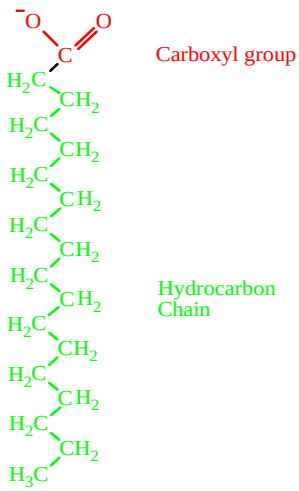
Chapter 9 Lipids

Display a diversity of structures and functions:

Energy storage, membrane components, coenzymes, electron carriers, light-absorbing pigments, hormones, intracellular messengers, detergents.



All are insoluble in water but soluble in organic solvents – hydrophobic.

I - Fatty Acids Carboxylic acids with 4-36 carbons. They have a **hydrophobic** and a **hydrophilic** segment – **Amphipathic**

Stearic acid = octadecanoic acid = 18:0

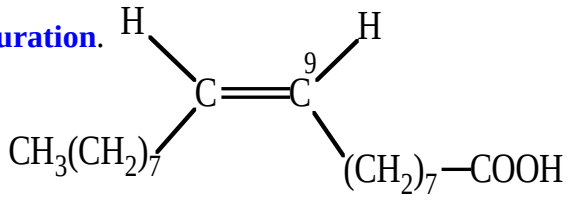
18 C and 0 double bonds. So this is a **saturated** fatty acid. *i.e.* it is saturated with H. It makes up 5% of human body fat.

Shown above is the most stable conformation. It is a high melting (70^{o}C) waxy solid.

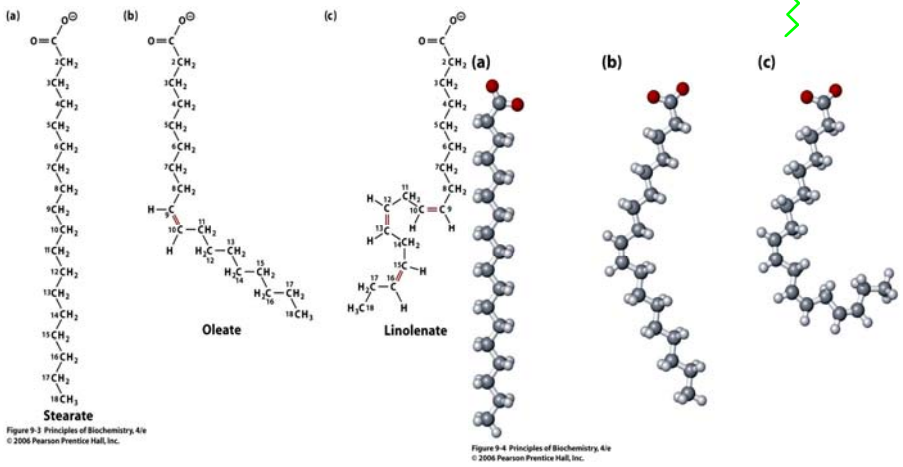
Palmitic acid is 16:0. It makes up ~ 25% of human fat.

Oleic acid = *cis*-9-Octadecenoic acid. 18:1 (Δ^9).

C^9 is the site of **unsaturation**.



The double bond puts a bend in the hydrocarbon tail. It is a low melting oil ($13^{o}C$) because the chains do not pack well together. It makes up bout 46% of human fat.



Linoleic acid is 18:2($\Delta^{9,12}$). The MP is -5^{o} C. It is an essential FA in the diets of mammals.

It is called an ω-3 FA because the last double bond is at C-12 which is 3 atoms from the end of the chain. ω is the last letter in the Greek alphabet.

Linolenic acid is 18:3($\Delta^{9,12,15}$) and has a melting point of -17^{o}C. It is an ω-3 polyunsaturated FA.

TABLE 9.1 Some common fatty acids (anionic forms)

Number of carbons	Number of double bonds	Common name	IUPAC name	Melting point, °C	Molecular formula
12	0	Laurate	Dodecanoate	44	$CH_3(CH_2)_{10}COO^{\ominus}$
14	0	Myristate	Tetradecanoate	52	$CH_3(CH_2)_{12}COO^{\ominus}$
16	0	Palmitate	Hexadecanoate	63	$CH_3(CH_2)_{14}COO^{\ominus}$
18	0	Stearate	Octadecanoate	70	$CH_3(CH_2)_{16}COO^{\ominus}$
20	0	Arachidate	Eicosanoate	75	$CH_3(CH_2)_{18}COO^{\ominus}$
22	0	Behenate	Docosanoate	81	$CH_3(CH_2)_{20}COO^{\ominus}$
24	0	Lignocerate	Tetracosanoate	84	$CH_3(CH_2)_{22}COO^{\ominus}$
16	1	Palmitoleate	*cis*-Δ^9-Hexadecenoate	−0.5	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COO^{\ominus}$
18	1	Oleate	*cis*-Δ^9-Octadecenoate	13	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COO^{\ominus}$
18	2	Linoleate	*cis, cis*-$\Delta^{9,12}$-Octadecadienoate	−9	$CH_3(CH_2)_4(CH{=}CHCH_2)_2(CH_2)_6COO^{\ominus}$
18	3	Linolenate	all *cis*-$\Delta^{9,12,15}$-Octadecatrienoate	−17	$CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6COO^{\ominus}$
20	4	Arachidonate	all *cis*-$\Delta^{5,8,11,14}$-Eicosatetraenoate	−49	$CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2COO^{\ominus}$

Table 9-1 Principles of Biochemistry, 4/e

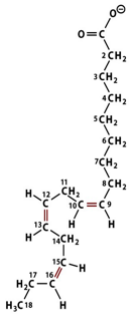
1. All have an even # of C's; some marine organisms have an odd # of C's.

2. None have conjugated double bonds.

3. Double bonds are always in the ***cis*** configuration.

4. The long-chain saturated FA are the least soluble in water. FA are made soluble in serum by binding to a protein – **albumin**.

5. The carboxyl pK_a is 4.5-5.0.



Linolenate

6. The melting points increase with chain length. C4 = Butyric acid; it melts at -8°C

7. Amphipathic FA form **micelles** in water. Water **entropy** (hydrophobic) effects drive the hydrocarbon chains to associate whereas the polar head groups interact with water. Lipids will also place their hydrocarbon chains in air and their head groups at the water surface forming a **monolayer**.

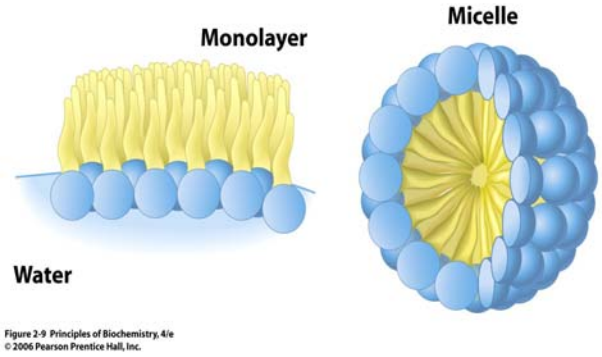
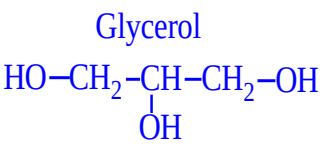
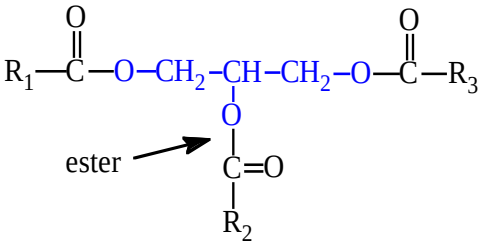


Figure 2-9 Principles of Biochemistry, 4/e
© 2006 Pearson Prentice Hall, Inc.

II - Triacyl Glycerols: neutral fats, triglycerides

Glycerol





R = saturated or unsaturated and the R groups may be identical or different.

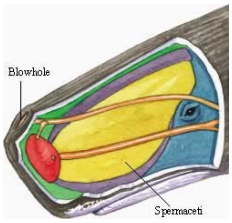
Functions: 1. Energy storage, fat cells (adipocytes), seeds.

Since the C is more **reduced** than in carbohydrate, fat has about 2x more energy.

2. Insulation. Stored under the skin in seals, walruses, penguins.

3. Echo location or Buoyancy in Sperm Whales - spermaceti oil crystallizes at 31° C.

4. Water repellent. Water fowl and plants secrete wax.



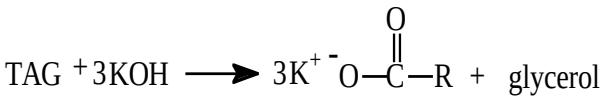
http://www.bookhouse.co.uk/web_books/whaling/trying/images/spermaceti.jpg

http://www.valdosta.edu/~mtrejo/duck.jpeg

http://news.thomasnet.com/IMT/archives/lotus%20leaf,%20water%20droplets.jpg

Soap

This is called **saponification**.

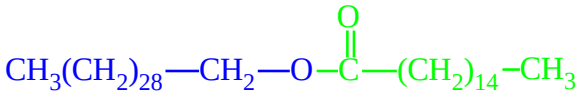


The micelles formed in water can carry oil in their interiors and still be soluble in water.

In cells, intestinal **lipases** catalyze enzymatic hydrolysis of TAGs releasing FA and glycerol.

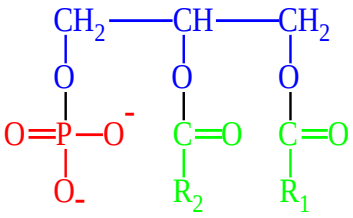
III - Other FA Storage Forms

Bee's Wax = triacontanylpalmitate



IV - Glycerophospholipids They are the main components of cell membranes.

Phosphatidic Acid = diacylglycerolphosphate



Generally, R1 is saturated, R2 is unsaturated. The # of C is usually 16 or 18.

In membrane lipids, one of the O on the phosphate bonds to a "*head*" group to give a **Glycerophospholipid**.

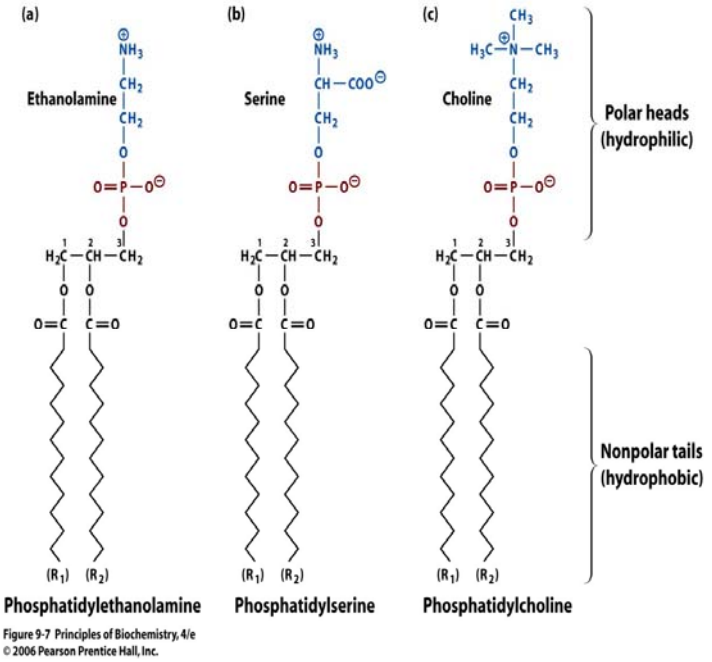


Figure 9-7 Principles of Biochemistry, 4/e

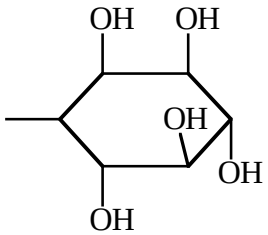
Phosphatidylethanolamine: $—CH_2–CH_2NH_3^+$

Phosphatidylserine: $—CH_2–\underset{\displaystyle COO^-}{\underset{|}{CH}}—NH_3^+$

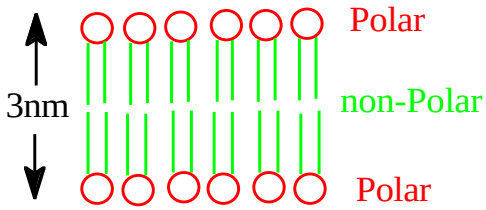
Phosphatidylcholine: $—CH_2–CH_2–N^+(CH_3)_3$

Phosphatidylglycerol: $—CH_2–\underset{\displaystyle OH}{\underset{|}{CH}}—CH_2OH$

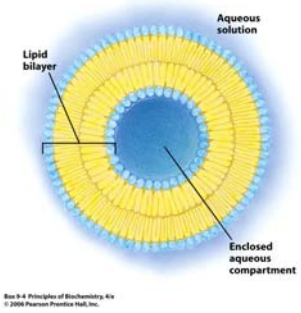
Phosphatidylinositol:

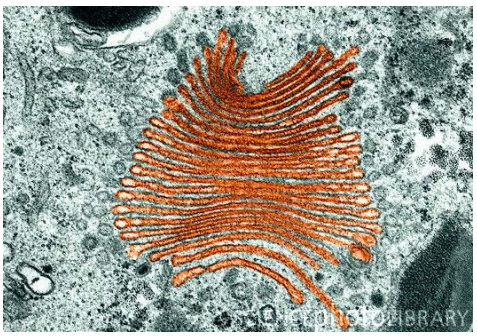


Glycerophospholipids form **bilayers** due to the hydrophobic effect (water entropy):



Curved bilayers can form **vesicles** AKA **liposomes**.

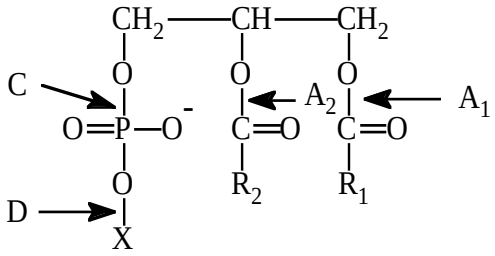




http://www.sciencephoto.com/media/214898/enlarge

On the right, is an electron micrograph of a cell's golgi apparatus composed of stacked lipid bilayers.

Specific **Phospholipases** located in **lysosomes** degrade P-lipids.



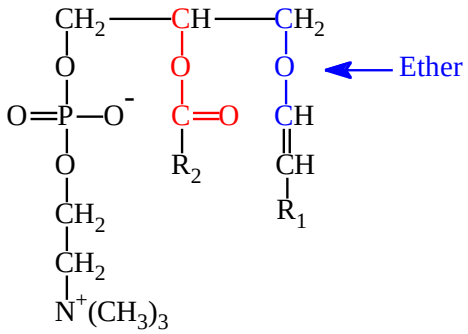
A **lysophospholipid** is a P-lipid from which one of the FA chains has been removed.

Phospholipase A2 releases arachidonic acid 20:4 ($\Delta^{5,8,11,14}$) which serves as a presursor to **prostaglandins**, **thromboxanes**, and **leukotrienes** called **eicosanoids**.

They are involved in inflammation, fever, pain, reproduction *etc*.

V - Ether-linked FA:

Plasmalogen



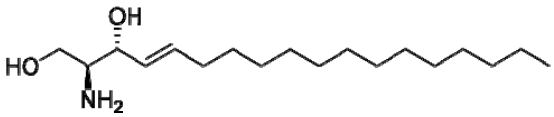
Platlet-Activating Factor is an ether-linked phospholipid hormone and a major cause of Toxic Shock Syndrome.

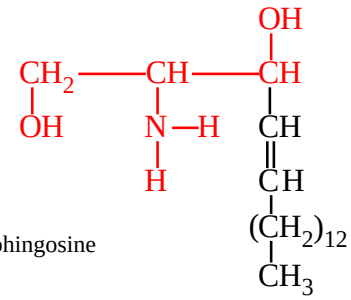
VI - Sphingolipids

Sphingolipids are NOT glycerol derivatives but derivatives of **sphingosine** which is derived from the amino acid **serine**.

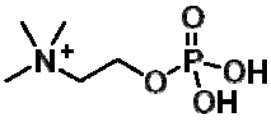
When a **FA** is added in amide linkage
this is called **Ceramide**.

When the head group is **phosphocholine**
this is called **Sphingomyelin**.



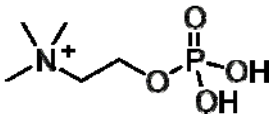


Two representations of sphingosine

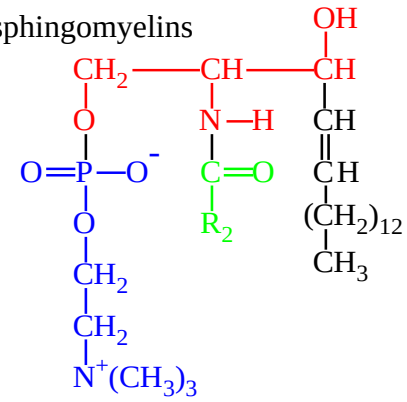


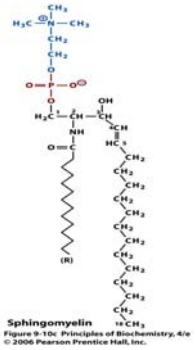
phosphocholine

The size and shape of sphingomyelins is similar to glycerophospholipids.

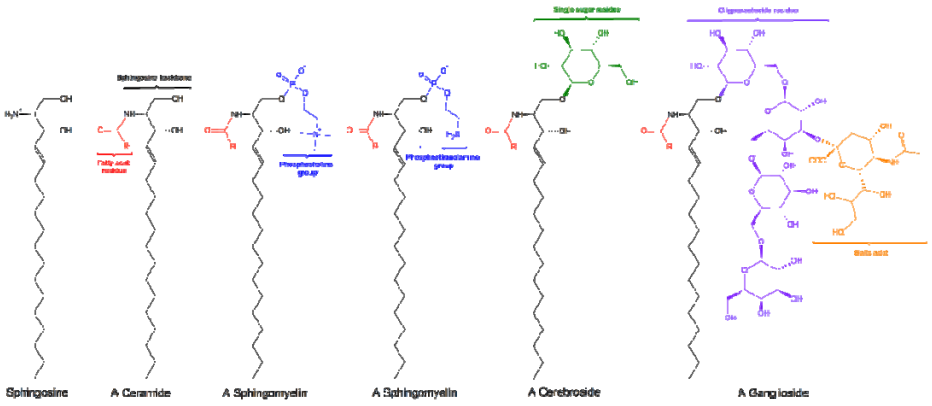


phosphocholine





They are found in the plasma membrane and in the myelin sheath of axons.



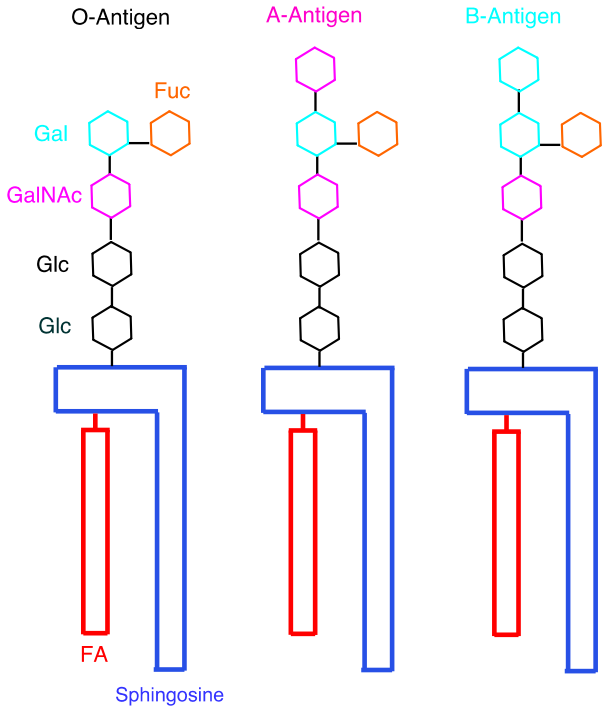
Gangliosides are glycosphingolipids that have complex oligosaccharides as head groups.

Abnormal metabolism of a ganglioside results in several genetic diseases that lead to mental retardation.

Tay-Sachs, Fabry, Sandhoff, Gaucher, Nieman-Pick….

O, A, and B **Blood Group Antigens** are glycosphingolipids with different complex carbohydrate head groups.

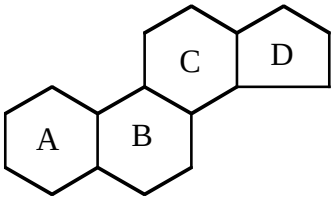
They are important in cell surface recognition events.



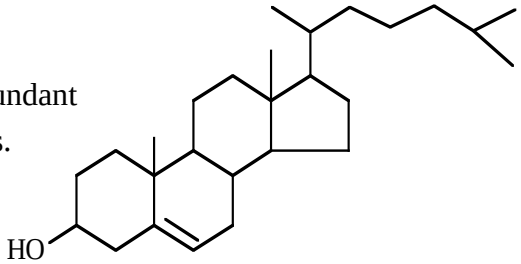
VII - Terpenes and Steroids

They are *non-saponifiable* lipids.

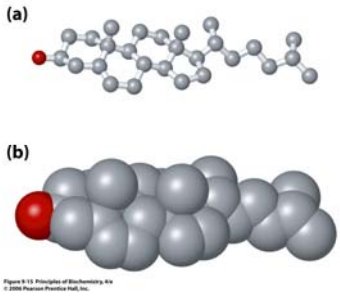
Sterols are lipids containing a 4-fused ring **steroid** nucleus.



Cholesterol is the most abundant sterol in human membranes.



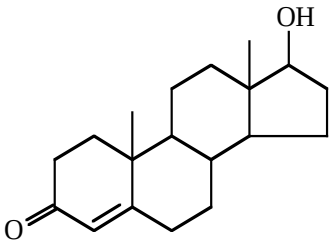
To the right are a ball-&-stick and a space-filling model of cholesterol.



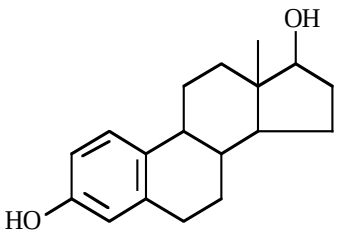
Sterols include the **hormones** testosterone, estradiol, progesterone, cortisol, aldosterone.

They bind to receptors and change gene expression.

Testosterone

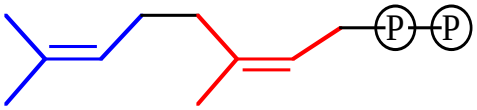


Estradiol



Sterols and Terpenes are synthesized from Δ^3-isopentenyl pyrophosphate (activated isoprene).

Head to tail condensation yields the monoterpene geranyl pyrophosphate.



Geranyl pyrophosphate

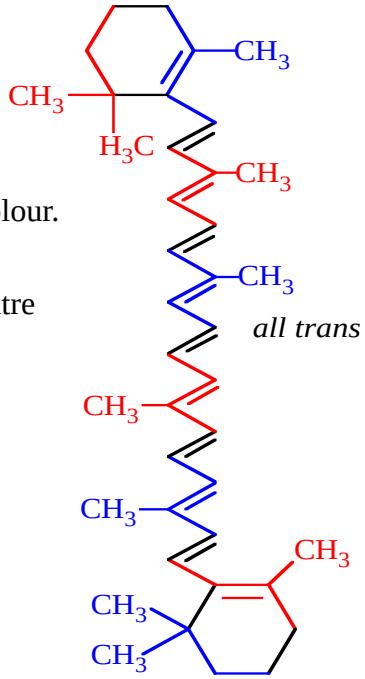
2 units form a monoterpene – 10 C's
3 units form a sesquiterpene – 15 C's
4 units is a diterpine – 20 C's
6 units is a triterpene – 30 C's
8 units is a tetraterpene – 40 C's *e.g.* β-carotene.

Fat-Soluble Vitamins

β-carotene is a tetraterpene **pigment:**

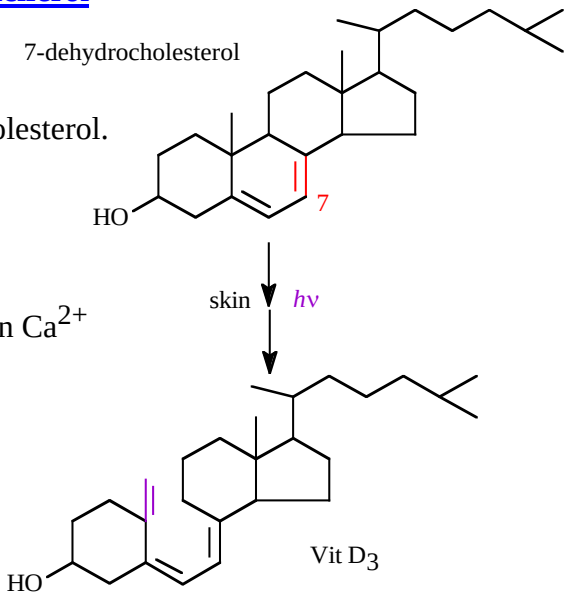
Each 5-carbon isoprene is indicated in colour.

Animals can cleave β-carotene in the centre to produce 2 Retinols = Vitamin A1 – needed for vision.



Vitamin D3 – **Cholecalciferol**

is formed in skin by an uv-light photochemical reaction on 7-dehydrocholesterol.

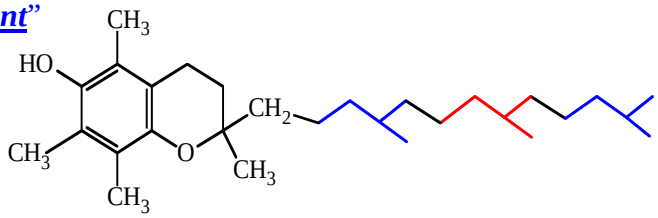


Vitamin D is important in Ca^{2+} and PO_4^{3-} metabolism.

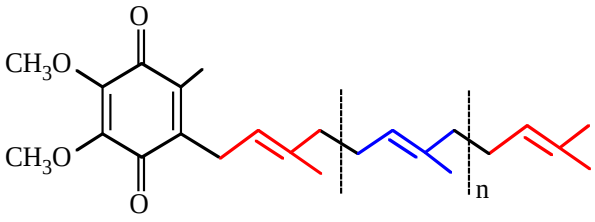
Vitamin E - A Tocopherol

Redox reactions on the aromatic rings prevent oxidative damage to lipid. *"**Antioxidant**"*

A sesquiterpene.



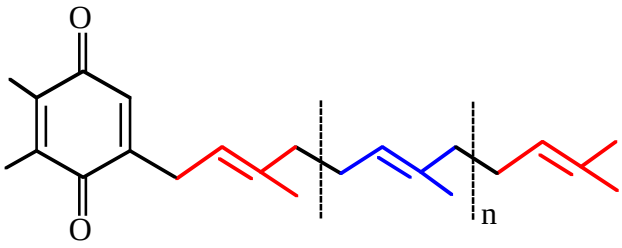
Coenzyme Q = **ubiquinone** is a mitochondrial electron carrier.



n = 4 - 8

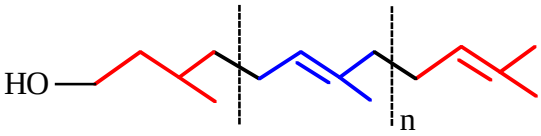
Vitamin K is a blood-clotting co-factor and sesquiterpene.

Plastoquinone is a chloroplast electron carrier.



Dolichol is a sugar carrier.

n = 4 - 8



n = 9 - 22

Trees in the Blue Ridge Mountains in Virginia emit large amounts of isoprene that oxidise forming aerosols creating a blue haze.

Garrett & Grisham, Biochemistry 3rd ed.

A high level of serum **cholesterol** is a risk factor for **atherosclerosis**.

Diets rich in **saturated fatty acids** and **trans fatty acids** are a risk factor for cornory artery disease.

Both increase serum levels of "*bad*" LDL cholesterol.

http://www.doctorsecrets.com/your-medicine/heart-attack-picture.gif

LDL = Low Density Lipoprotein. A large protein called Apolipoprotein B-100 carries fats and cholesterol in the bloodstream.

Trans fats also lower levels of "*good*" HDL cholesterol.

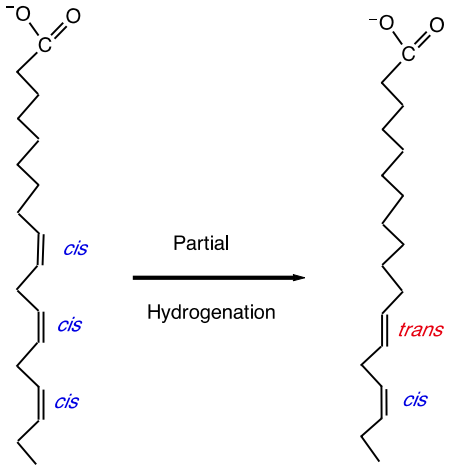
HDL = High Density Lipoprotein. Apolipoprotein A1 and ApoA2 carry triglycrides and cholesterol.

Trans fats are found naturally in meats and dairy products, in small amounts.

Large amounts are present in foods produced by **partial hydrogenation** of plant oils and animal fats.

Hydrogenation raises the MP and produces semi-solid fats for margarine and other foods.

Semi-solid fats are preferred for baking because of the way they mix with flour and alter the texture of food.



Hydrogenation raises the MP and produces semi-solid fats for margarine and other foods.

Semi-solid fats are preferred for baking because of the way they mix with flour and alter the texture of food.

Lipid Purification

1. Extract tissue with an organic solvent.

Lipids will be soluble, polar molecules will not.

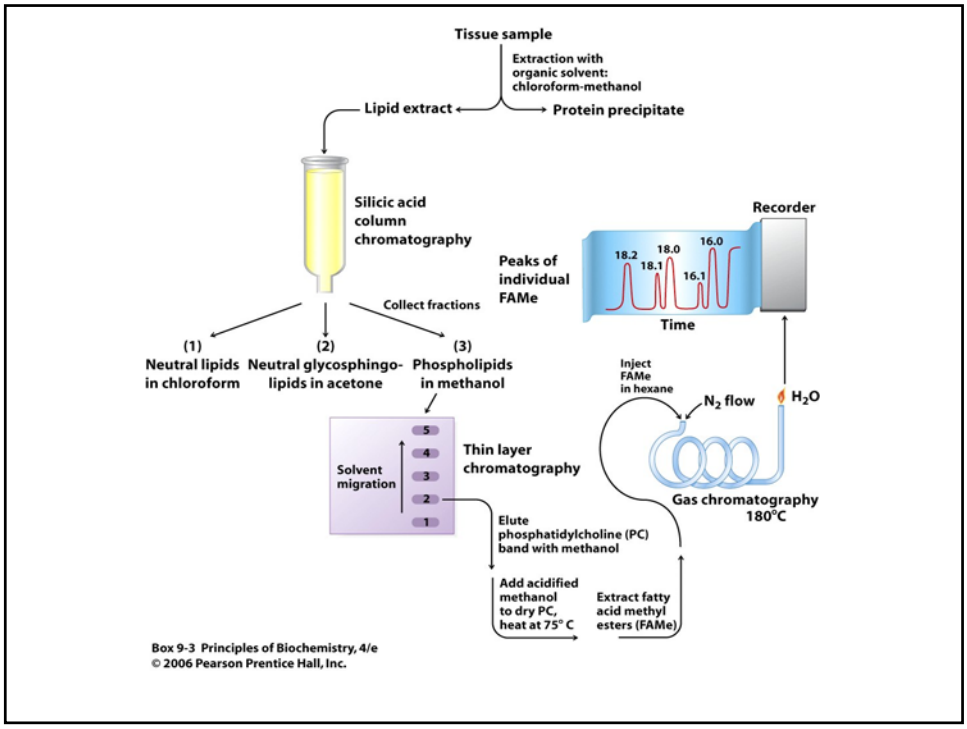
Separate the lipids by **Thin Layer Chromatography**, or adsorption chromatography using silica gel.

Polar and charged lipids bind to silica but neutral lipids do not.

Silicic Acid: $Si(OH_4)$

Polar lipids are eluted with acetone: $CH_3-C(=O)-CH_3$

Charged lipids are eluted with methanol: CH_3OH


Tissue sample
Extraction with organic solvent: chloroform-methanol
Lipid extract
Protein precipitate
Silicic acid column chromatography
Collect fractions
(1) Neutral lipids in chloroform
(2) Neutral glycosphingo-lipids in acetone
(3) Phospholipids in methanol
Solvent migration
5
4
3
2
1
Thin layer chromatography
Elute phosphatidylcholine (PC) band with methanol
Add acidified methanol to dry PC, heat at 75° C
Extract fatty acid methyl esters (FAMe)
Inject FAMe in hexane
N_2 flow
H_2O
Gas chromatography 180°C
Recorder
Peaks of individual FAMe
18.2
18.0
18.1
16.0
16.1
Time
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