Lipids

- Molecules of Mr = 150 - ≈ 2000 composed of saturated, unsaturated and/or aromatic or aliphatic hydrocarbon moieties - Non-polar lipids
- When water-binding functional groups (-OH, -COOH, -NH, -C=O, etc.) are covalently linked - Polar Lipids
- Biologically-relevant lipids are molecules with aliphatic chains of at least 12C atoms and/or aromatic/aliphatic structures with at least 3 rings which may be fused
- Old system of classification based on solubility in organic solvents is neither strictly true nor useful (e.g., bile salts)
OCTADECANOL

Graphic representations of a Polar Lipid
Lipid soluble portion of molecule

Water soluble portion of molecule

Figure by MIT OCW.
Classification of Polar Lipids Based on Interactions with $\text{H}_2\text{O}$*

*D. M. Small (1968)
<table>
<thead>
<tr>
<th>Class</th>
<th>Surface and Bulk Interactions with Water</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-Polar Lipids</strong></td>
<td>Will Not Spread To Form A Monolayer</td>
</tr>
<tr>
<td></td>
<td>Insoluble In Bulk</td>
</tr>
<tr>
<td><strong>Polar Lipids</strong></td>
<td></td>
</tr>
<tr>
<td><strong>A</strong>. Insoluble Non-Swelling Amphiphiles</td>
<td>Forms A Stable Monolayer</td>
</tr>
<tr>
<td></td>
<td>Insoluble In Bulk</td>
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<tr>
<td><strong>B</strong>. Insoluble Swelling Amphiphiles</td>
<td>Forms A Stable Monolayer</td>
</tr>
<tr>
<td></td>
<td>Bulk Phase-pure liquid crystals in pure water</td>
</tr>
<tr>
<td><strong>C</strong>. Soluble Amphiphiles</td>
<td></td>
</tr>
<tr>
<td>1. with lyotropic mesomorphism</td>
<td>Forms An Unstable Monolayer</td>
</tr>
<tr>
<td></td>
<td>Bulk Phase-a micellar solution</td>
</tr>
<tr>
<td>2. without lyotropic mesomorphism</td>
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<tr>
<td></td>
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</tr>
</tbody>
</table>

Self-Aggregated States

i) LIQUID CRYSTALS (L.C.)

- Intermediate Physical States (mesophases) with properties of both liquids and solid crystals.
- Long rage order in at least 1 dimension
  - Lyotropic L.C.
  - Thermotropic L.C.
- Have distinct optical textures by polarizing microscopy
Self Aggregated States

ii) MICELLES

Thermodynamically stable aggregates of soluble amphiphilic lipids that form spontaneously above a critical micellar concentration (CMC) and critical micellar temperature (CMT)

- in aqueous systems: regular micelles
  “The hydrophobic effect”
- in organic solvents: reverse micelles
Solution of monomers

Micellar solution

Krafft point

Crystalline suspension

Temperature

Concentration of Detergent

Figure by MIT OCW.
iii) EMULSIONS

Dispersions of one liquid in a continuous phase of another liquid: O/W, W/O systems
The dispersed (discontinuous) phase consists of microscopic droplets, usually 0.1-100 µm in diameters
Self-Aggregated States

iv) SOLID CRYSTALS

Classically lipids such as Cholesterol (Gallstones, Atheroma), fatty acids + bile acids (Enteroliths), glycolipids (neural storage diseases) – all are pathologic
Anhydrous Cholesterol and Cholesterol Monohydrate

Figures removed due to copyright reasons. Please see:


Principal Mixed Lipid Systems in Living Organisms

- Stable Emulsions (dietary fat, plasma lipoproteins, intracellular fat droplets, gut luminal lipids pre-digestion, etc.)
- Mixed Micelles (bile, gut lumen, certain brain lipid storage diseases)
- Mixed Liquid Crystals (biologic membranes, serum lipoprotein X in cholestasis, myelin sheet, mixed vesicles in gut lumen, etc.)
Figure removed due to copyright reasons.
ADDITION OF BILE SALT TO LECITHIN - CHOLESTEROL LIQUID CRYSTAL

Figure removed due to copyright reasons.
The 3 “P” Rules

• Predictability Rule

• Predominance Rule

• Phase Rule \((F=C-P+2)\)
How Lipids Traverse Biological Membranes

• As single molecules (molecule need not be water soluble)
• As aggregated particles (i.e., stable emulsions)
• Transporter control: Genomic (slow), nongenomic (fast)
CELLULAR CHOLESTEROL HOMEOSTASIS

- Increased Cholesterol Influx
  - LDL Receptor
  - HMG CoA Reductase
  - ACAT

- Lysosomal cholesterol ester hydrolase
- Neutral cholesterol ester hydrolase
- ACAT
- HMG CoA Reductase
- LDL receptor
- LDL
- HDL
- Free cholesterol
- Acetate
- Cholesterol ester
- Cell membrane
- Lipoprotein
- Bile Salt
- Bile

Figure by MIT OCW.
1. All VLDL made in liver.

2. ~ 80% of LDL removed by liver.
CHEMICAL COMPOSITIONS OF HUMAN PLASMA LIPOPROTEINS

Figure by MIT OCW.
### GI Movements of Single Molecules: Examples

<table>
<thead>
<tr>
<th></th>
<th><strong>Bile Salts</strong> (soluble)</th>
<th><strong>Cholesterol/Phytosterols</strong> (insoluble)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Enterocytes:</strong></td>
<td>Distal Ileocytes</td>
<td>Proximal &gt; Distal</td>
</tr>
<tr>
<td></td>
<td>Influx: ASBT, FABP6, OATα/β</td>
<td>Influx: NPC1L1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Efflux: ABCG5/ABCG8</td>
</tr>
<tr>
<td><strong>Transport:</strong></td>
<td>Portal Blood</td>
<td>Lymphatics</td>
</tr>
<tr>
<td><strong>Binding:</strong></td>
<td>Albumen, HDL</td>
<td>ChE and free Ch in chylomicrons and nascent HDL</td>
</tr>
<tr>
<td><strong>Hepatic Uptake:</strong></td>
<td>NTCP – 80%</td>
<td>ApoB/E receptor</td>
</tr>
<tr>
<td></td>
<td>OATPs – 20%</td>
<td>LRP receptor</td>
</tr>
<tr>
<td><strong>Nuclear Control:</strong></td>
<td>FXR/RXR</td>
<td>SREBP’s</td>
</tr>
<tr>
<td></td>
<td>SHP, LRH1</td>
<td>LXR/RXR</td>
</tr>
<tr>
<td><strong>Biliary Secretion:</strong></td>
<td>BSEP, MRP2</td>
<td>ABCG5/ABCG8, (others unknown)</td>
</tr>
<tr>
<td><strong>Facilitators:</strong></td>
<td>Needs intact FIC1 function</td>
<td>Same + hydrophobic “sink” in bile</td>
</tr>
</tbody>
</table>
That’s All Folks!