Lipids of Physiological Significance

Dr. Sumbul Fatma
Objectives

• By the end of this lecture the first year students will be able to:
  • Define and classify lipids
  • Understand the physiological importance of lipids
  • List the examples of simple and complex lipids
  • Correlate implications of lipids in clinical conditions
Overview

• What are lipids?
• Classification of lipids
• Functions of lipids
• Simple lipids: Fatty acids, triacylglycerols, steroids
• Complex lipids: Phospholipids, sphingolipids, glycolipids
• Plasma lipid transport: types and functions of lipoproteins
What are lipids?

• A heterogeneous group of hydrophobic (water-insoluble) organic molecules that are soluble only in organic solvents

• Body lipids are compartmentalized (packed) in cell membranes, tissue and plasma
Functions of Lipids

• Lipids are essential components of biological membranes
• Lipids with hydrocarbon chains serve as major energy stores
• Cell signaling involves lipid molecules
  • e.g. Inositol tri-phosphate
• Fat-soluble vitamins, steroid hormones and prostaglandins are formed of lipids
Lipids and disease

Diseases that are strongly associated with abnormality in lipid metabolism:

- Atherosclerosis
- Coronary artery disease
- Obesity
- Metabolic syndrome
- Hypertension
Classification of Lipids

- **Simple lipids:**
  - Fatty acids
  - Triacylglycerols
  - Steroids (cholesterol)

- **Complex lipids**
  - Phospholipids
  - Sphingolipids
  - Glycolipids
**Fatty Acids (FAs)**

- FAs are carboxylic acids with long-chain hydrocarbon side groups

- They are **amphipathic** in nature (both hydrophilic and hydrophobic)
  - The carboxylic group (COOH) is **hydrophilic**
  - The hydrocarbon chain is **hydrophobic**
Fatty Acids (FAs)

- FAs are highly insoluble in water
- Must be transported in plasma with proteins
- Majority of plasma FAs are esters of:
  - Triacylglycerol
  - Cholesterol
  - Phospholipids

**Chain length**

- In mammals it varies from $C_{16} - C_{18}$
- Examples: palmitic, oleic, linoleic, stearic acids
Fatty Acids (FA)

Degree of saturation

- FAs may contain:
  - No double bonds (Saturated / trans form)
  - One or more double bonds (Mono or Polyunsaturated / cis form)
<table>
<thead>
<tr>
<th>Saturated FAs</th>
<th>Unsaturated FAs</th>
</tr>
</thead>
<tbody>
<tr>
<td>12:0 Lauric acid</td>
<td>18:1 Oleic acid</td>
</tr>
<tr>
<td>16:0 Palmitic acid</td>
<td>18:2 Linoleic acid</td>
</tr>
<tr>
<td>18:0 Stearic acid</td>
<td>20:4 Arachidonic acid</td>
</tr>
</tbody>
</table>

- **16:0**
  - No. of carbon atoms: 16
  - Zero double bonds

- **20:4**
  - No. of carbon atoms: 20
  - Four double bonds
Essential Fatty Acids (FA)

- Linoleic acid (precursor of arachidonic acid)
  - α-Linolenic acid
- Body cannot synthesize
- Must be supplied in the diet
- Deficiency can cause dermatitis, membrane function loss
- Arachidonic acid is essential when linoleic acid is deficient in the diet
ω-3 and ω-6 fatty acids

ω = Omega

- Long-chain polyunsaturated FAs with first double bond starting with 3rd carbon from the methyl end
- They reduce serum triglycerides, blood pressure and risk for heart disease
- Major source: Fish
- Examples: α-linolenic acid, EPA (eicosapentaenoic acid), DHA (Docosahexaenoic acid)
ω-3 and ω-6 fatty acids
ω-3 and ω-6 fatty acids

- Long-chain polyunsaturated FAs with first double bond starting with 6th carbon from the methyl end
- They reduce serum cholesterol
- Major source: Vegetable oils, nuts
- Examples:
  - Linoleic acid 18:2
Triacylglycerols (TGs)

- TGs are tri-esters of fatty acids also called fats
- Three fatty acids are bonded to a glycerol molecule
- Constitutes majority of dietary lipids
- Stored in adipocytes (fat cells) as energy reservoir
- Not a component of cell membranes
- Subcutaneous layer of fats provides thermal insulation
Structure of a triacylglycerol
Steroids

- Derivatives of cyclopentanoperhydrophenanthrene ring
- Consists of four fused rings called steroid nucleus with an 8-carbon chain
- Steroids with a hydroxyl group are called sterols
- Cholesterol is a major sterol in humans and animals
- Cholesterol in plasma is bound to fatty acids called cholesteryl esters
Functions of cholesterol

- Component of cell membranes
- Precursor for:
  - Bile acids / Bile salts
  - Vitamin D
  - Steroid hormones (Aldosterone, cortisol, testosterone, estrogen, progesterone)
- High levels of plasma cholesterol is strongly associated with coronary artery disease and atherosclerosis
Phospholipids

- Two classes of phospholipids:
  - Glycerophospholipids (contain glycerol backbone)
  - Sphingophospholipids (contain sphingosine)

Glycerophospholipids

- Glycerol-3-PO$_4$ is bonded to two fatty acid chains
- The PO$_4$ group is linked to a hydrophilic group
- Amphiphilic in nature
  - Hydrophobic tail
  - Hydrophilic phosphoryl heads
Glycero-phospholipids
Phospholipids

- Major components of biological membranes
- Examples: phosphatidic acid, phosphatidyl – choline and serine

Sphinogosphospholipids

- Long-chain fatty acids attached to sphingosine
- Example: Sphingomyelin
- An important component of myelin that protects and insulates nerve fibers
Figure 17.4
Structure of sphingomyelin, showing sphingosine (in green box) and ceramide components (in dashed box).
Glycolipids

• Contain both carbohydrate and lipid components
• Derivatives of ceramide
• A long chain fatty acid is attached to sphingosine
• Also called glycosphingolipids
• Examples: Ganglioside, glactocerebroside
• Act as: Blood group antigens, cell surface receptors for bacteria/viruses
Transport of plasma lipids

- Plasma lipids are transported as lipoprotein particles (lipids + protein)
- Protein part: Apoproteins or apolipoproteins
  - Examples: Apolipoproteins A, B, C
  - Functions: lipid transport, enzymatic functions, ligands for receptors
- Lipid part: Contains lipids of various types
## Types and functions of lipoproteins

<table>
<thead>
<tr>
<th>Lipoprotein</th>
<th>Transports</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chylomicrons</td>
<td>Dietary TGs</td>
</tr>
<tr>
<td>Very low density lipoprotein (VLDL)</td>
<td>Endogenous TGs</td>
</tr>
<tr>
<td>Low density lipoprotein (LDL)</td>
<td>Free cholesterol</td>
</tr>
<tr>
<td>High density lipoprotein (HDL)</td>
<td>Cholesteryl esters</td>
</tr>
</tbody>
</table>
Take home message

- Lipids are a group of hydrophobic molecules
- Perform essential physiological functions in the body
- Simple lipids include: fatty acids, TGs and steroids
- Complex lipids include: phospholipids, sphingolipids and glycolipids
- A number of diseases are associated with abnormal lipid metabolism
References

• Lippincott’s Illustrated Reviews, Biochemistry, 6th edition, Denise R. Ferrier, Lippincott Williams & Wilkins, USA.
  • Chapter 16: pages 181-182, 195-198
  • Chapter 17, page 201-202, 205-206
  • Chapter 18, page: 219-220, 226-232