LIPID CHEMISTRY

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Definitions of Lipids, Fatty acids, Saponifiable and Non-Saponifiable lipids, Saponification number and Iodine number

What are Lipids?

• **Lipids** are bio-molecules that are:
  • Hydrophobic in nature because of the high amount of Hydrocarbons in their structure,
  • Relatively insoluble in water but readily soluble in non-polar solvents such as Chloroform, Benzene and Ether,
  • Easily separated from other biological materials by extraction into organic solvents because of their hydrophobic properties,
  • Examples of lipids:
    • Fats, Oils, Steroids, Waxes, Fat-soluble Vitamins (Vitamins A, D, E and K),
What are fatty acids?

- Aliphatic Carboxylic Acids containing Long Hydrocarbon chains that may be Saturated or Unsaturated,
- Fatty acid has both Hydrophobic and Hydrophilic properties, thus are Amphipathic in nature,
- Fatty acid can be separated into two distinct parts:
  - Non-polar Hydrophobic Hydrocarbon Chain (Tail)
  - Polar (-COOH) group (Hydrophilic Head)
- Most naturally occurring fatty acids, obtained from hydrolysis of natural fats and oils contain **Even number of carbon atoms** because they are synthesized from Two-carbon units,
- Examples of fatty acids: Palmitic Acid, Oleic Acid, Arachidonic Acid, Linoleic Acid, Linolenic Acid, etc.
What are Saponifiable Lipids?

• Lipids that can be hydrolyzed either by Heat, Alkaline or Acid solutions,

• The hydrolyzed products usually include:
  • Fatty Acids (salts of fatty acids),
  • Glycerol, and in some cases other molecular components contained in the lipid,

• Examples:
  • Neutral fats,
  • Phospholipids,
What are Non-Saponifiable Lipids?

• Non-Saponifiable lipids are those lipids that cannot be hydrolyzed,

• Examples:
  • Terpenes,
  • Steroids
  • Fat-soluble Vitamins
What is the Saponification Number of a Lipid?

• Saponification Number is the number of milligrams of KOH that is needed to Saponify one gram of Fat;
• Since each molecule of fat regardless of its size requires 3 molecules of KOH to Saponify it, the Saponification number also indicates the number of molecules of fat in one gram of fat;
Simple diagram to illustrate the structure of Fat
What is the Iodine Number of Fat?

• Iodine Number of fat is the number of grams of iodine that is absorbed by 100 grams of Fat,
• It is a measure of the degree of un-saturation of the fatty acids in the structure of the Fat,
**NOMENCLATURE OF SATURATED FATTY ACIDS**

Systematic nomenclature of saturated fatty acids

- **IUPAC system** (Systematic name or Genevan system) and **Common names**
- **IUPAC or Systematic name** of a fatty acid is formed by replacing the ending \(-e\) with suffix \(-oic\ acid\) in the name of the Alkane with the same number of carbon atoms,
- Carboxyl Carbon is Carbon number one,
- **Examples:**
  - 16C fatty acid is: Hexadecan\(oic\ acid\) (from Hexadecane)
  - 18C fatty acid is: Octadecan\(oic\ acid\) (from Octadecane)
Common Names of Saturated fatty acids

• **Common names** of fatty acids are generally derived from either the Latin or Greek name of their source of origin,

• Greek letters or symbols ($\alpha, \beta, \gamma, \delta, \varepsilon$, etc.) can be used to number Carbon atoms in fatty acid molecules,

• Examples of Common names:
  • Palmitic acid from Latin - Palma (palm tree);
  • Arachidic acid from Greek - Arachne (spider), etc.
IMPORTANT TO NOTE

• Nomenclature of fatty acids should not mix Greek letters or symbols with Systematic names of fatty acids, nor should numerals be mixed with Common names of fatty acids;

• Carboxyl Carbon in a fatty acid molecule is always considered as the First Carbon (C-1) in Systematic name, it has no corresponding Greek letter or symbol in Common name,

• In Systematic name:
  • Second Carbon atom (C-2) in Fatty Acid molecule corresponds to the $\alpha$-Carbon in Common name,
  • Third Carbon atom (C-3) in Fatty Acid molecule corresponds to $\beta$-Carbon atom in Common name and so on,

• Last or Terminal Carbon atom in a fatty acid molecule is considered as the $\omega$-Carbon or the n-carbon atom,
# Common names, Systematic names and Short Hand Formula of some Saturated Fatty Acids

<table>
<thead>
<tr>
<th>Common Name</th>
<th>Systematic Name</th>
<th>Short-hand Structural formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valeric acid</td>
<td>Pentanoic acid</td>
<td>CH$_3$(CH$_2$)$_3$COOH</td>
</tr>
<tr>
<td>Caproic acid</td>
<td>Hexanoic acid</td>
<td>CH$_3$(CH$_2$)$_4$COOH</td>
</tr>
<tr>
<td>Caprylic acid</td>
<td>Octanoic acid</td>
<td>CH$_3$(CH$_2$)$_6$COOH</td>
</tr>
<tr>
<td>Capric acid</td>
<td>Decanoic acid</td>
<td>CH$_3$(CH$_2$)$_8$COOH</td>
</tr>
<tr>
<td>Lauric acid</td>
<td>Dodecanoic acid</td>
<td>CH$_3$(CH$_2$)$_10$COOH</td>
</tr>
<tr>
<td>Myristic acid</td>
<td>Tetradecanoic acid</td>
<td>CH$_3$(CH$_2$)$_12$COOH</td>
</tr>
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<td>Palmitic acid</td>
<td>Hexadecanoic acid</td>
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<tr>
<td>Stearic acid</td>
<td>Octadecanoic acid</td>
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</tr>
<tr>
<td>Arachidic acid</td>
<td>Eicosanoic acid</td>
<td>CH$_3$(CH$_2$)$_18$COOH</td>
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<tr>
<td>Behenic acid</td>
<td>Docosanoic acid</td>
<td>CH$_3$(CH$_2$)$_20$COOH</td>
</tr>
<tr>
<td>Lignoceric acid</td>
<td>Tetracosanoic acid</td>
<td>CH$_3$(CH$_2$)$_22$COOH</td>
</tr>
</tbody>
</table>
NOMENCLATURE OF UNSATURATED FATTY ACIDS

OMEGA-numbering and n-numbering systems:
• In all naturally occurring Unsaturated fatty acids the double bond is always in the cis-configuration,
• Nomenclature of Unsaturated fatty acids uses:
  • Systematic names
  • Common names
• Common names of Unsaturated fatty acids are derived from the Latin or Greek names of their source of origin;
• Replace ending -e with suffix -enoic acid in the name of the Alkyne with the same number of carbon atoms
SYSTEMATIC NOMENCLATURE OF UNSATURATED FATTY ACIDS

• Carboxyl Carbon is the First Carbon Atom (C-1)

• Systematic Nomenclature indicates:
  • Number of Carbon atoms in the Fatty acid,
  • Number of Double bonds (unless it has only one double bond),
  • Position of the Double bonds,
  • Contain the suffix enoic,

• The \textbf{delta (Δ) numbering system} is used to indicate the position of the double bond in fatty acids,
Examples for unsaturated fatty acids:

- Oleic acid, 18C with one double bond between C9 and C10;
  - Systematic name is: cis-$\Delta$9-Octadecenoic acid;
- Linoleic acid, an 18C with two double bonds, between C9 and C10, and also between C12 and C13;
  - Systematic name is: cis-$\Delta$9,12-Octadecadienoic acid,
- Systematic nomenclature can be used without delta sign,
  - Oleic acid is: cis-9-octadecenoic acid,
  - Linoleic acid is: cis-9, 12-octadecadienoic acid,
- **Shortened form of nomenclature can be used:**
  - Oleic acid it is: 18:1; 9;
    - It means 18C atoms, one double bond between C9 and C10,
  - Linoleic acid it is: 18:2;9,12;
Explain the Omega numbering system for unsaturated fatty acids

- **ω-numbering system** is used to indicate the position of a double bond by counting from the ω-Carbon;

Examples:

- **Oleic acid: ω 9, C18:1**
  - ω 9 means Oleic acid contains a double bond between C9 and C10 counting from the ω-carbon atom (i.e., from the last Carbon atom in the fatty acid molecule);
  - C18:1, means 18C atoms, one double bond;

- **Linoleic acid: ω 6, C18:2**
  - ω 6 means Linoleic acid contains a double bond between C6 and C7 counting from the ω-carbon atom,
  - C18:2, means 18C atoms, two double bonds, the first double bond is between C6 and C7 counting from the ω-carbon;
Omega Nomenclature

ω-9 C18:1

ω-6 C18:2

ω-3 C18:4
Schematic diagrams of Saturated and Unsaturated Fatty Acids

Saturated Fatty Acid

Unsaturated Fatty Acid
OMEGA NUMENCLATURE: IMPORTANT TO NOTE

• In Omega numbering system the position of the second double bond is not indicated;

• General principle is that in Polyunsaturated fatty acids, double bonds occur at every Third Carbon atom towards the Methyl end of the molecule:

  - CH = CH - CH2 - CH = CH - CH2 - CH = CH -

• In other words, double bonds in Polyunsaturated fatty acids are NOT in the Conjugated form such as:

  - CH = CH - CH = CH –

• Double bonds are separated by at least Two single bonds, not by just one single bond ,

• Thus, in Linoleic acid (\(\omega\) 6, C18:2) the second double bond will be between C9 and C10 from the \(\omega\)-carbon;
What are the groups of polyunsaturated fatty acids?

- Polyunsaturated fatty acids are grouped into Three series or families based on the Omega nomenclature. The groups are:

  - **ω 9 or n-9 series:**
    - Fatty acids in which the first double bond is between C9 and C10 counting from the ω-carbon;
    - Examples: Oleic acid and Gondoic acid

  - **ω 6 or n-6 series:**
    - Fatty acids in which the first double bond is between C6 and C7 counting from the ω-carbon;
    - Examples: Linoleic acid and Arachidonic acid

  - **ω 3 or n-3 series:**
    - Fatty acids in which the first double bond is between C3 and C4 counting from the ω-carbon;
    - Examples: α-Linolenic acid and Timnodonic acid
Can polyunsaturated fatty acids be produced in mammalian tissues?

• Mammals can biosynthesize the ω 9 series of polyunsaturated fatty acids because of the presence of Δ9-Desaturase enzyme in liver and other tissues;
• The enzyme can introducing double bonds only between C-9 and the Carboxyl group;
• The ω 6 series and ω 3 series of polyunsaturated fatty acids cannot be biosynthesized by most animals including humans, because of lack of the Desaturase enzyme system capable of introducing double bonds beyond C-9 (carbon atom number 9 counting from the Carboxyl carbon);
<table>
<thead>
<tr>
<th>Common names</th>
<th>Systematic names (all-cis-)</th>
<th>Shortened names</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palmitoleic acid</td>
<td>9-Hexadecenoic acid</td>
<td>16:1;9</td>
</tr>
<tr>
<td>Oleic acid</td>
<td>9-Octadecenoic acid</td>
<td>18:1;9</td>
</tr>
<tr>
<td>Vaccenic acid</td>
<td>11-Octadecenoic acid</td>
<td>18:1;11</td>
</tr>
<tr>
<td>Linoleic acid</td>
<td>9,12-Octadecadienoic acid</td>
<td>18:2;9,12</td>
</tr>
<tr>
<td>γ-Linolenic acid</td>
<td>6,9,12-Octadecatrienoic acid</td>
<td>18:3;6,9,12</td>
</tr>
<tr>
<td>α-Linolenic acid</td>
<td>9,12,15-Octadecatrienoic acid</td>
<td>18:3;9,12,15</td>
</tr>
<tr>
<td>Gondoic acid</td>
<td>11-Eicosenic acid</td>
<td>20:1;11</td>
</tr>
<tr>
<td>Arachidonic acid</td>
<td>5,8,11,14-Eicosatetraenoic acid</td>
<td>20:4;5,8,11,14</td>
</tr>
<tr>
<td>Timnodonic acid</td>
<td>5,8,11,14,17-Eicosapentaenoic acid (EPA)</td>
<td>20:5;5,8,11,14,17</td>
</tr>
<tr>
<td>Erucic acid</td>
<td>13-Docosenoic acid</td>
<td>22:1;13</td>
</tr>
<tr>
<td>Clupanodonic acid</td>
<td>7,10,13,16,19-Docosapentaenoic acid</td>
<td>22:5;7,10,13,16,19</td>
</tr>
<tr>
<td>Cervonic acid</td>
<td>4,7,10,13,16,19-Docosahexaenoic acid (DHA)</td>
<td>22:6;4,7,10,13,16,19</td>
</tr>
<tr>
<td>Nervonic acid</td>
<td>15-Tetracosenoic acid</td>
<td>24:1;15</td>
</tr>
</tbody>
</table>
What are the essential fatty acids?

• ESSENTIAL FATTY ACIDS are **Unsaturated** fatty acids that **cannot** be biosynthesized in tissues of some animals including humans, thus they must be obtained in the diet. Examples:
  
  • Linoleic acid (18:2;9,12) and
  • \(\alpha\)-Linolenic acid (18:3;9,12,15)

• Most of the essential fatty acids are members of the \(\omega\) 6 and \(\omega\) 3 series;

• Some animals including humans can biosynthesize **Arachidonic acid** from Linoleic acid obtained in the diet;

• Thus, **Linoleic acid** is called **True Essential Fatty Acid**;
State some of the physical properties of fatty acids

• Fatty acids are Amphipathic, because of the Hydrophobic tail and Hydrophilic (–COOH) head,
• The longer the Hydrocarbon chain the higher the melting point of the fatty acid,
• The greater the number of double bonds in the fatty acid the lower the melting point of the fatty acid,
• Unsaturated fatty acids have substantially lower melting points than saturated fatty acids,
• Example, melting point of:
  • Stearic acid (18:0) is 70o C
  • Oleic acid (18:1;9) is 13o C,
  • Linoleic acid (18:2;9,12) is -11o C.
CLASSIFICATION OF LIPIDS:  
What are the major classes of lipids?

Lipids can be separated into 3 major classes:

• **Simple lipids**: Esters that fatty acids form with various alcohols;

• Simple lipids are made up of:
  • Fats,
  • Oils,
  • Waxes

• Fats and oils are esters of Fatty Acids and Glycerol;

• Waxes are esters of fatty acids and higher molecular weight monohydric alcohols,
• **Complex lipids**: Esters made up of Fatty Acids, Alcohol and other chemical compounds,

• Complex lipids are made up of:
  
  • Phospholipids,
  • Glycolipids,
  • Glycosphingolipids,
  • Sulfolipids,
  • Aminolipids
  • Lipolipids,
• **Precursor and derived lipids:**
  
  • They include the following:
  
  • Fatty acids,
  • Glycerol,
  • Steroids,
  • Sterols,
  • Fatty Aldehyde,
  • Ketone bodies,
  • Hydrocarbons,
  • Lipid-soluble vitamins
  • Hormones
Simple Lipids:
What is the stereospecific (sn-) numbering system?

• Triacylglycerols (Triglycerides or Neutral Fats) are Tri-esters of Glycerol and 3 Fatty acids,

• General structure of a Triacylglycerol contains 3 Fatty Acyl groups linked by ester bonds to Glycerol (Propane-1, 2, 3-triol),

• If the fatty acyl groups that are esterified to C-1 and C-3 of the glycerol molecule are different, then the C-2 of the Glycerol molecule is asymmetric (Chiral center),
• Fatty Acyl group esterified to C-2 is written to the left of C-2 in a Fisher projection formula to designate the L-configuration of naturally occurring Triacylglycerols,
• Spatial arrangements of the -OH groups in C-1 and C-2 of Glycerol molecule are not identical,
• Therefore, the 3 carbon atoms in a Glycerol molecule are usually designated either by:
• **Stereospecific numbering** system (sn-, 1, 2, 3) or by
• An older numbering system that uses the symbols $\alpha$, $\beta$ and $\alpha'$
Sterospecific numbering of Glycerol

\[
\begin{align*}
H_2 & - C - OH \\
HO & \quad ^2 C - H \\
H_2 & - ^3 C - OH
\end{align*}
\]

Sn - GLYCEROL
Why is the stereospecific (sn-) numbering system of Glycerol important?

- sn- numbering of Glycerol is significant because some enzymes can readily distinguish sn-3 Carbon from sn-1 Carbon in Glycerol,

- Example: Glycerol kinase catalyzes the addition of a Phosphate group to -OH on sn-3 Carbon of Glycerol to produce Glycerol-3-Phosphate and not Glycerol-1-Phosphate,
Sn-Glycerol-3-Phosphate
Why are Simple Triacylglycerols different from Mixed Triacylglycerols?

• Triacylglycerol that contains identical fatty acyl groups that are esterified to the three-ester positions of Glycerol is called a **Simple Triacylglycerol**;

• Example,

• Triolein (Tri-oleoyl-glycerol) contains three molecules of Oleic acid residues esterified to a molecule of Glycerol,

• Tri-stearin (Tri-stearoyl-glycerol) contains three Stearic acid residues esterified to a molecule of glycerol,
Diagrams of Simple Tri-acyl-glycerols
• **Mixed Triacylglycerols** contain two or three different types of fatty acid residues esterified to a molecule of Glycerol,

• Such compounds are named according to the placement of the fatty acid residues on the glycerol molecule,

• Examples:
  • 1-palmitoleoyl-2-linoleoyl-3-stearoyl-glycerol;
  • 1,3-dipalmitoleoylstearylglycerol.
How are Fats different from Oils?

- Fats and Oils are called Neutral fats,
- They are complex mixtures of simple and mixed Triacylglycerols, whose composition of fatty acid residues varies with the organism that produced them
- Fats are solid or semi-solid at room temperature;
- Oils are liquid at room temperature,
- Triacylglycerols in oils contain mainly unsaturated fatty acids
- Triacylglycerols in fats contain mainly saturated fatty acid,
- Melting points of unsaturated fatty acids are lower than those for saturated fatty acids,
What are Phospholipids (give examples)?

- Phospholipids: Lipids containing Phosphate; eg:
  - Phospho-Glycerides,
  - Sphingosine (e.g., Sphingomyelin),
- Major lipids in cellular membranes of Glandular organs, Blood plasma, Egg yolk and Seeds of legumes,
- Phospho-glyceride (Glycero-phospho-lipids or Phospho-acyl-glycerol) are major components of the Biological Membranes,
Give the general structure of Phospholipids

• General structure of Phosphoglyceride (see diagram)

• Phosphoglyceride is made up of:
  • sn-3-Phosphorylated Glycerol (sn-Glycerol-3-Phosphate) esterified at C-1, C-2 with Fatty acids;
  • A Third ester bond is formed between the Phosphate group at sn-C-3 and a Polar Alcohol ("X");

• Phosphoglycerides are Amphipathic they contain:
  • Two non-polar aliphatic hydrophobic chains ("Tails") and
  • Polar hydrophilic (Phosphoryl-X group) ("Head").,
    • Saturated fatty acid r with either 16C or 18C are esterified to sn-C-1 of Glycerol; while sn-C-2 in Glycerol is esterified unsaturated fatty acid that contains between 16C to 20C;
Diagram of Phosphoglyceride

Phosphatidic acid
Diagram of Phospholipid
Diagram of Phosphoglyceride
Structures and names of some Phosphoglycerides and their corresponding polar alcohol groups;
Phosphatidic acid: simplest Phosphoglyceride with "X" = -H

<table>
<thead>
<tr>
<th>Phosphoglyceride (Glycerophospholipid)</th>
<th>Polar alcohol group (&quot;X&quot;)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphatidic acid</td>
<td>-H</td>
</tr>
<tr>
<td>Phosphatidylethanolamine (Cephaline)</td>
<td>Ethanolamine</td>
</tr>
<tr>
<td>Phosphatidylcholine (Lecithin)</td>
<td>Choline</td>
</tr>
<tr>
<td>Phosphatidylserine</td>
<td>Serine</td>
</tr>
<tr>
<td>Phosphatidylinositol</td>
<td>Myo-inositol</td>
</tr>
<tr>
<td>Phosphatidylglycerol</td>
<td>Glycerol</td>
</tr>
</tbody>
</table>
What are Lysophospholipids?

- **Lysophospholipids** are Glycerophospholipids that contain only one fatty Acyl residue in their molecule,

- Example: **Lecithin (Phosphatidylcholine)** contains 2 Fatty Acyl residues in its molecule, while Lysolecithin contains only One Fatty Acyl residue,
Diagram of Lyso-phospholipid

Lysophosphatidic acid
What is Plasmalogen?

- **Plasmalogens** are Glycerophospholipids (Phosphoglycerides)
- They are structurally different from other Glycerophospholipids,
- The sn-1-C of Glycerol is linked by Ether bond to a **cis-α, β -Unsaturated Alcohol** instead of a saturated fatty acid as in other Glycerophospholipids,
- Plasmalogen: Polar alcohol (Head) group "X" can either be Ethanolamine, Choline or Serine,
What is Sphingolipid

• All Sphingolipids are derived from Sphingosine,
• Different types of Sphingolipids are:
  • Sphingomyelin, (which are the only Sphingolipid that contain phosphate and have no sugar moiety),
  • Glycosphingolipids.
• Sphingosine (also called 4-Sphingenine) is an 18 carbon unsaturated amino alcohol (a diol),
Diagram of Sphingosine & Sphingomyelin
What is Ceramide?

• **Ceramide**: Compound formed when a fatty acid molecule is linked to -NH2 group in Sphingosine via amide bond,

• Ceramides are the N-fatty acyl derivatives of Sphingosine,

• Ceramides form the core structure of naturally occurring Sphingolipids,
Diagram of Ceramide

GENERAL STRUCTURE OF A CERAMIDE
EICOSANOIDs

• Eicosanoids are a group of compounds derived from metabolism of Eicosapopolyenoic fatty acids (Polyunsaturated fatty acids with 20 Carbons).

Examples:
  • Prostanoids,
  • Leukotrienes (LTs) and
  • Lipoxins (LXs)

• Prostanoids are a group of compounds that include:
  • Prostaglandins (PGs),
  • Prostacyclins (PGIs) and
  • Thromboxanes (TXs)
Diagram of Cholesterol