Introduction, Fatty Acid Properties and Triglyceride Synthesis

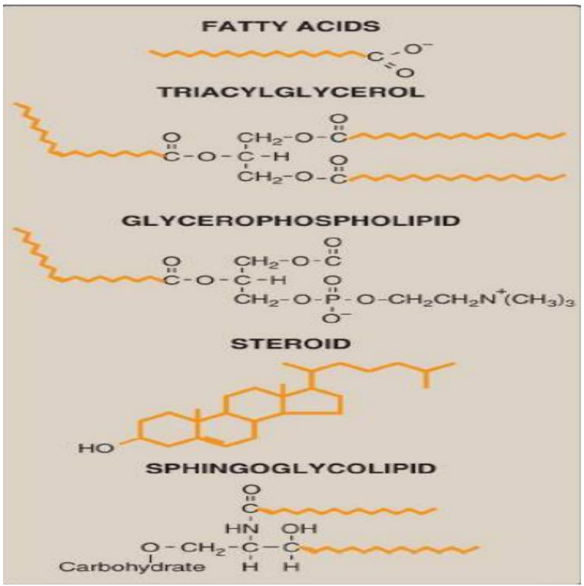
Introduction:

Lipids are a heterogeneous group of water-insoluble (hydrophobic) organic molecules but soluble in nonpolar solvents such as ether and chloroform.

- Lipids are a major source of energy for the body.
- Dietary supplementation with long-chain ω3 fatty acids is believed to have beneficial effects in a number of chronic diseases, including cardiovascular disease and rheumatoid arthritis

- Classification of lipids according chemical structure

1. Fatty acids
2. Cholesterol
3. Acylglycerols
4. Sphingolipids
5. Prostaglandins
6. Others

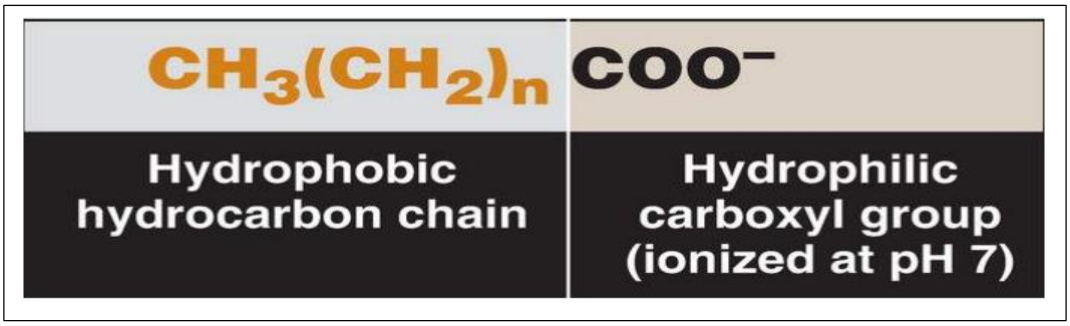


Fatty acids (F.As) Properties

1- Free FA or esterified

- Fatty acids exist free in the body (that is, they are **nonesterified**) and as fatty acyl esters in more complex molecules such as triacylglycerol (TAG).
- Low levels of free fatty acids (FFA) occur in all tissues, but substantial amounts can sometimes be found in the plasma, particularly during fasting.

- Fatty acids are simply linear chains of C-H bonds that terminate with a carboxyl group (-COOH).
- RCOOH is the general chemical formula for a fatty acid, where "R" is an alkyl chain. It consists of a hydrophobic hydrocarbon chain with a terminal carboxyl group (figure below)



2- Long and short chain FAs

- Long chain-length fatty acids (LCFA) are mostly found in body, the hydrophobic portion is predominant. These molecules are highly water insoluble and must be transported in the circulation in association with protein.
- More than 90% of the fatty acids found in plasma are in the form of fatty acid esters (primarily TAG, cholesteryl esters, and phospholipids) contained in circulating lipoprotein particles.
- Long chain FFA are transported in the circulation in association with albumin, the most abundant protein in serum.
- Short chain fatty acids can be really free.

3- Even or odd numbered FAs

- In humans, fatty acids with an even number of carbon atoms (16, 18, or 20) predominate, with longer fatty acids (>22 carbons) being found in the brain.
- In natural fats, FAs contain an even number of carbon atoms because they are synthesized from two carbon units (Ie, acetyl COA)

4- Fatty acid saturation and saturation

- Fatty acid chains may contain no double bonds (that is, be saturated) or contain one or more double bonds (that is, be mono- or polyunsaturated). In humans, the majority are saturated or monounsaturated.

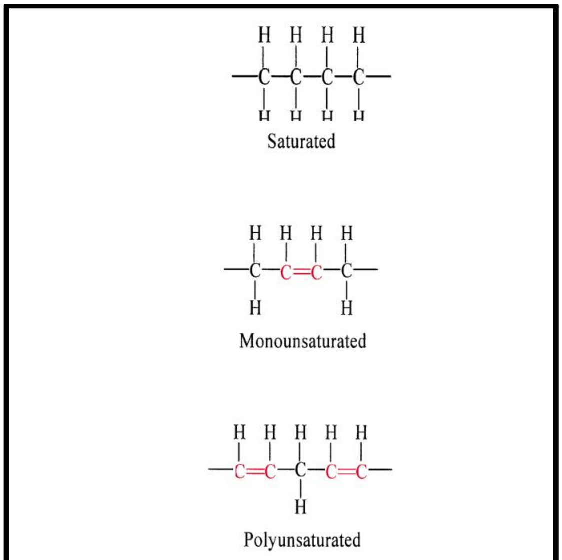
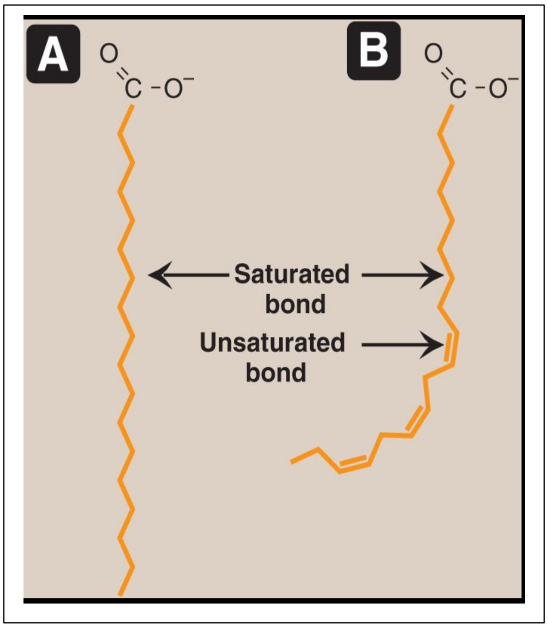
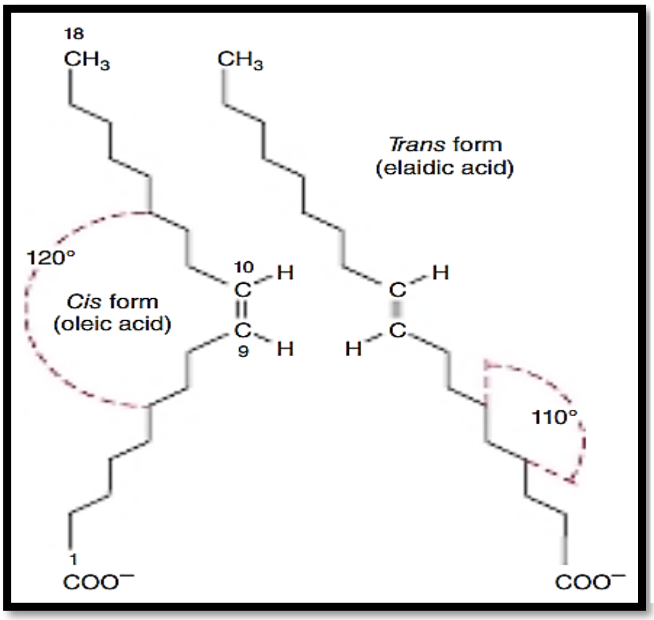


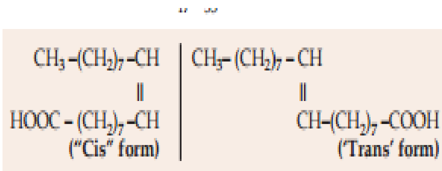
Figure 23-7 Saturated and unsaturated fatty acids.



5- Cis and trans

- When double bonds are present, they are nearly always in the cis rather than in the trans configuration. The introduction of a cis double bond causes the fatty acid to bend **120 degrees at the double bond position**





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6- Melting points of a FAs

Depends on two factors, 1- LCFA and 2- double bond

- In general, addition of double bonds decreases the melting temperature (Tm) of a fatty acid, whereas increasing the chain length of FA lead to increases the Tm. Because membrane lipids typically contain LCFA, the presence of double bonds in some fatty acids helps maintain the fluid nature of those lipids.

- **Fatty Acid - Nomenclature (Systemic name)**
- The carbon atoms are numbered, beginning with the carboxyl carbon as carbon 1
- Saturated: parent hydrocarbon + oic e.g. C18: Octadecanoic acid
- Unsaturated: with one double bond: + enoic e.g. C18: Octadecenoic acid
- Unsaturated: with two double bonds: + dienoic e.g.C18: Octadecadienoic acid
- Unsaturated: with three double bonds: + trienoic e.g. C18: Octadecatrienoic acid

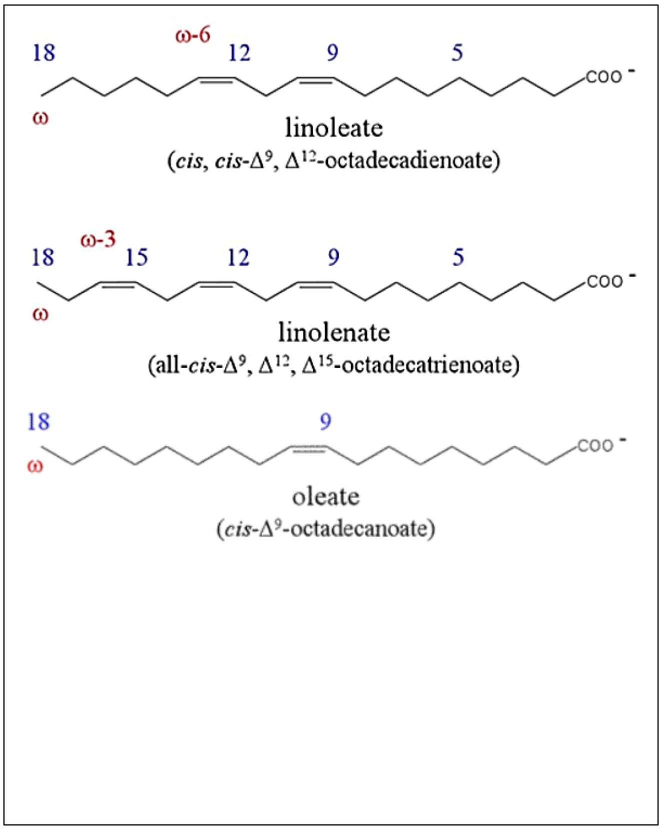
Fatty acids with chain lengths of four to ten carbons are found in significant quantities in milk.

Structural lipids and triacylglycerols contain primarily fatty acids of at least 16 carbons.

COMMON NAME	STRUCTURE
Formic acid	1
Acetic acid	2:0
Propionic acid	3:0
Butyric acid	4:0
Capric acid	10:0
Palmitic acid	16:0
Palmitoleic acid	16:1(9)
Stearic acid	18:0
Oleic acid	18:1(9)
Linoleic acid	18:2(9,12)
α-Linolenic acid	18:3(9,12,15)
Arachidonic acid	20:4(5, 8,11,14)
Lignoceric acid	24:0
Nervonic acid	24:1(15)

Precursor of prostaglandins

Essential fatty acids



- Essential Fatty Acids

- Three polyunsaturated fatty acids, linoleic acid, linolenic acid and arachidonic acid are called "essential fatty acids" (EFA).

- These FAs cannot be synthesized in the body and must be provided in the diet.
- Lack of EFA in the diet can produce growth retardation and other deficiency manifestation symptoms.

- Linoleic acid is most important, arachidonic acid can be synthesized from linoleic acid.

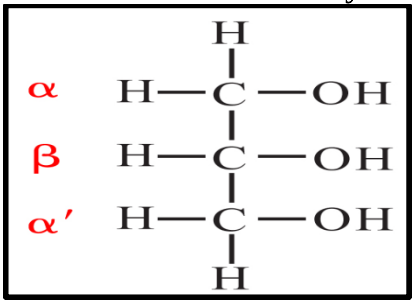
- Biologically arachidonic acid is very important as it is precursor from which prostaglandins

Triacylglycerol (TAG)

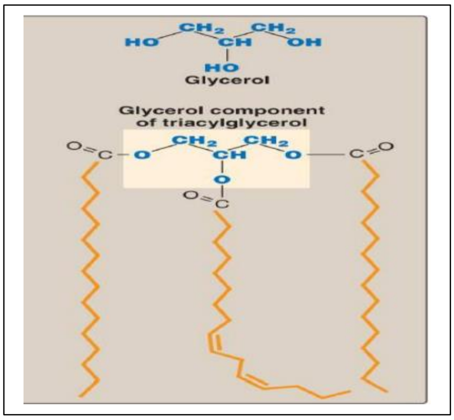
- Triglycerides are the predominant form of glycerol ester in plasma.

1- Acylglycerols

A three-carbon alcohol that contains a hydroxyl group on each of its carbons and is classified by the number of fatty acyl groups present;



- Mono-, di-, and triacylglycerols consist of one, two, or three molecules of fatty acid esterified to a molecule of glycerol.



The three fatty acids esterified to a glycerol molecule to form a TAG are usually not of the same type. The fatty acid on carbon 1 is typically saturated, that on carbon 2 is typically unsaturated, and that on carbon 3 can be either saturated. The presence of the unsaturated fatty acid(s) decrease(s) the Tm of the lipid

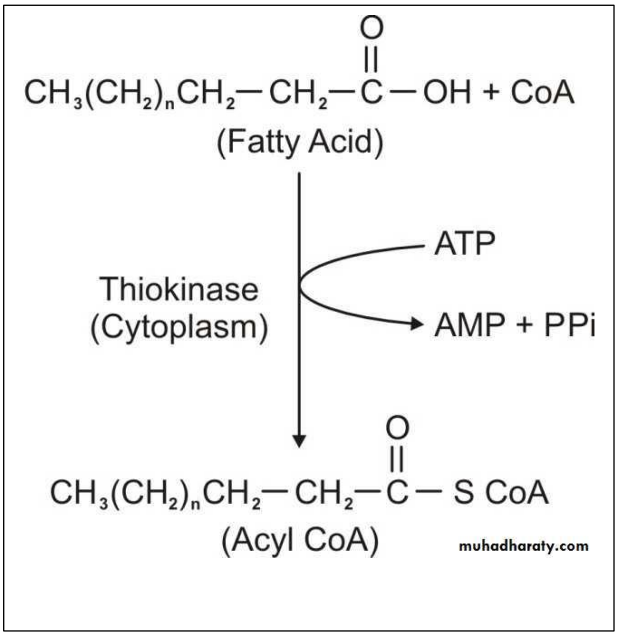
- Triacylglycerol storage: Because TAG are only slightly soluble in water, they coalesce within white adipocytes to form large oily droplets that are nearly anhydrous.

Synthesis of Triacylglycerol (TAG)

Note: Synthesis of TAGs requires activation of fatty acids and glycerol

- **Activation of FAs**

A free fatty acid must be converted to its activated form (bound to CoA through a thioester link) before it can participate in metabolic processes such as TAG synthesis. This reaction is catalyzed by Thiokinase (acyl CoA synthetases).



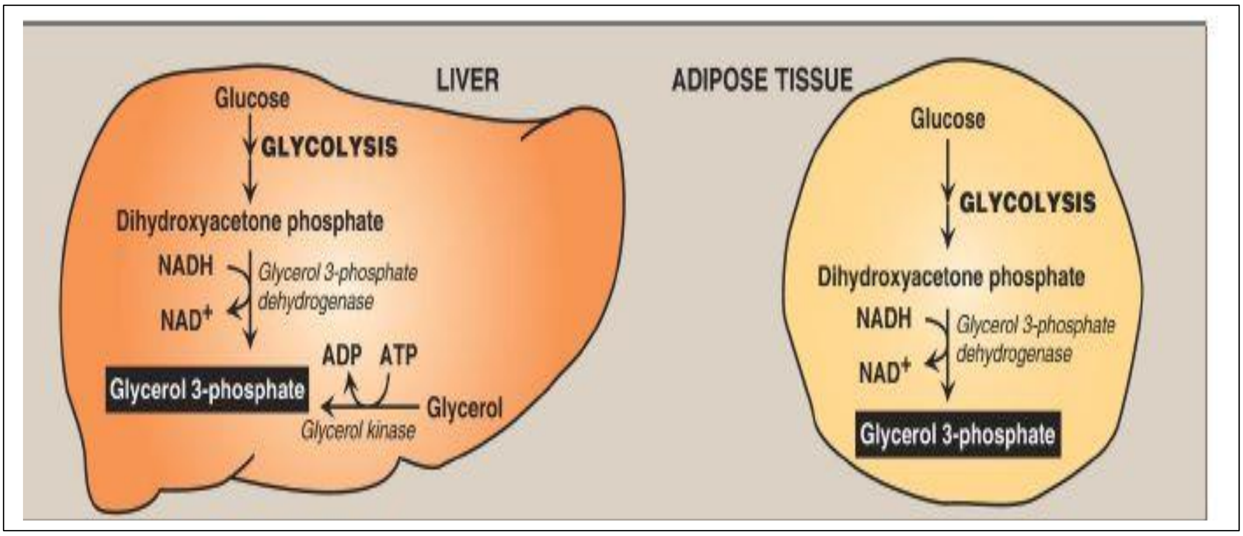
- **Activation of glycerol**
- Activation of glycerol through phosphate attachment
- Glycerol 3-phosphate synthesis: Glycerol 3-phosphate is the initial acceptor of fatty acids during TAG synthesis.
- There are two major pathways for its production

  1- In liver (the primary site of TAG synthesis)

  2- In adipose tissue

- In both liver and adipose tissues glycerol the 3-phosphate can be produced from glucose, first using the reactions of the glycolytic pathway to produce dihydroxyacetone phosphate [DHAP].

- DHAP is reduced by glycerol 3-phosphate dehydrogenase to glycerol 3- phosphate.
- A second pathway found in the liver, but not in adipose tissue, uses glycerol kinase to convert free glycerol to glycerol 3- phosphate.



Steps of synthesis of a TAG molecule:

The pathway involves 4 reactions that include sequential Addition of fatty acids (as fatty acyl CoAs), the removal of phosphate and an addition of a third fatty acyl.

Clinical correction: Adipocytes can take up glucose only in the presence of insulin hormone. Thus, when plasma glucose is low, such as in fasting and insulin level is low, and no glucose enters. Adipocytes the adipocytes have only a limited ability to synthesis glycerol phosphate and can't produce TGAs. In diabetes mellitus no glucose enters adipocytes in spite of hyperglycemia because insulin is inactivating or low in level, and again no triglycerides are produced.