

## Chapter 10 Homework Assignment

- I have decided to alter the homework assignment for Chapter 10. The following problems will be due once we finish the chapter:

**2, 4, 5, 6, 9**

Chapter 10

1

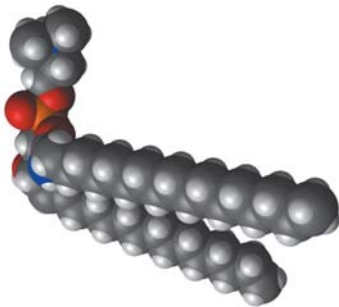
## Lipids are Good (and not always greasy)

- **Lipids** are a chemically diverse group of compounds, the common and defining feature being their insolubility in water
- Important for energy storage (fats & oils)
  - Fatty acids
  - Triacylglycerols (TAG's)
- Crucial to membrane structure
  - Phospholipids
  - Sterols
- Many other functions in various guises
  - Cofactors
  - Pigments
  - Hormones

Chapter 10

3

## Chapter 10 Lipids



## Storage Lipids

### Fatty Acids are Self-Descriptive

- **Fatty Acids** are the fundamental building blocks of lipids
- They are in a low oxidation state, and thus conversion to carbon dioxide and water is highly exergonic (lots of energy in fats!)
- They are *carboxylic acids* with hydrocarbon chains ranging from 4 to 36 carbons long
- Chains may be fully saturated (no double bonds), or have some unsaturated double bonds
  - The unsaturated FAs can be cis or trans (trans fats!)
- Chains are usually unbranched

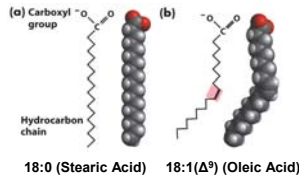
Chapter 10

4

## Storage Lipids

### The Naming of Fatty Acids

- Most natural fatty acids have an **even** number of backbone carbons (from synthesis in 2-carbon units)
- Nomenclature: Carbon chain length: # of double bonds (position)**
  - 20:2(Δ<sup>9,12</sup>)** is a FA with 20 carbons and 2 double bonds, between C9-10, C12-13
- With 2 or more unsaturated double bonds:
  - FAs are rarely conjugated,
  - Double bonds are usually at 3 carbon intervals, starting at C9, e.g. α-linolenic acid is 18:3 (Δ<sup>9,12,15</sup>)
  - Double bonds are (almost) always in the **cis** configuration



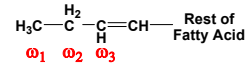
Chapter 10

5

## Storage Lipids

### The Omega (ω) Designation

- The end of the fatty acid chain is called the omega end
- The omega designation indicates the position of the double bond closest to the omega end of the chain, and furthest from the carbonyl group



This would be an omega-3 fatty acid

- The health benefits of these essential fatty acids (EFAs) is in their ability to act as a competitive inhibitor in the production of Arachidonic Acid (20:4(Δ<sup>5,8,11,14</sup>), a precursor of the eicosanoids
- These eicosanoids are signaling molecules promote inflammation of the tissues in which they are located.
- The diet of early man was rich in these omega-3 fatty acids
- This is no longer the case, resulting in an increase in a number of diseases called the **diseases of civilization**

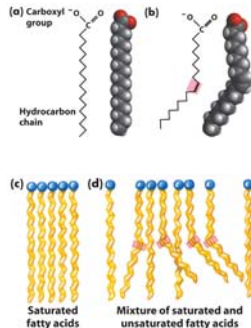
Chapter 10

7

## Storage Lipids

### Saturated versus Unsaturated

- Why are any fatty acids soluble in water?
- Why does m.p. increase with length?
- Why does m.p. decrease with more unsaturation (i.e. more double bonds)?
- Why does solubility decrease with length?
- Which bonds in the hydrocarbon chain can rotate freely, and which cannot?
- What kinds of forces contribute to these behaviors?
- Which types of FAs do you think make up oils? What about solid fats like shortening?
- Why does this difference occur?
- What is so bad about trans-fats?



Chapter 10

6

## Storage Lipids

TABLE 10-1 Some Naturally Occurring Fatty Acids: Structure, Properties, and Nomenclature

Carbon number	Structure*	Systematic name†	Common name (abbreviation)	Melting point (°C)	Solubility at 30°C (mg/g solvent)
12:0	<chem>CH3(CH2)10COOH</chem>	→ Dodecanoic acid	Lauric acid (Latin laurus, "lavender plant")	44.2	0.083
14:0	<chem>CH3(CH2)12COOH</chem>	→ Tetradecanoic acid	Myristic acid (Latin Myrica, "myrtle berries")	53.9	0.024
16:0	<chem>CH3(CH2)14COOH</chem>	→ Hexadecanoic acid	Palmitic acid (Latin Palmaria, "palm tree")	63.1	0.0083
18:0	<chem>CH3(CH2)16COOH</chem>	→ Octadecanoic acid	Stearic acid (Greek steira, "wool fat")	69.6	0.0034
20:0	<chem>CH3(CH2)18COOH</chem>	→ Eicosanoic acid	Arachidic acid (Latin Arachis, "peanut")	76.5	—
24:0	<chem>CH3(CH2)22COOH</chem>	→ Tetracosanoic acid	Lignoceric acid (Latin lignum, "wood")	86.0	—
18:1(Δ <sup>7</sup> )	<chem>CH3(CH2)7CH=CH(CH2)9COOH</chem>	→ 9-Hexadecenoic acid	Palmitoleic acid (Latin palmaria, "palm")	5.5	—
18:1(Δ <sup>9</sup> )	<chem>CH3(CH2)7CH=CH(CH2)9COOH</chem>	→ 9-Octadecenoic acid	Oleic acid (Latin oleum, "oil")	13.4	—
18:2(Δ <sup>7,11</sup> )	<chem>CH3(CH2)5CH=CHCH2CH=CH(CH2)7COOH</chem>	→ 9,12-Octadecadienoic acid	Linoleic acid (Greek linon, "flax")	−5.5	—
18:3(Δ <sup>7,11,15</sup> )	<chem>CH3(CH2)5CH=CHCH2CH=CHCH2CH=CH(CH2)4COOH</chem>	→ 9,12,15-Octadecatrienoic acid	α-Linolenic acid (Latin linon, "flax")	−11	—
20:4(Δ <sup>5,8,11,14</sup> )	<chem>CH3(CH2)4CH=CHCH2CH=CHCH2CH=CHCH2CH=CH(CH2)2COOH</chem>	→ 5,8,11,14-Eicosatetraenoic acid	Arachidonic acid (Latin Arachis, "peanut")	−49.5	—

You should be able to draw the structure of the following FAs:  
**Palmitic Acid**  
**Stearic Acid**  
**Palmitoleic Acid**  
**Oleic Acid**  
**Linoleic Acid**

**Note trends:**  
**MP vs length**  
**MP vs saturation**  
**Solubility vs length**

\*12:0 acids are shown in their zwitterionic form, [O-]C(=O)CH2(CH2)10NH3+. All the fatty acids have an overall net neutral charge. †The prefix "n" indicates the "normal" unbranched structure. For instance, "9-tetradecenoic" simply indicates 14 carbon atoms, which could be arranged in a variety of branched forms. "9-tetradecenoic" indicates the most unbranched form. For unsaturated fatty acids, the configuration of each double bond is indicated, as "cis" or "trans" if the configuration is about double bond.

Chapter 10

Glucose MW 180 Sol = 1100 mg/g  
 Lauric Acid MW 200 Sol = 0.063 mg/g

8

## Storage Lipids

### Fuel: Fat vs. Sugar?

TABLE 16-1 Stoichiometry of Coenzyme Reduction and ATP Formation in the Aerobic Oxidation of Glucose via Glycolysis, the Pyruvate Dehydrogenase Complex Reaction, the Citric Acid Cycle, and Oxidative Phosphorylation

Reaction	Number of ATP or reduced coenzyme directly formed	Number of ATP ultimately formed*
Glucose → glucose 6-phosphate	-1 ATP	-1
Fructose 6-phosphate → fructose 1,6-bisphosphate	-1 ATP	-1
2 Glucose-derived 3-phosphoglycerate → 2 1,3-bisphosphoglycerate	2 NADH	3 or 3'
2 1,3-bisphosphoglycerate → 2 3-phosphoglycerate	2 ATP	2
2 Phosphoenolpyruvate → 2 pyruvate	2 ATP	2
2 Pyruvate → 2 acetyl CoA	2 NADH	5
2 Isocitrate → 2 α-ketoglutarate	2 NADH	5
2 α-ketoglutarate → 2 succinyl CoA	2 NADH	5
2 Succinyl CoA → 2 succinate	2 ATP (or 2 GTP)	2
2 Succinate → 2 fumarate	2 NADH	5
2 Malate → 2 oxaloacetate	2 NADH	5
<b>Total</b>		<b>30-32</b>

TABLE 17-1 Yield of ATP during Oxidation of One Molecule of Palmitoyl-CoA to CO<sub>2</sub> and H<sub>2</sub>O

Enzyme catalyzing the oxidation step	Number of NADH or FADH <sub>2</sub> formed	Number of ATP ultimately formed*
Acyl CoA dehydrogenase	7 FADH <sub>2</sub>	10.5
β-Hydroxyacyl-CoA dehydrogenase	7 NADH	17.5
Isocitrate dehydrogenase	8 NADH	20
α-Ketoglutarate dehydrogenase	8 NADH	20
Succinyl-CoA synthetase	8 NADH	18'
Succinate dehydrogenase	8 FADH <sub>2</sub>	12
Malate dehydrogenase	8 NADH	20
<b>Total</b>		<b>108</b>

Chapter 10

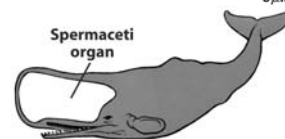
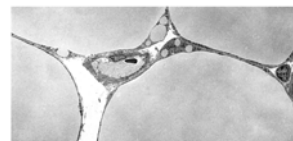
So why don't we just eat a fat FULL diet?

9

## Storage Lipids

### TAGs Provide Stored Energy and Other Functions

- TAGs form oily droplets in the aqueous cytosol in the cells of most eukaryotes
- In addition, specialized cells (**adipocytes** or **fat cells**) store large amounts of TAGs
- These stores of TAGs can serve both as energy sources and insulation sources
- How do you think whales utilize their stores of TAGs?



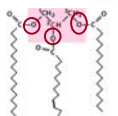
Chapter 10

11

## Storage Lipids

### The Simplest Lipids: Triacylglycerols (TAGs)

- A TAG is a triester of glycerol and three fatty acids
- If all three FAs are the same (a simple TAG), it is named after the FA, e.g. tripalmitin
- If the FAs are different, a name and position of each must be given
- How will the solubility of a TAG compare to its parent molecules (the FAs and the Glycerol)?
- Note the physical consequence of a pair of double bonds in *cis*



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

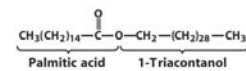
Chapter 10

10

## Storage Lipids

### Waxes

- Biological **waxes** are esters of long-chain (C<sub>14</sub> to C<sub>36</sub>) saturated and unsaturated FAs with long chain (C<sub>16</sub> to C<sub>30</sub>) alcohols
- Their MPs are generally higher than TAGs
- Waxes can serve as energy sources; water repellent; and structural components
- What animals can you think of that use waxes as water repellants? Why would a plant want its leaves to be coated in wax?



Chapter 10

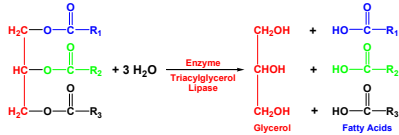
12

## Storage Lipids

### Chemical Properties of TAGs

- TAGs undergo several reactions including **hydrolyzation**, **saponification** and **hydrogenation**

#### Hydrolysis



- This reaction is catalyzed by an enzyme called a **lipase**
- When the TAGs are digested, hydrolysis is usually incomplete
- You get a mixture of products including MAGs, free fatty acids, glycerol and some DAGs

Chapter 10

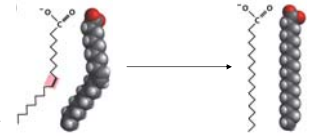
13

## Storage Lipids

### Chemical Properties of TAGs

#### Hydrogenation

- When you add hydrogen to the double bonds found in the lipids of most vegetable oils, the oils become solids similar to those of animal lipids.
- Basically, you are saturating all of the double bonds to form a fully saturated fat.
- Partial hydrogenation (partial saturation of the double bonds) results in compounds such as margarine and peanut butter.
- A side effect of incomplete hydrogenation having implications for human health is the isomerization of the remaining unsaturated carbon bonds.
- The cis configuration of these double bonds predominates in the unprocessed fats in most edible fat sources, but incomplete hydrogenation partially converts these molecules to trans isomers, which have been implicated in circulatory diseases including heart disease (see trans fats).
- The catalytic hydrogenation process favors the conversion from cis to trans bonds because the trans configuration has lower energy than the natural cis one.



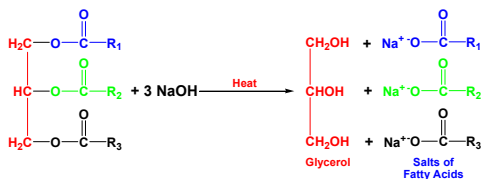
Chapter 10

15

## Storage Lipids

### Chemical Properties of TAGs

#### Saponification



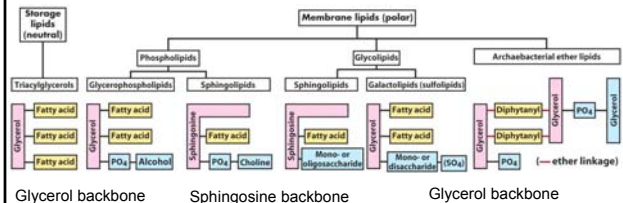
- TAGs are **saponified** to form soaps
- Here, the hydrolysis reaction occurs through the addition of a base (OH<sup>-</sup>) to form glycerol and the anionic forms of the three fatty acids.
- The first soap was likely made accidentally by the saponification of animal fat in a fire by the KOH present in wood ash

Chapter 10

14

## Classification of Lipids

- In addition to the storage lipids, there are lipids involved in membranes
- These lipids can be split into five different groups with either a glycerol or sphingosine backbone



Glycerol backbone

Sphingosine backbone

Glycerol backbone

**Know this chart!**

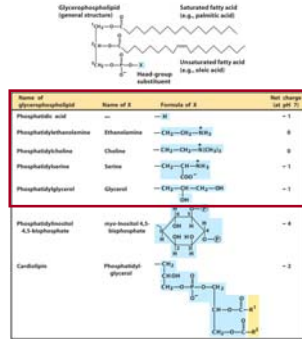
Chapter 10

16

## Structural Lipids

### Phospholipids: Glycerophospholipids

- Glycerophospholipids** (GPLs) are structural lipids in which one of the FAs from a TAG is replaced with a highly polar or charged group attached via a phosphodiester linkage
- The fatty acids vary within each group, but usually are sat'd C16/18 at C1, and unsat'd C18/20 at C2
- Note the GPL can carry a charge that may be positive, negative, or neutral
- Depends on the head group substituent

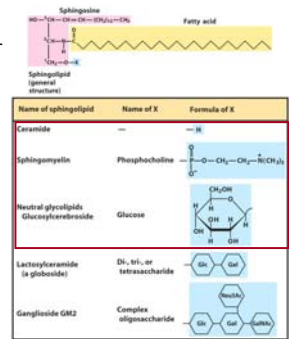


Chapter 10

## Structural Lipids

### Sphingolipids

- Sphingolipids** (SPLs) also have a polar head group and two non-polar tails but do not contain glycerol
- Instead, the backbone is **sphingosine**, a long-chain amino alcohol
- Some derivatives are Ceramide, Sphingomyelin, and Glycosphingolipids

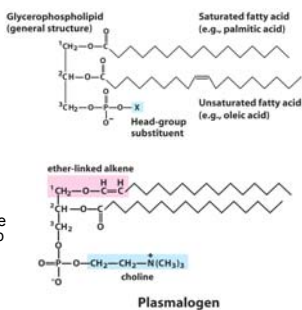


Chapter 10

## Structural Lipids

### Phospholipids: Glycerophospholipids

- GPLs can be further into the **phosphatides** and the **plasmalogens**
- Both are esters of glycerol (meaning glycerol is the backbone to which the other groups are attached)
- Phosphatides** are those listed on the previous slide
- Plasmalogens** have both ether and ester groups
- These compounds occur widely in the membranes of both nerve and muscle cells
- They differ from the phosphatides by the presence of an unsaturated **ether** group in addition to the ester groups.
- Similar to the phosphatides, these compounds will carry electrical charges on the oxygen of the phosphate group and the attached alcohol group.

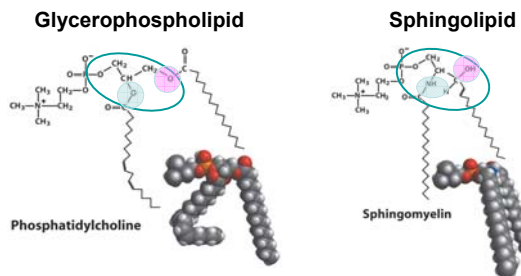


Chapter 10

18

## Structural Lipids

### GPL's and SL's Actually Look Alike!

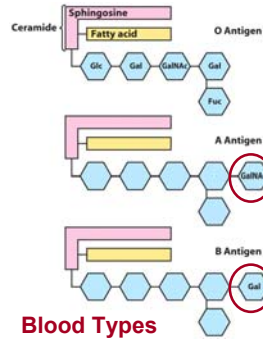


Chapter 10

20

## Structural Lipids

### Cell Surface Recognition is Mediated by Sphingolipids



### Blood Types

Chapter 10

21

- When the sphingolipids were discovered by Johann Thudichum, he said their biological function seemed as enigmatic as the Sphinx (hence their name!)
- In humans, at least 60 different SPLs have been identified, but only a handful have known functions attached.
- The sugar moieties of certain SPLs are used to define blood type
- Other SPLs are concentrated on the surface of cells and used for recognition by extracellular molecules and entities

## Lipids as Signals, Cofactors & Pigments

### Beyond the Passive Roles of Lipids in Storage & Structure

- Active roles for lipids and their derivatives
  - Intracellular signaling – Phosphatidylinositol
  - Paracrine hormones – Eicosanoids
  - Steroid hormones – polar cholesterol derivatives
  - Vitamins – A, D, E, and K
- Provide crucial parameters of membrane fluidity

Chapter 10

23

## Structural Lipids

### Sterols



### The Dreaded Cholesterol

Chapter 10

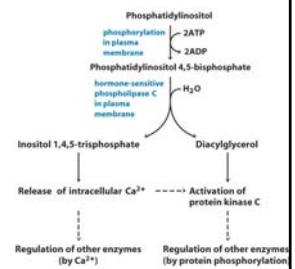
22

- **Sterols** are structural lipids that consists of an **aliphatic** core structure of four fused rings ( 3 hexa- and 1 penta-carbon)
- Sterols have a many roles:
  - A structural role in most eukaryotic membranes (*we'll see why later*)
  - Hormone derivatives that regulate gene expression
  - Bile acids are polar derivatives that help emulsify dietary fats

## Lipids as Signals, Cofactors & Pigments

### Phosphatidylinositols & Sphingosine Derivatives Act as Intracellular Signals

- These molecules can serve as sources for intracellular signals when acted upon by enzymes
- When substituents are added and bonds broken, the resulting molecules can initiate and regulate other processes within the cell
  - Release of secondary messengers (*i.e.* Calcium ions)
  - Regulation of protein kinases
  - Regulation of cell division, proliferation and apoptosis

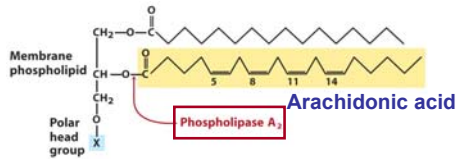


Chapter 10

24

## Lipids as Signals, Cofactors & Pigments

### Where Do Eicosanoids Come From?



- **Eicosanoids** are paracrine hormones that act on cells near their point of synthesis to affect inflammation, blood clotting, gastric acid secretion, etc.
- They are derived from arachidonic acid (20:4( $\Delta^{5, 8, 11, 14}$ )) liberated from particular membrane phospholipids by phospholipase  $A_2$
- This group includes **prostaglandins**, **thromboxanes** and **leukotrienes**

Chapter 10

25

## Lipids as Signals, Cofactors & Pigments

### Steroid Hormones Derived from Cholesterol

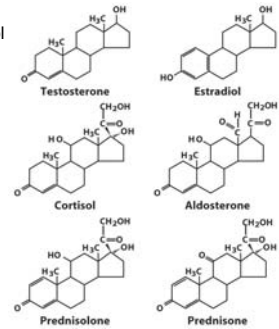
- They lack the alkyl chain of cholesterol and as oxidized derivatives are more polar

*How does this affect solubility?*

- These molecules can move through the bloodstream and thus act at a distance - unlike paracrine hormones, which act locally

- Very tiny amounts needed because of very high affinities for their receptors

- They include the sex hormones, and those produced by the adrenal cortex

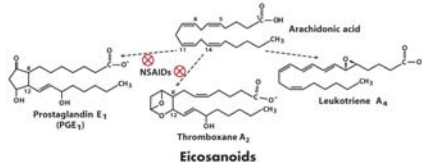


Chapter 10

27

## Lipids as Signals, Cofactors & Pigments

### Eicosanoids



- **Prostaglandins** act in many tissues by regulating the synthesis of the intracellular messenger 3',5' - cyclic AMP (cAMP)
- **Thromboxanes** are produced by platelets and act in the formation of blood clots and the reduction of blood flow to the site of the clot
  - Their formation can be inhibited by compounds like aspirin
- **Leukotrienes** were originally found in leukocytes and serve as powerful biological signals
  - Overproduction of leukotrienes causes asthmatic attacks and is a main contributor to the contraction of smooth muscle in the lungs during anaphylactic shock

Chapter 10

26

## Lipids as Signals, Cofactors & Pigments

### Fat-Soluble Vitamins

- Remember, a **vitamin** is a compound that is essential to the health of humans but cannot be synthesized internally and must be obtained through diet.
- **Vitamins A and D** are precursors of hormones:
  - **Vitamin D** is a cholesterol derivative that is converted into a hormone regulating calcium metabolism in the intestine, kidney, and bone (deficiency leads to rickets)
  - **Vitamin A** (aka. **retinol**) derivatives can absorb light (retinal + opsin = rhodopsin, a vision thing), and control epithelial tissue development

Chapter 10

28

## Lipids as Signals, Cofactors & Pigments

### Fat-Soluble Vitamins

- **Vitamin K** – a cofactor essential for activating prothrombin, needed to promote blood clotting
- **Vitamin E** – group of lipids called tocopherols, which as antioxidants, protect unsaturated fatty acids, and scavenge damaging free radicals
- **Warfarin** is a synthetic compound that inhibits the formation of active prothrombin (excellent rat poison or human anticoagulant!)
- **Ubiquinone** (aka Coenzyme Q) and **Plastiquinone** function as lipophilic electron carriers in the redox reactions that drive ATP synthesis

Chapter 10

29