DRUG-RECEPTOR INTERACTIONS
FORCES INVOLVED

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Covalent Bonds

- Often found between two nonmetals.
- Typical of molecular species.
- Atoms bonded together to form molecules.
  - Strong attraction.
- **Atoms share pairs of electrons** to attain octets.
- Molecules generally weakly attracted to each other.
  - Observed physical properties of molecular substance due to these attractions.

Covalent bonds form when atoms share 2 or more valence electrons.

Covalent bond strength depends on the number of electron pairs shared by the atoms.

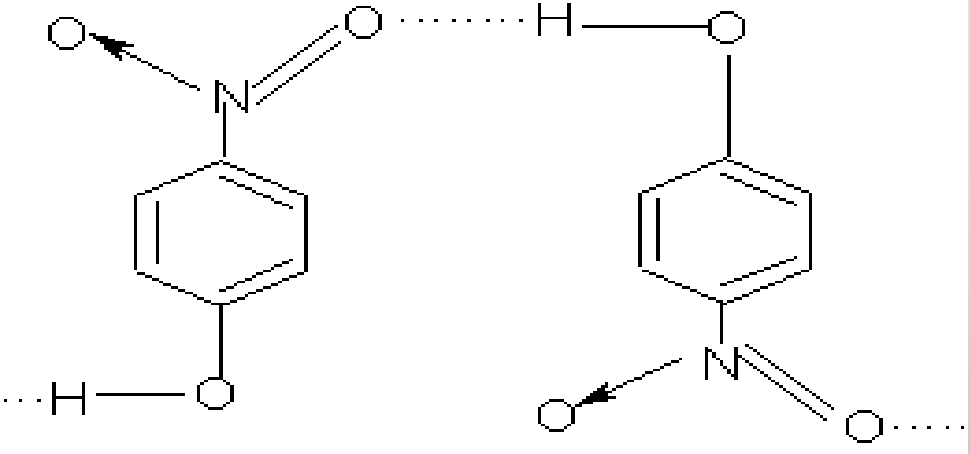
single bond < double bond < triple bond

Ionic Bonding

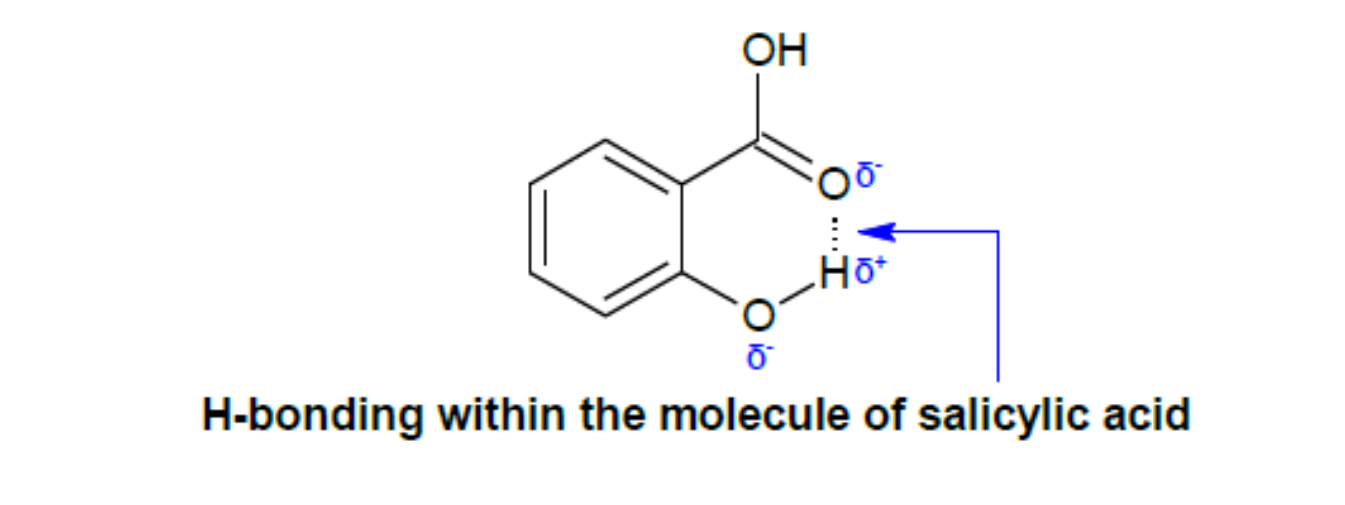
- Formed by the attraction of oppositely charged atoms or groups of atoms
- Important because many of the functional groups will be in the ionized form at the physiological pH
- Usually reversible
- Ubiquitous
- Effective at greater distances when compared to the other bonding types

There are two types of hydrogen bonds, namely
1- intermolecular hydrogen bond
2- intramolecular hydrogen bond

When the hydrogen bond is present between two atoms of two different molecules,then it is known **intermolecular** hydrogen bond.



When the hydrogen bond is present between two atoms of the same molecule, then it is known as **intramolecular** hydrogen bond.



H-bonding within the molecule of salicylic acid

- Intermolecular H-bonds are much weaker than intramolecular H-bonds.

Ionic or electrostatic interactions

- This type of bond is weaker than covalent bond (-5 Kcal/mol).
- At the same time, it is one of the most prevalent bonds in drug-receptor interaction.
- The drug molecule must have opposite charge compared to the ionized amino acids found in the receptor or enzyme.
  - Extent of ionization affects the occurrence of this bond.
  - The distance between opposite charges has a role as well.

IONIC OR ELECTROSTATIC INTERACTIONS

- Electronic dipole is formed when we have polarized bond.
- In the polarized bond one of the pole will be partially positive and the other partially negative.
- These partially positive or negative charges might form an electrostatic bond with either partially charged atoms or ionized elements.

Charge-Transfer bonds

- Occurs between an electron donor group in one molecule and an electron acceptor in another.
  - Electron donors such as alkenes, alkynes and aromatic ring bearing an electron donating group, and atoms having pairs of non-bonded electrons such as O, N and S
  - Electron acceptors such as aromatic ring bearing an electron withdrawing group,
  - These groups might exist in the receptor binding sites:
    - Electron donor a.a such as tyrosine and carboxylates
    - Electron acceptor a.a such as cysteine
    - Having both: such as Histidine, tryptophan and sparagine

affinity, efficacy, and potency

- **Affinity:** how strongly the drug binds to the receptor; depends on the molecular complementarily of drug and receptor.

- **Efficacy:** the maximum biological effect the drug can produce. A compound with high affinity does not necessarily have high efficacy (e.g. antagonists).

- **Potency:** the amount of drug needed to achieve a defined biological effect. The smaller the dose required, the more potent the drug. It is possible to have potent drugs with low efficacy. Potency depends in part on the affinity of the receptor for binding the drug, and in part on the efficiency with which the drug-receptor interactions is coupled to response.

Receptor's agonist

- Agonists ***mimic the natural messenger of a receptor***
- Agonists bind ***reversibly to the binding site and produce the same induced fit as the natural messenger - receptor is activated.***
- ***Similar intermolecular bonds formed as with natural messenger.***
- Agonists are often ***similar in structure to the natural messenger***

Antagonist:

A receptor ligand that either directly (competitive) or indirectly (allosteric) prevents the binding of an agonist

Functional antagonist:

A substance that prevents a receptor response by another mode of action

Competitive Antagonists:

Compete with agonist for receptor binding => Agonist appears less potent, but can still achieve 100% effect but at higher concentrations.

Non-competitive