Lecture 3: Chiral Drugs, Polar Bonds, Functional Groups

Chiral Drugs:
- If a drug contains one chiral center, it will exist in two forms, one enantiomer will have biological activity, the other enantiomer could have no activity, or actually be toxic.
- An equal mixture of the two enantiomers is called a *racemic mixture*. If one enantiomer is toxic it is necessary to produce a *chiral drug*—consisting of just one enantiomer.
- Existing racemic drugs, which were patented, have been awarded new patents for the chiral drug.

Naproxen
(*Aleve*):

![Naproxen structure]

**Thalidomide.** This drug was prescribed as a sedative in the late 50s and early 60s. It was withdrawn because it causes birth defects by interfering with the development of the baby (compounds that affect development are called teratogens). This activity is associated with only one enantiomer. The other enantiomer is perfectly safe as a sedative and available in Europe.

Polar (and non-polar) bonds:

**Electronegativity:** The ability of an atom to attract electrons.

The degree of sharing of electrons by atoms depends on the difference in their electronegativity. The atom with the higher electronegativity will pull electrons from the atom with the lower electronegativity. One atom will develop a partial positive charge and the more electronegative atom will develop a partial negative charge. Bonds with large differences in partial charges are called polar bonds.

<table>
<thead>
<tr>
<th>Bond</th>
<th>Electronegativity difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>C—C</td>
<td>2.5 2.5 0.0</td>
</tr>
<tr>
<td>C—H</td>
<td>2.5 2.1 0.4</td>
</tr>
<tr>
<td>N—H</td>
<td>3.0 2.1 0.9</td>
</tr>
<tr>
<td>C—O</td>
<td>2.5 3.5 −1.0</td>
</tr>
<tr>
<td>O—H</td>
<td>3.5 2.1 1.4</td>
</tr>
</tbody>
</table>

**Aromatic Compounds:**
- Atoms connected in a ring formation, can contain nitrogen.
- Form single bonds + ¼ double bond with each other.
- Ring is planar cannot be chiral because none of the carbons are bound to four different atoms.

C₆H₆
*benzene*
Organic molecules and Functional Groups:
Functional groups are subsets of atoms within a larger molecule, e.g., methyl group, ethyl group. Functional groups have unique properties, e.g., methyl and ethyl are non-polar, alcohols polar, etc.

Note the “short hand” notation:
- Carbons are located at the end of lines and at kinks in the line.
- Hydrogens are not drawn, you need to add sufficient hydrogens to satisfy the number of bonds of the other atoms, e.g., 4 for carbon.

Non-Polar Functional Groups

Alkanes
- Methane (methyl)
- Ethane (ethyl)
- Propane (propyl)
- Butane (butyl)

Alkene

Aromatic
- Ethene
- Benzene (phenyl)

Polar Functional groups

Alcohols
- Methanol
- Ethanol

Thiols (sulfhydryl)

Carbonyl group
- Aldehyde
- Ketone
- Ester

Example: Identifying functional groups:
a) What functional groups are common to all four of these amino acids?
b) What functional groups are different between each amino acid?

Review:
1. What is a chiral center, can you identify it, what are the implications in biological reactivity?
2. What is a racemic mixture?
3. How does a polar bond differ from a non-polar bond? Can you identify polar bonds?
4. What makes a group aromatic and what are the geometrical properties of the aromatic group?
5. Do you know the structure of a methyl group, phenyl group and recognize that it is non-polar.
6. What is an alcohol, thiol, carboxylate, amine, and an amide?
7. Can you identify functional groups on biological molecules?