كيمياء حياتية سريرية

قسم تقنيات العلاج الطبيعي

المرحلى الاولى

اعداد

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Clinical Biochemistry
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First stage
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Biochemistry can be defined as the science concerned with the chemical basis of life. The **cell** is the basic structural and functional unit of all known living organisms. It is the smallest unit of life that is classified as a living thing. There are two types of cells: **eukaryotic** and **prokaryotic**. Organisms can be classified as **unicellular** (consisting of a single cell; including most bacteria) or **multicellular** (including plants and animals). Thus, biochemistry can also be described as the science concerned with the chemical constituents of living cells and with the reactions and processes they undergo. By this definition, biochemistry encompasses large areas of **cell biology, molecular biology,** and **molecular genetics.**

The maintenance of health is that there be optimal dietary intake of a number of chemicals; the chief of these are **vitamins, amino acids, fatty acids,** various **minerals,** and **water.** Because much of the subject matter of both biochemistry and nutrition is concerned with the study of various aspects of these chemicals, there is a close relationship between these two sciences.

We believe that most if not all diseases are the result of abnormalities of molecules, **chemical reactions**, or **biochemical processes**. The major factors responsible for causing diseases in animals and humans are:-

1. Physical agents: Extremes of temperature, sudden changes in atmospheric pressure, radiation, electric shock.

2. Chemical agents, including drugs: Certain toxic compounds, etc.

3. Biologic agents: Viruses, bacteria, fungi, higher forms of parasites.

4. Oxygen lack: Loss of blood supply, depletion of the oxygen-carrying capacity of the blood, poisoning of the oxidative enzymes.

5. Genetic disorders: Congenital, molecular.

6**. Immunologic reactions:** Autoimmune disease.

7. Nutritional imbalances: Deficiencies, excesses.

8. Endocrine imbalances: Hormonal deficiencies, excesses.

All of them affect one or more chemical reactions or molecules in the body.

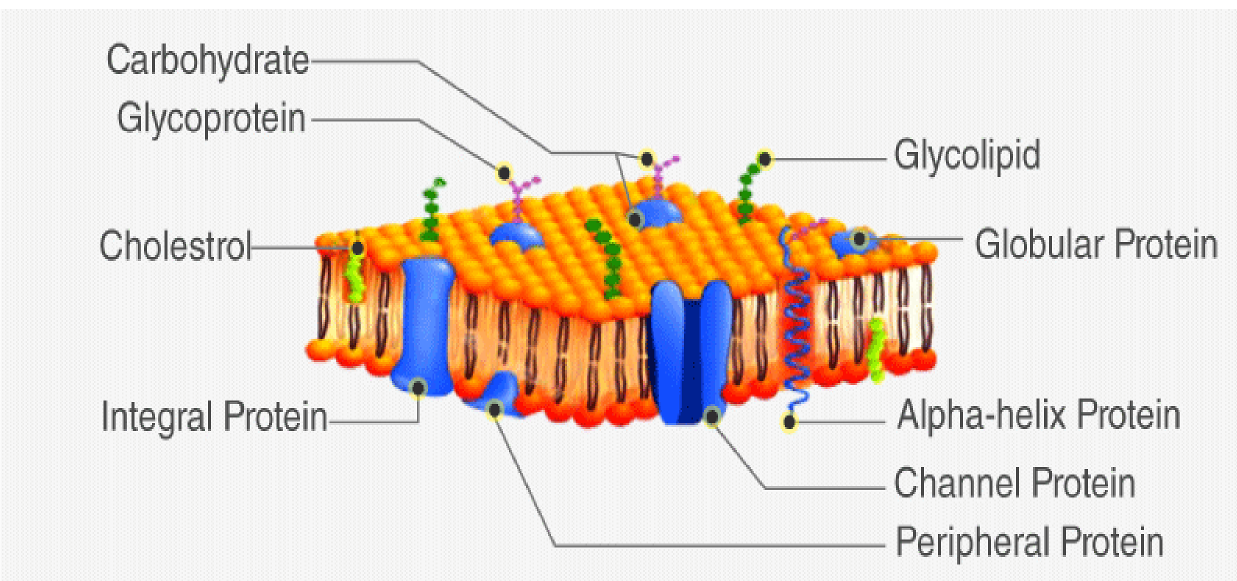
Cell Structure & Function

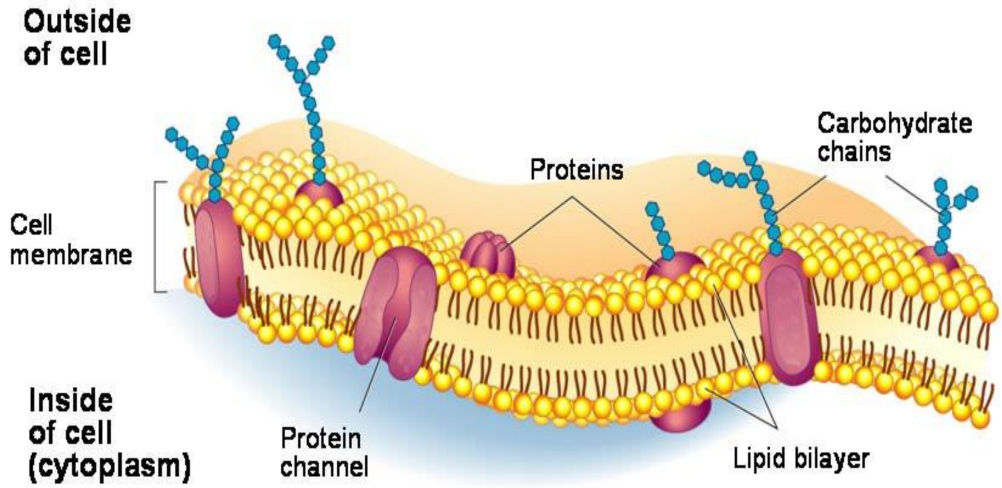
The smallest organisms consist of single cells and are microscopic. Larger, multicellular organisms contain many different types of cells, which vary in size, shape, and specialized function. All cells of the simplest and most complex organisms share certain fundamental properties, which can be seen at the biochemical level.

Major Cell organelles are as follows:-

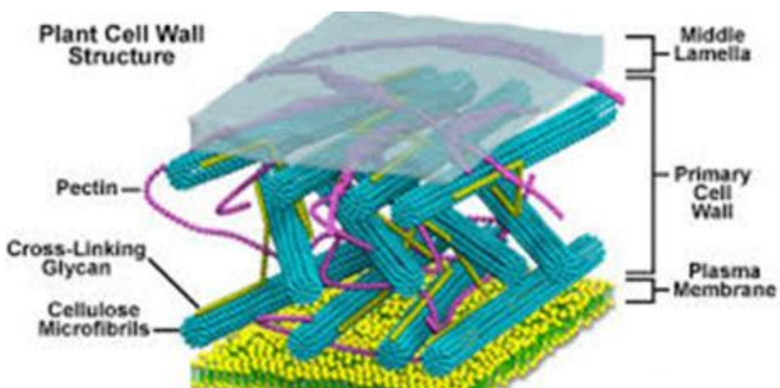
1. Cell Membrane- The cell membrane encloses the cell and regulates the in and outflow of substances. It is also known as the plasma membrane which forms the covering of animal cells. It is an elastic, living, double-layer, and permeable membrane. It is made up of protein and lipid molecules.

Function regulated movement of molecules inside and outside the cell.





2. Cell Wall – The outer layer in the plant cell is called cell wall. The cell wall lies outside the plasma membrane. The plant cell wall is mainly composed of cellulose and pectin. Cellulose is a complex substance and provides structural strength to plant.

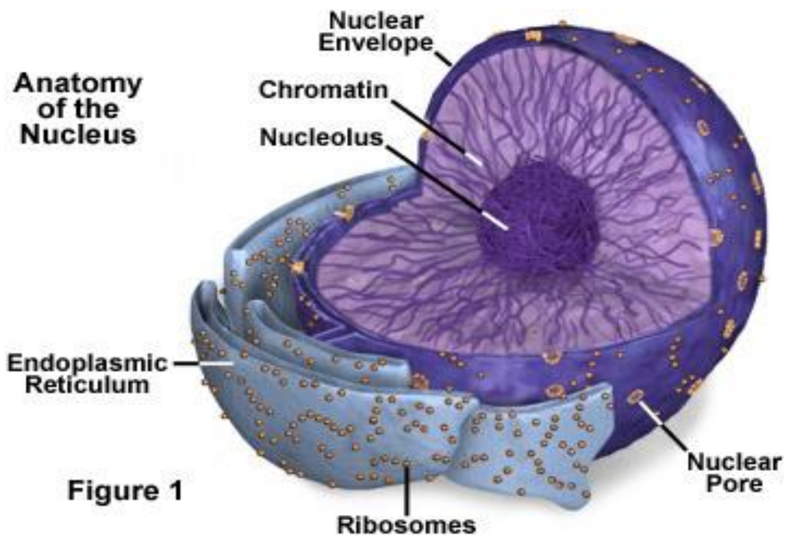


3. Protoplasm –The whole fluid present inside the plasma membrane is protoplasm. Protoplasm is made up of various chemical substances like water, ions, salt, and organic molecules. Protoplasm is divided into two parts:-

a) Cytoplasm – The fluid found outside the nuclear membrane.
b) Nucleoplasm – The fluid found inside the nuclear membrane.

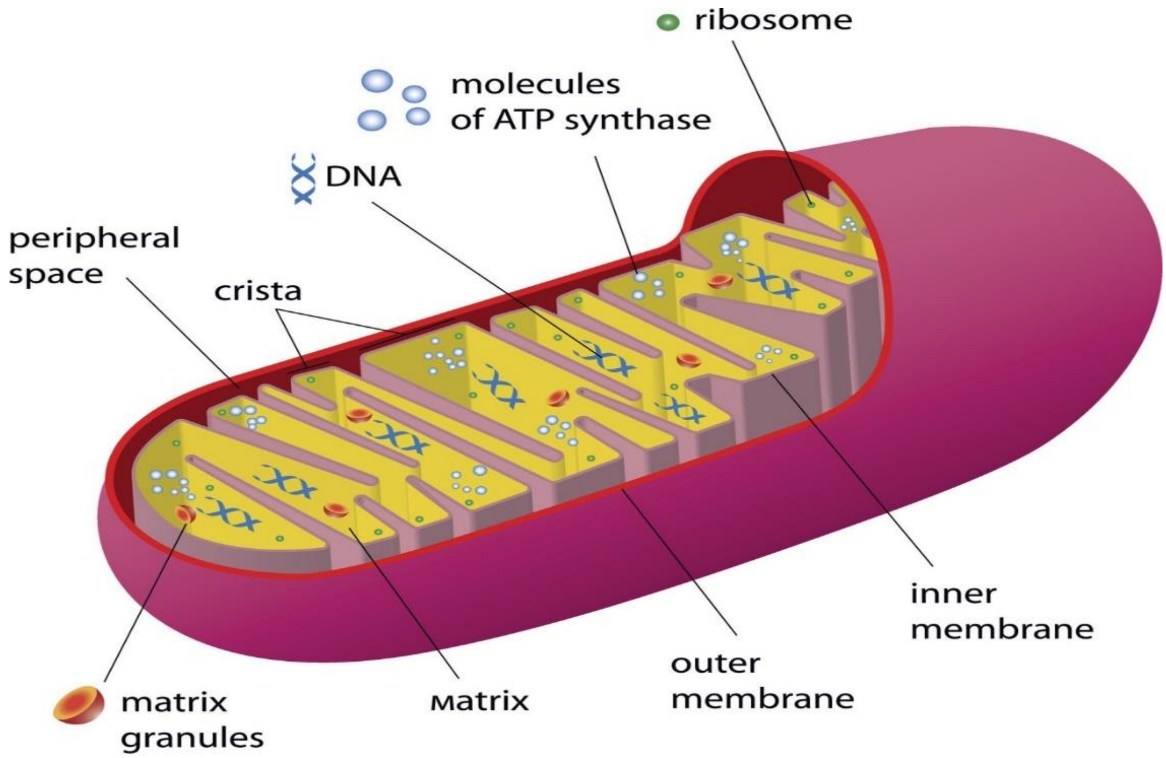
4. Nucleus- It is the most important organelle of a cell and usually lies in the center. Its basic function is cell division and multiplication. The nucleus has a double-layered covering called a nuclear membrane. The nucleus contains chromosomes Chromosomes contain information for the inheritance of parents to the next generation in the form of DNA (Deoxyribonucleic Acid) molecules.

Function- It controls all activity of cells. It is also known as the "control room "of the cell. Chromatin transmits hereditary characters from a parent to their offspring.



5. Mitochondria–These are cylinder rod-shaped or spherical structures found in the cytoplasm. It is surrounded by a double double-layered membrane. The inner membrane has many folds. The area present inside mitochondria is called the matrix, which contain many enzyme and co-enzymes.

Function- Mitochondria is the respiratory site of cellular respiration. Mitochondria synthesize energy-rich compound ATP (Adenosine Triphosphate). Mitochondria are known as the Powerhouse of the cell.



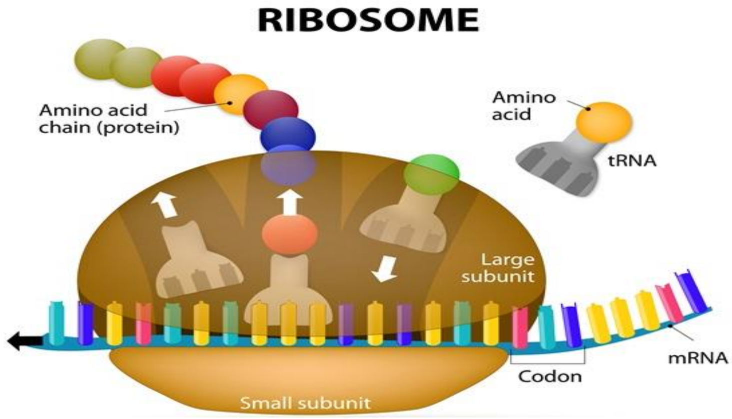
Mitochondrion

6. Ribosome- Small granules-like structure found attached to the endoplasmic reticulum or in Free State. It is made up of ribonucleic acid (RNA).

Function- Ribosome helps in protein Synthesis.

7. Lysosomes – Single membrane and contain hydrolytic enzyme.

Function- Digestive the proteins, fats, and carbohydrates.
- Transports undigested material to cell membrane for removal.
- Cell breaks down if lysosome explodes.



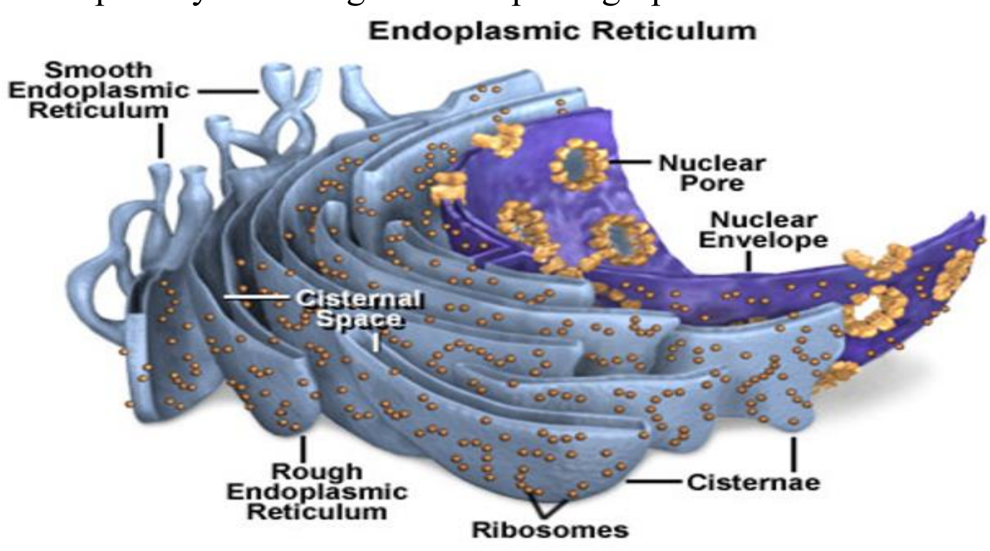
8. Endoplasmic Reticulum (ER)- Large network of tubules found in the cytoplasm.it is attached to the nucleus on one side and on the other side it is joined with the plasma membrane. There are two types of ER:-

a) Rough Endoplasmic reticulum (RER)- looks rough under a microscope because it has particles called ribosomes attached to its surface.

Function- RER is concerned with protein synthesis and transport.

b) Smooth Endoplasmic reticulum (SER) – looks smooth under a microscope because it has free ribosome particles on its surface.

Function- Helps in synthesizing and transporting lipids and steroids.

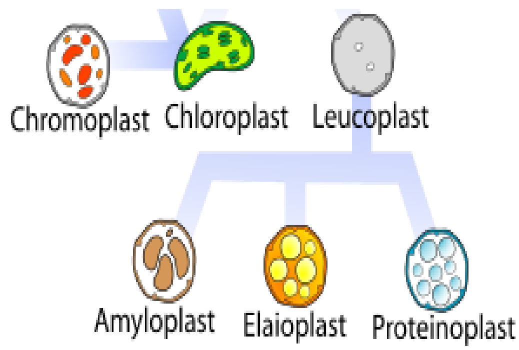


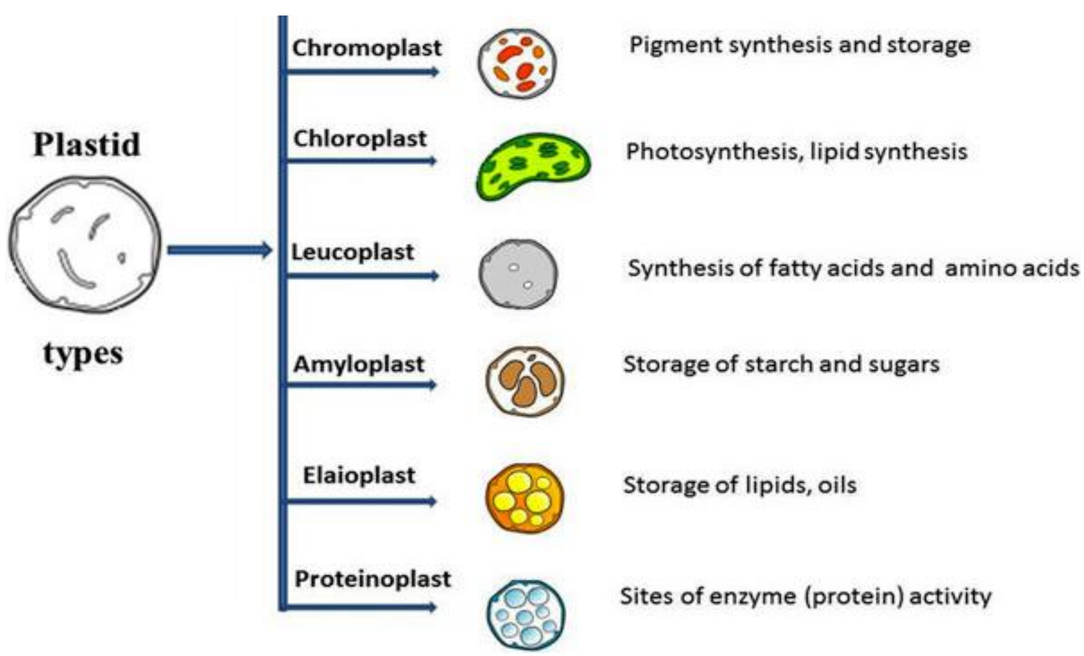
9. Plastids- Plastids are present only in plant cells. There are three types of plastids:-

a) Chromoplast (colored plastids) –It provides various colors to the plant.

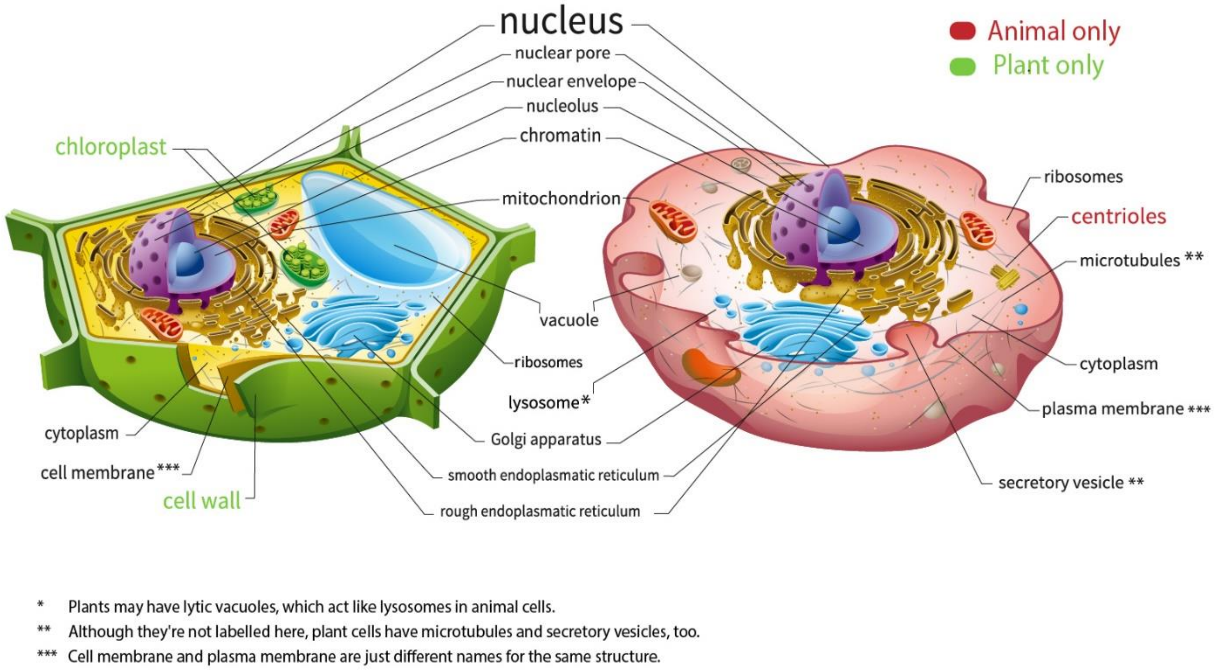
b) Chloroplasts– Plastids containing the pigment chlorophyll are known as chloroplast. Chloroplasts are important for photosynthesis in plants.

c) Leucoplast (white or colorless plastids) – Leucoplasts are primarily organelles. It stores the food in the form of starch, fat, and protein.





10. Vacuoles- Vacuoles are storage sacs for solid or liquid contents vacuoles are small-sized in animal cells while plant cells have very large vacuoles.
Many substances of importance in the life of the plant cell are stored in vacuoles. These include amino acids and some proteins.



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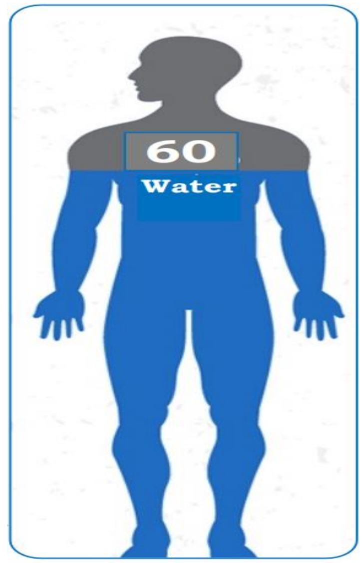
Lecture.2 Body Fluids

The human body is primarily composed of water. In males, **about 60%** of body weight is water (and in females, it is **about 55%**). The percentage of body water varies inversely with the body's fat content and age.

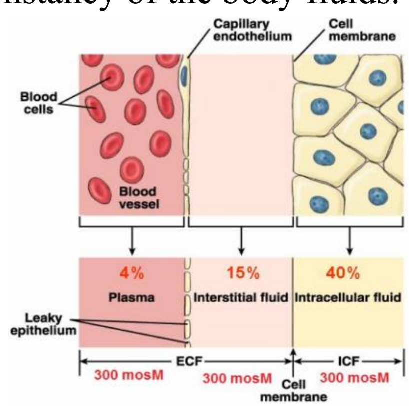


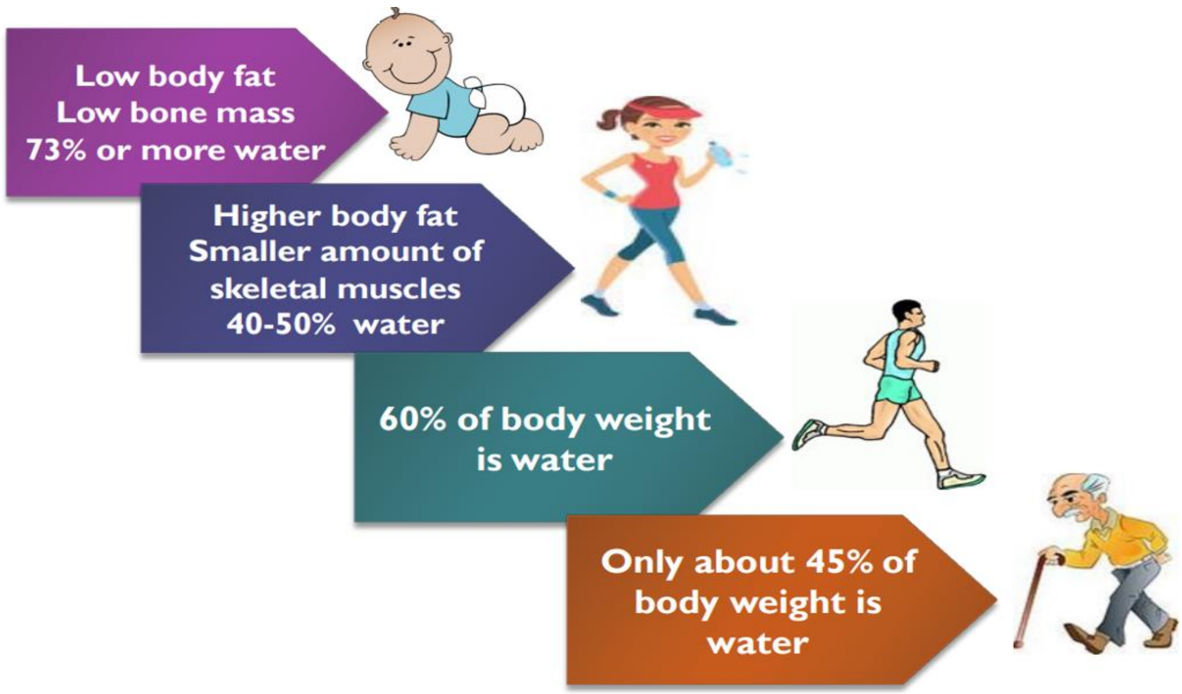
The **Total Body Water (TBW)** in males is larger than in females because the latter has a somewhat larger amount of subcutaneous fat. In both sexes, the percentage of body water decreases with age, which can be attributed primarily to an increase in adipose tissue.

Adipose tissue is low in water content; thus, obese individuals have less body water than normal-weight individuals.

The body water is distributed into two major fluid compartments, **Extracellular fluid** (ECF), which contains approximately **20%** of TBW, and **Intracellular fluid** (ICF), which contains approximately **40%** of the TBW.

The maintenance of a relatively constant volume and a stable composition of the body fluids is essential for homeostasis. Some of the most common and important problems in clinical medicine arise because of abnormalities in the control systems that maintain this relative constancy of the body fluids.





Body fluids = water + dissolved solutes.

Solutes = **Electrolytes** (Na^+, K^+, Cl^-, $HCO3^-$, Mg^{+2}, Ca^{+2}…)
Non-electrolytes (Glucose, Urea, Creatinine...)

Normal Daily Fluid Input and Output

Inputs	Outputs
Ingestion	Gut (Faeces 100ml)
Fluid (1.25 Liters)	Urine (1.5 Liters)
Food (1 Liter)	Breathing/Skin (900ml)
Metabolism (350 ml)	Sweating (100ml)
Total (2.6 Liters)	Total (2.6 Liters)

***Factors Affecting (TBW)**

Physiological:

-Age

-Sex

-Body Fat

Pathological:

-Vomiting

-Diarrhea

-Diseases With Excessive loss of water (DM = Diabetes Mellitus, excessive Sweating)

-Blood loss

-Burns

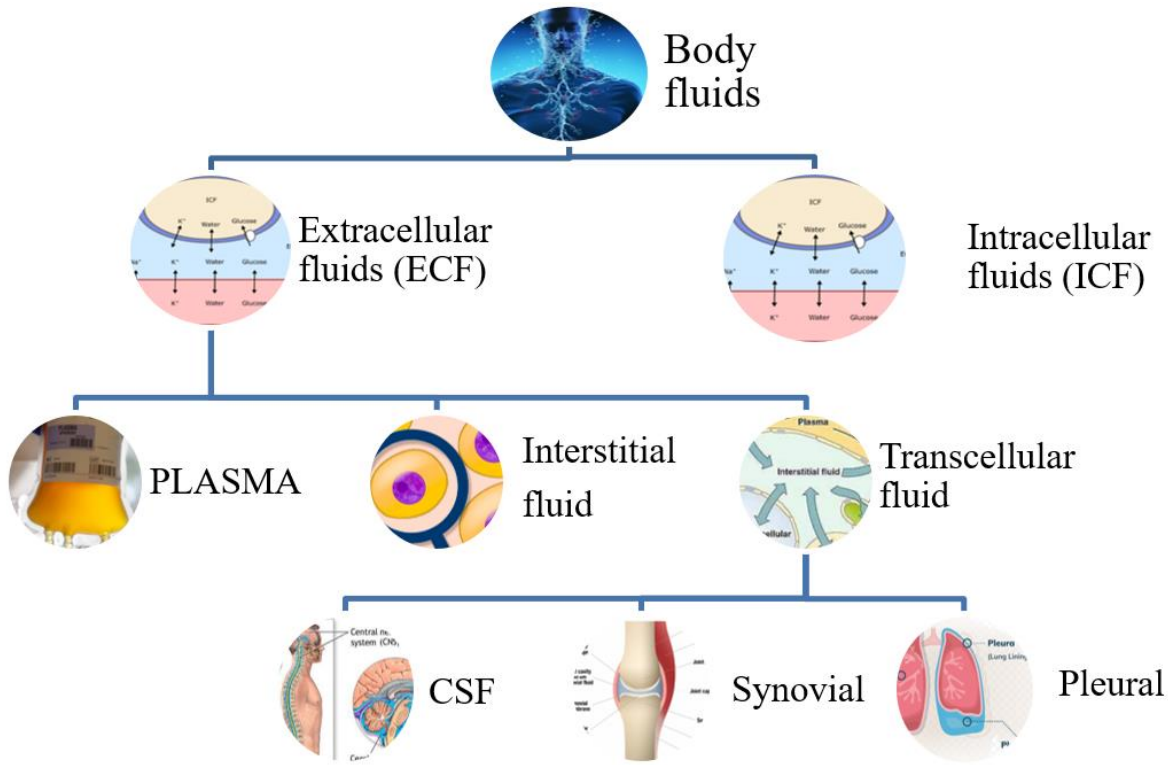
Other:

-Climate

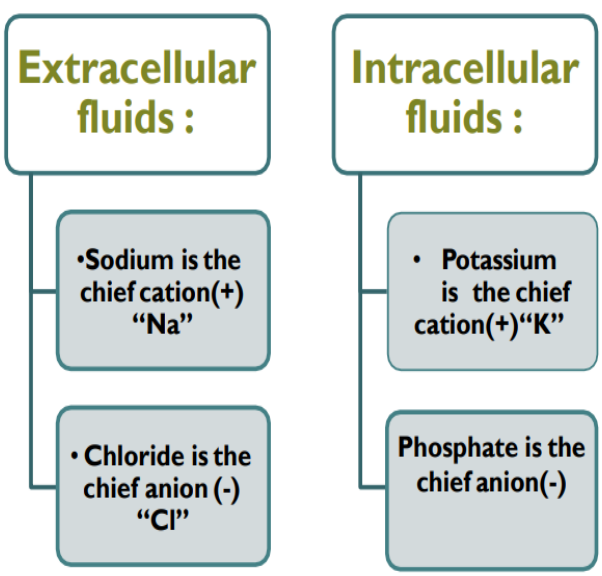
-Habits

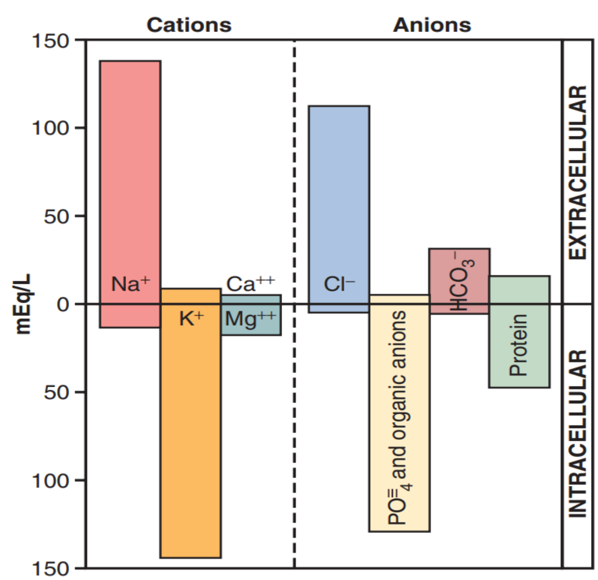
-Physical Activity

FLUID COMPARTMENTS



*The different compartments between electrolytes extracellular and intracellular.

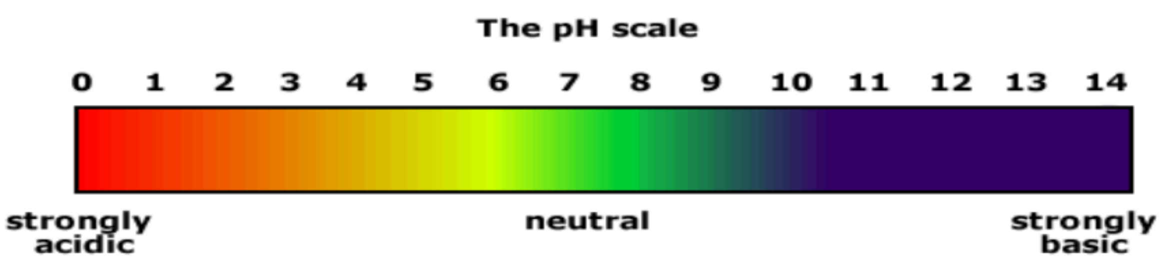




pH is a unit of measure that describes the degree of acidity or basicity of a solution.

The pH scale

- The scale ranges from 1 to 14.
- The pH of water is 7.0 which is neutral.
- The normal range of the human body fluids is 7.35 - 7.45.



pH Value

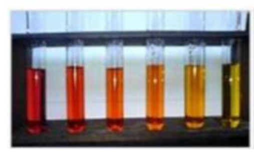
- The pH value of a substance is directly related to the ratio of the hydrogen ion and hydroxyl ion concentrations.
- If the H+ concentration is higher than OH- the material is **acidic.**
- If the OH- concentration is higher than H+ the material is **basic.**
- High H+ ion concentration = **low pH.**
- Low H+ ion concentration = **high pH.**

Measurement of pH

The pH can be measured by:

1. pH strips

2. pH indicators



3. pH meter

Body Buffer

Buffer solutions are extremely important in biology and medicine because most biological reactions and enzymes need very specific pH ranges in order to work properly.

Type of Buffers

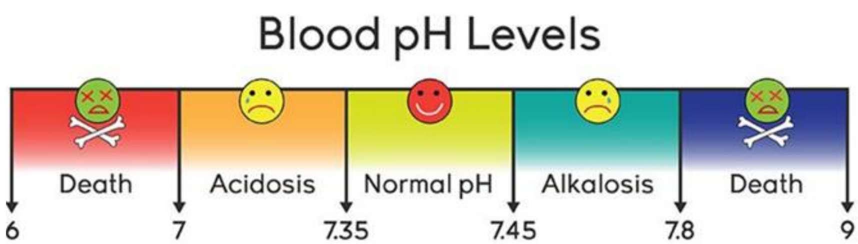
- Acidic buffers: Solution of a mixture of a weak acid and a salt of this weak acid with a strong base.
  e.g. $CH_3COOH + CH_3COONa$
  (weak acid) (Salt)

- Basic buffers: Solution of a mixture of a weak base and a salt of this weak base with a strong acid.
  e.g. NH_4OH + NH_4Cl
  (Weak base) (Salt)

A **buffer** is a solution that can resist pH change upon the addition of acidic or basic components. It is able to neutralize small amounts of added acid or base, thus maintaining the pH of the solution relatively stable.

This is important for processes and/or reactions that require specific and stable pH ranges. Buffer solutions have a working pH range and capacity which dictate how much acid/base can be neutralized before pH changes, and the amount by which it will change.

Blood contains buffers that maintain a consistent pH of about 7.4 If the pH of the blood goes slightly above or below 7.4, changes in oxygen levels and metabolic processes can be drastic enough to cause death



Alkalosis or alkalemia: arterial blood pH rises above 7.45.

Acidosis or acidemia: arterial pH drops below 7.35.

Alteration outside these boundaries affects all body systems Can result in coma, cardiac failure, and circulatory failure.

The body constantly produces acids through metabolism

These acids must be constantly eliminated from the body. Three systems perform this task

1. Buffer system
2. Respiratory system
3. Renal system

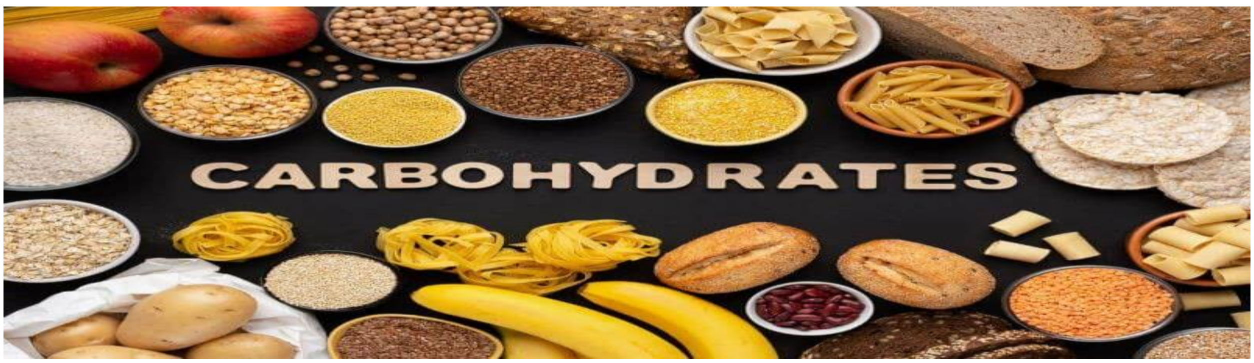
***Clinical Abnormalities of Body Fluid**

Edema

Edema is an abnormal accumulation of fluid in the interstitium or in one or more cavities of the body. It is clinically shown as swelling. Edema may be due to increased pressure differences (e.g. hypertension and pregnancy, hypoalbuminemia, liver cirrhosis, and inflammation). It may be caused by increased blood vessel wall permeability (e.g. in inflammation and allergy). Another cause of edema is the obstruction of the lymphatic system (e.g. tumors or surgical removal of lymph nodes).

Lecture.3 Carbohydrates

Carbohydrates are a class of naturally occurring organic compounds of carbon, hydrogen, and oxygen which are primarily produced by plants. the chemical formula is (Cn(H2O)n. Carbohydrates are also called saccharides (Greek: saccharo means sugar). the simple sugar glucose is an essential constituent of blood and occurs in a polymeric form as glycogen in the liver and muscle.



Importance of carbohydrates

- Carbohydrates serve as energy stores and metabolic intermediates.
- Ribose and deoxyribose sugars form part of the structural framework of RNA and DNA.
- Carbohydrates are important for tissue formation.
- Carbohydrates form the basis of human blood groups.
- Polysaccharides are structural elements in the cell walls of bacteria and plants and in the connective tissues of animals.
- Carbohydrates are linked to many proteins and lipids, where they play key roles in mediating interactions among cells and interactions between cells and other elements in the cellular environment.
- As a structural material (cellulose in plants, chitin in insects, building blocks of nucleotides).
- Certain carbohydrate derivatives are used as drugs, like cardiac glycosides(such as Digitoxin) or antibiotics.

Classification of Carbohydrates

1- **Monosaccharides:** simple sugars with multiple OH groups.
2- **Disaccharides:** two monosaccharides covalently linked by a glycosidic bond.
3- **Oligosaccharides:** several monosaccharides (3-9) joined by glycosidic bonds.
4- **Polysaccharides:** polymers consisting of chains of monosaccharide or disaccharide units.

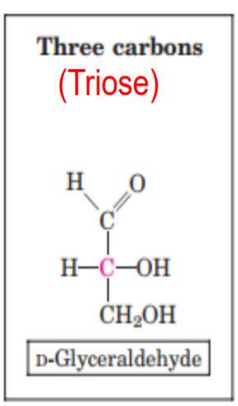
1- Monosaccharides:

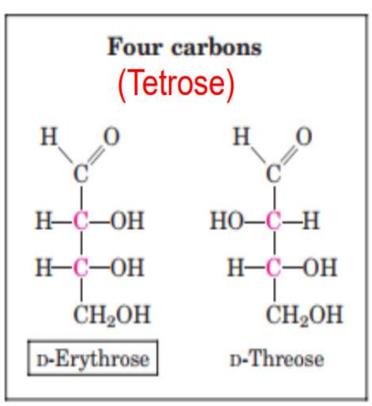
- Simple sugar, Cannot be further hydrolyzed into simple carbohydrates
- Usually, colorless, water-soluble, crystalline solids and Some monosaccharides have a sweet taste.
- Categorized by the number of carbon (typically 3-8) and whether an aldehyde or ketone.
- So it`s classified according to number of carbon atoms:

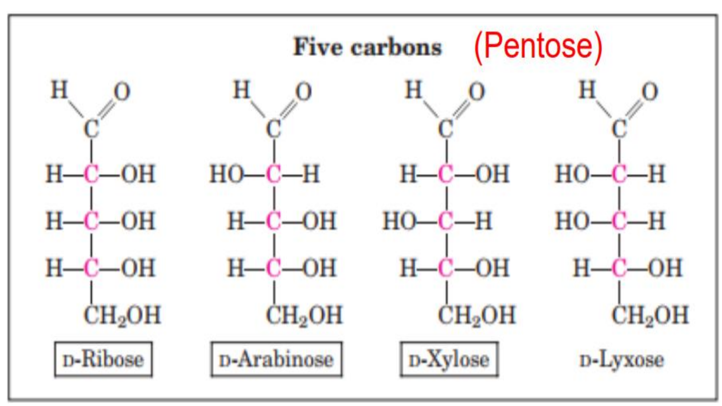
Trioses, Tetroses, Pentoses, hexoses, Heptoses, and Octoses, or according to

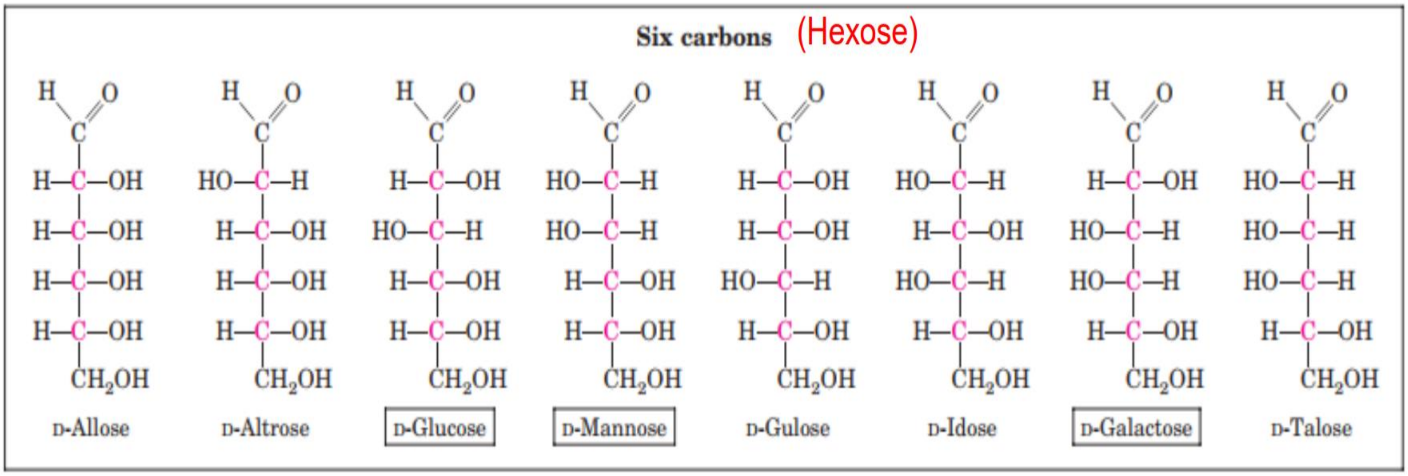
✓ functional group to

- **Aldose** (e.g., glyceraldehyde, ribose, glucose, mannose, galactose) has an aldehyde group at one end.
- **Ketose** (e.g., dihydroxy acetone, fructose) has a keto group, usually at C_2.

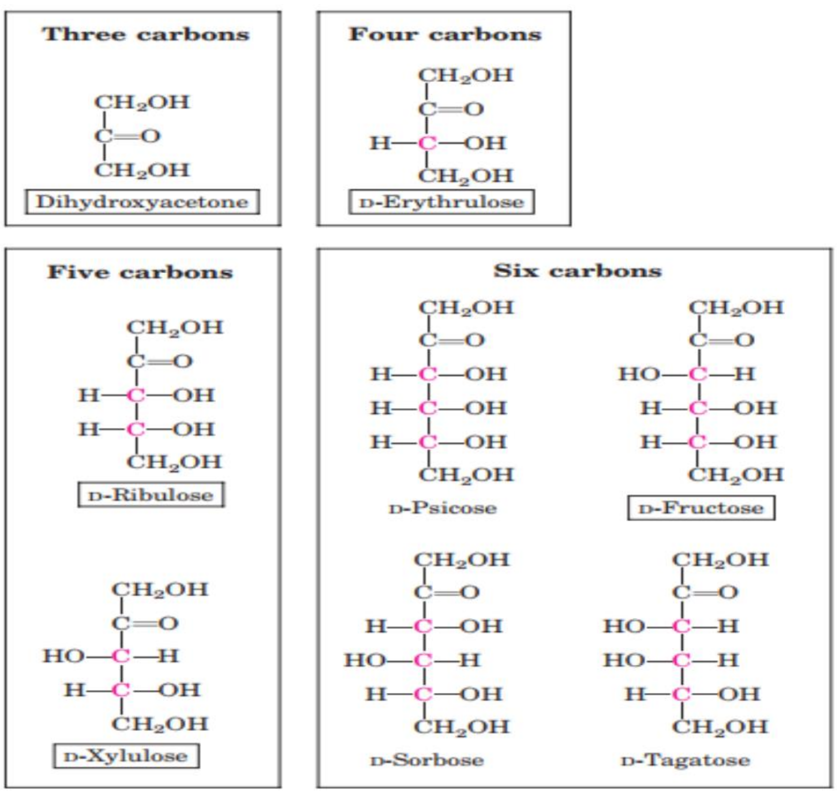








Aldoses



Ketoses

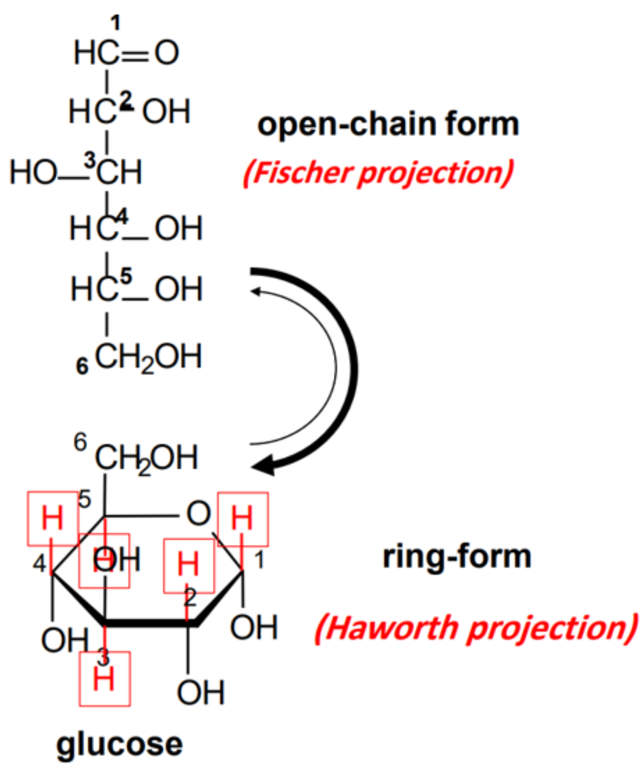
MONOSACCHARIDE STRUCTURES

1-FISCHER PROJECTIONS:

- In a Fischer projection, the carbohydrate is shown in its open-chain form, rather than a cyclical one.
- Carbon atoms in the main chain of the carbohydrate molecule are connected vertically, whilst hydrogen atoms and hydroxyl groups are bonded horizontally.

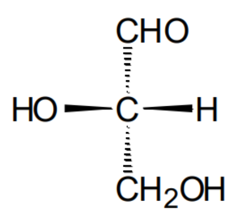
2-HAWORTH PERSPECTIVE FORMULAS:

- A Haworth projection differs from a Fischer projection in that it is used to represent the carbohydrate in its cyclical form. This is especially useful for sugars that have a ring structure.

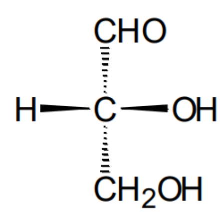


D and L isomerism

- Isomers are molecules with the same kinds and numbers of atoms joined up in different ways.
- A carbon atom that contains 4 different chemical groups forms an asymmetric (chiral) center.
- The prefixes D and L designate the absolute configuration of the asymmetric carbon farthest from the aldehyde or keto group.
- When the OH group on this carbon is on the right, the sugar is the D-isomer; when it is on the left, it is the L-isomer.
- Glyceraldehyde has a single asymmetric carbon and, thus, there are 2 stereoisomers of this sugar.
- D-glyceraldehyde and L-glyceraldehyde are mirror images of each other (enantiomers).

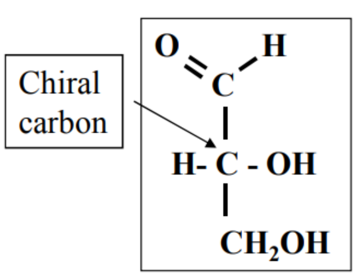


L-glyceraldehyde

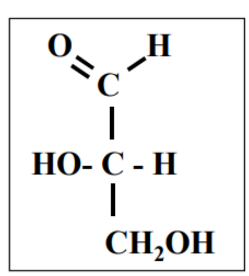


D-glyceraldehyde

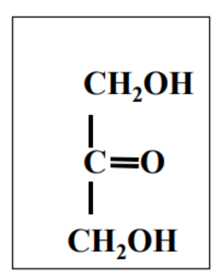
- Glyceraldehyde is used as a reference for optical isomers because it is the simplest monosaccharide with an asymmetric carbon.



D-Glyceraldehyde



L-Glyceraldehyde



Dihydroxyacetone

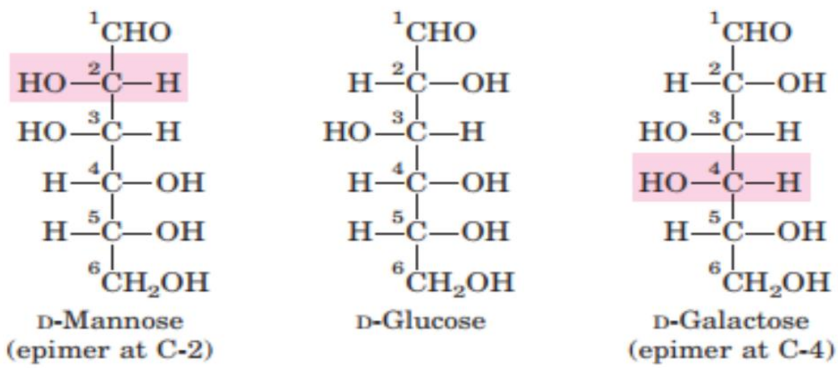
Stereoisomers and Epimers

*Stereoisomers have the same chemical formula but differ in the position of the OH group on 1 or more of their asymmetric carbons.

*Epimers are stereoisomers that differ in the position of the OH group at only 1 of their asymmetric carbons.

*D-glucose and D-galactose are epimers of each other, differing only at C_4, and can be interconverted in human cells by enzymes called epimerase.

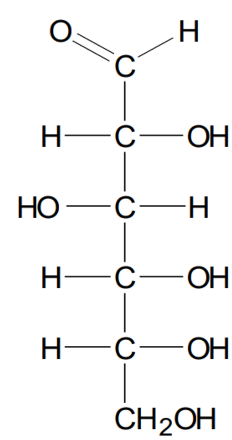
*D-mannose and D-glucose are also epimers of each other, differing only at C_2.



Some important monosaccharide

1-Glucose:

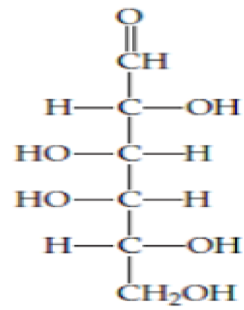
- Glucose is an aldohexose.
- It is the major source of energy for humans and animals.
- It is the main sugar in the blood.
- It is converted into other carbohydrates in the liver and other tissue.



glucose

2-Galactose:

- Galactose is an aldohexose.
- It is synthesized in the mammary gland.
- It binds to glucose to form the disaccharide lactose (sugar of milk).
- It can be converted into glucose in the liver.



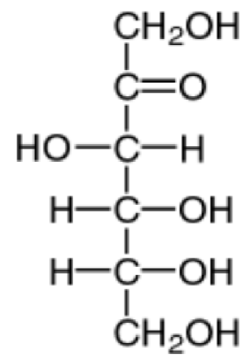
Galactose

3-Fructose:

- Fructose is a ketohexose.
- It is present in semen acting as the main energy source for the spermatozoa.
- It is a constituent of disaccharide sucrose (cane sugar).
- It can be converted into glucose in the liver.

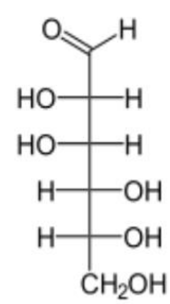
Small amounts are converted into glycogen, lactic acid, or fat
Found in fruit, honey, and high fructose corn syrup.

Fructose

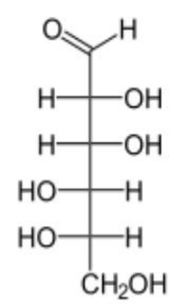


4- Mannose:

- It is not found free in nature.
- In the human body, it is found as a constituent of glycoproteins.
- It is a reduction product that is mannitol.



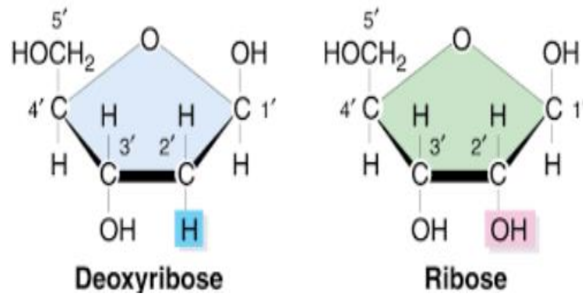
D-Mannose



L-Mannose

5-Ribose and deoxyribose:

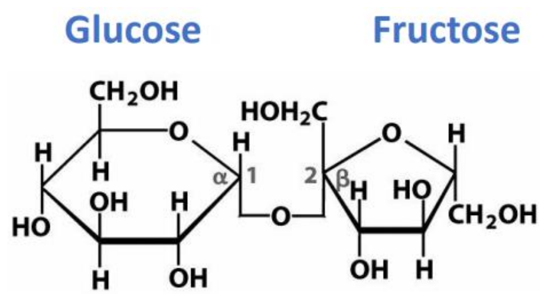
- Ribose and deoxyribose are aldopentoses.
- They enter in nucleic acids structure.
- Ribose enters the structure of high-energy phosphate compounds such as ATP, GTP, and CTP.
- Ribose in the structure of coenzymes such as NAD and FAD.



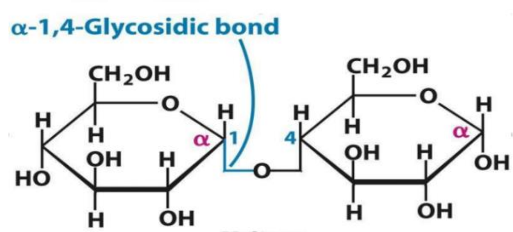
2- **Disaccharides:** Two monosaccharides can be linked together through a glycosidic linkage to form a disaccharide.

The most common disaccharides are:

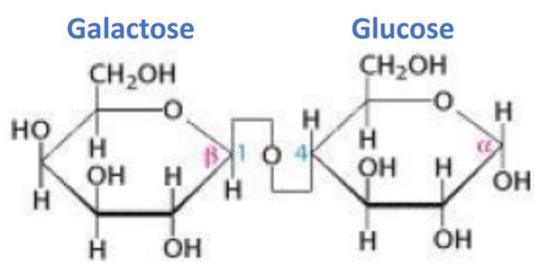
Sucrose (cane or beet sugar - made from one glucose and one fructose)



Maltose (made from two glucose)



Lactose (milk sugar - made from one glucose and one galactose)

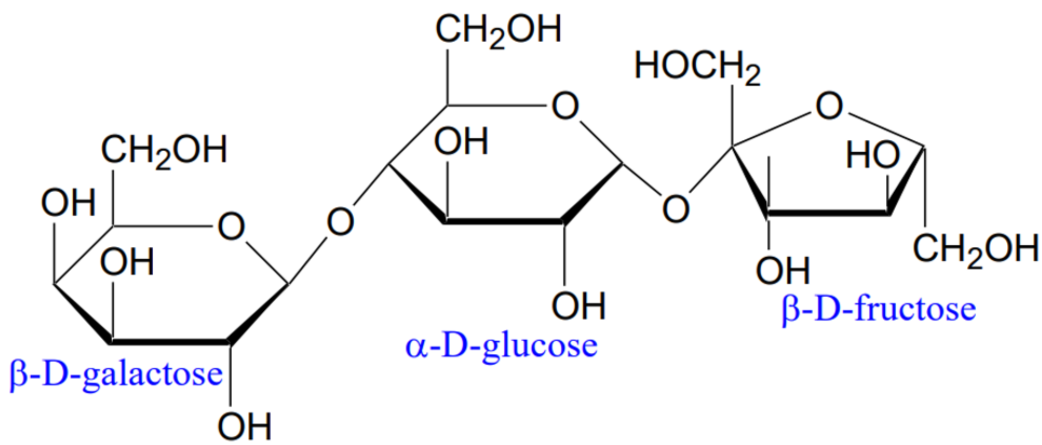


The formula of these disaccharides is **$C_{12}H_{22}O_{11}$.**

Disaccharides can be hydrolyzed into their mono-saccharide building blocks by boiling them with dilute acids or reacting them with the appropriate enzymes.

3- **Oligosaccharides:**

Oligosaccharides contain from 3 to 10 monosaccharide units.



Raffinose

An oligosaccharide found in peas and beans; largely undigested until reaching the intestinal flora in the large intestine, releasing hydrogen, carbon dioxide, and methane)

4- **Polysaccharides:**

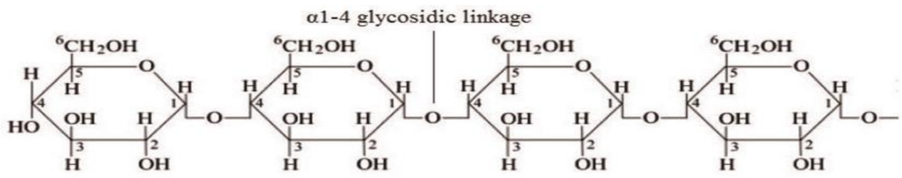
- ❖ Most carbohydrates found in nature occur as polysaccharides, polymers of medium to high molecular weight.
- ❖ Homopolysaccharides are polymers of a single monosaccharide, whereas heteropolysaccharides contain more than one type of monosaccharide.
- ➢ Three important Polysaccharides are starch, glycogen, and cellulose.

Starch :

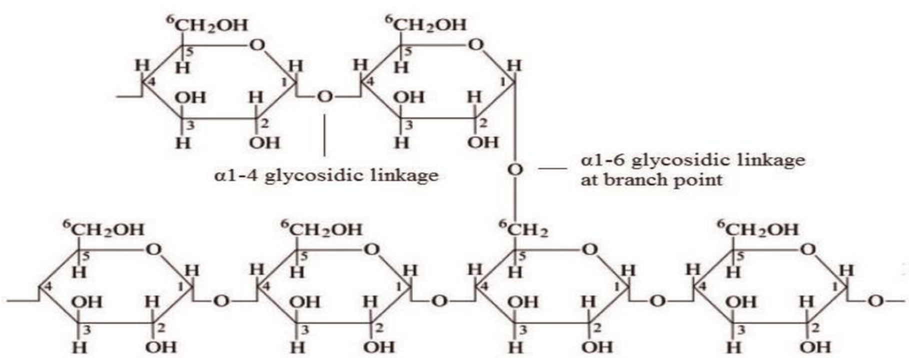
- large molecule with a variable number of glucose units; storage carbohydrate of plant cells.
- Starch is a polymer consisting of D-glucose units.
- There are two forms of starch: amylose and amylopectin.

❖ Amylose – is a linear polymer of glucose linked with mainly (α-1,4) bonds.

❖ Amylopectin – a chain of glucose molecules (α -1,4), every 30th glucose branch to other glucose residues (α-1,6).



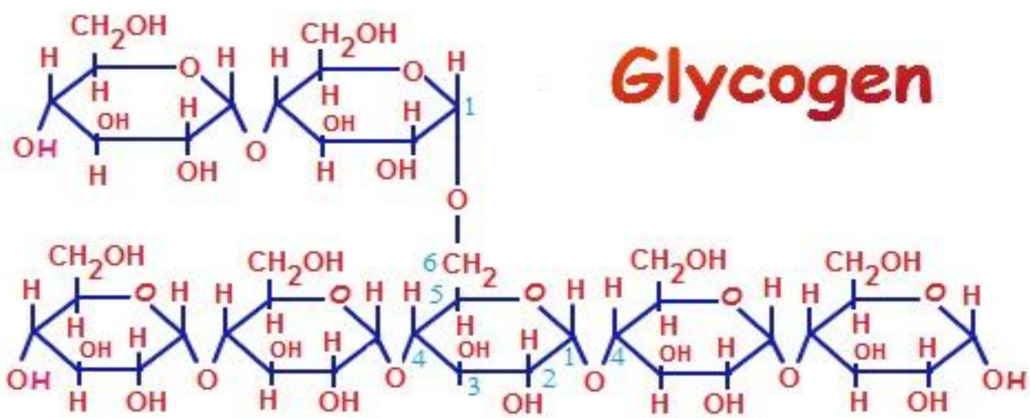
Amylose



Amylopectin

Glycogen:

- Glycogen, also known as animal starch, is structurally similar to amylopectin, containing both α(1→4) glycosidic linkages and α(1→6) branch points. Glycogen is even more highly branched, with branches occurring every 8 to 12 glucose units.
- Glycogen is abundant in the liver and muscles; on hydrolysis, it forms D-glucose, which maintains normal blood sugar level and provides energy.

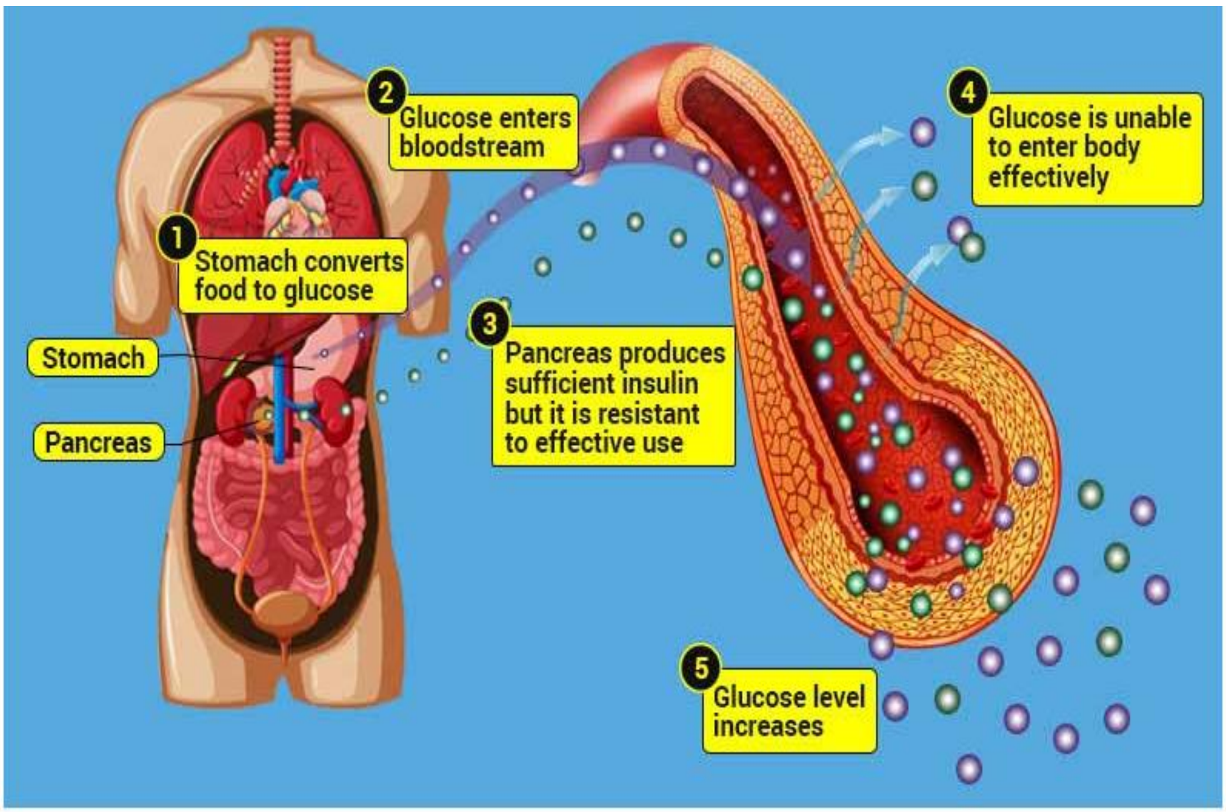


Cellulose:

- Cellulose is a polymer consisting of long, unbranched chains of D-glucose connected by β(1→4) glycosidic linkages; it may contain from 300 to 3000 glucose units in one molecule.
- Because of the β-linkages, cellulose has a different overall shape from amylose, forming extended straight chains that hydrogen bond to each other, resulting in a very rigid structure.
- Cellulose is the most important structural polysaccharide and is the single most abundant organic compound on earth. It is the material in plant cell walls that provides strength and rigidity; wood is 50% cellulose.

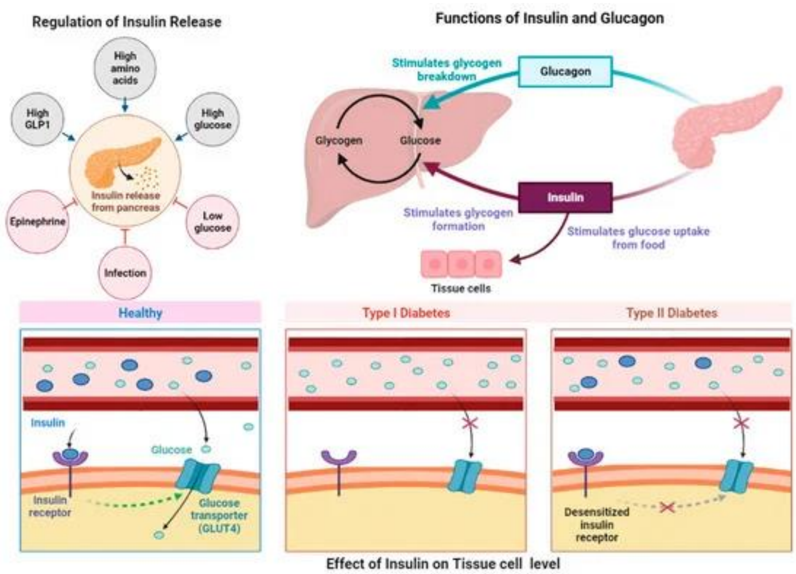
***Clinical Abnormalities:**

Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which leads over time to serious damage to the heart, blood vessels, eyes, kidneys, and nerves.



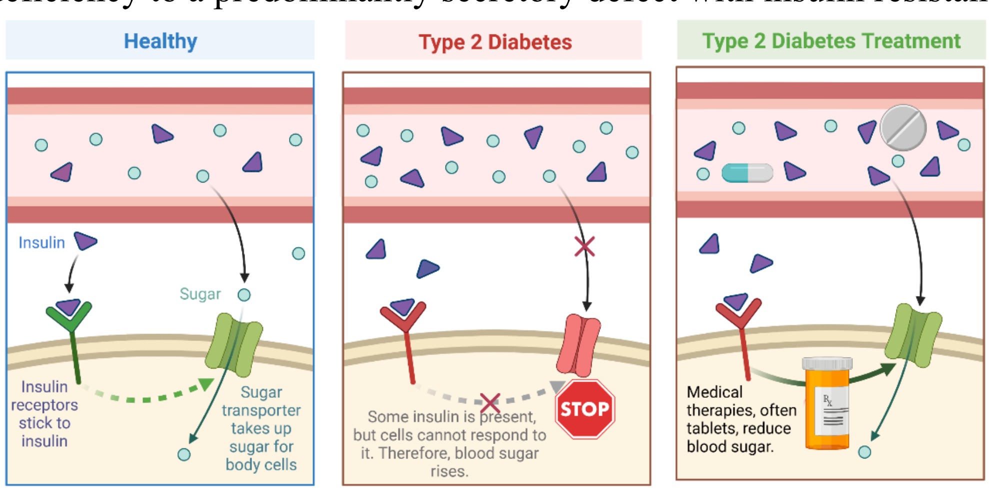
Type 1 diabetes mellitus

Previously called insulin-dependent diabetes mellitus, this is the term used to describe the condition in patients for whom insulin therapy is essential because they are prone to develop ketoacidosis. It usually occurs during childhood or adolescence. Most of these cases are due to immune-mediated processes and may be associated with other autoimmune disorders such as Addison's disease, vitiligo, and Hashimoto's thyroiditis. which has damaged the β-cells of the pancreatic islets.



Type 2 diabetes mellitus

Previously called non-insulin-dependent diabetes mellitus, this is the most common variety worldwide (about 90 percent of all diabetes mellitus cases). Patients are much less likely to develop ketoacidosis than those with type 1 diabetes, although insulin may sometimes be needed. Onset is most common during adult life; there is a familial tendency and an association with obesity. There is a spectrum of disorders ranging from mainly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance.



The main symptoms of Diabetes Mellitus

- Increased thirst
- Weight loss
- Increased urination
- Hunger due to starvation of cells
- Fatigue
- Slow healing of wounds

Complications of Diabetes Mellitus

The smallest blood vessels of the body are damaged due to the production of high blood sugar levels. This, in turn, leads to a decrease in the blood flow level in the body resulting in the death of tissues. This condition also affects the other parts of the body such as the heart, kidneys, and nervous system. Hence it has a large effect on the immune system of the body by completely damaging it.

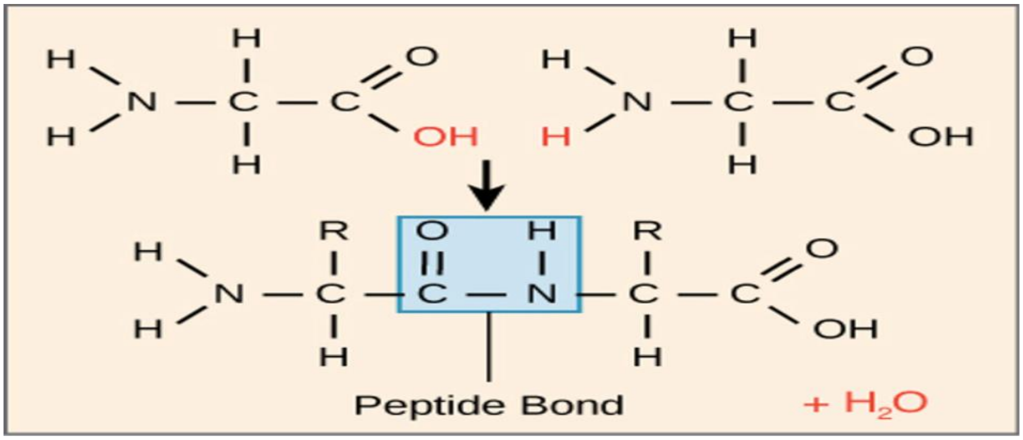
Lecture.4 Peptides, and Proteins: part 2

Introduction to Peptides

- Peptides are short polymers of amino acid (monomers) linked by peptide bonds,
- the covalent chemical bonds formed between two molecules when the carboxyl group of one molecule reacts with the amino group of the other molecule.
- Peptides are distinguished from proteins on the basis of size, typically containing fewer than 50 monomer (amino acid) units.
- The shortest peptides are dipeptides, consisting of two amino acids joined by a single peptide bond, There are also tripeptides, tetrapeptides, etc.
- Amino acids that have been incorporated into a peptide are termed "residues"; every peptide has an N-terminus and C-terminus residue on the ends of the peptide.
- A polypeptide is a long, continuous, and unbranched peptide.
- Proteins consist of one or more polypeptides arranged in a biologically functional way and are often bound to cofactors or other proteins.

Peptide Bond Formation

- Amino acids are linked together by condensation reaction between carboxylic and amino groups from two different amino acids (with elimination of water).
- The amide bond formed is called a peptide bond.
- The product is called a peptide, and named according to the number of amino acids involved: e.g. dipeptide (2), tripeptide (3), decapeptide (10).
- Big peptides are called polypeptides.



Characteristics of Peptide Bonds

 Peptide bonds are strong with partial double bond character:

 They are not broken by usual denaturing agents like heating or high salt concentration.

They can be broken by:

• Prolonged exposure to strong acids or the base at elevated temperatures.

• Specific enzymes such as digestive enzymes(pepsin, trypsin, chymotrypsin).

 Peptide bonds are rigid and planner-resisting free rotation, therefore they stabilize protein structure.

Some important peptides

1-Glutathione: (L-glutamyl-L-cysteinyl-glycine) is widespread in animals, plants, and microorganisms.

-Beef (200), broccoli (140), spinach (120), chicken (95), potatoes (71), paprika (49), tomatoes (49), and oranges (40) are especially rich in glutathione (mg/kg).

-The peptide is the coenzyme of glyoxalase.

-Present in oxidized and reduced state.

-Functions of glutathione component of an antioxidant which is required for free radical scavenging.

-Protect the integrity of the RBC membrane.

-Protect Hb from oxidation by H_2O_2.
-transport of amino acids (meister cycle).
-Detoxification formation and stabilization of disulfide linkage in proteins.

2-Thyrotropin-releasing hormone-TRH
- is a tripeptide hormone (p-Glu-His-Pro-NH_2) produced in the hypothalamus.
- It stimulates the release of TSH, which then increases thyroid hormones(T3 and T4).

Roles of TRH in Health and Disease:
1-Learning and Memory: TRH is widely found in the brains of mammals and is considered a neurotransmitter.
2-Mental Health
3-Blood Sugar Control: TRH is also made in the pancreas. It inhibits amylase secretion and increases glucagon secretion from the pancreas.

3-Enkephalin
- An enkephalin is a pentapeptide.
- Found in the brain.
- Inhibits the sense of pain.

4-Angiotensin- II:
-Angiotensin- II (8 AAs) Pressor or hypertensive peptide.
-Stimulates release of aldosterone from the adrenal cortex.

5-Oxytocin :
-Oxytocin secreted by the posterior pituitary gland
-Contains 9 amino acids(nonapeptide).
-Oxytocin causes contraction of the uterus.

6-Vasopressin:
-also called antidiuretic hormone (ADH).
-is a nonapeptide(9 amino acids) synthesized in the hypothalamus as a prohormone and then Secreted by the posterior pituitary gland.
-effect on the kidney and cause reabsorb of solute-free water and return it to the circulation from the tubules of the nephron.

Proteins

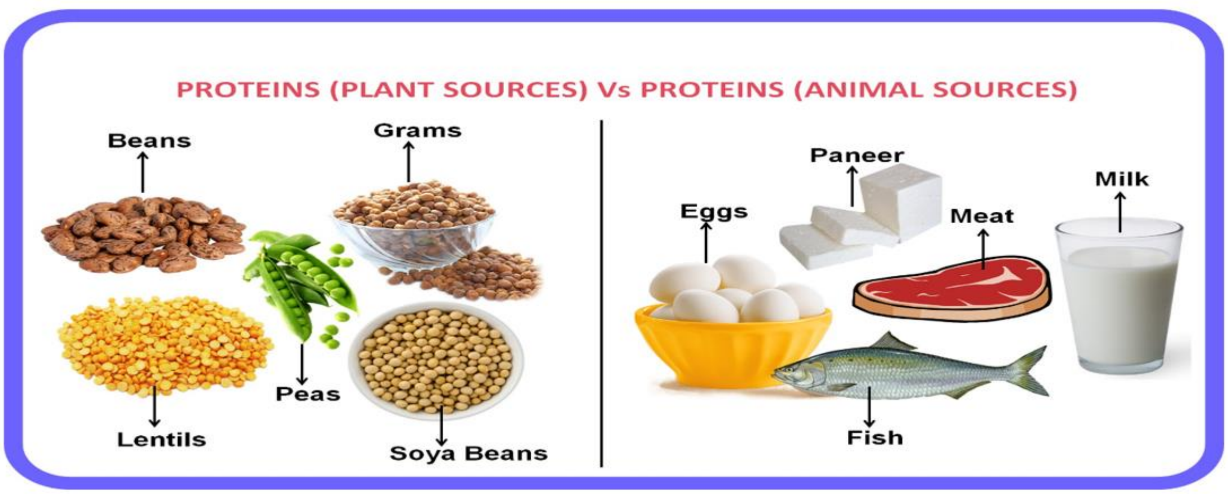
The word protein is derived from the Greek word, proteious meaning primary. So, proteins are the major components of any living organism.

Proteins are natural substances with high molecular weights ranging from 5,000 to many millions. Besides Carbon, Hydrogen, and Oxygen, they also contain Nitrogen, and sometimes, Sulfur and Phosphorous.

Proteins are the most important constituent of cell membranes and cytoplasm. Muscle and blood plasma also contain certain specific proteins.

Protein-containing foods are essential for living organisms, because protein is the most important biological molecule in building up and maintenances of the structure of the body, giving as much energy as carbohydrates in the course of metabolism in the body. Many of the body's proteins perform innumerable chemical reactions constantly taking place inside the body.

Proteins are the molecular instruments in which genetic information is expressed; hormones, antibodies, transporters, muscle, lens protein, antibiotics.



Definition

Proteins are macromolecules with a backbone formed by the polymerization of amino acids in a polyamide structure.

Classification

Even though there is no universally accepted classification system, proteins may be classified on the basis of their composition, solubility, shape, biological function, and on their three-dimensional structure.

1. Composition:-

A. Simple protein: Yields only amino acids and no other major organic or inorganic hydrolysis products i.e. most of the elemental compositions.

B. Conjugated Proteins: Yields amino acids and other organic and inorganic components. E.g. **Nucleoprotein** (a protein containing Nuclei acids).
Lipoprotein (a protein containing lipids).
Phosphoprotein (a protein containing phosphorous).
Metalloprotein (a protein containing metal ions of Fe_2^+).
Glycoprotein (a protein containing carbohydrates).

2. Solubility:-

A. Albumins:
These proteins such as egg albumin and serum albumin are readily soluble in water and coagulated by heat.

B. Globulins:
these proteins are present in serum, muscle, and other tissues and are soluble in dilute salt solution but sparingly in water.

C. Histones:
are present in glandular tissues (thymus, pancreas) and soluble in water; they combine with nucleic acids in cells and on hydrolysis yield basic amino acids.

3- Shape

A. Fibrous proteins:
the molecules are constituted by several coiled cross-linked polypeptide chains, are insoluble in water, and are highly resistant to enzyme digestion.
A few subgroups are listed below.

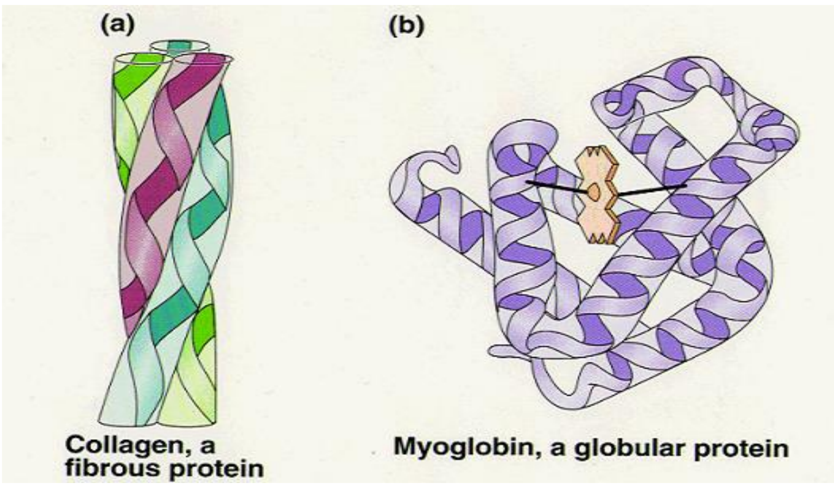
1. Collagens: the major protein of the connective tissue, insoluble in water, acids, or alkalis. But they are convertible to water-soluble gelatin, easily digestible by enzymes.

2. Elastins: present in tendons, arteries, and other elastic tissues, not convertible to gelatin.

3. Keratins: protein of hair, and nails.

B. Globular proteins:

These are globular or ovoid in shape, soluble in water, and constitute the enzymes, oxygen-carrying proteins, and hormones. Subclasses include:- Albumin, globulins, and histones.



4- Biological Functions:

Proteins are sometimes described as the "workhorses" of the cell

- **Enzymes:** kinases, transaminases.
- **Storage proteins:** myoglobin, ferritin
- **Regulatory proteins**: peptide hormones, DNA binding proteins
- **Structural protein:** collagen, proteoglycan
- **Protective proteins**: blood clotting factors, Immunoglobins,
- **Transport protein:** Hemoglobin, plasma lipoproteins
- **Contractile or motile Proteins:** Actin, tubulin

Conformation of Proteins

The conformation of a protein refers to the three-dimensional structure in its native state. There are many different possible conformations for a molecule as large as a protein. Four types of structural organization can be distinguished in proteins:

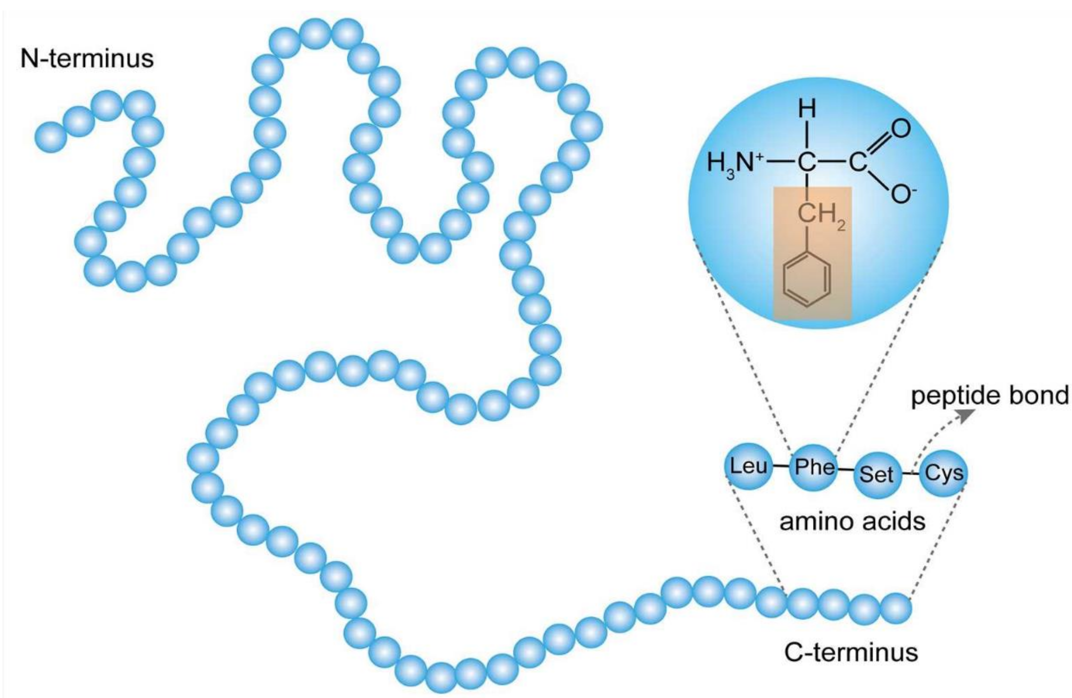
1. **Primary Structure of Proteins:**

The primary structure of a protein is defined by the linear sequences of amino acid residues. Protein contains between 50 and 2000 amino acid residues.

The amino acid composition of a peptide chain has a profound effect on the physical and chemical properties of proteins.

Proteins rich in polar amino acids are more water-soluble. Proteins rich in aliphatic or aromatic amino groups are relatively insoluble in water and more soluble in cell membranes (can easily cross the cell membrane).

The primary structure cannot represent the 3D nature of a protein molecule since the extended chain of amino acids is co-planar as the covalent bond of the peptide is right.



2. Secondary Structure of Proteins:

The secondary structure of a protein refers to the local structure of a polypeptide chain, which is determined by the Hydrogen bond. The Interactions are between the carbonyl oxygen group of one peptide bond and the amide hydrogen of another nearby peptide bond.

There are two types of secondary structures, the ∝ - helix, and the β- pleated sheet.

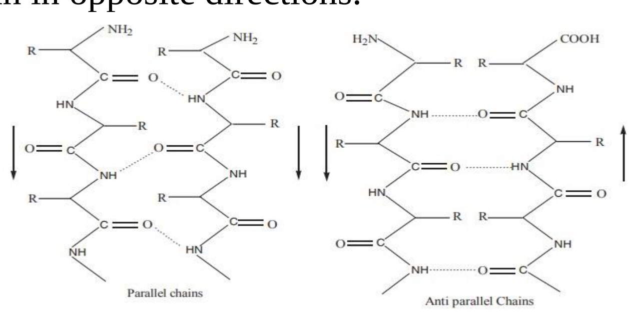
The α - helix

The α-helix is a rod-like structure with peptide chains tightly coiled and the side chains of amino acid residues extending outward from the axis of the spiral. Each amide carbonyl group is hydrogen bonded to the amide hydrogen of a peptide bond. This enables every = NH group to bind with a carbonyl O, fourth in line behind the primary structure, and the helix winds in a right-handed manner in almost all natural protein, i.e. turns in a clockwise fashion around the axis.

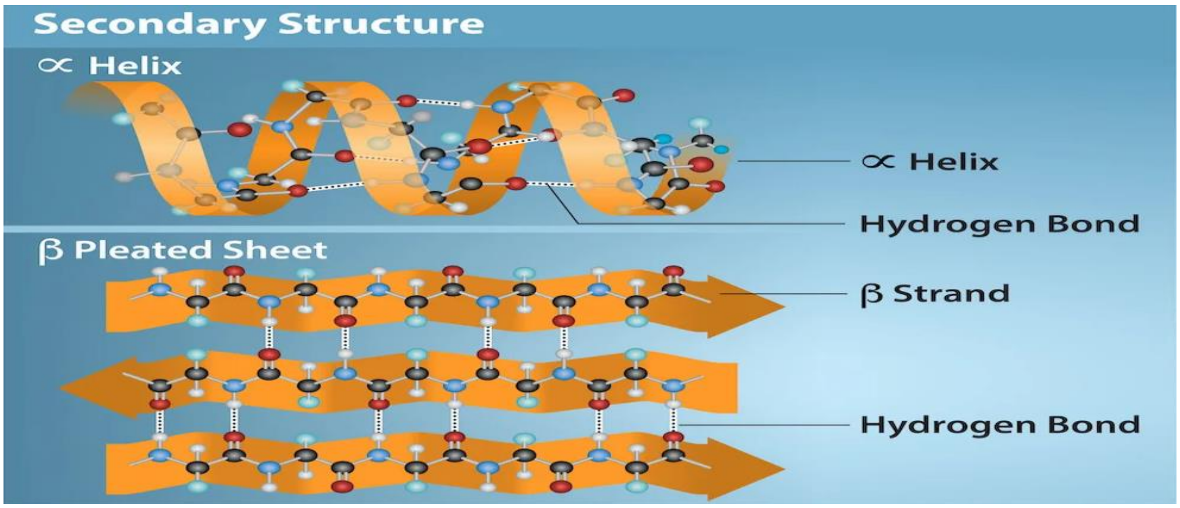
The β-pleated Sheet Structure

Pauling and Corey also proposed a second-order structure, the p-pleated sheet. for polypeptide. This structure is a result of intermolecular hydrogen bonding between the polypeptide chains to form a sheet-like arrangement.

There are two ways in which protein chains can form the pleated sheet structure. One is with the chains running in the same direction i.e. the -COOH or NH2 ends of the polypeptide chains lying all at the top or all at the bottom of the sheet. This is called a parallel pleated sheet structure. In another type, known as anti-parallel β-pleated sheet structure, the polypeptide chains alternate in such a way that the -COOH end of the one polypeptide is next to the -NH2 end of the other i.e., polypeptide chains run in opposite directions.



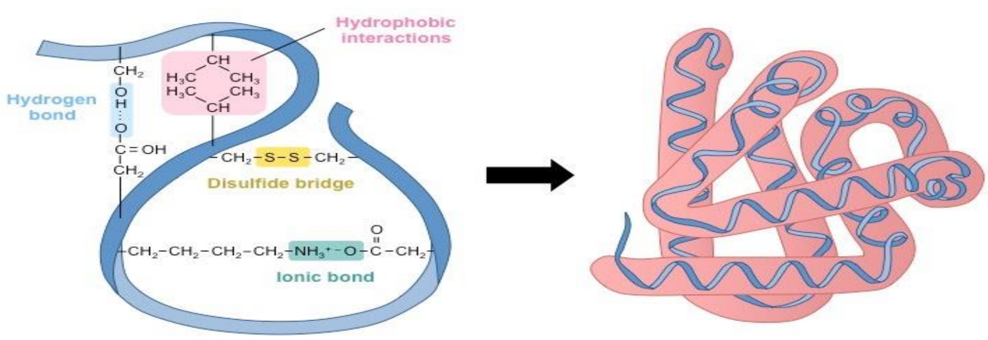
β-pleated sheet structure



3. Tertiary Structure of Proteins:

The three-dimensional, folded, and biologically active conformation of a protein is referred to as tertiary structure. The structure reflects the overall shape of the molecule. The three-dimensional tertiary structure of a protein is stabilized by interactions between sides. Chain functional group, covalent, disulfide bonds, hydrogen bonds, salt bridges, and hydrophobic interactions.

In the tertiary structure, the side chains of Tryptophan and Arginine serve as both hydrogen bond donors and acceptors. Lysine, aspartic acid Glutamic acid, tyrosine, and Histidine also can serve as both donors and acceptors in the formation of ion pairs (salt bridges). Two opposite-charged amino acids, such as glutamate with a γ -carboxyl group and lysine with an ε - amino group, may form a salt bridge, primarily on the surface of proteins.

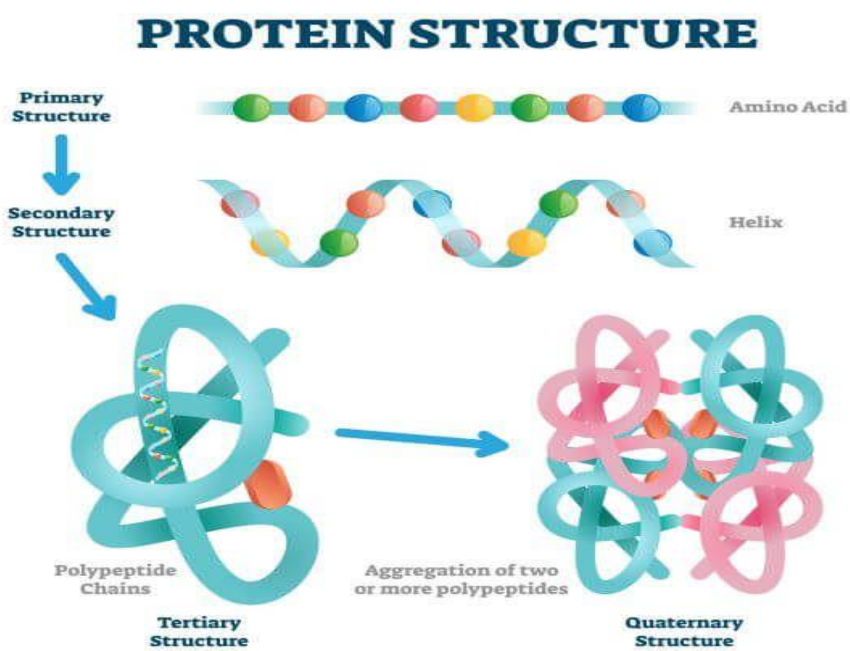


Types of side chain interactions   Overall 3D shape (3° Structure)

4. Quaternary Structure of Proteins:

Quaternary structure refers to a complex or an assembly of two or more separate peptide chains that are held together by non-covalent or, in some cases, covalent interactions.

If the subunits are identical, it is a homogeneous quaternary structure; but if there are dissimilarities, it is heterogeneous. For instance, insulin consists of A and B chains which are different. Hemoglobin has 4 chains, two of them are α and two are β. these, the polymers may be dimers, trimers, or tetramers.



Denaturation of Proteins

Proteins have finite lifetimes. They are also subject to environmental damage like oxidation proteolysis, denaturation, and other irreversible modifications.

A denatured protein loses its native physico-chemical and biological properties since the bonds that stabilize the protein are broken down. Thus the polypeptide chain unfolds itself and remains in solution in the unfolded state.

Factors that Affect Denaturation

1. physical factors

Temperature, pressure, mechanical shear force, ultrasonic vibration, and ionizing radiation cause the protein to lose its biological activity.

2. chemical factors

Acids and alkalis, organic solvents (acetone, ethanol), detergents (cleaning agents), and heavy metal salts (Hg, Cu, Ba, Zn, Cd) Cause the denaturation.

DIGESTION OF PROTEINS

The process of digestion is defined as the „process by which macromolecules in food are broken down into their component small-molecule subunits"

Digestion is the disintegration of complex nutrients into simple, soluble and assimilable forms.

Proteins are too large to be absorbed. The dietary proteins are hydrolyzed to amino acids by proteolytic enzymes, which can be easily absorbed.

Proteolytic enzymes responsible for degrading proteins are produced by three different organs; The stomach, pancreas, and the small intestine.

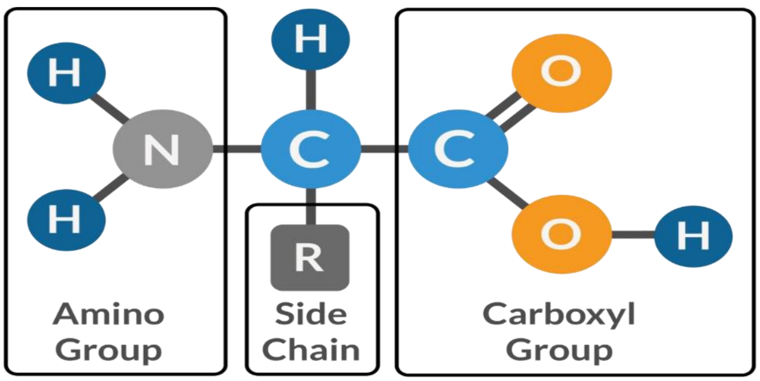
Some important enzyme effects on proteins

1- **Mouth:** no enzymes.
2- **Stomach:** Pepsin, Renin.
3- **Pancreas:** Trypsin, Chymotrypsin, Elastase, Carboxypeptidase A, Carboxypeptidase B.
4- **Intestine:** Aminopeptidase, Dipeptidase.

Lecture.4 Amino Acids, part 1

There are approximately 300 amino acids present in various animals, plants, and microbial systems, but only 20 amino acids are coded by DNA to appear in proteins.

Amino acids are the basic structural units of proteins consisting of an amino group, (-NH2) a carboxyl (-COOH) group a hydrogen (H) atom, and a (variable) distinctive (R) group. All of the substituents in an amino acid are attached (bonded) to a central (α-carbon atom). This carbon atom is called α because it is bonded to the carboxyl (acidic) group. The general formula ($H_2NCHRCOOH$) for the naturally occurring amino acids would be :

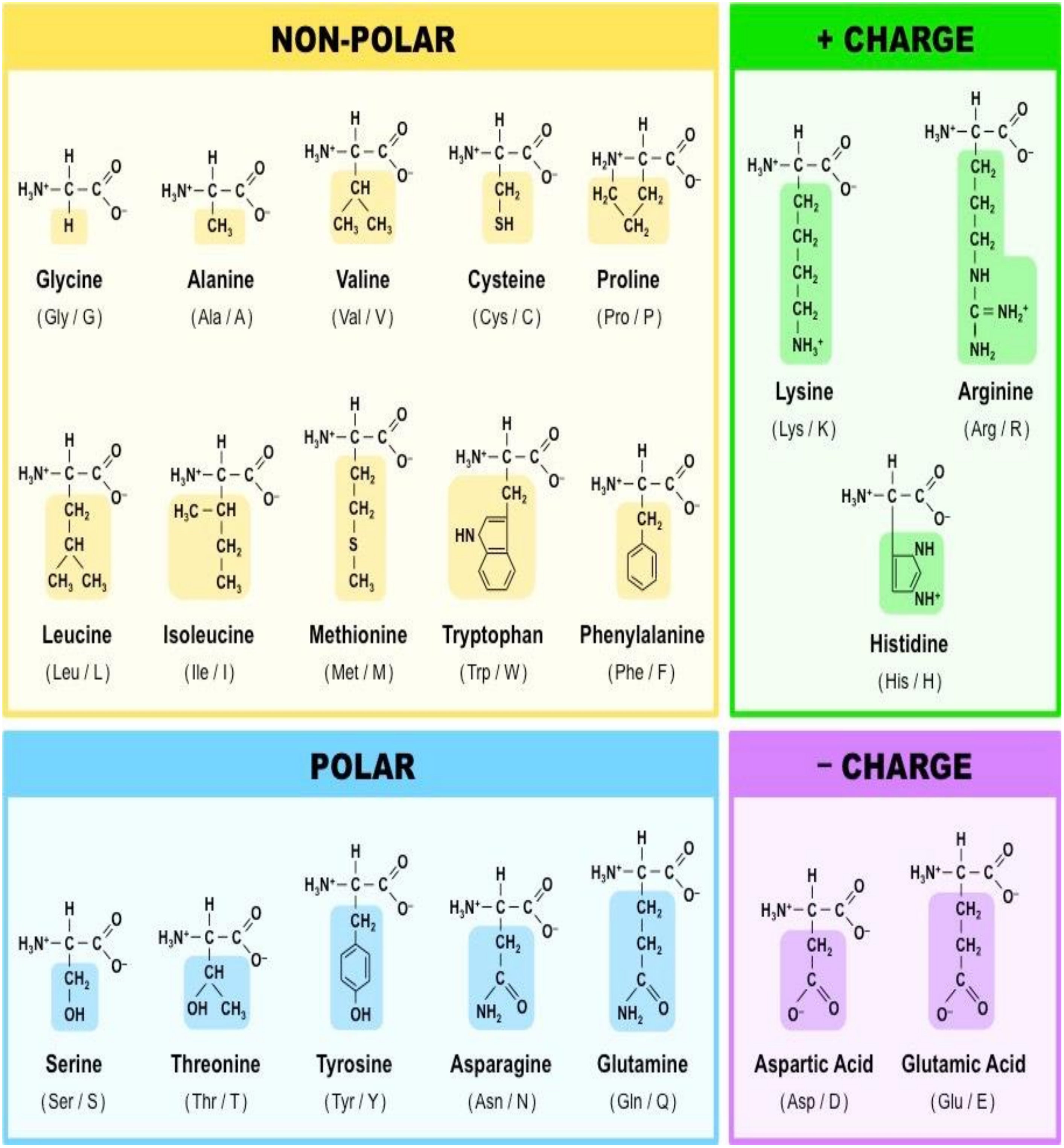


CLASSIFICATION OF AMINO ACIDS

1-Structural Classification

This classification is based on the side chain radicals (R-groups) amino acid is designated by three letter abbreviation eg. Aspartate as Asp.

Amino Acid	3-Letter	1-Letter	Amino Acid	3-Letter	1-Letter
Alanine	Ala	A	Leucine	Leu	L
Arginine	Arg	R	Lysine	Lys	K
Asparagine	Asn	N	Methionine	Met	M
Aspartic acid	Asp	D	Phenylalanine	Phe	F
Cysteine	Cys	C	Proline	Pro	P
Glutamic acid	Glu	E	Serine	Ser	S
Glutamine	Gln	Q	Threonine	Thr	T
Glycine	Gly	G	Tryptophan	Trp	W
Histidine	His	H	Tyrosine	Tyr	Y
Isoleucine	Ile	I	Valine	Val	V


NON-POLAR
Glycine
(Gly / G)
Alanine
(Ala / A)
Valine
(Val / V)
Cysteine
(Cys / C)
Proline
(Pro / P)
Leucine
(Leu / L)
Isoleucine
(Ile / I)
Methionine
(Met / M)
Tryptophan
(Trp / W)
Phenylalanine
(Phe / F)
+ CHARGE
Lysine
(Lys / K)
Arginine
(Arg / R)
Histidine
(His / H)
POLAR
Serine
(Ser / S)
Threonine
(Thr / T)
Tyrosine
(Tyr / Y)
Asparagine
(Asn / N)
Glutamine
(Gln / Q)
- CHARGE
Aspartic Acid
(Asp / D)
Glutamic Acid
(Glu / E)

i) Based on Chemical Properties				
Non Polar Amino acids	**Polar**	**Aromatic**	**Positively Charged**	**Negatively Charged**
Glycine Alanine Valine Leucine Isoleucine Methionine	Serine Threonine Cysteine Proline Aspargine Glutamine	Phenylalanine Tyrosine Tryptophan	Lysine Arginine Histidine	Aspartic Acid Glutamatic Acid

2-Electrochemical classification

Amino acids could be classified based on their acid-base properties.

- Acid amino acids
- Basic amino acids
- Neutral amino acid

Acid-Base Behavior of Amino Acids:

Amino acids exist as a zwitterion: a dipolar ion having both a formal positive and formal negative charge (overall charge neutral).

Amino acids are amphoteric:

They can react as either an acid or a base. Ammonium ion acts as an acid, the carboxylate as a base.

Note: At a certain compound-specific pH known as the isoelectric point (pI), the number of protonated ammonium groups with a positive charge and deprotonated carboxylate groups with a negative charge are equal, resulting in a net neutral charge.

- If pH >pI, amino acid would be negatively charged.
- If pH <pI, amino acid would be Positively charged.
- If pH= pI, amino acid would have no charged.

3-Biological or Physiological Classification

This classification is based on the functional property of amino acids for the organism.

❖ **Essential Amino Acids**

Amino acids which are not synthesized in the body and must be provided in the diet to meet an animal's metabolic needs are called essential amino acids. About ten of the amino acids are grouped under this category indicating that mammals require about half of the amino acids in their diet for growth and maintenance of normal nitrogen balance.

❖ **Non- Essential Amino Acids**

These amino acids do not need to be provided through diet, because they can be biosynthesized in adequate amounts within the organism.

❖ **Semi-essential amino acids**

Two amino acids are grouped under semi-essential amino acids since they can be synthesized within the organism but their synthesis is not in sufficient amounts. In that, they should also be provided in the diet. Semi-essential amino acids include Arginine and Histidine.

ii) Based on Nutritional Requirements

Essential amino acids	Semi-essential amino acids	Non-essential amino acids
Isoleucine Leucine Lysine, Methionine Phenylalanine Threonine Tryptophan, Valine	Arginine Histidine	Alanine, Aspargine, Tyrosine, Aspartic acid, Cysteine, Glutamic acid, Glycine, Proline, Serine, Hydroxylysine, Glutamine, Hydroxyproline

➢ **Classification Based on the Fate of Each Amino acid in Mammals.**

Amino acids can be classified here as Glucogenic (potentially converted to glucose), ketogenic (potentially converted to ketone bodies), and both glucogenic and ketogenic.

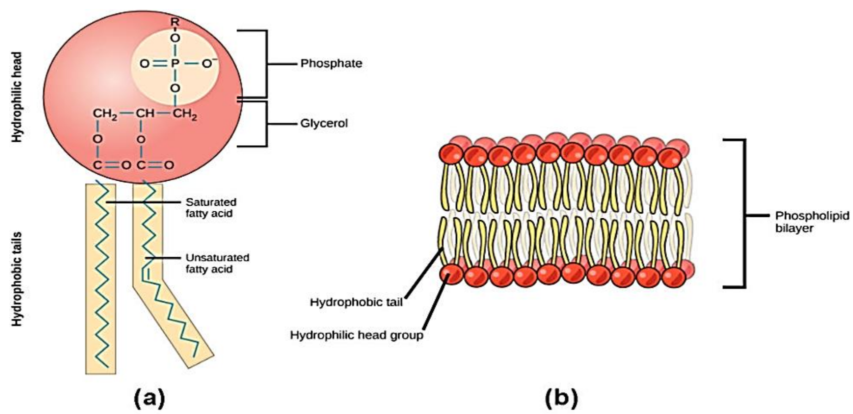
- Glucogenic Amino Acids
- Ketogenic Amino Acids

<u>IMPORTANCE OF AMINO ACIDS</u>

1. Formation of proteins: amino acids joined by peptide bonds to form proteins and peptides.
2. Formation of Glucose: Glucogenic amino acids are converted to Glucose in the body.
3. Transport and storage of ammonia: Glutamine plays a role in the transport and storage of amino nitrogen in the form of ammonia.
4. Enzyme activity: Cysteine has an important role in the activity of certain enzymes.
5. Buffer: both free amino acids and some amino acids found in protein can potentially act as buffers. Histidine can serve as the best buffer at physiological pH.
6. Detoxification reactions: Glycine, Cysteine, and Methionine are involved in the detoxification of toxic substances.
7. Formation of Biologically important compounds in the body.

Lecture.5 Lipids

Organic substances are relatively insoluble in water but soluble in organic solvents(chloroform, ether, alcohol, benzene), actually or potentially related to fatty acid and utilized by living cells.



Lipid Properties

•Lipids are oily or greasy nonpolar molecules, stored in the adipose tissue of the body.

• Lipids are energy-rich organic molecules, which provide energy for different life processes.

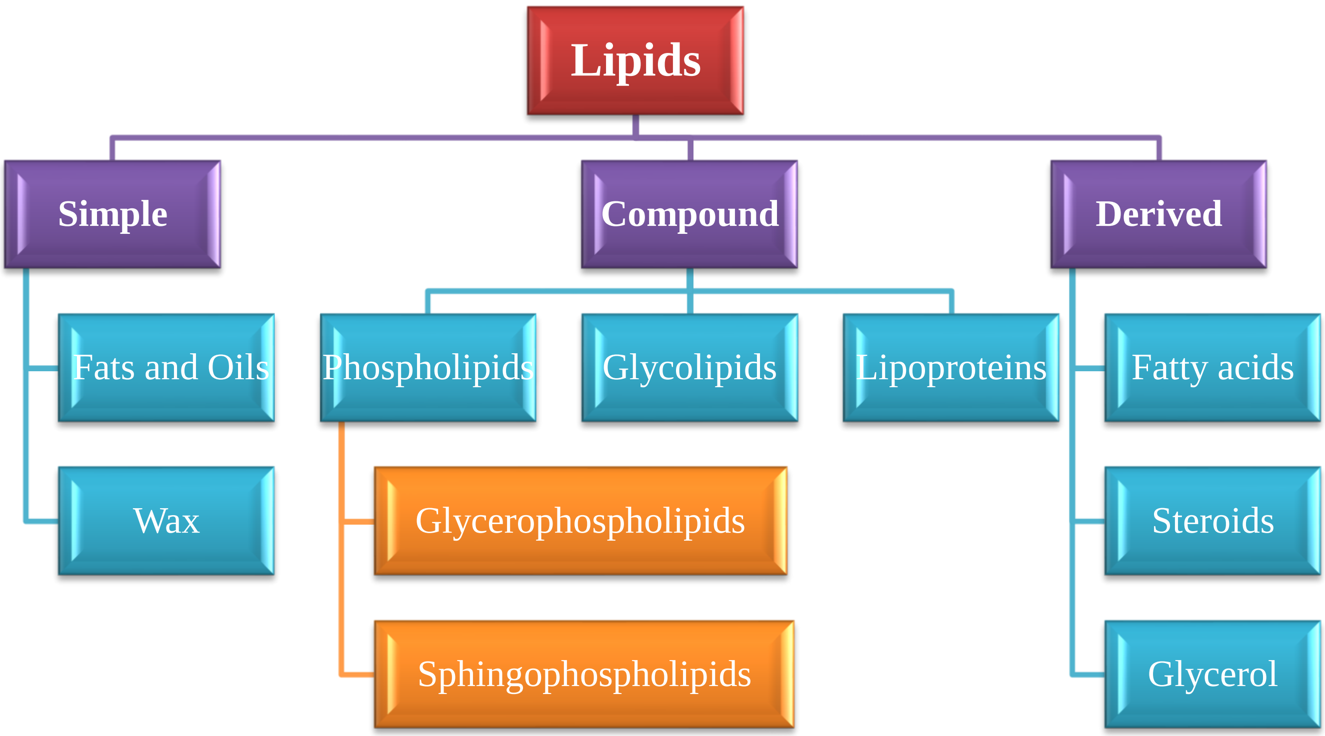
• Lipids are a class of compounds characterized by their solubility in nonpolar solvents and insolubility in water.

• Lipids are significant in biological systems as they form a mechanical barrier dividing a cell from the external environment known as the cell membrane.

• Lipids are the waxy, greasy, or oily compounds found in plants and animals.
– wax coating that protects plants
– structural components (cell membranes)
– insulation against cold

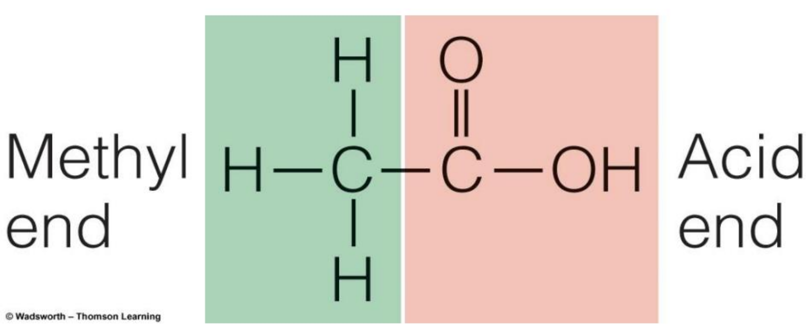
Classification of Lipids

Based on the composition of lipids are classified as:-



Fatty Acids

Fatty acids are long-chain hydrocarbon molecules that terminate with carboxylic acid groups, The fundamental building blocks of many lipids. The numbering of carbons in fatty acids begins with the carbon of the carboxylate group (COOH).

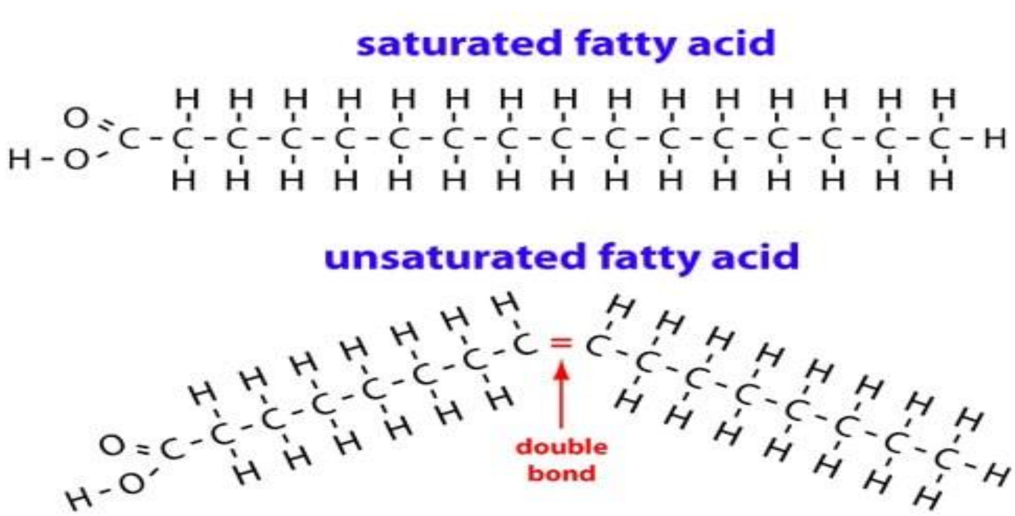


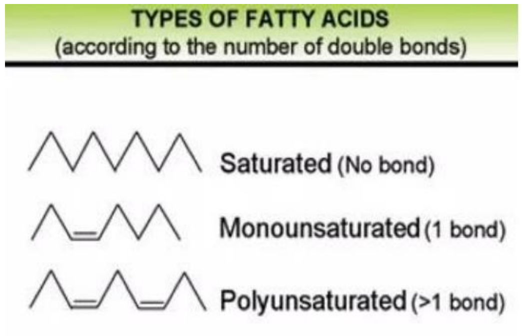
Properties of fatty acids:-

• The long nonpolar tail of fatty acids that are responsible for most of the fatty or oily characteristics of fats.
• Carboxylic group, the polar head of fatty acid is very hydrophilic under conditions of physiological pH and it exists as the carboxylate anion COO^-.
• The fatty acid chains in membranes usually contain between 14 and 24 carbon atoms; they may be **saturated** or **unsaturated**.
• The 16- and 18-carbon fatty acids are **most common**. The hydrocarbon chain is almost **unbranched** in animal fatty acids.
• Fatty acids that contain no carbon-carbon double bonds are termed **saturated fatty acids**; those that contain double bonds are **unsaturated fatty acids** and fatty acids with multiple sites of unsaturation are termed polyunsaturated fatty acids (PUFAs).

Classification of fatty acids:-

Fatty acids can be classified in many ways:
1) According to the nature of the hydrophobic chain-
a)Saturated
b) Unsaturated
Saturated fatty acids do not contain double bonds, while **unsaturated fatty acids** contain double bonds





Saturated Fatty Acids

Number of C atoms	Common Name	Systemic Name	Formula
2	Acetic acid	Ethanoic acid	CH3COOH
4	Butyric acid	Butanoic acid	$CH_3(CH_2)_2COOH$
6	Caproic acid	Hexanoic acid	$CH_3(CH_2)_4COOH$
8	Caprylic acid	Octanoic acid	$CH_3(CH_2)_6COOH$
10	Capric acid	Decanoic acid	$CH_3(CH_2)_8COOH$
12	Lauric acid	Dodecanoic acid	$CH_3(CH_2)_{10}COOH$
14	Myristic acid	Tetradecanoic acid	$CH_3(CH_2)_{12}COOH$
16	Palmitic acid	Hexadecanoic acid	$CH_3(CH_2)_{14}COOH$
18	Stearic acid	Octadecanoic acid	$CH_3(CH_2)_{16}COOH$
20	Arachidic acid	Eicosanoic acid	$CH_3(CH_2)_{18}COOH$
22	Behenic acid	Docosanoic acid	$CH_3(CH_2)_{20}COOH$

Unsaturated fatty acids

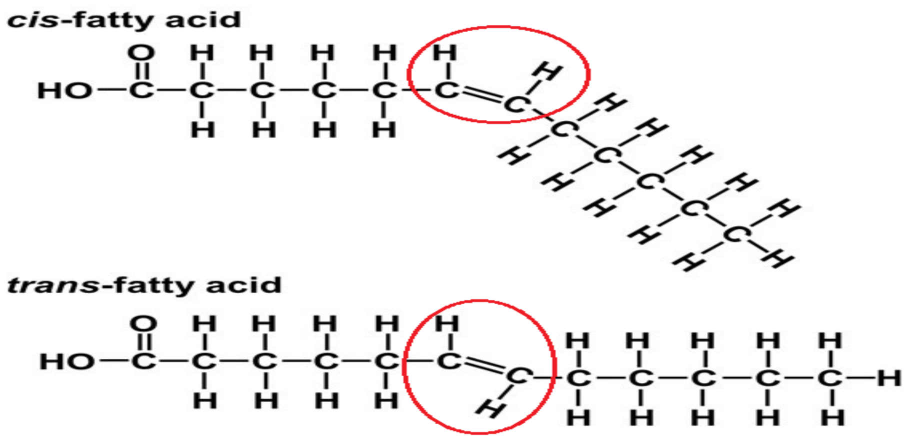
Unsaturated fatty acids may further be divided as follows-

(1) Monounsaturated (monoenoic) acids, containing one double bond.

(2) Polyunsaturated (polyenoic) acids, containing two or more double bonds.

- The configuration of the double bonds in most unsaturated fatty acids is **cis**.

- The double bonds in polyunsaturated fatty acids are separated by at least one methylene group.



<u>Essential and non- Essential fatty acids:-</u>

1-Essential Fatty acids:

-Must be supplied in the diet because the body can not form them.

They are present mainly in vegetable oils; They are the polyunsaturated fatty acids:

» linoleic acid 18:2 Δ9,12

» linolenic acid 18:3 Δ9,12,15

<u>Importance of essential fatty acids:</u>

1- Membrane structure and functions.

2- Transport of cholesterol.

3- Formation of lipoproteins.

4- Prevention of fatty liver.

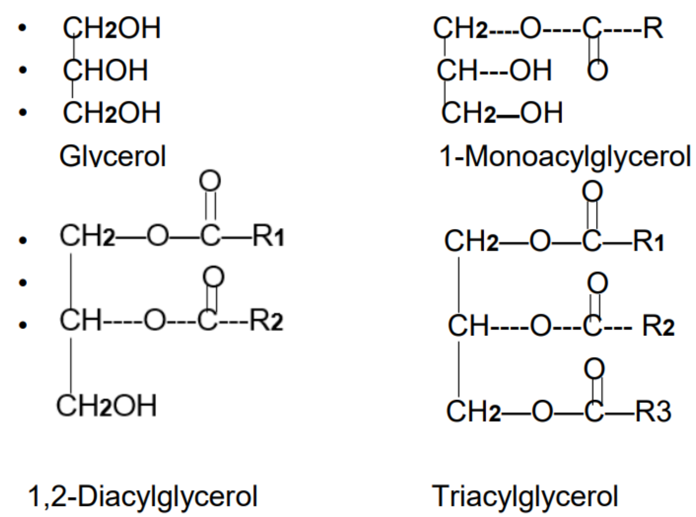
5-They are also needed for the synthesis of eicosanoids (prostaglandins, prostacyclins). It is derived from arachidonic acid (20) carbon.

2-Non essential Fatty acids:

They can be formed in the body; An example of a non-essential Fatty acid is **palmitic acid.**

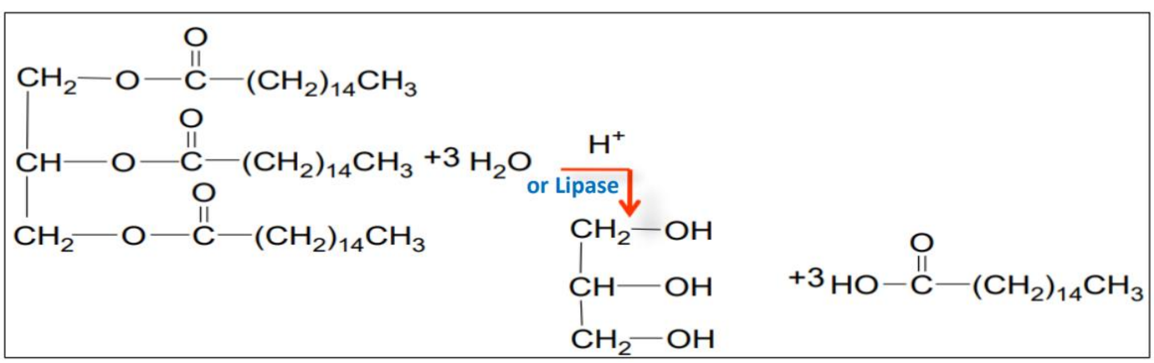
<u>Triacylglycerols</u>

Animal fats and vegetable oils are esters composed of three molecules of a fatty acid connected to a glycerol molecule, producing a structure called a triglyceride or a triacylglycerol:



<u>Properties of triacylglycerols:-</u>

- **Hydrolysis:** (Triacylglycerols) **lipase:-** Free fatty acids + glycerol.

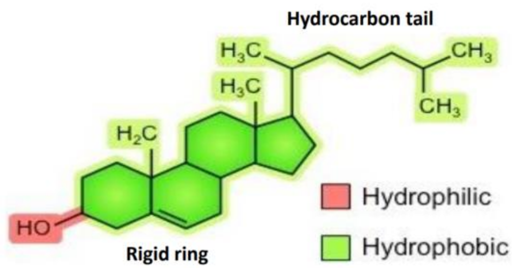


- **Antioxidants:** prevent the occurrence of oxidative rancidity.

- **Lipid peroxidation in vivo:** In living cells, lipids undergo oxidation to produce peroxides and free radicals which can damage the tissue. The free radicals are believed to cause inflammatory diseases, aging, cancer, and atherosclerosis.

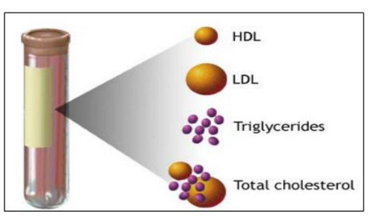
Cholesterol:-

Cholesterol is the most abundant steroid in the body (myelin sheath, brain, and nerve tissues). It is an essential component of **cell membranes** and is a precursor for other steroids, such as **bile salts**, **sex hormones**, **vitamin D**, and **adrenocorticoid hormones**.



Coronary Heart Diseases

• Usually; saturated fat in diet causes high blood cholesterol levels and these are considered risk factors for coronary heart disease.



A lipoprotein profile measures the level of cholesterol in the blood