STUDY MATERIAL

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BIOCHEMISTRY

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Optical activity and its application in Biochemistry

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Optical activity and its application in Biochemistry

History :

❖Stereochemistry is the branch of chemistry concerned with the three dimensional nature of molecules. This branch of chemistry originated as an offshoot of the research of the French physicist Jean Baptiste Biot (1774-1862).

Biot was investigating the nature of **"plane - polarized light"** when he accidentally discovered **optical activity**. This discovery eventually led to the development of stereochemistry.


Jean-Baptiste Biot
(1774-1862)

❖In 1815, Biot discovered that when a beam of plane polarized light is passed through solutions of certain organic molecules, such as sugar or camphor, the plane of polarization is rotated. We call molecules that exhibit this property optically active.

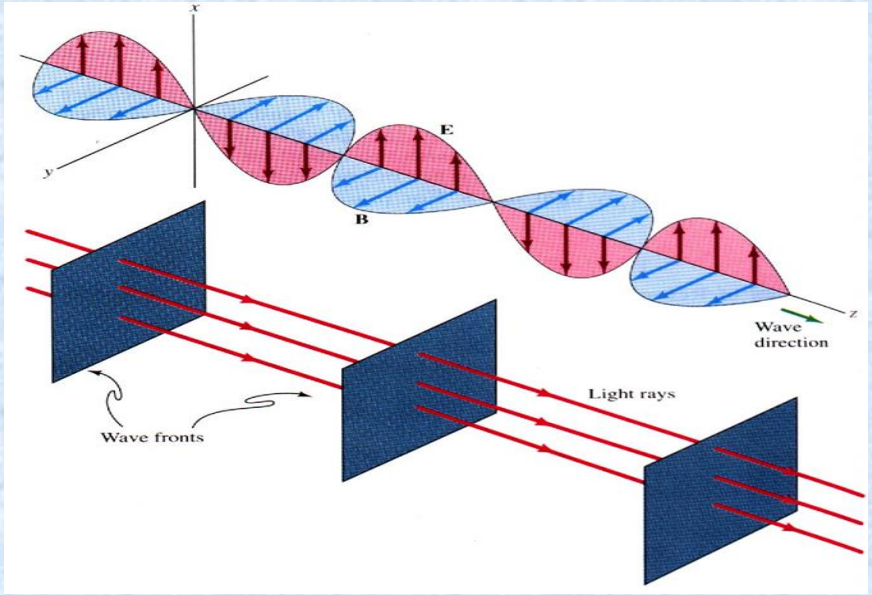
❑Electromagnetic Wave :

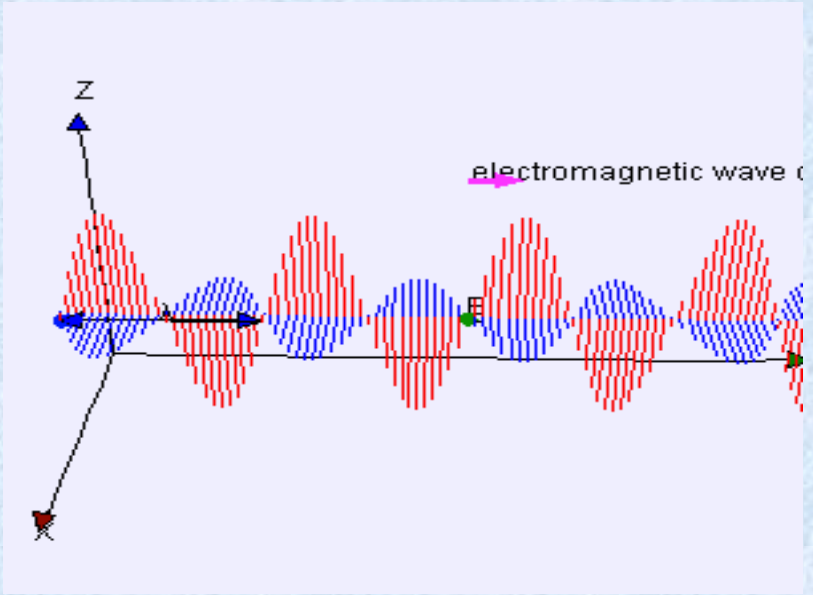
➢Light is an electromagnetic wave.

➢It consists of vibrations of electric field and magnetic field.

➢The electric field and magnetic field are perpendicular to each other and in phase.

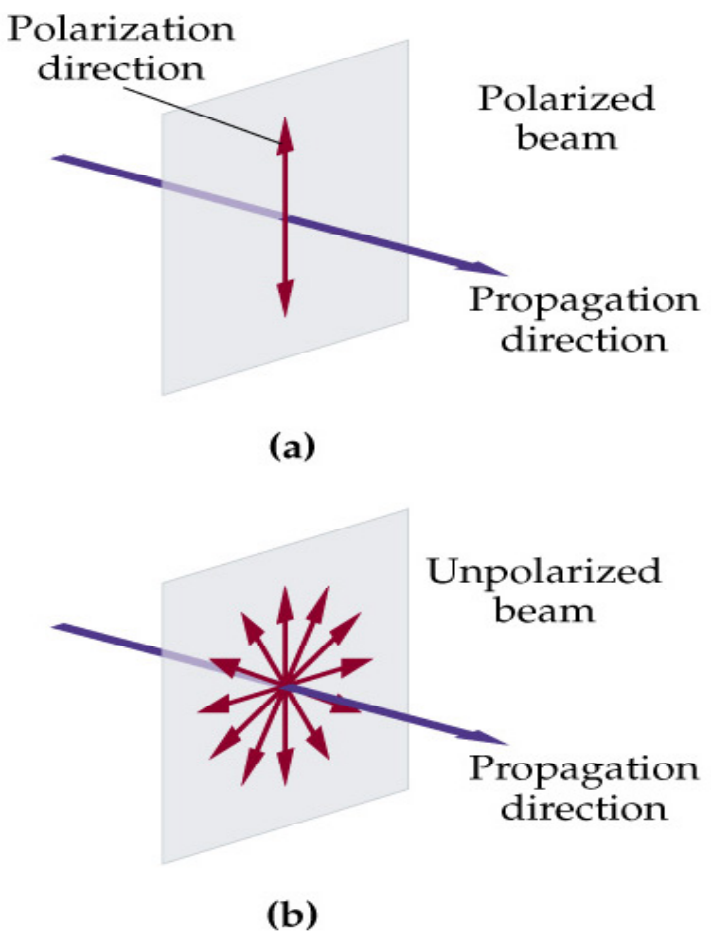
➢E.M wave is a transverse wave.





❑ **The polarization** is defined as the direction of oscillation of the electric field

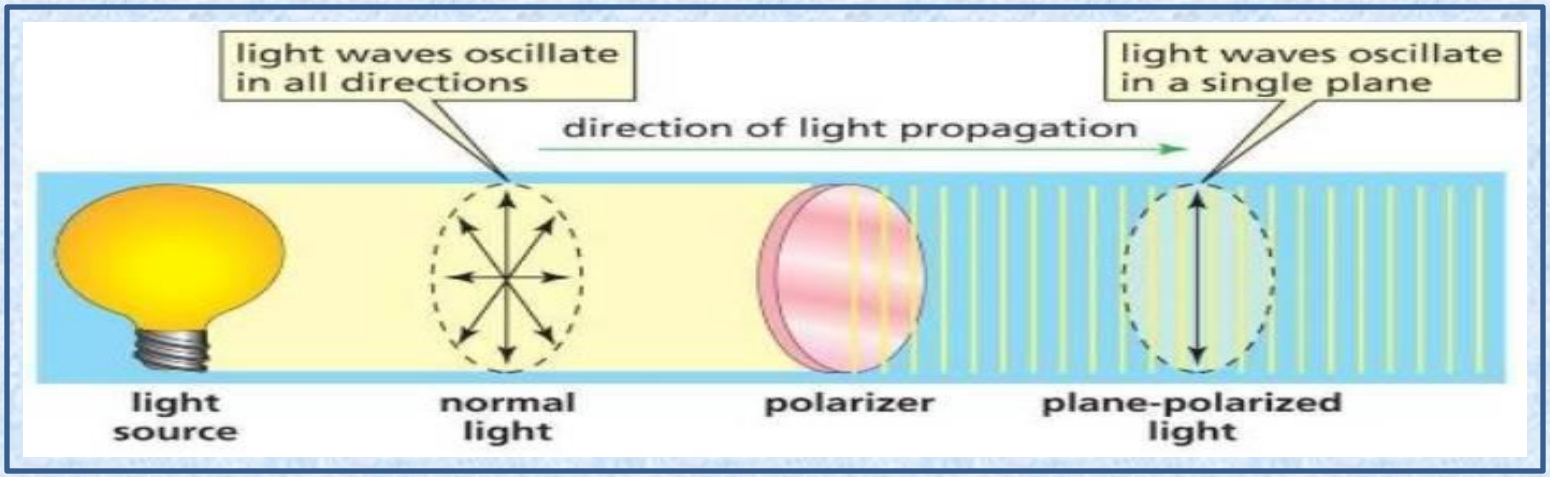
❑**Plane polarized light** : light that has been passed through a nicol prism or other polarizing medium so that all of the vibrations are in the same plane.



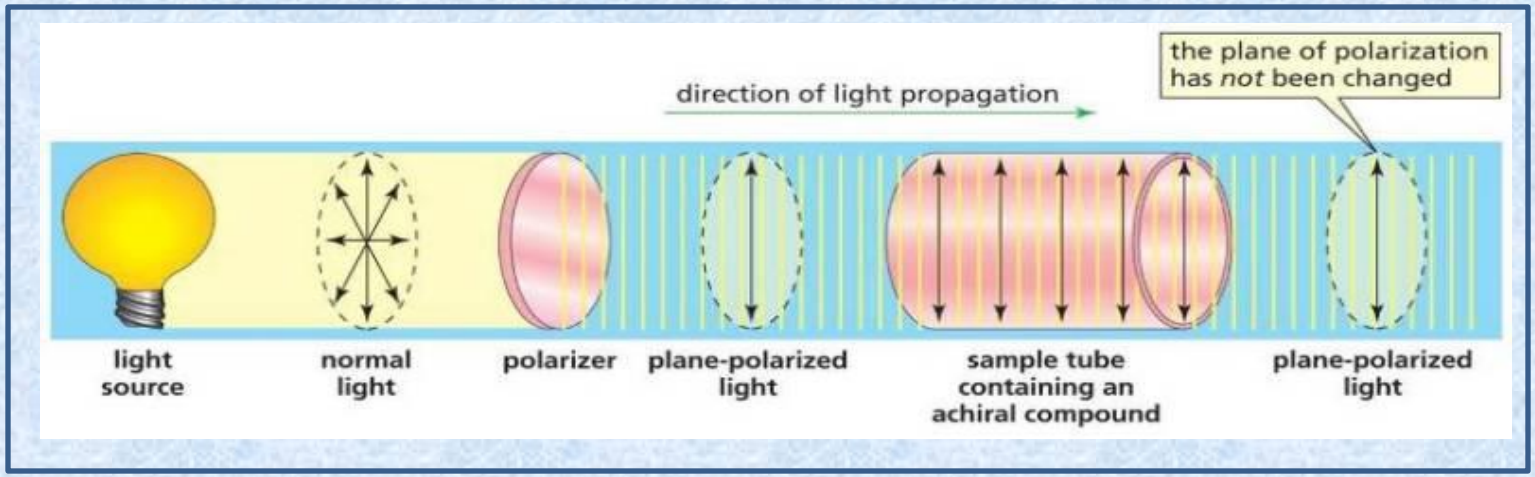
Polarized Light
Vibrations lie on
one single plane only.

Unpolarized Light
consists of many beams
vibrating in different planes

❖ **Plane-polarized light is produced by passing normal light through a polarizer.**



❖ When plane-polarized light passes through a solution of achiral molecules, the light emerges from the solution with its plane of polarization unchanged**.**

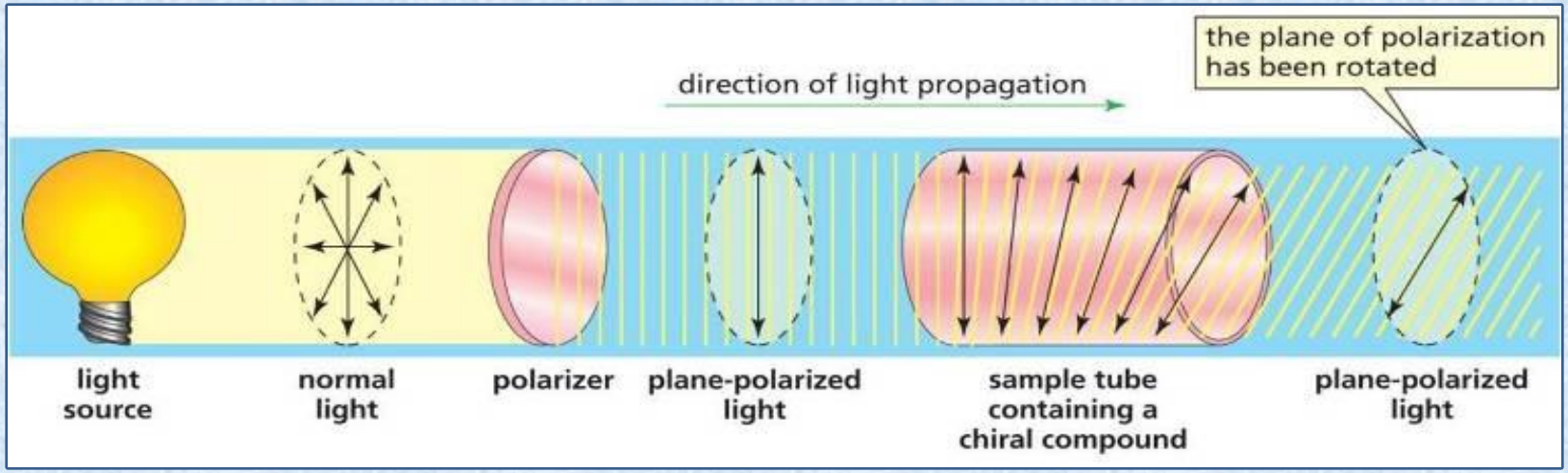


❑ Definition of optical activity :

Optical activity is a physical property of a substance by virtue of which it is able to rotate the plane of polarization of plane polarized monochromatic ray passing through it.

When a sample of material able to rotate the plane of polarization of a beam of transmitted plane-polarized light is said to possess optical activity (or to be optically active).

❖ **Plane-Polarized monochromatic light through an optically active Compound**



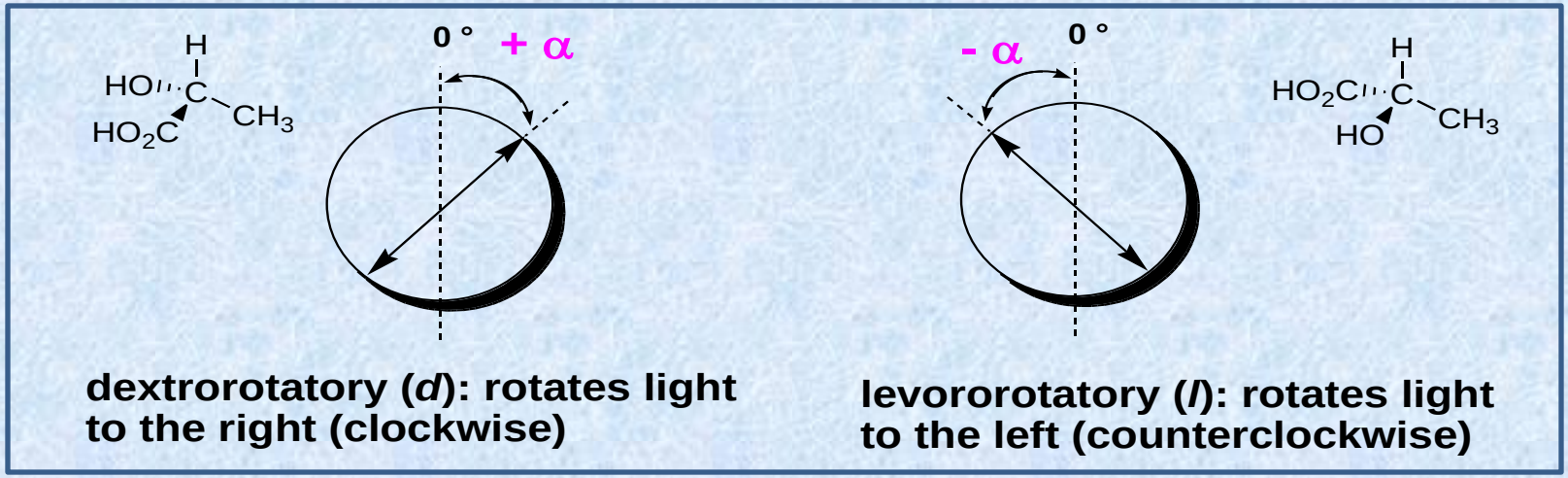
Optically Active compounds rotate plane polarized light. Chiral compounds (compounds non-superimposable on their mirror objects) are expected to be optically active.

Optically Inactive compounds do not rotate plane polarized light. Achiral compounds are optically inactive.

❑ Direction of optical rotation in a Polarimeter :

The optical rotation is the classical distinguishing characteristic (sufficient but not necessary) of systems containing unequal amounts of corresponding enantiomers.

- ❖ An enantiomer causing rotation in a clockwise direction (when viewed in the direction facing the on coming light beam) under specified conditions is called **dextrorotatory** and its chemical name or formula is designated by the prefix (+)-;
- ❖ one causing rotation in the opposite sense is **levorotatory** and designated by the prefix (-)-.



❑ Measurement of optical rotation :

The optical rotation of a dissolved solute is expressed in terms of Specific rotation, the angle of rotation of plane polarized light by a 1.00 gram /ml sample in a 1 dm tube. $[\alpha]_D$ (D = sodium lamp, λ = 589 mμ).

$$[\alpha]_D = \frac{\alpha}{l \times c}$$

where α = observed rotation

l = length (dm)

c = concentration (g/ml)

❑ Specific Rotations of some Common Bio-molecules :

Compound	**[α]**
Penicillin V	(+)233.0
Sucrose	(+)66.5
Camphor	(+)44.3
MSG	(+)25.5
Cholesterol	(-)31.3
Morphine	(-)132.0

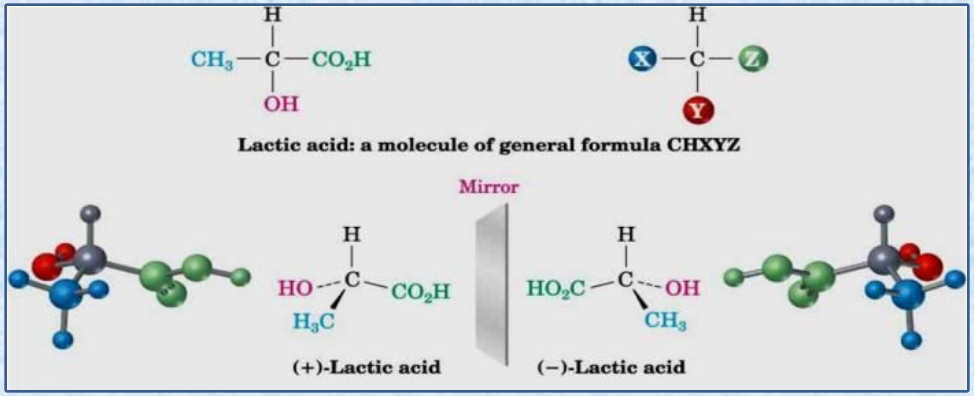
❑ Causes of Optical activity :

It results from the following two types of structural asymmetry of the optically active substance.

❖If a substance is optically active in its crystalline state, but not in its molten state, or in solution, its optical activity arises from the asymmetric 3-dimensional molecular arrangement in the crystal.

❖But the optical activity of a dissolved solute or a liquid results from the presence of asymmetric carbon (s) in its molecule.

Because the electromagnetic field around an asymmetric carbon is not uniform in all directions, it influences unequally the polarized light passing through that field and thereby rotates the plane of its vibration either to the right(dextrorotation) or to the left (levorotation)



❑The factors affecting extent of rotation :

The amount of rotation obtained from a polarimeter is depend upon the number of optically active molecules the beam encounters and the nature of the light source. Consequently, the amount of rotation is dependent upon:

- length of sample tube
- concentration of optically active molecules in solution
- the wavelength of the light used

Because optical rotation is dependent upon these three variables, we must choose standard conditions so that comparisons can be made.

❑Criteria for optical activity :

In order for a molecule to exist as a pair of optical isomers it must meet the following two criteria:

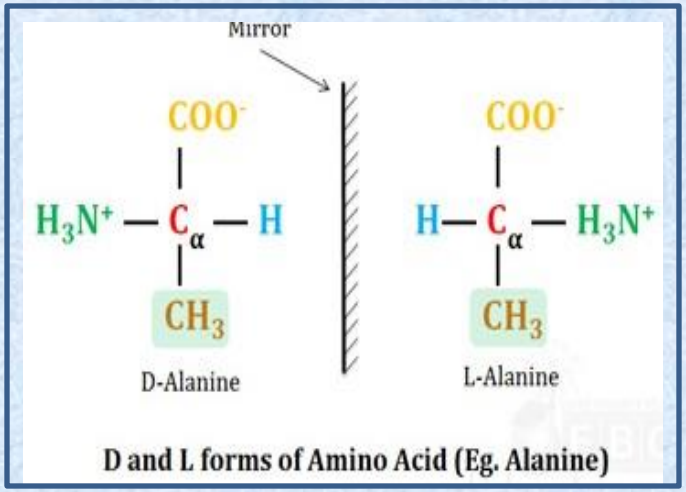
- It must contain at least one carbon bonded to **four different groups**
- It must **not** **contain a plane of symmetry**

❑ Optical Isomerism :

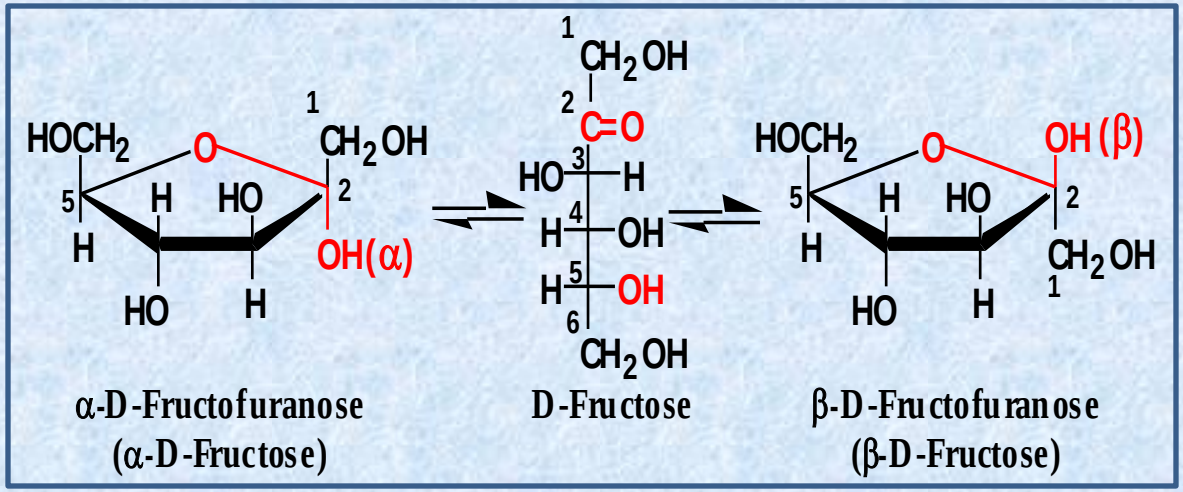
❖ A molecule that exhibits optical isomerism is called *chiral*. Most of the bio-molecules are chiral, often with one isomer performing important biological functions while the other may be biologically inactive.

❖ Optical isomers are also called *enantiomers*. A pair of enantiomers are identical in many respects. They have the same melting point, density, polarity and solubility.

❖ The two differences are that they bend plane polarized light in opposite directions, and they behave differently in a chiral environment.



D and L forms of Amino Acid (Eg. Alanine)



❑ Biological applications :

❖ Most of the carbohydrates, amino acids (except glycine), proteins and nucleic acids and some vitamins are optically active.
❖ Generally only one of the optical isomers of each of these compounds is biologically active.

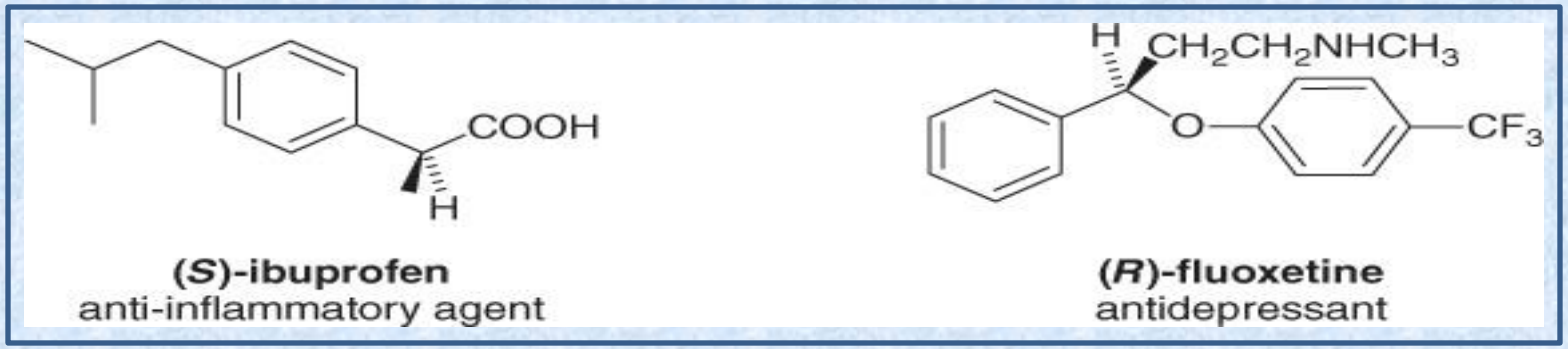
Dextrorotatory bio-molecules	**Levorotatory bio-molecules**
Glucose	Fructose
Galactose	Ribose
Lactose	Proline
Glycogen	Leucine

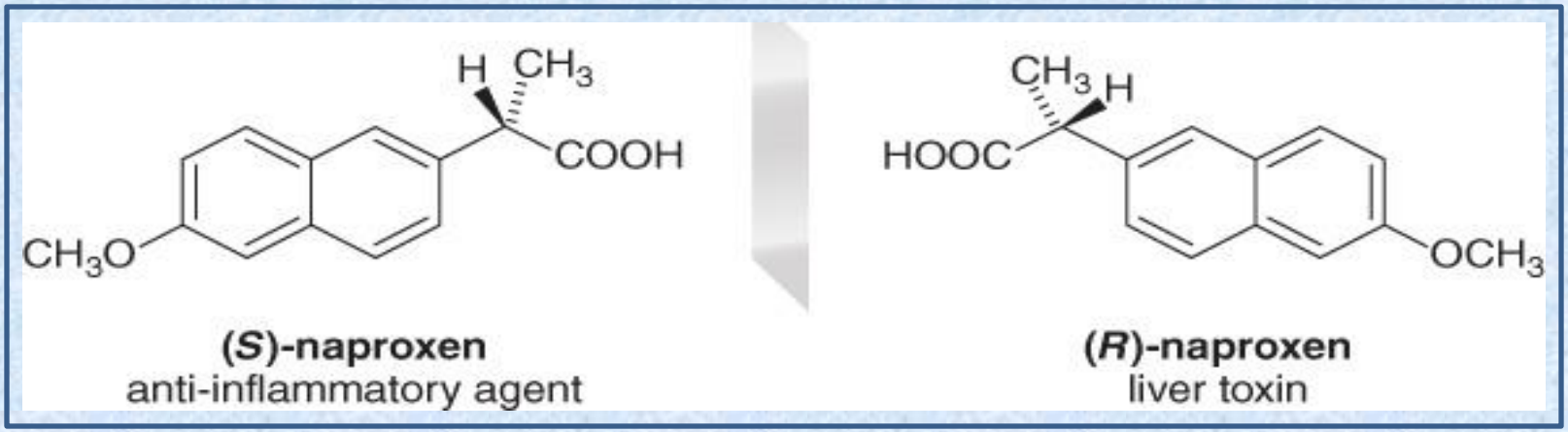
❖Optical activity of a small peptide or a denatured protein approximates the algebraic sum of the optical activities of its amino acid residues.
❖The secondary and tertiary structures of a native protein give it additional optical activity.
❖The right handed alpha-helices make the native protein more dextrorotatory.
❖The asymmetric double helix makes the native DNA dextrorotatory. In Its denature form less assymetric single strands decreases the dextrorotation,

❑ Biological applications :

•Two enantiomers have exactly the same chemical properties except for their reaction with chiral non-racemic reagents.

•Many drugs are chiral and often must react with a chiral receptor or chiral enzyme to be effective. One enantiomer of a drug may effectively treat a disease whereas its mirror image may be ineffective or toxic.

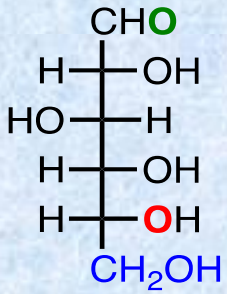


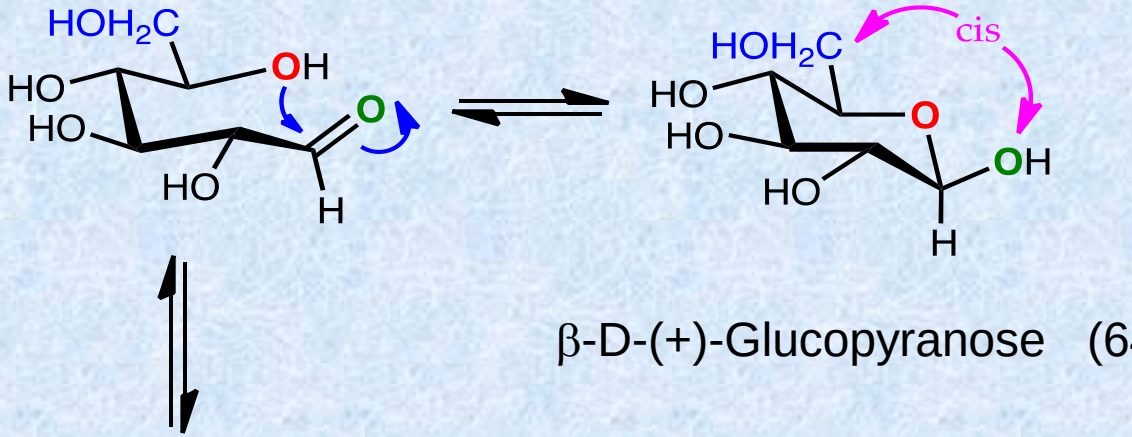


❑ Biological applications :

❖ Mutarotation :

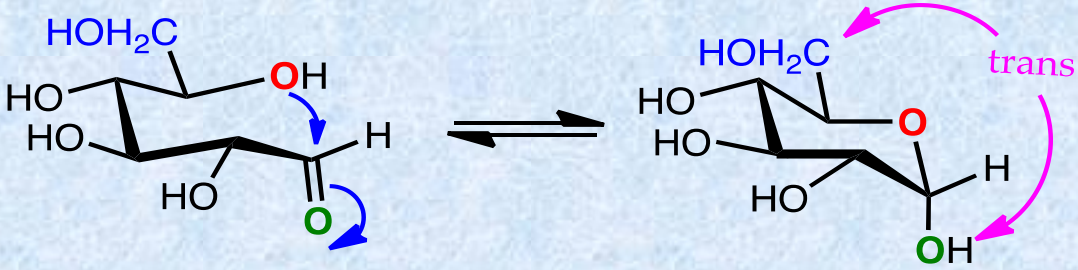
It is the change of optical rotation of a fresh aqueous solution of a reducing sugar until it attains a constant value. Mutarotation results from the spontaneous interconversion of one anomer to other until the attainment of equilibrium mixture





β-D-(+)-Glucopyranose (64%)

$[\alpha]_D$ +18.7



α-D-(+)-Glucopyranose (36%)

$[\alpha]_D$ +112.2

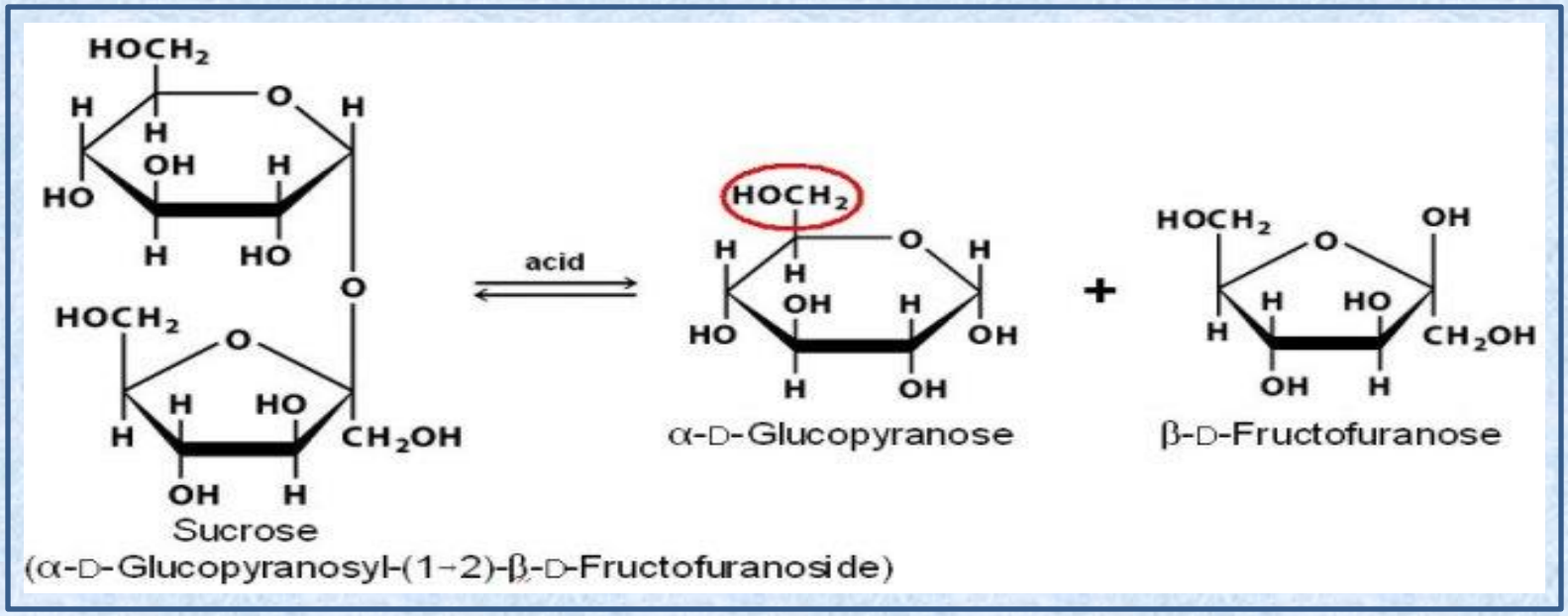
❖In water each anomer mutarotates to an equilibrium with [α] = +52.7

❑ Biological applications :

❖Inversion of cane sugar :

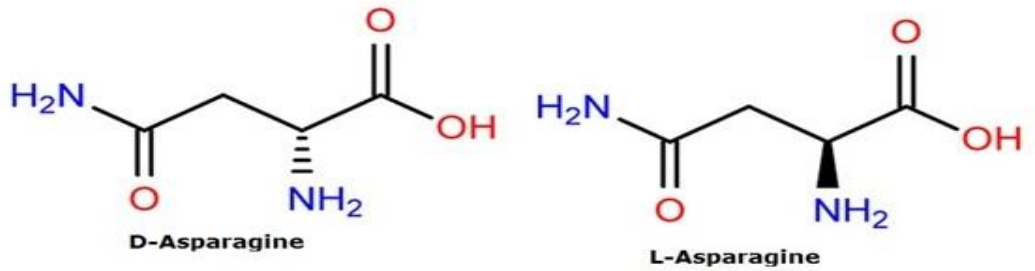
- Upon hydrolysis by invertase or sucrase , detrorotatory sucrose ($\alpha = +66.5^{o}$) yields an equimolecular mixture of α-D-Glucose and β-D-Fructose.

- Since the magnitude of laevorotation of D-Fructose ($\alpha = -92.3^{o}$) exceeds the magnitude of dextrorotion of D-Glucose ($\alpha = +52.7^{o}$) the resultant mixture is levorotatory ($\alpha = -21.2^{o}$) , therefore the phenomenon is called **inversion of cane sugar** and mixture is called **invert sugar.**

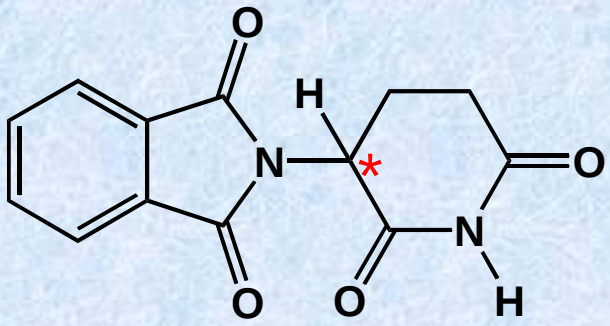


❑ Some optically active Bio-molecules :

❖ Asparagine is an amino acid having two enantiomers. One tastes bitter & other is sweet.



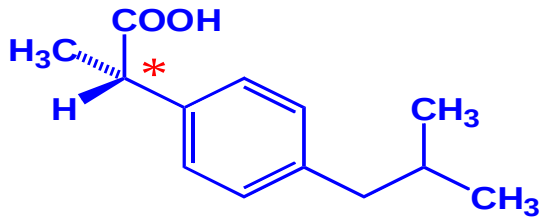
Biochemical effects arise when molecules interact with biomolecules such as enzymes or receptors. These are constructed of chiral building blocks called amino acids.Therefore, the biomolecule only accepts molecules of a certain configuration or shape. Thus, only one enantiomer will fit into the receptor or enzyme active site



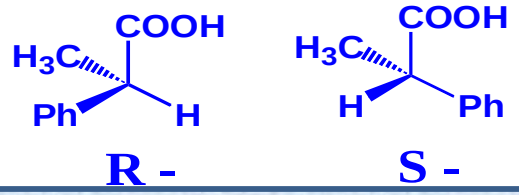
thalidomide

S – induces a teratogenic response
R – induces a hypnotic or seductive response

Only the S- is pharamacologically active



Ibuprofen - anti-inflammatory drug

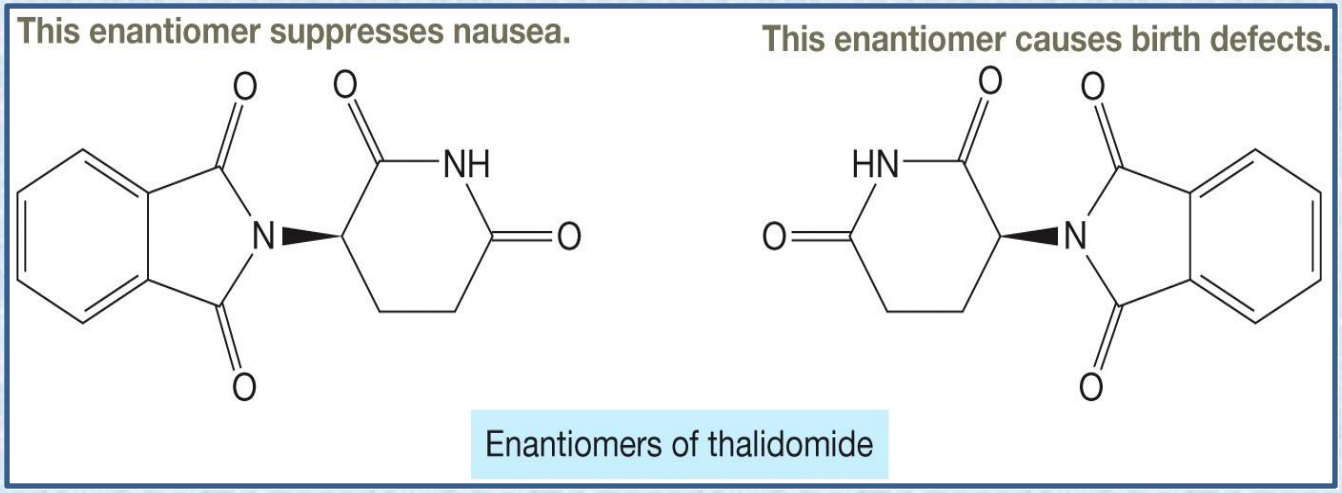


❑ Some optically active Bio-molecules :

- Thalidomide is teratogenic (causes birth defects).

- It is estimated that more than 10,000 children worldwide were born with deformed or missing limbs.

- Thalidomide is chiral and was sold as a racemic mixture of its two enantiomers.



Enantiomers of thalidomide

- The enantiomer on the left is primarily responsible for reducing nausea, whereas the one on the right is responsible for the teratogenic properties.

❑ References :

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