

# Chapter 10 Lipids

Problems: 1, 2, 3, 4, 6, 8, 10, 13  
Extra Credit homework available

## 10.0 Introduction

Lipids include all compounds insoluble in water. Hence very diverse

Functions also diverse

Fats & oils storage of E

phospholipids - cell membranes

some cofactors, pigments, hydrophobic anchors, hormones, intracellular signals

## 10.1 Storage Lipids

Fatty acid derivatives

### A. Fatty acids

4-36 C long with COOH at one end

may be no saturations or a few

A few with 3C rings, hydroxyl, or methyl groups

Most common are unbranched 12-24 (usually even # C) with up to 3 saturations

(Usually 9, 12, 15)

### Table 10-1

simplified nomenclature give chain length:# of saturations

### Figure 10-1

Position of saturations given as superscript following a delta  
18:2 ( $\Delta^{9,12}$ )

Saturations are usually separated by a methylene so NOT conjugated

The longer the chain and the fewer the double bonds the less soluble in water

The COOH is then only thing that makes them soluble

Lauric acid 12:0 MP 44 Solubility .063 mg/ml

Solubility of Glucose 1,100 g/ml

Longer the chain the higher the MP

Adding saturations lower MP

Why? Figure 10-2

Double bonds are made CIS not trans

With no double bonds can freeze to long perfect array

With cis kinks can't get as nice an array so less van der

Waals interaction between molecules and lower MP

Free fatty acids can circulate in vertebrates when bound to carrier protein  
serum albumin

Also in esterified or amidated, but then less soluble

### B. Triacylglycerols

simplest lipid

triglycerides fats, neutral fats

3 fatty acids linked to glycerol **Figure 10-3**

if all three the same, name is simple ... tristerin, tripalmitin

in nature usually mixed, but won't get into that nomenclature

insoluble in water

less dense than water so float

### C. Triacylglycerols as E storage and insulation

in eukaryotic cells separate phase of oil drop in cytoplasm

specialized cells adipocytes for mass storage

Fat nearly fills cell

also stored as oils in seed. Seed cells usually contain lipases to hydrolyze  
triacyl into free FA so can be easily exported

Why so good E storage

1 C fully reduced, so gives off more E in oxidation

2 unhydrated so don't carry extra weight of water of hydration

Body stores E needed to Months in fat supply

E for about a day in glycogen

Also acts as insulation in bears and walruses

in sperm whales acts to match buoyancy (as dives deep gets cold, fats  
solidify, get more dense to match water density)

### D. Many food contain triacylglycerols

Natural fats, animal fats, vegetable oils

compositions vary (**see figure 10-5**)

Vegetable oils tend to have more unsaturated to make liquid

As get saturated become more solid

Industrial hydrogenation to make solid - Crisco

Unsaturated may be air oxidized

-becomes rancid

Cleavage to acids and aldehydes can be poisonous

### E. Waxes as water repellents

Waxes long chain fatty acid esterified to long chain alcohol

**Figure 10-6a** Beeswax

generally higher MP than triacylglycerols  
energy storage for plankton

vertebrate skin cells secrete to keep hair & skin flexible and pliable  
bird, particularly waterfowl use for feathers to keep water repellent  
many tropical plant use to keep evaporation down

(Holly, Poison ivy)

May pharmaceutical and household uses

### 10.2 Structural Lipid in membranes

membranes double layer of lipids

membrane lipids are amphipathic

hydrophobic ends interact with each other

hydrophilic end interact with water

A variety of polar head groups

As little as a single OH

Or much more complex, sugars, small charged or polar  
compounds, phosphates, or combinations

If have a phosphate polar group, called phospholipid

If have a sugar polar group, called glycolipid

General organization (**figure 10-7**)

Phospholipids - Contain a phosphate in polar group

glycerophospholipids

2 FA on glycerol, then phospho- on other OH of glycerol

Sphingolipids

1 FA joined to Fatty amine called sphingosine

Glycolipid - Contain a sugar in the polar group

Sphingolipids

1 FA joined to Fatty amine called sphingosine

Hold it didn't we just see this guy in the Phospholipids

That's right Sphingolipids refer to the sphingosine backbone,  
can be with a glyco- or a phospho- lipid depending on polar  
group that you attach. Book is organized to lump both  
together

Galactolipids

Galactose sugar - seen in plants only

Archaeobacterial lipids

Real oddballs

steroids (**not on 10-6**)

Rigid 4 , fused 4 ring systems

(Won't follow organization just described in 10-6, will skip around a bit so pay attention)

### A. Glycerophospholipids

Also called phosphoglycerides

2 lipids to C1 and C2 of glycerol

highly polar or charged group attached via a phosphodiester to C3

see fig 10-9

glycerol itself is achiral

But attaching phosphate makes chiral

L-glycerol 3 phosphate

D glycerol 1 phosphate both correct names (fig 10-8)

Also name the group attached to the phosphate

Ethanolamine choline, serine, glycerol (figure 10-9) are common

Note that these groups can be +, +/-, -. Neutral so this gives cells lots of flexibility when making a membrane

FA part is also variable

In general C1 is C16 or C18 and unsaturated

C2 is C18 or 20 and unsaturated

Variation here is not well understood can vary from tissue to tissue

### B. Ether linked phospholipids (not on 10-6, a sub class of glycerophospho-)

Some animal tissues and some unicellular organism have ether linked phosphoglycerol lipids (For instance, your heart)

Usually on C1

either an ether or an ether - C=C

see figure 10-10

Plasmalogens are example of ether -C=C

Found in vertebrate heart

1/2 of phospholipids are plasmalogens

Role not known

Maybe because can't be cleaved by phospholipase

Platelet activation factor (same figure, not a plasmalogen)

Is a signal so more like a hormone!

### C. Galactolipids & Sulfolipids (Chloroplasts) Figure 10-11

Unique to plants

In particular the chloroplast of plants

70-80% of total membrane lipids in plant

Makes about most abundant lipid in biosphere

Galactolipid **Upper two of figure**

Glycerol backbone

FA's on C1 and C2

1 or 2 galactose on C3

Sulfolipid (**figure bottom**)

Glycerol backbone

FA's on C1 and C2

Sulfonated glucose on C3

Sulfate is negatively charged, speculation that it works like phospholipid without the phosphate

### D. Lipids in Archaeobacteria

real oddball

**Figure 10-12**

GDGT's Glycerol Dialkyl glycerol tetraethers

terpene (isoprene) based lipid (called Diphytanyl)

ETHER linked Diacyl glycerol at BOTH ends

Glycerol at 1 end linked to glycerol phosphate

Glycerol at other end linked to sugar

Glycerol in R config instead of normal S

Why? (Speculation)

Archaeobacteria - Extreme environments

Ether linkages, more stable

Membrane of organism more stable

1 lipid across middle instead of 2

Branches prevent from crystalizing

R instead of S Who knows?

### E. Sphingolipids

derivatives of Sphingosine

structure of sphingosine **Figure 10-13 MEMORIZE**

Long chain amino alcohol

similar in overall shape to phosphoglycerol

**BUT NO GLYCEROL**

Polar group attached to alcohol

FA attached to NH via a peptide linkage

When this occurs call it a ceramide

### 3 major subclasses

Sphingomyelins (a phospho lipid)- contain phosphatidyl choline or phosphatidyl ethanolamine Thus included as phospholipids

Present in plasma membrane of animal cells

Prominent in myelin membrane sheath that surrounds and insulated axon of some neurons

Glycosphingolipids (a glycolipid)- have polar head of 1 or more sugars

Do not contain phosphate

Dominate on outer face of PM

Cerebrosides

Only 1 sugar

If neural tissue - usually galactose

If non-neural usually glucose

Globosides

2 or more sugars

Cerebrosides and globosides called neutral glycolipids because no charge at pH 7

Gangliosides (also a glycolipid, but more complicated)

Oligosaccharides as polar head

Typically sialic acid at terminus

### F. Sphingolipids at cell surface site of biological recognition

(But it is the sugar, not the lipid that is recognized)

have been recognized for over 100 years

60 different have been isolated

Many found on PM of neurons

several are recognition sites

few have specific known function at this point

are responsible for Blood type (**figure 10-15**)

See dramatic changes in embryo development and in tumor formation

Area of active research

### G. phospholipids and sphingolipids degraded by lysosomes

cells usually degrading and replacing cell membrane

for each hydrolyzable bond there is a specific hydrolytic enzyme

**see figure 10-16**

Gangliosides sugars removed by a set of enzymes

If any is defective, start to accumulate

A variety of diseases **See box 10-2** generally ending in mental

retardation for child who inherits

### H. Sterols

found in membranes of most eucaryotic  
 characteristic fused ring structure (figure 10-17)  
 Not a flat ring  
 cholesterol major steroid in animal tissue  
 Only slightly polar  
 synthesized from 5C isoprene units  
 used in membranes (to stiffen)  
 Precursor to steroid hormones  
 Bile salts (detergent in intestine for emulsifying fats)  
 will see cholesterol again a few times

### 10.3 Lipids as signals, cofactors & pigments

Membrane lipids (structural lipids)

5-5% of dry weight of cell

Storage lipids >80% mass of adipose cell

Now look at lipids present in lower amounts

signals

Intracellular and extracellular  
 enzyme cofactors for electron transfer reactions  
 intermediate in glycosylation transfer reactions  
 lipids with conjugated double bonds use as pigments  
 fat soluble vitamins

### A. Phosphatidylinositols as intracellular signals

(Note: this is a membrane phospholipid, so nothing new, just used in a new way)

Structure glycerol 2FA's, Phosphate, inositol sugar

Phosphatidyl inositol 4,5 biphosphate

On inner side of PM

Serves as binding site for certain cytoskeleton proteins

Also a reserve that is released by extracellular signals that interact with protein on surface

**Figure 10-9 again**

Inositol triphosphate - soluble- release of CA in cytosol

Diacylglycerol - membrane bound- activated protein kinase C

Kinase C adds P to several proteins and alters cells metabolism

Membrane sphingolipids also sources for intracellular messengers

## B. Eicosanoids

This is somebody new. Pay attention

paracrine hormone - only works on cells near host cell - not transported by blood

wide variety of cellular responses associated with injury or disease

Based on 20 C polyunsaturated arachadonic acid 20:4( $\Delta^{5,8,11,14}$ )

Figure 10-18b

3 classes

Prostaglandins

Thromboxanes

Leukotrienes

### **I. Prostaglandins**

5 C ring in center

First isolated from prostate gland (duh)

2 main types

PGE (ether soluble)

PGF buffer soluble (fosfat-Swedish for buffer)

Subtypes numbered i.e. PGE<sub>2</sub>

Acts on many tissues by regulating synthesis of cAMP internal messenger

Lots of cellular effects

Contraction of uterus (menstruation and labor)

Produce fever cause inflammation and pain

Blood flow to organs, wake/sleep response to epinephrine

### **II. Thromboxanes**

6 membered ring with an ether

Produced by platelets when forming blood clot

Nonsteroidal anti-inflammatory drugs (NSAID's)

(Aspirin, ibuprofen, acetaminophen)

Inhibit prostaglandin H<sub>2</sub> synthase also called COX

Early step in synthesis of both thromboxane and

Prostaglandins So shut down synthesis

Why aspirin is a blood thinner? And pain reliever (see part 2 prostagladins above)

### **III. Leukotrienes**

Contains 3 conjugated double bonds

Leukotriene D<sub>4</sub> induces contraction of muscle lining airways of lungs

Overproduction causes asthma

Target of drug to suppress asthma  
Also involve in anaphylactic shock

### C. Steroid Hormones

generally oxidized derivatized sterols  
Lack chain attached to D loop

Figure 10-19 for some

Bloodstream hormones so activate cells far from site of release  
actually enter cell, bind to receptors in nucleus and change gene  
expression to modulate metabolism

Male and female sex hormones

adrenal cortex hormones (cortisol and aldosterone)

Prednisone and prednisolone steroid drugs inhibit release of arachonic  
acid so inhibit release of leukotrienes, prostaglandins and  
thromboxanes

Lots of medical implications

### D. Plants use Phosphatidylinositols, Steroids, and Eicosanoidslike compounds in signaling

Just in case you thought that ths hormone signal stuff was just for  
animals, plants do it too!

Phosphatidylinositol for Ca regulation very similar

Steroid equivalent - Brassinolide 10-19 also

Growth regulators

Stem elongation cellulase orientation

Eicosanoid equivalent - Jasmonate Fig 12-32

Derived from 18:3( $\Delta^{9,12,15}$ )

Instead of 20:4( $\Delta^{5,8,11,14}$ ) arachidonic acid

Trigger plant defense response for insect damage

Methyl ester of Jasmonate is jasmine smell used in perfume

Also many, many volatiles based of the isoprene unit

(bottom right column page 359

Note animals use isoprene too! This is what cholestrol is made  
from!

### E. Vitamins A and D

vitamin compound essential to health not synthesized in body

Fat soluble A, D, E, K

D<sub>3</sub> or cholecalciferol

**Figure 10-20**

Built from isoprenoids like sterols  
 Formed in skin via as UV reaction  
 Need further process by liver and kidney to active form  
 Regulates Ca uptake in intestine  
 Deficiency lead to lack of Ca adsorption lead to rickets

D<sub>2</sub> made commercially by UV radiation of ergosterol from yeast  
 Then added to mild and butter  
 Has same effect as D<sub>3</sub>

## Vitamin A (retinol)

**Fig 10-21**

Build from isoprenoids like sterols  
 Retinoic acid

Regulated gene expression in epithelial tissue  
 Active ingredient in Retin-A  
 Used for acne and wrinkled skin

## Retinal

Pigment that starts response of rod and cone in eye  
 Described in detail in chapter 13 if you want to read ahead  
 First isolated from fish liver and liver  
 Now know that  $\beta$ -carotene (carrots-sweet potatoes and yellow  
 veggies)  
 Can be converted to Vit A in body  
 Many various problems if you lack

F. Vit E & K**Figure 10-22**

Also derived from isoprenoid, but not cyclized into sterol system  
 E - tocopherols

Membrane soluble  
 Aromatic ring used as antioxidant  
 Keeps unsaturated membrane lipids from oxidizing

## K

Similar structure  
 Oxidation and reduction part of activation of prothrombin  
 Prothrombin essential to blood clot formation  
 Lack of K slows blood clotting can be fatal

Warfarin structurally similar

Acta as agonist  
 Stop blood clotting  
 Rat poison rat die from internal bleeding  
 Also used as treatment for excess blood clotting

Surgery patients  
 Ubiquinone (Co enzyme Q) & plastoquinone  
 Lipophilic electron carriers  
 Used in Mitochondria and chloroplasts  
 Will see again next semester

### G. Dolichols

Another isoprenoid  
 Used to anchor sugars to membranes as intermediate in making  
 glycolipids and glycoproteins

## 10.4 Separation and analysis of Lipids Figure 10-24

### A. Extraction with organic solvents

Neutral lipids - readily extracted with diethyl ether, chloroform or benzene  
 Membrane lipids usually extracted methanol or ethanol  
 common extraction chloroform methanol water 1:2:0.8  
 At this ratio a single phase  
 Homogenize cell so get all into solution  
 Add more water  
 Now water MeOH phase separate to top  
 Chloroform stays on bottom with lipids

### B. Adsorption chromatography

yet another chromatography  
 use a polar solid phases (silica gel  $\text{Si(OH)}_4$ )  
 Nonpolar liquid phase  
 Material will move quickly if non polar because will dissolve in  
 organic  
 More slowly if polar because attracted to solid  
 Neutral lipids come out first  
 Will need a more polar solvent to pull of the more polar lipids  
 can do with HPLC (smaller column higher pressure  
 this is what are doing on tlc!  
 Visualize by spraying with dye that fluoresces in presence of lipid  
 $\text{I}_2$  (binds to double bond to give temporary color  
 Other reagent for other lipids

### C. GC

Volatile compound can be separated by GC  
 Gas chromatography  
 partition between carrier gas and solid or liquid phase  
 FA made volatile by turning into methyl esters with MeOH and acid or  
 base

see figure 11-21  
make fancy by adding a mass spec

#### D. Specific hydrolysis

most lipids contain hydrolyzable bonds - ester linkage between groups  
can take apart with mild acid or base  
not good for a triglyceride because all come off  
so use enzymes to achieve hydrolysis at specific bonds  
(see figure 10-16 again for specifics)

Combine all of above for complete analysis

#### E. Mass Spec Figure 10-25

Identification of individual lipids based on above methods can be difficult  
The physical difference between an 18:0 and an 18:1  
Or an 18:2( $\Delta^{9,12}$ ) or 18:2( $\Delta^{12,15}$ ) is pretty minimal  
Mass Spectrum of a compound gives a pattern that is unique  
Much easier to identify (but still can be tricky)