LIPIDS

Lipid

- Lipids are organic compounds of biological nature that includes fats, oils and waxes. They are insoluble in water but soluble in nonpolar solvents such as ether, chloroform and benzene. Lipids are utilizable by living organisms.
- In the normal mammal at least 10 to 20 percent of the body weight is lipid. They form important dietary constituent on account of their high calorific value and fat soluble vitamins (vitamins A, D, E and K) along with the essential fatty acids.
- Lipids are distributed in all organs, particularly in adipose tissues in which lipids represent more than 90 percent of the cytoplasm of a cell.

Biological functions of lipids:-

- 1. Body lipids are reservoir of potential chemical energy. Lipids can be stored in the body in almost unlimited amount in contrast to carbohydrates. Furthermore, lipids have a high calorific value (9.3 calories per gram) which is twice as great as carbohydrate. Large amount of energy is stored as lipid than as carbohydrates
- 2. Lipids which forms the major constituent of bio-membranes are responsible for membrane integrity and regulation of membrane permeability.
- 3 The subcutaneous lipids serve as insulating materials against atmospheric heat and cold and protect internal organs.

- They serve as a source of fat soluble vitamins (Vitamin A, D, E and K) and essential fatty acids. (Linoleic, Linolenic and Arachidonic acid).
- 5. Lipids serve as metabolic regulators of steroid hormones and prostaglandins.
- 6. Lipids present in inner mitochondrial membrane actively participate in electron transport chain.
- 7. Polyunsaturated fatty acids help in lowering blood cholesterol.
- 8. Squalamine, a steroid, is an potential antibiotic and antifungal agent

Fatty acids

- The fatty acids

are the basic units of lipid molecules.

Fatty acids are derivatives of aliphatic hydrocarbon chain that contains a carboxylic acid group.

Over 200 fatty acids have been isolated from various lipids.

- They differ among themselves in hydrocarbon chain length, number and position of double bonds as well as in the nature of substituents such asoxy-, keto-, epoxy groups and cyclic structure.

Depending on the absence,or presence of double bonds, they are classified into saturated andunsaturated fatty acids.

- Saturated fatty acids, do not contain double bonds. The hydrocarbon chain may contain 12 to 18 carbon atoms. eg. palmitic andstearic acids.

- $CH_3(CH_2)_{14}COOH$ - Palmitic acid (C-16).
- $CH_3(CH_2)_{16}COOH$ - Stearic acid (C-18).

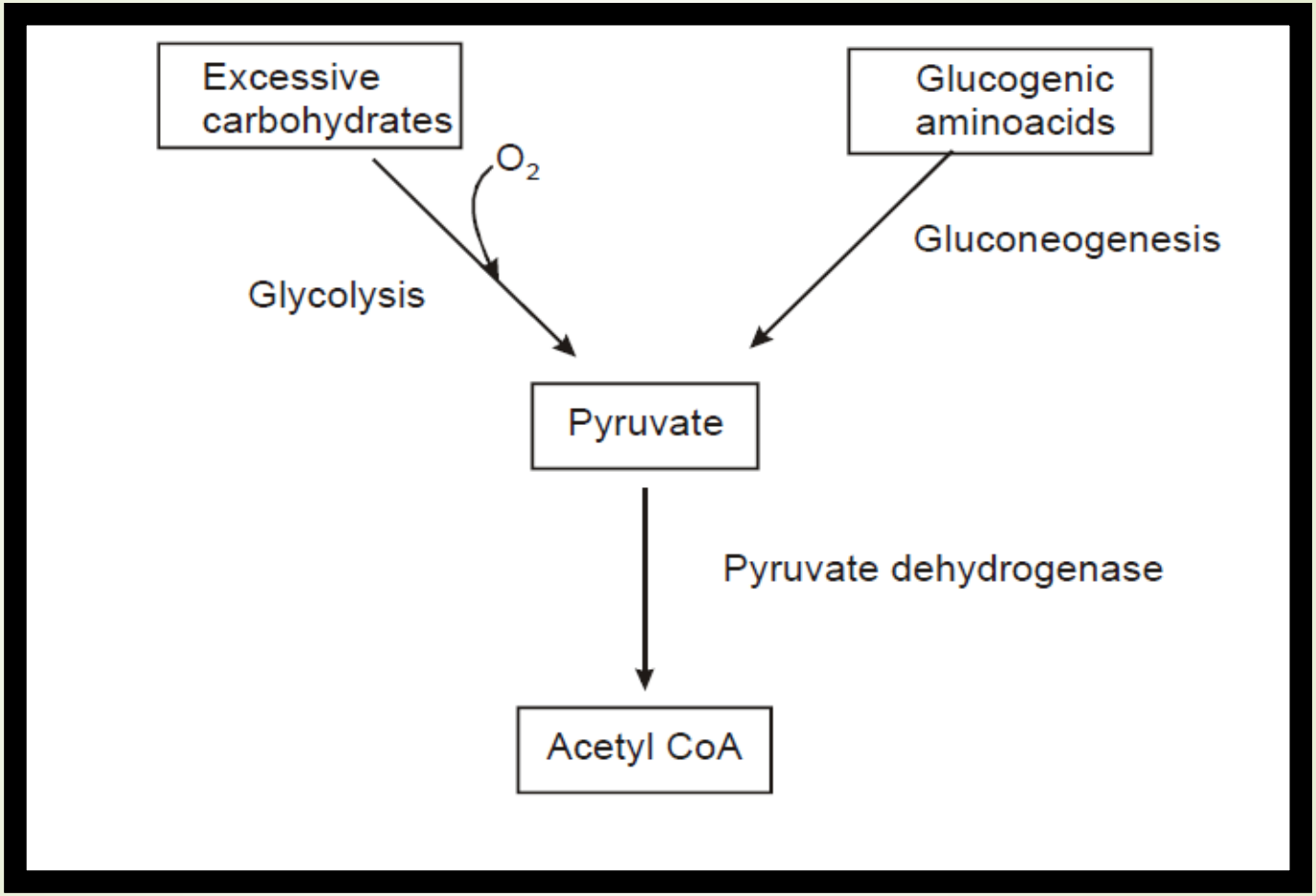
- **Unsaturated fatty acids** are classified into different types depending on the number of double bonds present in the hydrocarbon chain. These fatty acids are mainly found in plant lipids.

- **Essential fatty acids**
- Fatty acids required in the diet are called essential fatty acids (EFA). They are not synthesized by the body and are mainly polyunsaturated fatty acids (PUFA).
- **eg. Linoleic acid**
- **Linolenic acid**
- **Arachidonic acid**

- **Functions of essential fatty acids**
- They are required for membrane structure and function, transport of cholesterol, formation of lipoproteins and prevention of fatty liver.
- **Deficiency of essential fatty acids**
- The deficiency of essential fatty acid results in phrynoderma or toad skin.

Biosynthesis of fatty acids

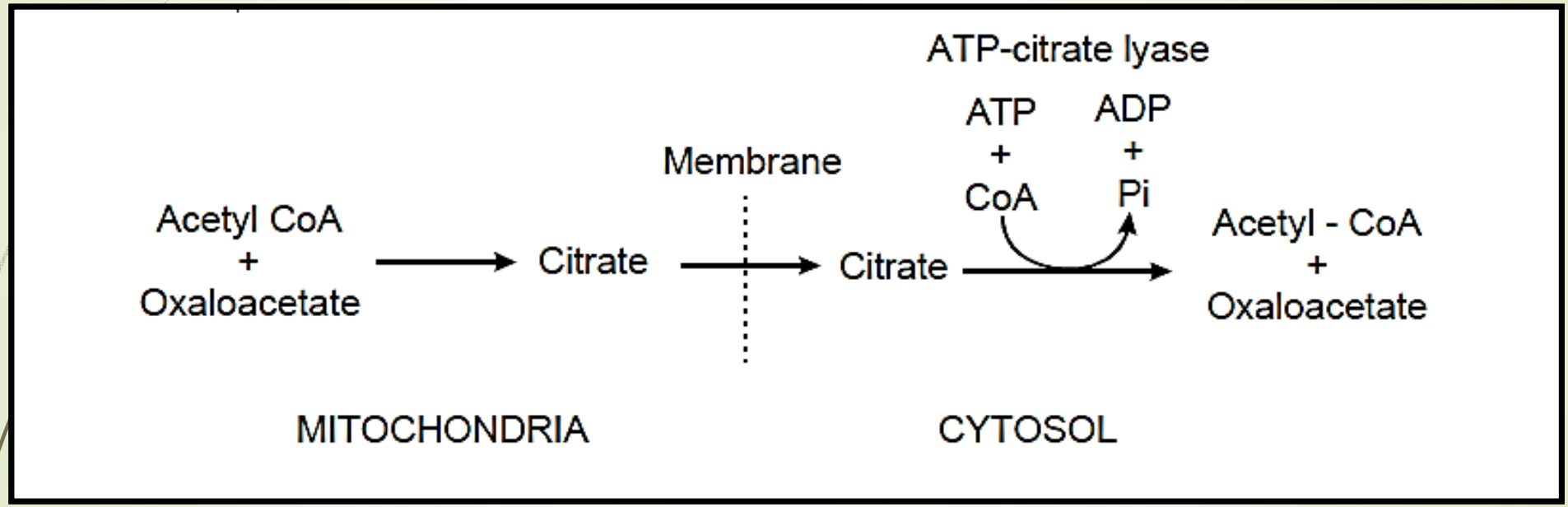
- 1. Biosynthesis of fatty acids occurs in all organisms and in mammals it occurs mainly in adipose tissue, mammary glands, and liver.
- 2. Fatty acid synthesis takes place in the cytosol in two steps.
- a) Formation of medium chain fatty acid of chain length 16 carbon atoms.
- b) Lengthening of this carbon chain in microsomes for larger fatty acids.
- 3. Acetyl CoA serves as a source of carbon atoms for saturated as well as unsaturated fatty acids.
- Acetyl CoA can be formed from excessive dietary glucose and glucogenic amino acids (amino acids which can be converted to glucose).
- Carbohydrates and amino acids in the presence of oxygen is converted to pyruvate which in turn can be converted to acetyl CoA.


Excessive carbohydrates
O_2
Glucogenic aminoacids
Glycolysis
Gluconeogenesis
Pyruvate
Pyruvate dehydrogenase
Acetyl CoA

- The synthesis of fatty acid from acetyl CoA takes place with aid of a multi-enzyme complex termed as **fatty acid synthetase complex.**
- Palmitic acid is the major product of the fatty acids synthetase complex mediated reaction and hence it is also called as palmitate synthetase.
- It is a dimer with two identical subunits namely subunit-1 and subunit-2 arranged in a head to tail fashion.
- Each monomer of this enzyme complex contains seven enzymes; of these, each is assigned a definite function.

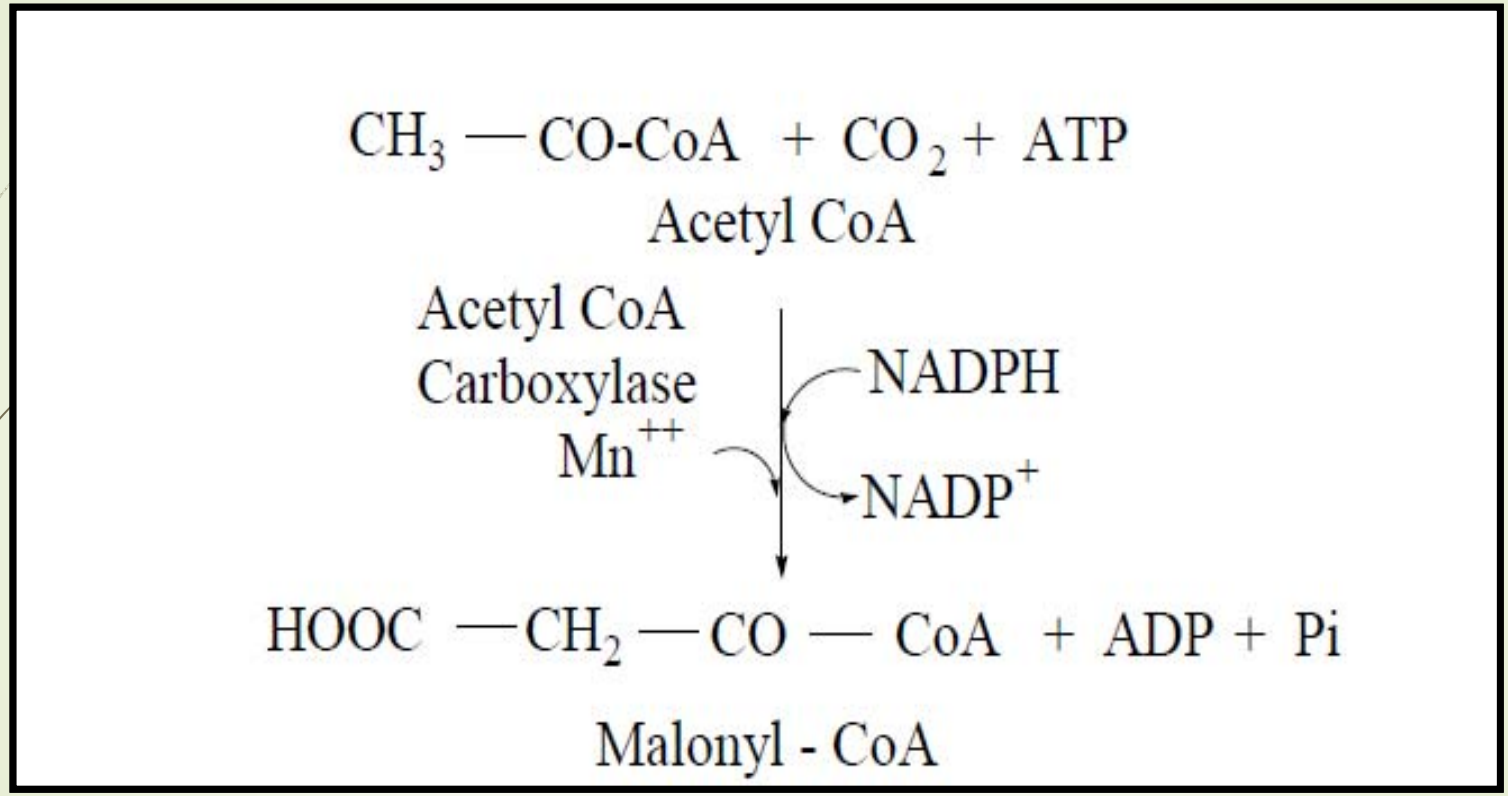
Migration of Acetyl CoA for the bio synthesis of Fatty acids

- Formation of acetyl CoA from pyruvate takes place in mitochondria.
- Mitochondrial membrane is impermeable to acetyl CoA.
- Migration of acetyl CoA from the mitochondria to the cytoplasm is facilitated by the condensation of the acetyl CoA with oxaloacetate to form citrate which is permeable to mitochondrial membrane.
- In the cytoplasm, citrate readily decomposed back to acetyl CoA and oxaloacetate in the presence of ATP and co-enzyme A by the action of an enzyme called ATP – Citrate lyase.

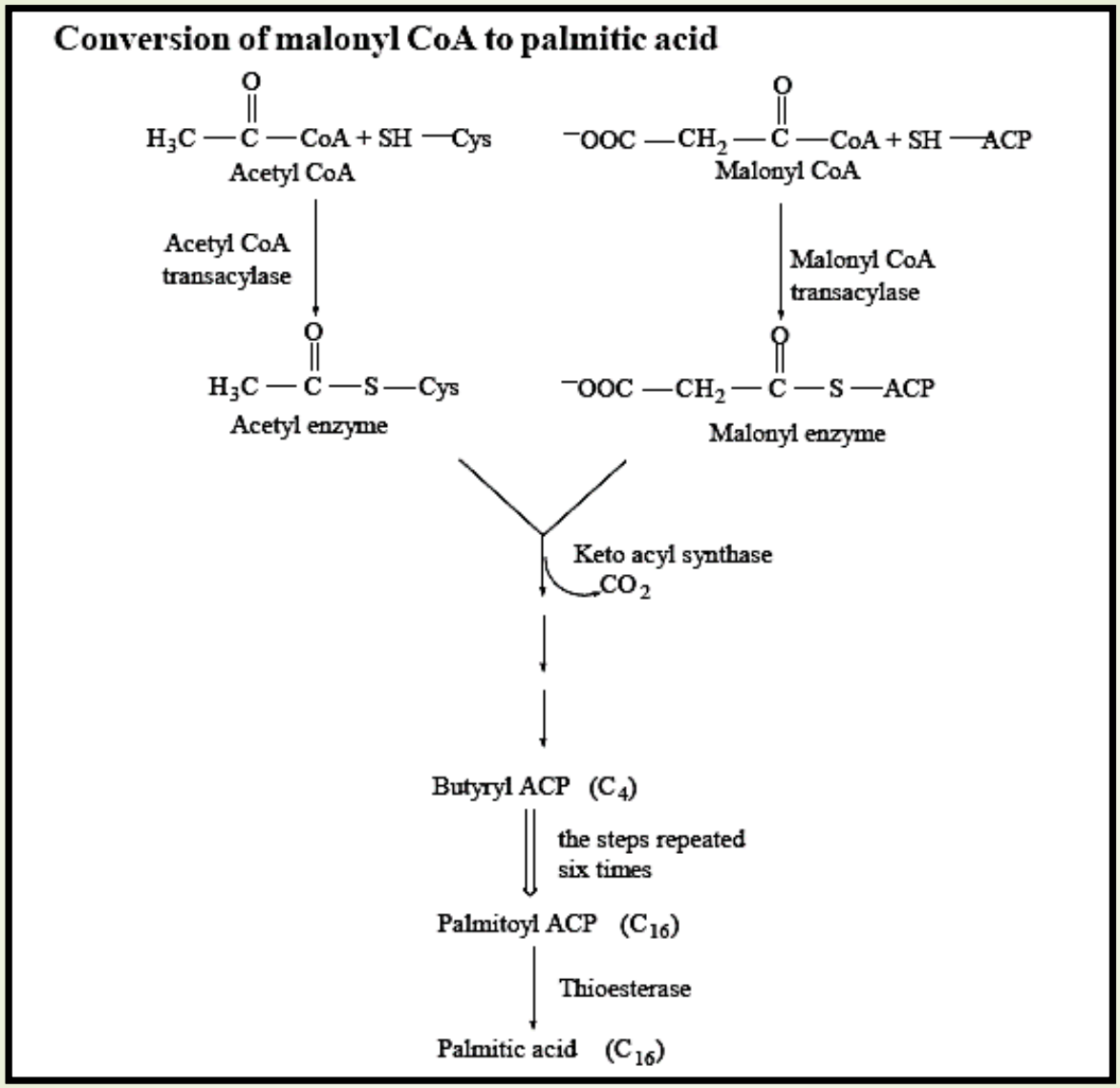

ATP-citrate lyase
ATP
+
CoA
ADP
+
Pi
Membrane
Acetyl CoA
+
Oxaloacetate
Citrate
Citrate
Acetyl - CoA
+
Oxaloacetate
MITOCHONDRIA
CYTOSOL

Conversion of Acetyl CoA to Malonyl CoA

- The acetyl - CoA is carboxylated in the cytoplasm in the presence of **acetyl CoA carboxylase,** a vitamin Biotin containing enzyme, which helps in carbon dioxide fixation. Acetyl CoA carboxylase is the regulatory enzyme in the fatty acid biosynthesis.


CH3 — CO-CoA + CO2 + ATP
Acetyl CoA
Acetyl CoA
Carboxylase
Mn++
NADPH
NADP+
HOOC — CH2 — CO — CoA + ADP + Pi
Malonyl - CoA

- The malonyl CoA is converted to palmitic acid by several steps and each of these steps are catalysed by different enzymes of fatty acid synthetase complex.
- Acetyl CoA and malonyl CoA condenses to form butyryl-ACP with the formation of intermediates.
- This cycle repeats itself six times and in each cycle two carbon atoms (malonyl CoA) is added to butyryl ACP, ultimately resulting in the formation of palmitoyl CoA, a 16 carbon molecule.


Conversion of malonyl CoA to palmitic acid
H3C — C — CoA + SH — Cys
Acetyl CoA
⁻OOC — CH2 — C — CoA + SH — ACP
Malonyl CoA
Acetyl CoA transacylase
Malonyl CoA transacylase
H3C — C — S — Cys
Acetyl enzyme
⁻OOC — CH2 — C — S — ACP
Malonyl enzyme
Keto acyl synthase
CO2
Butyryl ACP (C4)
the steps repeated six times
Palmitoyl ACP (C16)
Thioesterase
Palmitic acid (C16)

Oxidation of Fatty Acids

- The digestion of fats starts in the small intestine.
- Fats are emulsified by the bile salts and hydrolysed by the pancreatic lipases to form free fatty acids.
- These free fatty acids combine with glycerol (produced by the glycolytic process) to form triglycerides.
- They combine with proteins to form lipoproteins and enter into circulation to perform various biolological functions such as oxidation, storage and formation of new lipids.
- Fatty acids are the immediate source for oxidation of fats in various tissues viz. liver, adipose tissue, muscles, heart, kidney, brain, lungs and testes.

β-Oxidation

- Fatty acids are oxidized to CO2 and water with the liberation of large amount of energy.
- Oxidation is brought about in the mitochondria because all the enzymes required for oxidation are present in the mitochondria.
- Oxidation of fatty acids is of three types, based on the position of the carbon atom which gets oxidised (γ, β and α).
- R- CH2- CH2- CH2- COOH fatty acid
- γ β α
- However ββ-oxidation of fatty acids is predominant and widely prevalent and it provides large amount of energy than α and γ oxidation.