Lecture 1

Organic Pharm. Chemistry for Pharmacy Students

By

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Why to study medicinal chemistry?

- **Medicinal chemistry** and/or **pharmaceutical chemistry** is a discipline of chemistry includes studying the synthesis and analysis of pharmaceutical compounds, pharmacology and various other biological aspects, where they are involved with design, chemical synthesis, and development of pharmaceutical agents.
- The **key difference** between medicinal chemistry and pharmaceutical chemistry is that **medicinal chemistry** deals with the designing, optimization, and development of **new chemical compounds** to use them as drugs whereas pharmaceutical chemistry deals with the study of **drugs** and their development**.**

- **Organic Pharmaceutical Chemistry IV**
- Course number: 511
- Level: 5th Class,
- 1st Semester
- Credit hours/week : Theory 2
- Reference text: Wilson and Gisvold Textbook of Organic Medicinal and Pharmaceutical Chemistry; Delgado JN, Remers WA, (Eds.); 10th ed., 2004.
- **Objectives:**

To give the students knowledge and experience in **pro-drug** and hormones as part of their medicinal and pharmaceutical field. It includes classification, synthesis, biotransformation and/or formulation of certain drugs to improve their action as well as to avoid some side effect.

كيمياء دوائية 4 : مقرر رقم 511

يختص هذا المقرر بدراسة :

الروابط الكيميائية . الادوية الاولية وانواعها . وسائل توصيل الدواء الي العضو المستهدف . دراسة الادوية من حيث استهداف دواء جديد .تسميتها وتشييدها المعملي وخواصها الكميائيه والفيزيائية . البناء الكيمائي وتأثيره علي الدواء .

تحسين الاداء وتقليل الاثار الجانبية واستخدام الطرائق الكومبيوترية الحديثة.

وهي تكملة للكيمياء الدوائية 1 - 3

No Lecture	title	hours
1	Basic concept of prodrugs; Covalent bonds (cleavable); Prodrugs of functional groups; Types of prodrugs.	6
2	Chemical delivery systems; Polymeric prodrugs; Types and structure of polymers; Cross-linking reagents.	6
3	Drug targeting.	4
4	Project.	4
5	Combinatorial chemistry; Peptides and other linear structures; Drug like molecules; Support and linker; Solution-phase combinatorial chemistry.	5
6	Detection, purification and analgesics; Encoding combinatorial libraries; High-throughput screening; Virtual screening; Chemical diversity and library design.	5

Types of Chemical Bonds
Introduction to Bonding

- Chemical bonding describes a variety of interactions that hold atoms together in chemical compounds.
- **Chemical bonds are forces that hold atoms together to make compounds or molecules.**
- Chemical bonds include **covalent**, **polar covalent**, and **ionic** bonds.
- Atoms with relatively similar electronegativities **share** electrons between them and are connected by covalent bonds.
- Atoms with large differences in electronegativity **transfer** electrons to form ions. The ions then are attracted to each other. This attraction is known as an ionic bond.
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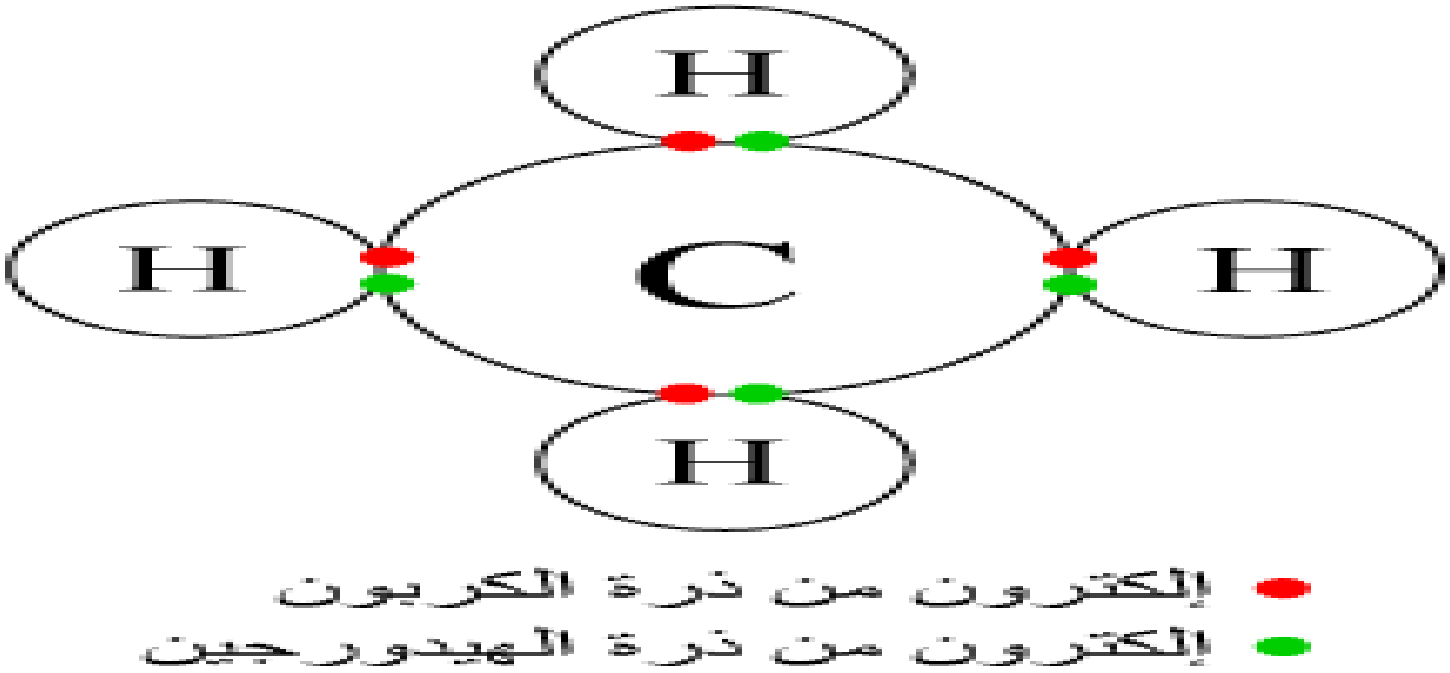
- **bond**: A link or force between neighboring atoms in a molecule or compound.
- **ionic bond**: An attraction between two ions used to create an ionic compound. This attraction usually forms between a metal and a non-metal.
- **covalent bond**: An interaction between two atoms, which involves the sharing of one or more electrons to help each atom satisfy the octet rule. This interaction typically forms between two non-metals.
- **intramolecular**: Refers to interactions within a molecule.
- **intermolecular forces**: Refers to interactions between two or more molecules.

- **Chemical bonds**
- Chemical bonds are the connections between atoms in a molecule.
- These bonds include both strong *intramolecular* interactions, such as covalent and ionic bonds.
- They are related to weaker *intermolecular* forces, such as dipole-dipole interactions, the London dispersion forces, and hydrogen bonding.

A. Covalent Bonds

- Chemical bonds are the forces of attraction that tie atoms together.
- Bonds are formed when valence electrons, the electrons in the outermost electronic "shell" of an atom, interact.
- The nature of the interaction between the atoms depends on their relative electronegativity. Atoms with equal or similar electronegativity form covalent bonds, in which the valence electron density is **shared** between the two atoms. The electron density resides between the atoms is equal and is attracted to both nuclei. This type of bond forms most frequently between two non- metals.



This pictures shows examples of chemical bonding using Lewis dot notation. Hydrogen and carbon are not bonded, while in water there is a single bond between each hydrogen and oxygen. Bonds, especially covalent bonds, are often represented as lines between bonded atoms. Acetylene has a triple bond, a special type of covalent bond that will be discussed later.

- When there is a greater electronegativity difference than between covalently bonded atoms, the pair of atoms usually forms **a polar covalent bond**. The electrons are still shared between the atoms, but the electrons are not equally attracted to both elements. As a result, the electrons tend to be found near one particular atom most of the time. Again, polar covalent bonds tend to occur between non-metals.

- **Forming Covalent Bonds**
- Covalent bonds are a class of chemical bonds where valence electrons are shared between two atoms, typically two nonmetals.
- The formation of a covalent bond allows the nonmetals to obey the octet rule and thus become more stable.
- For example:
- A fluorine atom has seven valence electrons. If it shares one electron with a carbon atom (which has four valence electrons), the fluorine will have a full octet (its seven electrons plus the one it is sharing with carbon).
- Carbon will then have five valence electrons (its four and the one its sharing with fluorine).
- Covalently sharing two electrons is also known as a "**single bond**."

  Carbon will have to form four single bonds with four different fluorine atoms to fill its octet. The result is CF_4 or carbon tetrafluoride.

- Covalent bonding requires a specific orientation between atoms in order to achieve the overlap between bonding orbitals.
- Covalent bonding interactions include **sigma-bonding (σ)** and **pi-bonding (π)**.
- **Sigma bonds** are the strongest type of covalent interaction and are formed via the overlap of atomic orbitals along the orbital axis. The overlapped orbitals allow the shared electrons to move freely between atoms.
- **Pi bonds** are a weaker type of covalent interactions and result from the overlap of two lobes of the interacting atomic orbitals above and below the orbital axis.

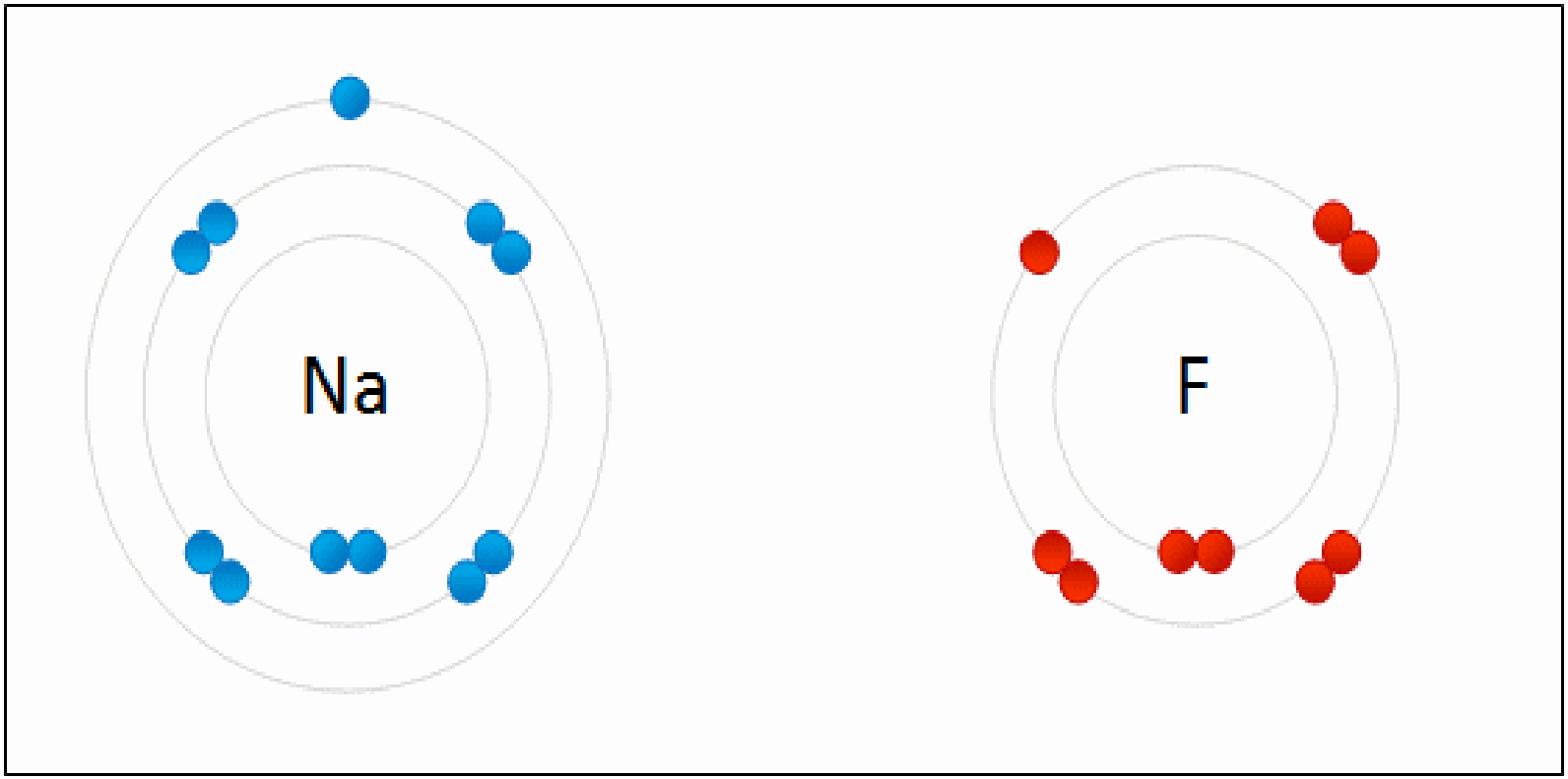
- Covalent bonds can be **single**, **double**, and **triple** bonds.
- **Single bonds** occur when two electrons are shared and are composed of one sigma bond between the two atoms.
- **Double bonds** occur when four electrons are shared between the two atoms and consist of one sigma bond and one pi bond.
- **Triple bonds** occur when six electrons are shared between the two atoms and consist of one sigma bond and two pi bonds.

B. Ionic Bonds

- Finally, for atoms with the **largest** electronegativity differences (such as metals bonding with nonmetals), the bonding interaction is called ionic, and the valence electrons are typically represented as being **transferred** from the metal atom to the nonmetal.
- Once the electrons have been transferred to the non-metal, both the metal and the non-metal are considered to be ions.
- The two oppositely charged ions attract each other to form an ionic compound.

- **Forming an Ion**
- Ionic bonds are a class of chemical bonds that result from the exchange of one or more valence electrons from one atom, typically a metal, to another, typically a nonmetal.
- This electron exchange results in an electrostatic attraction between the two atoms called an ionic bond.
- An atom that loses one or more valence electrons to become a positively charged ion is known as a **cation,** while an atom that gains electrons and becomes negatively charged is known as an **anion**.

- **A cation** is indicated by a positive superscript charge (+ something) to the right of the atom. **An anion** is indicated by a negative superscript charge (- something) to the right of the atom. **For example**, if a sodium atom loses one electron, it will have one more proton than electron, giving it an overall +1 charge.
- The chemical symbol for the sodium ion is Na^{+1} or just Na^{+}.
- Similarly, if a chlorine atom gains an extra electron, it becomes the chloride ion, Cl^{-}.
- Both ions form neutral molecule .
- The ion is more stable than the atom due to the octet rule.


Na
F

- **Forming an Ionic Bond**
- Once the oppositely charged ions are formed, they are attracted by their positive and negative charges and form an ionic compound. Ionic bonds are also formed when there is a large electronegativity difference between two atoms. This difference causes an unequal sharing of electrons such that one atom completely loses one or more electrons and the other atom gains one or more electrons, such as in the creation of an ionic bond between a metal atom (sodium) and a nonmetal (fluorine).

- **Determining the Formula of an Ionic Compound**
- To determine the chemical formulas of ionic compounds, the following two conditions must be satisfied:
- Each ion must obey the octet rule for maximum stability.
- Ions will combine in a way that the overall ionic compound will be neutral. In other words, the charges of the ions must balance out.

- **Magnesium and fluorine** combine to form an ionic compound. What is the formula for the compound?
- **Mg** most commonly forms a 2+ ion. This is because Mg has two valence electrons and it would like to get rid of those two ions to obey the octet rule.
- **Fluorine** has seven valence electrons and usually forms the F^- ion because it gains one electron to satisfy the octet rule.
- When Mg^{2+} and F^- combine to form an ionic compound, their charges must cancel out. Therefore, one Mg^{2+} needs two F^- ions to neutralize the charge. The 2+ of the Mg is balanced by having two -1 charged ions.
- Therefore, the formula of the compound is MgF_2.
- The subscript two indicates that there are two fluorines that are ionically bonded to magnesium.
- On the macroscopic scale, ionic compounds form crystalline lattice structures that are characterized by high melting and boiling points and good electrical conductivity when melted or solubilized.

- **Bonds, Stability, and Compounds**
- Covalent interactions are directional and depend on orbital overlap, while ionic interactions have no particular directionality.
- Each of these interactions allows the atoms involved to gain eight electrons in their valence shell, satisfying the octet rule and making the atoms more stable.
- These atomic properties help describe the macroscopic properties of compounds.
- For example, smaller **covalent compounds** that are held together by weaker bonds are frequently soft and malleable.
- On the other hand, longer-range covalent interactions can be quite strong, making their compounds very durable.
- **Ionic compounds**, though composed of strong bonding interactions, tend to form brittle crystalline lattices.

- **Ionic Compounds v. Molecular Compounds**
- Unlike an ionic bond, a **covalent bond** is stronger between two atoms with similar electronegativity.
- For atoms with equal electronegativity, the bond between them will be a non- polar covalent interaction.
- In non-polar covalent bonds, the electrons are equally shared between the two atoms.
- For atoms with differing electronegativity, the bond will be a polar covalent interaction, where the electrons will not be shared equally.
- **Ionic** solids are generally characterized by high melting and boiling points along with brittle, crystalline structures.
- **Covalent compounds**, on the other hand, have lower melting and boiling points. Unlike ionic compounds, they are often not soluble in water and do not conduct electricity when solubilized.

- **Quesions :**

1. Define each of the followings : bond, ionic bond, covalent bond, Intramolecular, intermolecular forces, valence electrons

2. What is the differences between covalent and ionic bonds ?

3. What are the main characters of covalent compounds ?

4. What are the main characters of ionic compounds ?