بسمه تعالی

کارشناسی ارشد
بیوشیمی و بیولوژی سلول

چربی ها و اسیدهای چرب

ابراهیم قاسمی

lipids

- The common and defining feature of which is their insolubility in water.

- Hydrophobic or amphiphilic

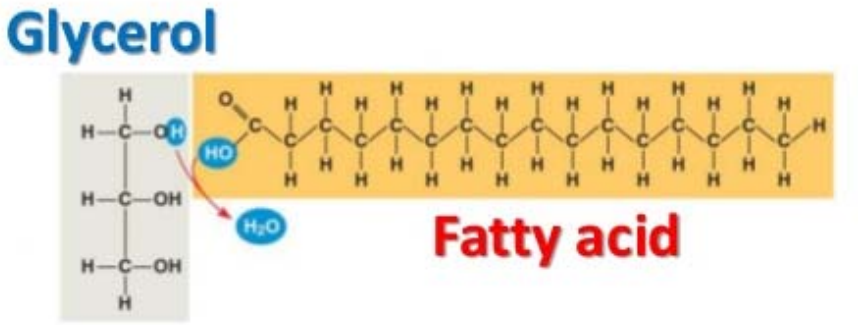
Importance

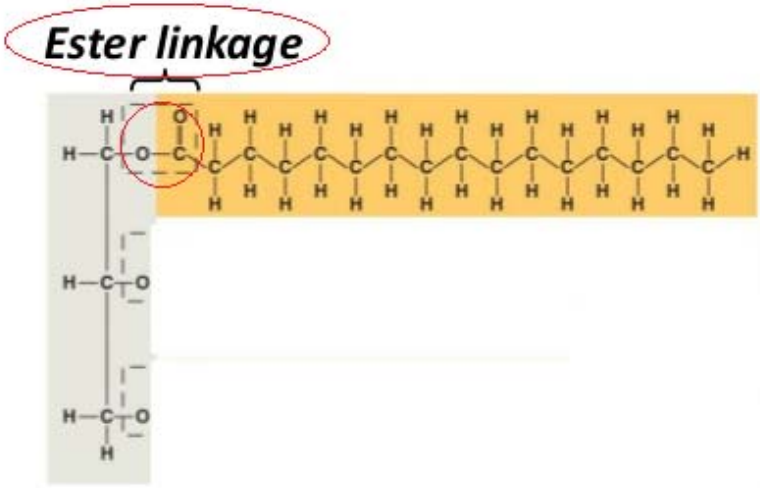
- stored forms of energy
- Structural elements of biological membranes
- electrical insulators
- hormones, and intracellular messengers
- enzyme cofactors, electron carriers, light absorbing pigments

Classification

- **Simple lipids**
  - **Fats and Oils (triacylglycerols)**
  - **Waxes**
- **Complex lipids**
  - **Phospholipids**
  - **Glycolipids**
  - **Sphingolipids**
- **Sterols**

Condensation reaction





Fatty acids

- hydrocarbon derivatives (carboxylic acids)
- carbons length (C4 to C36).
- even numbers
- Saturated
- One or more double bonds (unsaturated)
- Unconjugated (double bonds, are separated by a methylene group)
- cis configuration

Table 14–1. Saturated fatty acids.

Common Name	Number of C Atoms	
Acetic	2	Major end product of carbohydrate fermentation by rumen organisms[1]
Propionic	3	An end product of carbohydrate fermentation by rumen organisms[1]
Butyric	4	In certain fats in small amounts (especially butter). An end product of carbohydrate fermentation by rumen organisms[1]
Valeric	5	
Caproic	6	
Lauric	12	Spermaceti, cinnamon, palm kernel, coconut oils, laurels, butter
Myristic	14	Nutmeg, palm kernel, coconut oils, myrtles, butter
Palmitic	16	Common in all animal and plant fats
Stearic	18	

Table 14–2. Unsaturated fatty acids of physiologic and nutritional significance.

Number of C Atoms and Number and Position of Double Bonds	Family	Common Name	Systematic Name	Occurrence
Monoenoic acids (one double bond)				
16:1;9	ω7	Palmitoleic	*cis*-9-Hexadecenoic	In nearly all fats.
18:1;9	ω9	Oleic	*cis*-9-Octadecenoic	Possibly the most common fatty acid in natural fats.
18:1;9	ω9	Elaidic	*trans*-9-Octadecenoic	Hydrogenated and ruminant fats.
Dienoic acids (two double bonds)				
18:2;9,12	ω6	Linoleic	all-*cis*-9,12-Octadecadienoic	Corn, peanut, cottonseed, soybean, and many plant oils.
Trienoic acids (three double bonds)				
18:3;6,9,12	ω6	γ-Linolenic	all-*cis*-6,9,12-Octadecatrienoic	Some plants, eg, oil of evening primrose, borage oil; minor fatty acid in animals.
18:3;9,12,15	ω3	α-Linolenic	all-*cis*-9,12,15-Octadecatrienoic	Frequently found with linoleic acid but particularly in linseed oil.
Tetraenoic acids (four double bonds)				
20:4;5,8,11,14	ω6	Arachidonic	all-*cis*-5,8,11,14-Eicosatetraenoic	Found in animal fats and in peanut oil; important component of phospholipids in animals.
Pentaenoic acids (five double bonds)				
20:5;5,8,11,14,17	ω3	Timnodonic	all-*cis*-5,8,11,14,17-Eicosapentaenoic	Important component of fish oils, eg, cod liver, mackerel, menhaden, salmon oils.
Hexaenoic acids (six double bonds)				
22:6;4,7,10,13,16,19	ω3	Cervonic	all-*cis*-4,7,10,13,16,19-Docosahexaenoic	Fish oils, phospholipids in brain.

Nomenclature

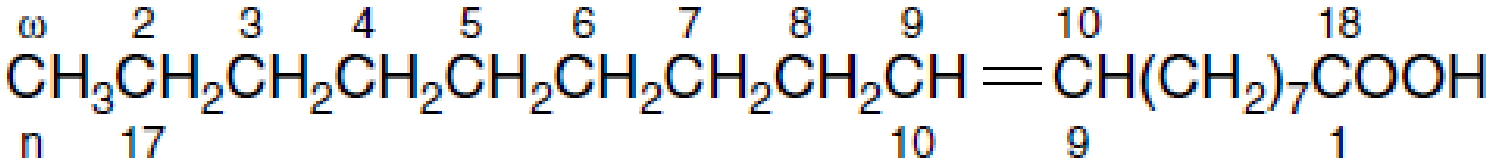
- **Carbon**
  - The carbon atoms adjacent to the carboxyl carbon (No. 2, 3, and 4) are also known as the α, β, and γ carbons, the terminal methyl carbon is known as the ω or n-carbon.

- **names of hydrocarbon (saturated acids end in -anoic, and unsaturated acids with double bonds end in -enoic)**
  - octadecenoic acid (oleic acid)

- **the chain length, number of double bonds, positions of any double bonds**
  - $18:2(\Delta^{9,12})$

Oleic acid

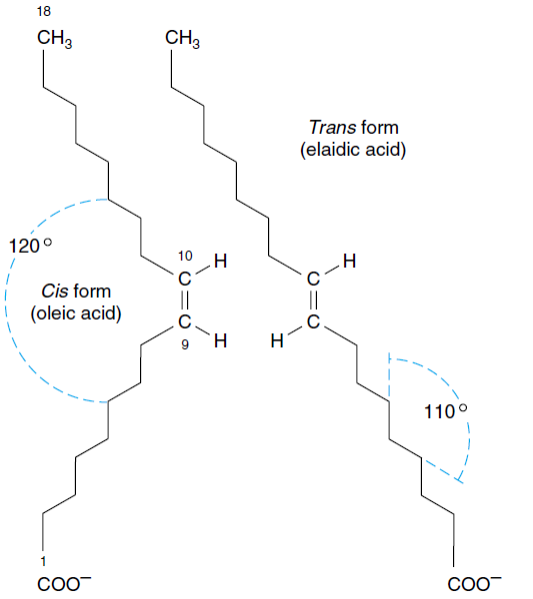
ω9,C18:1 *or* n–9, 18:1



α, β, and γ

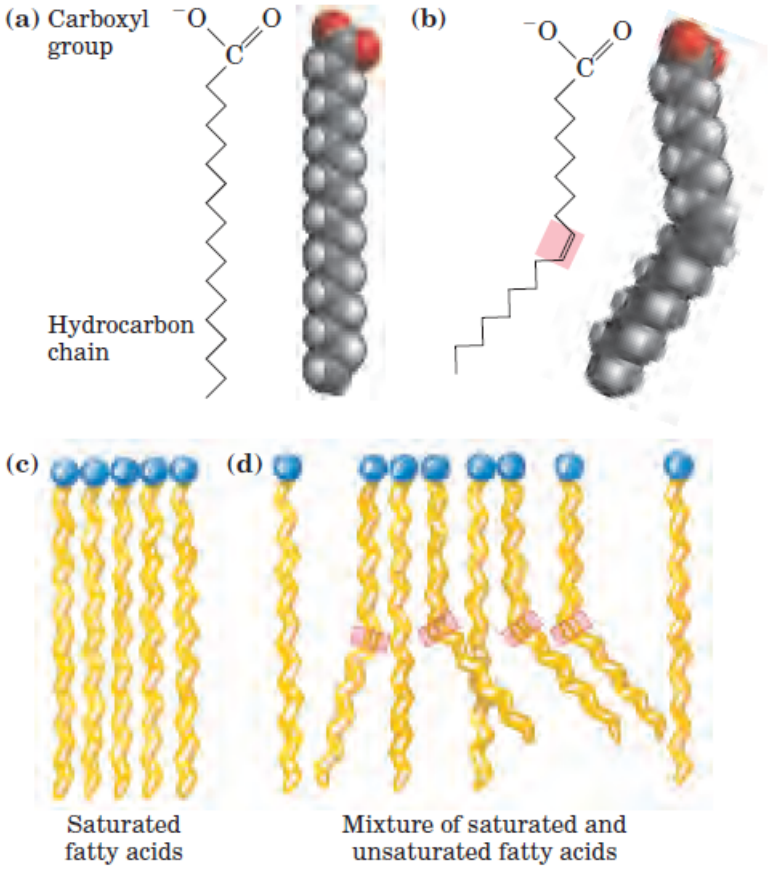
Trans fatty acids

- increased blood levels of LDL (bad cholesterol) and decreased HDL (good cholesterol)
  - French fries, doughnuts, and cookies
  - during hydrogenation, or “hardening,” of natural oils
- Improved health
  - Dairy products and meat



Physical properties of the fatty acids

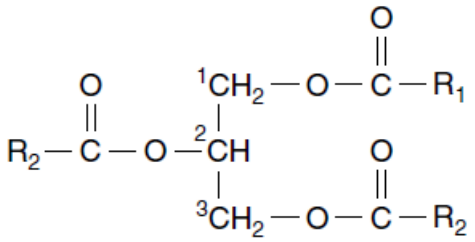
- the length and degree of unsaturation
  - solubility of fatty acids in water
  - Melting points



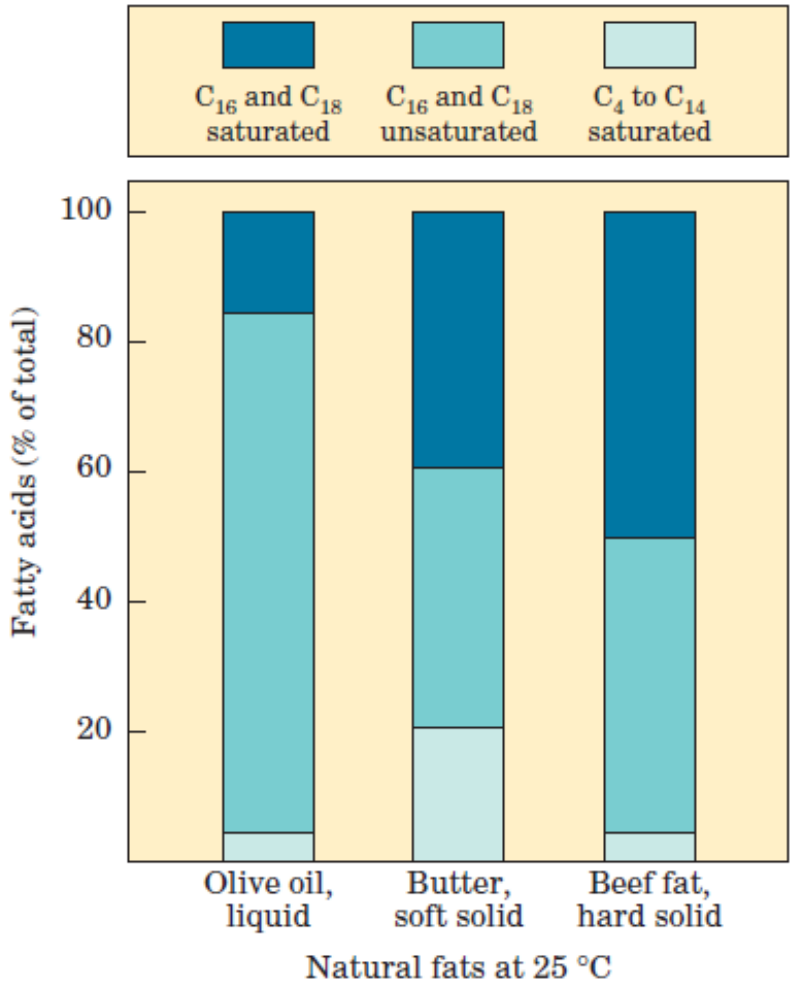
Carbon skeleton	Structure*	Systematic name†	Common name (derivation)	Melting point (°C)	Solubility (mg/g solvent)	
					Water	Benzene
12:0	$CH_3(CH_2)_{10}COOH$	*n*-Dodecanoic acid	Lauric acid (Latin *laurus*, "laurel plant")	44.2	0.063	2,600
14:0	$CH_3(CH_2)_{12}COOH$	*n*-Tetradecanoic acid	Myristic acid (Latin *Myristica*, nutmeg genus)	53.9	0.024	874
16:0	$CH_3(CH_2)_{14}COOH$	*n*-Hexadecanoic acid	Palmitic acid (Latin *palma*, "palm tree")	63.1	0.0083	348
18:0	$CH_3(CH_2)_{16}COOH$	*n*-Octadecanoic acid	Stearic acid (Greek *stear*, "hard fat")	69.6	0.0034	124
20:0	$CH_3(CH_2)_{18}COOH$	*n*-Eicosanoic acid	Arachidic acid (Latin *Arachis*, legume genus)	76.5		
24:0	$CH_3(CH_2)_{22}COOH$	*n*-Tetracosanoic acid	Lignoceric acid (Latin *lignum*, "wood" + *cera*, "wax")	86.0		
16:1(Δ^9)	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	*cis*-9-Hexadecenoic acid	Palmitoleic acid	1–0.5		
18:1(Δ^9)	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	*cis*-9-Octadecenoic acid	Oleic acid (Latin *oleum*, "oil")	13.4		
18:2($\Delta^{9,12}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-9,12-Octadecadienoic acid	Linoleic acid (Greek *linon*, "flax")	1–5		
18:3($\Delta^{9,12,15}$)	$CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-,*cis*-9,12,15-Octadecatrienoic acid	α-Linolenic acid	−11		
20:4($\Delta^{5,8,11,14}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_3COOH$	*cis*-,*cis*-,*cis*-,*cis*-5,8,11,14-Icosatetraenoic acid	Arachidonic acid	−49.5		

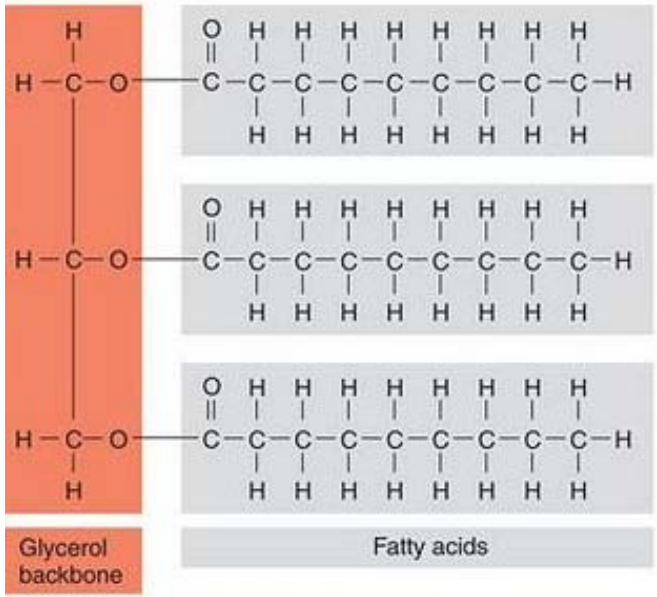
TRIACYLGLYCEROLS (TRIGLYCERIDES)

- **Esters of fatty acids with glycerol**
- **mixed triacylglycerols**
  - **Triacylglycerols that are composed largely of unsaturated fatty acids are called oil and those from saturated FA are called Fat.**
- **Stored forms of energy: are highly exergonic**
  - **In vertebrates (adipocytes)**
  - **Germinating seeds**
- **Insulation**

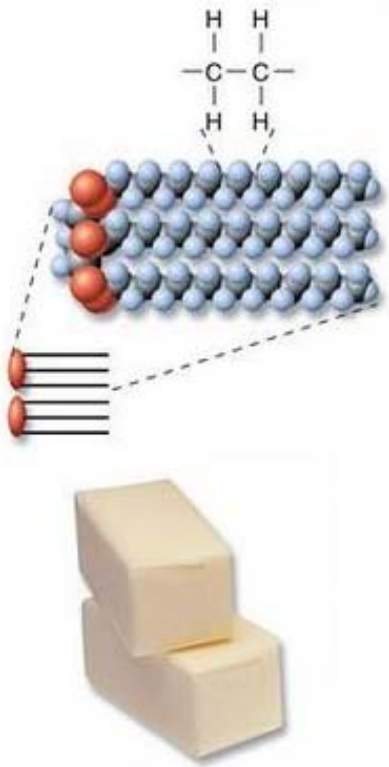


Triacylglycerol.

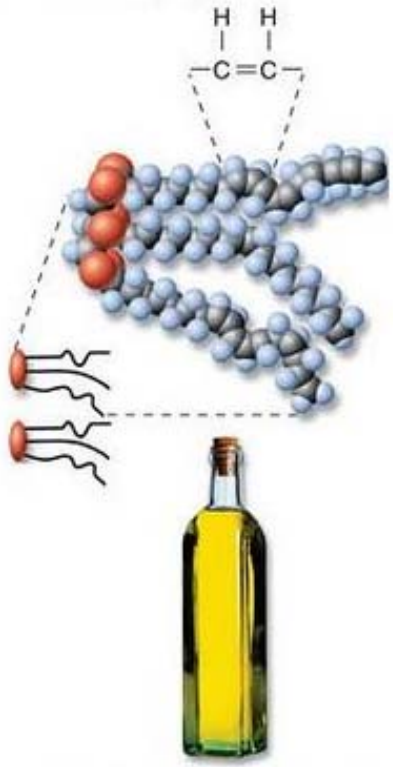

C_{16} and C_{18} saturated
C_{16} and C_{18} unsaturated
C_4 to C_{14} saturated
Fatty acids (% of total)
100
80
60
40
20
Olive oil, liquid
Butter, soft solid
Beef fat, hard solid
Natural fats at 25 °C



(a) Fat molecule (triacylglycerol)



(b) Hard fat (saturated): Fatty acids with single bonds between all carbon pairs

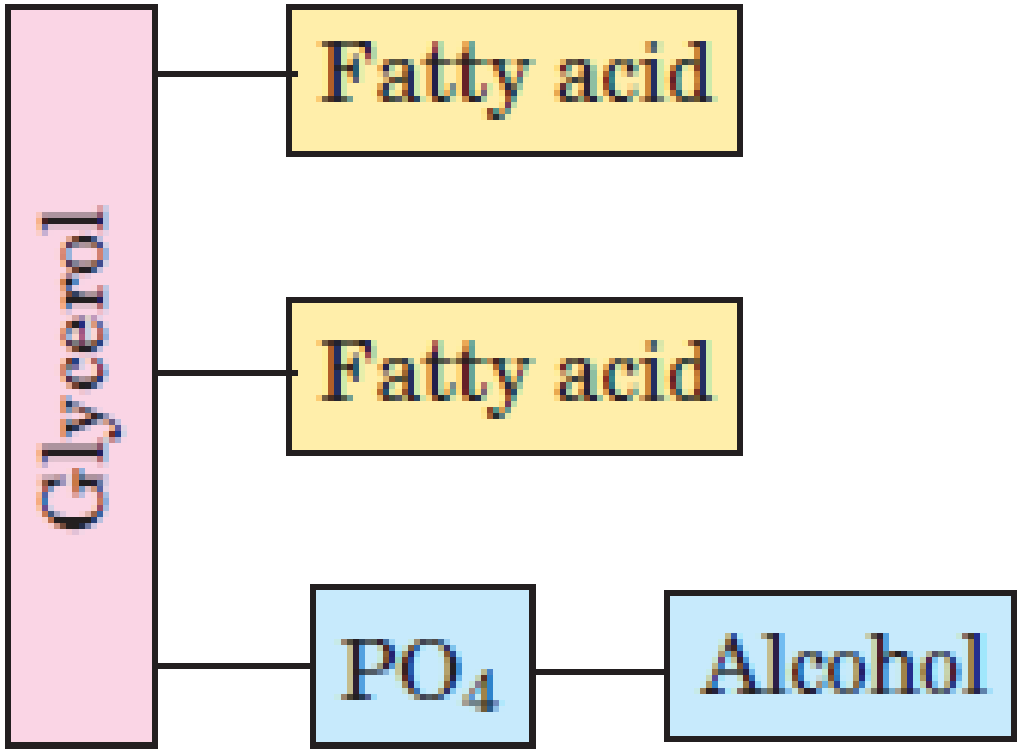


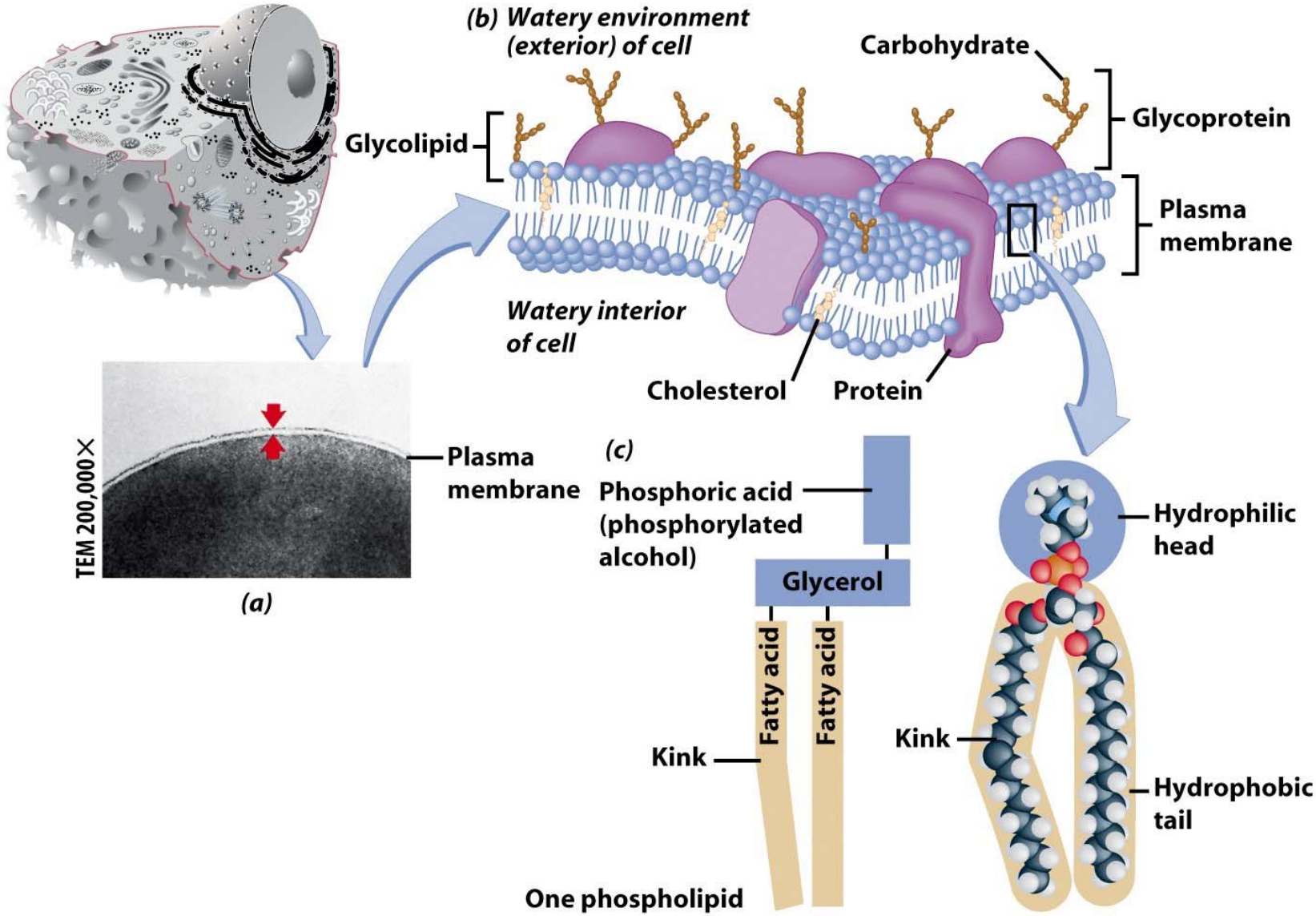
(c) Oil (unsaturated): Fatty acids that contain double bonds between one or more pairs of carbon atoms

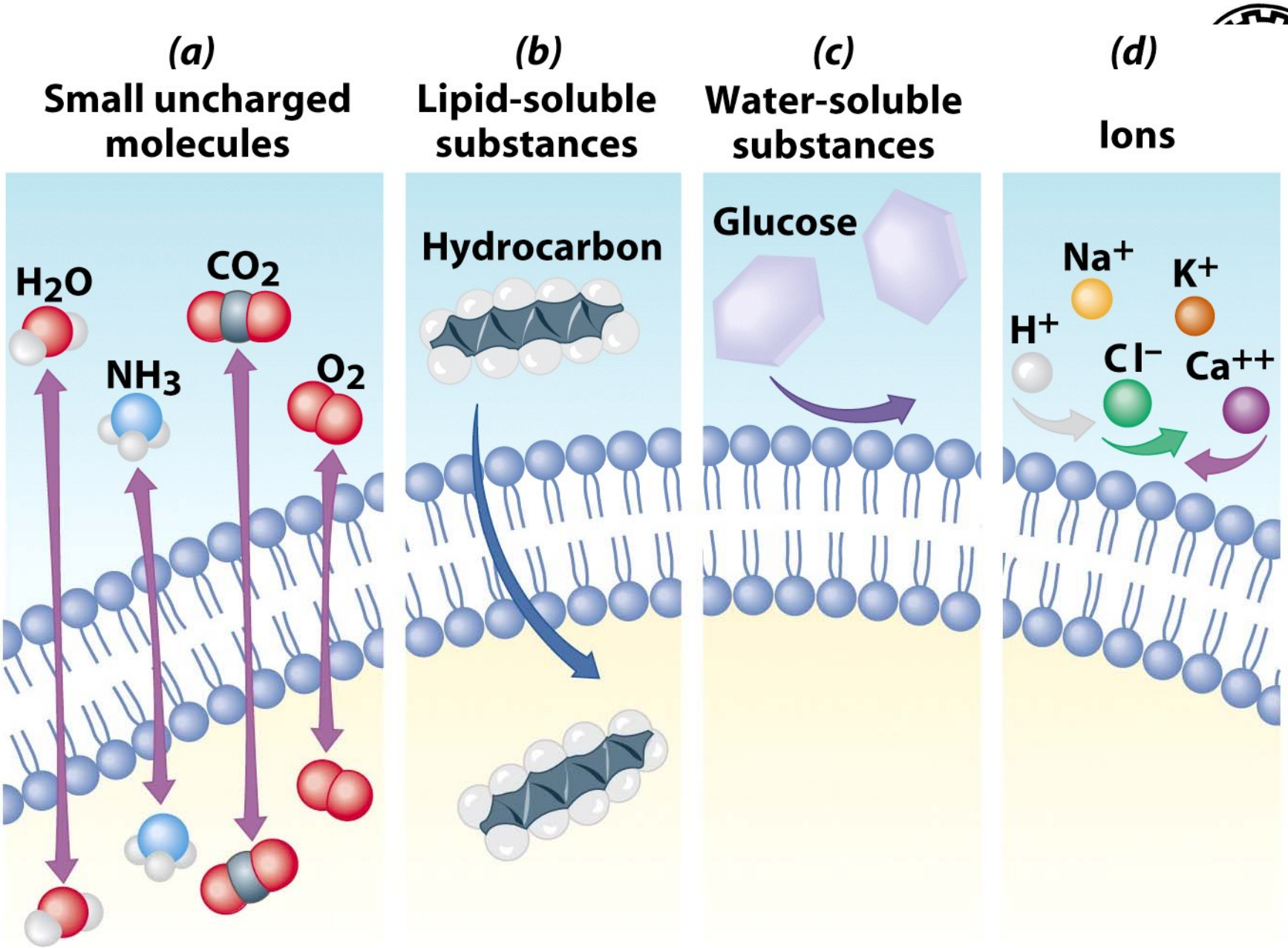
Waxes

- long-chain (C14 to C36) saturated and unsaturated fatty acids with long-chain (C16 to C30) alcohols
- Energy Stores
  - Plankton
- Water Repellents
  - Birds
  - tropical plants
  - Lanolin
  - beeswax

Phospholipids

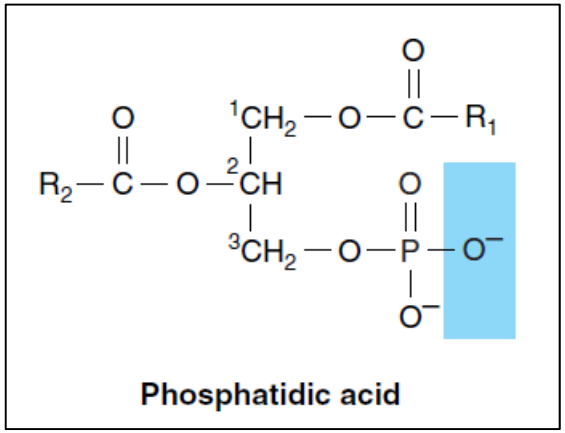


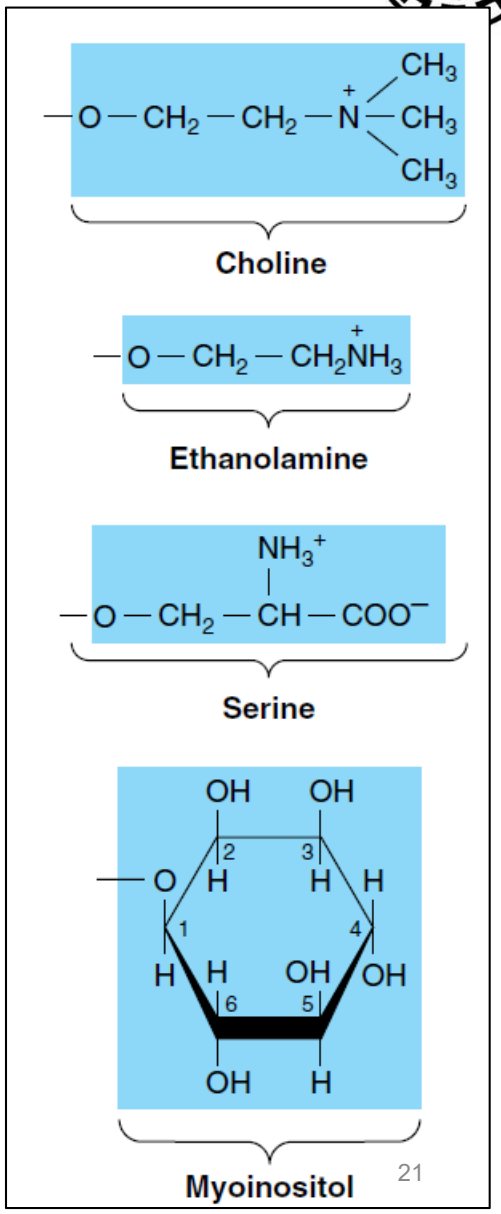

(b) Watery environment (exterior) of cell
Carbohydrate
Glycoprotein
Glycolipid
Plasma membrane
Watery interior of cell
Cholesterol
Protein
TEM 200,000×
Plasma membrane
(a)
(c)
Phosphoric acid (phosphorylated alcohol)
Glycerol
Fatty acid
Fatty acid
Kink
Kink
Hydrophilic head
Hydrophobic tail
One phospholipid

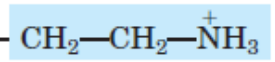
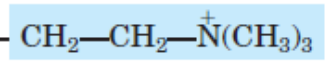
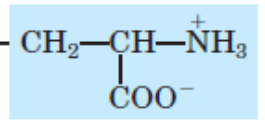
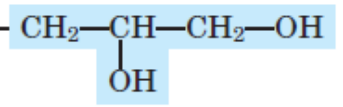
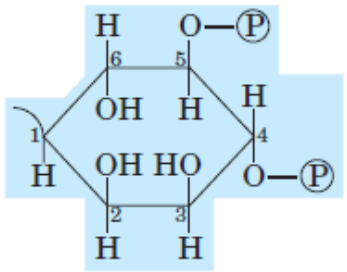
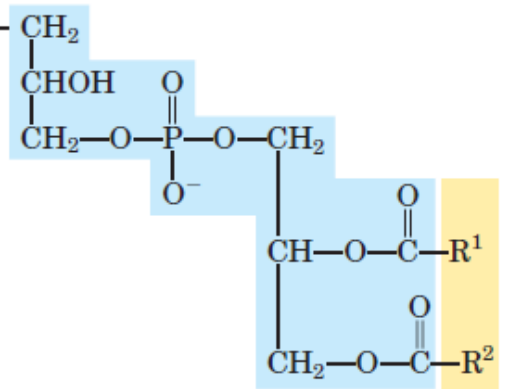

(a)
Small uncharged molecules
(b)
Lipid-soluble substances
(c)
Water-soluble substances
(d)
Ions
H2O
CO2
NH3
O2
Hydrocarbon
Glucose
Na+
K+
H+
Cl−
Ca++

…Phospholipids

- **Derivatives of phosphatidic acid**
- **Phosphatidic acid as an intermediate in the synthesis of phosphoglycerols**

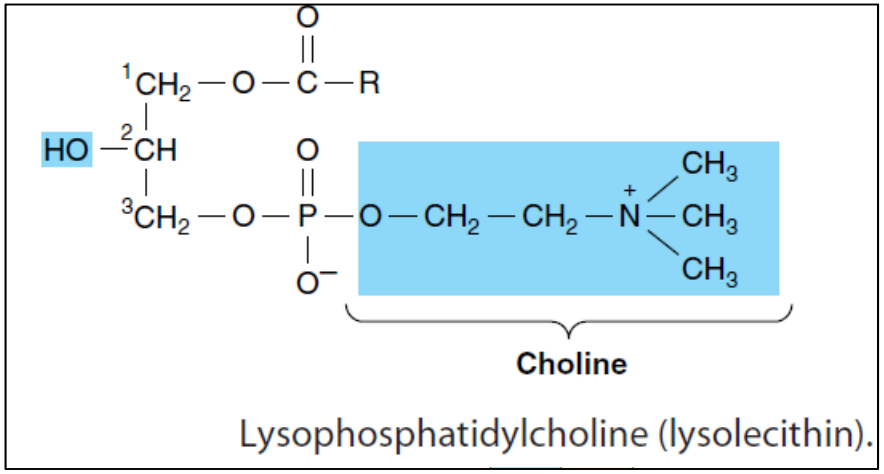




Name of glycerophospholipid	Name of X	Formula of X	Net charge (at pH 7)
Phosphatidic acid	—		−1
Phosphatidylethanolamine	Ethanolamine		0
Phosphatidylcholine	Choline		0
Phosphatidylserine	Serine		−1
Phosphatidylglycerol	Glycerol		−1
Phosphatidylinositol 4,5-bisphosphate	*myo*-Inositol 4,5-bisphosphate		−4
Cardiolipin	Phosphatidyl-glycerol		−2

…Phospholipids

- **Lysophospholipids as Intermediates in the Metabolism of Phosphoglycerols**



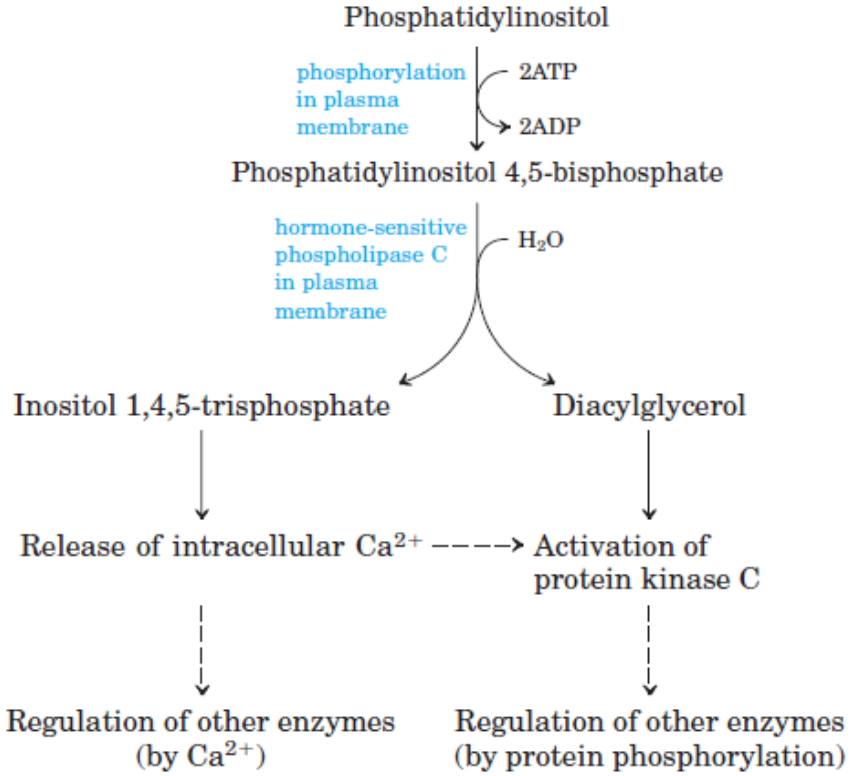
Lysophosphatidylcholine (lysolecithin).

…Phospholipids

- **Phosphatidylcholines (Lecithins)**
  - **Membrane bilayers**
  - **Surfactant**

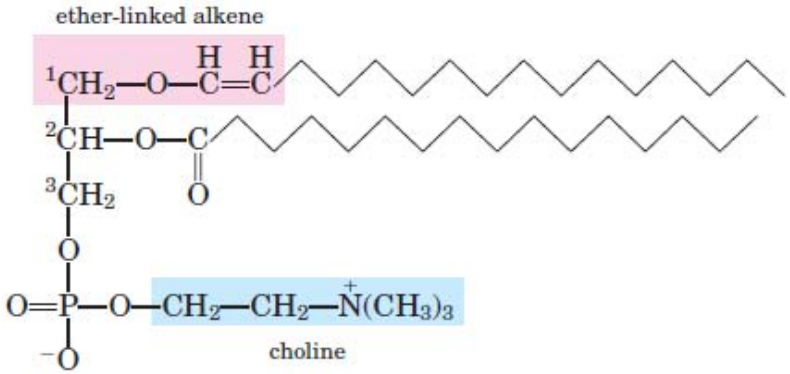
…Phospholipids

- **Phosphatidylinositol**
  - reservoir of messenger molecules

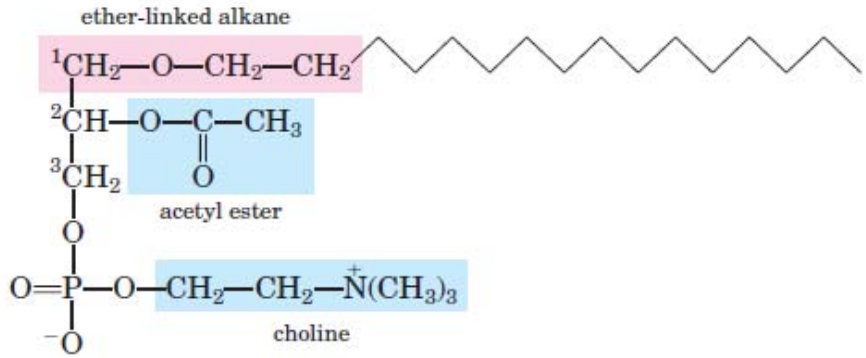


Some Phospholipids Have Ether-Linked Fatty Acids

- Heart tissue, membranes of halophilic bacteria, ciliated protists, and certain invertebrates



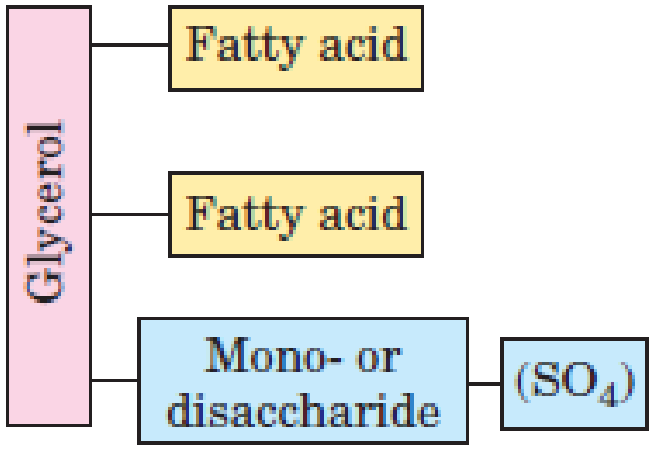
Plasmalogen



Platelet-activating factor

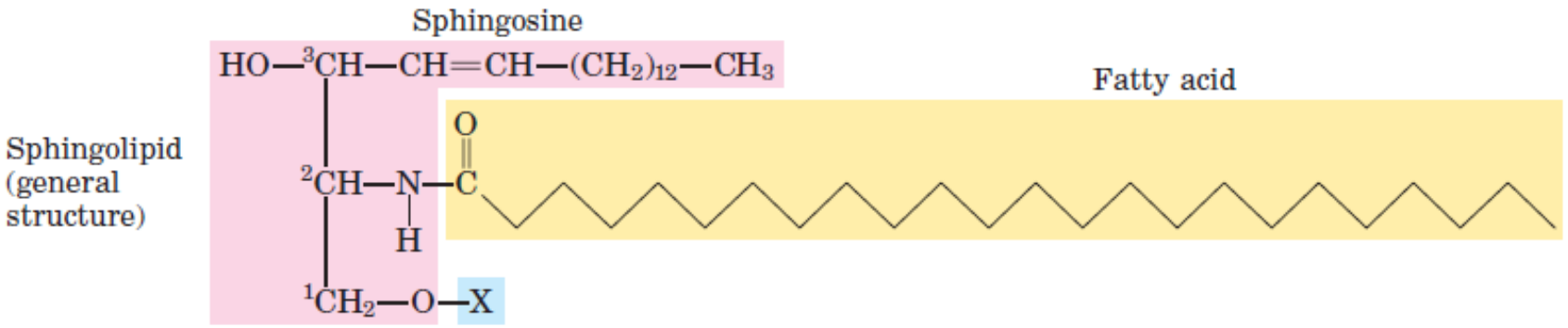
GLYCOLIPIDS

- **Membrane lipids in plant cells**
  - **Chloroplasts Contain Galactolipids and Sulfolipids**



Sphingolipids

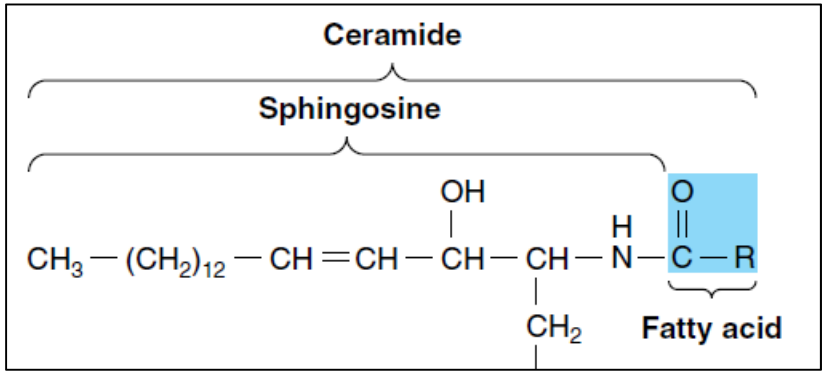
- **Derivatives of Sphingosine**
  - **long-chain amino alcohol sphingosine**



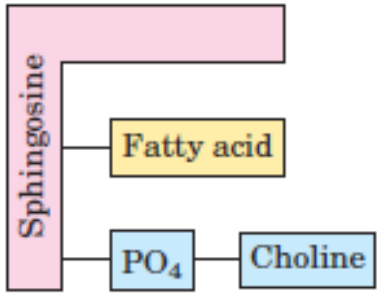
…Sphingolipids

- **Ceramide: The combination of sphingosine plus fatty acid**

- **Ceramide is the structural parent of sphingolipids**



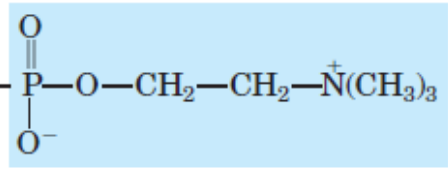
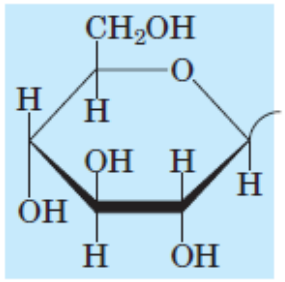
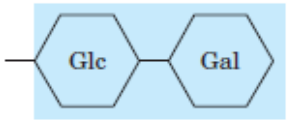
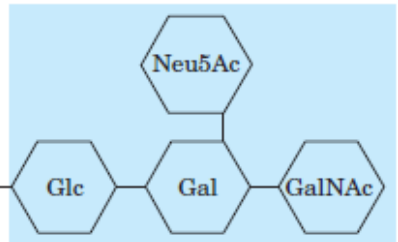
…Sphingolipids



- **Phosphosphingolipids**
  - **Sphingomyelins**
    - **Found in the Nervous System**

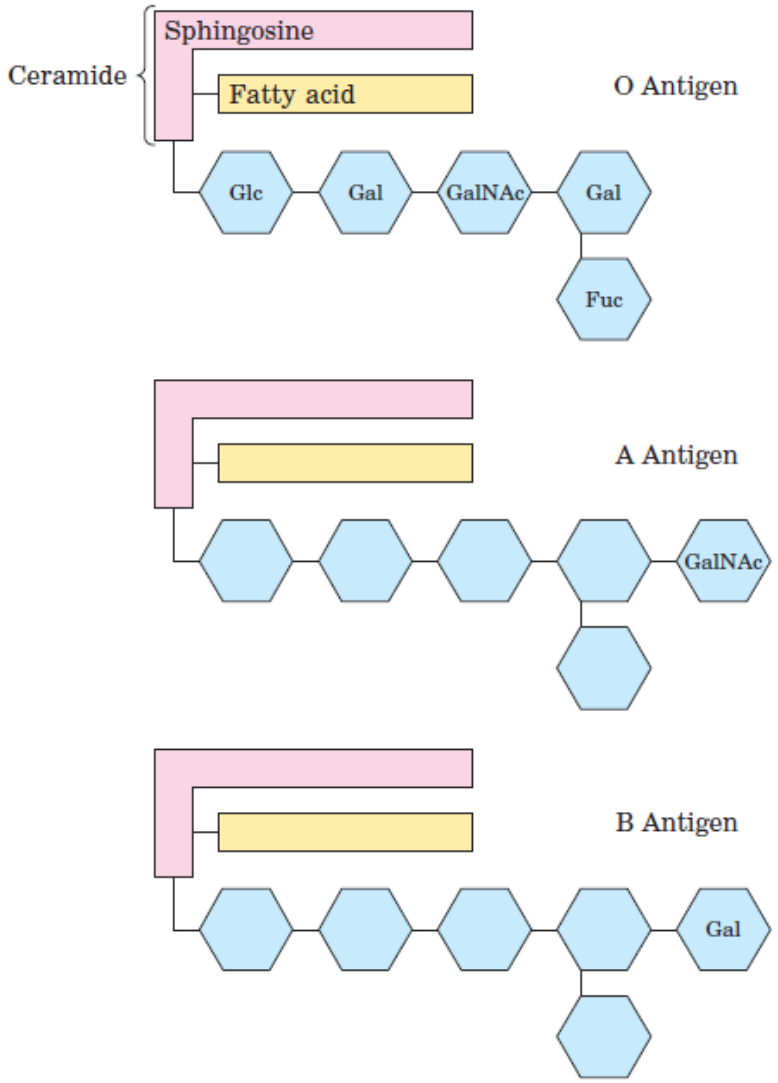
- **Glycosphingolipids**
  - **Neutral (uncharged) glycolipids**
    - **They have no charge at pH 7.**
    - **Cerebrosides have a single sugar**
    - **Globosides have two or more sugars**
  - **Gangliosides**
    - **have oligosaccharides as their polar head groups and one or more residues of N-acetylneuraminic acid (Neu5Ac), a sialic acid**

…Sphingolipids

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

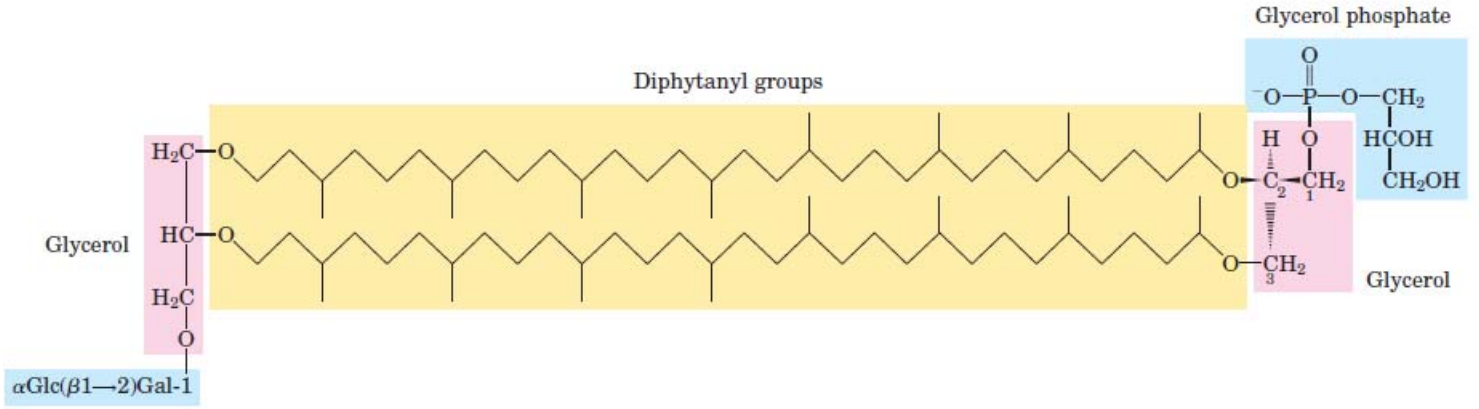
…Sphingolipids

- **Glycosphingolipids**



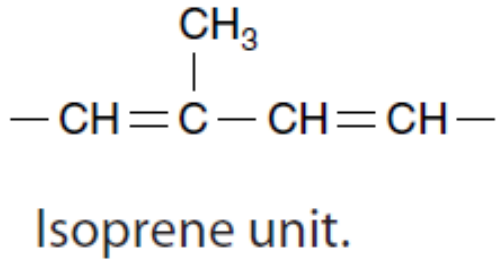
Archaebacteria

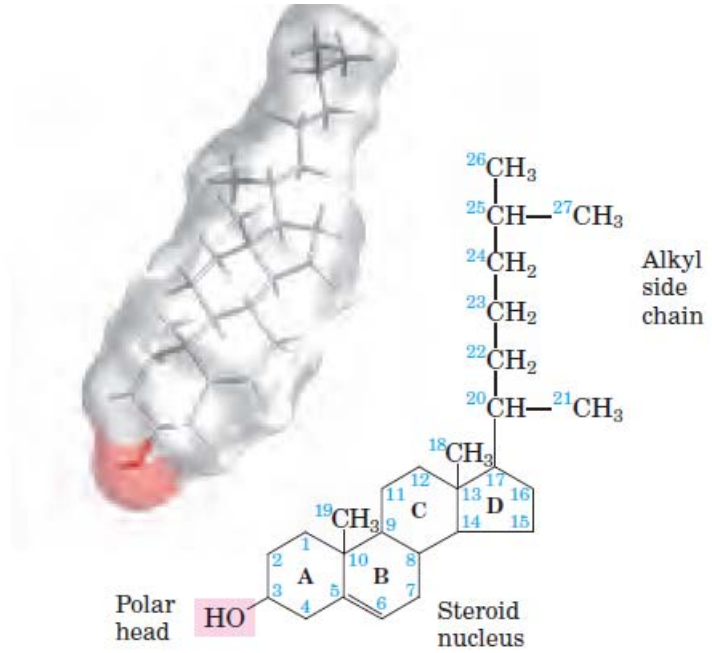
- Extreme conditions (high temperatures, low pH, high ionic strength)
- Contain Unique Membrane Lipids
  - long-chain (32 carbons)
  - branched hydrocarbons
  - ether bonds



Isoprene derivatives

- **Sterol**
  - **Cholesterol**
    - **isoprene subunits**





…sterols

- **Structural lipids**
  - Plasma membrane

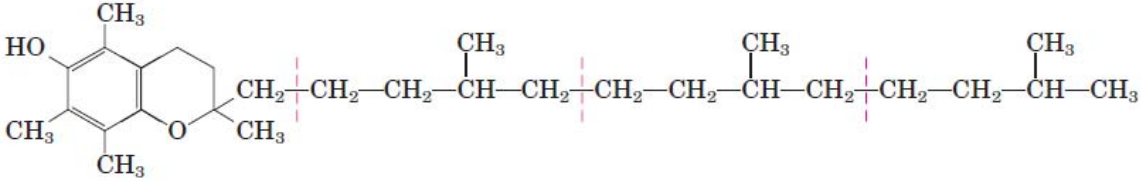
- **precursors for a variety of products with specific biological activities**
  - Steroid hormones
  - Bile acids
  - as a precursor of vitamin D

Other isoprene derivatives

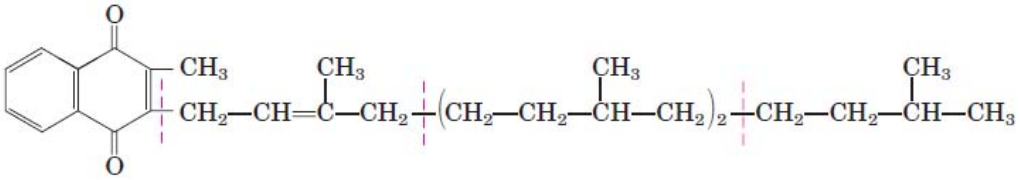
- rubber,
- camphor,
- the fat-soluble vitamins A, E, and K,
- β-carotene (provitamin A).
- Ubiquinone

Some other biologically active isoprenoid compounds or derivatives

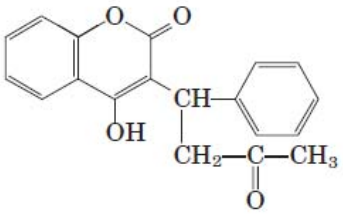
(a)
Vitamin E: an antioxidant



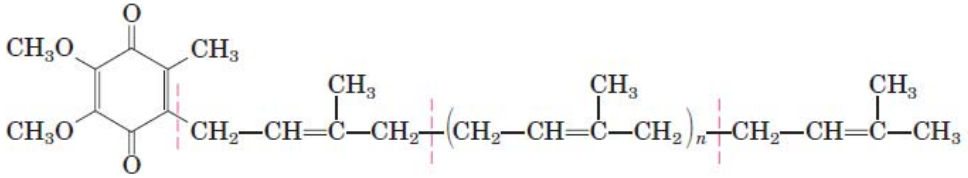
(b)
Vitamin K_1: a blood-clotting cofactor (phylloquinone)



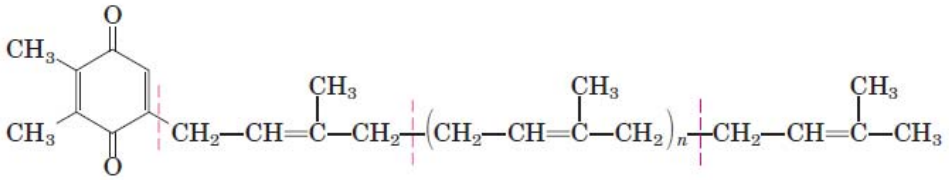
(c)
Warfarin: a blood anticoagulant



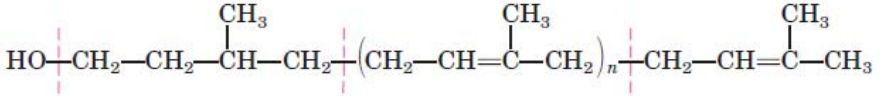
(d)
Ubiquinone: a mitochondrial electron carrier (coenzyme Q) ($n = 4$ to 8)



(e)
Plastoquinone: a chloroplast electron carrier ($n = 4$ to 8)

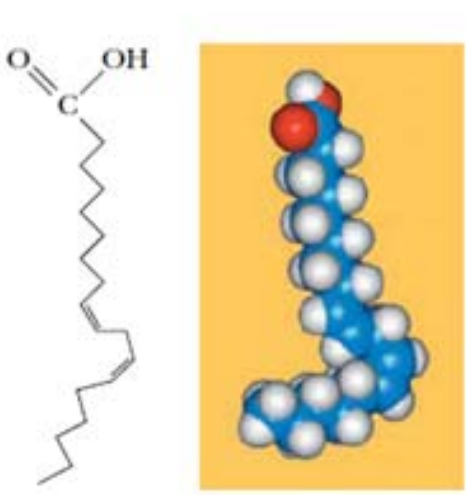


(f)
Dolichol: a sugar carrier ($n = 9$ to 22)

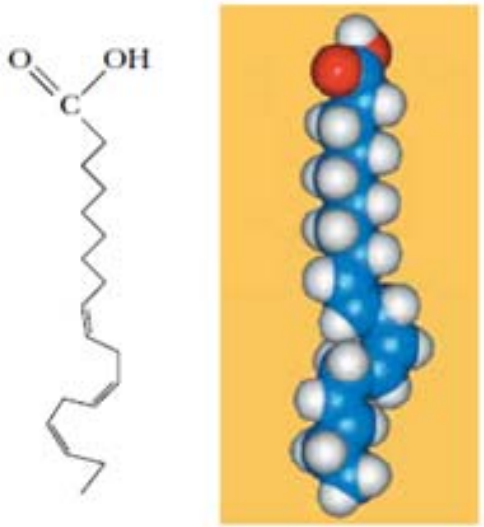


Essential fatty acids (EFA)

- Alpha-linolenic acid (ALA), an omega-3 fatty acid
- linoleic acid (LA), an omega-6 fatty acid



Linoleic acid



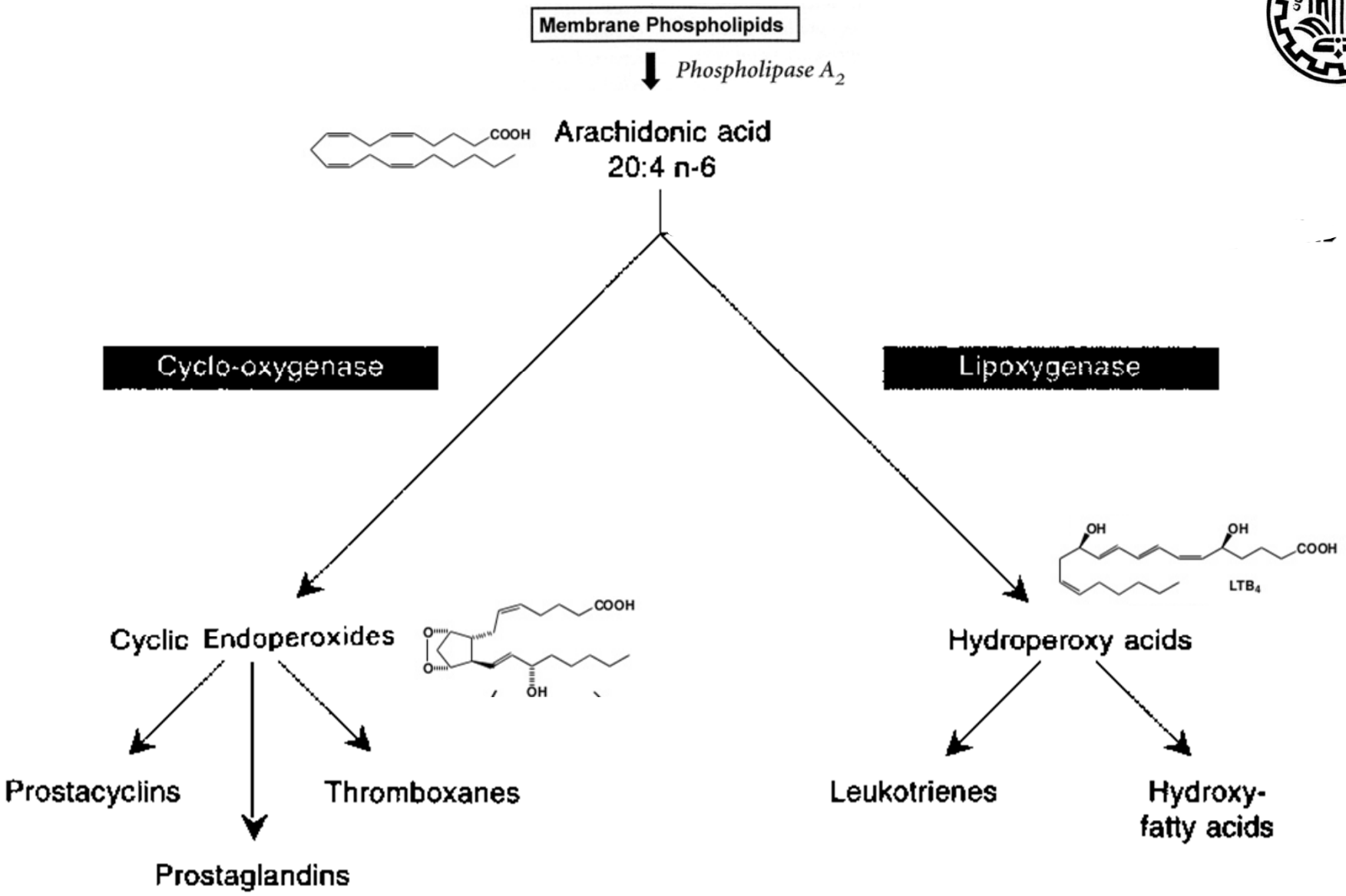
α-Linolenic acid

Essential fatty acids (EFA)

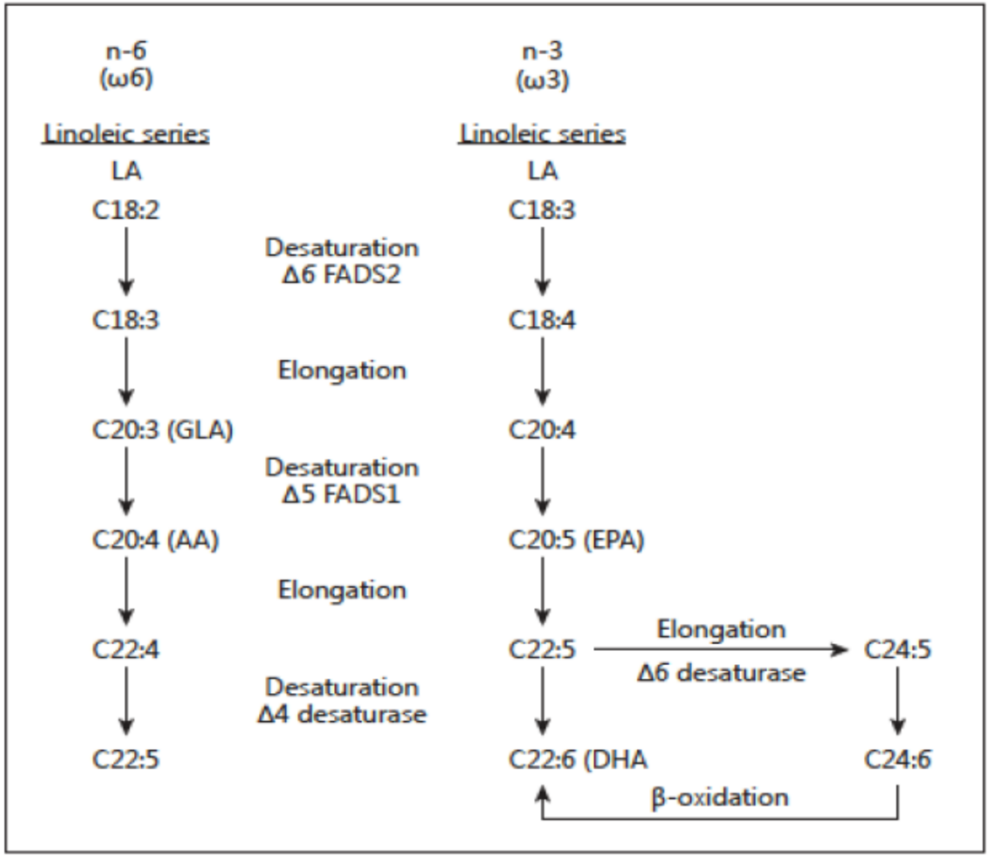
- Structure of cell membranes
- biological processes
- gene expression

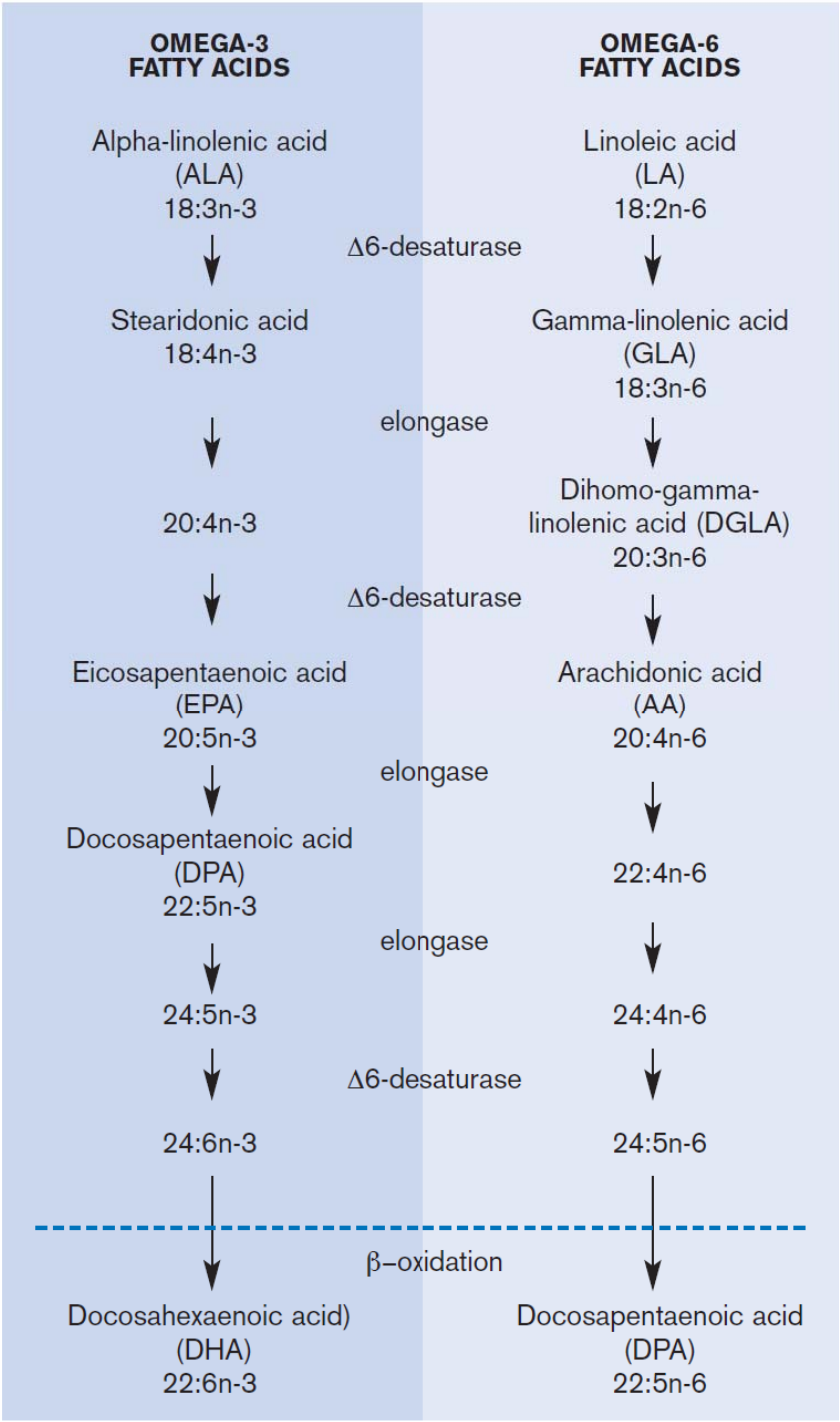
Eicosanoids Carry Messages to Nearby Cells

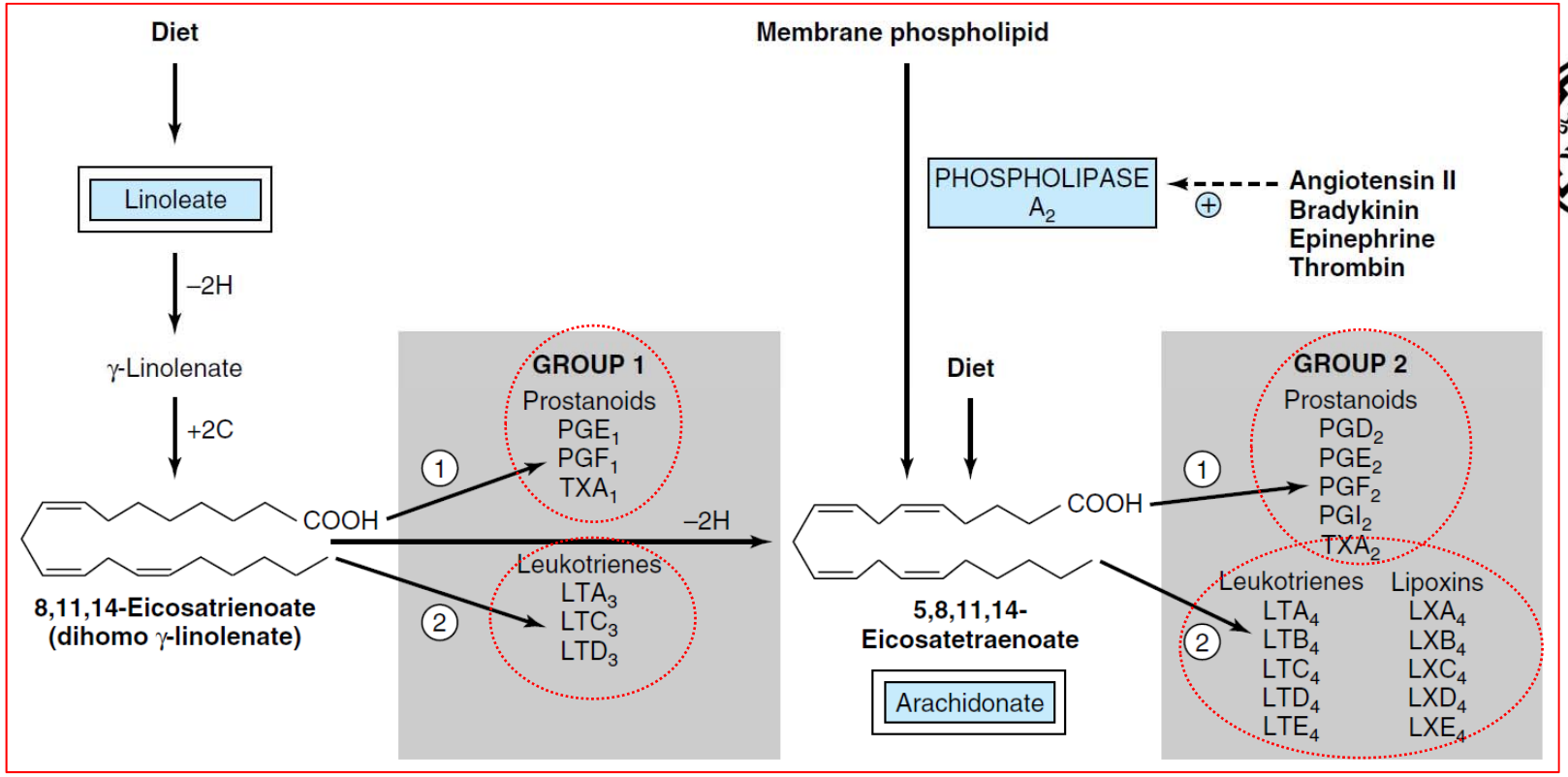
- Signaling molecules made of polyunsaturated fatty acids with 20 carbon units in length
- Paracrine hormones
- in a variety of processes important in human health or disease
  - Reproductive function
  - inflammation
  - fever and pain
  - the formation of blood clots
  - the regulation of blood pressure
  - Gastric acid secretion

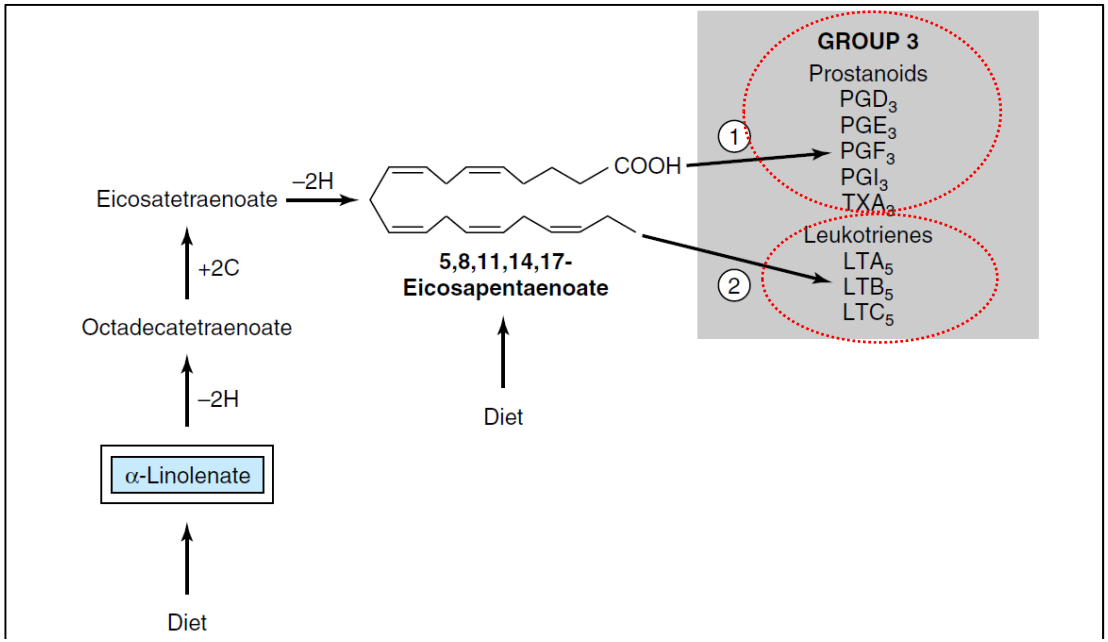

Membrane Phospholipids
Phospholipase A_2
COOH
Arachidonic acid
20:4 n-6
Cyclo-oxygenase
Lipoxygenase
OH
OH
COOH
LTB_4
COOH
Cyclic Endoperoxides
O
O
OH
Hydroperoxy acids
Prostacyclins
Thromboxanes
Prostaglandins
Leukotrienes
Hydroxy-
fatty acids

Omega 3, 6


n-6
(ω6)
Linoleic series
LA
C18:2
C18:3
C20:3 (GLA)
C20:4 (AA)
C22:4
C22:5
Desaturation
Δ6 FADS2
Elongation
Desaturation
Δ5 FADS1
Elongation
Desaturation
Δ4 desaturase
n-3
(ω3)
Linoleic series
LA
C18:3
C18:4
C20:4
C20:5 (EPA)
C22:5
Elongation
Δ6 desaturase
C24:5
C24:6
C22:6 (DHA
β-oxidation


Site of Activity
Endoplasmic Reticulum
Peroxisome
OMEGA-3 FATTY ACIDS
OMEGA-6 FATTY ACIDS
Alpha-linolenic acid (ALA) 18:3n-3
Linoleic acid (LA) 18:2n-6
Δ6-desaturase
Stearidonic acid 18:4n-3
Gamma-linolenic acid (GLA) 18:3n-6
elongase
20:4n-3
Dihomo-gamma-linolenic acid (DGLA) 20:3n-6
Δ6-desaturase
Eicosapentaenoic acid (EPA) 20:5n-3
Arachidonic acid (AA) 20:4n-6
elongase
Docosapentaenoic acid (DPA) 22:5n-3
22:4n-6
elongase
24:5n-3
24:4n-6
Δ6-desaturase
24:6n-3
24:5n-6
β–oxidation
Docosahexaenoic acid) (DHA) 22:6n-3
Docosapentaenoic acid (DPA) 22:5n-6

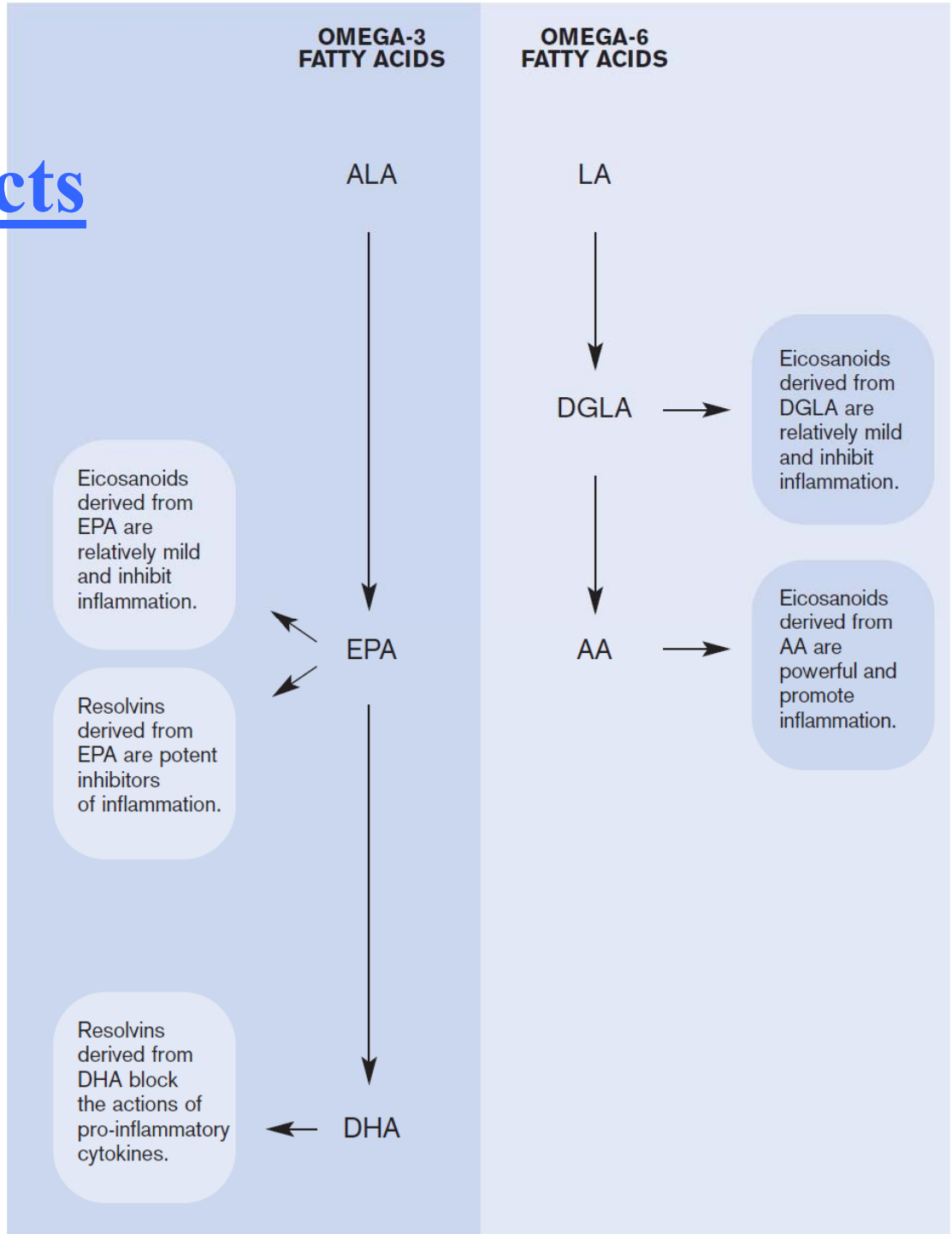

Diet
Membrane phospholipid
Linoleate
–2H
γ-Linolenate
+2C
8,11,14-Eicosatrienoate
(dihomo γ-linolenate)
COOH
1
2
GROUP 1
Prostanoids
PGE1
PGF1
TXA1
Leukotrienes
LTA3
LTC3
LTD3
–2H
PHOSPHOLIPASE
A2
Angiotensin II
Bradykinin
Epinephrine
Thrombin
Diet
5,8,11,14-
Eicosatetraenoate
Arachidonate
GROUP 2
Prostanoids
PGD2
PGE2
PGF2
PGI2
TXA2
Leukotrienes
LTA4
LTB4
LTC4
LTD4
LTE4
Lipoxins
LXA4
LXB4
LXC4
LXD4
LXE4


GROUP 3
Prostanoids
PGD3
PGE3
PGF3
PGI3
TXA3
Leukotrienes
LTA5
LTB5
LTC5
COOH
1
2
Eicosatetraenoate
–2H
+2C
Octadecatetraenoate
–2H
α-Linolenate
Diet
5,8,11,14,17-
Eicosapentaenoate
Diet

Omega-3 fatty acids

- Maintaining the nervous system
- ALA is a precursor of EPA, which is tend not to promote inflammation.
- interferes with the conversion of LA to AA and blocks the formation of cytokines and blood levels of C-reactive protein (CRP)
  - have biologic effects that make them useful in preventing and managing chronic conditions such as type 2 diabetes, kidney disease, rheumatoid arthritis, high blood pressure, coronary heart disease, stroke, Alzheimer disease, alcoholism and certain types of cancer.

Omega 3, 6 effects



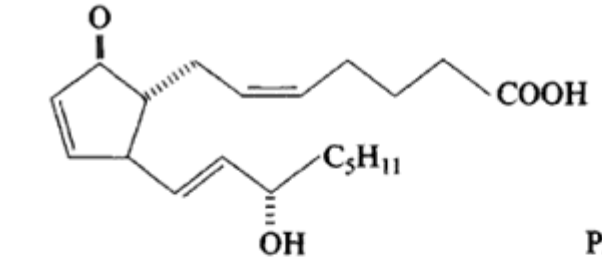
Oil	Omega-6 Content	Omega-3 Content
Safflower	75%	0%
Sunflower	65%	0%
Corn	54%	0%
Cottonseed	50%	0%
Sesame	42%	0%
Peanut	32%	0%
Soybean	51%	7%
Canola	20%	9%
Walnut	52%	10%
Flaxseed	14%	57%
Fish*	0%	100%

Table 4. Omega-6/Omega-3 Ratios in Different Populations.

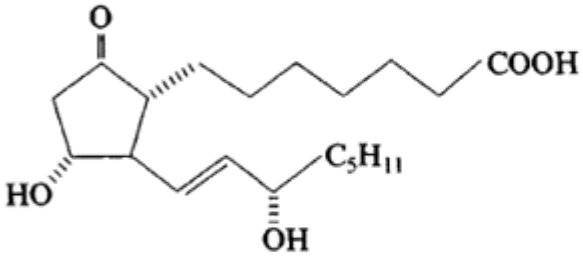
Population	ω-6/ω-3
Paleolithic	0.79
Greece prior to 1960	1.00–2.00
Current Japan	4.00
Current India, rural	5–6.1
Current UK and northern Europe	15.00
Current US	16.74
Current India, urban	38–50

…Eicosanoids

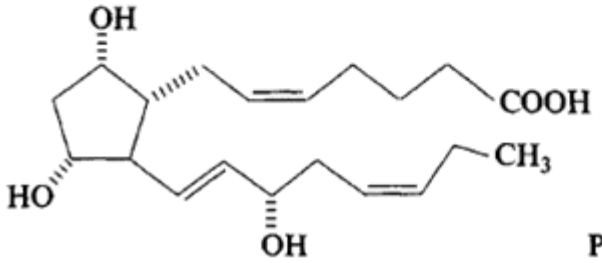
- **Prostaglandins (PG)**
  - Five-carbon ring
  - PGE: ether-soluble, and PGF, for: phosphate buffer–soluble
  - Each group contains numerous subtypes



Prostaglandin A_2



Prostaglandin E_1



Prostaglandin $F_{3\alpha}$

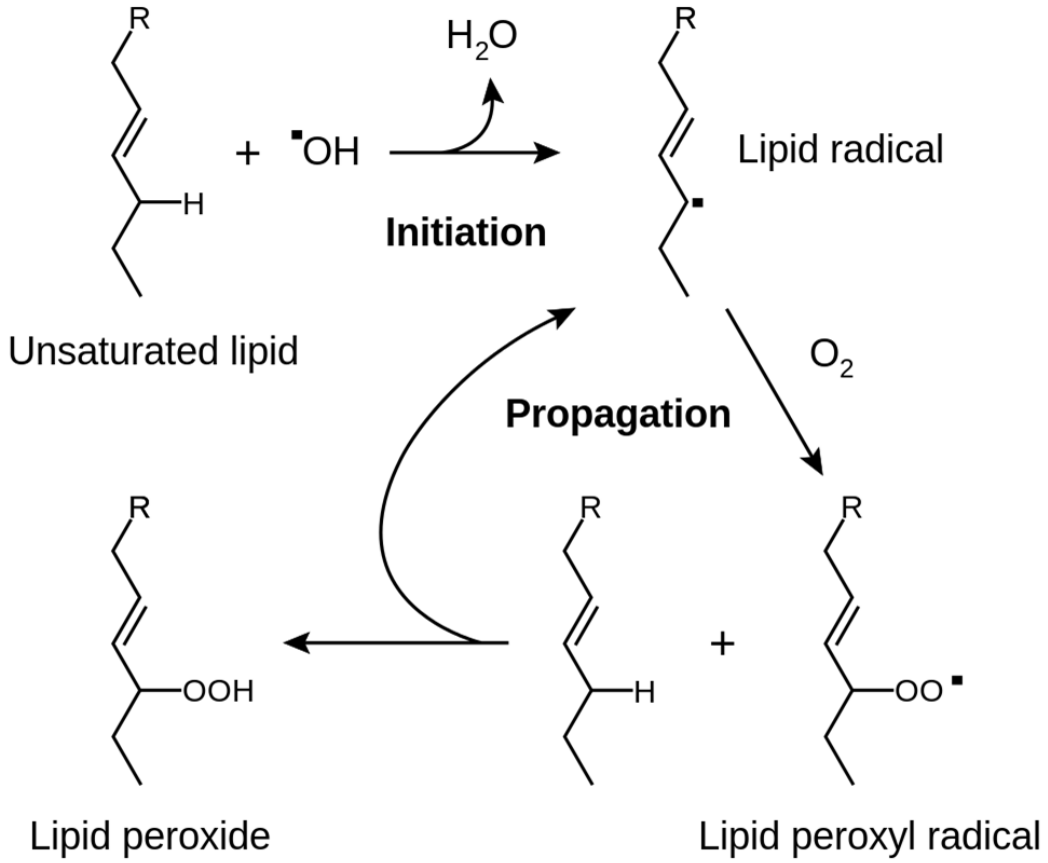
…Eicosanoids

- **Thromboxanes**
  - six-membered ring
  - Blood clots and the reduction of blood flow
- **Leukotrienes**
  - Contain three conjugated double bonds
  - anaphylactic shock (Overproduction of leukotrienes causes asthmatic attacks, hypersensitive to bee stings, penicillin)

Type	Receptor	Receptor type	Function
PGI_2	IP	G_s	•vasodilation •inhibit platelet aggregation •bronchodilation
PGE_2	EP_1	G_q	•bronchoconstriction •GI tract smooth muscle contraction
	EP_2	G_s	•bronchodilation •GI tract smooth muscle relaxation •vasodilation
	EP_3	G_i	•↓ gastric acid secretion •↑ gastric mucus secretion •uterus contraction (when pregnant) •GI tract smooth muscle contraction •lipolysis inhibition •↑ autonomic neurotransmitters [12] •↑ platelet response to their agonists [13] and ↑ atherothrombosis in vivo [14]
	Unspecified		•hyperalgesia[12] •pyrogenic
$PGF_{2\alpha}$	FP	G_q	•uterus contraction •bronchoconstriction

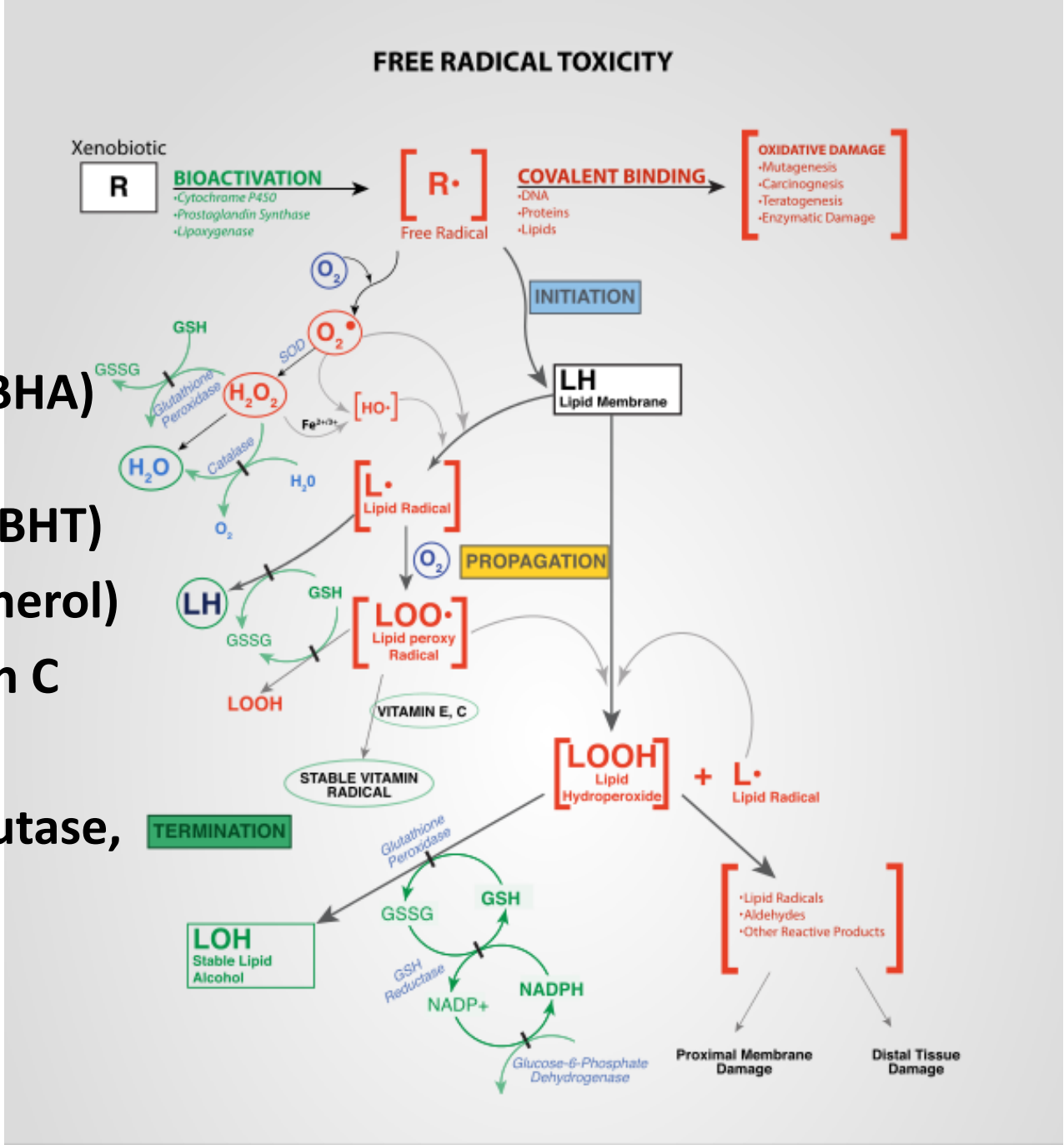
LIPID PEROXIDATION

- **Oxidative degradation of lipids**



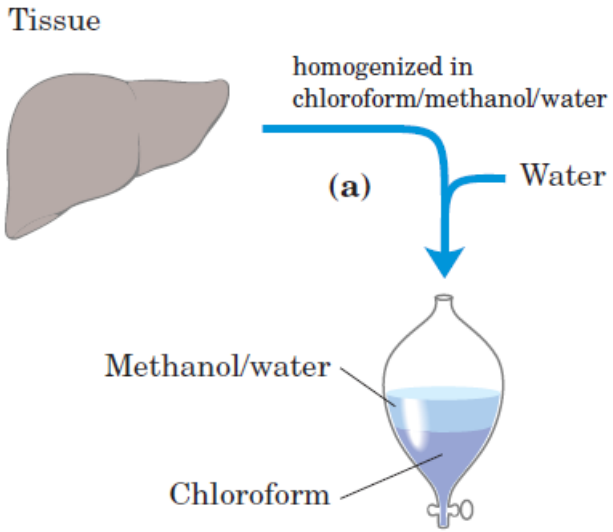
Antioxidants

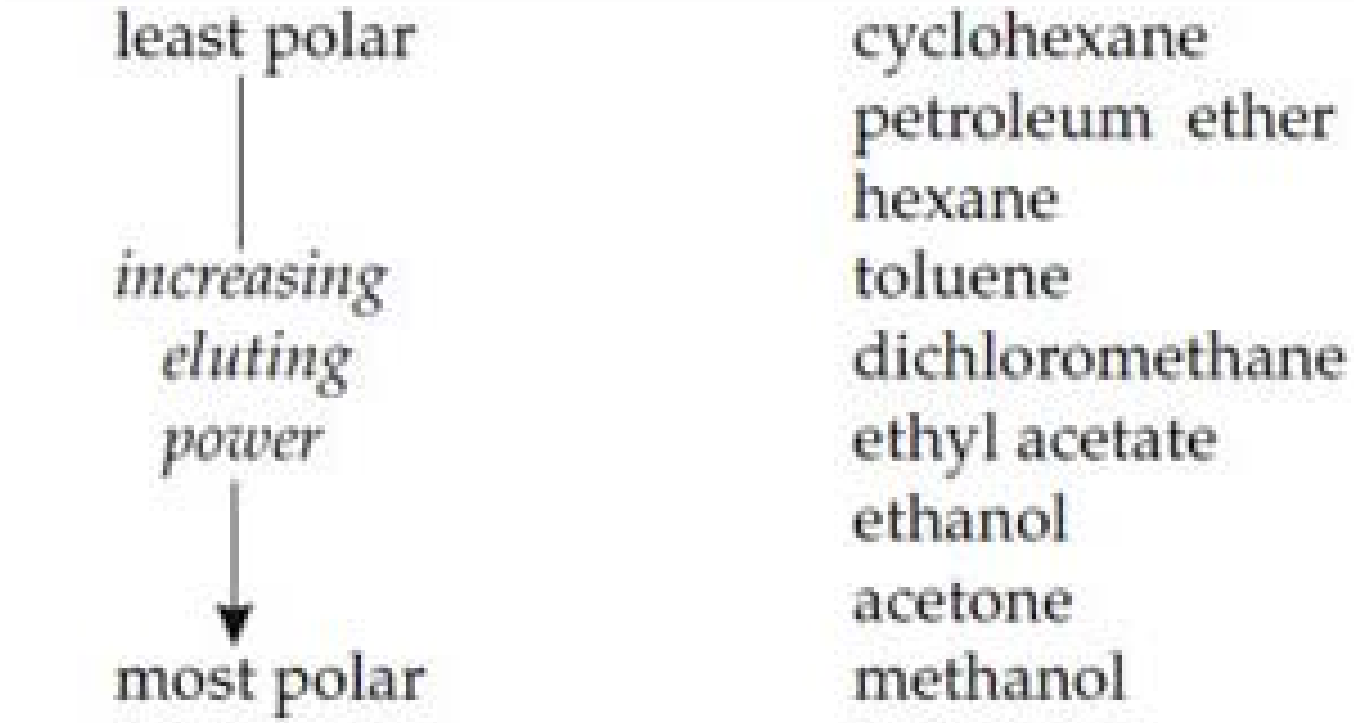
- Butylated hydroxyanisole (BHA)
- Butylated hydroxytoluene (BHT)
- Vitamin E (tocopherol)
- Urate and vitamin C
- Beta-carotene
- Superoxide dismutase, catalase, and peroxidase



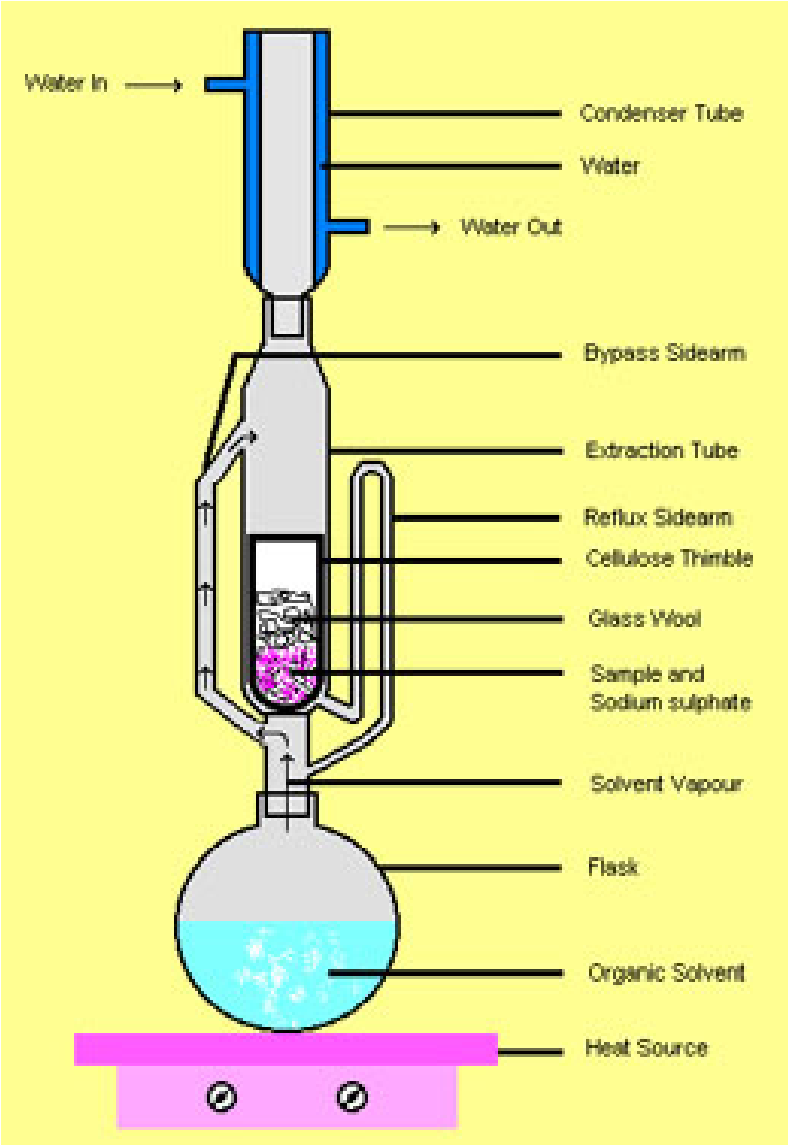
Working with Lipids

- **Lipid Extraction Requires Organic Solvents**
  - **Neutral lipids are extracted with ethyl ether, chloroform, or benzene**
  - **Membrane lipids are extracted by more polar organic solvents, such as ethanol or methanol.**
  - **A commonly extractant is a mixture of chloroform, methanol, and water (1:2:0.8)**



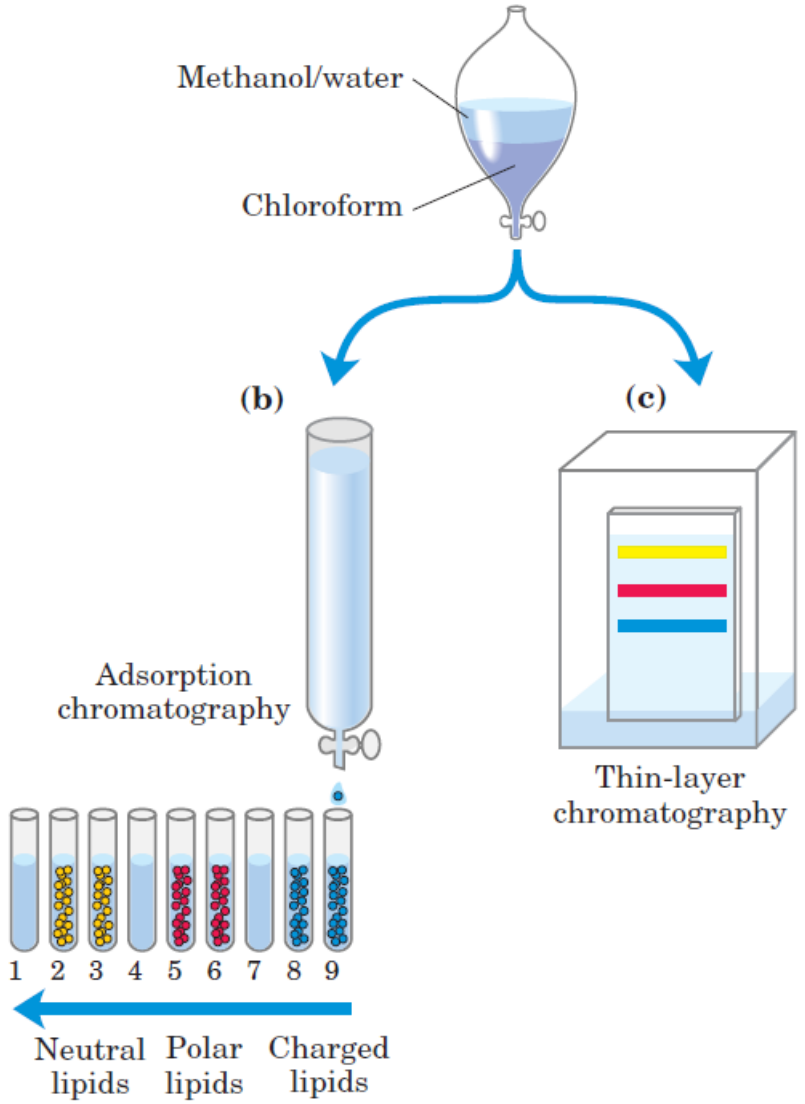

least polar
increasing
eluting
power
most polar
cyclohexane
petroleum ether
hexane
toluene
dichloromethane
ethyl acetate
ethanol
acetone
methanol

Lipid extraction



Separation of Lipids

- **Stationary phase: polar material such as silica gel**
- **Mobile phase: washing the column with solvents of progressively higher polarity (chloroform, acetone, Methanol.)**



Separation of Fatty Acids

- Gas-liquid chromatography separates volatile components of a mixture
- heated in a methanol/HCl or methanol/NaOH mixture, which converts fatty acids esterified to glycerol into their methyl esters
- Stationary phase:
- Mobile phase: an inert gas such as helium.
- column is heated