CHAPTER 10 LIPIDS

10.1 Storage Lipids
10.2 Structural Lipids in Membranes
10.3 Lipids as Signals, Cofactors, and Pigments
10.4 Working with Lipids

Classification of Lipids

• Based on the structure and function
  • Lipids that do not contain fatty acids: cholesterol, terpenes, …
  • Lipids that contain fatty acids (complex lipids)
    – Storage lipids and membrane lipids
10.1 Storage Lipids

- The fats and oils used almost universally as stored forms of energy in living organisms are derivatives of fatty acids.

Fatty Acids Are Hydrocarbon Derivatives

- Fatty acids are carboxylic acids with hydrocarbon chains ranging from 4 to 36 carbons long (C$_4$ to C$_{36}$).
- A simplified nomenclature for unbranched fatty acids specifies the chain length and number of double bonds, separated by a colon (Fig. 10–1a).

FIGURE 10–1 Two conventions for naming fatty acids.

(a) 18:1(Δ$^9$) **cis-9-Octadecenoic acid**

(b) 20:5(Δ$^5,8,11,14,17$) **Eicosapentaenoic acid (EPA)**, an omega-3 fatty acid
The most commonly occurring fatty acids have even numbers of carbon atoms in an unbranched chain of 12 to 24 carbons.

The family of polyunsaturated fatty acids (PUFAs) with a double bond between the third and fourth carbon from the methyl end of the chain are of special importance in human nutrition.

PUFAs with a double bond between C-3 and C-4 are called omega-3 (ω-3) fatty acids, and those with a double bond between C-6 and C-7 are omega-6 (ω-6) fatty acids.
Triacylglycerols Are Fatty Acid Esters of Glycerol

- The simplest lipids constructed from fatty acids are the triacylglycerols, also referred to as triglycerides, fats, or neutral fats. Triacylglycerols are composed of three fatty acids each in ester linkage with a single glycerol (Fig. 10–3).
FIGURE 10–7 Some common types of storage and membrane lipids.

FIGURE 10–3 Glycerol and a triacylglycerol.
Triacylglycerols Provide Stored Energy and Insulation

- In vertebrates, specialized cells called adipocytes, or fat cells, store large amounts of triacylglycerols as fat droplets that nearly fill the cell (Fig. 10–4a).

- Triacylglycerols are also stored as oils in the seeds of many types of plants, providing energy and biosynthetic precursors during seed germination (Fig. 10–4b). Adipocytes and germinating seeds contain lipases, enzymes that catalyze the hydrolysis of stored triacylglycerols, releasing fatty acids for export to sites where they are required as fuel.

**FIGURE 10-4(a) 4 guinea pig adipocytes**
Two significant advantages to using triacylglycerols as stored fuels:

(1) the carbon atoms of fatty acids are more reduced than those of sugars, and oxidation of triacylglycerols yields more than twice as much energy.

(2) Triacylglycerols are hydrophobic and therefore unhydrated, the organism that carries fat as fuel does not have to carry the extra weight of water of hydration.
Partial Hydrogenation of Cooking Oils Produces Trans Fatty Acids

- Most natural fats, such as those in vegetable oils, dairy products, and animal fat, are complex mixtures of simple and mixed triacylglycerols. These contain a variety of fatty acids differing in chain length and degree of saturation (Fig. 10–5).

- Many fast foods are deep-fried in partially hydrogenated vegetable oils and therefore contain high levels of trans fatty acids (Table 10–2).
Trans Fatty Acids in Foods

- partial dehydrogenation of unsaturated fatty acids
- A trans double bond allows a given fatty acid to adopt an extended conformation.
- Trans fatty acids can pack more regularly, and show higher melting points than cis forms.
- Consuming trans fats increases risk of cardiovascular disease
  - Avoid deep-frying partially hydrogenated vegetable oils
  - Current trend: reduce trans fats in foods
    (Wendy’s, KFC)

<table>
<thead>
<tr>
<th>Trans fatty acid content</th>
<th>In a typical serving (g)</th>
<th>As % of total fatty acids</th>
</tr>
</thead>
<tbody>
<tr>
<td>French fries</td>
<td>4.7 - 6.1</td>
<td>28 - 36</td>
</tr>
<tr>
<td>Breaded fish burger</td>
<td>5.6</td>
<td>28</td>
</tr>
<tr>
<td>Breaded chicken nuggets</td>
<td>5.0</td>
<td>25</td>
</tr>
<tr>
<td>Pizza</td>
<td>1.1</td>
<td>9</td>
</tr>
<tr>
<td>Corn tortilla chips</td>
<td>1.6</td>
<td>22</td>
</tr>
<tr>
<td>Doughnut</td>
<td>2.7</td>
<td>25</td>
</tr>
<tr>
<td>Muffin</td>
<td>0.7</td>
<td>14</td>
</tr>
<tr>
<td>Chocolate bar</td>
<td>0.2</td>
<td>2</td>
</tr>
</tbody>
</table>

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**Waxes**

- Waxes are esters of long-chain saturated and unsaturated fatty acids with long-chain alcohols.
- Insoluble and have high melting points.
- Variety of functions:
  - Storage of metabolic fuel in plankton (浮游生物)
  - Protection and pliability for hair and skin in vertebrates.
  - Waterproofing of feathers in birds.
  - Protection from evaporation in tropical plants and ivy.
  - Used by people in lotions, ointments, and polishes.

**Wax: the material of the honeycomb**

- Beeswax is a mixture of a large number of lipids, including esters of triacontanol, and a long-chain palmitic acid.

![Beeswax structure](image)
10.2 Structural Lipids in Membranes

- In glycerophospholipids and some sphingolipids, a polar head group is joined to the hydrophobic moiety by a phosphodiester linkage; these are the phospholipids.

- Other sphingolipids lack phosphate but have a simple sugar or complex oligosaccharide at their polar ends; these are the glycolipids (Fig. 10–7).

**FIGURE 10–7** Some common types of storage and membrane lipids.
Glycerophospholipids Are Derivatives of Phosphatidic Acid

Glycerophospholipids, also called phosphoglycerides, are membrane lipids in which two fatty acids are attached in ester linkage to the first and second carbons of glycerol.

\[
\begin{align*}
\text{L-Glycerol 3-phosphate} & \quad \text{(sn-glycerol 3-phosphate)} \\
\end{align*}
\]

**FIGURE 10–8** the backbone of phospholipids.  p.350

backbone of phospholipids

**FIGURE 10–9** Glycerophospholipids.  p.351
The properties of head groups determine the surface properties of membranes

Different organisms have different membrane lipid head group compositions

Different tissues have different membrane lipid head group compositions

Examples of Glycerophospholipids:
Phosphatidylcholine (磷脂酰膽鹼，卵磷脂)

Phosphatidylcholine is the major component of most eukaryotic cell membranes

Many prokaryotes, including *E. coli* cannot synthesize this lipid; their membranes do not contain phosphatidylcholine
Some Glycerophospholipids Have Ether-Linked Fatty Acids

- Some animal tissues and some unicellular organisms are rich in \textit{ether lipids}, in which one of the two acyl chains is attached to glycerol in ether, rather than ester, linkage.
Ether lipids:
Plasmalogen

- Vinyl ether analog of phosphatidylethanolamine
- Common in vertebrate heart tissue
- Also found in some protozoa and anaerobic bacteria
- Function is not well understood
  - Resistant to cleavage by common lipases but cleaved by few specific lipases
  - Increase membrane rigidity?
  - Sources of signaling lipids?
  - May be antioxidants?

Ether lipids:
Platelet-activating factor

- Aliphatic ether analog of phosphatidylcholine
- Acetic acid has esterified position C2
- First signaling lipid to be identified
- Stimulates aggregation of blood platelets
- Plays role in mediation of inflammation
Chloroplasts Contain Galactolipids and Sulfolipids

- The second group of membrane lipids are those that predominate in plant cells: the galactolipids, in which one or two galactose residues are connected by a glycosidic linkage to C-3 of a 1,2-diacylglycerol.

Fig. 10–11 Three glycolipids of chloroplast thylakoid membranes
Archaea contain unique membrane lipids

- Most of the archaea live in ecological extreme conditions (e.g. high temperatures, low pH, high ionic strength).
- They have membrane lipids containing long-chain branched hydrocarbons linked at each end to glycerol through [ether bonds](#).
- Ether bonds are more stable to hydrolysis at low pH and high temperatures.
- These archaea lipids are twice the length of phospholipids and sphingolipids, and can span the full width of the surface membrane.

**FIGURE 10–12**

A typical membrane lipid of archaea. 

Linked at each end to glycerol through [ether bonds](#)  
**General name:** glycerol dialkyl glycerol tetraethers

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Sphingolipids Are Derivatives of Sphingosine

- Sphingolipids (神經鞘脂質), the fourth large class of membrane lipids, also have a polar head group and two nonpolar tails.
- The backbone of sphingolipids is NOT glycerol. The backbone of sphingolipids is a long-chain amino alcohol, sphingosine.
- A fatty acid is joined to sphingosine via an amide linkage rather than an ester linkage as usually seen in lipids.
- A polar head group is connected to sphingosine by a glycosidic or phosphodiester linkage.
- The sugar-containing glycosphingolipids are found largely in the outer face of plasma membranes.
There are three subclasses of sphingolipids.

1. **Sphingomyelins** (神經鞘磷脂質) contain phosphocholine or phosphoethanolamine as their polar head group and are therefore classified along with glycerophospholipids as phospholipids (Fig. 10–7). Sphingomyelin is abundant in myelin sheath(髓鞘) that surrounds some nerve cells in animals.

2. **Glycosphingolipids**, which occur largely in the outer face of plasma membranes, have head groups with one or more sugars connected directly to the —OH at C-1 of the ceramide moiety.

3. **Gangliosides**, the most complex sphingolipids, have oligosaccharides as their polar head groups and one or more residues of N-acetylneuraminic acid (Neu5Ac), a sialic acid, at the termini.
FIGURE 10–7 Some common types of storage and membrane lipids.
Glycosphingolipids and Blood Groups

- The blood groups are determined in part by the type of sugars located on the head groups in glycosphingolipids.
- The structure of sugar is determined by an expression of specific glycosyltransferases:
  - Individuals with no active glycosyltransferase will have the O antigen.
  - Individuals with a glycosyltransferase that transfers an N-acetylgalactosamine group have A blood group.
  - Individuals with a glycosyltransferase that transfers a galactose group to phosphate will have B blood group.
Phospholipids and sphingolipids are degraded in lysosome

- For each hydrolyzable bond in glycerophospholipids, there is a specific hydrolytic enzyme in lysosome.
- **Phospholipases** of the A type remove one of the two fatty acids (These esterases do not attach the ether bond of plasmalogens), producing a lysophospholipid. Lysophospholipases remove the remaining fatty acid.
- Gangliosides are degraded by a set of lysosomal enzymes the remove sugar units. A genetic defect leads to accumulation of gangliosides in the cell with severe medical consequences. (see box 10-2)

**FIGURE 10–16 The specificities of phospholipases.**
Sterols (固醇) Have Four Fused Carbon Rings

- **Sterols** are structural lipids present in the membranes of most eukaryotic cells. The characteristic structure of this fifth group of membrane lipids is the steroid (類固醇) nucleus, consisting of four fused rings, three with six carbons and one with five (Fig. 10–17).

- **Cholesterol (膽固醇)**, the major sterol in animal tissues, is amphipathic, with a polar head group (the hydroxyl group at C-3) and a nonpolar hydrocarbon body, about as long as a 16-carbon fatty acid in its extended form.
Bile acids (膽酸) are polar derivatives of cholesterol that act as detergents in the intestine, emulsifying dietary fats to make them more readily accessible to digestive lipases.
Physiological Role of Sterols

- Cholesterol and related sterols are present in the membranes of most eukaryotic cells.
  - Modulate fluidity and permeability
  - Thicken the plasma membrane
  - Most bacteria lack sterols
- Mammals obtain cholesterol from food and synthesize it de novo in the liver
- Cholesterol, bound to proteins, is transported to tissues via blood vessels
  - Cholesterol in low-density lipoproteins tends to deposit and clog arteries
- Many hormones are derivatives of sterols

Steroid Hormones

- Steroids are oxidized derivatives of sterols
- Steroids have the sterol nucleus, but lack the alkyl chain found in cholesterol. This makes them more polar than cholesterol.
- Steroid hormones are synthesized in gonads and adrenal glands from cholesterol
- They are carried through the body in the blood stream, usually attached to carrier proteins
- Many of the steroid hormones are male and female sex hormones
Eicosanoids Carry Messages to Nearby Cells
Eicosanoids are paracrine hormones, are present in small amounts but play vital roles as signaling molecules between nearby cells.

- All eicosanoids are derived from arachidonic acid (花生酸) (20:4(Δ5,8,11,14)) (Fig. 10–18), the 20-carbon polyunsaturated fatty acid from which they take their general name. There are three classes of eicosanoids:

  1. Prostaglandins (PG) contain a five-carbon ring originating from the chain of arachidonic acid.
(2) **Thromboxanes** have a six-membered ring containing an ether. They are produced by platelets (also called thrombocytes) and act in the formation of blood clots and the reduction of blood flow to the site of a clot.

(3) **Leukotrienes** contain three conjugated double bonds.

**Functions:**
- Inflammation and fever (prostaglandins)
- Formation of blood clots (thromboxanes)
- Smooth muscle contraction in lungs (leukotrienes)
- Smooth muscle contraction in uterus (prostaglandins)
Vitamins A and D Are Hormone Precursors

- **Vitamin D₃**, also called **cholecalciferol**, is normally formed in the skin from 7-dehydrocholesterol in a photochemical reaction driven by the UV component of sunlight (Fig. 10–20a).

- **Vitamin A (retinol)**, in its various forms, functions as a hormone and as the visual pigment of the vertebrate eye (Fig. 10–21).

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**FIGURE 10–20** Vitamin D₃ production and metabolism.
Vitamins E and K and the Lipid Quinones Are Oxidation-Reduction Cofactors

- **Vitamin E** is the collective name for a group of closely related lipids called *tocopherols*, all of which contain a substituted aromatic ring and a long isoprenoid side chain (Fig. 10–22a).

- The aromatic ring of **vitamin K** (Fig. 10–22b) undergoes a cycle of oxidation and reduction during the formation of active prothrombin, a blood plasma protein essential in blood clotting.
FIGURE 10-22 Some other biologically active isoprenoid compounds or derivatives.

(a) Vitamin E, an antioxidant

(b) Vitamin K, a blood-clotting cofactor (phyloquinone)

(c) Warfarin, a blood anticoagulant

(d) Ubiquinone, a mitochondrial electron carrier (coenzyme Q) \( (n = 4 \text{ to } 8) \)

(e) Plastoquinone, a chloroplast electron carrier \( (n = 4 \text{ to } 8) \)

(f) Dolichol, a sugar carrier \( (n = 9 \text{ to } 22) \)
10.4 Working with Lipids

Some methods commonly used in lipid analysis are shown in Figure 10–24.

(1) Lipid Extraction Requires Organic Solvents

(2) Adsorption Chromatography Separates Lipids of Different Polarity

(3) Gas-Liquid Chromatography Resolves Mixtures of Volatile Lipid Derivatives

(4) Specific Hydrolysis Aids in Determination of Lipid Structure
FIGURE 10–24 Part 1

Tissue homogenized in chloroform/methanol/water

(a) Water

Methanol/water

Chloroform

(b) Adsorption chromatography

Neutral Polar Charged lipids lipids lipids lipids

(c) Thin-layer chromatography

FIGURE 10–24 Part 2

Neutral Polar Charged lipids lipids lipids

(d) NaOH/methanol

Fatty acyl methyl esters

(e) Gas-liquid chromatography

(f) High-performance liquid chromatography

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FIGURE 10–24 Part 3

(5) Mass Spectrometry Reveals Complete Lipid Structure

(6) Lipidomics Seeks to Catalog All Lipids and Their Functions

- The structural lipids of membranes include both glycerophospholipids and sphingolipids, separate categories in Table 10–3. Each method of categorization has its advantages.
<table>
<thead>
<tr>
<th>Category</th>
<th>Category code</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatty acids</td>
<td>FA</td>
<td>Oleate, stearoyl-CoA, palmitoylcarnitine</td>
</tr>
<tr>
<td>Glycerolipids</td>
<td>GL</td>
<td>Di- and triacylglycerols</td>
</tr>
<tr>
<td>Glycerophospholipids</td>
<td>GP</td>
<td>Phosphatidylcholine, phosphatidylserine, phosphatidylethanolamine</td>
</tr>
<tr>
<td>Sphingolipids</td>
<td>SP</td>
<td>Sphingomyelin, ganglioside GM2</td>
</tr>
<tr>
<td>Sterol lipids</td>
<td>ST</td>
<td>Cholesterol, progesterone, bile acids</td>
</tr>
<tr>
<td>Prenol lipids</td>
<td>PR</td>
<td>Farnesol, geraniol, retinol, ubiquinone</td>
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<td>Saccharolipids</td>
<td>SL</td>
<td>Lipopolysaccharide</td>
</tr>
<tr>
<td>Polyketides</td>
<td>PK</td>
<td>Tetracycline, aflatoxin B₁</td>
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