LIPIDS

Introduction

Lipids are a heterogeneous group of compounds that are related more by their physical than by their chemical properties.

Lipid Properties

1- Insoluble in water.
2- Soluble in nonpolar solvents such as ether & chloroform.

Importance of Lipids

1- Important dietary constituents because:
   A- They give high energy value.
   B- Fatty food contains fat-soluble vitamins & essential fatty acids.
2- Stored in adipose tissue where it serves as a thermal & mechanical insulator.
3- Act as electrical insulators in nerve action.

Classification of Lipids

1. **Simple lipids:** Esters of fatty acids with various alcohols. eg, fats, oils & waxes.
2. **Complex lipids:** Esters of fatty acids with various alcohols with additional group, eg. Phospholipids, glycolipids, sulfolipids, aminolipids & lipoproteins.
3. **Precursor & derived lipids:** Include fatty acids, glycerol, other alcohols, steroids, fatty aldehydes, ketone bodies, hydrocarbons, lipid-soluble vitamins & hormones.

Fatty Acids

Fatty acids are aliphatic carboxylic acids.

Presence of Fatty Acids

It present in two forms:
1- Esterified form: The main form, eg, triacylglycerol.
2- Unesterified form [free fatty acids or nonesterified fatty acids (NEFA)] combined with albumin in the blood & in the cell attached to a fatty acid-binding protein, so that in fact they are never ”free."

Classification of Fatty Acids

1- Saturated fatty acids: They have no double bonds.

2- Unsaturated Fatty Acids: Contain one (monounsaturated, monoenoic) or more double bonds (polyunsaturated, polyenoic).

Nomenclature of Fatty Acids

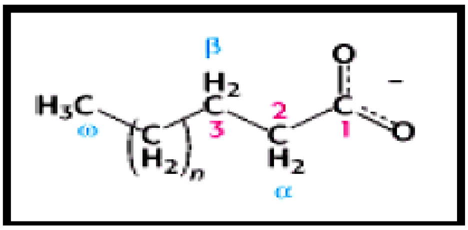
I- Systematic Nomenclature:

1- Name according to number of carbon atoms that form the fatty acid with **oic** being substituted for the final **e**.

a- In saturated acids end in **-anoic,** eg, octanoic acid.

b- Unsaturated acids with single double bond **(monoenoic acids)** end **-enoic,** eg, octadecenoic acid, if two double bonds (**dienoic acids)** end in **-adienoic**, eg, octadecadienoic, if three double bonds (**trienoic acids**) end in **-atrienoic**, eg, octadecatrienoic & so on.

2- Carbon atoms are numbered from the carboxyl carbon (carbon No. 1). The carbon atoms adjacent to the carboxyl carbon (Nos. 2, 3 & 4) are also known as α, β & γ carbons respectively & the terminal methyl carbon is known as the ω or n-carbon.



3- The number & position of the double bonds are indicated by:

a- Δ using the number of preceding carbon atom in the double bond eg, Δ^9 indicates a double bond between carbons 9 & 10 of the fatty acid counting from the carboxyl carbon.

b- ω using the number counting from the ω -carbon eg, ω^7 indicates a double bond on the seventh carbon counting from the ω -carbon.

c- Write number of carbon atoms that form the fatty acid (eg, 16): number of double bonds (eg, 1); number of preceding carbon atom in the double bond (eg, 9), therefore, it written **16: 1; 9**

II- Common Nomenclature:

1- Common name for saturated fatty acids.

Common Name	Number of C Atoms
Acetic	2
Butvric	4
Caproic	6
Palmitic	16
Stearic	18

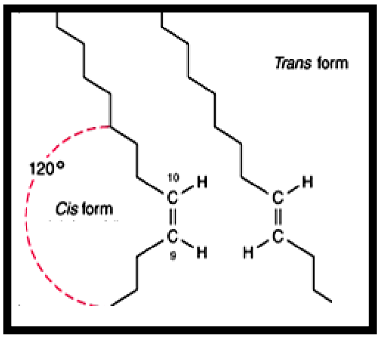
2- Common name for unsaturated fatty acids.

Number of C Atoms and Number and Position of Common Double Bonds	Family	Common Name	Systematic Name
Monoenoic acids (one double bond)			
16:1;9	ω7	Palmitoleic	*cis*-9-Hexadecenoic
18:1;9	ω9	Oleic	*cis*-9-Octadecenoic
Dienoic acids (two double bonds)			
18:2;9,12	ω6	Linoleic	all-*cis*-9,12-Octadecadienoic
Trienoic acids (three double bonds)			
18:3;9,12,15	ω3	Linolenic	all-*cis*-9,12,15-Octadecatrienoic
Tetraenoic acids (four double bonds)			
20:4;5,8,11,14	ω6	Arachidonic	all-*cis*-5,8,11,14-Eicosatetraenoic

Geometric Isomerism of Fatty Acids

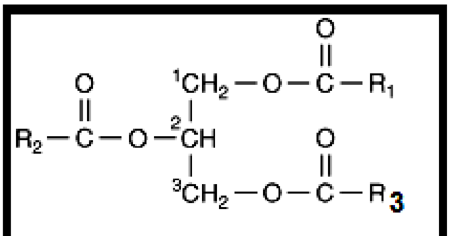
The carbon chains of saturated fatty acids form a zigzag pattern when extended at low temperatures. At higher temperatures, some bonds rotate causing chain shortening.

A type of **geometric isomerism** occurs in the unsaturated fatty acids, depending on the orientation of atoms or groups around the axes of double bonds which do not allow rotation. If the acyl chains are on the same side of the bond, it is *cis-,* if on opposite sides, it is *trans-,* Double bonds in naturally occurring unsaturated long-chain fatty acids are nearly all in the *cis* configuration, the molecules being "bent" 120 degrees at the double bond.



Triacylglycerols (Triglycerides)

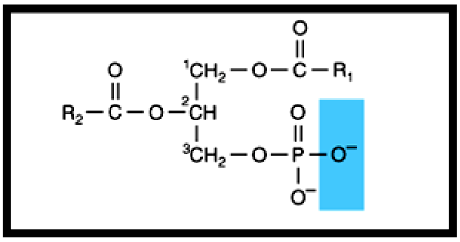
They are esters of glycerol with three fatty acids. It constitutes the majority of lipids in the body & in food.



Triacylglycerol

Phospholipids

They are esters of glycerol with fatty acid with additional phosphate group.



Phospholipids include mainly:
1- Phosphatidylcholines (Lecithins).
2- Phosphatidylinositol.
3- Cardiolipin.
4- Lysophospholipids.
5- Plasmalogens.
6- Sphingomyelins.

Glycolipids

They are lipids with a carbohydrate attached to it, widely distributed in every body tissue particularly in nervous tissue.

Steroids

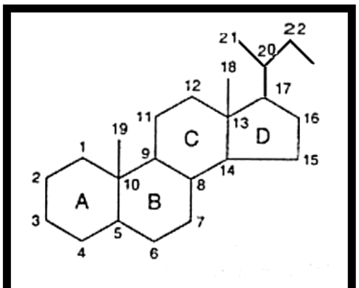
Clinically cholesterol is the best-known steroid because of its association with atherosclerosis & heart disease. Biochemically it is also of significance because it is the precursor of a large number of equally important steroids including bile acids, adrenocortical hormones, sex hormones & vitamin D.

Steroids are characterize by having **cyclopentanoperhydrophenanthrine** that have four rings (17-carbon atoms) with additional carbon atom at position 13(C18) & at position 10 (C19) & carbon atoms at position 17 (C20 , 21,….).

If the side-chain of steroid above (front) hormone plane it's called **β cis** while if it's below (behind) hormone plane it's called **α trans**.

Double-bond in steroid represented by Δ (Delta) with number of preceding carbon atom (example Δ5 mean double bond between C5 & C6).

On drawing the structure of steroid, the carbon positions on the steroid nucleus are numbered. All double bonds are shown as such. Methyl side chains are shown as single bonds unattached at the farther (methyl) end. β- bonds are shown with bold solid lines whereas α -bonds are indicated with broken lines.



The steroid nucleus.

Fatty Acids Oxidation

Only free fatty acids are subjected to oxidation, which occur in mitochondria through the following steps:

Step 1: Activation of fatty acid: In this step which occurs in the outer mitochondrial membrane, the fatty acids are converted to an active intermediate called "active fatty acid" or acyl-CoA" This is the only step that requires energy from ATP (two ATP) in the presence of coenzyme A & the enzyme **acyl-CoA synthetase (thiokinase)** which catalyzes the reaction.

Step 2: Penetration of inner mitochondrial membrane: Long-chain acyl-CoA (more than 12 carbon atoms) cannot penetrate inner mitochondrial membrane, however, **carnitine palmitoyltransferase-I (carnitine acyltransferase-I)** enzyme**,** located in outer mitochondrial membrane, converts long-chain acyl-CoA to acylcarnitine that is able to penetrate the inner mitochondrial membrane by the action of **carnitine-acylcarnitine translocase** enzyme which acts as an inner membrane exchange transporter, acylcarnitine is transported in coupled with the transport out of carnitine.

Step 3: Reformation of acyl-CoA: The acylcarnitine reacts with CoA, catalyzed by **carnitine palmitoyltransferase-II (carnitine acyltransferase-II)** enzyme, located on the inside of the inner membrane, reforming acyl-CoA in the mitochondrial matrix & carnitine is liberated.

Step 4: β-oxidation: In β-oxidation, two carbons at a time are cleaved from acyl-CoA molecule start from carboxyl end with addition of one molecule of Co-A-SH. Chain is broken between α(2)- & β(3)-carbon atoms hence the name β-oxidation. The two-carbon units formed are acetyl-CoA; thus, the number of acetyl-CoA produced depends on the number of carbon atoms that form acyl-CoA for example palmitoyl-CoA (16 carbons , forms 8 acetyl-CoA molecules).

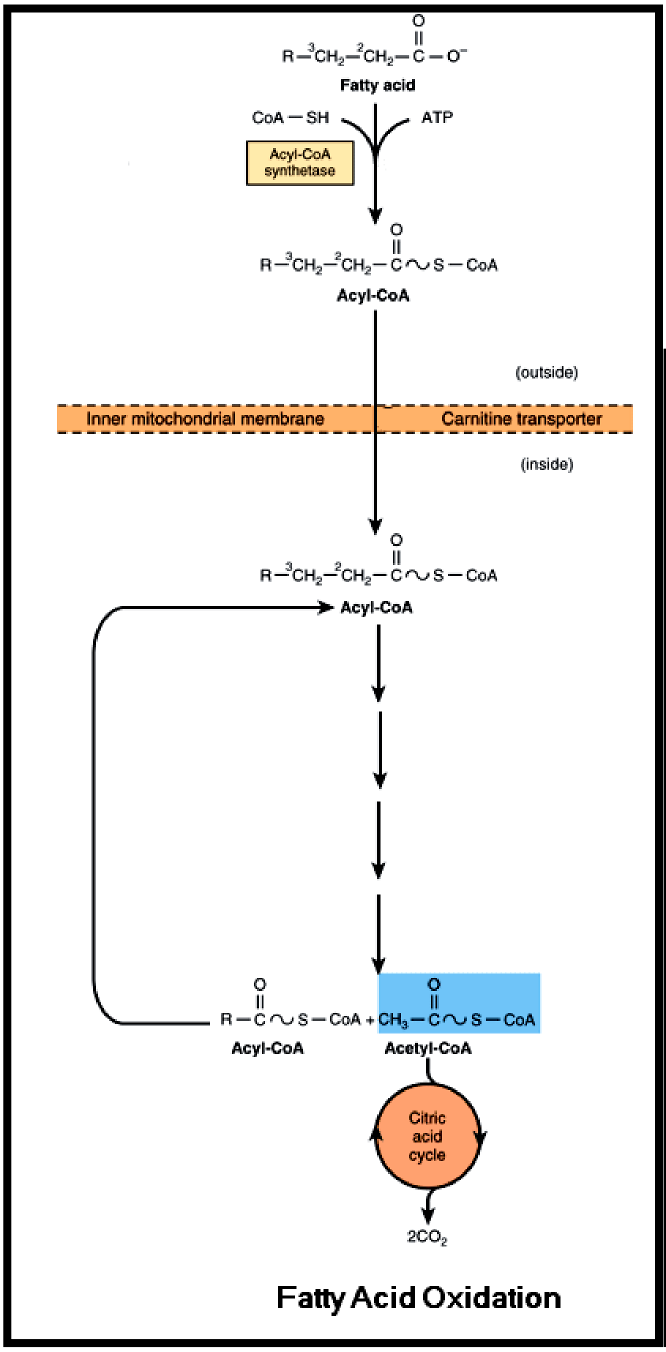
β-oxidation is catalyzed by several enzymes, known collectively as **"fatty acid oxidase" ,** found in the mitochondrial matrix or inner membrane adjacent to the respiratory chain with generation of one mol of $FADH_2$ & NADH + H^+ for each acetyl-CoA produced from β-oxidation.

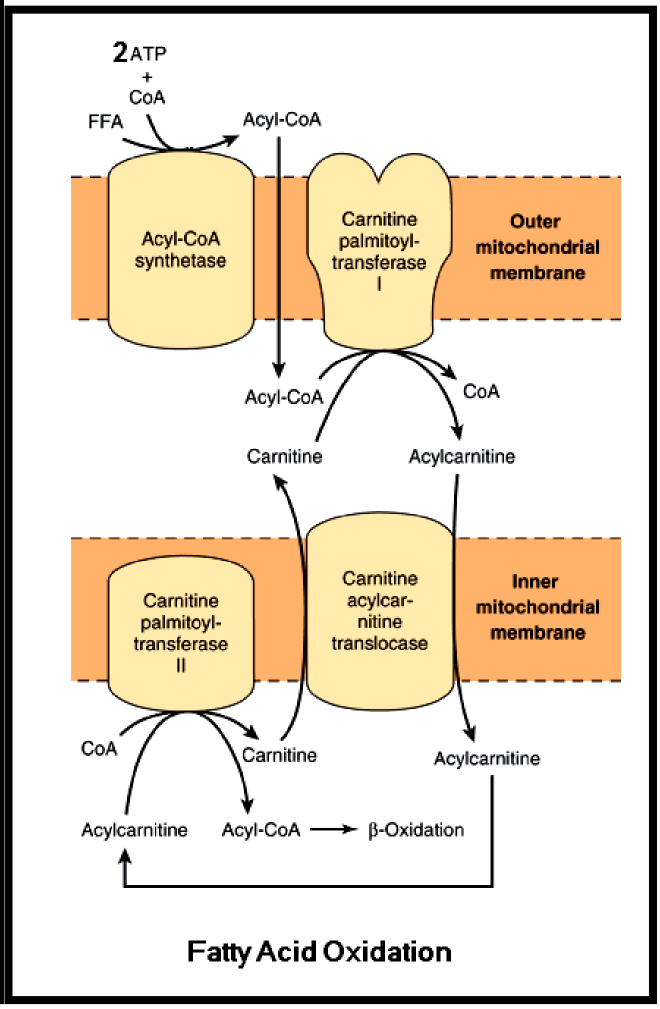
Note: Fatty acids shorter than 12 carbons can cross the inner mitochondrial membrane without the aid of carnitine.

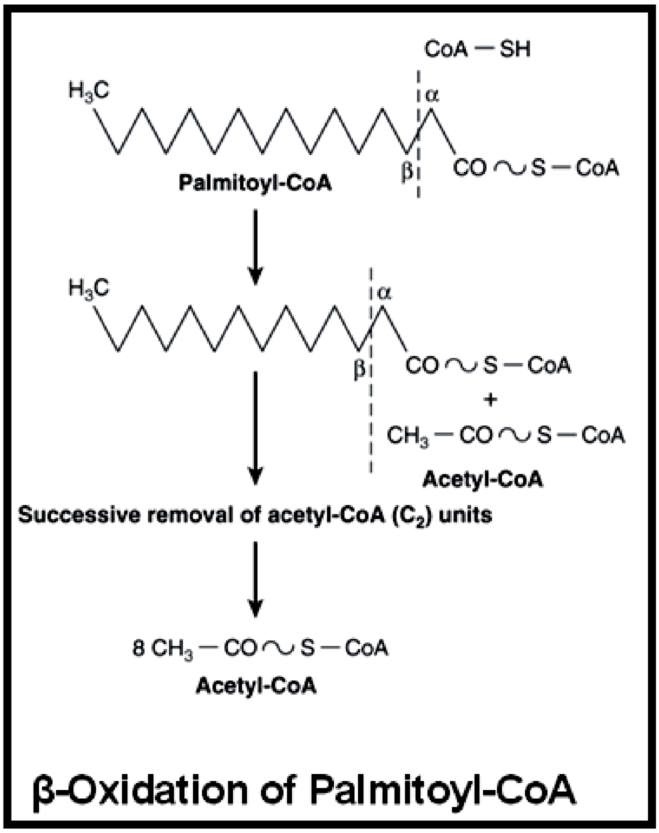
Energy Produced From Fatty Acid Oxidation

1- In β-oxidation, for each 2 carbons cleaved from acyl-CoA molecule to produce acetyl-CoA there is a release of one mol of $FADH_2$ & one mol of NADH + H^+ that enter respiratory chain producing 4 mol ATP (1.5 ATP from $FADH_2$ + 2.5 ATP from NADH + H^+), e.g., 7 cycles of β-oxidation are needed for palmitate breakdown (16 carbons) to acetyl-CoA producing 7X4=28 mol ATP.

2- Each mol of acetyl-CoA produced from β-oxidation enters citric acid cycle producing 10 mol of ATP, e.g., since in β-oxidation of palmitate 8 mol of acetyl-CoA is formed & each gives rise to 10 mol of ATP on oxidation in the citric acid cycle, making 8 x 10 = 80 mol of ATP produced, therefore the total mol of ATP produced per one mole of palmitate undergoes oxidation are (28+80) – 2ATP(consumed in step 1)=106 mol of ATP.


Fatty acid
CoA — SH
ATP
Acyl-CoA synthetase
Acyl-CoA
(outside)
Inner mitochondrial membrane
Carnitine transporter
(inside)
Acyl-CoA
Acyl-CoA
Acetyl-CoA
Citric acid cycle
2CO2
Fatty Acid Oxidation


2ATP
+
CoA
FFA
Acyl-CoA
Acyl-CoA synthetase
Carnitine palmitoyl-transferase I
Outer mitochondrial membrane
Acyl-CoA
CoA
Carnitine
Acylcarnitine
Carnitine palmitoyl-transferase II
Carnitine acylcar-nitine translocase
Inner mitochondrial membrane
CoA
Carnitine
Acylcarnitine
Acylcarnitine
Acyl-CoA
β-Oxidation
Fatty Acid Oxidation



Clinical Aspects of Fatty Acid Oxidation

Impaired fatty acids oxidation gives rise to diseases often associated with hypoglycemia as occur in:

1- Carnitine deficiency.
2- CPT-I deficiency.
3- CPT-II deficiency .
4- Inherited defects in the enzymes of β-oxidation.