Chapter 10 Lipids

Biological Functions of Lipids:

(1) storage of energy

(2) structural elements of biological membranes

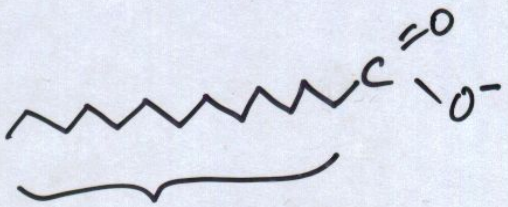
(3) signals, cofactors, and Pigments hormones, ... 等等

Storage Lipids (包含 fats and oils)

fats and oils are derivatives of

fatty acids.

Structure =



Hydrocarbon Chain (4 to 36 carbons)

see Table 10.1 for the nomeclature

Fatty acids

Hydrocarbon chain 愈長 double bond 愈少 Melting temp ↑

table 10–1

Some Naturally Occurring Fatty Acids

Carbon skeleton	Structure*	Systematic name†	Common name (derivation)	Melting point (°C)	Solubility at 30 °C (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	−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")	−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		

*All acids are shown in their nonionized form. At pH 7, all free fatty acids have an ionized carboxylate. Note that numbering of carbon atoms begins at the carboxyl carbon.

†The prefix *n*- indicates the "normal" unbranched structure. For instance, "dodecanoic" simply indicates 12 carbon atoms, which could be arranged in a variety of branched forms; "*n*-dodecanoic" specifies the linear, unbranched form. For unsaturated fatty acids, the configuration of each double bond is indicated; in biological fatty acids the configuration is almost always cis.

e.g. palmitic acid

① 16:0

↑ # of carbons : # of double bonds

② 20:2 ($\Delta^{9,12}$)

同上 2个 double bond 的位置在 C9, 以及 C12

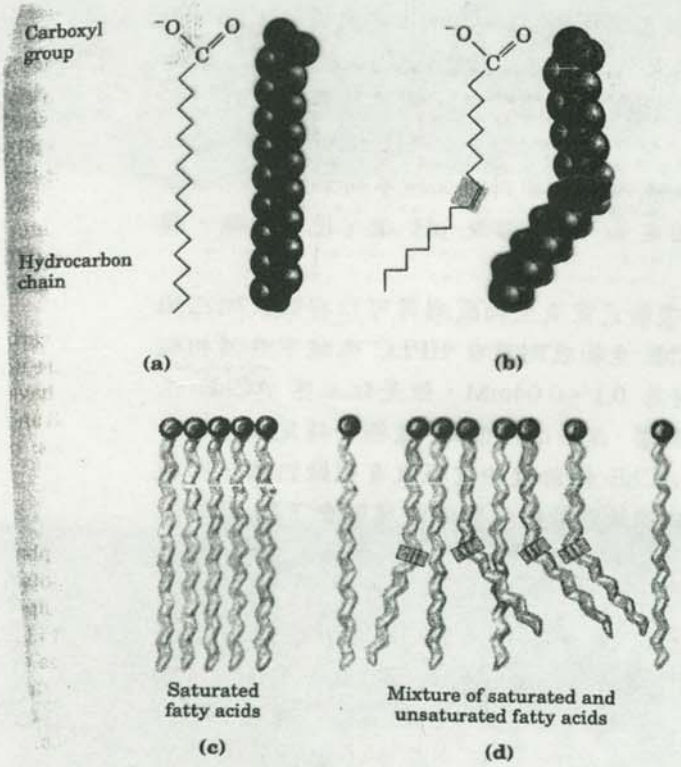


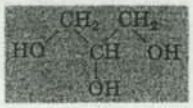
figure 10-1

The packing of fatty acids into stable aggregates. The extent of packing depends on the degree of saturation. **(a)** Two representations of the fully saturated acid stearic acid (stearate at pH 7) in its usual extended conformation. Each line segment of the zig-zag represents a single bond between adjacent carbons. **(b)** The cis double bond (shaded) in oleic acid (oleate) does not permit rotation and introduces a rigid bend in the hydrocarbon tail. All other bonds in the chain are free to rotate. **(c)** Fully saturated fatty acids in the extended form pack into nearly crystalline arrays, stabilized by many hydrophobic interactions. **(d)** The presence of one or more cis double bonds interferes with this tight packing and results in less stable aggregates.

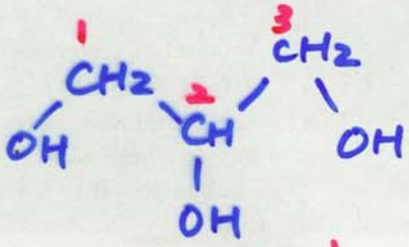
Triacylglycerols Are Fatty Acid Esters of Glycerol

simplest lipids constructed from fatty Acids

Structure:



Glycerol



glycerol

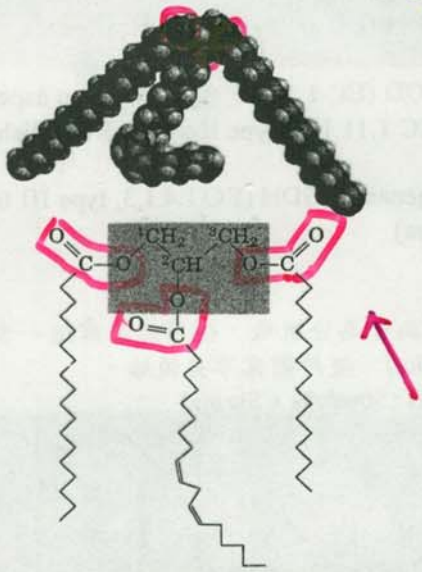
+

fatty acid

↓

triacylglycerols

(形成 ester linkage)



1-Stearoyl, 2-linoleoyl, 3-palmitoyl glycerol, a mixed triacylglycerol

figure 10–2
Glycerol and a triacylglycerol. The mixed triacylglycerol shown here has three different fatty acids attached to the glycerol backbone. When glycerol has two different fatty acids at C-1 and C-3, the C-2 is a chiral center (p. 59).

triacylglycerols (or triglycerides, fats, or neutral fats)

Triacylglycerols Provide stored Energy and Insulation

see Fig 10-3 (a) guinea pig adipocytes (脂肪方法田胞)

(b) 植物种子内法田胞

皆储存 "fat droplets" lipases hydrolysis of stored fats

Triacylglycerols Provide Stored Energy and Insulation

Using triacylglycerols as stored fuels :

(1) 產生 more energy / gram than polysaccharides

(2) 不需攜帶 hydration water when transfer (2 g H_2O / g polysaccharides bound)

Triacylglycerols stored under skin can serve as "insulator" in addition to energy storage.

Many Foods Contain Triacylglycerols

vegetable oils, dairy products, animal fat are composed of triacylglycerols

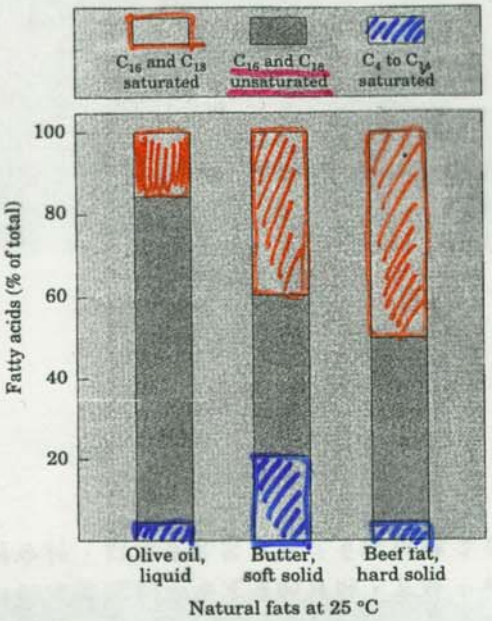


figure 11–4
Fatty acid composition of three food fats. Olive oil, butter, and beef fat consist of mixtures of triacylglycerols, differing in their fatty acid composition. The melting points of these fats—and hence their physical state at room temperature (25 °C)—are a direct function of their fatty acid composition. Olive oil has a high proportion of long-chain (C_{16} and C_{18}) unsaturated fatty acids, which accounts for its liquid state at 25 °C. The higher proportion of long-chain (C_{16} and C_{18}) saturated fatty acids in butter increases its melting point, so butter is a soft solid at room temperature. Beef fat, with an even higher proportion of long-chain saturated fatty acids, is a hard solid.

Waxes Serve as Energy Stores and Water Repellents

Wax:

e.g. $CH_3(CH_2)_{14}-\overset{O}{\overset{\|}{C}}-O-CH_2-(CH_2)_{28}-CH_3$

Palmitic acid (通常 14-36 C)

1-Triacotanol alcohol (C_{16}-C_{30})

Structual Lipids in Membranes

Double layers of lipids ← biological membrane

与 storage lipids 比较：

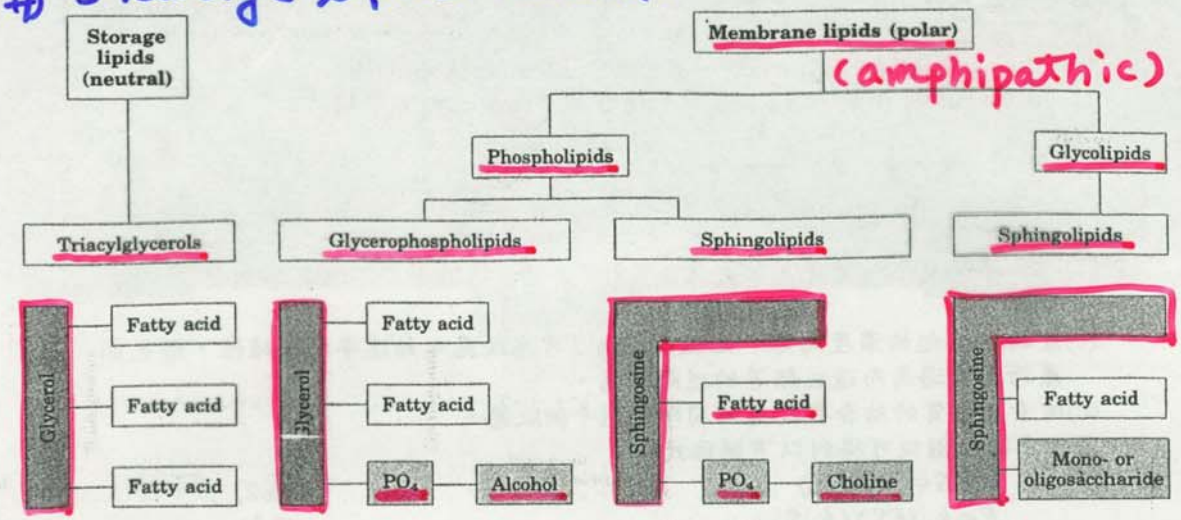


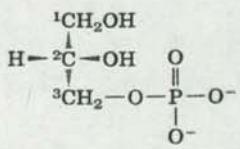
figure 11–6
The principal classes of storage and membrane lipids. All the lipids shown here have either glycerol or sphingosine as the backbone. A third class of membrane lipids, the sterols, is described later (see Fig. 11–14).

Membrane lipids:

(1) phospholipids < glycero phospho lipids / sphingo lipids

(2) glycolipids - sphingo lipids

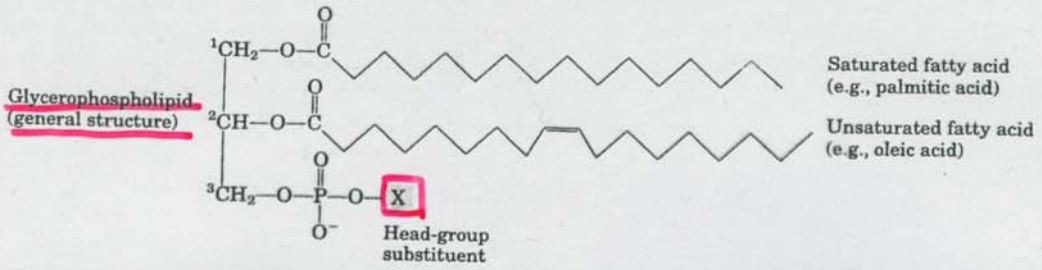
Glycerophospholipids:



Derivatives of

Glycerol-3-phosphate

figure 11–7
L-Glycerol 3-phosphate, the backbone of phospholipids. Note that this compound can also be called D-glycerol 1-phosphate.



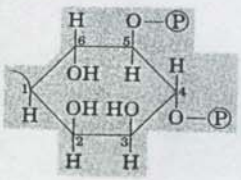
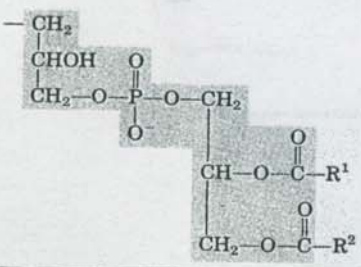
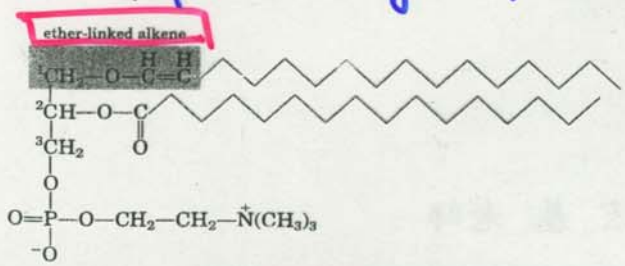
Name of glycerophospholipid	Name of X	Formula of X	Net charge (at pH 7)
Phosphatidic acid	—	—H	−1
Phosphatidylethanolamine	Ethanolamine	$-CH_2-CH_2-\overset{+}{N}H_3$	0
Phosphatidylcholine	Choline	$-CH_2-CH_2-\overset{+}{N}(CH_3)_3$	0
Phosphatidylserine	Serine	$-CH_2-\underset{COO^-}{CH}-\overset{+}{N}H_3$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

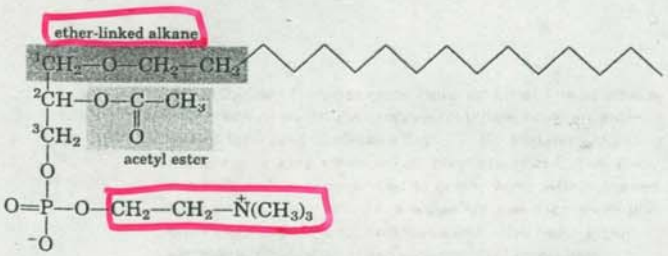
figure 11–8
Glycerophospholipids. The common glycerophospholipids are diacylglycerols linked to head-group alcohols through a phosphodiester bond. Phosphatidic acid, a phosphomonoester, is the parent compound. Each derivative is named for the head-group alcohol (X), with the prefix "phosphatidyl-." In cardiolipin, two phosphatidic acids share a single glycerol.

除了 phosphatidylethanolamine 不带电外
phosphatidyl choline
其餘的 glycerophospholipid 皆带电

Some Phospholipids Have Ether-Linked Fatty Acids

e.g. plasmalogen :
ether-linked alkene (在C1 and C2 間为 double bond)
(about 50% heart phospholipids 为 plasmalogen)





(PAF)

figure 11–9
Ether lipids. Plasmalogens have an ether-linked alkenyl chain where most glycerophospholipids have an ester-linked fatty acid (compare Fig. 11–8). Platelet-activating factor has a long ether-linked alkyl chain at C-1 of glycerol, but C-2 is ester-linked to acetic acid, which makes the compound much more water-soluble than most glycerophospholipids and plasmalogens. The head-group alcohol is choline in plasmalogens and in platelet-activating factor.

Platelet-activating factor released from leukocytes (白血球)
↓
stimulates platelet aggregation
release of serotonin from platelet
(血清素，一种血管收缩剂)
↓
smooth muscle, heart, ... 都会有反應

Sphingolipids Are Derivatives of Sphingosines

神經鞘氨醇

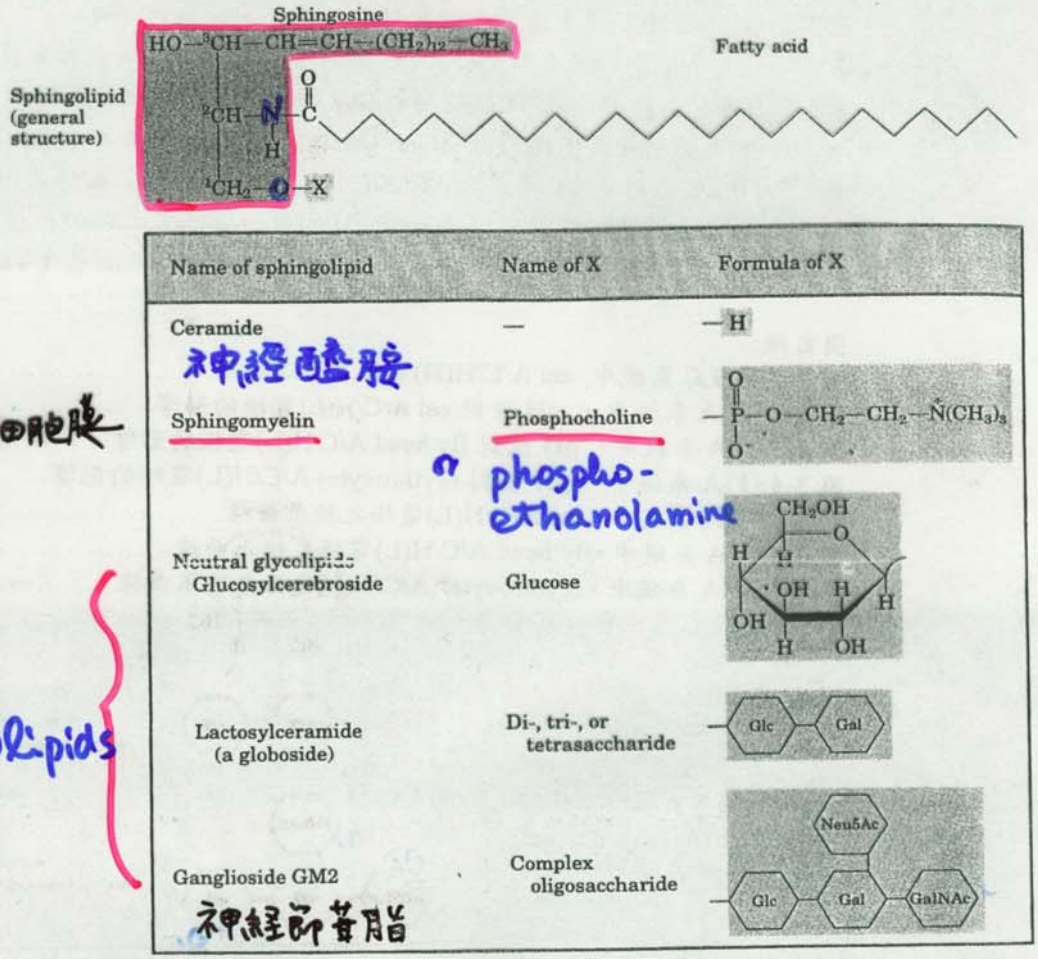


figure ~~11-10~~ 10-12

Sphingolipids. The first three carbons at the polar end of sphingosine are analogous to the three carbons of glycerol in glycerophospholipids. The amino group at C-2 bears a fatty acid in amide linkage. The fatty acid is usually saturated or monounsaturated, with 16, 18, 22, or 24 carbon atoms. Ceramide is the parent compound for this group. Other sphingolipids differ in the polar head group (X) attached at C-1. Gangliosides have very complex oligosaccharide head groups. Standard abbreviations for sugars are used in this figure: Glc, D-glucose; Gal, D-galactose; GalNAc, *N*-acetyl-D-galactosamine; Neu5Ac, *N*-acetylneuraminic acid (sialic acid).

sphingolipids composed:

① a long-chain amino alcohol sphingosine

② a long-chain fatty acid

③ a polar head group that is joined by a glycosidic or phosphodiester linkage

There are three subclasses of sphingolipids:

(1) Sphingomyelins
(2) neutral (uncharged) glycolipids
(3) gangliosides

(1)

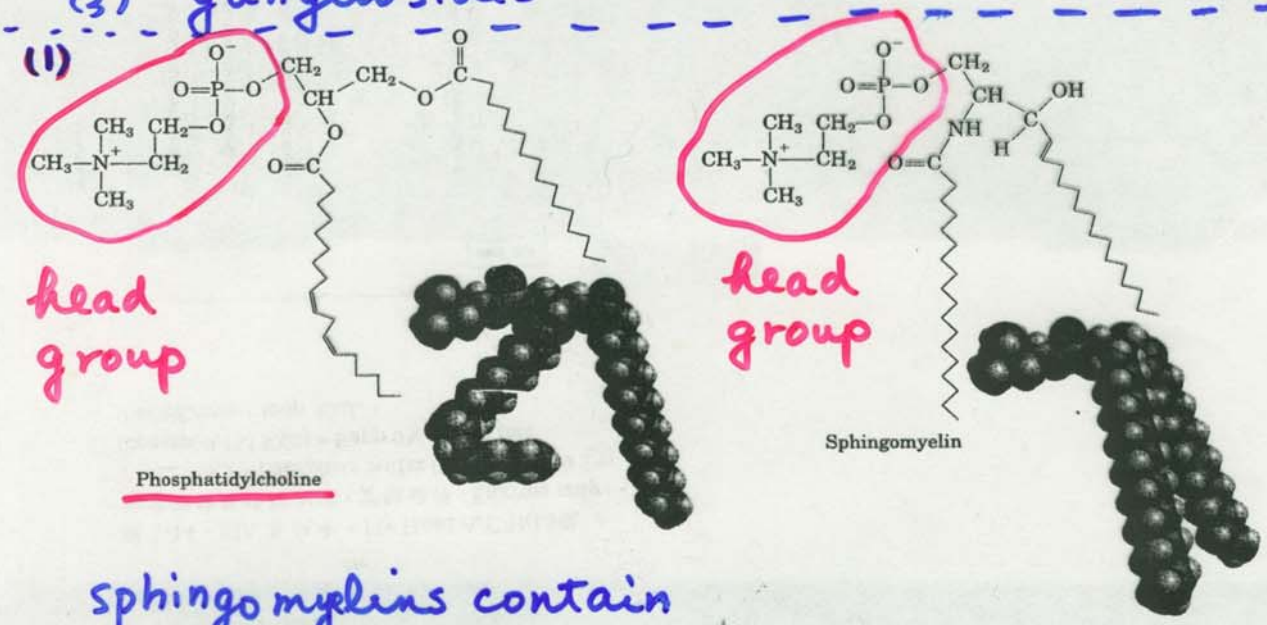
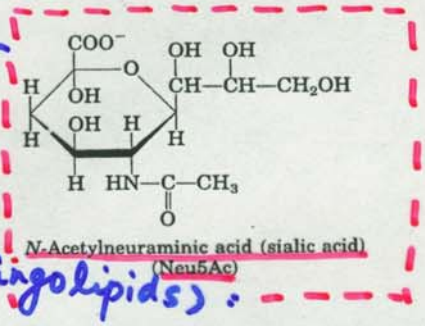


figure 10-12
The similarities in shape and in molecular structure of phosphatidylcholine (a glycerophospholipid) and sphingomyelin (a sphingolipid) are clear when their space-filling and structural formulas are drawn as here.

sphingomylins contain phosphocholine or phosphoethanolamine

head group → no net charge

(structurally similar to phosphatidycholin)



(2) glycolipids (or glycosphingolipids):

- largely occur in the out face of plasma membrane
- contain one or more sugars (connected to C1 of ceramide moiety), no phosphate

(3) gangliosides: contain oligosaccharides and one or more N-acetylneuraminic acid ↑

Sphingolipids at Cell Surfaces Are Sites of Biological Recognition

. More than 60 different Sphingolipids found in human, only a few sphingolipids has a specific function been discovered.

e.g. The carbohydrate moieties of certain sphingolip define the human blood groups.

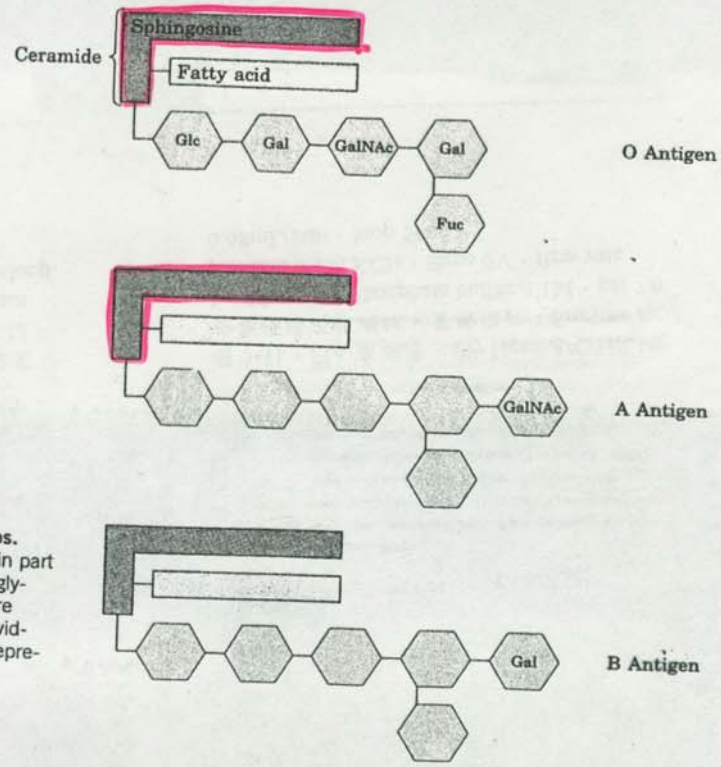


figure 10-14
Glycosphingolipids as determinants of blood groups. The human blood groups (O, A, B) are determined in part by the oligosaccharide head groups (blue) of these glycosphingolipids. The same three oligosaccharides are also found attached to certain blood proteins of individuals of blood types O, A, and B, respectively. (Fuc represents the sugar fucose.)

gangliosides :

The kinds and amounts of gangliosides in plasma membrane change dramatically w/ embryonic development.

Some cultured neuronal tumor cells induce some specific gangliosides.

↓

reasons unknown

Phospholipids and Sphinogolipids Are Degraded in Lysosomes

Membrane lipids are continually degraded and replaced.

Each hydrolyzable bond in glycerophospholipids → there is a specific hydrolytic enzyme in the lysosome

e.g. :

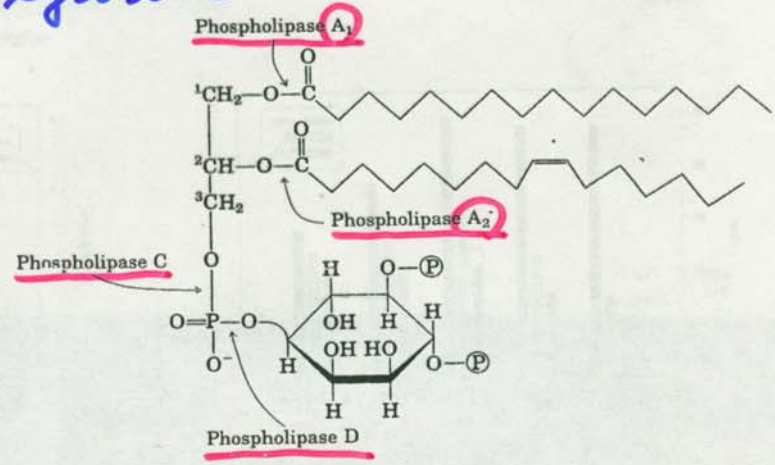


Figure ~~11-12~~ 10-15
The specificities of phospholipases. Phospholipases A_1 and A_2 hydrolyze the ester bonds of intact glycerophospholipids at C-1 and C-2 of glycerol, respectively. Phospholipases C and D each split one of the phosphodiester bonds in the head group. Some phospholipases act on only one type of glycerophospholipid, such as phosphatidylinositol 4,5-bisphosphate (shown here) or phosphatidylcholine; others are less specific. When one of the fatty acids has been removed by a type A phospholipase, the second fatty acid is cleaved from the molecule by a lysophospholipase (not shown).

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gangliosides

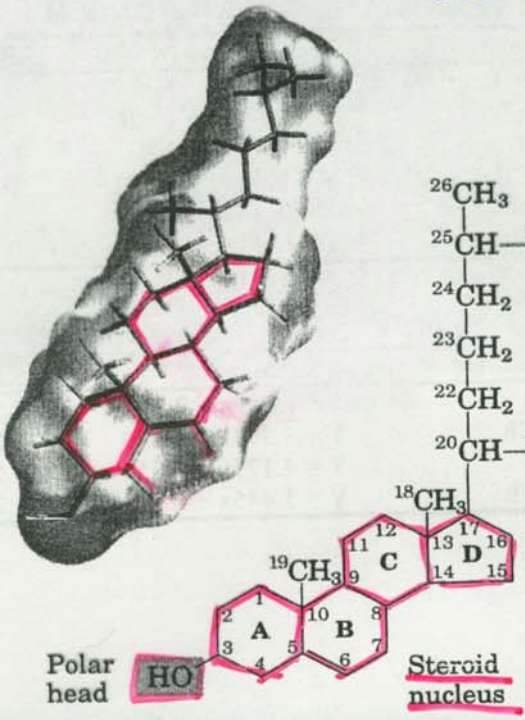
↓ by a series of lysosomal enzymes

removal of sugar units, yielding a ceramid

A genetic defect in any of these hydrolytic enzymes lead to the accumulation of gangliosides in the cells, w/ severe medical consequences

Sterols Have Four Fused Carbon Rings

固醇 Structural lipids present in most eukaryotic cells.



含三个 6C ring
一个 5C ring

cholesterol (膽固醇)

major sterol in animal tissue

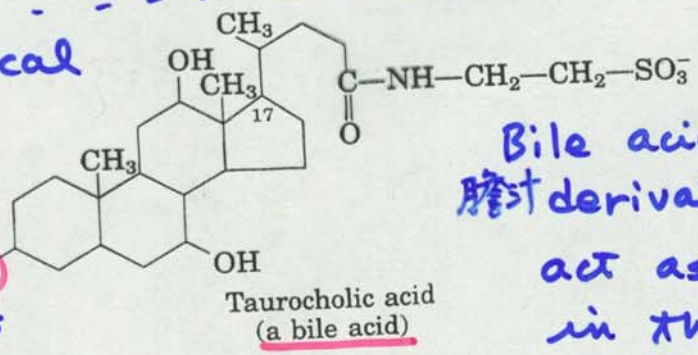
amphipathic:
polar head OH
nonpolar hydrocarbon tail

figure 10-16

Cholesterol. The stick structure of cholesterol is visible through a transparent surface contour model of the molecule. In the chemical structure, the rings are labeled A through D to simplify reference to derivatives of the steroid nucleus and the carbon atoms are numbered in blue. The hydroxyl group on C-3 (red in both representations) represents the polar head group. For storage and transport of the sterol, this hydroxyl group condenses with a fatty acid to form a sterol ester.

Other biological funcs:

1. Hormone
2. detergent in intestines



Taurocholic acid (a bile acid)

Bile acids: polar 膽汁 derivatives of cholesterol

act as detergents in the intestine

↓ emulsifying dietary fats

↓ more accessible for lipase

Lipids as Signals, Cofactors, and Pigments

Lipids:

(1) storage & structural lipids
e.g. adipocyte 內 80% 以上為 lipids
membrane 內 5-10% 為 lipids

(2) Metabolic traffic (as metabolites and messengers)
e.g. Hormones
enzyme cofactors

(3) Pigment molecules:
lipids w/ a system of conjugated double bonds
absorbs light
e.g. light-capturing pigments in vision and photosynthesis
natural colorations (如南瓜、紅蘿蔔的顏色)

Phosphatidylinositols Act as Intracellular Signals

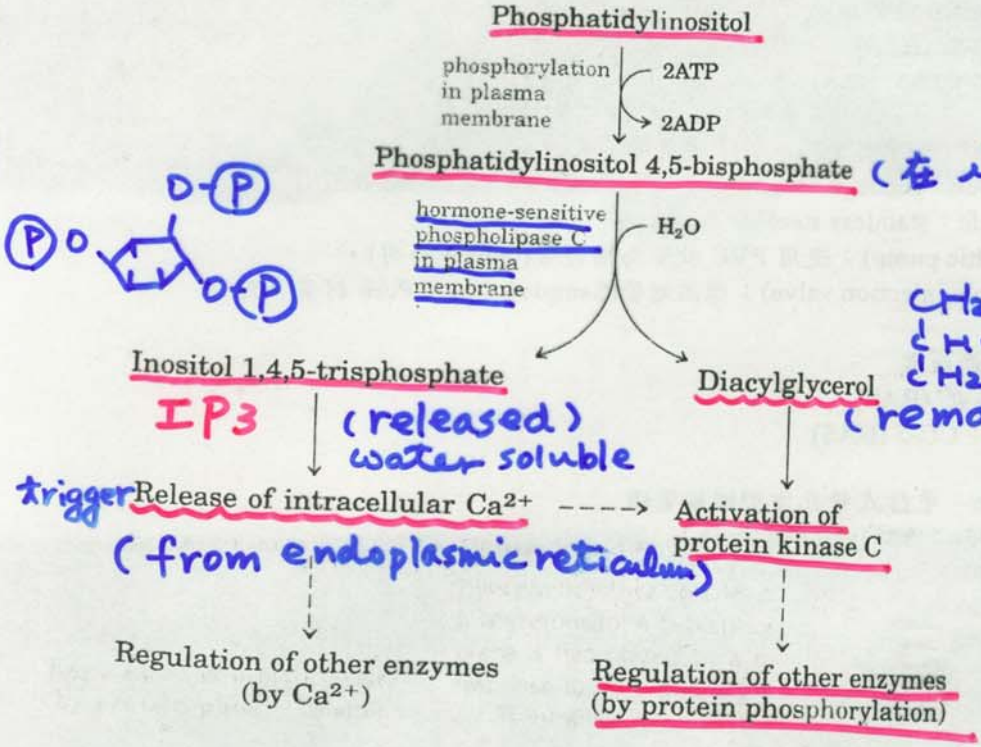


figure 10-15 17

Phosphatidylinositols in c
phatidylinositol 4,5-bispho
brane is hydrolyzed by a sp
response to hormonal signa
act as intracellular messen

(Eico)sanoids Carry Messages to Nearby Cells

a-17

20的意思 類花生酸

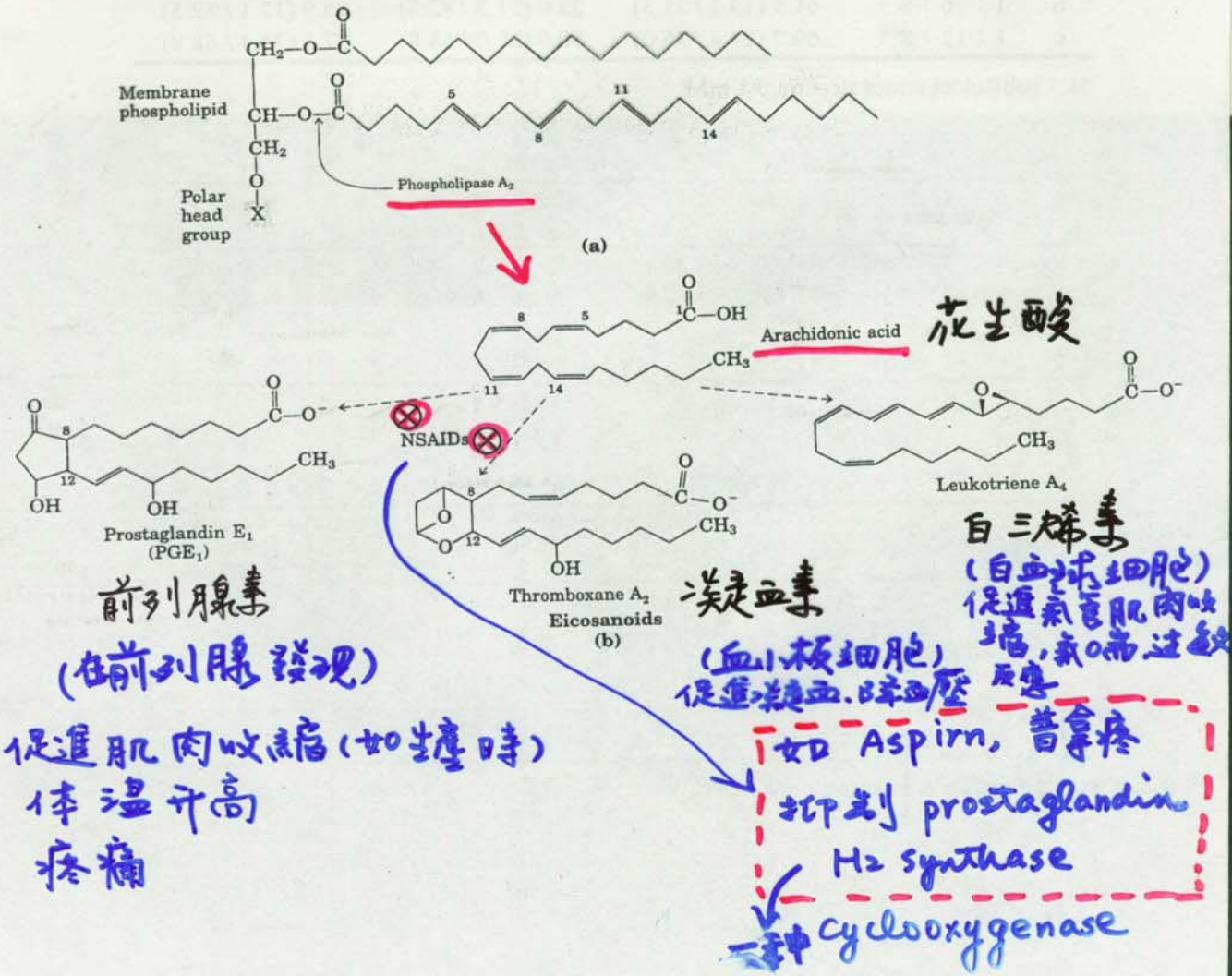
arachidonic acid acid 的 derivative

20 : Δ (Δ^{5,8,11,14})

1. paracrine hormone (作用在附近的 cells)
2. 与 inflammation, fever, pain … 等 processes 的 signal 有関

figure ~~11-16~~ 10-18

Arachidonic acid and some eicosanoid derivatives. **(a)** In response to hormonal signals, phospholipase A_2 cleaves arachidonic acid–containing membrane phospholipids to release arachidonic acid (arachidonate at pH 7), the precursor to various eicosanoids. **(b)** These include prostaglandins such as PGE_1, in which C-8 and C-12 of arachidonate are joined to form the characteristic five-membered ring. In thromboxane A_2, the C-8 and C-12 are joined and an oxygen atom is added to form the six-membered ring. Leukotriene A_4 has a series of three conjugated double bonds. Nonsteroidal antiinflammatory drugs (NSAIDs) such as aspirin, acetaminophen, and ibuprofen block the formation of prostaglandins and thromboxanes from arachidonate by inhibiting the enzyme cyclooxygenase (prostaglandin H_2 synthase).



前列腺素

(在前列腺发现)

促进肌肉收缩(如生產時)

体温升高

疼痛

凝血素

(血小板细胞)

促进凝血、血压/压

白三烯素

(白血球细胞)

促进氣管肌肉收縮，氣喘，過敏反應

如 Aspirn, 普拿疼

抑制 prostaglandin H2 synthase

一种 cyclooxygenase

Steroid Hormones Carry Messages between Tissues

11-18

Steroid 是 sterol 的衍生物（但沒有 aliphatic chain attached to ring D）

（類固醇）

∴ 易溶於水

↓

隨血液傳至 target tissues（可傳至非鄰近）

↓

進入細胞

↓

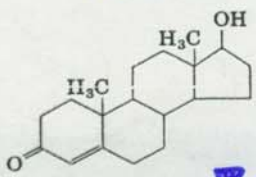
binds to receptor in nucleus

↓

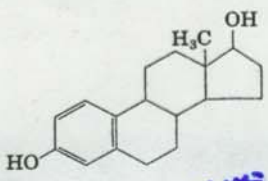
trigger gene expression & metabolism

figure 11–17

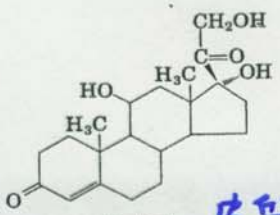
Steroids derived from cholesterol. Testosterone, the male sex hormone, is produced in the testes. Estradiol, one of the female sex hormones, is produced in the ovaries and placenta. Cortisol and aldosterone are hormones synthesized in the cortex of the adrenal gland; they regulate glucose metabolism and salt excretion, respectively. Prednisolone and prednisone are steroid drugs used as antiinflammatory agents.



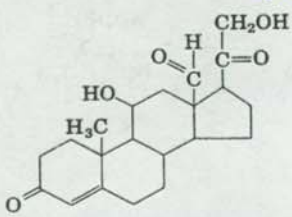
Testosterone 睪固酮



Estradiol 雌二醇

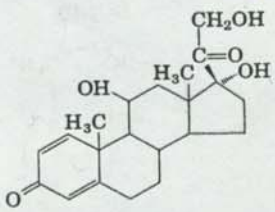


Cortisol 皮質醇

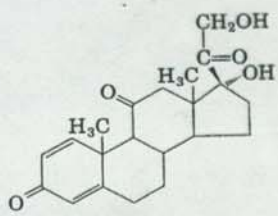


Aldosterone

醛固酮



Prednisolone



Prednisone

類固醇類抗發炎藥

Steroid drug

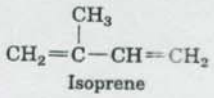
(inhibit phospholipase A_2

∴ inhibit arachidonic acid production)

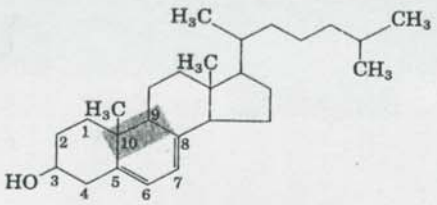
Vitamins A and D Are Hormone Precursors

維他命

生活必需但必須仰賴食物

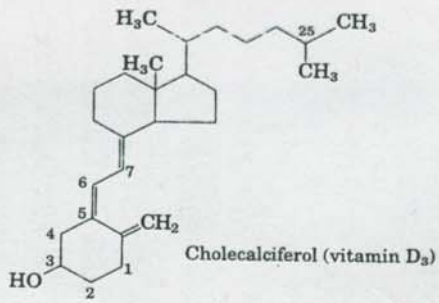


Isoprene


7-Dehydrocholesterol

UV light

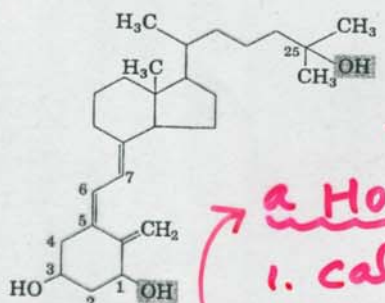
2 steps (in skin)


Cholecalciferol (vitamin D_3)

在 skin 合成
(∵ need UV light)
並無 Biological activity
必須經過 liver & kidney
的酵素反應
變成 1,25-dihydroxyvitamin D_3

1 step in the liver

1 step in the kidney


1,25-Dihydroxycholecalciferol
(1,25-dihydroxyvitamin D_3)
(a)

a Hormone regulates
1. calcium levels in bone & kidney
2. calcium uptake in intestines.

缺乏 → 佝僂症

regulates gene expression
↓
Turning on the synthesis of an intestinal Ca^{2+}-binding protein

Vitamin A (retinol 視黃醇)

hormone that regulate gene expression in skin (治療痤瘡)

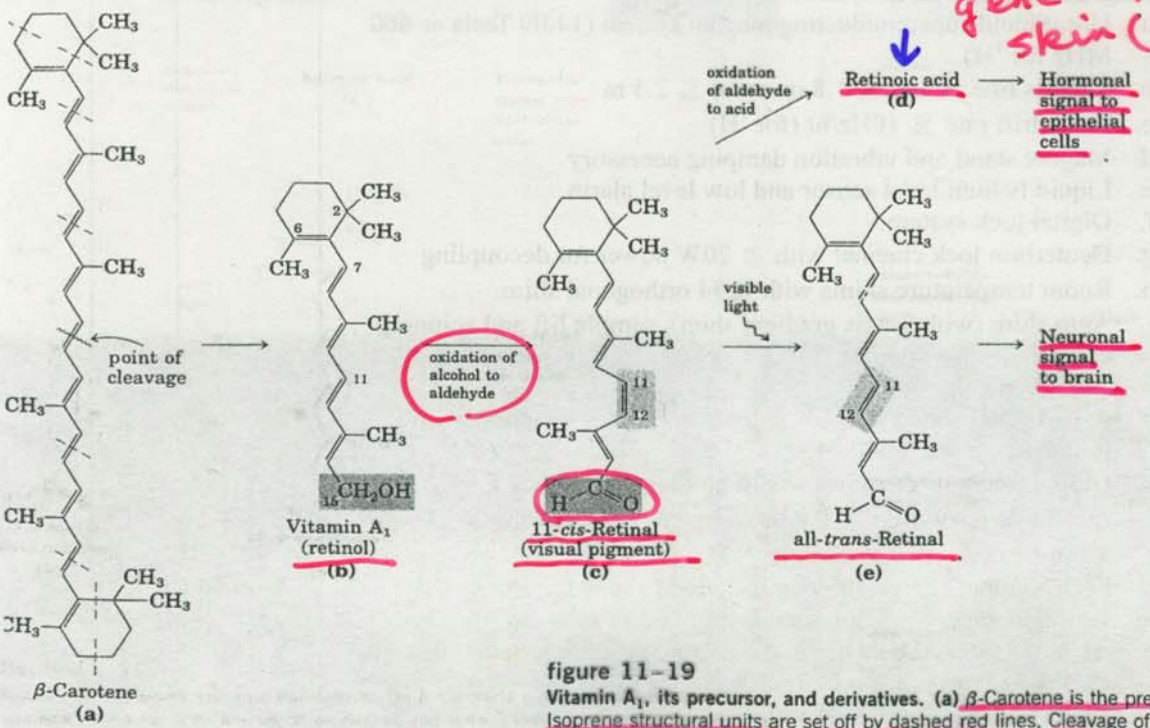
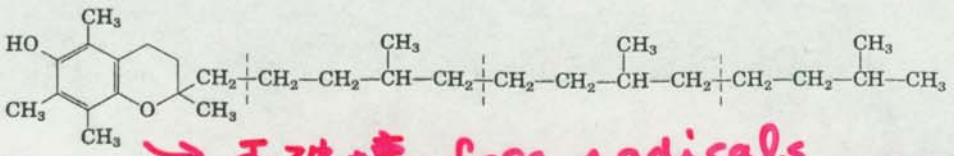


figure 11–19

Vitamin A_1, its precursor, and derivatives. (a) β-Carotene is the precursor of vitamin A_1. Isoprene structural units are set off by dashed red lines. Cleavage of β-carotene yields two molecules of vitamin A_1 (retinol) **(b).** Oxidation at C-15 converts retinol to the aldehyde, retinal **(c),** and further oxidation produces retinoic acid **(d),** a hormone that regulates gene expression in skin. Retinal combines with the protein opsin to form rhodopsin (not shown), a visual pigment widely employed in nature. In the dark, retinal of rhodopsin is in the 11-*cis* form **(c).** When a rhodopsin molecule is excited by visible light, the 11-*cis*-retinal undergoes a series of photochemical reactions that convert it to all-*trans*-retinal **(e),** forcing a change in the shape of the entire rhodopsin molecule. This transformation in the rod cell of the vertebrate retina sends an electrical signal to the brain that is the basis of visual transduction, a topic we address in more detail in Chapter 13.

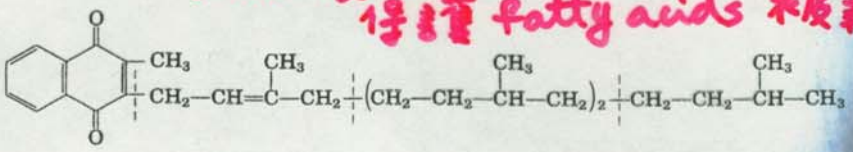
Vitamins E & K and Lipid Quinones Are Oxidation-Reduction Cofactors

(a) Vitamin E: an antioxidant

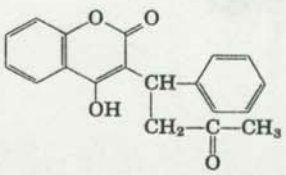


→ 可破壞 free radicals 保護 fatty acids 被氧化

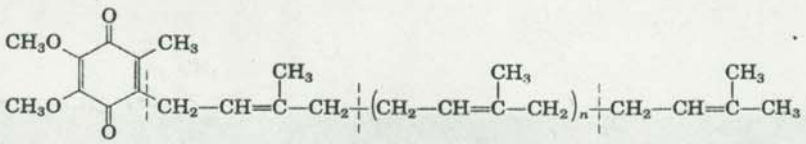
(b) Vitamin K_1: a blood-clotting cofactor (phylloquinone)



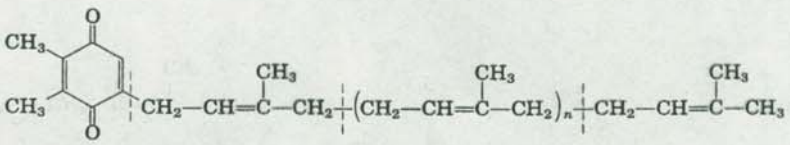
(c) Warfarin: a blood anticoagulant



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



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



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

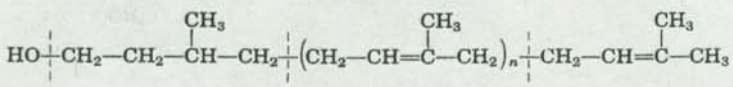
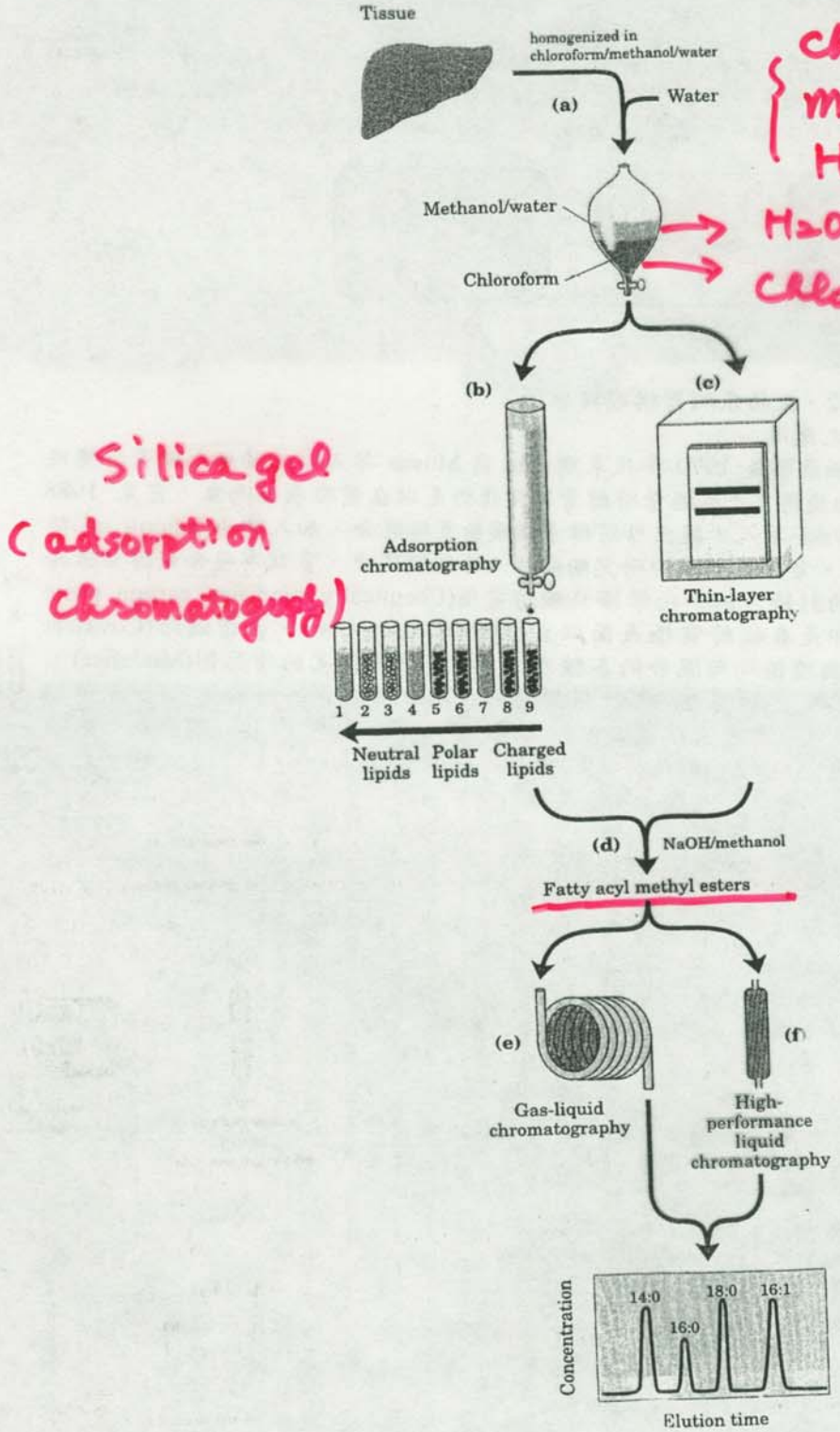


figure 11–20
Some other biologically active isoprenoid compounds or derivatives. Isoprene structural units are set off by dashed red lines. In most mammalian tissues, ubiquinone (also called coenzyme Q) has ten isoprene units. Dolichols of animals have 17 to 21 isoprene units (85 to 105 carbon atoms), bacterial dolichols have 11, and those of plants and fungi have 14 to 24.

Lipid Extraction



chloroform
methanol
H_2O

H_2O / methanol

Chloroform

Silica gel
(adsorption chromatography)

TLC