LIPID CHEMISTRY (I)

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- **PROPERTIES OF LIPIDS**
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INTRODUCTION

- The word ‘lipid’ is used by Biochemists to denote a chemically heterogeneous group of substances having in common the property of insolubility in water, but solubility in non-aqueous solvents such as chloroform, hydrocarbon or alcohols.
- It is necessary to use this definition based on physical properties since there may be little or no chemical relationship between the numerous compounds now classified as lipids
- The biological functions of the lipids are as diverse as their chemistry

CLASSIFICATION OF LIPIDS

LIPIDS

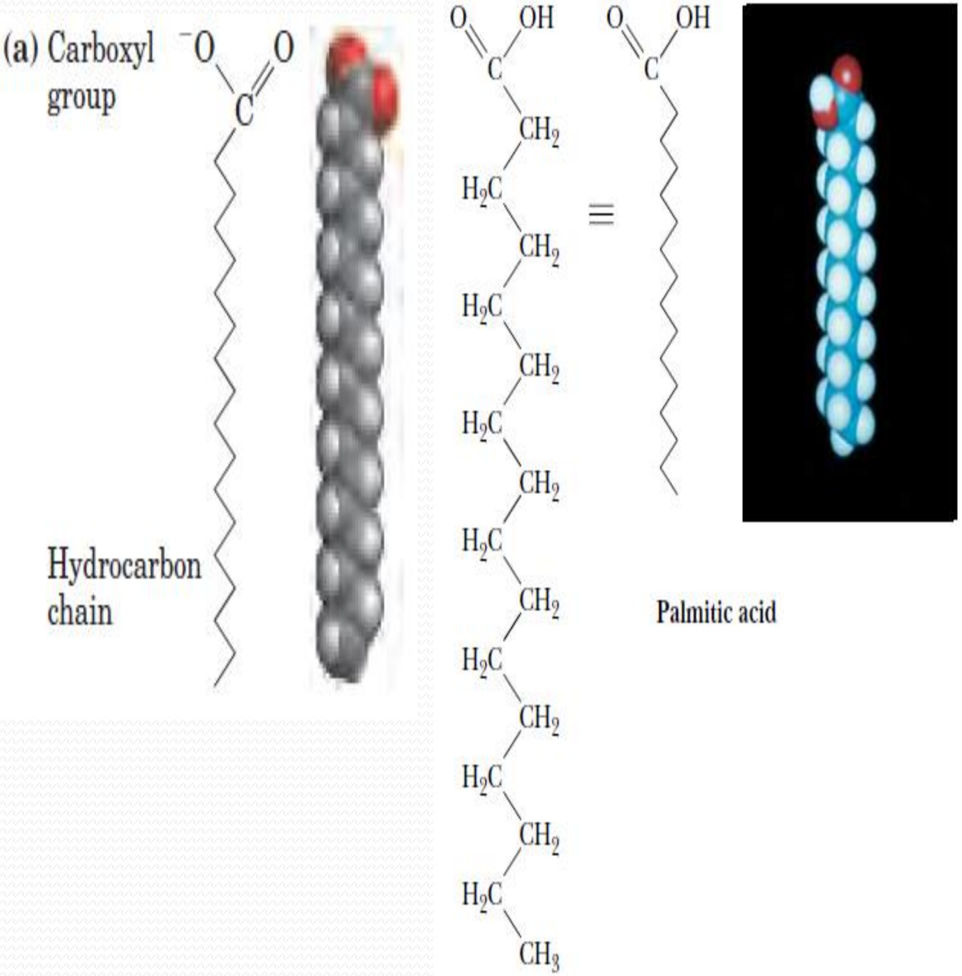
- SIMPLE LIPIDS or HOMOLIPIDS
  - **Fats and oils** (Triglycerides)
    - Simple triglycerides
    - Mixed triglycerides
  - **Waxes**
    - Sperm whale wax
    - Beeswax
    - Carnauba wax
- COMPOUND LIPIDS or HETEROLIPIDS
  - **Phospholipids** (Phosphatids)
    - Phosphoglycerides
      - Lecithins
      - Cephalins
      - Plasmalogens
    - Phosphoinositides (Phosphatidyl inositols)
    - Phosphosphingosides (Sphingomyelins)
  - **Glycolipids** (Cerebrosides)
    - Kerasin
    - Phrenosin
    - Nervon
    - Oxynervon
- DERIVED LIPIDS
  - **Steroids**
    - C 29, C 28, C 27 steroids
    - C 24 steroids
    - C 21, C 19, C 18 steroids
  - **Terpenes**
    - Monoterpenes
    - Sesquiterpenes
    - Diterpenes
    - Triterpenes
    - Tetraterpenes
    - Polyterpenes
  - **Carotenoids**
    - Lycopene
    - Carotenes
    - Xanthophylls

SIMPLE LIPIDS

These are esters of fatty acids with glycerol or higher alcohols. Examples are fatty acids, Acylglycerols and Waxes.

(A) FATTY ACIDS: A fatty acid is composed of a long hydrocarbon (tail) and a terminal carboxyl group(head).

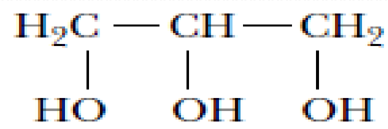
- Fatty acids occur in large amounts in biological systems, but rarely in the free, uncomplexed state.
- They are esterified to glycerol or other backbone structure.



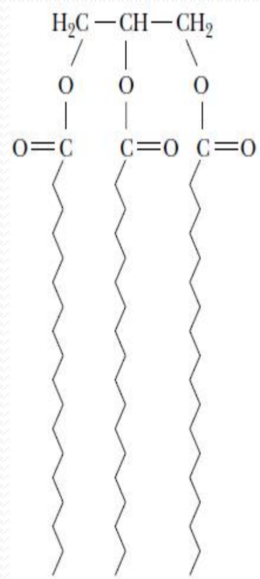
SIMPLE LIPIDS

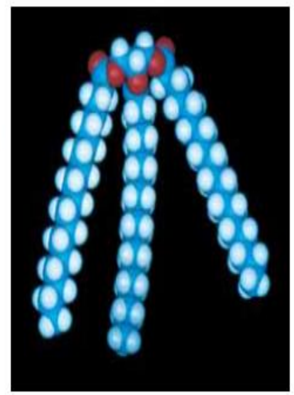
(B) ACYLGLYCEROLS: these are glycerol esters of fatty acids. They include tri-, di- and monoacylglycerols.

- **The triglycerides are the most abundant of all lipids.**
- **If all three fatty acid groups are the same, the molecule is called a simple triglyceride**
- **Mixed triglycerides contain two or more different fatty acids.**

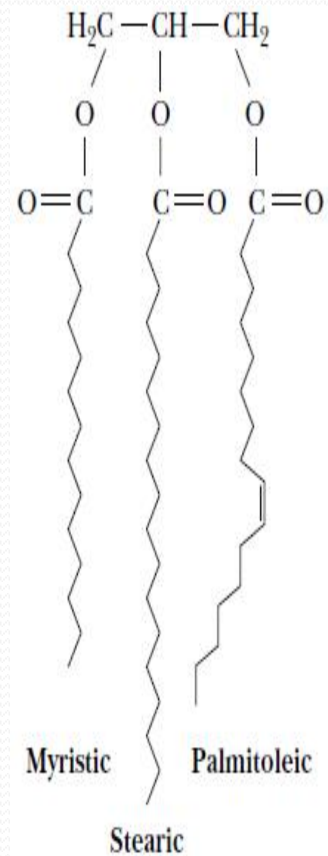


Glycerol





Tristearin
(a simple triacylglycerol)

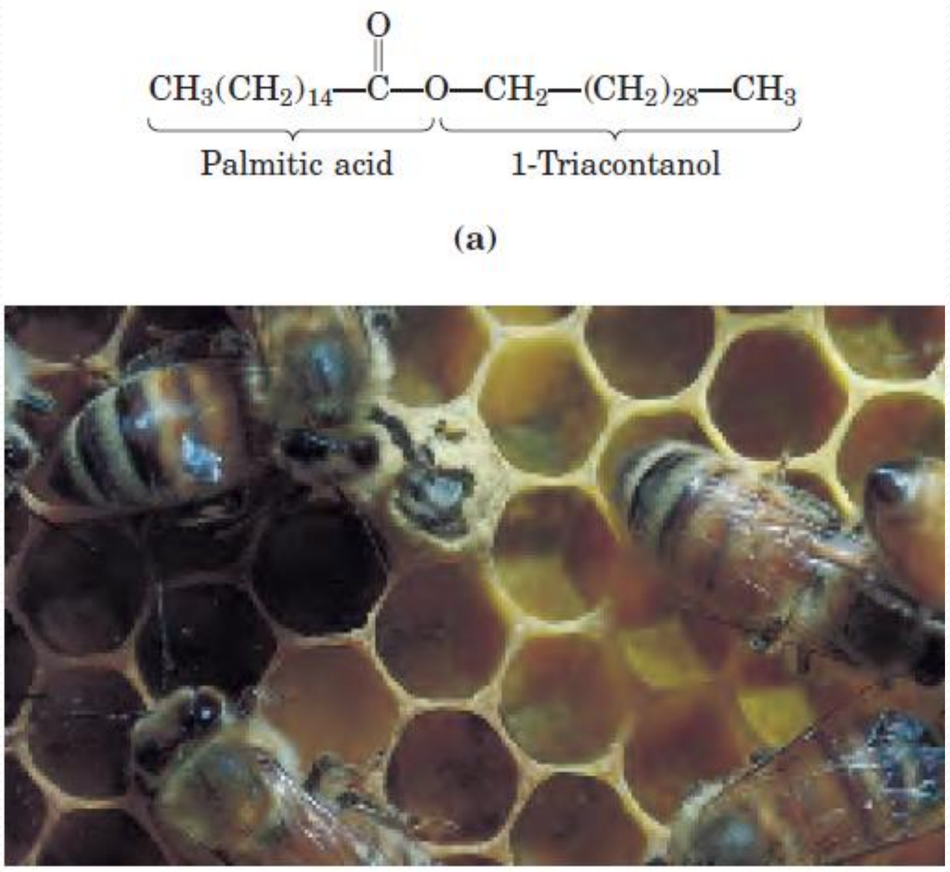


A mixed triacylglycerol

SIMPLE LIPIDS

(C) WAXES are esters of long-chain alcohols with long-chain fatty acids.

- **The resulting molecule can be viewed as having a weakly polar head (the ester moiety itself) and a long, non polar tail (the hydrocarbon chain).**
- **Fatty acids found in waxes are usually saturated.**
- **The alcohols found in waxes may be saturated or unsaturated and may include sterols**
- **Waxes are water insoluble . As a result, they confer water-repellant character to animal skin, to the leaves of certain plants and to bird feathers**
- **Examples include Carnauba wax, Beeswax and Lanolin**



(a)

(b)

COMPOUND/COMPLEX LIPIDS

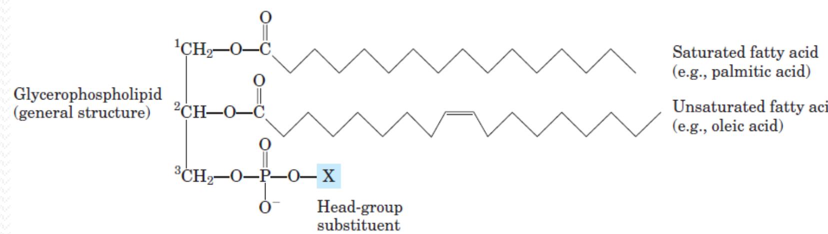
They are esters of fatty acid with one of the various alcohols in addition, they contain other groups (non-lipid component). The subclasses are: phospholipids and glycolipids

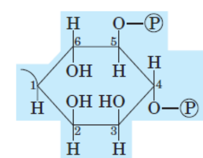
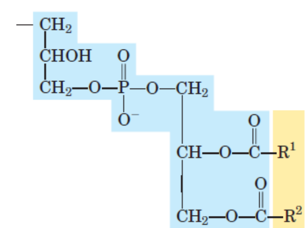
- **(A) PHOSPHOLIPIDS: these are compound/complex lipids containing alcohol, phosphoric acid and a nitrogenous base or other alcoholic group. There are mainly two classes of phospholipids (i) glycerophospholipids and (ii) Sphingophospholipids**

PHOSPHOLIPIDS

(1)GLYCEROPHOSHOLIPIDS: A 1,2-diacylglycerol that has a phosphate group esterified at carbon atom 3 of the glycerol backbone is a glycerophospholipids also known as a phoshoglyceride or a glycerol phosphatide

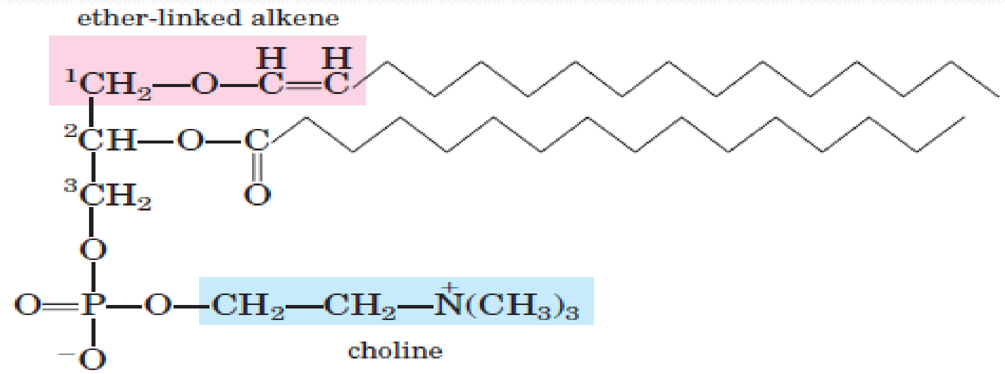
- **These lipids form one of the largest classes of natural lipids and one of the most important**
- **They are essential components of cell membranes**
- **In these compounds, a variety of polar groups are esterified to the phosphoric acid moiety of the molecule**
- **The phosphate, together with such esterified entities, is referred to as a “head "group**
- **Common head groups found in phosphatides are choline, ethanolamine,glycerol, serine and inositol.**



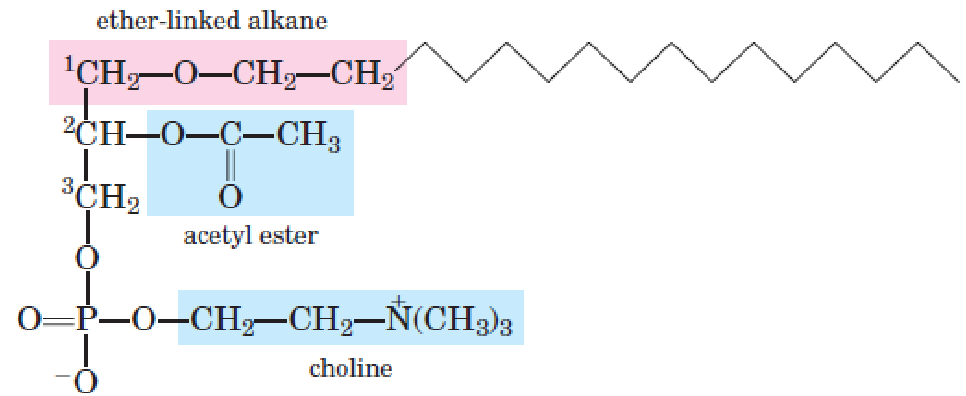
Name of glycerophospholipid	Name of X	Formula of X	Net charge (at pH 7)
Phosphatidic acid	—	$-H$	−1
Phosphatidylethanolamine	Ethanolamine	$-CH_2-CH_2-\overset{+}{N}H_3$	0
Phosphatidylcholine	Choline	$-CH_2-CH_2-\overset{+}{N}(CH_3)_3$	0
Phosphatidylserine	Serine	$-CH_2-CH(COO^-)-\overset{+}{N}H_3$	−1
Phosphatidylglycerol	Glycerol	$-CH_2-CH(OH)-CH_2-OH$	−1
Phosphatidylinositol 4,5-bisphosphate	*myo*-Inositol 4,5-bisphosphate		−4
Cardiolipin	Phosphatidyl-glycerol		−2

PHOSHOLIPIDS CONT'D

- Ether Glycerophospholipids posses an ether linkage instead of an acyl group at C-1 position of glycerol. Platelet activating factor (PAF) and plasmalogen are examples of ether glycerophospholipids



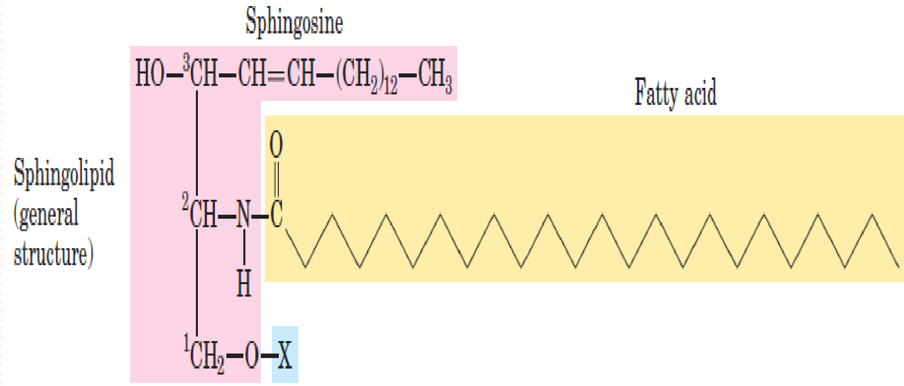
Plasmalogen



Platelet-activating factor

PHOSPHOLIPIDS

- **(II) SPHINGOLIPIDS/SPHINGOPHOSHOLIPIDS: sphingolipids represent another class of lipids found frequently in biological membranes. An 18 carbon amino alcohol, sphingosine, forms the backbone of these lipids rather than glycerol. Typically, a fatty acid is joined to a sphingosine via an amide linkage to form a ceramide**
- **Sphingomyelins represent a phosphorous-containing subclass of sphingolipids and are especially important in the nervous tissue of higher animals**

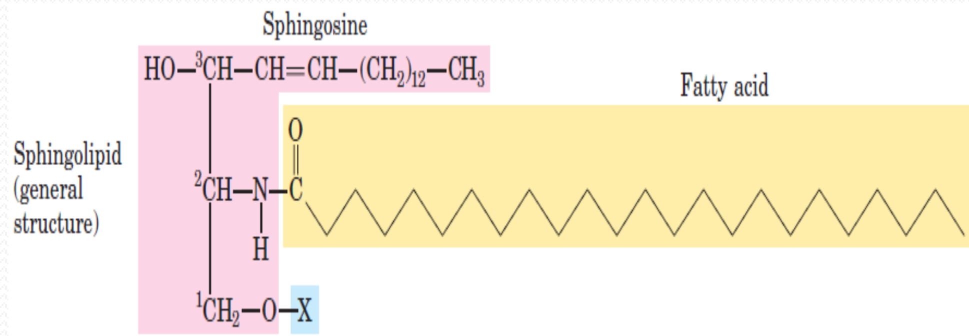


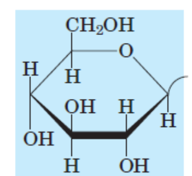
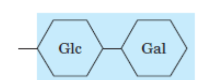
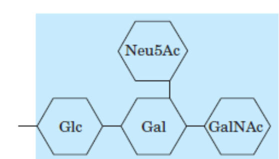
Name of sphingolipid	Name of X	Formula of X
Ceramide	–	$-H$
Sphingomyelin	Phosphocholine	$-P(=O)(O^-)-O-CH_2-CH_2-\overset{+}{N}(CH_3)_3$

COMPOUND/COMPLEX LIPIDS

(B) GLYCOSPHINGOLIPIDS/ GLYCOLIPIDS:

Glycosphingolipids consist of a ceramide with one or more sugar residues in a β-glycosidic linkage at 1-hydroxyl moiety. Examples are cerebroside, sulfatide and gangliosides

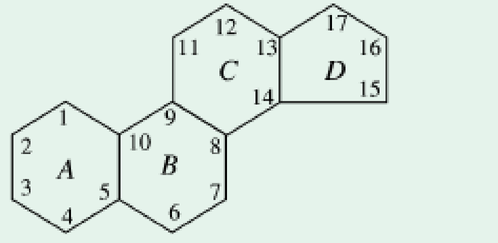


Name of sphingolipid	Name of X	Formula of X
Neutral glycolipids Glucosylcerebroside	Glucose	
Lactosylceramide (a globoside)	Di-, tri-, or tetrasaccharide	
Ganglioside GM2	Complex oligosaccharide	

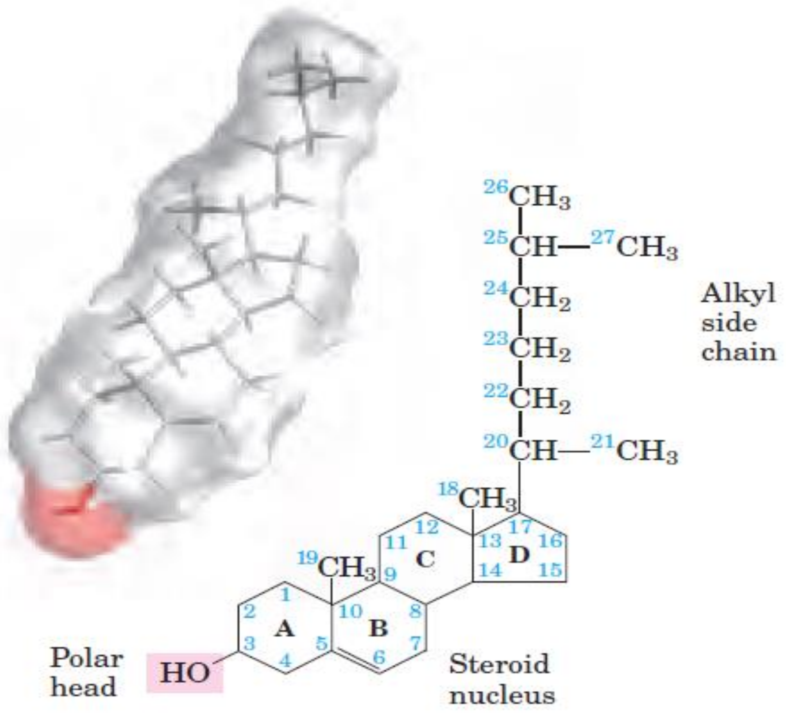
DERIVED LIPIDS

These are substances derived from simple and compounds lipids by hydrolysis. These include steroids, terpenoids and carotenoids

- (A) STEROIDS: All steroids may be considered as derivatives of a fused and fully saturated ring system called CYCLOPENTANOPERHYDROPHENATHRENE or STERANE
- This system consists of 3 cyclohexane rings (A,B and C) fused in nonlinear or phenathrene manner and a terminal cyclopentane ring (D)
- Cholesterol, the principal sterol of higher animal is undoubtedly the most publicized lipid in nature, because of the strong correlation between high levels of cholesterol in the blood and the incidence of diseases of the cardiovascular system.



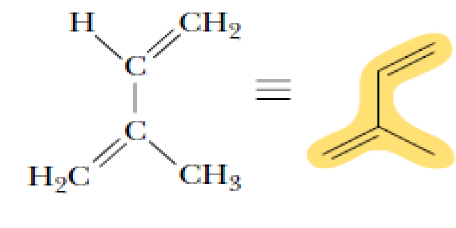
Cyclopentanoperhydrophenanthrene or sterane nucleus



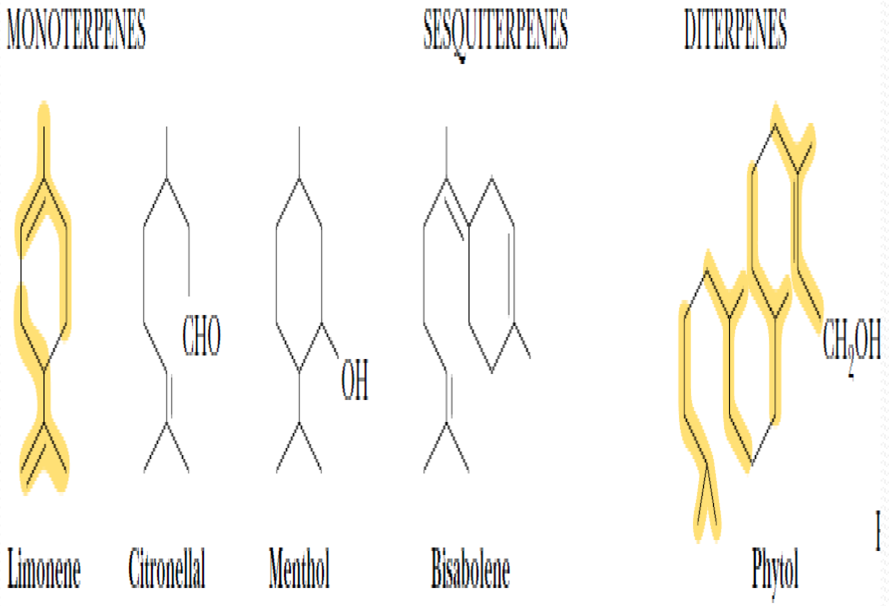
DERIVED LIPIDS

(B) TERPENES: the terpenes are a class of lipids formed from the combination of two or more molecules of 2methyl 1,3-butadiene,better know as isoprene (a five-carbon unit that is abbreviated C5)

The simplest terpenes are called monoterpenes ($C_{10}H_{16}$), followed by sesquiterpenes ($C_{15}H_{24}$), diterpenes ($C_{20}H_{32}$) and triterpenes ($C_{30}H_{48}$)



Isoprene

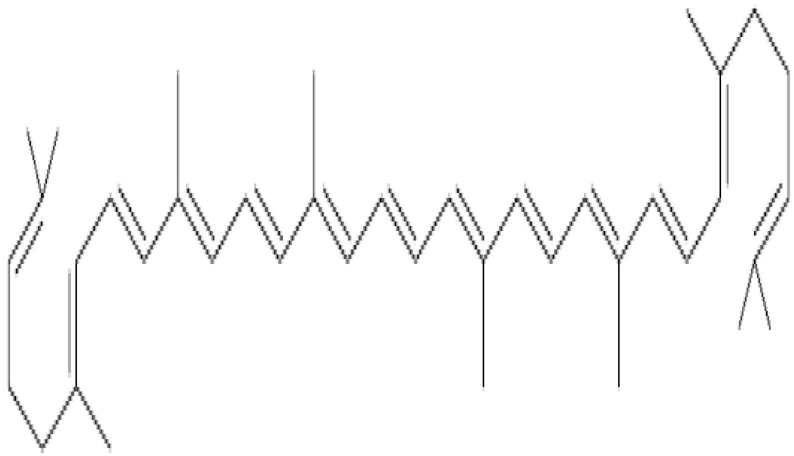


DERIVED LIPIDS

(C) CAROTENOIDS

Carotenoids are tetraterpenes, these are widely distributed in both the plant and animal kingdoms but are exclusively of plant origin. They are isoprene derivatives with high degree of unsaturation. Because of the many conjugated double bonds, they are coloured red or yellow examples are lycopene (in tomato), α- andβ- carotene (in carrot) and xanthophyll

TETRATERPENES



Lycopene

PROPERTIES (PHYSICAL) OF FATS

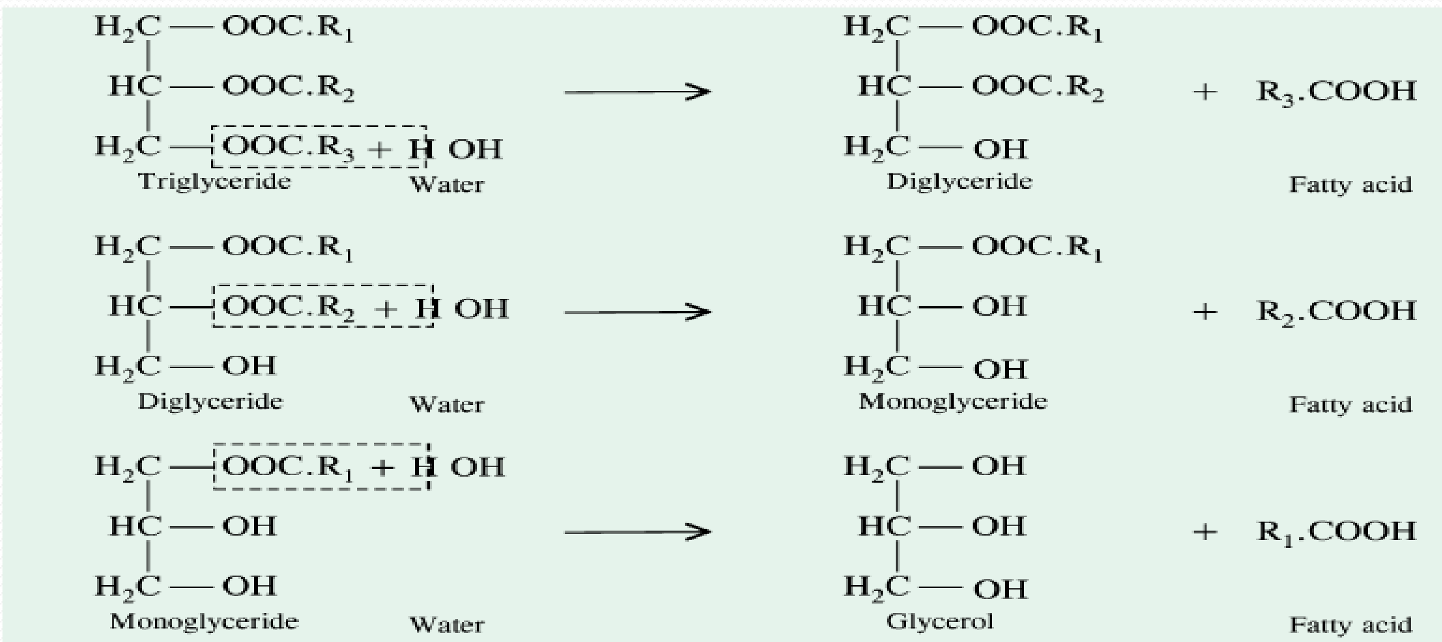
- **The fats and oils owe the manifestation of their physical properties to the fatty acids and alcohols, the two major components**

- ✓ **STATE:**
- ✓ **COLOUR, ODOUR AND TASTE**
- ✓ **SOLUBILITY**
- ✓ **MELTING POINT**
- ✓ **SPECIFIC GRAVITY**
- ✓ **GEOMETRIC ISOMERISM**
- ✓ **INSULATION**
- ✓ **EMULSIFICATION**
- ✓ **SURFACE TENSION**

CHEMICAL PROPERTIES/REACTIONS OF LIPID

The chemical reactions of the fats reflect the reactivities of the ester linkage and the degree of unsaturation of the hydrocarbon chain

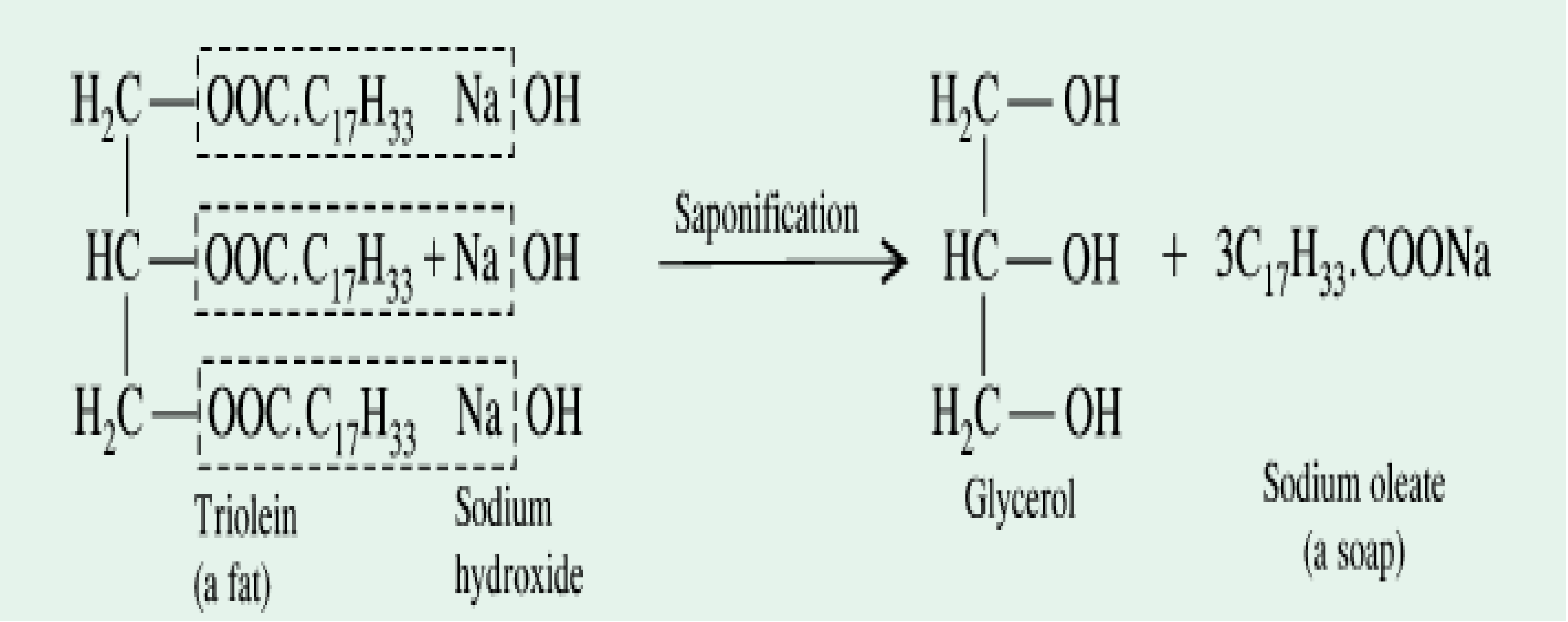
- **HYDROLYSIS: the fats are hydrolyzed by the enzymes lipases to yield mixtures of fatty acids and glycerol.**



[Radicals R_1, R_2 and R_3 may be similar or dissimilar.]

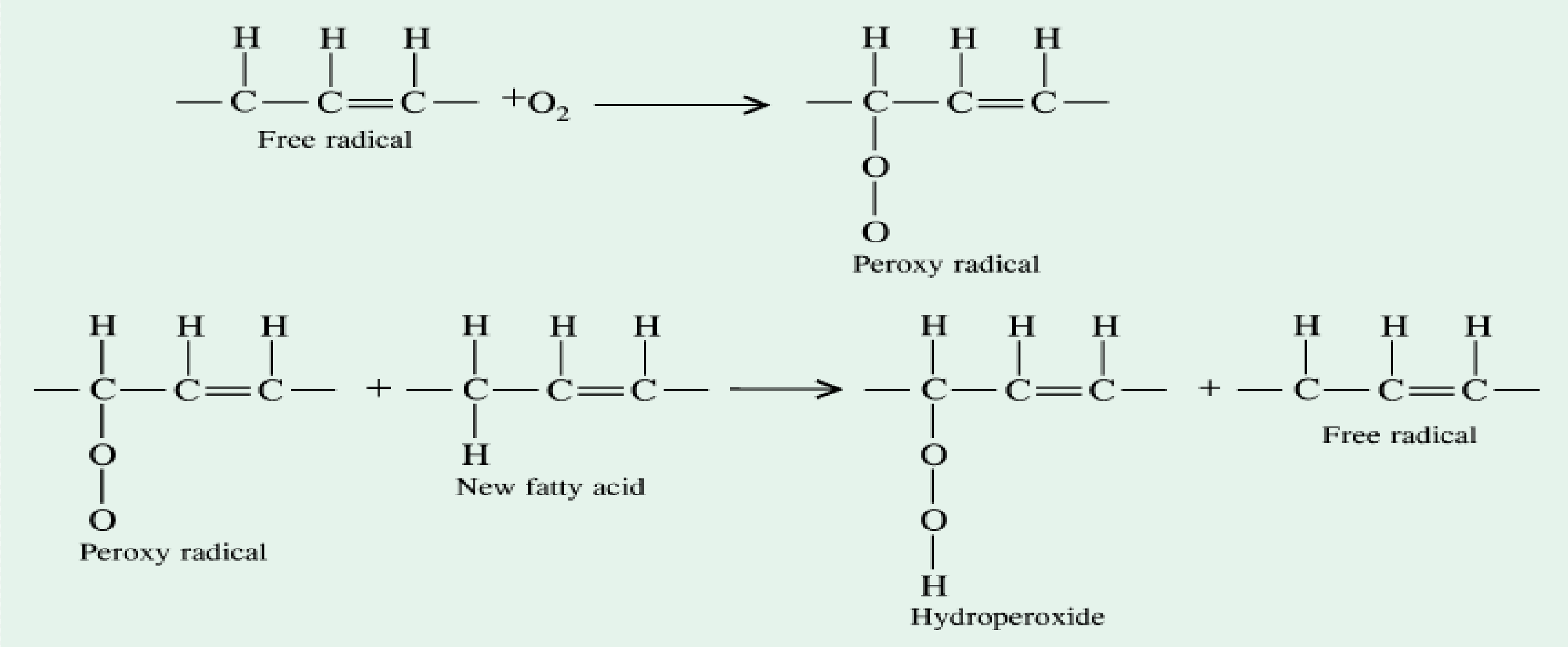
CHEMICAL PROPERTIES/REACTIONS OF LIPID

- **SAPONIFICATION: The hydrolysis of fats by alkali is called saponification. This reaction results in the formation of glycerol and salts of fatty acids which are called soaps**



CHEMICAL PROPERTIES/REACTIONS OF LIPID

- **RANCIDITY: there are two types of rancidity (1) Oxidative rancidity (2) hydrolytic rancidity**
- **(1) Oxidative rancidity/lipid peroxidation: oils containing highly unsaturated fatty acids are spontaneously oxidized by atmospheric oxygen at ordinary temperatures. This is due to a reaction called autoxidation. Autoxidation proceeds by a free radical mechanism in which the α-methylene group is attacked**



CHEMICAL PROPERTIES/REACTIONS OF LIPID

- **(2) Hydrolytic rancidity: when butter or other fats are stored, they often become rancid and hence unpalatable. This is caused by the growth of micro-organisms which secrete enzymes like lipases. This may be prevented by refrigeration or by exclusion of water**

SOME QUANTITATIVE TESTS FOR FATS AND OILS

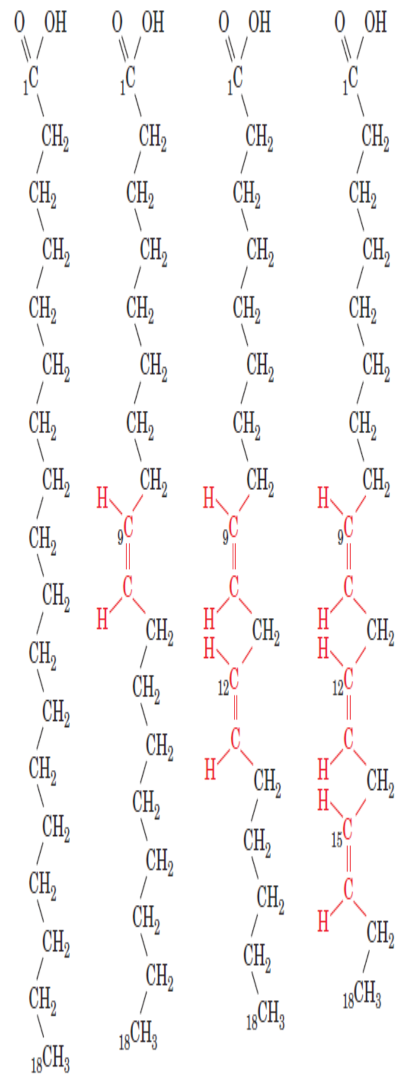
- **IODINE VALUE: It is the number of grams of iodine absorbed by 100g of fats. The iodine number is thus, a measure of the degree of unsaturation of the fatty acids in fats.**
- **PEROXIDE VALUE: Peroxides (R-OOH) are primary reaction products formed in the initial stages of oxidation, and therefore give an indication of the progress of lipid oxidation. One of the most commonly used methods of determining peroxide values utilizes the ability of peroxides to liberate iodine from potassium iodide**

$$R\text{-}OOH + KI_{excess} \longrightarrow ROH + KOH + I_2$$

Other quantitative tests include Acid value, saponification number, oxygen uptake etc.

CHEMISTRY AND PROPERTIES OF FATTY ACIDS

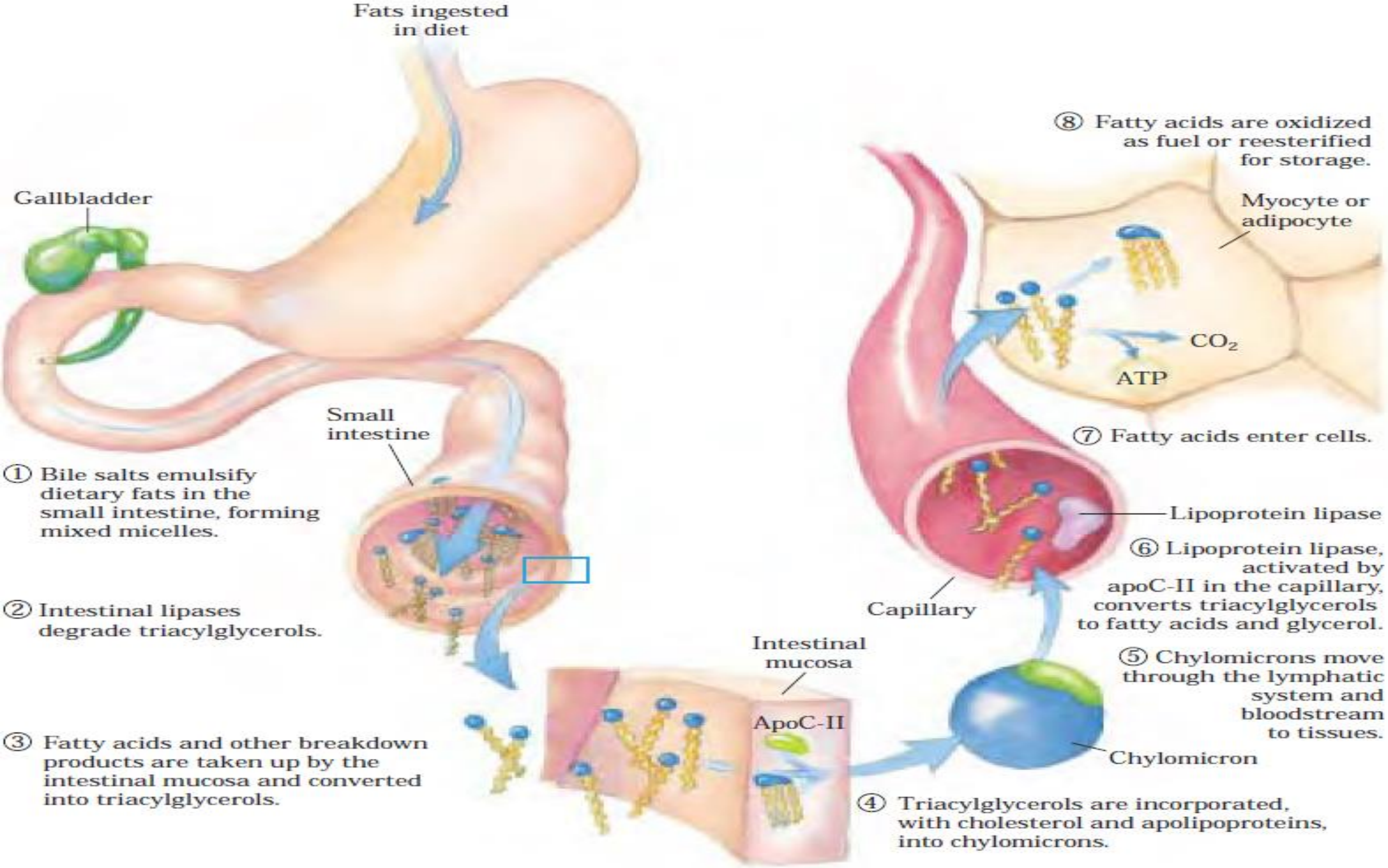
- **Fatty acids are carboxylic acids with hydrocarbon chains ranging from 4 to 36 carbon long.**
- **In most monounsaturated fatty acids, the double bond is between C-9 and C-10 (Δ9) and the other double bonds of polyunsaturated are generally Δ12 andΔ15**
- **The double bonds of polyunsaturated fatty acids are almost never conjugated but are separated by a methylene group**
- **In nearly all naturally occurring unsaturated fatty acids, the double bonds are in the cis configuration**



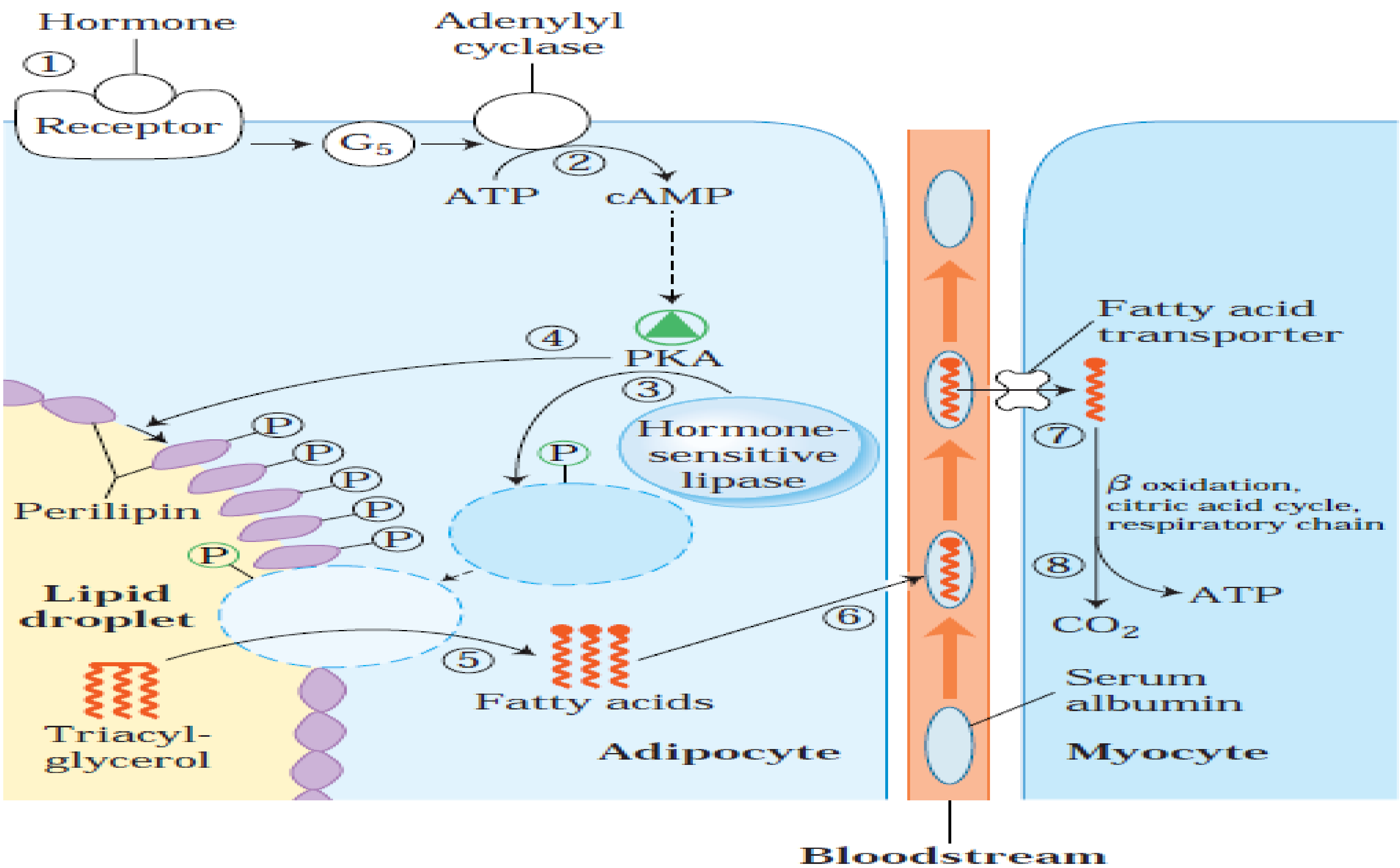
Stearic acid Oleic acid Linoleic acid α-Linolenic acid

Number of Carbons	Common Name	Systematic Name	Symbol	Structure
Saturated fatty acids				
12	Lauric acid	Dodecanoic acid	12:0	$CH_3(CH_2)_{10}COOH$
14	Myristic acid	Tetradecanoic acid	14:0	$CH_3(CH_2)_{12}COOH$
16	Palmitic acid	Hexadecanoic acid	16:0	$CH_3(CH_2)_{14}COOH$
18	Stearic acid	Octadecanoic acid	18:0	$CH_3(CH_2)_{16}COOH$
20	Arachidic acid	Eicosanoic acid	20:0	$CH_3(CH_2)_{18}COOH$
22	Behenic acid	Docosanoic acid	22:0	$CH_3(CH_2)_{20}COOH$
24	Lignoceric acid	Tetracosanoic acid	24:0	$CH_3(CH_2)_{22}COOH$
Unsaturated fatty acids (all double bonds are *cis*)				
16	Palmitoleic acid	9-Hexadecenoic acid	16:1	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$
18	Oleic acid	9-Octadecenoic acid	18:1	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$
18	Linoleic acid	9,12-Octadecadienoic acid	18:2	$CH_3(CH_2)_4(CH{=}CHCH_2)_2(CH_2)_6COOH$
18	α-Linolenic acid	9,12,15-Octadecatrienoic acid	18:3	$CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6COOH$
18	γ-Linolenic acid	6,9,12-Octadecatrienoic acid	18:3	$CH_3(CH_2)_4(CH{=}CHCH_2)_3(CH_2)_3COOH$
20	Arachidonic acid	5,8,11,14-Eicosatetraenoic acid	20:4	$CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2COOH$
24	Nervonic acid	15-Tetracosenoic acid	24:1	$CH_3(CH_2)_7CH{=}CH(CH_2)_{13}COOH$

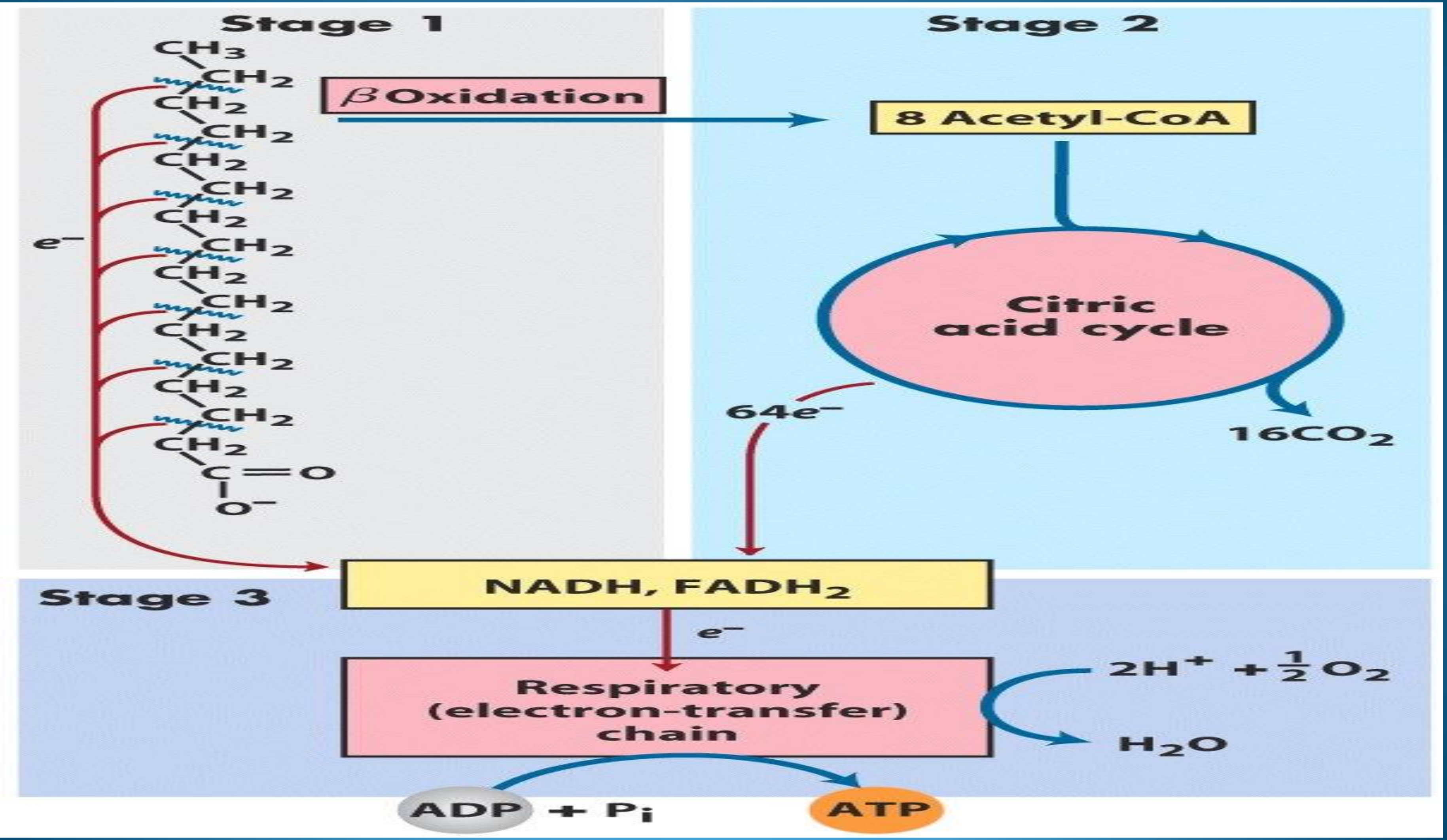
DIGESTION AND ABSORPTION OF FATS



HORMONES TRIGGER MOBILIZATION OF STORED TRIACYLGLYCEROL

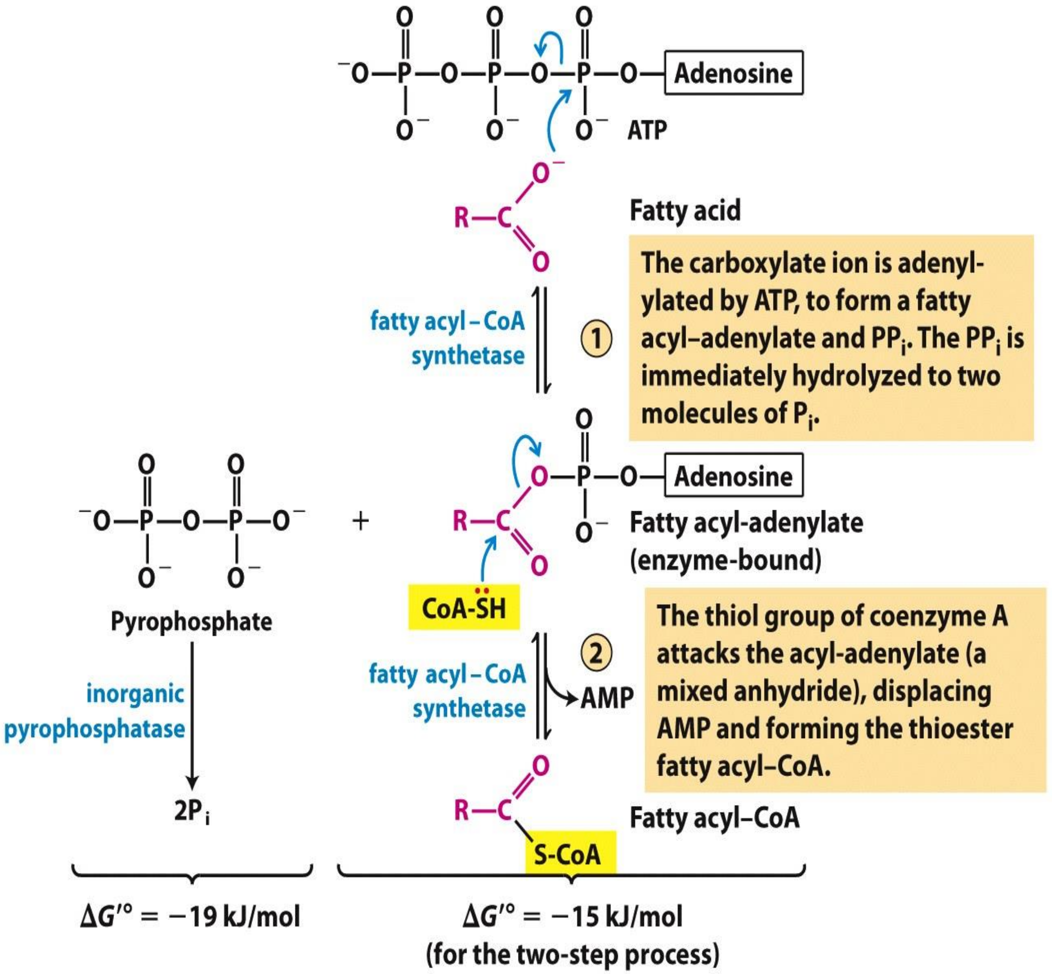


OVERVIEW OF FATTY ACID OXIDATION



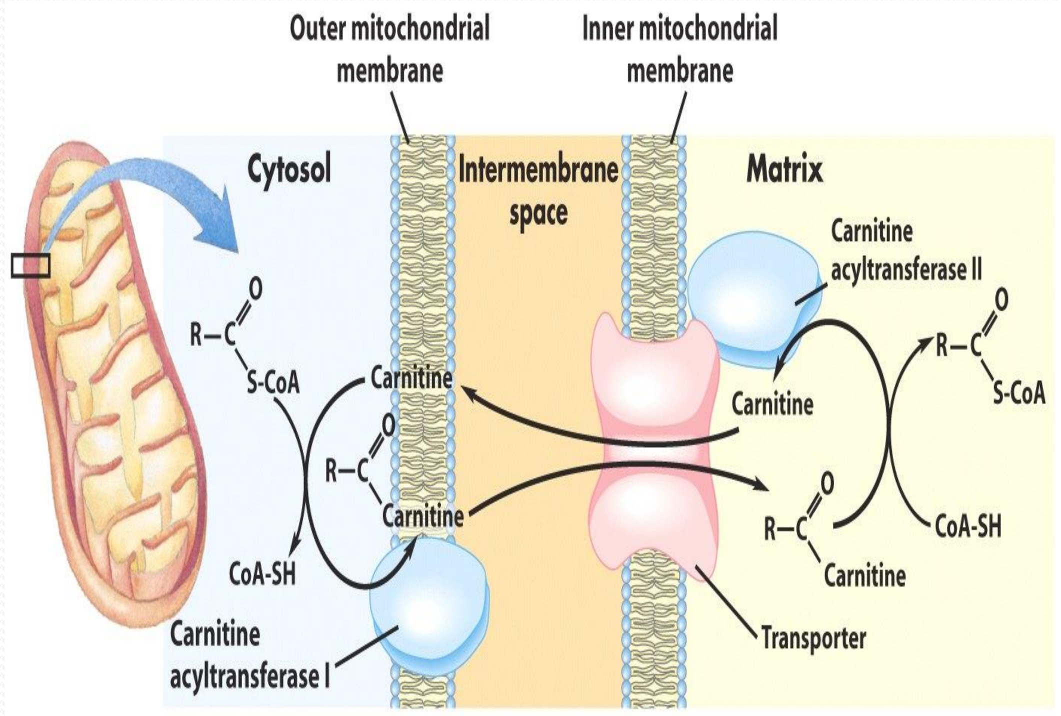
FATTY ACID ACTIVATION

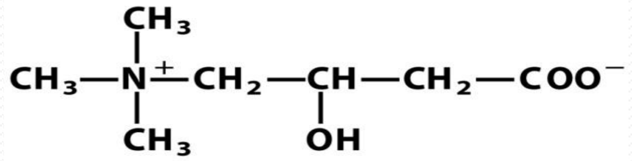
- **Before fatty acids can be oxidized, they must be "primed" for reaction in an ATP-dependent acylation to form fatty acyl-coA**.



TRANSPORT ACROSS MITOCHONDRIAL MEMBRANE

- **Although fatty acids are activated for oxidation in the cytosol, they are oxidized in the mitochondrial matrix**

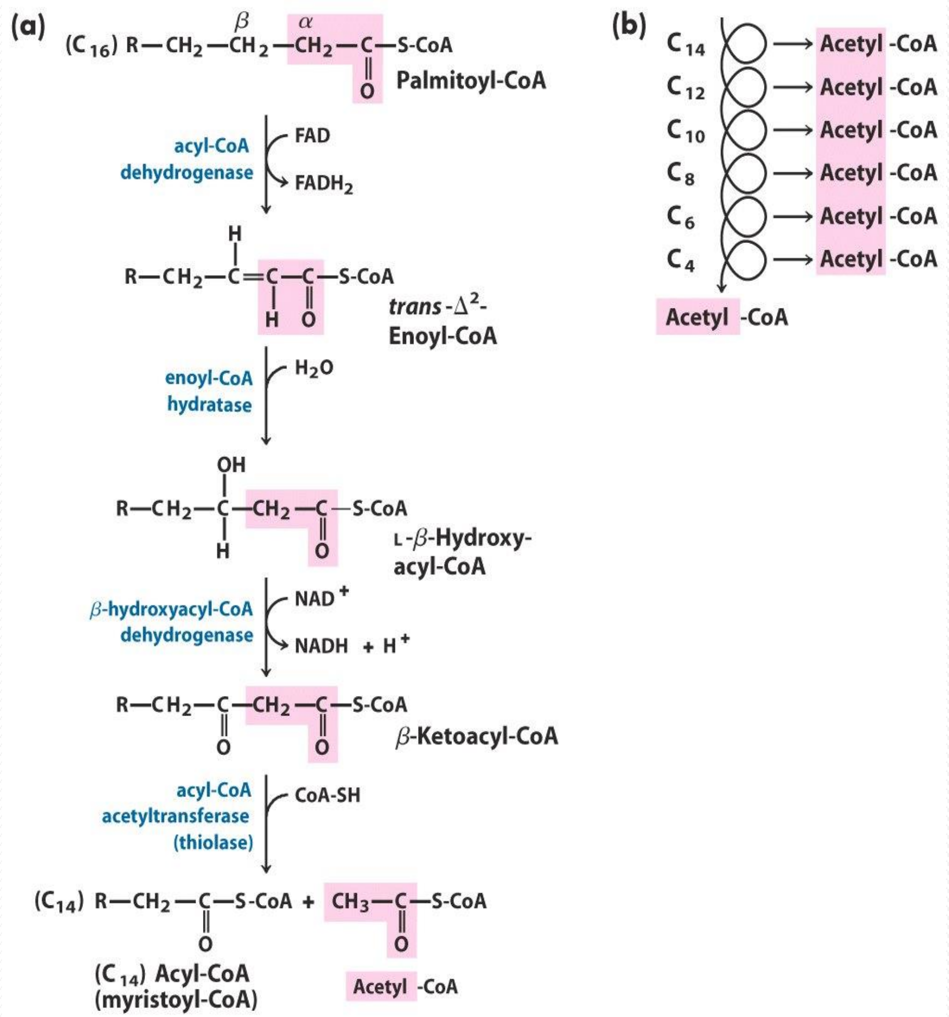




Carnitine

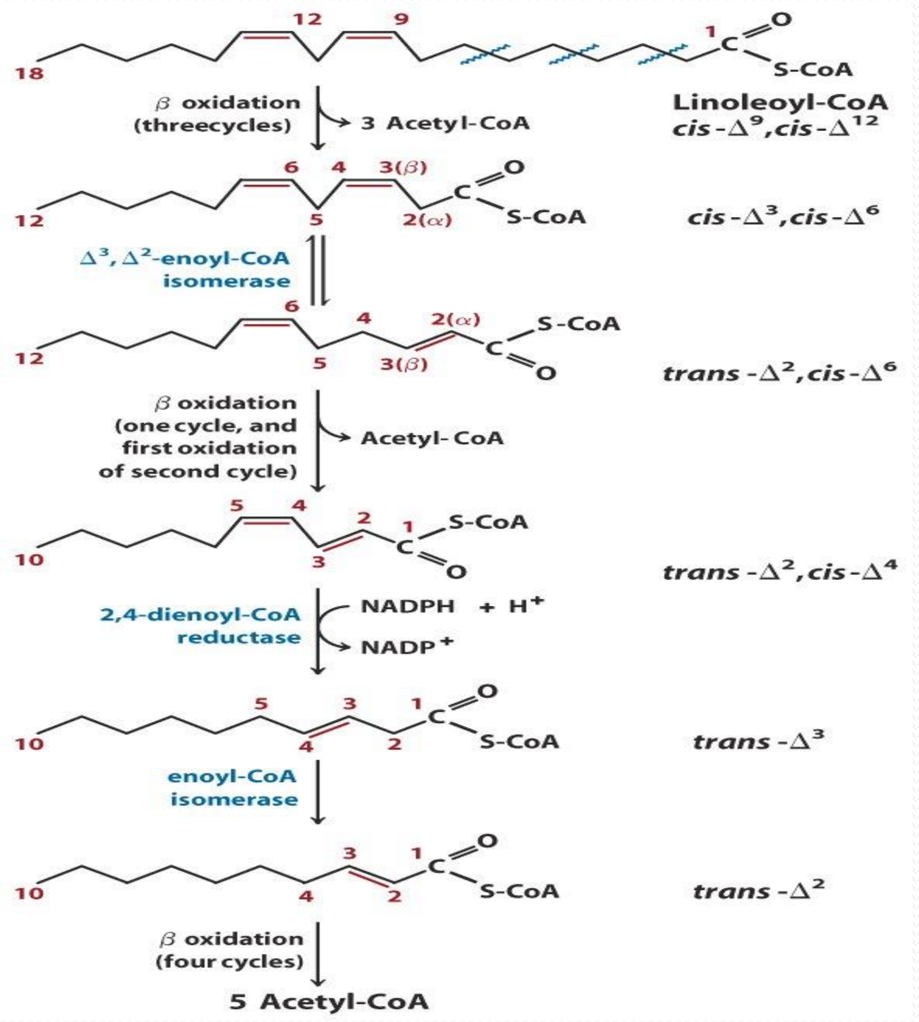
β OXIDATION OF SATURATED FATTY ACIDS

- **Fatty acids are dismembered through the β oxidation of fatty acyl coA, a process that occurs in four reactions**

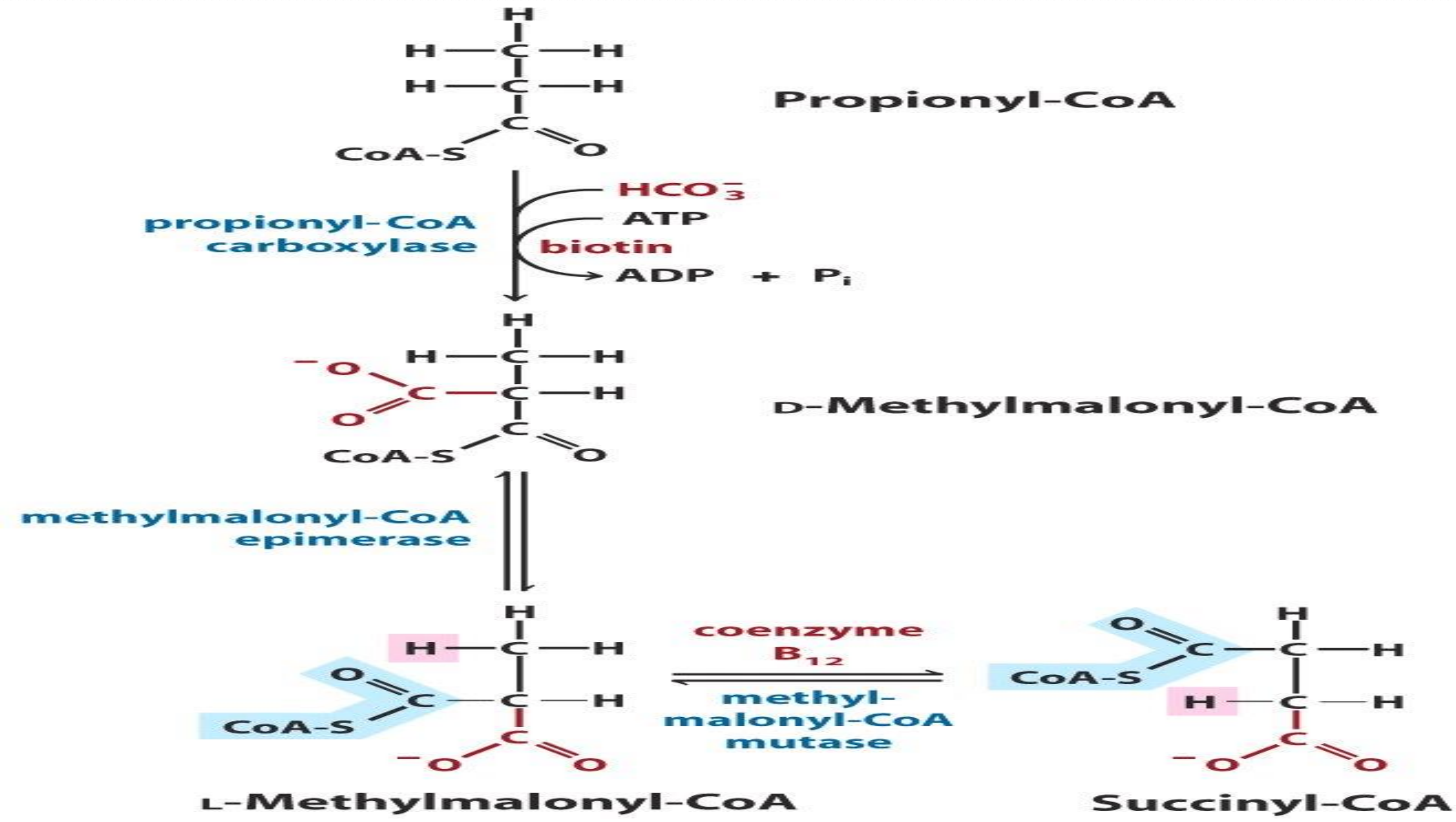


OXIDATION OF UNSATURATED FATTY ACIDS

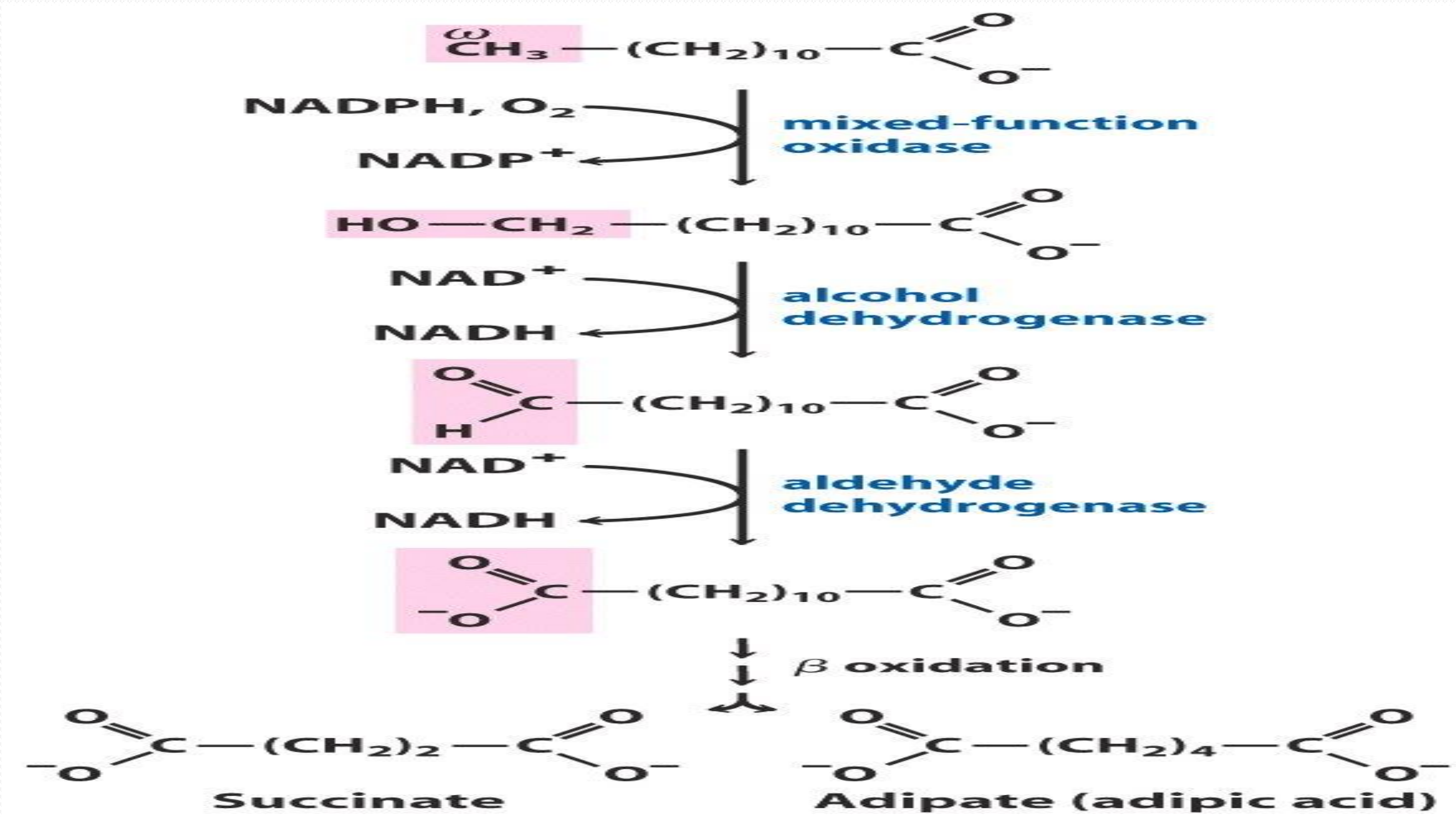
- **Two auxiliary enzymes are needed for complete β oxidation of the common unsaturated fatty acids**
- **Δ3,Δ2-enoyl-coA isomerase and 2,4 dienoyl-coA reductase allows reentry of intermediates generated into the β oxidation pathway**



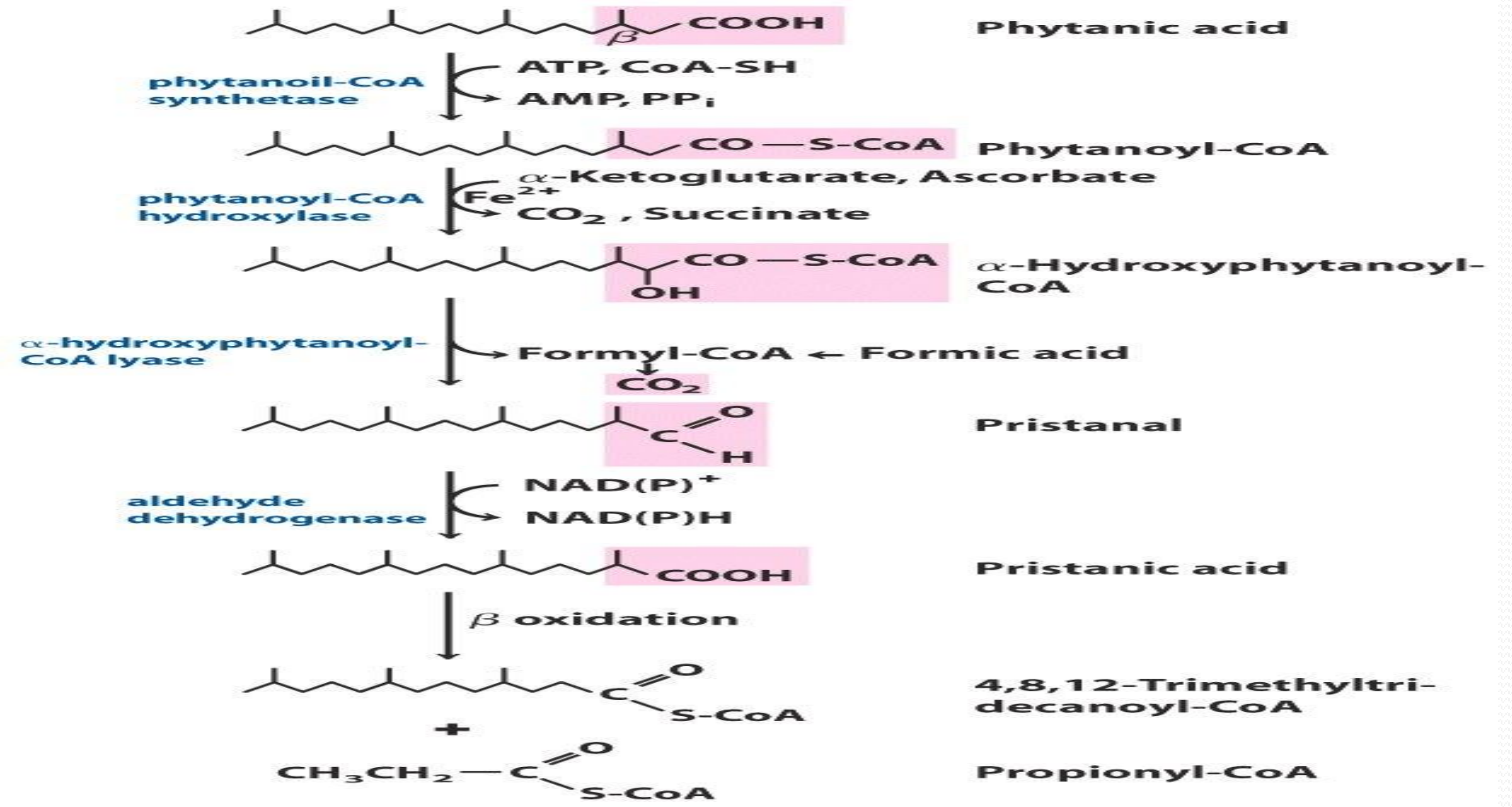
COMPLETE OXIDATION OF ODD NUMBER FATTY ACIDS REQUIRES THREE EXTRA REACTIONS



OMEGA OXIDATION OF FATTY ACIDS OCCURS IN THE ENDOPLASMIC RETICULUM



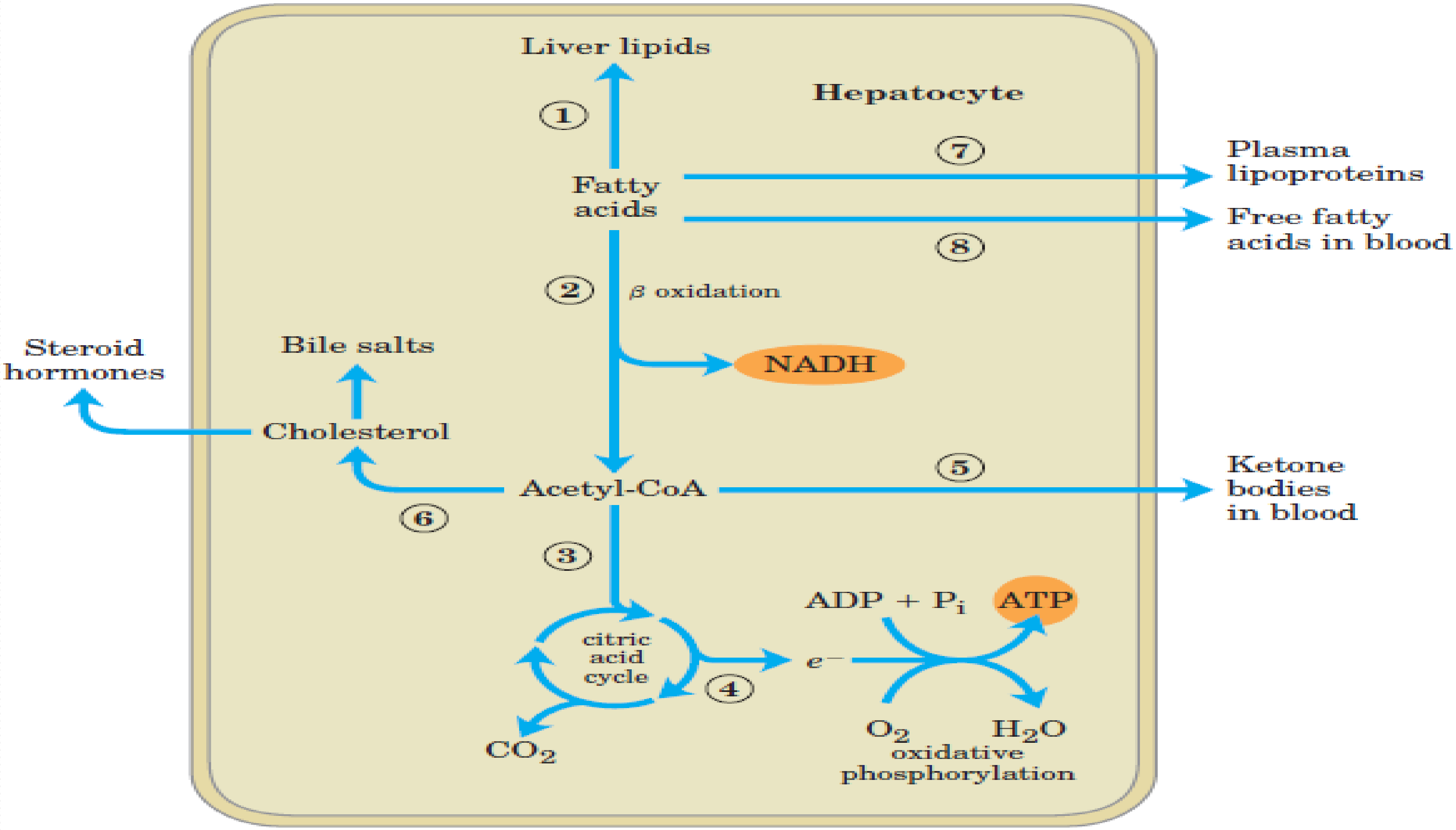
α OXIDATION OF BRANCHED-CHAIN FATTY ACIDS IN PEROXISOMES



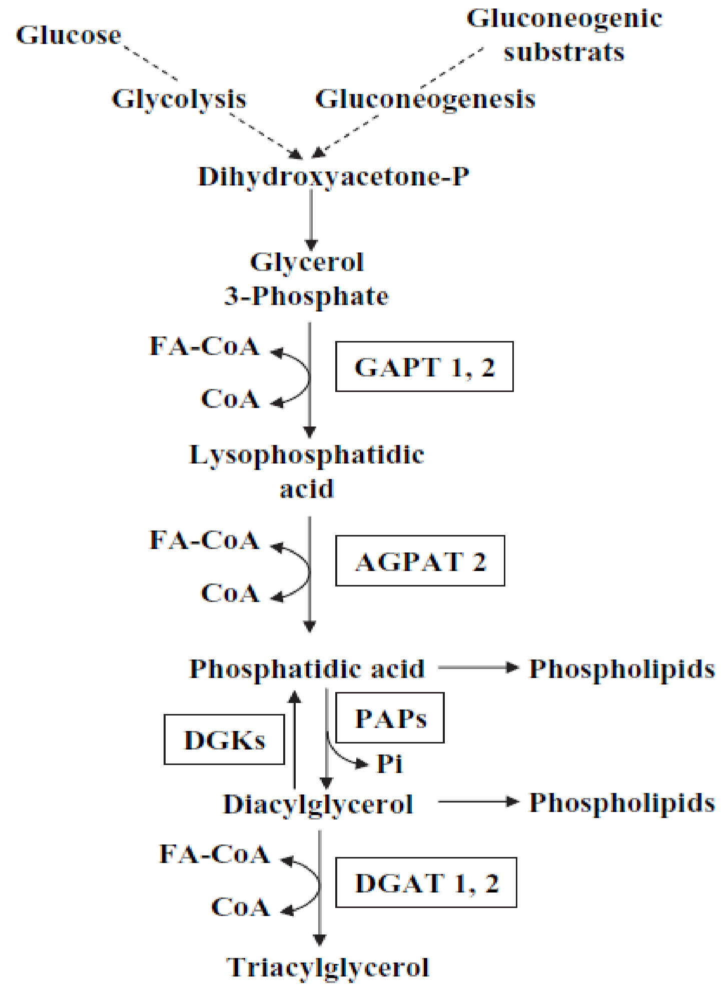
OXIDATION OF PHOSPHOLIPIDS

- There is increasing evidence that oxidized phospholipids (OxPLs) play an important role in atherosclerosis and attendant CVDs. these phospholipids accumulate in human and mouse lesions
- Specific OxPLs have been identified as major regulators of many cell types
- OxPLs regulate vascular cell function:
  - Endothelial cells
  - Dendritic cells
  - Smooth muscle cells
  - Platelets
- Oxidative breakdown of biological phospholipids occurs in most cellular membranes including mitochondria, microsomes, peroxisomes and plasma membrane.

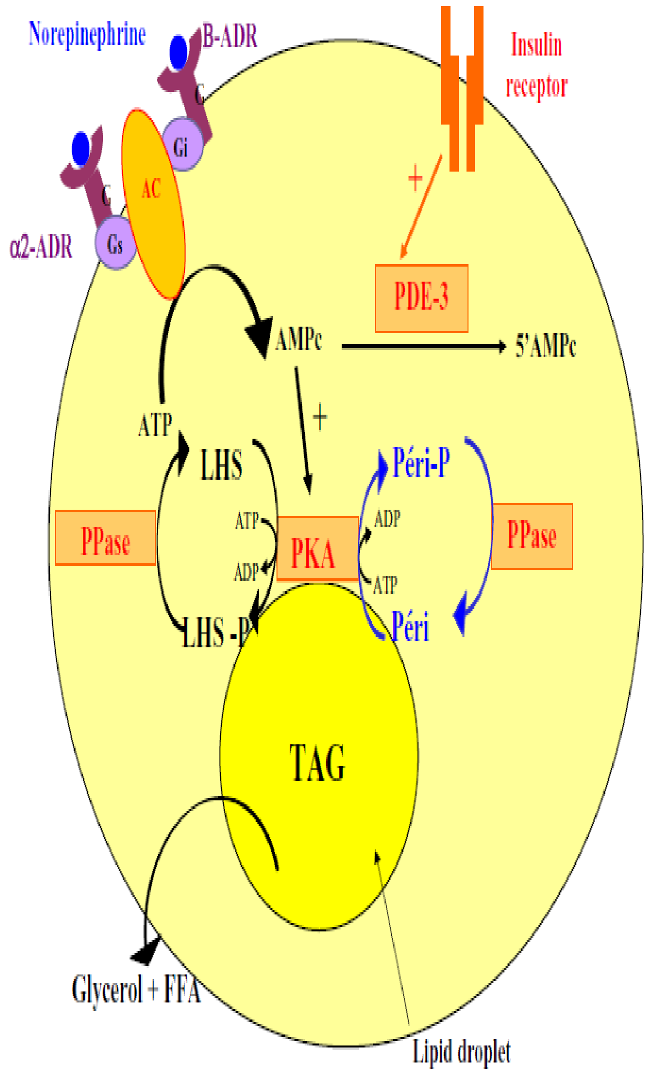
THE ROLE OF THE LIVER IN LIPID METABOLISM



LIPID METABOLISM IN ADIPOSE TISSUE



Triglyceride synthesis pathway in adipocytes. FA-CoA: acyl CoenzymeA; GAPT: glycerol-3-phosphate acyltransferase; AGPAT: 1-acylglycerol-3-phosphate acyltransferase; PAPs: phosphatidate phosphohydrolase; DGKs: diacylglycerol kinase; DGAT: diacylglycerol acyltransferase.



The lipolytic cascade in adipocyte. ADR: adrenoceptor, AC: adenylyl cyclase, FFA: free fatty acid, G: G protein, LHS: hormone-sensitive lipase, PDE: phophodiesterase, Peri: perilipin, PKA: protein kinase A, PPase: protein phos-phatase, TAG: triacylglycerol.

QUESTIONS AND COMMENTS