Topic: **Physicochemical properties of drug molecules**

By:

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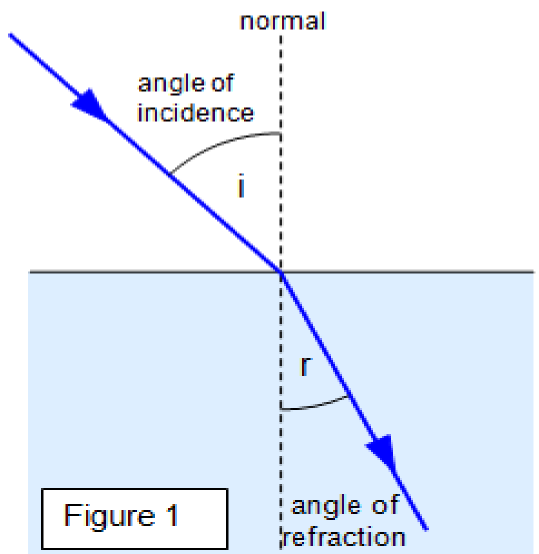
1: Refractive index:

When a ray of light passes from one medium to another medium it bends. This is called refraction.

The refractive index of a substance is given by **Snell's law**. The refractive index is constant for a substance.

n= Sin i / Sin r.

i = angle of incidence, r = angle of refraction, n = refractive index.



The velocity of light is different in different mediums. This is the reason for bending of light rays, when it passes from one medium to another. The medium takes the energy from light rays and so its velocity decreases. Example: the velocity of light in air is 3×10^{10} cm/sec and in water is 2.26×10^{10} m/sec.

Another formula for refractive index is

Refractive index = Velocity of light in air / velocity of light in medium.

For water, n = velocity of light in air / velocity of light in water

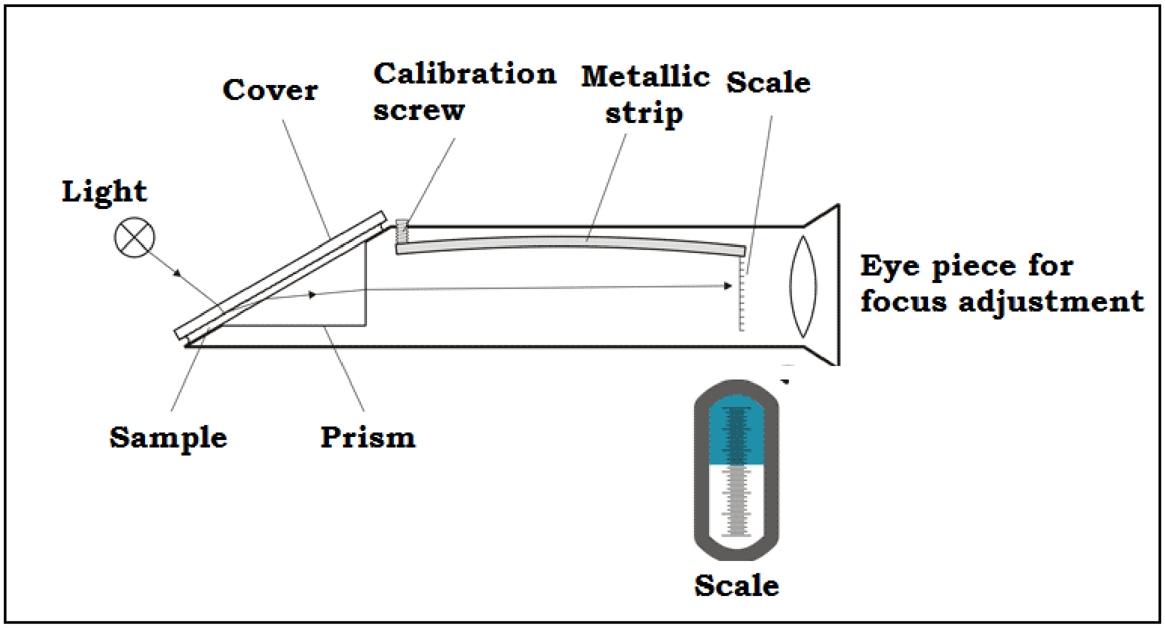
$= 3 \times 10^{10} / 2.26 \times 10^{10} = 1.33$

Example: Refractive index of water is 1.33, benzene is 1.50, chloroform is 1.44, acetone is 1.37 at 20 degree centigrade.

Refractive index can be determined using a refractometer. A refractometer is shown below. It has a prism with a cover, a calibration screw, metallic strip, scale and eye piece.

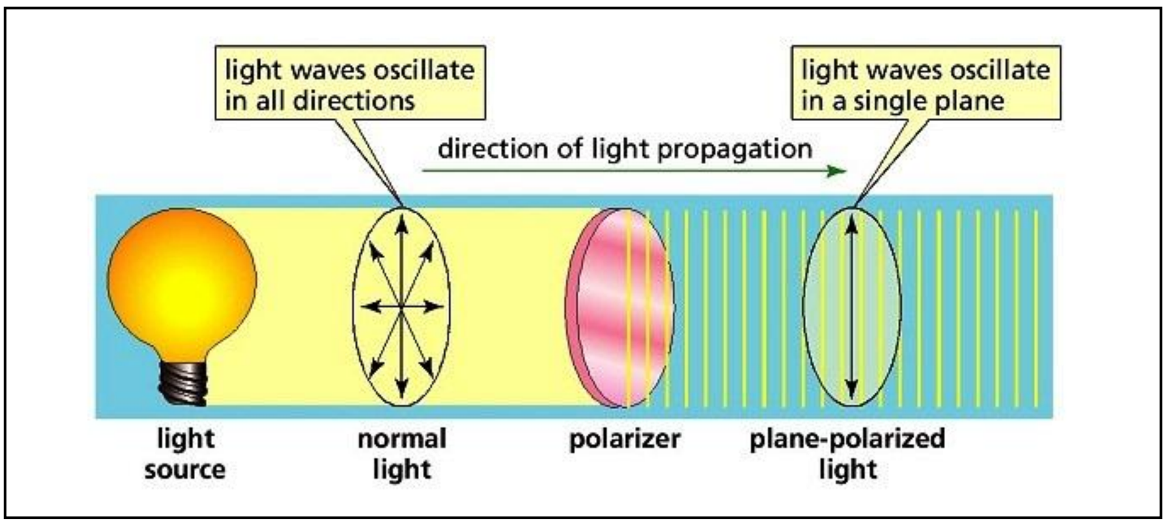
A drop of liquid sample is placed between cover and prism surface. Light passes through the sample and prism and falls on the scale. The light ray bends depending on the refractive index of the liquid sample. The scale will give the refractive index value.

It is used for qualitative analysis, quantitative analysis, and to determine molecular structure of drugs.



2: Optical rotation:

When **ordinary light** is passed through a **nicol prism**, plane polarized light is produced.



When plane polarized light is passed through an optically active substance, it is rotated to left or right.

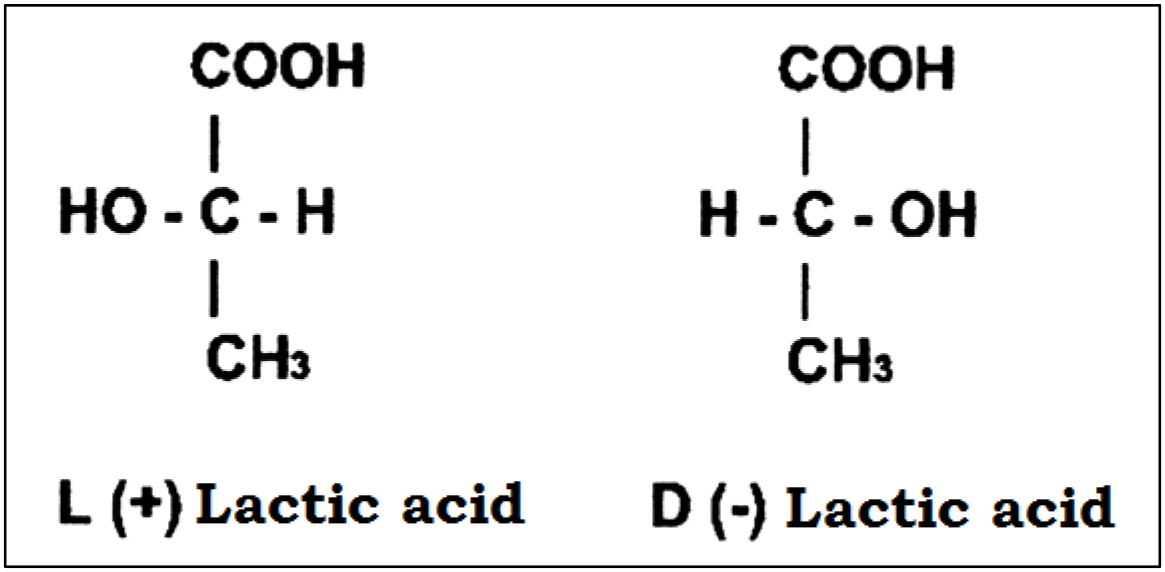
If the substance, rotates the plane polarized light to left, it is called laevo compound.

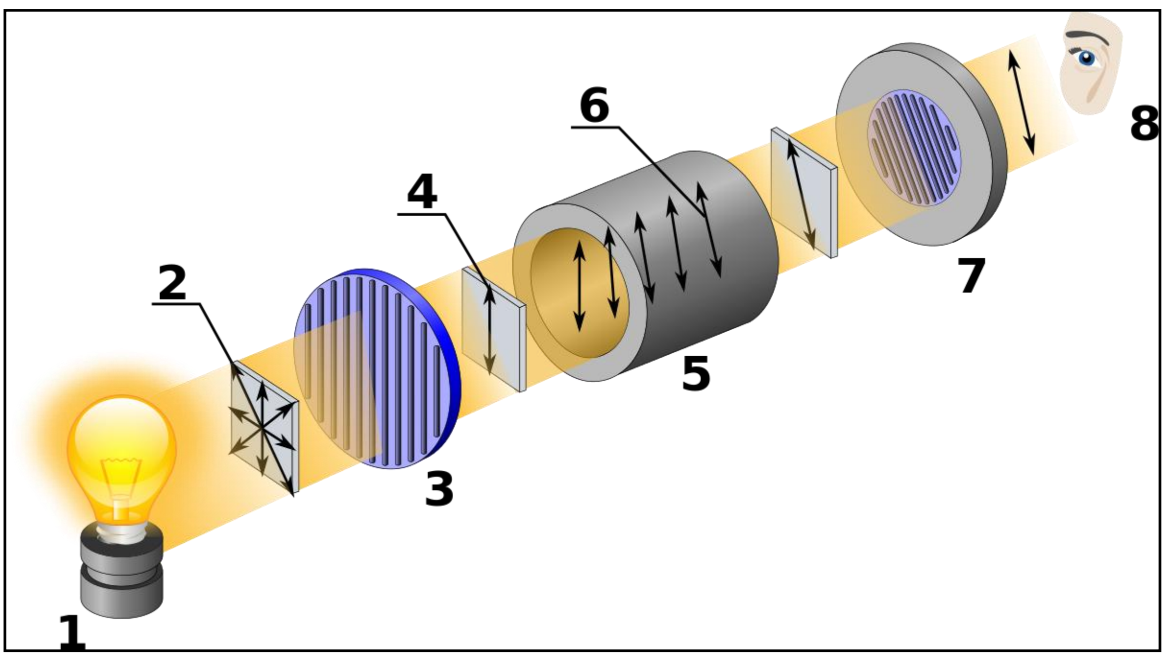
If the substance, rotates the plane polarized light to right, it is called dextrocompound.

The angle of rotation is called optical rotation. This angle depends on the concentration of optically active substance.

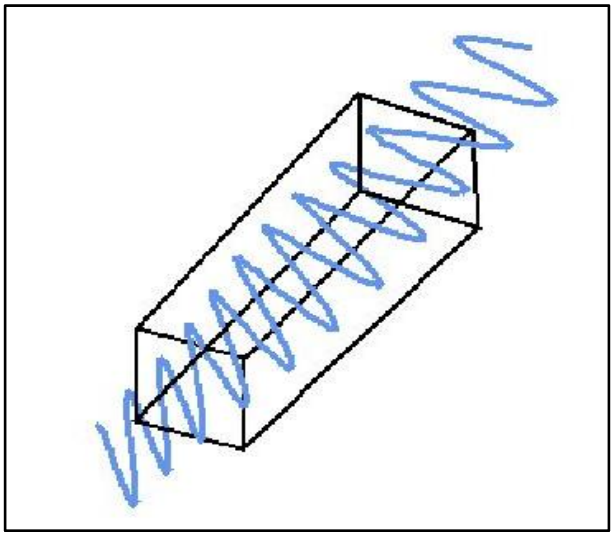
Chiral compounds show optical activity. A chiral compound has a carbon atom attached to four different groups.

Example: D-lactic acid has an optical rotation of – 2.5 ^{0}, L – tartaric acid has an optical rotation of +2.5 ^{0}.





A polarimeter has a light source, a nicolprism to produce plane polarized light. This light passes through a solution in the sample holder. The light rotates and angle of rotation is observed from the other side.



The **rotatory power** of a solution is given by **specific rotation**.

Specific rotation = Angle of rotation / L C

L = path length of light in solution, C = Concentration of solution.

The angle of rotation is found out by using a polarimeter.

Specific rotation is an **additive and constitutive property** and is used for qualitative and quantitative analysis of drugs.

3: Dielectric constant, [ε]:

It is a very important property of liquids. Liquids have capacity to separate ions and keep them in solution. This capacity is measured in terms of dielectric constant values. Water has a dielectric constant of **80**, alcohol has a dielectric constant of **25** and chloroform has a dielectric constant of 5.

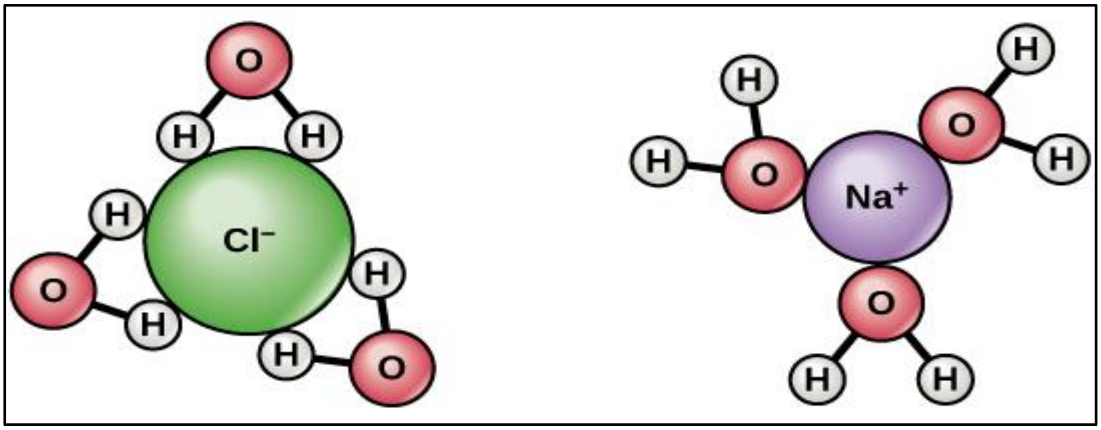
Importance of dielectric constant in pharmacy:

1. The higher the dielectric constant, the higher is the capacity to dissolve polar substances. Water has a high dielectric constant and can dissolve **sodium chloride** easily when compared with alcohol and chloroform.

2. Polar substances dissolve in liquids having high dielectric constant values.

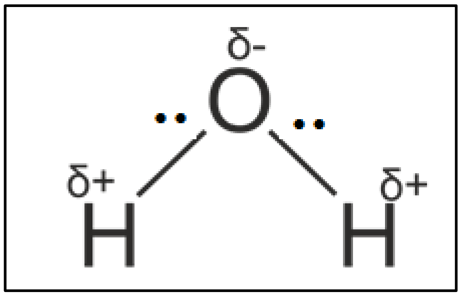
3. Non – polar substances dissolve in liquids having low dielectric constant values.

4. Dielectric constant is an **additive property** and can be used to select liquid blends for preparing elixirs.



4: Dipole moment, [μ]:

In some molecules, there is **unequal** sharing of electrons between atoms. So, they will have a **small positive** and negative charge. Example:HCl, H_2O, have **dipoles** and are called polar molecules. The polarity of a molecule is measured using dipole moment.

a. 

Dipole moment, μ = Charge X distance between charges, Units – **Debye**.

b. Greater the dipole moment, greater is the polarity of the molecule.

c. Lesser the dipole moment, lesser is the polarity of the molecule.

d. Dipole moment is an **additive property** and symmetrical molecules like CO_2, benzene have zero dipole moment.

e. Dipole moments of some molecules are given below.

Water	– 1.84	Debye,	Alcohol	– 1.69	Debye
CO_2	– 0	Debye,	Benzene	– 0	Debye

Importance of dipole moment in pharmacy:

1. **Symmetrical molecules** have zero dipole moment.

2. Drug – receptor binding is due to dipole – dipole attractive forces.

3. Cis isomers have dipole moment,**trans isomers** do not have dipole moment.

4. **DDT** has three isomers. Para isomer has low dipole moment, is fat soluble, can easily cross the insect cell membrane and kill it. Hence it has more activity than other isomers.

5. The **crystalline structure** of solids is due to dipole – dipole attractive forces.

6. Polar substances are soluble in **polar solvents** and non-polar substances are soluble in non-polar solvents.

5: Dissociation / Ionization constant:

Ionization of Weak Acids: The ionization of a weak acid (acetic acid), in water can be written as

$$CH_3COOH + H_2O \rightleftharpoons CH3COO^- + H3O^+$$

The dissociation constant for this acid is given by

$$K_a = [CH_3COO^-]\,[H_3O^+] \,/\, [CH_3COOH]$$

If ***K*$_a$ is more,** the acid is **stronger.** K_a value of salicylic acid is greater than the K_a value of acetic acid. So, salicylic acid is stronger than acetic acid.

If an acid ionizes to a greater extent, it is a stronger acid.

Negative logarithm of K_a is called **pK_a**. If pK_a of an acid is less it is a strong acid.

pK_a can be determined by half neutralization method using the Henderson Hassel Bach equation.

For weakly acidic drugs

$$pH = pK_a + \log \frac{\text{[Ionized Form]}}{\text{[Un Ionized form]}}$$

In this method, acetic acid solution is half neutralized with NaOH solution, and the pH of this solution is measured using a pH meter. The pH is equal to the pKa of the acid.

Ionization of Weak Bases: The ionization of a weak base (ammonium hydroxide), in water can be written as

$$NH_4OH + H_2O \rightleftharpoons NH_4^+ + OH^-$$

1. The *ionization constant* or the *dissociation constant or basicity constant* of ammonium hydroxide is given by the below equation.

   $$K_b = [NH_4^+]\,[OH^-] / [NH_4OH]$$

2. K_b values can be used to compare strength of weak bases. If K_b is more the base is stronger than the other.
3. Negative logarithm of K_b is called pK_b. If pK_b of a base is less, it is a strong base.
4. pK_b can be found by half neutralization method. In this method, the base is half neutralized and the pH will be equal to the pKb of the base.