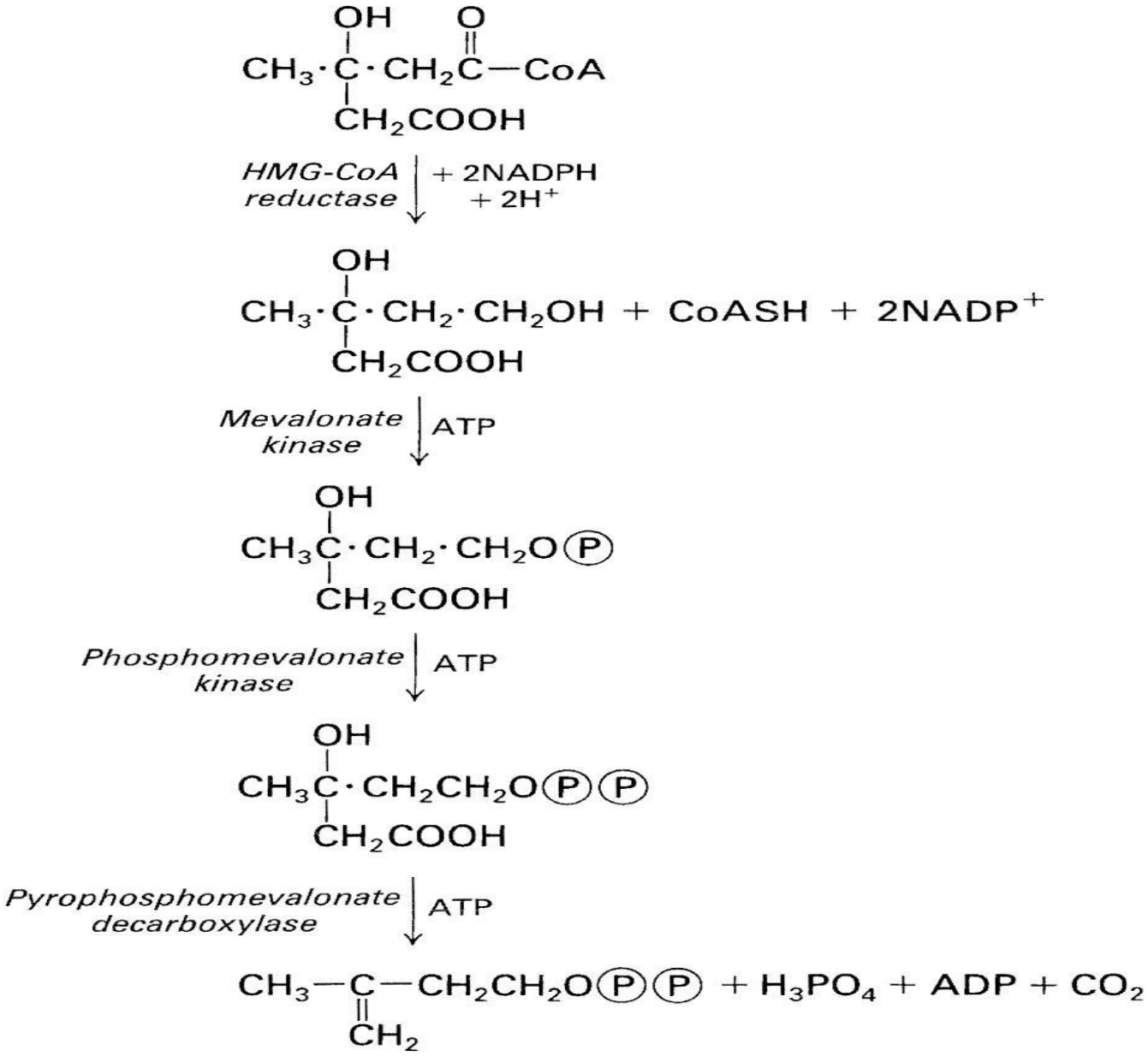
c) Cholesterol synthesis:

- Synthesis of 3-hydroxy-3-methyglutaryl-CoA (HMG-CoA).
- Condensation of acetyl-CoA takes place in the ***cytoplasm***.
- HMG-CoA synthase is a ***microsomal*** enzyme.



Role of HMG-CoA reductase

- The microsomal enzyme that converts HMG-CoA to mevalonate
- It is rate-limiting and regulatory enzyme for cholesterol synthesis



Ketone body synthesis

Three types of ketone bodies are synthesized in our body that is acetone, β-hydroxybutyrate and acetoacetate.

- Supply of fatty acids in the liver → ketone body synthesis
- In liver mitochondria do not have enough oxaloacetate to oxidize all of the acetyl-CoA produced from fatty acid oxidation. Acetyl-CoA is used to produce ketone bodies in the mitochondria.

Ketone body synthesis