Chapter 1: *Structure of Matter*

CHAPTER OUTLINE: The student will be able to:-

The atom-*size; weight*
Inside the atom
Fundamentals particles
Atomic weight
Atomic number
Mass number
Numbers of neutrons in the nucleus
Isotopes
The periodic table

The Atom:

The smallest portion of an element that retains all of the properties of the element.

Consider a bar of iron. Iron is an element. It has certain properties. Cutting the bar in half produces two pieces of iron. Both pieces have the same properties as the original bar. Continued cutting produces smaller and smaller pieces, all with identical properties. In time, we could theoretically arrive at the smallest piece of iron attainable. This smallest piece of iron is an atom-an atom of iron.

A piece of iron is made up of many atoms of iron, a piece of copper of many atoms of copper, and a piece of silver of many atoms of silver. The atoms of one element differ from those of another and so give characteristic properties of each element.

Size: An atom has a diameter of approximately (1/ 100, 000,000 cm).
Weight: An atom weights very little.

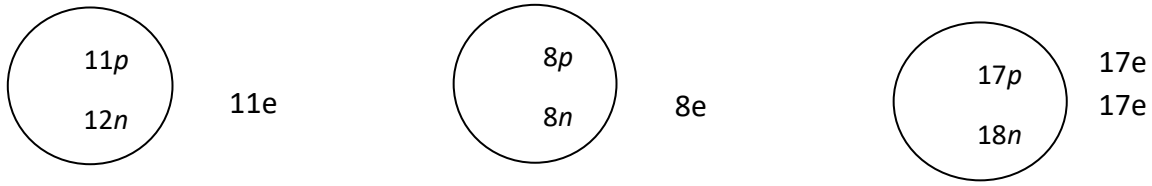
Fundamental particles:

Atoms are considered to be made of three fundamental particles, the proton, the neutron, and the electron. The proton (*p*) has a charge of positive one (+1) and mass (weight) of approximately one atomic mass unit (amu ≈ 1.6605×10^{-24} g.). Protons are located inside the nucleus of the atom. The electron (*e*) has a negative charge (-1) and a mass (weight) of 1/1837 amu. Electrons are located outside the nucleus. The neutron (*n*) has no charge; it is neutral. It has a mass (weight) of approximately 1 amu. Neutrons are located inside the nucleus (see table 1-1).

particle	Symbol & charge	Weight amu	Location in the atom
Proton	*p* or P^+	1	Inside nucleus
Electron	*e* or e^-	1/1837	Outside nucleus
Neutron	*n* or n^0	1	Inside nucleus

Atomic weight: The relative weight of an atom. The chemist uses atomic weights rather than exact weight. What does the term relative weight mean? The chemist has given the carbon-12, sodium-23, oxygen-16…..and so on.

Na=23 O=16 Cl=35



The atomic weight of carbon is 12, that of oxygen is 16, and that of sodium is 23. For precise, however, the exact atomic weights must be used. The atomic weights of all the elements are listed in the periodic table.

The atomic number: It indicates the number of protons in the nucleus of an atom of that element. However, since all atoms are electrically neutral. Therefore, the atomic number also tells the number of electrons in the atom, these electrons being located outside the nucleus. [why the atoms are neutral? There must be as many electrons (negative charge) as protons (positive charge)].

Mass number: The mass number of a nucleus is equal to the total number of protons and neutrons in that nucleus.

Number of the neutrons in the nucleus: The number of neutrons can be found by subtracting the atomic number of an element from its mass number. Knowing that each neutron weights 1 amu.

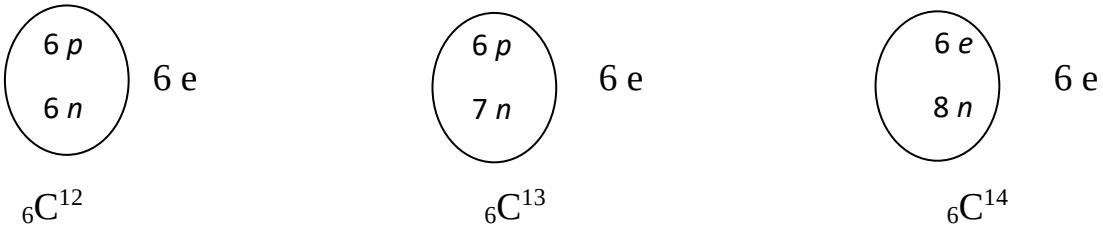
Isotopes: Are defined as atoms of an element having the same atomic numbers but different mass numbers. The first isotope of chlorine (Cl)-atomic number 17 and mass number 35-has 17 protons in its nucleus, 17 electrons outside its nucleus, and 18 neutrons (35-17) in its nucleus. The second isotope of chlorine-atomic number 17 and mass number 37-has 17 protons in its nucleus, 17 electrons outside its nucleus, and 20 neutrons (37-17) in its nucleus.

$_{17}Cl^{35}$ $_{17}Cl^{37}$

The atomic weight is the average weight of all the isotopes: If the two isotopes of chlorine , mass number (atomic weight) 35 and 37, were present in equal amounts, the atomic (average) weight would be 36. However, since the atomic weight is listed as 35.5 must be *predominant* one *because the atomic weight is closer to 35 than to 37*.

The element carbon-atomic number 6 has three isotopes. Their mass number are 12, 13, and 14. They all have atomic number 6, which means that they all have 6 protons in their

nucleus and 6 electrons outside their nucleus. The isotope of mass number 12 has 6 neutrons in its nucleus; the isotope of mass number 13 has 7 neutrons in its nucleus; and the isotope of mass number 14 has 8 neutrons in its nucleus. The carbon-12 is the most *abundant since the atomic weight of carbon is 12.011*, indicating small amounts of the other isotopes.



$_6C^{12}$ $_6C^{13}$ $_6C^{14}$

Three isotopes of carbon

Isotopes have been defined as atoms of an element having the same atomic number but different mass number; therefore isotopes of an element must have the same number of protons and electrons but different number of neutrons. In general, isotopes have identical chemical properties because they contain the same number of electrons as well as protons. However, isotopes have different physical properties.

Radioactive: **Substance like uranium that spontaneously give off radiation**. ***Radioactivity:*** **is the property that causes an element to emit radiation. This radiation comes from the nucleus of the atom**. Radiations produced by a radioactive element are *alpha, beta (electrons)* , and *gamma(neutrons)*.

Radioisotopes: The isotopes produced artificially by bombardment with one of the various particles (radioactive isotopes or radioisotopes). Some radioisotopes used in medicine and in biochemistry ^{131}I, ^{60}Co, ^{99}Tc, ^{14}C, and ^{59}Fe.

Biologic effects of radiation: Externally, alpha and beta particles are relatively harmless to humans since they have slight penetrating power. Gamma rays, with their great penetrating power, have a very definite effect upon the body. If a radioactive substance is taken inside the body, it is the alpha particles that are most harmful. **protection by** shielding, distance, and limiting exposure are the only effective preventative methods against radiation exposure.

Sources of radiation: The body receives radiation externally from three principal sources: *natural background radiation, medical radiation, and fallout and radioactive waste*. Background radiation comes from space and from radioactive material present in the soil, in the air, in the water, and in the building materials of the our houses.

Chapter 2- *Chemical Bonding*

CHAPTER OUTLINE: The student will be able to:-

Molecules
Stability of the atoms
Symbols and formulas
Formation of ions
Ionic bonds
Covalent bonds
Oxidation numbers
Molecular weight

Molecules: It is a combination of two or more atoms. These atoms may be the same elements, as in the oxygen molecule (O_2), or of different elements, as in the hydrogen chloride molecule (HCl). A more complicated molecule is that of glucose, $C_6H_{12}O_6$. Atoms are held together by bonds that may be classified into two main types-ionic and covalent bond.

Stability of atoms: Most atoms are considered stable (nonreactive) when their highest (outer) energy level is filled to eight (electrons). The noble gases-neon, argon, krypton, xenon, and radon-all have eight electrons in their highest energy level. They are stable.

Atoms that do not have eight outer electrons may lose, gain, or share their valence electrons with other atoms in order to reach a more stable structure with lower chemical potential energy. **This process of rearrangement of the *valence electrons* is responsible of chemical reactions between atoms.**

Symbols and Formulas:

A symbol not only identifies an element but also represents one atom of that element. Thus, the symbol Cu designates the element copper and also indicates one atom of copper (two atoms of copper are designated as 2Cu). [2O, 2Cl….].

A formula consists of a group of symbols that represents the elements present in a substance. It also indicates one molecule of that substance. Thus the formula NaCl indicates that the compound (sodium chloride) consists of one atom of sodium (Na) and one atom of chlorine (Cl). In the compound HNO_3 (nitric acid) there is one atom of hydrogen (H), one atom of nitrogen (N), and three atoms of oxygen (3O). [$K_2Cr_2O_7$ Potassium dichromate]. ***To designate more than one molecule of that substance $2HNO_3$, $6K_2Cr_2O_7$*** , **a number (a coefficient)** is placed in front of the formula for that substance.

Diatomic molecules: O_2, H_2, N_2, Cl_2, Br_2, and I_2.

Formation of ions:

Table 2-1 Electron-dot structures of the first 18 elements

^{1}H.							^{2}He:
^{3}Li.	^{4}Be:	^{5}B…	• ^{6}C • •	• ^{7}N • • •	:^{8}O : • •	: ^{9}F : • •	: ^{10}Ne : • •
^{11}Na•	^{12}Mg:	^{13}Al…	• ^{14}Si • •	• ^{15}P • • •	:^{16}S : ••	: ^{17}Cl : ••	:^{18}Ar: ••

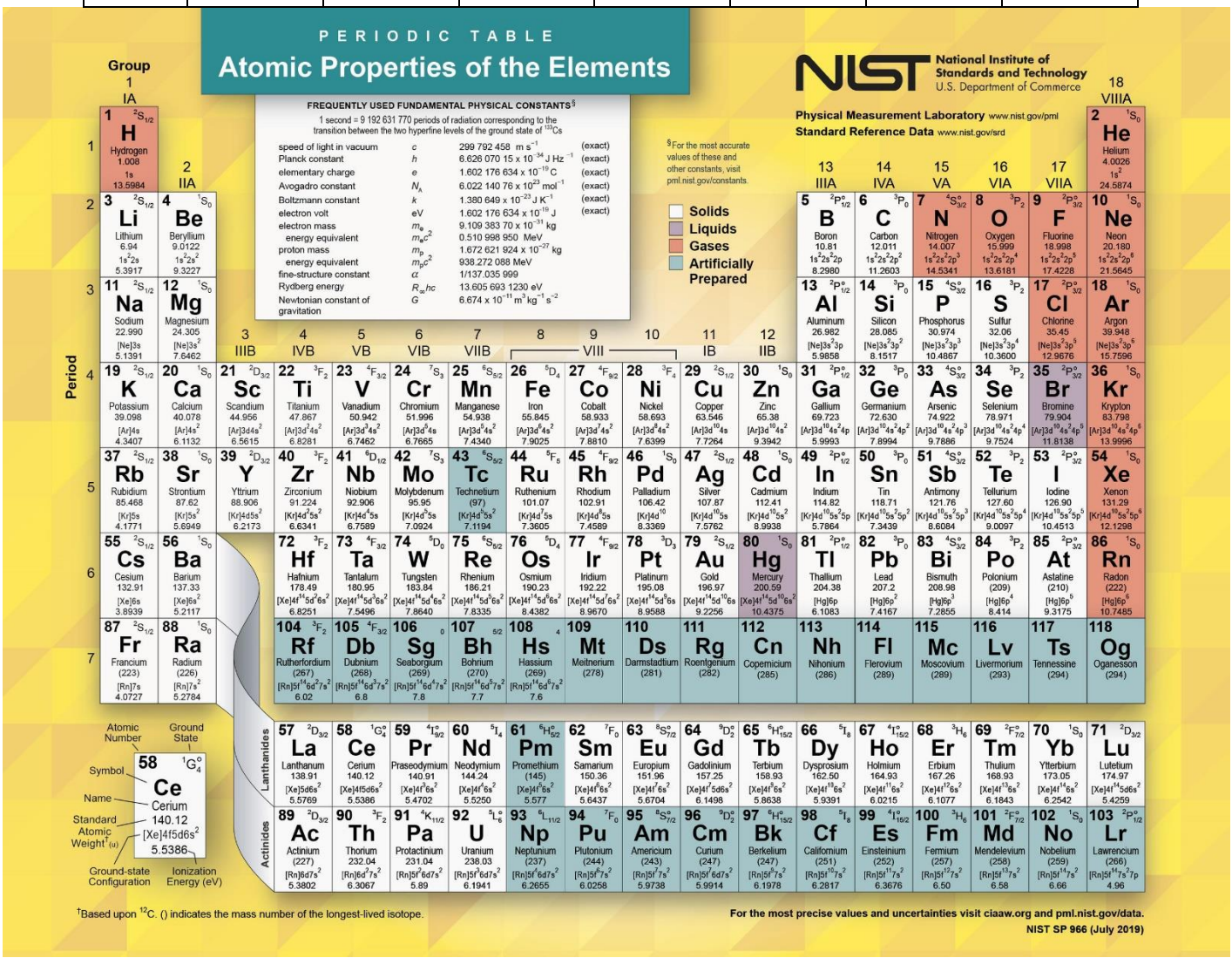


Table 2-1 indicates the electron-dot structures of the elements in the first three periods of the periodic chart.

Consider the sodium ion with the electron structure 2e) 8e) 1e). if the sodium atom **loses** its one outer electron, it will reach a noble gas structure of eight electrons in its outer energy level. Such a noble gas structure has great stability. When a sodium atom loses an electron, it becomes a positively charged particle called a sodium ion. this reaction may be written as

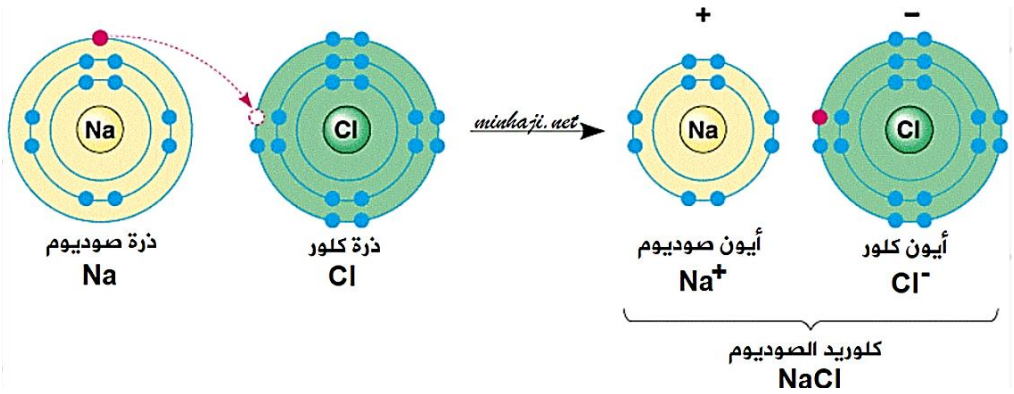
$$Na^{\bullet} - 1e \longrightarrow Na^{+}$$

Or, with the electron-dot being understood,

$$Na - 1e \longrightarrow Na^{+}$$

Consider the element chlorine, 2e) 8e) 7e). the electron atom will tend to gain one electron to fill its outer energy level to eight, reaching a stable (noble gas) structure. Chlorine will thus form an ion with a charge of (-1), or omitting the dots,

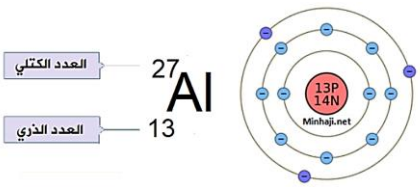
$$Cl + 1e \longrightarrow Cl^{-}$$



Where the positive sign indicates a charge of (+ 1) on the sodium ion. (note that the number 1 is understood and not written.) **The charge on the sodium ion is positive <u>because the sodium ion still has (11) protons in its nucleus but now has only (10) electrons outside that nucleus</u>**.

Likewise, the aluminum atom, which has the electron structure of 2e) 8e) 3e), **<u>loses</u>** all three outer electrons when it forms an aluminum ion with a charge of (+3) [written above the symbol as 3+].

$$Al^{\cdot}_{\cdot} - 3e \longrightarrow Al^{3+} \quad \text{or simply} \quad Al - 3e \longrightarrow Al^{3+}$$



<u>A **metal**</u> that has one valence electron forms an ion with a (*1+ charge*); a metal with two valence electrons forms an ion with a (*2+ charge*), and so on. The positive charge on a metallic ion is equal to the number of electrons lost by the metal.

Elements that have (6 or 7) outer electrons tend to **gain** electrons to each a stable noble gas of eight. Such element are called **nonmetals**. Most elements having 4 or 5 outer electrons are also **nonmetals**.

Since the ion has one more electron that the atom, it will have a charge of (-1), again with the 1 being understood and not written. Likewise, the sulfur atom, 2e) 8e) 6e), can gain 2 electrons to form an ion with a charge of (-2).

$$S + 2e \longrightarrow S^{2-}$$

The S^{2-} ion has a **full outer energy level**, reaching a **noble gas** structure.

An atom that has either lost or gained in its outer energy level is called **ions**. Ions formed from a **metal** will have a **positive charge** equal to the number of **electrons lost**. Ions formed from **nonmetal** will have a negative charge equal to the number of **electrons gained**.

Positive ions are attracted toward a negatively charged electrode called a **cathode**. Such ions are called **cations**. Likewise, **negative ions** are attracted toward a positively charged electrode, called an **anode**. These ions are called **anions**. Common cations in body fluids are the sodium ion, Na^+, the potassium ion, K^+, and the calcium ion, Ca^{2+}. **The chloride ion, Cl^-, is the most common anion in the body fluids.**

Ionic Bonds: When a sodium atom (Na) combines with a chlorine atom (Cl) to form a sodium chloride molecule (NaCl), the sodium atom loses one electron to form a positively charged sodium ion (Na^+). At the same time the chlorine atom gains that one electron to form a negatively charged chloride ion (Cl^-). The reaction is

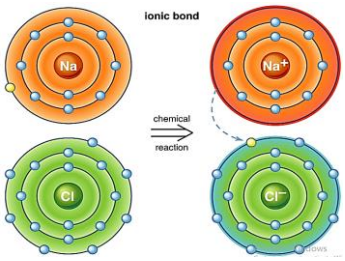
$$Na^{\bullet} + {\cdot}\underset{\bullet\bullet}{\overset{\bullet\bullet}{Cl}}: \longrightarrow :\underset{\bullet\bullet}{\overset{\bullet\bullet}{Cl}}:^{-} + Na^+ \quad \text{or} \quad Na + Cl \longrightarrow Na^+ + Cl^-$$

Another example of a transfer of electrons from a metal to a nonmetal is in the reaction between magnesium (Mg) and chlorine (Cl_2, here written as 2Cl):

$$Mg: + \begin{matrix} Cl^{7-} \\ Cl^{7-} \end{matrix} \longrightarrow Mg^{2+} + \begin{matrix} Cl^{8-} \\ Cl^{8-} \end{matrix} \quad \text{or} \quad Mg + 2Cl \longrightarrow Mg^{2+} + 2Cl^- = MgCl_2$$

Again each ion has a completed outer energy level of eight.

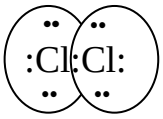
***The positively charged of metal ion (sodium ion, magnesium ion) and the negatively charged (chloride ion) will be attracted to each other and will be held together by electrostatic attraction of their charges (opposite charges attract each other). This type of bonding is called an* ionic bond.** Ionic compounds or electrolytes are acids, bases, and salts. ***Ionic bond*, type of linkage formed from the electrostatic attraction between oppositely charged ions in a chemical compound.**

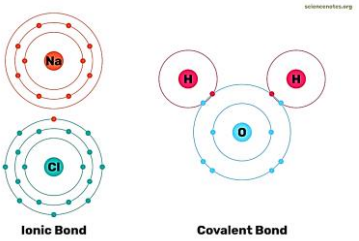


Covalent Bonds*: Ionic bonding results from the loss or gain of electrons**. However, there is another method by which atoms can be bonded together. ***This is by sharing of electrons (**covalent bonding)**. Involve the sharing of a pair of valence electrons by two atoms.

In the chlorine molecule, Cl_2, each of the chlorine atoms has seven outer electrons. In this case both atoms will share electrons so that each will have a completed outer energy level of eight electrons.

Cl-Cl, O=C=O, N≡N or Cl:Cl, O::C::O, N⁝⁝N





Note that in CO_2 and in N_2 there are eight electrons around each atom.

Oxidation numbers:

For ionic compounds, the oxidation number, sometimes called the *charge* of an element, is equal to the of electrons lost or gained and so is the same as the charge on the ion. that is, in sodium chloride, Na^+Cl^-, the oxidation number of sodium is +1, and that of chlorine -1. In the compound $MgBr_2$, where the magnesium ion has a charge of 2+ and each bromide ion a charge of 1-, the oxidation number of magnesium is +2 and that of each bromine -1.

For covalent compounds, where electrons are shared and not transferred, oxidation numbers are assigned to elements using the following rules:

1. All elements in their free state have an **oxidation number of zero**.
2. The oxidation number of oxygen is **-2** (except in peroxide where it is **-1**).
3. The oxidation number of hydrogen is **+1**.
4. The sum of oxidation number in all compounds **must equal zero**. (That is, all compounds are **electrically neutral**).
5. All elements in group **1A** have an oxidation number of **+1**.

Table 2-2 indicates the oxidation numbers of various elements.

? -2=0 +1 +? +4(-2)= 0 ? + 3 (-2)= 0

Zn O , K Mn O_4 , As_2 S_3

In order for the sum of oxidation numbers to be zero, the number of **Mn** must be **+7**, of **As +6** applies to two **As** atoms, so that the oxidation of each **As** is **+3**.

Table 2-2. Oxidation Numbers of Elements

Positive oxidation number			Negative oxidation number		
Name and Symbol		Oxidation Number	Name and Symbol		Oxidation Number
Hydrogen	H^+	+1	Chloride	Cl^-	-1
Sodium	Na^+	+1	Bromide	Br^-	-1
Potassium	K^+	+1	Iodide	I^-	-1
Silver	Ag^+	+1	Sulfide	S^{2-}	-2
Calcium	Ca^{2+}	+2	Oxide	O^{2-}	-2
Magnesium	Mg^{2+}	+2			
Aluminum	Al^{3+}	+3			
Ammonium	NH^+	+1			
Iron	$Fe^{2+}$and Fe^{3+}	+2 and +3			
Copper	$Cu^+$and Cu^{2+}	+1 and +2			
Tin	$Sn^{2+}$and Sn^{4+}	+2 and + 4			

Molecular weight: The molecular weight of any compound is the sum of the **atomic weights** of all of the atoms present in the molecule of that compound. Examples:

NaBr = (23+80)= 123; H_2O= (2×1 + 16) =18; $C_6H_{12}O_6$ =(6×12 + 12×1 + 6×16)= 180;

$Ca_3(PO_4)_2$ = (3×40 + 2×31+ 8×16) = 310

Percentage Composition: The percentage composition of a compound can be calculated **from the relative atomic weights of the elements present in the compound**. Consider the compound $Ca_3(PO_4)_2$, calcium phosphate whose molecular weight was found to be 310. Of this weight, calculate the percentage of Ca, P, and O in the upper compound.

$$\% \text{ Ca} = \frac{\text{Weight of calcium in compound}}{\text{Weight of compound}} \times 100 = \frac{120}{310} = 38.7\ \%;$$

$$\% \text{ P} = \frac{62}{310} = 20.0\ \%;$$

$$\% \text{ O} = \frac{128}{310} = 41.3\ \%$$

Chapter 3- *Liquid Mixture-Solutions*

CHAPTER OUTLINE: The student will be able to:-

Solutions
Preparation of Standards units
Concentration
percentage
Formal solution
Molar solution
Normal solution

Solutions: *A solution is a homogenous mixture of two or more substances evenly distributed in each other*.

Solubility: The quantity of **solute** that will dissolve in a definite quantity of **solvent**, the solubility of a substance is measured by ***the concentration of its saturated solution***.

***Preparation of standard solution unit*:**

Standard solution: *is one whose concentration (the quantity of reagent in a given volume) is known*. The concentration of a standard solution is usually expressed in grammes or equivalents of the active constituent in each liter of the solution. The process by which the concentration of a solution is determined is called **standardization**

Requirements of a primary standard substance:

1. It must be of highest purity.
2. A primary standard substance should be stable, it should not be attracted by constituent of the atmosphere.
3. It should be readily available and not too expensive.
4. It should not be hygroscopic.
5. Finally, it should have a reasonably high equivalent weight. *A high equivalent weight tend to minimize weighing errors*.

Preparation a standard solution is always prepared by dissolving the standard material in a small volume. Generally, the standard substance is weighed directly on to a clock-glass, or if hygroscopic, in a weighing bottle, and then transferred to the graduated flask. the volume is carefully adjusted to the mark, and the stopper flask is inverted 30-40 times to sure mixing of the contents.

Factors affecting solubility of a solute:

1. Temperature:

Most solid solutes are more soluble in hot water than in cold water. There is variation of solubility of various substances in a water as a function of temperature.

For example-KNO_3 becomes much more soluble with an increase of temperature; however $Ce_2(SO_4)_3$, gases such as HCl and SO_2 become less soluble with increasing temperature, and NaCl shows little change in solubility. The solubility of Br_2, a liquid, is practically unaffected by temperature.

2. Pressure:

The pressure will affect the solubility of a gaseous solute. ***The greater the pressure, the greater the solubility of a gas in a liquid.***

3. Surface area:

It does affect the rate of dissolution. ***The greater the amount of surface area, the quicker a solute will dissolve in a solvent.***

4. Stirring:

The rate at which solute dissolves can also be increased by stirring the mixture. The process of stirring brings fresh solvent in contact with solute and so ***permits more rapid solution.***

5. Nature of solvent:

In general, polar liquids ***dissolve*** polar compounds, and non-polar liquids ***dissolve*** non-polar compounds. Some polar liquids (H_2O, CH_3OH, and C_2H_5OH) . Some non-polar liquids (benzene, carbon tetrachloride (CCl_4), and ether).

Importance of solutions:

During digestion, foods are changed to soluble substances so that they may pass into the bloodstream and be carried to all parts of the body. At the same time the waste products of the body are dissolved in the blood and carried to other parts of the body where they can be eliminated. Plants obtain minerals from the groundwater in which those minerals have dissolved.

Many chemical reactions take place in solution. ***This reaction occurs because the ions in the solution are free to move and react with other ions.***

$$AgNO_3 + NaCl \longrightarrow Ag^+ + Cl^- + Na^+ + NO_3^-$$

Many medications are administered orally, subcutaneously, or intravenously as solutions. Drugs must be in solution before they can be absorbed from the gastrointestinal (GI) tract. As you might expect, when drugs are taken in solution, such as syrups and elixirs, they are absorbed more rapidly than drugs in a solid form, such as tablets and capsules.

Strength of Solutions:

when a few crystals of sugar are placed in a beaker of water, a ***dilute*** sugar solution is produced (solvent more than solute). As more and more sugar is added to the water, the solution becomes more ***concentrated*** (solute more than solvent). However, both dilute and concentrated are *relative terms.* A dilute sugar solution may contain 5 g of sugar per 100 ml of solution, whereas 5 g (the same amount) of boric acid per 100 ml of solution will produce a concentrated boric acid solution. That is, the term
dilute and concentrated usually have no specific quantitative meaning and so are not generally used for medical applications. Dilution law C_1V_1 X C_2V_2

Concentration Expressions:

Table 3-1: CONCENTRATION EXPRESSIONS

Expression	***symbol***	**Definition**
Molarity	*M,c*	Moles (gram molecular weights) of solute in 1 liter of sol.
Normality	*N*	Gram equivalent weights of solute in 1 liter of solution
Molality	*m*	Moles of solute in 1000 g of solvent
Mole fraction	*X*	Ratio of the moles of one constituent (e.g., the solute) of a solution to the total moles of all constituents (solute & solvent
Mole percent		Moles of one constituent in 100 moles of solution; mole percent is obtained by multiplying mole fraction by 100
Percent by weight	% w/w	Grams of solute in 100 g of solution
Percent by volume	% v/v	Milliliter of solute in 100 mL of solution
Percent weight-in-volume	% w/v	Grams of solute in 100 mL of solution
Milligram percent	—	Milligrams of solute in 100 mL of solution

The concentration of a solution can be expressed either in terms of the quantity of solute in a definite *volume of solution* or as the quantity of solute in a definite *mass of solvent or solution.*

Percentage solution: The weight-volume method express *the weight of solute in a given volume of solvent, usually water*. A 10 percent glucose solution will contain 10 g glucose per 100 ml of solution. A 0.9 percent saline solution will contain 0.9 g sodium chloride per 100 ml of solution. The **percentage** ***indicates the number of grams of solute per 100 ml of solution (% w/v).***

Ex1*:* prepare 500 ml of 2 percent citric acid solution.

500 ml X 2 (g citric acid) / 100 ml = 10 g citric acid

1. Weight out exactly 10 g citric acid.
2. Dissolve 10 g citric acid in a small amount of water contained in a 500-ml graduated cylinder.
3. Add water to the 500-ml mark and stir.

Ex2: a patient is given 1000 ml 0.9 percent NaCl intravenously. How many grams of NaCl did the patient receive?

0.9 % means 0.9 g NaCl/100 ml solution

1000 ml X 0.9 g NaCl / 100 ml = 9 g NaCl

In clinical work involving dilute solutions, concentrations sometimes expressed in terms of milligrams percent **(mg %)**, *which indicates the number of milligrams of solute per 100 ml of solution.* Milligrams percent is also referred to as milligrams per deciliter (mg/dl). The values of blood components in these units. Hint (1 dL = 100 mL).

Parts per Million (ppm): low concentration may be expressed in units *milligrams per liter* (mg/L). Another method of expressing low concentration is parts per million (ppm). *One part per million is equivalent to (1 mg/L).* that is, if a solution has a concentration of 40 mg/L, its concentration may be expressed as 40 ppm.

ppm = wt of solute / wt of solution X 1000.000

$$c_{ppm} = \frac{\text{mass of solute}}{\text{mass of solution}} \times 10^6 \text{ ppm}$$

Ratio Solutions*:* Another method of expressing concentration is a ratio solution . A 1:1000 merthiolate solution contains 1 g in 1000 ml solution. A 1:10.000 $KMnO_4$ solution contains 1 g in 10.000 ml solution.

Molar Solutions (molarity): *Moles (gram molecular weights) of solute in 1 liter of solution* . Molar used the symbol (*M*). A 1 molar (1*M*) solution of glucose ($C_6H_{12}O_6$) will contain 1 mol glucose (180 g) in 1L solution. (*M* = moles of solute per 1 liter of solution)

$$M = \frac{\text{Moles of solute}}{\text{Liters of solution}} = \frac{\text{Weight of solute}}{\text{Molecular weight of solute}} \times \frac{1000}{\text{Volume of solution (ml)}}$$

Ex3*:* Prepare 3L of 2*M* (2molar) KCl (molecular weight 74.5).
M = wt/m.wt X 1000/vol. of solution (ml)
2 = wt/74.5 X 1000/3000 = 447 g KCl

Ex4*:* Prepare 500 ml 0.1 *M* NaOH (m.wt, 40).
M = wt/ m.wt X 1000/vol. of solution (ml)

0.1 = wt/40 X 1000/500 = 2 g NaOH (Thus, we should dissolve 2 g NaOH in water and dilute to 500 ml.)

Ex5: How many grams of glucose are present in 0.5L of 2.0 *M* of glucose solution?

2.0 *M* = wt/180 X 1000/500 (ml) = 180 g glucose

Ex6*:* What is the molarity (molar concentration) of sodium carbonate (m.wt, 106), in which the % w/v 0.85.?
%w/v is the number of grams of solute in 100 ml of solution.
M = 0.85/106 X 1000/100 = 0.08 *M*

Molality: *is the number of moles of solute per 1000 grams of solvent (water).*The **molal** contains 1 g molecular weight (mole) dissolve in 1000 g of water.

Molality (*m*) = moles of solute/kg of solvent

Ex7: what are the molality of KOH solution, if dissolve 23 g of KOH in 500 g water.

Normal solution: *Gram equivalent weights of solute in 1 liter of solution* (symbol *N*). A 1 normal (1*N*) solution contains one gram equivalent weight of solute per liter of solution. **The gram equivalent weight is represent the molecular weight of atoms or molecules to the *valence* of atoms or molecules**.

$$\text{Equivalent weight (g/Eq)} = \frac{\text{Atomic weight}}{\text{Number of equivalents (valence)}} \quad \textit{for atom}$$

Equivalent weight (g/Eq) = $\frac{\text{Molecular weight (g/mole)}}{\text{Equivalent/mole}}$ *for molecules*

The valence (oxidation number) for hydrogen 1; potassium K, 1; sodium Na, 1; fluorine F, 1; calcium Ca, 2; magnesium Mg, 2; oxygen O, 2; aluminum Al, 3;….and so on.
The equivalent weight of F, H, K, and Na; is identical to the molecular weight, according to the upper equation for atom. Therefore, the valence for Ca, Mg, and O, are 2 and its equivalent weight one half of its atomic weight, aluminum is 3 and its equivalent weight is one third of its atomic weight, or 27/3 = 9 g/Eq.

Equivalent weight of acid: *The gram equivalent weight of an acid can be calculated by dividing the weight of 1 mol of that acid by the number of replaceable hydrogen that it contains*. For example, hydrochloric acid HCl, contains one replaceable H. the grams equivalent weight is the weight of 1 mol (36.5 g) divided by 1. The gram equivalent weight of sulfuric acid H_2SO_4, is the weight of 1 mol of H_2SO_4 (98 g) divided by 2, or 49 g.

Equivalent weight of base: *The gram equivalent weight of a base can be calculated by dividing the weight of 1 mol of that base by the number of OH^- groups it contains*. The gram equivalent weight of sodium hydroxide (NaOH), is the weight of 1 mol of NaOH (40 g) divided by 1, or 40 g. the gram equivalent of calcium hydroxide $Ca(OH)_2$ (74 g), is the weight of 1 mol of $Ca(OH)_2$ divided by 2, or 37 g.

Equivalent weight of salt: The equivalent weight of sodium chloride (NaCl) is identical to its molecular weight, 58.5 g/Eq. that is, the equivalent weights of NaCl is the sum of the equivalent weights of sodium (23 g) and chlorine (35.5 g), or 58.5 g/Eq. The g/Eq of NaCl is identical to its molecular weight, 58.5 g, because the valence of sodium and chlorine is each1in the compound. The Eq of Na_2CO_3 is numerically half of its molecular weight. The valence of the carbonate ion, CO_3^{2-}, is 2 and its equivalent weight is 60/2 = 30 g/Eq. although the valence of sodium is 1, two atoms are present in Na_2CO_3. Providing a weight of 2 x 23 g = 46 g ; its equivalent weight is one half of this, or 23 g/Eq. the equivalent weight of sodium carbonate is therefore 30 + 23 = 53 g, which is one the molecular weight.

Eq for salt = m. wt of salt / oxidation of salt

Eq for reducing and oxidizing agent = m.wt / no. of electrons gained or lost

$$N = \frac{\text{Weight of solute}}{\text{Equivalent weight}} \times \frac{1000}{\text{Volume of solution (ml)}}$$

Ex8: Prepare 2L of 1.5 *N* H_2SO_4.

N = wt/Eq. wt X 1000/vol. (ml)

Equivalent weight of H_2SO_4 = 98 / 2 = 49 g/Eq

1.5 = wt/49 X 1000/ 2000 = 147 g dissolve it in water, and dilute to a total of 2 L.

Ex9: Prepare 100 ml of 0.2 *N* NaOH (Na:23 ; O: 16; H: 1).
Molecular weight of sodium hydroxide = 23 + 16 + 1 = 40
Equivalent weight (g/Eq) for NaOH = m. wt/equivalent = 40/1 = 40
N = wt/equivalent X 1000/vol. (ml)
0.2 = wt/40 X 1000/100
Wt = 0.8 g NaOH thus we should dissolve 0.8 g NaOH in water and dilute to 100 ml.

Ex12: Prepare 250 ml of 0.1 *N* sodium carbonate solution. (Na:23; C: 12; O: 16) Results: wt: 1.325 gm.

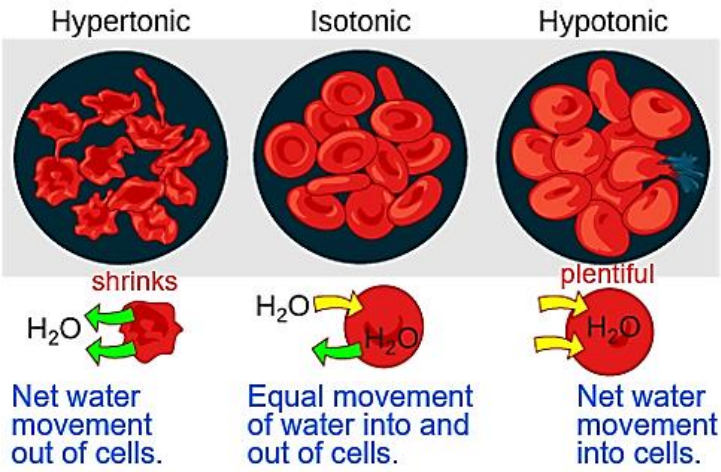
Ex13: Dissolve 5.3 gm of sodium carbonate in water, then complete the volume of the solution to ¼ liter. Compute molarity of solution. (Na: 23; C: 12; O: 16). Results: 0.2 mol/liter.

Ex14: Compute the molarity of 100 milliliter of solution of 0.001 mol of KOH.

M = moles/liter = 0.001/ (100/1000) = 0.01 *M*

Some definitions:

Diffusion: The movement of solute into a solvent or through a solution.
Osmosis: The flow of solvent through a semipermeable membrane.
Osmotic pressure: The pressure exerted during osmosis. Osmotic pressure is expressed in terms of the **osmolarity** of the solution.
Isotonic solution: Solution has the same salt concentration as the salt concentration of blood and is used for transfusion.
Hypotonic solution: Solution has a solute concentration less than that sodium chloride of the blood. If injected into the bloodstream, a **hypotonic solution** can cause hemolysis- the bursting RBC.
Hypertonic solution: Solution has a solute concentration greater than that salt concentration of the blood. If injected into the bloodstream, a **hypertonic solution** may cause crenation or plasmolysis-the shrinking of the RBC.



Osmotic pressure changes the shape of red blood cells in hypertonic, isotonic, and hypotonic solutions.

Questions and Problems:

A. Preparation of Liquid - Liquid Solutions

General method for preparation of diluted acid solution

The normality of concentrated acid can be calculated from the information written on the bottle (percentage % w/w , specific gravity , equivalent weight) according to the equation:-

$$N = \frac{\% \; x \; sp.gr \; x \; 1000}{eq.wt}$$

To calculate the volume of conc. acid that should be taken (diluted) to prepare a specific volume of diluted acid in the selected normality we have to use the equation below:

$N_1 \times V_1 = N_2 \times V_2$

of conc. acid of dilute acid

Notes

1.Dilution is usually carried out by a factor of ten exactly.

2.Density and Specific Gravity

Density = mass/volume (The units are usually grams/mL).

Specific Gravity = (mass of substance)/(mass of equal volume water)

= (Density of substance)/Density of water)

Note that the temperature must be specified for specific gravity. Specific gravity is a unit less ratio (i.e., it doesn't matter what the units are so long the same units are used for

the substance and water). **Specific gravity** is more often used in commerce and commercial reagent labeling than **density**.

Procedure

Transfer (x) mL of concentrated acid into volumetric flask (x) mL using cylinder or pipette, complete to the mark with distilled water and mix well.

A. *Preparation of Approximately 0.1 N Hydrochloric acid*

For HCl

$\%= 37\%$ $Sp.gr=1.18$ $eq.wt=36.5$

So that

Normality = 1.18 × 0.37 × 1000 / 36.5 = 11.96 N ~ 12N

To calculate the volume of conc. HCl that should be taken to prepare (250) mL of (0.1) N HCl

$$12N \times V_1 = 0.1N \times 250\ mL$$

So

V_1 = 2.08 mL should be diluted with distilled water in 250 mL volumetric flask to obtain 0.1N HCl.

B. Preparation of Solid - Liquid Solutions

We can expressed the concentration of solution prepared by dissolving a specific amount of solid substance in a specific volume of solution, in two ways **formal concentration**, and **normal concentration**.

$$\mathbf{M} = \frac{\mathbf{wt\ (g)}}{\mathbf{M.wt}\ (\frac{\mathbf{g}}{\mathbf{mol}})} \times \frac{\mathbf{1000}}{\mathbf{V\ (mL)}} \qquad normality = \frac{no.of\ equivalents}{1 liter\ of\ solution}$$

To calculate the weight need to prepare any one of these concentration in specific volume of solvent we use the equations:

The normality of a solution is the gram equivalent weight of a solute per liter of solution. It may also be called the **equivalent concentration**. It is indicated using the symbol N.

$$N = \frac{Gram\ eq.of\ Solute}{Volume\ of\ sol.in\ litre} = \frac{Weight}{Equivalent\ weight} \times \frac{1000}{V\ ml}$$

$$\text{Equivalent Weight} = \frac{Molar\ Mass}{n}$$

1-Acids :

The molecular formula of sulfuric acid is H_2SO_4.

Its molecular mass is =(1×2)+32+(16×4)=2+32+64=98

The expression for the equivalent weight of an acid is as given below.

$$\text{Equivalent weight} = \frac{\text{Molecular mass}}{\text{Number of replaceable H}}$$

sulfuric acid contains two replaceable hydrogens.

Substitute values in the above expression.

Equivalent weight =98/2=49

2-Bases :

The weight which will furnish 1 mole of H+ or 1 mole of OH- ions is called the **Equivalent weight.**

$Ba(OH)_2 = Ba^{2+} + 2OH^-$

i.e 1 mole of $Ba(OH)_2$ will produce 2 moles of OH^-

The molar mass of $Ba(OH)_2$ is

1(137.3) + 2(16) + 2(1) = 171.3 gm/mole

$Ba(OH)_2$ = Equivalent Weight = $molar\ mass/mole\ factor$ = 171.3/2 = **85.7 g/eq**

3- Salts:

$$\text{Equivalent weight of salt} = \frac{\text{Molecular weight of salt}}{\text{Charge present on ionic form}}$$

$$\text{Molecular weight of } Na_2CO_3 = 106$$

$$Na_2CO_3 \longrightarrow 2Na^+ + CO_3^{2-}$$

$$\text{Charge} = 2$$

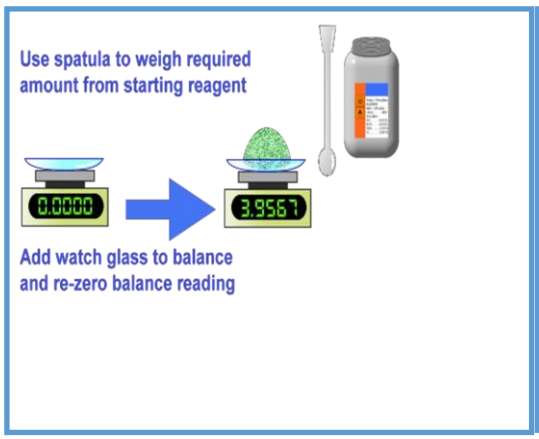
$$\text{Eq. Wt.} = \frac{106}{2} = 53 \text{ g/eq}$$

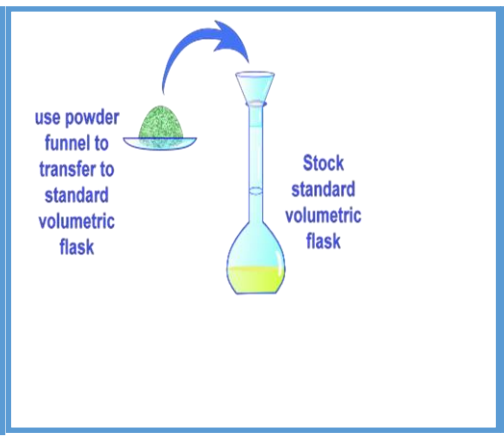
$$\mathbf{wt} = \frac{\mathbf{M} \times \boldsymbol{Mwt} \times \mathbf{V}(\boldsymbol{mL})}{\mathbf{1000}}$$ For formal concentration

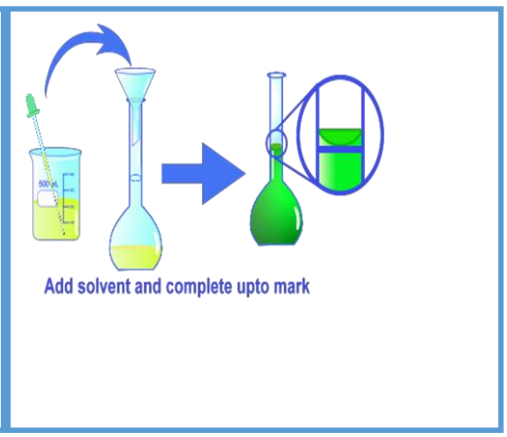
$$Weight = \frac{eq.wt \times N \times v(mL)}{1000}$$ For normal concentration

Procedure

Dissolve (x) gm of solid substance into a small beaker with distilled water and transfer the solution after dissolution into the volumetric flask (x) mL , washing the beaker many times and adding the washing into the volumetric flask for quantitative transferring of the solution, complete to the mark and mix well.





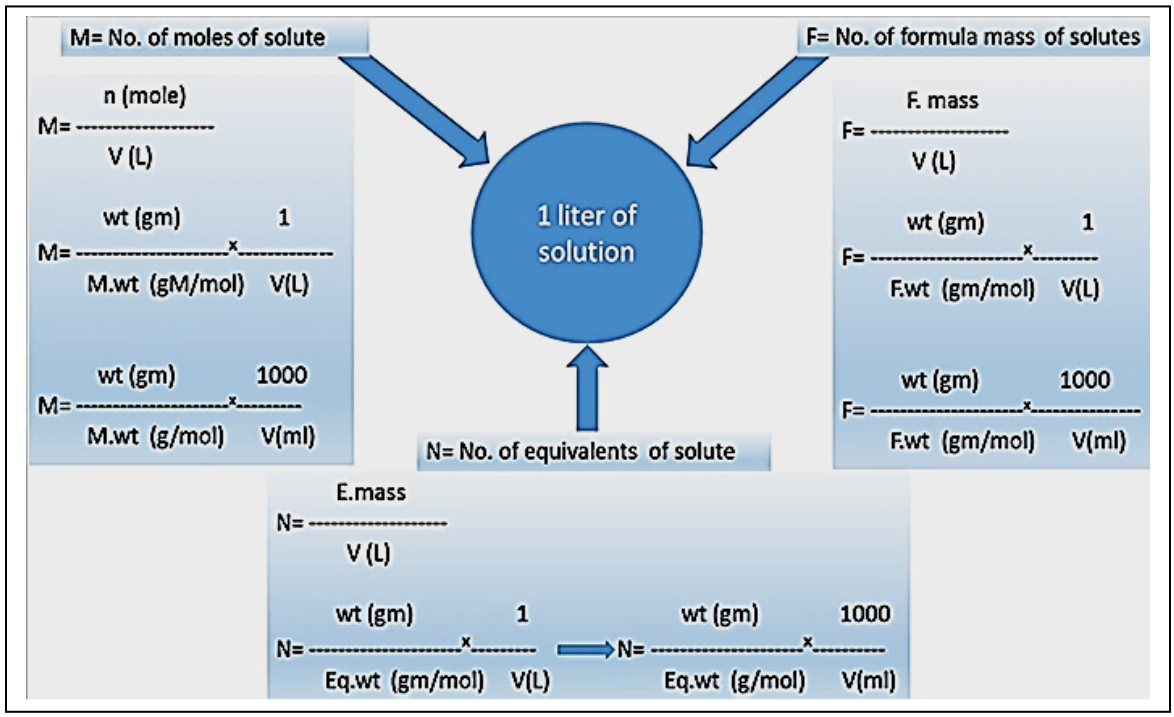


Methods of Expressing the Concentration of a Solution

The concentration of a solution can be expresses in a number of ways. The important methods are:

1- Molarity: is the number of moles of a solute dissolved in a liter of solution.

2- Normality : is the number of equivalents of a solute dissolved in a liter of solution.



Q/ what are the molarity of (125 ml) solution containing of 0.050 moles of HCl ?

A/ before anything : convert ml to L

125ml/1000 = 0.125 L

M= n(mole) / V(L)

M= 0.050 / 0.125= 0.40 mol/L

Q/ you dissolve 152.5 gm of $CuCl_2$ in water to make solution with final volume of 2.25 L what is the molarity ?

A/ M.wt ($CuCl_2$)= 63.55 + (2×35.44)= 134.45 gm/mol

n= wt/M.wt

n=152.5 / 134.45= 1.134 mol M=

n/v (L) = 1.134 / 2.25

M= 0.504 mol/L

Chapter 4: *Oxidation-Reduction*

CHAPTER OUTLINE: The student will be able to:-

Oxidation-reduction
Oxidizing agents & reducing agents
Importance of oxidation-reduction: *cleaner Effects, Effects on hair protein, and Stain removal*

Oxidation: May be defined as "a loss of electrons". Consider the electron-dot structures in reaction 4-1. The sodium atom has one outer electron. When the sodium atom loses this one electron, it forms a sodium ion with a +1 charge: **This loss of an electron is defined as oxidation**. Therefore, the sodium atom was oxidized.

$$Na\bullet + \bullet\ddot{Cl}: \longrightarrow Na^{+} + :\ddot{Cl}:^{-} \qquad (4\text{-}1)$$

A second definition of **oxidation** states that it is **an increase in oxidation number**. Consider reaction 4-2.

$$2Na + Cl_2 \longrightarrow 2NaCl \qquad (4\text{-}2)$$

An uncombined element has an oxidation number of zero. The oxidation number of sodium in sodium chloride (NaCl) is +1 and that of chlorine -1. Therefore, reaction 4-2 may be written as follows.

$$\overset{0}{2Na} + \overset{0}{Cl_2} \longrightarrow \overset{+1}{2Na} + \overset{-1}{2Cl}$$

The sodium has changed in oxidation number from zero to +1, This is oxidation. The sodium atom was oxidized. The cells in the body burn glucose producing carbon dioxide (CO_2), water, and energy.

$$\underset{\text{glucose}}{\overset{0}{C_6H_{12}O_6}} + \overset{0}{6O_2} \longrightarrow \overset{+4}{6CO_2} + 6\overset{-2}{H_2O} + \text{energy}$$

The oxidation number of each carbon atom in glucose is zero. The oxidation number of the carbon atom in carbon dioxide is +4. † Therefore, the carbon atom increased in oxidation number. A gain in oxidation number is oxidation; therefore, the carbon atom in glucose was oxidized, or it can be said that the glucose, which contain the carbon atom, was oxidized.

A third definition of **oxidation** is "**addition of oxygen**." Consider reaction 4-3, which involves the oxidation of formaldehyde to formic acid.

$$\underset{\text{Formaldehyde}}{HCHO} + [O] \longrightarrow \underset{\text{formic acid}}{HCOOH} \qquad (4\text{-}3)$$

Note that this reaction involves the addition of oxygen.

A fourth definition of **oxidation** involves the "**removal of hydrogen**" in reaction 4-4

$$\underset{\text{ethanol}}{CH_3CH_2OH} + [O] \longrightarrow \underset{\text{acetaldehyde}}{CH_3CHO} + H_2O \qquad (4\text{-}4)$$

The following oxidation reactions take place in the body.

$$\text{Carbohydrate} + O_2 \longrightarrow CO_2 + H_2O + \text{energy}$$

$$\text{fat} + O_2 \longrightarrow CO_2 + H_2O + \text{energy}$$

$$\text{protein} + O_2 \longrightarrow CO_2 + H_2O + \text{urea} + \text{energy}$$

Thus, oxidation may be defined as

1. A loss of electrons
2. An increase in oxidation number
3. A gain of oxygen
4. A loss of hydrogen

Reduction: reduction is the opposite of oxidation;

1. A gain of electrons
2. A decrease in oxidation number
3. A loss of oxygen
4. A gain of hydrogen

$$\underset{\text{acetic acid}}{CH_3COOH} + H_2 \longrightarrow \underset{\text{ethanol}}{CH_3CH_2OH} + H_2O \qquad (4\text{-}5)$$

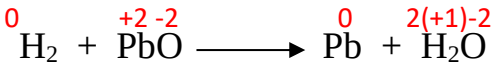
$$\underset{\text{acetone}}{CH_3COCH_3} + H_2 \longrightarrow \underset{\text{isopropyl alcohol}}{CH_3CH(OH)CH_3} \qquad (4\text{-}6)$$

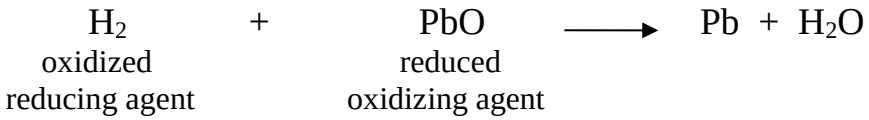
- Oxidation is when there is an increase in oxidation number; Reduction is when there is a decrease in oxidation number.

Oxidizing agents & Reducing agents:

Reducing agent- The substance that causes the reduction of an element or compound.

Oxidizing agent- The substance that causes the oxidation of an element or compound.





Oxidation and reduction reactions produce the energy the body needs to carry out its normal functions. Oxidation-reduction in the body involves either oxygen or hydrogen, or both.

Enzymes involved in oxidation-reduction reactions in the body is called **oxidoreductases**. Many of these enzymes are present in the mitochondria. These enzymes are responsible for the production of heat and energy.

Importance of oxidation-reduction:

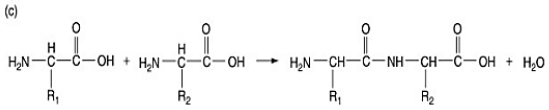
Antiseptic effects- Because they are oxidizing agents, many antiseptics have the property of killing bacteria. Among these is *chlorine*, which oxidizes organic matter and bacteria and so is used in the treatment of water to make it potable. *Calciumhypochlorite* $Ca(OCl)_2$, another commonly used oxidizing agent and bleaching powder, is used as disinfectant for clothes and hospital beds. Tab. 4-1 lists some of the common antiseptics that are oxidizing agents.

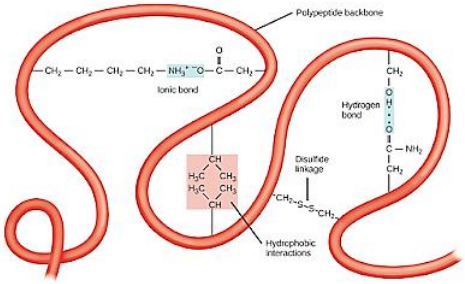
Table 4-1, Antiseptic agents

Formula	Name	Use
3%H_2O_2	Hydrogen peroxide	More cuts and scratches
$KMnO_4$	Potassium permanganate	Treatment of infection in urethra & bladder
$KClO_3$	Potassium chlorate	Treatment of sore throat
I_2 in H_2O	Lugol's solution	Treatment of minor cuts
NaOCl	Sodium hypochlorite (Dakin's solution)	Treatment of wounds

Formaldehyde and sulfur dioxide are two reducing agents used in disinfecting rooms formerly occupied by patients with contagious diseases.

Effects on hair protein- Oxidizing and reducing agents denature protein by affecting the disulfide bonds of the amino acid cysteine.





Stain removal-Oxidizing and reducing agents are used to remove most stains that cannot otherwise be removed. Common stain removers and indicates where they may be used safely (H_2O_2, $KMnO_4$, and sodium hypochlorite, NaOCl;) are oxidizing agent. ($Na_2S_2O_3$), sodium thiosulfate and oxalic acid $[COOH]_2$ are reducing agent.

Redox Reactions in Biology

What is the purpose of redox reactions in the cell?

Many biological processes involve redox reactions, such as in cellular respiration and photosynthesis.

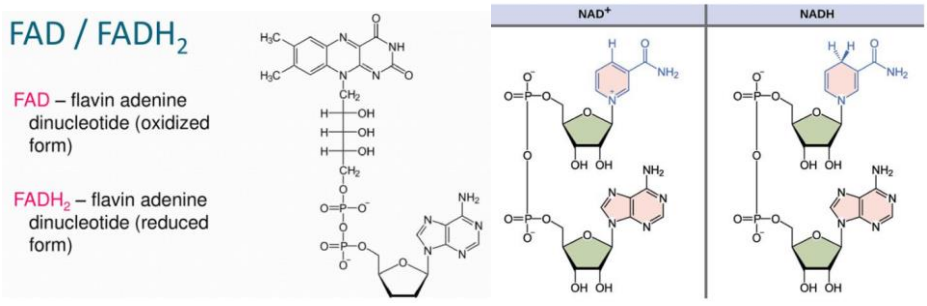
Cellular respiration

Cellular respiration ($C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O$) is the oxidation

of glucose into carbon dioxide (CO2) and reduction of oxygen (O2) to water (H2O).

The method of cellular respiration redox is related to the reduction and oxidation of NAD+ into NADH and vice versa. Below is a schematic diagram of cellular respiration. schematic diagram of cellular respiration.

(NADH) nicotinamide adenine dinucleotide



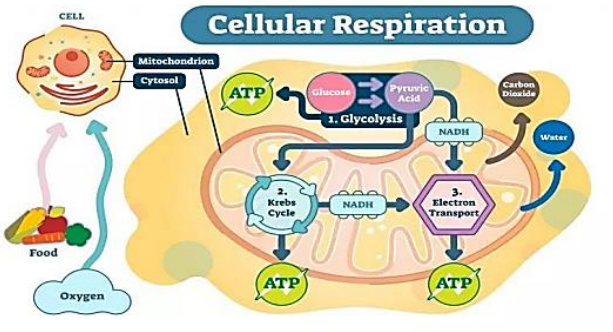


Figure 1: Schematic diagram of aerobic respiration as a form of cellular

Respiration. There are many instances where in redox occurs in this biological process. An example is the oxidation of glucose during glycolysis where NAD+ is reduced, thereby, producing NADH. This is is reduced, thereby, producing NADH. This is also, what occurs involving the other electron carriers, such as FAD producing FADH2. And the steps of the citric acid cycle are, in fact, a series of redox reactions.

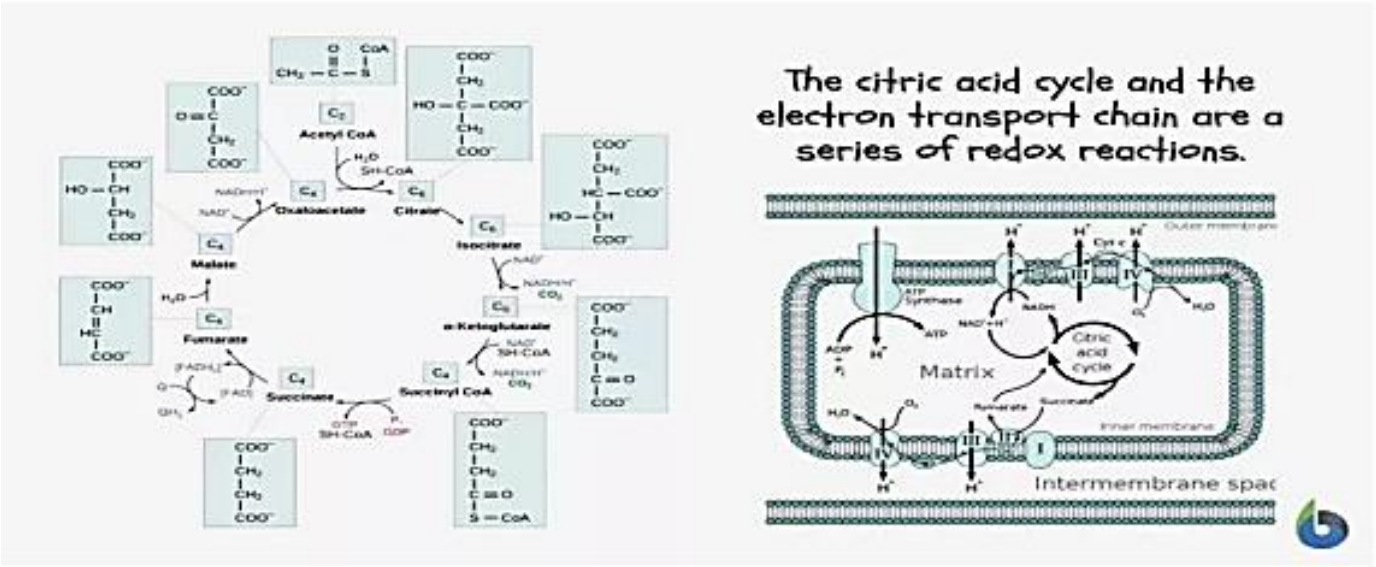


Figure 2: Citric acid cycle (left) and electron transport chain (right) are

shown to illustrate redox reactions. Photosynthesis In redox reactions in photosynthesis ($6\ CO_2 + 6\ H_2O$ + light energy $\rightarrow C_6H_{12}O_6 + 6\ O_2$),

Carbon dioxide is reduced into sugar and water oxidation gives molecular oxygen. The number of electrons in oxygen is 8. Although cellular respiration and photosynthesis appear like opposite reactions, these two processes are not reverse of each other.

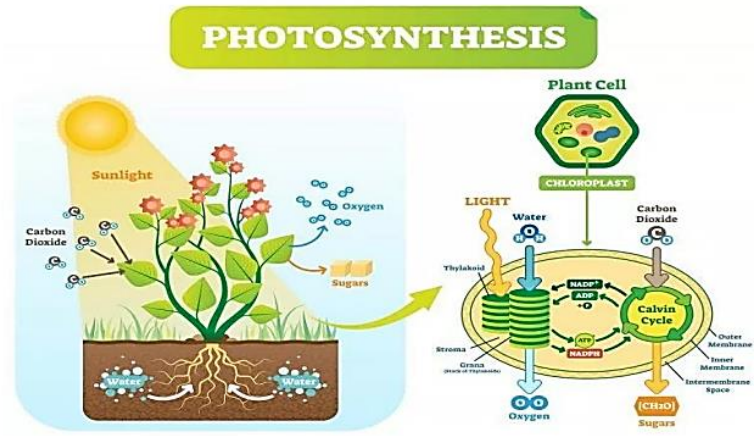


Figure 3: Photosynthesis involves the losing and gaining of electrons, which unlike in cellular respiration, is driven by light (photon)

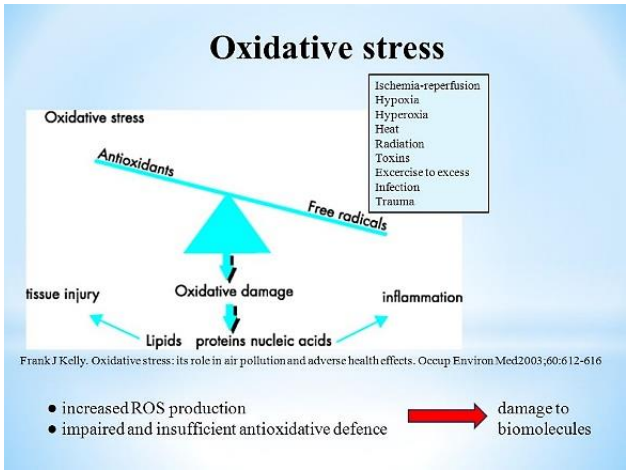
References:

1. Dickson, T. R. *introduction to chemistry*, 4th ed. John Wiley & Sons, Int., New York, 1983, chapter 13.
2. McQUARRIE, DONALD A. and Peter A. Rock. *General chemistry* , W. H. Freeman and Company, New York, 1984, chapter 24.
3. Chemistry for the Health Sciences, George, 5th ed., 1985.

Oxidation stress in the eye

What is oxidative stress?

- Oxygen is necessary for life. Our bodies constantly react withoxygen as we breathe and our cells produce energy, resulting in theproduction of free radicals such as Reactive Oxygen Species (ROS)and Reactive Nitrogen Species (RNS).
- Free radicals are "live wires" and interact with other molecules inside cells, harming cells if the interactions are uncontrolled.
- Oxidative stress occurs during normal respiration, digestion, and metabolism, and is necessary for living cells to survive.
- It also drives critical signaling pathways that create normal tissues,heal wounds, and allow adaptation to stress and disease.
- There is no way to avoid oxidative stress because it is a normal process occurring during routine living and aging, from exposure to UV (ultraviolet) light, and from normal cellular metabolism.
- In healthy tissues, the body balances the normal oxidative stress of daily living by using antioxidants (such as grapeseed extract and omega 3 fatty acids) to control and balance free radicals.
- Damage and disease occur when this balance is lost. The formationof unbalanced free radicals from oxidative stress can set off a chainreaction that damages DNA or cell membranes, often causing cell death.
- Many antioxidants, such as vitamin C and green tea extract, are well-proven to provide protection against oxidative stress.



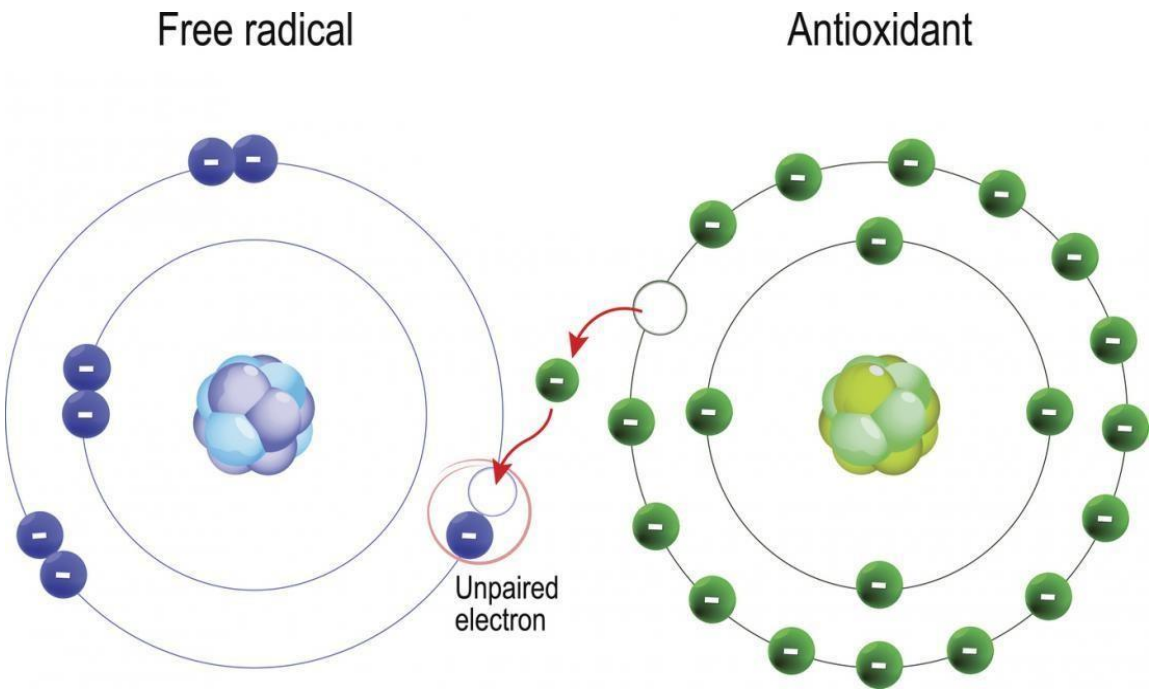
Free radical

A free radical is a molecule or molecular fragment that contains one or more unpaired electrons in its outer orbital .

Free radical is generally represented by a superscript dot, (R•).

Oxidation reactions ensure that molecular oxygen is completely reduced to water.

The products of partial reduction of oxygen are highly reactive and createhavoc in the living systems. Hence, they are also called Reactive oxygen species or ROS.

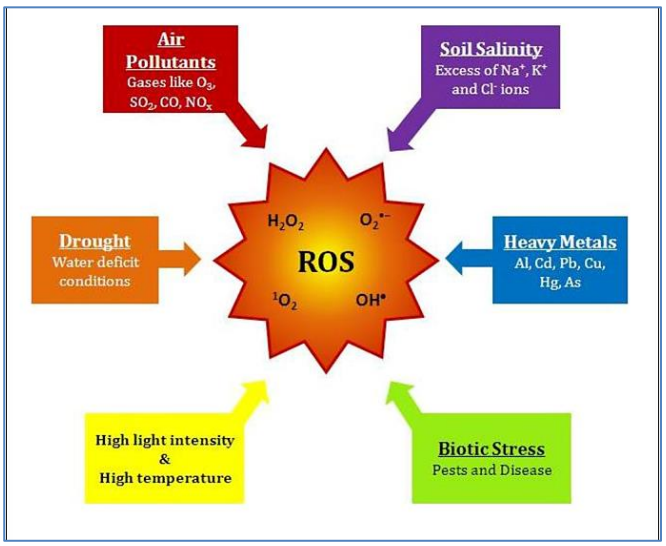


Formation of Free Radicals

- By Reduction-Oxidation reactions during normal metabolicprocess.
- Primary source is our body during energy production
- Enzymatic Metabolism of exogenous chemicals and drugs.
- During Inflammation.
- Prolonged low blood flow states (atherosclerosis, heart attacks &stroke)
- Environmental contaminants
- Tobacco (Smoking) is a major oxidative stress, that is a source ofmutagens.
- Absorption of Radiation energy
- Diet (fatty and processed foods)
- Low levels of antioxidants

The following are members of this group:

1. Superoxide anion radical (O2 --•)
2. Hydroperoxyl radical (HOO•)
3. Hydrogen peroxide (H2O2)
4. Hydroxyl radical (OH•) Lipid peroxide radical (ROO•)
5. Singlet oxygen (1O2)
6. Nitric oxide (NO•)
7. Peroxy nitrite (ONOO--•).



- **What is the main cause of oxidative stress?**

Oxidative stress is a phenomenon caused by an imbalance between production and accumulation of oxygen reactive species (ROS) in cells and tissues and the ability of a biological system to detoxify these reactive products.

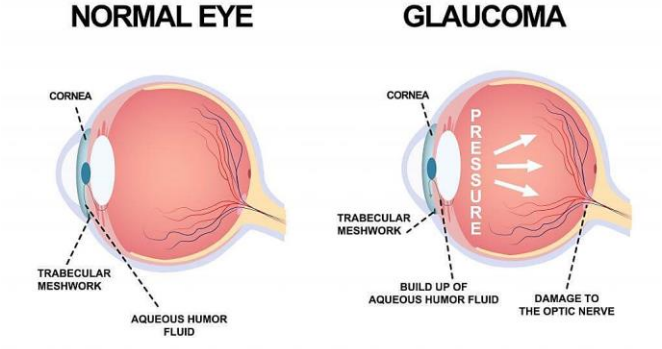
- Oxidative Stress • It is imbalance between free radicals and antioxidants in the body.

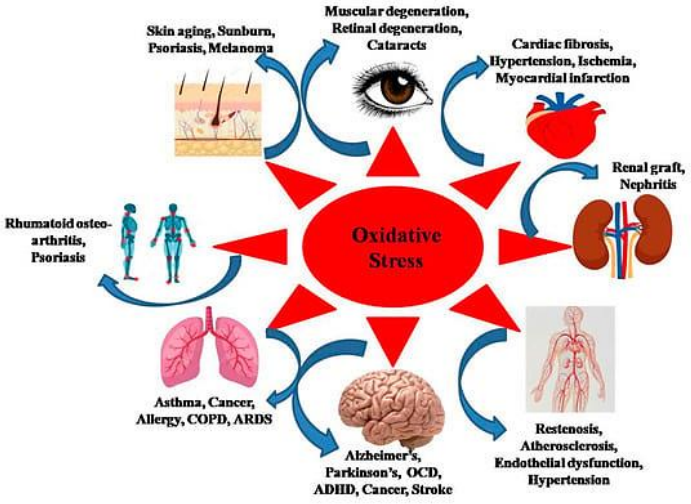
  • Under normal conditions, cells are able to balance the productionof oxidants and antioxidants. Oxidative stress occurs when cells aresubjected to excess levels of ROS or as a result of antioxidant depletion.

  • It is harmful because ROS attack biological molecules such as lipids, proteins, and DNA that involved in the pathogenesis oflifestyle-related diseases.

- **Risks and consequences of oxidative stress**.

The eye is an organ that is predisposed to great levels of oxidative stress. The eye is constantly exposed to factors such as radiation, chemicals, oxygen, drugs, which induce the formation of reactive oxygen species (ROS) that can ultimately damage cells.





What are the symptoms of oxidative stress?

Why is it a problem?

- Fatigue.
- Memory loss and/or brain fog.
- Muscle and/or joint pain.
- Decreased eye sight.
- Headaches and sensitivity to noise.
- Susceptibility to infections.

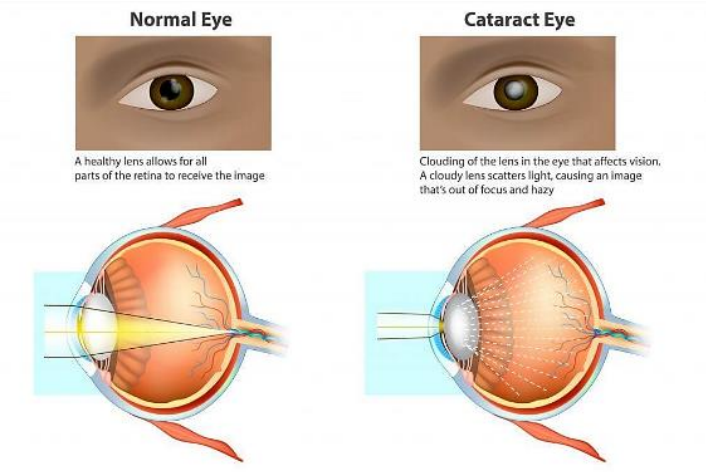
Does oxidative stress cause glaucoma?

These findings suggest that intraocular pressure increase, which characterizes most glaucomas, is related to oxidative and degenerative processes affecting the more specifically, its endothelial cells.

This supports the theory that glaucomatous damage is the pathophysiological consequence of oxidative stress.

Does oxidative stress cause cataracts?

Cataracts are the leading cause of blindness . Opacity of the lens is a direct result of oxidative stress. Cataracts occur primarily due to age, but also are common in diabetes where superoxide in the mitochondria is elevated as a result of hyperglycemia.



Cataracts are a clouding of the lens. Medical illustration of a normal eye and an eye with a cataract, clouded lens

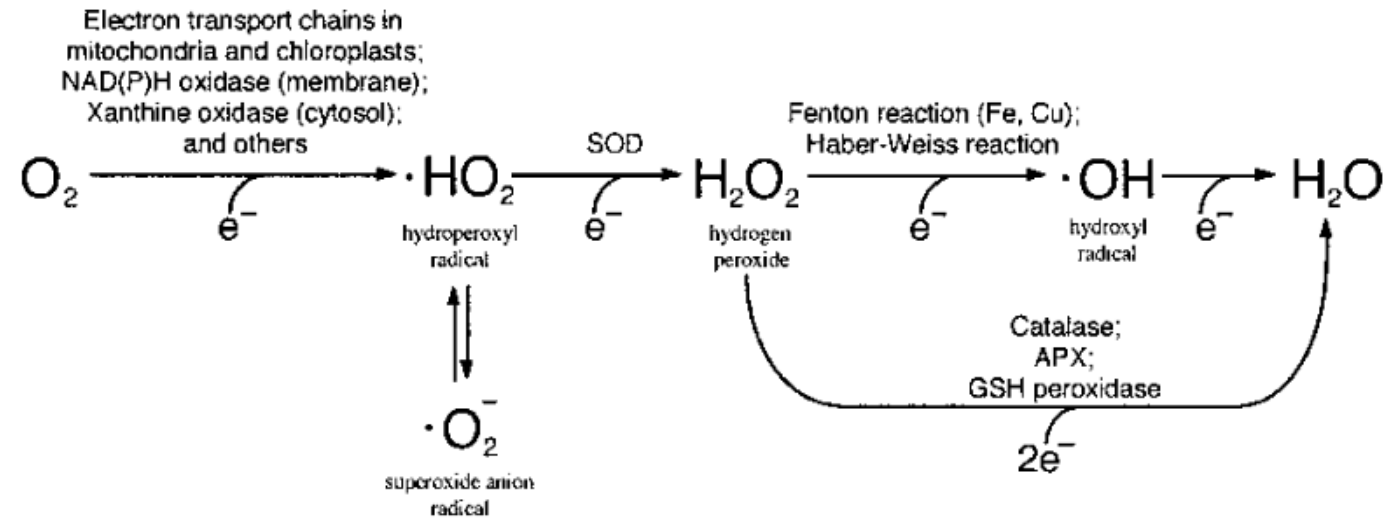
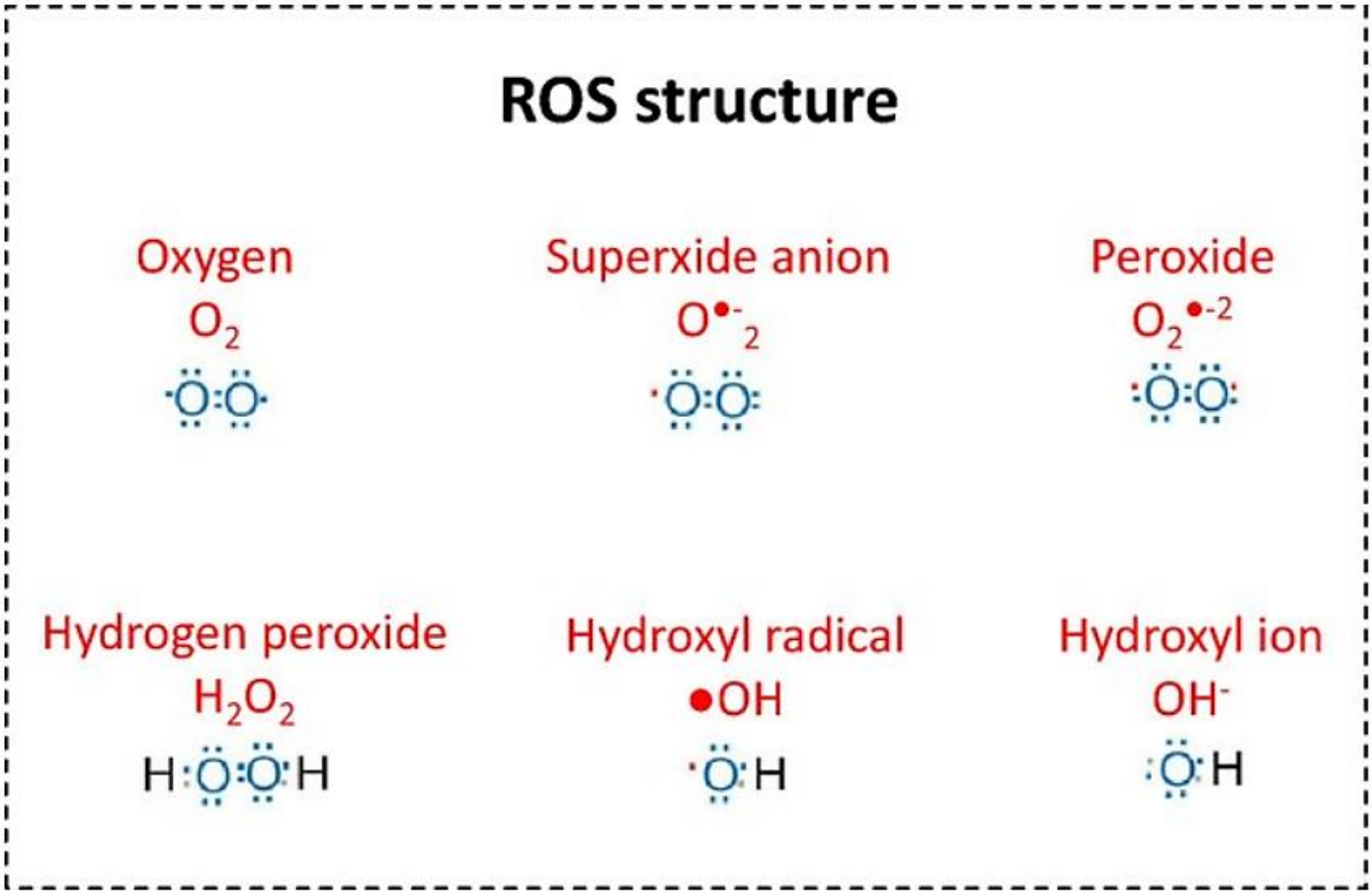


Figure 1. Metabolic pathways of reactive oxygen species in plants. Some of the important enzymes in reactive oxygen species metabolic pathways are illustrated. APX, ascorbate peroxidase; GSH, glutathione; SOD… Expand

Published in 2004

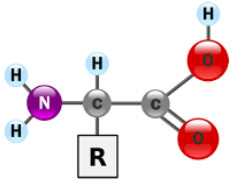
Update on Reactive Oxygen Species Activation of Ca 2 1 Channels Reactive Oxygen Species Activation of Plant Ca 2 1 Channels . A Signaling Mechanism in Polar Growth , Hormone Transduction , Stress Signaling , and Hypothetically Mechanotransduction 1



D. Hayder K. Khattar Althalme

2023

Amino Acids



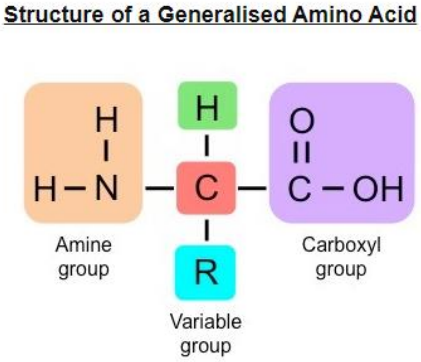
- Amino Acids are the building units of proteins. Proteins are polymers of amino acids linked together by what is called " Peptide bond" (see latter).
- There are about 300 amino acids occur in nature. Only 20 of them occur in proteins.

Structure of amino acids:

Each amino acid has 4 different groups attached to α- carbon (which is C-atom next to COOH). These 4 groups are : amino group, COOH gp,

Hydrogen atom and side

Chain (R)



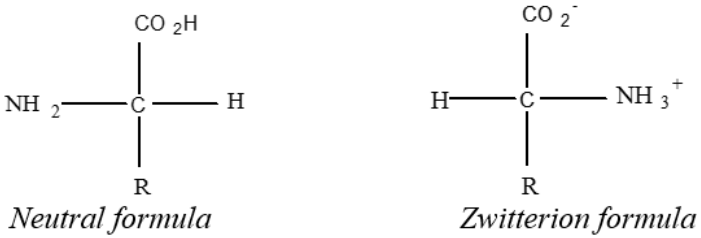
- **At physiological PH (7.4), -COOH gp is dissociated forming a negatively charged carboxylate ion (COO^-) and amino gp is protonated forming positively charged ion (NH_3^+) forming Zwitter ion**
- **N.B. Proline is an imino acid not amino acid (see latter)**

Classification of amino acids

I- Chemical classification: According to number of COOH and NH_2 groups i.e. according to net charge on amino acid.

A- Monobasic, monocarboxylic amino acids i.e. neutral or uncharged:

The α-amino acids in peptides and proteins (excluding proline) consist of a carboxylic acid (**-COOH**) and an amino (**-NH_2**) functional group attached to the same tetrahedral carbon atom. This carbon is the α-carbon.
Distinct R-groups, that distinguish one amino acid from another, also are attached to the alpha-carbon (except in the case of glycine where the R-group is hydrogen). The fourth substitution on the tetrahedral α-carbon of amino acids is hydrogen.



Neutral formula *Zwitterion formula*

General structure of amino acids. Neutral formula never found in the body.

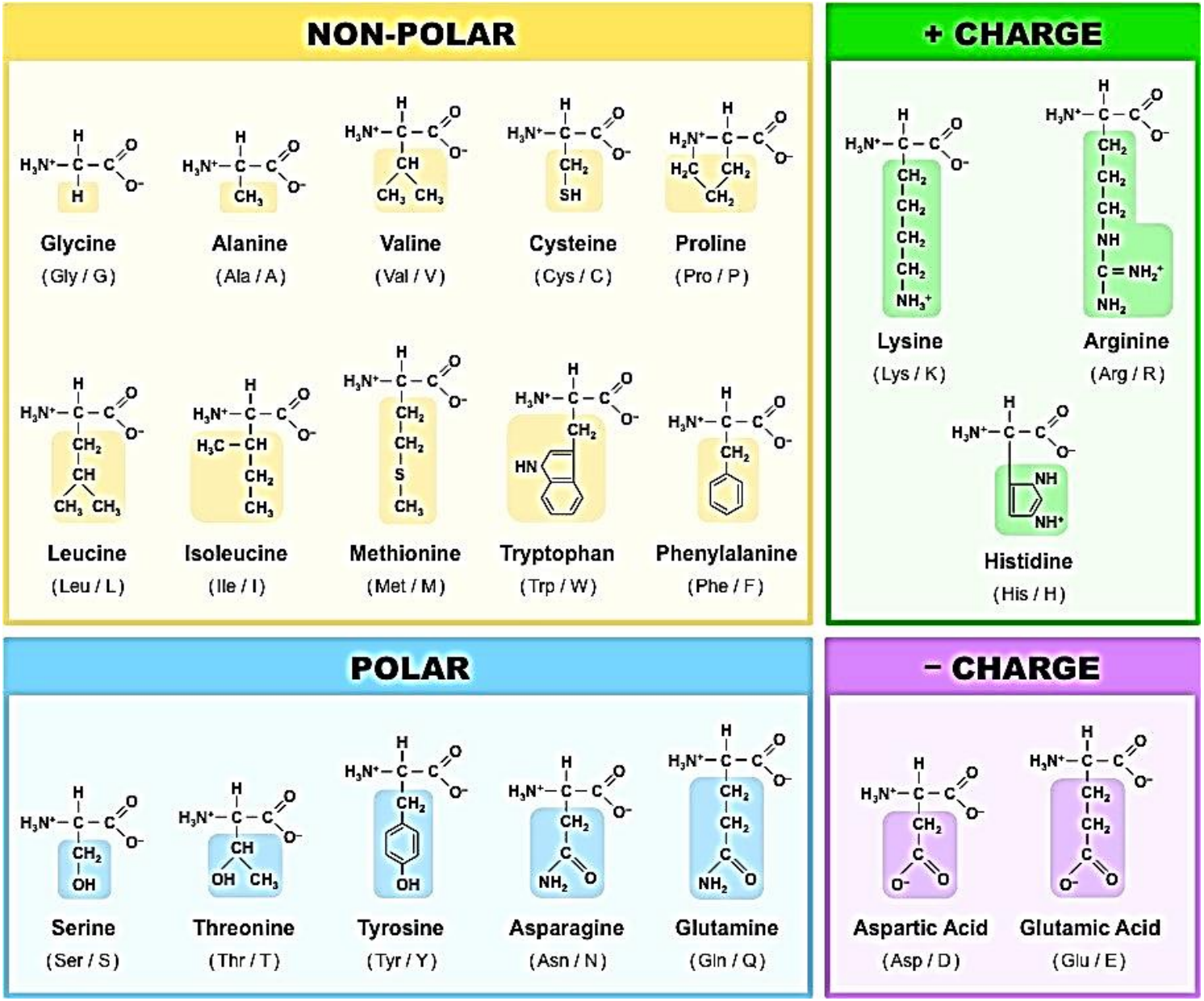
Acid-Base Properties of the Amino Acids

The α -COOH and α -NH_2 groups in amino acids are capable of ionizing (as are the acidic and basic R-groups of the amino acids). As a result of their ionizability the following ionic equilibrium reactions may be written:

R-COOH = R-COO^- + H^+

R-NH_3^+ = R-NH_2 + H^+

#-At physiological pH (around 7.4) the carboxyl group will be unprotonated and the amino group will be protonated. An amino acid with no ionizable R-group would be electrically neutral at this pH. This species is termed a **zwitterion**.



The 20 Universal Amino Acids

Subclassification of neutral amino acids:

All structures are required (See structures in hand out)

1- Glycine R= H

2- Alanine R= CH_3

3- Branched chain amino acids: R is branched such as in:

a -**Valine** R= isopropyl gp

b- **Leucine** R= isobutyl gp

c- **Isoleucine** R = is isobutyl

R is isobutyl in both leucine and isoleucine but branching is different:

in leucine → branching occurs on γ carbon

in isoleucine→ branching occurs on β- carbon

4- Neutral Sulfur containing amino acids:

e.g. Cysteine and Methionine. What is cystin?

5- Neutral, hydroxy amino acids:

e.g. Serine and Threonine

Optical Properties of the Amino Acids

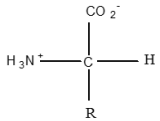
A tetrahedral carbon atom with 4 distinct constituents is said to be **chiral**. The one amino acid not exhibiting chirality is glycine .

&&-Chirality describes the handedness of a molecule that is observable by the ability of a molecule to rotate the plane of polarized light either to the right (**dextrorotatory**) or to the left (**levorotatory**).

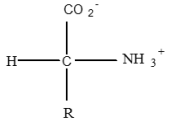
All of the amino acids in proteins exhibit the same absolute steric configuration as **L-glyceraldehyde**. Therefore, they are all L-α-amino acids.

&&-D-amino acids are never found in proteins, although they exist in nature. D-amino acids are often found in polypetide antibiotics.

The aromatic R-groups in amino acids absorb ultraviolet light with an absorbance maximum in the range of 280nm. The ability of proteins to absorb ultraviolet light is predominantly due to the presence of the tryptophan which strongly absorbs ultraviolet light.



L-amino acid



D-amino acid

6- Neutral aromatic amino acids:

a- Phenyl alanine : It's alanine in which one hydrogen of CH_3 is substituted with phenyl group. So it's called phenyl alanine

b- Tyrosine: - it is P- hydroxy phenyl alanine

- it is classified as **phenolic amino acid**

c-Tryptophan: as it contains indole ring so it is classified as **heterocyclic amino acid**

7- Neutral heterocyclic amino acids:

a- Tryptophan: contains indole ring

b- Proline: In proline, amino group enters in the ring formation being α-imino gp so proline is an α-imino acid rather than α-amino acid

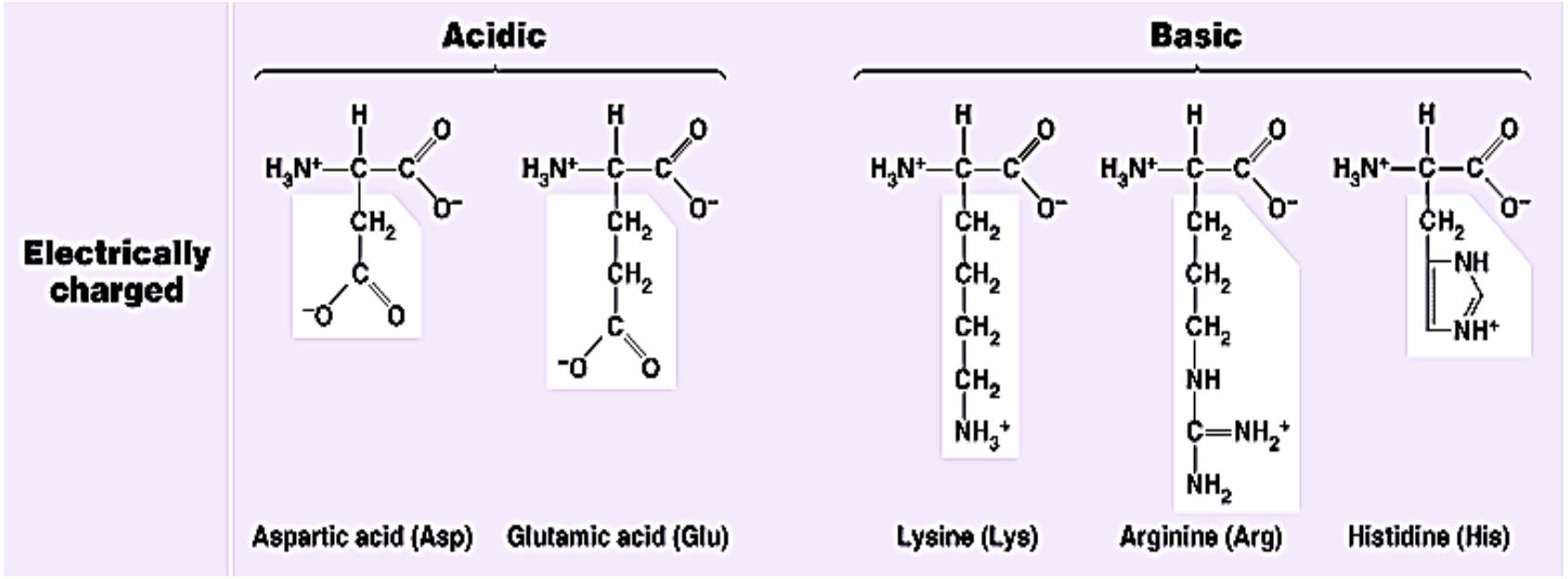
B- Basic amino acids: Contain two or more NH_2 groups or nitrogen atoms that act as base i.e. can bind proton.

At physiological pH, basic amino acids will be **positively charged** e.g.

a- Lysine

b-Arginine: contains guanido group

c-Histidine: is an example on basic heterocyclic amino acids



C- Acidic Amino acids: at physiological pH will carry negative charge.
e.g. Aspartic acid (aspartate) and Glutamic acid (glutamate). see structures in hand out.

Aspargine and Glutamine: They are amide forms of aspartate and glutamate in which side chain COOH groups are amidated.
They are classified as neutral amino acids.

II- Classification according to polarity of side chain (R):

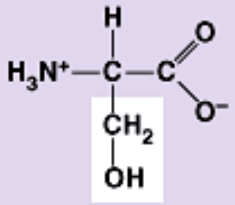
A- Polar amino acids: in which **R** contains polar **hydrophilic group** so can forms hydrogen bond with H_2O. In those amino acids, **R** may contain:

1- OH group : as in serine, threonine and tyrosine
2- SH group : as in cysteine
3- amide group: as in glutamine and aspargine
4- NH_2 group or nitrogen act as a base (basic amino acids): as lysine, arginine and histidine
5- COOH group (acidic amino acids): as aspartic and glutamic .

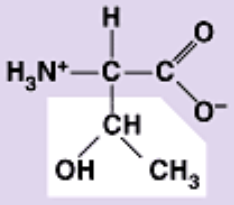
B- Non polar amino acids:

R is alkyl **hydrophobic group** which can't enter in hydrogen bond formation. **9 amino acids** are non polar (glycine, alanine, valine, leucine, isoleucine, phenyl alanine, tryptophan, proline and methionine)

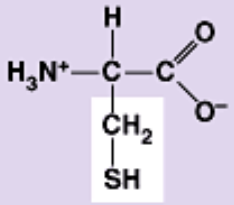
Polar



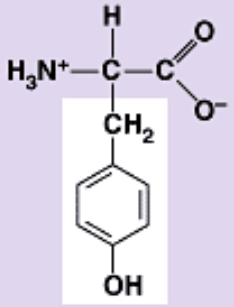
Serine (Ser)



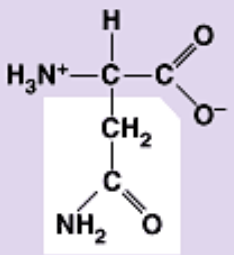
Threonine (Thr)



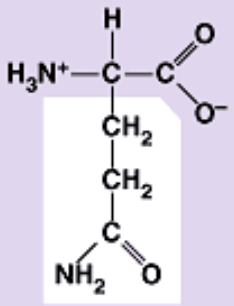
Cysteine (Cys)



Tyrosine (Tyr)

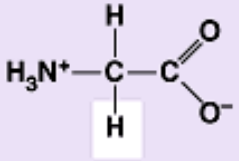


Asparagine (Asn)

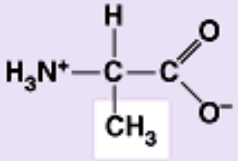


Glutamine (Gln)

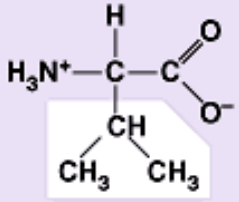
Nonpolar



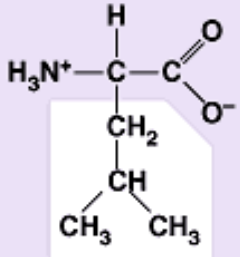
Glycine (Gly)



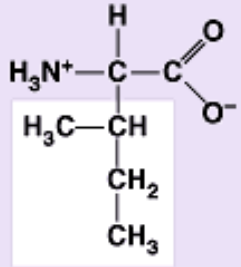
Alanine (Ala)



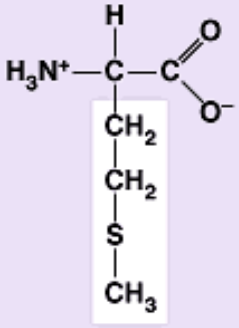
Valine (Val)



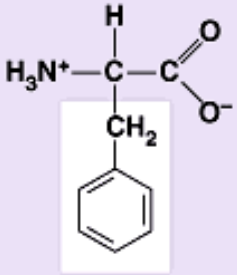
Leucine (Leu)



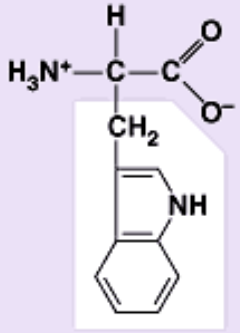
Isoleucine (Ile)



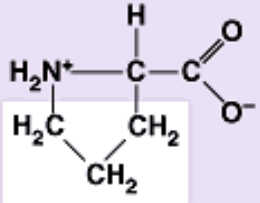
Methionine (Met)



Phenylalanine (Phe)



Tryptophan (Trp)



Proline (Pro)

III- Nutritional classification:

1- Essential amino acids: These amino acids can't be formed in the body and so, it is essential to be taken in diet. Their deficiency affects growth, health and protein synthesis.

2- Semiessential amino acids: These are formed in the body but not in sufficient amount for body requirements especially in children.

Summary of essential and semiessential amino acids:

V= valine i= isoleucine l= lysine l= leucine

A = arginine* H= histidine* M= methionine

T= tryptophan Th= threonine P= phenyl alanine

*= arginine and histidine are semiessential

3- Non essential amino acids: These are the rest of amino acids that are formed in the body in amount enough for adults and children. They are the remaining 10 amino acids.

IV- Metabolic classification: according to metabolic or degradation products of amino acids they may be:

1- Ketogenic amino acids: which give ketone bodies. **Lysine** and **Leucine** are the only pure ketogenic amino acids.

2- Mixed ketogenic and glucogenic amino acids: which give both ketonbodies and glucose. These are: **isoleucine, phenyl alanine, tyrosine and tryptophan.**

3- Glucogenic amino acids: Which give **glucose**. They include the rest of amino acids. These amino acids by catabolism yields products that enter in **glycogen and glucose formation**.

Amphoteric properties of amino acids: that is they have both basic and acidic groups and so can act as base or acid.

Neutral amino acids (monobasic, monocarboxylic) exist in aqueous solution as " Zwitter ion" i.e. contain both positive and negative charge. Zwitter ion is electrically neutral and can't migrate into electric field.

Isoelectric point (IEP) = is the pH at which the zwitter ion is formed.

e.g IEP of alanine is 6

Chemical properties of amino acids:

1- Reactions due to COOH group:

-Salt formation with alkalis, ester formation with alcohols, amide formation with amines and decarboxylation

2- Reactions due to NH_2 group:

deamination and reaction with ninhydrin reagent.

-Ninhydrin reagent reacts with amino group of amino acid yielding blue colored product. The intensity of blue color indicates quantity of amino acids present. Ninhydrine can react with imino acids as proline and hydroxy proline but gives **yellow color.**

3- Reactions due to side chain (R):

1- Millon reaction: for tyrosine gives red colored mass

2- Rosenheim reaction: for trptophan and gives violet ring.

3- Pauly reaction: for imidazole ring of histidine: gives yellow to reddish product

4- **Sakagushi test:** for guanido group of arginine andgives red color.

5- Lead sulfide test (sulfur test): for sulfur containing amino acids as cysteine give brown color.

Fate of α-amino group:

Q/ what is the fate of α-amino group?

A/ In times of dietary surplus, the potentially toxic nitrogen of amino acids is eliminated

1-Transamination to other α-keto acids. 2-Glutamate by oxidative demination releases free amino group to produce α-ketoglutarate (α-KG) 3-(-NH_4^+) converted into urea by urea cycle.

Peptides and Proteins

20 amino acids are commonly found in protein.

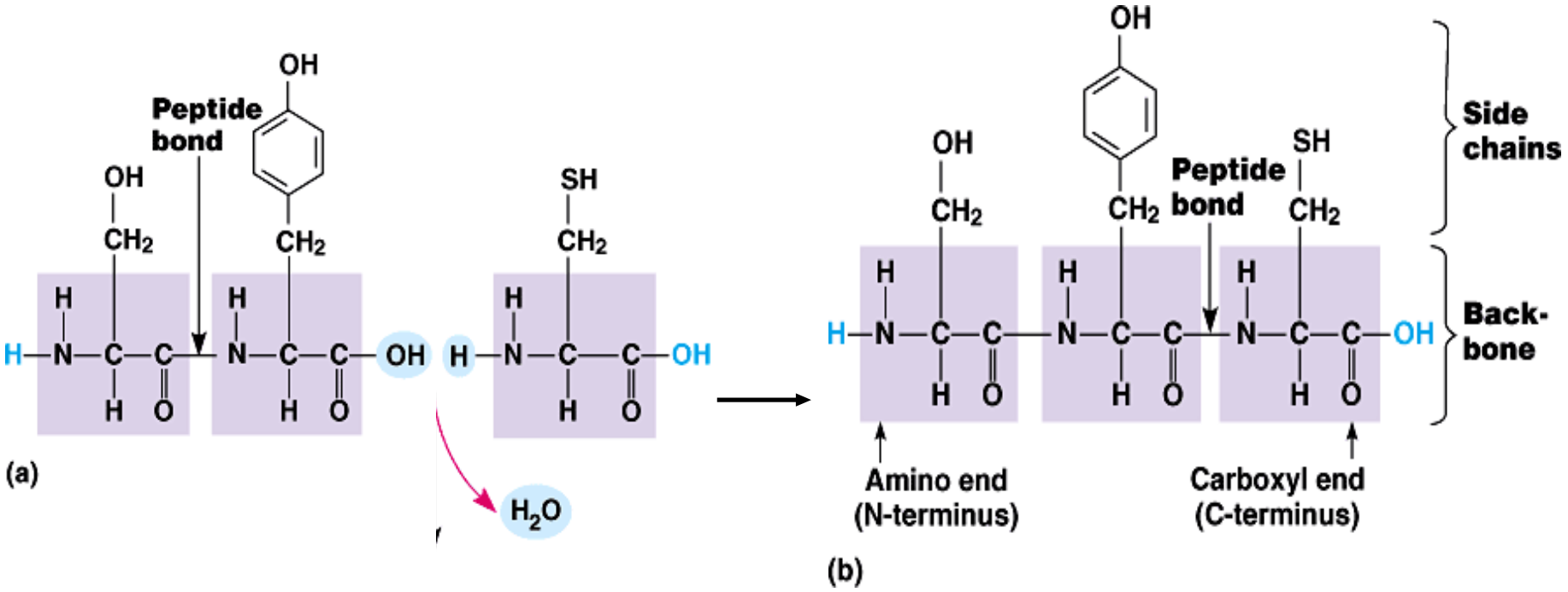
These 20 amino acids are linked together through "peptide bond forming peptides and proteins (what's the difference?).

- The chains containing less than 50 amino acids are called **"peptides",** while those containing greater than 50 amino acids are called **"proteins".**

Peptide bond formation:

α-carboxyl group of one amino acid (with side chain R1) forms a covalent peptide bond with α-amino group of another amino acid (with the side chain R2) by removal of a molecule of water. The result is : **Dipeptide** (i.e. Two amino acids linked by one peptide bond). By the same way, the dipeptide can then forms a second peptide bond with a third amino acid (with side chain R3) to give **Tripeptide.** Repetition of this process generates a polypeptide or protein of specific amino acid sequence.

Peptide bond formation:



- Each polypeptide chain starts on the left side by free amino group of the first amino acid enter in chain formation . It is termed (N- terminus).
- Each polypeptide chain ends on the right side by free COOH group of the last amino acid and termed (C-terminus).

***Importance of Peptides:**

1. A number of hormones (e.g. Insulin) and some neurotransmitters are peptides.
2. Several antibiotics (e.g. Gramacidin and Valinomycin) are peptides.
3. Some antitumor agents are peptides (e.g.Bleomycin).

#-The presence of the carbonyl group in a peptide bond allows electron resonance stabilization to occur such that the peptide bond exhibits rigidity not unlike the typical -C=C- double bond. The peptide bond is, therefore, said to have **partial double-**

Examples on Peptides:

1- Dipeptide (tow amino acids joined by one peptide bond):

Example**:** **Aspartame** which acts as **sweetening agent** being used in replacement of cane sugar. It is composed of **aspartic acid** and **phenyl alanine.**

2- Tripeptides (3 amino acids linked by two peptide bonds).

Example: **GSH** which is formed from 3 amino acids: **glutamic acid, cysteine** and **glycine**. It helps in absorption of amino acids, protects against hemolysis of RBC by breaking H_2O_2 which causes cell damage.

3- octapeptides: (8 amino acids)

Examples: Two hormones; oxytocine and vasopressin (ADH).

4- polypeptides: 10- 50 amino acids: e.g. Insulin hormone

Protein structure:

There are four levels of protein structure (primary, secondary, tertiary and quaternary), Protein is a polymer of more than 100 amino acids. Each of them is called residue. There are 4 basic levels of structure in protein architecture.

Primary structure:

- The **primary structure** of a protein is its unique sequence of amino acids.

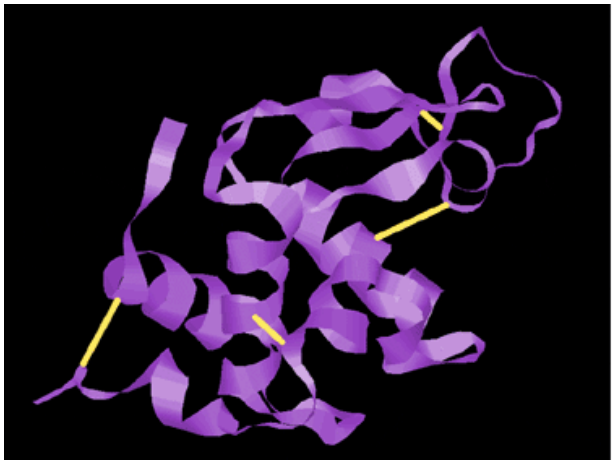
– Lysozyme, an enzyme that attacks bacteria, consists of a polypeptide chain of 129 amino acids.

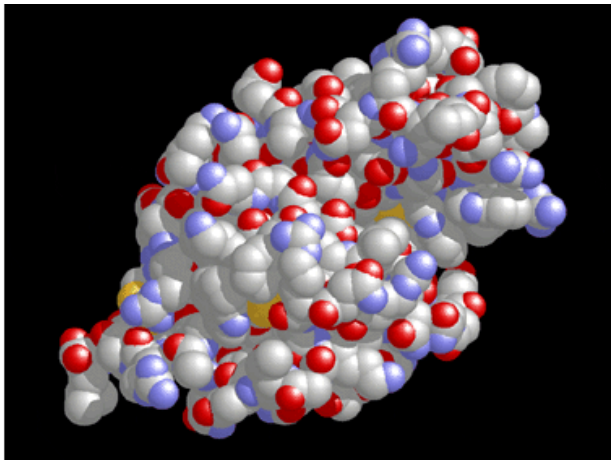
– The precise primary structure of a protein is determined by inherited genetic information.

– At one end is an amino acid with a free amino group the (the N-terminus) and at the other is an amino acid with a free carboxyl group (the C-terminus).

High orders of Protein structure

- **A functional protein** is **not just** a polypeptide chain, but **one or more** polypeptides precisely **twisted, folded and coiled** into a molecule of unique shape (**conformation).** This conformation is essential for some protein function e.g. Enables a protein to recognize and bind specifically to another molecule e.g. hormone/receptor; enzyme/substrate and antibody/antigen.





2- Secondary structure:

Results from hydrogen bond formation between hydrogen of –NH group of peptide bond and the carbonyl oxygen of another peptide bond. According to H-bonding there are two main forms of secondary structure:

α-helix: It is a spiral structure resulting from hydrogen bonding between one peptide bond and the fourth one.

β-sheets: is another form of secondary structure in which two or more polypeptides (or segments of the same peptide chain) are linked together by hydrogen bond between H- of NH- of one chain and carbonyl oxygen of adjacent chain (or segment).

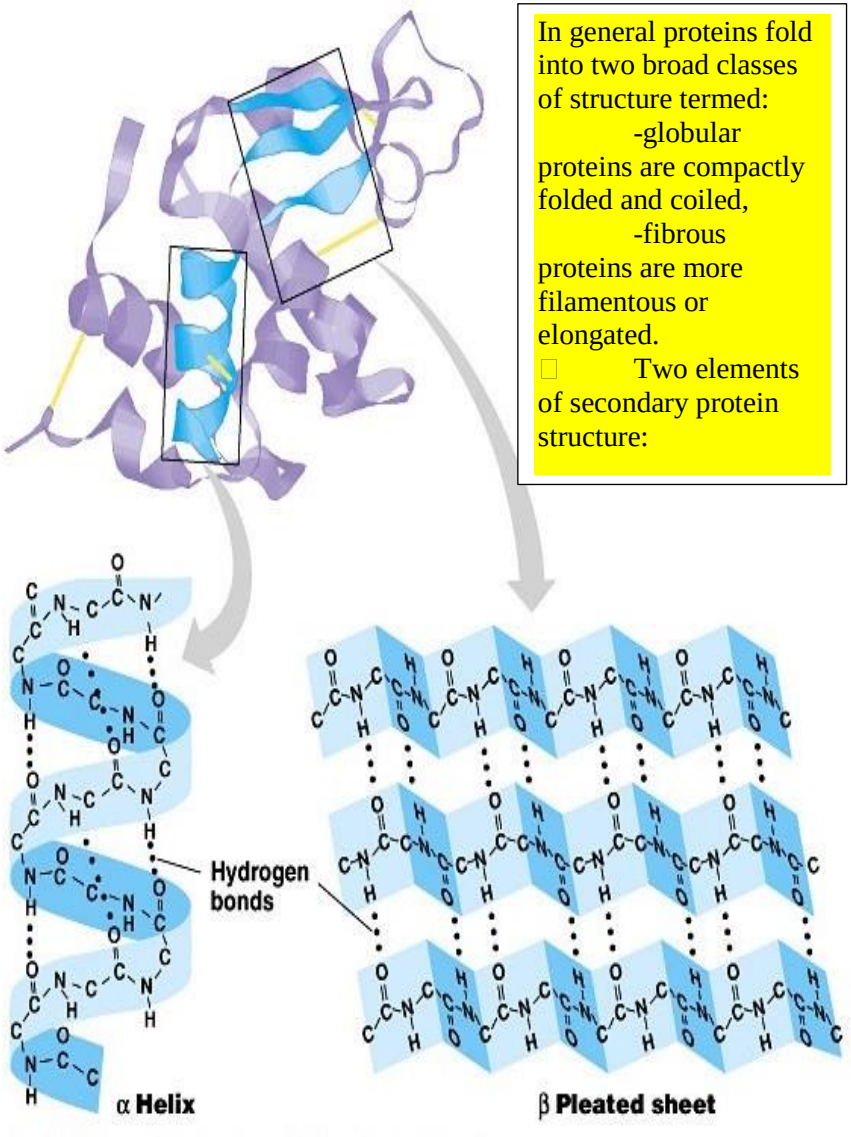
- α -Helix: Right-handed helix with 3.6 amino acid residues per turn. Hydrogen bonds are formed parallel to the helix axis.
- β -Sheet: A parallel or antiparallel arrangement of the polypeptide chain. Hydrogen bonds are formed between the two (or more) polypeptide strands.
- β -Turn: A structure in which the polypeptide backbone folds back on itself. Turns are useful for connecting helices and sheets.
- β -Sheets are either parallel or antiparallel.

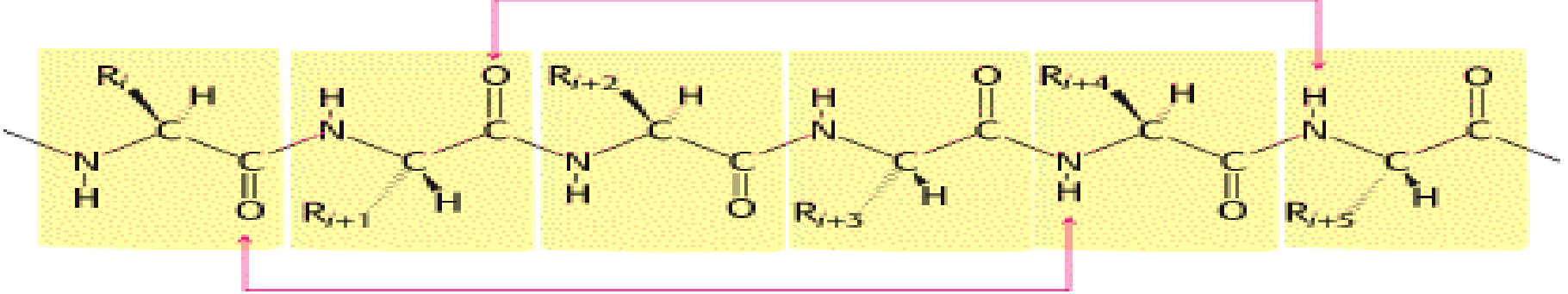
In general proteins fold into two broad classes of structure termed:

-globular proteins are compactly folded and coiled,

-fibrous proteins are more filamentous or elongated.

- Two elements of secondary protein structure:





Hydrogen bonding in α-helix: In the α-helix CO of the one amino acid residue forms H-bond with NH of the fourth one.

Supersecondary structure or Motifs :

occurs by combining secondary structure.

The combination may be: α-helix- turn- α-helix- turn…..etc

Or: **β**-sheet -turn- **β**-sheet-turn……etc

Or: **α**-helix- turn- **β**-sheet-turn- **α**-helix

Turn (or bend): is short segment of polypeptides (3-4 amino acids) that connects successive secondary structures.

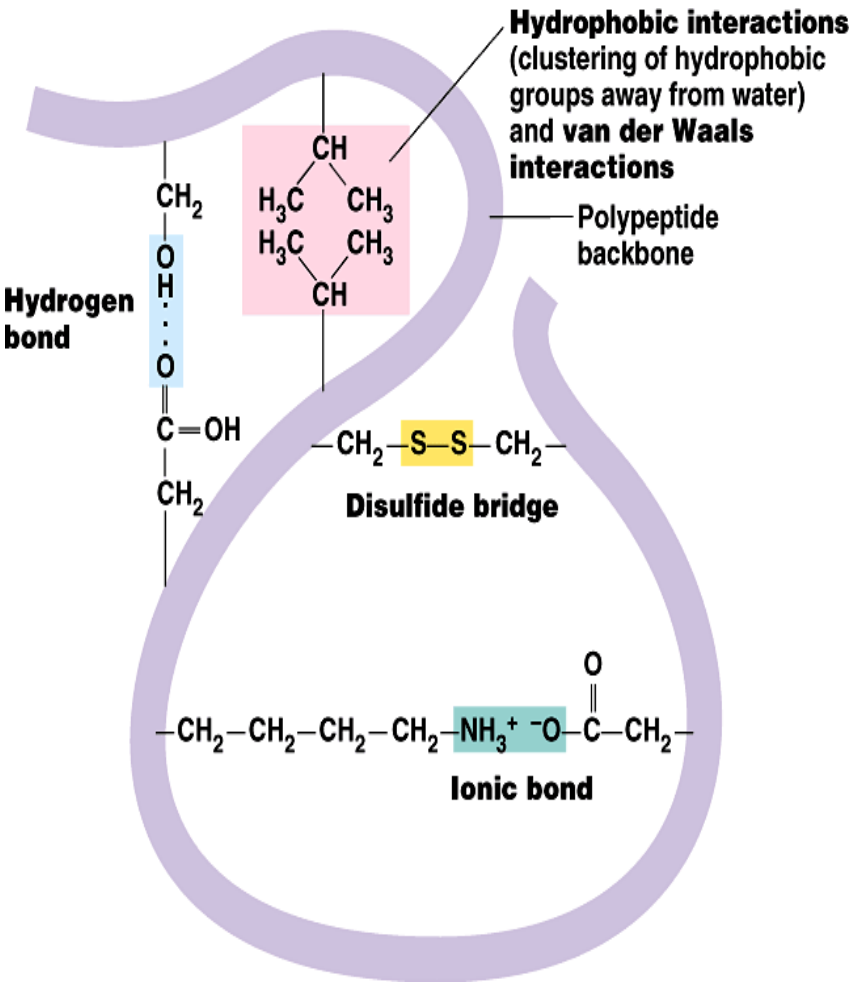
e.g. β-turn: is small polypeptide that connects successive strands of β- sheets.

- # Tertiary structure

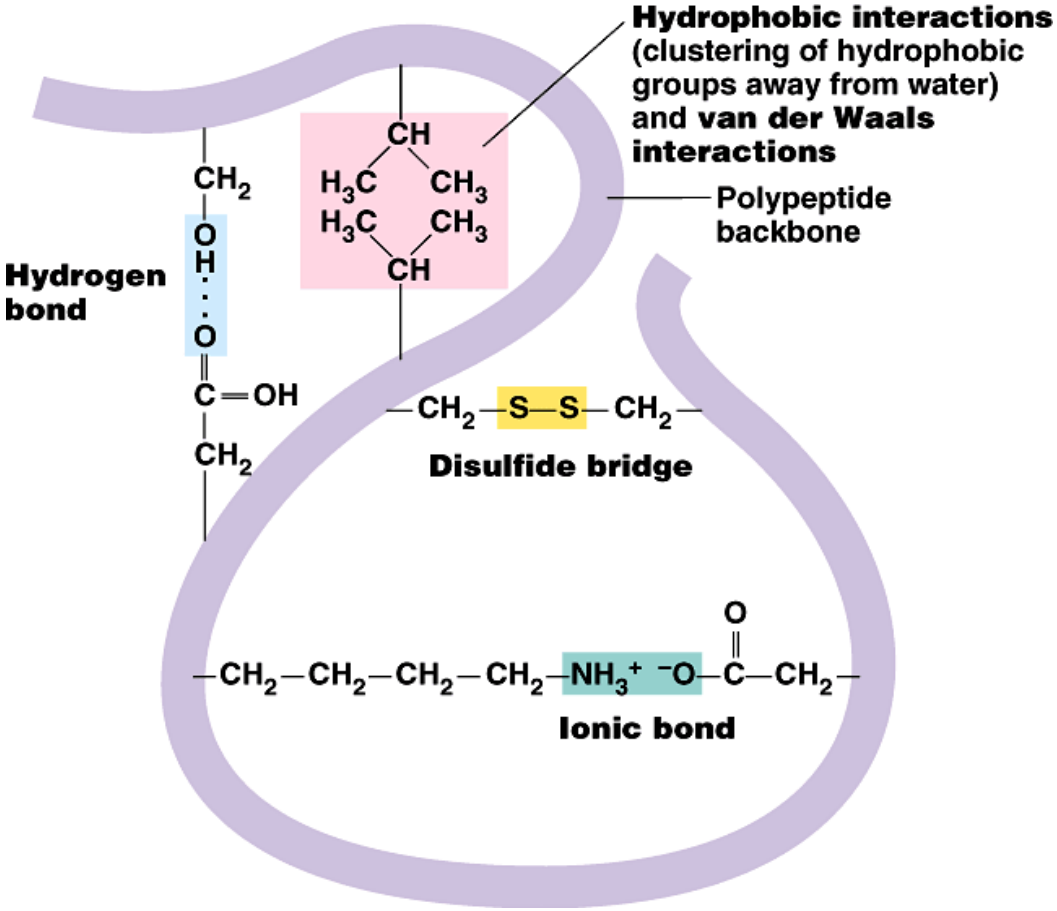
Is determined by a variety of interactions (bond formation) among R groups and between R groups and the polypeptide backbone.

a. **The weak interactions** include:

- **Hydrogen bonds** among polar side chains
- **Ionic bonds** between charged R groups (basic and acidic amino acids)
- **Hydrophobic interactions** among hydrophobic (non polar) R groups.



b. **Strong covalent bonds** include **disulfide bridges**, that form between the sulfhydryl groups (SH) of cysteine monomers, stabilize the structure.



Quaternary structure: results from the aggregation (combination) of two or more polypeptide subunits held together by non-covalent interaction like H- bonds, ionic or hydrophobic interactions.

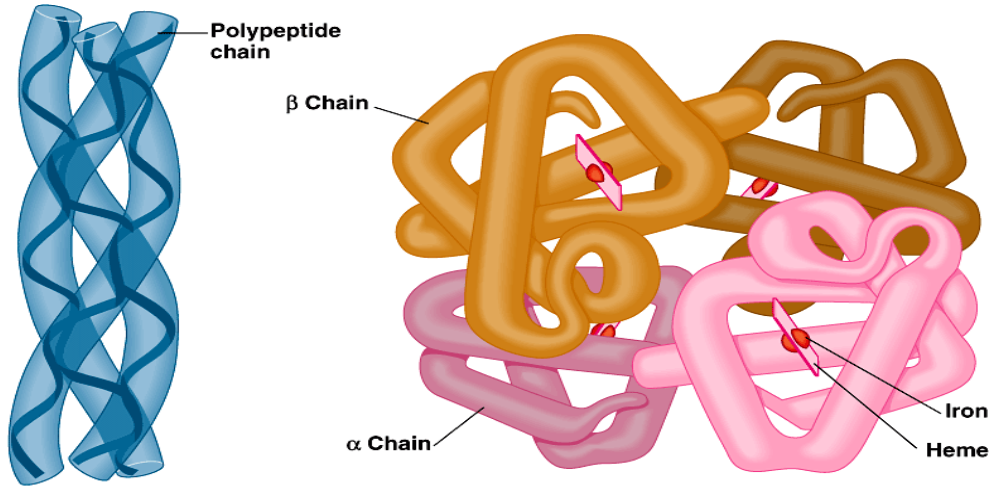
- Examples on protein having quaternary structure:

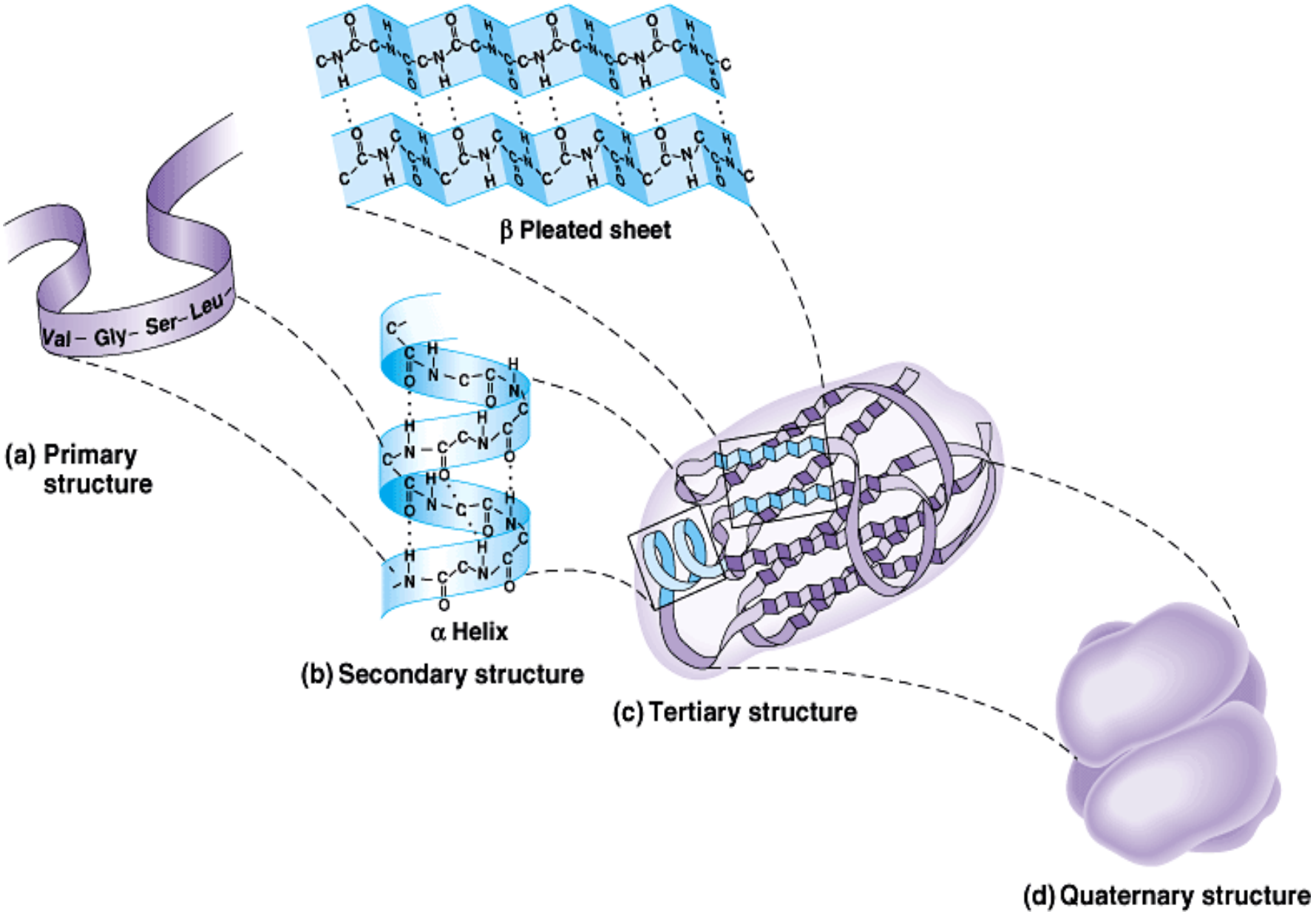
– **Collagen** is a fibrous protein of three polypeptides (trimeric) that are supercoiled like a rope.

This provides the structural strength for their role in connective tissue.

– **Hemoglobin** is a globular protein with four polypeptide chains (tetrameric)

– **Insulin** : two polypeptide chains (dimeric)




β Pleated sheet
Val – Gly – Ser – Leu
(a) Primary structure
α Helix
(b) Secondary structure
(c) Tertiary structure
(d) Quaternary structure

Classification of proteins

I- Simple proteins:

i.e. on hydrolysis gives only amino acids Examples:

1- Albumin and globulins: present in egg, milk and blood

They are proteins of high biological value i.e. contain all essential amino acids and easily digested.

Types of globulins:

α1 globulin: e.g. antitrypsin: see later

α2 globulin: e.g. hepatoglobin: protein that binds hemoglobin to prevent its excretion by the kidney

β-globulin: e.g. transferrin: protein that transport iron

γ-globulins = **Immunoglobulins** (antibodies): responsible for immunity.

Protein Functions:

1. Enzyme catalysis: e.g. All enzymes that catalyze cell reactions are proteins.
2. Transport and storage: Hemoglobin transport oxygen, Ferritin store iron.
3. Coordinated motions: e.g. muscles contain two motion proteins (myosin and actin)
4. Mechanical support: e.g. collagen (a fibrous protein)
5. Immune and Protection: e.g. Antibodies (immunoglobulin-A,-G,-M, and-E)
6. Generation and transmission of nerve pulses: e.g.Rhodopsin (a light-sensitive protein in retinal rod cells.
7. Control of growth and differentiation: e.g.(Hormones: insulin, growth hormone…)

2- Globins (Histones): They are basic proteins rich in histidine amino acid.

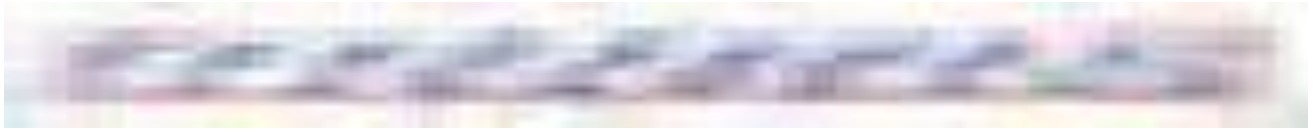
They are present in : a - combined with DNA
b - combined with heme to form hemoglobin of RBCs.

3-Gliadines are the proteins present in cereals.

4-Scleroproteins: They are structural proteins, not digested.
include: keratin, collagen and elastin.

α-keratin: protein found in hair, nails, enamel of teeth and outer layer of skin.

a-It is α-helical polypeptide chain, rich in cysteine and hydrophobic (non polar) amino acids so it is water insoluble.

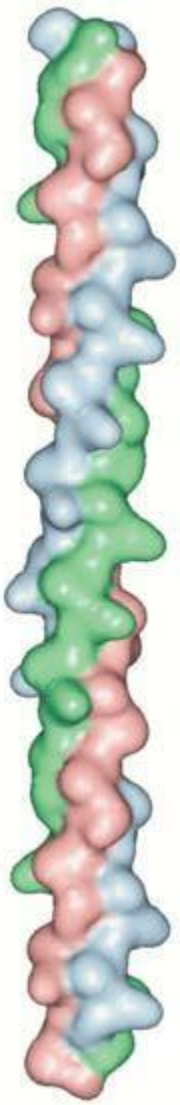


b- collagens: protein of connective tissues found in bone, teeth, cartilage, tendons, skin and blood vessels.

• Collagen may be present as gel e.g. in extracellular matrix or in vitreous humor of the eye.

• Collagens are the most important protein in mammals. They form about 30% of total body proteins.

• There are more than 20 types of collagens, the most common type is **collagen I** which constitutes about 90% of cell collagens.



• **Structure of collagen:** three helical polypeptide chains (trimeric) twisted around each other forming triplet-helix molecule.

• ⅓ of structure is glycine, 10% proline, 10% hydroxyproline and 1% hydroxylysine. Glycine is found in every third position of the chain. The repeating sequence –Gly-X-Y-, where X is frequently proline and Y is often hydroxyproline and can be hydroxylysine.

Solubility: collagen is insoluble in all solvents and not digested.

- When collagen is heated with water or dil. HCl it will be converted into **gelatin** which is soluble , digestible and used as diet (as jelly). Gelatin is classified as derived protein.

Some collagen diseases:

1- Scurvy: disease due to deficiency of vitamin C which is important coenzyme for conversion of proline into hydroxyproline and lysine into hydroxylysine. Thus, synthesis of collagen is decreased leading to abnormal bone development, bleeding, loosing of teeth and swollen gum.

2- Osteogenesis Imperfecta (OI): Inherited disease resulting from genetic deficiency or mutation in gene that synthesizes collagen type I leading to abnormal bone formation in babies and frequent bone fracture in children. It may be lethal.

C- Elastin: present in walls of large blood vessels (such as aorta). It is very important in lungs, elastic ligaments, skin, cartilage,
It is elastic fiber that can be stretched to several times as its normal length.

Structur e: composed of 4 polypeptide chains (tetramer), similar to collagen being having 33% glycine and rich in proline but in that it has low hydroxyproline and absence of hydroxy lysine.

Emphysema: is a chronic obstructive lung disease (obstruction of air ways) resulting from deficiency of α1-antitrypsin particularly in cigarette smokers.

Role of α1-antitrypsin: Elastin is a lung protein. Smoke stimulate
enzyme called elastase to be secreted form neutrophils (in lung). Elastase cause destruction of elastin of lung.

α1-antitrypsin is an enzyme (secreted from liver) and inhibit elastase and prevent destruction of elastin. So deficiency of α1-antitrypsin especially in smokers leads to degradation of lung and destruction of lung (loss of elasticity of lung, a disease called emphysema.

Conjugated proteins

i.e. On hydrolysis, give protein part and non protein part and subclassified into:

1- Phosphoproteins: These are proteins conjugated with phosphate group. Phosphorus is attached to oh group of serine or threonine.
e.g. Casein of milk and vitellin of yolk.

2- Lipoproteins:

These are proteins conjugated with lipids.

Functions: a- help lipids to transport in blood

b- Enter in cell membrane structure helping lipid soluble substances to pass through cell membranes.

3- Glycoproteins:

proteins conjugated with sugar (carbohydrate)

e.g. – Mucin

- Some hormones such as erythroproeitin
- present in cell membrane structure
- blood groups.

4- Nucleoproteins: These are basic proteins (e.g. histones) conjugated with nucleic acid (DNA or RNA).

e.g. a- chromosomes: are proteins conjugated with DNA

b- Ribosomes: are proteins conjugated with RNA

5- Metalloproteins: These are proteins conjugated with metal like iron, copper, zinc, ……

a- Iron-containing proteins: Iron may present in heme such as in

- hemoglobin (Hb)
- myoglobin (protein of skeletal muscles and cardiacmuscle),
- cytochromes,
- catalase, peroxidases (destroy H_2O_2)
- tryptophan pyrrolase (desrtroy indole ring of tryptophan).

Iron may be present in free state (not in heme) as in:

- Ferritin: Main store of iron in the body. ferritin is present in liver, spleen and bone marrow.
- Hemosidrin: another iron store.
- Transferrin: is the iron carrier protein in plasma.

b- Copper containing proteins:

e.g. - Ceruloplasmin which oxidizes ferrous ions into ferric ions.

- Oxidase enzymes such as cytochrome oxidase.

c- Zn containing proteins: e.g. Insulin and carbonic anhydrase

d- Mg containing proteins: e.g. Kinases and phosphatases.

Chromoproteins: These are proteins conjugated with pigment. e.g.

- All proteins containing heme (Hb, myoglobin, ……..)
- - Melanoprotein:e.g proteins of hair or iris which contain melanin.

Derived proteins

Produced from hydrolysis of simple proteins.

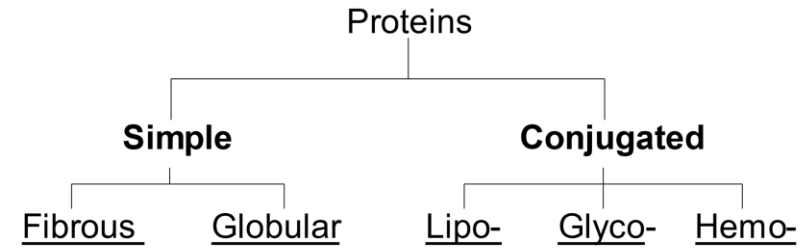
e.g. - Gelatin: from hydrolysis of collagen

- Peptone: from hydrolysis of albumin

PROTEIN DENATURATION

- Heat
- Mechanical agitation
- pH change
- Inorganic salts
- polar organic solvents
- Soaps and detergents

Proteins by Structure



insoluble soluble
'structural' ' reactive'

hair, horn enzymes HDL, interferon hemo -
LDL globin

Proteins by Structure

Fibrous

Collagens Elastins Keratins Myosins

bones lungs hair/feathers muscles
tendons ligaments horn/nails
cartilage

Proteins by Structure

Globular

Albumins Globulins

egg whites antibodies(γ -globulin)
enzymes

Proteins by Function

Enzymes	- the biological catalysts
Contractile	- muscle
Hormones	- insulin, growth hormone
Neurotransmitters	- endorphins
Storage	- store nutrients, eg. seeds, casein in milk
Transport	- hemoglobin
Structural	- collagen, keratins
Protective	- antibodies
Toxins	- snake venom, botulinum

Role of protein in the: cornea, lens , retina The lenses in the eyes are built of long cells, this means crystalline cells are elongated. The cells are deprived of cell nuclei and mitochondria. This leaves the protein to be a smooth and transparent solution. The crystalline proteins are of three types: alpha, beta, and gamma. The crystalline solutions in the eyes are the mixture of all three. Crystalline is a water-soluble structural protein, found in the lens and the cornea of the eye accounting for the transparency of the structure. The crystallins are water-soluble structural proteins that occur in high concentration in the cytoplasm of eye lens fiber cells. Four major groups of crystalline have been distinguished on the basis of size, charge and immunological properties: alpha-, beta- and gamma-crystalline occur in all vertebrate classes (though gamma-crystalline are low or absent in avian lenses); and delta-crystalline is found exclusively in reptiles and birds.

What are eye proteins called? a crystalline is a water-soluble structural protein found in the lens and the cornea of the eye accounting for the transparency of the

structure. **What does the eye lens protein do?** Crystallins are the most prevalent proteins in the lens. Comprising of two families, α- and β and γ-crystallins, they make up 90% of water-soluble proteins of the mammalian lens. They are highly organized and provide a refractive index gradient, which allows for transparency of the lens.

A cataract occurs when there is a buildup of proteins in the lens, creating protein clumps. These clumps, or deposits, prevent light from passing clearly through the lens, thus disrupting normal vision. There are several reasons why a cataract may form including: Aging – The eyes mainly consist of water and protein Traumatic Cataract – Another common cause of cataracts is trauma Diabetes – People with diabetes are 60% more likely to develop cataracts. Congenital Cataract – While cataracts are normally associated with the aging process High Blood Pressure – High blood pressure (HBP) is known to cause elevated inflammation which may result in cataracts. Excessive Alcohol Consumption – Studies have shown that high alcohol consumption significantly increases the risk of cataracts.

Lipids & Lipoproteins

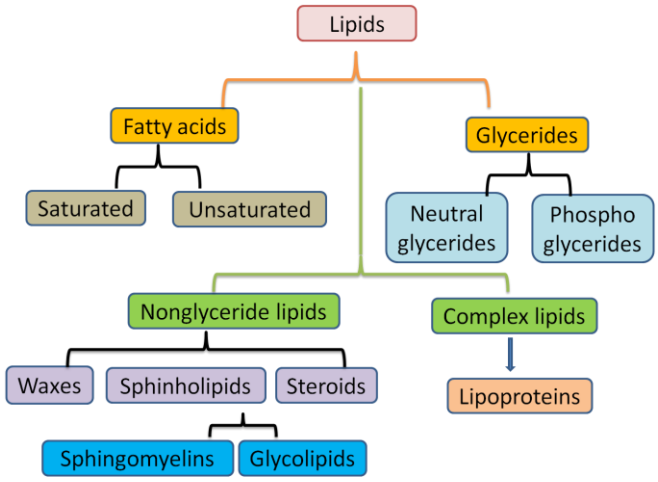
Lipids: Biological molecules that are insoluble in aqueous solutions and soluble in organic solvents are classified as lipids.

***-Neutral lipids(e.g. cholesterol esters, triglyceride..) are uncharged molecules.

Major Roles of Biological of Lipids:

1. They serve as structural components of biological membranes.
2. They provide energy reserves, predominantly in the form of triacylglycerols.
3. Both lipids and lipid derivatives serve as vitamins and hormones.
4. Lipophilic bile acids aid in lipid solubilization.
5. Serve as thermal and electrical insulator.

Classification of Lipids:



The types of lipids that we will look at include.

- Fatty Acids
- In the carboxylic acid family
- Waxes
- Fatty Acids + Alcohols
- Triglycerides
- 3 Fatty acids + glycerol
- Phospholipids and glycolipids
- 2 fatty acids + glycerol + phosphate + X
- Steroids
- Derivatives of cholesterol
- Eicosanoids
- Derivatives of the Fatty acid arachidonic acid
- Membranes
- Formed from phospholipids and glycolipids

1-Fatty Acids:

Fatty acids are long-chain hydrocarbon molecules containing a carboxylic acid moiety at one end.

*Fatty acids fill two major roles in the body:

1. As the components of more complex membrane lipids.
2. As the major components of stored fat in the form of triacylglycerols.

* **Saturated fatty acids:** Fatty acids that contain no carbon-carbon double bonds.
* **Unsaturated fatty acids:** Fatty acids that contain double bonds.

Fatty acids may be further subdivided as follows:

(1) Monounsaturated (monoethenoid, monoenoic) acids, containing one double bond.
(2) Polyunsaturated (polyethenoid, polyenoic) acids, containing two or more double bonds.
(3) Eicosanoids: These compounds, derived from eicosa- (20-carbon) polyenoic fatty acids, comprise the **prostanoids, leukotrienes (LTs),** and **lipoxins (LXs).** Prostanoids include **prostaglandins (PGs), prostacyclins (PGIs),** and **thromboxanes (TXs).**

#The site of unsaturation in a fatty acid is indicated by the symbol **Δ** and the number of the first carbon of the double bond (e.g. palmitoleic acid is a 16-carbon fatty acid with one site of **unsaturation** between **carbons 9** and 10, and is designated by $16:1^{\Delta 9}$).

@ Naturally occurred unsaturated FA occurs in cis-form.

@ Body can biosynthesize lipids and can supply the body with all the various fatty acid structures needed except the **essential FA.**

***Essential fatty acids**; must be provided in the diet (the highly unsaturated fatty acids: these are all **polyunsaturated fatty acids**: the **C20** fatty acid **arachidonic acid** (20:4;5,8,11,14), and the two **C18 acids linoleic acid** (18:2;9,12) and **linolenic acid** (18:3;9,12,15). **linoleic acid** and **linolenic acid**) because they containing unsaturation sites beyond carbons 9 and 10.

Physiologically Relevant Fatty Acids:

Numerical Symbol	Common Name	Structure	Comments
14:0	Myristic acid	$CH_3(CH_2)_{12}COOH$	
16:0	Palmitic acid	$CH_3(CH_2)_{14}COOH$	End product of mammalian F.A. synthesis
$16:1^{\Delta 9}$	Palmitoleic acid	$CH_3(CH_2)_5C=C(CH_2)_7COOH$	
18:0	Stearic acid	$CH_3(CH_2)_{16}COOH$	
$18:1^{\Delta 9}$	Oleic acid	$CH_3(CH_2)_7C=C(CH_2)_7COOH$ Physiologically most important omega-9 monounsaturated fatty acid (MUFA)	
$18:2^{\Delta 9,12}$	Linoleic acid	$CH_3(CH_2)_4C=CCH_2C=C(CH_2)_7COOH$ Essential fatty acid, an omega-6 PUFA	**Essential fatty acid**
$18:3^{\Delta 9,12,15}$	Linolenic acid	$CH_3CH_2C=CCH_2C=CCH_2C=C(CH_2)_7COOH$ Essential fatty acid, an omega-3 PUFA	**Essential fatty acid**
$20:4^{\Delta 5,8,11,14}$	Arachidonic acid Essential fatty acid	$CH_3(CH_2)_3(CH_2C=C)_4(CH_2)_3COOH$ An omega-6 PUFA, precursor for eicosanoid synthesis	**Precursor for eicosanoid synthesis**

&&Prostaglandines:

Synthesized *in vivo* by cyclation of the center of the (20C-atoms unsaturated FA that called Eicosanoic acid) to form cyclopentane cycle. Examples of prostaglandins: thromboxane,

prostaglandine 2 (PGE2)

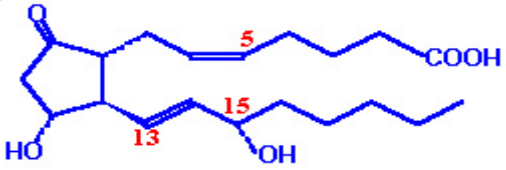


Figure : PEG2

2-Basic Structure of Triacylglycerides

Triacylglycerides (TG) are composed of a glycerol backbone to which 3 fatty acids are esterified. TG are the stored lipids in the **body tissues**.

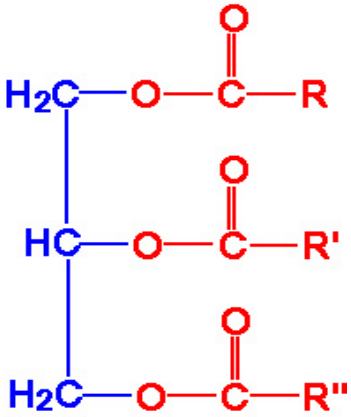


Figure: Basic composition of a triacylglyceride

3-Basic Structure of Phospholipids

The basic structure of phospolipids is very similar to that of the triacylglycerides except that C-3 of the glycerol backbone is esterified to **phosphoric acid.**

*The building block of the phospholipids is **phosphatidic acid** (X= hydrogen atom).

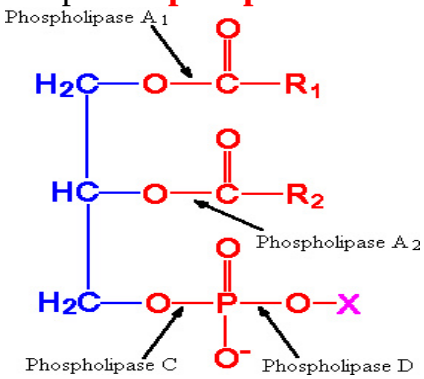
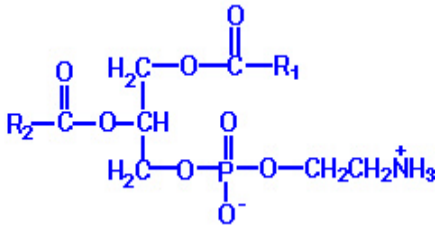
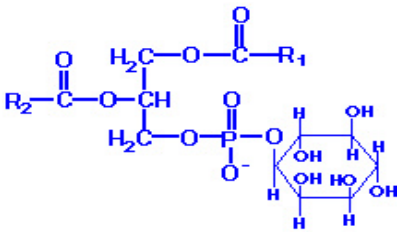


Figure: Basic composition of a phospholipid. X can be a number of different substituents.

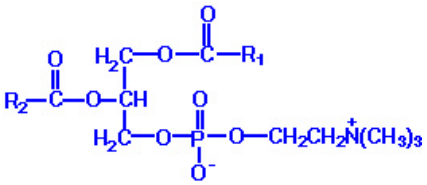
*Substitutions include ethanolamine (**phosphatidylethanolamine**), choline (**phosphatidylcholine**, also called **lecithins**), serine (**phosphatidylserine**), glycerol (**phosphatidylglycerol**), *myo*-inositol (**phosphatidylinositol**,, and phosphatidylglycerol (**diphosphatidylglycerol** more commonly known as **cardiolipins**).



Phosphatidylethanolamine



Phosphatidylinositol



Phosphatidylcholine (lecithins)

4-Basic Structure of Plasmalogens

Plasmalogens are phospholipids substituted at C-1 (*sn*1) of glycerol contain either an *O*-alkyl or *O*-alkenyl ether species. One of the most potent biological molecules is **platelet activating factor**.

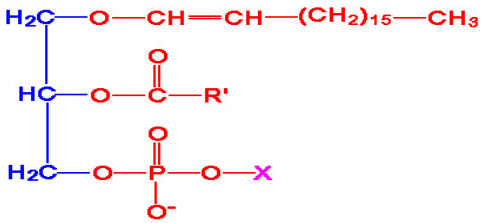


Figure: basic composition of *O*-alkenyl plasmalogens.

5-Basic Structure of Sphingolipids

*Sphingolipids are composed of a backbone of sphingosine which is derived itself from glycerol.

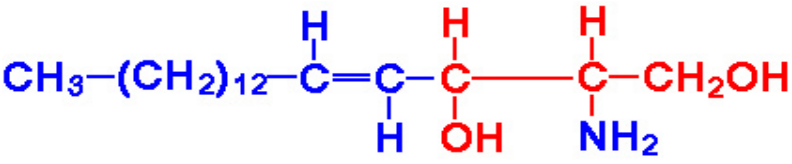
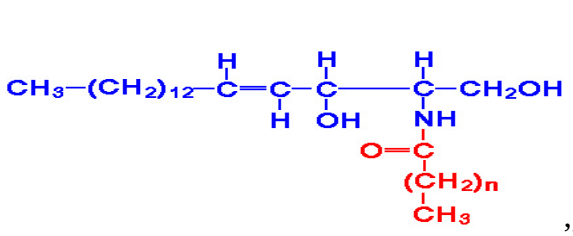


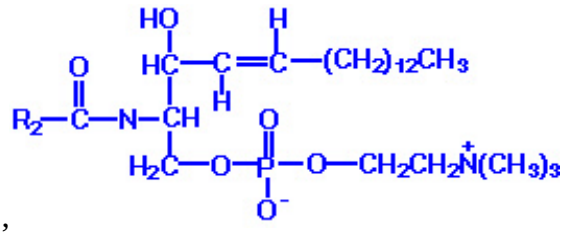
Figure: Sphingosine

* **Ceramides:** A family of molecules composed of sphingosine when N-acetylated by a variety of fatty acids. Sphingolipids predominate in the myelin sheath of **nerve fibers**.



Ceramide

,,,,,



Sphingomyelin

***Sphingomyelin** is an abundant sphingolipid generated by transfer of the phosphocholine moiety of phosphatidylcholine to a ceramide, thus sphingomyelin is a unique form of a phospholipid.

The other major class of sphingolipids (besides the sphingomyelins) are the **glycosphingolipids** generated by substitution of carbohydrates to the *sn1* carbon of the glycerol backbone of a ceramide. There are 4 major classes of glycosphingolipids:

Cerebrosides: contain a single moiety, principally galactose.

Sulfatides: sulfuric acid esters of galactocerebrosides.

Globosides: contain 2 or more sugars.

Gangliosides: similar to globosides except also contain sialic acid.

6- Steroids:

Steroids are lipids derived from the cyclopentanophenanethrine.

Cholesterol is an extremely important biological steroids: 1-Constituent of plasma membrane and lipoproteins 2- precursor for the synthesis of the steroid hormones, sex hormones, vitamine D, and bile acids.

- Both dietary cholesterol and that synthesized *de novo* are transported through the circulation in lipoprotein particles. The same is true of cholesteryl esters, the form in which cholesterol is stored in cells.

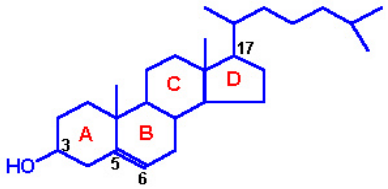


Figure: Cholesterol

Lipid Peroxidation:

It is a chain reaction providing continuous supply of free radicals ($ROO^{\cdot}$, $RO^{\cdot}$, and $OH^{\cdot}$) that initiates further peroxidation. This process causes **different disorders**: **rancidity** (auto oxidation of lipids by oxygen), **aging**, **cancer**, **atherosclerosis**, **inflammation**, **damage to tissue in vivo.**

Notes:

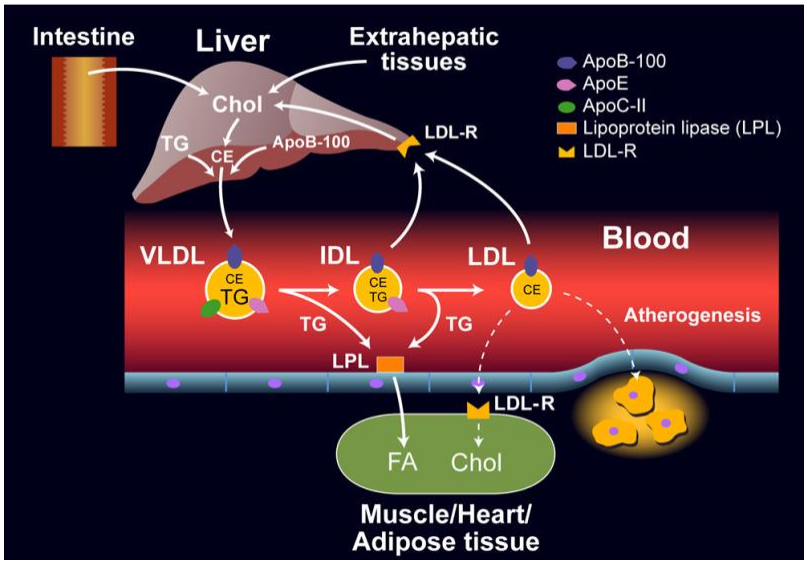
Amphipathic molecule: Part of the molecule is hydrophilic (polar) and the other is hydrophobic (non-polar). Polar group faces the water phase and the non-polar faces the hydrophobic phases (oil); this is the main feature of **plasma membrane.**

- **Micelles**: Critical concentration of polar lipids in aqueous medium.
- **Liposome**: Consist of spheres of lipid layers that enclose part of water.
  - **Emulsion**: Larger particles formed by non-polar lipids in an aqueous medium.

#-**Aggregation of bile salts into micelles and liposomes** with th product of fat digestion are important in facilitating absorption of lipids from intestine.

Lipoproteins: Macromolecular complex of lipids and proteins . They are the transport vehicles for lipids in the circulation. There are five types of lipoproteins.

1. **Chylomicrons:** transport primarily triglycerides from the digestive track to liver.
2. **VLDL**: transport triglycerides from liver to other tissues. transport the lipids (endogenously synthesized) mainly TG from liver to peripheral tissues).
3. **IDL:** Intermediate density lipoproteins, are formed from the degradation of **very low-density lipoproteins** as well as **high-density lipoproteins,** that enable fats and cholesterol to move within the water-based solution of the bloodstream.
4. **LDLs:** (low density lipoproteins) transport cholesterol, triglycerides and phospholipids from the liver to other tissues ("**bad" cholesterol**).
5. **HDLs:** (high density lipoproteins "**good" cholesterol**) transport cholesterol and phospholipids back carry from peripheral tissues to the liver.



ApoB-48

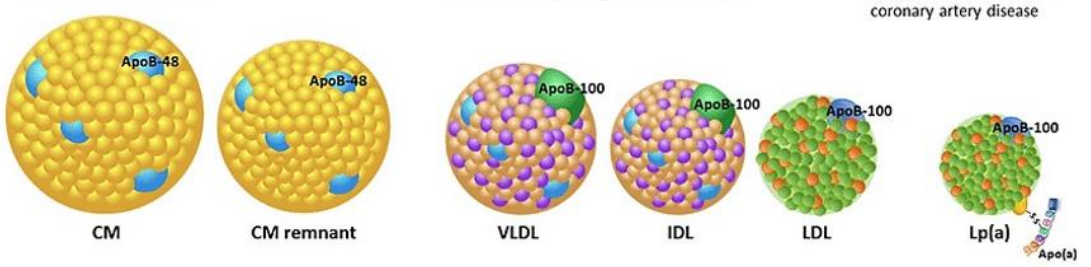
- MW: 264,000 daltons
- Metabolic function: assembly and secretion of CMs from the small intestine; structural protein of CMs and CM remnants

ApoB-100

- MW: 540,000 daltons
- Metabolic function: assembly and secretion of VLDL from the liver; structural protein of VLDL, IDL, LDL and Lp(a); ligand for LDL receptor

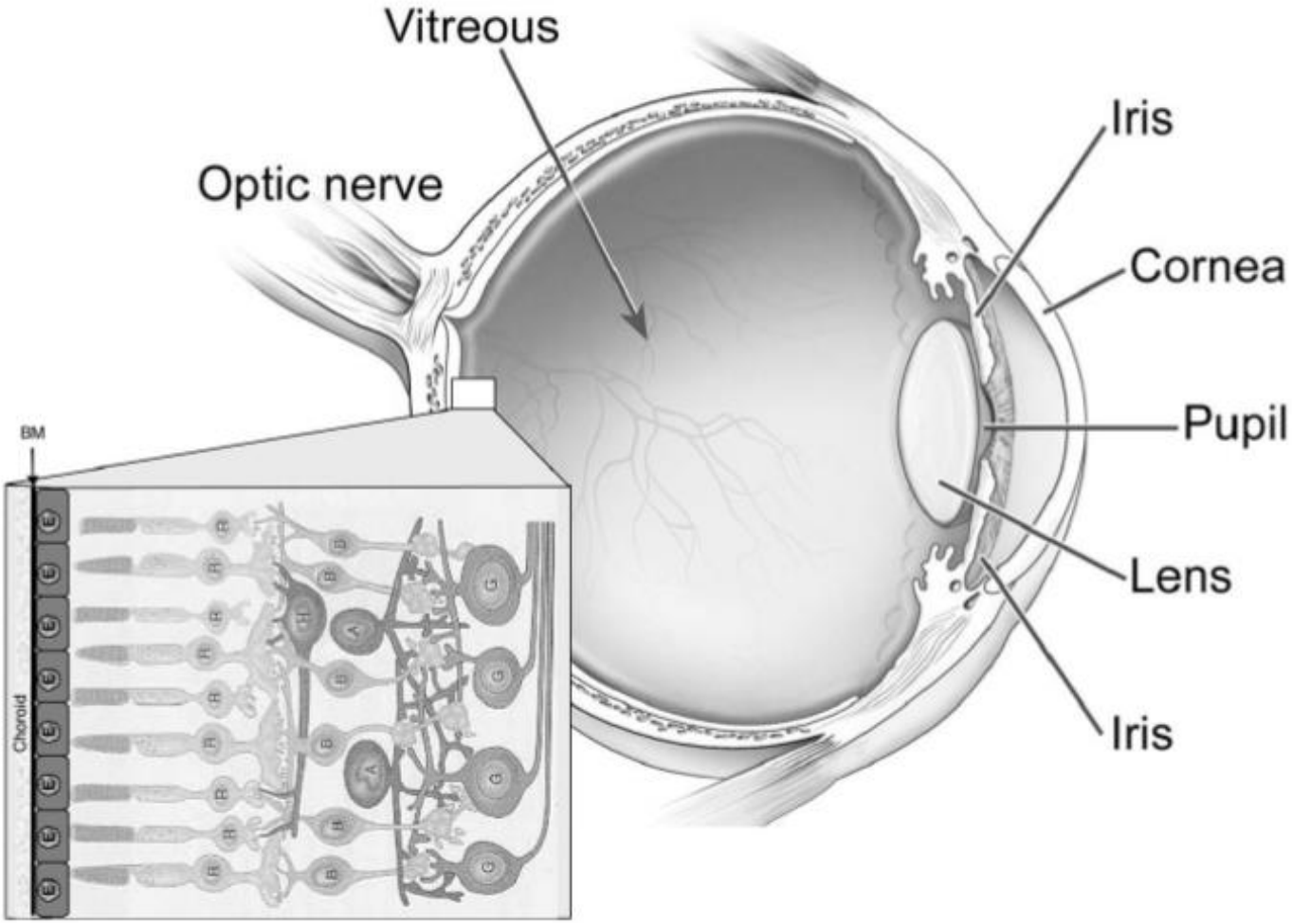
Apo(a)

- MW: 250,000-800,000 daltons
- Metabolic function: not completely defined, but it is an independent predictor of coronary artery disease



	CM	CM remnant	VLDL	IDL	LDL	Lp(a)
Source	intestine	CM	liver (intestine)	VLDL	VLDL	liver
Density (g/dl)	< 0.95	< 1.006	0.95-1.006	1.006-1.019	1.019-1.063	1.05-1.12
Diameter (nm)	75-1200	45-150	30-80	25-35	18-25	about 25
Molecular weight (daltons)	400×10^6	unknown	$10\text{-}80 \times 10^6$	$5\text{-}10 \times 10^6$	2.3×10^6	about 4×10^6
Structural components	99-98% total lipid and 1-2% total protein	94-92% total lipid and 6-8% total protein	93% total lipid and 7% total protein	85% total lipid and 15% total protein	80% total lipid and 20% total protein	80% total lipid and 20% total protein
Apolipoprotein composition	A-I, A-II, A-IV, B-48, C-I, C-II, C-III, E	B-48, E	B-100, C-I, C-II, C-III, E	B-100, C-I, C-II, C-III, E	B-100	B-100, Apo(a)

•Lipids are key components of the retina, and are closely associated with the aging processes.
•Omega-3 fatty acids show protective properties against inflammation and neurodegeneration in retinal aging and the development of Age-related macular degeneration (AMD).
•The eye retina is a part of the central nervous system, together with the brain and the spinal cord and as such is also naturally rich in lipids



•The human eye and retina

BM, Bruch's membrane;

E, retinal pigment epithelium;

R, photoreceptor (rods and cones);

H, horizontal cell;

B, bipolar cell;

A, amacrinecell;

G, ganglion cell

Lipids as crucial components of the retina

•The retina covers the internal side of the posterior chamber of the eye

•The retina is composed of
•neurosensory tissue: neuroretina,

•a pigment epithelium: retinal pigment epithelium (RPE)
•The main function of the neuroretinais to convert the light stimulus into an electrical signal that can be decoded by the brain

•The RPE creates a physical and metabolic barrier between the neuroretina and the choriocapillar is that limits the entry of exogenous compounds in the neuroretina.

•One of the primary function of the RPE is to eliminate the metabolic debris generated by photoreceptors.

•The RPE exhibits an endogenous capacity to synthesize and secrete lipoprotein-like particles

•Low density lipoprotein particles (LDL) participate significantly in retinal lipid supply.

Lipids as crucial components of the retina

•Lipids account for about 25% of the dry matter in the neuroretina.

•Phospholipids are the prominent lipids therein (more than 85%), while cholesterol is present as free cholesterol (10%), and to a lesser extent as cholesteryl esters (less than 2%)

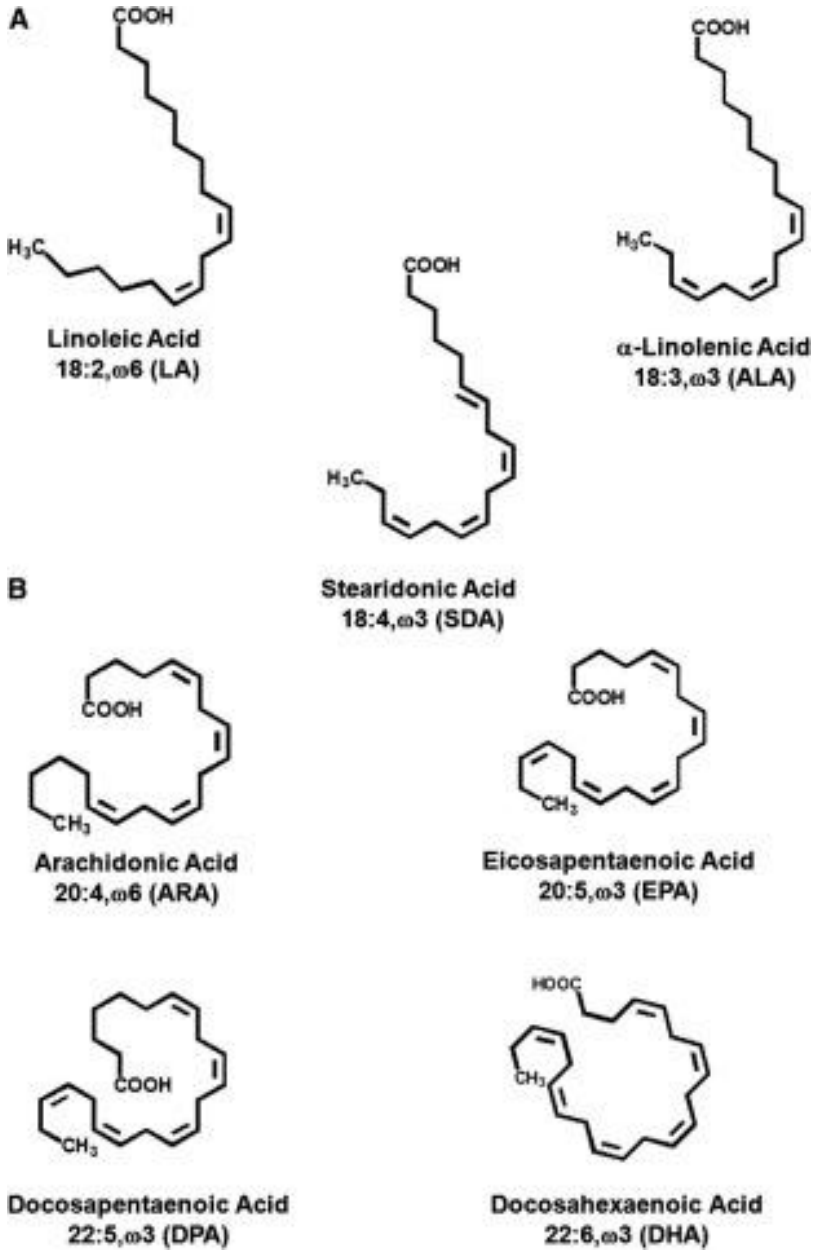
•Phospholipids are present in great quantity in the outer segment of rods and cones.

•Docosahexaenoic acid (DHA) is the main long-chain polyunsaturated fatty acid in the phospholipids of the neuroretina: 12–20% of the fatty acids in human and more than 30% in rodent

•The potential of a diet enriched in DHA and EPA (eicosapentaenoicacid) to increase the level of the longer chain omega-3 fatty acids (EPA; DPA, docosapentaenoicacid; and DHA) in the retina has clearly been demonstrated

•Intervention trials have been conducted in pregnant and lactating women and premature and at-term babies in order to evaluate the efficacy of dietary long chain omega-3 fatty acids to improve vision performance in infants.

•The positive effect of omega-3 fatty acids was obvious only in studies where the intake of DHA was higher than 1g daily



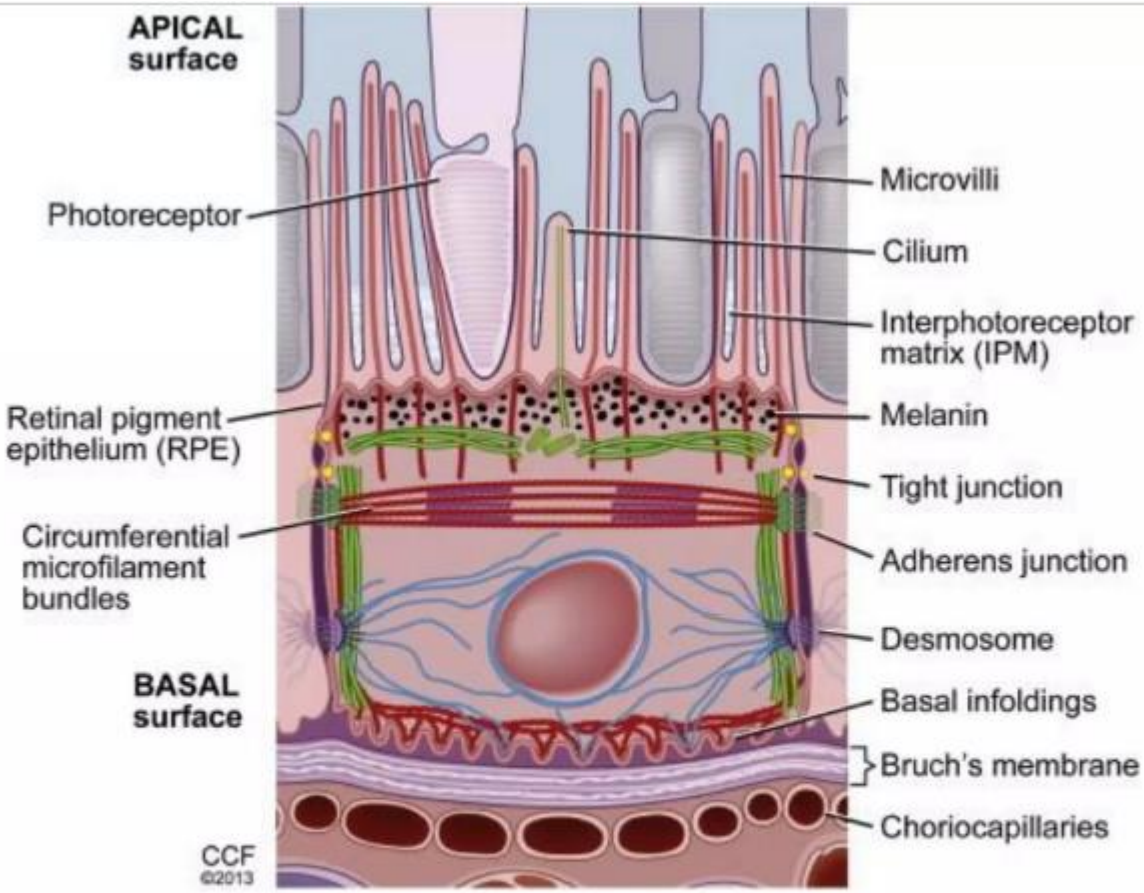
Aging of the retina & Lipids

•The “lipid wall”, made of cholesterol, participates in the age associated thickening of Bruch's membrane that increases hydraulic resistance and may reduce the fluxes of nutrients to the retina.

•AMD targets a specific area of the retina: the macula.

•High fat intake has been associated with higher risk for AMD.

•Smoking and light exposure are, for instance, recognized as promoting factors

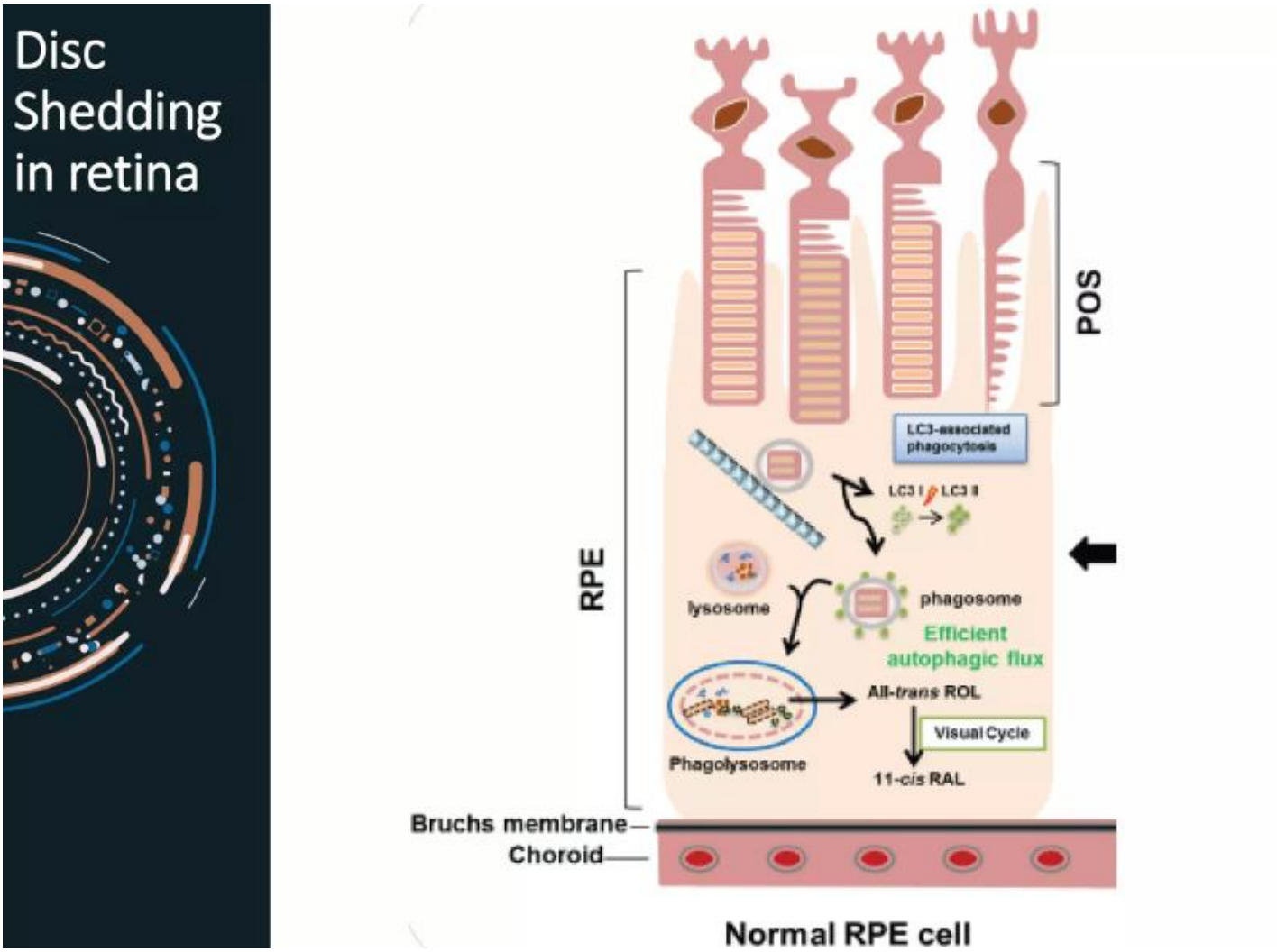


choriocapillaries supply → retinal pigment epithelial → interphotoreceptor matrix → photoreceptor cells

- **choriocapillaries supply** the nutrients to the **retinal pigment epithelial** (RPE) cells, which delivers them to the interphotoreceptor matrix.
- **Low density lipoprotein (LDL)** is the main carrier of DHA, and since the RPE cells contain LDL receptors
- it is likely that the **uptake and delivery of DHA to the photoreceptor cells are receptor mediated** with subsequent release of DHA phospholipids, or free DHA, into the interphotoreceptor matrix.
- **Fatty acid-binding proteins (FABPs)** present in the interphotoreceptor matrix bind DHA, and are believed to be involved in the transport of DHA to the photoreceptor cells.

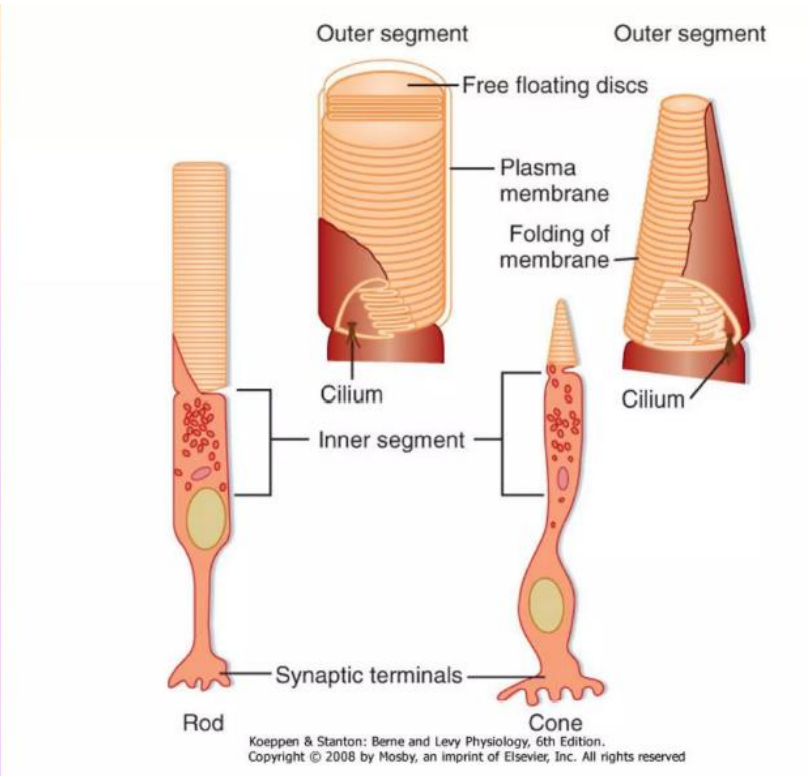
- RPE is a single layer of **hexagonal pigmented cells** located in the outmost part of the neurosensory retina.
- the **supplement of nutrients and oxygen to retina**
- the **sustainment of visual cycle** through metabolizing vit- A
- the absorbing of scattered light to **reduce photo-oxidation** via melanosomes
- the performance of **receptor-mediated phagocytosis of photoreceptor outer segment (POS) fragments** for assuring viability and functionality of photoreceptors
- **Dysfunction of RPE** resulted from consistent exposures to oxidative stress has been reportedly to cause retinal degenerations, such as age-related macular degeneration (AMD).

- The **heterophagy of Photoreceptor Outer Segment** by RPE is essential to the longevity of photoreceptors.
- The **renewal of POS is regulated by circadian rhythms** via the shedding of distal tips POS, which are degraded and engulfed by RPE, and are eventually digested by lysosomal enzymes.
- **All-trans-retinol (ROL) are recycled and converted to 11-cis-retinal (11CR) by visual cycle** to replenish chromophore for reproduction of photobleached pigments.



- Disc membranes are assembled at the inner segment, and form discs at the base of the outer segment
- These membranes have a short lifetime, and **are replaced every 9–14 days**
- The discs move outward toward the tip apical region where they are shed into the **adjacent RPE, *phagocytosed and digested*** by the lysosomal system.
- However, the retina conserves its **DHA by retrieving it from the phagosomal membranes** within the RPE and recycling it for incorporation into newly forming disc membranes

DHA accumulation in the retina



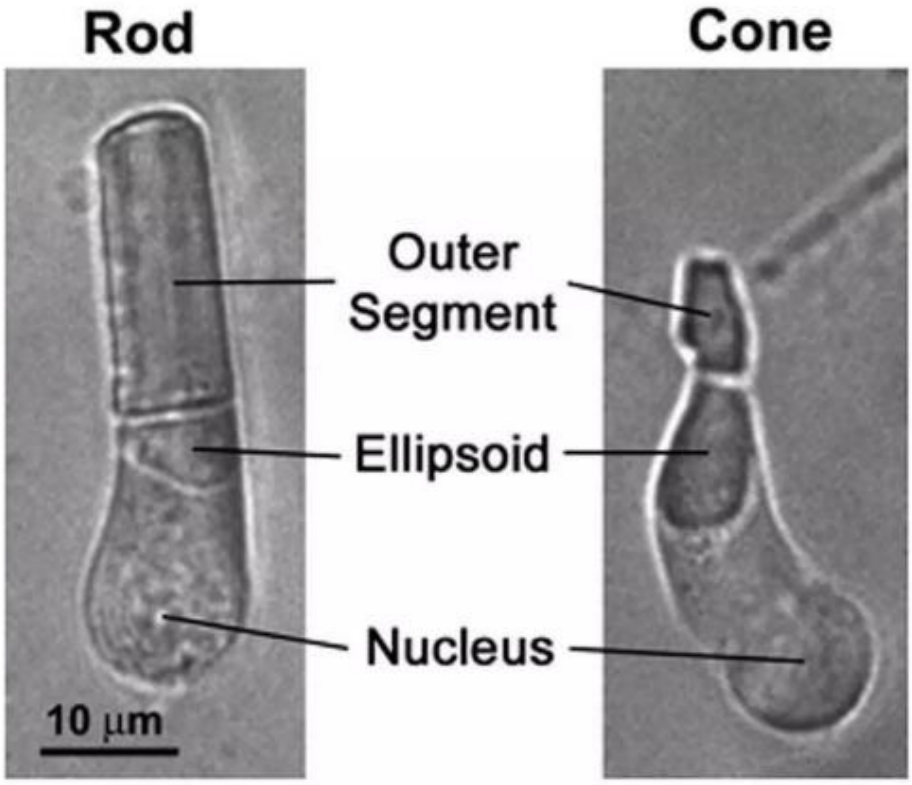
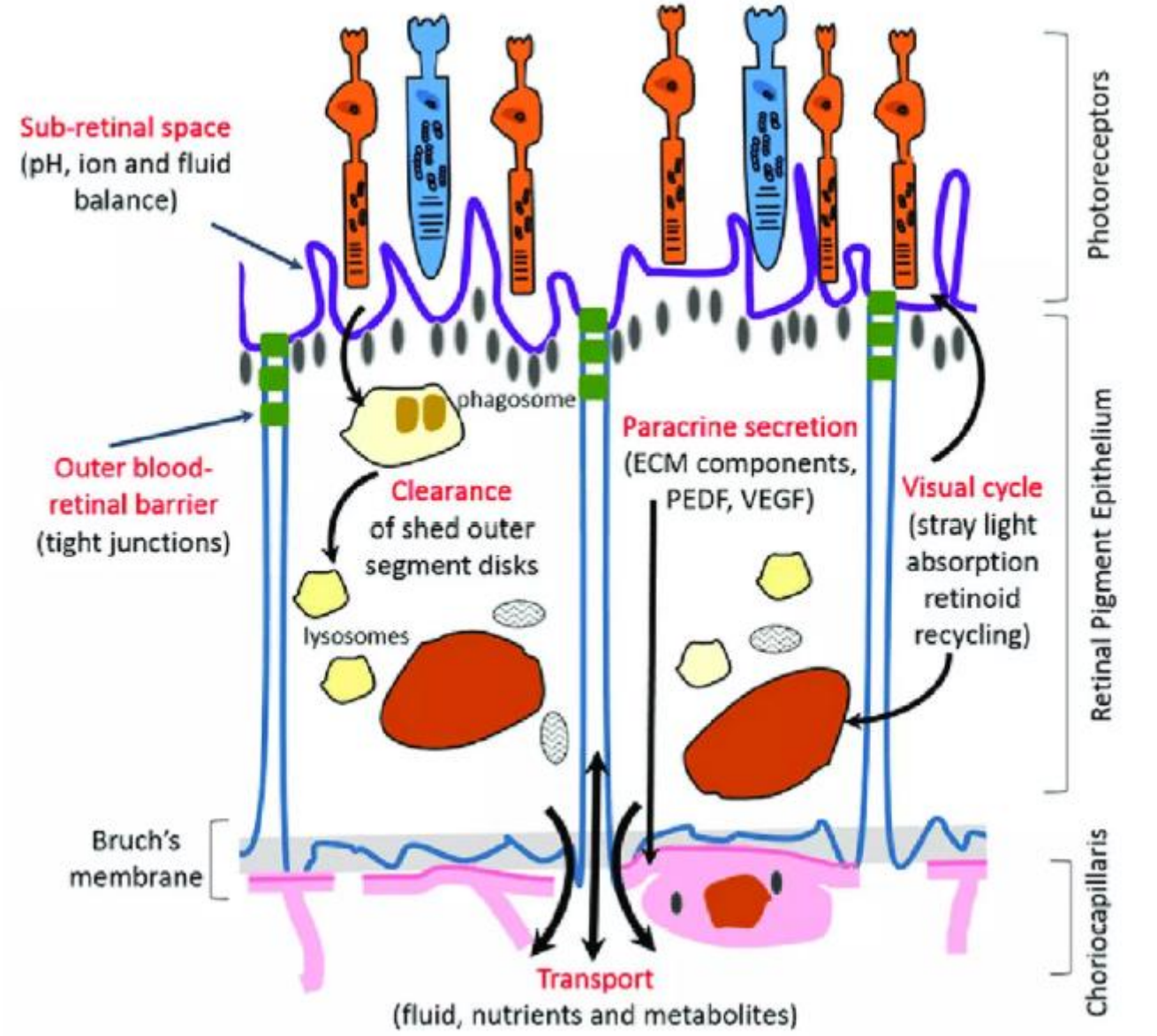


Figure 1. Brightfield images of living rod and cone photoreceptors isolated from a salamander retina. Phototransduction takes place in the outer segment, while the ellipsoid is densely packed with mitochondria. Rods are responsible for dim light vision, cones for bright light vision.
Courtesy of Yiannis Koutalos.



- The recycling mechanism is not fully understood, but it has been postulated to occur via one of the two following mechanisms:

- (1) by **returning the DHA** from the RPE back to the photoreceptors (short-loop)
- (2) by **entry of DHA into the systemic circulation**, where it follows a similar pathway to cellular and dietary DHA via the liver, and reuptake by the RPE cells, with delivery to photoreceptor cells for new disc formation (long-loop)

- This selective retention of lipid is unique to the photoreceptor cells.

Role of DHA

1. **DHA affects the membrane structure** by altering its **permeability, fluidity, thickness and lipid-phase properties** while increasing the rate of rhodopsin activation
2. **DHA surrounds rhodopsin** (approximately 60 molecules of phospholipid for each rhodopsin), excluding cholesterol from **creating a fluid microenvironment** within the rod outer-segment membranes
3. **membrane fluidity is an important biophysical factor** of the disc membranes, and this fluidity is brought about by the presence of DHA and other PUFAs on the constituent phospholipids

4. **The membrane's fluid state allows Brownian movement** of the protein components within the plane of the disc membrane, enabling transduction and amplification of the signal
5. *membranes containing DHA have higher MII formation, MII–transducing interaction and activation and, finally, PDE activation.*

DHA and retinal oxidative stress

- DHA has high degree of unsaturation
- It is **susceptible to oxidation** within the photoreceptor disc membranes
- the membrane stabilising substances, vitamin E and taurine, along with the retinal antioxidants, vitamin C, carotenoids, superoxide dismutase and glutathione (and its associated enzymes) helps in fighting against oxidative damage of eye
- However a constant cellular and dietary supply is required to maintain the disc membranes.
- studies have demonstrated that depletion of DHA from the developing retina leads to **abnormalities in electroretinogram (ERG) and visual evoked potential (VEP), resulting in reduced visual function**

Dietary deficiency of DHA and visual function

- diets low in Omega-3 fatty acids led **to impaired visual acuity**
- The retinal dysfunction occurs due to **inadequate disc membrane DHA phospholipids to support rhodopsin in light capture**, and hence MII formation
- Cells compensate this lack of DHA by converting omega-6 EFA linoleic acid to decosapentanoic acid, which is not efficient in supporting rhodopsin.
- The retinal abnormalities due to DHA deficiency are reversible
- but the **responsiveness of the visual cortex, and the higher cortical centres involved in visual function**, appear long-lasting and irreversible
- In infants: supplementation should be approached with caution as these infants have low retinal levels of vitamin E and **increased retinal DHA concentration could increase susceptibility to retinal oxidative damage**

Aging of the retina & Lipids

•The “lipid wall”, made of cholesterol, participates in the age associated thickening of Bruch's membrane that increases hydraulic resistance and may reduce the fluxes of nutrients to the retina

•AMD targets a specific area of the retina: the macula.

•High fat intake has been associated with higher risk for AMD.

•Smoking and light exposure are, for instance, recognized as promoting factors

•In a study it was observed that participants who have the highest omega-3 long-chain polyunsaturated fatty acid (EPA and DHA) intake (0.11% of total energy intake) were 30% less likely to develop Geographic atrophy and neovascularAMD than low consumers (0.01% of total energy intake)

Lipids in tears

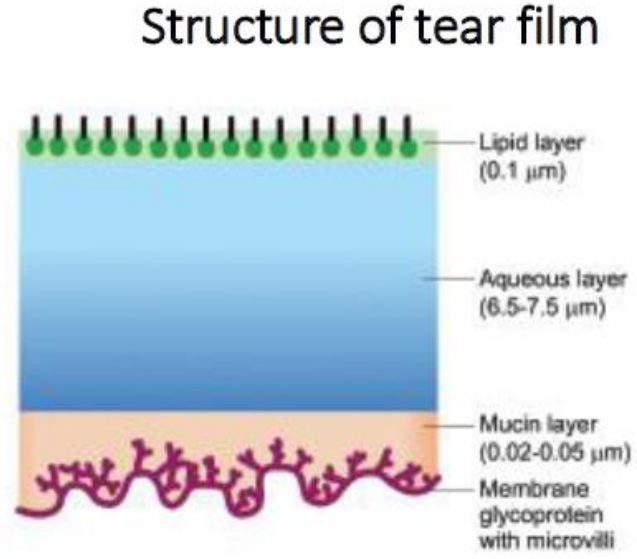
•Tear film is actually composed of three basic layers: mucin, water and lipids from posterior to anterior.

•**Lipid or oily layer** is the outermost layer of tear film formed at air-tear interface from the secretions of Meibomian, Zeis, and Moll glands.

•This layer prevents the overflow of tears, retards their evaporation and lubricates the eyelids as they slide over the surface of the globe.

•Lipids within tears help prevent water evaporation from the ocular surface and protect the eye against infection

•Prolonged dry eyes leads to cloudy cornea, inhibiting self repair of the damaged cornea



Eye Diseases linked to lipids

•**Arcus senilis**refers to an annular lipid infiltration of corneal periphery. This is an age-related change occurring bilaterally in 60 percent of patients between 40 and 60 years of age and in nearly all patients over the age of 80.

•**Fatty degeneration (Lipoid keratopathy)of cornea** is characterisedby whitish or yellowish deposits. The fat deposits mostly consist of cholesterol and fatty acids

•**Diabetic retinopathy**: hyperlipidemia is a risk factor

•**Seborrhoeicor squamous blepharitis:** glands of Zeissecrete abnormal excessive neutral lipids which are split by *Corynebacteriumacne* into irritating free fatty acids

Eye Diseases linked to lipids

•**Xanthelasma:**

•Thesearecreamy-yellowplaque-likelesionswhichfrequentlyinvolvetheskinofupperandlowerlidsneartheinnercanthus.

•Xanthelasmarepresentslipiddepositsinhistiocytesinthedermisofthelid.

•Thesemaybeassociatedwithdiabetesmellitusorhighcholesterollevels.

•**THE DRY EYE:**

•Lipid deficiency is extremely rare.

•It has only been described in some cases of congenital anhidrotic ectodermal dysplasia along with absence of meibomianglands.

•However, lipid abnormalities are quite common in patients with chronic blepharitis and chronic meibomitis

•Lipid soluble drugs have better permeability in eyes

•***Asteroid hyalosis.***

•It is characterisedby small, white rounded bodies suspended in the vitreous gel.

•These are formed due to accumulation of calcium containing lipids.

•Asteroid hyalosisis a unilateral, asymptomatic condition usually seen in old patients with healthy vitreous.

•There is a genetic relationship between this condition, diabetes and hypercholesterolaemia.

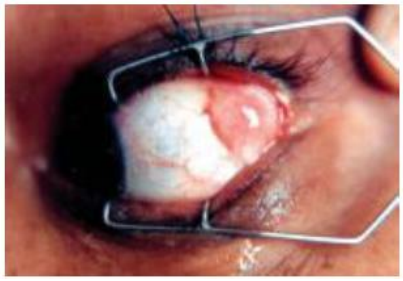
•The genesis is unknown and there is no effective treatment

Lipodermoids.

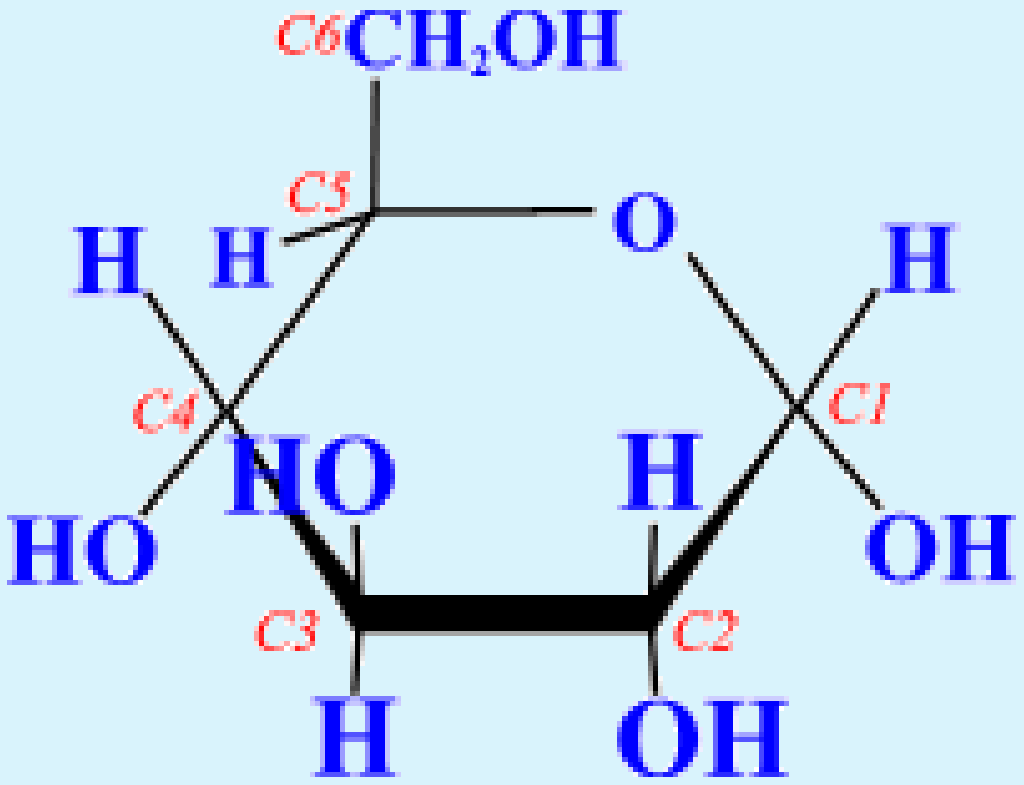
•These are solid tumours usually seen beneath the conjunctiva.

•These are mostly located adjacent to the superior temporal quadrant of the globe.

•These do not require any surgical intervention unless they enlarge significantly



Carbohydrate (CHO)



2023

D. Hayder K. Khattar Althalme

Outline of carbohydrate lecture

- Introduction to carbohydrate
- Functions of carbohydrates
- Classification of carbohydrates
- Carbohydrate metabolism
- Hormonal regulation of glucose

Carbohydrates

Introduction

- Constructed from Carbon - carbon-
- Hydrogen & O_2 – (hydrates, or water)
- General formula ($C_nH_{2n}O_n$).

- **Carbohydrate Nomenclature-Monosaccharides - Disaccharides-Polysaccharides-Glycogen-Starch**

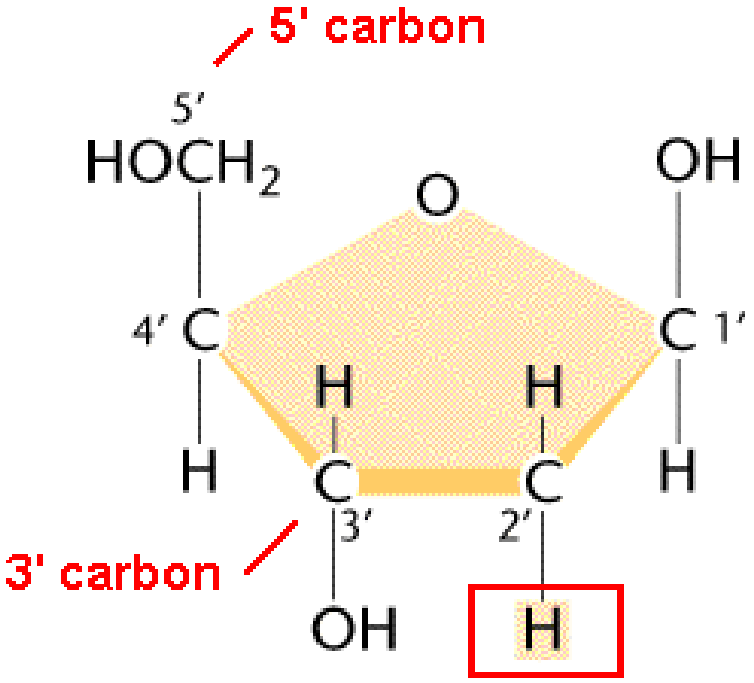
- Carbohydrates are organic compounds that contain large quantities of hydroxyl groups. It has the general formula ($C_nH_{2n}O_n$). The simplest carbohydrates also contain either an **aldehyde moiety** (these are termed polyhydroxy aldehydes) or a **ketone moiety** (polyhydroxy ketones).

Function of carbohydrates

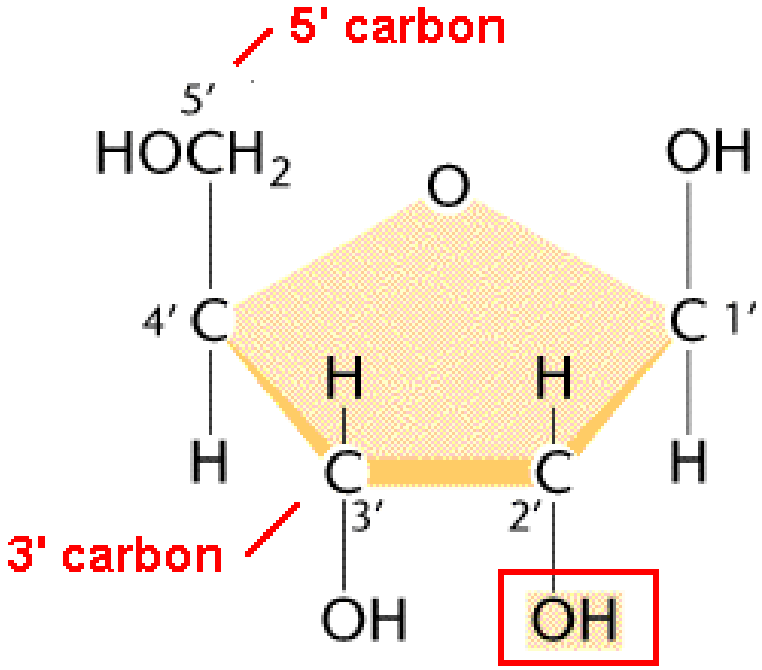
- Energy source- 1g= 4kcal - 17kj
- by conversion of glucose→ CO_2 +H_2O + ATP
- Stored as glycogen in the **liver** and **muscles** or triglyceride in **adipose tissue**
- Cell structure (plants-cellulose & animals- chitin)
- Recognition markers - eg. A,B,O blood types
- Structural component of nucleic acids
- Part of plasma membrane

Importance of Carbohydrates:

1. Glucose is a major fuel of the tissues of **mammals** and can be stored as glycogen for energy.
2. Ribose and deoxyribose is a component of **RNA** and **DNA**, respectively.
3. **Galactose** is the main component of milk.
4. Many diseases associated with defects in CHO metabolism e.g. {**diabetes mellitus (DM), glycogen storage diseases**}.
5. Polysaccharides are structural elements in the cell wall of **bacteria**, **plants**, and **exoskeleton** of **arthropods**.
6. CHO play a key role in **cell-cell** recognition process.



2-Deoxyribose



Ribose

3. Classification

1. **Monosaccharides,**

2. **Disaccharides,**

3. **Oligosaccharides** (from two to ten monosaccharide units, linked by **glycosidic bonds**),

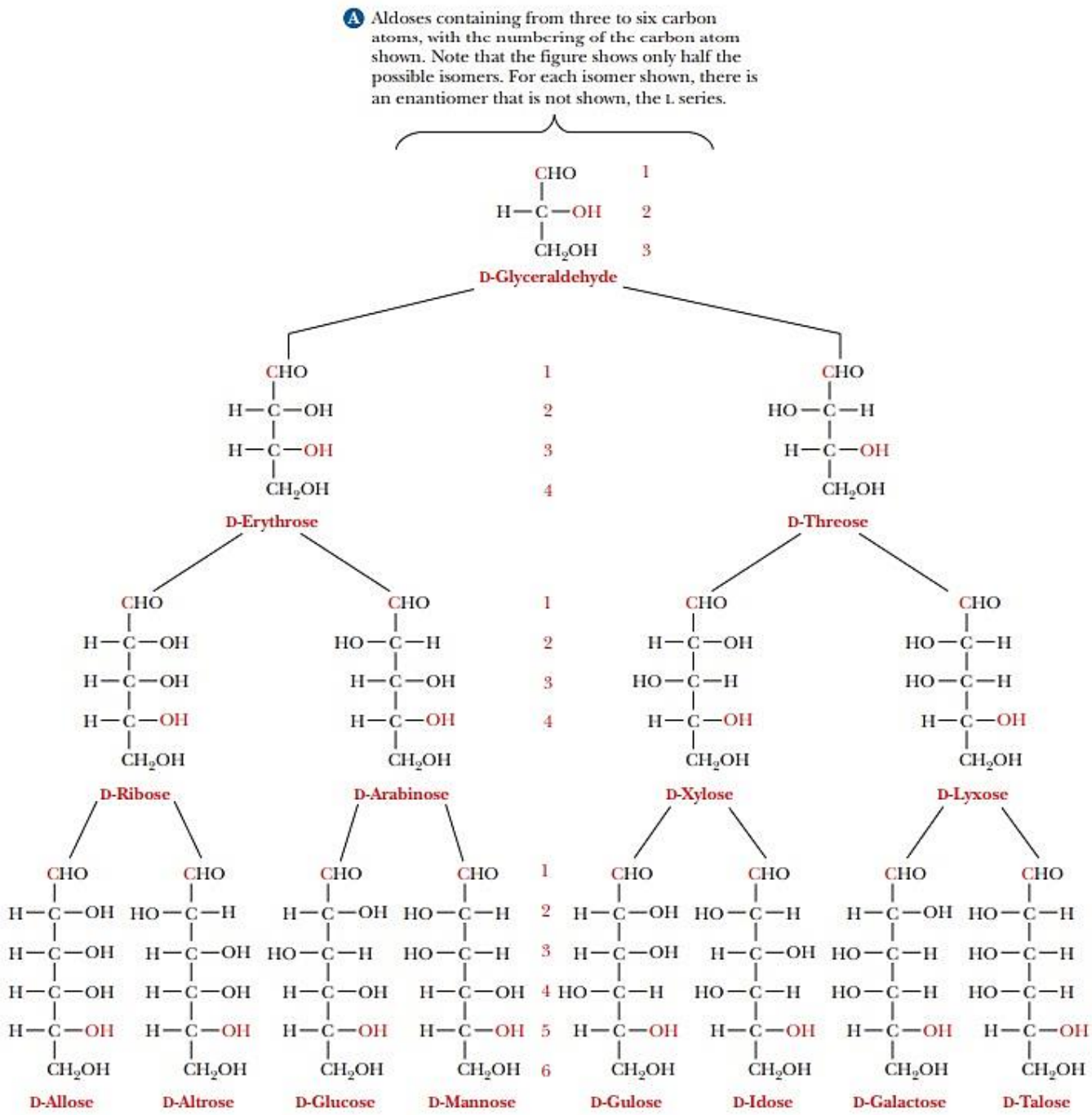
4. **Polysaccharides** (hundreds of monosaccharide units).

- Carbohydrates can combine with lipid to form **glycolipids** or with protein to form **glycoproteins**.

Monosaccharides and Disaccharides

Stereoisomerism in Sugars

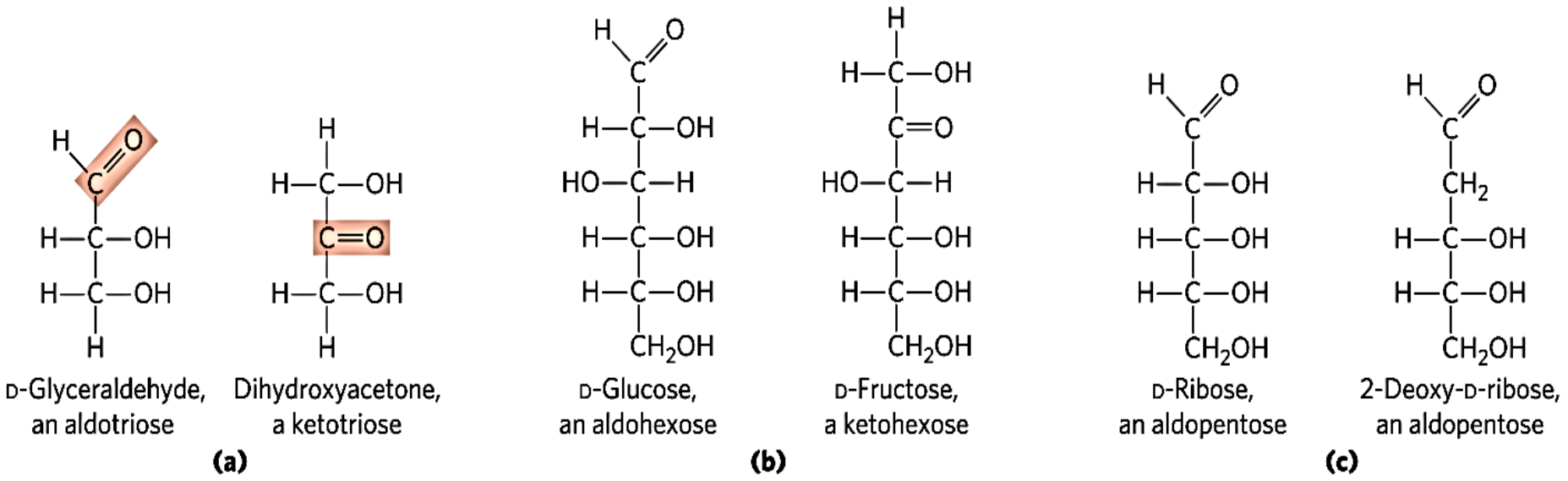
- sugar stereoisomers arise because many of the carbon atoms to which the **hydroxyl groups** are attached are **chiral centers.**
- enzymes that act on sugars are **stereospecific** .


A Aldoses containing from three to six carbon atoms, with the numbering of the carbon atom shown. Note that the figure shows only half the possible isomers. For each isomer shown, there is an enantiomer that is not shown, the L series.
D-Glyceraldehyde
D-Erythrose
D-Threose
D-Ribose
D-Arabinose
D-Xylose
D-Lyxose
D-Allose
D-Altrose
D-Glucose
D-Mannose
D-Gulose
D-Idose
D-Galactose
D-Talose

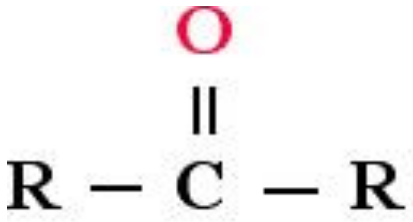
Aldoses and Ketoses

- **aldose** = carbonyl group is at an end of the carbon chain (in an aldehyde group)

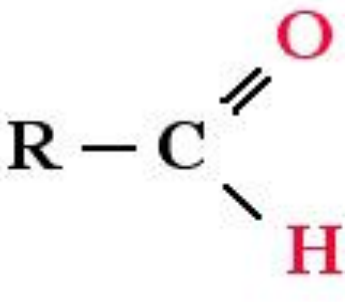
- **ketose** = carbonyl group is at any other position (in a ketone group)



- Two functional groups
  1. hydroxyl (- OH)
  2. Carbonyl
     - one of the carbon atom is double bonded to an oxygen atom to form a **carbonyl group**
     - Two types:

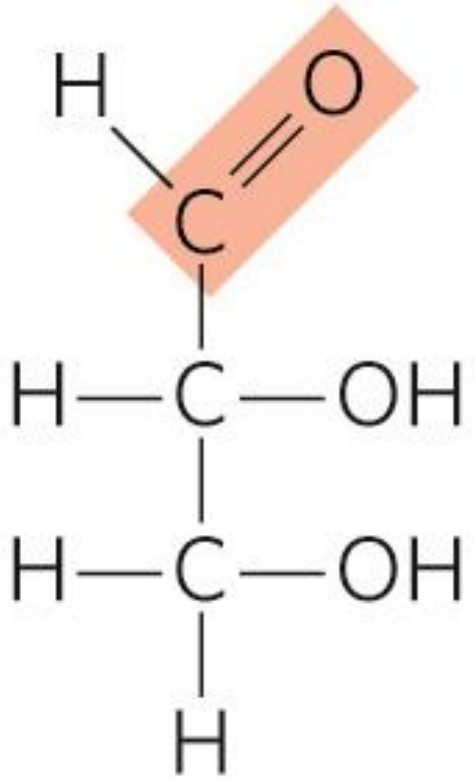


Ketone Group

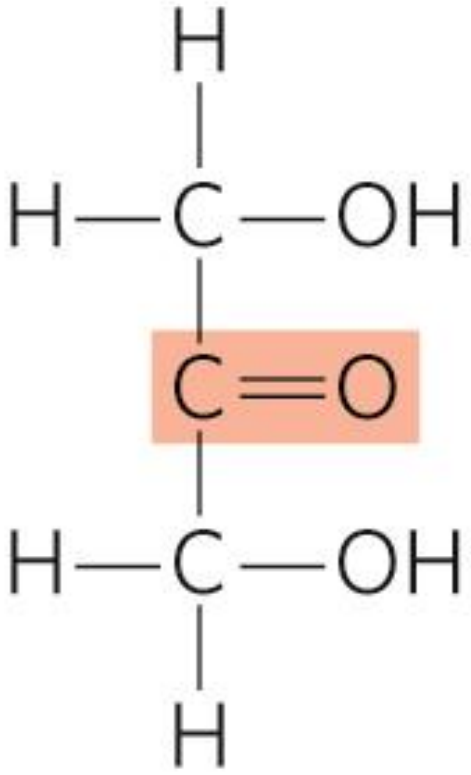


Aldehyde Group

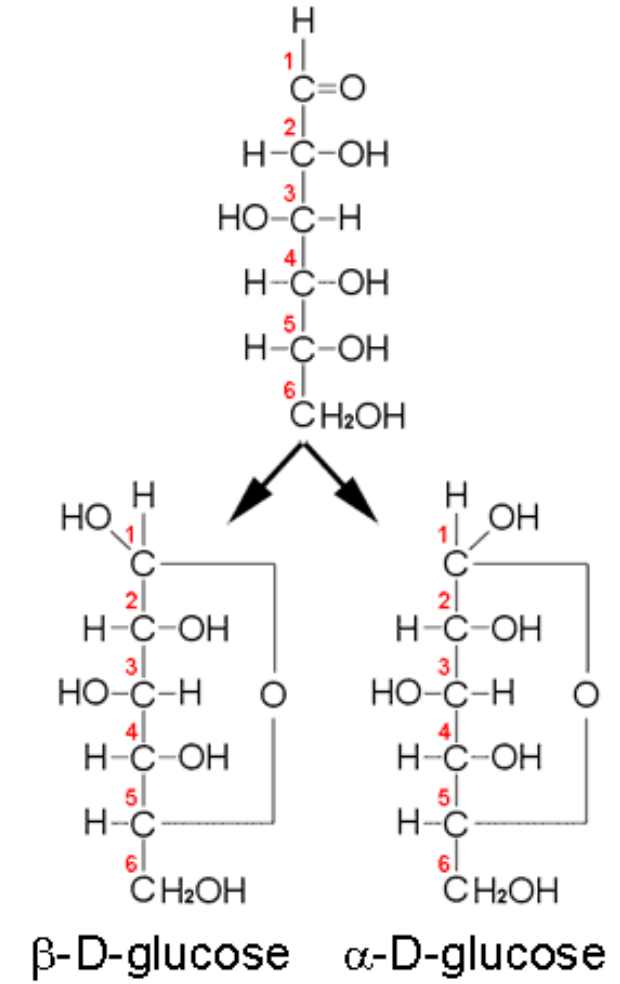
Note: A carbon atoms (or any other) atoms bonded to four **dissimilar atom** is asymmetric or **chiral** carbon

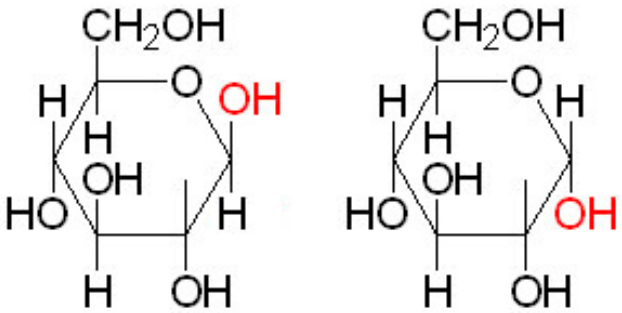


D-Glyceraldehyde, an aldotriose

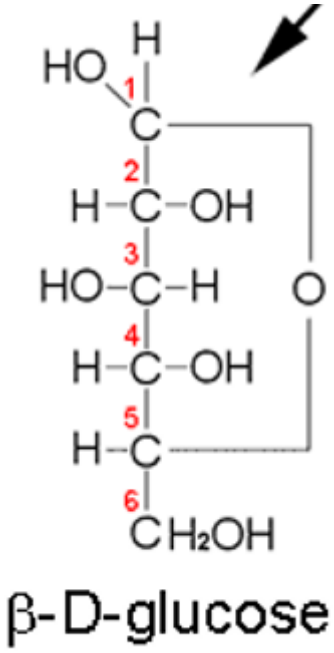


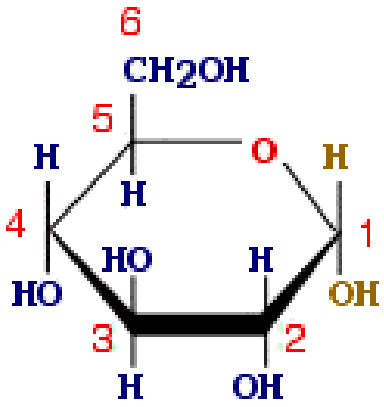
Dihydroxyacetone, a ketotriose

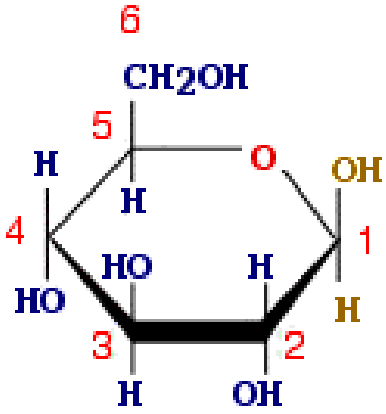

β-D-glucose
α-D-glucose

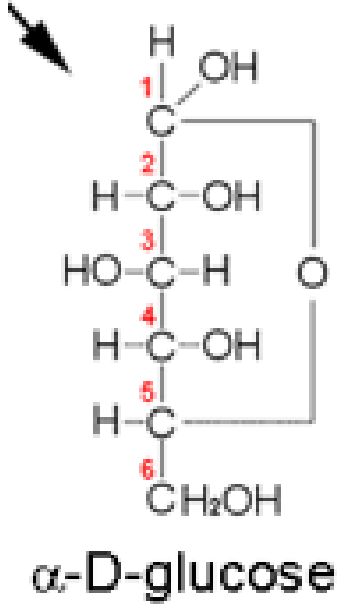


- α- form: if the hydroxyl group on carbon 1 written to the right or below the plane of the ring, it is an **alpha form .**
- β-form: If the –OH on the carbon 1 written to the left or above the plan of the ring. it is an **Beata form .**







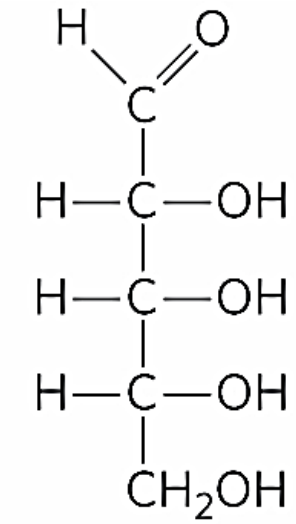


Tetroses and Pentoses

- tetroses = four carbon backbone

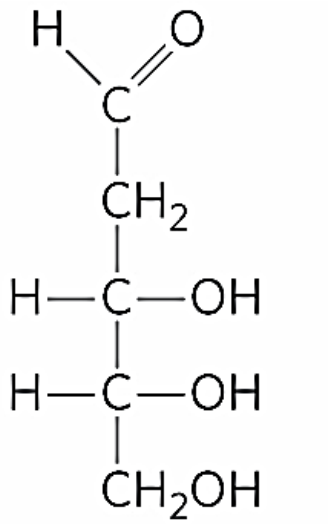
- pentoses = five carbon backbone

component of RNA



D-Ribose, an aldopentose

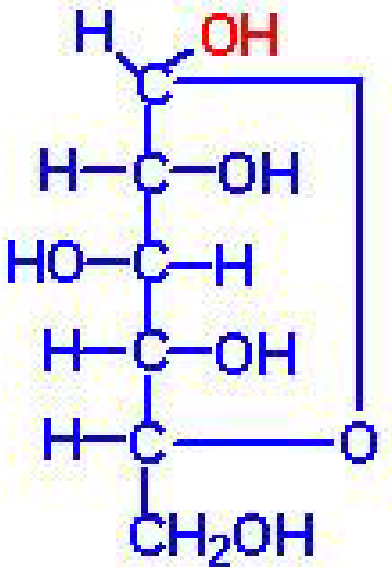
component of DNA



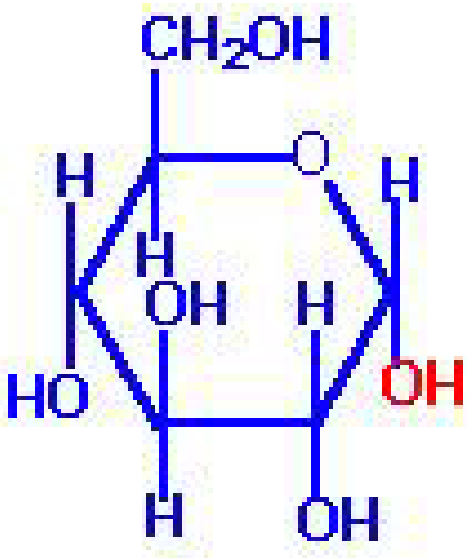
2-Deoxy-D-ribose, an aldopentose

*Plotting methods: such structures can be depicted by either **Fischer** or **Haworth** style diagrams.

*Numbering: the numbering of the carbons in carbohydrates proceeds from the carbonyl carbon, for aldoses, or the carbon **nearest** the carbonyl, for ketoses.



Cyclic Fischer Projection of α-D-Glucose



Haworth Projection of α -D-Glucose

Stereoisomerism: Compounds have the same structural formula but differ in spatial configuration.

Number of isomers=2Number of asymmetric atoms

The rings can open and re-close, allowing rotation to occur about the carbon bearing the reactive carbonyl yielding two distinct configurations **(α and β) of the hemiacetals** and **hemiketals**.

anomeric carbon: the carbon about which this rotation occurs and forming the sugar types (α and β) and its carbon number (1) in glucose.

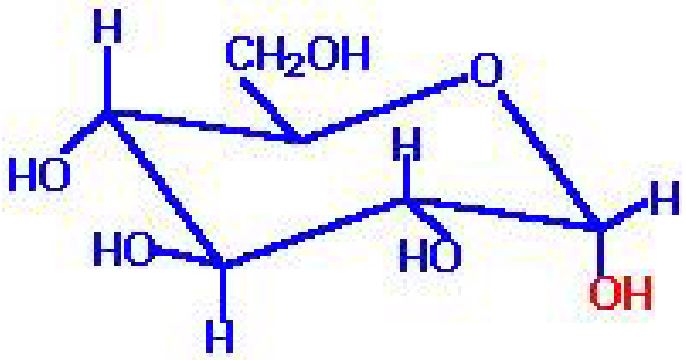
Mutarotation: Carbohydrates can change spontaneously between the (α and β) configurations.

- ❖ When drawn in the Fischer projection, the α configuration places the hydroxyl attached to the anomeric carbon to the right, towards the ring.
- ❖ When drawn in the Haworth projection, the α configuration places the hydroxyl downward.

The spatial relationships of the atoms of the furanose and pyranose ring structures are more correctly described by the two conformations identified as the **chair form** and the **boat form**.

* The chair form is the more stable of the two.

- ❖ In the chair conformation, the orientation of the hydroxyl group about the anomeric carbon of α -D-glucose is axial and equatorial in **α** -D-glucose.

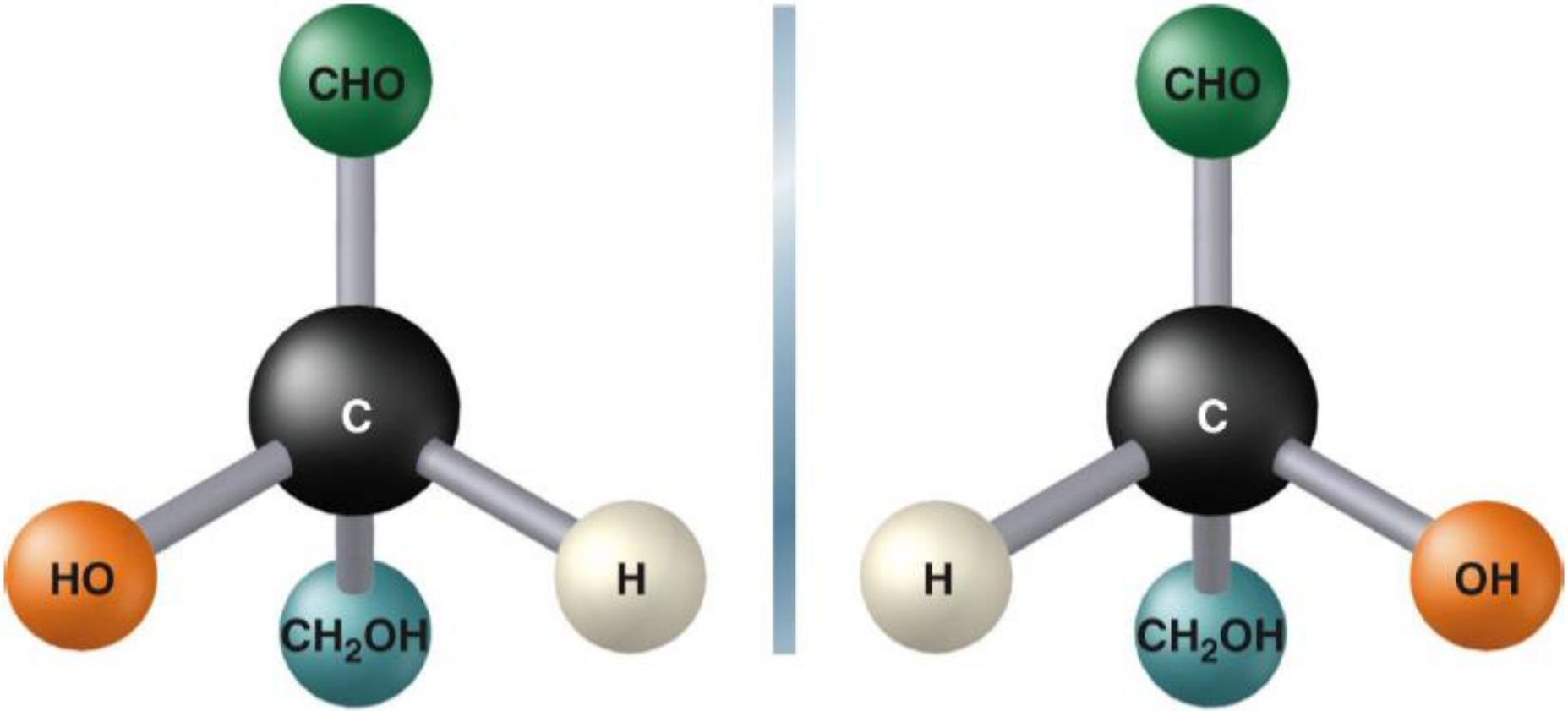


* The simplest carbohydrates encountered in the body are **glyceraldehyde** (aldotriose) and to the **dihydroxyacetone**(ketotriose).

*All carbohydrates contain at least one asymmetrical **(chiral carbon)** (carbon atom attached to four different groups) and are, therefore, optically active (can rotate the plane of the polarized light to the right =dextro (+) and to the left (-) Levo).

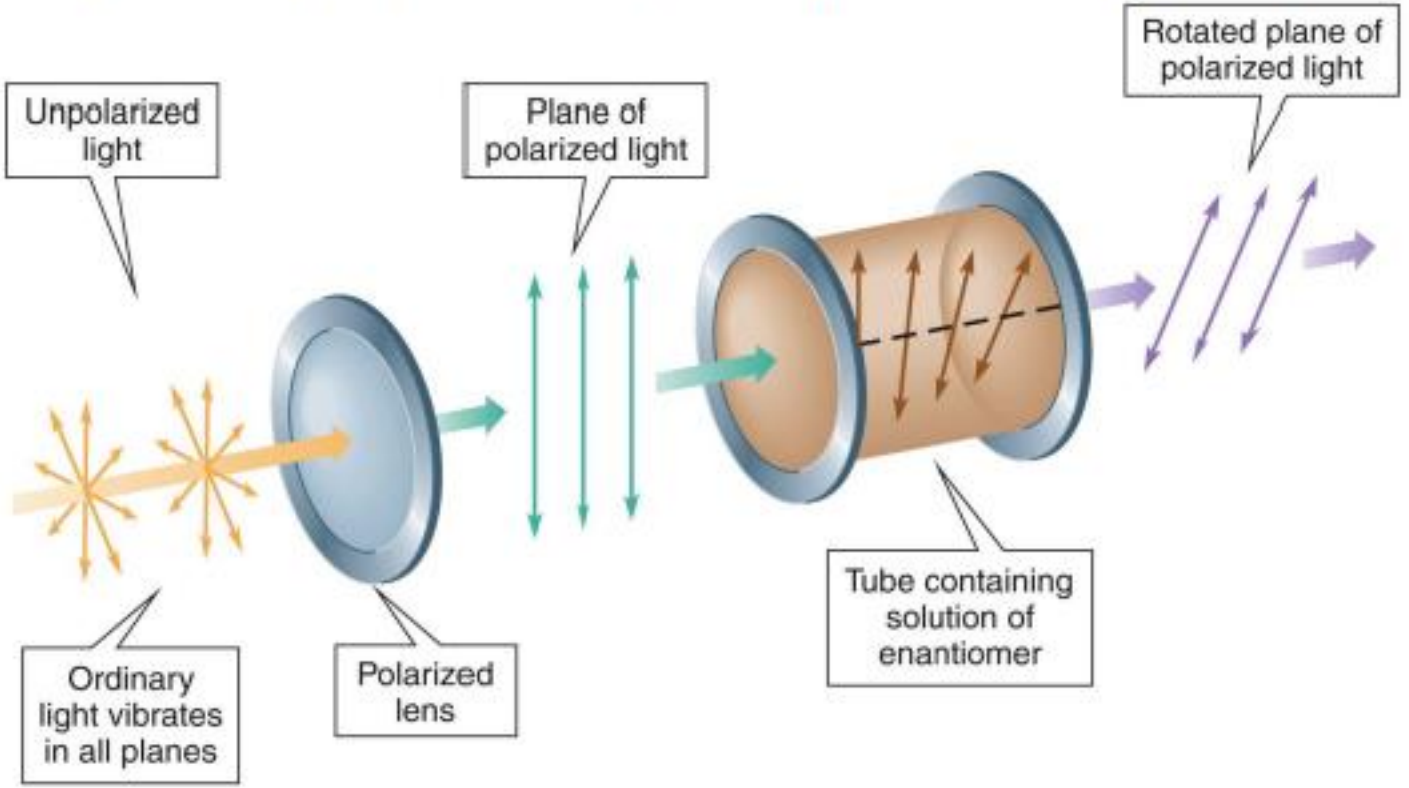
Two Forms of Glyceraldehyde

- Glyceraldehyde, the simplest carbohydrate, exists in two isomeric forms that are mirror images of each other:



What's So Great About Chiral Molecules?

- Molecules which are enantiomers of each other have exactly the **same** physical properties (melting point, boiling point, index of refraction, etc.) but not their interaction with **polarized light**.
- Polarized light vibrates only in one plane; it results from passing light through a **polarizing filter**.



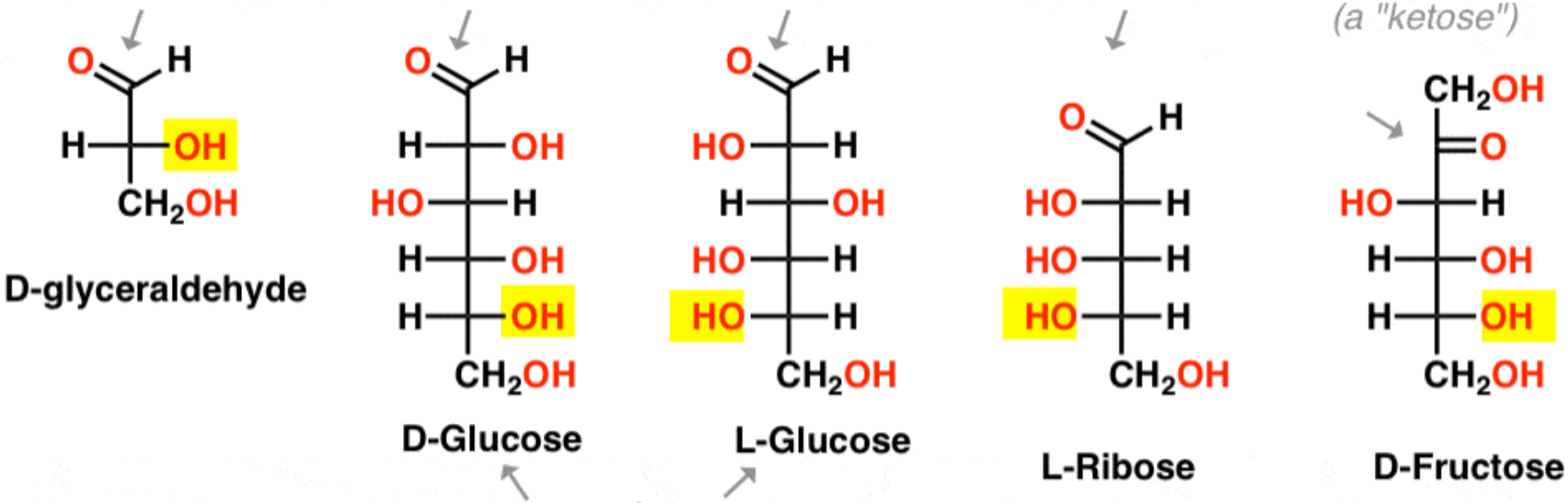
D- and L- Sugars

For a sugar drawn in the Fischer projection with the most oxidized carbon at the top:

- If the OH on the bottom chiral center points to the **right**, the sugar is **D**
- If the OH on the bottom chiral center points to the **left**, the sugar is **L**

most oxidized carbon (aldehyde) at top: these are "aldoses"

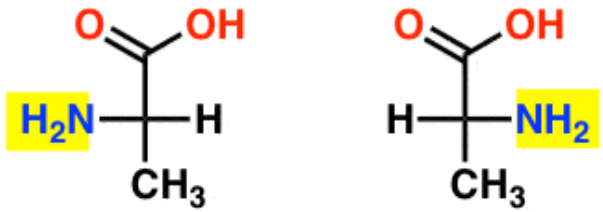
ketone (a "ketose")



L- and D- is a means of describing the **absolute configuration** of a molecule that pre-dates *R* and *S* but is still used for some biological molecules (sugars, amino acids). It's a quick way of denoting enantiomers: e.g. L-glucose and D-glucose are enantiomers.

L- and D- have no relation to the optical rotation of a molecule.

The D- L- system can also be applied to other chiral molecules, e.g. amino acids:



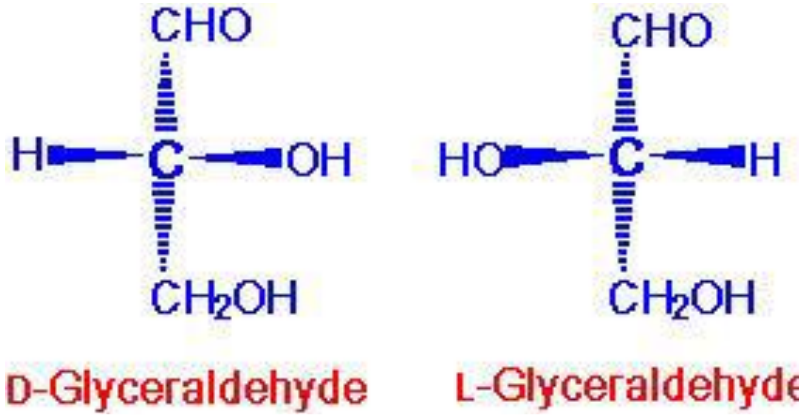
The form of glucose present in the human body is D-glucose. This is the naturally occurring form of glucose, and it is the form that is utilized by **cells** for energy production and metabolic processes.

The reason for this is that the enzymes responsible for metabolizing glucose in the body are specific for D-glucose and cannot effectively use the mirror-image isomer, L-glucose. Additionally, D-glucose is the form that is transported across cell membranes, **incorporated into glycogen (a storage form of glucose in the body),** and used as a building block for other sugars and carbohydrates.

In summary, D-glucose is the form of glucose found in the human body because it is the form that is metabolically active and utilized by the body's cells for energy and other processes.

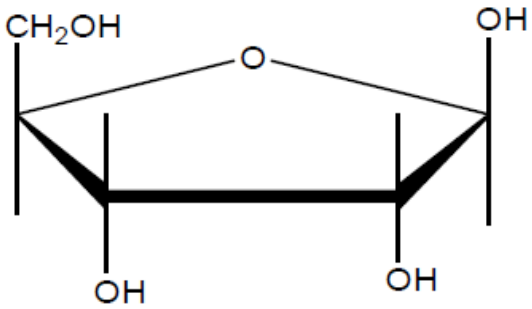
*** Racemic mixture :** When equal amounts of D and L isomers are present in solution cause elimination of optical activity.

***Enantiomers:** The mirror-image conformations of the same compound depending on the orientation of the hydroxyl group about the asymmetric carbon farthest from the carbonyl. (e.g. carbon atom number 5 in glucose). They are in the **L-conformation** (hydroxyl group to the left) and **D-conformation** (hydroxyl group to the right).



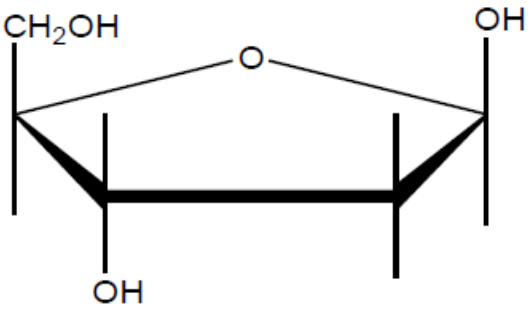
Structures of Glyceraldehyde Enantiomers

❖ **Deoxy sugars**: One of the hydroxyl groups of the sugars reduced (**-OH into -H**) . The most important example is **ribose** (present in **RNA**) and **deoxyribose** (**present** in **DNA**)



β-D-Ribose

present in RNA)



β-D-Deoxyribose

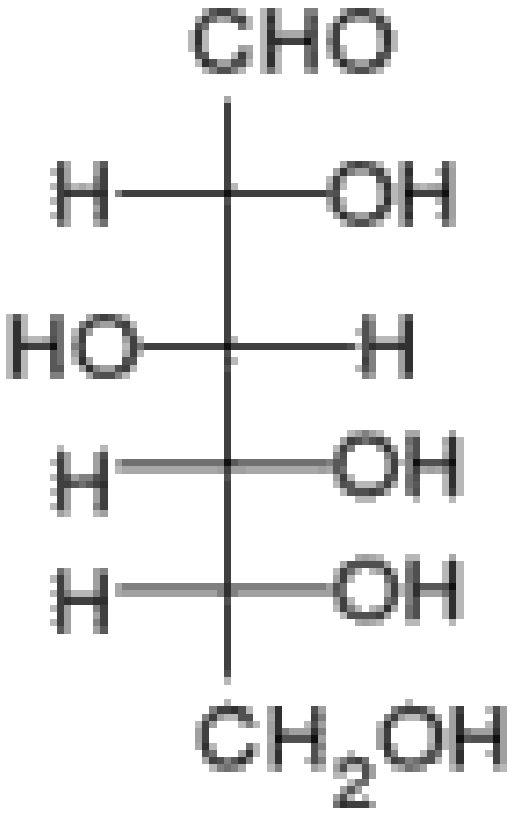
(present in DNA)

Monosaccharides Have Asymmetric Centers

- all monosaccharides (except dihydroxyacetone) contain 1+ chiral carbon atom
  - occur in optically active isomeric forms

- **Enantiomers** = two different optical isomers that are mirror images

- In general, a molecule with n chiral centers can have $\mathbf{2^n}$ stereoisomers
- **Most natural sugars are D- and most natural amino acids are L- .**



- carbons are numbered beginning at the end of the chain near the carbonyl group

Diasteriomers: compound that have the same chemical formula but they are not mirror image for each other.

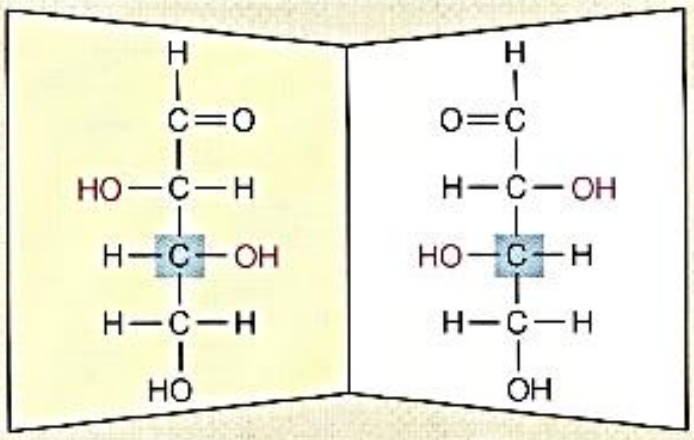
*__Epimers__: Isomers differ in the orientation of –OH groups around carbon atoms number 2, 3, or 4. For examples (glucose, galactose are epimers)

*__Epimerization__: Conversion of one sugar to another as a result of rotation of hydroxyl groups around carbon atoms number 2, 3, or 4.

Configurational isomers

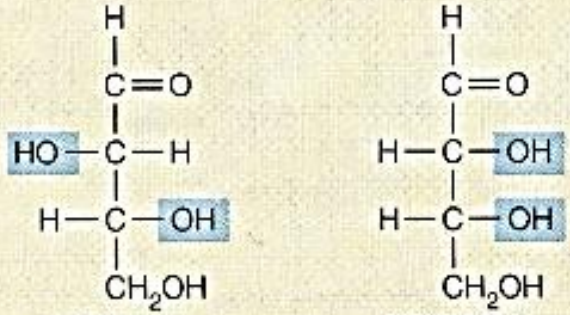
Enantiomers
Stereoisomers that are mirror images of one another

The boxed asymmetric carbon (farthest from aldehyde) determines D/L designation



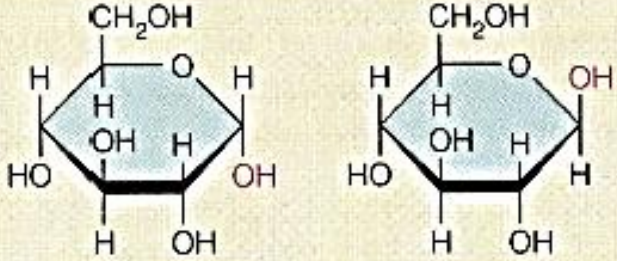
D-Threose L-Threose

Diastereomers
Stereoisomers that are not mirror images of one another



D-Threose D-Erythrose

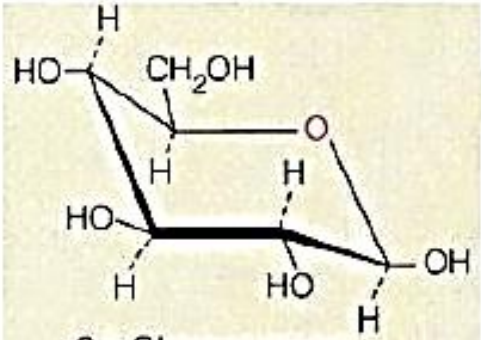
Anomers
Stereoisomers that differ in configuration at the anomeric carbon



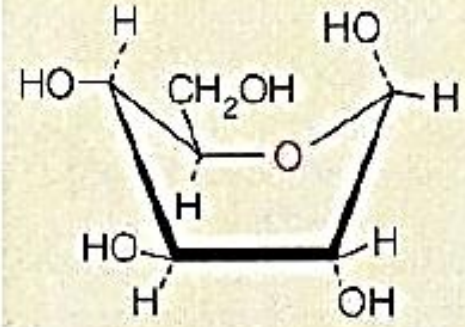
α-D-Glucopyranose β-D-Glucopyranose

Conformational isomers

Molecules with the same stereochemical configuration, but differing in three-dimensional conformation



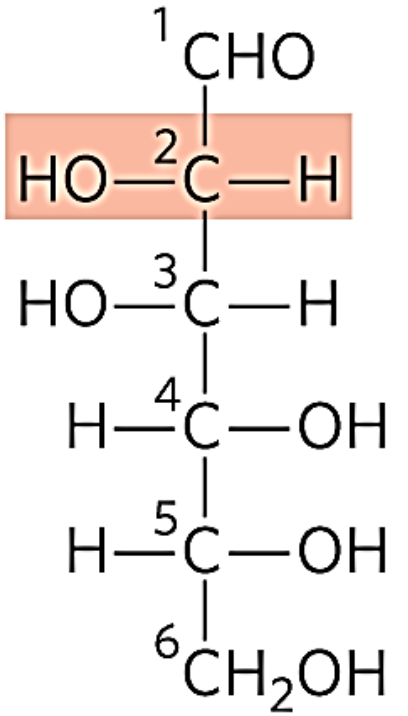
β-D-Glucopyranose chair form



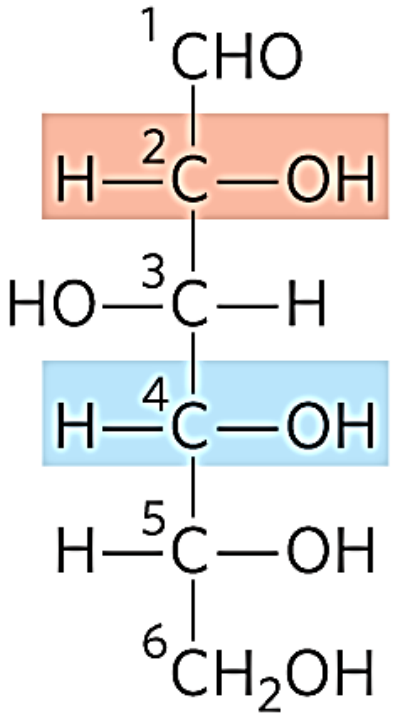
β-D-Glucopyranose boat form

Epimers

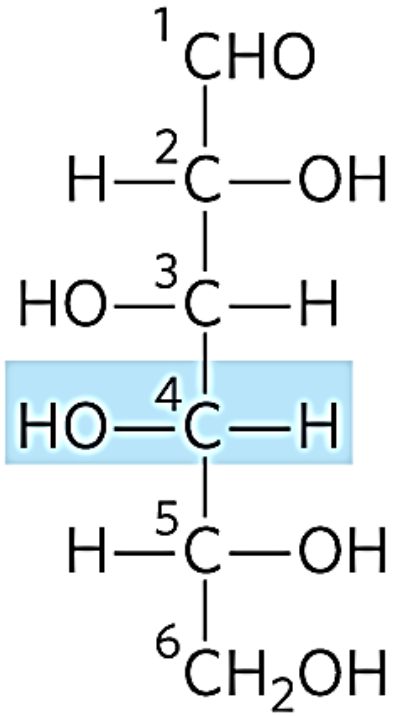
- **Epimers** = two sugars that differ only in the configuration around one carbon atom



D-Mannose
(epimer at C-2)

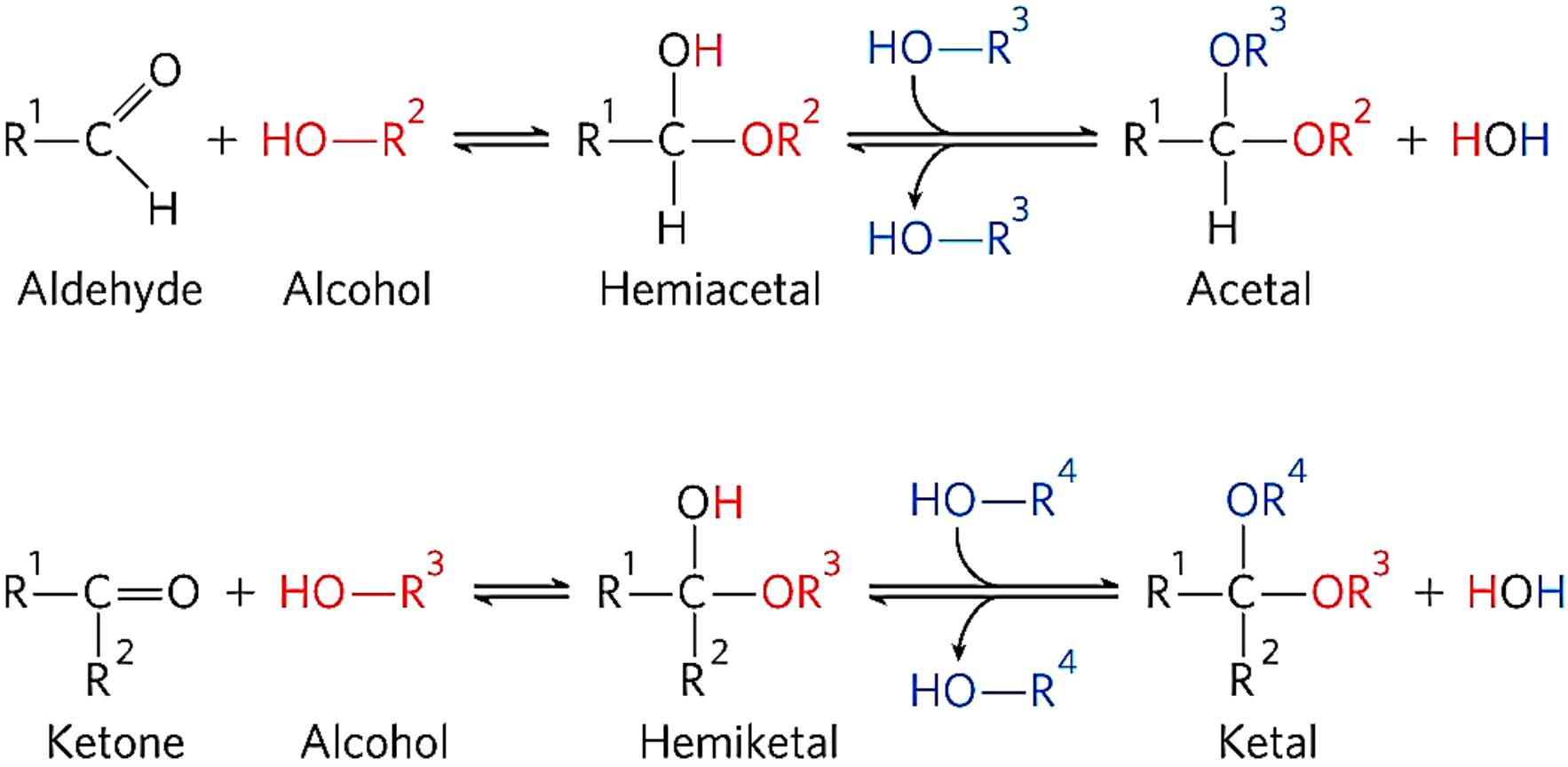


D-Glucose



D-Galactose
(epimer at C-4)

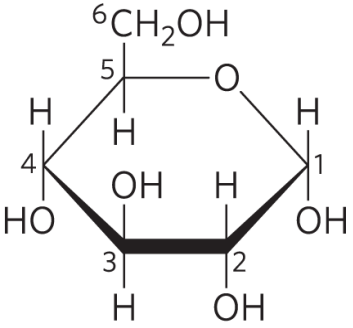
Formation of Hemiacetals and Hemiketals



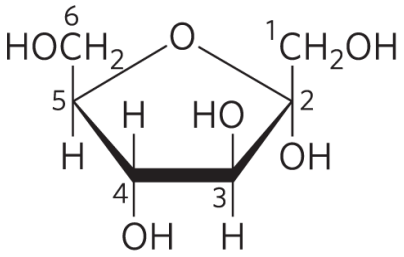
Pyranoses and Furanoses

- **pyranoses** = six-membered ring compounds
  - form when the hydroxyl group at C-6 reacts with the keto group at C-2

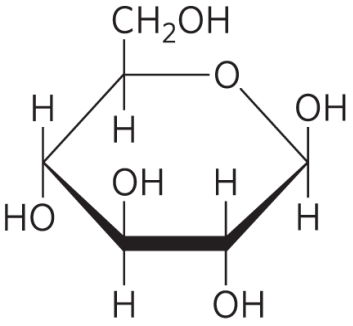
- **furanoses** = five-membered ring compounds
  - form when the hydroxyl group at C-5 reacts with the keto group at C-2



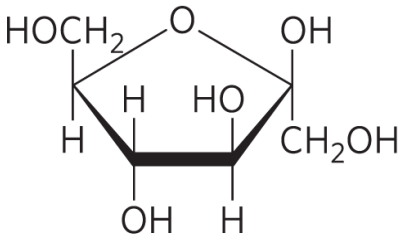
α-D-Glucopyranose



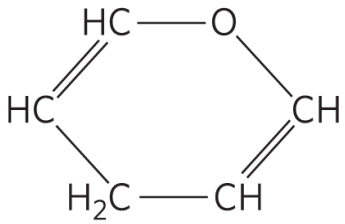
α-D-Fructofuranose



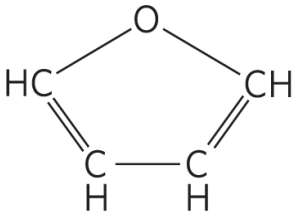
β-D-Glucopyranose



β-D-Fructofuranose

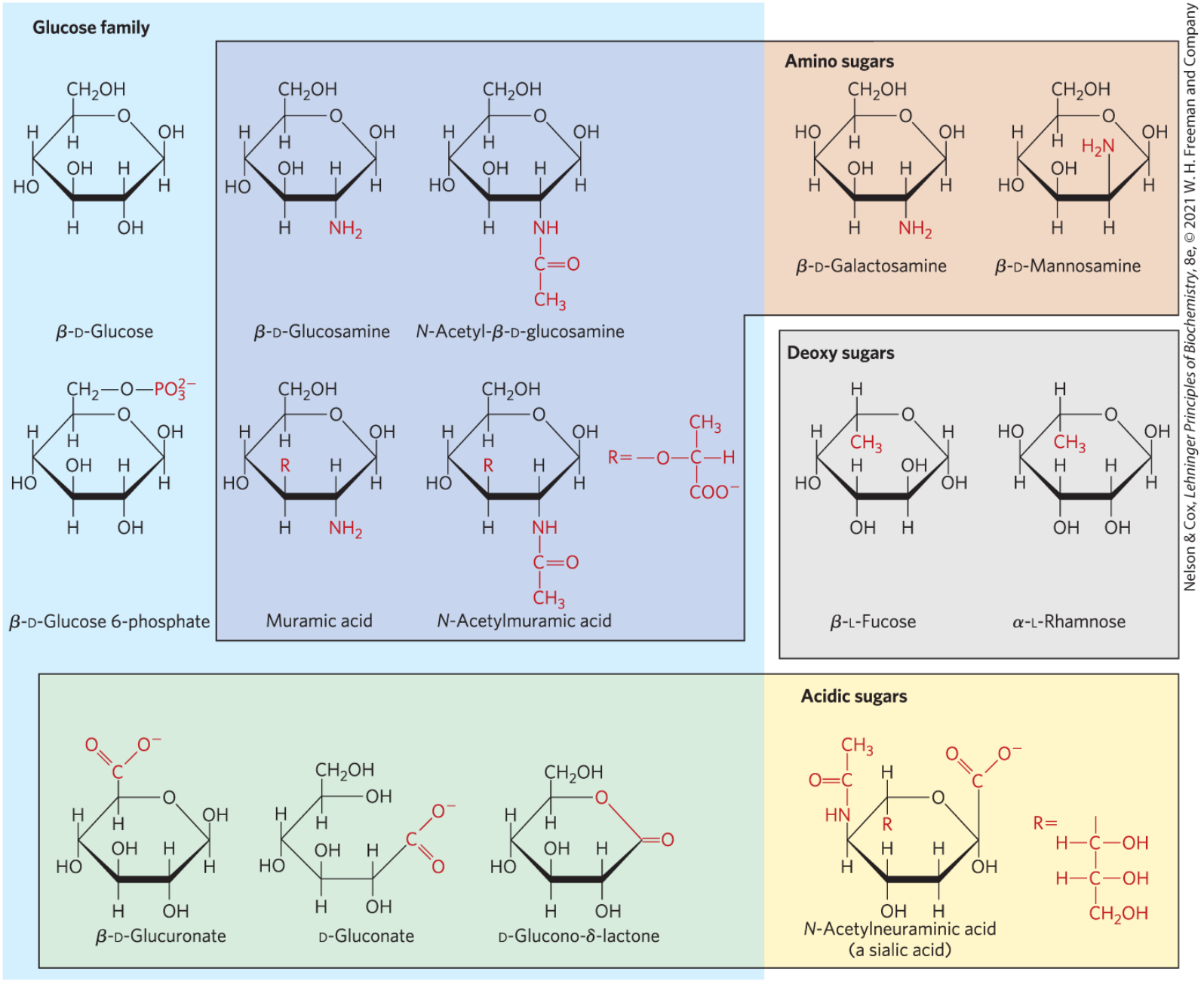


Pyran



Furan

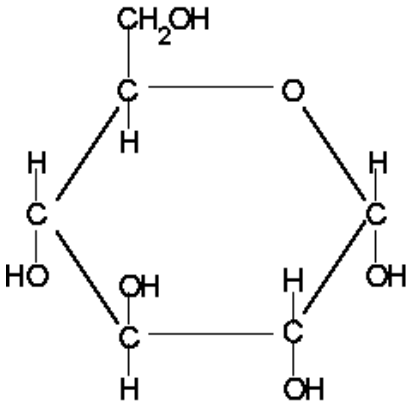
Organisms Contain a Variety of Hexose Derivatives



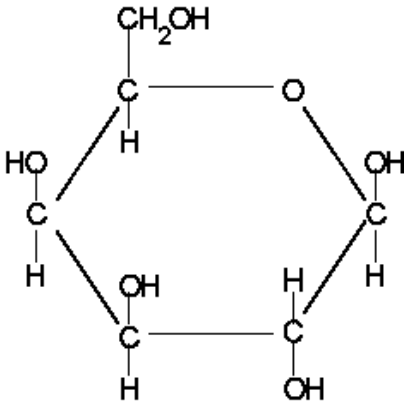
Simple Carbohydrate

- monosaccharides
  - All are 6 carbon hexes
    - 6 carbons
    - 12 hydrogens
    - 6 oxygens
    - arrangement differs
      - accounts for varying sweetness
  - glucose, fructose, galactose

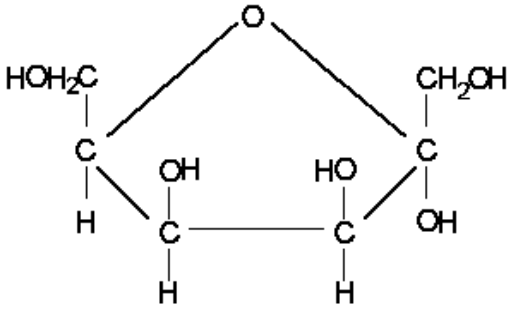
Structures of Common Monosaccharides



Glucose

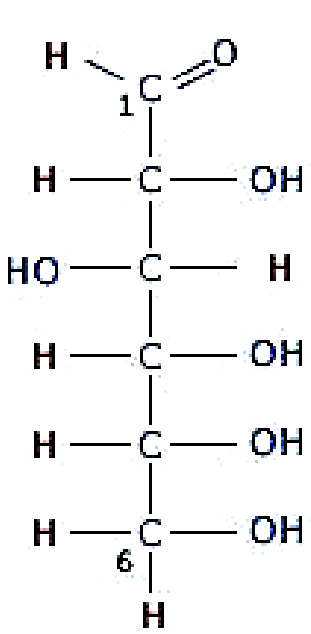


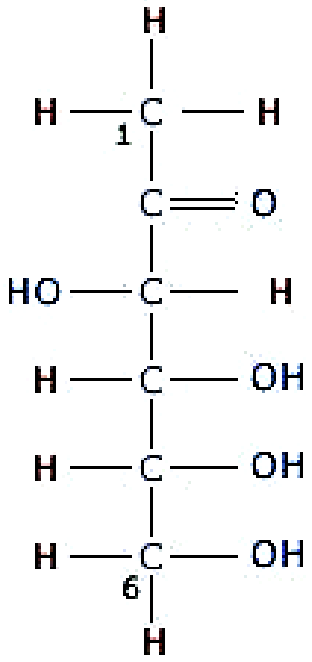
Galactose

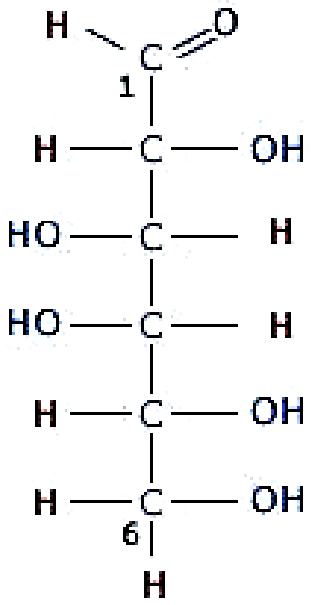


Fructose

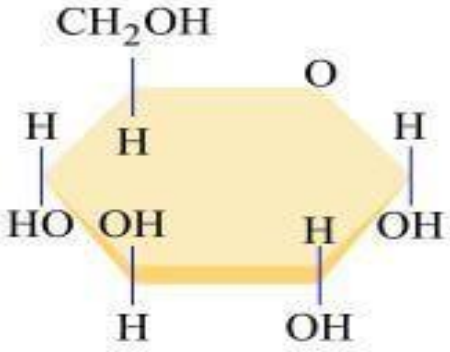
Three Monosaccharides $C_6H_{12}O_6$



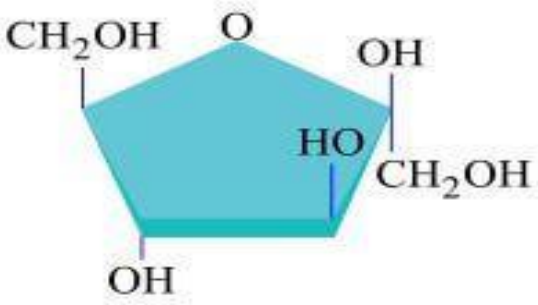




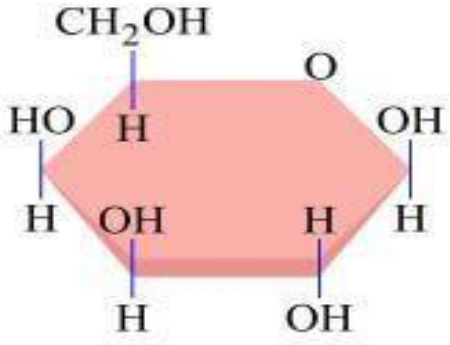
Monosaccharide



Glucose



Fructose



Galactose

Sugars That Are, or Can Form, Aldehydes Are Reducing Sugars

- **reducing sugars** = undergo a characteristic redox reaction where free aldehyde groups react with Cu^{2+} under alkaline condition reduction of Cu^{2+} to Cu^{+} forms a brick-red precipitate .
- ketoses that can tautomerize to form aldehydes are also **reducing sugars**

❖ **Reducing sugar** : A molecule containing **free carbonyl group** that can **reduce** the indicators such as **cupric ions** reagent into **cuprous ions**. (**Lactose** and **Mannose** are reducing sugars while **sucrose** are not reducing sugar).

O-Glycosidic Bonds

O-glycosidic bond =

covalent linkage joining

two monosaccharides

formed when a **hydroxyl**

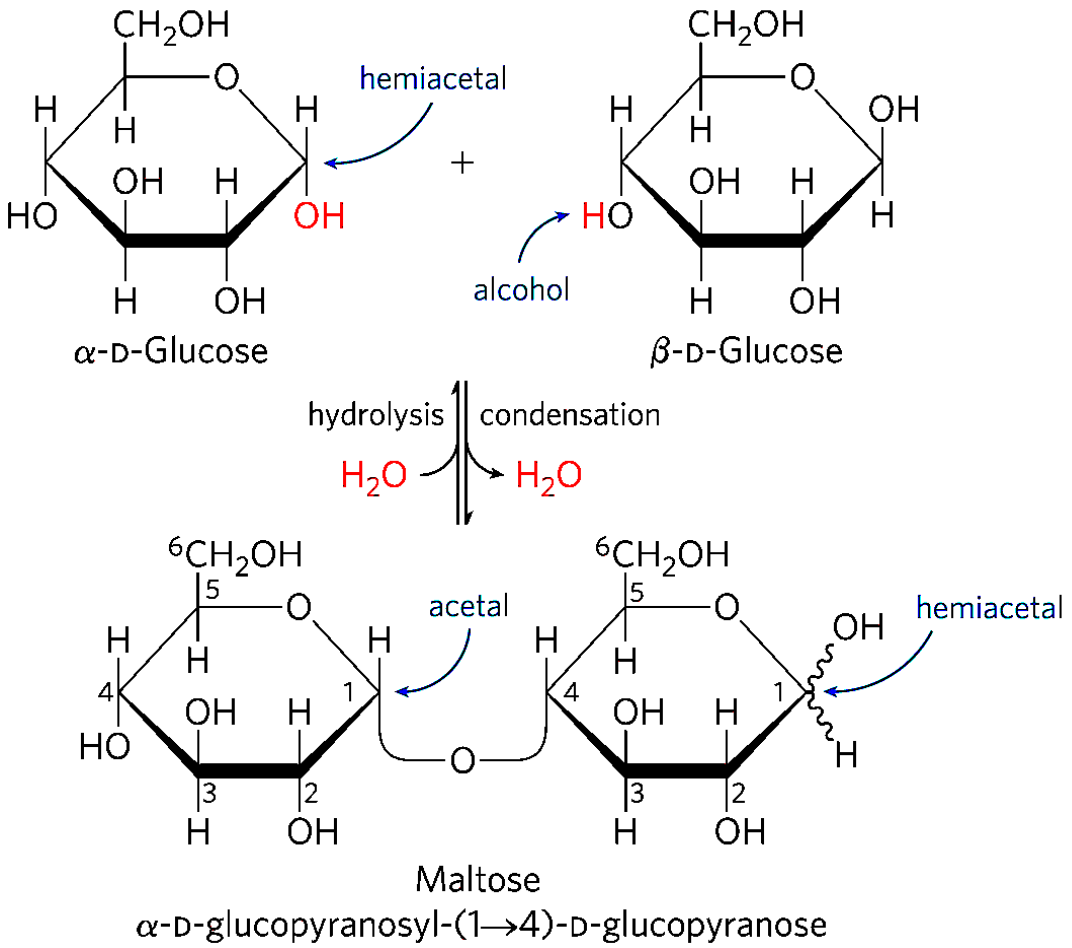
group of one sugar

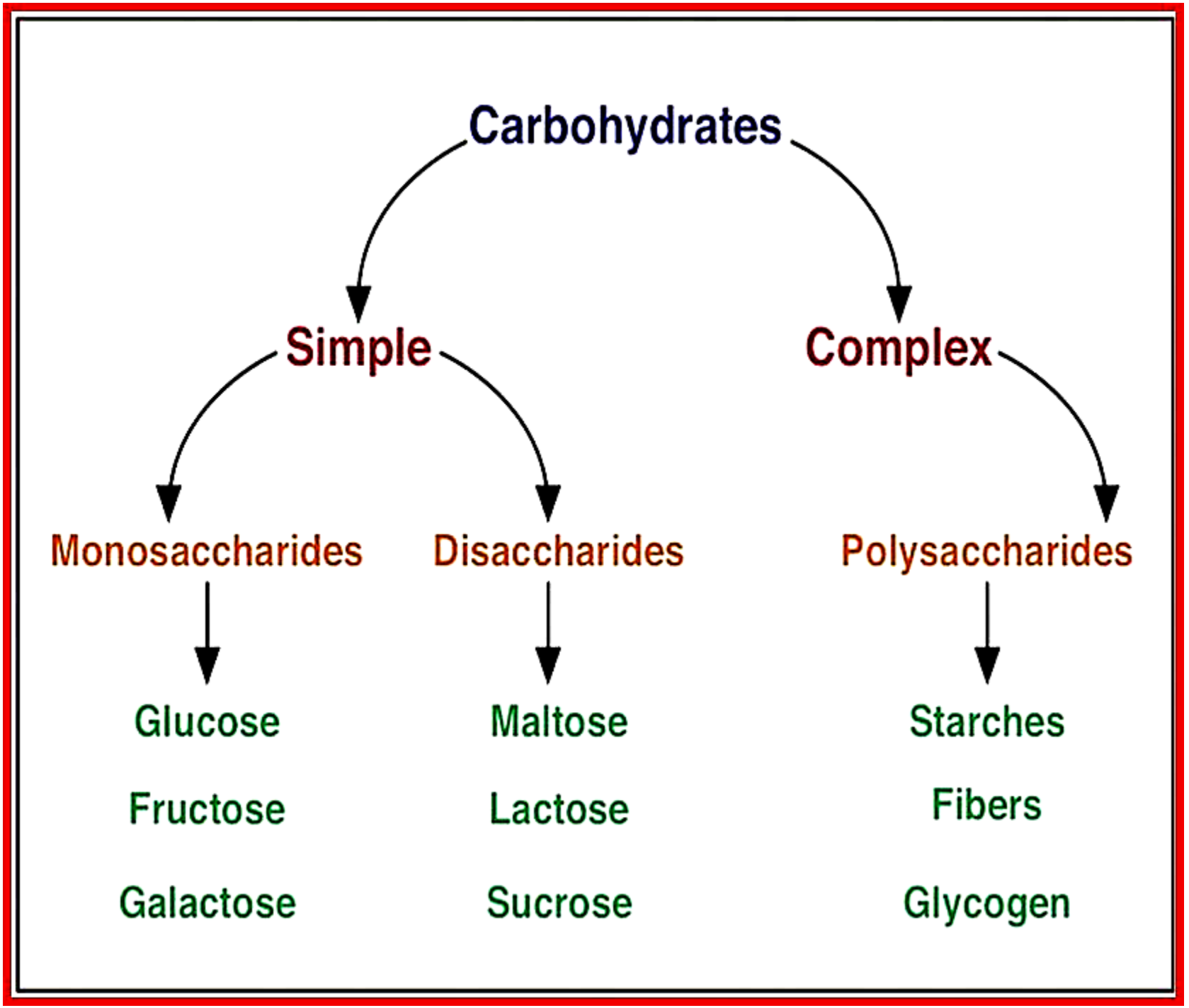
molecule reacts with the

anomeric carbon of the

other readily hydrolyzed by

acid .




Carbohydrates
Simple
Complex
Monosaccharides
Disaccharides
Polysaccharides
Glucose
Fructose
Galactose
Maltose
Lactose
Sucrose
Starches
Fibers
Glycogen

Carbohydrate Classifications

Simple carbohydrates

1. **Monosaccharides**, Glucose, fructose, galactose

2. **Disaccharides**, Lactose, sucrose, maltose

Complex carbohydrates

3. **Oligosaccharides** (from two to ten monosaccharide units, linked by glycosidic bonds), (3-10 monomers).

4. **Polysaccharides** (hundreds of monosaccharide units). (> 10 monomers).

Carbohydrates can combine with lipid to form **glycolipids** or with protein to form **glycoproteins**.

Starch , glycogen , cellulose

Simple Carbohydrates

Monosaccharides ($C_6H_{12}O_6$)

Glucose Fructose Galactose

Glucose – **dextrose** or blood sugar

1. Primary fuel for the body
2. Found in all disaccharides & polysaccharides

Fructose – fruit sugar

1. Found in fruit, honey, syrup
2. Converts to glucose in the body

Galactose – part of lactose

1. Found in milk
2. Converts to glucose in the body

Types of Disaccharides

Simple Carbohydrates

Disaccharides Sucrose Lactose Maltose

Sucrose – table sugar

1. Glucose + Fructose
2. Refined from sugar beets &cane

Maltose – malt sugar

1. Glucose + Glucose
2. Found in germinating seeds & used in fermentation to produce malted beverages (beer, whiskey)

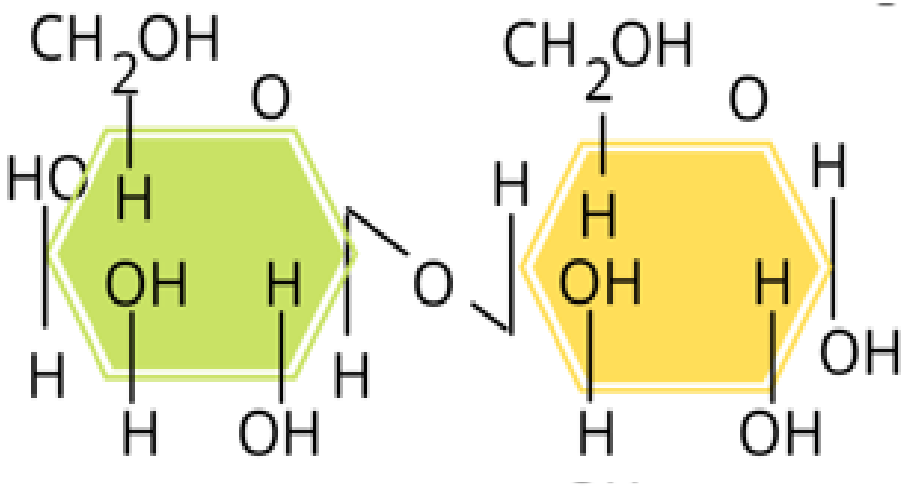
Lactose – milk sugar

1. Glucose + Galactose
2. Lactose intolerance – missing digestive enzyme needed to split into two monosaccharide parts to absorb it.

• **Sucrose**: prevalent in sugar **cane** and sugar **beets**, is composed of glucose and fructose through an **α** (1,2) -glycosidic bond.

• **Maltose**: the major degradation product of starch, is composed of 2 glucose monomers in an **α** (1,4) glycosidic bond.

• **Lactose**: is found exclusively in the milk of mammals and consists of galactose and glucose in a **β** (1,4) glycosidic bond.



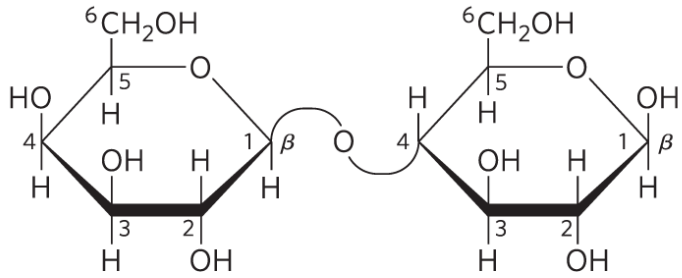
Lactose
galactose + glucose

Three Common Disaccharides

- **Lactose (milk sugar)=**

1 glucose + 1 galactose

- **with β (1-4) linkage from the anomeric OH of galactose. Its full name is β -D-galactopyranosyl-(1-4)-α-D-glucopyranose**

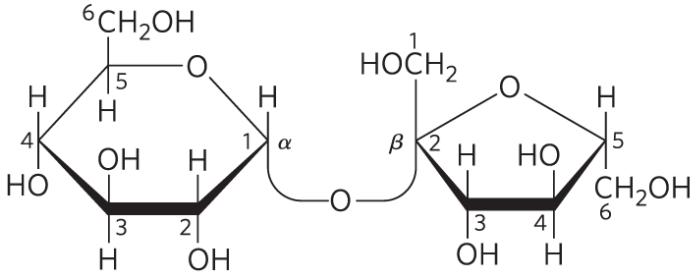


Lactose (β form)
β-D-galactopyranosyl-(1→4)-β-D-glucopyranose
Gal(β1→4)Glc

- **Sucrose (table sugar)=**

1 glucose + 1 fructose (fruit sugar)

- **Because the configuration at the anomeric C of glucose is α (O points down from ring), the linkage is α (1→2).**

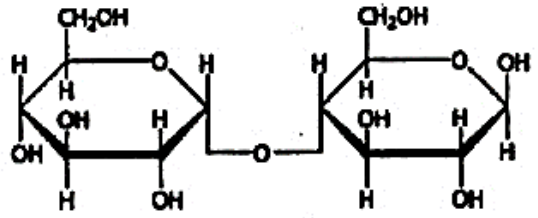


Sucrose
β-D-fructofuranosyl α-D-glucopyranoside
Fru(2β↔α1)Glc ≡ Glc(α1↔2β)Fru

- **Maltose (malt-sugar)=**

glucose + glucose (blood sugar)

- **Malt sugar. Produced during the course of digestion of starch by the enzyme amylase. Two α-D-glucose units held together by α(1→4) glycosidic bond.**



Maltose
(α-D-glucopyranosyl-(1→4) α-D-glucopyranose)

Structure of Maltose

Source / Occurrence Of Lactose

- Milk and Milk products.
- Lactating Mothers body.

Biomedical Importance Of Lactose

- Lactose has dietary and calorific value.
- **Enzyme Lactase digests** Lactose by cleaving β (1-4) glycosidic bond and releases free **Galactose** and **Glucose**.

Polysaccharides

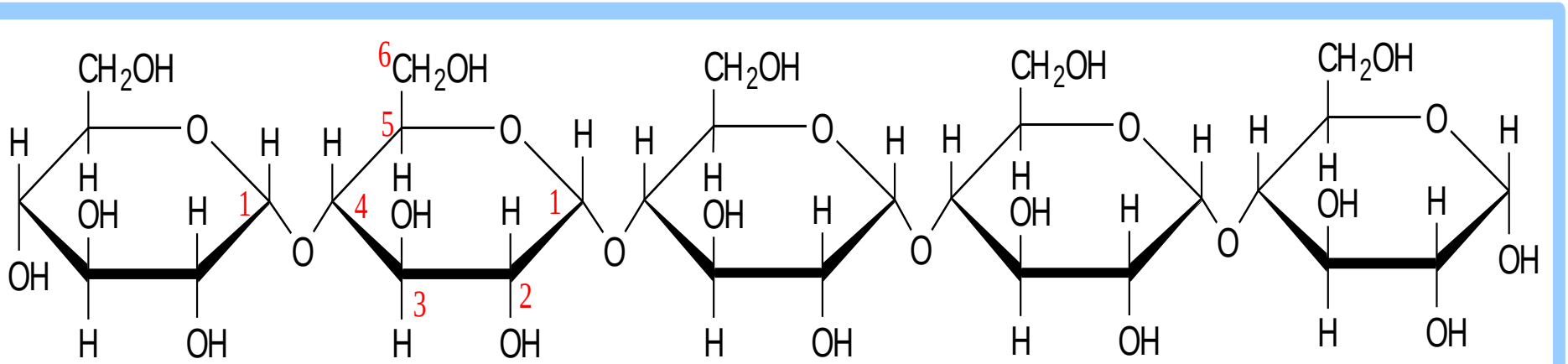
Complex Polysaccharides

Macromolecules consisting of >10 monosaccharides joined together by glycosidic bond **storage polysaccharide**

1- Starch- plant

Consists entirely of glucose monomers contain two types

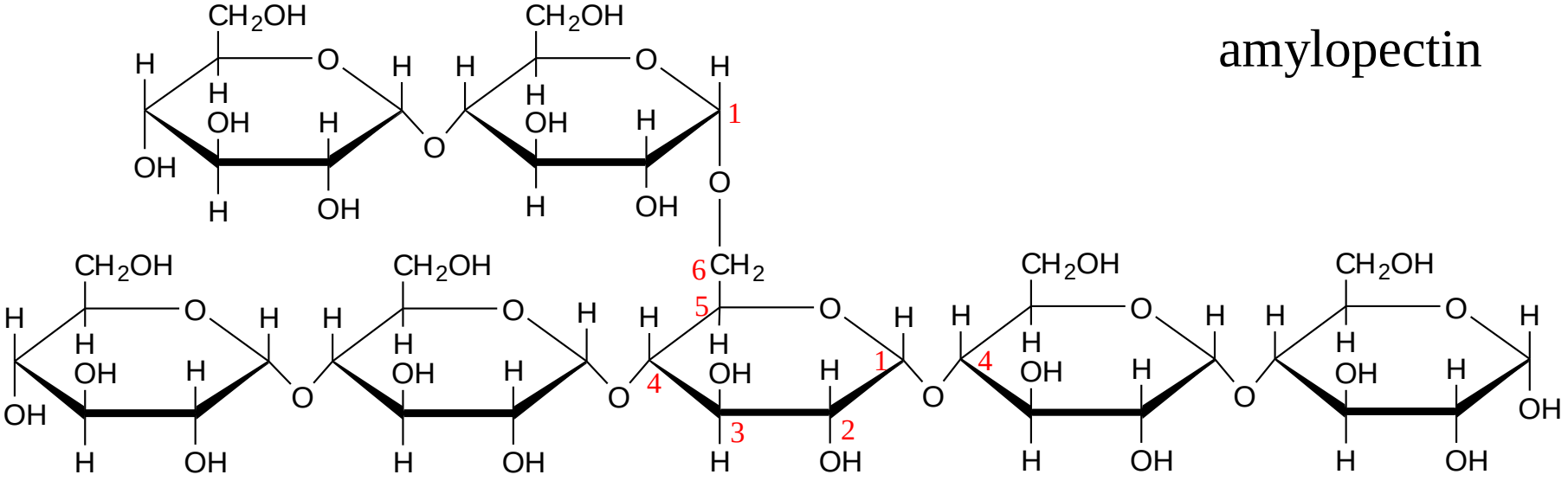
- **unbranched starch** – amylose- joined by α-1,4- glycosidic bond
- **Branched starch**- amylopectin - joined by α-1,4- & α-1,6- glycosidic bond



2- Glycogen - animal starch (liver & muscle) . Made up of glucose monomers but more extensively branched.

Amylopectin- is a glucose polymer with mainly α (1→4) linkages, but it also has branches formed by α (1→6) linkages. Branches are generally longer than shown above.

The branches produce a compact structure & provide multiple chain ends at which **enzymatic cleavage can occur.**



3. Cellulose: The main polysaccharide in plants. It is is a homopolymer of glucose in β-glycosidic linkage**s.**

4. **Inulin** :Present in Dahlias. Consists of fructose only.

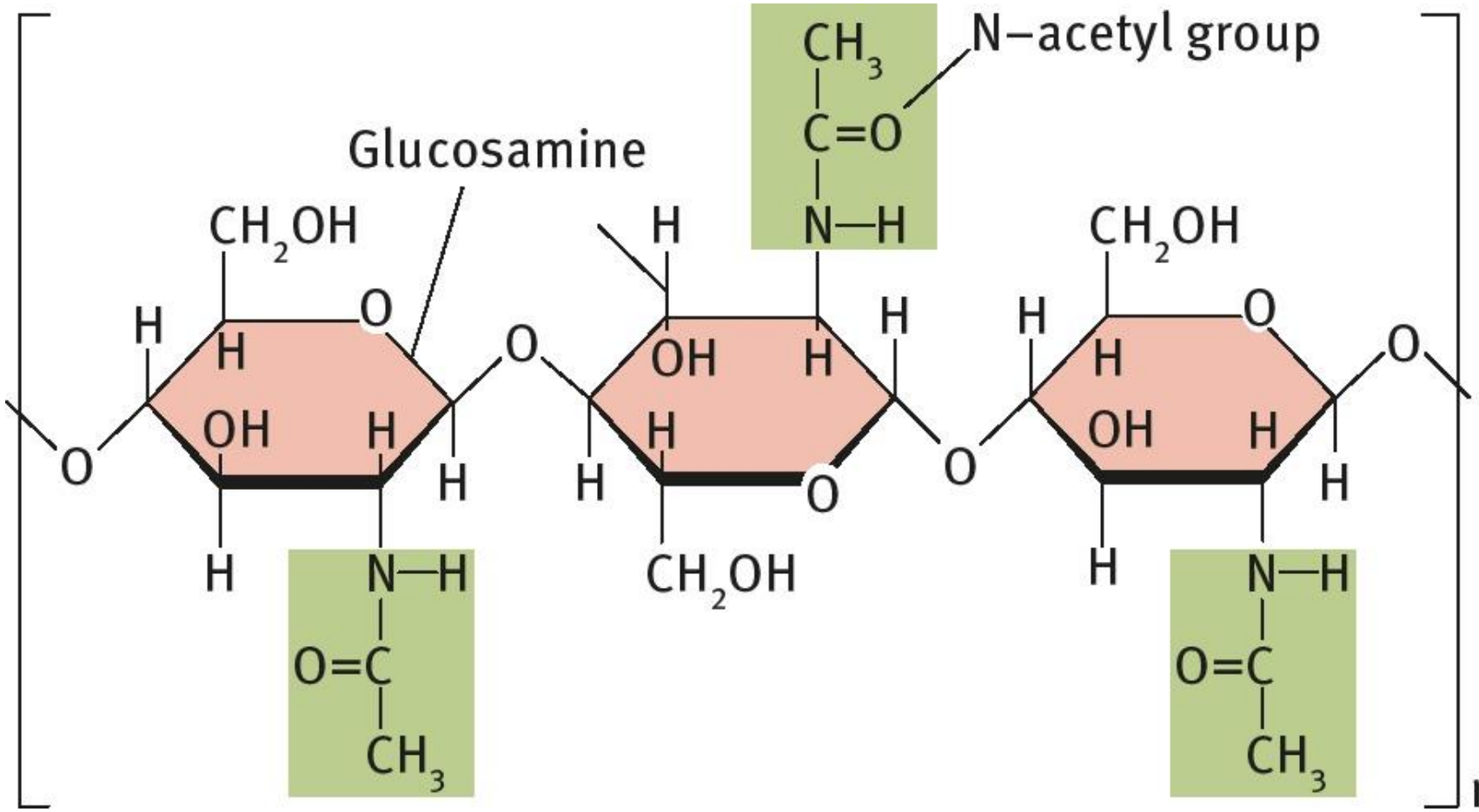
5. **Chitin**: structural elements of invertebrates and in the exoskeleton of arthropods. It is poly(N-acetyl-D-glucosamine units) joined by β(1,4) linkages.

6. **Dextrin** : bacteria consists of glucose linked formed during the coarse of starch hydrolysis.

7. **Dextran**: A storage polysaccharide present in yeast and by (α-(1,6) linkages and for branches (α-(1,2) α-(1,3) and α-(1,4).

Chitin

- Made of glucose with a nitrogen containing group
- Major component of arthropod exoskeleton & fungal cell



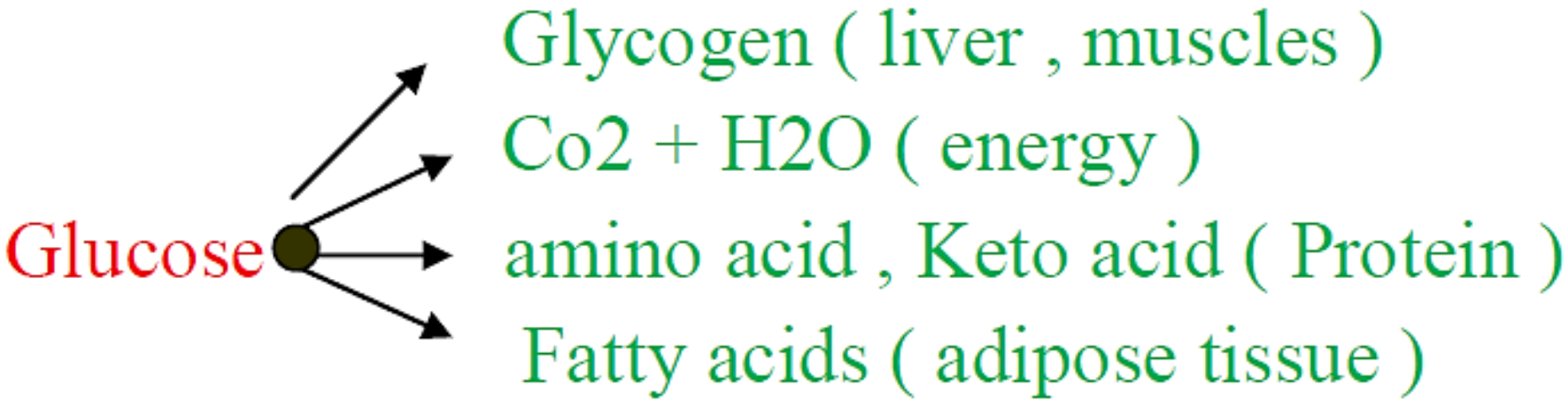
Digestion of Dietary Carbohydrates

In mouth by **lingual amylase** in salive & in the small intestine is **α-amylase**. This enzyme is secreted by the **pancreas** and has the same activity as **salivary amylase**, producing disaccharides and trisaccharides. The latter are converted to monosaccharides by **intestinal saccharidases**, including **maltases** that hydrolyze di - and trisaccharides, and the more specific disaccharidases (**sucrase**, **lactase**, and **trehalase**). The net result is the almost complete conversion of digestible carbohydrate to its constituent monosaccharides

$$Polysaccharide \xrightarrow{Amylases} Di-Trisaccharide \xrightarrow{Disaccharideases} Monosaccharides \longrightarrow Absorption, through, intestinl, wall$$

The resultant glucose and other simple carbohydrates are transported across the intestinal wall to the hepatic portal vein and then to liver parenchymal cells and other tissues.

Glucose was absorbed across intestinal wall and transported to the hepatic portal vein and them to liver parenchymal cells and other tissues . then they are converted to glycogen , fatty acids and amino acids or else oxidize by the various catabolic pathways of cells .



1- **Glycolysis :-** Conversion of **glucose** to **lactate** or **pyruvate**.

2- **Glycogenesis :-** The process refers to conversion of **glucose** to **glycogen**.

3- **Glycogenolysis :-** The process refers to breakdown of **glycogen** to **glucose** and other intermediate products .

4- **Gluconeogenesis :-** The formation of **glucose** from **non-carbohydrate** such as **amino acids** and **fatty acid .**

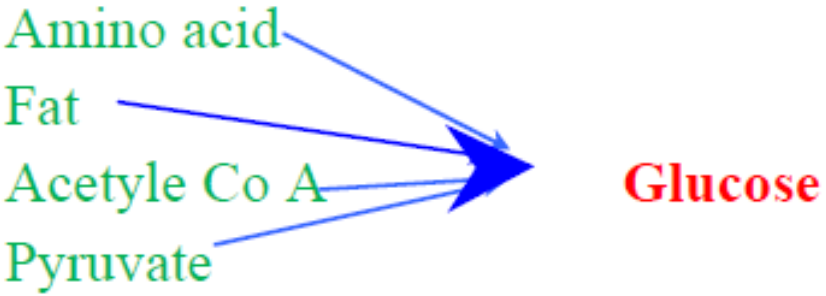
1- Glycogenesis :-

Glucose $\xrightarrow{\text{G –6 –phosphatase}}$ g – 6 – p $\xrightarrow{\text{glycogen synthetase}}$ Glycogen

2- Glycogenolysis :-

Glycogen $\xrightarrow[\text{Or glucokinase}]{\text{Hexokinase}}$ Glucose

3- Gluconeogenesis :-



4- Glycolysis : -

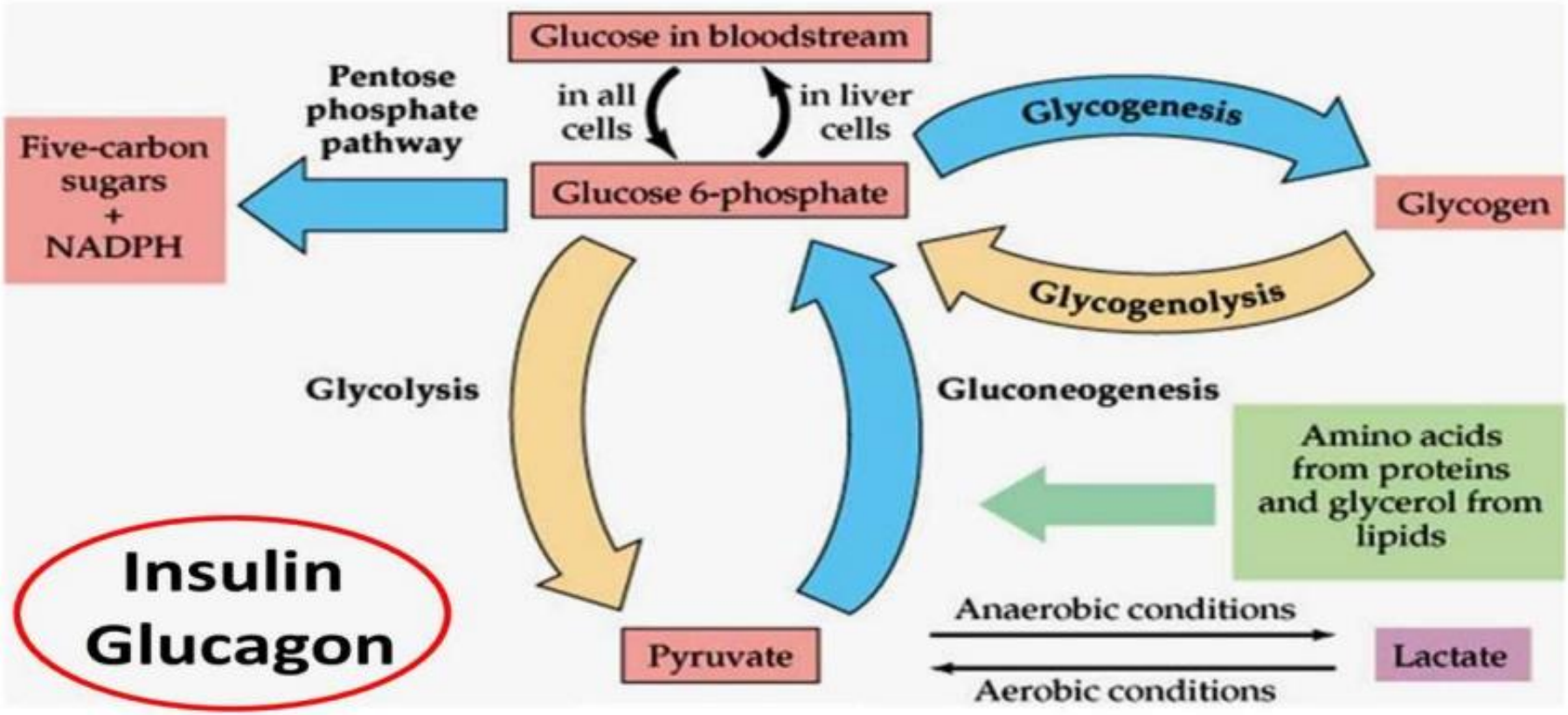
a- aerobic glycolysis

glucose ------ □ pyruvate ------ □ acetyl co A **(highly Oxygen)**

b- anaerobic glycolysis

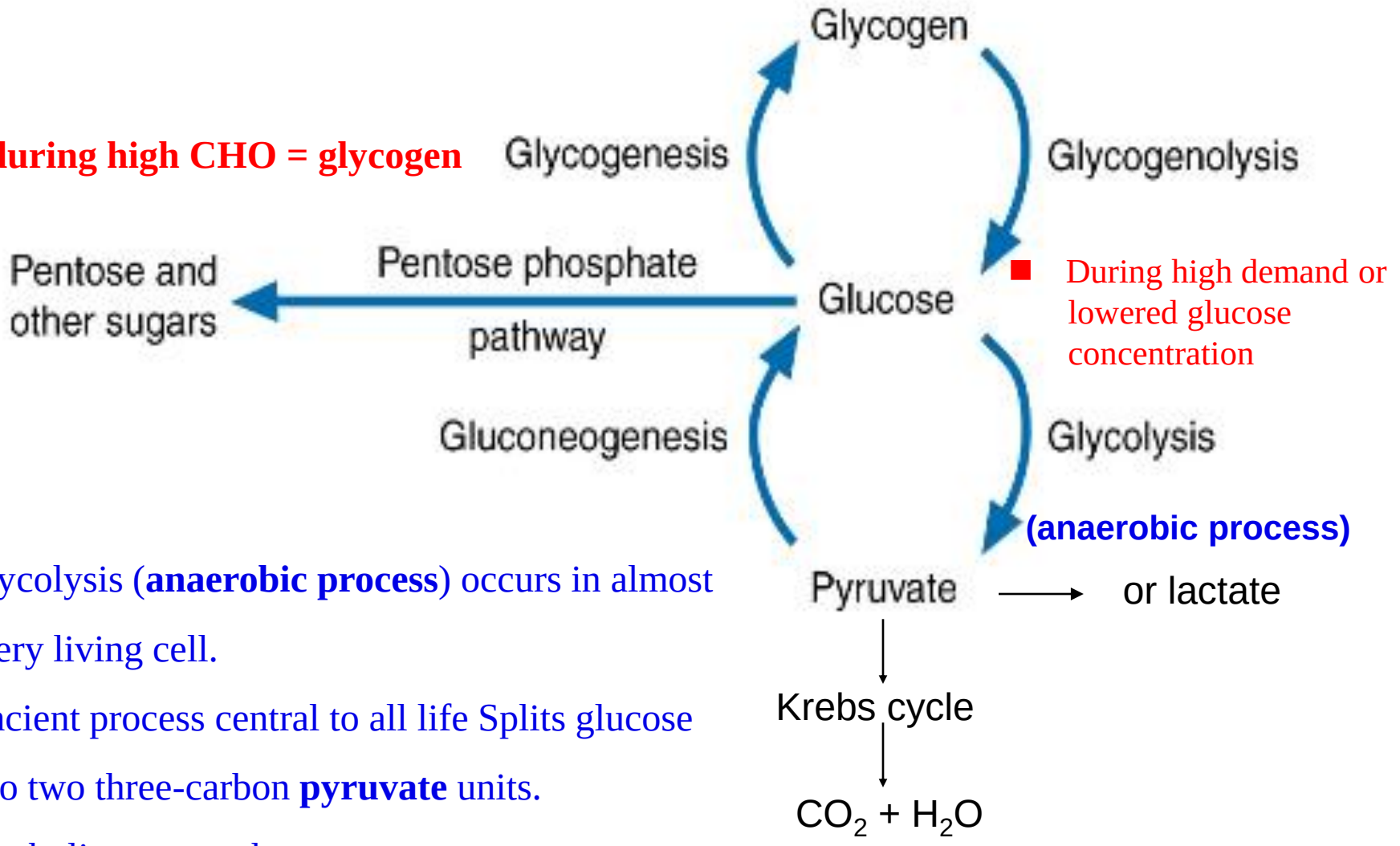
glucose ------ □ Lactate ----- □ Ketone bodies (**hypoxia**)

Main pathways of carbohydrate metabolism



Carbohydrate Metabolism

- **during high CHO = glycogen**



1. Glycolysis (**anaerobic process**) occurs in almost every living cell.
2. Ancient process central to all life Splits glucose into two three-carbon **pyruvate** units.
3. Catabolic process that captures some energy as 2 ATP and 2 NADH.

Note

Through the process of glycolysis, one molecule of glucose breaks down to form two molecules of pyruvate. Depending on the microcellular environment (specifically, **oxygen availability**, energy demand, and the presence or absence of mitochondria), pyruvate has several separate fates:

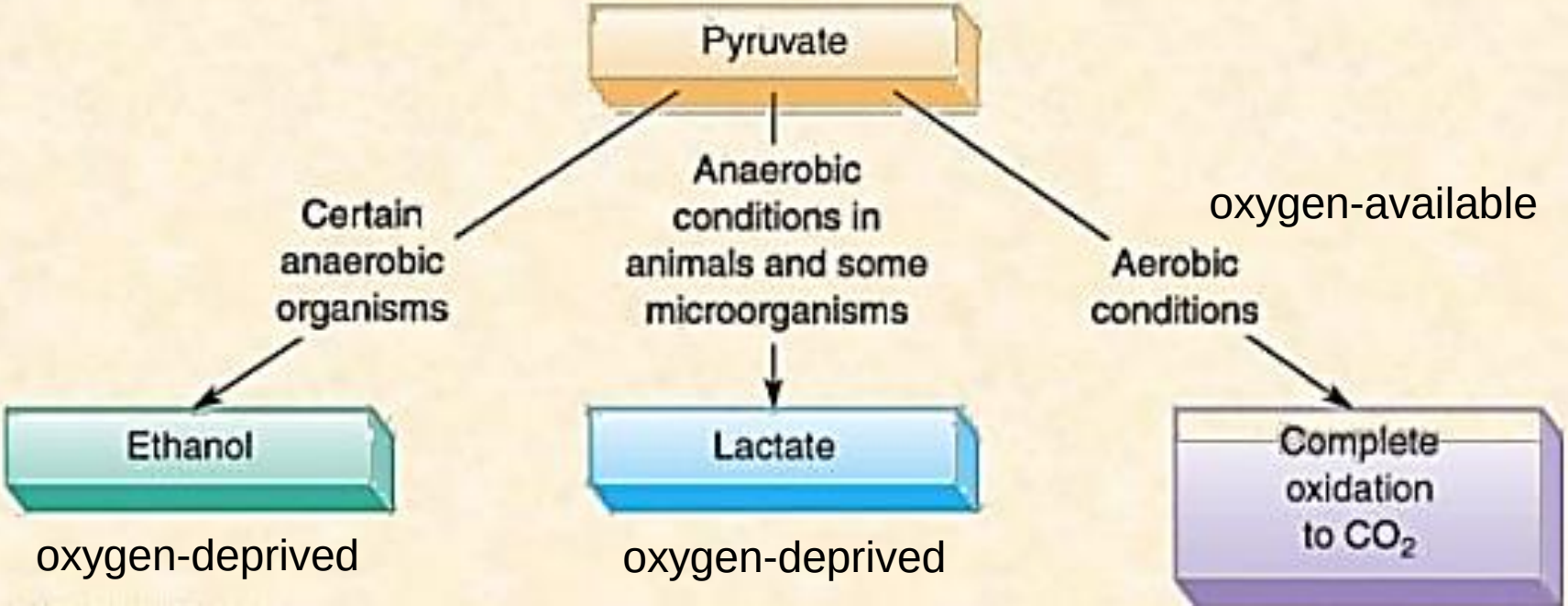
In mitochondria-containing cells, pyruvate can enter the citric acid cycle within the mitochondrial matrix and undergo oxidative phosphorylation. Aptly named due to its dependence on oxygen as the final electron acceptor, oxidative phosphorylation cannot take place in the absence of oxygen. Moreover, as the enzymes of both the citric acid cycle and electron transport chain are within the mitochondria, cells lacking mitochondria (e.g., erythrocytes) cannot rely on oxidative phosphorylation for energy production.

In **erythrocytes** and **oxygen-deprived** tissue, pyruvate remains within the cytoplasm and converts to lactate, a process referred to as **anaerobic glycolysis**. This final reaction allows for the regeneration of NAD+, a cofactor that must be available in high enough intracellular concentrations for the earlier reactions of glycolysis to remain favorable. Compared to oxidative phosphorylation, however, anaerobic glycolysis is **significantly less efficient**, providing a net production of only 2 ATP per glucose molecule (versus 32 ATP per glucose molecule produced during oxidative phosphorylation.

After glycolysis, pyruvate can be:

- Oxidized to acetyl CoA (aerobic conditions).
- Reduced to lactate (anaerobic conditions).
- Reduced to ethanol (anaerobic conditions for some prokaryotic organisms).

- Note: All processes must regenerate NAD^+ from NADH so glycolysis can continue.



Thank you for your Attention

Introduction to Vitamins

* Vitamins are organic molecules that function in a wide variety of capacities within the body.

** The most prominent function is as cofactors for enzymatic reactions.

The distinguishing feature of the vitamins is that they generally cannot be synthesized by mammalian cells and, therefore, must be supplied in the diet. The vitamins are of two distinct types:

1. **Water Soluble Vitamins:** Thiamin (B_1) -Riboflavin (B_2) -Niacin (B_3) -Pantothenic Acid (B_5)-Pyridoxal, Pyridoxamine, Pyridoxine (B_6)-Biotin-Cobalamin (B_{12})-Folic Acid -Ascorbic Acid.
2. **Fat Soluble Vitamins**: Vitamin A-Vitamin D, Vitamin E, Vitamin K.

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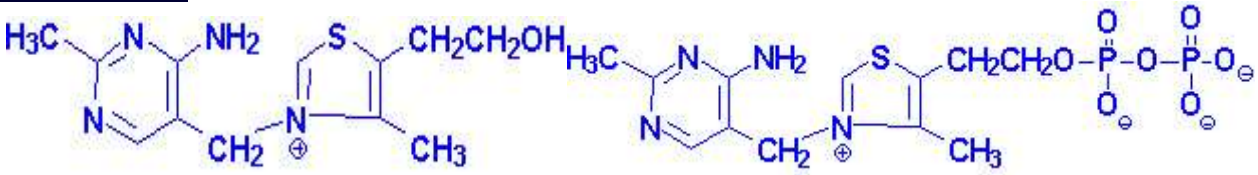
1. Thiamin (vitamin B_1)



Thiamin structure **Thiamin pyrophosphate**

- Thiamin is rapidly converted to its active form, **thiamin pyrophosphate, TPP**, in the brain and liver by a specific enzymes, ***thiamin diphosphotransferase***.

TPP is necessary as a cofactor for: 1-***pyruvate dehydrogenase*** 2-***α-ketoglutarate dehydrogenase*** 3- ***transketolase***

@ A deficiency in thiamin intake leads to a severely reduced capacity of cells to generate energy as a result of its role in these reactions.

The dietary requirement for thiamin ranges **from 1.0 - 1.5 mg/day** for normal adults.

- **Beriberi:** The severe thiamin deficiency disease
- Wernicke-Korsakoff syndrome. This disease is most commonly found in chronic alcoholics due to their poor dietetic lifestyles.

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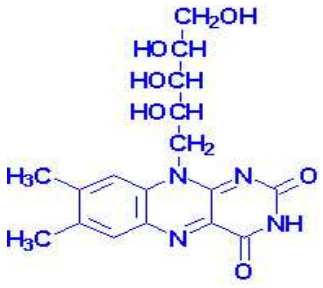
2. Riboflavin (vitamin B_2)

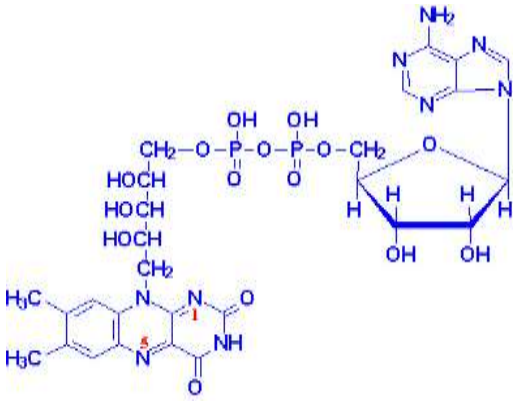


Riboflavin structure

- Riboflavin is the precursor for the coenzymes, **flavin mononucleotide (FMN)** and **flavin adenine dinucleotide (FAD)**.

@@The enzymes that require FMN or FAD as cofactors are termed flavoproteins. Several flavoproteins also contain metal ions and are termed metalloflavoproteins.

- Both classes of enzymes are involved in a wide range of redox reactions, e.g. ***succinate dehydrogenase*** and ***xanthine oxidase***. During the course of the enzymatic reactions involving the flavoproteins the reduced forms of FMN and FAD are formed, $FMNH_2$ and $FADH_2$, respectively.
- The normal daily requirement for riboflavin is **1.2 - 1.7 mg/day** for normal adults.
- Riboflavin decomposes when exposed to visible light. This characteristic can lead to riboflavin deficiencies in newborns treated for hyperbilirubinemia by phototherapy.



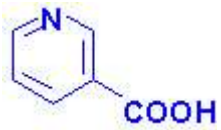
Structure of FAD-------nitrogens 1 & 5 carry hydrogens in $FADH_2$

Q/ Why Riboflavin deficiencies are rare.

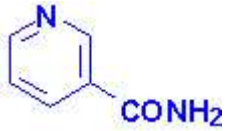
A/ Due to the presence of adequate amounts of the vitamin in eggs, milk, meat and cereals.

- Riboflavin deficiency is often seen in chronic alcoholics due to their poor dietetic habits.

3. Niacin



Nicotinic Acid



Nicotinamide

- Niacin (nicotinic acid and nicotinamide) is also known as **vitamin B_3**.
- Niacin is required for the synthesis of the active forms of vitamin B_3, **nicotinamide adenine dinucleotide (NAD^+)** and **nicotinamide adenine dinucleotide phosphate ($NADP^+$)**. Both NAD^+ and $NADP^+$ function as cofactors for numerous dehydrogenase, e.g., ***lactate*** and ***malate dehydrogenases***.

Q/ Why Niacin is not a true vitamin in the strictest definition.

A/ Because it can be derived from the amino acid tryptophan.

The recommended daily requirement for niacin is **13 - 19 mg** of free niacin.

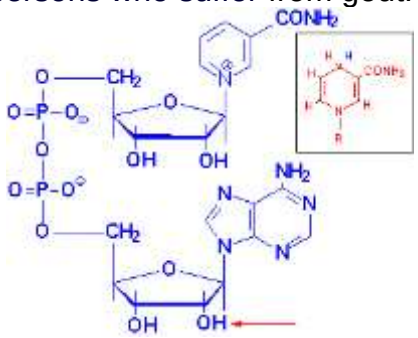
- Causes of Niacin deficiency: **1**-**Pellagra** **2**-Hartnup disease and malignant carcinoid syndrome) **3**-drug therapies (e.g. isoniazid).

@@ nicotinic acid therapy causes:

1- lowers blood cholesterol

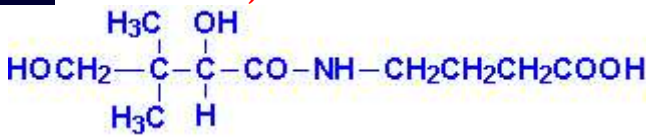
2- depletion of glycogen stores and fat reserves in skeletal and cardiac muscle

3-an elevation in blood glucose and uric acid production. For these reasons nicotinic acid therapy is not recommended for diabetics or persons who suffer from gout.



Structure of NAD^+----NADH is shown in the box insert.
The -OH phosphorylated in $NADP^+$ is indicated by the red arrow.

4. Pantothenic Acid (vitamin B_5)

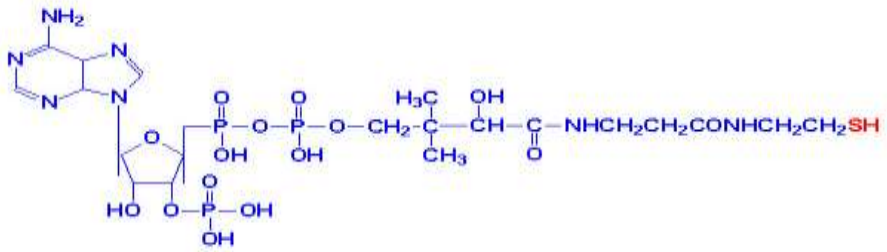


Pantothenic Acid

- Pantothenic acid is formed from β-alanine and pantoic acid.

- Pantothenate is required for: **1-**Synthesis of coenzyme A(CoA) **2-**Component of the acyl carrier protein (ACP) domain of fatty acid synthase **3-**required for the metabolism of carbohydrate via the TCA cycle and all fats and proteins.
- At least 70 enzymes have been identified as requiring CoA or ACP derivatives for their function.

@Deficiency of pantothenic acid is extremely rare.



Coenzyme A

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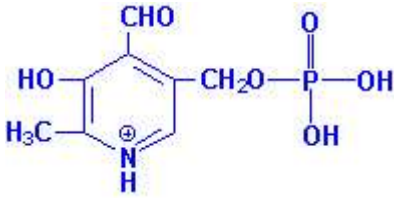
5. Vitamin B_6

Pyridoxine

Pyridoxal

Pyridoxamine

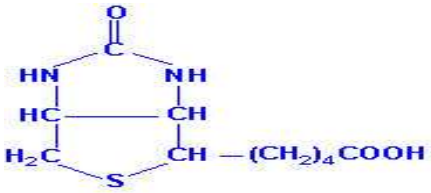


Pyridoxal Phosphate

- **Pyridoxal, pyridoxamine** and **pyridoxine** are as a group known as **vitamin B_6**.
- All three compounds are efficiently converted by ***pyridoxal kinase*** to the biologically active form of vitamin B_6, **pyridoxal phosphate**.
- Pyridoxal phosphate functions as **1-**cofactor in enzymes involved in transamination reactions **2-**required for the synthesis and catabolism of the amino acids **3-** in glycogenolysis as a cofactor for ***glycogen phosphorylase***.
- The requirement for vitamin B_6 in the diet is proportional to the level of protein consumption ranging from **1.4 - 2.0 mg/day** for a normal adult.

#During pregnancy and lactation the requirement for vitamin B_6 increases approximately 0.6 mg/day.

6-Biotin



Biotin

- Biotin is the cofactor required of enzymes that are involved in carboxylation reactions, e.g. ***acetyl-CoA carboxylase*** and ***pyruvate carboxylase***.
- Deficiencies of the vitamin are rare because **1-**Biotin is found in numerous foods **2-** synthesized by intestinal bacteria.
- Note: Deficiencies are generally seen only after 1- long antibiotic therapies which deplete the intestinal fauna 2-following excessive consumption of raw eggs because of the affinity of the egg white protein, **avidin**, for biotin preventing intestinal absorption of the biotin.

7-Cobalamin (vitamin B_{12})

- Vitamin B_{12} is composed of a complex tetrapyrrol ring structure (corrin ring) and a cobalt ion in the center.
- The vitamin must be hydrolyzed from protein in order to be active. Hydrolysis occurs in the stomach by gastric acids or the intestines by trypsin digestion following consumption of animal meat. The vitamin is then bound by **intrinsic factor**, a protein secreted by parietal cells of the stomach, and carried to the ileum where it is absorbed. Following absorption the vitamin is transported to the liver in the blood bound to **transcobalamin II**.
  ##There are only two clinically significant reactions in the body that require vitamin B_{12} as a cofactor:1-. ***methylmalonyl-CoA mutase***, 2- ***methionine synthase***.

Clinical Significances of B_{12} Deficiency

1. The liver can store up to six years worth of vitamin B_{12}, hence deficiencies in this vitamin are rare.
2. Pernicious anemia: is a megaloblastic anemia resulting from vitamin B_{12} deficiency that develops as a result a lack of intrinsic factor in the stomach leading to malabsorption of the vitamin. The anemia results from impaired *DNA synthesis due to a block in purine and thymidine biosynthesis*. The block in nucleotide biosynthesis is a consequence of the effect of vitamin B_{12} on folate metabolism. When vitamin B_{12} is deficient essentially all of the folate becomes trapped as the N^5-methylTHF derivative as a result of the loss of functional ***methionine synthase***. This trapping prevents the synthesis of other THF derivatives required for the purine and thymidine nucleotide biosynthesis pathways.

---

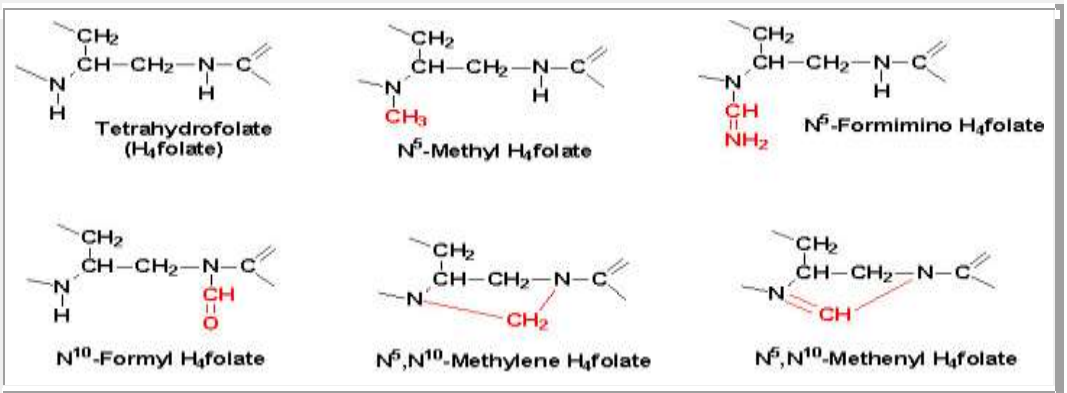
8. Folic Acid

- Folic acid is obtained primarily from yeasts and leafy vegetables as well as animal liver.
- Folic acid is reduced within cells (principally the liver where it is stored) to tetrahydrofolate (THF also H_4folate) through the action of ***dihydrofolate reductase*** **(DHFR)**, an NADPH-requiring enzyme.

Folic Acid

positions 7 & 8 carry hydrogens in dihydrofolate (DHF)
positions 5-8 carry hydrogens in tetrahydrofolate (THF)

- The function of THF derivatives is to carry and transfer various forms of one carbon units during biosynthetic reactions. The one carbon units are either methyl, methylene, methenyl, formyl or formimino groups.



Active center of tetrahydrofolate (THF). Note that the N^5 position is the site of attachment of methyl groups, the N^{10} the site for attachment of formyl and formimino groups and that both N^5 and N^{10} bridge the methylene and methenyl groups.

- These one carbon transfer reactions are required in the biosynthesis of serine, methionine, glycine, choline and the purine nucleotides and dTMP.

Clinical Significance of Folate Deficiency

Folate deficiencies are rare due to the adequate presence of folate in food

a) The most pronounced effect of folate deficiency on cellular processes is upon DNA synthesis. This is due to an impairment in dTMP synthesis which leads to cell cycle arrest in S-phase of rapidly proliferating cells, in particular hematopoietic cells. The result is **megaloblastic anemia** as for vitamin B_{12} deficiency.

b) The inability to synthesize DNA during erythrocyte maturation leads to abnormally large erythrocytes termed **macrocytic anemia**.
metabolism.

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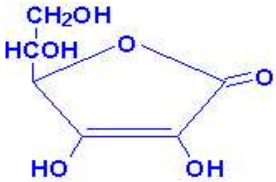
9. Ascorbic Acid (vitamin C)



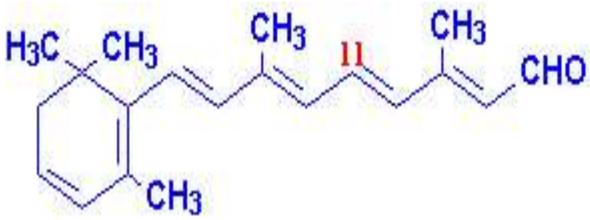
Ascorbic Acid

- Ascorbic acid is derived from glucose via the uronic acid pathway. The enzyme responsible for the conversion of gulonolactone to ascorbic acid is ***L-gulonolactone oxidase***.
- The main function of ascorbate is as a reducing agent in a number of different reactions.
  1. To reduce cytochromes a and c of the respiratory, molecular oxygen.
  2. As a cofactor in the hydroxylation of proline residues in collagen.
  3. Maintenance of normal connective tissue- wound healing since synthesis of connective tissue is the first event in wound tissue remodeling.
  4. as a cofactor for 1-catabolism of tyrosine 2- synthesis of epinephrine from tyrosine3- Synthesis of the bile acids.
  5. It is also believed that vitamin C is involved in the process of steroidogenesis.

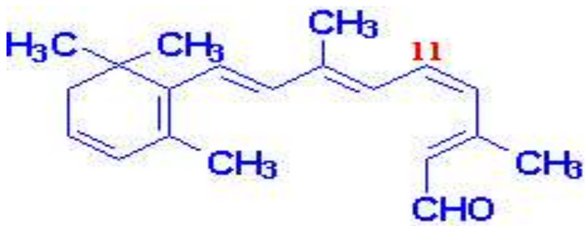
##Deficiency in vitamin C leads to the disease **scurvy** due to the role of the vitamin in the post-translational modification of collagens. Scurvy is characterized by easily bruised skin, muscle fatigue, soft swollen gums, decreased wound healing and hemorrhaging, osteoporosis, and anemia.
$$

10.Vitamin A

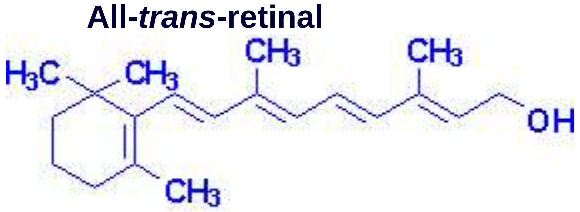
Vitamin A consists of three biologically active molecules, **retinol, retinal** (retinaldehyde) and **retinoic acid**.



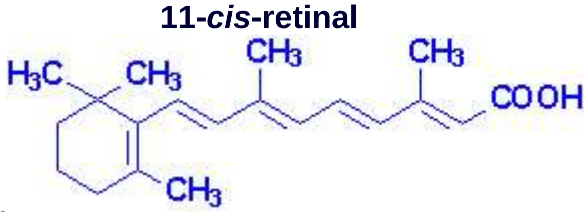
All-*trans*-retinal



11-*cis*-retinal



Retinol



Retinoic Acid

- All derived from the plant precursor molecule, **β-carotene** (a member of a family of molecules known as **carotenoids**).
- β-carotene dioxygenase → retinaldehyde reductase
- Ingested β-carotene ——→ Retinal ——→ Retinol
- NADPH → NAD^+

- Retinol also functions in the synthesis of certain glycoproteins and mucopolysaccharides necessary for mucous production and normal growth regulation.

Vision and the Role of Vitamin A

- The rod and cone cells in retina (specialized cells in the retina) contain a photoreceptor pigment in their membranes.
- **opsin** The photosensitive compound of most mammalian eyes. It is a protein covalently coupled with an aldehyde of vitamin A.
- **scotopsin**: The opsin of rod cells.
- **rhodopsin** or **visual purple:** The photoreceptor imbedded in the membrane of the rod cells. This compound is a complex between scotopsin and the 11-*cis*-retinal (also called 11-*cis*-retinene) form of vitamin A.

Q/ How the vision occurs?

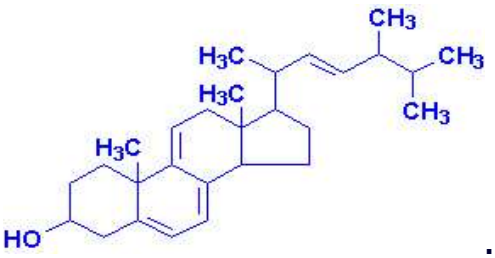
A/ When the rhodopsin is exposed to light it is **bleached** releasing the **11-*cis*-retinal** from **opsin.** Absorption of photons by 11-*cis*-retinal triggers a series of conformational changes on the way to conversion **all-*trans*-retinal**. This conformational change activates transducin, leading to an increased GTP-binding by the a-subunit of transducin. Binding of GTP releases the α-subunit from the inhibitory β- and γ-subunits. The GTP-activated α-subunit in turn activates an associated ***phosphodiesterase***; an enzyme that hydrolyzes cyclic-GMP (cGMP) to GMP. Cyclic GMP is required to maintain the Na^+ channels of the rod cell in the open conformation. The drop in cGMP concentration results in complete closure of the Na^+ channels. Metarhodopsin II appears to be responsible for initiating the closure of the channels. The closing of the channels leads to hyperpolarization of the rod cell with concomitant propagation of nerve impulses to the brain.

Clinical Significances of Vitamin A Deficiency

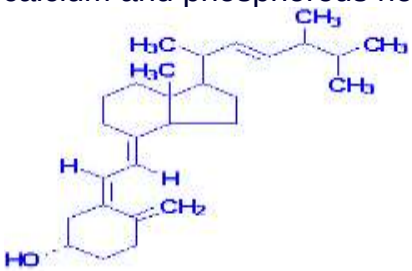
- Vitamin A is stored in the liver and deficiency of the vitamin occurs only after prolonged lack of dietary intake.
- The earliest symptoms of vitamin A deficiency are **night blindness**.
- Additional early symptoms include (follicular hyperkeratinosis, increased susceptibility to infection and cancer and anemia equivalent to iron deficient anemia).

11-Vitamin D

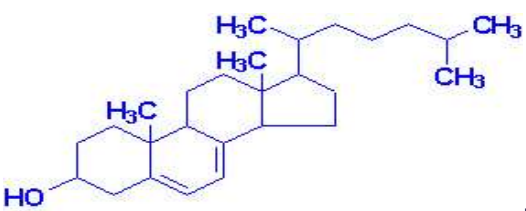
- Vitamin D is a steroid hormone.
- The biologically active form of the hormone is **1,25-dihydroxy vitamin D_3** ($1,25\text{-}(OH)_2D_3$, also termed **calcitriol**).
- Calcitriol functions: primarily to regulate calcium and phosphorous homeostasis.



Ergosterol



Vitamin D_2



7-Dehydrocholesterol

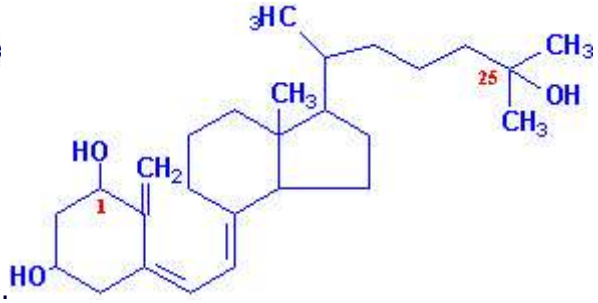
Vitamin D_3

- **in plants**: Active calcitriol is derived from **ergosterol** (produced in plants) and form **Ergocalciferol** (vitamin D_2) by uv irradiation of ergosterol.
- **In the skin: 7-dehydrocholesterol** is converted to **cholecalciferol** (vitamin D_3) following *uv* irradiation.

Synthesis of active Vitamin D:

Cholecalciferol (or egrocalciferol) → Intestine → liver (D_3-25-hydroxylase) → 25-hydroxy-D_3 [25-(OH)D_3] → (D_3-1-hydroxylase) In (kidneys bone and placenta) → **calcitriol**

25-hydroxyvitamin D_3



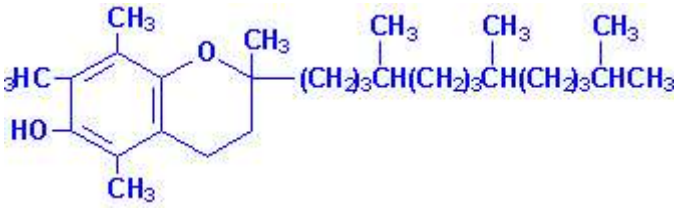
1,25-dihydroxyvitamin D_3

Calcitriol functions in concert with **parathyroid hormone (PTH)** and **calcitonin** to regulate serum calcium and phosphorous levels.

Clinical Significance of Vitamin D Deficiency

1. Vitamin D deficiency in children causes **rickets** Rickets is characterized improper mineralization during the development of the bones resulting in soft bones.
2. Vitamin D deficiency in adults causes **osteomalacia**. Osteomalacia is characterized by demineralization of previously formed bone leading to increased softness and susceptibility to fracture.

12.Vitamin E



α-Tocopherol

Vitamin E is a mixture of several related compounds known as **tocopherols**.

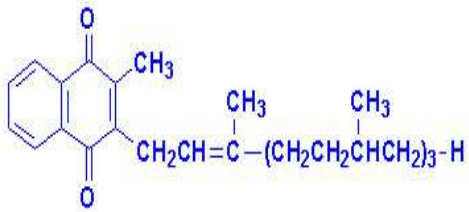
@ **The major function of vitamin E is:** to act as a natural **antioxidant** by scavenging free radicals and molecular oxygen. In particular vitamin E is important for preventing peroxidation of polyunsaturated membrane fatty acids.

@ **Clinical significances of Vitamin E Deficiency**:

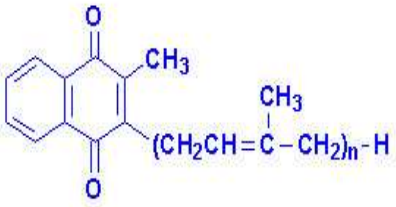
1-an increase in red blood cell fragility. 2-Neurological disorders have been associated with vitamin E deficiencies associated with fat malabsorptive disorders.

13.Vitamin K

The K vitamins exist naturally as: **1**-K_1 (phylloquinone) in green vegetables **2**-K_2 (menaquinone) produced by intestinal bacteria **3**-K_3 is synthetic water soluble menadione. When administered, vitamin K_3 is alkylated to one of the vitamin K_2 forms of menaquinone.



Vitamin K_1



VitaminK_2

Vitamin K_3

"n" can be 6, 7 or 9 isoprenoid groups

##The major function of the K vitamins is:

1. in the maintenance of normal levels of the blood clotting proteins, **factors II, VII, IX, X**.

2. Vitamin K reactions are the site of action of the **dicumarol** based anticoagulants such as **warfarin**.

Clinical significance of Vitamin K Deficiency

- Naturally occurring vitamin K is absorbed from the intestines only in the presence of bile salts and other lipids through interaction with chylomicrons. Therefore, fat malabsorptive diseases can result in vitamin K deficiency.

@The synthetic vitamin K_3 is water soluble and absorbed regardless of the presence of intestinal lipids and bile.

- Since the vitamin K_2 form is synthesized by intestinal bacteria, deficiency of the vitamin in adults is rare. However, long term antibiotic treatment can lead to deficiency in adults.

@ The intestine of newborn infants is sterile, therefore, vitamin K deficiency in infants is possible if lacking from the early diet. The primary symptom of a deficiency in infants is a **hemorrhagic syndrome**.

Lipids & Lipoproteins

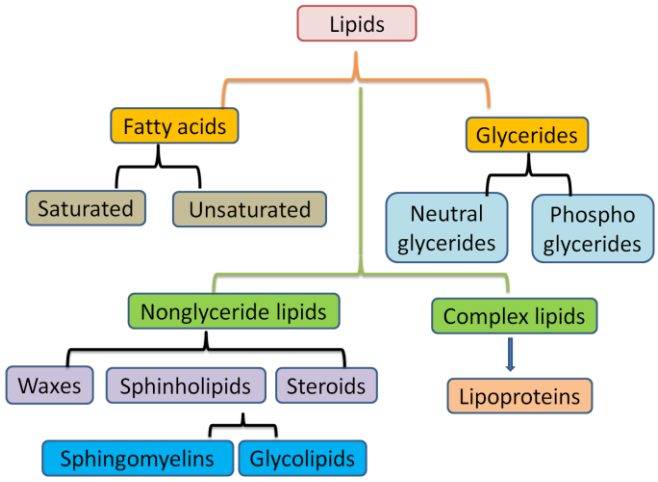
Lipids: Biological molecules that are insoluble in aqueous solutions and soluble in organic solvents are classified as lipids.

***-Neutral lipids(e.g. cholesterol esters, triglyceride..) are uncharged molecules.

Major Roles of Biological of Lipids:

1. They serve as structural components of biological membranes.
2. They provide energy reserves, predominantly in the form of triacylglycerols.
3. Both lipids and lipid derivatives serve as vitamins and hormones.
4. Lipophilic bile acids aid in lipid solubilization.
5. Serve as thermal and electrical insulator.

Classification of Lipids:



The types of lipids that we will look at include.

- Fatty Acids
- In the carboxylic acid family
- Waxes
- Fatty Acids + Alcohols
- Triglycerides
- 3 Fatty acids + glycerol
- Phospholipids and glycolipids
- 2 fatty acids + glycerol + phosphate + X
- Steroids
- Derivatives of cholesterol
- Eicosanoids
- Derivatives of the Fatty acid arachidonic acid
- Membranes
- Formed from phospholipids and glycolipids

1-Fatty Acids:

Fatty acids are long-chain hydrocarbon molecules containing a carboxylic acid moiety at one end.

*Fatty acids fill two major roles in the body:

1. As the components of more complex membrane lipids.
2. As the major components of stored fat in the form of triacylglycerols.

* **Saturated fatty acids:** Fatty acids that contain no carbon-carbon double bonds.
* **Unsaturated fatty acids:** Fatty acids that contain double bonds.

Fatty acids may be further subdivided as follows:

(1) Monounsaturated (monoethenoid, monoenoic) acids, containing one double bond.
(2) Polyunsaturated (polyethenoid, polyenoic) acids, containing two or more double bonds.
(3) Eicosanoids: These compounds, derived from eicosa- (20-carbon) polyenoic fatty acids, comprise the **prostanoids, leukotrienes (LTs),** and **lipoxins (LXs).** Prostanoids include **prostaglandins (PGs), prostacyclins (PGIs),** and **thromboxanes (TXs).**

#The site of unsaturation in a fatty acid is indicated by the symbol **Δ** and the number of the first carbon of the double bond (e.g. palmitoleic acid is a 16-carbon fatty acid with one site of **unsaturation** between **carbons 9** and 10, and is designated by $16:1^{\Delta 9}$).

@ Naturally occurred unsaturated FA occurs in cis-form.

@ Body can biosynthesize lipids and can supply the body with all the various fatty acid structures needed except the **essential FA.**

***Essential fatty acids**; must be provided in the diet (the highly unsaturated fatty acids: these are all **polyunsaturated fatty acids**: the **C20** fatty acid **arachidonic acid** (20:4;5,8,11,14), and the two **C18 acids linoleic acid** (18:2;9,12) and **linolenic acid** (18:3;9,12,15). **linoleic acid** and **linolenic acid**) because they containing unsaturation sites beyond carbons 9 and 10.

Physiologically Relevant Fatty Acids:

Numerical Symbol	Common Name	Structure	Comments
14:0	Myristic acid	$CH_3(CH_2)_{12}COOH$	
16:0	Palmitic acid	$CH_3(CH_2)_{14}COOH$	End product of mammalian F.A. synthesis
$16:1^{\Delta 9}$	Palmitoleic acid	$CH_3(CH_2)_5C=C(CH_2)_7COOH$	
18:0	Stearic acid	$CH_3(CH_2)_{16}COOH$	
$18:1^{\Delta 9}$	Oleic acid	$CH_3(CH_2)_7C=C(CH_2)_7COOH$ Physiologically most important omega-9 monounsaturated fatty acid (MUFA)	
$18:2^{\Delta 9,12}$	Linoleic acid	$CH_3(CH_2)_4C=CCH_2C=C(CH_2)_7COOH$ Essential fatty acid, an omega-6 PUFA	**Essential fatty acid**
$18:3^{\Delta 9,12,15}$	Linolenic acid	$CH_3CH_2C=CCH_2C=CCH_2C=C(CH_2)_7COOH$ Essential fatty acid, an omega-3 PUFA	**Essential fatty acid**
$20:4^{\Delta 5,8,11,14}$	Arachidonic acid Essential fatty acid	$CH_3(CH_2)_3(CH_2C=C)_4(CH_2)_3COOH$ An omega-6 PUFA, precursor for eicosanoid synthesis	**Precursor for eicosanoid synthesis**

&&Prostaglandines:

Synthesized *in vivo* by cyclation of the center of the (20C-atoms unsaturated FA that called Eicosanoic acid) to form cyclopentane cycle. Examples of prostaglandins: thromboxane,

prostaglandine 2 (PGE2)

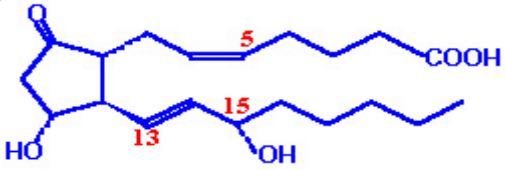


Figure : PEG2

2-Basic Structure of Triacylglycerides

Triacylglycerides (TG) are composed of a glycerol backbone to which 3 fatty acids are esterified. TG are the stored lipids in the **body tissues**.

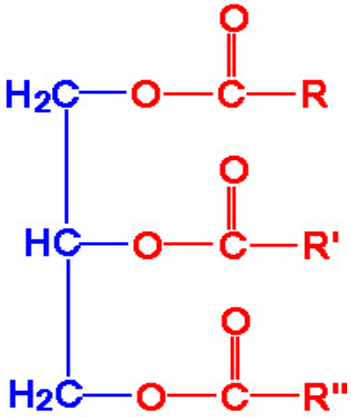


Figure: Basic composition of a triacylglyceride

3-Basic Structure of Phospholipids

The basic structure of phospolipids is very similar to that of the triacylglycerides except that C-3 of the glycerol backbone is esterified to **phosphoric acid.**

*The building block of the phospholipids is **phosphatidic acid** (X= hydrogen atom).

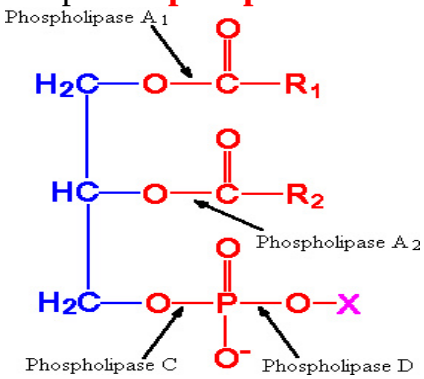
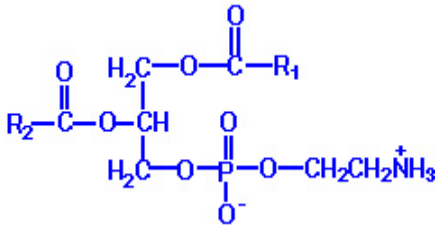
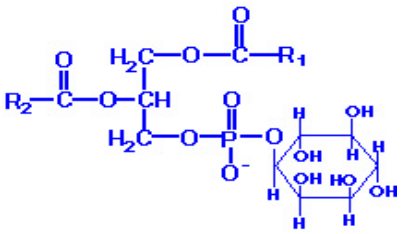


Figure: Basic composition of a phospholipid. X can be a number of different substituents.

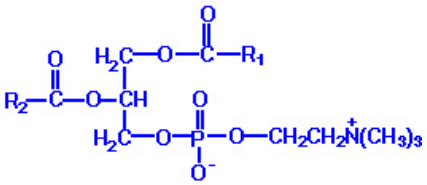
*Substitutions include ethanolamine (**phosphatidylethanolamine**), choline (**phosphatidylcholine**, also called **lecithins**), serine (**phosphatidylserine**), glycerol (**phosphatidylglycerol**), *myo*-inositol (**phosphatidylinositol**,, and phosphatidylglycerol (**diphosphatidylglycerol** more commonly known as **cardiolipins**).



Phosphatidylethanolamine



Phosphatidylinositol



Phosphatidylcholine (lecithins)

4-Basic Structure of Plasmalogens

Plasmalogens are phospholipids substituted at C-1 (*sn*1) of glycerol contain either an *O*-alkyl or *O*-alkenyl ether species. One of the most potent biological molecules is **platelet activating factor**.

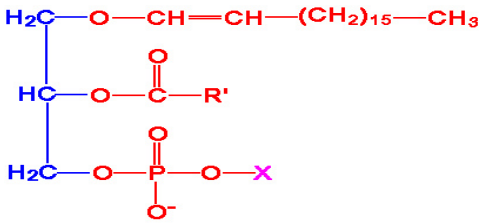


Figure: basic composition of *O*-alkenyl plasmalogens.

5-Basic Structure of Sphingolipids

*Sphingolipids are composed of a backbone of sphingosine which is derived itself from glycerol.

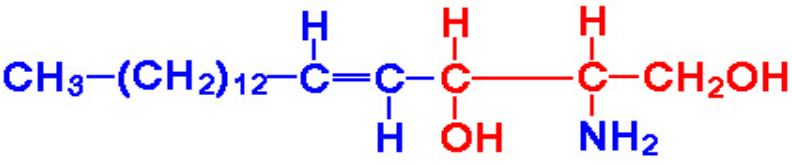
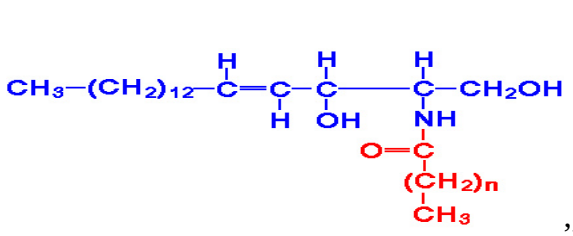


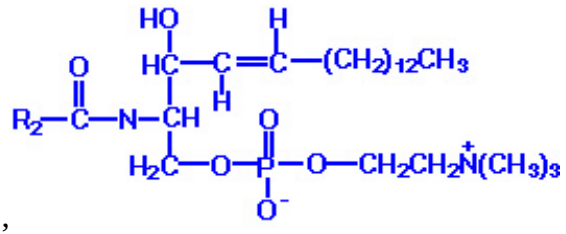
Figure: Sphingosine

* **Ceramides:** A family of molecules composed of sphingosine when N-acetylated by a variety of fatty acids. Sphingolipids predominate in the myelin sheath of **nerve fibers**.



Ceramide

,,,,,



Sphingomyelin

***Sphingomyelin** is an abundant sphingolipid generated by transfer of the phosphocholine moiety of phosphatidylcholine to a ceramide, thus sphingomyelin is a unique form of a phospholipid.

The other major class of sphingolipids (besides the sphingomyelins) are the **glycosphingolipids** generated by substitution of carbohydrates to the *sn1* carbon of the glycerol backbone of a ceramide. There are 4 major classes of glycosphingolipids:

Cerebrosides: contain a single moiety, principally galactose.

Sulfatides: sulfuric acid esters of galactocerebrosides.

Globosides: contain 2 or more sugars.

Gangliosides: similar to globosides except also contain sialic acid.

6- Steroids:

Steroids are lipids derived from the cyclopentanophenanethrine.

Cholesterol is an extremely important biological steroids: 1-Constituent of plasma membrane and lipoproteins 2- precursor for the synthesis of the steroid hormones, sex hormones, vitamine D, and bile acids.

- Both dietary cholesterol and that synthesized *de novo* are transported through the circulation in lipoprotein particles. The same is true of cholesteryl esters, the form in which cholesterol is stored in cells.

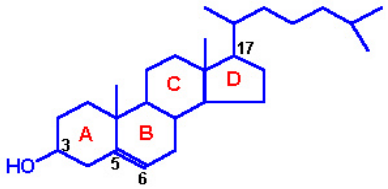


Figure: Cholesterol

Lipid Peroxidation:

It is a chain reaction providing continuous supply of free radicals ($ROO^{\cdot}$, $RO^{\cdot}$, and $OH^{\cdot}$) that initiates further peroxidation. This process causes **different disorders**: **rancidity** (auto oxidation of lipids by oxygen), **aging**, **cancer**, **atherosclerosis**, **inflammation**, **damage to tissue in vivo.**

Notes:

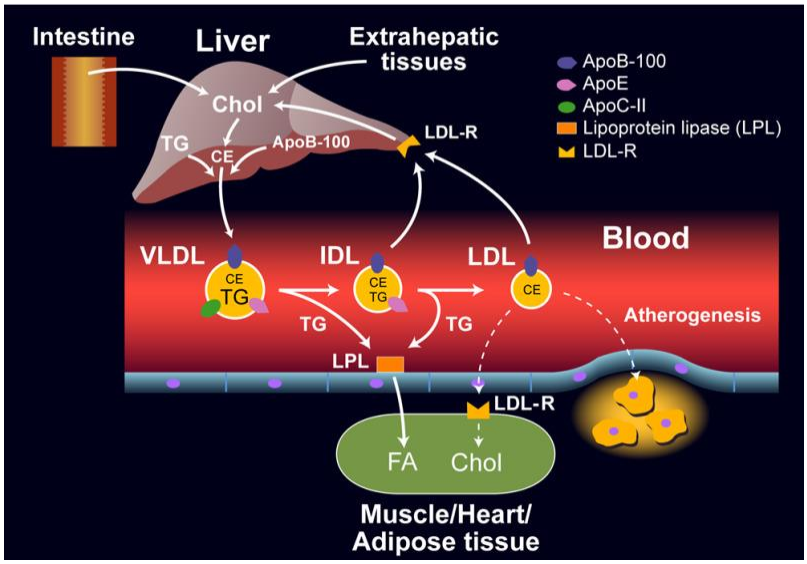
Amphipathic molecule: Part of the molecule is hydrophilic (polar) and the other is hydrophobic (non-polar). Polar group faces the water phase and the non-polar faces the hydrophobic phases (oil); this is the main feature of **plasma membrane.**

- **Micelles**: Critical concentration of polar lipids in aqueous medium.
- **Liposome**: Consist of spheres of lipid layers that enclose part of water.
  - **Emulsion**: Larger particles formed by non-polar lipids in an aqueous medium.

#-**Aggregation of bile salts into micelles and liposomes** with th product of fat digestion are important in facilitating absorption of lipids from intestine.

Lipoproteins: Macromolecular complex of lipids and proteins . They are the transport vehicles for lipids in the circulation. There are five types of lipoproteins.

1. **Chylomicrons:** transport primarily triglycerides from the digestive track to liver.
2. **VLDL**: transport triglycerides from liver to other tissues. transport the lipids (endogenously synthesized) mainly TG from liver to peripheral tissues).
3. **IDL:** Intermediate density lipoproteins, are formed from the degradation of **very low-density lipoproteins** as well as **high-density lipoproteins,** that enable fats and cholesterol to move within the water-based solution of the bloodstream.
4. **LDLs:** (low density lipoproteins) transport cholesterol, triglycerides and phospholipids from the liver to other tissues ("**bad" cholesterol**).
5. **HDLs:** (high density lipoproteins "**good" cholesterol**) transport cholesterol and phospholipids back carry from peripheral tissues to the liver.



ApoB-48

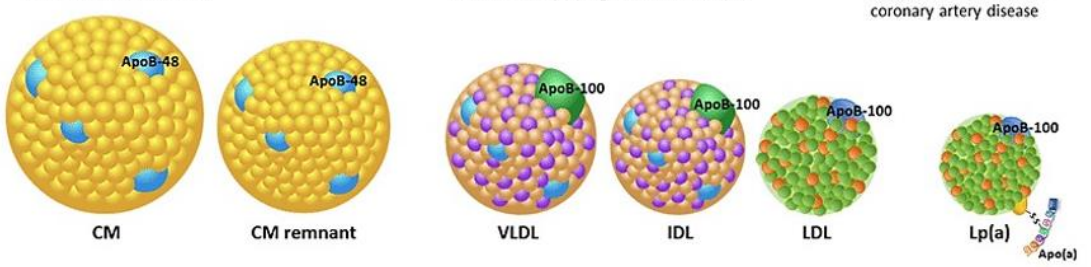
- MW: 264,000 daltons
- Metabolic function: assembly and secretion of CMs from the small intestine; structural protein of CMs and CM remnants

ApoB-100

- MW: 540,000 daltons
- Metabolic function: assembly and secretion of VLDL from the liver; structural protein of VLDL, IDL, LDL and Lp(a); ligand for LDL receptor

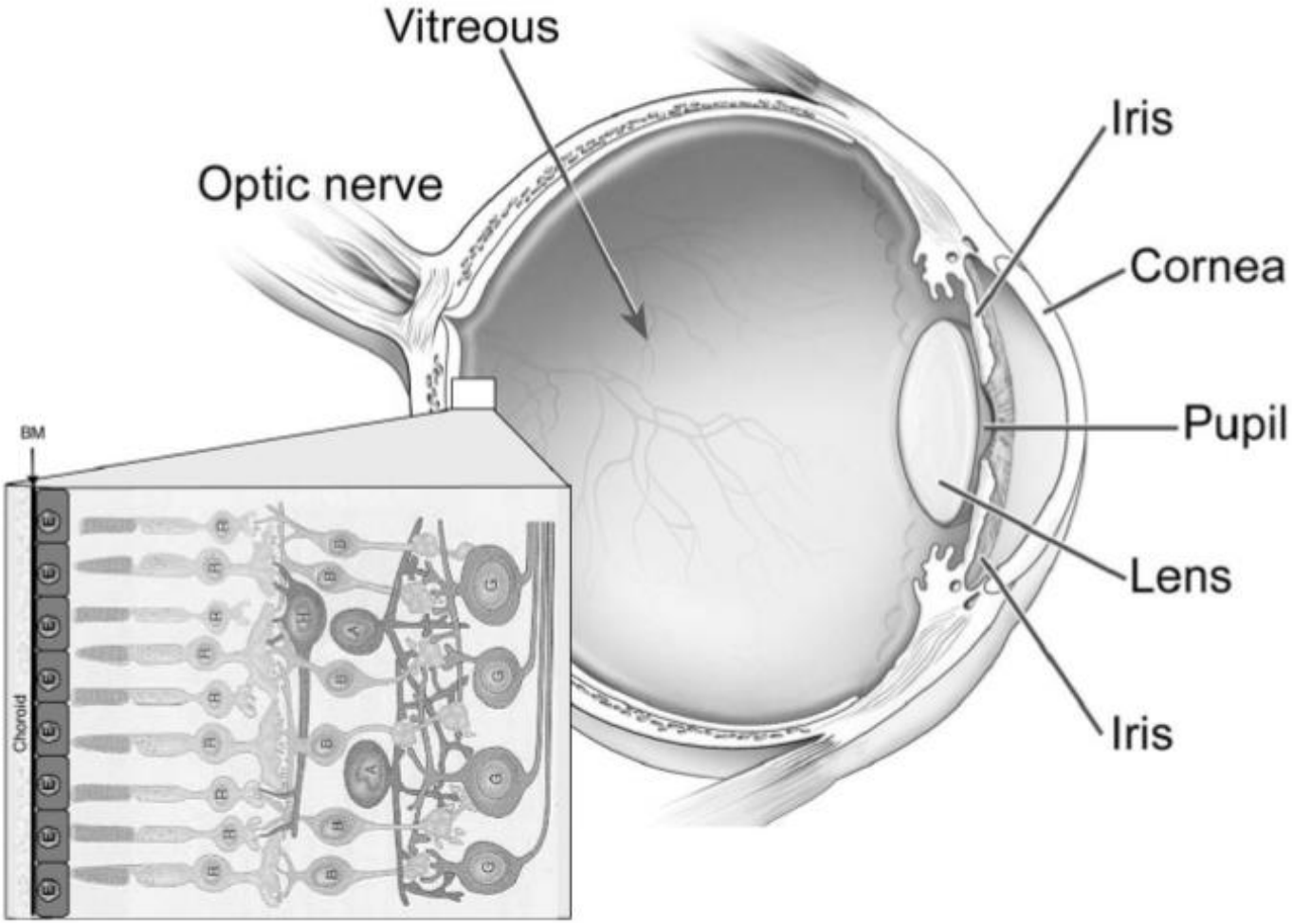
Apo(a)

- MW: 250,000-800,000 daltons
- Metabolic function: not completely defined, but it is an independent predictor of coronary artery disease



	CM	CM remnant	VLDL	IDL	LDL	Lp(a)
Source	intestine	CM	liver (intestine)	VLDL	VLDL	liver
Density (g/dl)	< 0.95	< 1.006	0.95-1.006	1.006-1.019	1.019-1.063	1.05-1.12
Diameter (nm)	75-1200	45-150	30-80	25-35	18-25	about 25
Molecular weight (daltons)	400×10^6	unknown	$10\text{-}80 \times 10^6$	$5\text{-}10 \times 10^6$	2.3×10^6	about 4×10^6
Structural components	99-98% total lipid and 1-2% total protein	94-92% total lipid and 6-8% total protein	93% total lipid and 7% total protein	85% total lipid and 15% total protein	80% total lipid and 20% total protein	80% total lipid and 20% total protein
Apolipoprotein composition	A-I, A-II, A-IV, B-48, C-I, C-II, C-III, E	B-48, E	B-100, C-I, C-II, C-III, E	B-100, C-I, C-II, C-III, E	B-100	B-100, Apo(a)

•Lipids are key components of the retina, and are closely associated with the aging processes.
•Omega-3 fatty acids show protective properties against inflammation and neurodegeneration in retinal aging and the development of Age-related macular degeneration (AMD).
•The eye retina is a part of the central nervous system, together with the brain and the spinal cord and as such is also naturally rich in lipids



•The human eye and retina

BM, Bruch's membrane;

E, retinal pigment epithelium;

R, photoreceptor (rods and cones);

H, horizontal cell;

B, bipolar cell;

A, amacrinecell;

G, ganglion cell

Lipids as crucial components of the retina

•The retina covers the internal side of the posterior chamber of the eye

•The retina is composed of
•neurosensory tissue: neuroretina,

•a pigment epithelium: retinal pigment epithelium (RPE)
•The main function of the neuroretinais to convert the light stimulus into an electrical signal that can be decoded by the brain

•The RPE creates a physical and metabolic barrier between the neuroretina and the choriocapillar is that limits the entry of exogenous compounds in the neuroretina.

•One of the primary function of the RPE is to eliminate the metabolic debris generated by photoreceptors.

•The RPE exhibits an endogenous capacity to synthesize and secrete lipoprotein-like particles

•Low density lipoprotein particles (LDL) participate significantly in retinal lipid supply.

Lipids as crucial components of the retina

•Lipids account for about 25% of the dry matter in the neuroretina.

•Phospholipids are the prominent lipids therein (more than 85%), while cholesterol is present as free cholesterol (10%), and to a lesser extent as cholesteryl esters (less than 2%)

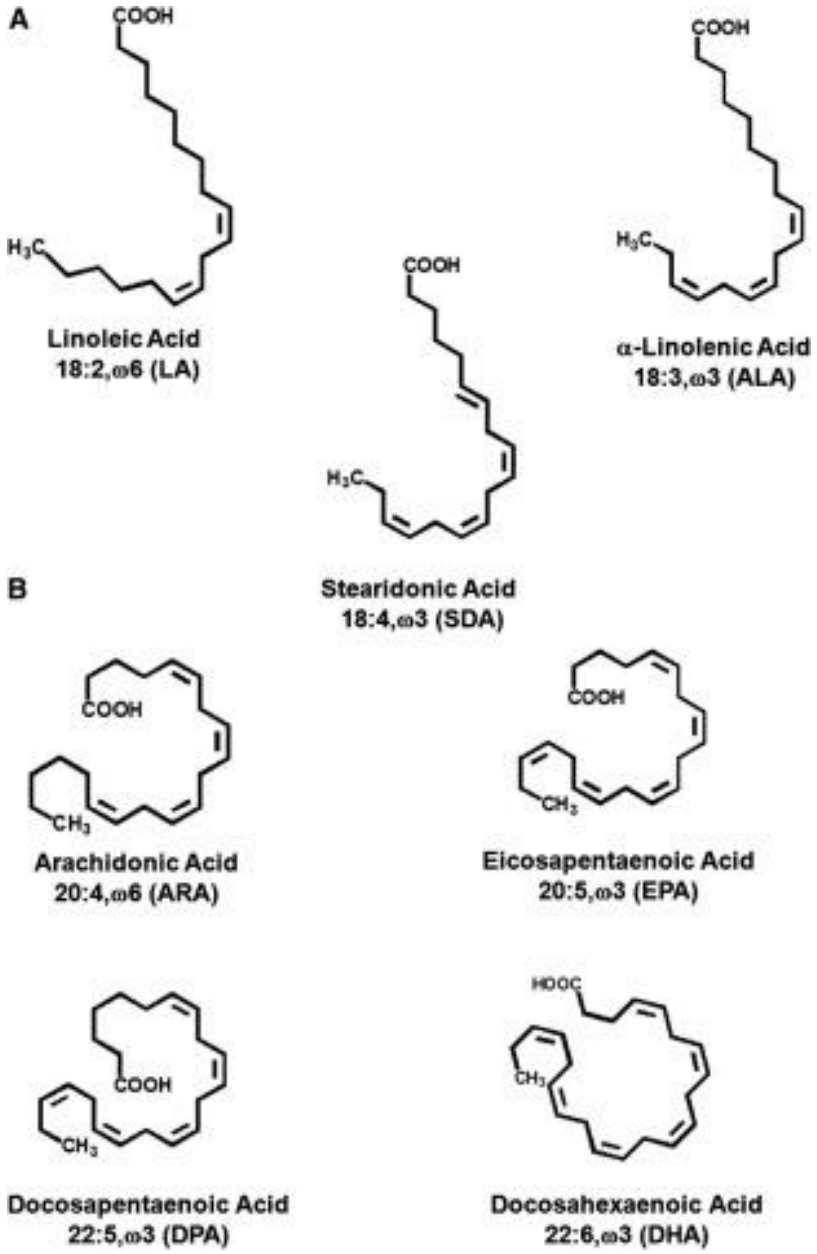
•Phospholipids are present in great quantity in the outer segment of rods and cones.

•Docosahexaenoic acid (DHA) is the main long-chain polyunsaturated fatty acid in the phospholipids of the neuroretina: 12–20% of the fatty acids in human and more than 30% in rodent

•The potential of a diet enriched in DHA and EPA (eicosapentaenoicacid) to increase the level of the longer chain omega-3 fatty acids (EPA; DPA, docosapentaenoicacid; and DHA) in the retina has clearly been demonstrated

•Intervention trials have been conducted in pregnant and lactating women and premature and at-term babies in order to evaluate the efficacy of dietary long chain omega-3 fatty acids to improve vision performance in infants.

•The positive effect of omega-3 fatty acids was obvious only in studies where the intake of DHA was higher than 1g daily



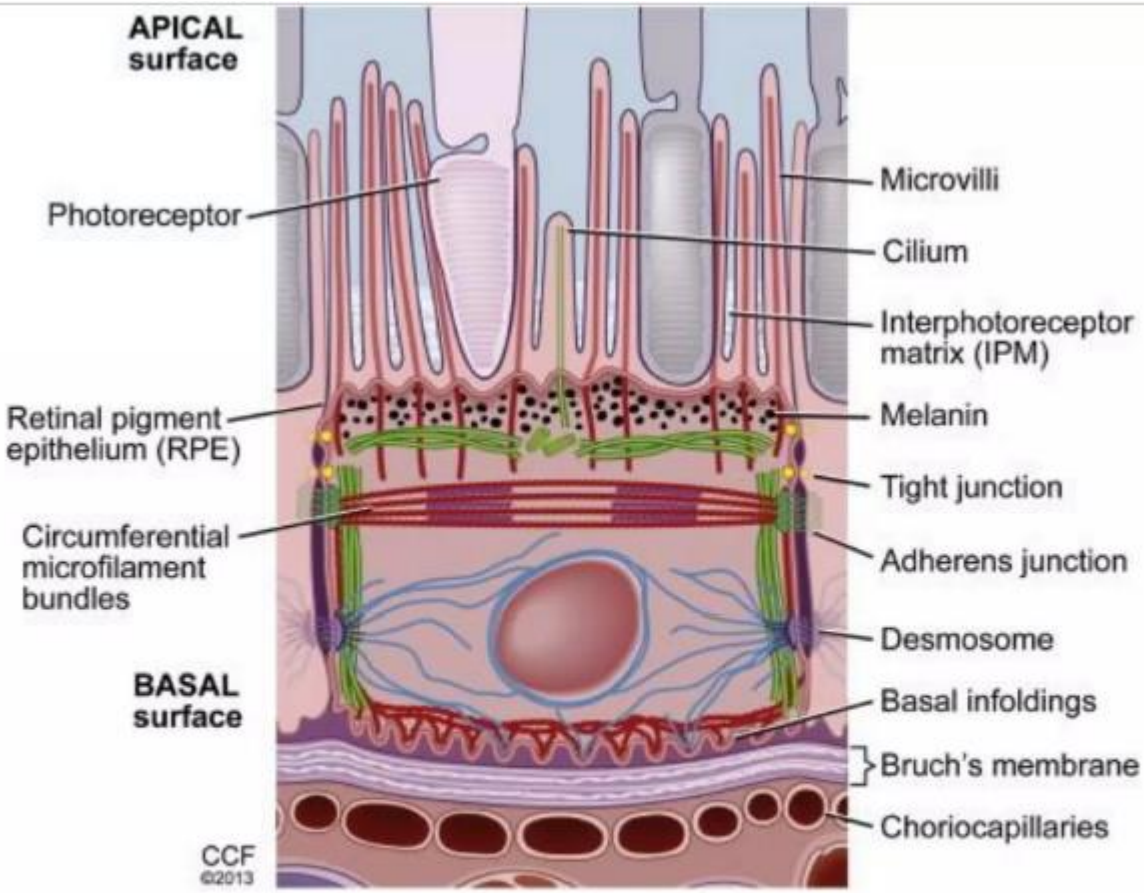
Aging of the retina & Lipids

•The “lipid wall”, made of cholesterol, participates in the age associated thickening of Bruch's membrane that increases hydraulic resistance and may reduce the fluxes of nutrients to the retina.

•AMD targets a specific area of the retina: the macula.

•High fat intake has been associated with higher risk for AMD.

•Smoking and light exposure are, for instance, recognized as promoting factors

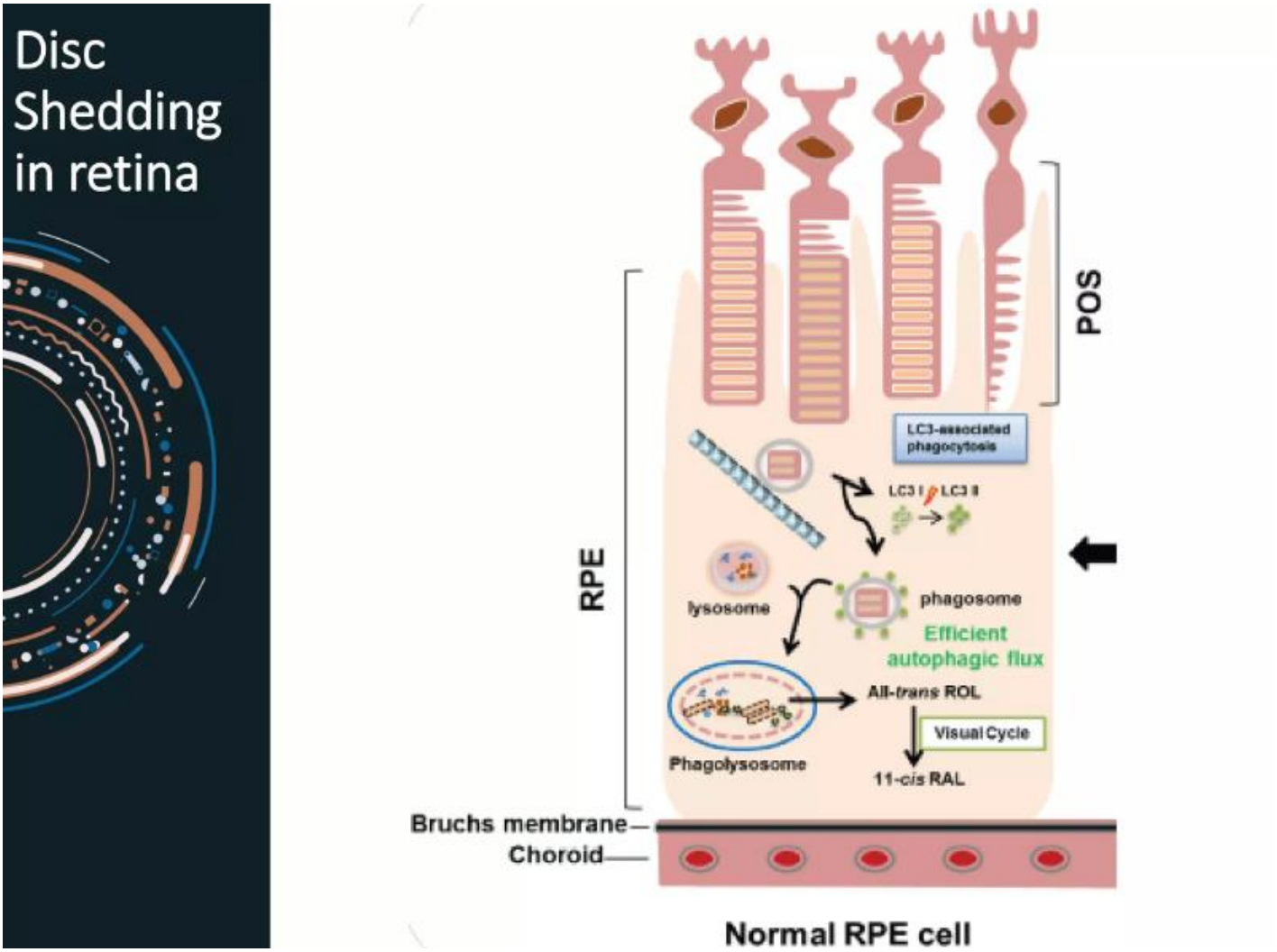


choriocapillaries supply → retinal pigment epithelial → interphotoreceptor matrix → photoreceptor cells

- **choriocapillaries supply** the nutrients to the **retinal pigment epithelial** (RPE) cells, which delivers them to the interphotoreceptor matrix.
- **Low density lipoprotein (LDL)** is the main carrier of DHA, and since the RPE cells contain LDL receptors
- it is likely that the **uptake and delivery of DHA to the photoreceptor cells are receptor mediated** with subsequent release of DHA phospholipids, or free DHA, into the interphotoreceptor matrix.
- **Fatty acid-binding proteins (FABPs)** present in the interphotoreceptor matrix bind DHA, and are believed to be involved in the transport of DHA to the photoreceptor cells.

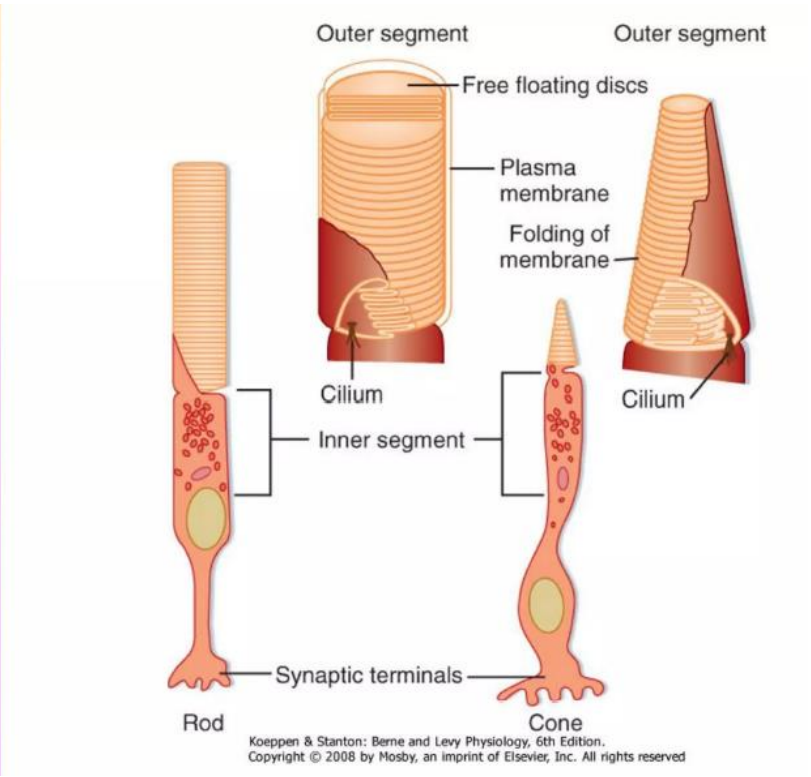
- RPE is a single layer of **hexagonal pigmented cells** located in the outmost part of the neurosensory retina.
- the **supplement of nutrients and oxygen to retina**
- the **sustainment of visual cycle** through metabolizing vit- A
- the absorbing of scattered light to **reduce photo-oxidation** via melanosomes
- the performance of **receptor-mediated phagocytosis of photoreceptor outer segment (POS) fragments** for assuring viability and functionality of photoreceptors
- **Dysfunction of RPE** resulted from consistent exposures to oxidative stress has been reportedly to cause retinal degenerations, such as age-related macular degeneration (AMD).

- The **heterophagy of Photoreceptor Outer Segment** by RPE is essential to the longevity of photoreceptors.
- The **renewal of POS is regulated by circadian rhythms** via the shedding of distal tips POS, which are degraded and engulfed by RPE, and are eventually digested by lysosomal enzymes.
- **All-trans-retinol (ROL) are recycled and converted to 11-cis-retinal (11CR) by visual cycle** to replenish chromophore for reproduction of photobleached pigments.



- Disc membranes are assembled at the inner segment, and form discs at the base of the outer segment
- These membranes have a short lifetime, and **are replaced every 9–14 days**
- The discs move outward toward the tip apical region where they are shed into the **adjacent RPE, *phagocytosed and digested*** by the lysosomal system.
- However, the retina conserves its **DHA by retrieving it from the phagosomal membranes** within the RPE and recycling it for incorporation into newly forming disc membranes

DHA accumulation in the retina



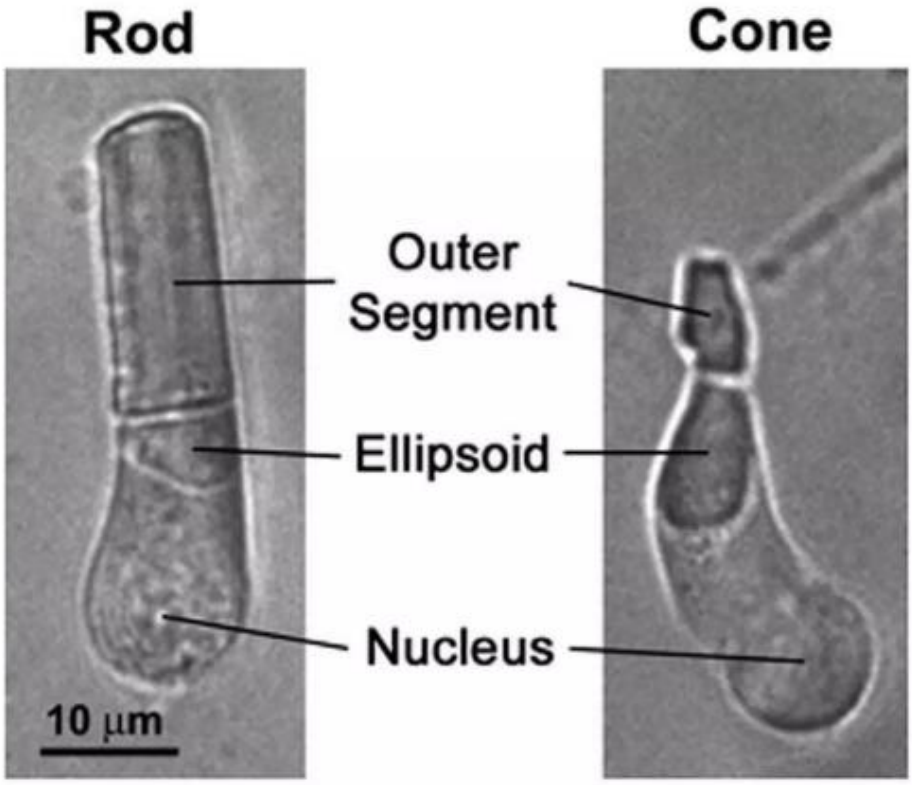
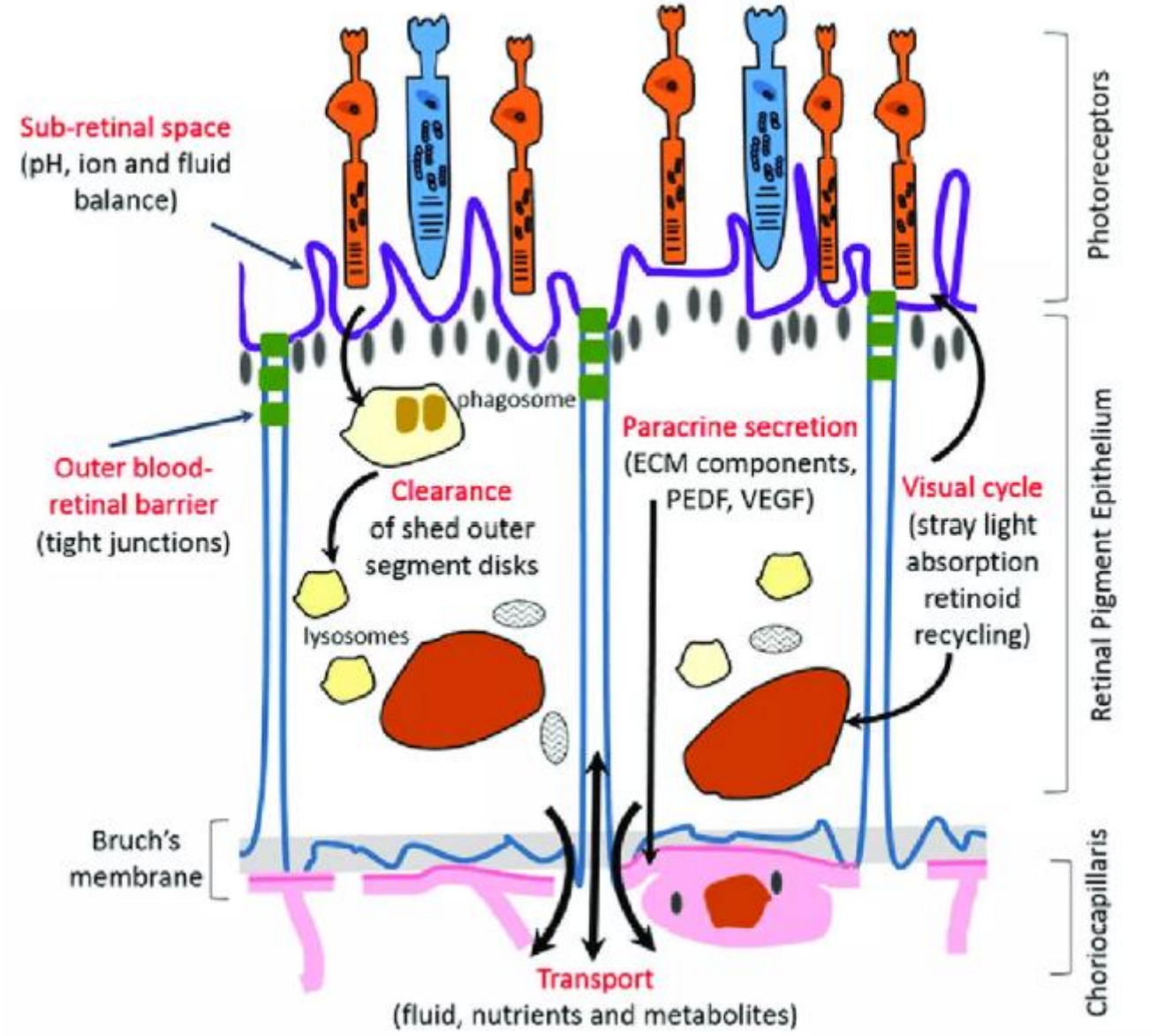


Figure 1. Brightfield images of living rod and cone photoreceptors isolated from a salamander retina. Phototransduction takes place in the outer segment, while the ellipsoid is densely packed with mitochondria. Rods are responsible for dim light vision, cones for bright light vision.
Courtesy of Yiannis Koutalos.



- The recycling mechanism is not fully understood, but it has been postulated to occur via one of the two following mechanisms:

- (1) by **returning the DHA** from the RPE back to the photoreceptors (short-loop)
- (2) by **entry of DHA into the systemic circulation**, where it follows a similar pathway to cellular and dietary DHA via the liver, and reuptake by the RPE cells, with delivery to photoreceptor cells for new disc formation (long-loop)

- This selective retention of lipid is unique to the photoreceptor cells.

Role of DHA

1. **DHA affects the membrane structure** by altering its **permeability, fluidity, thickness and lipid-phase properties** while increasing the rate of rhodopsin activation
2. **DHA surrounds rhodopsin** (approximately 60 molecules of phospholipid for each rhodopsin), excluding cholesterol from **creating a fluid microenvironment** within the rod outer-segment membranes
3. **membrane fluidity is an important biophysical factor** of the disc membranes, and this fluidity is brought about by the presence of DHA and other PUFAs on the constituent phospholipids

4. **The membrane's fluid state allows Brownian movement** of the protein components within the plane of the disc membrane, enabling transduction and amplification of the signal
5. *membranes containing DHA have higher MII formation, MII–transducing interaction and activation and, finally, PDE activation.*

DHA and retinal oxidative stress

- DHA has high degree of unsaturation
- It is **susceptible to oxidation** within the photoreceptor disc membranes
- the membrane stabilising substances, vitamin E and taurine, along with the retinal antioxidants, vitamin C, carotenoids, superoxide dismutase and glutathione (and its associated enzymes) helps in fighting against oxidative damage of eye
- However a constant cellular and dietary supply is required to maintain the disc membranes.
- studies have demonstrated that depletion of DHA from the developing retina leads to **abnormalities in electroretinogram (ERG) and visual evoked potential (VEP), resulting in reduced visual function**

Dietary deficiency of DHA and visual function

- diets low in Omega-3 fatty acids led **to impaired visual acuity**
- The retinal dysfunction occurs due to **inadequate disc membrane DHA phospholipids to support rhodopsin in light capture**, and hence MII formation
- Cells compensate this lack of DHA by converting omega-6 EFA linoleic acid to decosapentanoic acid, which is not efficient in supporting rhodopsin.
- The retinal abnormalities due to DHA deficiency are reversible
- but the **responsiveness of the visual cortex, and the higher cortical centres involved in visual function**, appear long-lasting and irreversible
- In infants: supplementation should be approached with caution as these infants have low retinal levels of vitamin E and **increased retinal DHA concentration could increase susceptibility to retinal oxidative damage**

Aging of the retina & Lipids

•The “lipid wall”, made of cholesterol, participates in the age associated thickening of Bruch's membrane that increases hydraulic resistance and may reduce the fluxes of nutrients to the retina

•AMD targets a specific area of the retina: the macula.

•High fat intake has been associated with higher risk for AMD.

•Smoking and light exposure are, for instance, recognized as promoting factors

•In a study it was observed that participants who have the highest omega-3 long-chain polyunsaturated fatty acid (EPA and DHA) intake (0.11% of total energy intake) were 30% less likely to develop Geographic atrophy and neovascularAMD than low consumers (0.01% of total energy intake)

Lipids in tears

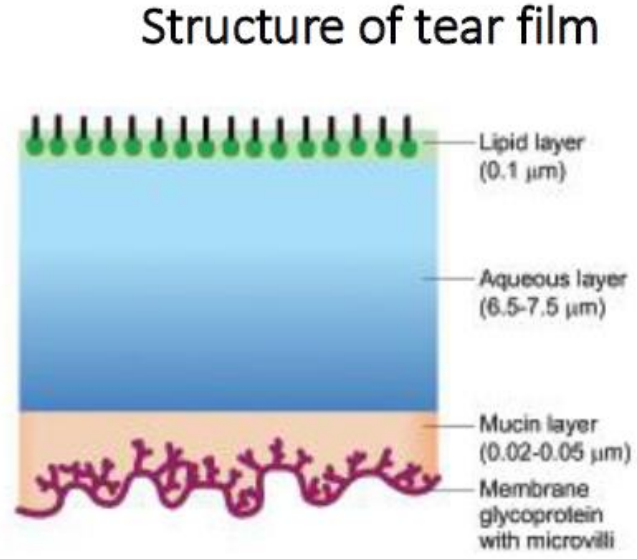
•Tear film is actually composed of three basic layers: mucin, water and lipids from posterior to anterior.

•**Lipid or oily layer** is the outermost layer of tear film formed at air-tear interface from the secretions of Meibomian, Zeis, and Moll glands.

•This layer prevents the overflow of tears, retards their evaporation and lubricates the eyelids as they slide over the surface of the globe.

•Lipids within tears help prevent water evaporation from the ocular surface and protect the eye against infection

•Prolonged dry eyes leads to cloudy cornea, inhibiting self repair of the damaged cornea



Eye Diseases linked to lipids

•**Arcus senilis**refers to an annular lipid infiltration of corneal periphery. This is an age-related change occurring bilaterally in 60 percent of patients between 40 and 60 years of age and in nearly all patients over the age of 80.

•**Fatty degeneration (Lipoid keratopathy)of cornea** is characterisedby whitish or yellowish deposits. The fat deposits mostly consist of cholesterol and fatty acids

•**Diabetic retinopathy**: hyperlipidemia is a risk factor

•**Seborrhoeicor squamous blepharitis:** glands of Zeissecrete abnormal excessive neutral lipids which are split by *Corynebacteriumacne* into irritating free fatty acids

Eye Diseases linked to lipids

•**Xanthelasma:**

•Thesearecreamy-yellowplaque-likelesionswhichfrequentlyinvolvetheskinofupperandlowerlidsneartheinnercanthus.

•Xanthelasmarepresentslipiddepositsinhistiocytesinthedermisofthelid.

•Thesemaybeassociatedwithdiabetesmellitusorhighcholesterollevels.

•**THE DRY EYE:**

•Lipid deficiency is extremely rare.

•It has only been described in some cases of congenital anhidrotic ectodermal dysplasia along with absence of meibomianglands.

•However, lipid abnormalities are quite common in patients with chronic blepharitis and chronic meibomitis

•Lipid soluble drugs have better permeability in eyes

•***Asteroid hyalosis.***

•It is characterisedby small, white rounded bodies suspended in the vitreous gel.

•These are formed due to accumulation of calcium containing lipids.

•Asteroid hyalosisis a unilateral, asymptomatic condition usually seen in old patients with healthy vitreous.

•There is a genetic relationship between this condition, diabetes and hypercholesterolaemia.

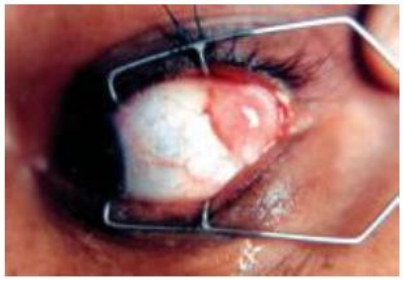
•The genesis is unknown and there is no effective treatment

Lipodermoids.

•These are solid tumours usually seen beneath the conjunctiva.

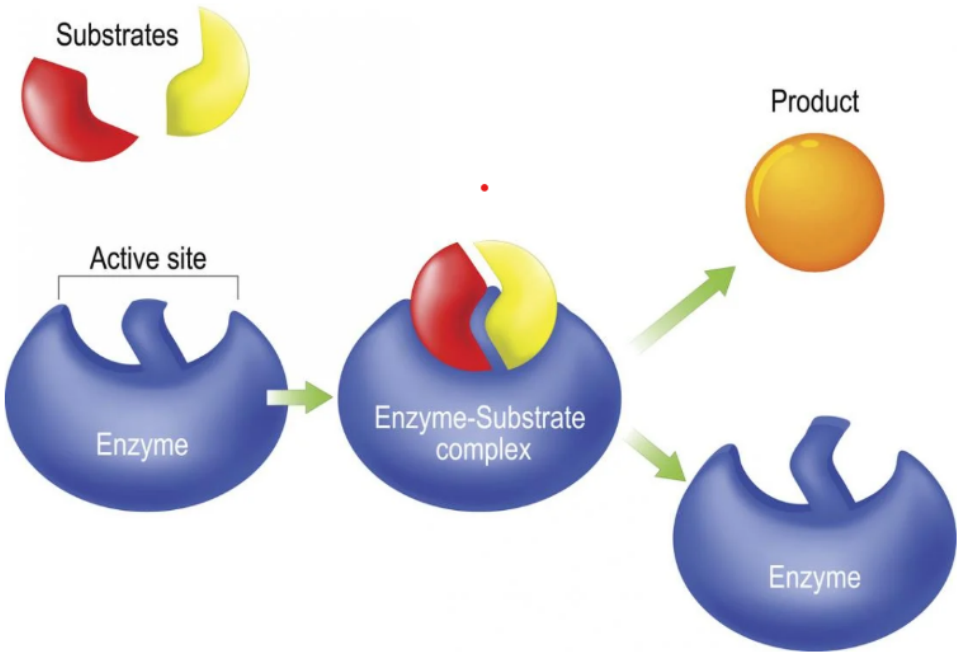
•These are mostly located adjacent to the superior temporal quadrant of the globe.

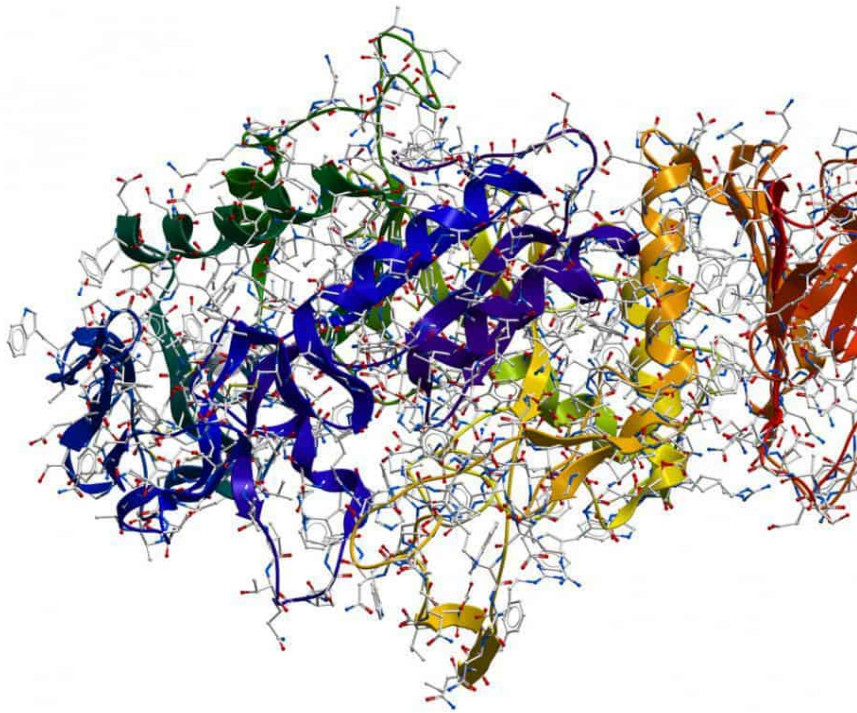
•These do not require any surgical intervention unless they enlarge significantly



Enzyme Structure, classification and mechanism of action

م.د حيدر خضير الظالمي





Definition : enzymes are biological catalysts which bring about chemical reaction in the living cell.

. produced by the living organism in small amounts.

. Functions: digestion, breathing, synthesis and break down of CHOS, proteins, fats

. enzymes acts upon substance called substrate.

. enzymes convert substrate into product. Ex: lactose **lactase** → galactose + glucose

. 16% of weight is nitrogen.

physical properties: **1**. Heat labile **2**. Soluble in water

3. Precipitate by precipitating agent (ammonium sulphate or trichloroacetic acid).

General properties of enzymes:

1. all enzymes are proteins.

2. enzymes accelerate the reaction but:

a. do not alter the reaction equilibrium

b. not consumed in overall reaction **c**. required in very small quantities.

3. enzymes are highly specific for their substrate.

4. enzymes possess active site, at which interaction with substrate take place.

Sources of enzymes:

Endoenzymes: enzymes that function within the cells, most of enzymes are these types.
Ex: metabolic oxidase.

Exoenzymes: enzymes that are liberated by cells and catalyze reactions outside the cell.
Ex: digestive enzymes (amylase, lipase, protease).

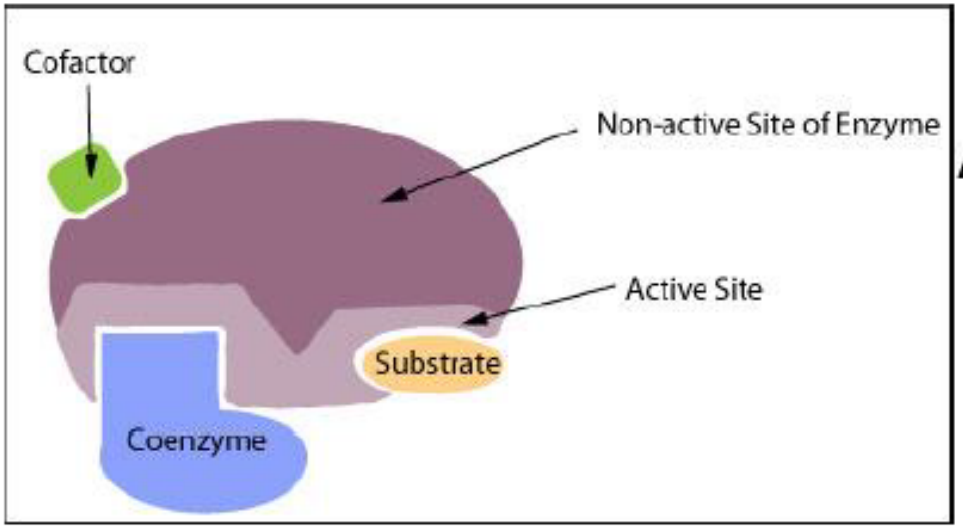
Chemical composition of enzymes:

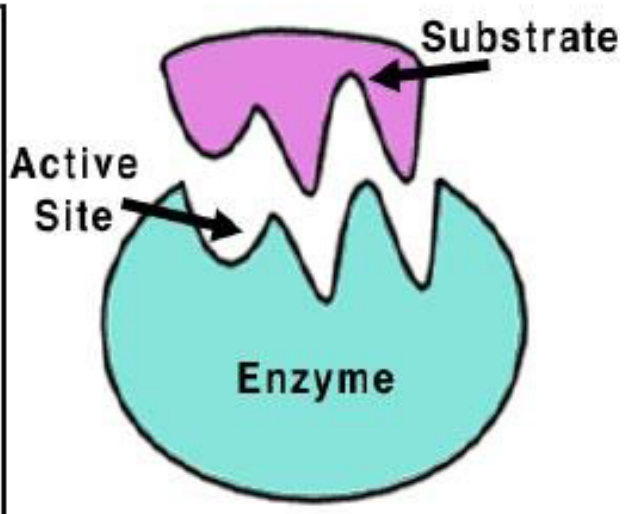
Enzymes classified according to their chemical composition into.

1. **Enzyme consist of only protein.**

   Ex: pepsin, trypsin (amino acids binding peptide bonds).

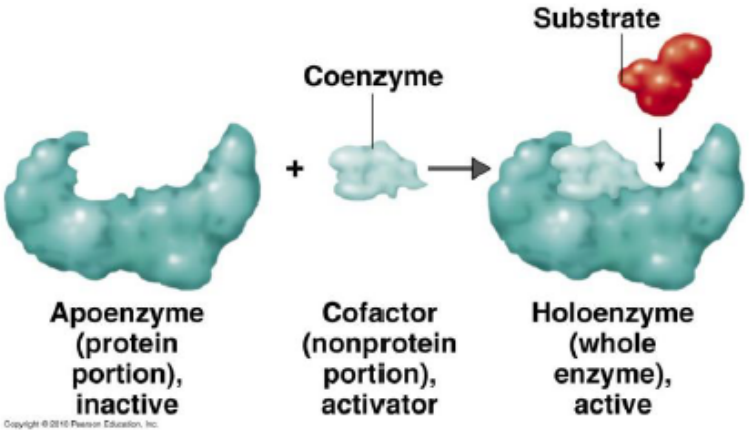
2. **Enzyme consist of** : protein (enzyme) + Co - Enzyme = **Holoenzyme**
   (apoenzyme**)**





3. Enzyme consist of:

Protein (enzyme) + prosthetic group (Co – factor) = **Holoenzyme**



Coenzymes : are typically organic molecules, used by enzymes to help catalyse reactions, contain functionalities not found in proteins,

cofactors : are catalytically essential molecules or ions that are covalently bound to the enzyme

Holoenzyme : enzyme consist of Apoenzyme + prosthetic group

Apoenzyme : term refers to the protein part of enzyme.

Active site of enzyme: the point in the enzyme which interaction with substrate, co-enzyme, inhibitor take place.

Zymogen: the active form of enzyme.

Ex: pepsinogen —**Hcl**→ pepsin (active)

Ex: trypsinogen —**enterokinase**→ trypsin (active)

The difference between Co-enzymes and Co- factors:

Co-enzymes	Co - factors
1. binds loosely and can easily separated from enzyme by dialysis.	**1**.conjugated with protein(enzyme)
2. organic compounds (ex: water soluble vitamins such as Vit C and B	**2**. metallic ions (Fe, Mn, Cu,Mg)
4. non protein.	**3**. has low molecular weight
5. heat resistance.	
6. their function as co-substrate.	

(Enzymes as Biological Catalysts)

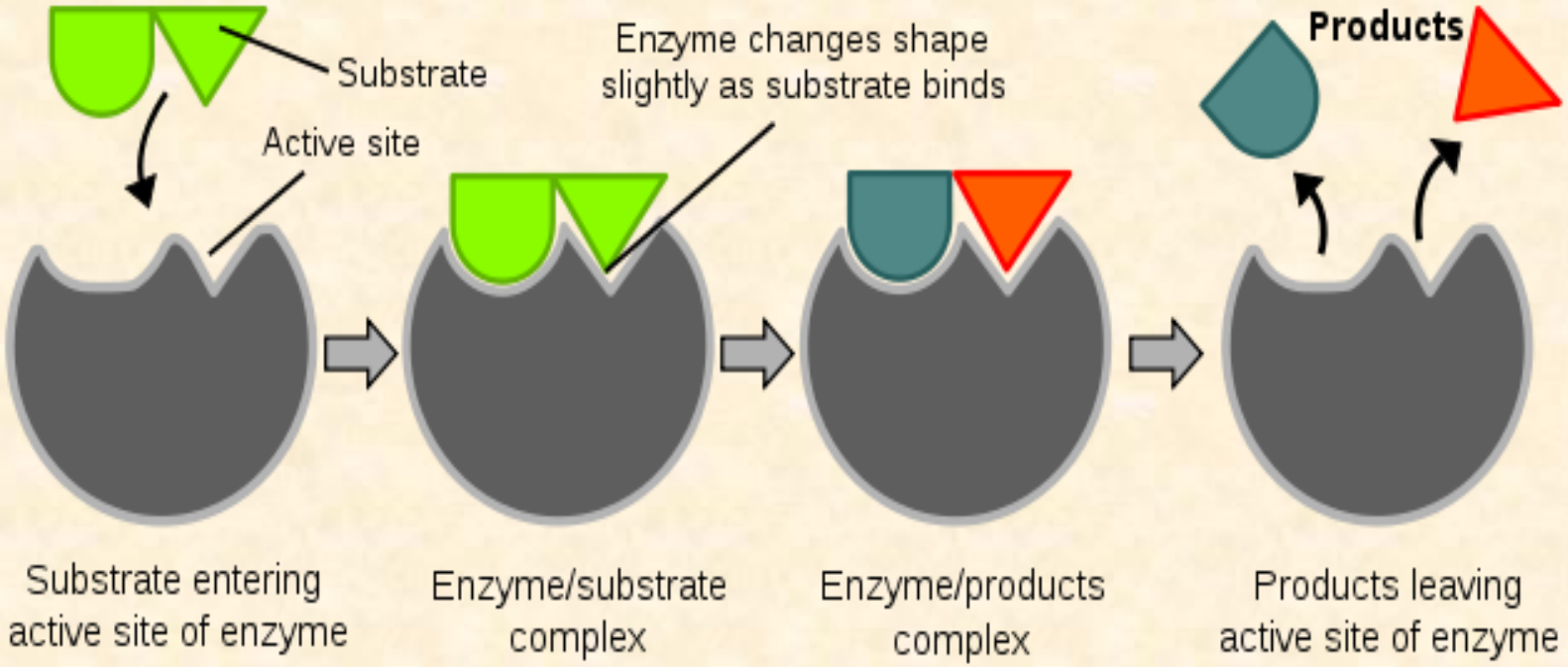
- **Enzymes** are proteins that increase the rate of reaction by lowering the energy of activation
- They catalyze nearly all the chemical reactions taking place in the cells of the body.
- Not altered or consumed during reaction.
- Reusable

Importance

- Enzymes play an important role in Metabolism, Diagnosis, and Therapeutics.
- All biochemical reactions are enzyme catalyzed in the living organism.
- Level of enzyme in blood are of diagnostic importance e.g. it is a good indicator in disease such as myocardial infarction.
- Enzyme can be used therapeutically such as digestive enzymes.

ACTIVE SITES

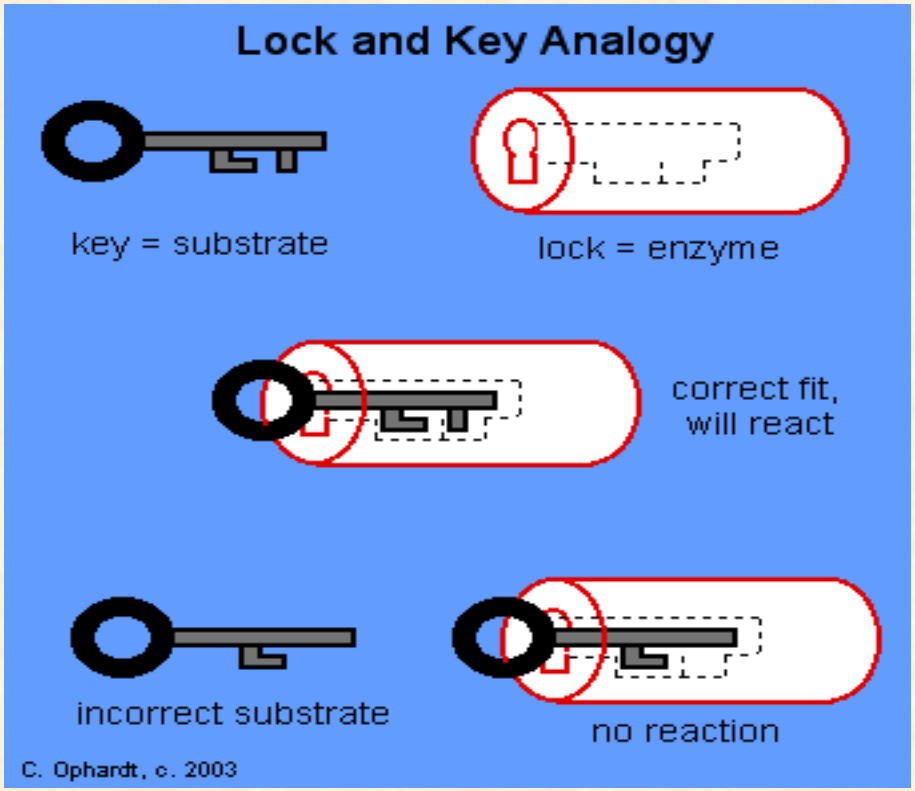
- Enzyme molecules contain a special pocket or cleft called the active sites.



Lock-and-Key Model

- **In the lock-and-key model of enzyme action:**
  - the active site has a rigid shape
  - only substrates with the matching shape can fit
  - the substrate is a key that fits the lock of the active site

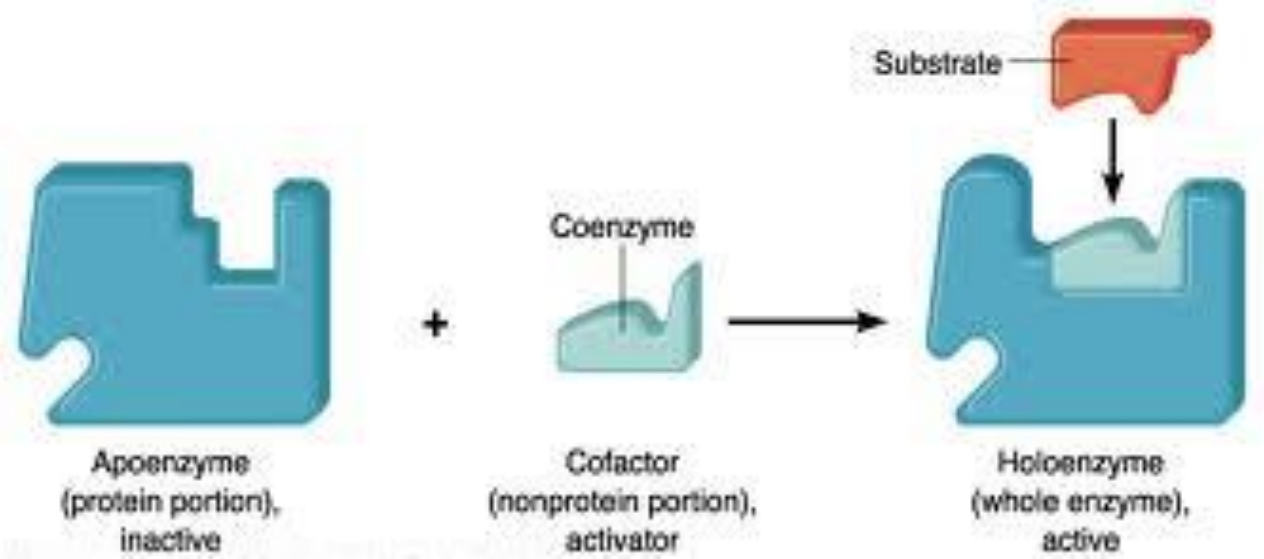
This explains enzyme specificity
This explains the loss of activity when enzymes denature



APOENZYME and HOLOENZYME

Apoenzyme or apoprotein is an enzymatically inactive protein part of an enzyme, which requires a cofactor for its activity. Apart from catalytic RNA, most of the enzymes are proteins. Not all the enzymes require a cofactor. Enzymes that do not require any cofactor are known as simple enzymes, e.g. pepsin, trypsin, etc

Holoenzyme is a complete, functional enzyme, which is catalytically active. Holoenzyme consists of an apoenzyme together with its cofactors. Holoenzyme contains all the subunits required for the functioning of an enzyme, e.g. DNA polymerase III, RNA polymerase .



Important Terms to Understand Biochemical Nature And Activity of Enzymes

- **Cofactor:**
  - A cofactor is a non-protein chemical compound that is bound (either tightly or loosely) to an enzyme and is required for catalysis.
  - Types of Cofactors:
    - Coenzymes.
    - Prosthetic groups.

Types of Cofactors

- **Coenzyme:**
  The non-protein component, loosely bound to apoenzyme by non-covalent bond.
- **Examples : vitamins or compound derived from vitamins.**

Coenzymes are a specific type of helper or partner that are organic molecules required for enzyme function that bind loosely to an enzyme. They are often, though not always, derived from vitamins. Prosthetic groups are enzyme partner molecules that bind tightly to an enzyme.

- **Prosthetic group**
  The non-protein component, tightly bound to the apoenzyme by covalent bonds is called a Prosthetic group.

This is a component of a conjugated protein that is required for the protein's biological activity, The prosthetic group may be organic (such as a vitamin, sugar, RNA, phosphate or lipid) or inorganic (such as a metal ion). Prosthetic groups are bound tightly to proteins and may even be attached through a covalent bond.

Enzyme Specificity

- Enzymes have varying degrees of **specificity** for substrates
- Enzymes may recognize and catalyze:
  - a single substrate
  - a group of similar substrates
  - a particular type of bond

Important Terms to Understand Biochemical Nature And Activity of Enzymes

Activation energy or Energy of Activation:

- All chemical reactions require some amount of energy to get them started.

OR

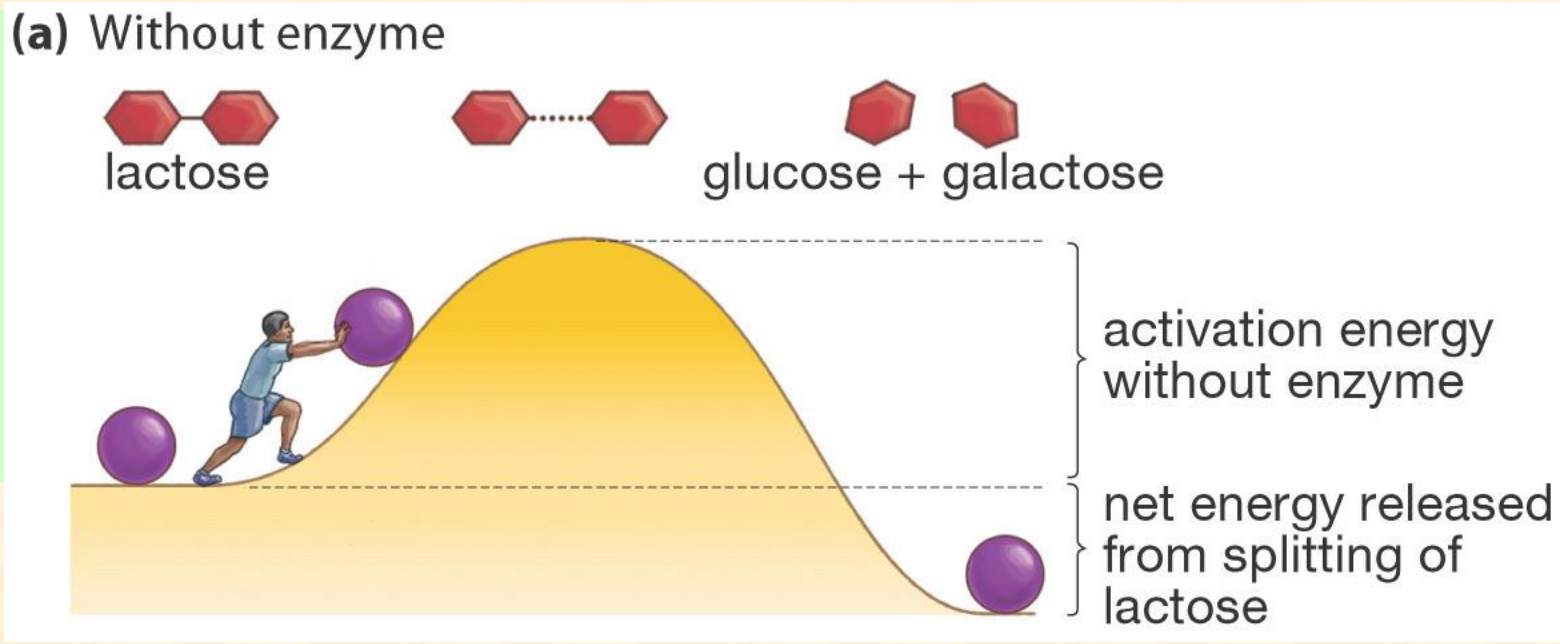
- It is First push to start reaction.

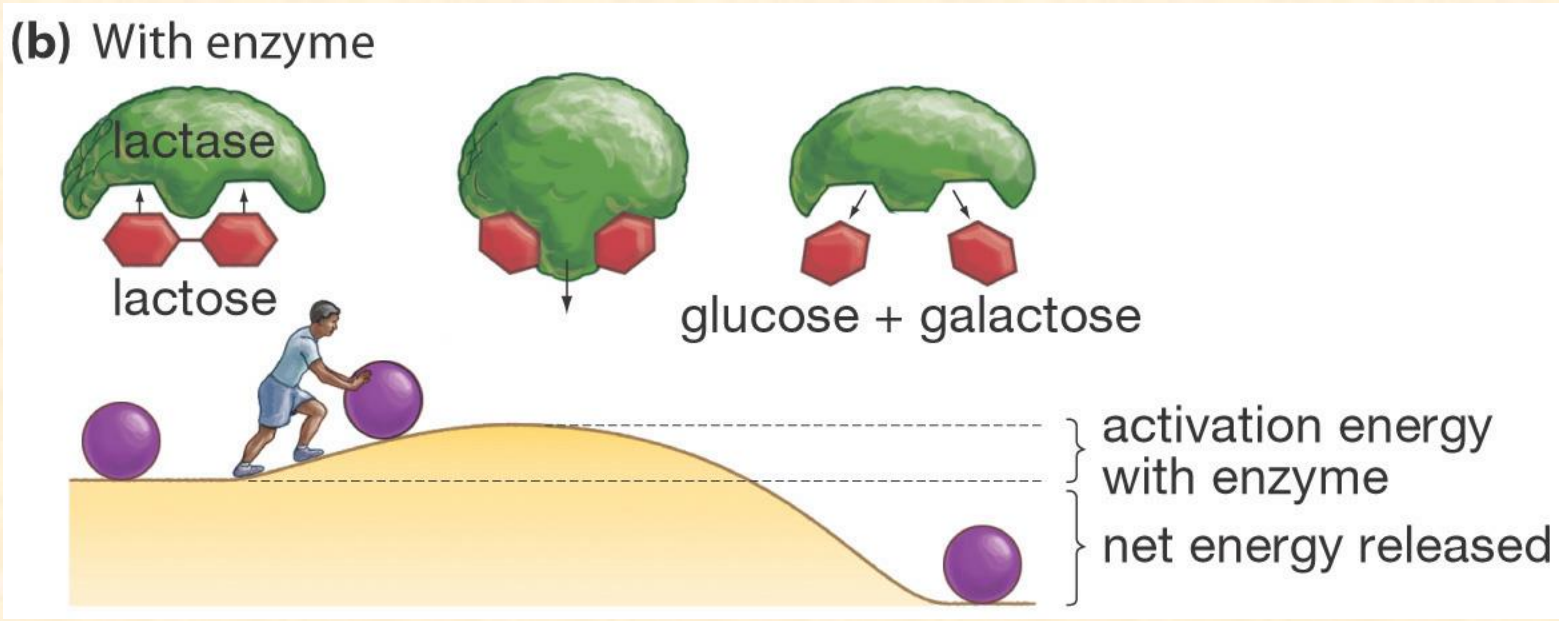
This energy is called activation energy.

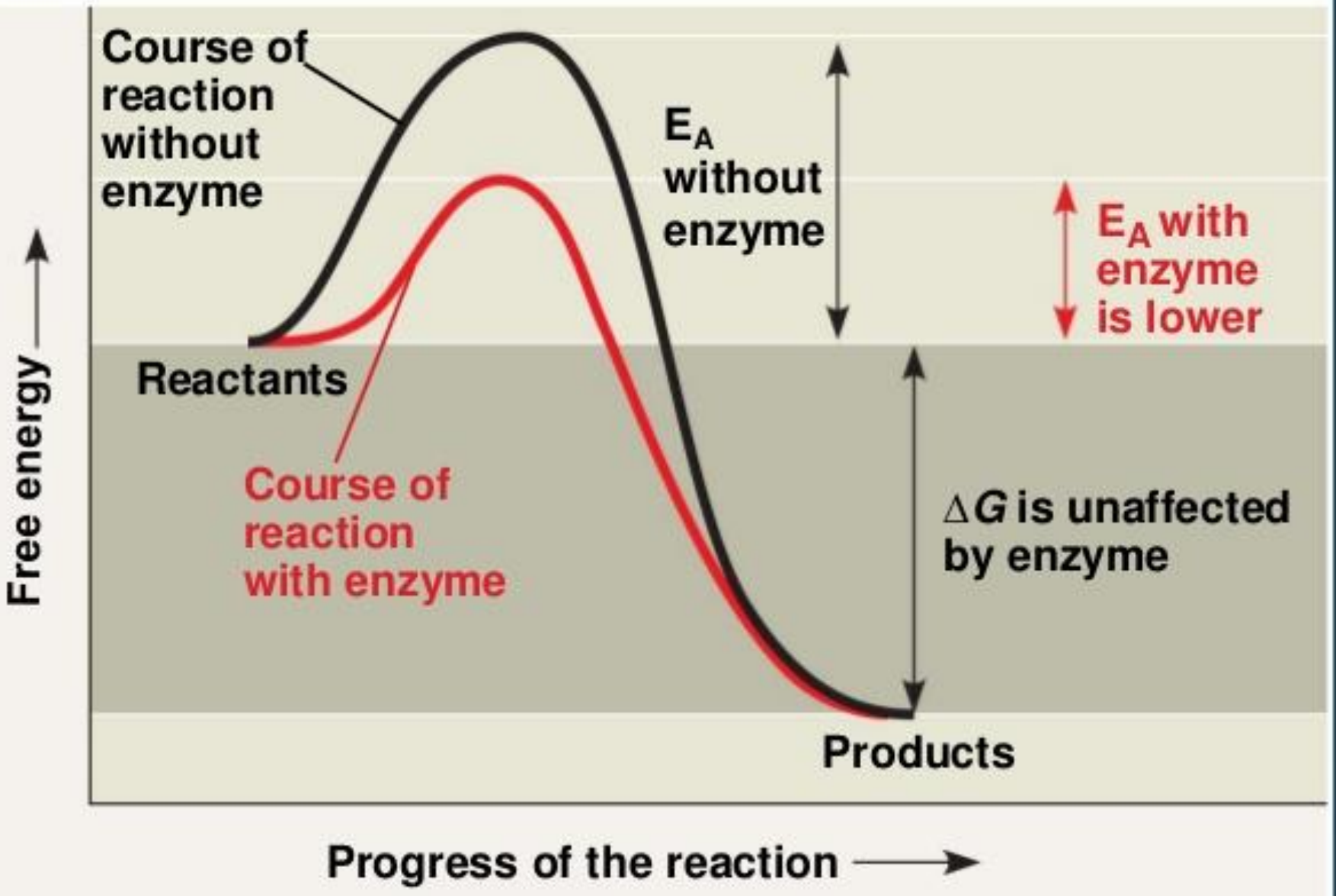
Mechanism of Action of Enzymes

- **Enzymes increase reaction rates by decreasing the Activation energy:**
- **Enzyme-Substrate Interactions:**
  - **Formation of Enzyme substrate complex by:**
  - Lock-and-Key Model
  - Induced Fit Model

Enzymes Lower a Reaction's Activation Energy





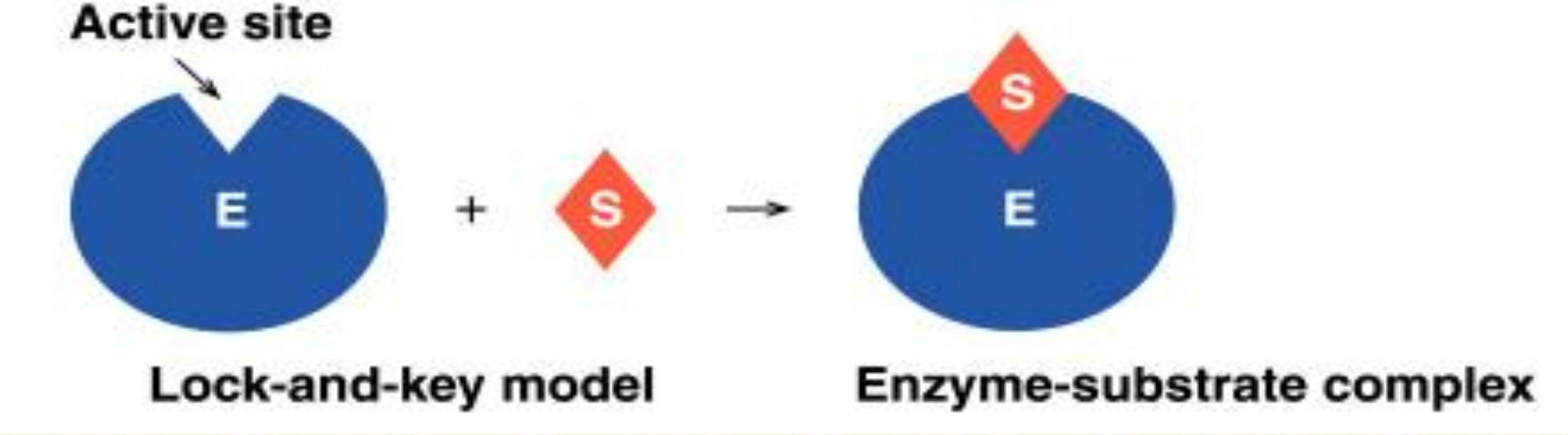

Course of reaction without enzyme
E_A without enzyme
E_A with enzyme is lower
Reactants
Course of reaction with enzyme
ΔG is unaffected by enzyme
Products
Free energy
Progress of the reaction

MECHANISM OF ACTION OF ENZYMES

1- Lock: Key model of enzyme action: implies that the active site of the enzyme is complementary in shape to that of its substrate, i.e. the shape of the enzyme molecule and the substrate molecule should fit each other like a lock and Key. In 1958, Daniel Koshland, postulated another model; which implies that the shapes & the active sites of enzymes are complementary to that of the substrate only after the substrate is bound.

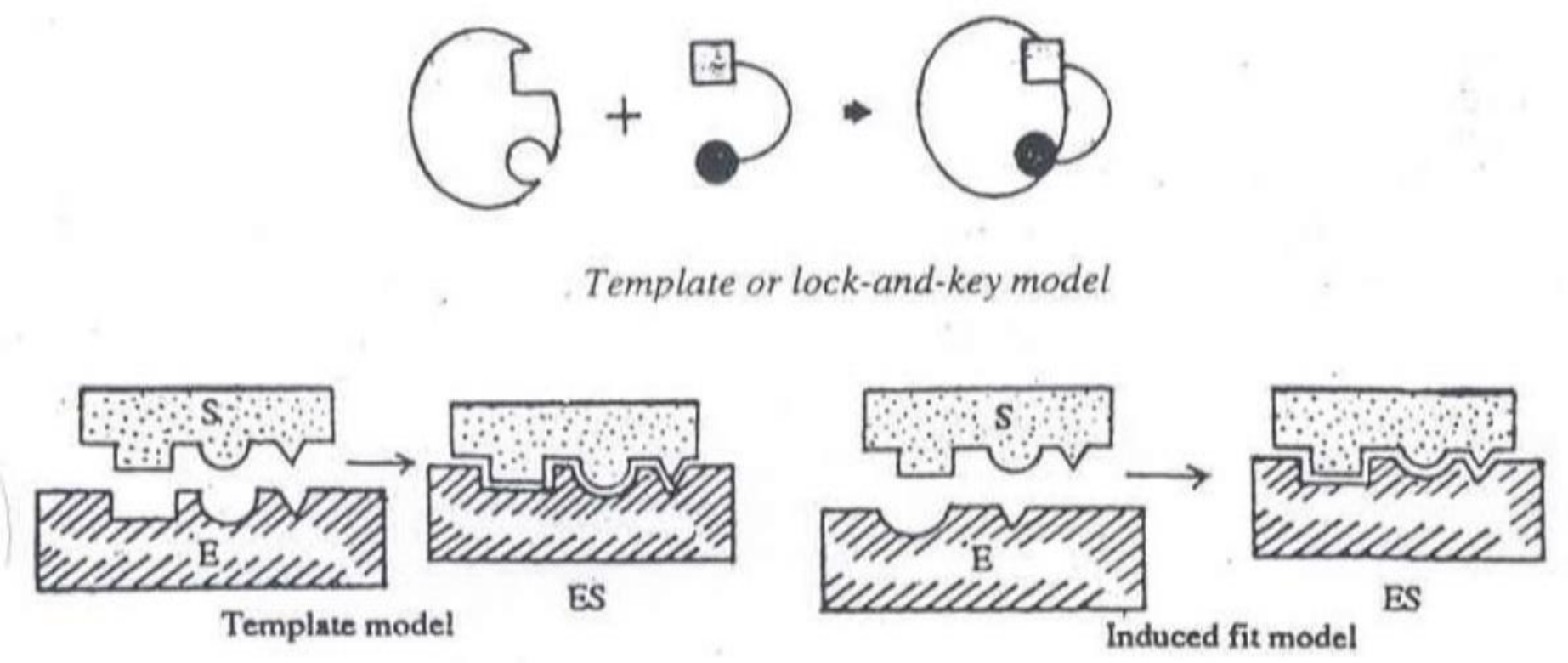
Lock-and-Key Model

- In the lock-and-key model of enzyme action:
  - the active site has a rigid shape
  - only substrates with the matching shape can fit
  - the substrate is a key that fits the lock of the active site
- This is an older model, however, and does not work for all enzymes



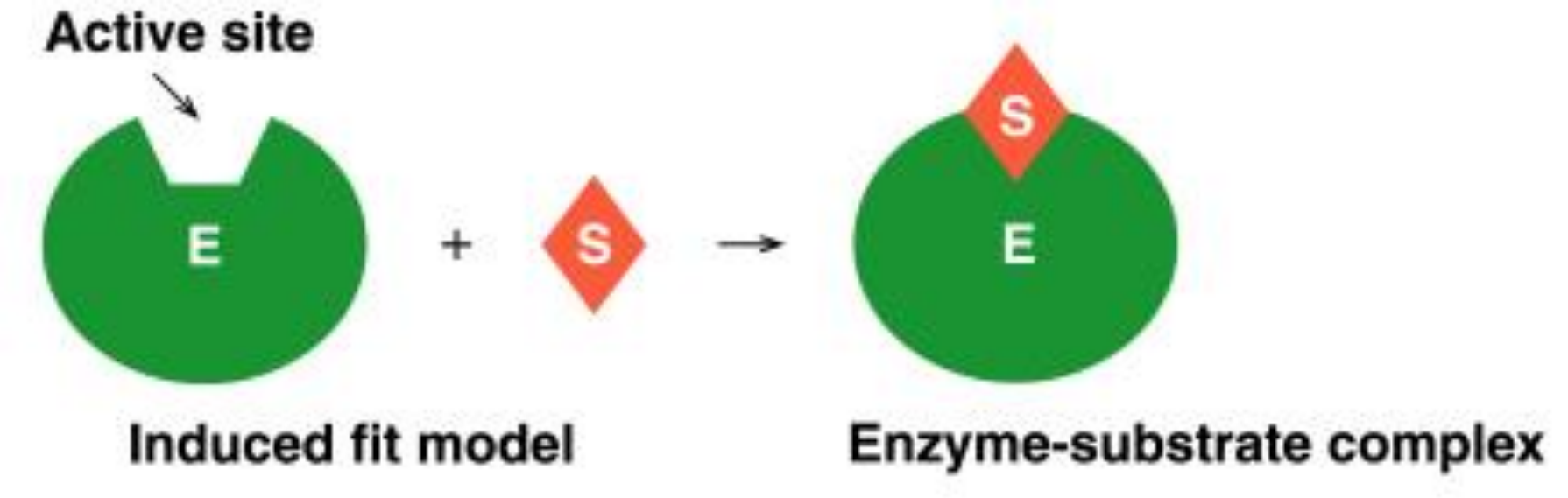
2-Induced fit Model :

is a model that implies the shapes & the active sites of enzymes are complementary to that of the substrate only after the substrate is bound.



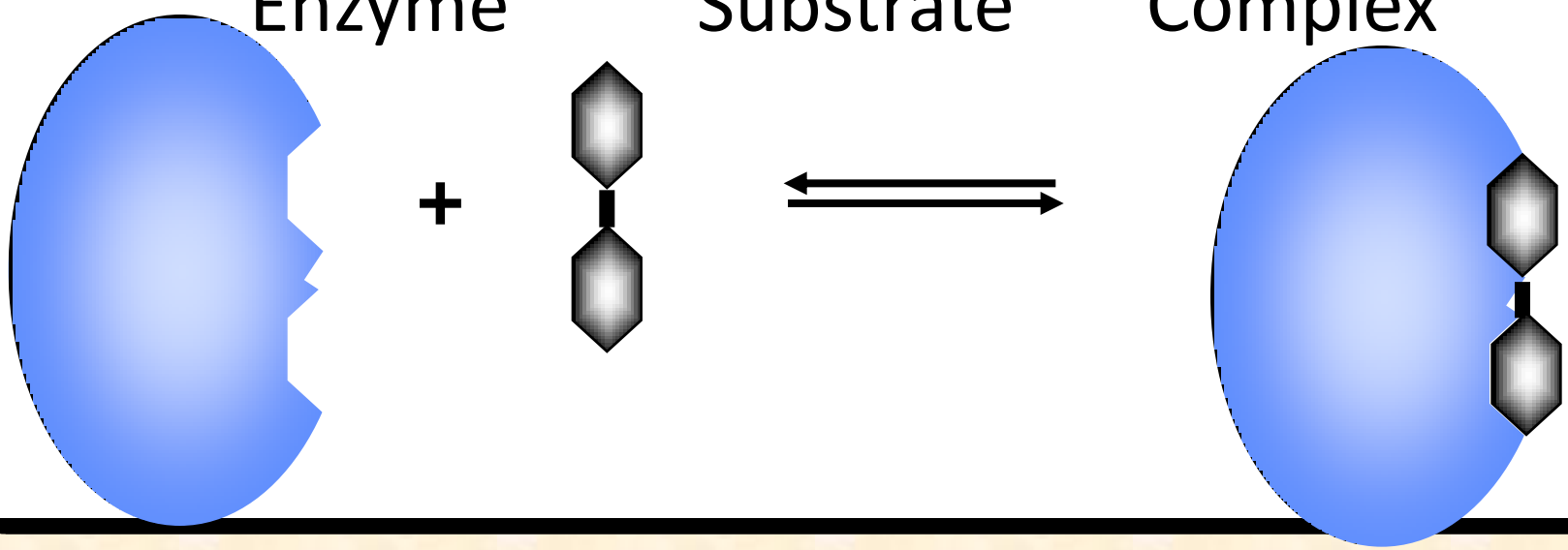
Induced Fit Model

- In the **induced-fit model** of enzyme action:
  - the active site is flexible, not rigid
  - the shapes of the enzyme, active site, and substrate adjust to maximumize the fit, which improves catalysis
  - there is a greater range of substrate specificity
- This model is more consistent with a wider range of enzymes



Enzyme-substrate complex

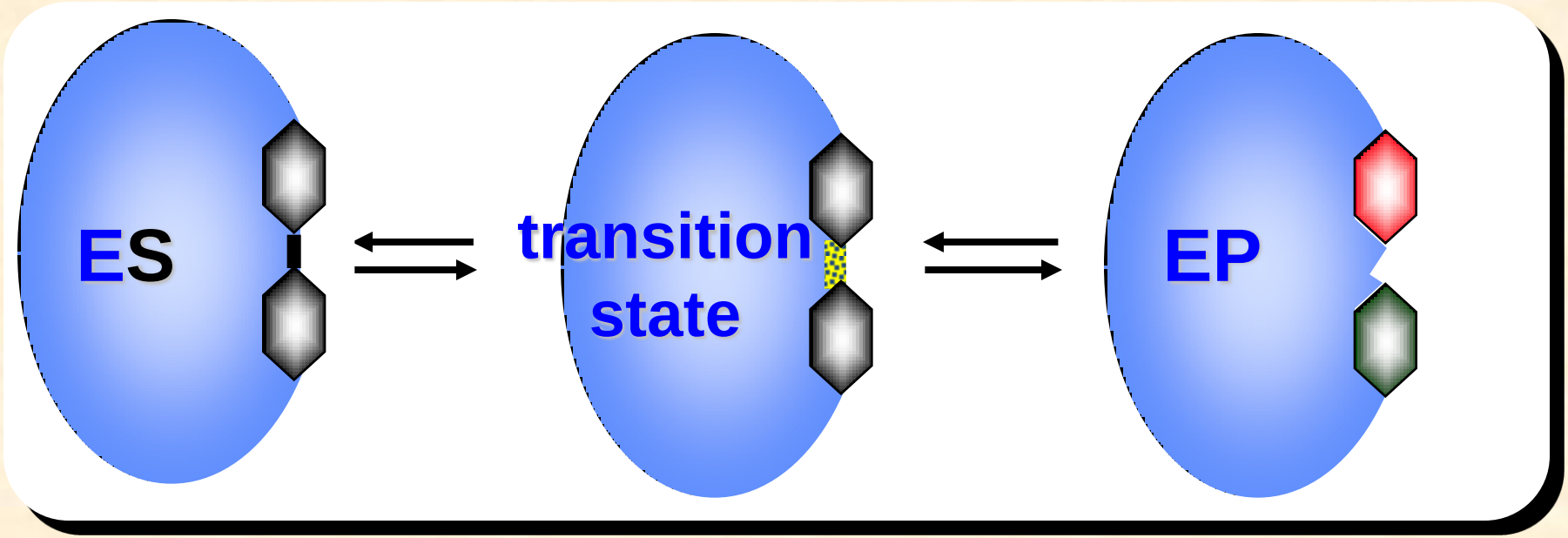
- Step 1:
- Enzyme and substrate combine to form complex
- E + S ⇌ ES
- Enzyme Substrate Complex



Enzyme-product complex

- Step 2:
- An enzyme-product complex is formed.

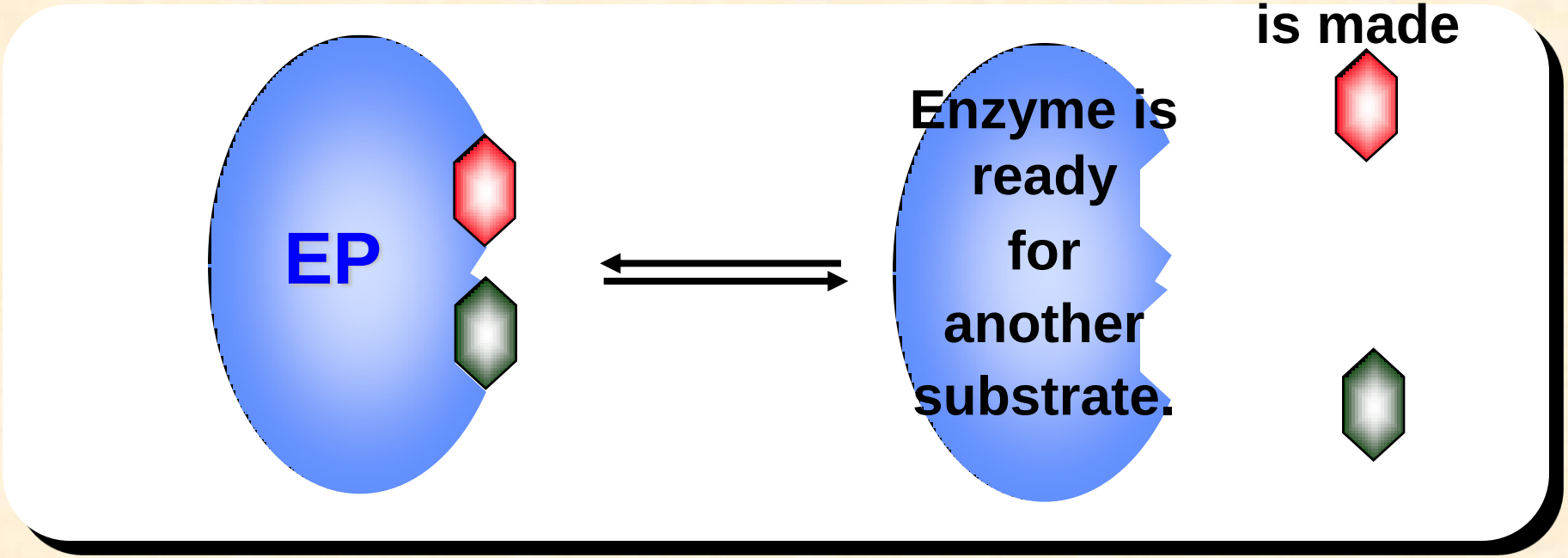
- ES ⇌ EP



Product

- The enzyme and product separate

- EP ⇌ E + P



What Affects Enzyme Activity?

- **Three factors:**
  1. **Environmental Conditions**
  2. **Cofactors and Coenzymes**
  3. **Enzyme Inhibitors**

1. Environmental Conditions

1. Extreme Temperature are the most dangerous

- high temps may denature (unfold) the enzyme.

2. pH (most like 6 - 8 pH near neutral)

3. substrate concentration .

2. Cofactors and Coenzymes

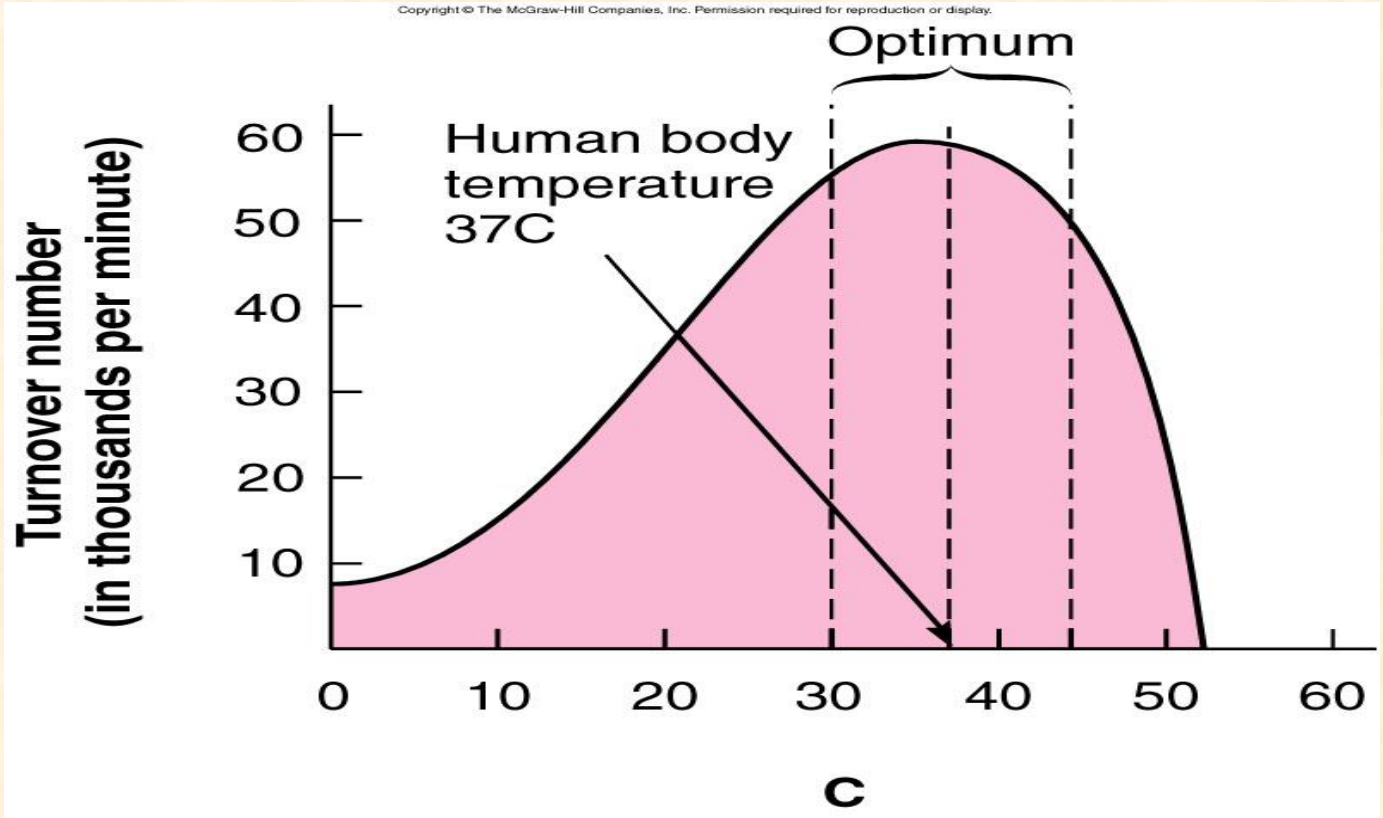
- **Inorganic substances (zinc, iron) and vitamins (respectively) are sometimes need for proper enzymatic activity.**

- **Example:**

  Iron must be present in the quaternary structure - hemoglobin in order for it to pick up oxygen.

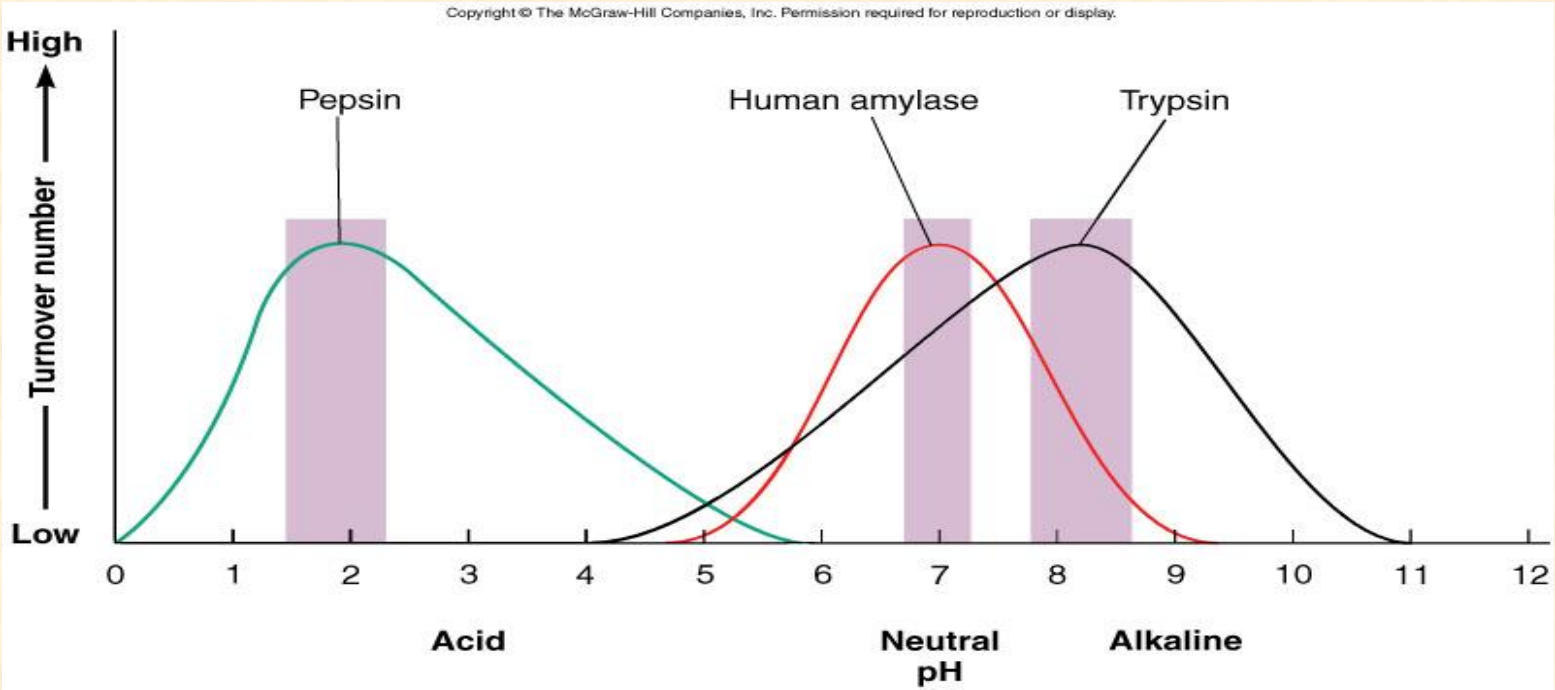
Environmental factors

- ***Optimum temperature*** The temp at which enzymatic reaction occur fastest.



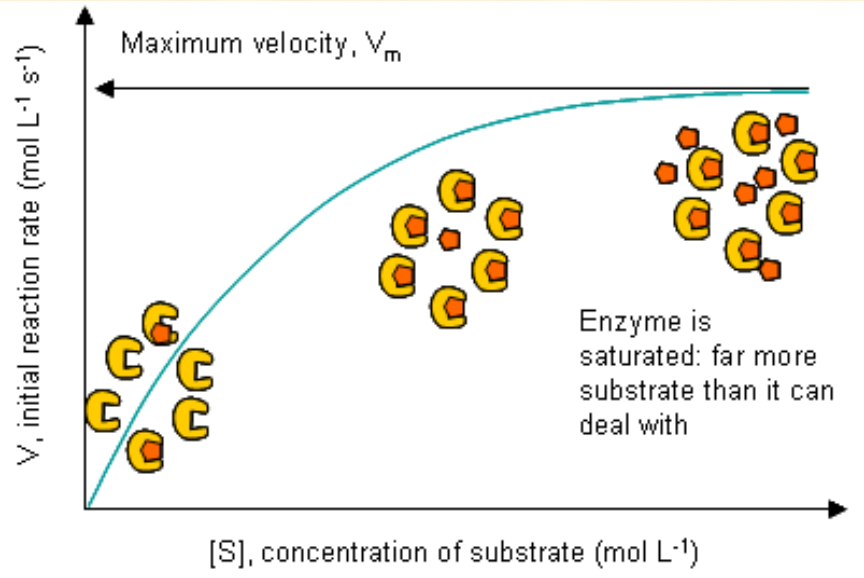
Environmental factors

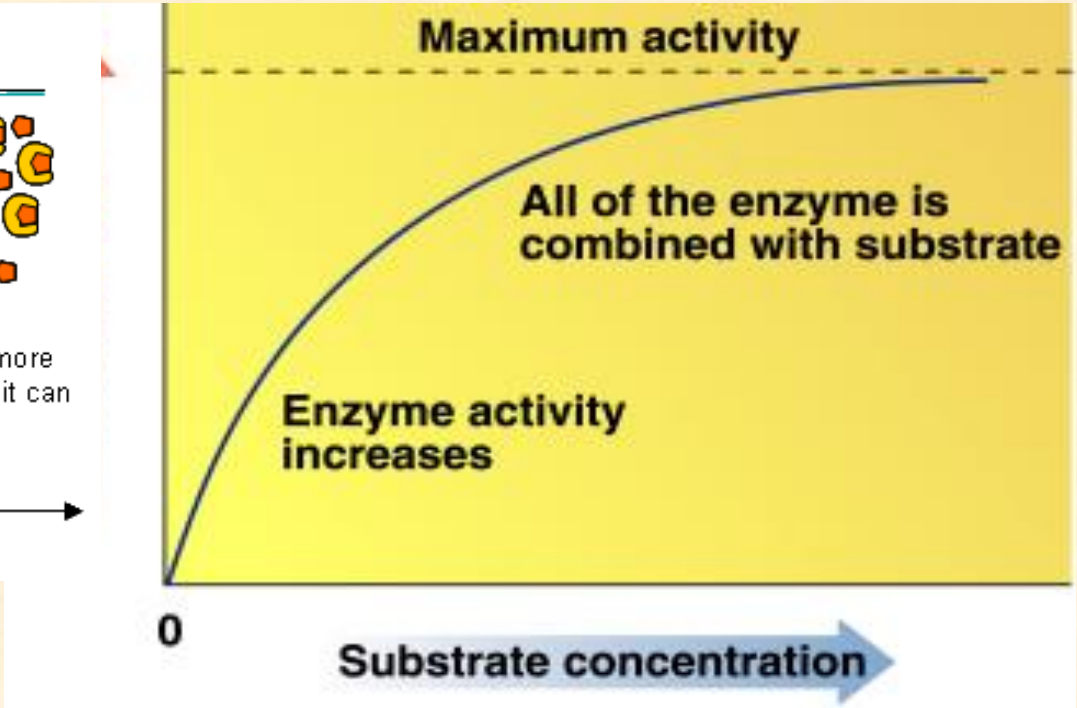
- pH also affects the rate of enzyme-substrate complexes
  - Most enzymes have an optimum pH of around 7 (neutral)
    - However, some prefer acidic or basic conditions



Substrate Concentration and Reaction Rate

- **The rate of reaction increases as substrate concentration increases (at constant enzyme concentration)**
- **Maximum activity occurs when the enzyme is saturated (when all enzymes are binding substrate)**





Enzyme Inhibition

Any substance that can diminish the velocity of an enzyme-catalyzed reaction is called an inhibitor and the process is known as inhibition. There are two major types of enzyme inhibition, Irreversible and Reversible.

1- Irreversible Inhibition

The type of inhibition that can not be reversed by increasing substrate concentration or removing the remaining free inhibitor is called Irreversible inhibition. Example: Acetyl cholinesterase catalyzes the hydrolysis of Acetylcholin (to acetic acid and choline) a neurotransmitter substance functioning in certain portions of the nervous system

2-REVERSIBLE INHIBITION

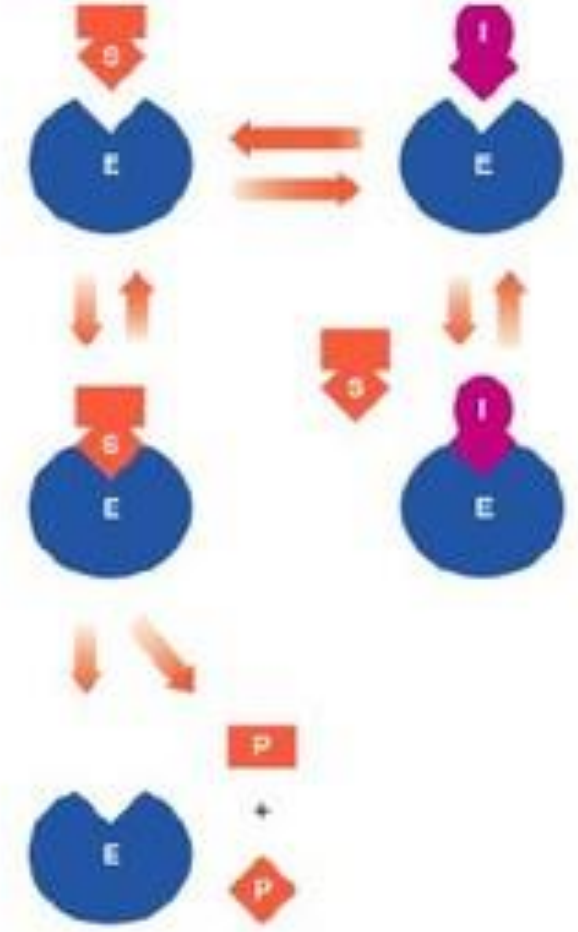
This type of inhibition can be Competitive, Non-competitive and uncompetitive Competitive Inhibition: This type of inhibition occurs when the inhibitor binds reversibly to the same site that the substrate would normally occupy, therefore, competes with the substrate for that site.

In competitive inhibition the inhibitor and substrate compete for the same active site on the enzyme as a result of similarity in structure. The enzyme substrate complex will be broken dawn to products (E+S → ES → E+P) where as enzyme inhibitor complex; (EI) will not be broken down to products.

Reversible Competitive Inhibition

A **competitive inhibitor**:

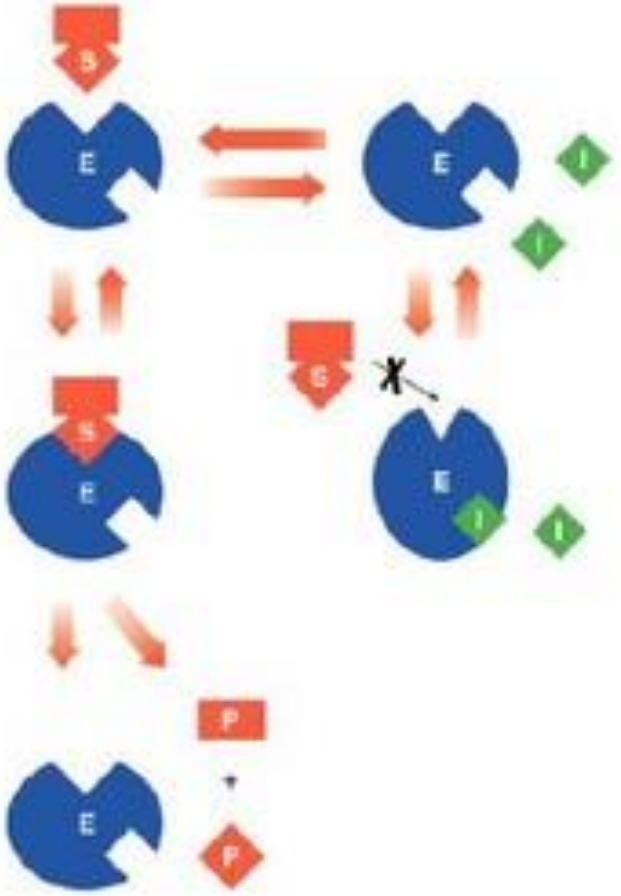
- Has a structure like the substrate.
- Competes with the substrate for the active site.
- Has its effect reversed by increasing substrate concentration.



Noncompetitive Inhibition

A **noncompetitive inhibitor**:

- Has a structure different than the substrate.
- Distorts the shape of the enzyme, which alters the shape of the active site.
- Prevents the binding of the substrate.
- Cannot have its effect reversed by adding more substrate.



Naming Enzymes

- **The name of an enzyme in many cases end in *–ase***
- **For example, *sucrase* catalyzes the hydrolysis of sucrose**

- **The name describes the function of the enzyme**
  For example, *oxidases* catalyze oxidation reactions

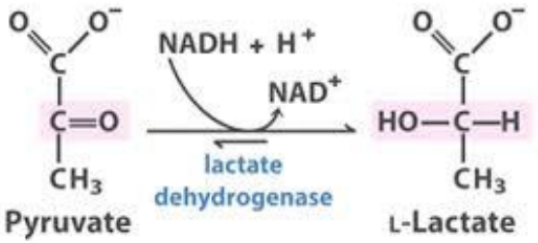
- **Sometimes common names are used, particularly for the digestion enzymes such as *pepsin* and *trypsin***

- **Some names describe both the substrate and the function**
- **For example, *alcohol dehydrogenase* oxides ethanol**

Enzymes Are Classified into six functional Classes (EC number Classification) by the International Union of Biochemists (I.U.B.). on the Basis of the Types of Reactions That They Catalyze

- **EC 1. Oxidoreductases**
- **EC 2. Transferases**
- **EC 3. Hydrolases**
- **EC 4. Lyases**
- **EC 5. Isomerases**
- **EC 6. Ligases**

1. Oxidoreductases: one compound oxidized, another reduced. Ex: lactate dehydrogenase, tyrosinase,

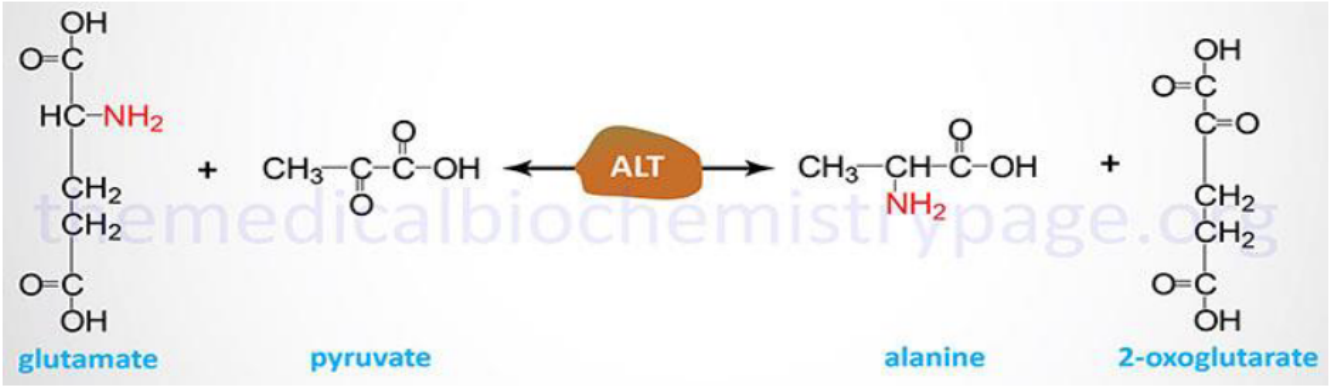


$\Delta G'^{\circ} = -25.1$ kJ/mol

2. Transferase:

Enzyme transfer group containing C, N or S, from one substrate to another substrate.

Ex: **Transaminase** (glutamate oxaloacetate transaminase(**GOT**) or Aspartate transaminase (**AST**). and glutamate pyruvate transaminase(**GPT**), alanine transaminase(**ALT**)
(transfer of amine group)

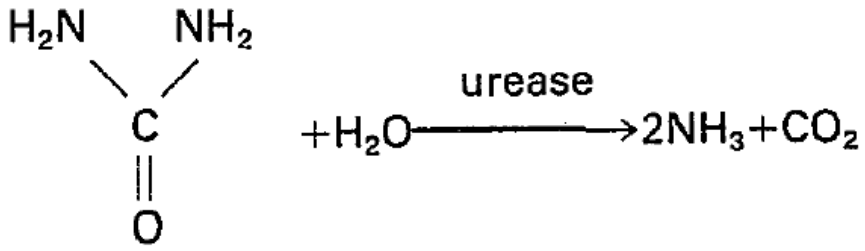


3. Hydrolyase:

Catalyse hydrolysis of ester, peptide or glycoside bound by addition of H2O across the bond.

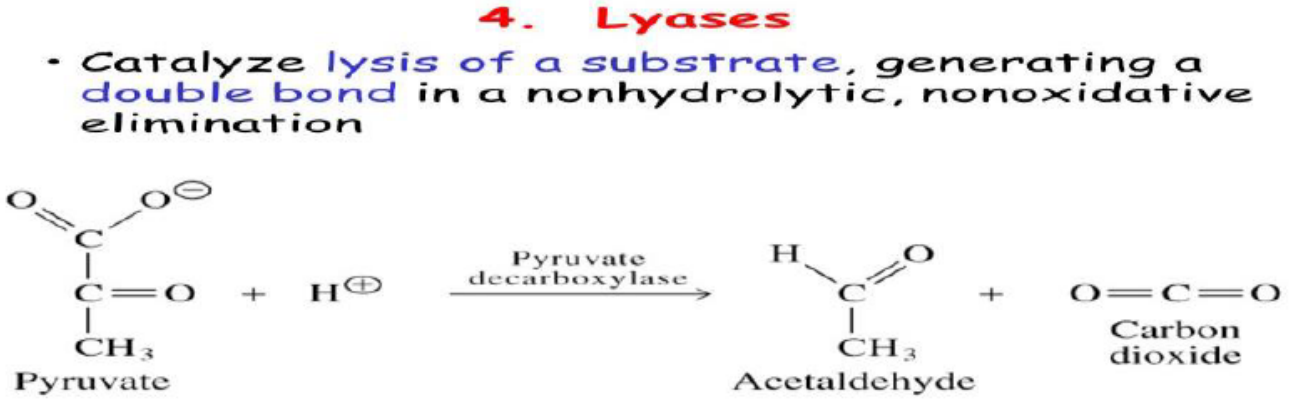
Urea + H2O —urease→ 2NH3 + CO2

Maltose + H2O —maltase→ glucose + glucose



4. Lyasis:

Additional or removal of group without hydrolysis, oxidation, reduction producing double Bond.



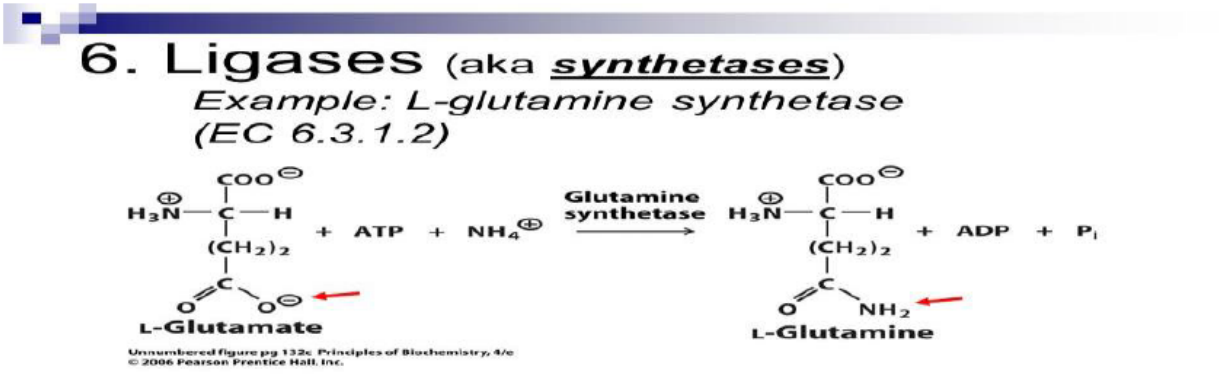
5. Isomerase:

Produce optical, geometric or position isomer of substrates by intermolecular rearrangement.

Ex: D- alanine —racemase→ **L – alanine**

6. Ligases or synthetase:

link two substrate together usually by pyrophosphate bound.



Principle of the international classification

Each enzyme has **classification number**

consisting of four digits:

Example, **EC:** (**2.7.1.1**) **HEXOKINASE**

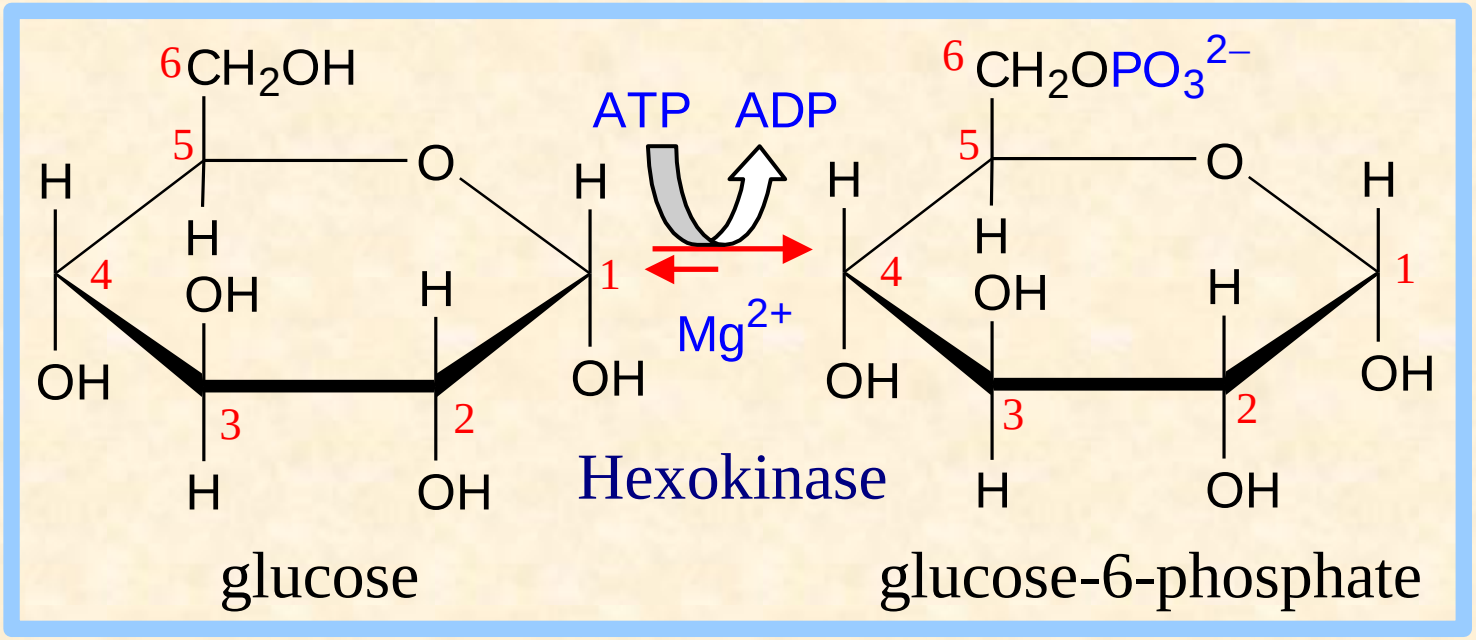
- **EC: (2.7.1.1) these components indicate the following groups of enzymes:**

- **2. IS CLASS (TRANSFERASE)**

- **7. IS SUBCLASS (TRANSFER OF PHOSPHATE)**

- **1. IS SUB-SUB CLASS (ALCOHOL IS PHOSPHATE ACCEPTOR)**
- **1. SPECIFIC NAME**

  ATP,D-HEXOSE-6-PHOSPHOTRANSFERASE (Hexokinase)



1. Hexokinase catalyzes:

Glucose + ATP → glucose-6-P + ADP

ENZYMES IN CLINICAL DIAGNOSIS:

Plasma enzymes can be classified into two major groups

1. Those relatively, small group of enzymes secreted into the plasma by certain organs (i.e. Enzymes those have function in plasma) For example: - the liver secretes zymogens of the enzymes involved in blood coagulation.

2. Those large enzyme species released from cells during normal cell turnover. These enzymes are normally intracellular and have no physiologic function in the plasma. In healthy individuals the levels of these enzymes are fairly constant and represent steady state in which the rate of release from cells into the plasma is balanced by an equal rate or removal from the plasma.

Many diseases that cause tissue damage result in an increased release of intracellular enzymes into the plasma. The activities of many of these enzymes are routinely determined for diagnostic purposes in diseases of the heart, liver, skeletal muscle, and other tissues.

The level of specific enzyme activity in the plasma frequently correlates with the extent of tissue damage. Thus, the degree of elevation of a particular enzyme activity in plasma is often useful in evaluating the diagnosis and prognosis for the patient.

Measurement of enzymes concentration of mostly the latter type in plasma gives valuable informatio0n about disease involving tissues of their origin.

1. Lipase:

It is an enzyme catalyzing the hydrolysis of fats. It is secreted by pancreas and Liver. The plasma lipase level may be low in liver disease, Vitamin A deficiency, some malignancies, and diabetes mellitus. It may be elevated in acute pancreatitis and pancreatic carcinoma.

2. α- Amylase

α- amylase is the enzyme concerned with the break down of dietary starch and glycogen to maltose. It is present in pancreatic juice and saliva as well as in liver, fallopian tubes and muscles. The enzyme is excreted in the Urine. The main use of amylase estimations is in the diagnosis of acute pancreatitis. The plasma amylase level may be low in liver disease and increased in high intestinal obstruction, mumps, acute pancreatitis and diabetes.

3. Trypsin: Trypsin is secreted by pancreas. Elevated levels of trypsin in plasma occur during acute pancreatic disease.

4. Alkaline phosphates (ALP)

The alkaline phosphates are a group of enzymes, which hydrolyze phosphate esters at an alkaline pH. They are found in bone, liver, kidney, intestinal wall, lactating mammary gland and placenta. In bone the enzyme is found in osteoblasts and is probably important for normal bone function. The level of these enzymes may be increased in rickets and osteomalacia, hyperparathyroidism, obstructive jaundice, and metastatic carcinoma. Serum alkaline phosphatase levels may be increase in congestive heart failure result of injury to the liver.

5. Acid Phosphatase (ACP)

Acid phosphatases catalyzing the hydrolysis of various phosphate esters at acidic pH is found in the prostate, liver, red cells, platelets and bone. It may be elevated in metastatic prostatic carcinoma.

6. Transaminases:

Two transaminases are of clinical interest.

A- Aspartate Transaminase, AST or (Glutamate oxaloacetate transaminase, GOT):

catalyzes the transfer of the amino group of aspartic acid to α- ketoglutarate forming glutamate and oxaloacetate.

AST or GOT is widely distributed, with high concentration, in the heart, liver, skeletal muscle, kidney and erythrocytes, and damage to any of these tissues may cause raised levels.

B. Alanine transaminase, ALT (Glutamate pyruvate transaminase, GPT):

Transfer the amino group of alanine to α- ketoglutarate, forming glutamate and pyruvate. It is present in high concentration in liver and to a lesser extent in skeletal muscle, kidney and heart.

- Serum levels of glutamate- pyruvate transaminase (SGOT) and Glutamateoxaloacetate- transaminase (SGOT) are useful in the diagnosis of liver parenchymal damage and myocardial damage respectively. In liver damage, both enzymes are increased, but SGPT increases more. In myocardial infarction SGOT is increased

7. Lactate Dehydrogenase (LDH)

It catalyzes the reversible interconversion of lactate and pyruvate. It is widely distributed with high concentrations in the heart, skeletal muscle, liver, kidney, brain and erythrocytes. The enzyme is increased in plasma in myocardial infarction, acute leukemias, generalized carcinomatosis and in acute hepatitis. Estimation of it isoenzymes is more useful in clinical diagnosis to differentiate hepatic disease and myocardial infarction.

8. Creatine kinase (CK) or creatine phosphokinase (CPK):

CK (CPK) is found in heart muscle, brain and skeletal muscle. Measurement of serum creatine phosphokinase activity is of value in the diagnosis of disorders affecting skeletal and cardiac muscle. The level of CPK in plasma highly increased in myocardial infarction.