Medical Biochemistry

Carbohydrate Chemistry

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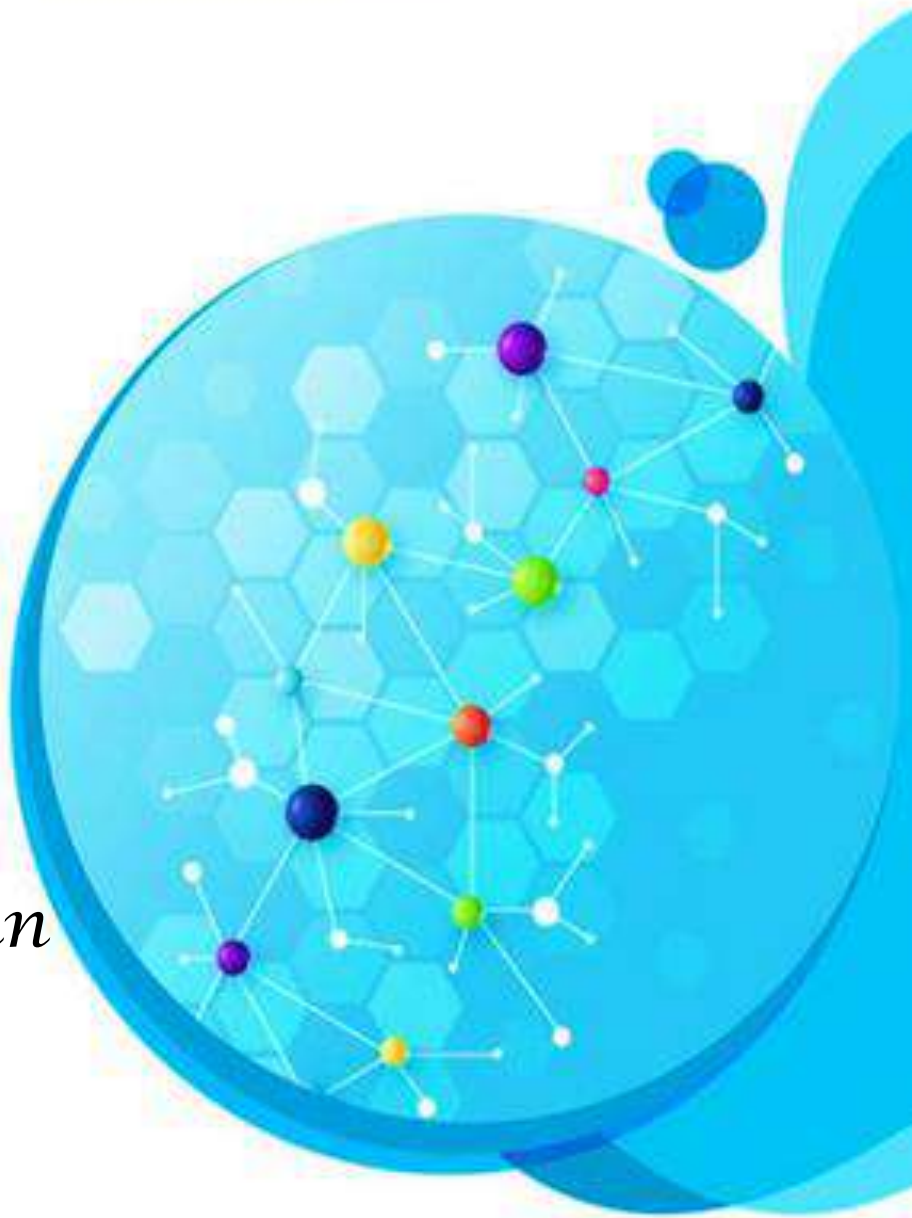
Faculty of Medicine

Al-Azhar University-Gaza



Contents

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- Chapter 3: Proteins of physiologic Importance
- Amino acids
- Peptides
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- Simple proteins
- Conjugated proteins
- Derived proteins

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Organic Functional groups

CATEGORY	FUNCTIONAL GROUP	GENERAL FORMULA	EXAMPLE
ALCOHOLS	$-OH$	$R-OH$	CH_3OH METHANOL
ETHERS	$-O-$	$R-O-R'$	CH_3OCH_3 *Dimethyl ether*
CARBOXYLIC ACIDS	$-\overset{O}{\overset{\|\|}{C}}-O-H$	$R-\overset{O}{\overset{\|\|}{C}}-O-H$	CH_3COOH *Acetic acid*
ESTERS	$-\overset{O}{\overset{\|\|}{C}}-O-$	$R-\overset{O}{\overset{\|\|}{C}}-O-R'$	CH_3COOCH_3 *Methyl acetate*
ALDEHYDES	$-\overset{O}{\overset{\|\|}{C}}-H$	$R-\overset{O}{\overset{\|\|}{C}}-H$	CH_3CHO *Acetaldehyde*
KETONES	$-\overset{O}{\overset{\|\|}{C}}-$	$R-\overset{O}{\overset{\|\|}{C}}-R'$	$CH_3CH_2COCH_3$ *methyl ethyl ketone*
AMINE	$-NH_2$	$R-NH_2$	CH_3NH_2 METHYLAMINE
AMIDE	$-\overset{O}{\overset{\|\|}{C}}-NH_2$	$R-\overset{O}{\overset{\|\|}{C}}-NH_2$	$CH_3CH_2CONH_2$ PROPYLAMIDE

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Chapter 1

Chemistry of carbohydrates

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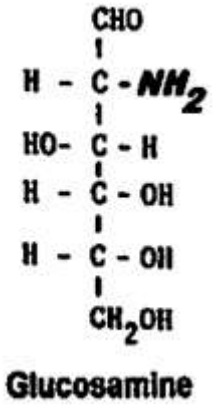
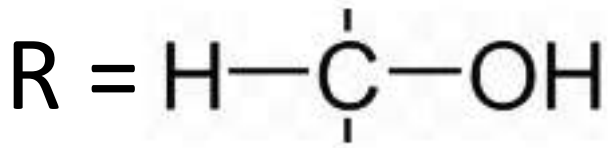
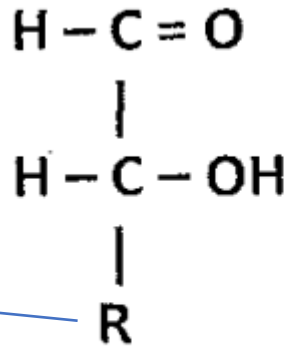
Definition: Carbohydrates (CHO) can be defined in deferent ways:

1. CHO are a large group of organic compounds composed of carbon, hydrogen, and oxygen atoms.
2. CHO are polyhydroxy aldehyde or ketone (simple sugar) or its derivatives.

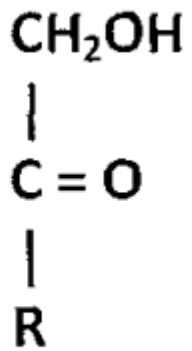


Glucosamine





Polyhydroxyaldehydes



Polyhydroxyketones

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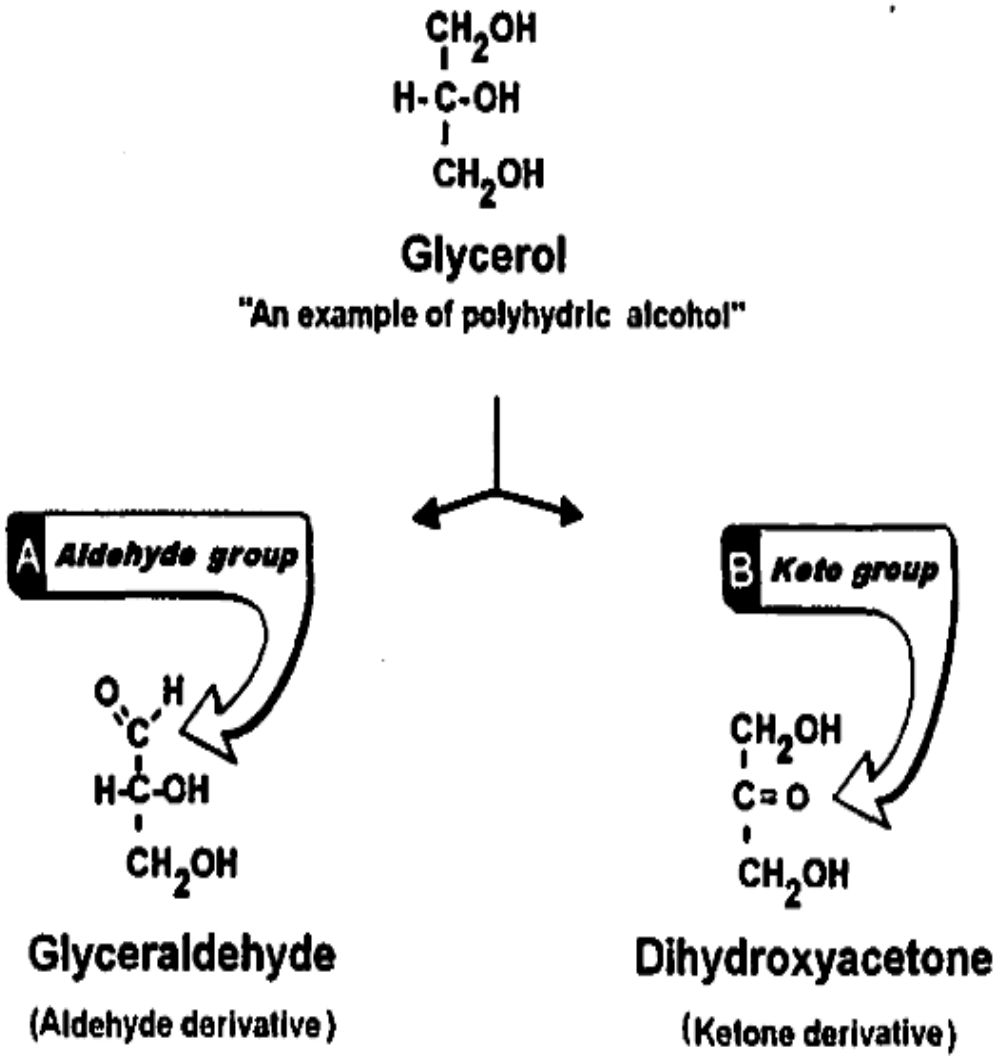
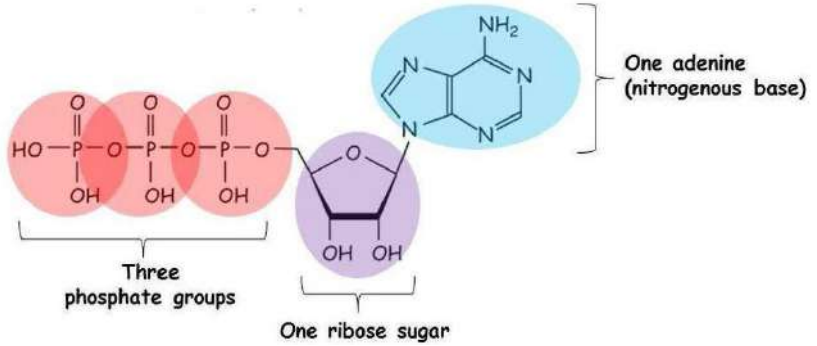
Definition: Carbohydrates (CHO) can be defined in deferent ways:

- CHO are aldehyde or ketone derivatives of polyhydric alcohols.
- Usually the ratio between Carbon & H_2O is 1. Hence the name carbohydrate



Importance of carbohydrates



1. Energy production e.g. glucose.
2. Formation of structural elements in animal and plant cells.
   - Formation of glycolipids (carbohydrates combined with lipids) and glycoproteins (carbohydrates combined with protein); both enter in the structure of cell membrane.

Classification of carbohydrates: according to the hydrolysis products

Monosaccharides	**contain a single unit (Can't be Hydrolyzed)**
Disaccharides	**contain two sugar units**
Oligosaccharide	**contain 3 - 10 sugar units**
Polysaccharides	• **contain more than 10 sugar units as in polymers** • **most contain glucose as the monosaccharide unit**

Monosaccharides (Single sugar units):

1. Glucose
2. Fructose
3. Galactose
4. Ribose
5. Deoxyribose

Disaccharides (Two monosaccharide units linked together):

1. Sucrose (Glucose + Fructose) - Common table sugar
2. Lactose (Glucose + Galactose) - Found in milk and dairy products
3. Maltose (Glucose + Glucose) - Produced during starch digestion

Oligosaccharides (Short chains of monosaccharide units, typically 3 to 10 sugar units):

1. Raffinose - Found in beans, and vegetables (cabbage).
   - Composed of three monosaccharide units (one molecule of galactose, one molecule of glucose, and one molecule of fructose)
2. Stachyose - Found in legumes
   - Composed of four monosaccharide units (Two molecules of galactose, One molecule of glucose, One molecule of fructose)

Polysaccharides (contain more than 10 sugar units):

1. Starch - A storage polysaccharide in plants, found in grains, and potatoes.
2. Glycogen - A storage polysaccharide in animals, stored in the liver & muscles.
3. Cellulose - A structural polysaccharide in plants, a major component of plant cell walls.

Monosaccharides

Monosaccharides

- Definition: They are the simplest units of carbohydrate containing one sugar unit.
- General formula is: $Cn(H_2O)n$.
- The general formula for glucose is $\mathbf{C_6H_{12}O_6}$. This means that each glucose molecule contains 6 carbon atoms, 12 hydrogen atoms, and 6 oxygen atoms.

Monosaccharides

Naming (nomenclature) of monosaccharides

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Naming of monosaccharides according to the presence of aldehyde or ketone group:

1. Aldoses: monosaccharides containing aldehyde group (-CHO).

2. Ketoses: monosaccharides containing ketone group (-C=O).

The suffix -ose means sugar.

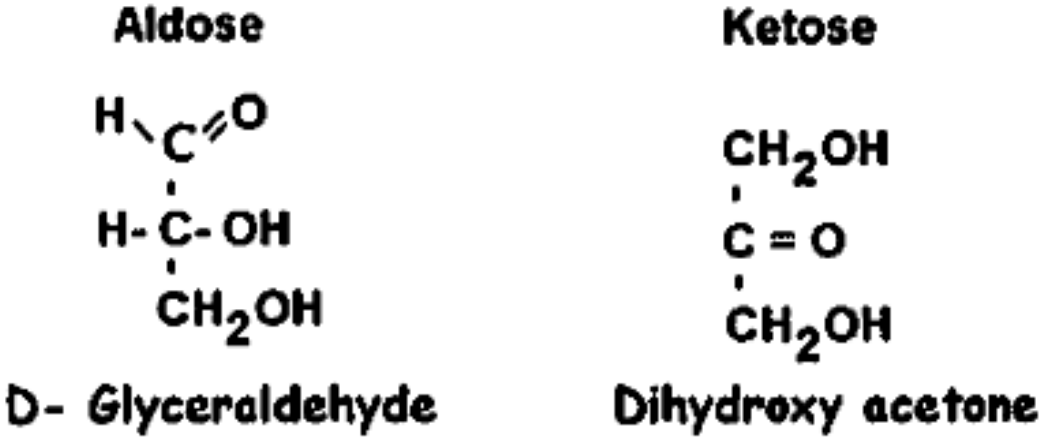
Naming of monosaccharides according to the Number of Carbon atoms:

Sugar	No. of Carbons	Includes
Trioses	3	Aldotrioses and ketotrioses
Tetroses	4	Aldotetroses and ketotetroses
Pentoses	5	Aldopentoses and ketopentoses
Hexoses	6	Aldohexoses and ketohexoses

Trioses: monosaccharides containing 3 carbons

1. Aldotriose: Glyceraldehyde "glycerose".
2. Ketotrioses: Dihydroxyacetone

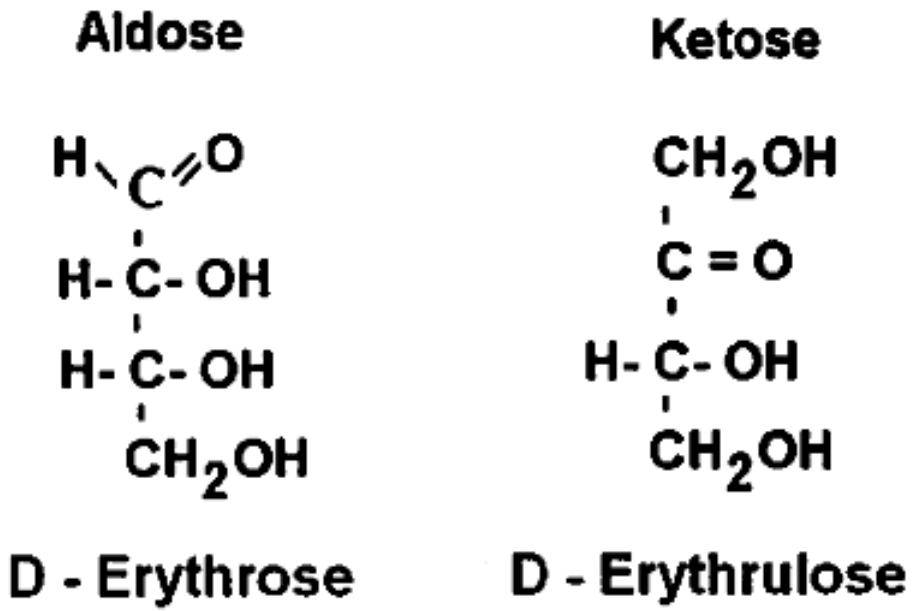
- Glyceraldehyde and dihydroxyacetone are the simplest sugars.
- Each of them contains only three carbon atoms (C3) in their molecular structure.



Tetroses: monosaccharides containing 4 carbon atoms:

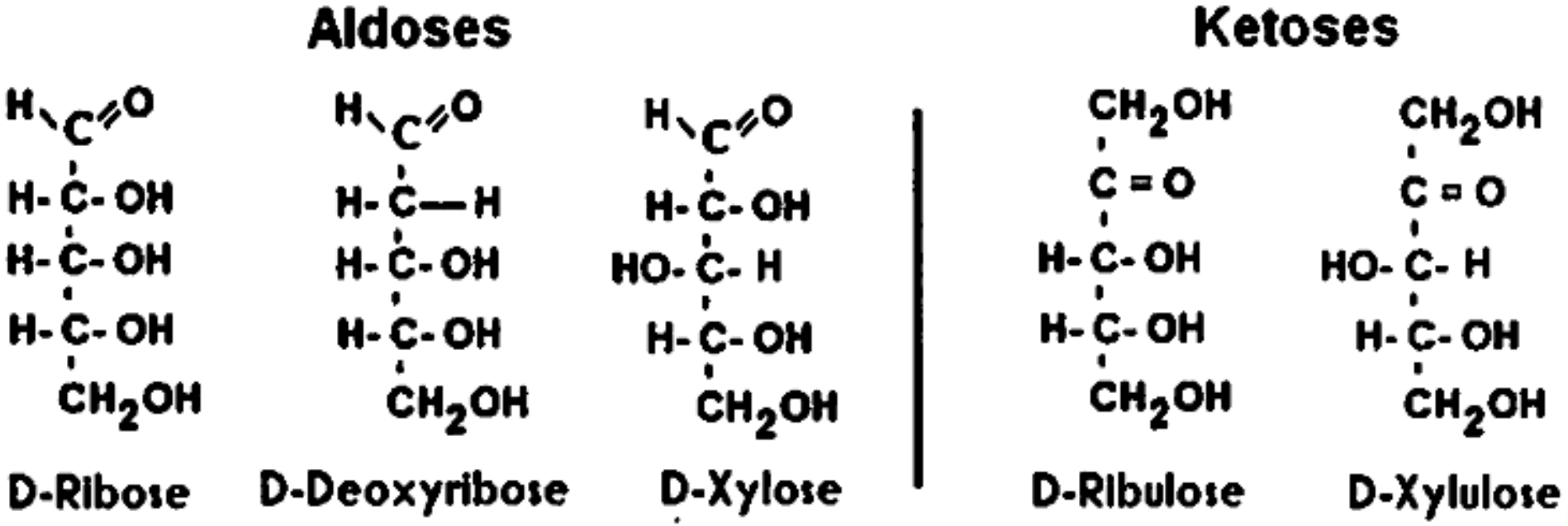
1. Aldotetroses: Erythrose.
2. Ketotetrose: Erythrulose.

- Note: The suffix –ulose means Keto group.



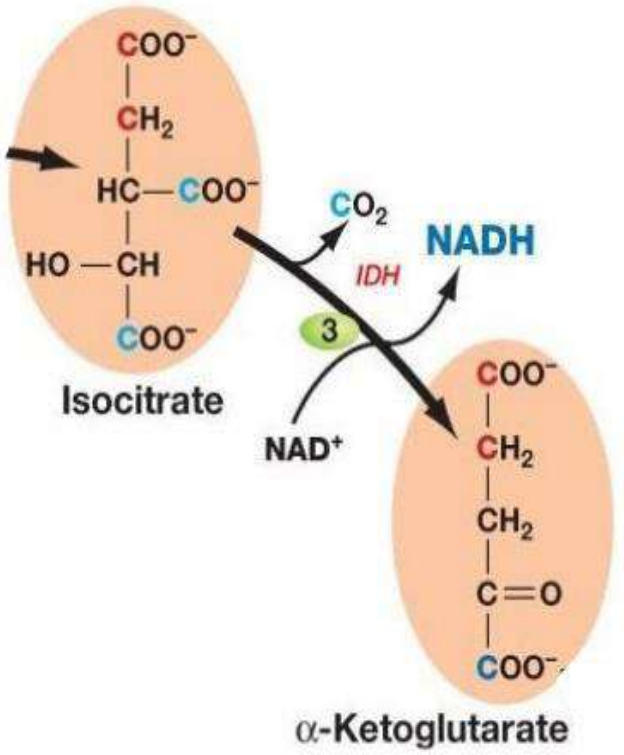
Pentoses: monosaccharides containing 5 carbon atoms.

- Aldopentoses: Ribose, arabinose, xylose and lyxose.
- Ketopentoses: Ribulose and xylulose.



Importance (functions) of Ribose

1. Enter in the structure of nucleic acids (RNA and DNA)
2. Enters in the structure of ATP, GTP.
3. Enters in the structure of coenzymes NAD, NADP and FAD.



Important Note: Arabinose and xylose are constituents of glycoproteins In plants and in animals.

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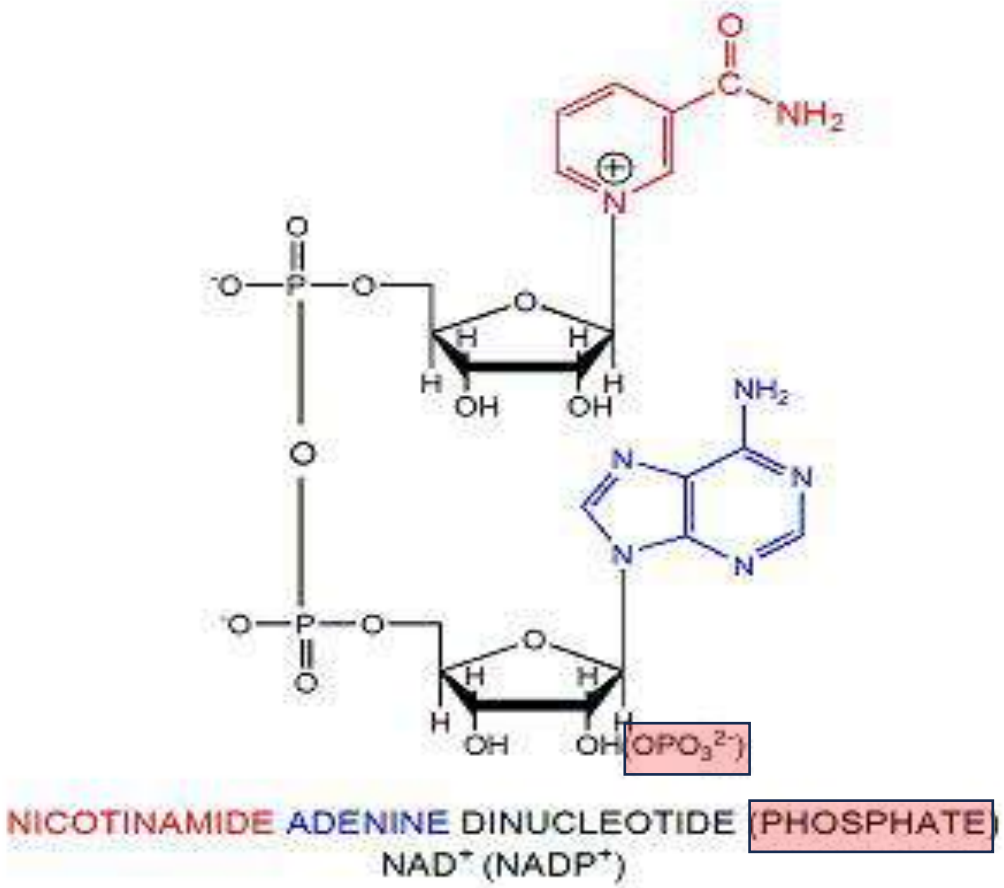
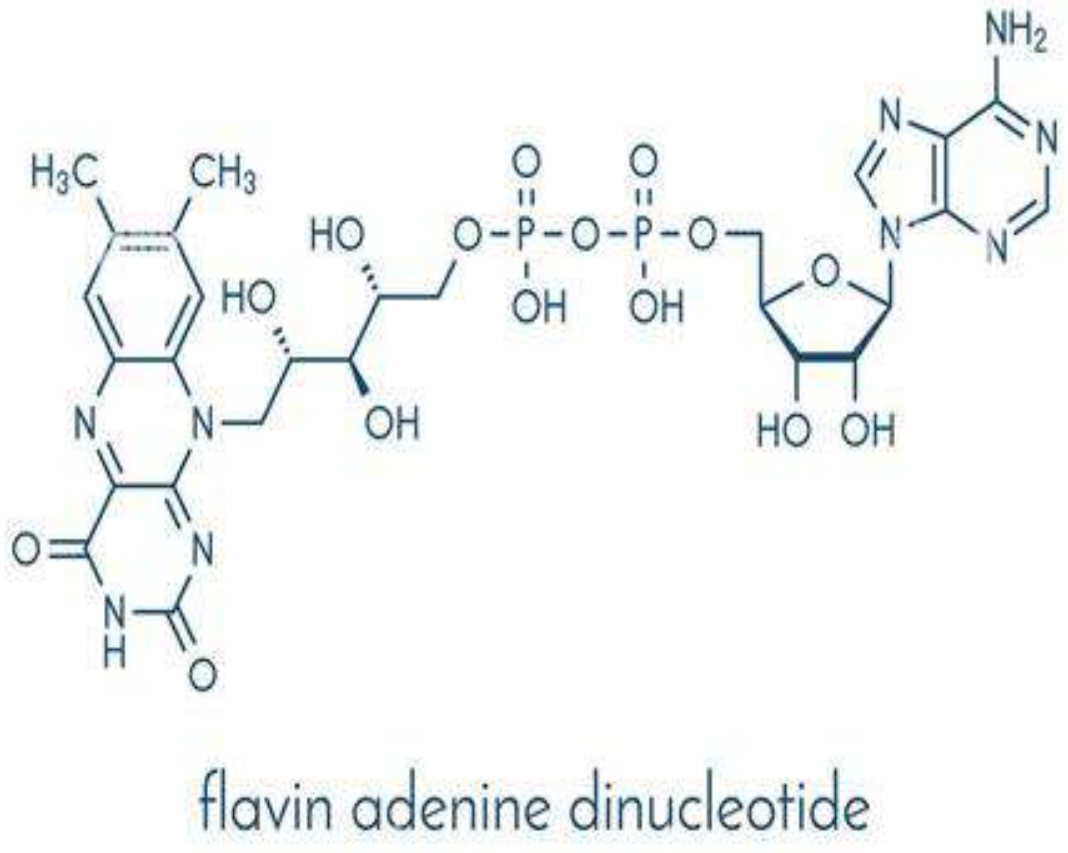
- **Nicotinamide adenine dinucleotide (NAD+)**
- **Flavin adenine dinucleotide (FAD+)**

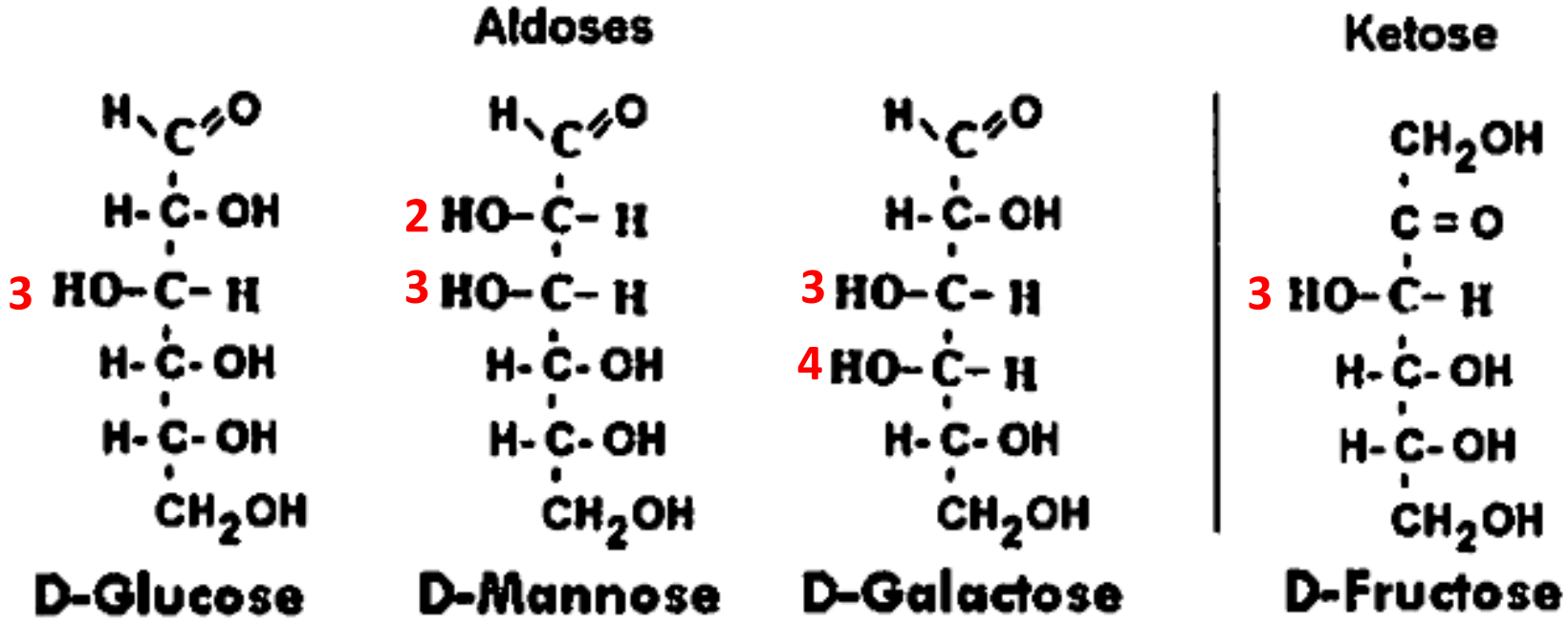




Hexoses: monosaccharides containing 6 carbon atoms

1. Aldohexose: glucose, mannose and galactose.

2. Ketohexose: fructose.



Importance (functions) of Glucose

1. Glucose: “grape sugar” is the most important sugar of carbohydrate.
2. Glucose is the main sugar in blood
3. Glucose is one of major sources of energy in the body.
4. In the liver, glucose is converted to all carbohydrates in the body e.g. glycogen, galactose,

Importance (functions) of Galactose

1. It can be converted into glucose in the liver.
2. It is synthesized in mammary gland to make the lactose of milk (milk sugar)

Importance (functions) of Fructose

1. Fructose "fruit sugar":
2. It can be converted into glucose in the liver.
3. It is the main sugar of semen.

Importance (functions) of Mannose

1. constituent of many glycoproteins.

THANK YOU

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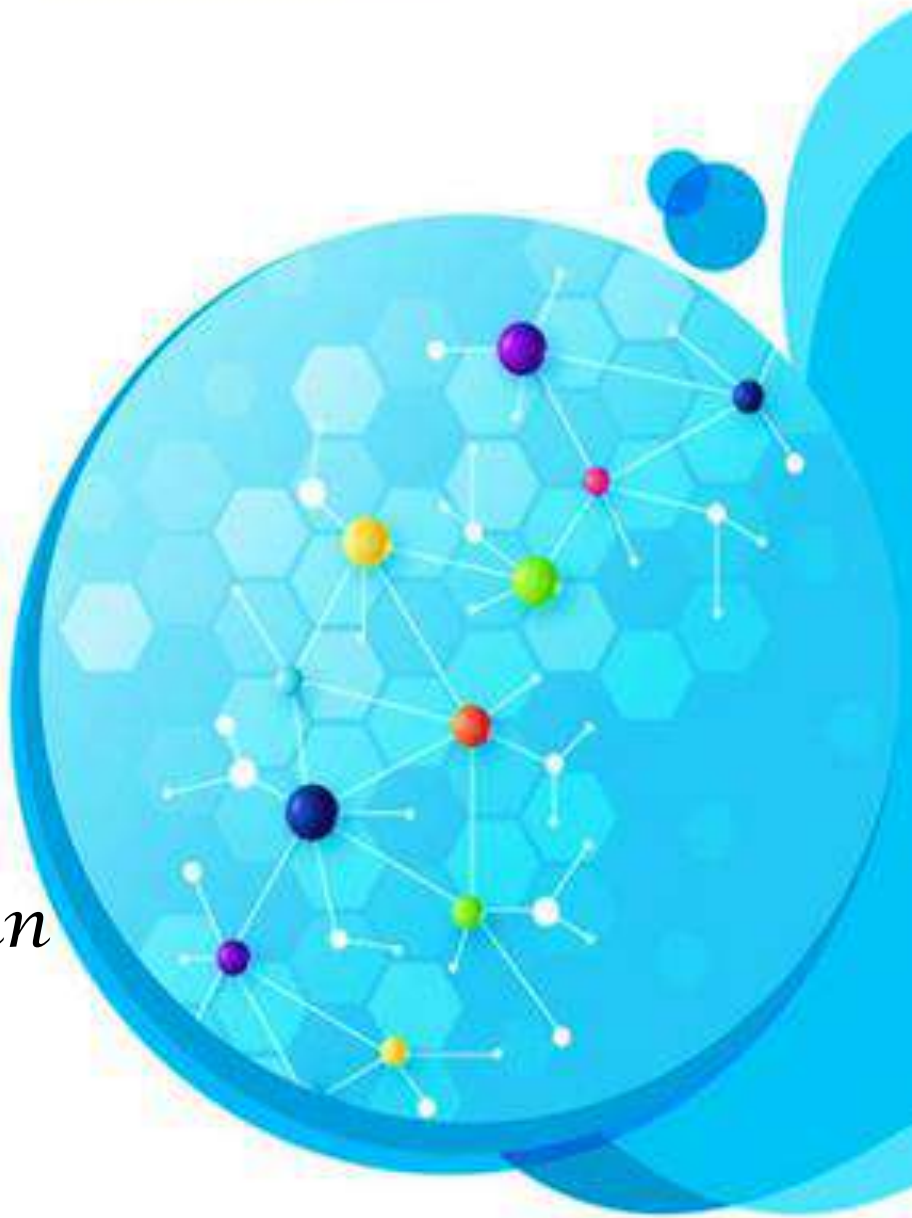

Monosaccharides

Properties of monosaccharides

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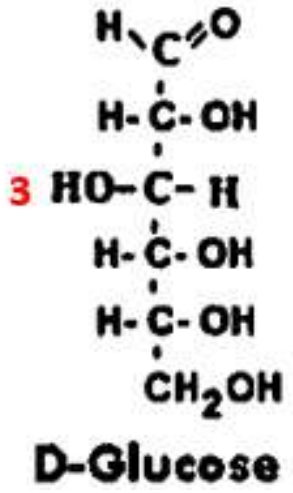
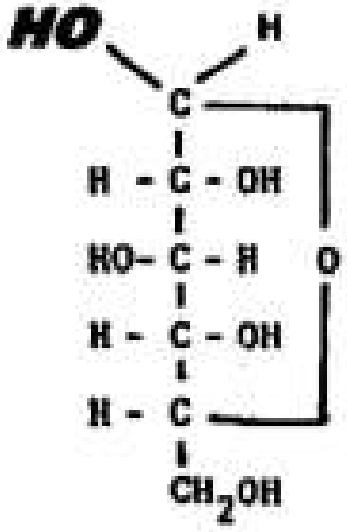
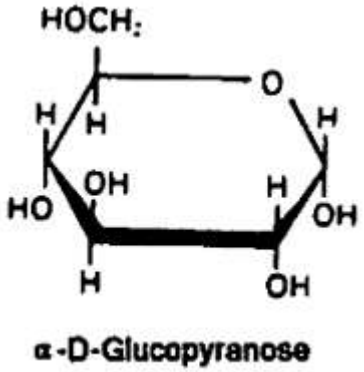
Ring (cyclic) structure

- In aqueous **solution, Monosaccharides** with **five or more carbon atoms**, such as **pentoses** and **hexoses**, commonly form **ring structures**.



open-chain (linear) form



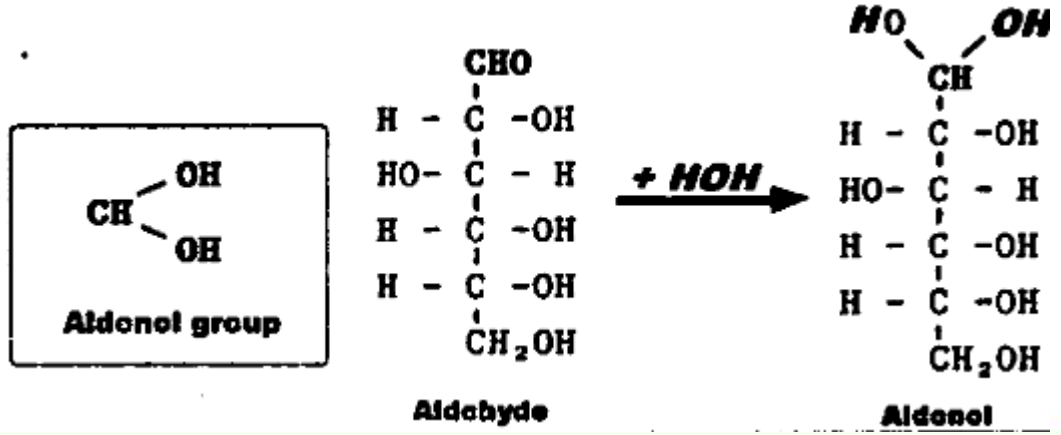


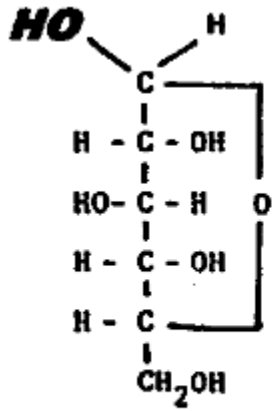
Ring (cyclic) structure

Ring (cyclic) structure of Glucose

- In solution, Glucose has an aldehyde group undergoes the following:

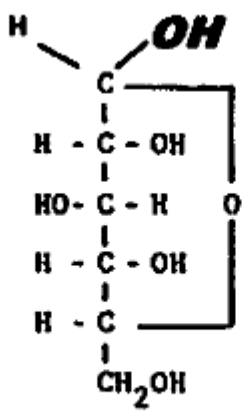
1. **Hydration of aldehyde group to form aldenol group (alcohol).**





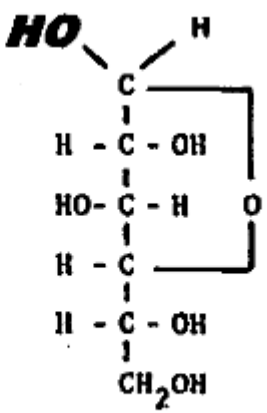
β - Glucose

(1-5 ring form)



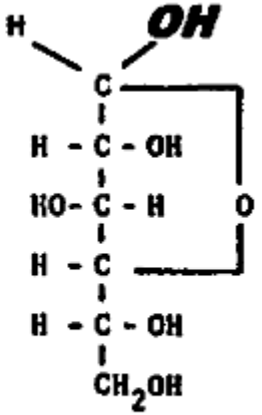
α - Glucose

(1-5 ring form)



β - Glucose

(1-4 ring form)



α - Glucose

(1-4 ring form)

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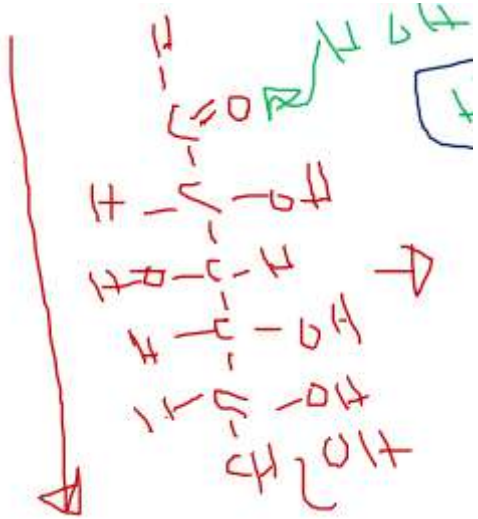
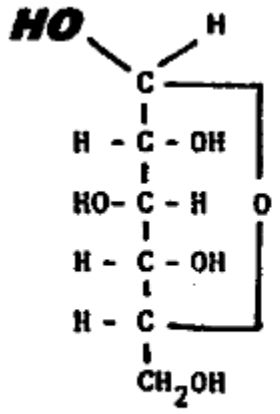
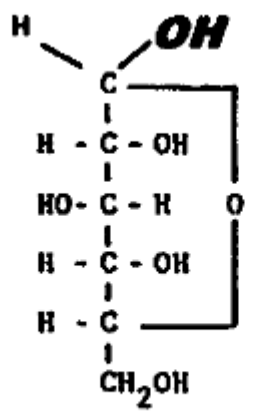
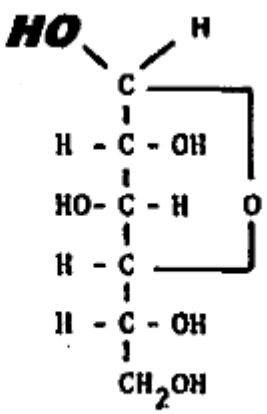




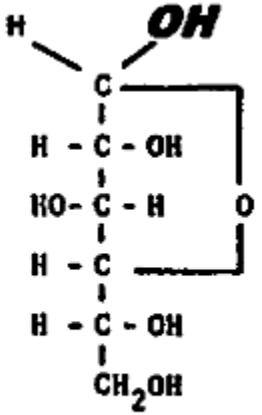
β - Glucose
(1-5 ring form)



α - Glucose
(1-5 ring form)



β - Glucose
(1-4 ring form)



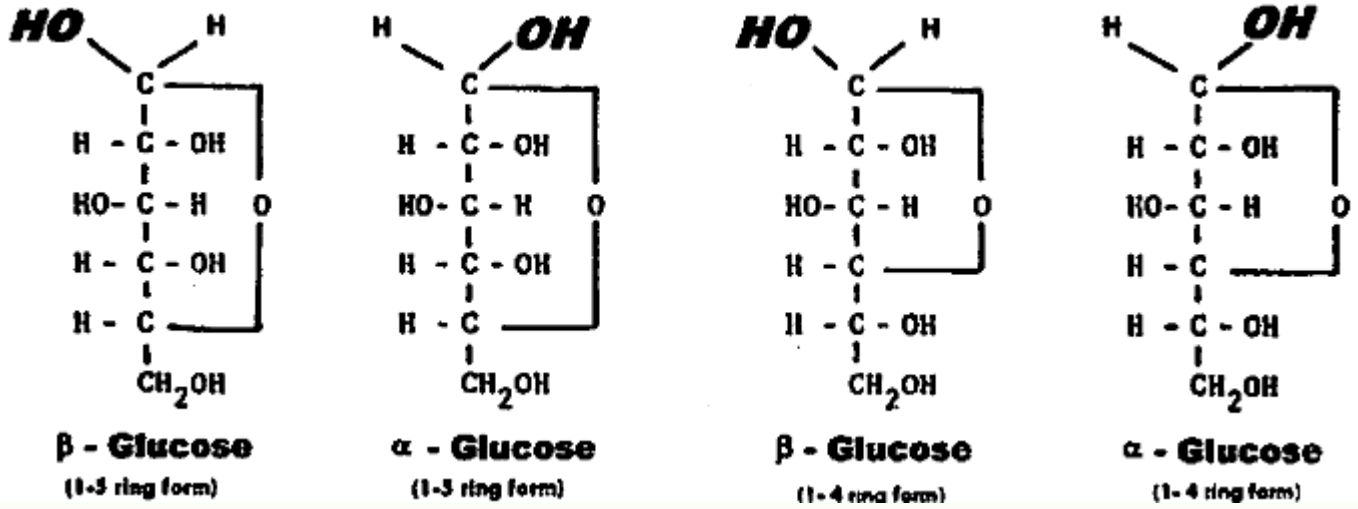
α - Glucose
(1-4 ring form)

Ring (cyclic) structure of Glucose

2. **Intra-molecular reactions (condensation) occur between one of the -OH of aldenol group and the -OH group of C4 or C5 to form ring structure.**
3. **If the remaining -OH is on the right side, it is α -sugar.**
4. **If the remaining -OH is on the left side, it is β- sugar.**

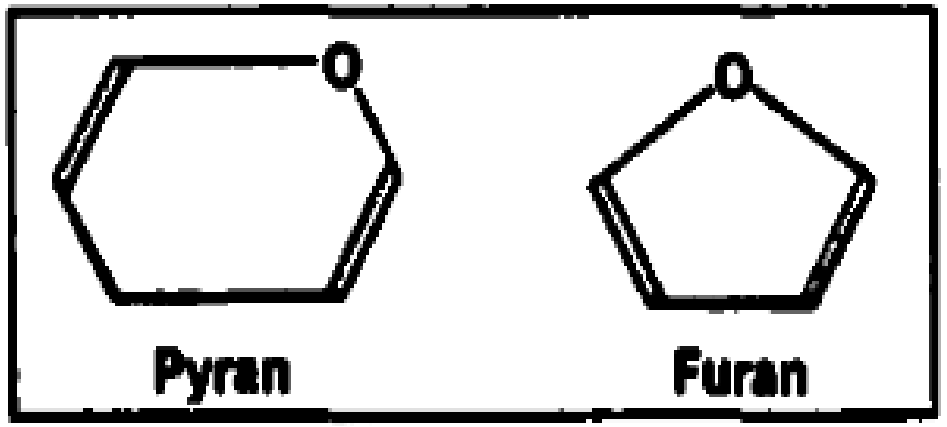
Old pyranose form

5. All the -OH groups on the right side are written downwards.
6. All the -OH groups on the left side are written upwards



Ring (cyclic) structure of Glucose

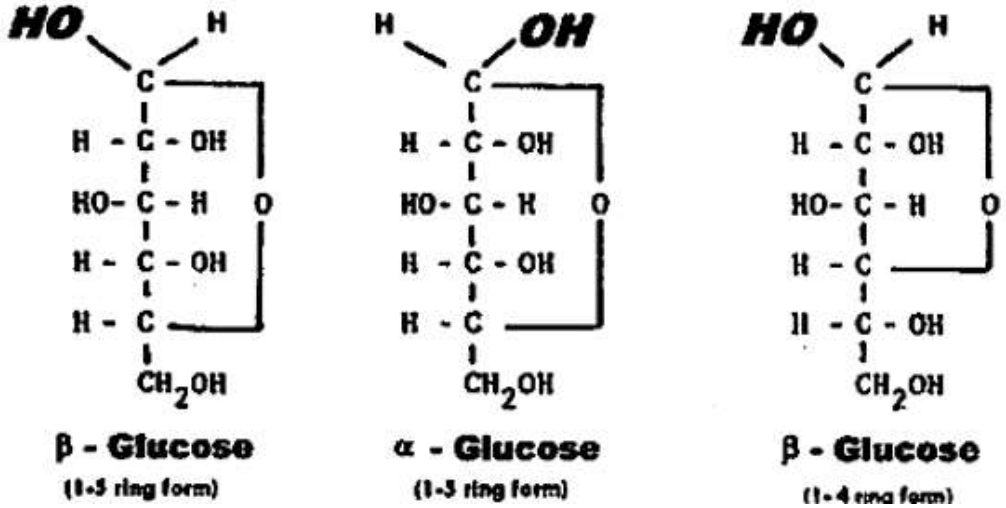
2. **The 1-5 ring form is called pyranose as it resembles an organic compound called pyran e.g. α and β glucopyranose**
3. **The 1-4 ring form is called furanose as It resembles an organic compound called furan e.g. α and β glucofuranose.**



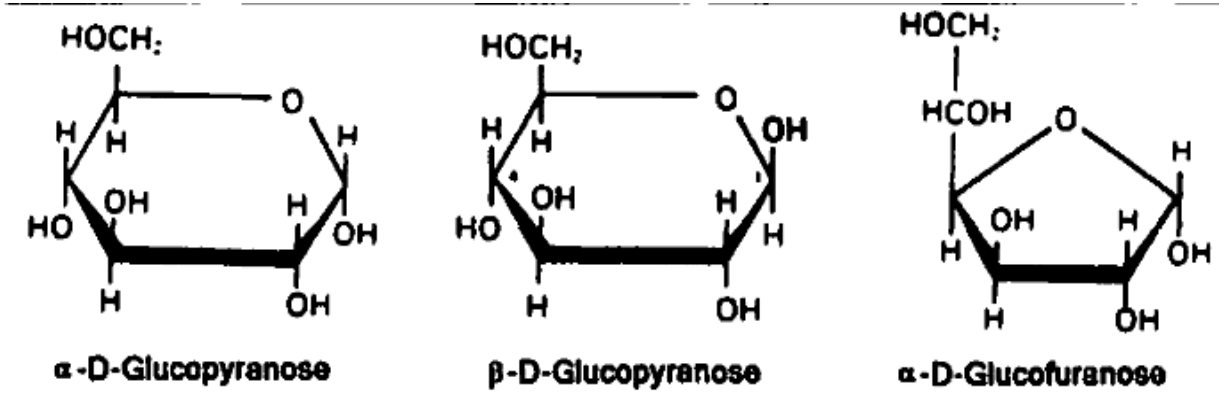
Ring (cyclic) structure of Glucose

5. All the -OH groups on the right side are written downwards.
6. All the -OH groups on the left side are written upwards

Old pyranose form



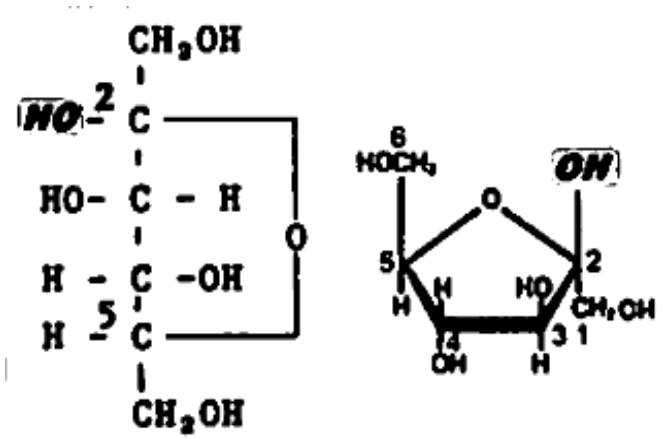
Haworth pyranose form



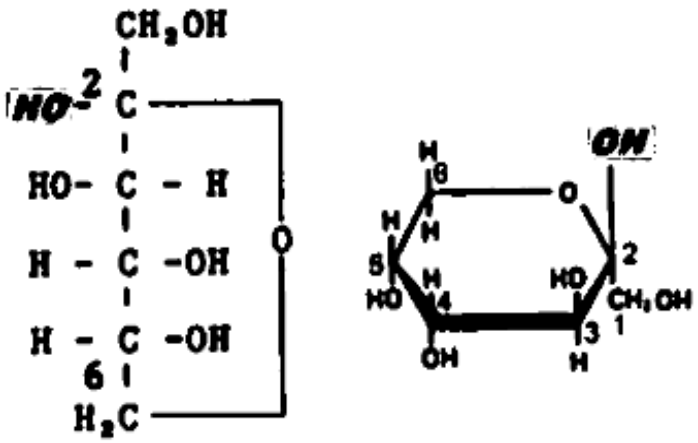
Formation of Fructose's Ring Structure:

- Fructose is a **ketohexose**, in its linear form, the carbonyl group (C=O) at **C-2** reacts with the hydroxyl group (-OH) at either **C-5** or **C-6**, depending on the type of ring that forms.

Ring (cyclic) structure of Fructose

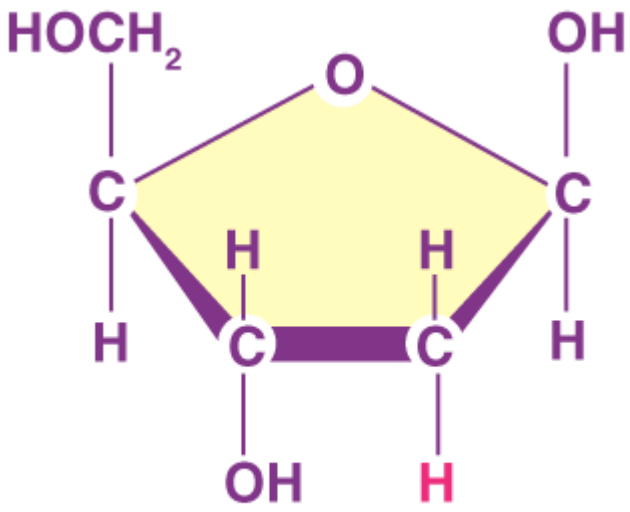


β – D – Fructofuranose
(2-5)

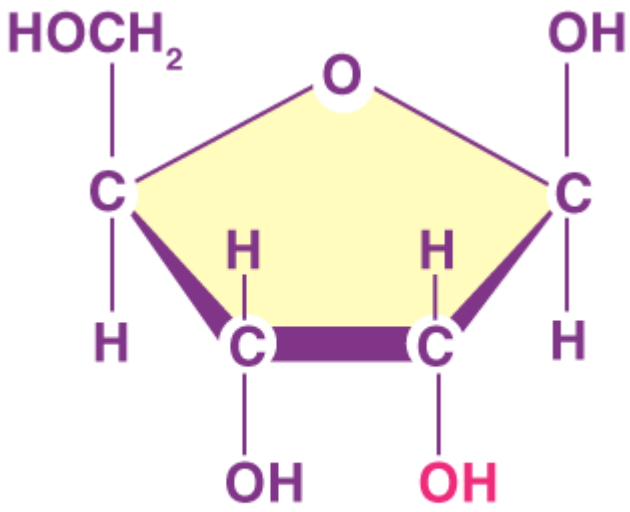


β – D – Fructopyranose
(2-6)

Ring (cyclic) structure of Ribose



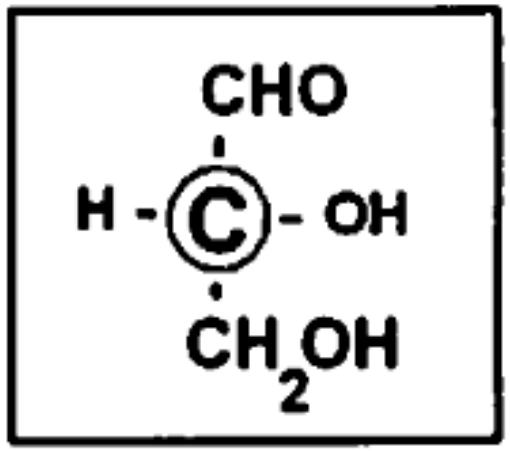
2- Deoxyribose

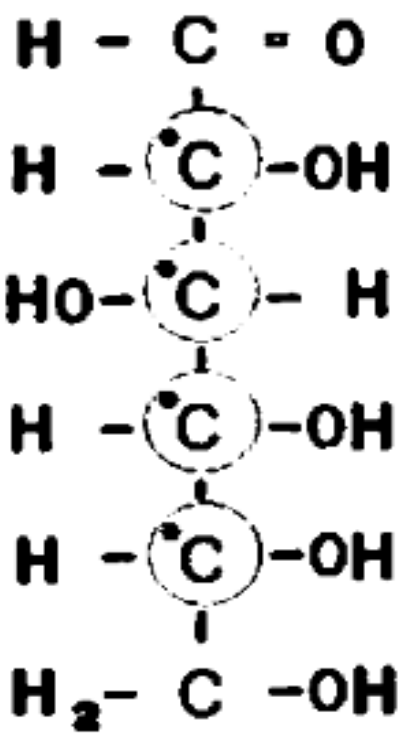


Ribose

Asymmetric carbon atom (chiral center)

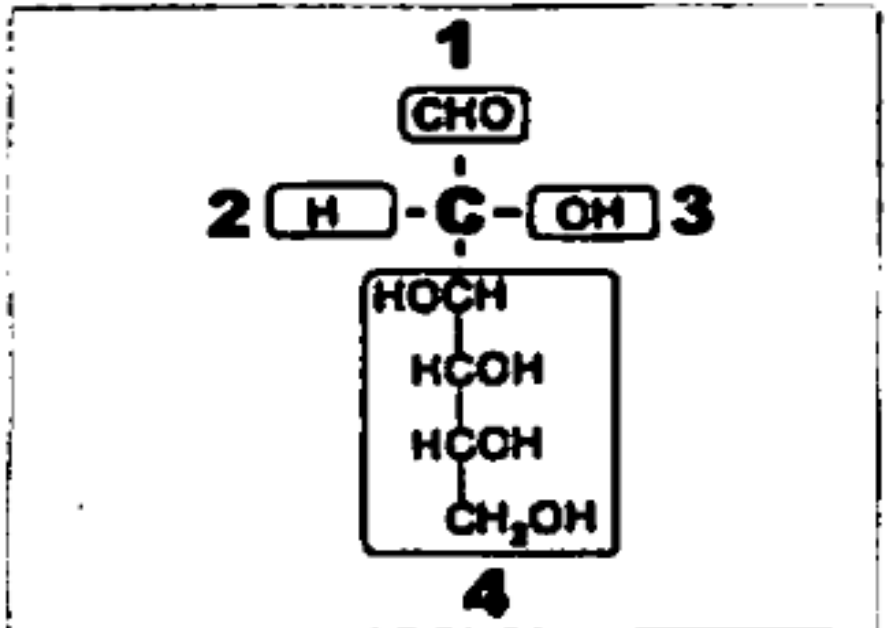
- Asymmetric carbon atom is the carbon atom to which 4 different groups or atoms are attached.
- Any substance containing asymmetric carbon atom shows 2 properties, optical activity and optical isomerism.



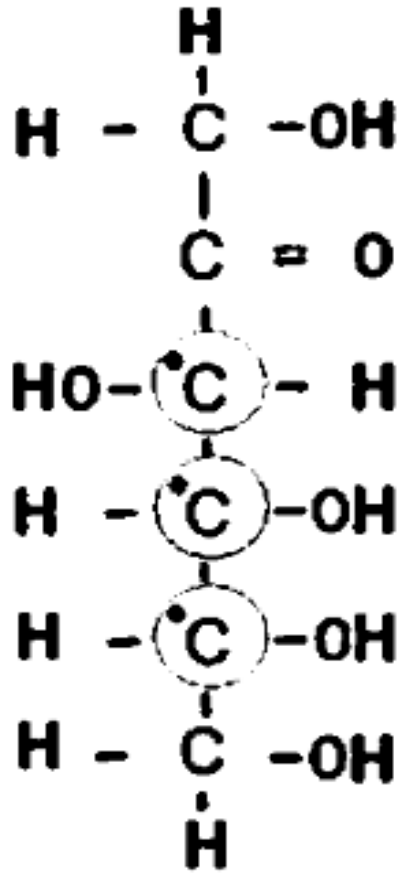


Glucose

*4 carbons labeled with
● are asymmetric*



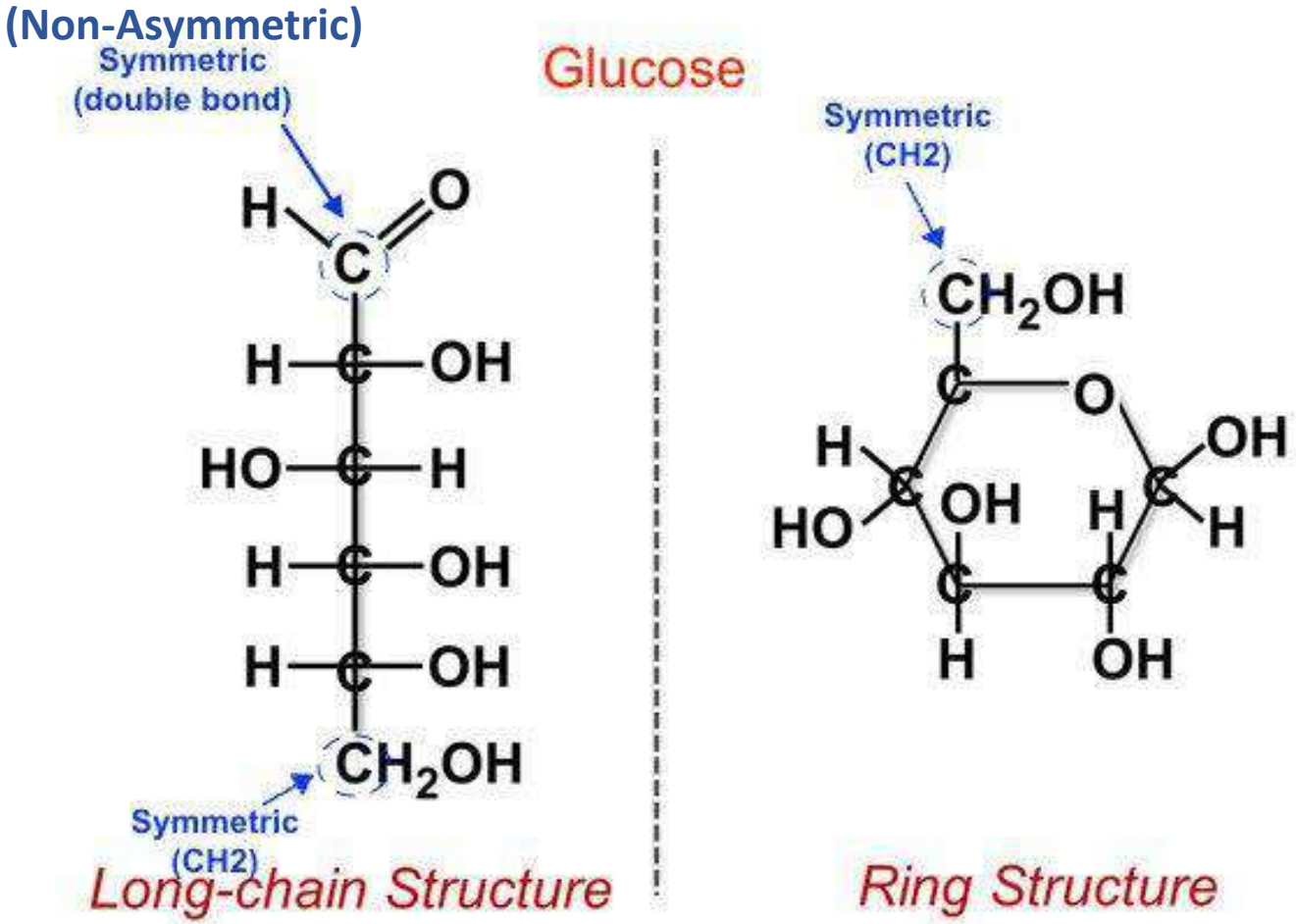
Representation of four different chemical groups attached to carbon #2 of glucose.



Fructose

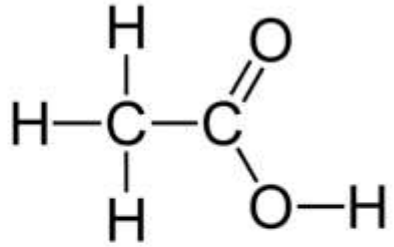
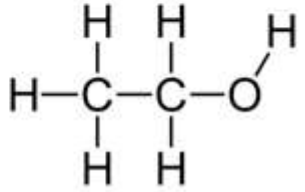
*3 carbons labeled with
● are asymmetric*

Asymmetric carbon atom (chiral center)



Molecular and structural formulas

- **Molecular formulas** give the kind and number of atoms of each element present in a molecular compound.
- **A structural formula** displays the atoms of the molecule in the order they are bonded.

Compound	Molecular Formula	Structural Formula
Acetic Acid	$C_2H_3O_2$	
Ethyl Alcohol	C_2H_6O	

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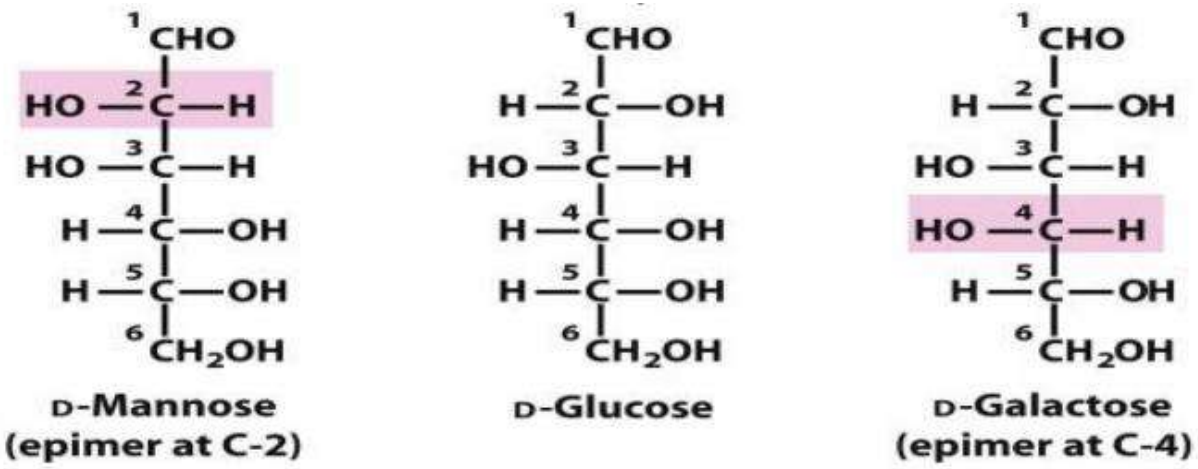
Isomers, epimers and Enantiomers

- Isomers are compounds that have the same chemical formula but different structures.
- For example, fructose, glucose, mannose, and galactose all have the same chemical formula, $C_6H_{12}O_6$, with different structures.

Epimers

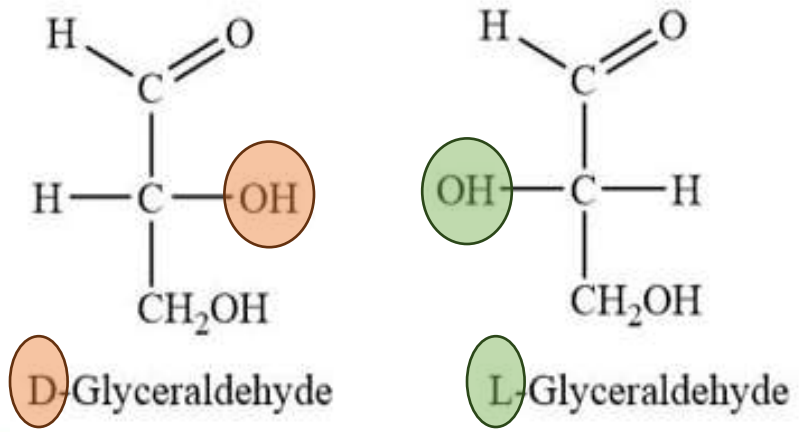
- Epimers are isomers having more than asymmetric carbon, all are same except only one is different.

    1. Glucose & Mannose are epimers at carbons 2.
    2. Glucose & Galactose are epimers at carbons 4



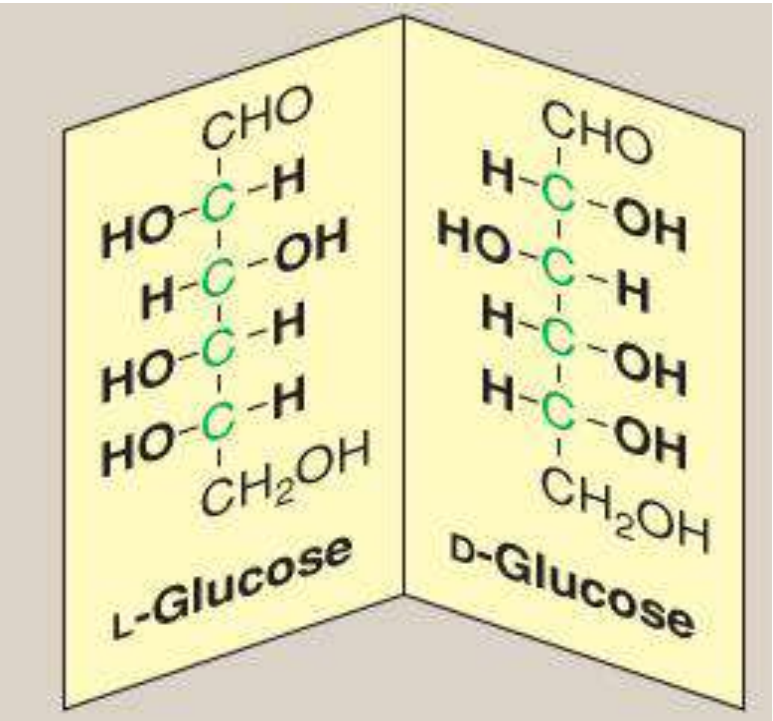
Enantiomers: D Vs L Designation

- A special type of isomerism is found in the pairs of structures that are mirror images of each other.
- D & L designations are based on the configuration about the single asymmetric C in glyceraldehyde.



Enantiomers: D Vs L Designation

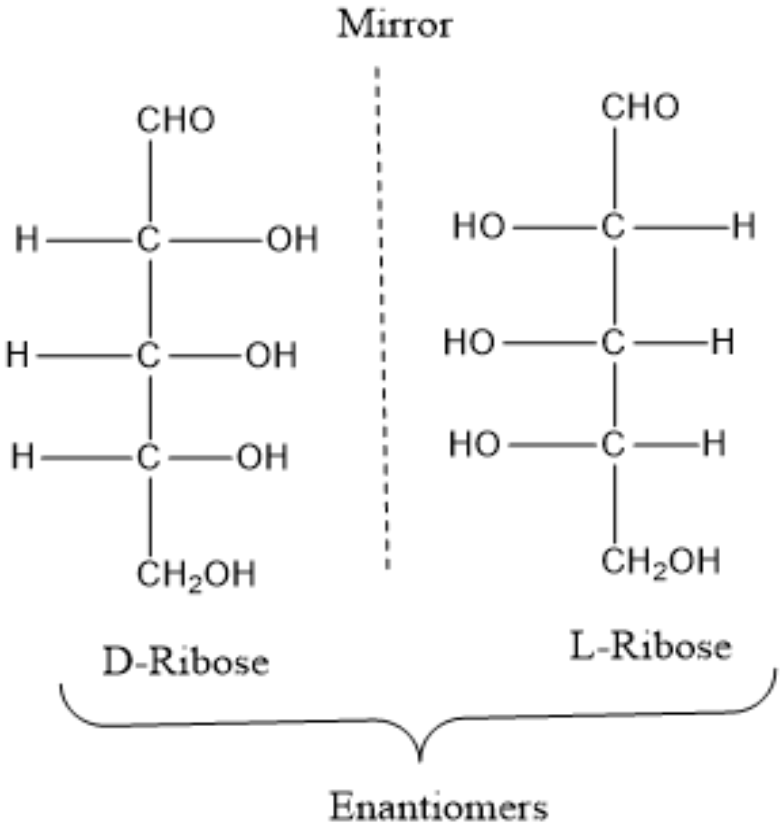
- For sugars with more than one chiral center, D or L refers to the asymmetric C farthest from the aldehyde or keto group.
- For example: They have the Same Name , e.g., D-glucose & L-glucose.

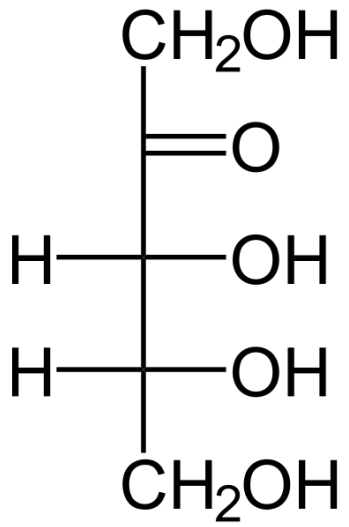


Enantiomers: D Vs L Designation

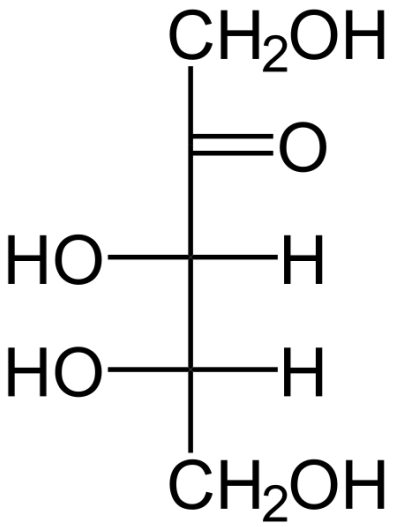
- The vast majority of the sugars in humans are D-isomers.
- In the D-isomeric form, the –OH group on the asymmetric carbon farthest from the carbonyl carbon is on the right, whereas in the L-isomer, it is on the left.
- Most enzymes are specific for either the D or the L form, but enzymes known as isomerases are able to interconvert D- and L-isomers.

Enantiomers: D Vs L Designation





D-Ribulose

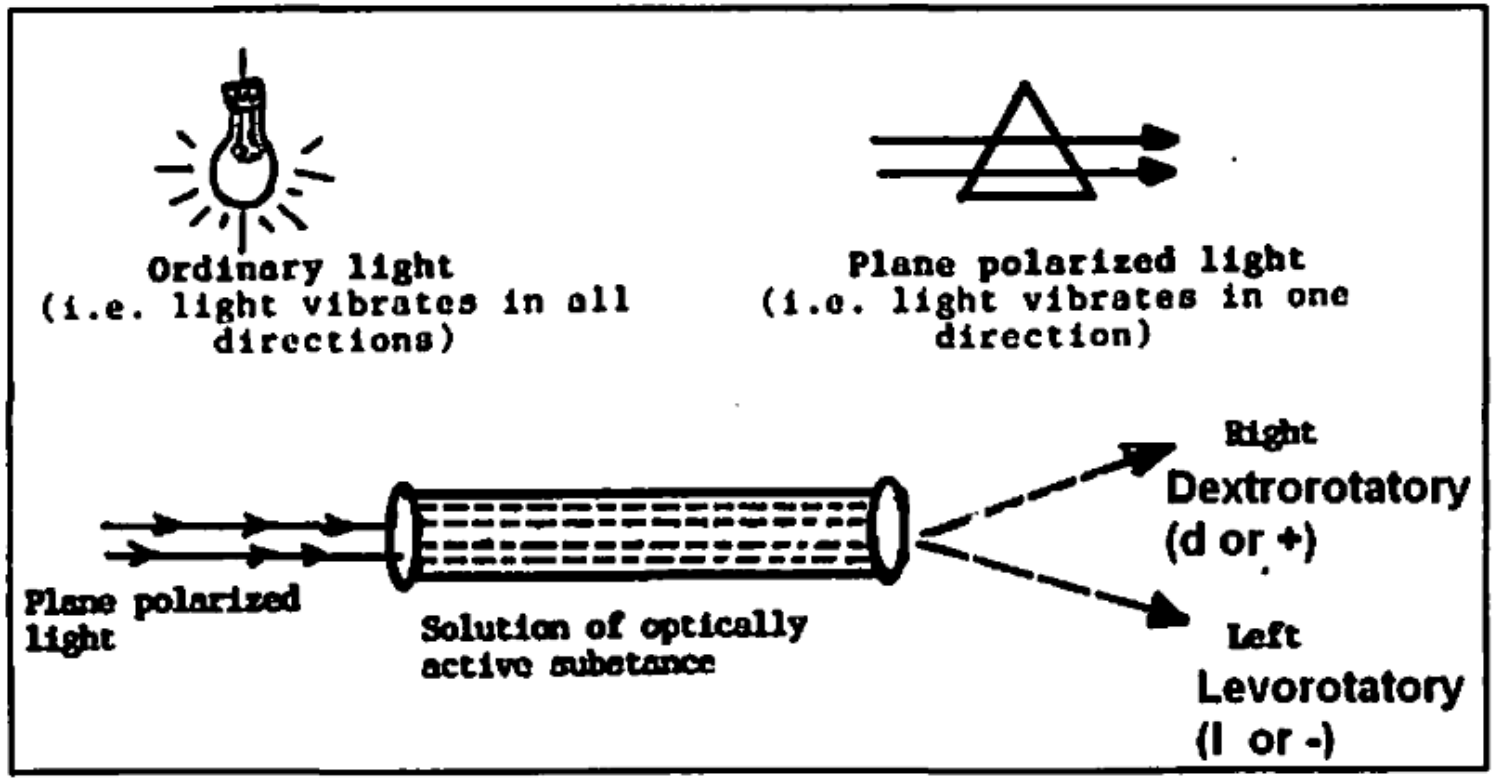


L-Ribulose

Optical activity

- It is the ability of substance to rotate plane-polarized light either to the right or to the left.

Polarimeter



Optical activity

- If the substance rotates plane polarized light to the right called: dextrorotatory or d or (+).
- If it rotates it to the left called: levorotatory or "l" or (-).

Optical activity

- D-Glucose
    1. It contains 4 asymmetric carbon atoms.
    2. It is dextrorotatory, so it is sometimes named dextrose.
- D-Fructose
    1. It contains 3 asymmetric carbon atoms.
    2. It is levorotatory so it is sometimes called: Levulose.

Optical activity

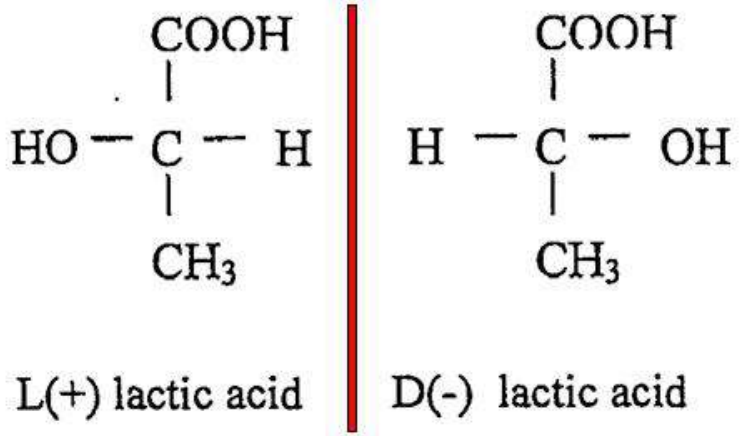
- The direction of rotation is independent of the stereochemistry of the sugar, so it may be designated D(-), D(+), L(-), or L(+).
- For example, the naturally occurring form of fructose is the D(-) isomer.

Optical isomers

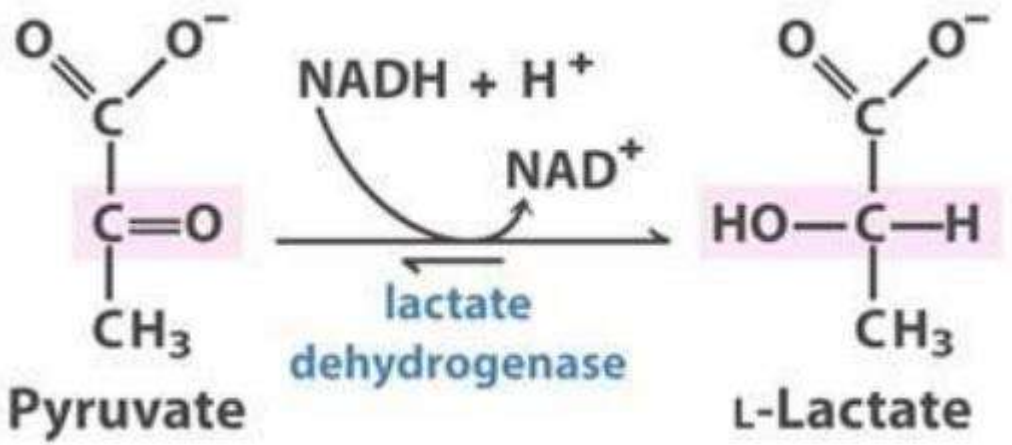
- L(+) Lactic acid and D(-) Lactic acid are optical isomers and

  Enantiomers because they differ in their:

  1. Ability to rotate plane-polarized light
  2. The position of OH group on the asymmetric carbon farthest from the functional group.

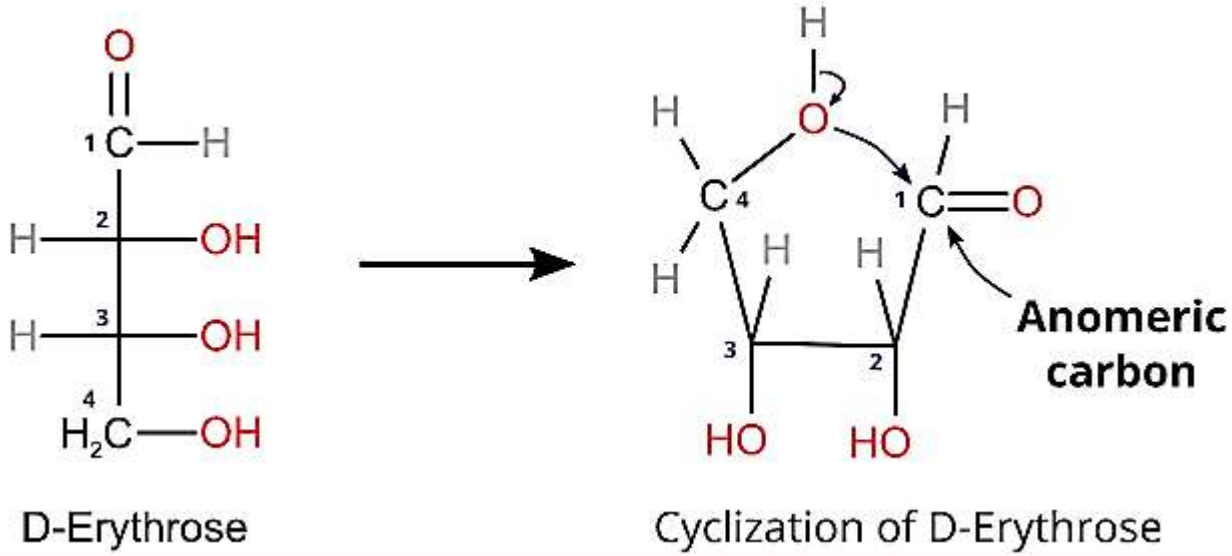


NOTE: Muscle cells convert pyruvate into lactate under anaerobic conditions



Anomeric carbons & anomers:

- In ring structure:
- Anomeric carbon: Formation of a ring results in the creation of an anomeric carbon at carbon 1 of an aldose or at carbon 2 of a ketose.

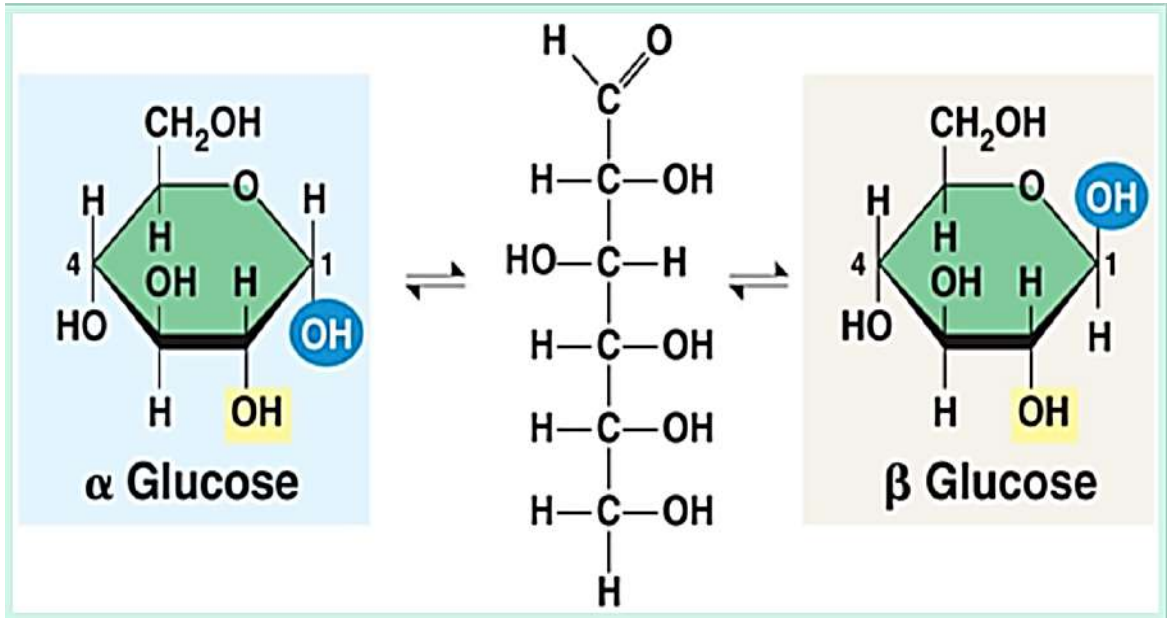


D-Erythrose

Cyclization of D-Erythrose

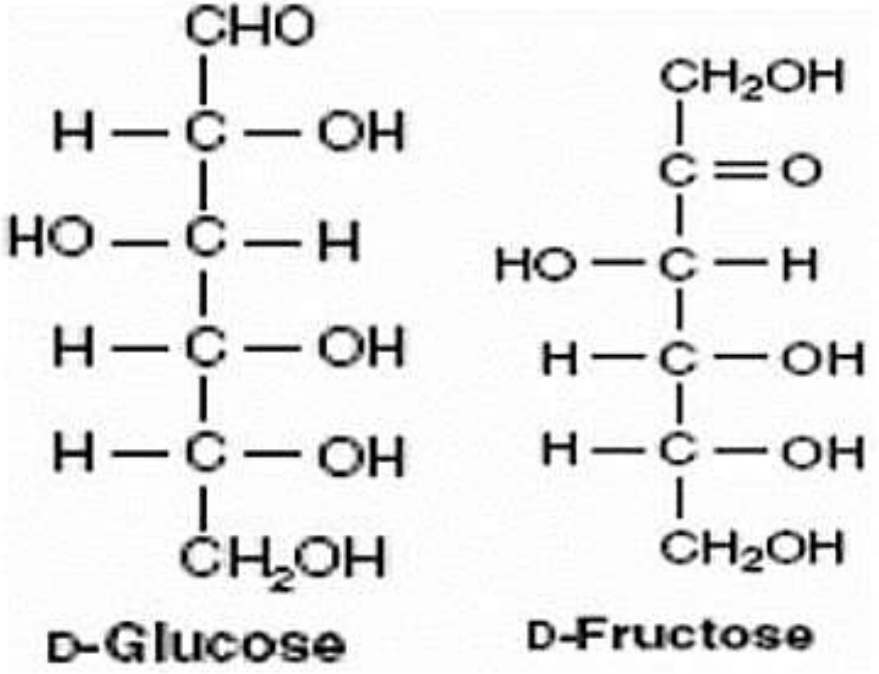
Anomeric carbons & anomers:

- Anomers: These are isomers obtained from the change of position of hydroxyl group attached to the anomeric carbon e.g. α and β glucose are 2 anomers.
- Also α and β fructose are 2 anomers.



Aldose-Ketose isomerism:

- Also kwon as (functional group isomerism): Have the same molecular formula but differs in functional group.
- EX: Fructose & glucose
  - One contains Ketone group (C=O) and the other contains aldehyde group (CHO).
  - Both are isomers.



THANK YOU

M.ELEYAN

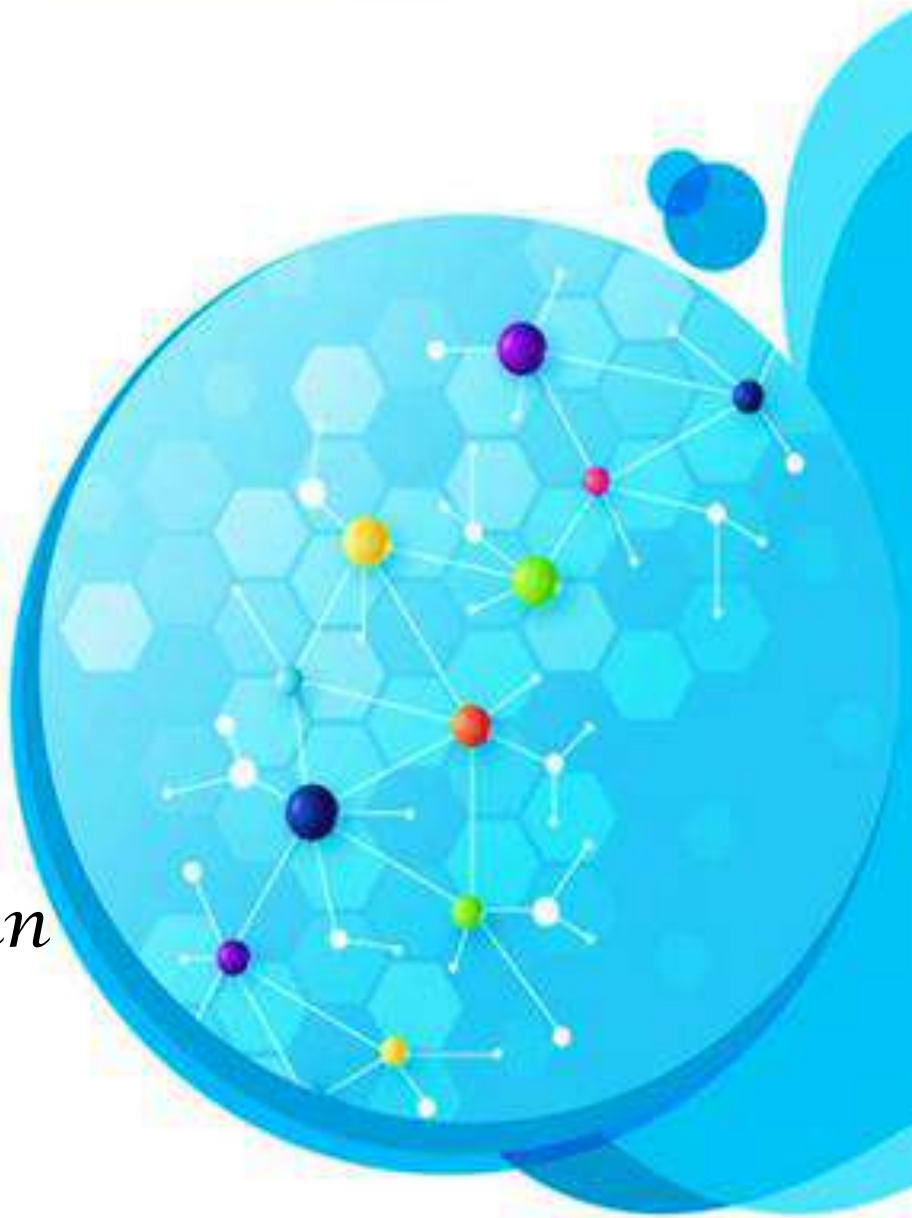
Medical Biochemistry

Carbohydrate Chemistry

Asst. Prof.Mohammed Hasan Eleyan

Faculty of Medicine

Al-Azhar University-Gaza



Properties of monosaccharides:

Chemical properties of monosaccharides :

Oxidation and reduction

Oxidation	Reduction
Addition of oxygen	Removal of oxygen
Removal of hydrogen	Addition of hydrogen
Loss (removal) of electrons	Gain of (Addition) of electrons

Sugar derivatives

- Sugar acids
- Sugar alcohols
- Inositol
- Deoxy sugars
- Amino sugars

Sugar derivatives

Sugar acids

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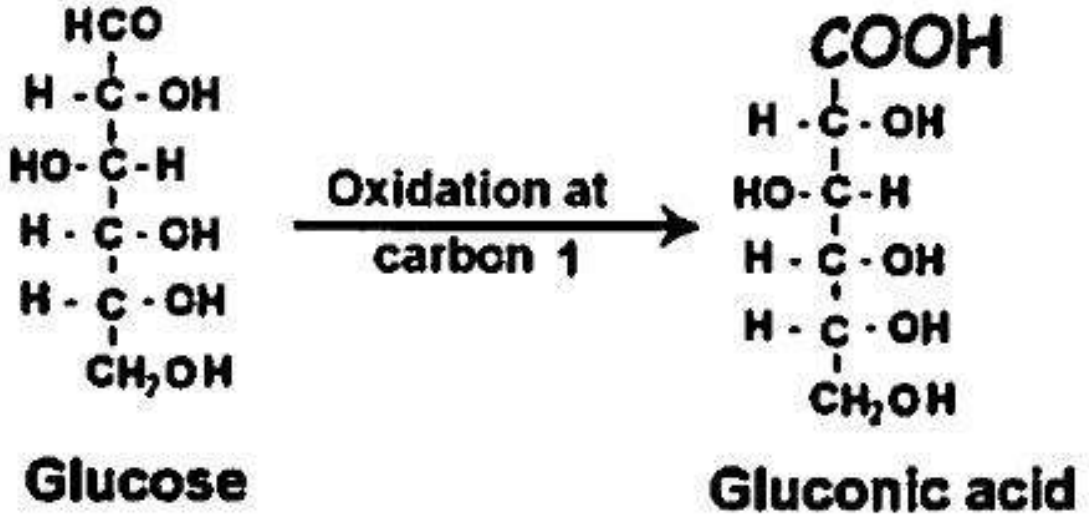
Sugar acids

- Are produced by oxidation of carbonyl carbon, last carbon or both.

Carbonyl carbon	Aldonic acid	Glucose	gluconic acid
Last hydroxyl carbon	uronic acid	Glucose	glucuronic acid
BOTH	Aldaric acids	Glucose	Glucaric (saccharic) acid

1.1. Aldonic acids

- Oxidation of the aldehyde group of an aldose sugar to a carboxylic acid group results in the formation of an aldonic acid.
- e.g. glucose is oxidized to gluconic acid.

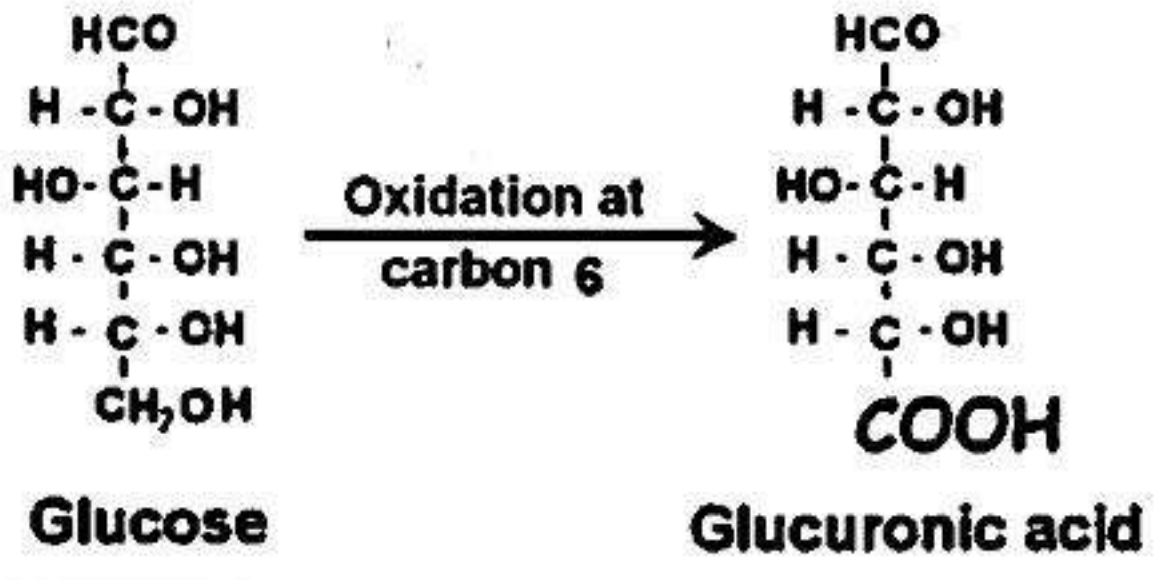


1.1. Aldonic acids

- **Hexoses:**
    1. **Mannose** is oxidized to **mannonic acid**.
    2. **Galactose** is oxidized to **galacturonic acid**.
- **Tetroses:**
    1. **Erythrose** is oxidized to **erythronic acid**.
- **Pentoses:**
    1. **Arabinose** is oxidized to **arabinonic acid**.
    2. **Ribose** is oxidized to **ribonic acid**.
    3. **Xylose** is oxidized to **xylonic acid**.

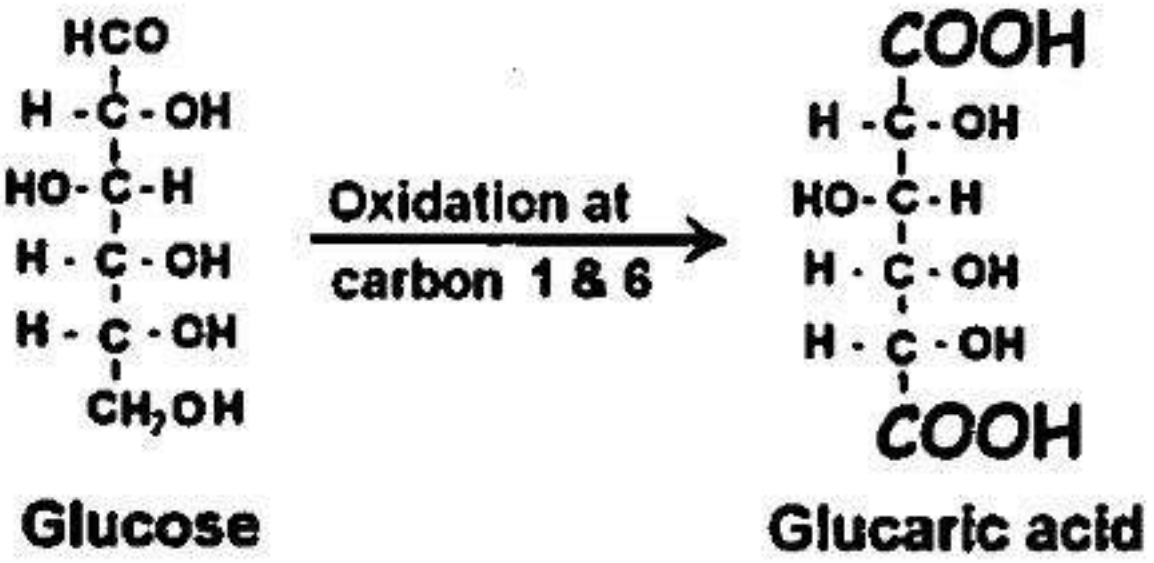
1.2. Uronic acids

- Oxidation of last hydroxyl carbon gives uronic acid e.g. glucose is oxidized to glucuronic acid.



1.3. Aldaric acids:

- These are dicarboxylic acids produced by oxidation of both carbonyl carbon and last hydroxyl carbon e.g. glucose Is oxidized to glucaric acid (saccharic acid).



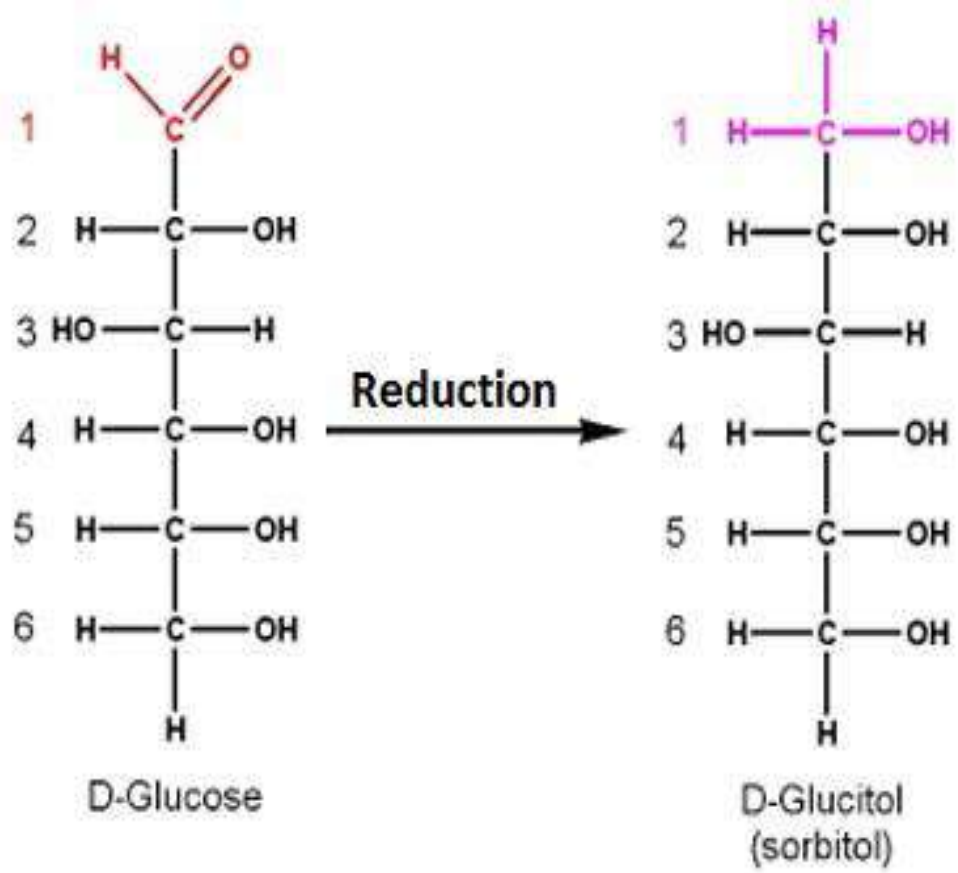
2- Sugar alcohols:

Monosaccharides, both aldoses and ketoses may be reduced at carbonyl carbon, to the corresponding alcohol:

Sugar	Sugar alcohols
Glucose	Glucitol (Sorbitol)
Galactose	Galactitol (dulcitol)
Mannose	Mannitol
Ribose	Ribitol
Fructose	Mannitol and Sorbitol

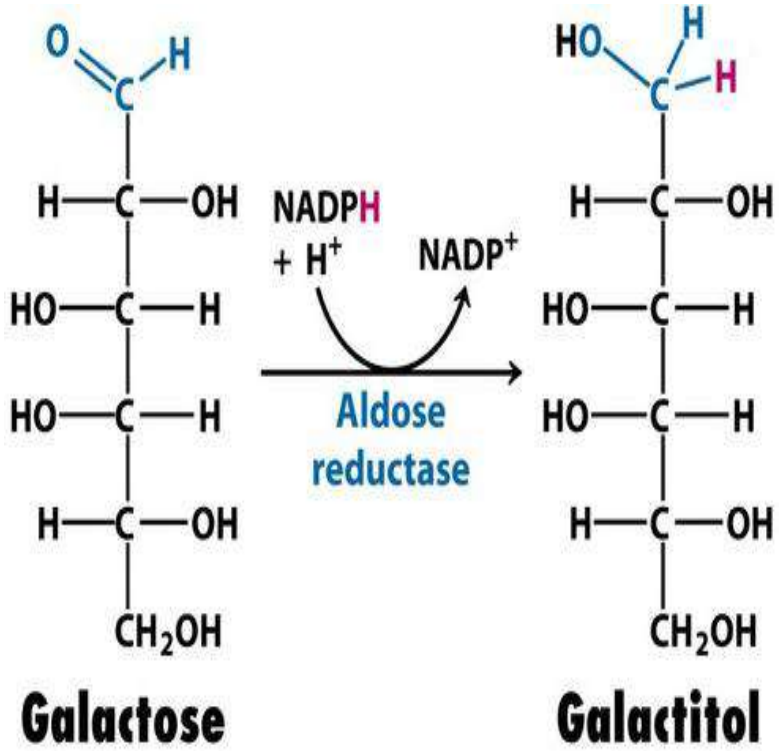
2- Sugar alcohols:

- Glucose is reduced to sorbitol (glucitol)
- Glucitol is used in the food industry as sweetener due to its sweetness and reduced caloric value compared to glucose.
- It is also used in various pharmaceutical and cosmetic products.



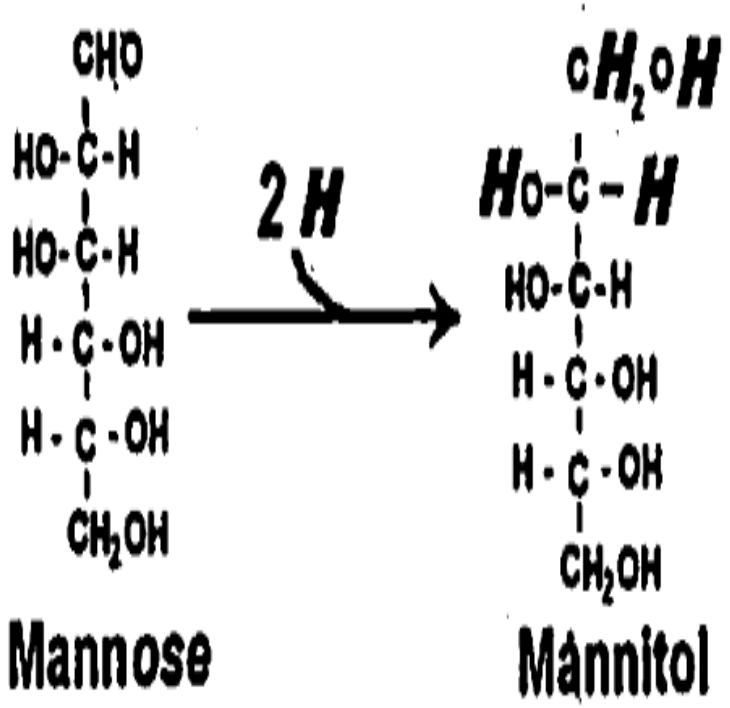
2- Sugar alcohols:

- Galactose is reduced to galactitol (dulcitol)
- It has a sweet taste but is not as sweet as sucrose.
- Galactitol is used as a sugar substitute in some food products, particularly in sugar-free and reduced-calorie foods.
- Additionally, it has applications in the pharmaceutical and medical fields.



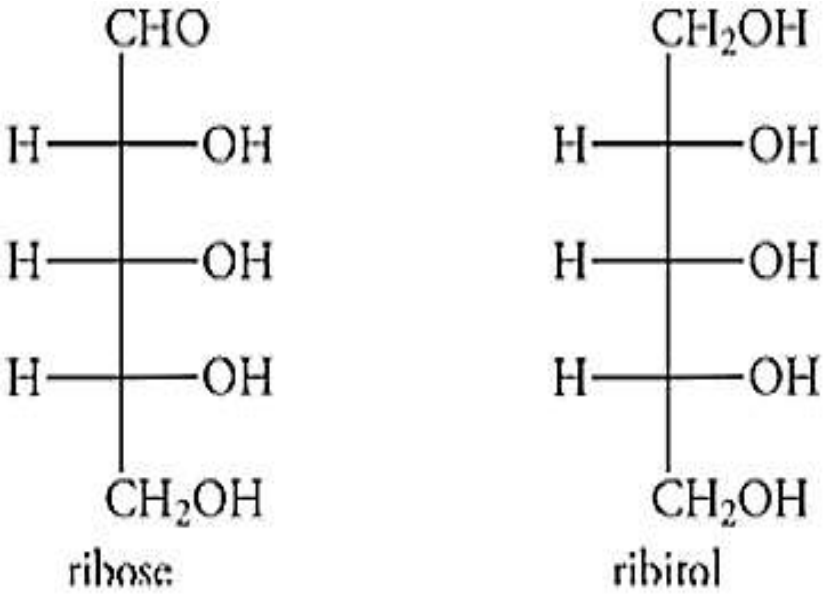
2- Sugar alcohols:

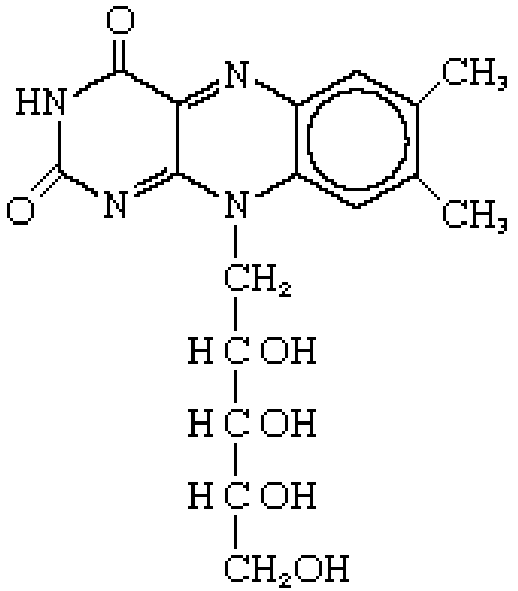
- Mannose is reduced to mannitol.
- Mannitol is a sugar alcohol and is commonly used in the food and pharmaceutical industries.
- It has medical applications, including its use as an osmotic diuretic and Reducing Intracranial Pressure (ICP).



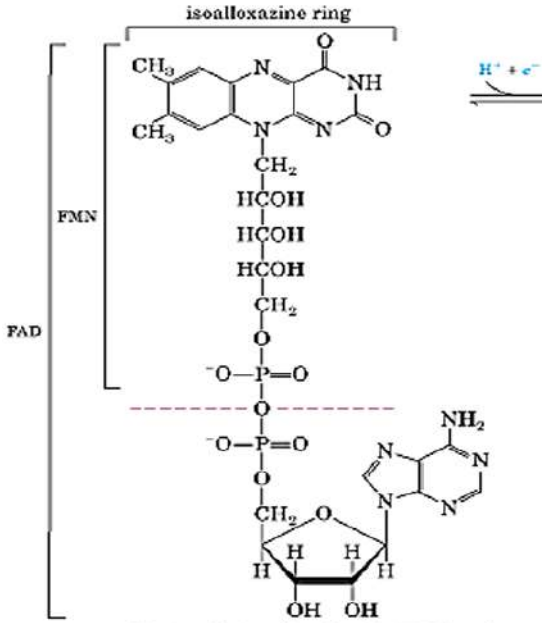
2- Sugar alcohols:

- Ribose is reduced to ribitol
- Ribitol is a constituent of vitamin B_2 (riboflavin) and coenzyme FAD.





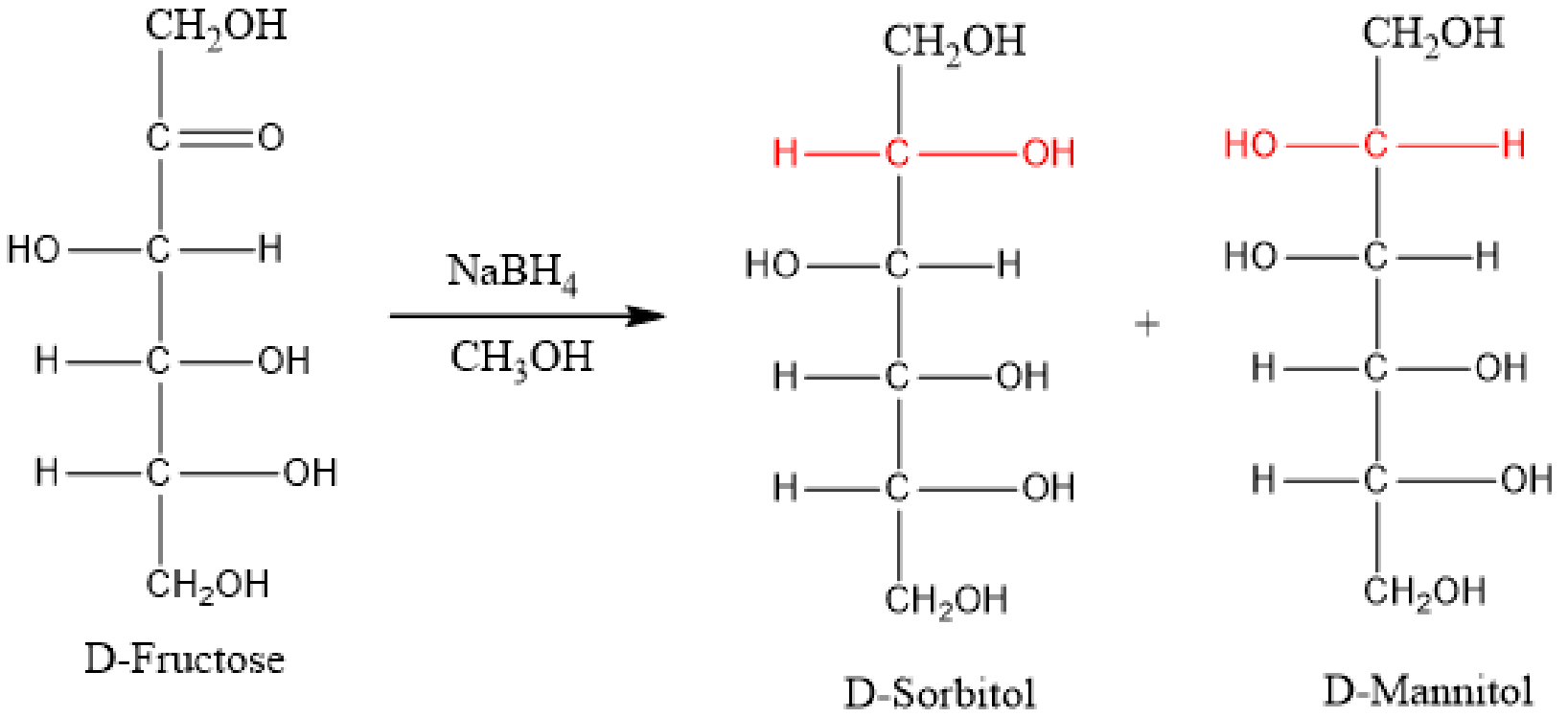
Vitamin B_2 (riboflavin)



Flavin adenine dinucleotide (FAD) and flavin mononucleotide (FMN)

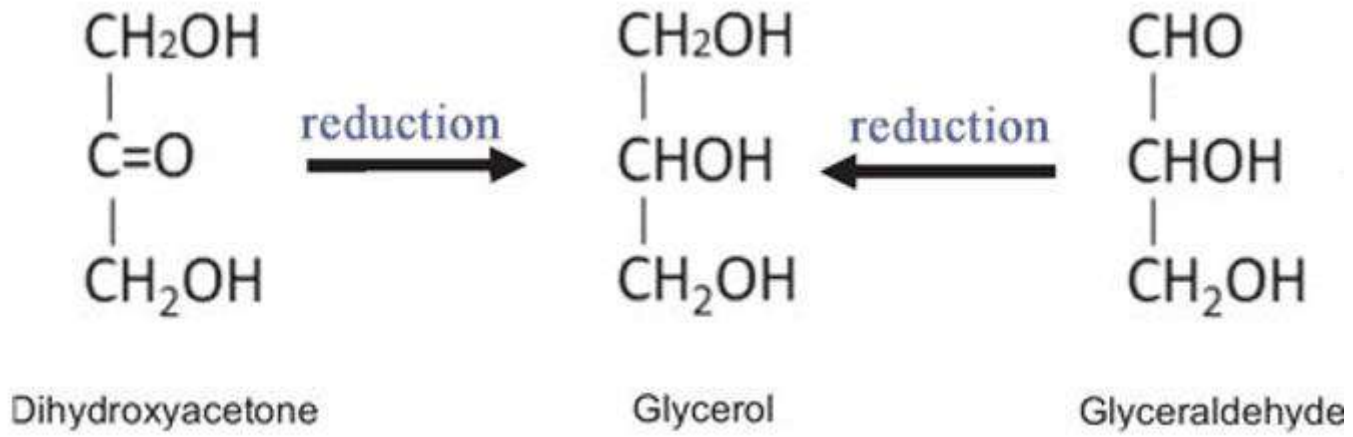
2- Sugar alcohols:

- Fructose is reduced to mannitol and sorbitol.



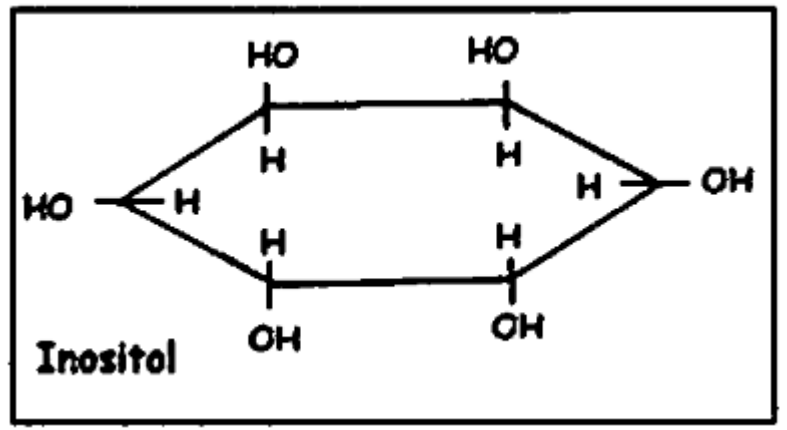
2- Sugar alcohols:

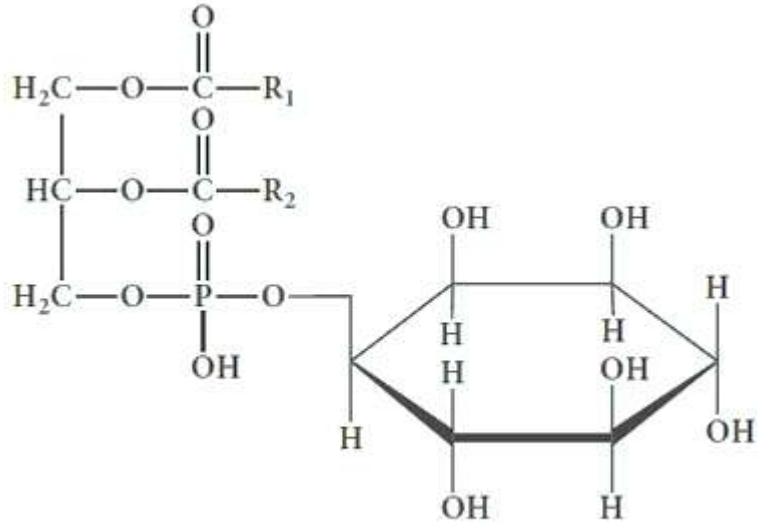
- Glyceraldehyde and dihydroxyacetone are reduced to glycerol
- Glycerol enters in the structure of Triacylglycerol (TAG) & phospholipid



3-Inositol

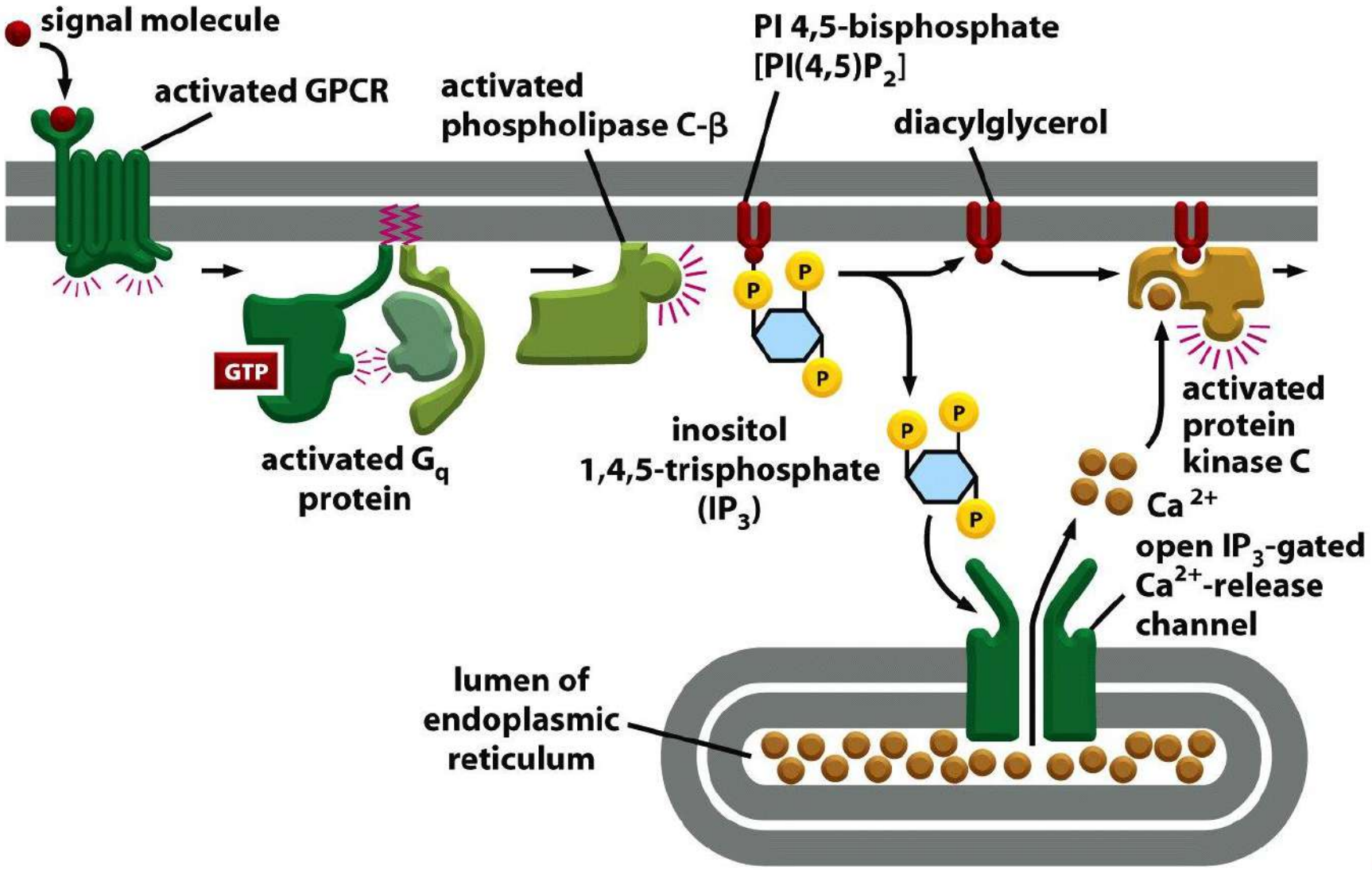
- Inositol is a sugar alcohol with six hydroxyl groups.
- Inositol enters in the structure of phospholipid), which is present in cell membrane.
- It acts as precursor of second messenger (inositol triphosphate), mediating hormonal action inside cells





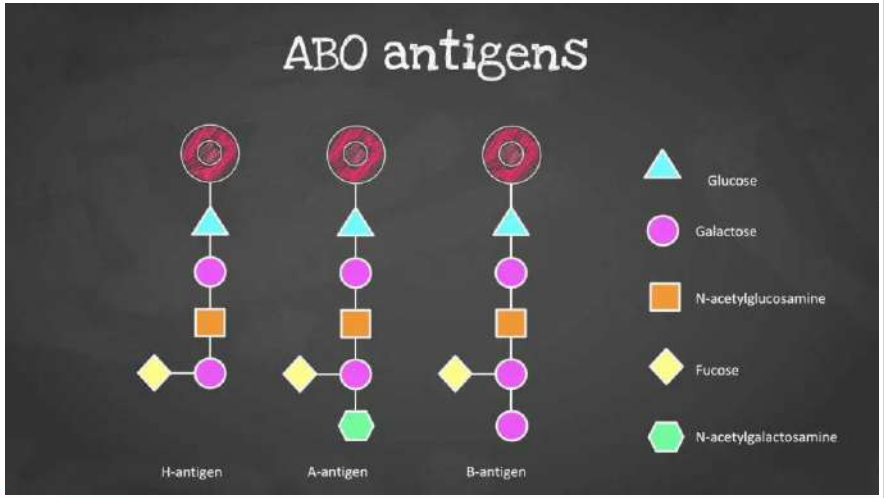
Phosphatidylinositol

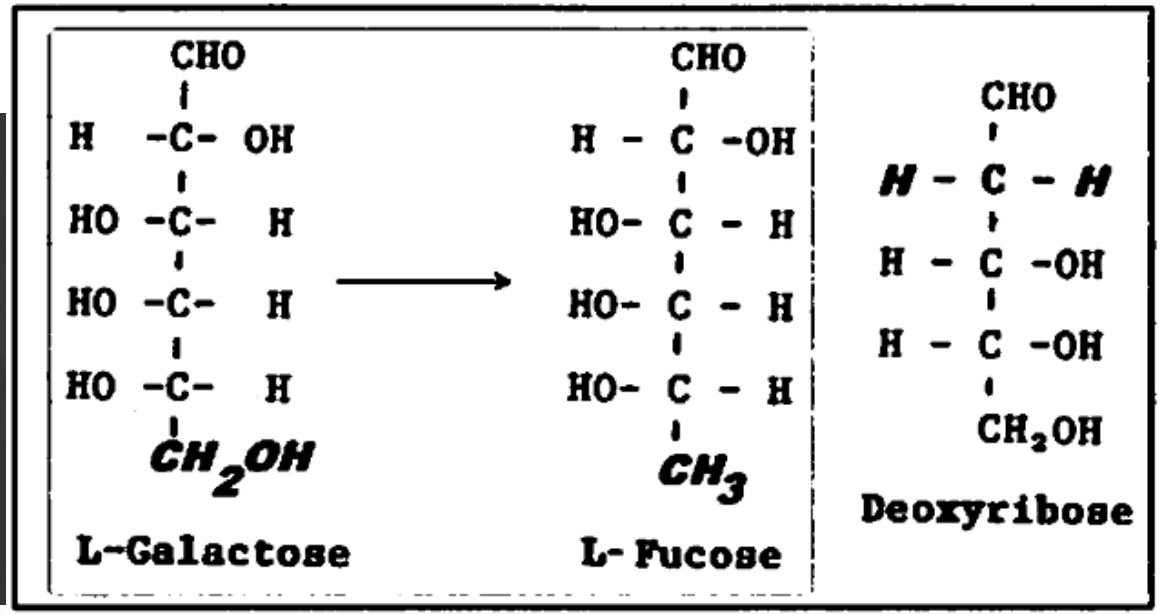
GPCRs increase cytosolic Ca^{2+} and activate PKC



4-Deoxy sugars:

- Are sugars in which one of the hydroxyl groups has been replaced by a hydrogen atom i.e. one oxygen is missed.
- L-Fucose (6-deoxygalactose): occurring in glycoproteins (Bl. Group AG).
- Deoxyribose: occurring in DNA.



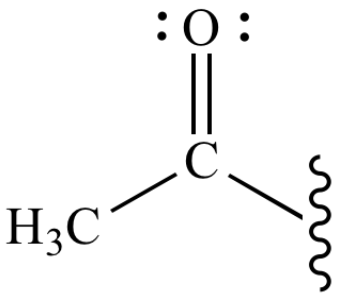


The ABO blood group system

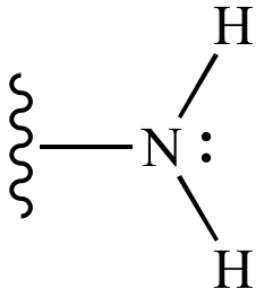
- The ABO blood group system is determined by a single gene that codes for glycosyltransferases responsible for adding specific sugar residues to the antigen precursor on the surface of red blood cells and other cells.

The ABO blood group system

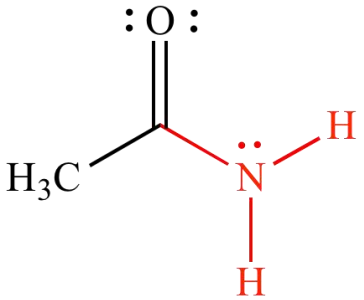
1. Blood Type A: Individual has the GTA enzyme, it will add N-acetylgalactosamine, resulting in the A antigen.
2. Blood Type B: Individual has the GTB enzyme, it will add galactose, resulting in the B antigen.
3. Blood Type AB: Individual has both GTA and GTB enzymes, both A and B antigens will be present on the red blood cell surface.
4. Blood Type O: Individual has neither the GTA nor GTB enzyme.



Acetyl group



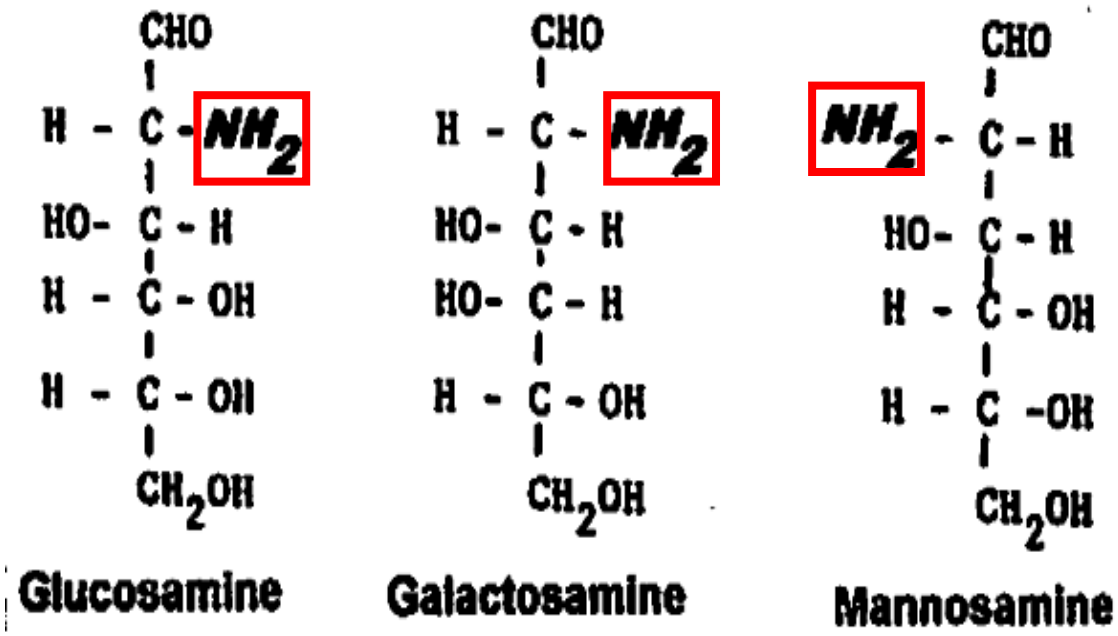
Amino group



Acetylamino group

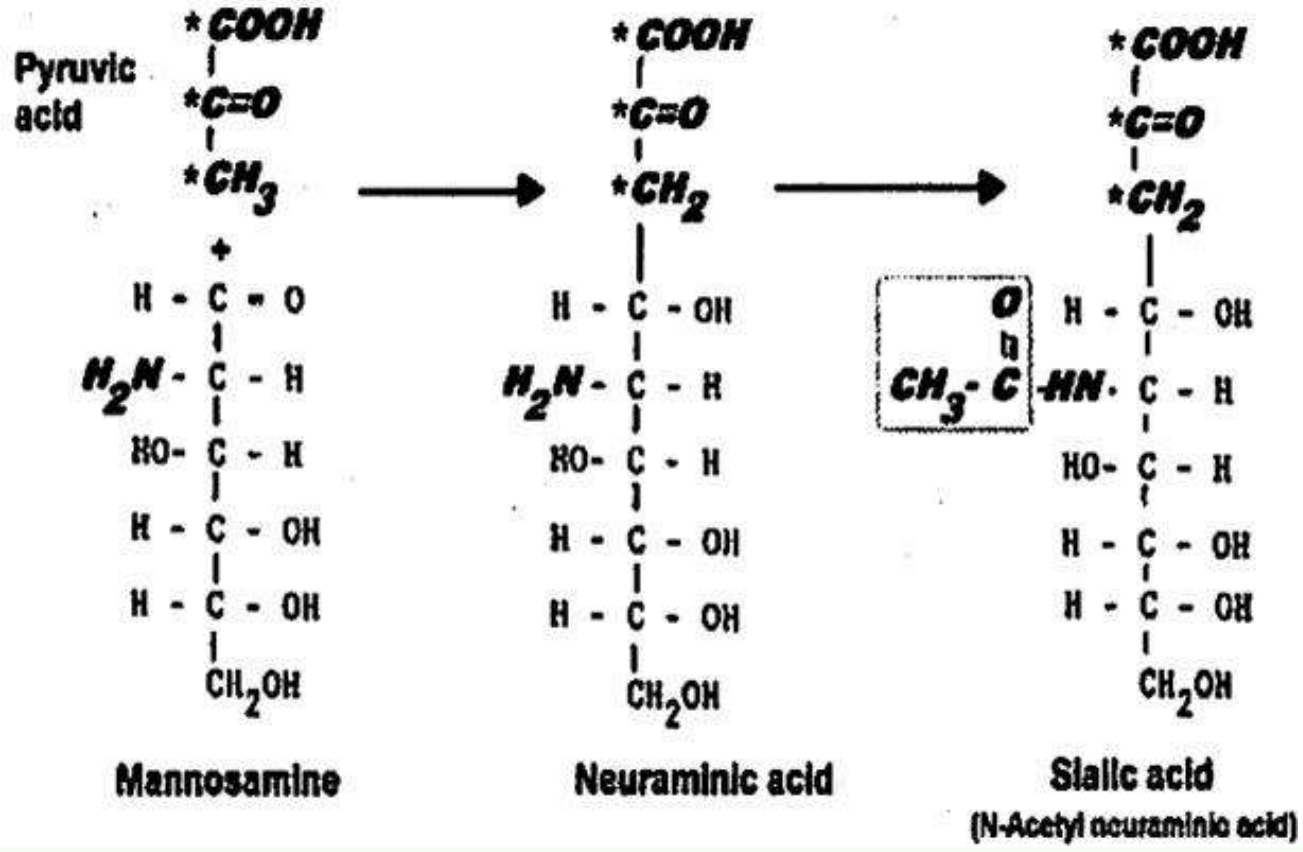
Amino sugars

- In these sugars, the hydroxyl group attached to carbon number 2 (C2) is replaced by an amino.



Amino sugar acids:

- These are condensation of amino sugars and some acids.
- Neuraminic acid
- Sialic acid (N-acetyl neuraminic acid or NANA).



Functions of Amino sugars & Amino sugar acids

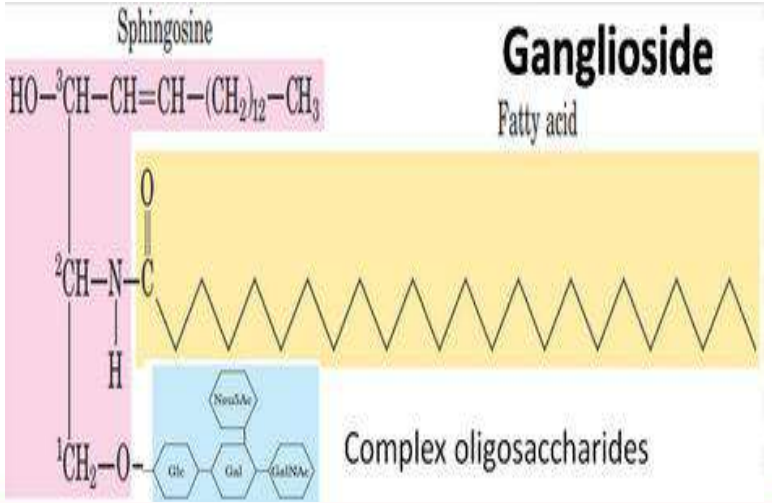
- Amino sugars and Amino sugar acids are constituents of:

1. Glycoproteins present in cell membrane
    1. These carbohydrate head groups also act as specific receptors for certain pituitary glycoprotein hormones and certain bacterial protein toxins such as cholera toxin.

Functions of Amino sugars & Amino sugar acids

2- Ganglioside (cell membranes of nervous system)

- The oligosaccharide groups on gangliosides projects outwards from the cell surface, and act as distinguishing surface markers that can serve as specific determinants in cellular recognition and cell-to-cell communication.
- Important in the biology of pathogenic bacteria and antibiotic (Erythromycin).



THANK YOU

M.ELEYAN

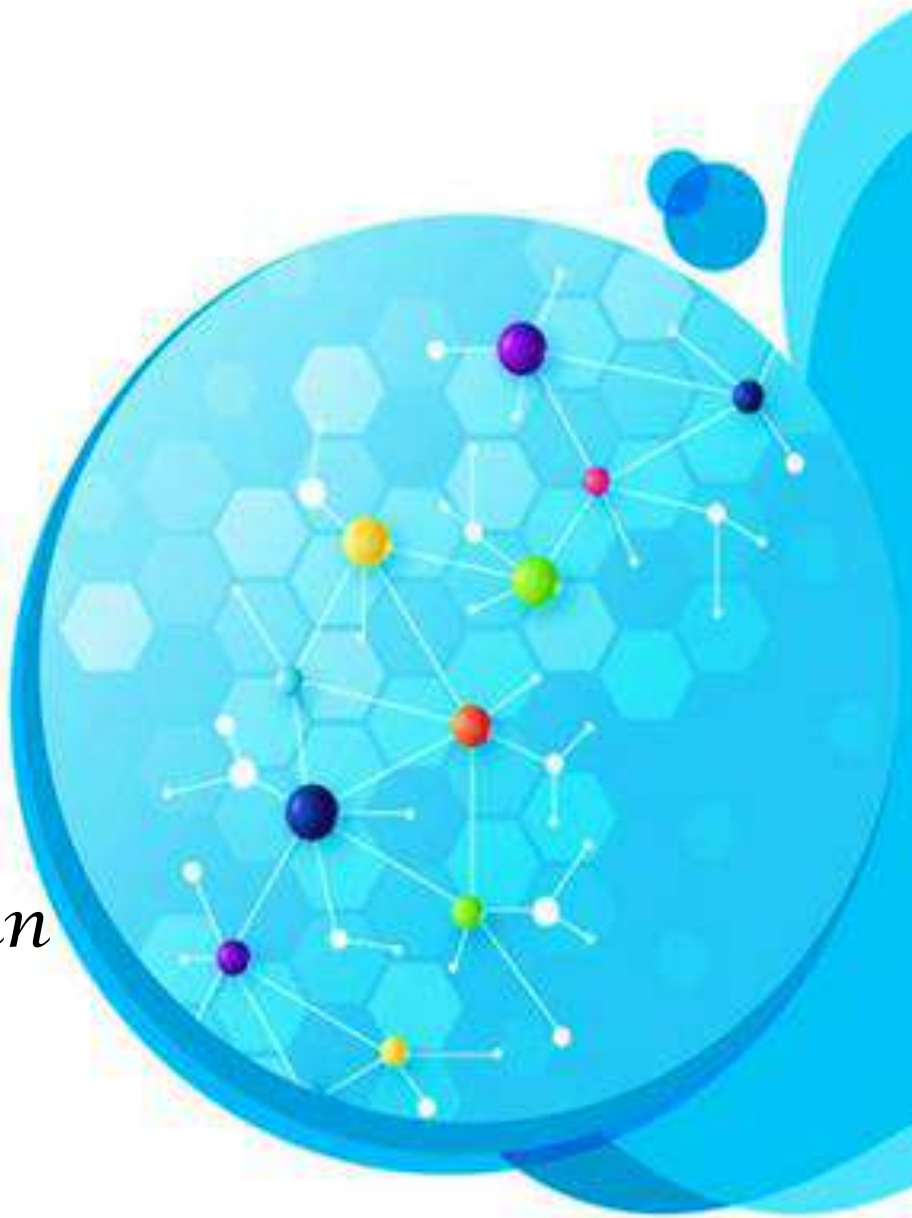
Medical Biochemistry

Carbohydrate Chemistry

Asst. Prof.Mohammed Hasan Eleyan

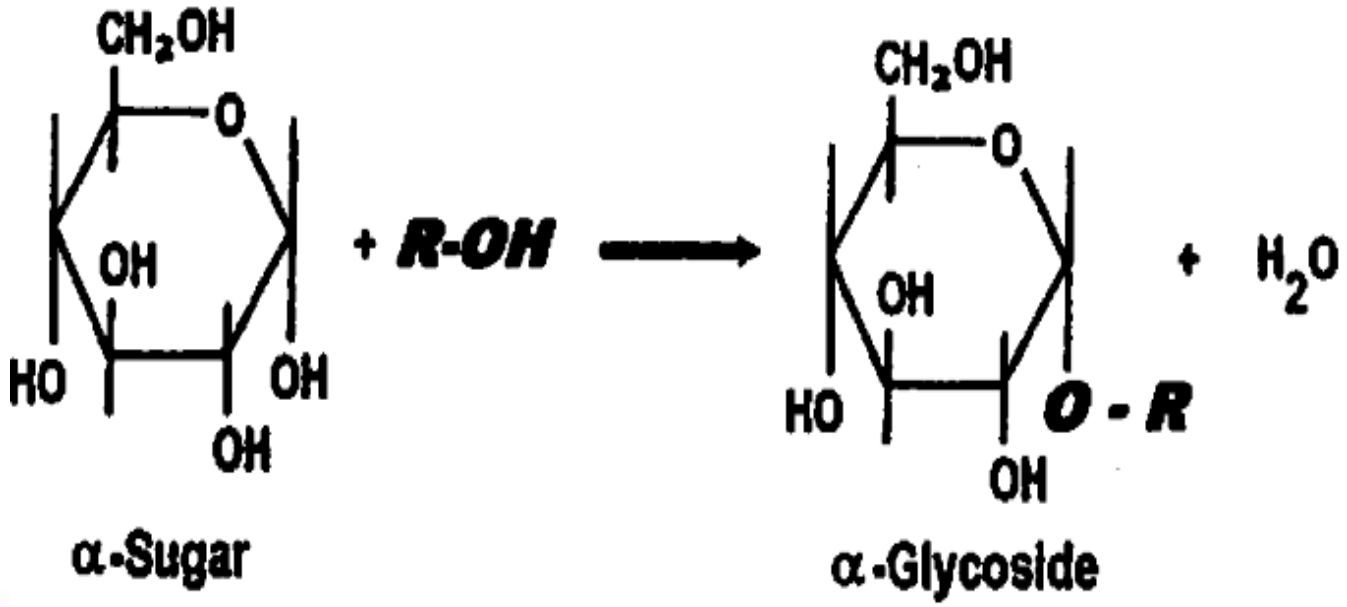
Faculty of Medicine

Al-Azhar University-Gaza



Glycosidic bond and glycosides

- Glycosidic bond: It is the bond between a carbohydrate and another compound to form a glycoside.



Glycosidic bond and glycosides

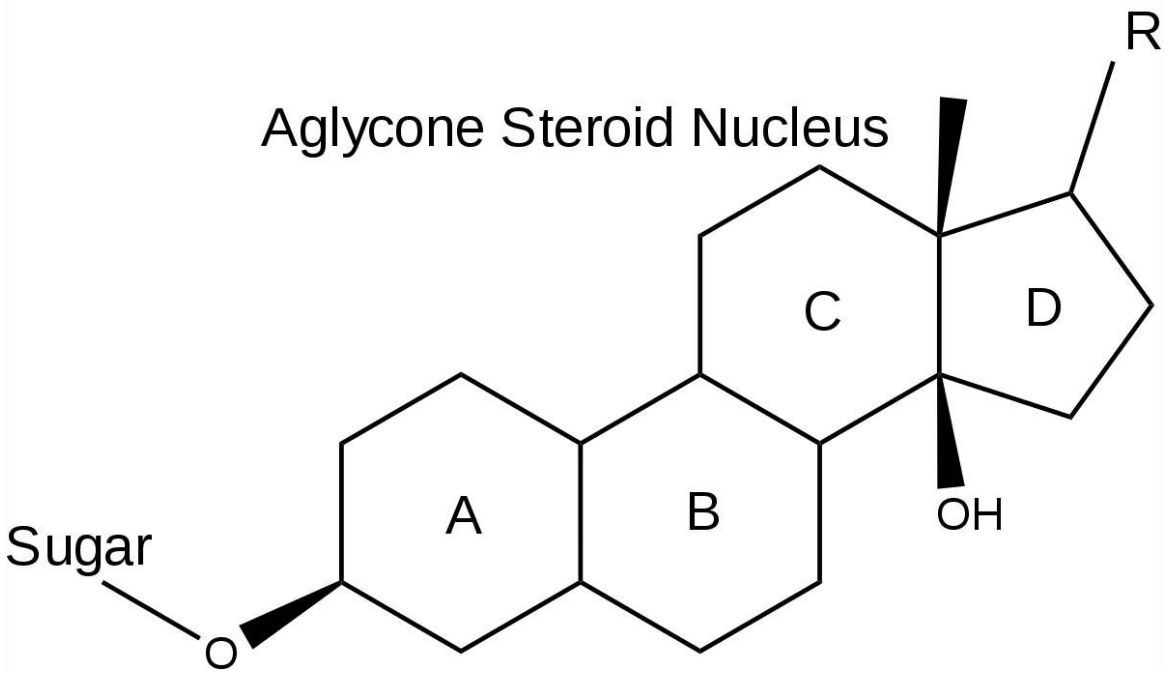
- This bond is between the hydroxyl group of anomeric carbon of monosaccharide (carbon 1 in aldoses or carbon 2 in ketoses) and another compound which may be:
  - ¶ Glycone (such as Another monosaccharide) to form disaccharide glycosides as maltose, lactose and sucrose.
  - ¶ Aglycone i.e. non-carbohydrate to form glycoside.

Examples of glycosides

- Disaccharide = monosaccharide + monosaccharide
- Nucleotide = monosaccharide + Nitrogen-containing base
- Glycolipids = monosaccharide + Lipid
- Glycoprotein = monosaccharide + protein
- Streptomycin (Next slide)
- Digitalis (Cardiac glycosides): Aglycone here is steroid.

✓Cardiac glycosides are important in treatment of heart failure.

Examples of glycosides



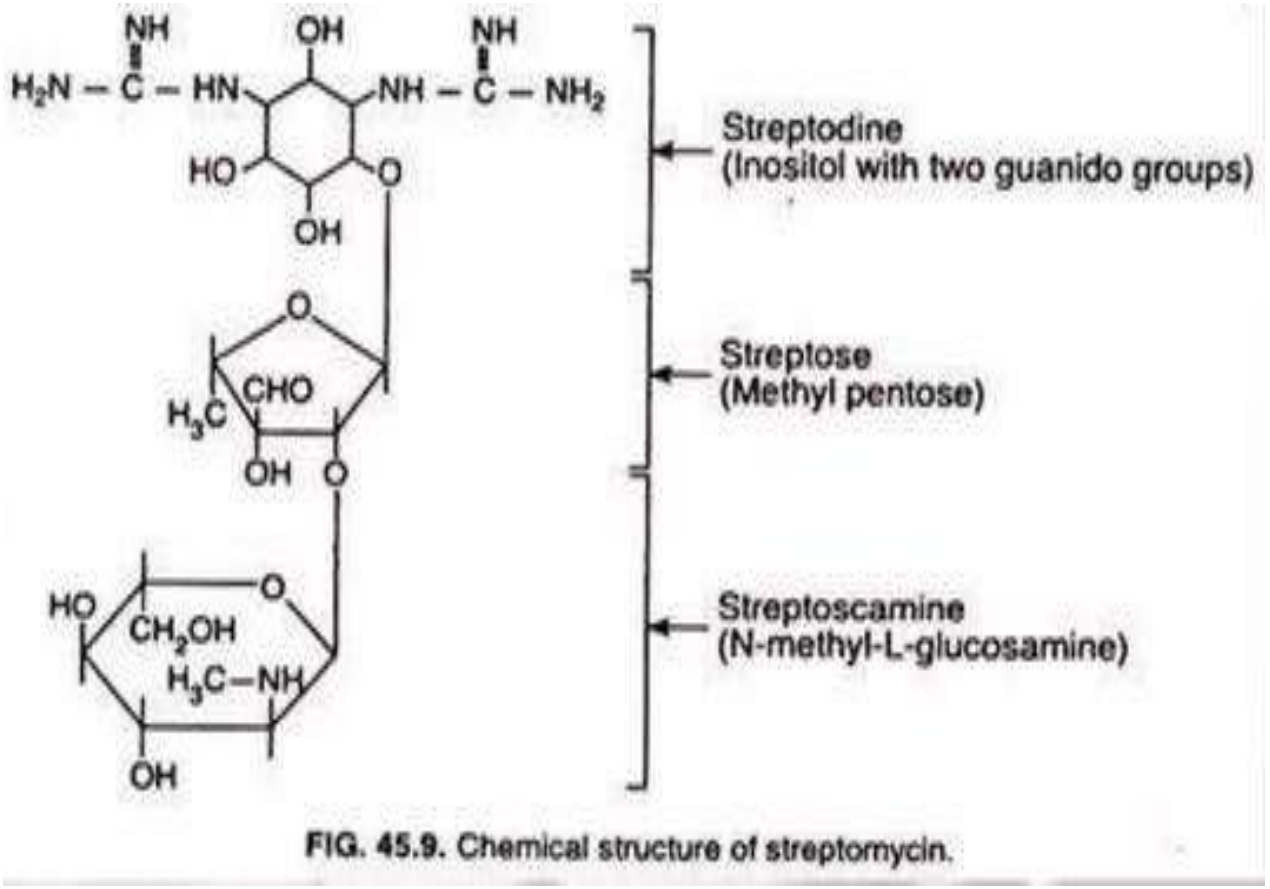
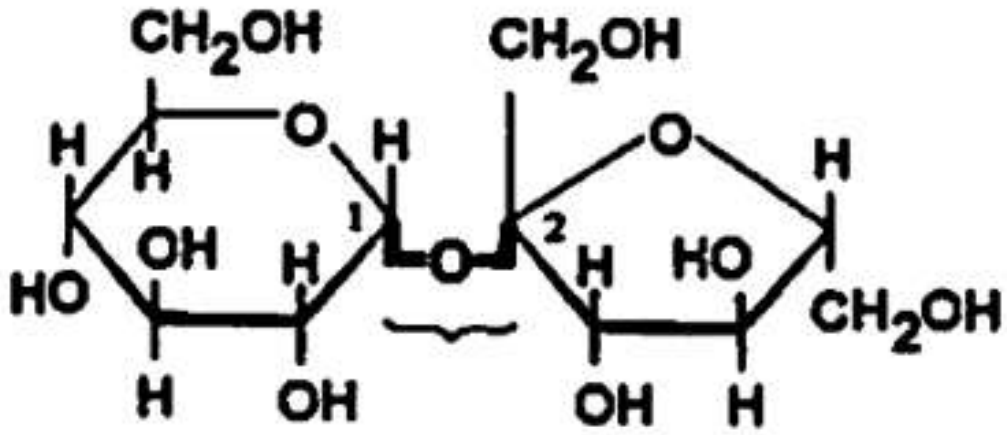


FIG. 45.9. Chemical structure of streptomycin.

N and O-glycosides:

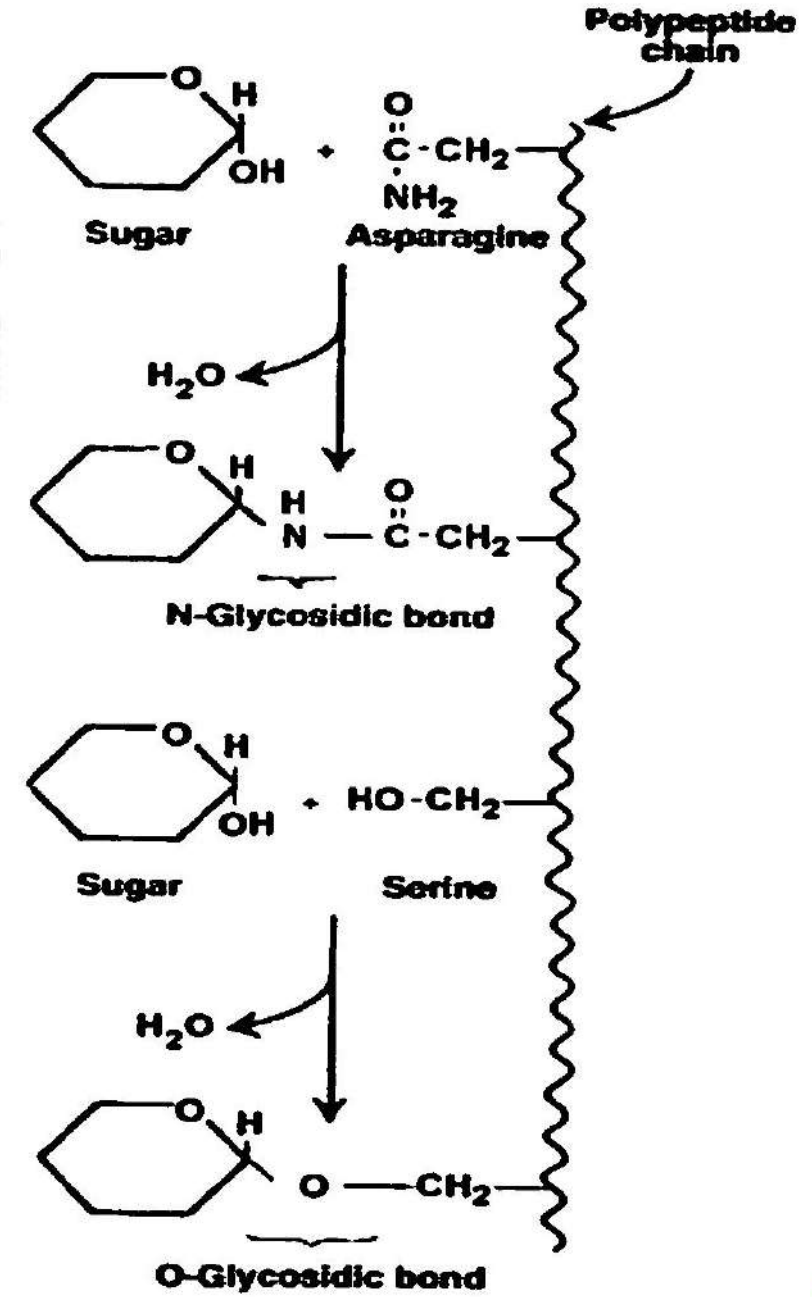
If the monosaccharide is attached to -OH group of another sugar or aglycone, the resulting structure is an o-glycoside.

All sugar-sugar glycosidic bonds are O-type linkage.



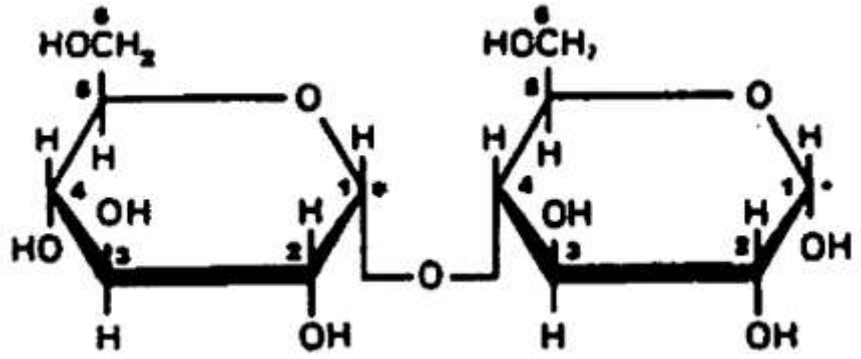
N and O-glycosides:

- If the monosaccharide is attached to - NH_2 of aglycone, the resulting structure is N-glycoside.



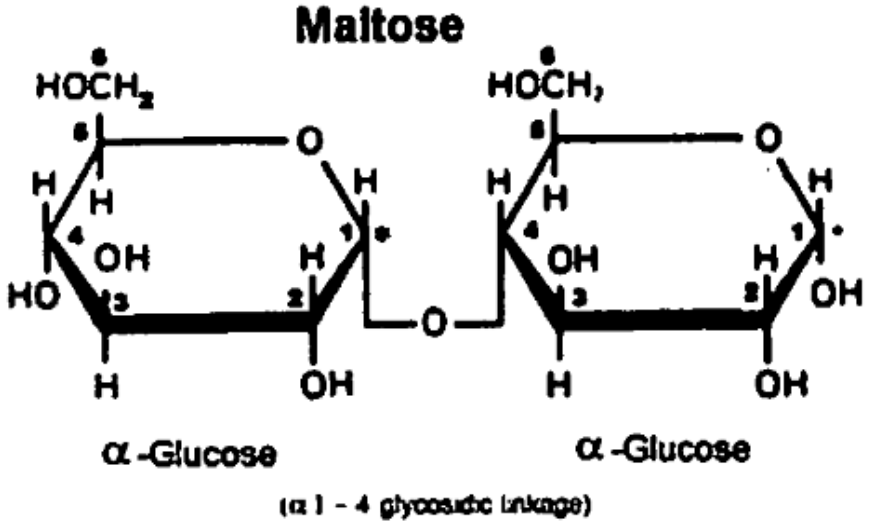
Disaccharides:

- These are formed by condensation of 2 molecules of monosaccharides bound together by glycosidic bond.
- Its general formula is $Cn(H_2O)_{n-1}$
- The most Important disaccharide& are: Maltose, Lactose, and Sucrose.



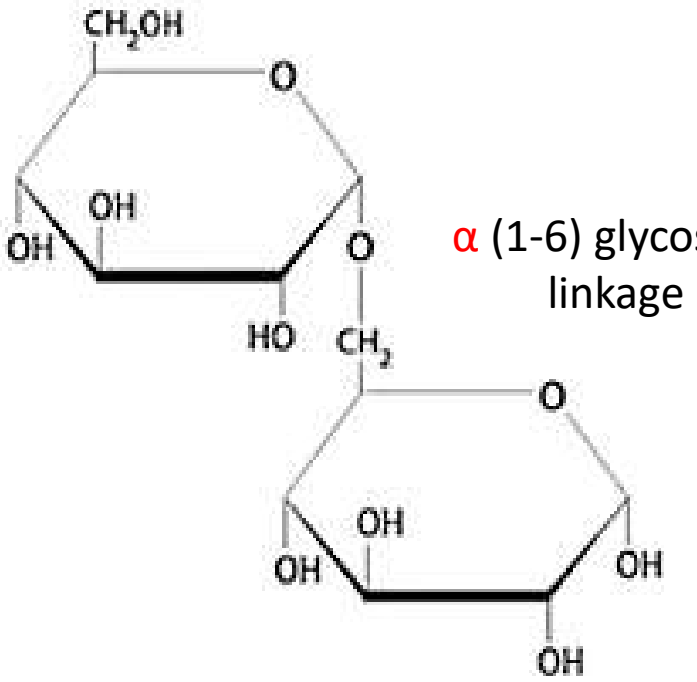
Maltose (malt sugar)

- Structure: it is formed of 2 molecules of α-D glucose linked together by α 1 - 4 glycosidic bond.
- Maltose is produced during digestion of starch by amylase enzyme.
- Sources: Malt.



Isomaltose

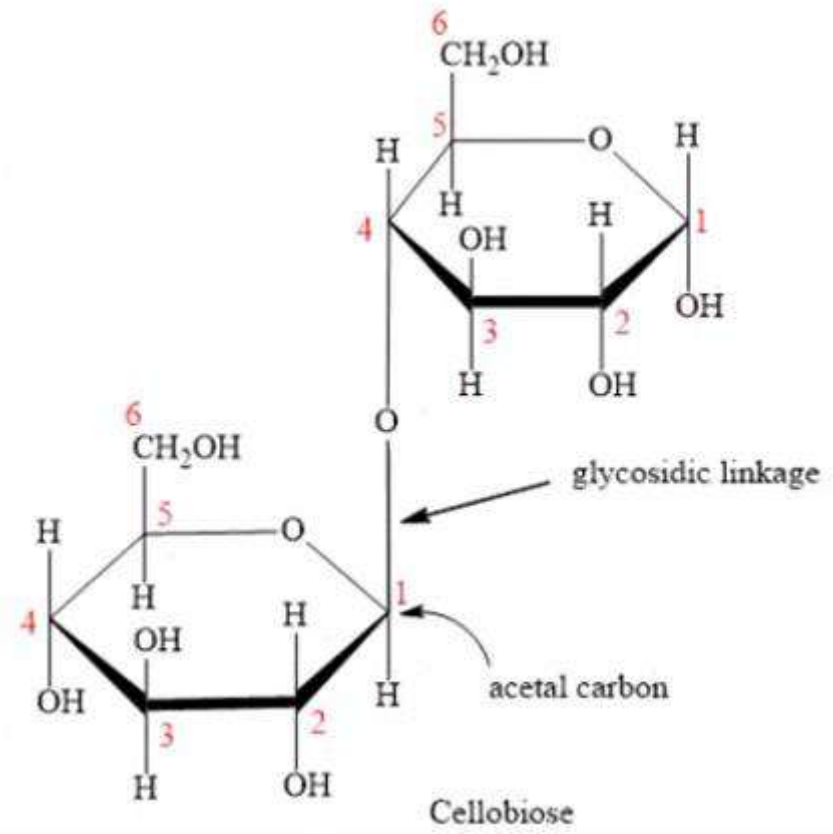
- The glucose units are held together by α (1-6) glycosidic linkage.
- Source and Formation: Isomaltose is typically formed as an intermediate during the breakdown of starch and glycogen by the enzyme α-amylase. It's also a byproduct in the digestion of dietary fibers.



Isomaltose

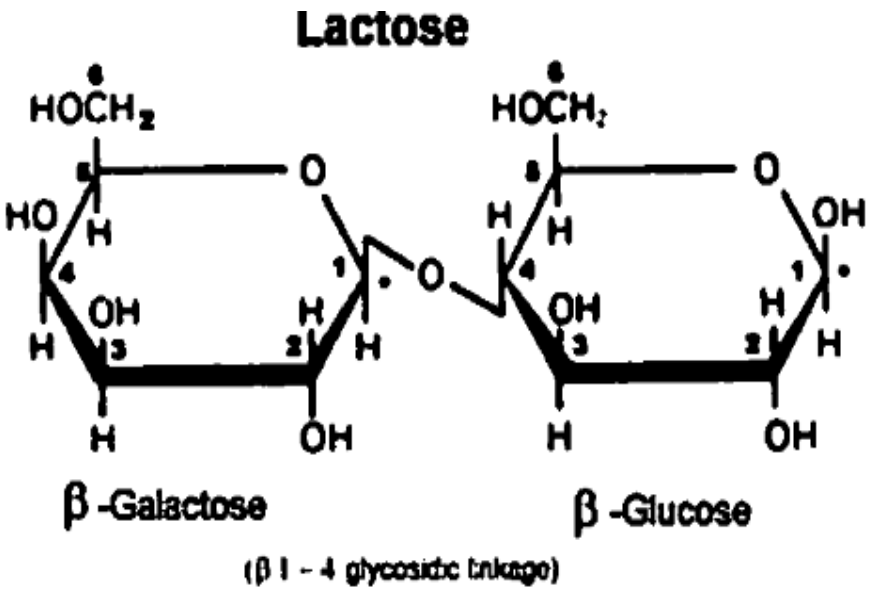
Cellobiose

- Cellobiose is another disaccharide identical in structure with maltose, except that the former has β 1-4 glycosidic bond.
- Cellobiose is formed during the hydrolysis of cellulose.



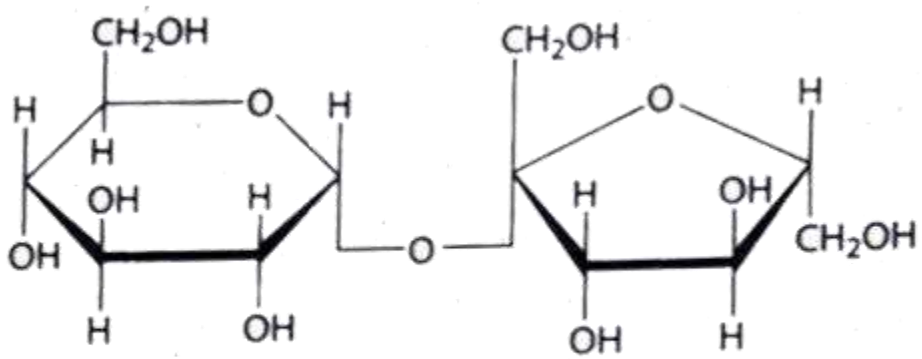
Lactose

- Structure: It is formed of 2 molecules of β-D-galactose and β -D-glucose linked together by β 1-4 glycosidic bond.
- Sources: It is the sugar present in milk.
- In human milk, its concentration is 7.4 g/dl.
- It may appear in urine in late pregnancy and during lactation.



Sucrose:

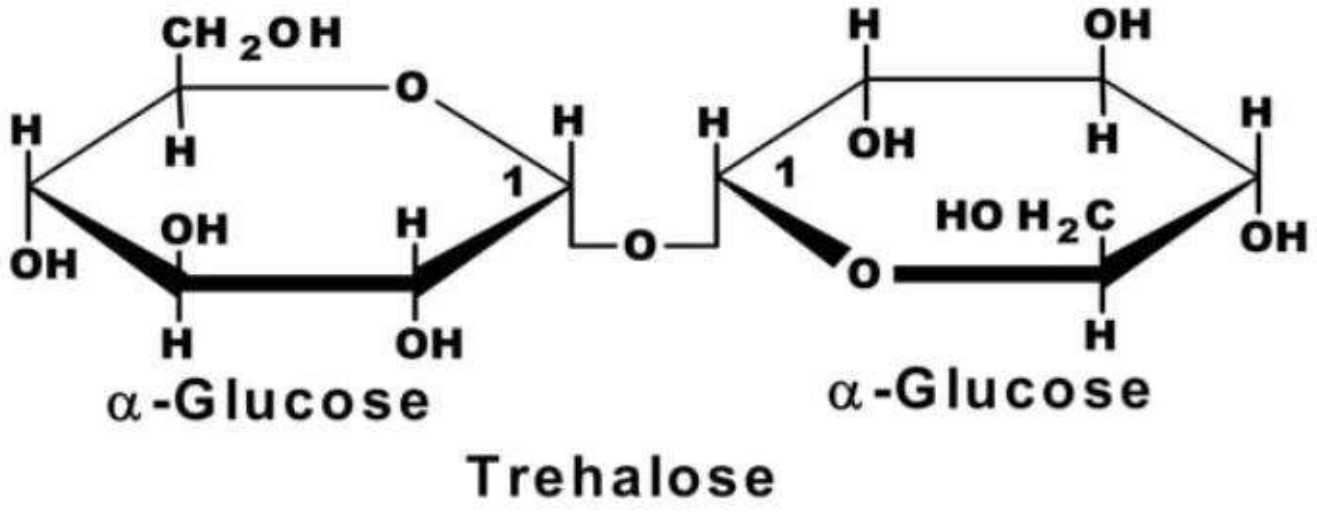
- Structure: it is formed of 2 molecules of α-D- glucose and β-D-fructose linked together by α1- β2-glycosidic bond.
- Sources:
- Cane and beet sugar.
- It is also present in pineapple and carrot.



Sucrose

Trehalose

- It is formed of 2 α-glucose units linked by α -1,1- glycosidic linkage.
- Some bacteria, fungi, plants and invertebrate animals synthesize it as a source of energy, and to survive freezing and lack of water.



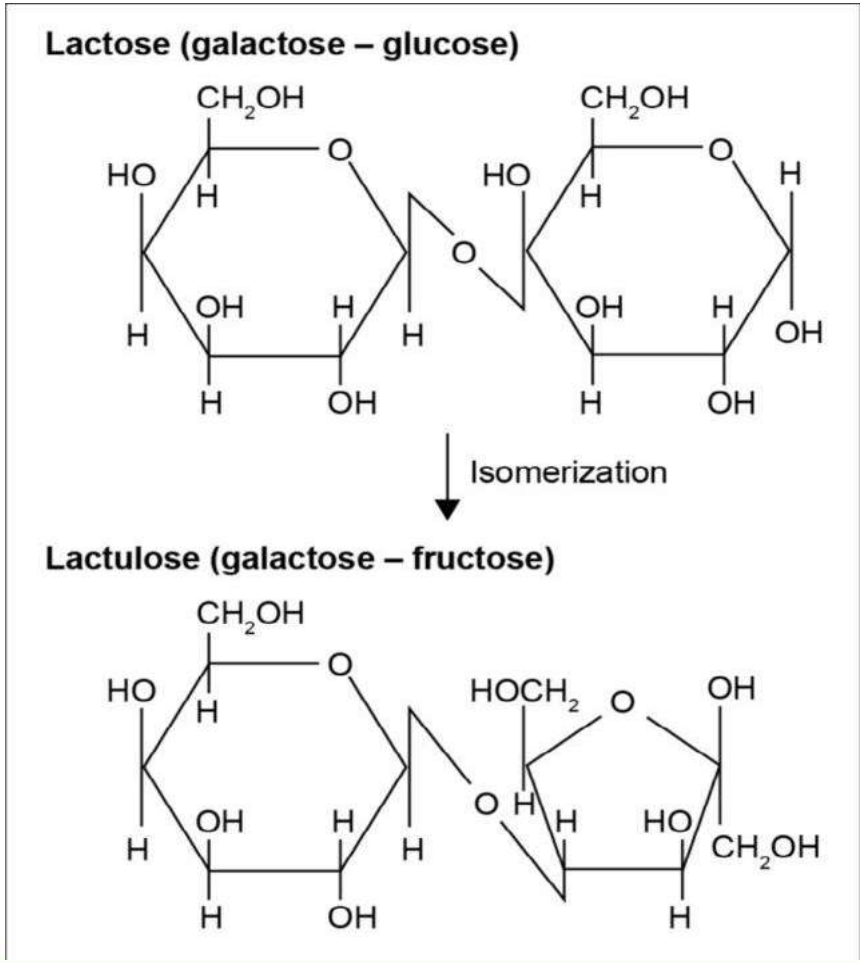
Lactulose

- Lactulose is a synthetic disaccharide sugar composed of two simple sugars, galactose, and fructose.
- The specific glycosidic bond in lactulose is a β(1→4) glycosidic bond.
- It is not naturally occurring in the human body but is produced through a chemical reaction from lactose

Lactulose

Lactulose is commonly used as a medication and a medical-grade laxative for the treatment of constipation and certain liver disorders.

It is not absorbed or broken down in the small intestine.



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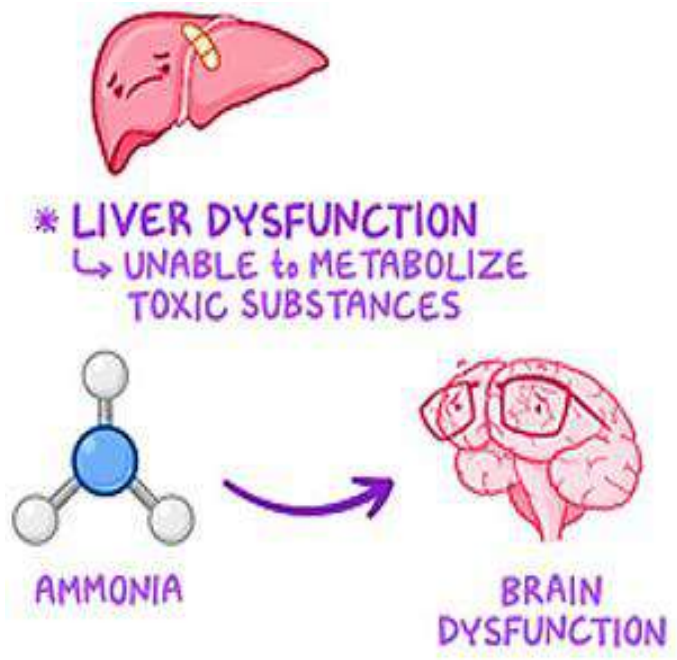
Lactulose used for hepatic encephalopathy treatment & reduction blood ammonia levels.

- Lactulose reaches the colon.
- In the colon, lactulose is fermented by gut bacteria, leading to the production of organic acids and gases, including lactic acid and acetic acid.
- These acids, creating an environment that favors the conversion of ammonia (NH3) into ammonium ions (NH4+).
- Ammonium ions are poorly absorbed in the colon, so they remain in the gut and are eventually excreted in the stool

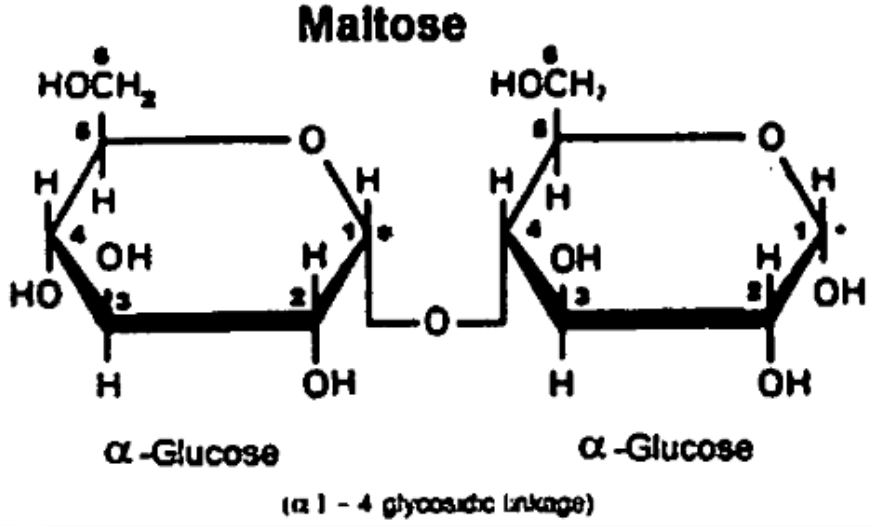


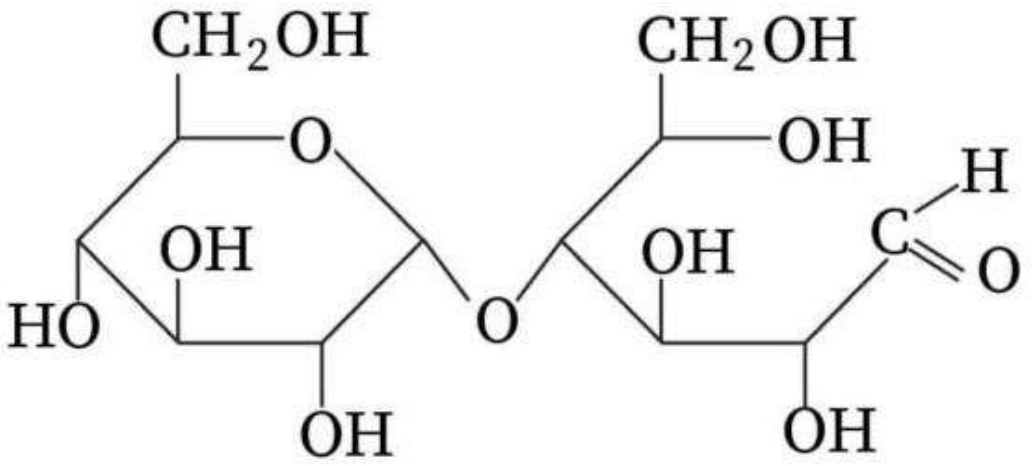
Disaccharides:

- As is evident from the name, a disaccharide consists of two monosaccharide units (similar or dissimilar) held together by a glycosidic bond.
- They are crystalline, water-soluble and sweet to taste.
- The disaccharides are of two types:
    1. Reducing disaccharides with free aldehyde or keto group e.g. **maltose and lactose**.
    2. Non-reducing disaccharides with no free aldehyde or keto group e.g. **sucrose and trehalose**.

Reducing disaccharides

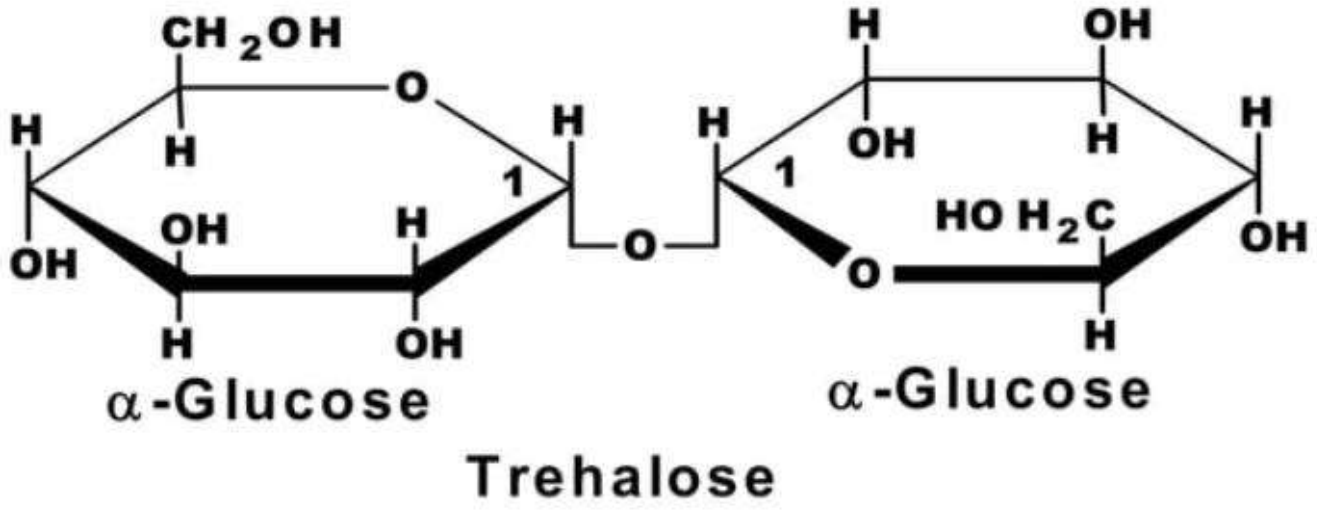
- In solution, these disaccharides can undergo mutarotation, where the free anomeric carbon can open and close, allowing them to reduce certain reagents, such as Benedict's which is used in tests for reducing sugars.





Non-reducing disaccharides

- Non-reducing disaccharides do not undergo mutarotation and do not react with reagents like Benedict’s solution, as they lack a free aldehyde or keto group.



Benedict's test- for reducing sugars

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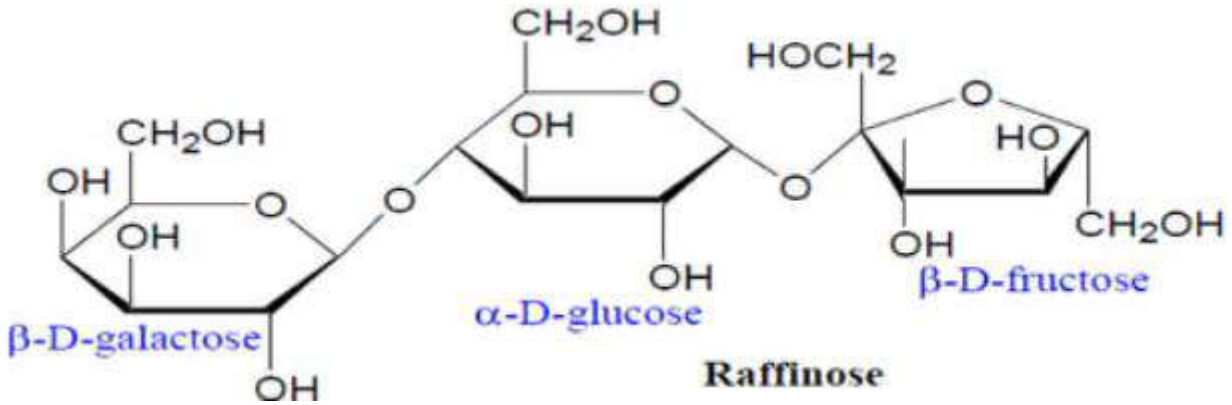
Oligosaccharides

- Oligosaccharides contain from 3 to 10 monosaccharide units.
- Raffinose an oligosaccharide found in peas and beans



Raffinose

THANK YOU

M.ELEYAN

Polysaccharides

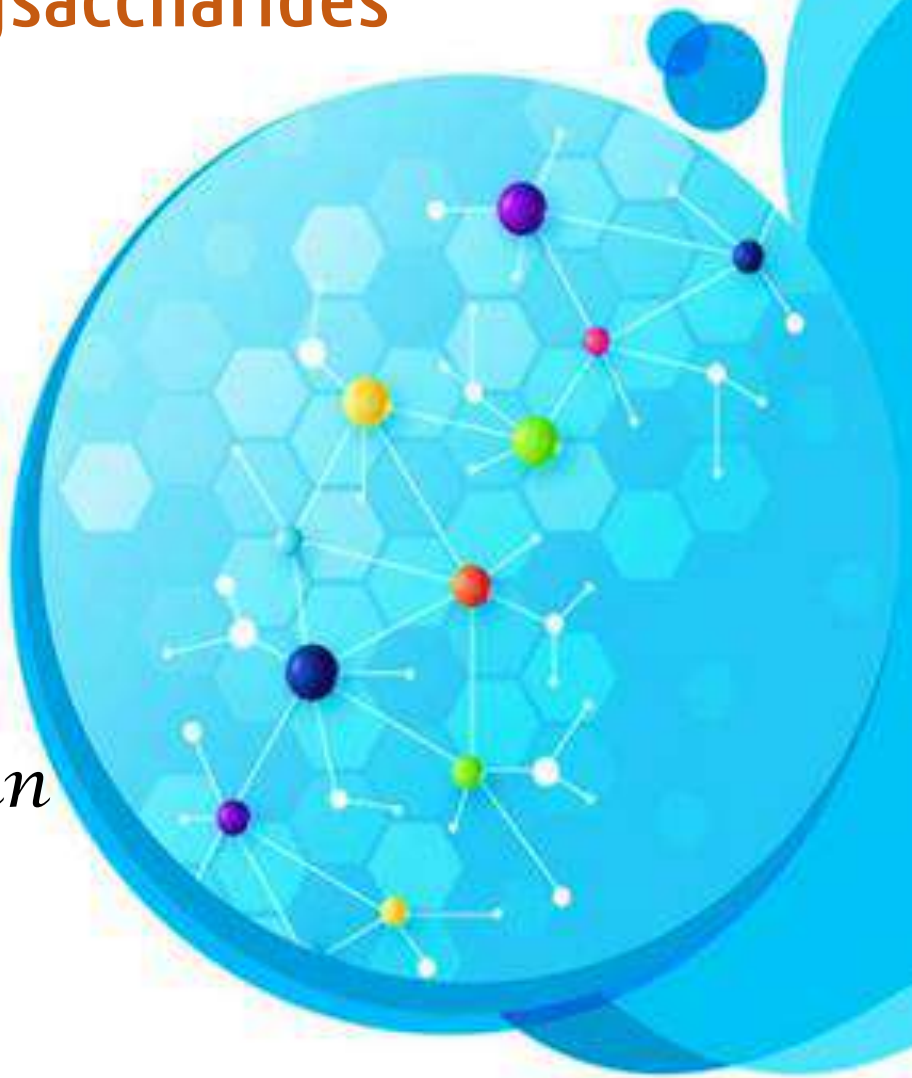
Medical Biochemistry

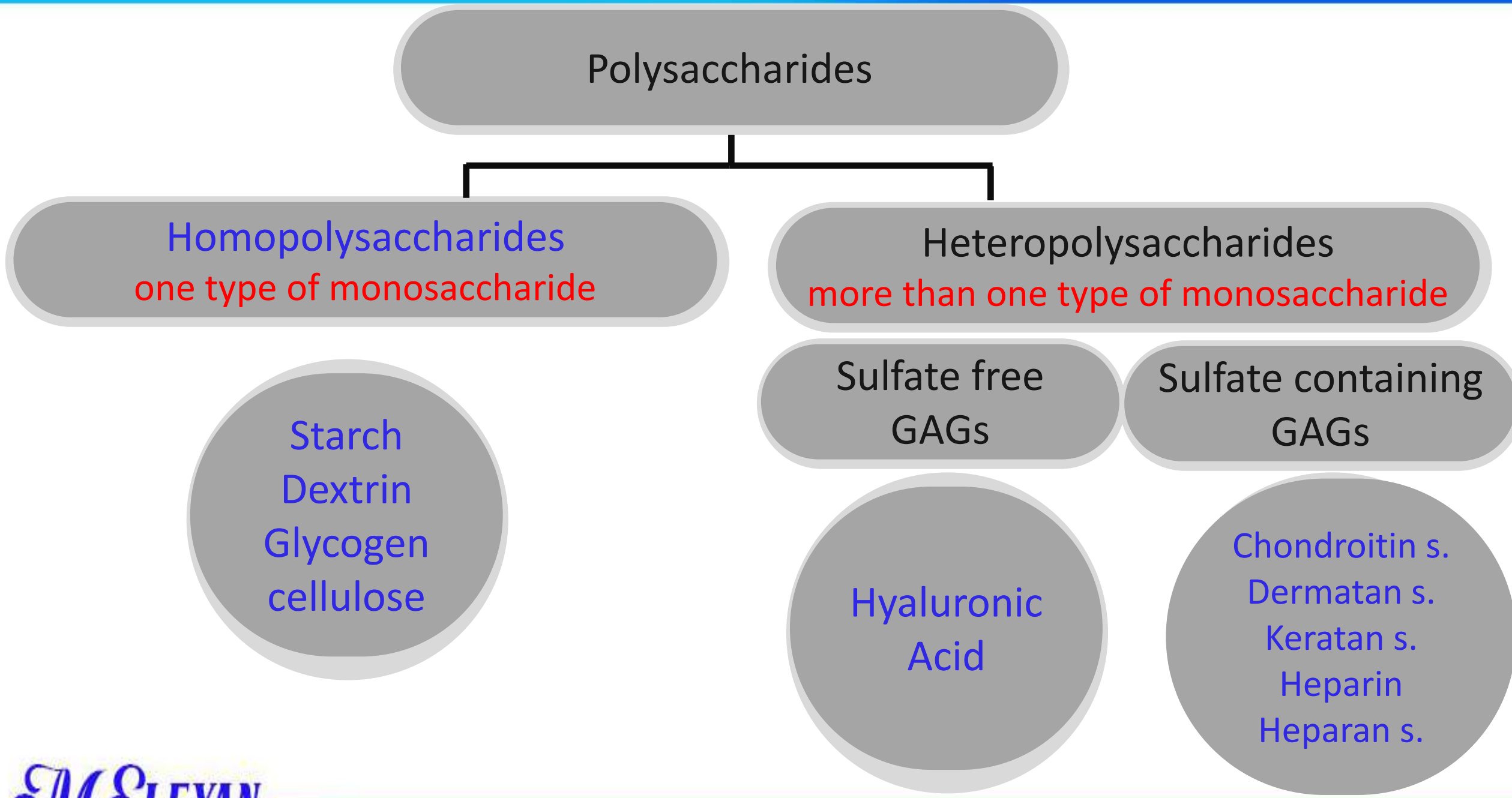
Carbohydrate Chemistry

Asst. Prof.Mohammed Hasan Eleyan

Faculty of Medicine

Al-Azhar University-Gaza

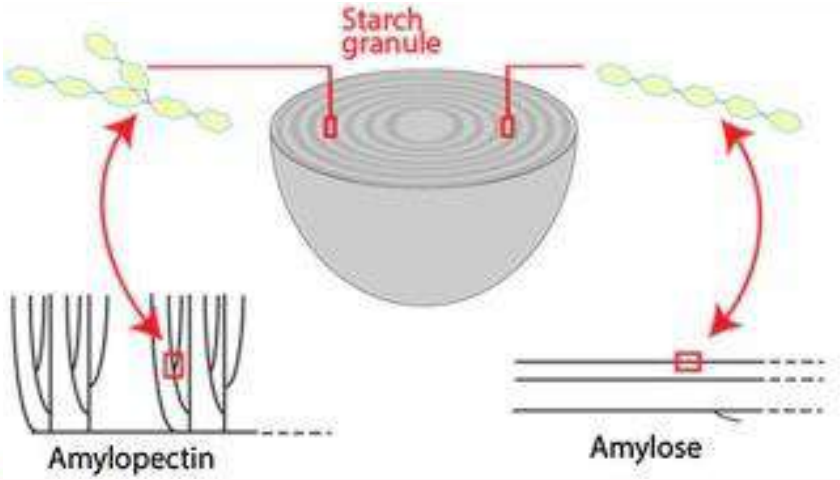



Polysaccharides
Homopolysaccharides
one type of monosaccharide
Heteropolysaccharides
more than one type of monosaccharide
Starch
Dextrin
Glycogen
cellulose
Sulfate free
GAGs
Sulfate containing
GAGs
Hyaluronic
Acid
Chondroitin s.
Dermatan s.
Keratan s.
Heparin
Heparan s.

Starch

- Starch is a homopolysaccharide that serves as the primary energy reserve in plants.
- It is made up of two polymers of glucose:

1. Amylose
2. Amylopectin

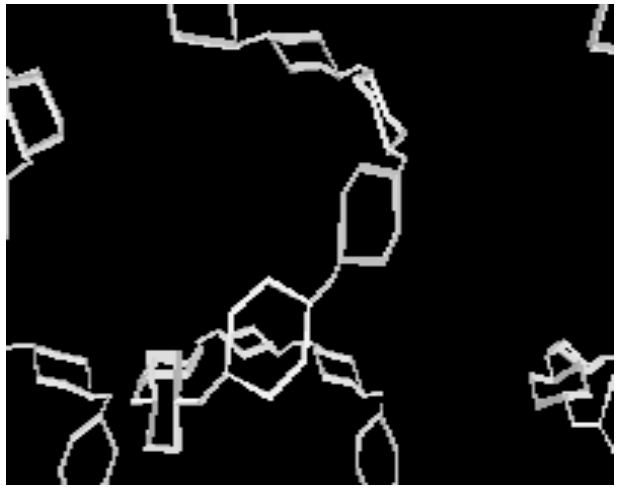


Starch (Amylose, Amylopectin)

1. Amylose is a continuous chain of glucose molecules linked by α-1,4 glycosidic bonds.
2. Amylopectin is a branched chain of glucose molecules linked by α-1,4- and α-1,6-glycosidic bonds.

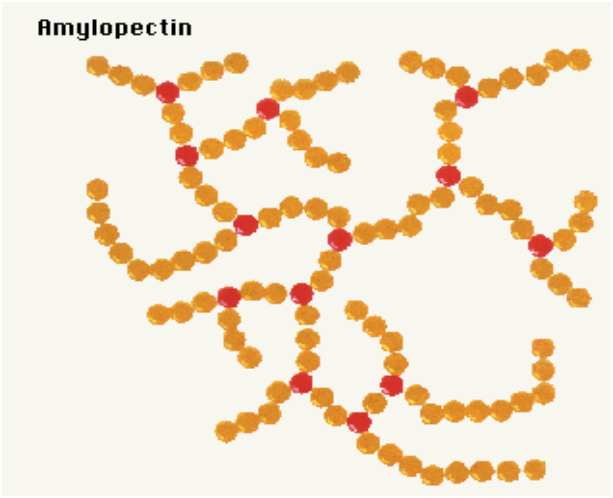
Starch

Amylose



- α-glucose
- 1,4 glycosidic bonds
- Spiral structure

Amylopectin

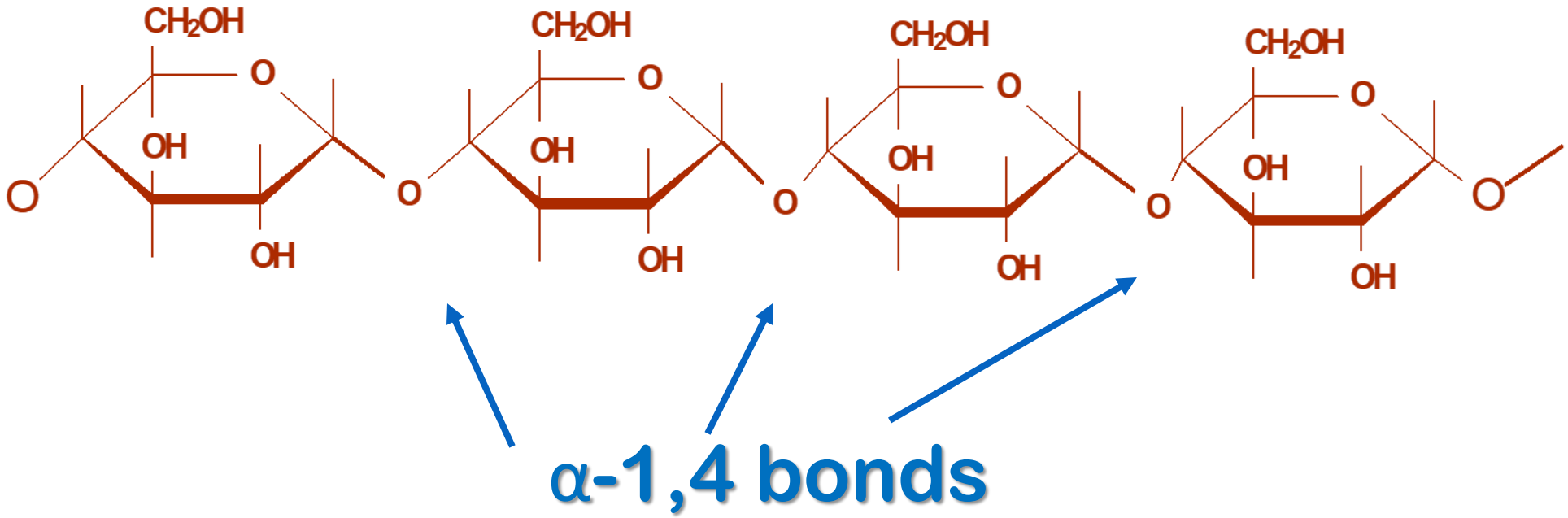


- α-glucose
- 1,4 and some 1,6 glycosidic bonds
- Branched structure

Structures of Amylose and Amylopectin

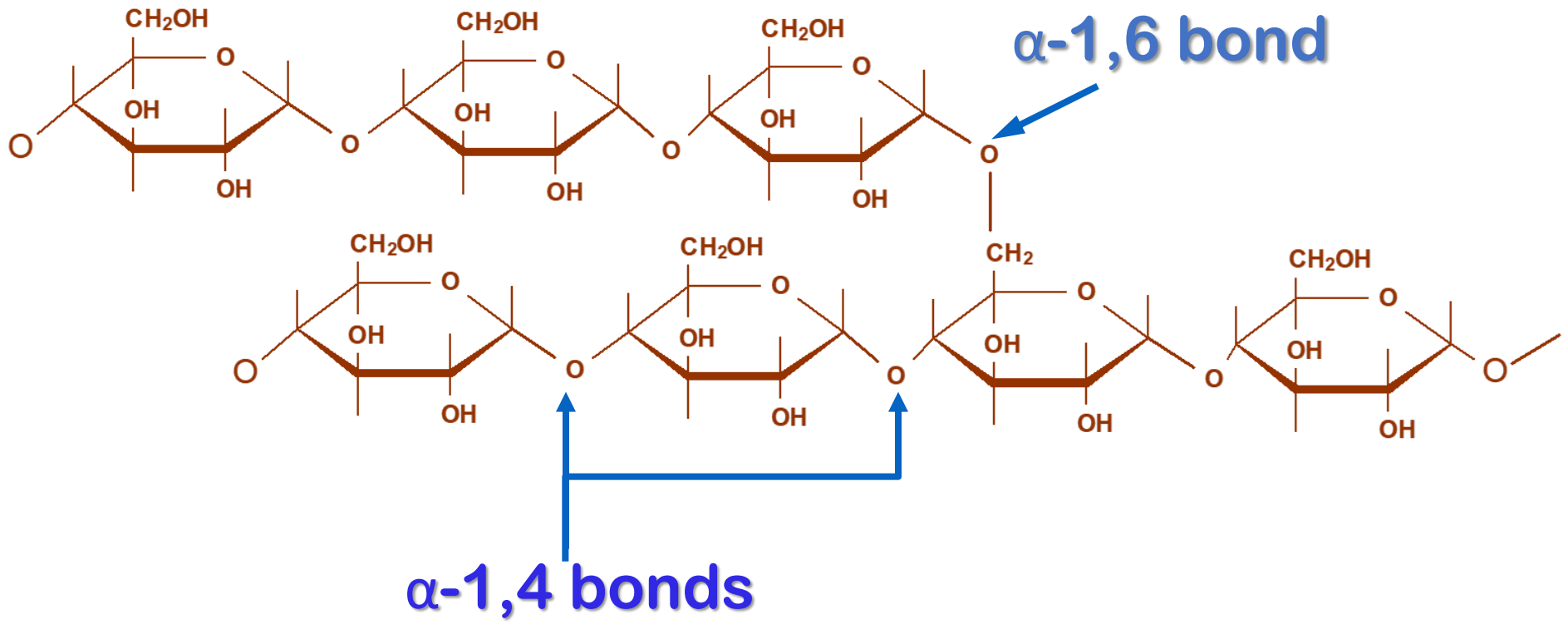
Amylose

Polymer with α-1,4 bonds



Amylopectin

Polymer with α-1,4 and α-1,6 bonds branches

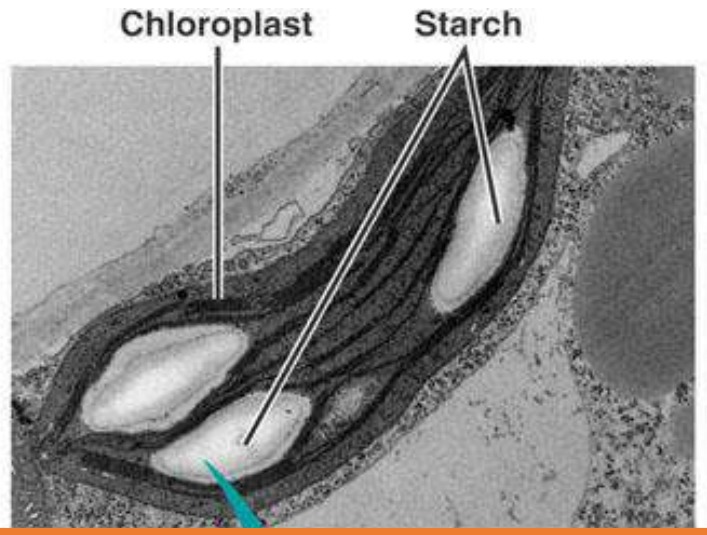


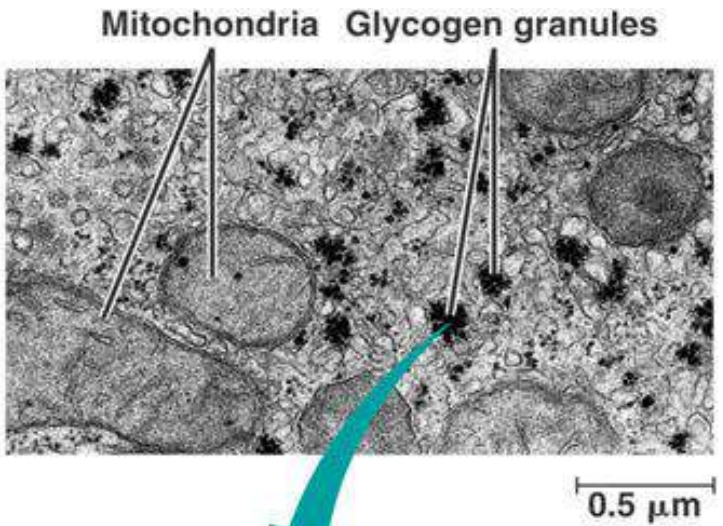
Glycogen

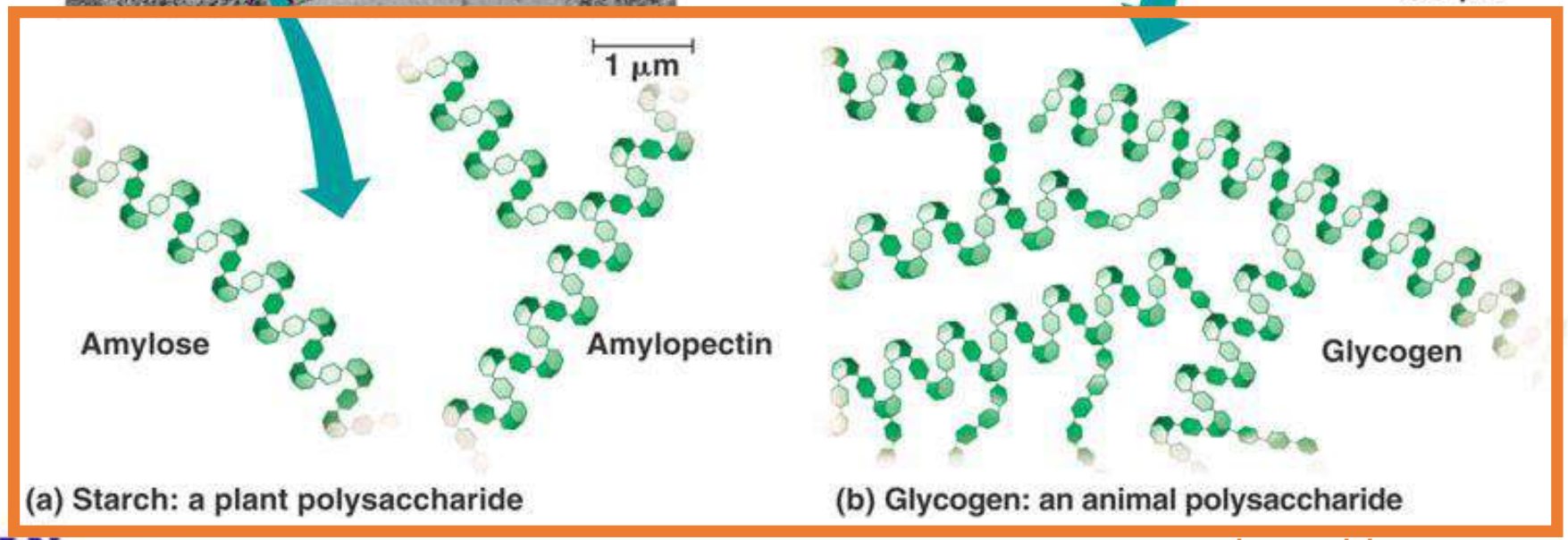
- Glycogen is similar to amylopectin, but more highly branched.
- In humans, glycogen is stored primarily in the cells of the liver and skeletal muscle.
- α-glucose units
- 1,4 and 1,6 glycosidic bonds
- Branched structure

Starches

Glycogen







more branching

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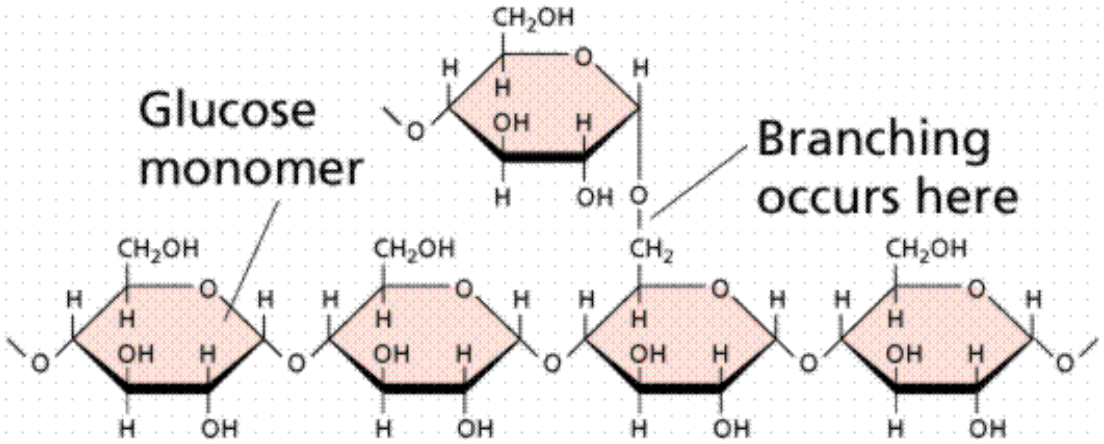
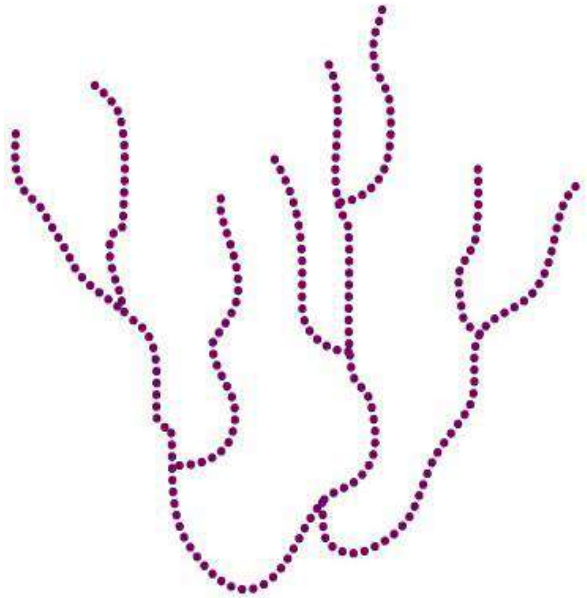
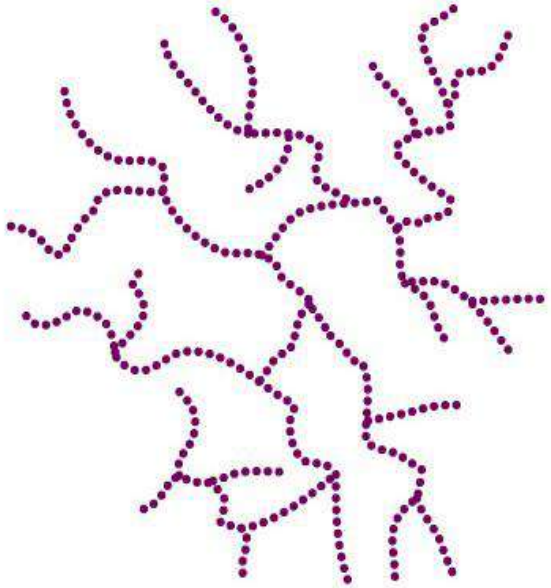
Starch/Glycogen





Amylopectin
(in plants)



Glycogen
(in animals)

Cellulose

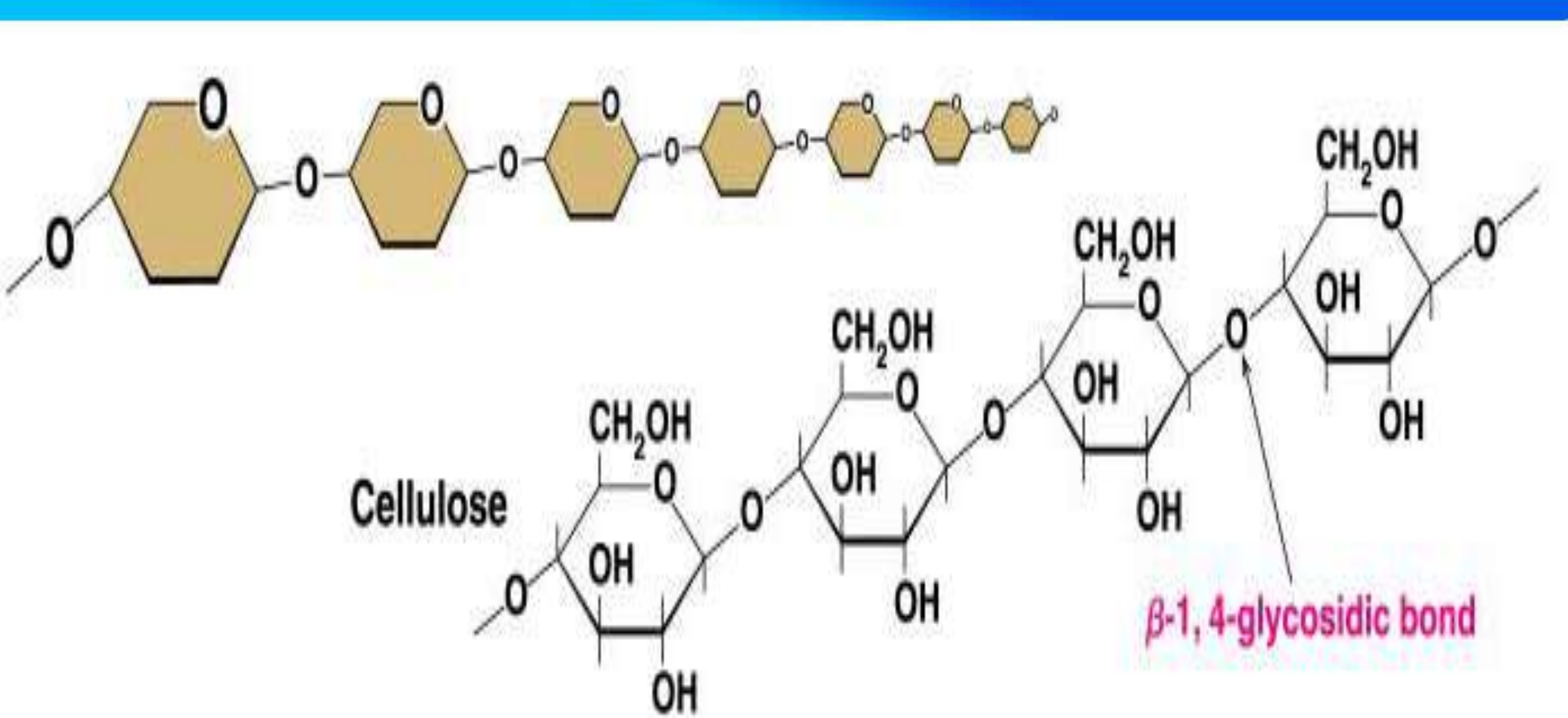
- Long linear chains of (β-D-glucopyranose) linked together by β-1-4 glycosidic bond.

1. Human cannot digest (hydrolyze) cellulose due to absence of digestive hydrolase enzyme that attacks β-linkage.
2. Other organisms can digest cellulose include the microorganisms living the gastrointestinal tract of cows and termites and many fungi.

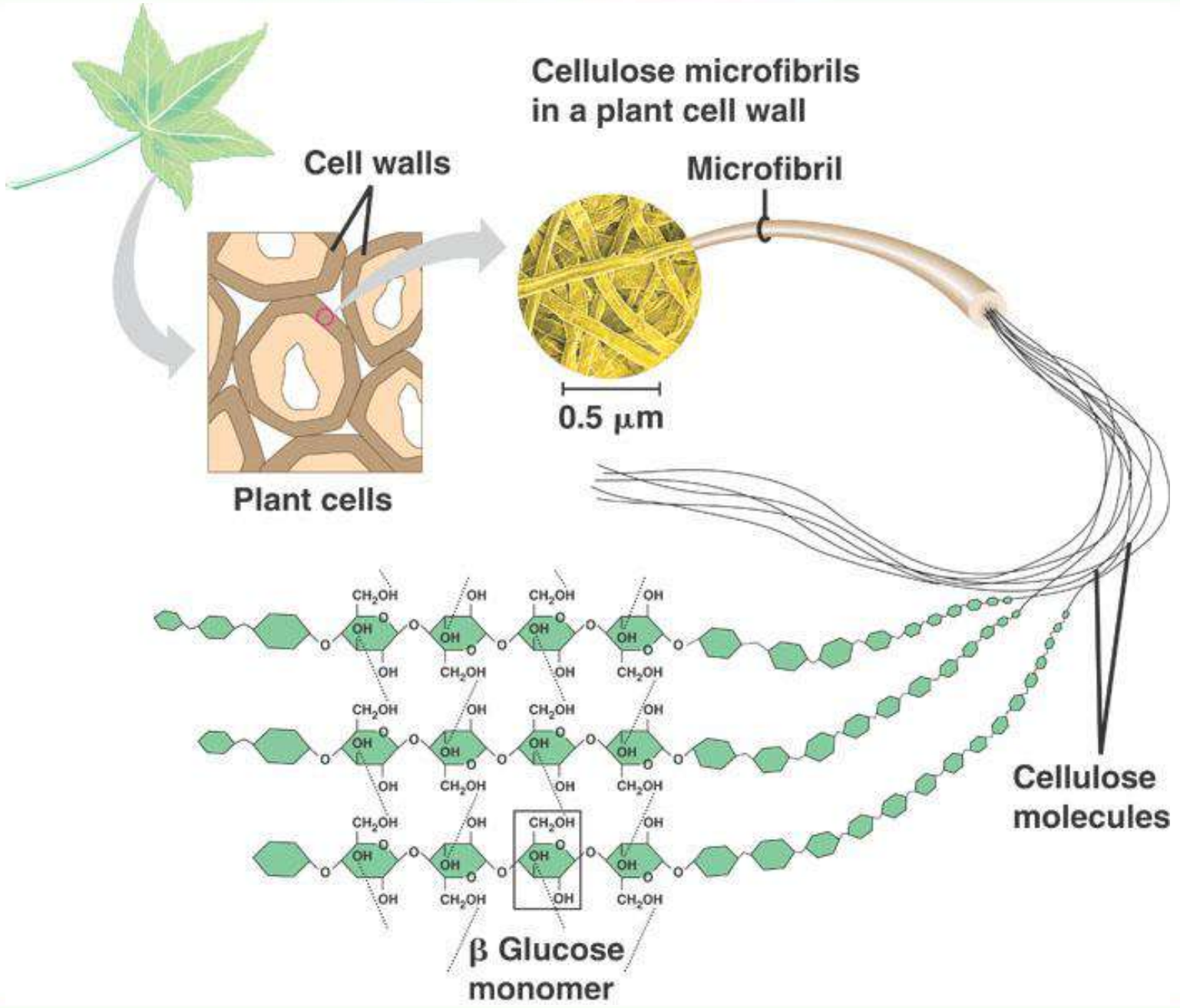
Cellulose

- It found in plants: vegetables, cotton
- The presence of cellulose in diet is important because it:

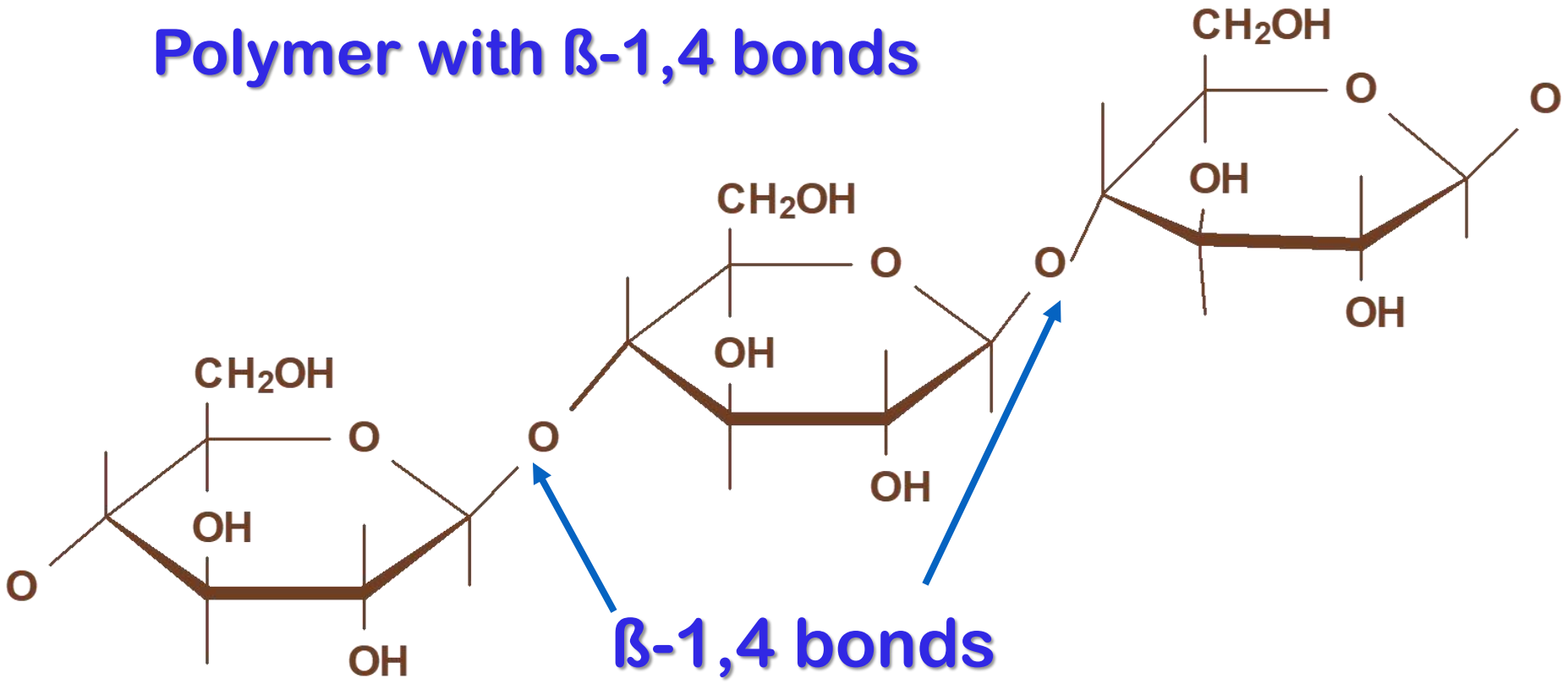
1. increases the bulk of stool.
2. This stimulates intestinal movement and prevents constipation.



Cellulose


Cellulose microfibrils
in a plant cell wall
Cell walls
Microfibril
0.5 μm
Plant cells
Cellulose
molecules
β Glucose
monomer

Cellulose



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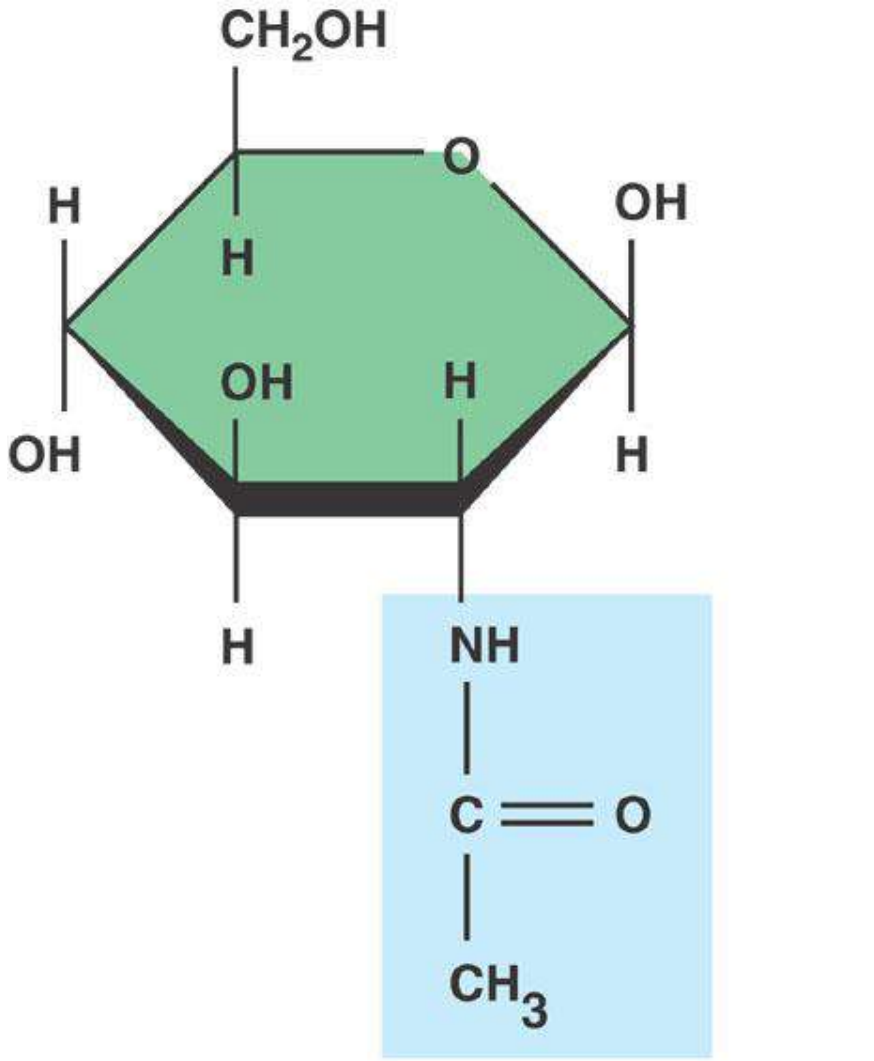
Chitin

- Chitin is another example of a structural carbohydrate.
- Chitin is composed of a repeating monomer called N-acetylglucosamine (GlcNAc or NAG).
- Chitin is found in the exoskeletons of insects and spiders.
- Chitin is also found in the cell walls of fungi.

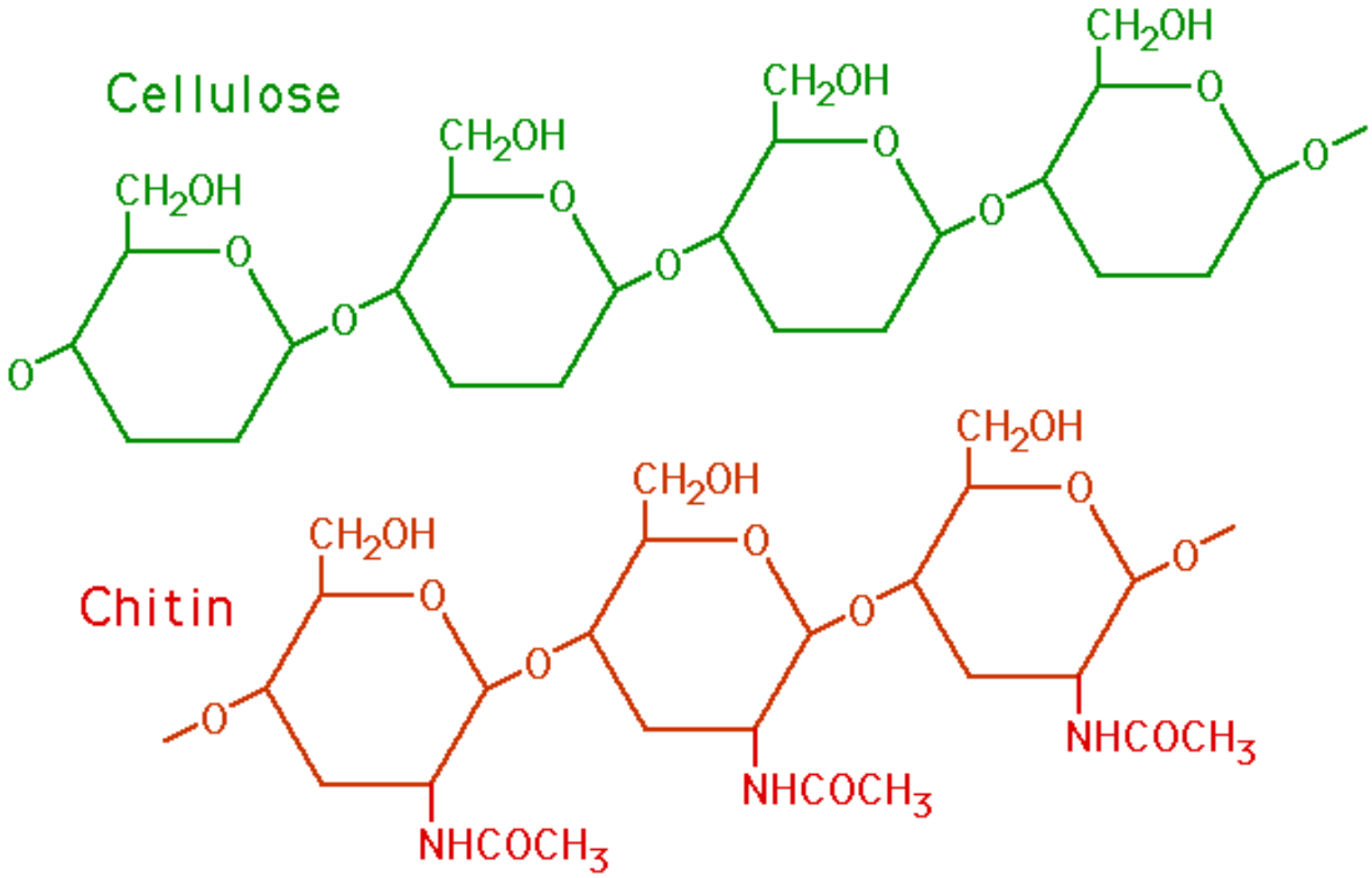
Chitin



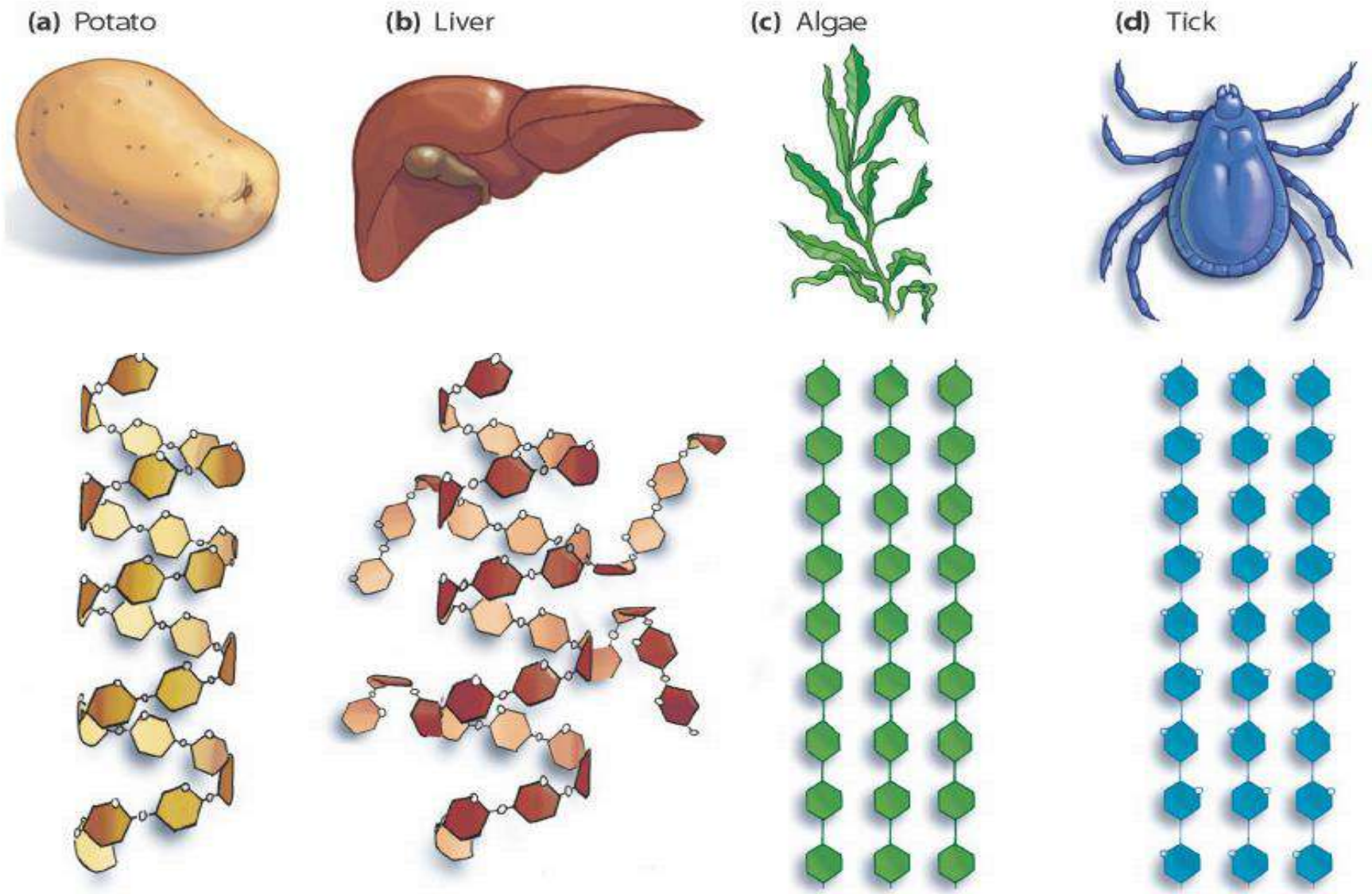
The structure of the chitin monomer

N-acetylglucosamine

Chitin

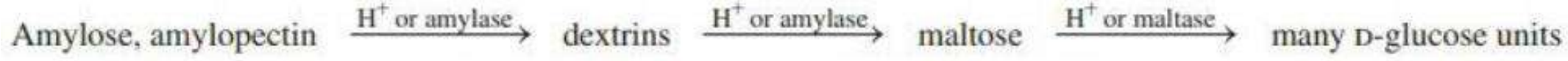


Some Familiar and Important Complex Carbohydrates

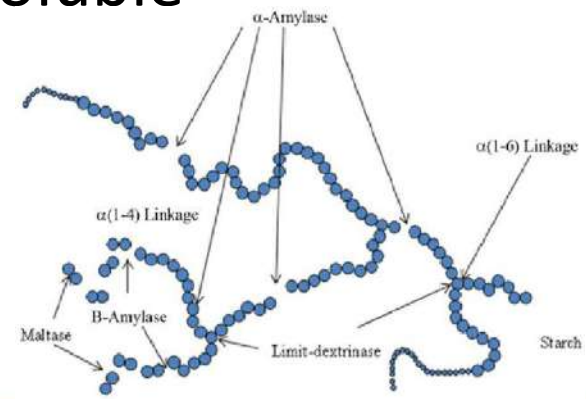


Dextrins

- Dextrins are a group of carbohydrates that are intermediate products formed during the partial hydrolysis (breakdown) of starch.



- Amylodextrin, Erythrodextrin and Achrodextrin (water-soluble nature)



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Dextrins

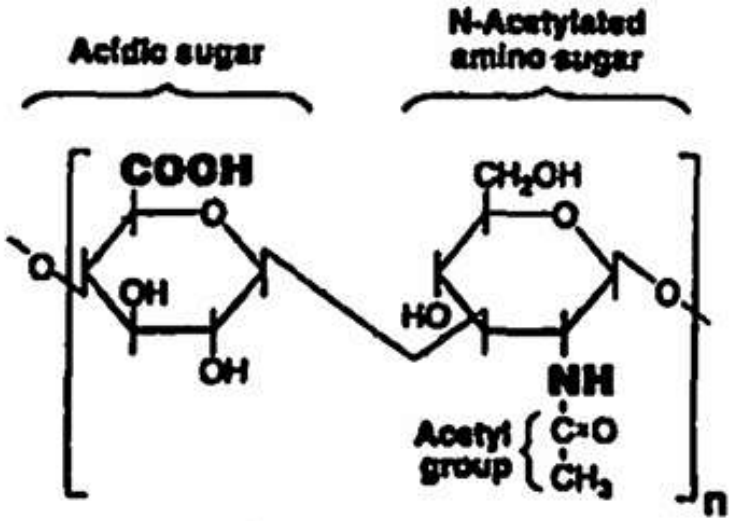
- Amylodextrin is shorter chains of glucose units than starch.
- Erythrodextrin is characterized by its reddish color and have a higher degree of polymerization (longer chains of glucose) compared to amylodextrins.
- Achrodextrin, is relatively colorless (achro means colorless), and consists of short chains of glucose units

Heteropolysaccharides: Glycosaminoglycans, GAGs (mucopolysaccharide)

- They are formed of repeating disaccharide units

(Amino sugar + Acidic sugar (uronic acid) or galactose)n

- They are unbranched and contain no N-acetyl neuraminic acid.

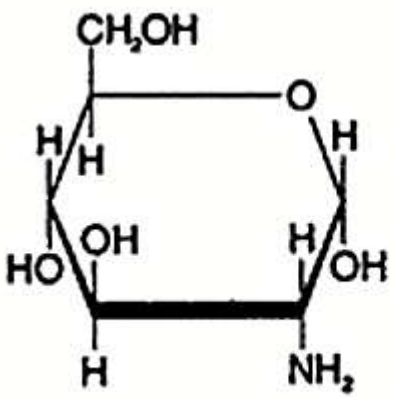


Repeating disaccharide unit.

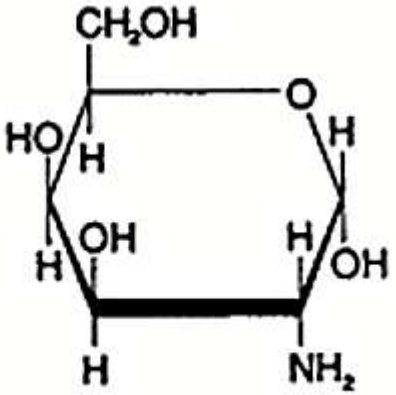
Heteropolysaccharides: Glycosaminoglycans, GAGs (mucopolysaccharide)

- Amino sugar :

1. D-glucosamine
2. D-Galactosamine



α-D-glucosamine



α-D-galactosamine

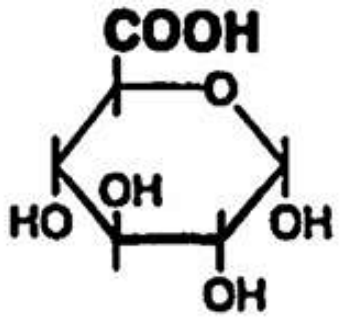
- In which the amino group is usually acetylated.
- The amino sugar may also be sulfated at carbon 4 or 6.

Heteropolysaccharides: Glycosaminoglycans, GAGs (mucopolysaccharide)

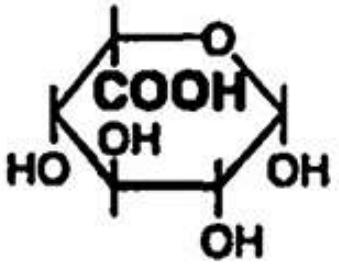
- The acidic sugar:

1. D-glucuronic acid or,
2. Its epimer, L-iduronic acid.

- Or: Galactose



D-Glucuronic acid

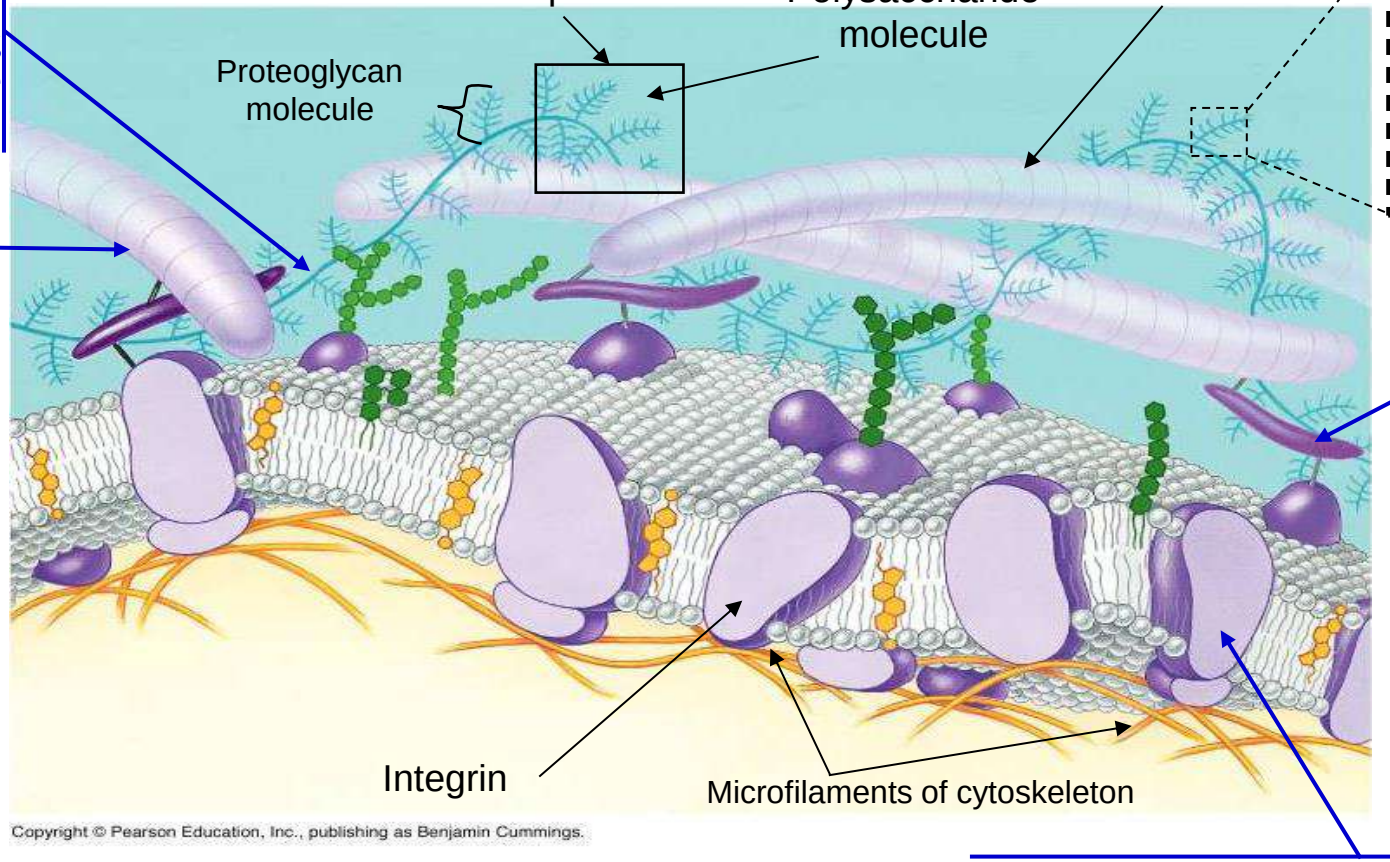


α-L-Iduronic acid

Heteropolysaccharides: Glycosaminoglycans, GAGs (mucopolysaccharide)

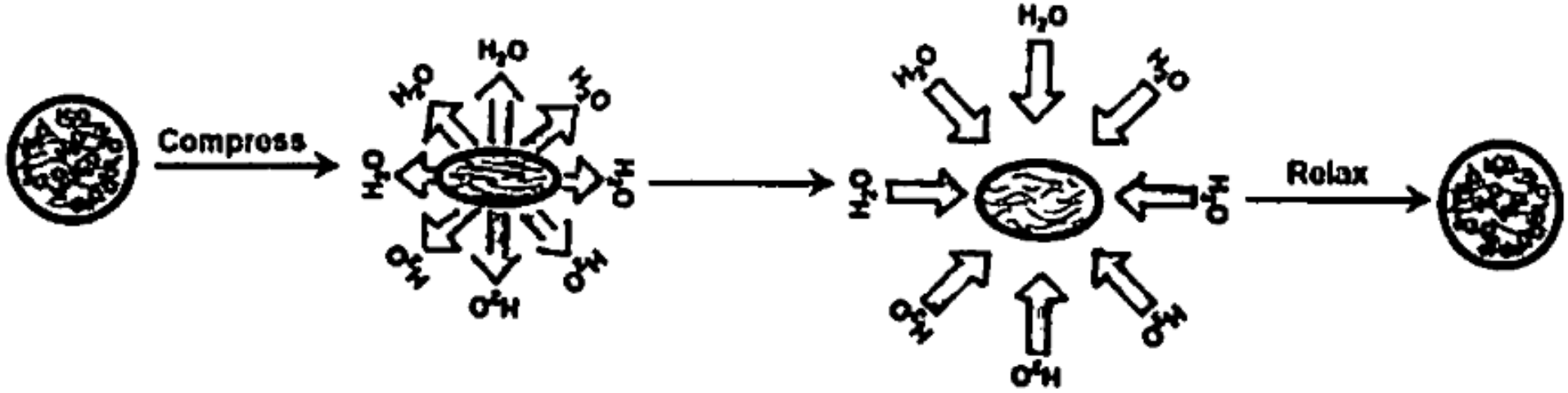
- Most of GAGs are present extracellularly except heparin.
- Most of them form the structural components of connective tissue such as bone, elastin and collagen.
- They act as Lubricants and cushion for other tissues because they have the property of holding large quantities of water.

Components of the extracellular matrix



Heteropolysaccharides: Glycosaminoglycans, GAGs (mucopolysaccharide)

- When a solution of glycosaminoglycans is compressed, the water is "squeezed out" and the glycosaminoglycans are forced to occupy a smaller volume,



Heteropolysaccharides: Glycosaminoglycans, GAGs (mucopolysaccharide)

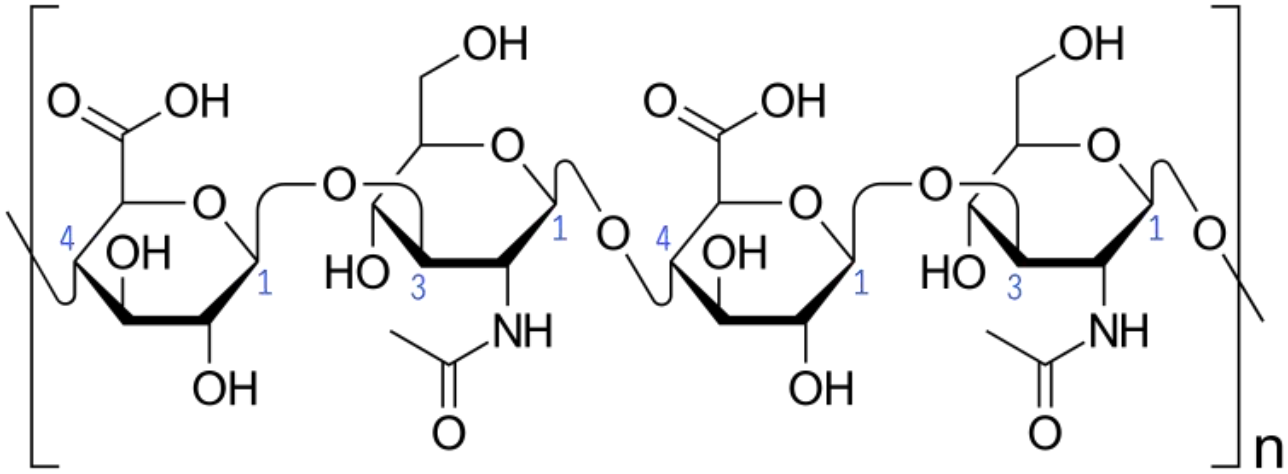
- When the compression is released, the glycosaminoglycans return to their original hydrated volume.
- This property is the cause of flexibility of synovial fluid.

There are 6 types:

1. Heparin.
2. Keratans
3. Heparan sulphate.
4. Chondroitins
5. Dermatan sulphate
6. Hyaluronic acid

Hyaluronic acid: structure

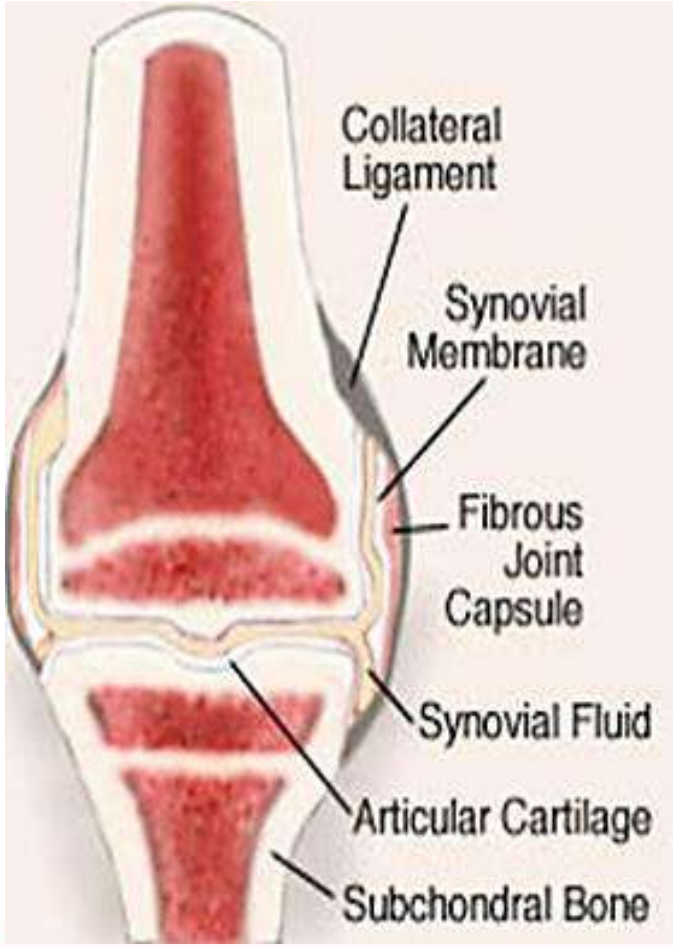
- Hyaluronic acid is the only GAGs which contains no sulfate group.
- Consists of repeats D-glucuronic acid and N-acetyl glucosamine.



Hyaluronic acid: Site and Function

1. Site: Cartilage, Connective tissue, and Synovial fluid
2. Function:

- It acts as a lubricant in joints.
- It makes cartilage compressible
- It makes extracellular matrix loose because of its ability to attract water.
- It permits cell migration during wound repair.



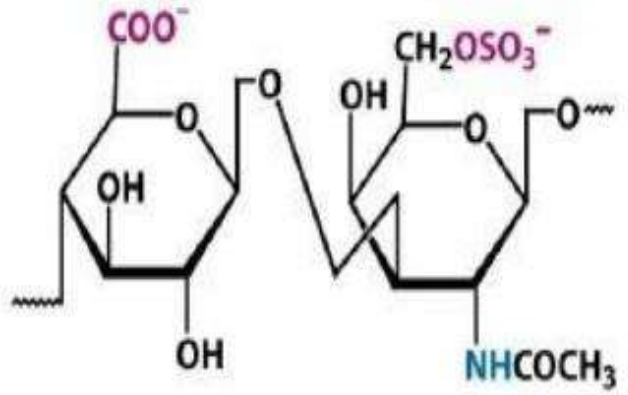
Hyaluronic acid: Role in disease:

- Hyaluronic acid facilitates cell migration.
- It is produced in increased amounts by tumor cells. This facilitates migration of these cells through the extra cellular matrix and spread of the tumor.

Chondroitin 4- and 6 sulfate: structure

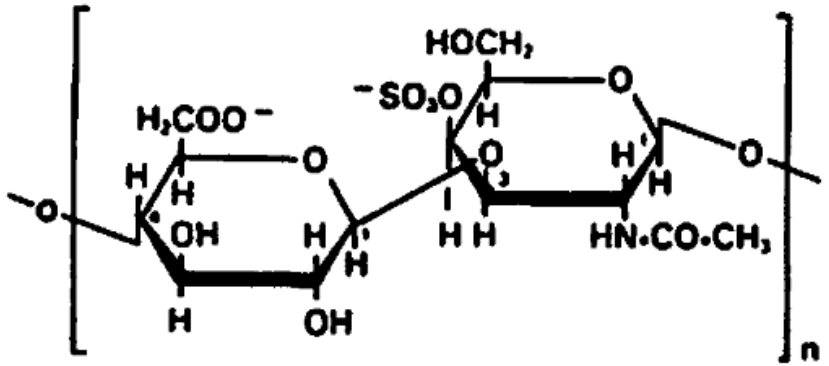
- The repeated disaccharide unit consists of:

1. Glucuronic acid.
2. N-acetylgalactosamine with sulfate on either C4 or C6.



Chondroitin 6-sulfate

Chondroitin 4-Sulfate
(Note There is also a 6-sulfate)

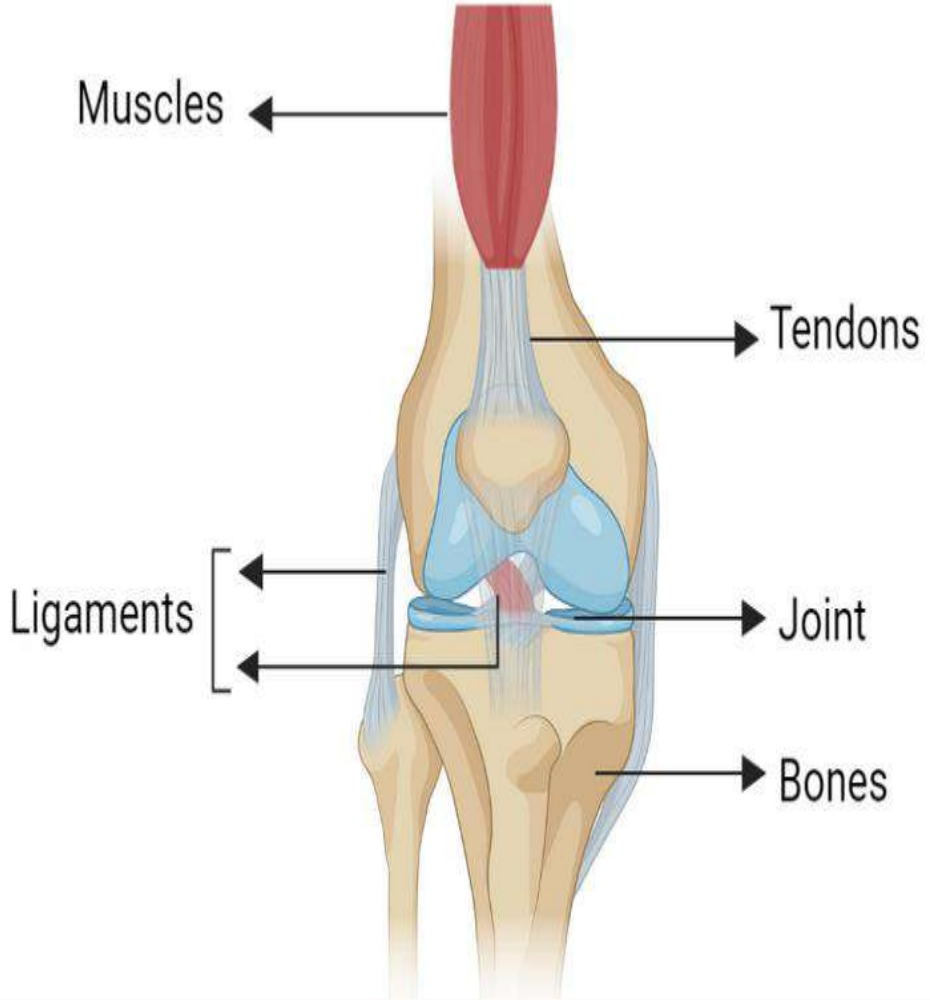


β-Glucuronic acid N-acetylgalactosamine sulfate

Chondroitin 4- and 6 sulfate: Site

- Site: It is the most abundant GAGs in the body.
- It is found in:

1. Cartilage, tendons, ligaments and bones.
2. Aorta, skin, cornea, and umblical cord.



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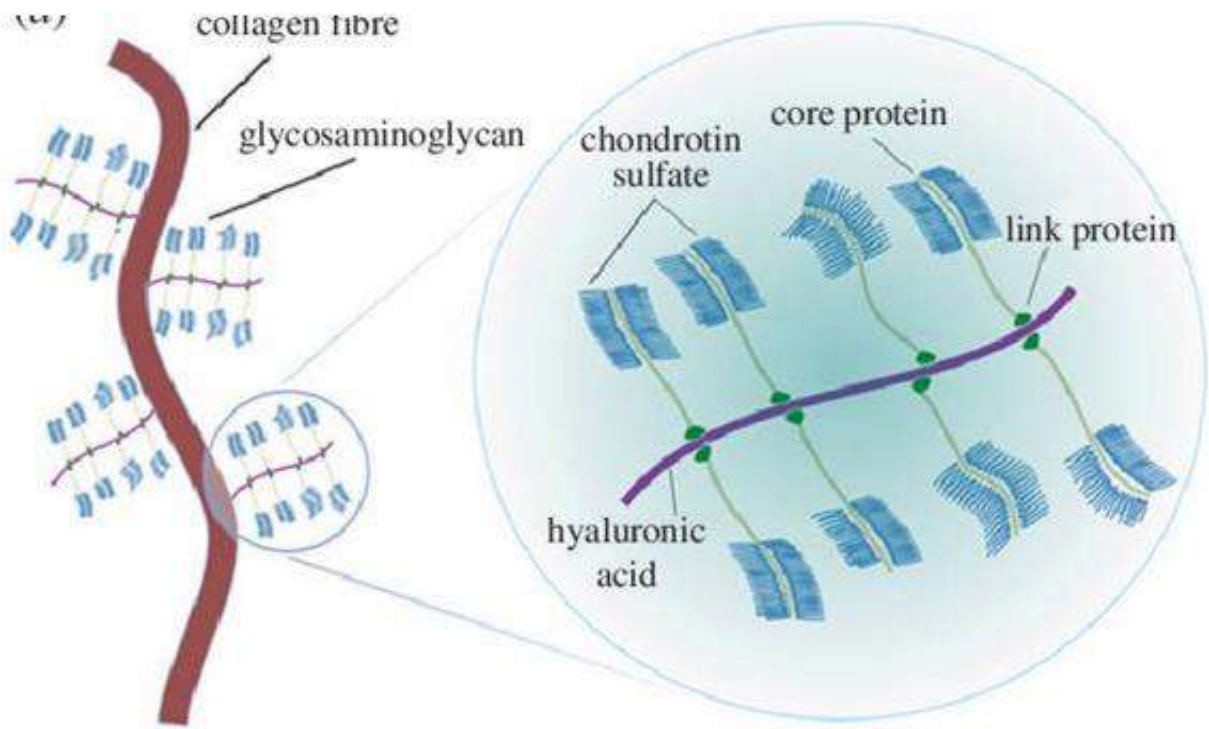
Chondroitin 4- and 6 sulfate: Function

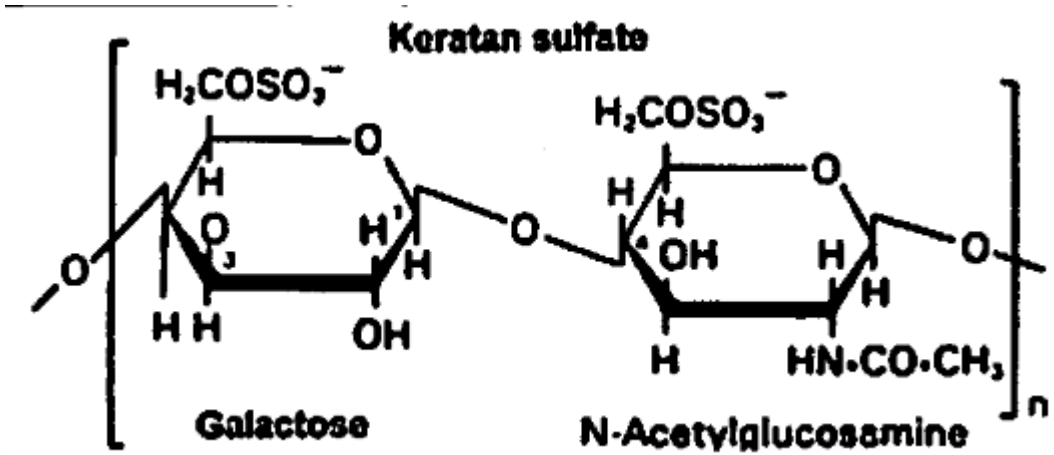
1. In cartilage: it binds collagen and hold fibers in strong network.
2. It makes cartilage compressible
3. Help to maintain the shape of skeletal system.



Keratan sulfate: Structure:

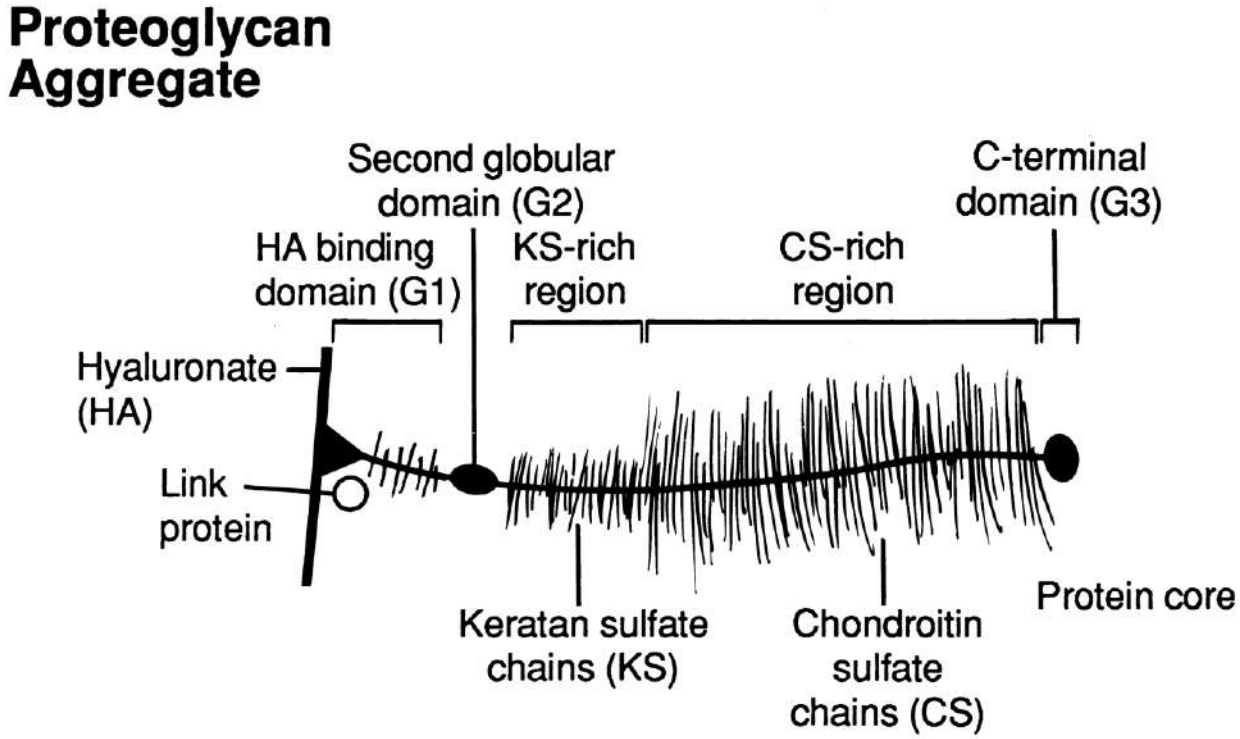
- The repeated disaccharide unit consists of:

1. Galactose (no uronic acid), with sulfate on C6.
2. N-acetylglucosamine with sulfate on C6.



Keratan sulfate: Site and Functions

- Site:
    1. Cornea.
    2. Cartilage.

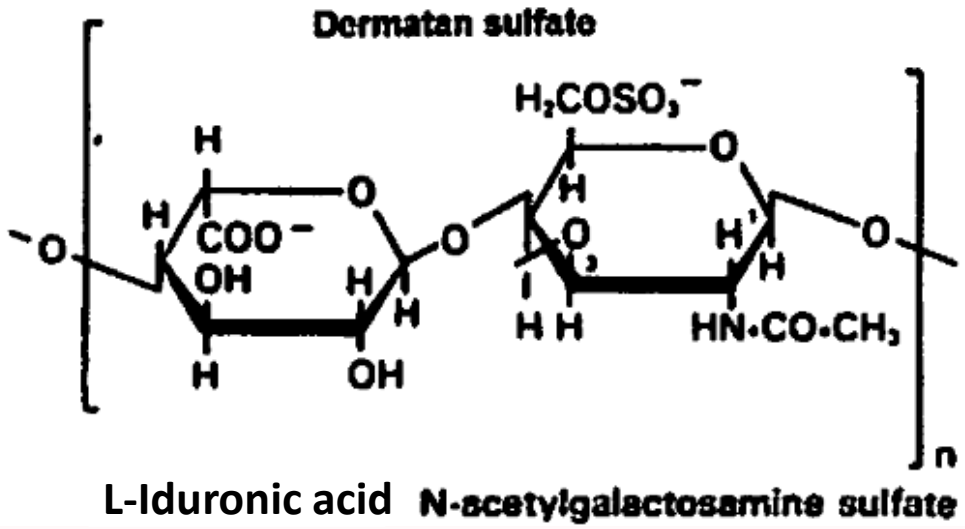


- Functions:
    1. It plays an important role in corneal transparency.

Dermatan sulfate:

- The repeated disaccharide unit consists of:

1. L-Iduronic acid.
2. N-acetylgalactosamine with sulfate on C6



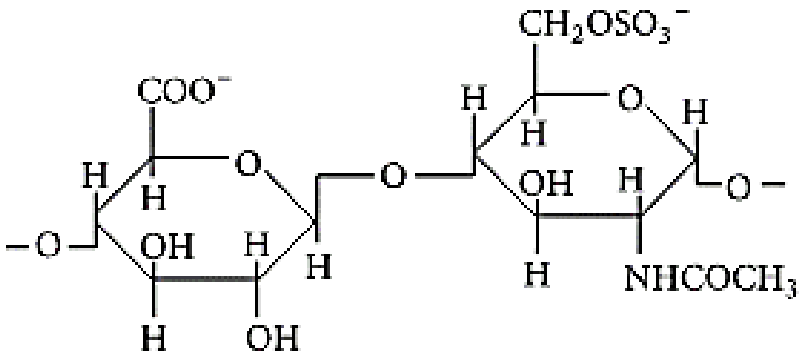
Dermatan sulfate: Site and Function

- Site:
  1. Cornea.
  2. Skin
  3. blood vessels
  4. heart valves.
- Functions:
  - In cornea, it plays-together with keratan sulfate, an important role in corneal transparency.

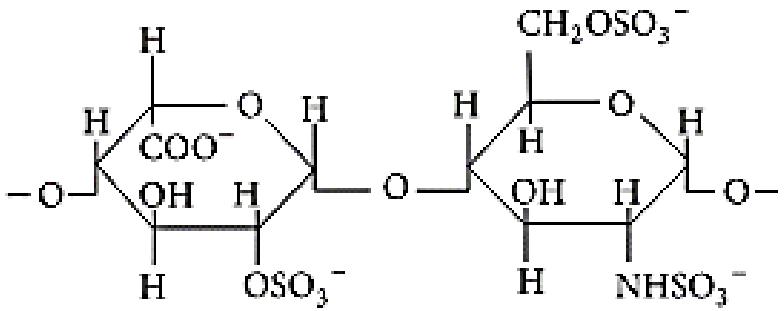
Heparin: Structure:

- The repeated disaccharide unit consists of:

1. Iduronic acid with sulfate on C2.
2. Glucosamine with sulfate on C2 and C6.



Heparan sulfate



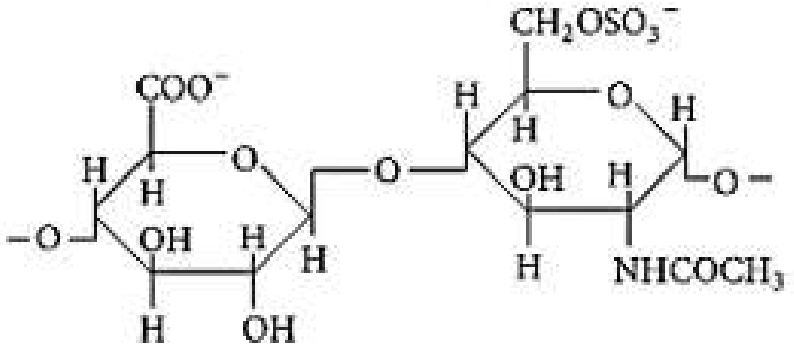
Heparin

Heparin: Structure:

- Site: Heparin present in mast cells (intracellular compound).
- Mast cells are located along the wall of blood vessels of liver, lungs, skin, heart, kidney and spleen.
- Functions:
- It acts as anticoagulant.

Heparan sulfate

- Heparan sulfate (which has the same structure as heparin except some glucosamines are acetylated and there are fewer sulfate groups, has the following functions:
- It acts as cell membrane receptors.
- It participates in cell adhesion and cell-cell interaction.



Heparan sulfate

THANK YOU

M.ELEYAN

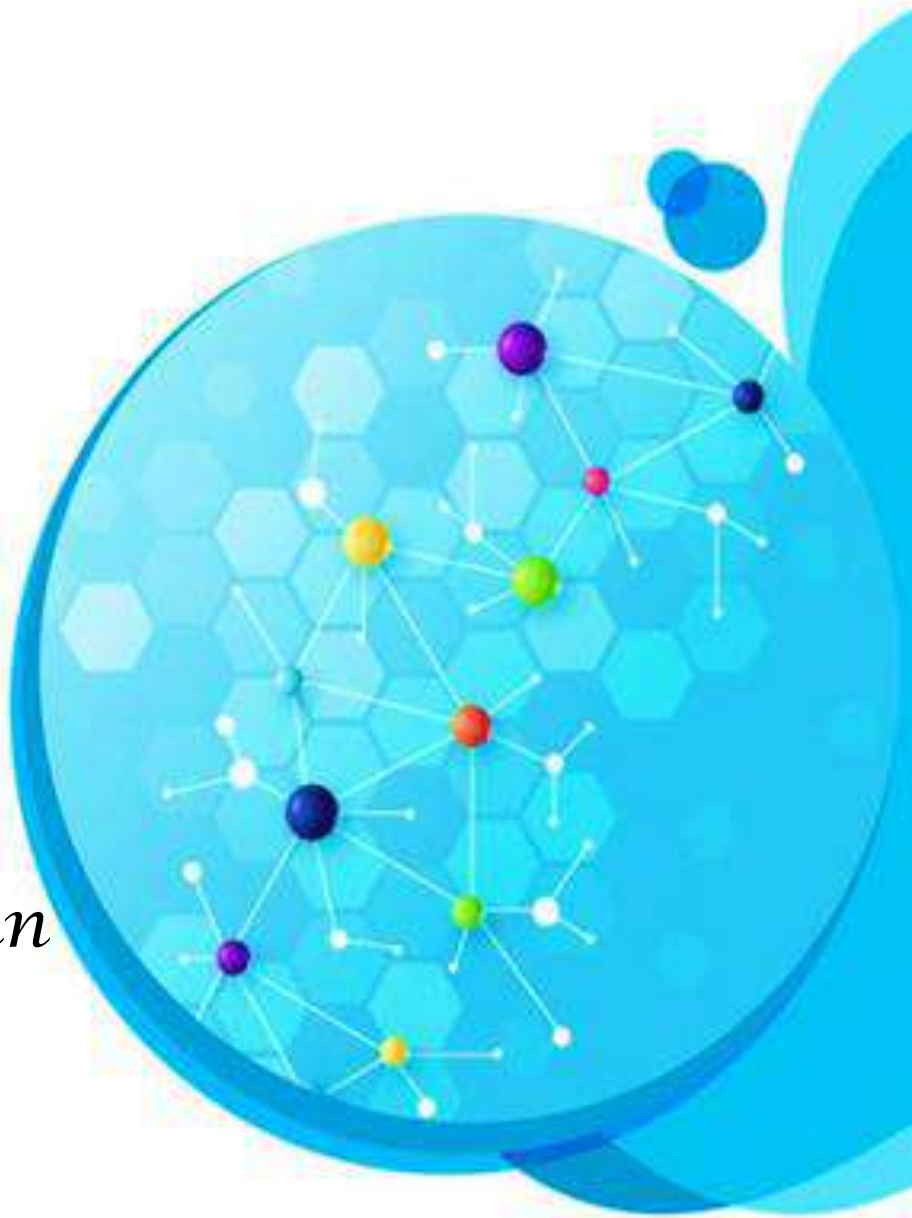
Medical Biochemistry

Lipid Chemistry

Asst. Prof.Mohammed Hasan Eleyan

Faculty of Medicine

Al-Azhar University-Gaza



Lipids Chemistry

Definition, function and classification of Lipids

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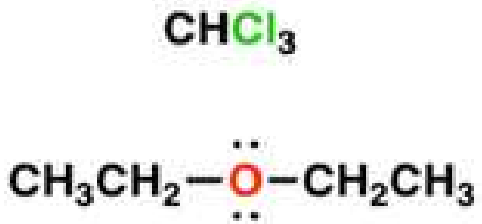
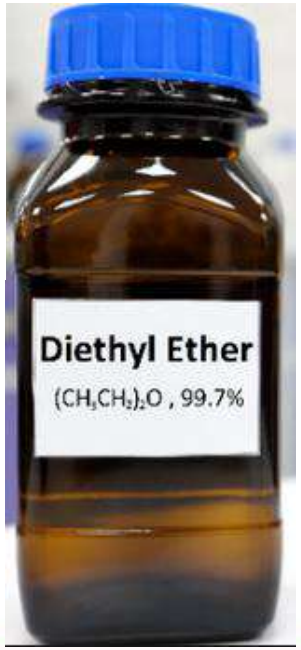
Definition of Lipids

- Lipids are a family of biomolecules that have the common property of being soluble in organic solvents, like ether or chloroform, but not in water.





- The hydrophobic nature of lipids is due to the predominance of hydrocarbon chains (- CH2-CH2-CH2-) in their structure.

Lipids, particularly triacylglycerols (TAGs), are the primary long-term energy storage molecules in animals.They provide more than twice the energy per gram compared to carbohydrates or proteins (9 kcal/g vs. 4 kcal/g).
Lipids in adipose tissue help maintain body temperature and protect organs against mechanical shock.
Lipids like eicosanoids, steroid hormones, and phosphatidylinositol derivatives play roles in cell signaling and regulation of physiological processes.
Lipids aid in the absorption and transport of vitamins A, D, E, and K.

- Storing energy (**fasting or physical exertion**).
- Protecting and insulating internal organs (**cushions & preventing heat loss)**
- Acting as chemical messengers (TAG)
- Because they are not soluble in water, lipids are components of cellular membranes (to separate the internal contents of cells from the external environment).

Classification of lipids

Simple

- **Fats (acylglycerols)**
  (Glycerol + FAs)
- **Waxes**
  (Higher alcohol + FA)

Compound

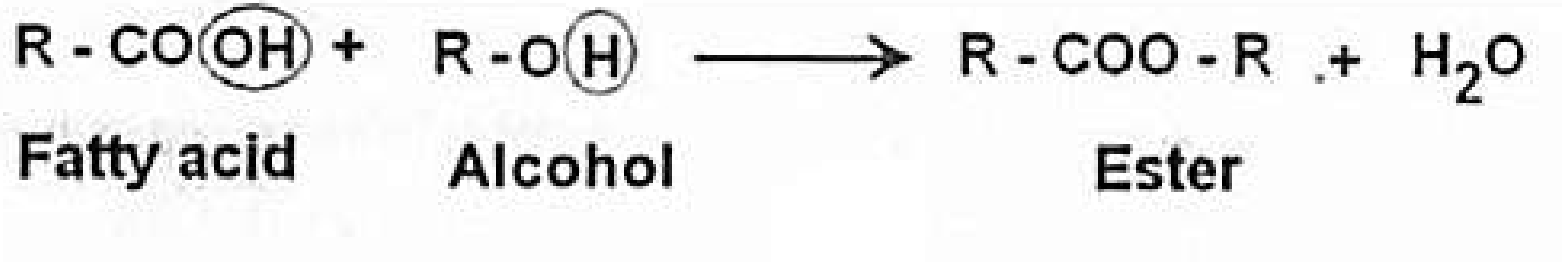
- **Phospholipids:**
  Glycerophospholipids
  Sphingophospholipids
- **Glycolipids**
  Cerbrosides
  Gangliosides
  Ceramide oligosaccharides
- **Lipoproteins**
  Chylomicrones
  VLDL
  LDL
  HDL

Derived

- Fatty acids
- Steroids
- Fat soluble vitamins
- Ketone bodies
- Carotenoids
- cholanthrenes

Simple lipids

- Simple lipids: are esters of fatty acids with various alcohols .
- (Ester bond = -COO-).
- They are either fats or waxes



Lipids Chemistry

Chemistry of fatty Acids, Alcohols and Simple Lipids

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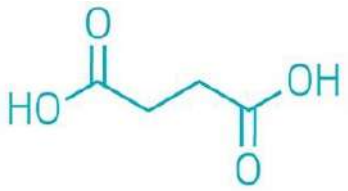
Fatty acids: R-COOH

- Fatty acids are water-insoluble especially “long chain hydrocarbons”.
- Fatty acids may be saturated (no double bonds) or unsaturated (containing one or more double bonds).
- They are mostly monocarboxylic i.e. having one carboxyl group at the end of the chain (-COOH)
- Short chain > 10 C or Long chain < 10 C



Succinic acid

Dicarboxylic

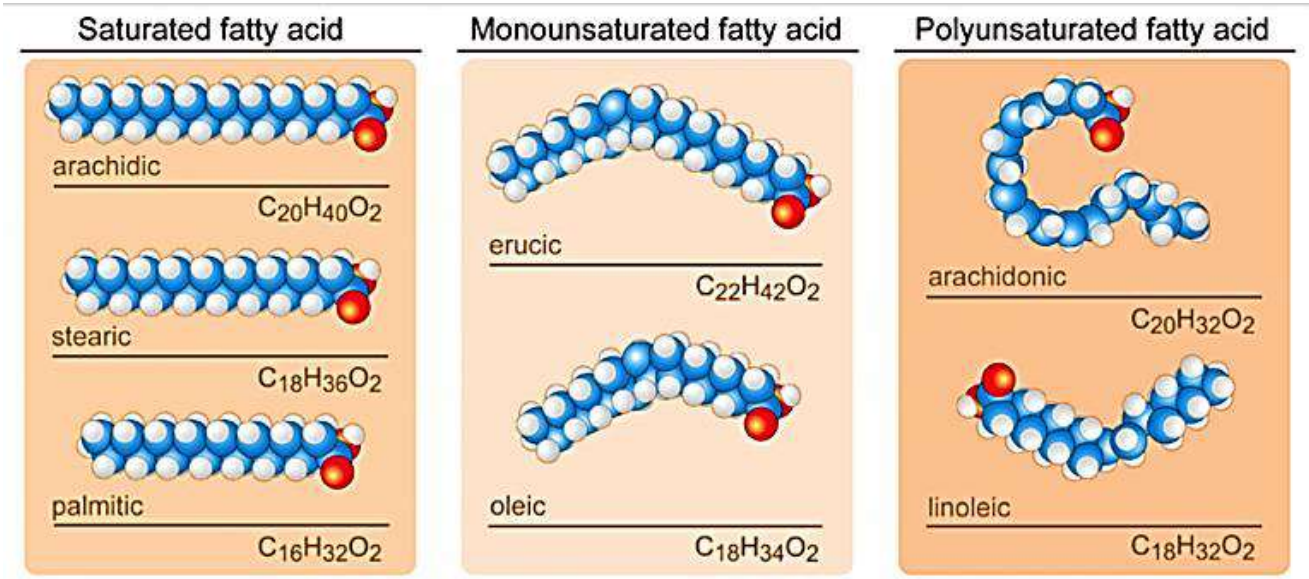
Fatty acids: R-COOH

- They are mostly aliphatic (i.e. not branched). A few branched chain fatty acids are more commonly associated with microorganisms.
- Fatty acids are most commonly found in natural fats and oils, where they are esterified to glycerol, forming **triacylglycerols** or other lipids.
- Fatty acids may also present as free fatty acids in the plasma carried by plasma proteins (serum albumin)

Fatty acids can be saturated, monounsaturated, or unsaturated.

Types of Fatty Acids

Type of Fatty Acid	Double Bonds	Diagram
Saturated	None	
Monounsaturated	One	
Polyunsaturated	Multiple (>1)	



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Saturated fatty acids :

- **Have no double bonds in the chain.**
- **Their general formula is CH_3-$(CH_2)_n$-COOH**

Butyric acid (4C) = $CH_3 - CH_2 - CH_2$ -COOH.

Caproic acid (6C) = $CH_3 - CH_2 - CH_2 - CH_2 - CH_2$ - COOH.

Palmitic acid (16C) = $CH_3 - (CH_2)_{14}$ - COOH.

Stearic acid (18C) = $CH_3 - (CH_2)_{16}$ - COOH.

Saturated fatty acids

Name	N.O of C	occurrence
Formic	1	Takes part in the metabolism of "C_1" units (formate) THF: 10-formyltetrahydrofolate Nucleotide Biosynthesis
Acetic	2	Major end product of carbohydrate fermentation by rumen organisms.
Propionic	3	
Butyric	4	In certain fats in small amounts (especially butter).
Palmitic acid	16	Common in all animal and plant fats
Stearic acid	18	
Arachidic	20	Peanut (arachis) oil

Numbering of carbon atoms:

- Counting starting from carboxylic (-COOH) group =carbon No.1
- Counting from carbon adjacent to carboxyl carbon as α, β, γ, δ, ε and so on.
- Counting from last methyl carbon (CH3) which is called omega carbon (ω). The carbon adjacent to it is carbon No.2 and so on

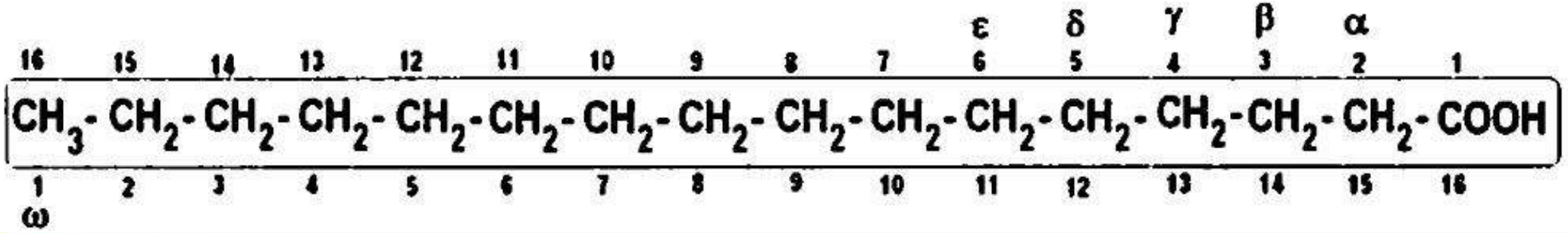
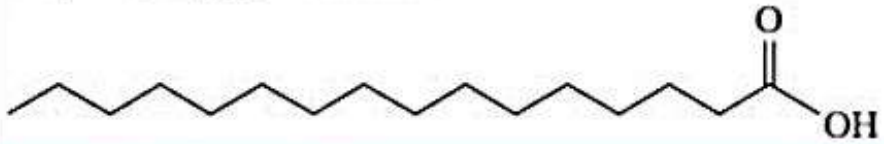


TABLE 17.1 Structures and Melting Points of Common Fatty Acids

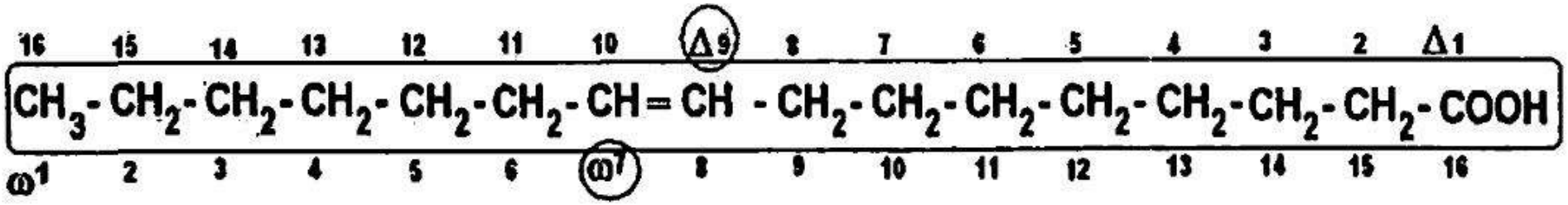
Name	Carbon Atoms: Double Bonds	Present in	Melting Point (°C)	Structures
Saturated Fatty Acids				
Palmitic acid	16:0	Palm	63	$CH_3—(CH_2)_{14}—COOH$ 
Stearic acid	18:0	Animal fat	69	$CH_3—(CH_2)_{16}—COOH$ 

Unsaturated fatty acids :

- Unsaturated fatty acids are fatty acid that contain one or more double bonds (C=C) in their hydrocarbon chain.
- Monounsaturated Fatty Acids (MUFA): have one double bond in their hydrocarbon chain.
- Polyunsaturated Fatty Acids (PUFA): have multiple double bonds in their hydrocarbon chain.

System of numbering and position of double bonds

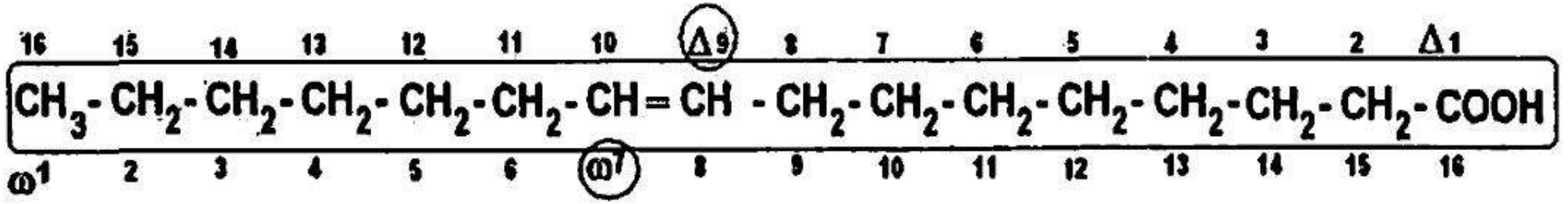
1. Numbering of carbon atoms; same as in saturated fatty acids
2. Position of double bonds:
   - **The delta(Δ) numbering system** e.g. palmitoleic acid, C16:1 Δ^9 (this acid contains 16 carbons and 1 double bond and it's position is between carbon number 9 and carbon number 10 starting from carboxyl carbon 1).



Palmitoleic acid (C 16:1 Δ^9) = (C 16:1 ω^7)

System of numbering and position of double bonds

- **Omega (ω) system** e.g. the palmitoleic acid may be Witten as: C16:1 , ω^7 which indicates a double bond on 7^{th} carbon counting from the ω-Carbon atom i.e. last $-CH_3$ carbon.



Palmitoleic acid (C 16:1 Δ^9) ≈ (C 16:1 ω^7)

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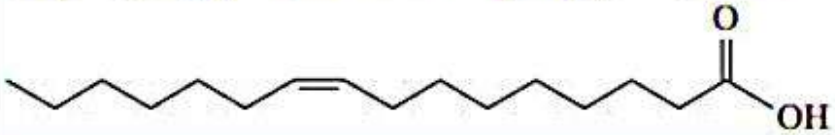
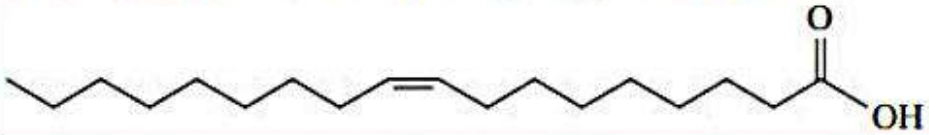
TABLE 17.1 Structures and Melting Points of Common Fatty Acids

Name	Carbon Atoms: Double Bonds	Present in	Melting Point (°C)	Structures
Monounsaturated Fatty Acids				
Palmitoleic acid	16:1	Butter	0	$CH_3-(CH_2)_5-CH=CH-(CH_2)_7-COOH$ 
Oleic acid	18:1	Olives, pecan, grapeseed	14	$CH_3-(CH_2)_7-CH=CH-(CH_2)_7-COOH$ 

Polyunsaturated fatty acids

- Polyunsaturated fatty acids (essential fatty acids): Containing more than one double bond: e.g

Linoleic acid (18:2 $\Delta^{9,12}$, ω^{6})

1) They are present in linseed oil.

$$CH_3-(CH_2)_4-CH=CH-CH_2-CH=CH-(CH_2)_7-COOH$$

Linolenic acid (18:3 $\Delta^{9,12,15}$, ω^{3}):

1) They are present in linseed oil.

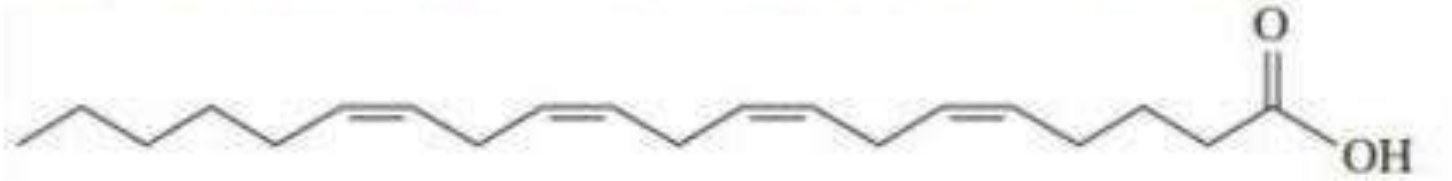
$$CH_3-CH_2-CH=CH-CH_2-CH=CH-CH_2-CH=CH-(CH_2)_7-COOH$$

Arachidonic acid (20:4 $\Delta^{5,8,11,14}$, ω^{6}):

It is present in peanut oil.

It is a component of phospholipids in animals.

$$CH_3-(CH_2)_3-(CH_2-CH=CH)_4-(CH_2)_3-COOH$$



Lipids Chemistry

Essential and nonessential fatty acids

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Nonessential fatty acids:

- These are fatty acids which can be synthesized in the body.
- Thus they are not necessary to be obtained from the diet.
- They include all saturated and monounsaturated fatty acids as palmitoleic and oleic acid.

Essential fatty acids:

- These are fatty acids that cannot be synthesized in the body. They must be obtained from the diet.
- They include fatty acids that contain more than one double bond (polyunsaturated fatty acids) e.g. linoleic, linolenic, arachidonic acids.
- The human body has enzyme system that can form only one double bond at the ninth carbon atom

Essential fatty acids:

- Sources:

1. Vegetable oils e.g. corn oil, soya bean oil, safflower oils, sunflower, linseed oil and cotton seed oil.
2. Fish oils: shark liver oils, which particularly contain the ω3 polyunsaturated fatty acids.

Essential fatty acids: Importance:

- Normal growth.
- They enter in the structure of phospholipids and cholesterol esters.
- They enter in the structure of cell membranes and are required for the fluidity of membrane structure.
- They protect against atherosclerosis and coronary heart disease by decreasing free cholesterol and LDL.

Thank you. We have completed the discussion on fatty acids as components of simple lipids

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Medical Biochemistry

Lipid Chemistry: Simple lipids

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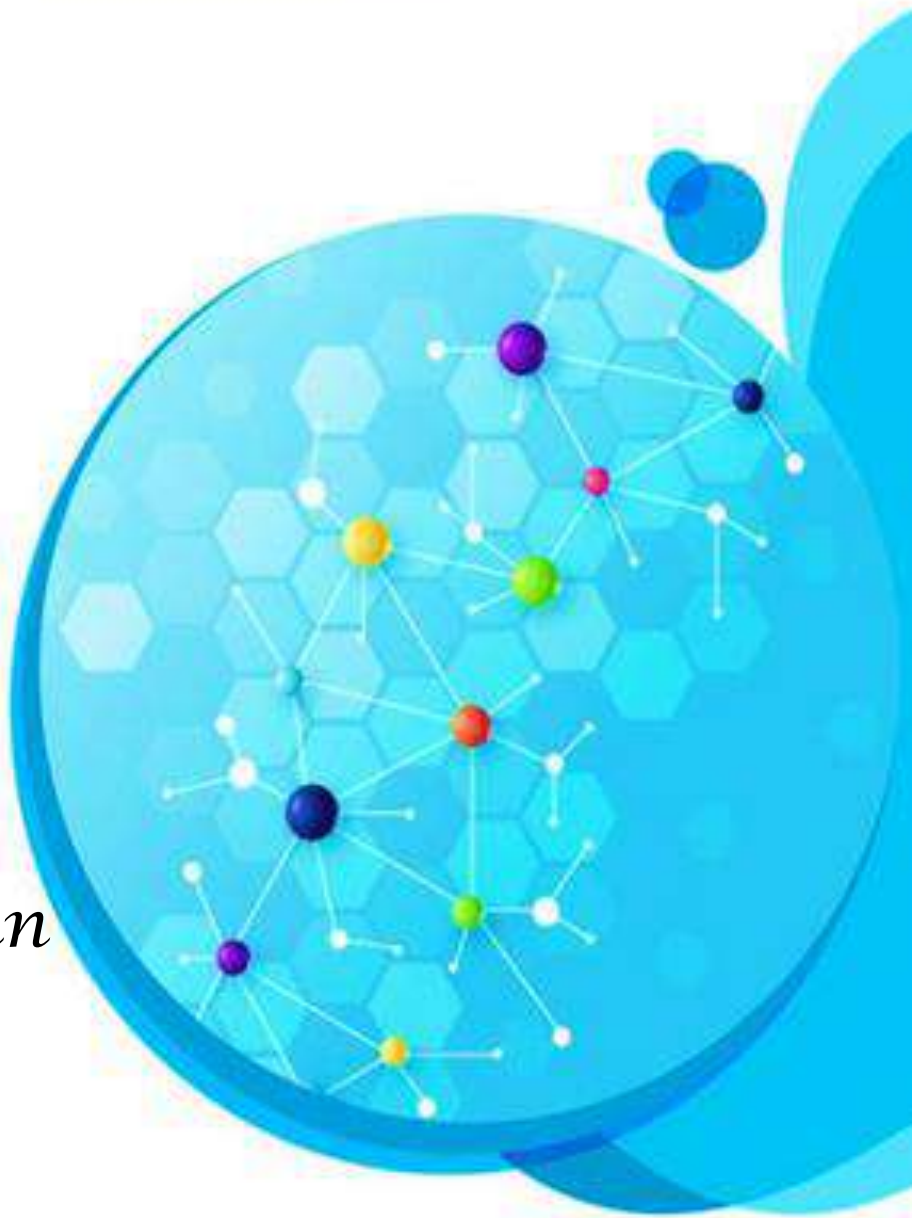
Faculty of Medicine

Al-Azhar University-Gaza

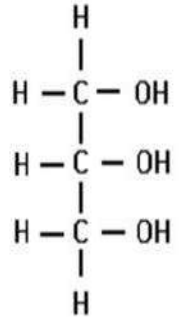


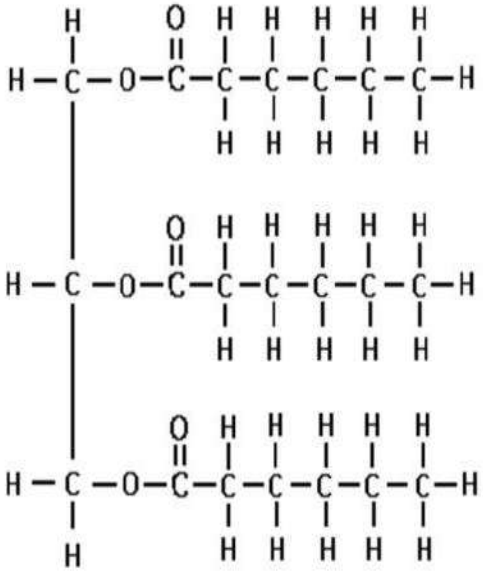
Lipids Chemistry

Alcohols: R. OH

Alcohols associated with lipids include:

1. Glycerol: A polyhydric alcohol containing three (-OH) groups
2. Cholesterol: An alcohol and classified as a derived lipid (discussed later).
3. Higher alcohol: These are alcohols with longer hydrocarbon chains, often monohydric (Cetyl alcohol ($C_{16}H_{33}OH$)





Lipids Chemistry

Simple lipids

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Simple lipids

- They are called simple because they are formed only from alcohols and Fatty acids.
- There are two classes of simple lipids (according to the type of alcohol): acylglycerols and waxes.

Lipids Chemistry

Simple lipids: Acylglycerols

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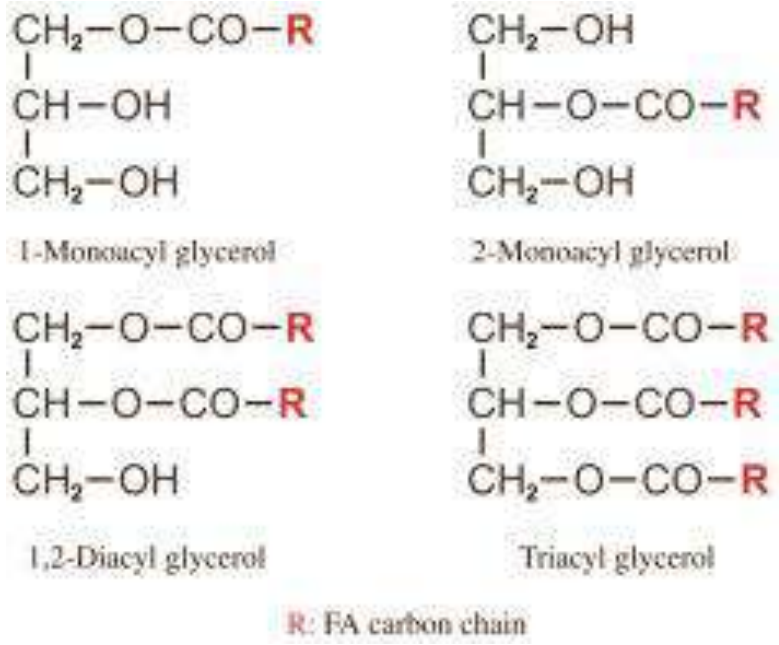
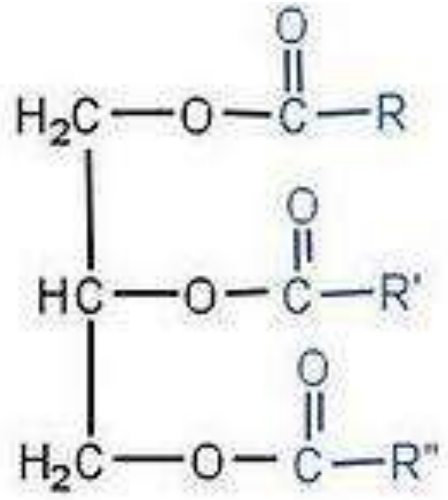
Acylglycerols

- **Acylglycerols**, also known as **Glycerides**, are esters formed from glycerol and fatty acids, and are generally very hydrophobic.
- Depending on the number of alcohol groups esterified by FAs, acylglycerols are designated monoacylglycerols, diacylglycerols, or triacylglycerols.
- Triacylglycerols are commonly called neutral fats



Triacylglycerols (triglycerides):

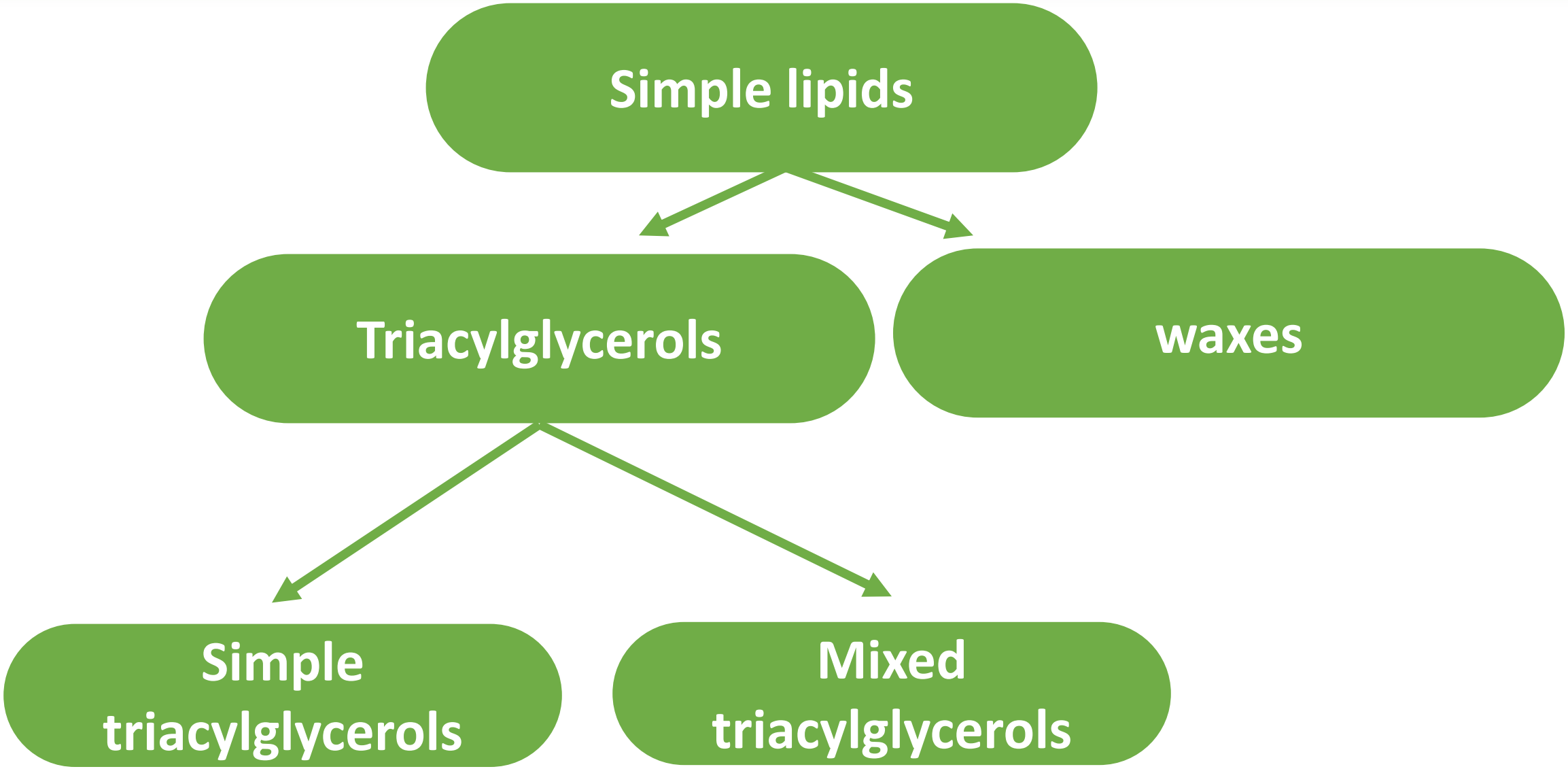
- They are called neutral fat because they carry no charge.
- They are stored mainly in cytoplasm of adipose tissue cells (which is located subcutaneously and around kidney and other organs).
- Body fat is important source of energy. Each gram fat gives 9.3 kcal.



Triglyceride

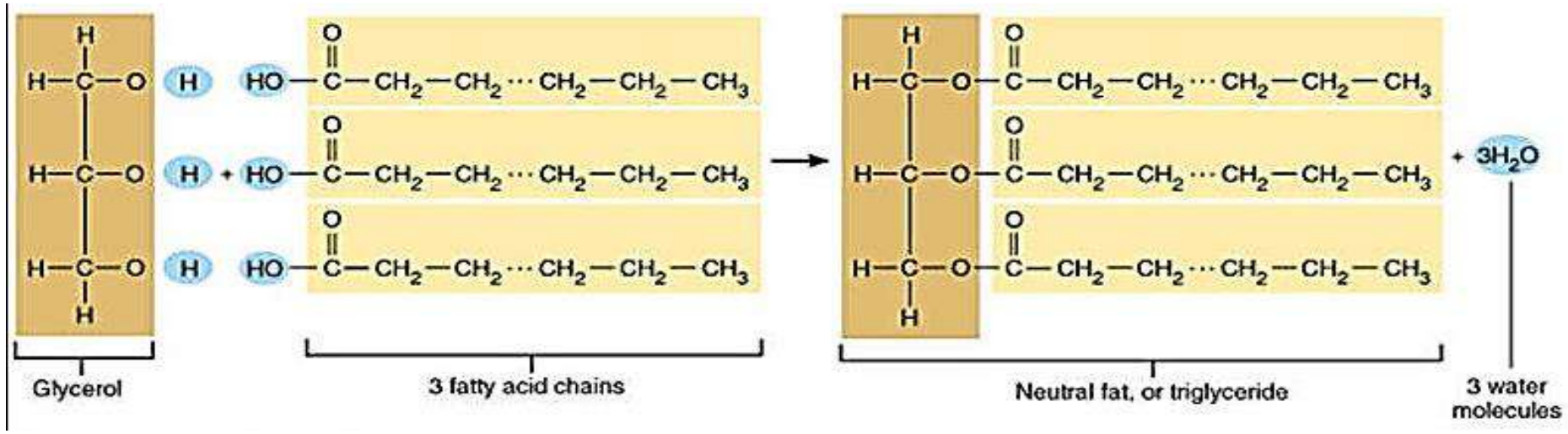
Dietary sources of triacylglycerols:

- In animals e.g. butter and lards.
- In plants e.g. cotton seed oil, linseed oil, sesame oil and olive oil.
- Marine oils e.g. cod-liver oil and shark liver oil


Simple lipids
Triacylglycerols
waxes
Simple triacylglycerols
Mixed triacylglycerols

Simple triacylglycerols

- They contain 3 similar fatty acids are attached to glycerol.



e.g. $CH_2\text{-}OOC\text{-}(CH_2)_{14}\text{-}CH_3$
$CH\ \ \text{-}OOC\text{-}(CH_2)_{14}\text{-}CH_3$
$CH_2\text{-}OOC\text{-}(CH_2)_{14}\text{-}CH_3$

Tripalmitin

$CH_2\text{-}OOC\text{-}(CH_2)_7\text{-}CH{=}CH\text{-}(CH_2)_7\text{-}CH_3$
$CH\ \ \text{-}OOC\text{-}(CH_2)_7\text{-}CH{=}CH\text{-}(CH_2)_7\text{-}CH_3$
$CH_2\text{-}OOC\text{-}(CH_2)_7\text{-}CH{=}CH\text{-}(CH_2)_7\text{-}CH_3$

Triolein

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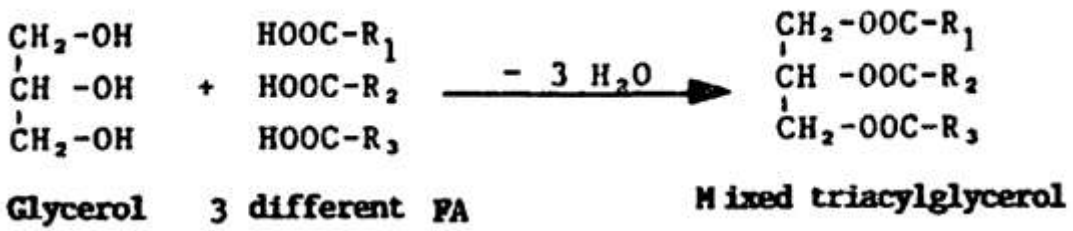
Mixed triacylglycerols

- They are triacylglycerols with different fatty acids are attached to glycerol.



e.g. CH_2-OOC-$(CH_2)_{16}$-CH_3
CH -OOC-$(CH_2)_{16}$-CH_3
CH_2-OOC-$(CH_2)_{14}$-CH_3

1,2-distearopalmitin

Properties of triacylglycerols:

1. Solubility: All triacylglycerols are insoluble in water, soluble in fat solvents.
2. Specific gravity: It is less than one. Specific gravity of water is one Therefore, triacylglycerols float on the surface of water.
3. Lipase enzymes can hydrolyze triacylglycerols into fatty acids and glycerol.

Properties of triacylglycerols:

4. Melting point:

- Triacylglycerols rich in unsaturated fatty acids are liquid at room temperature. They are called oils.
- Triacylglycerols rich in saturated fatty acids are solid at room temperature. They are called fats.

Lipids Chemistry

Chemical Properties of TAG depend on the presence of double bond

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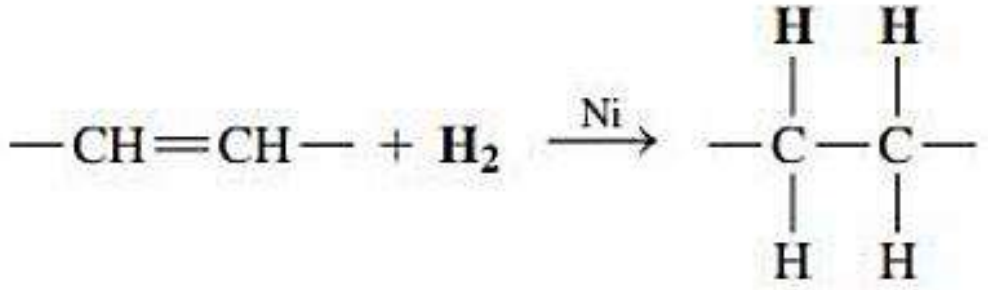
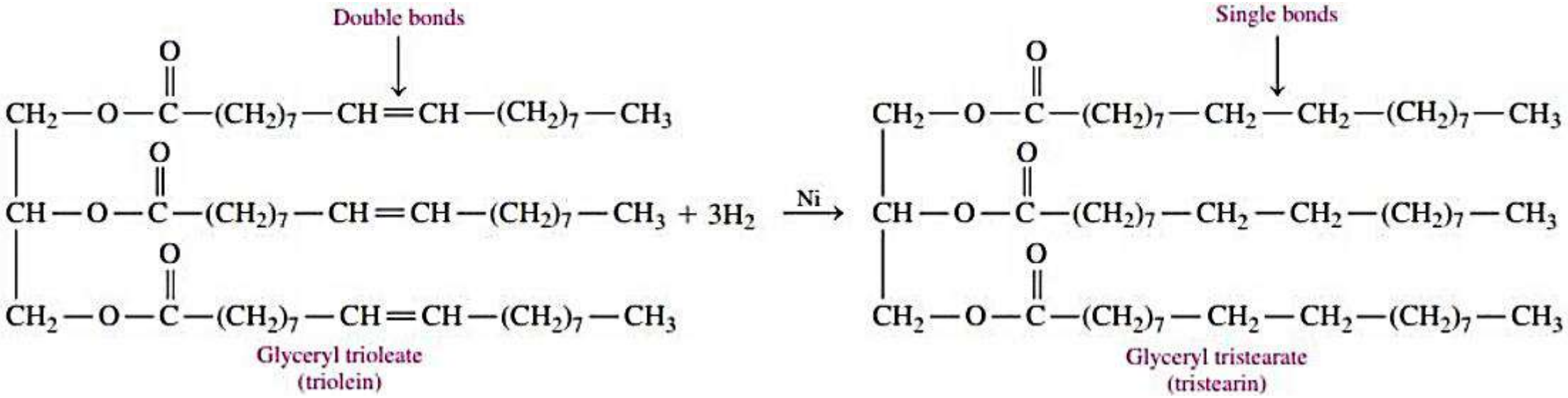
Hardening or Reduction or hydrogenation

- Def: Hydrogen gas is bubbled through a heated oil (presence of a nickel catalyst). As a result, H atoms add to one or more carbon-carbon double bonds to form carbon-carbon single bonds.



Hardening or Reduction or hydrogenation

- Hydrogenation of oils to form solid fat or margarine As: USFA are converted to SEA

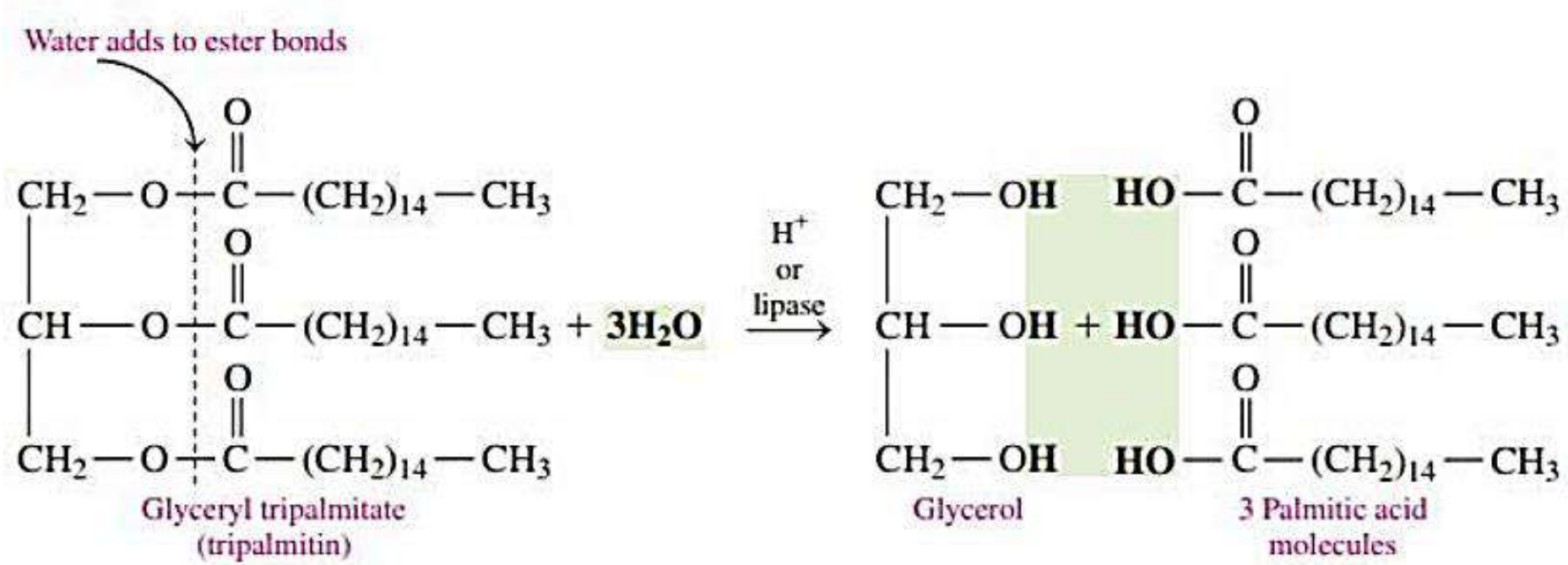


Hydrolysis

- Triacylglycerols are hydrolyzed (split by water) in the presence of strong acids such as HCl or H_2SO_4, or digestive enzymes called lipases.
- The products of hydrolysis of the ester bonds are glycerol and three fatty acids.
- The polar glycerol is soluble in water, but the fatty acids with their long hydrocarbon chains are not.

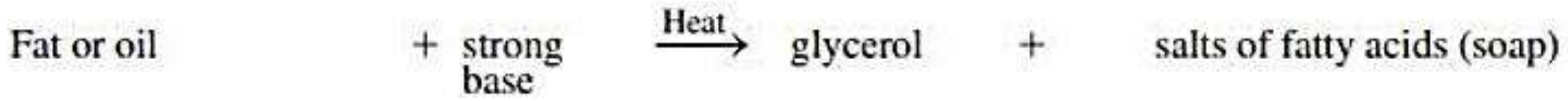
This is the fundamental process during digestion of fats.

Hydrolysis

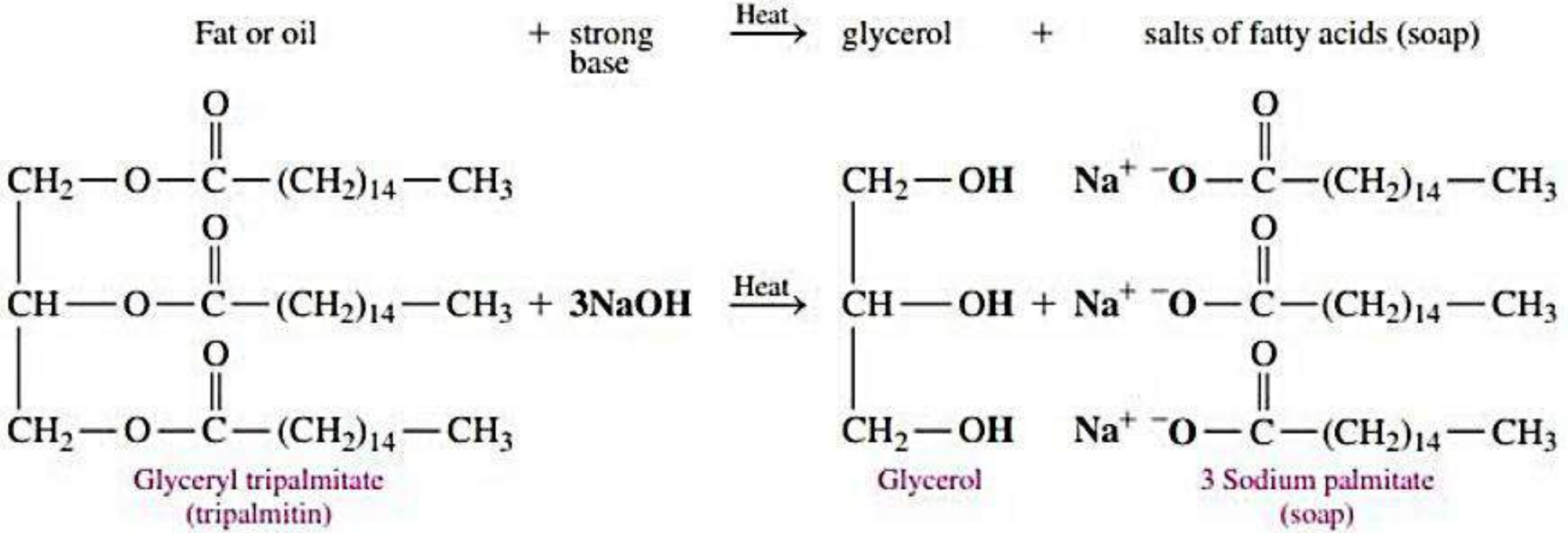

Water adds to ester bonds
$CH_2-O-C-(CH_2)_{14}-CH_3$
$CH-O-C-(CH_2)_{14}-CH_3$
$CH_2-O-C-(CH_2)_{14}-CH_3$
$+ 3H_2O$
H^+ or lipase
CH_2-OH
$CH-OH$
CH_2-OH
$HO-C-(CH_2)_{14}-CH_3$
Glyceryl tripalmitate (tripalmitin)
Glycerol
3 Palmitic acid molecules

Saponification

- Saponification occurs when a fat is heated with a strong base such as NaOH to form glycerol and the salts of the fatty acids.



Saponification



Saponification

- This is a process by which soap can be made.
- When NaOH is used as the base, a solid soap is produced that can be molded into a desired shape; KOH produces a softer, liquid soap.
- An oil that is polyunsaturated produces a softer soap.
- Names like "coconut" or "avocado shampoo" tell you the sources of the oil used in the reaction.

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Rancidity:

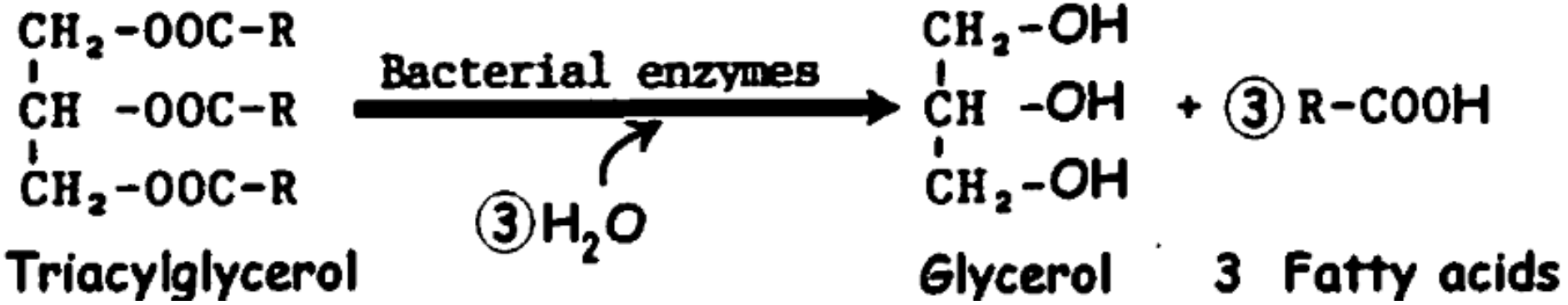
- Definition: It is a toxic reaction of triacylglycerols.
- It is due to oxidation of its unsaturated fatty acids content by oxygen of the air, bacteria or moisture.
- It leads to unpleasant odor or taste of oils and fats.

Rancidity:

- Oxidative rancidity: Fatty acids are oxidized at double bonds giving peroxide.

Rancidity:

- Hydrolytic rancidity: triacylglycerols are hydrolyzed by bacterial enzymes into glycerol and fatty acids.
- The free fatty acids can then undergo further auto-oxidation with a free radicals.



Waxes

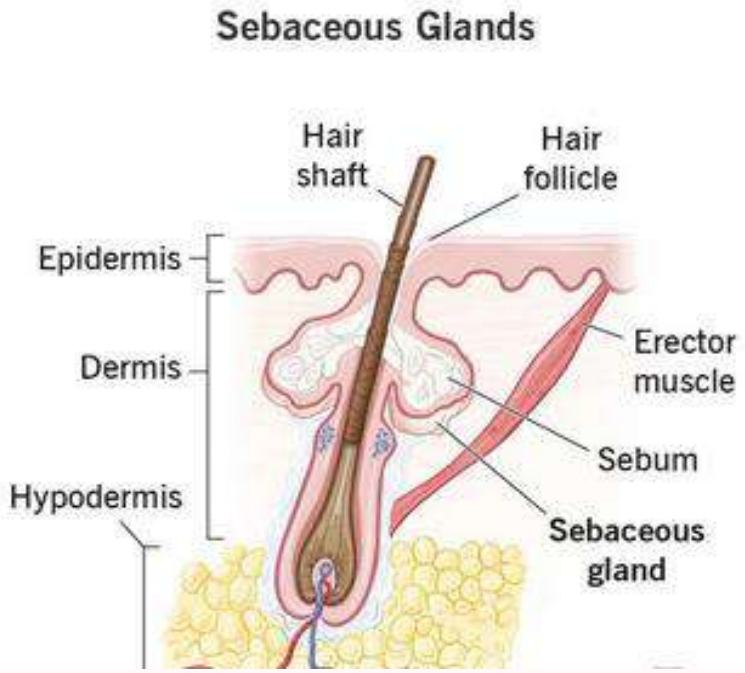
- These are esters of fatty acids with long chain alcohol other than glycerol.
- These alcohols contain one (-OH) group, i.e., monohydric alcohols e.g. bee wax
- They are not digested by lipase enzyme. Thus they are not utilized by the body.
- They are solids at room temperature.

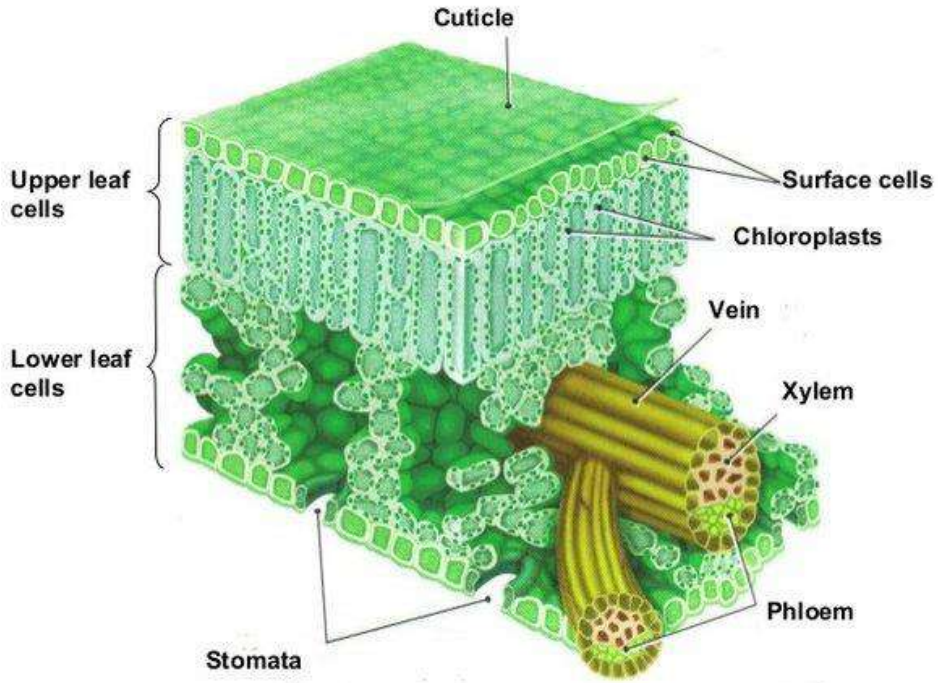
Differences between triacylglycerols and waxes:

	Triacylglycerols	*Waxes*
Composition	Contain glycerol	Contain no glycerol
Melting point	At room temperature: they are either solids or liquids.	At room temperature, they are solids.
Rancidity	They may undergo rancidity.	They do not undergo rancidity.

Sources of Waxes

- Waxes are excreted extracellularly in some plants and animals and has a protective function as in:
- Bee wax.
- Sebum.
- Cuticles of leaves.





THANK YOU

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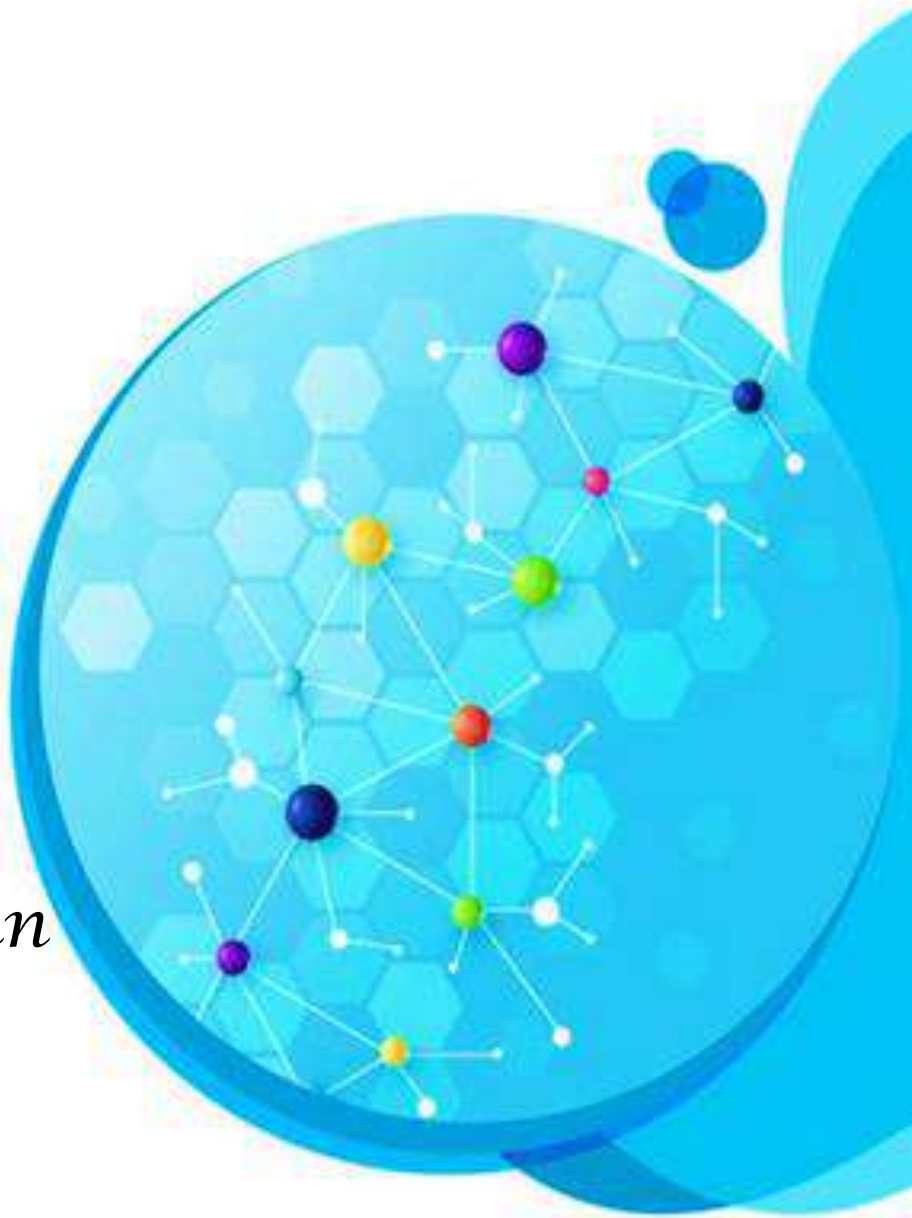
Medical Biochemistry

Lipid Chemistry

Asst. Prof.Mohammed Hasan Eleyan

Faculty of Medicine

Al-Azhar University-Gaza



Lipids Chemistry

Complex (compound) lipids

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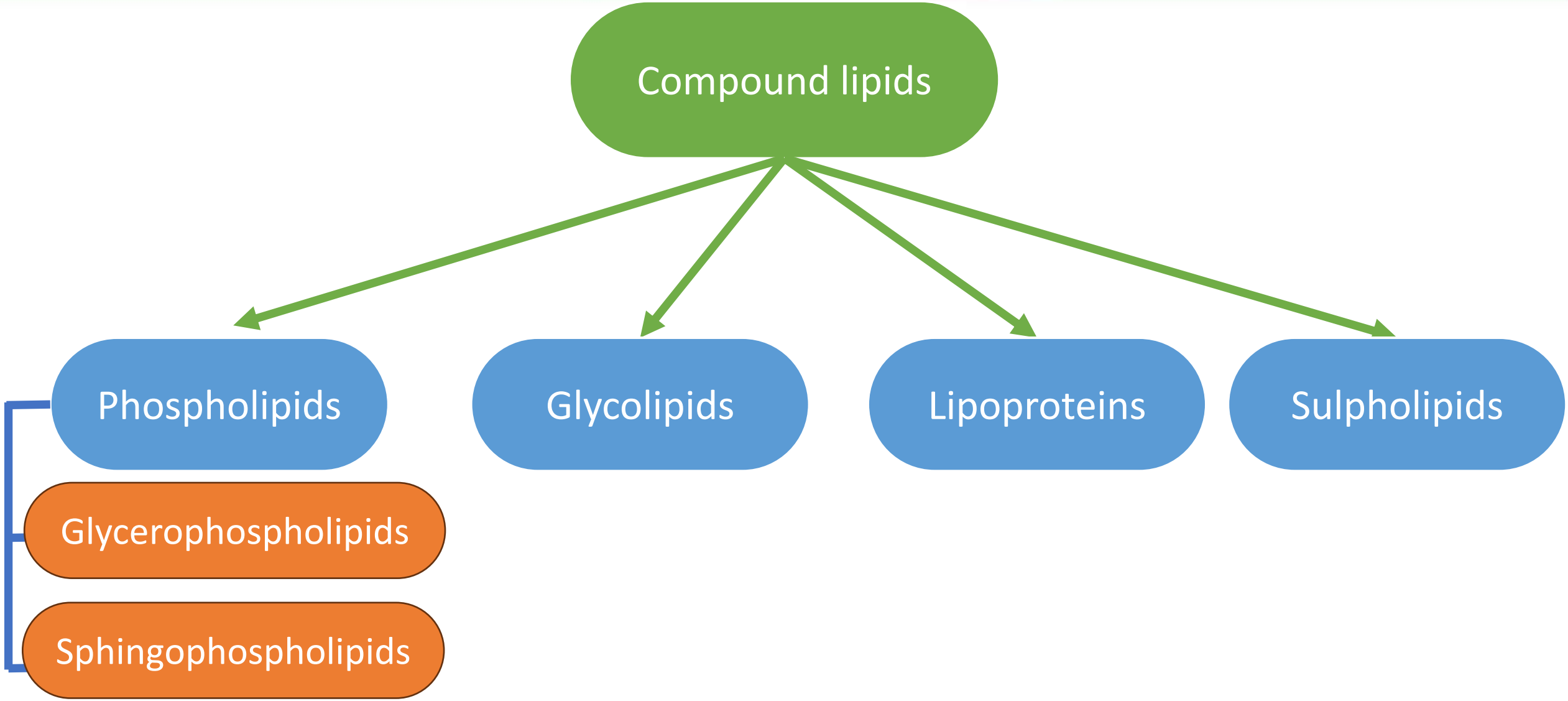
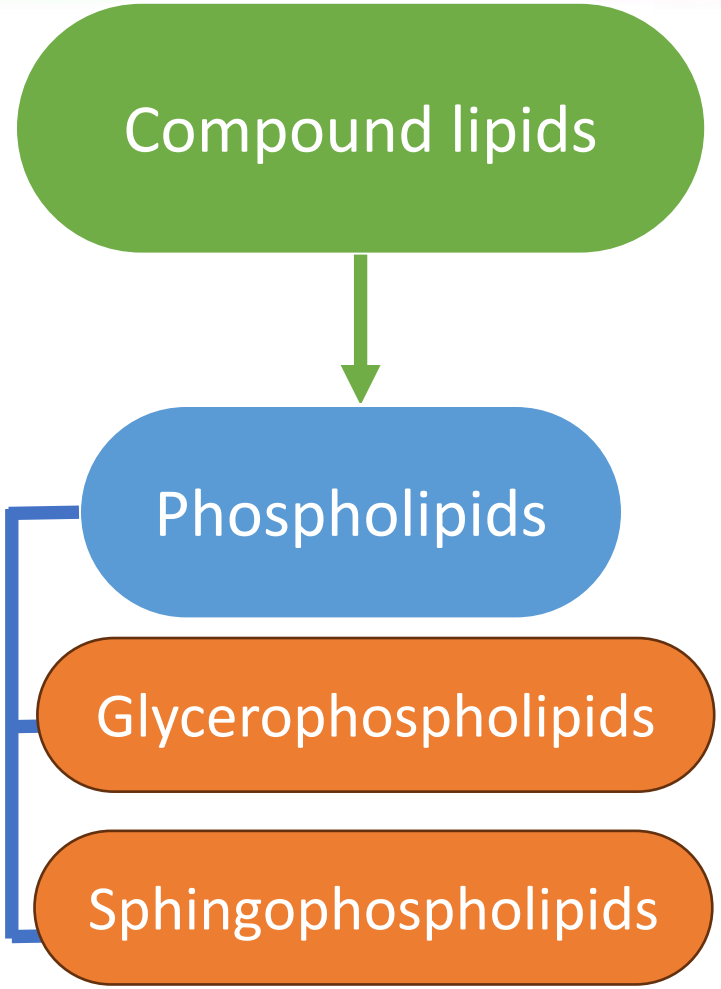
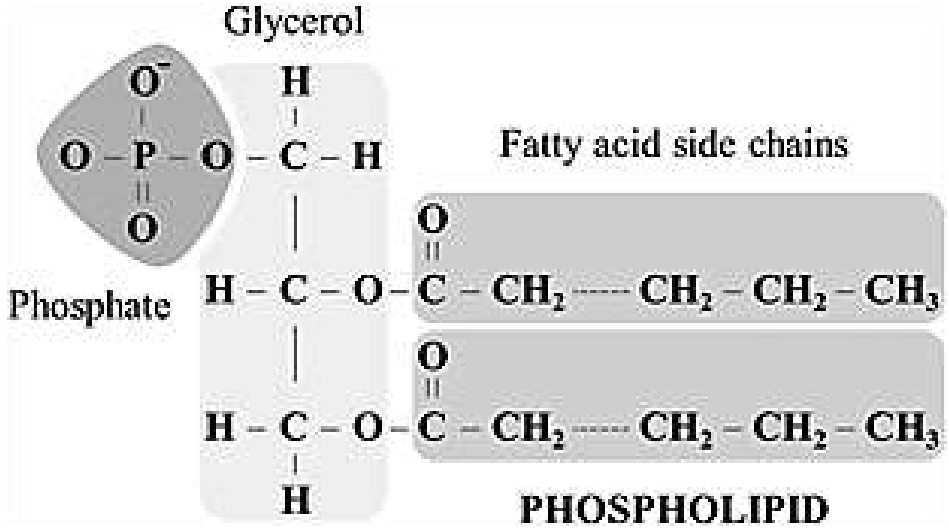

Compound lipids
Phospholipids
Glycolipids
Lipoproteins
Sulpholipids
Glycerophospholipids
Sphingophospholipids


Compound lipids
Phospholipids
Glycerophospholipids
Sphingophospholipids

Phospholipids

- The phospholipids are a family of lipids similar in structure to triacylglycerols;
- They contain phosphoric acid residues.
- They are classified into:

1. Glycerophospholipids (contain glycerol)
2. Sphingophospholipids (contain sphingosine).

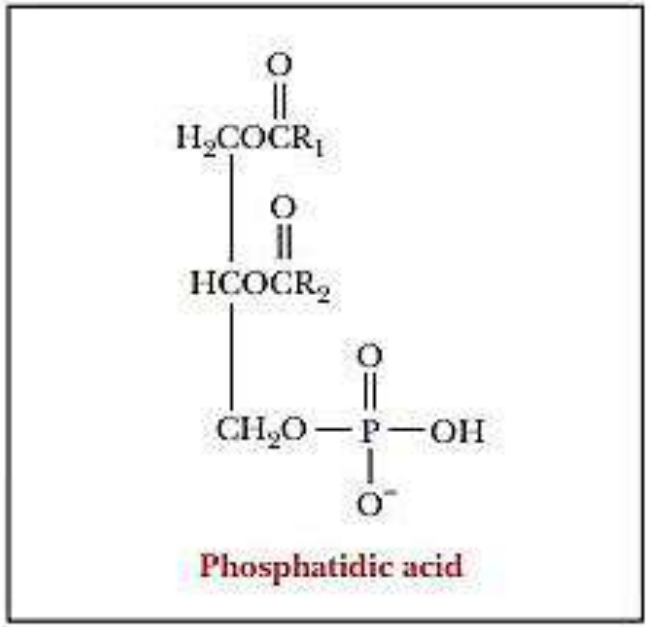


Lipids Chemistry

Complex (compound) lipids: Glycerophospholipids

Glycerophospholipids

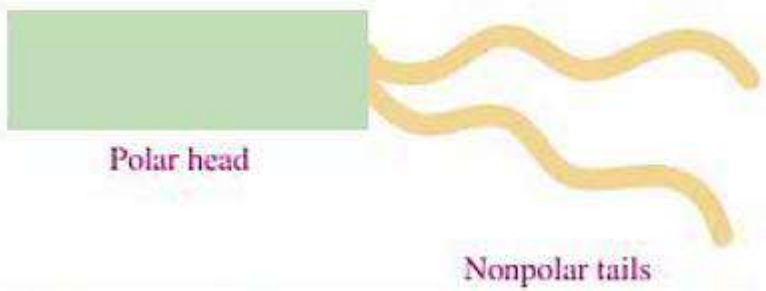
- Glycerophosphatides (Phosphoglycerides):
- Phospholipids containing glycerol as alcohol
- They are derivatives of phosphatidic acid.

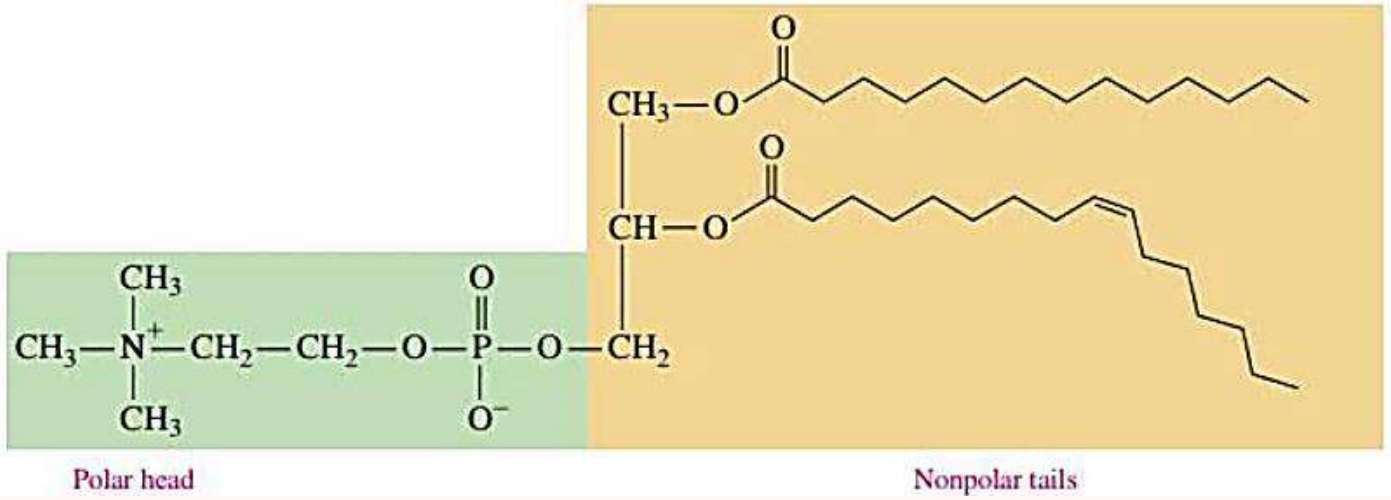


A A phosphatidic acid, in which glycerol is esterified to phosphoric acid and to two different carboxylic acids. R_1 and R_2 represent the hydrocarbon chains of the two carboxylic acids.

Glycerophospholipid contain both polar and nonpolar regions

- In a glycerophospholipid, a polar "head" contains the ionized amino alcohol and phosphate,
- While the hydrocarbon chains of two fatty acids make up the nonpolar "tails."

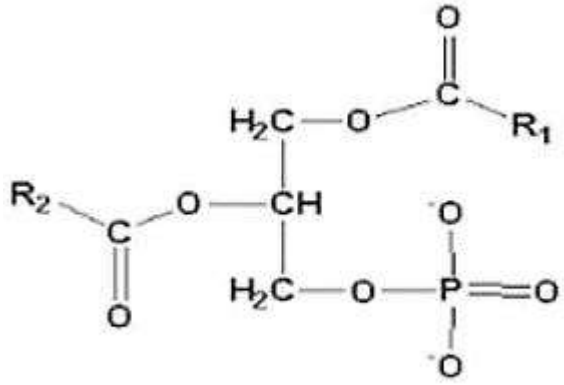


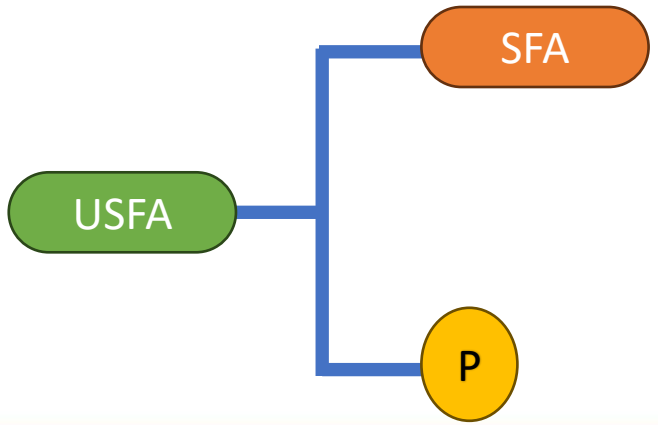


Phosphatidic acid (diacylglycerolphosphate):

- Structure:

1. Glycerol
2. Saturated fatty acid attached to 1 position
3. Unsaturated fatty acid attached to 2 position
4. Phosphoric acid residue at position 3.





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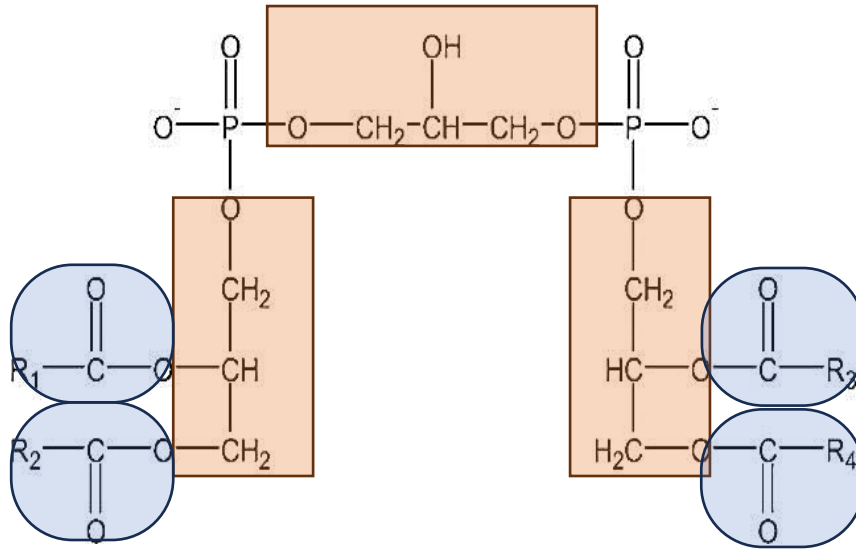
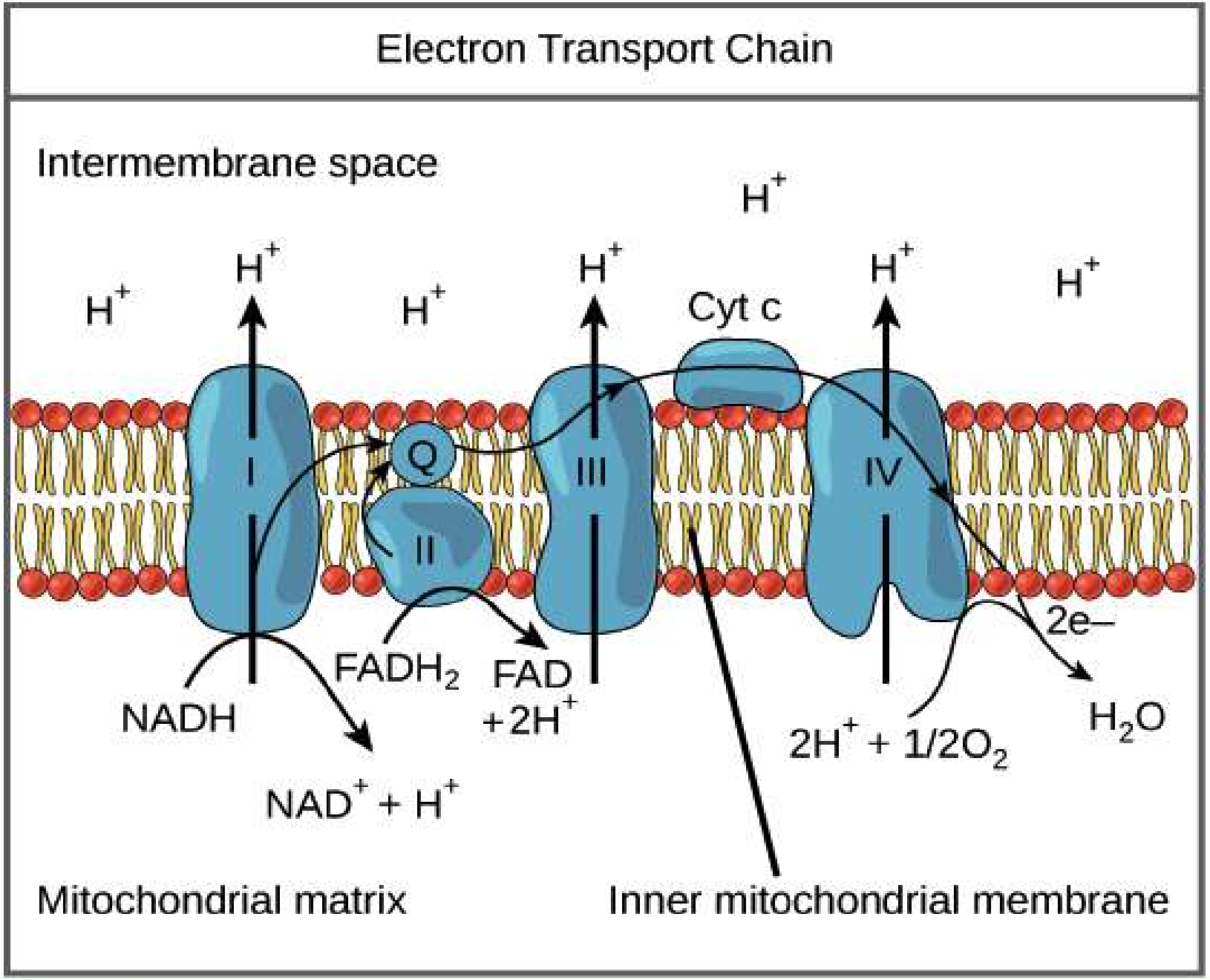
Phosphatidic acid (diacylglycerolphosphate):

- This is simplest phospholipids
- Does not occur in good concentration in tissues
- It is an intermediate in the synthesis of TAG and phospholipids (Other Phosphoglycerides are formed by conjugation of different groups to phosphate)

Cardiolipin

- Structure of cardiolipin.
- Cardiolipin is composed of three glycerol units and has four acyl side chains designated R 1-R 4 .
- Site: inner mitochondrial membrane
- Function: It plays roles in energy production, apoptosis and membrane organization.

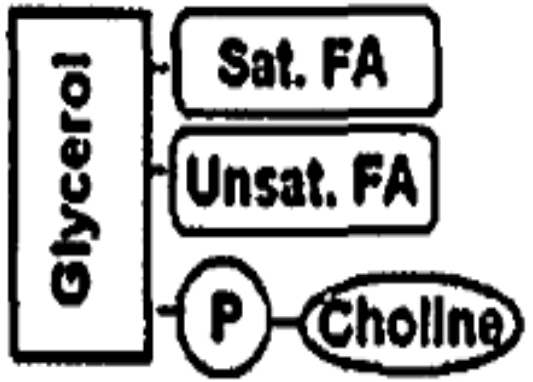



Electron Transport Chain
Intermembrane space
H+
H+
H+
H+
H+
H+
H+
Cyt c
I
II
Q
III
IV
NADH
NAD+ + H+
FADH2
FAD
+2H+
2H+ + 1/2O2
H2O
2e–
Mitochondrial matrix
Inner mitochondrial membrane

Lecithin (phosphatidyl choline):

a) **Structure:**

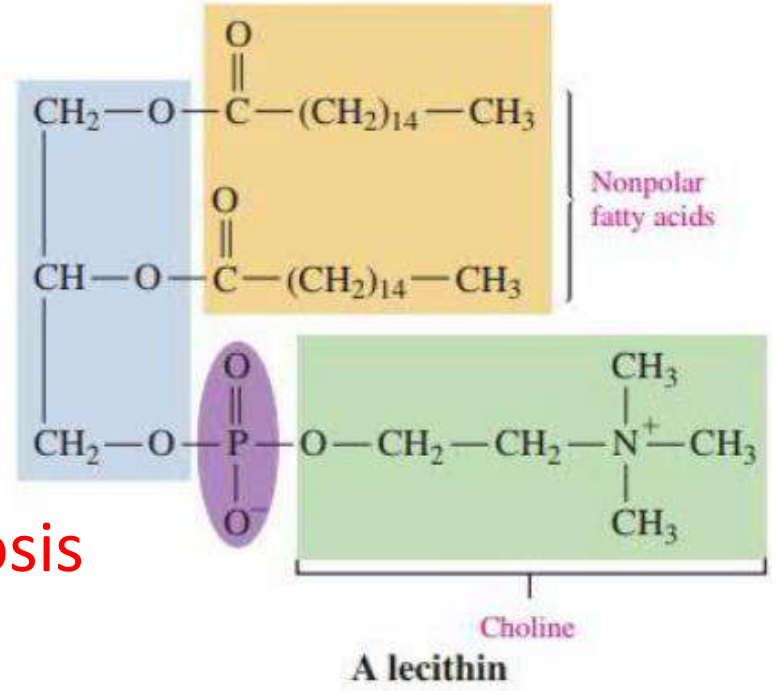
1) Glycerol.
2) Saturated fatty acid (attached to 1 (α) position.
3) Unsaturated fatty acid (attached to 2 (β) position.
4) Phosphoric acid (attached to 3(γ) position.
5) Choline base (attached to phosphoric acid).



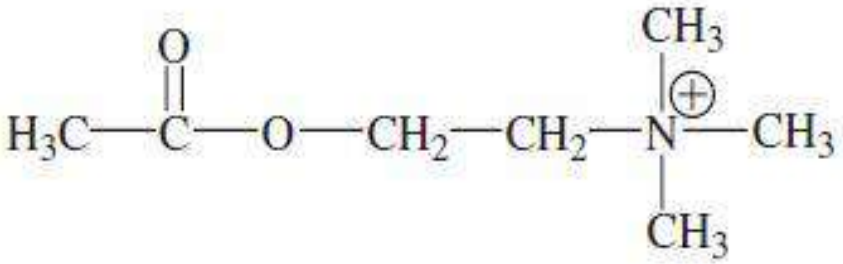
Lecithin

Lecithin (phosphatidyl choline) Functions:

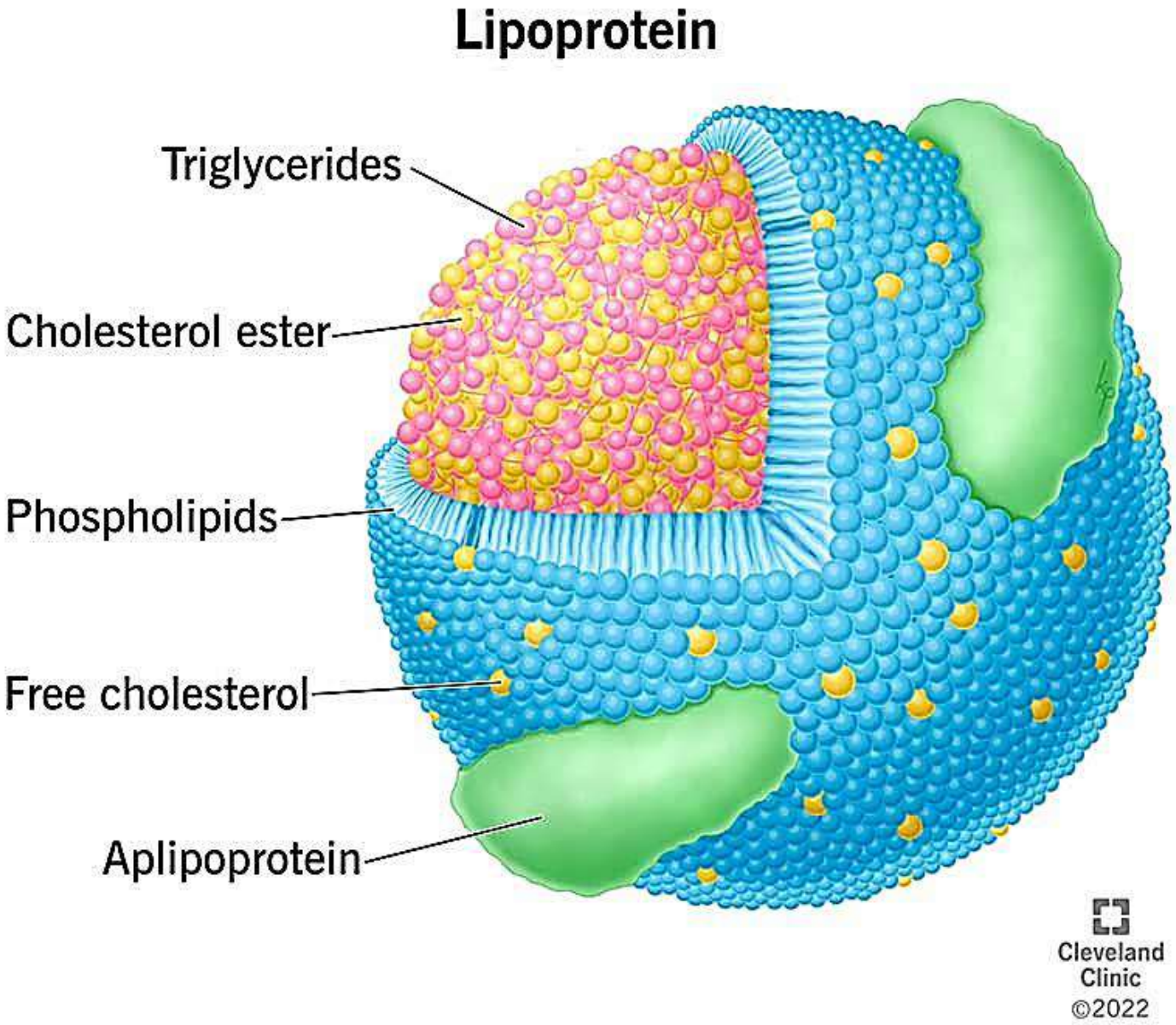
- Enters in the structure of cell membrane.
- Acts as lipotropic factor. i.e. prevent fatty liver
- Forms cholesterol ester, This prevent atherosclerosis
- Lecithin acts as body store of Choline (for nerve transmission)



A lecithin

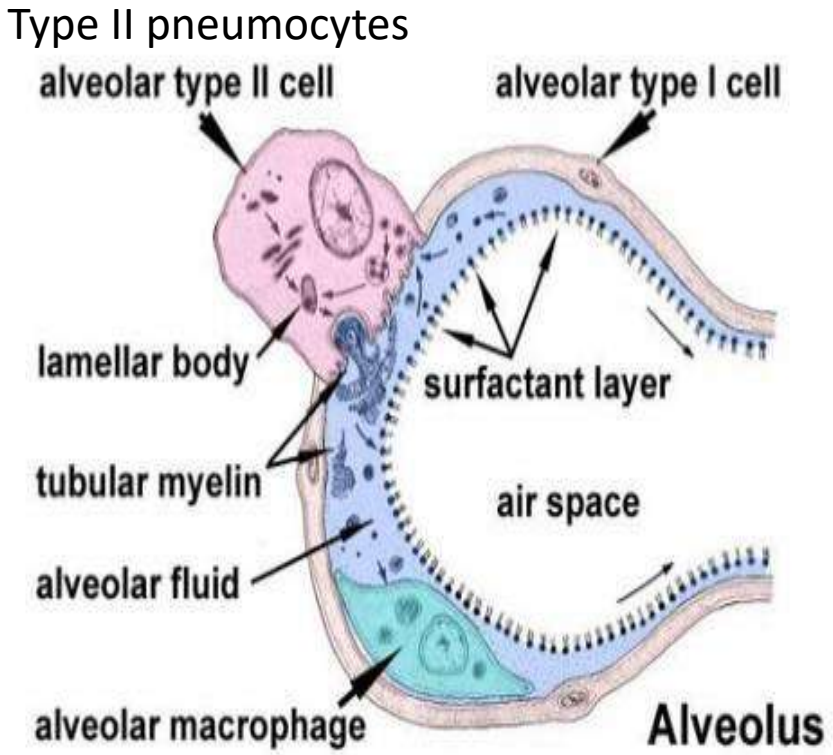


Acetylcholine



Dipalmitoyl lecithin (lecithin which contains 2 palmitic acid). Act as a surfactant in lung

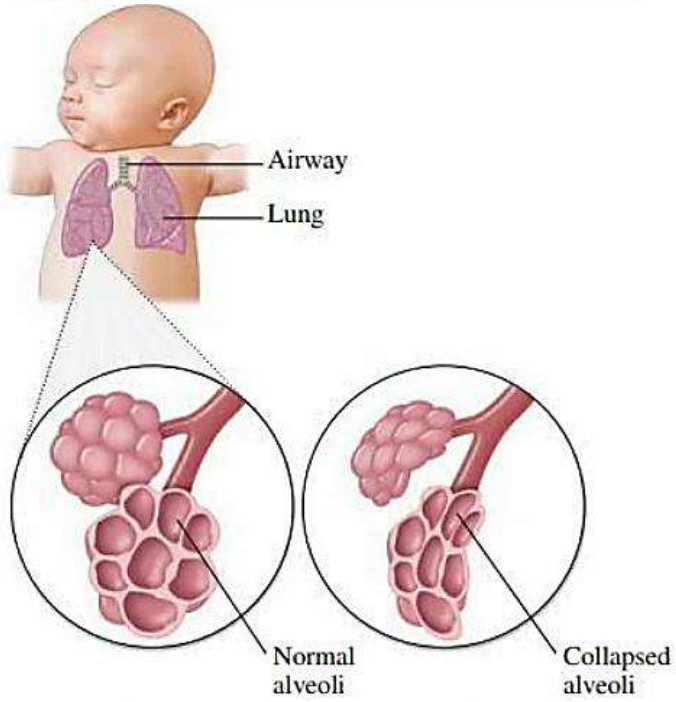
- Dipalmitoyl lecithin is continuously secreted by the lung cells in the alveolar wall, forming a monolayer over the watery surface of the alveolus and so lowers the surface tension this helps expiration and inspiration
- During expiration, the surfactant becomes solid under pressure. This prevents the adherence of alveolar wall.
- During inspiration, The surfactant makes the lung easier to expand.



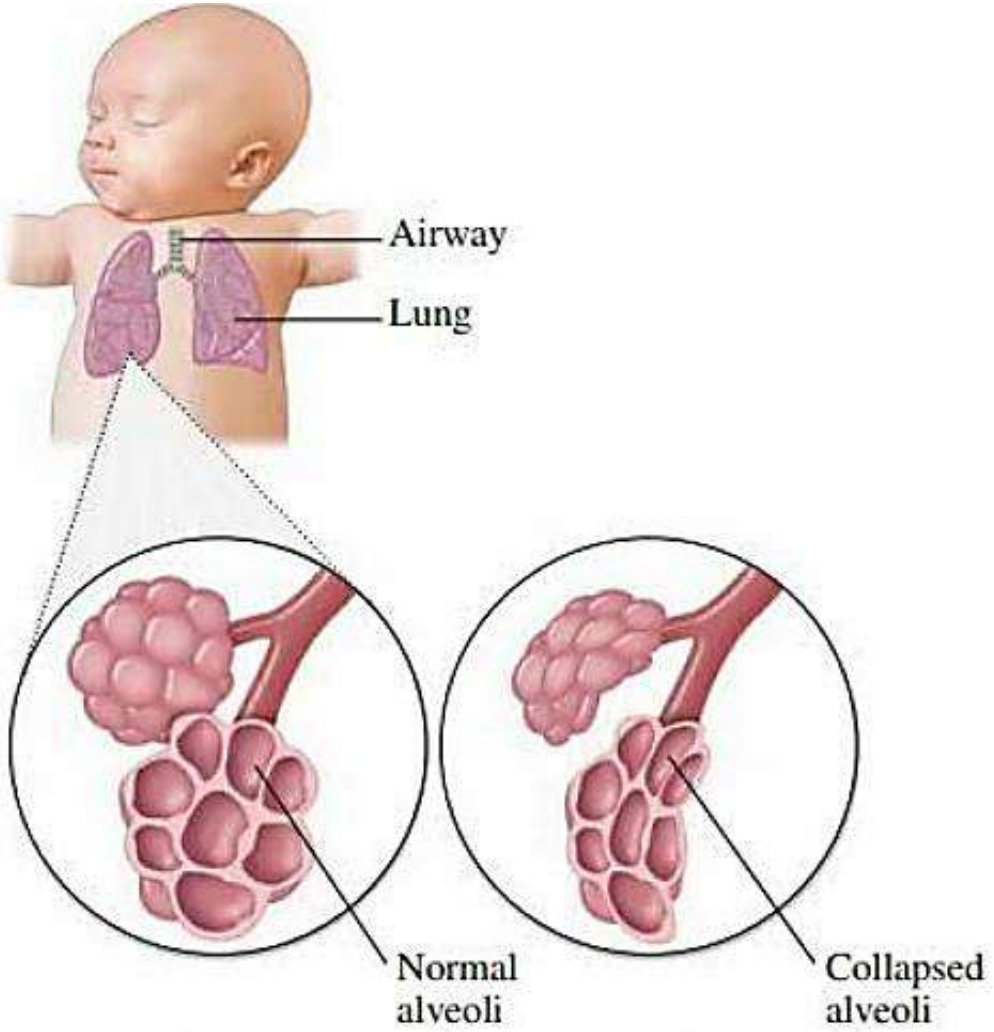
Respiratory distress syndrome (hyaline membrane disease):

- In premature babies, lungs do not secrete enough surfactant.
- This leads to lung collapse and death from respiratory failure (atelectasis).
- Treatment of this case needs putting the premature babies in incubator (ventilation) and administration of surfactant locally in the lung.

A premature infant with respiratory distress is treated with a surfactant and oxygen.



Without sufficient surfactant in the lungs of a premature infant, the alveoli collapse, which decreases pulmonary function.

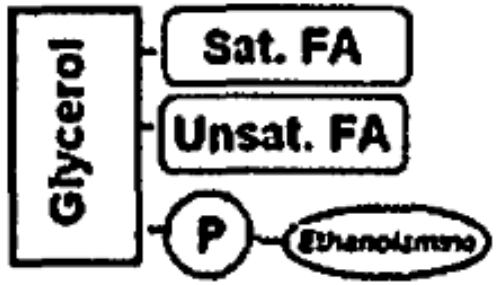


Without sufficient surfactant in the lungs of a premature infant, the alveoli collapse, which decreases pulmonary function.

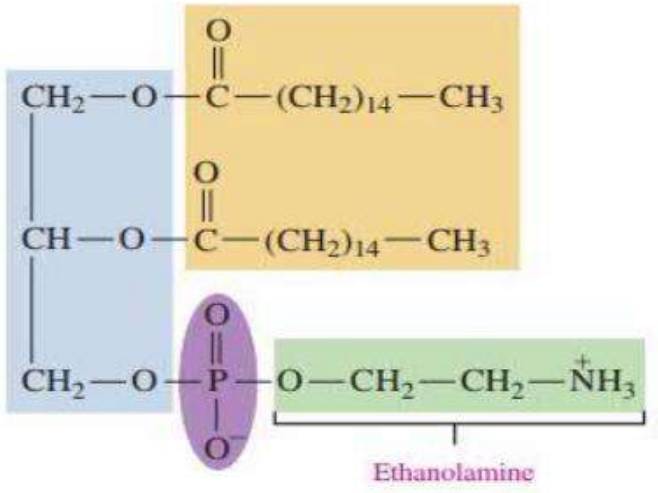
A premature infant with respiratory distress is treated with a surfactant and oxygen.

Cephalin (Phosphatidyl ethanolamine):

- Structure: Formed of phosphatidic acid + ethanolamine
- Lecithins and cephalins are two types of glycerophospholipids that are particularly abundant in brain and nerve tissue as well as in egg yolk, wheat germ, and yeast.



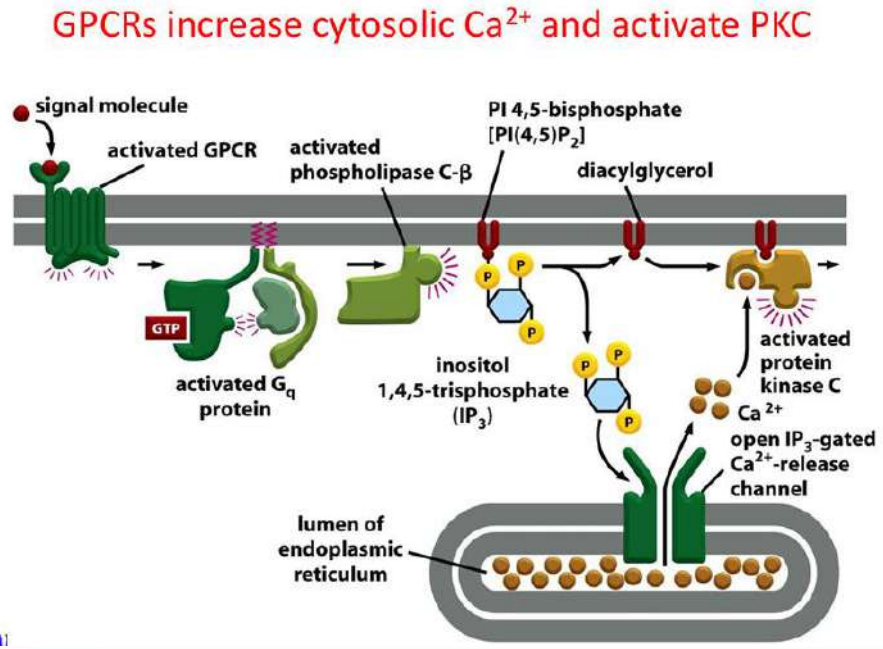
Cephalin

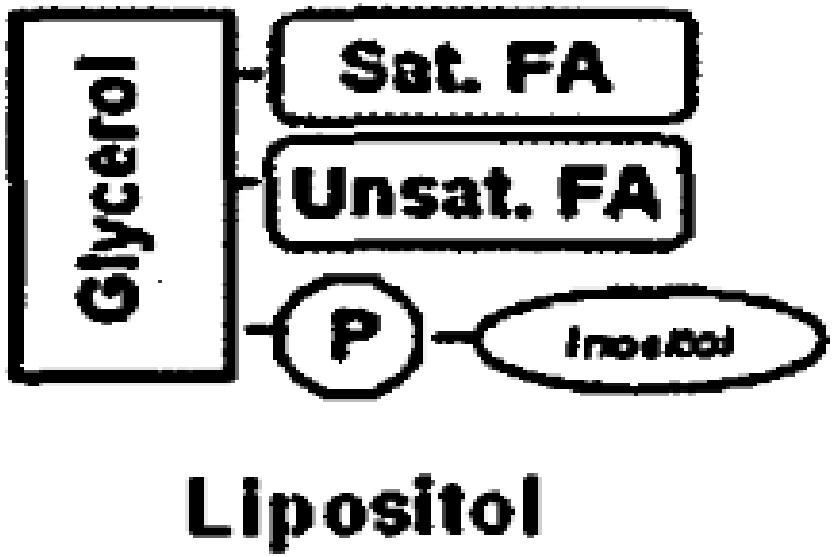


A cephalin

Phosphatidyl Inositol (Lipositol):

- Structure: Formed of phosphatidic acid + Inositol
- Functions: acts as precursor of 2nd messenger "IP3"



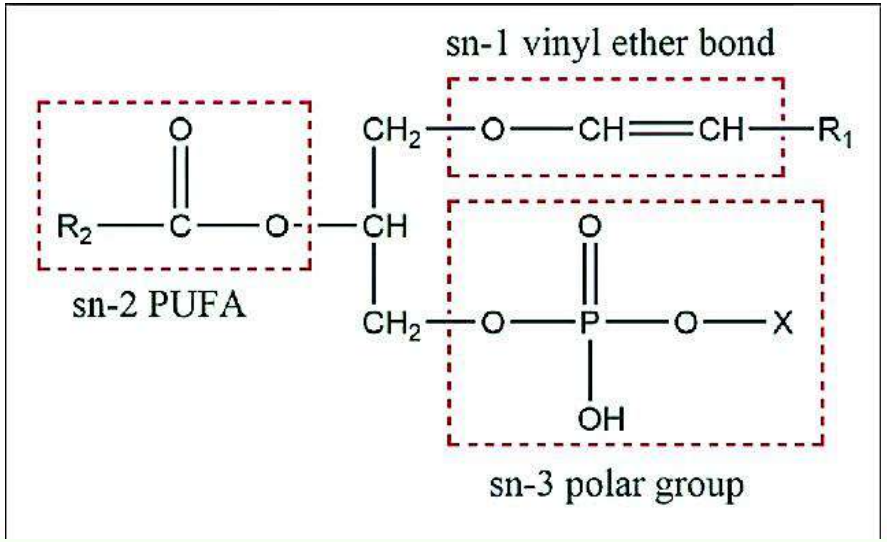


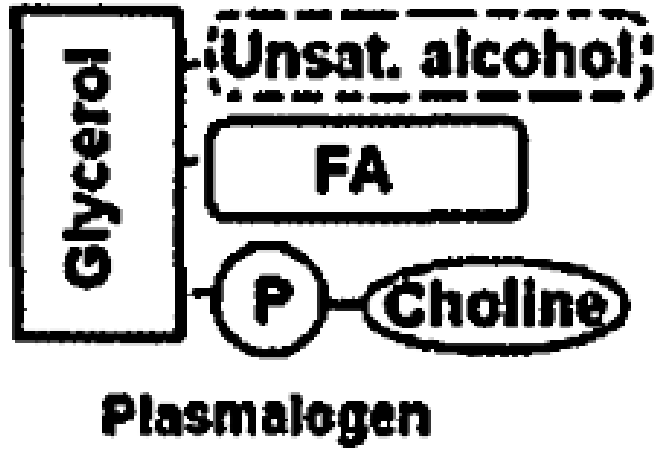
Plasmalogens:

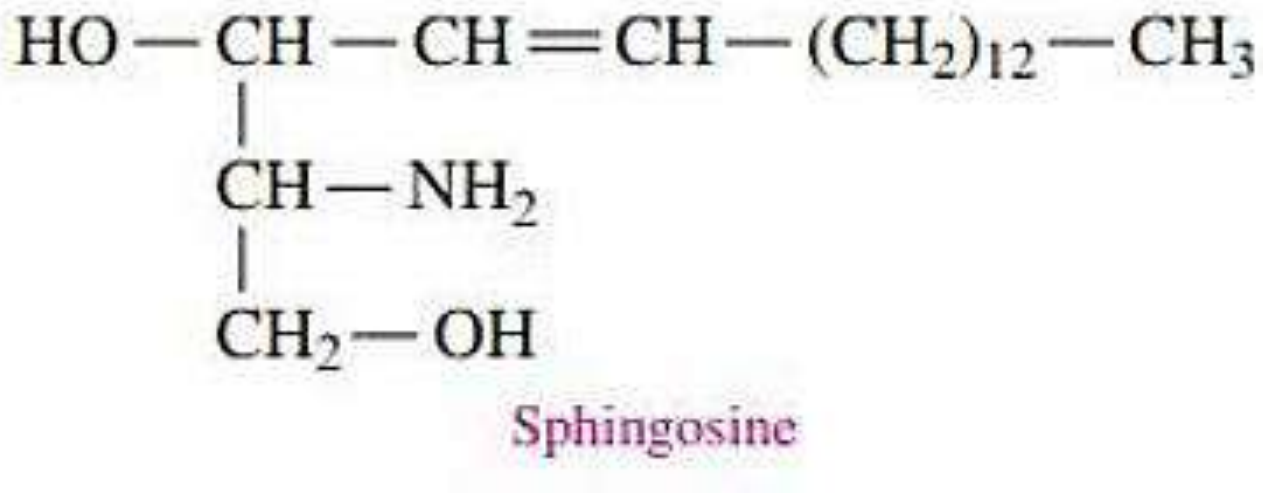
- Structure: Same structure as lecithin but FA at position 1 is replaced by unsaturated fatty alcohol

ischemia-reperfusion injury.

- Functions: present in brain & muscles "Lipophilic antioxidants"





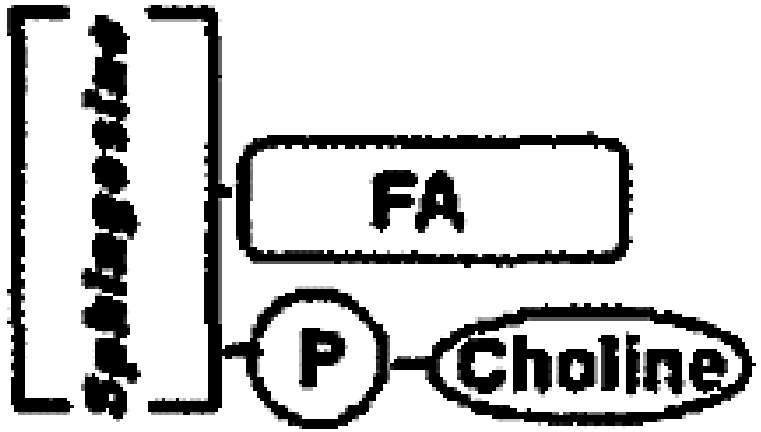


Lipids Chemistry

Complex (compound) lipids: Sphingophospholipids

Sphingophospholipids are a subclass of phospholipids that contain **sphingosine** (a long-chain amino alcohol) instead of glycerol as their backbone. They are key components of cell membranes, particularly in the nervous system.

Sphingomyelins

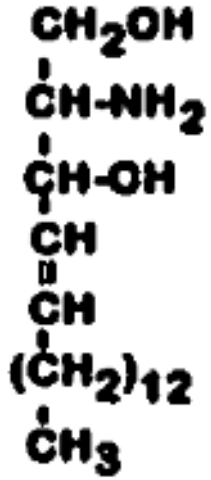


Sphingomyelin

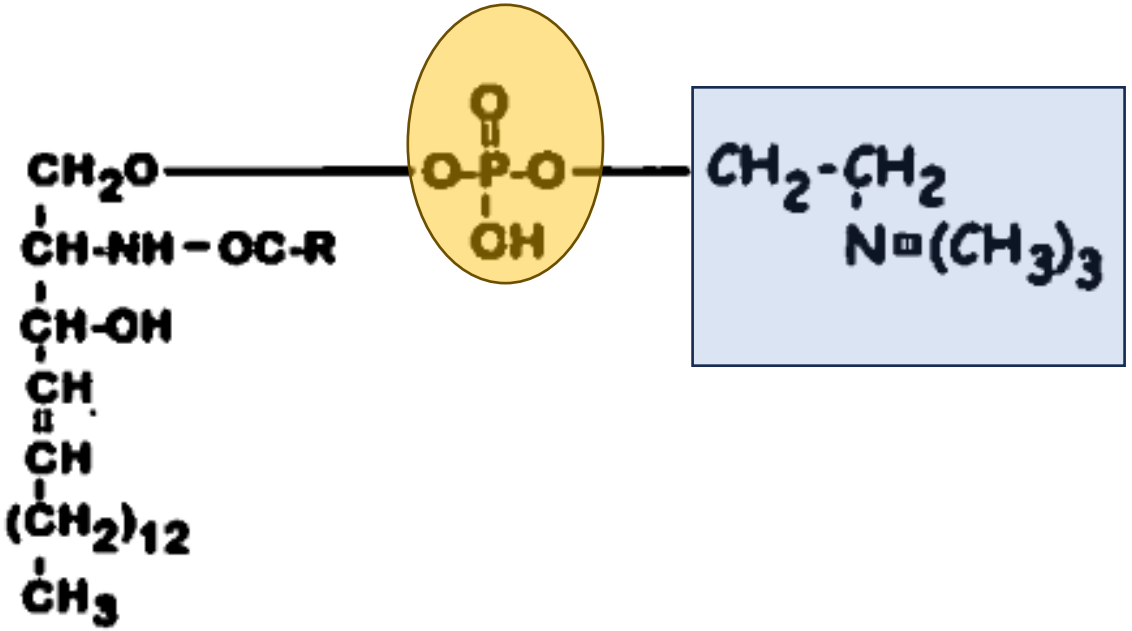
- Structure:

1. Sphingosine.
2. Fatty acid attached to amino group at position 2.
3. Phosphoric acid residue attached choline base
4. Function: It is present in high concentrations in brain and nerve tissue.

Sphingomyelins



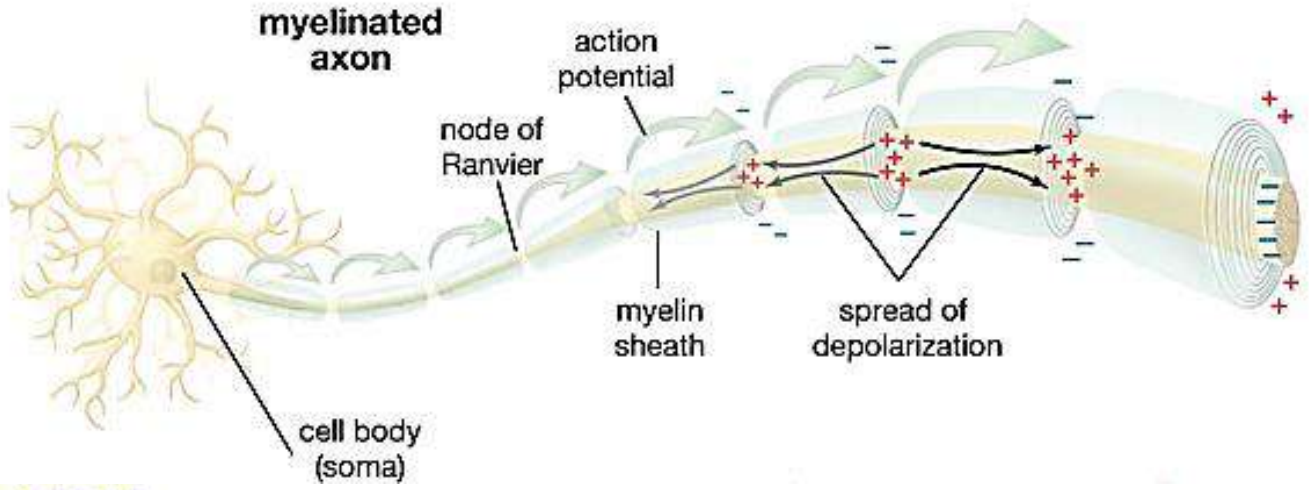
Sphingosine

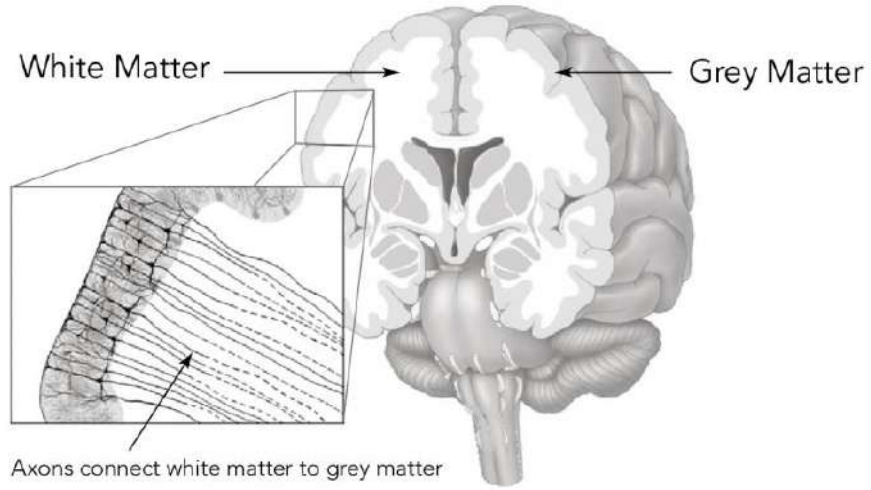


Sphingomyelin

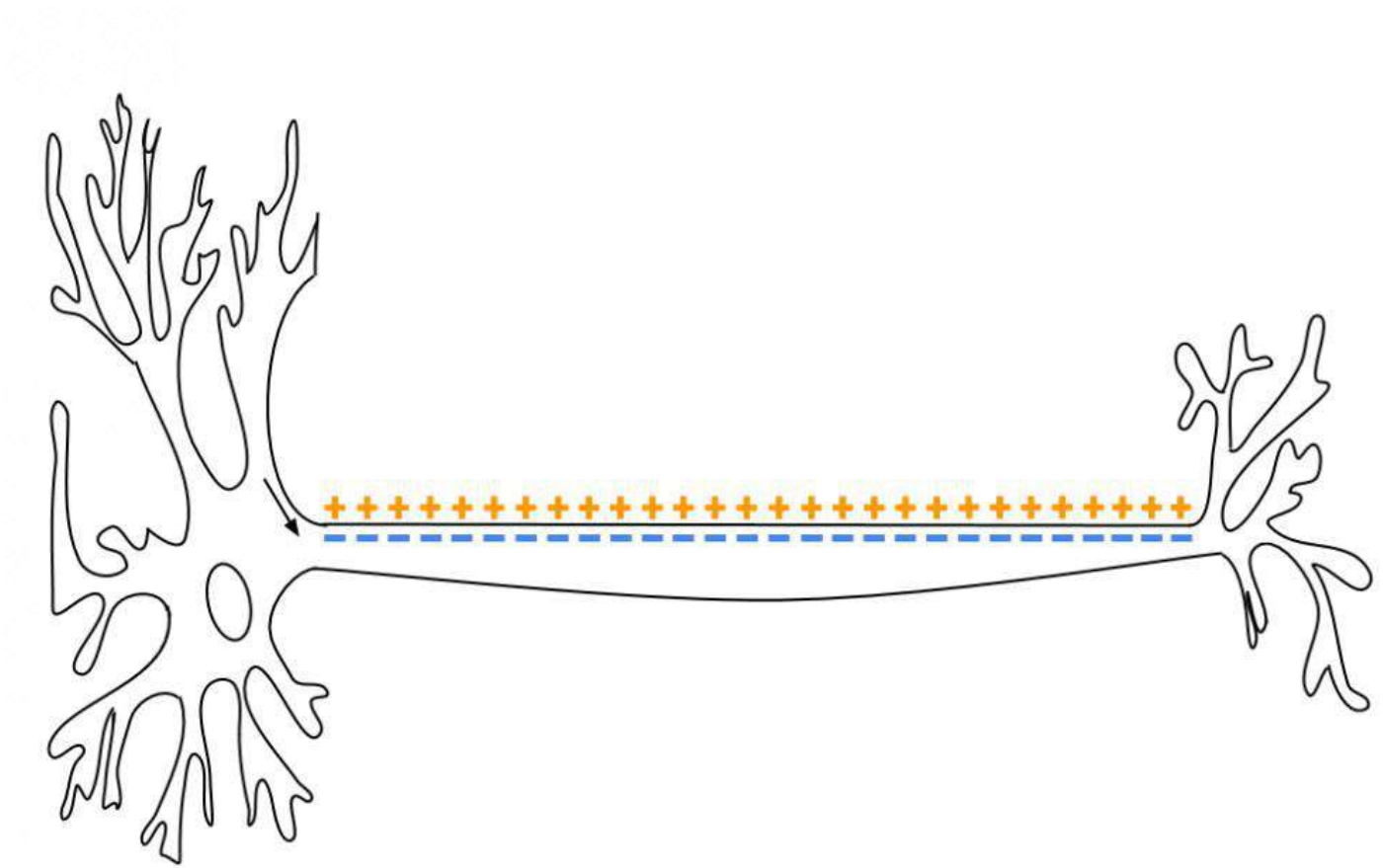
Sphingomyelins: Function

- The sphingomyelins are abundant in the white matter of the myelin sheath, a coating surrounding the nerve cells that increases the speed of nerve impulses and insulates and protects the nerve cells.





Nerve impulses

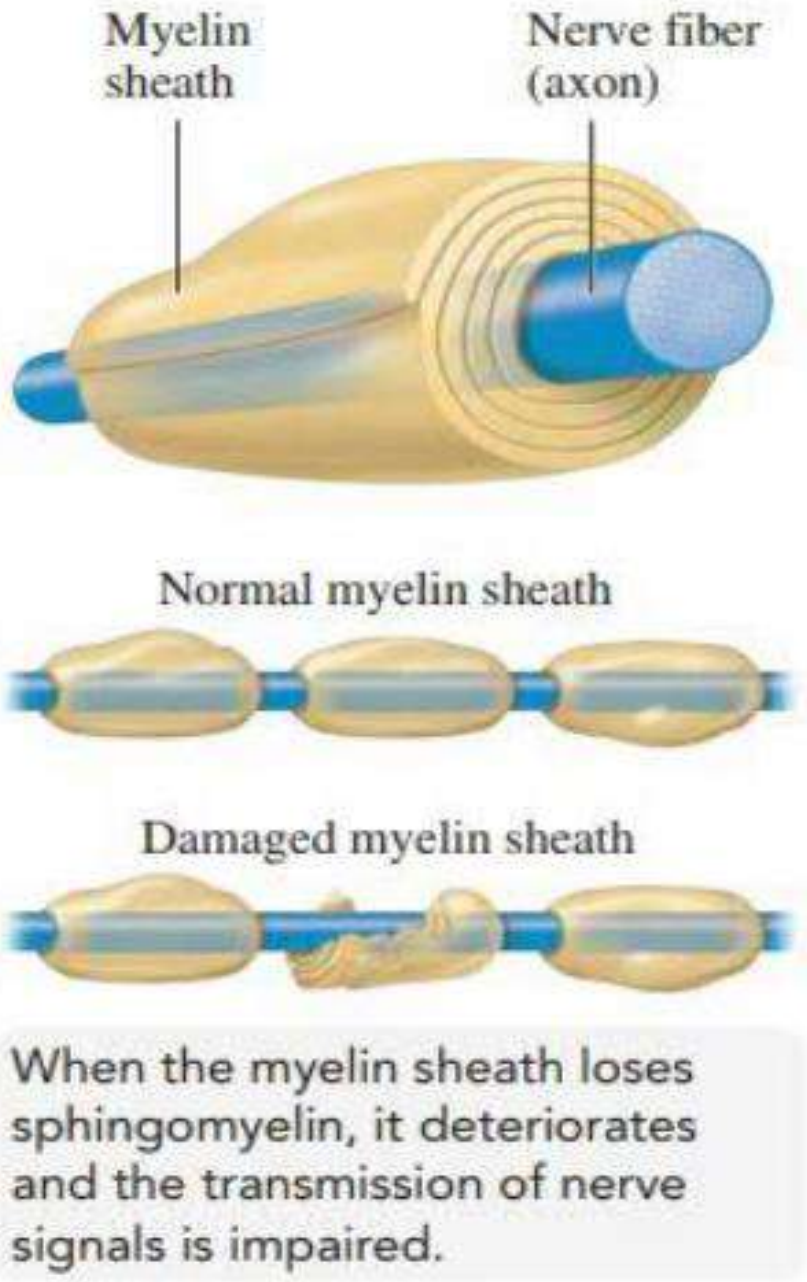


Multiple Sclerosis

- **Multiple Sclerosis (MS)** is a chronic autoimmune disease that affects the central nervous system (CNS), leading to the destruction of the **myelin sheath** surrounding nerve fibers.
- The symptoms of multiple sclerosis include muscle weakness with loss of coordination and vision, depending on the amount of damage.

Multiple Sclerosis

- Sphingomyelin is lost from the myelin sheath.
- As the disease progresses, the myelin sheath deteriorates.
- Scars form on the neurons and impair the transmission of nerve signals.



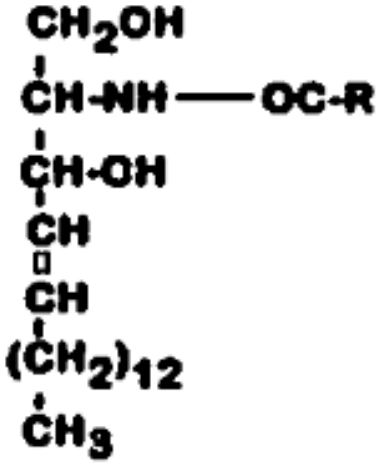
When the myelin sheath loses sphingomyelin, it deteriorates and the transmission of nerve signals is impaired.

Niemann Pick's disease

- It is accumulation of large amounts of sphingomyelin in brain, liver, spleen, and bone marrow due to deficiency of sphingomyelinase enzyme.
- It leads to mental retardation and death in early life.

Ceramides

- **Ceramide: It is not a phospholipid (**waxy lipid molecules)**.**
- **Structure: Sphingosine + fatty acid (usually polyunsaturated)**
- **Ceramides are found in high concentrations within the cell membrane of eukaryotic cells, since they are component lipids that make up sphingomyelin.**



Ceramide

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THANK YOU

M.ELEYAN

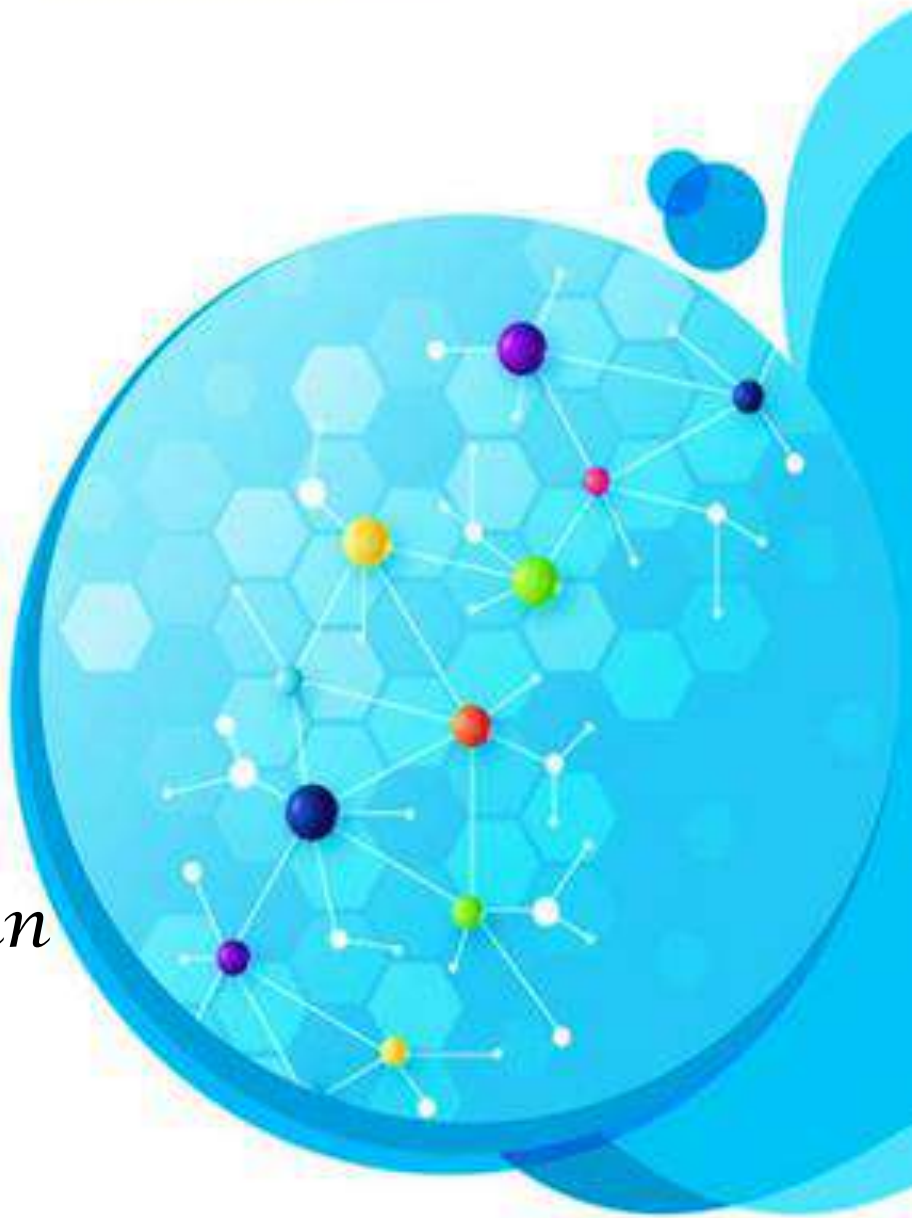
Medical Biochemistry

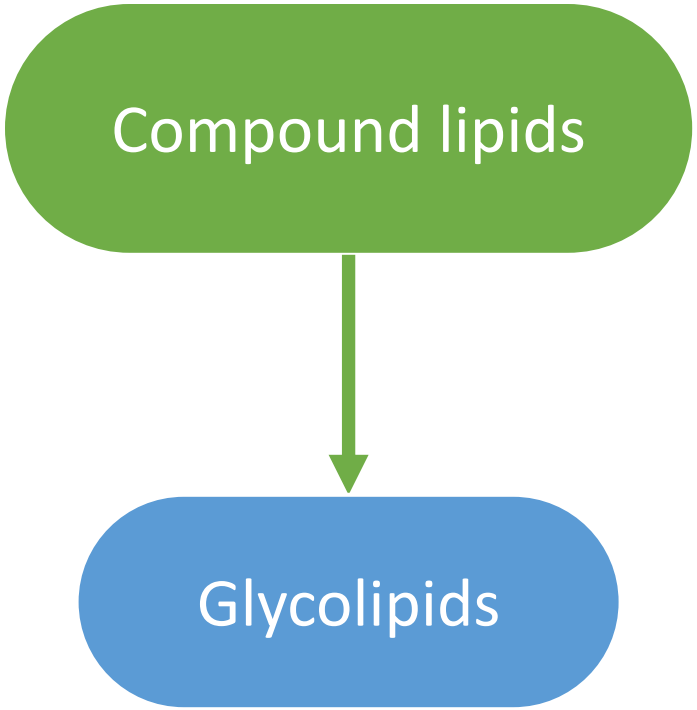
Lipid Chemistry

Asst. Prof.Mohammed Hasan Eleyan

Faculty of Medicine

Al-Azhar University-Gaza





Glycolipids

- Glycolipids: These are complex lipids containing ceramide (Sphingosine + fatty acid) & carbohydrate.
- Includes:
    1. Cerebrosides
    2. Sulfolipids
    3. Gangliosides.

Glycolipids

Cerebrosides

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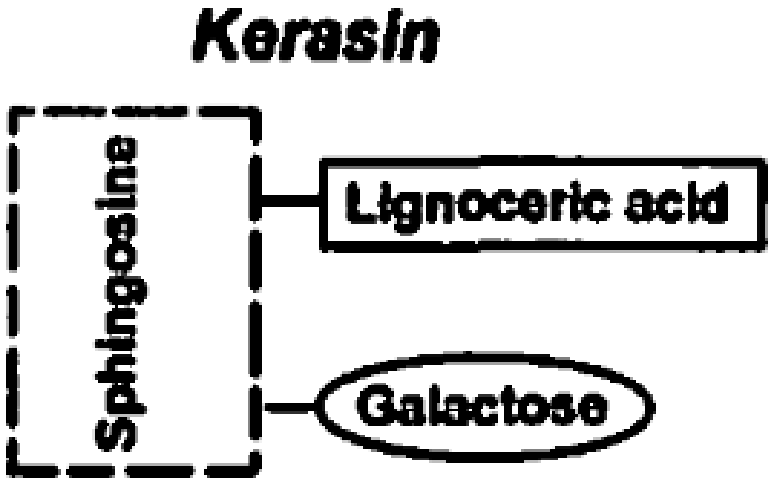
Cerebrosides

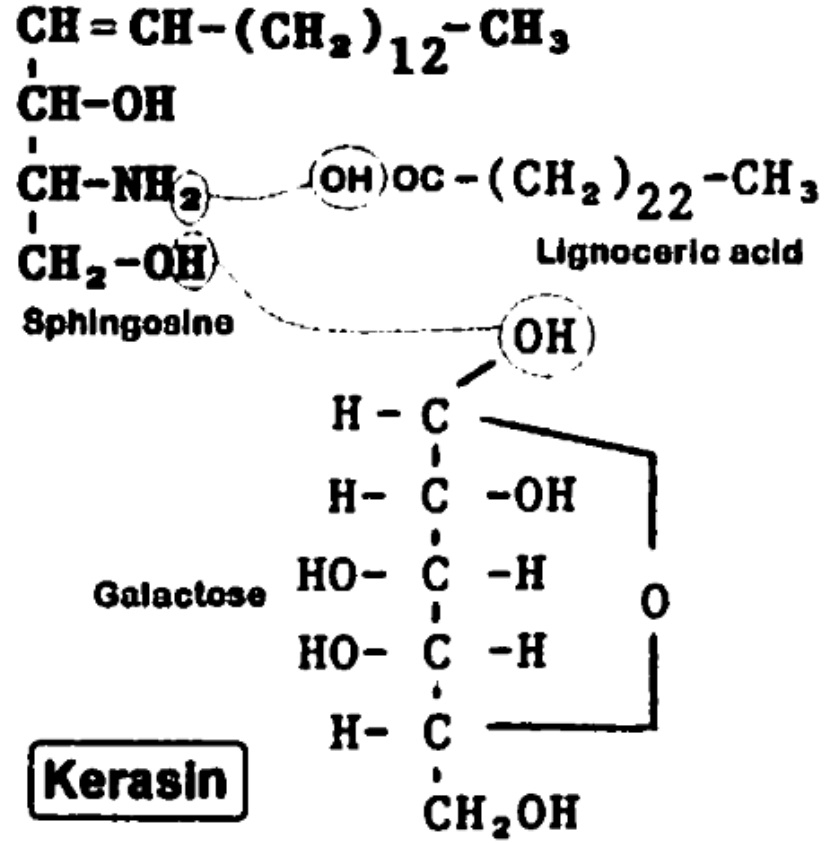
- They are called simple glycolipids.
- Upon hydrolysis ,they give:
    1. Sphingosine.
    2. Fatty acid.
    3. Sugar (usually galactose or glucose).
        - According to the type of fatty acid, they may be:

Kerasin

- Kerasin: The fatty acid is lignoceric acid

  (C24: saturated)

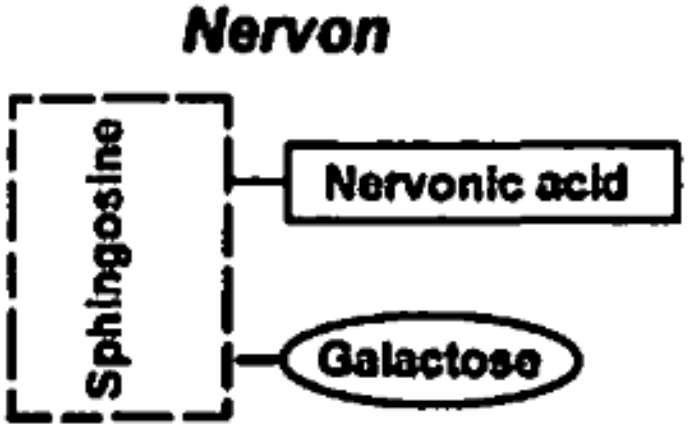




Nervon

- Nervon: The fatty acid is nervonic acid

  (C24 unsaturated ,ω^{9})

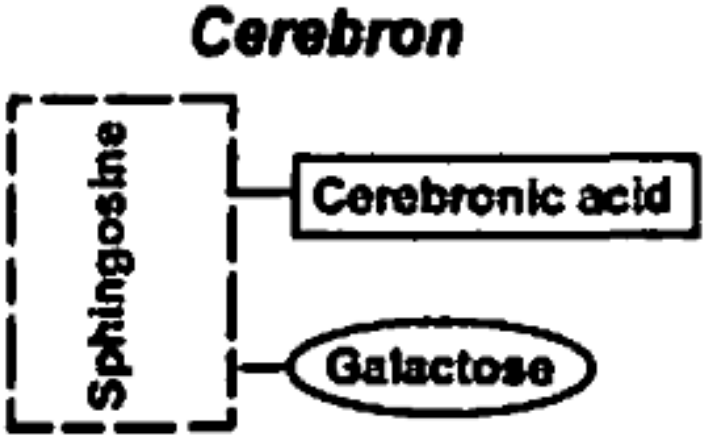


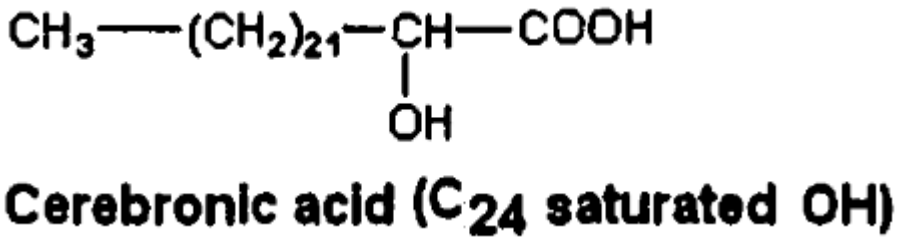
$$CH_3—(CH_2)_7—CH=CH—(CH_2)_{13}—COOH$$

Nervonic acid (C 24:1 Δ^{15})

Cerebron

- Cerebron: The fatty acid is cerebronic acid (C24-hydroxy saturated).

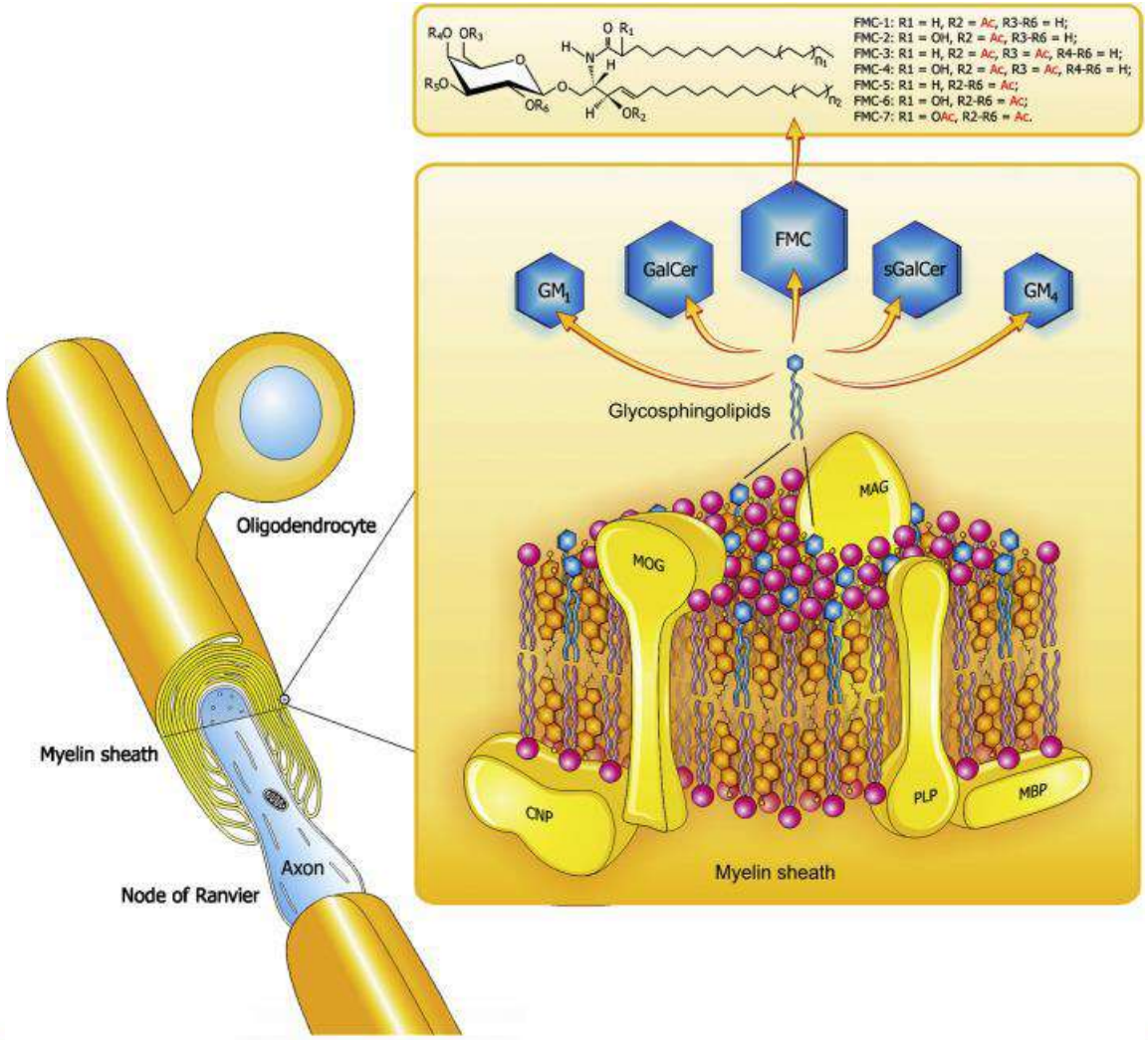




Cerebronic acid (C_{24} saturated OH)

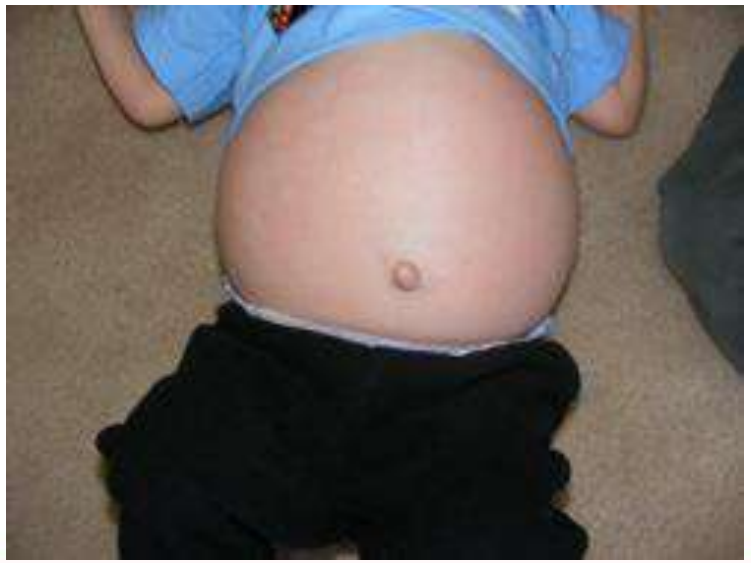
Functions of Cerebrosides

- Cerebrosides are present in many tissues especially in the brain and myelin of nerve fibers.
- They act as insulators of nerve impulse.



Gaucher's disease:

- **Def:** Accumulation of cerebrosides in tissues due to deficiency of "β glucocerebrosidase" enzyme.
- **Consequences:** **Affect normal function** of tissues where it is accumulated.
- **Manifestations**: mental retardation, hepatomegally and bone disorder.

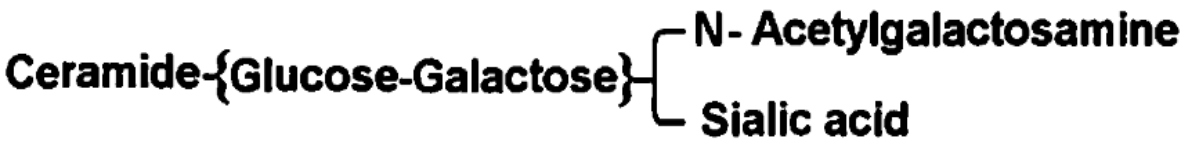


Glycolipids

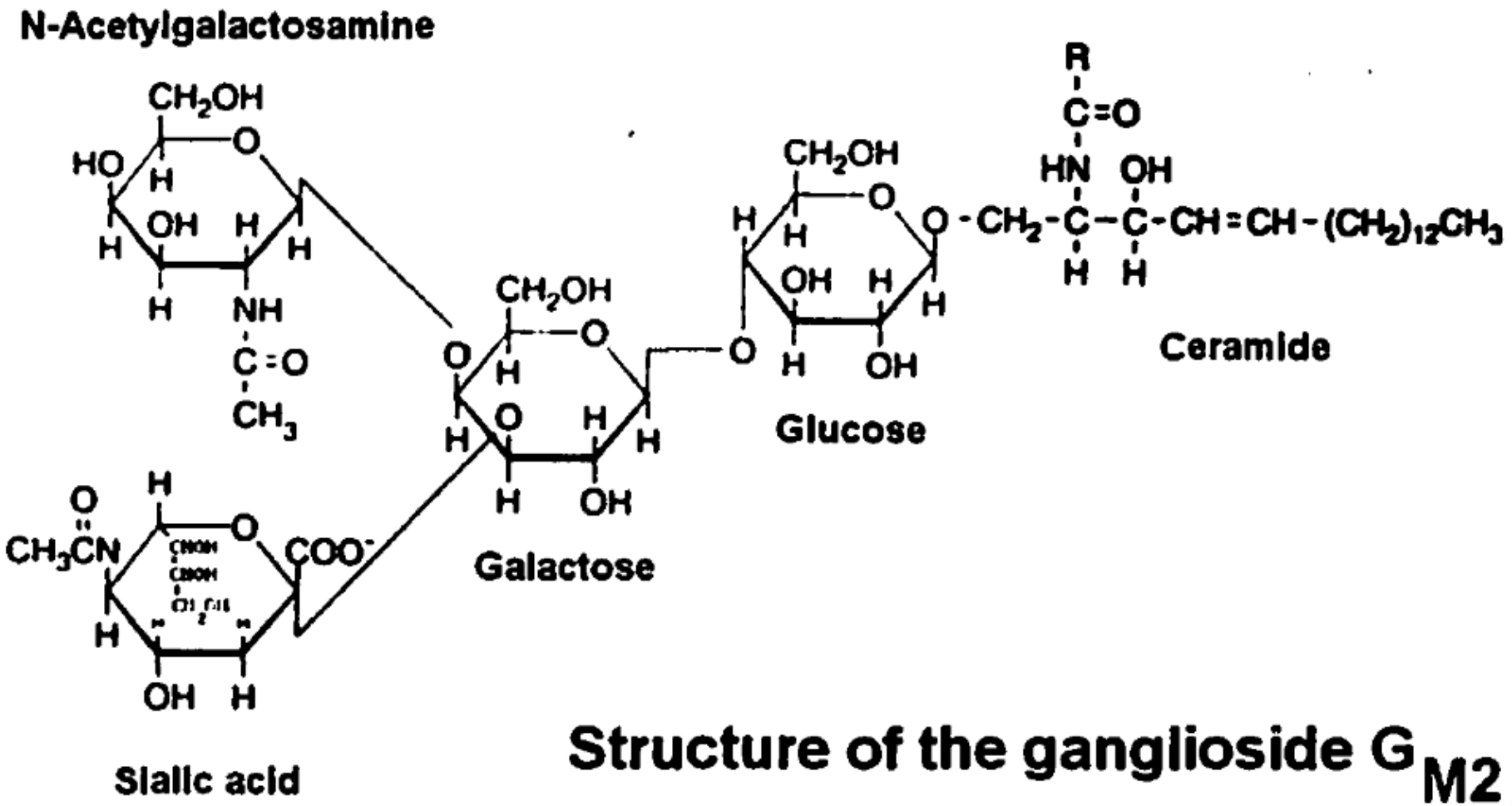
Gangliosides

Gangliosides:

- They are called complex glycolipids, because they contain in addition to hexose (glucose, galactose, and **N-acetylgalactosamine**), one or more sialic acid molecules.
- Upon hydrolysis they give:
    1. Ceramide (sphingosine and fatty acid).
    2. Hexoses (glucose and galactose).
    3. Hexosamines:
        - Sialic acid (N-acetylneuraminic acid).
        - N-acetylgalactosamine.



Ceramide-{Glucose-Galactose}
- N- Acetylgalactosamine
- Sialic acid



Structure of the ganglioside G_{M2}

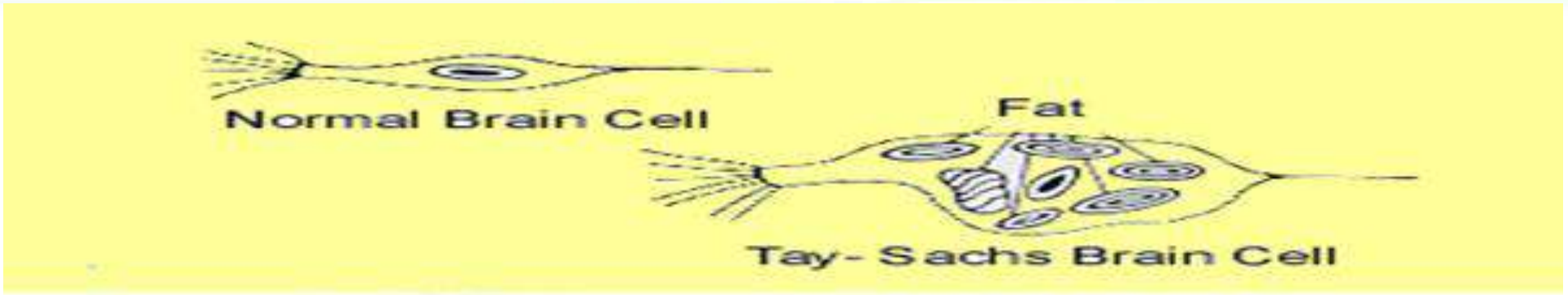
Functions of gangliosides:

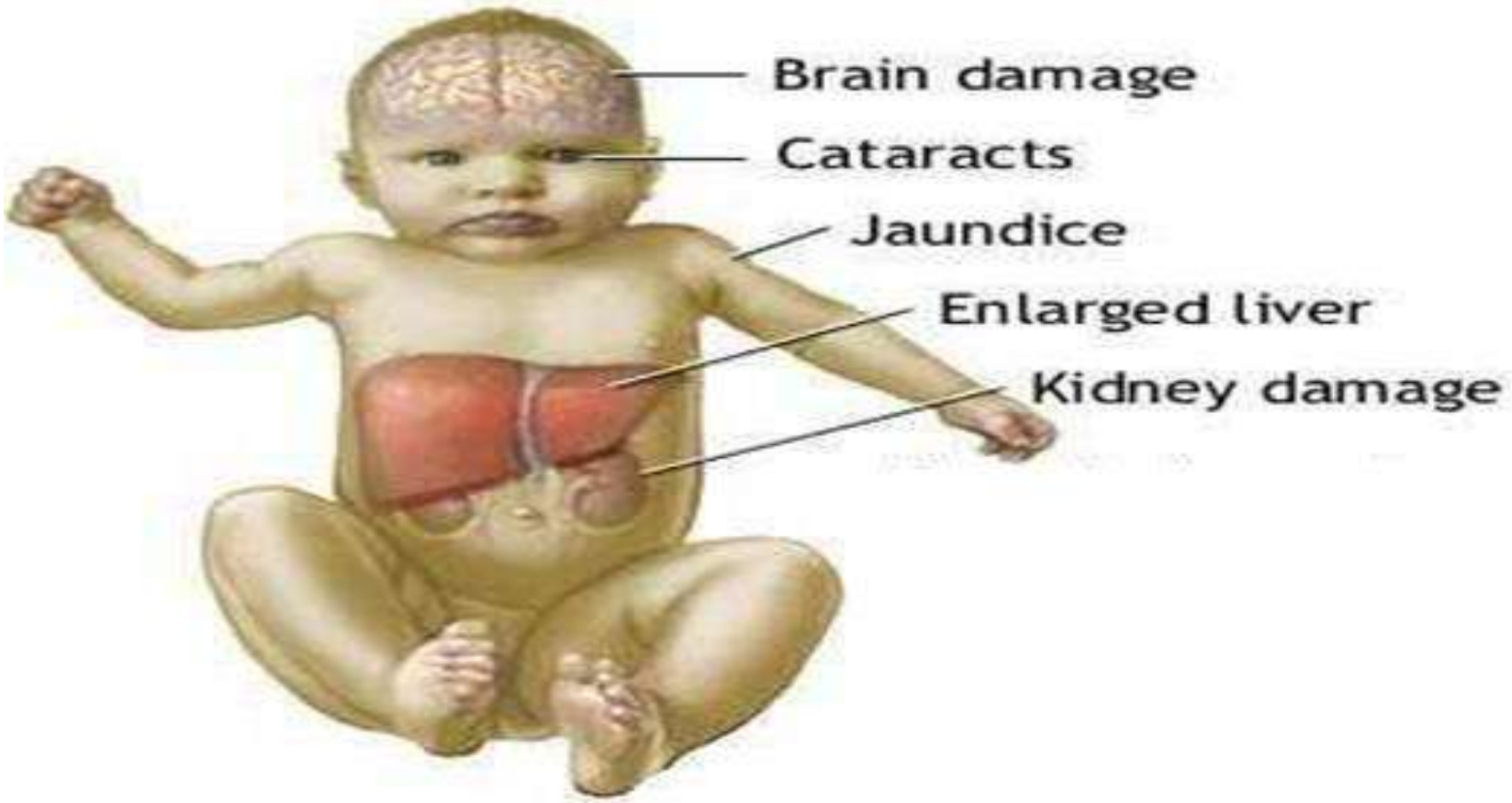
1. They act as receptors at cell membrane (back to CHO).
2. They are present in high concentration in brain.

- Degradation: By hexosaminidase enzyme.

Tay sachs disease:

- Accumulation of gangliosides in brain and intestine due to deficiency of hexosaminidase enzyme.
- Manifestations: mental retardation, hepatomegally, blindness and death in early life.


Normal Brain Cell
Fat
Tay- Sachs Brain Cell


Brain damage
Cataracts
Jaundice
Enlarged liver
Kidney damage

Glycolipids

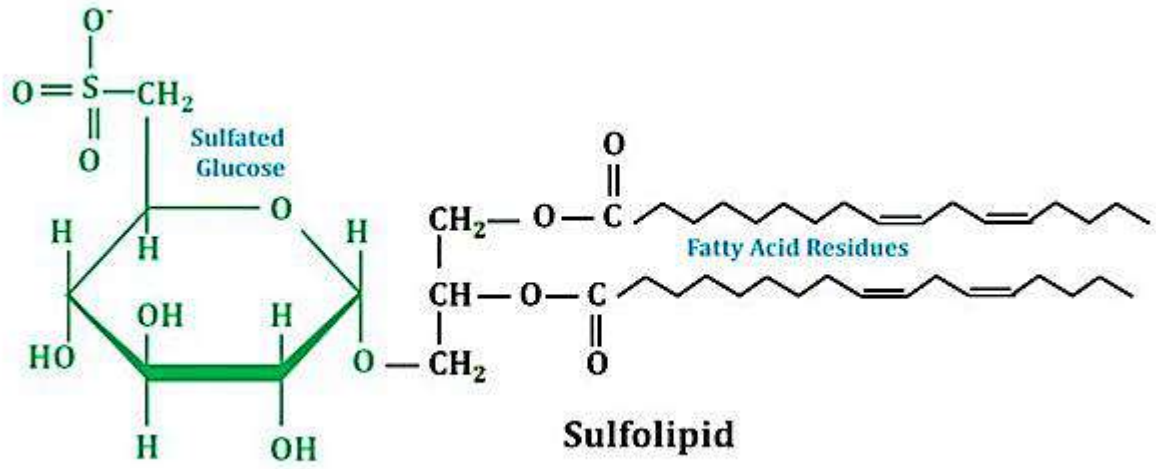
Sulpholipids

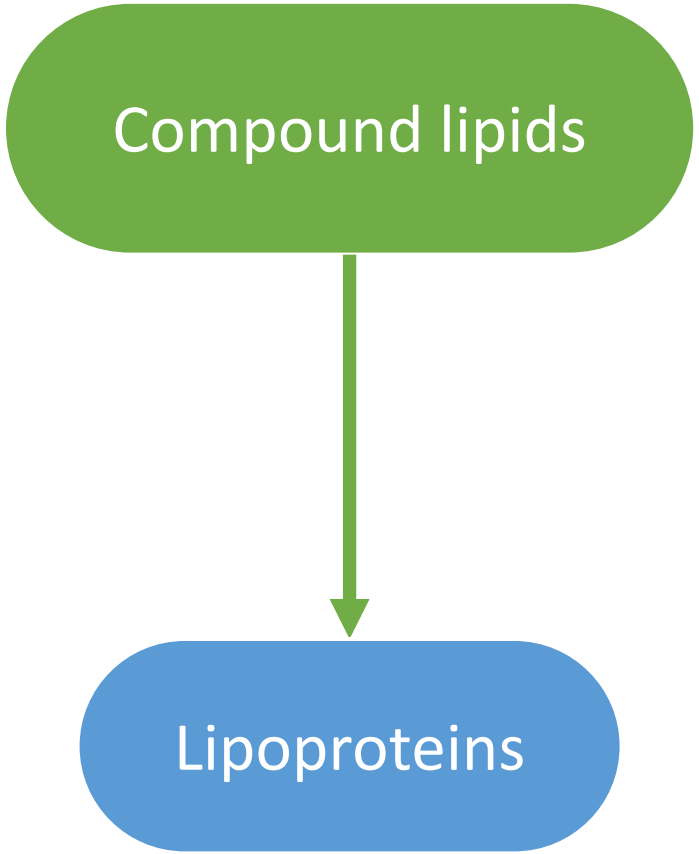
Sulfolipids

- Sulfolipids are a subclass of glycolipids containing a **sulfate group** attached to the sugar moiety.

contained in brain lipids and present in low levels in liver, lung, kidney, spleen, skeletal muscle and heart

Function: Membrane Stability and Antioxidant Properties





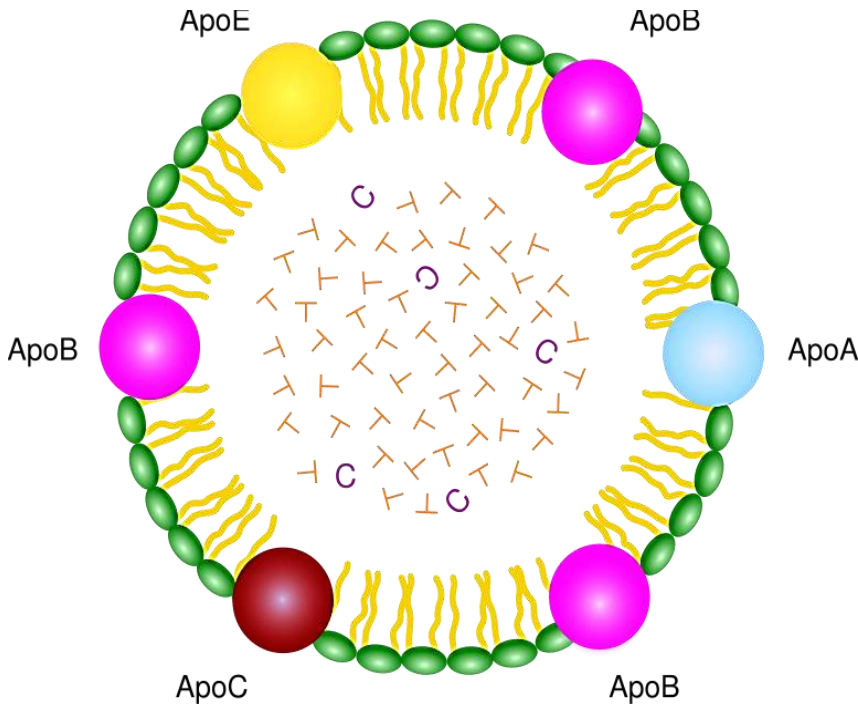
Lipoproteins

- These are complex lipids formed of lipids conjugated with protein.
- They are present in cell membrane, mitochondria and plasma (plasma lipoproteins).

Plasma Lipoproteins

- Plasma lipoproteins convert water insoluble lipids into water soluble complexes.

This facilitates transport of lipids between blood and different tissues.



Plasma Lipoproteins

The lipids present in plasma (total range: 360–820 mg/dL) include the following components:

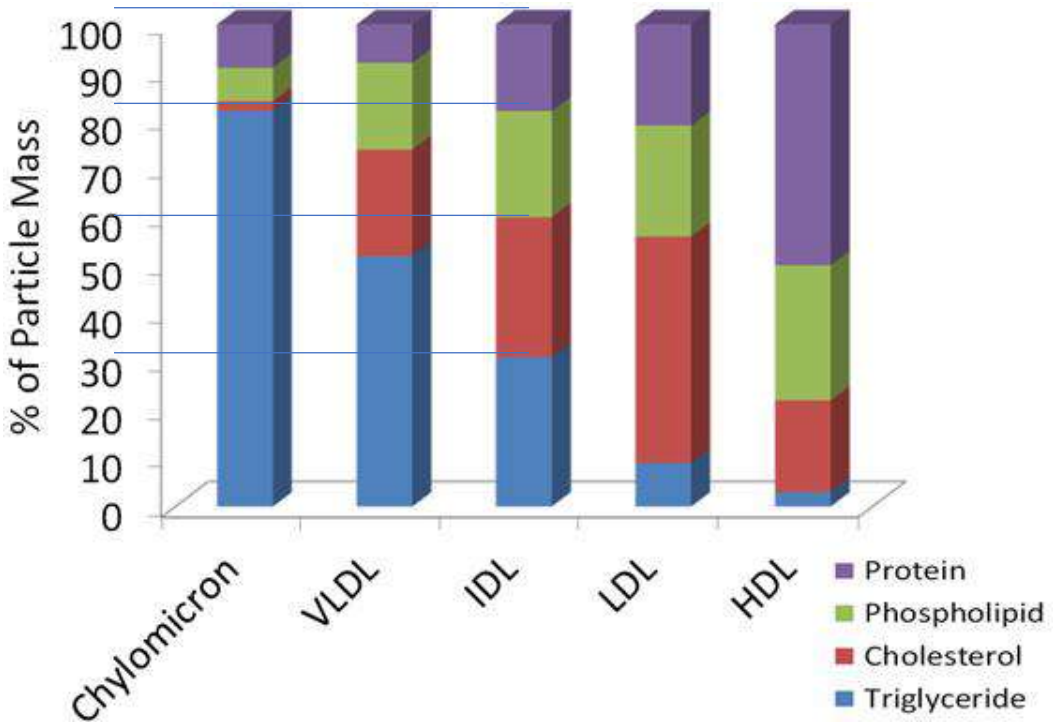
- The plasma lipids (360-820 mg/dl) are phospholipids, cholesterol (free and esterified) and lipids between triacylglycerols, free fatty acids.

1-Cholesterol :	140-220 mg/dl 70% Cholesteryl esters 30% Free cholesterol
2-Phospholipids :	150-200 mg/dl
3-Triacylglycerols :	40-160 mg/dl
4-Free fatty acids :	5-16 mg/dl

Plasma Lipoproteins

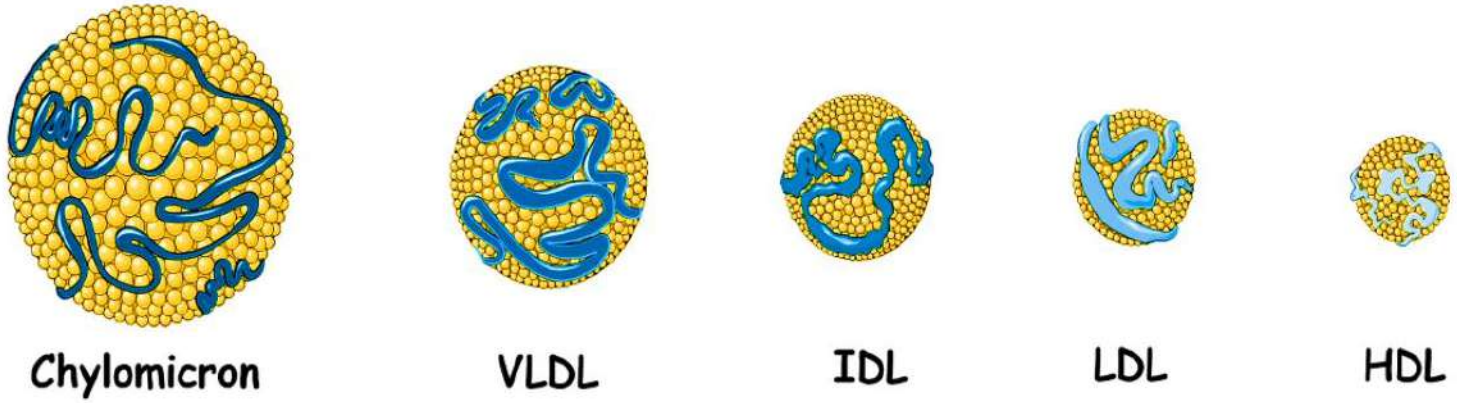
- The plasma lipoproteins are spherical macromolecular complexes of lipids and proteins (apolipoproteins).
- The lipoprotein particles include chylomicrons, very–low-density lipoproteins (VLDLs), intermediate-density lipoproteins (IDLs), low-density lipoproteins (LDLs), and high-density lipoproteins (HDLs).
- They differ in lipid and protein composition, size, density, and site of origin.

Composition of lipoproteins



		Composition (wt %)				
Lipoprotein	**Density (g/mL)**	**Protein**	**Phospholipids**	**Free cholesterol**	**Cholesteryl esters**	**Triacylglycerols**
Chylomicrons	<1.006	2	9	1	3	85
VLDL	0.95–1.006	10	18	7	12	50
LDL	1.006–1.063	23	20	8	37	10
HDL	1.063–1.210	55	24	2	15	4

Data from D. Kritchevsky, *Nutr. Int.* 2:290, 1986.



The density and diameter of different lipoproteins

Lipoprotein	Density (g/dL)	Diameter (nm)
Chylomicrons	0.95	75-1200
VLDL (very low-density lipoproteins)	0.95-1.006	30-80
IDL (intermediate-density lipoproteins)	1.006-1.019	25-35
LDL (low-density lipoproteins)	1.019-1.063	18-25
HDL (high-density lipoproteins)	1.063-1.21	5-12

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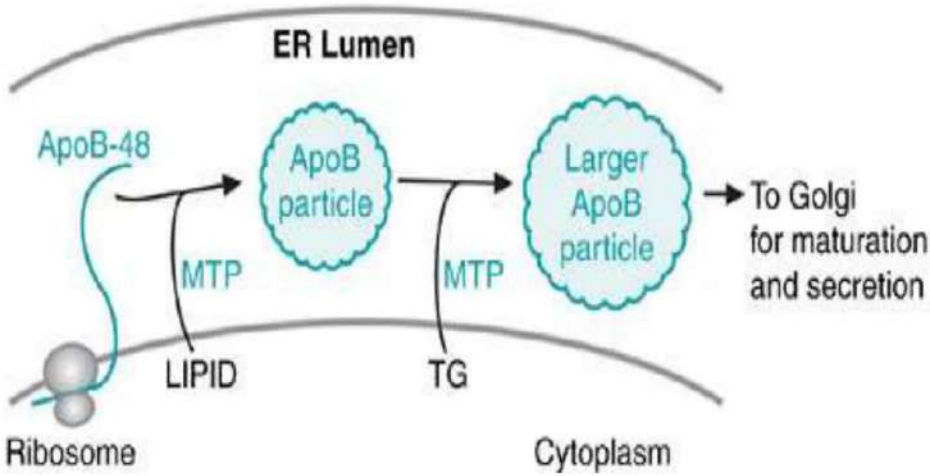
Chylomicrons

- **Chylomicrons** (TAG= 90%) are highly soluble in both lymphatic fluid and blood.
- **Function** in the transport of dietary triacylglycerol, cholesterol, and cholesteryl esters to other tissues.
- **Assembly of chylomicrons** occurs in the intestinal lining and results in a nascent chylomicron that contains lipids and apolipoproteins.

Chylomicron assembly in enterocytes

1. **Initial Assembly:**
   A. The synthesis begins with the translation of the apoB-48 protein.
   B. Lipid association occurs next, where small amounts of triglycerides and other lipids associate with the apoB-48 protein.
   C. This process is catalyzed by microsomal triglyceride transfer protein (MTP), leading to the formation of small apoB-containing particles.

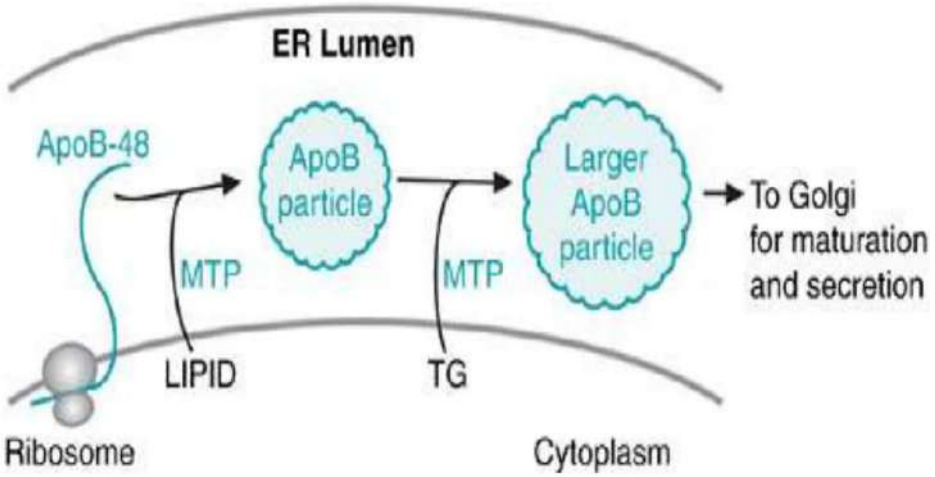
This process occurs within the endoplasmic reticulum (ER).



Chylomicron assembly in enterocytes

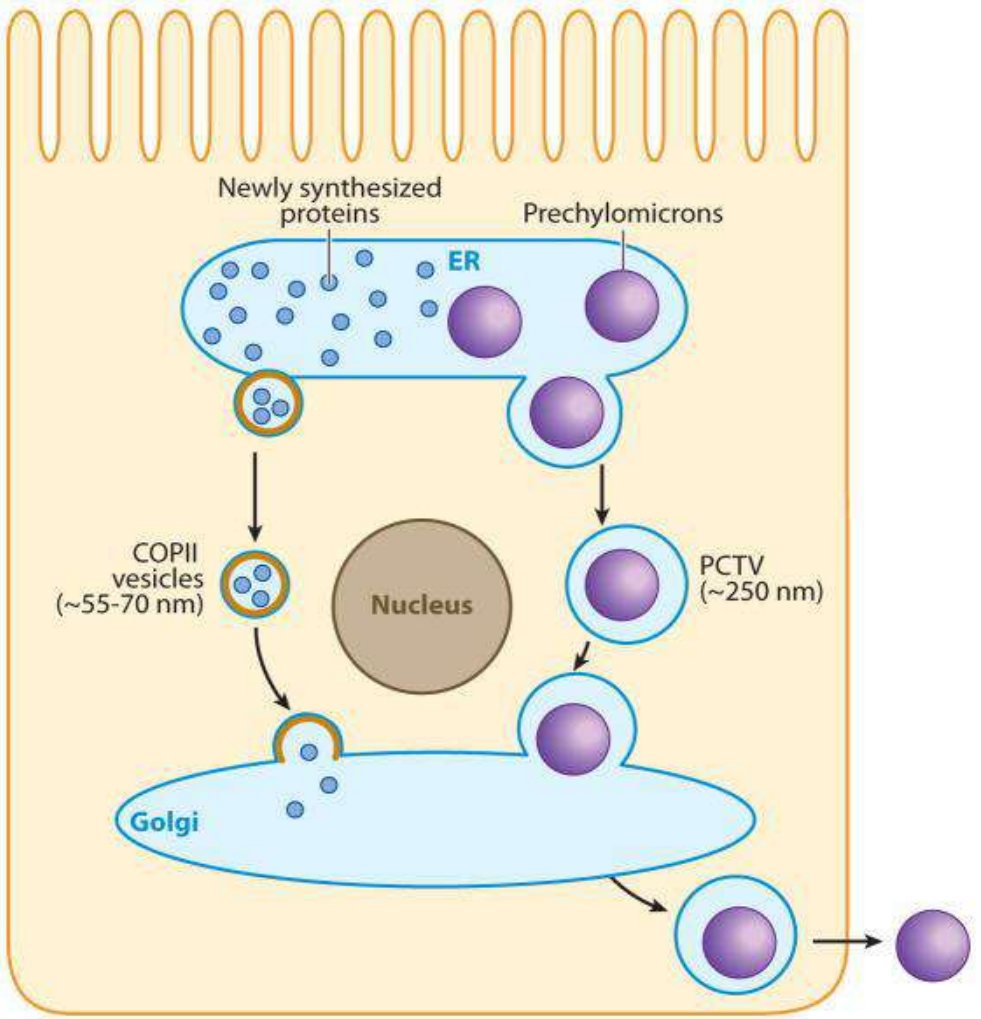
B. Particle Expansion:

- Large triacylglycerol droplets fuse with the initial apoB-containing particles.
- MTP also facilitates the transfer of additional triacylglycerol from the cytoplasm into the ER lumen, where it forms lipid droplets that are incorporated into the growing chylomicron.



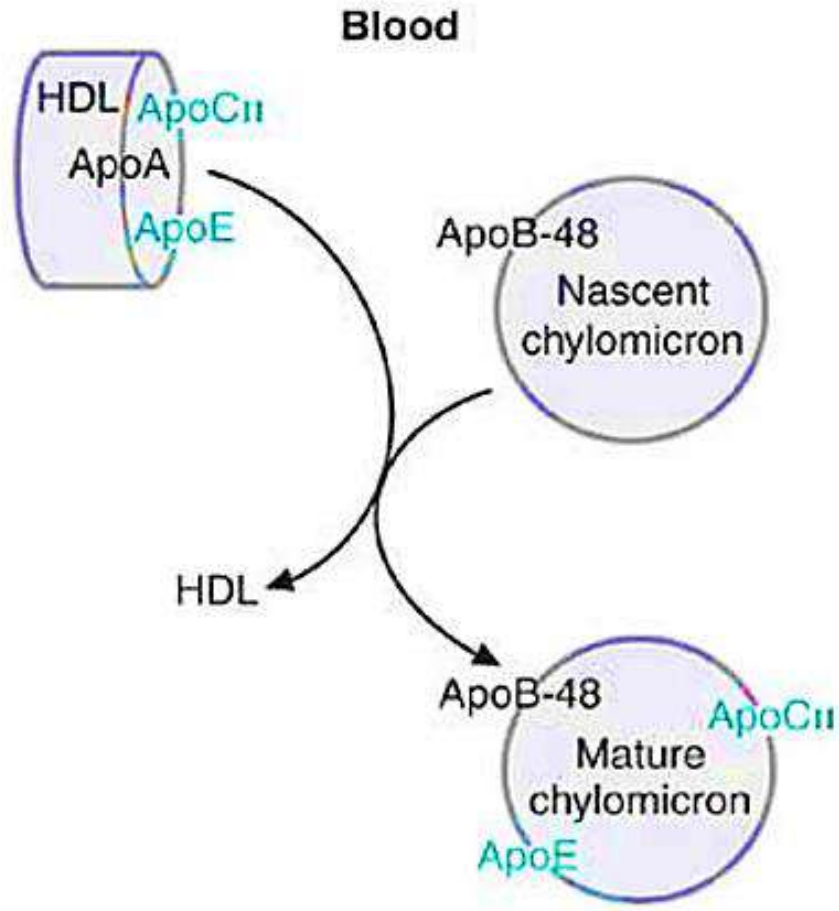
Chylomicron assembly in enterocytes

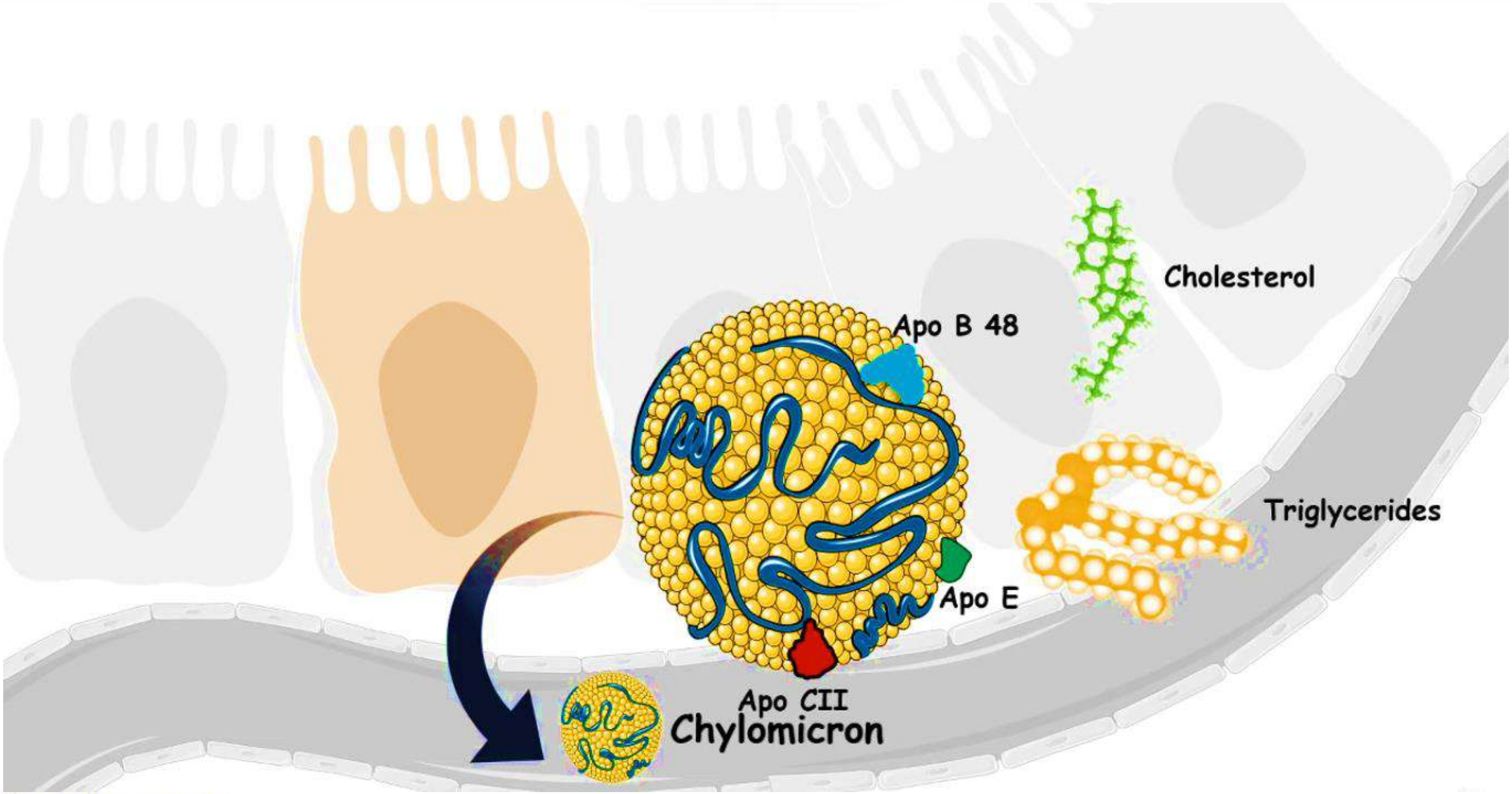
1. Transition of the chylomicrons to Golgi, where the particles are packaged in secretory vesicles.
2. These fuse with the plasma membrane releasing the lipoproteins to the blood.
3. When it reaches the plasma, the particle is rapidly modified, receiving apo E and apo C-II (The source of these apolipoproteins is circulating HDL).

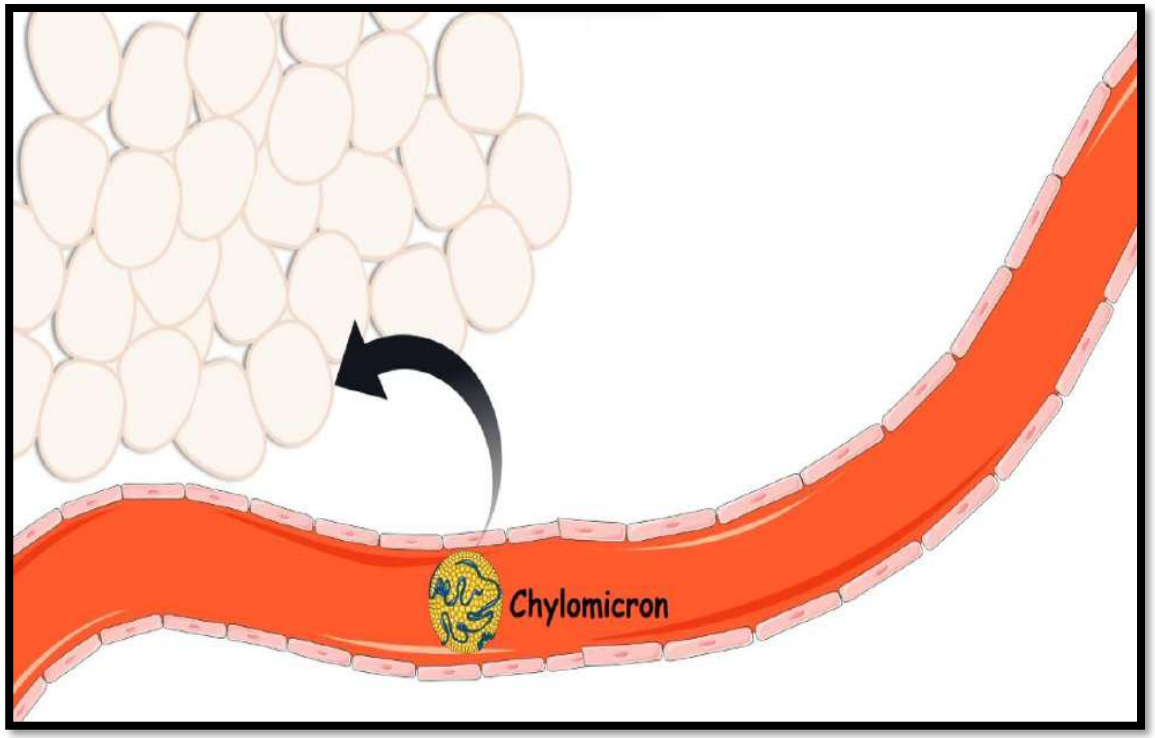


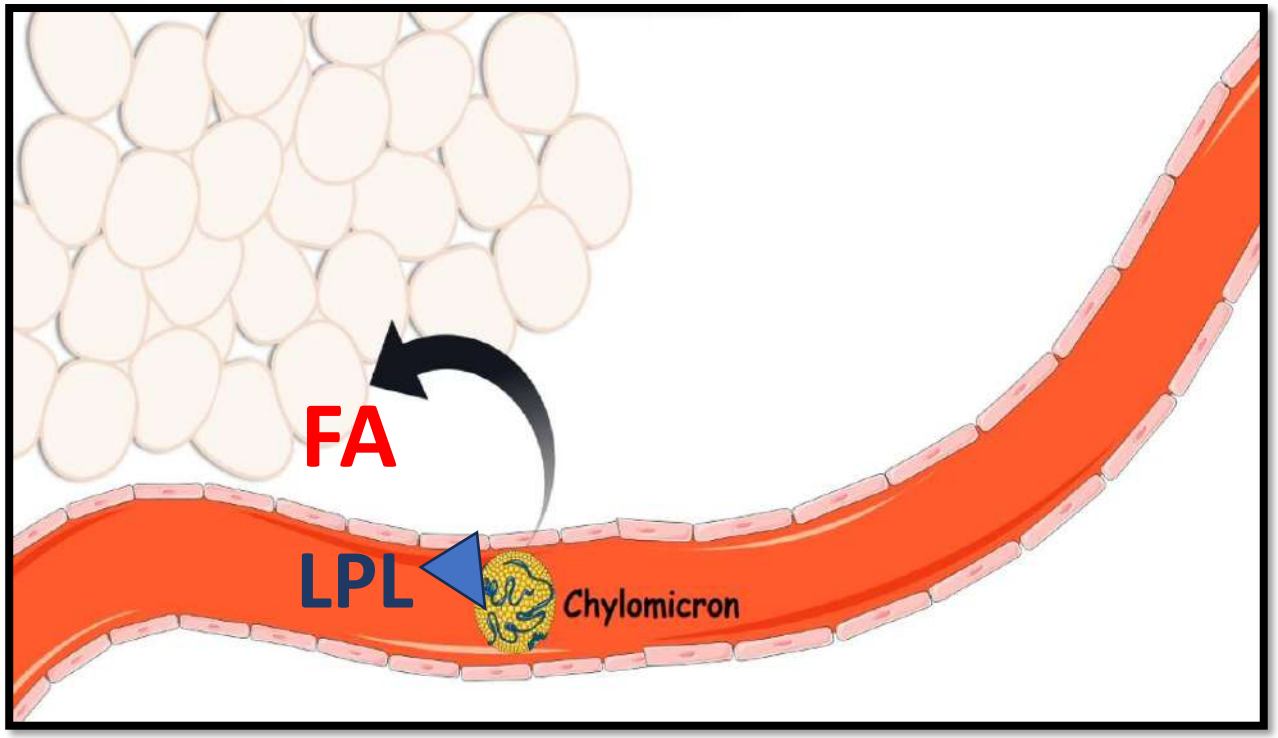
Transfer of proteins from HDL to chylomicrons

- Newly synthesized chylomicrons (nascent chylomicrons) mature as they receive apoC-ll and apoE from HDL.
- Roles of ApoC-II and ApoE:
  - ApoC-II: Essential for the activation of lipoprotein lipase (LPL), the enzyme responsible for hydrolyzing triglycerides in chylomicrons into free fatty acids and glycerol for uptake by tissues (e.g., muscle, adipose tissue).
  - ApoE: Serves as a ligand for receptors that mediate the uptake and clearance of chylomicron remnants by the liver.




Cholesterol
Apo B 48
Triglycerides
Apo E
Apo CII
Chylomicron





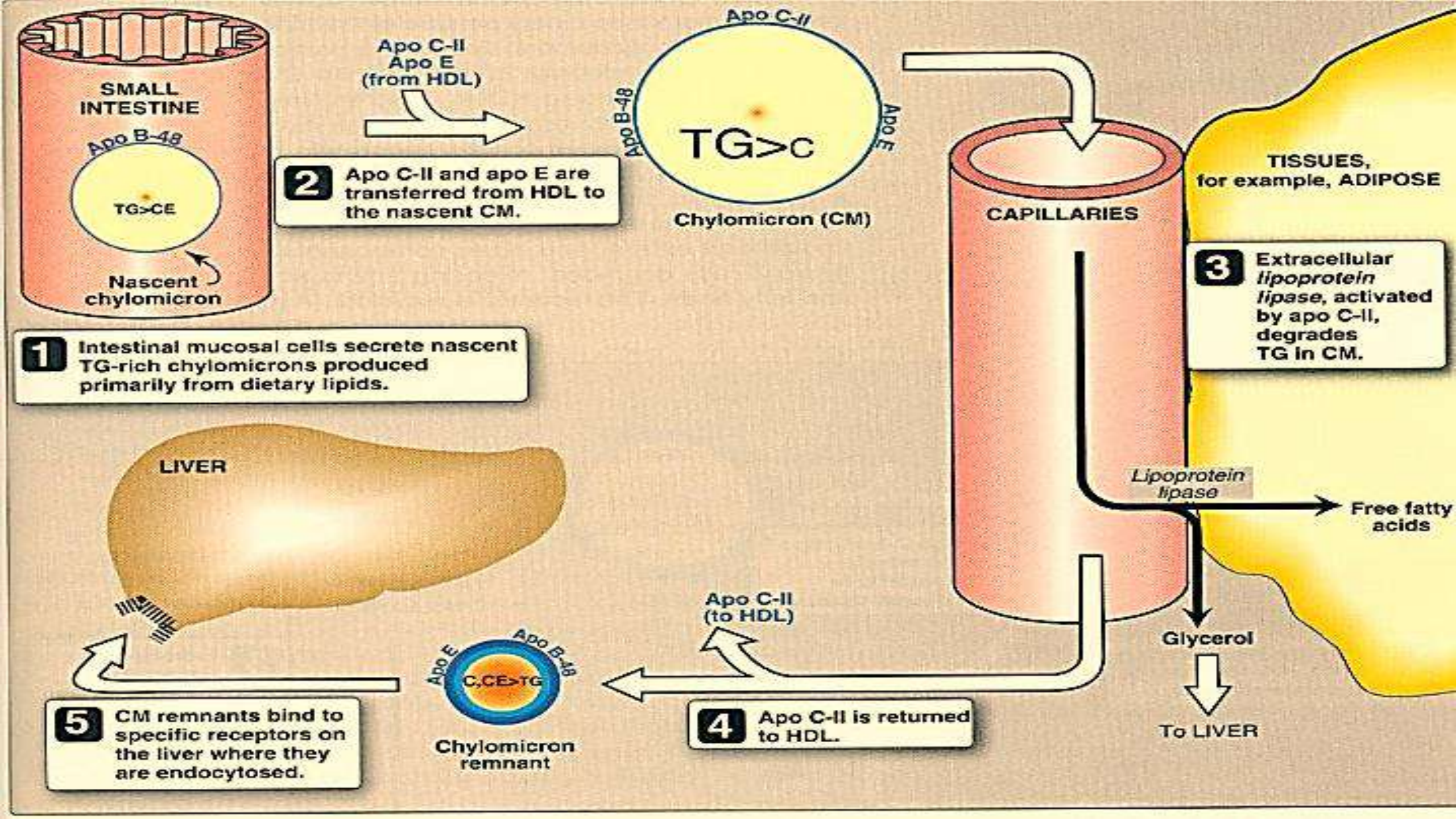
- **Lipoprotein lipase** (LPL) is an extracellular enzyme that is anchored to the capillary walls of most tissues but predominantly those of adipose tissue and cardiac and skeletal muscle.

Fate of Chylomicron

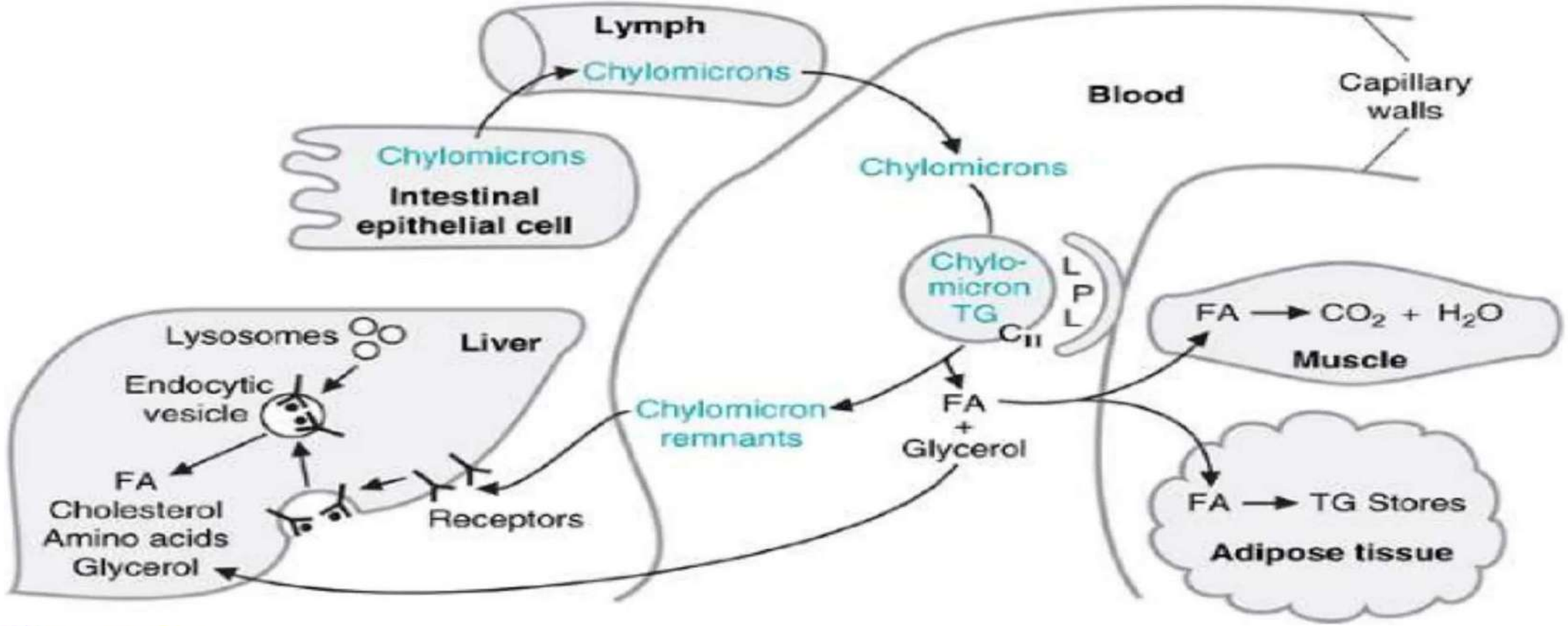
- LPL, activated by apo C-II on chylomicrons, hydrolyzes the TAG in these particles to FA and glycerol.
- The FA are stored (in adipose) or used for energy (in muscle).
- The glycerol is taken up by the liver, converted to dihydroxyacetone phosphate (an intermediate of glycolysis), and used in lipid synthesis or gluconeogenesis.

Fate of Chylomicron

- The remaining particle (remnant) is rapidly removed from the circulation by the liver, whose cell membranes contain lipoprotein receptors that recognize apo E and then taken into the hepatocytes by endocytosis.
- In the lysosome: the apolipoproteins, cholesteryl esters, and other components of the remnant are hydrolytically degraded, releasing amino acids, free cholesterol, and FA.


SMALL INTESTINE
Apo B-48
TG>CE
Nascent chylomicron
1 Intestinal mucosal cells secrete nascent TG-rich chylomicrons produced primarily from dietary lipids.
Apo C-II
Apo E
(from HDL)
2 Apo C-II and apo E are transferred from HDL to the nascent CM.
Apo C-II
Apo B-48
TG>C
Apo E
Chylomicron (CM)
CAPILLARIES
TISSUES, for example, ADIPOSE
3 Extracellular lipoprotein lipase, activated by apo C-II, degrades TG in CM.
Lipoprotein lipase
Free fatty acids
Glycerol
To LIVER
LIVER
Apo C-II
(to HDL)
4 Apo C-II is returned to HDL.
Apo E
Apo B-48
C,CE>TG
Chylomicron remnant
5 CM remnants bind to specific receptors on the liver where they are endocytosed.

Fate of chylomicrons. Chylomicrons are synthesized in intestinal epithelial cells, secreted into the lymph, pass into the blood, and become mature chylomicrons (see Fig.). On capillary walls in adipose tissue and muscle, lipoprotein lipase (LPL) activated by ApoC-II digests the triacylglycerols (TG) of chylomicrons to fatty acids and glycerol. Fatty acids (FA) are oxidized in muscle or stored in adipose cells as triacylglycerols. The remnants of the chylomicrons are taken up by the liver by receptor-mediated endocytosis. Lysosomal enzymes within the hepatocyte digest the remnants, releasing the products into the cytosol.

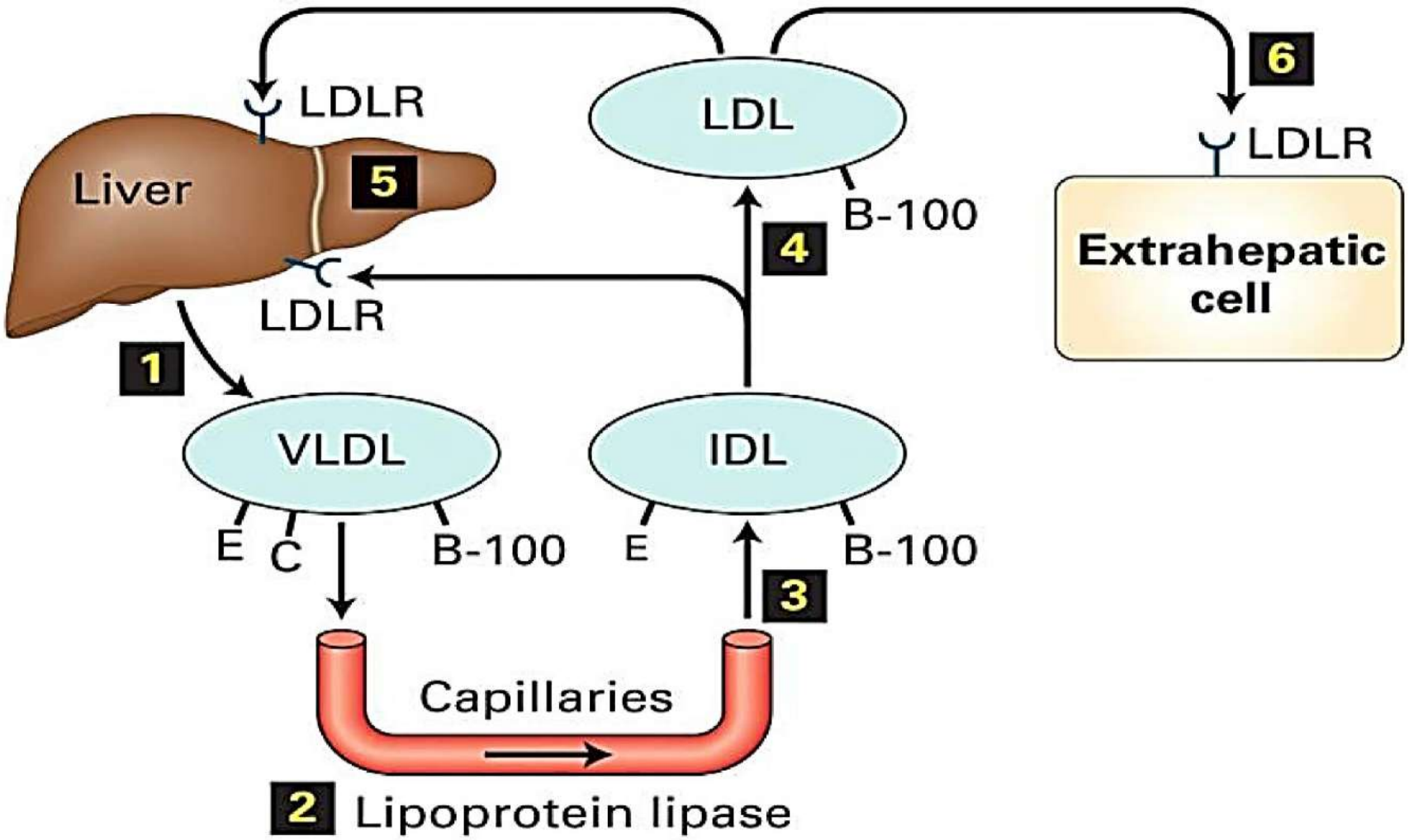


Type I Hyperlipoproteinemia (Familial Hyperchylomicronemia):

- Type I hyperlipoproteinemia is a rare autosomal recessive disorder characterized by the abnormal accumulation of chylomicrons in the plasma.
- Causes:

1. Deficiency of Lipoprotein Lipase (LPL), Deficiency or Mutation in ApoC-II:

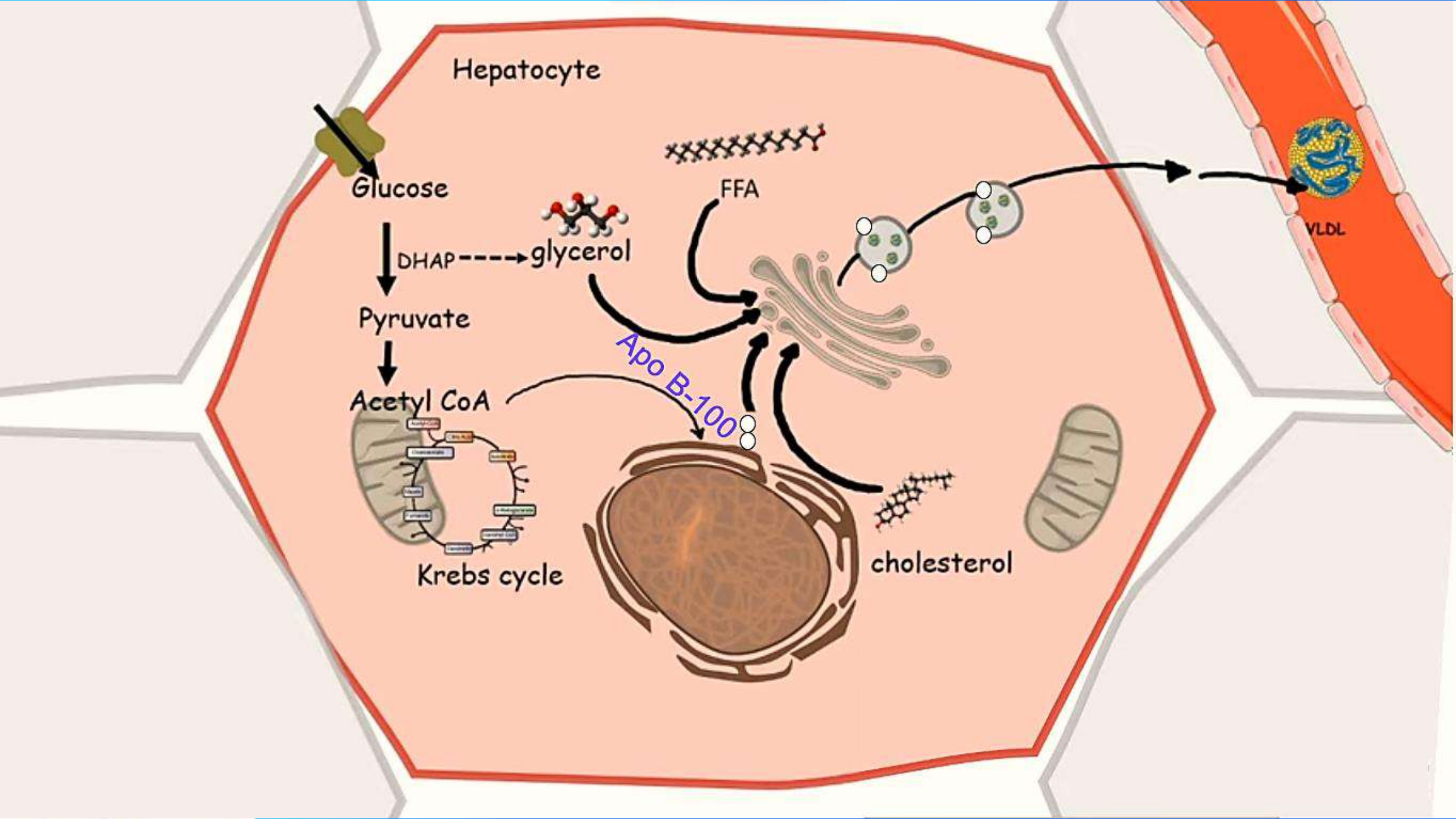
Endogenous Lipid Transport



Very–low-density lipoprotein metabolism (VLDLs)

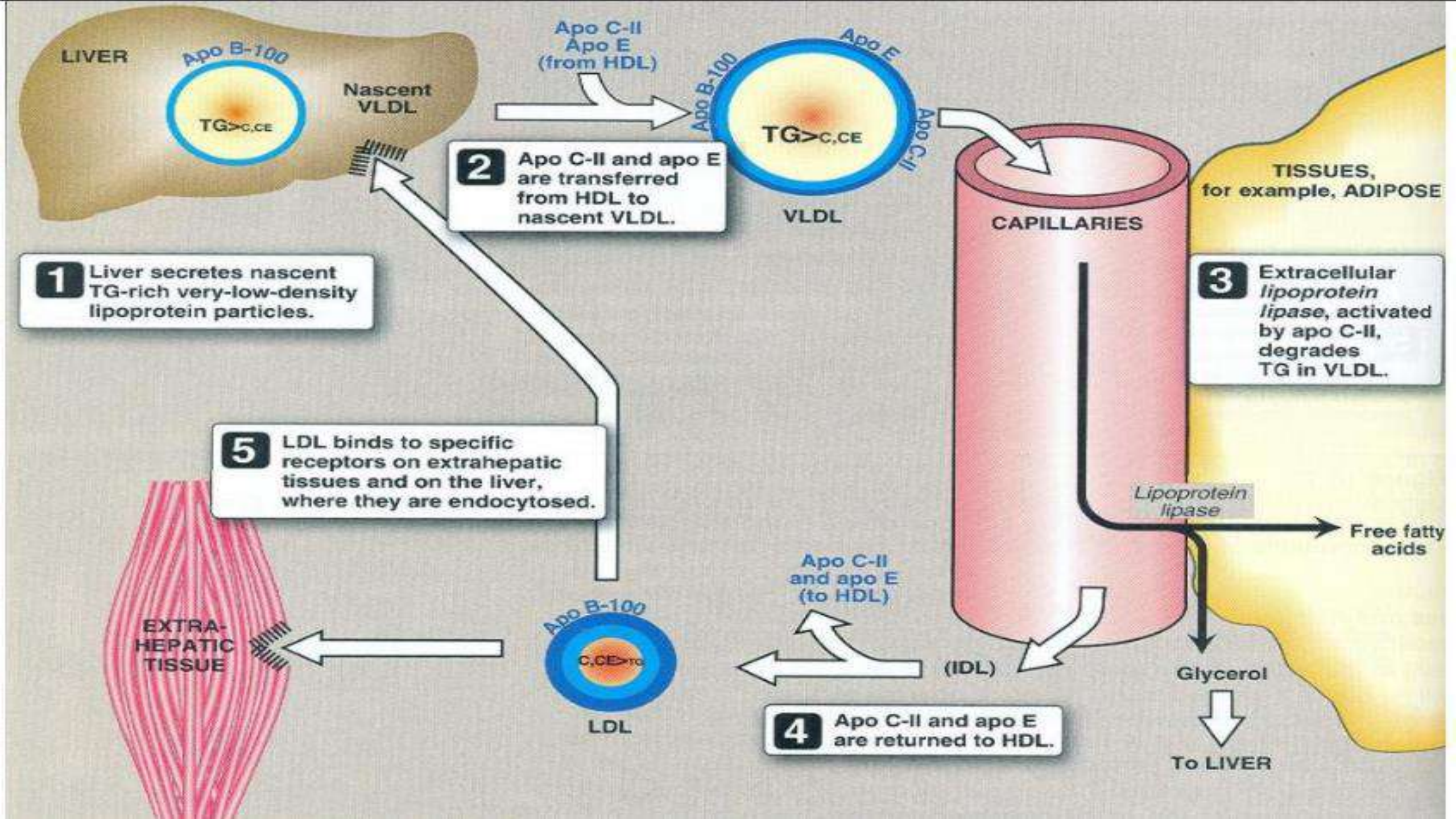
- VLDLs are produced in the liver.
- Their function is to carry this lipid from the liver (site of synthesis) to the peripheral tissues.
- There, the TAG is degraded by LPL, as discussed for chylomicrons.

Synthesis & Release of VLDLs from the liver


Hepatocyte
Glucose
DHAP
glycerol
FFA
Pyruvate
Acetyl CoA
Apo B-100
Krebs cycle
cholesterol
VLDL

Synthesis & Release of VLDLs from the liver

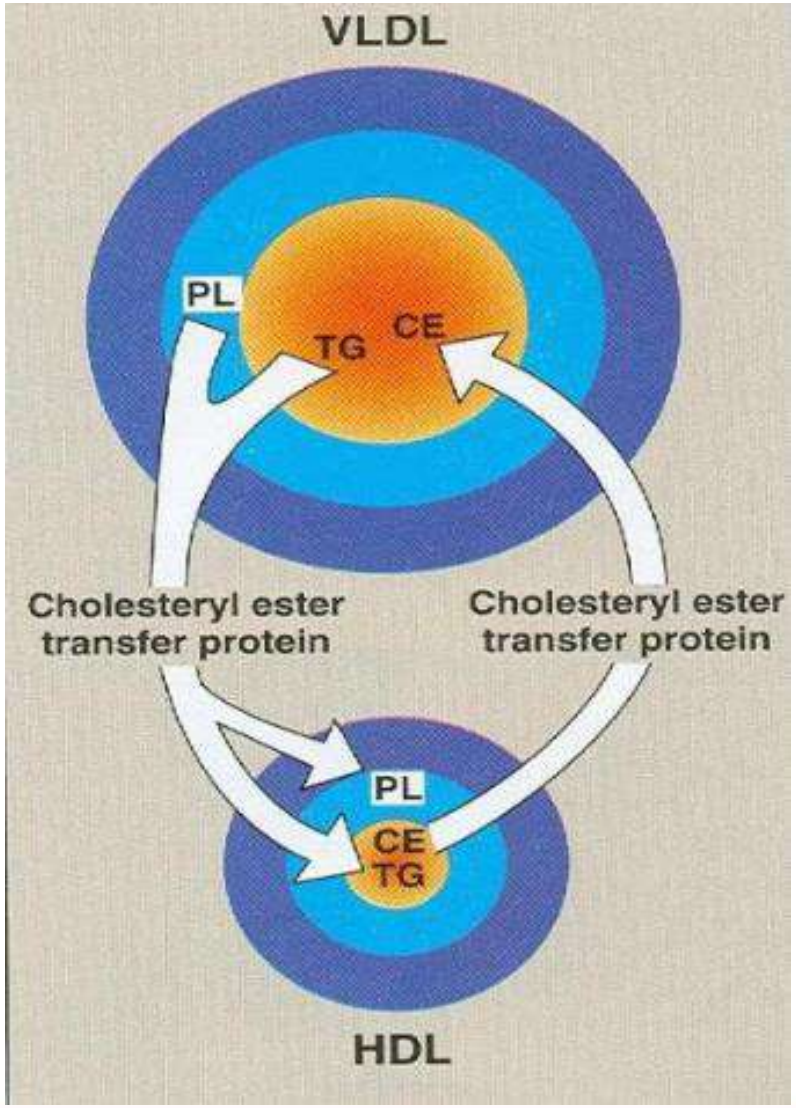
- They are composed predominantly of endogenous TAG (~60%).
- VLDLs are secreted directly into the blood by the liver containing apo B-100.
- They must obtain apo C-II and apo E from circulating HDL
- Apo C-II is required for activation of LPL.


LIVER
Apo B-100
TG>C,CE
Nascent VLDL
1 Liver secretes nascent TG-rich very-low-density lipoprotein particles.
Apo C-II
Apo E
(from HDL)
2 Apo C-II and apo E are transferred from HDL to nascent VLDL.
Apo E
Apo B-100
Apo C-II
TG>C,CE
VLDL
CAPILLARIES
TISSUES, for example, ADIPOSE
3 Extracellular lipoprotein lipase, activated by apo C-II, degrades TG in VLDL.
Lipoprotein lipase
Free fatty acids
Glycerol
To LIVER
(IDL)
Apo C-II and apo E (to HDL)
4 Apo C-II and apo E are returned to HDL.
Apo B-100
C,CE>TG
LDL
5 LDL binds to specific receptors on extrahepatic tissues and on the liver, where they are endocytosed.
EXTRA-HEPATIC TISSUE

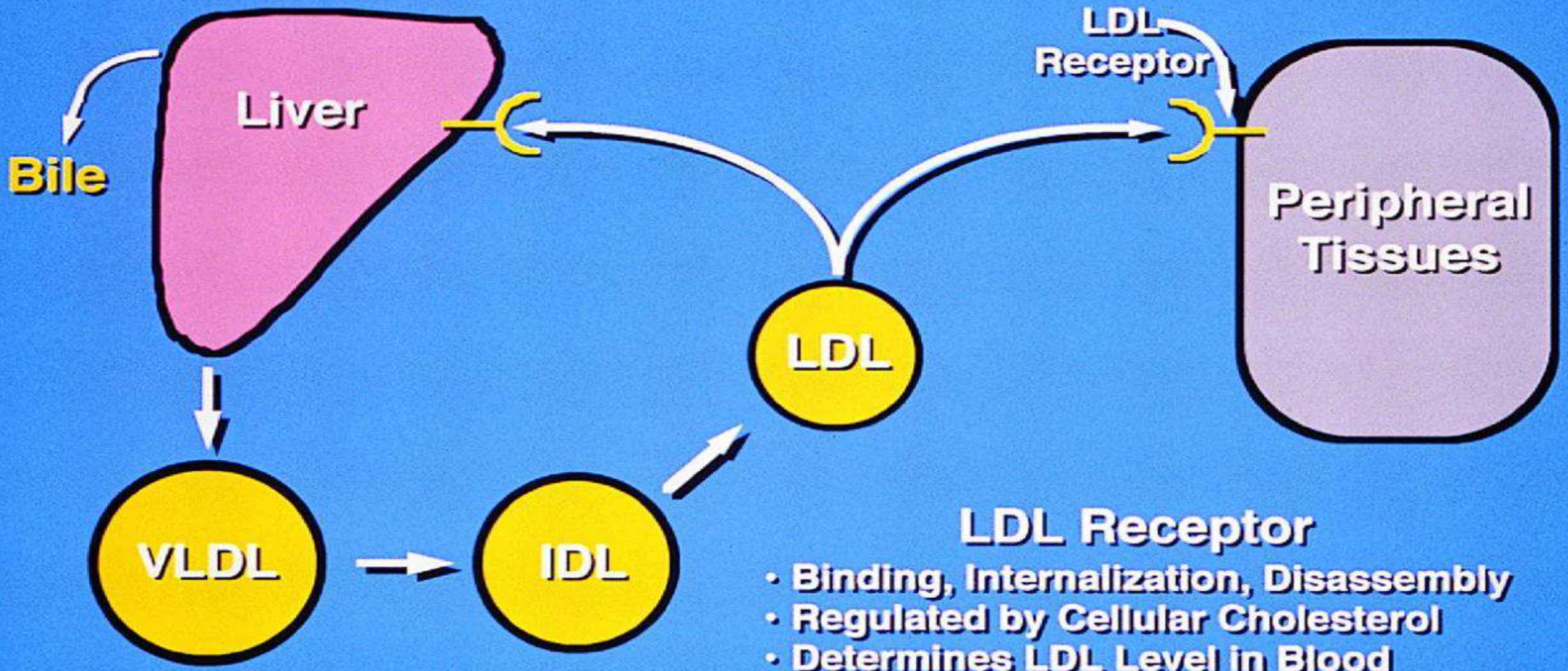
Modifications on VLDLs through their circulation

1. TAG is degraded by LPL.
2. The C and E apolipoproteins, are returned to HDL, but the particles retain apo B-100.
3. Additionally, some TAGs are transferred from VLDL to HDL in an exchange reaction that transfers cholesteryl esters from HDL to VLDL.
4. This exchange is accomplished by cholesteryl ester transfer protein (CETP)
5. With these modifications, the VLDL is converted in the plasma to LDL.

Transfer of cholesteryl ester (CE) from HDL to VLDL in exchange for triacylglycerol (TAG).



LDL and Cholesterol Transport

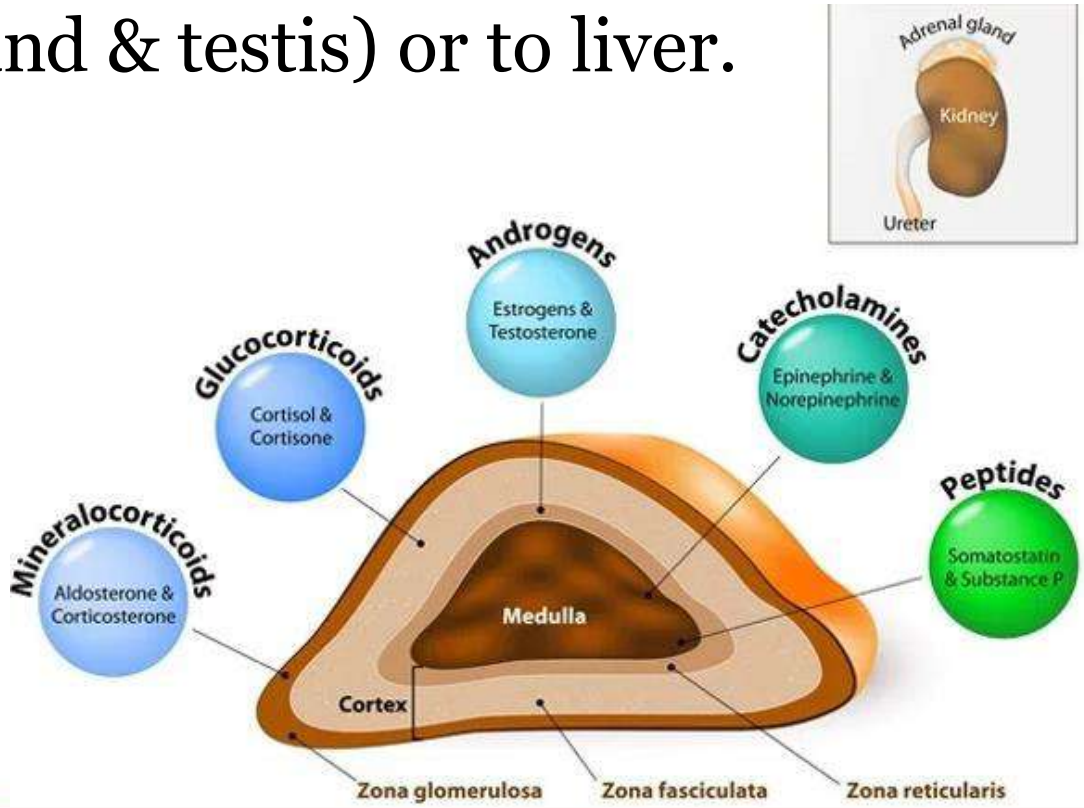


LDL Receptor

- Binding, Internalization, Disassembly
- Regulated by Cellular Cholesterol
- Determines LDL Level in Blood
- Defective in Familial Hypercholesterolemia
- Induced by 'Statin' Drugs

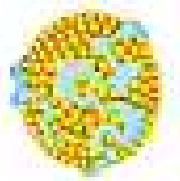
LDL and cholesterol transport

- The primary function of LDL particles is to provide cholesterol to the peripheral tissues (adrenal gland & testis) or to liver.
- They do so by binding to plasma membrane LDL receptors that recognize apo B-100 (but not apo B-48).



High-Density Lipoproteins (HDLs)

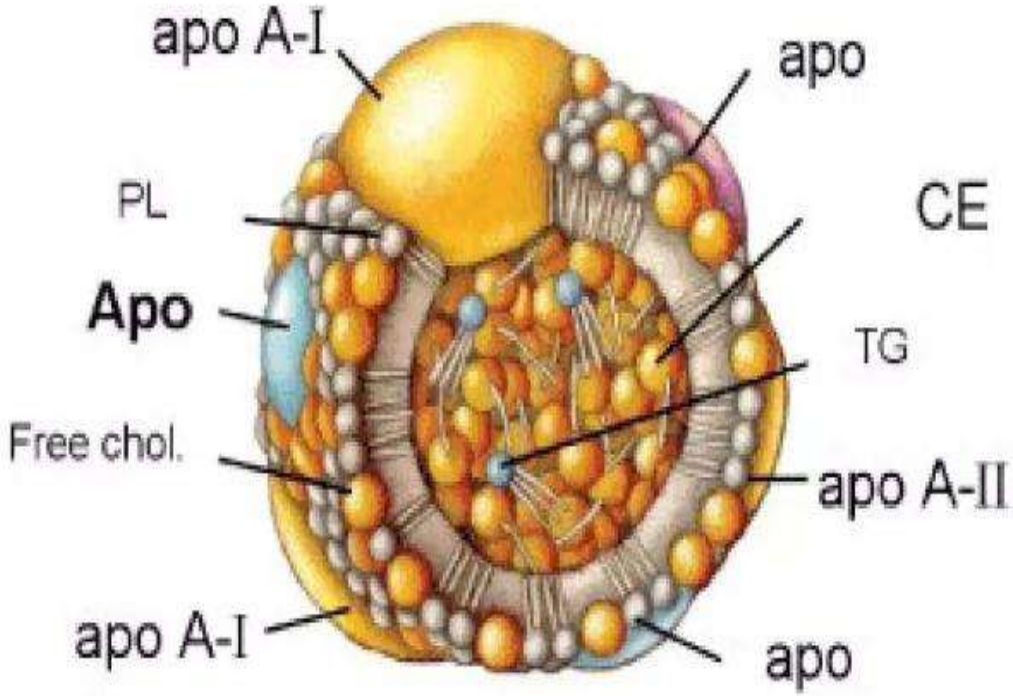
- HDLs are often referred to as "good cholesterol" because they play a critical role in reverse cholesterol transport—the process of transporting excess cholesterol from peripheral tissues back to the liver for excretion or recycling.



HDL

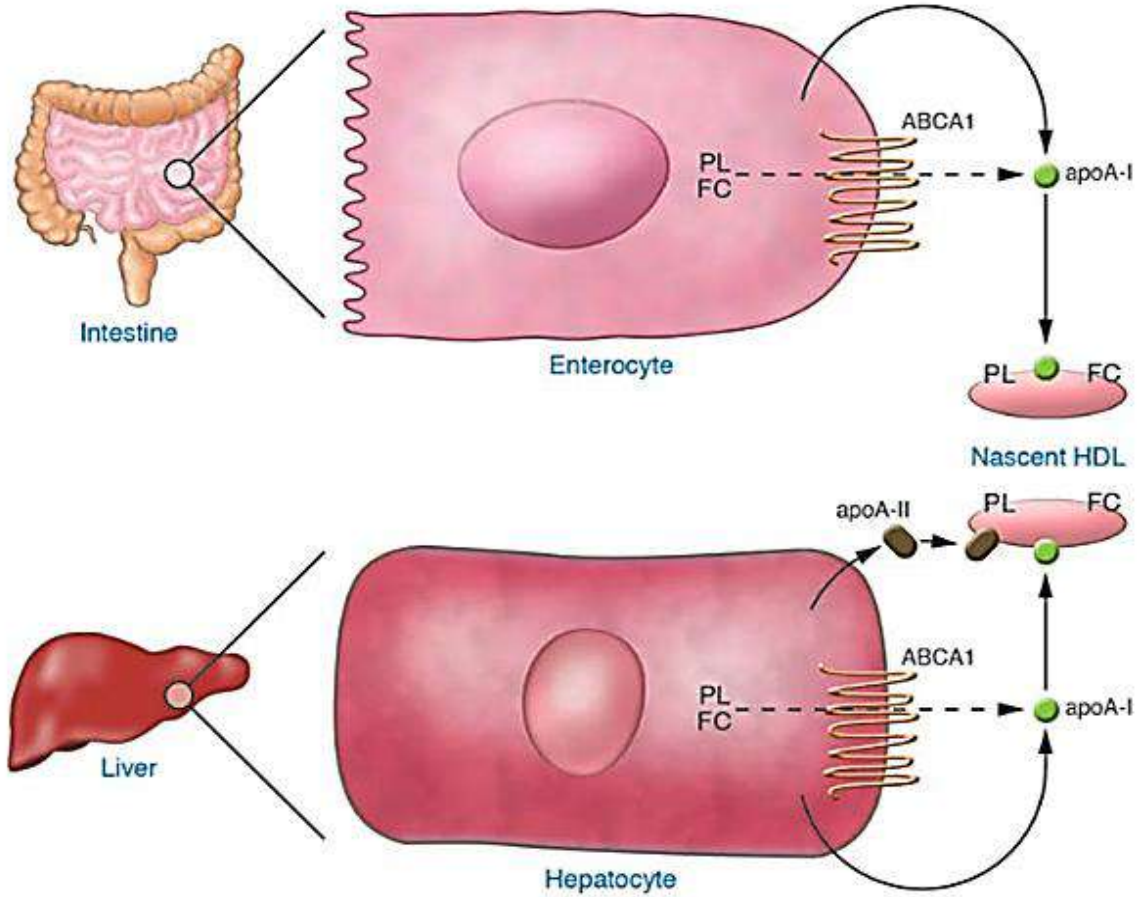
HDL contains several types of apolipoproteins

- apo-Al
- Apo-All
- apo-Cl
- apo-CII
- apo-D
- apo-E.
- Their most abundant apolipoproteins are apo A-I and apo A-II.



HDL Synthesis

- HDL particles are synthesized in two main locations:
- Liver: Produces nascent HDL particles containing phospholipids, cholesterol, and apolipoproteins (mainly apo A-I and apo A-II).
- Intestine: Produces nascent HDL with apo A-I.

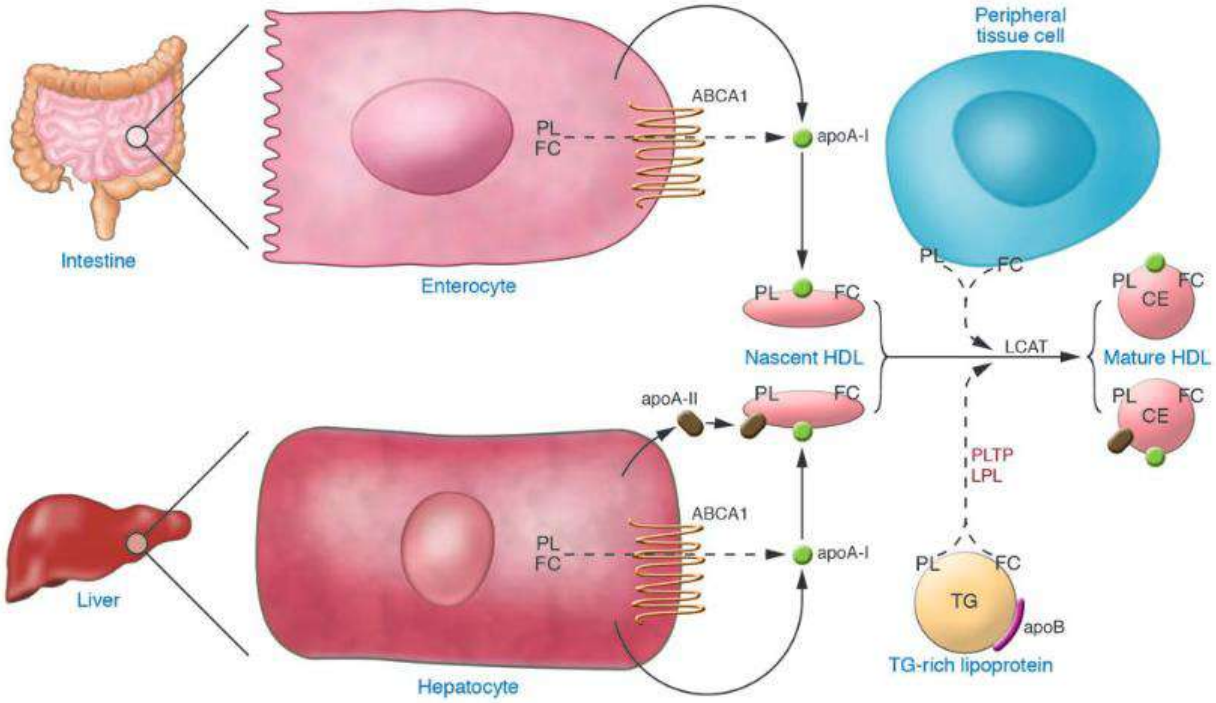


Maturation of HDL

- Nascent HDL collects additional lipids from:

1. Other peripheral tissues (via ABCA1 and ABCG1 transporters).
2. Other lipoproteins, such as VLDL and chylomicrons, during their metabolism.

1. Lecithin–cholesterol acyltransferase (LCAT)



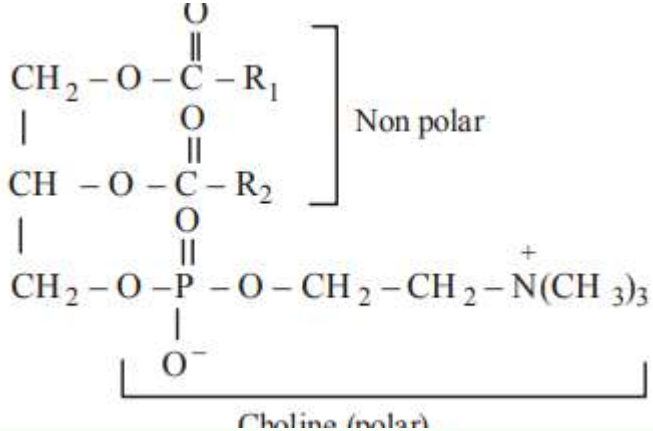
Storage of Cholesterol (Next lecture)

- Cholesterol ester is the storage form of cholesterol: It Is formed in both tissues and plasma.
- In tissues (liver), cholesterol is esterified by ACAT enzyme (acyl CoA cholesterol acyl transferase):

Cholesterol + Acyl CoA ➔ Cholesteryl ester + CoASH

- In plasma, cholesterol is esterified by LCAT enzyme (lecithin cholesterol acyl transferase). LCAT is associated with HDL.

Cholesterol + lecithin ➔ Cholesteryl ester + lysolecithin



Thanks

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Derived Lipids

Asst. Prof.Mohammed Hasan Eleyan

Faculty of Medicine

Al-Azhar University-Gaza

Derived Lipids

- **Derived lipids are compounds obtained from the hydrolysis of simple or conjugated lipids or substances that are naturally associated with lipids in biological systems. These include molecules that are structurally related to lipids or contribute to lipid metabolism.**
- **Includes:**

1. **Fatty Acids (FA)**
2. **Steroids.**
3. **Fat soluble vitamins (Vit. D, E, A and K)**

Lipids Chemistry

Derived Lipids: Steroids

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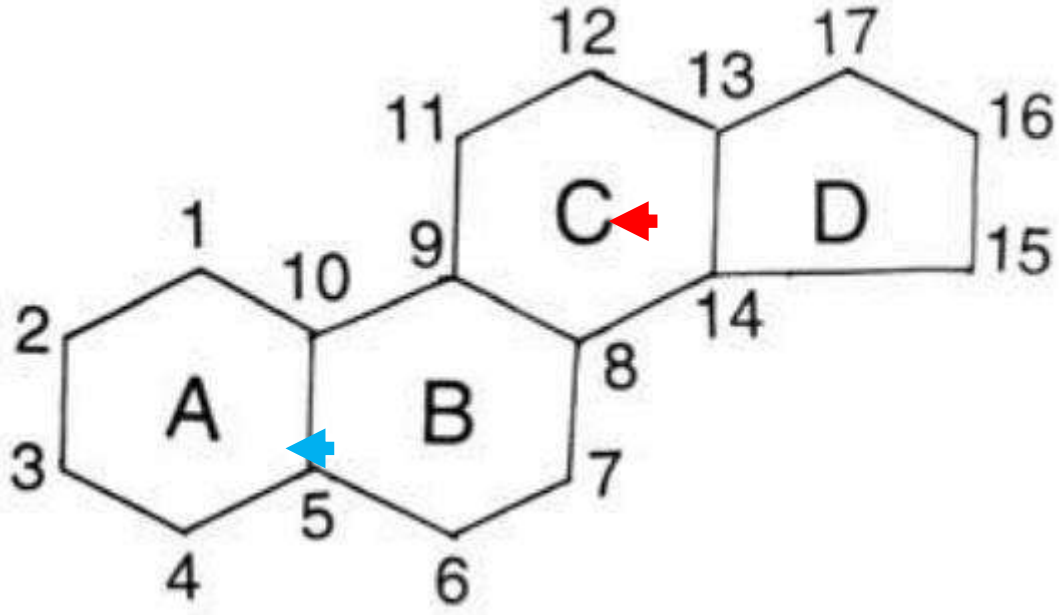
Steroids

- Compounds containing steroid nucleus (cyclopentano-perhydro-phenanthrene “CPPP”)

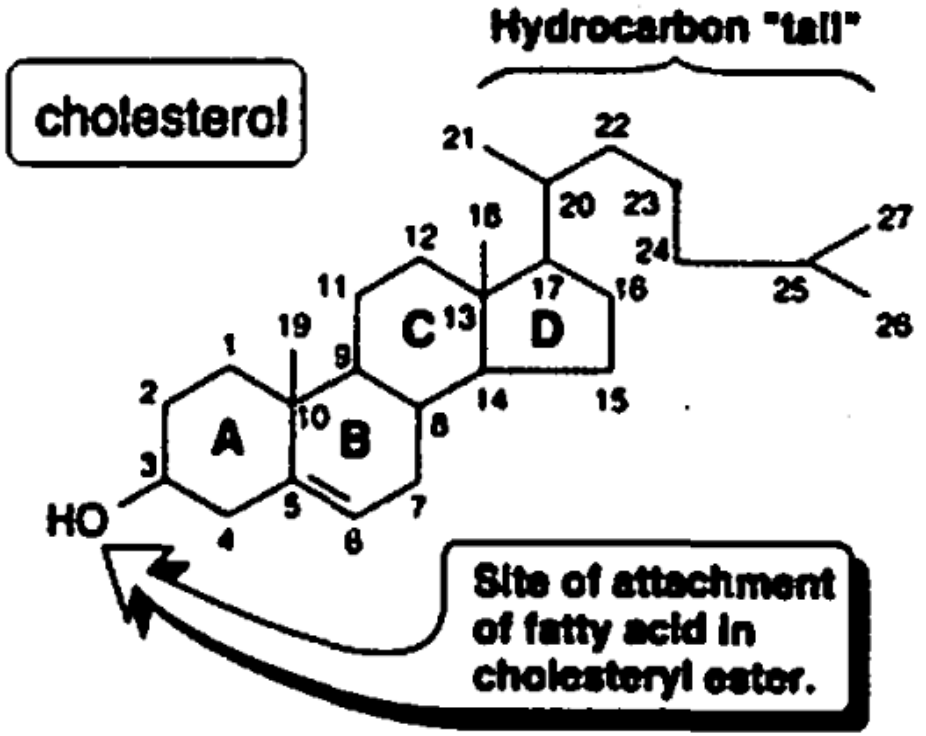


Examples of steroids

1. Cholesterol (animal origin).
2. Ergosterol (plant origin).
3. Vitamin D group (D2 and D3).
4. Bile salts.
5. Steroid hormones:
    1. Male sex hormones.
    2. Female sex hormones.
    3. Adrenocortical hormones.

Cholesterol

- Structure
  a) Cyclopentano-perhydro-phenanthrene ring
  b) -OH group at C3 (so it is an alcohol).
  c) Two methyl groups at C10 & C13.
  d) Long side chain at C17.



Body cholesterol

1. Cell membrane: it is present in everybody cell such as adrenal cortex, liver, brain and kidney.
2. Blood cholesterol: it occurs in the blood in 2 forms: free form and esterified form (combined to fatty acids to form ester)
   - The level of blood cholesterol is normally less than 220 mg/dl. Any increase above this level is called: **hypercholesterolemia**

Functions of cholesterol

Functions of cholesterol

1. Cholesterol enters in the structure of every body cell (e.g. cell membrane).

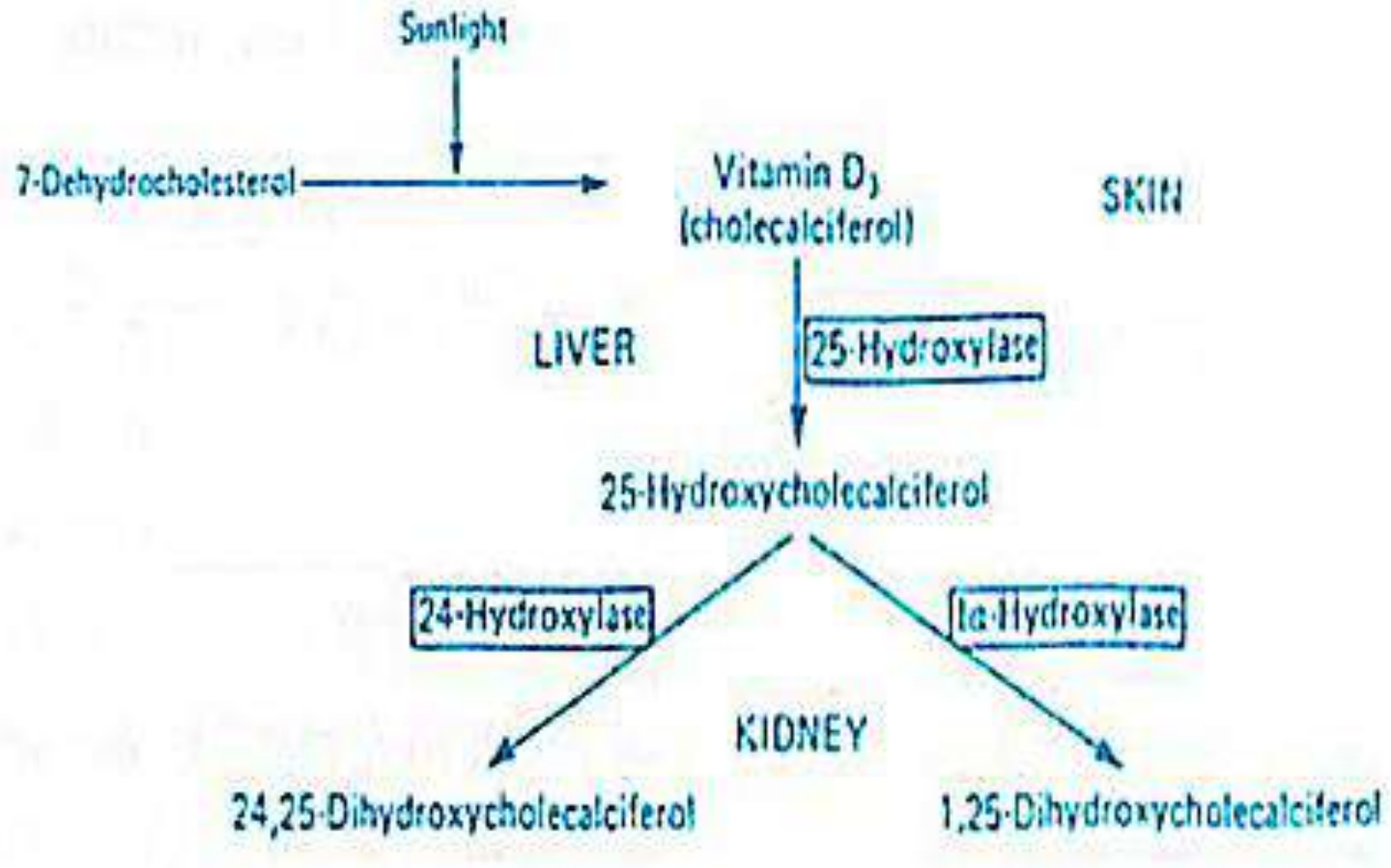
2. Cholesterol Is the precursor of:

1. **Vitamin D_3:** (subcutaneous fat) ➔ 7-dehydrocholesterol ➔ Vitamin D_3.
2. **Steroid hormones:**
   a) **Estrogens and progesterone** (ovaries).
   b) **Testosterone and androgens** (testes).
   c) **Glucocorticoids and mineralocorticoids** (Adrenal cortex).
3. **bile acids: (Liver)**

Generation the vitamin D_3 (1, 25 dihydroxycholecalciferol)

- Ultraviolet rays of sun generate the vitamin D_3 from the Provitamin 7-dehydrocholesterol (in human).
- 7-dehydrocholesterol is converted into cholecalciferol
- In the liver, cholecalciferol is converted into 25-hydroxyvitamin D3.
- Finally, the kidneys convert 25-hydroxyvitamin D into the active form of vitamin D, 1,25-dihydroxyvitamin D3.

Activation of vitamin D3 to 1,25 dihydroxycholccalcifcrol



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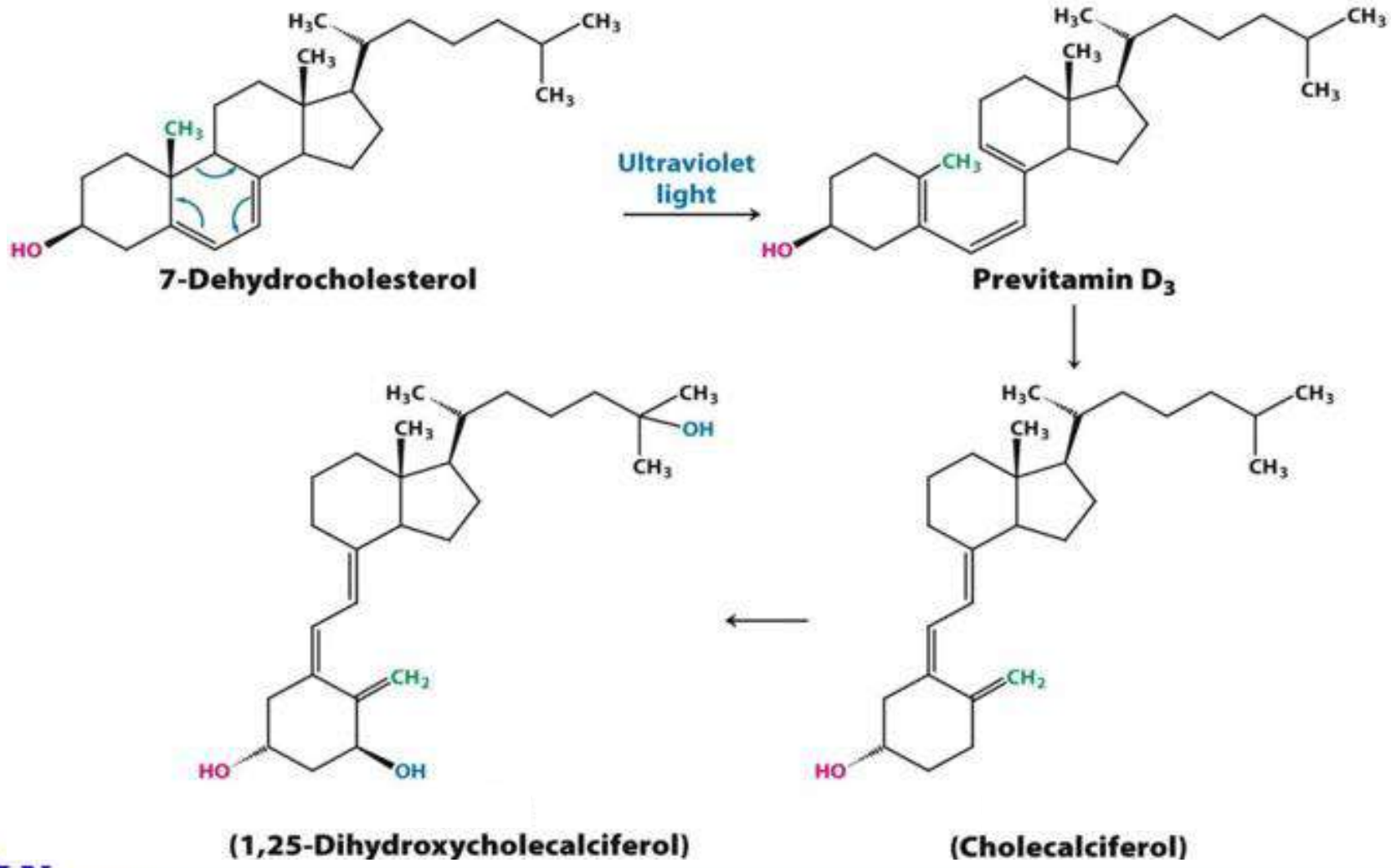
Activation of vitamin D3 to 1,25 dihydroxycholccalcifcrol



Bile, Bile acids and salts

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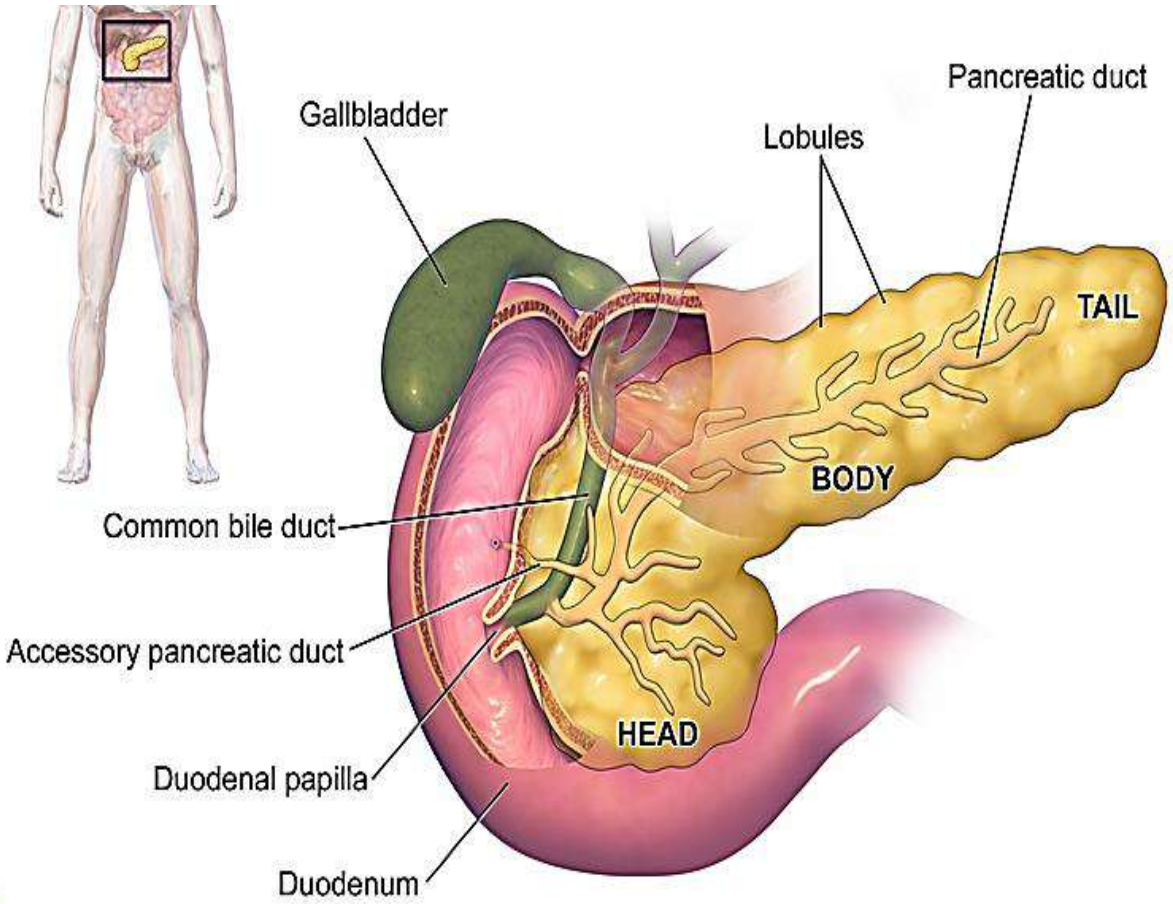
Bile definition and content

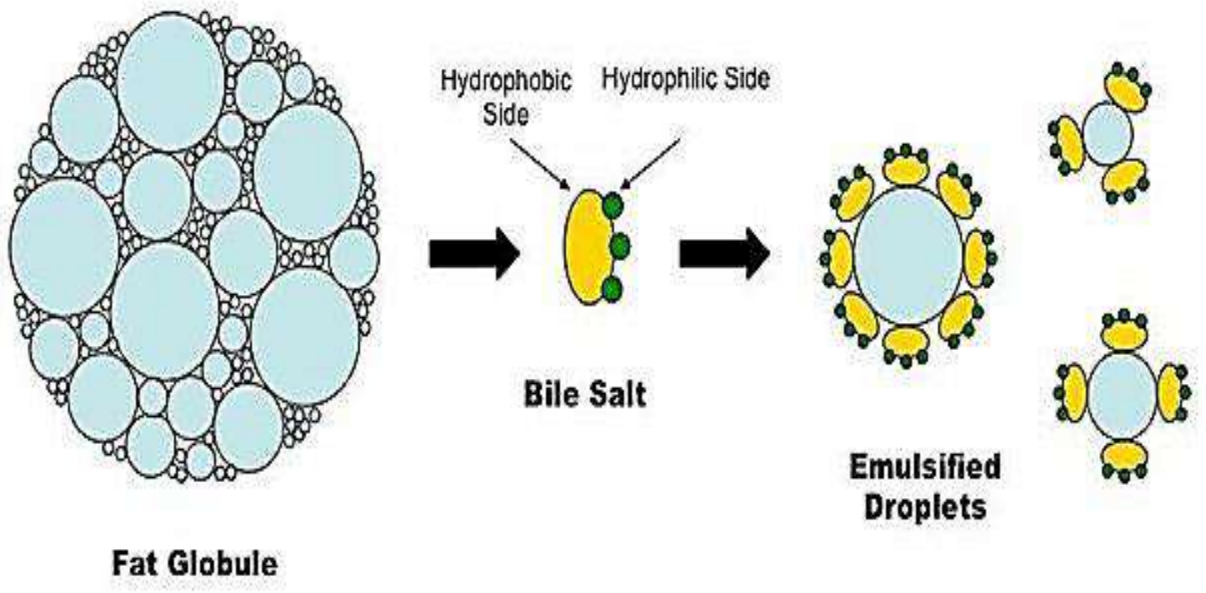
- Bile is a greenish-yellow fluid produced by the liver and stored in the gallbladder.
- It contains water, electrolytes, bile acids, bile salts, cholesterol, bilirubin, and phospholipid [phosphatidylcholine (lecithin)].



Importance of Bile

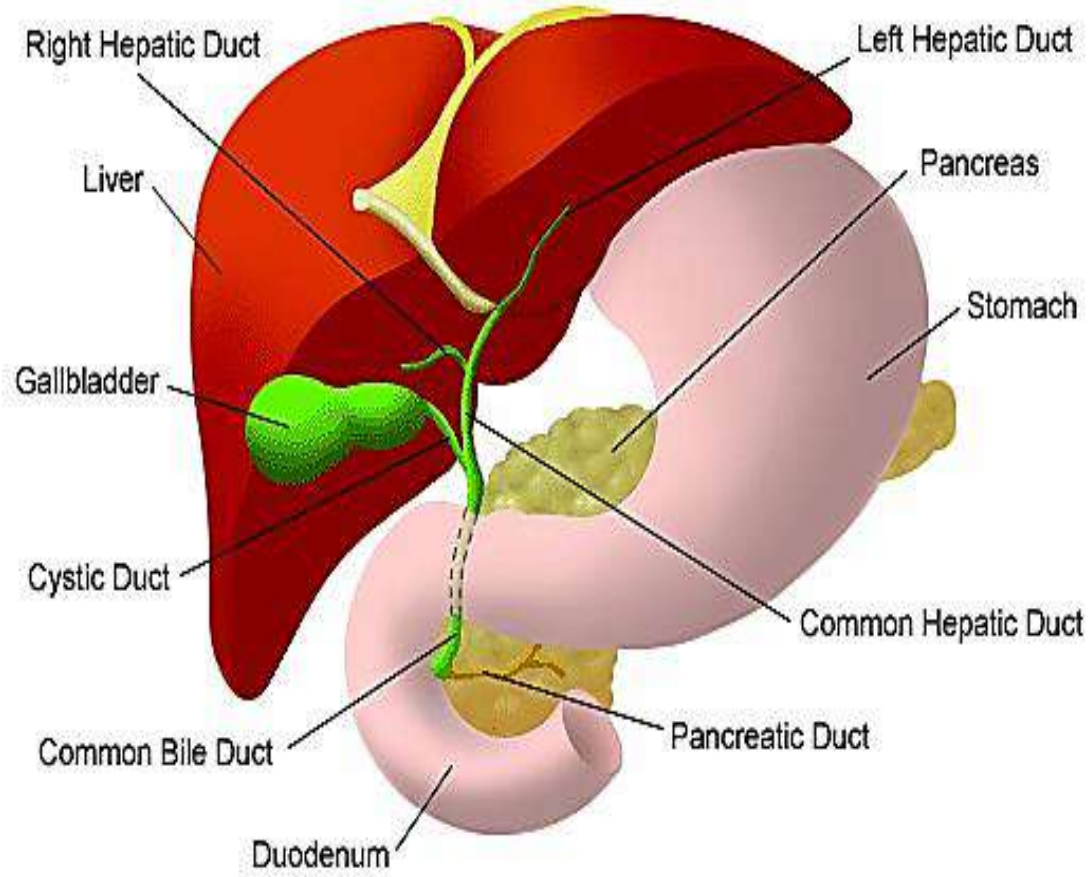
- Bile's role is to emulsify fats, which means it breaks down large fat drops into smaller droplets, making them more accessible to the action of enzymes.

- Bile is essential for the digestion and absorption of fats and fat-soluble vitamins (A, D, E, and K)



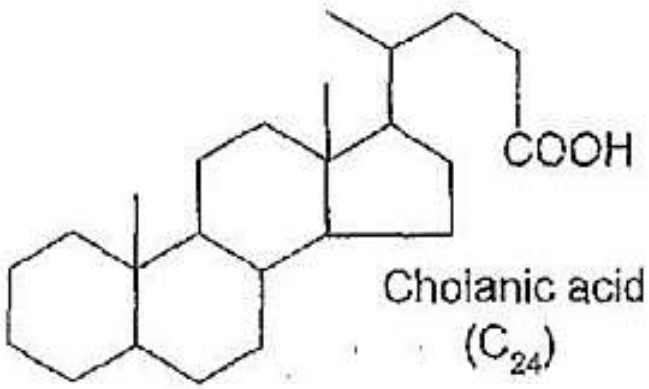
Bile has two potential pathways

- It can flow directly from the liver into the duodenum through the common bile duct, or it can be stored in the gallbladder for later use when immediate digestion is not required.



Bile acids

- Cholanic acid is a carboxylic steroidal compound (C24) that serves as the basis for the structure of various bile acids found in bile.
- Bile acids are hydroxyl derivatives of cholanic acid which is derived from cholesterol
- Types of bile acids: Primary & Secondary bile acids

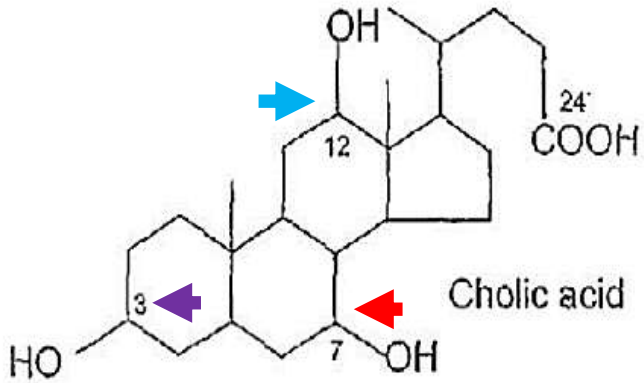


Cholanic acid
(C_{24})

Primary bile acids

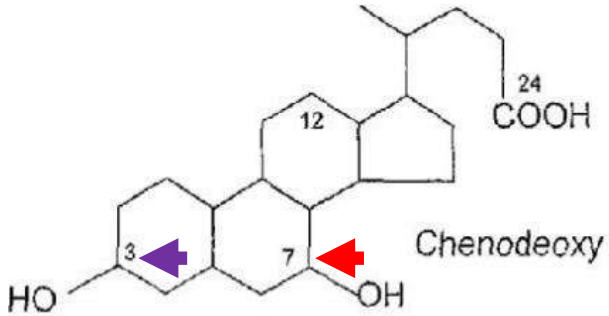
- Primary bile acids are synthesized in the liver:

1. Cholic acid (3, 7, 12 trihydroxy cholanic acid)
    - Cholic acid is one of the most abundant bile acids produced and is a major component of bile.



Cholic acid

2. Chenodeoxycholic Acid (3, 7 dihydroxycholanic acid)



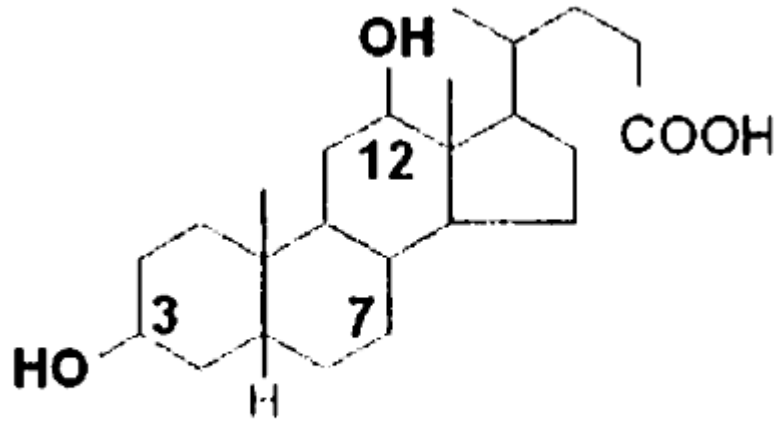
Chenodeoxy Cholic acid

Secondary bile acids

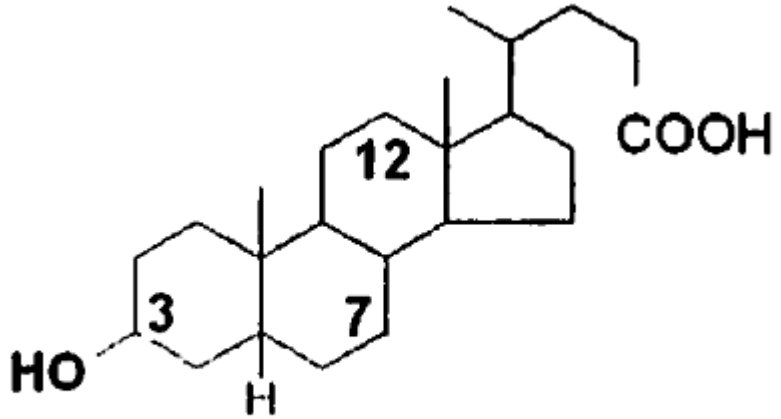
- **Secondary bile acids** are derived from primary bile acids in the intestine.
- This transformation occurs through the action of **intestinal bacteria**, which remove the hydroxyl group at the 7th carbon position (no OH on C7; contain 7α dehydroxylase).

Secondary bile acids

- Deoxycholic acid (3, 12 dihydroxy cholanic acid).
  - Formed from the primary bile acid **cholic acid** by bacterial dehydroxylation at the 7th carbon position.
- Lithocholic acid (3 monohydroxy cholanic acid).
  - It has a single hydroxyl group at the 3rd position.



Deoxycholic acid

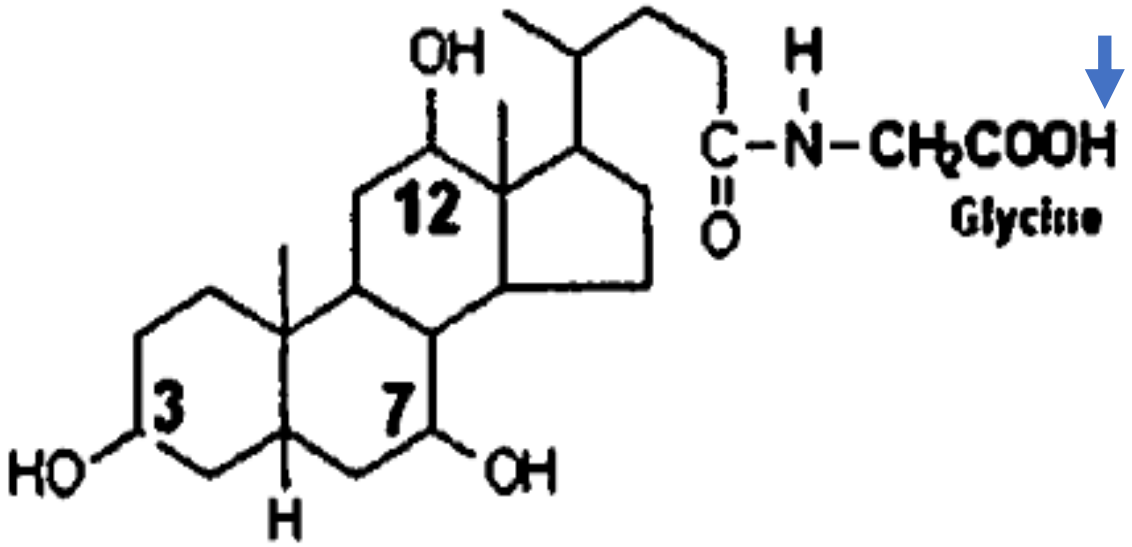


Lithocholic acid

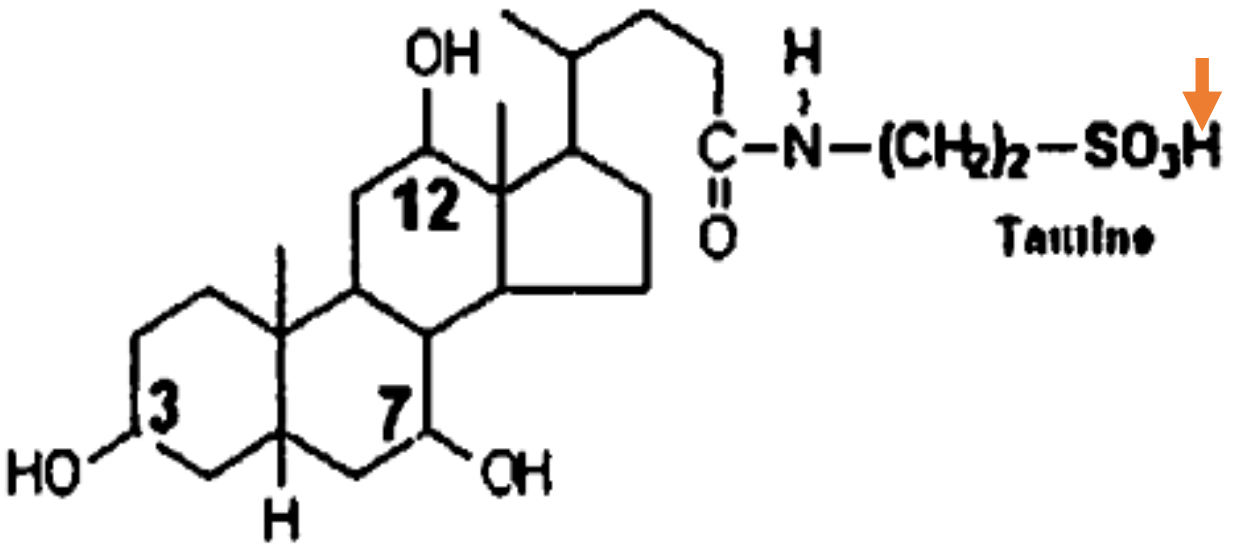
Bile salts

- Bile salts are bile acids conjugated with glycine (80%) and taurine (20%), they are excreted by liver in bile as sodium salts
  - Bile Acid + Glycine = Glycocholic OR Glycochenodeoxycholic acids
  - Bile Acid + Taurine = Taurocholic OR Taurochenodeoxycholic acids
    - sodium glycocholate and sodium taurocholate.

sodium glycocholate and sodium taurocholate.



Glycocholic acid

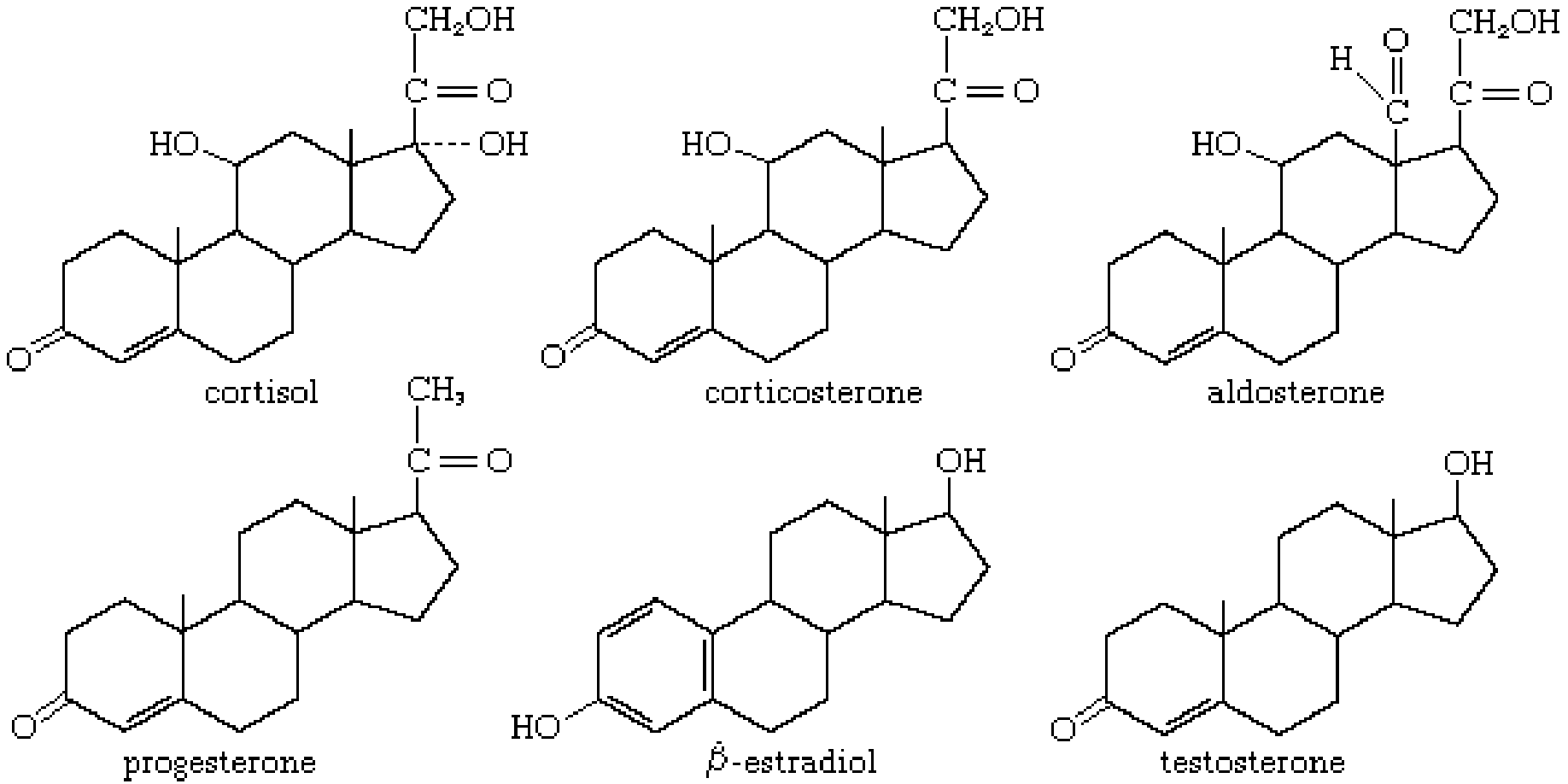


Taurocholic acid

Importance of bile salts

1. Main way for excretion of cholesterol.
   - Prevents precipitation of cholesterol & formation of cholesterol stones.
2. Digestion of fat due to emulsification.
3. Absorption of fat and fat soluble vitamins.

Steroid hormones



Thanks

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Proteins Chemistry

Amino Acids

Asst. Prof.Mohammed Hasan Eleyan

Faculty of Medicine

Al-Azhar University-Gaza

Proteins Chemistry

Amino Acids

There are 20 standard amino acids that are commonly found in the genetic code and are used to build proteins.

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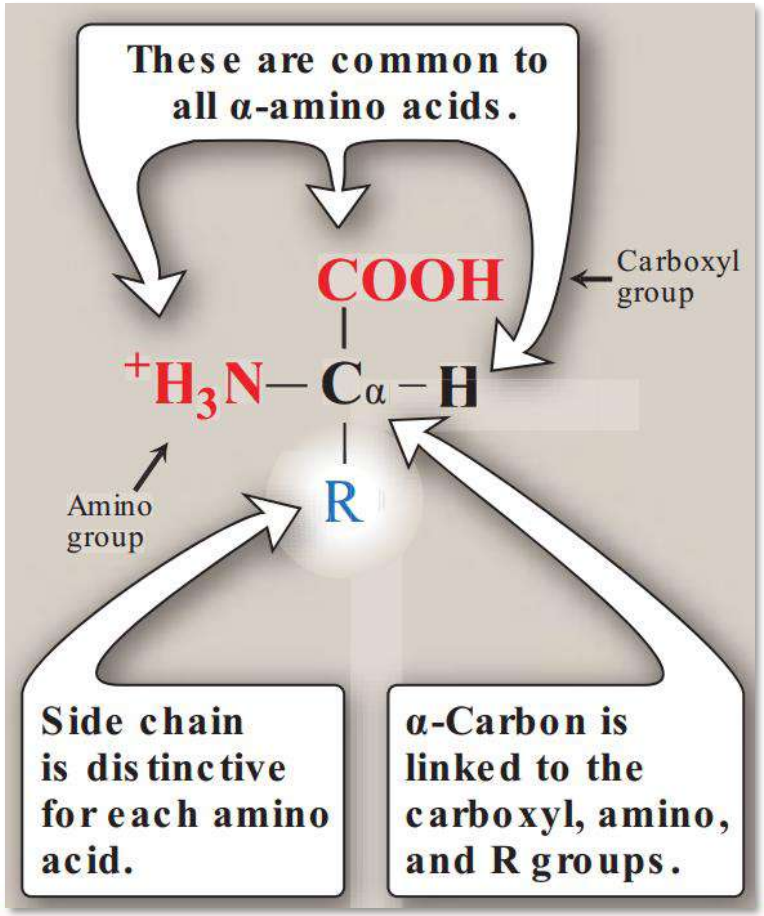
Alpha Amino Acids

- Structure: Each amino acid has the following 4 groups or atoms attached to alpha (α) carbon:



1. Amino group: (NH2).
2. Carboxyl group: (COOH).
3. Hydrogen atom (H).
4. Side chain (R).

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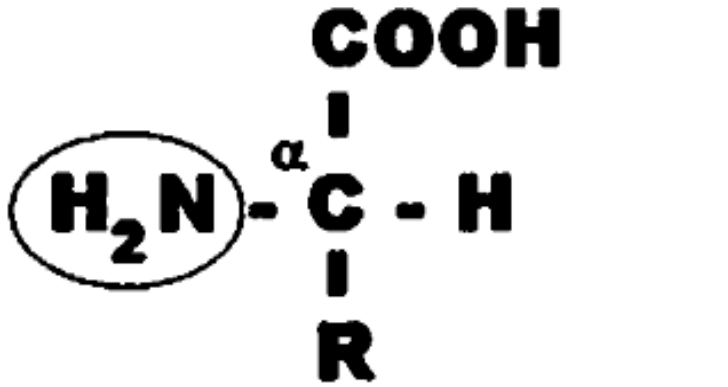
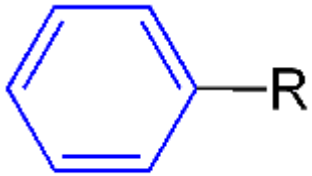
Structural characteristics of building blocks of proteins

1. α-Amino acids: the amino group attached to the second carbon (next to the carboxyl group).
2. L-Amino acid: α-amino group is on the left side configuration.

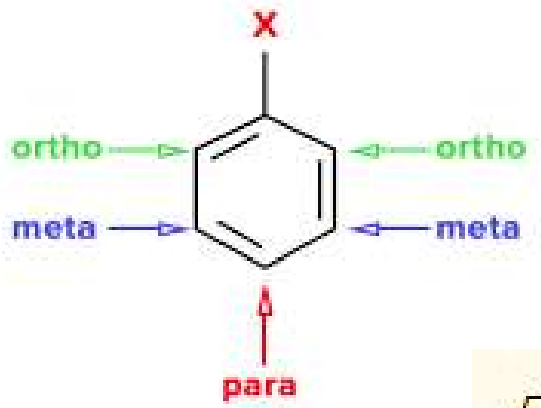


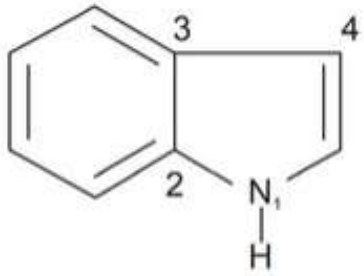
α - L - Amino acid

Some chemical groups may present in A.A.

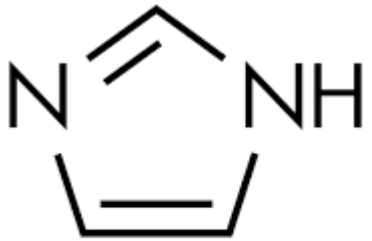


Phenyl group

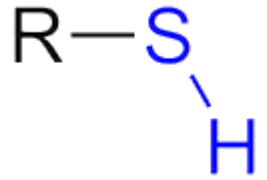




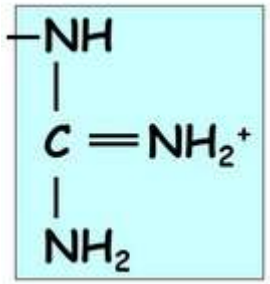
Indole



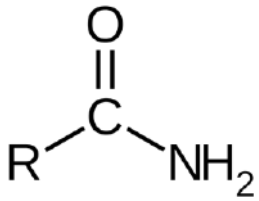
imidazole



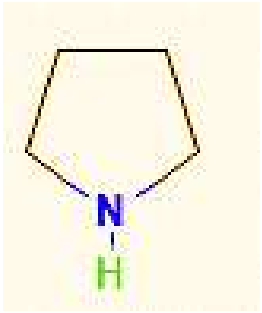
Thiol



guanido



carbamoyl



pyrrolidine ring

The indole ring is a six-membered benzene ring fused to a five-membered nitrogen-containing pyrrole ring.
Imidazole is a five-membered heterocyclic aromatic ring containing two nitrogen atoms

GREEK ALPHABET

LETTER	UPPERCASE	LOWERCASE	LETTER	UPPERCASE	LOWERCASE
Alpha	Α	α	Nu	Ν	ν
Beta	Β	β	Xi	Ξ	ξ
Gamma	Γ	γ	Omicron	Ο	ο
Delta	Δ	δ	Pi	Π	π
Epsilon	Ε	ε	Rho	Ρ	ρ
Zeta	Ζ	ζ	Sigma	Σ	σ
Eta	Η	η	Tau	Τ	τ
Theta	Θ	θ	Upsilon	Υ	υ
Iota	Ι	ι	Phi	Φ	ϕ
Kappa	Κ	κ	Chi	Χ	χ
Lambda	Λ	λ	Psi	Ψ	ψ
Mu	Μ	μ	Omega	Ω	ω

Chemical classification

- Structured approach to link specific amino acids to their respective fatty acid-derived precursors:

1. Amino acids derived from acetic acid, (2 carbons) (CH_3-COOH):

a) **Glycine:** (alpha amino acetic acid).

2. **Amino acids derived from propionic, (3 Carbons) (CH_3-CH_2-COOH):**

a) **Alanine:** (alpha amino propionic acid)

b) **Phenylalanine:** (alpha amino,beta phenylpropionic acid)

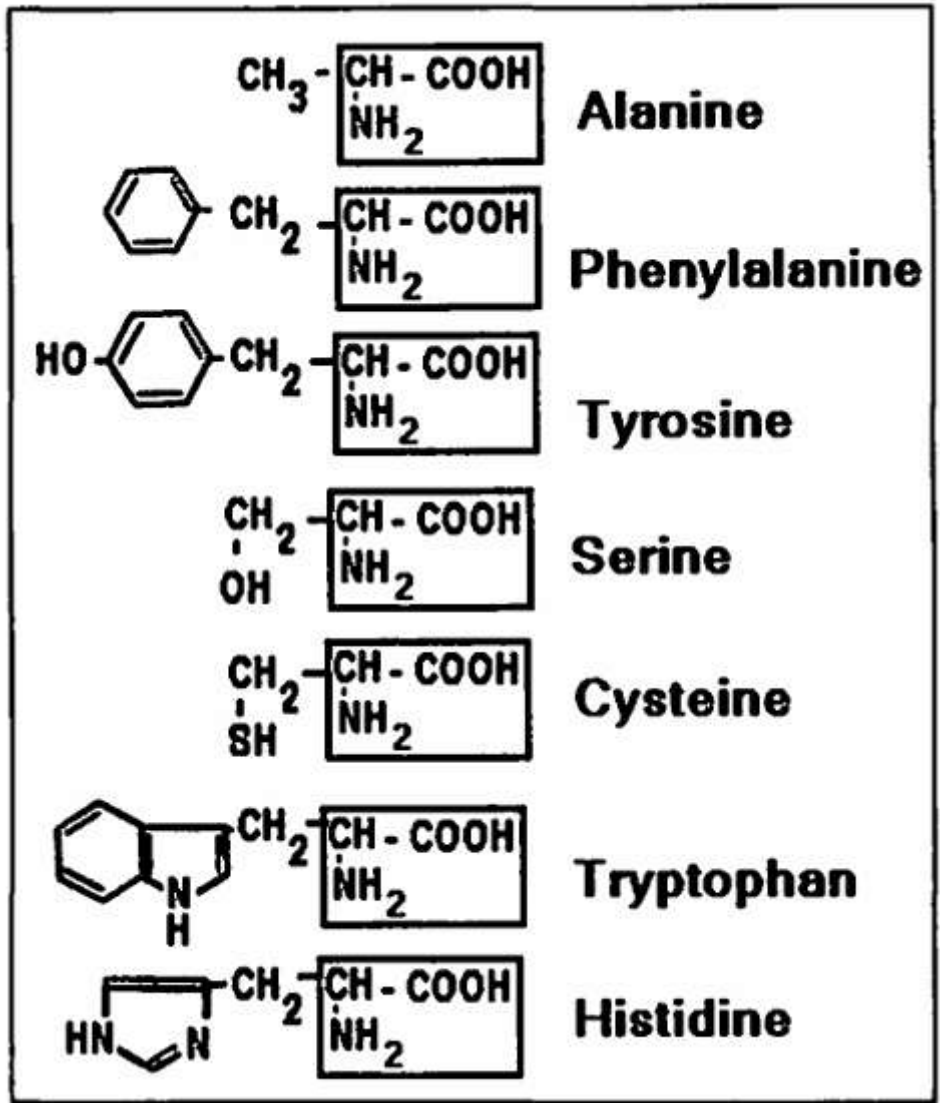
c) **Tyrosine:** (alpha amino, beta parahydroxy phenyl propionic acid)

d) **Serine:** (alpha mino betahydroxy propionic acid)

e) **Cysteine:** (alpha amino beta thiol,propionic acid)

f) **Tryptophan:** (alpha amino beta indole propionic acid)

g) **Histidine:** (alpha amino beta imidazol propionic acid)

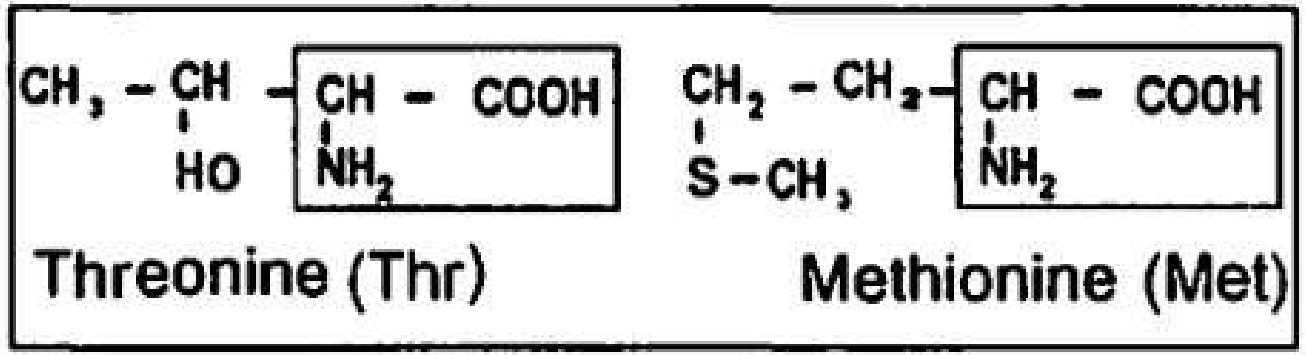


3. Amino acids derived from butyric acid, (4 Carbons)

(CH_3-CH_2-CH_2-COOH)

1) Threonine:(alpha amino,beta hydroxy butyric acid)

2) Methionine:(alpha amino, gamma methyl thiol butyric acid)

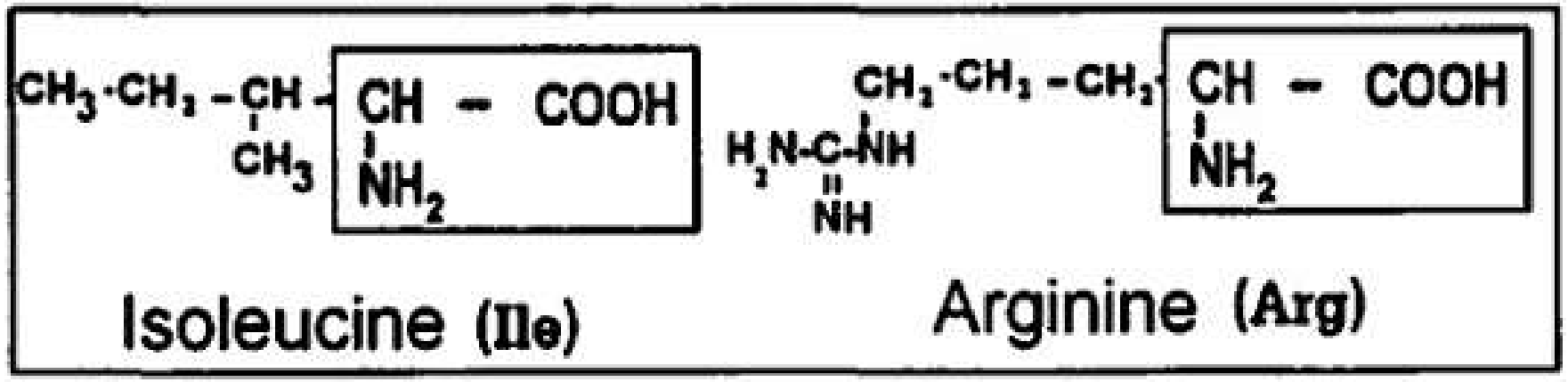


4. Amino acids derived from valeric acid (5 Carbons)

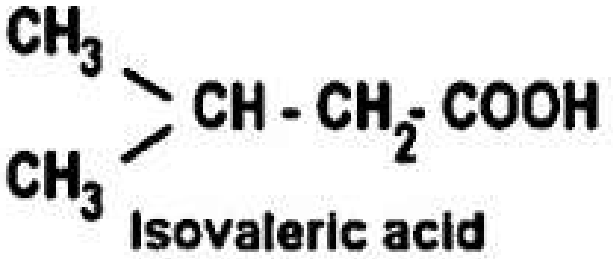
(CH_3-CH_2-CH_2- CH_2-COOH)

1) **Isoleucine:**(alpha amino, beta methyl valeric acid)

2) **Arginine:**(alpha amino, delta guanido valeric acid)

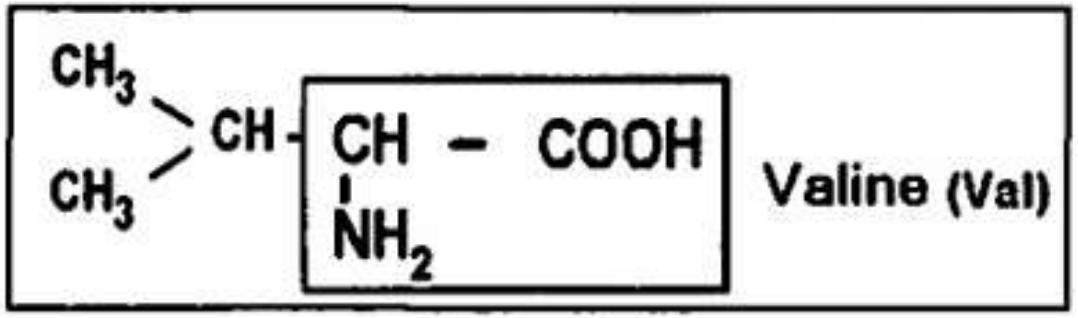


5. Amino acids derived from isovaleric acid (5 Carbons):



Isovaleric acid

1) Valine: alpha amino, isovaleric acid

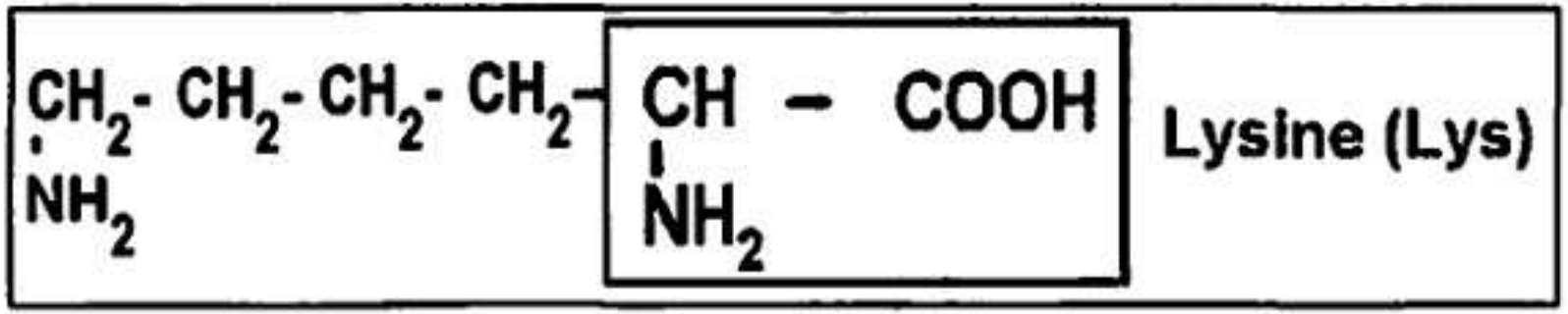


Valine (Val)

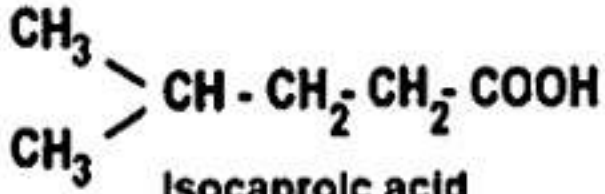
6. Amino acids derived from caproic acid (6 Carbons)

(CH_3-CH_2-CH_2- CH_2- CH_2- COOH)

1) Lysine:(alpha amino, epsilon amino caproic acid)

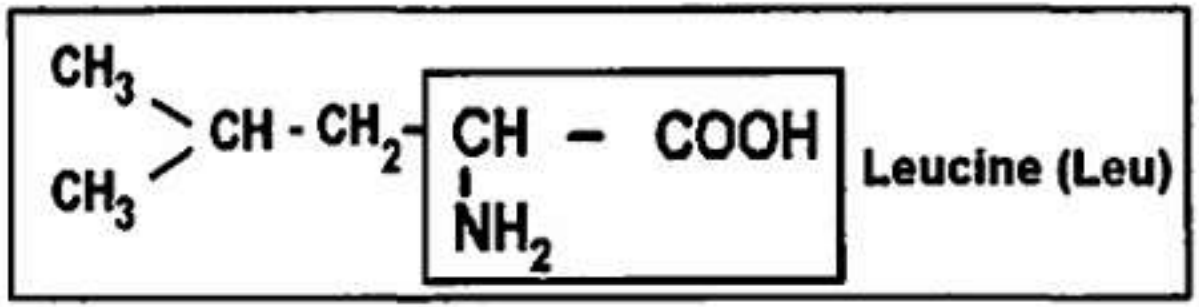


7. Amino acids derived from isocaproic acid (6 Carbons):



Isocaproic acid

1) **Leucine:** (alpha amino isocaproic acid)



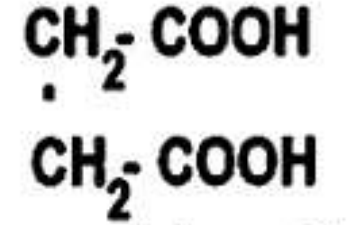
Leucine (Leu)

8. Amino acids derived from succinic acid

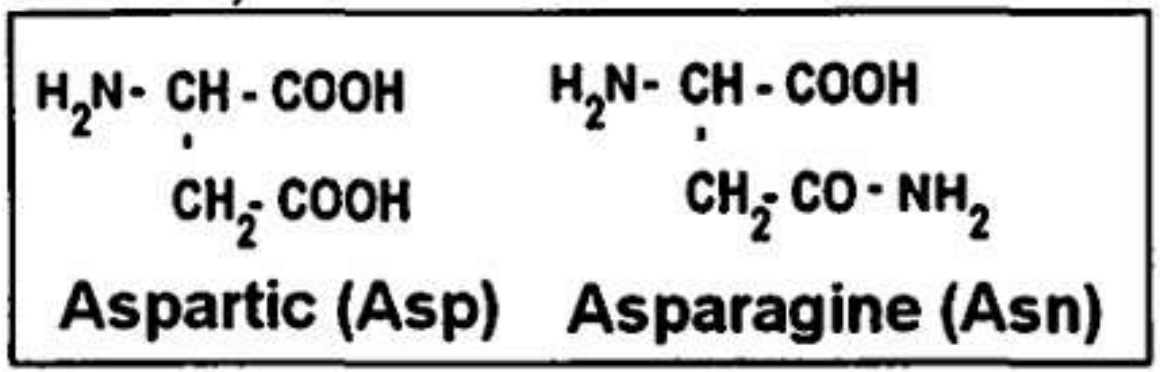
(4 Carbons):

1) **Aspartate:** (alpha amino succinic acid)

2) **Asparagine:**(alpha amino succinic acid amide)



Succinic acid



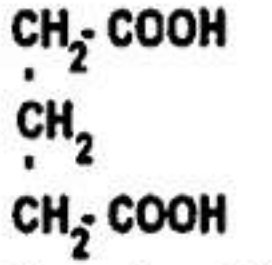
Aspartic (Asp) **Asparagine (Asn)**

9. Amino acids derived from glutaric acid:

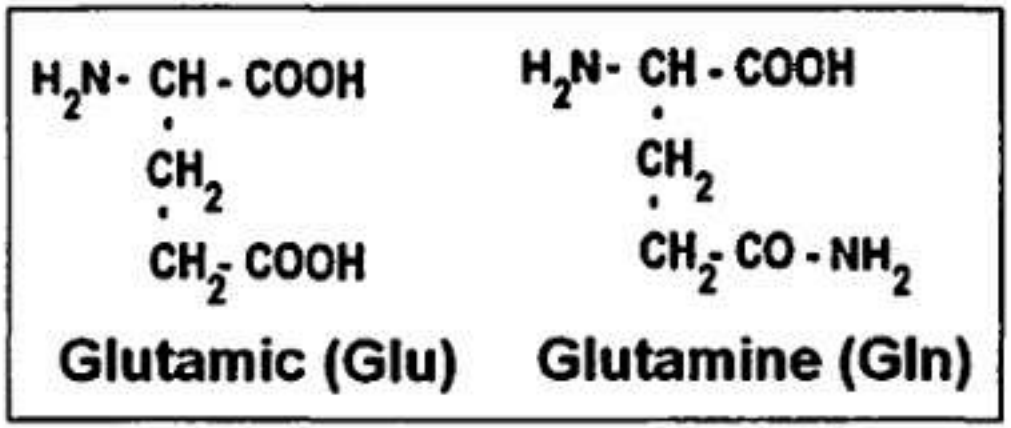
(5 Carbons):

1) **Glutamate:**(alpha amino glutaric acid)

2) **Glutamine:** (alpha amino glutaric acid amide)



Glutaric acid

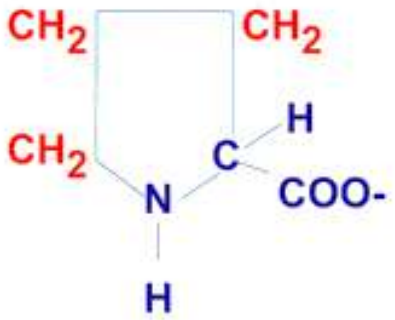


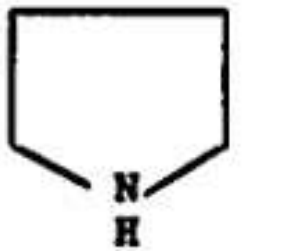
Glutamic (Glu) **Glutamine (Gln)**

10.Imino acids derived from pyrrolidine ring

(4 Carbons):

1) Proline (P):





Pyrrolidine

According to if the amino acid is acidic, basic or neutral amino acids

- Acidic amino acids: contain more than one -COOH group. e.g. aspartate and glutamate.
- Basic amino acids: contain more than one -NH2 group. e.g. lysine, arginine and histidine.
- Neutral amino acids: these are amino acids, which contain one COOH and one -NH2 groups. e.g. glycine, alanine, etc.

According to if amino acid is: aromatic, heterocyclic or aliphatic.

1. Aromatic amino acids: which contain phenyl or phenol ring:

   Phenylalanine (phenyl ring) and Tyrosine (phenol ring).

2. Heterocyclic amino acids: which contain other type of rings: Tryptophan (indole ring), Histidine (imidazol ring), Proline (pyrrolidine ring).

3. Aliphatic amino acids: include other amino acids which contain no ring.

According to if the amino acid is branched or non branched:

- Branched amino acids:
    1. valine
    2. Leucine
    3. Isoleucine.
- Non-branched amino acids: Rest of amino acids

- Imino and amino acids:
- Imino acids: Proline.
- Amino acids: Rest of amino acids.

- Sulfur and hydroxyl containing amino acids:
- Sulfer containing amino acids: cysteine and methionine.
- Hydroxyl containing amino acids: serine, threonine and Tyrosine.

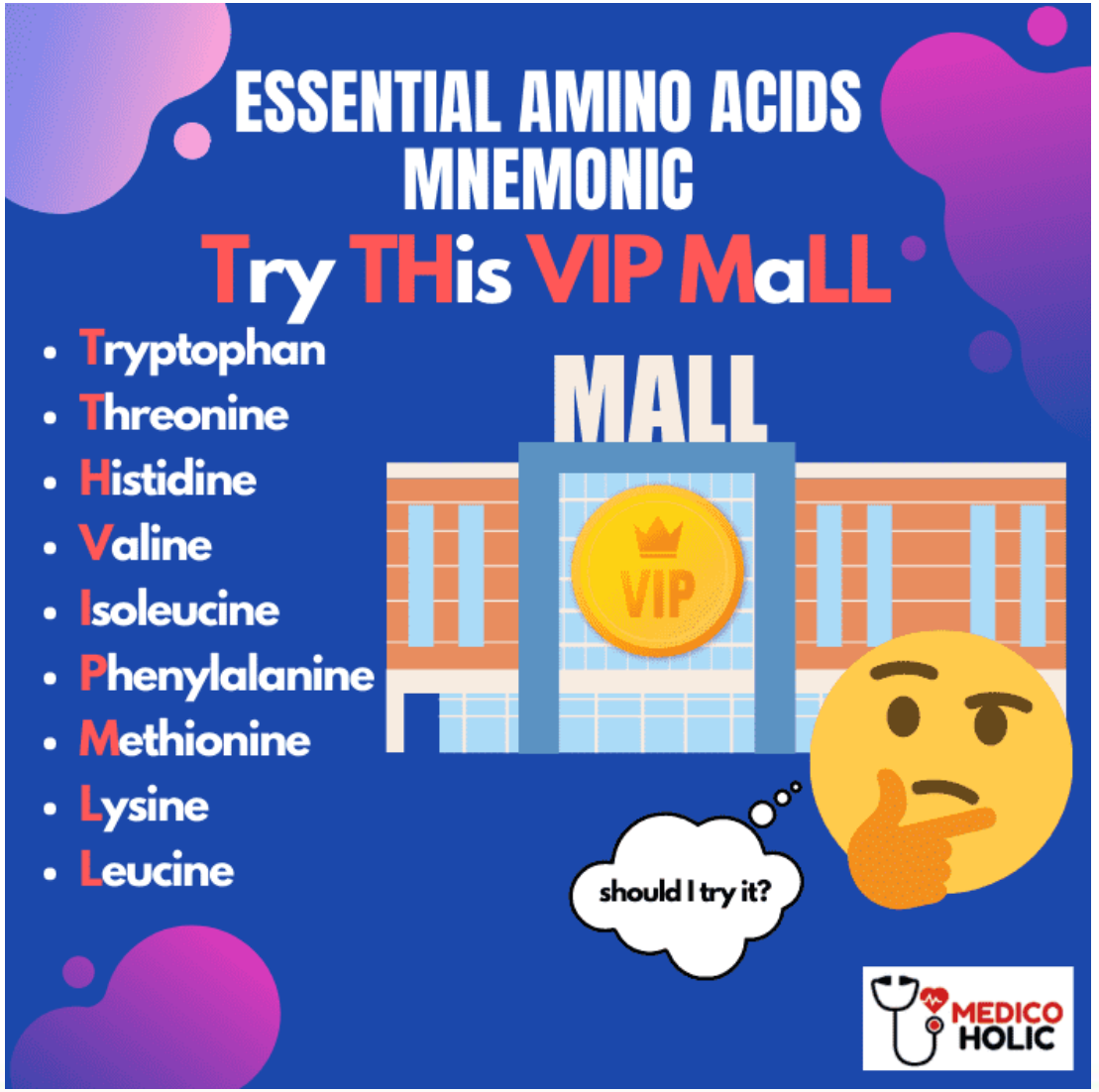
Nutritional classification of amino acids:

- They are classified into 3 main groups:

1. Essential amino acids
2. Half (semi) essential amino acids
3. Nonessential amino acids

Essential amino acids:

- These are amino acids that cannot be formed in the body. They are essential to be taken In diet.
- They are important for growth, health and protein synthesis.



Half (semi) essential amino acids:

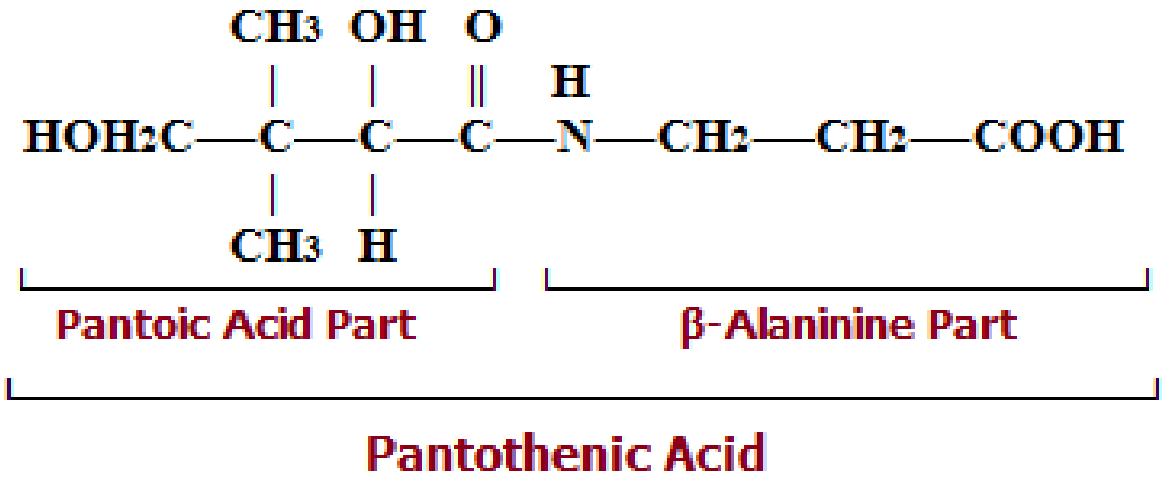
- These amino acids are formed in the body in amount enough for adults, but not for growing children.
- They include:
- Arginine.
- Histidine.

Nonessential amino acids:

- These are the rest of amino acids which are formed in the body, mostly formed from carbohydrate, in amount enough for adults and growing children.

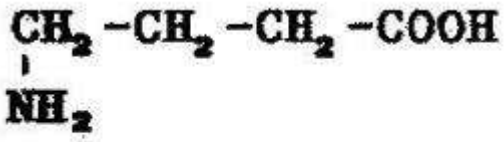
Non alpha amino acids:

- The amino group is not attached to α position.
- β-Alanine: It enters in the structure of vitamin B5 (pantothenic acid)

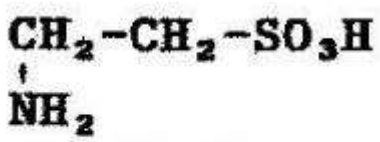


Non alpha amino acids:

- Gamma amino butyric acid (GABA): This is a neurotransmitter formed from glutamate in brain tissue.
- Taurine: This occurs in bile combined with bile acids.



GABA



Taurine

The amino group is attached to the γ-carbon (the third carbon from the carboxyl group). Acts as an **inhibitory neurotransmitter** in the central nervous system.

Structure: Contains a sulfonic acid group instead of a carboxylic acid group, making it unique among amino acids.

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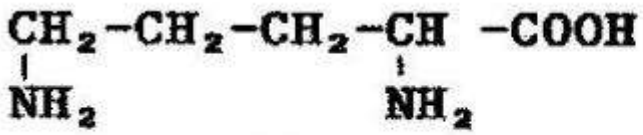
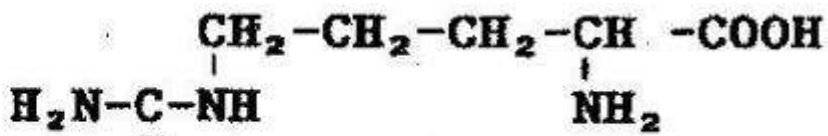
Amino acids which participate in Urea cycle

- Arginine: (α-amino δ-guanido Valeric acid).
- Ornithine: (α, δ- diamino Valeric acid).
- Citrulline: (α-amino δ- urido Valeric acid).



Ornithine



Citrulline

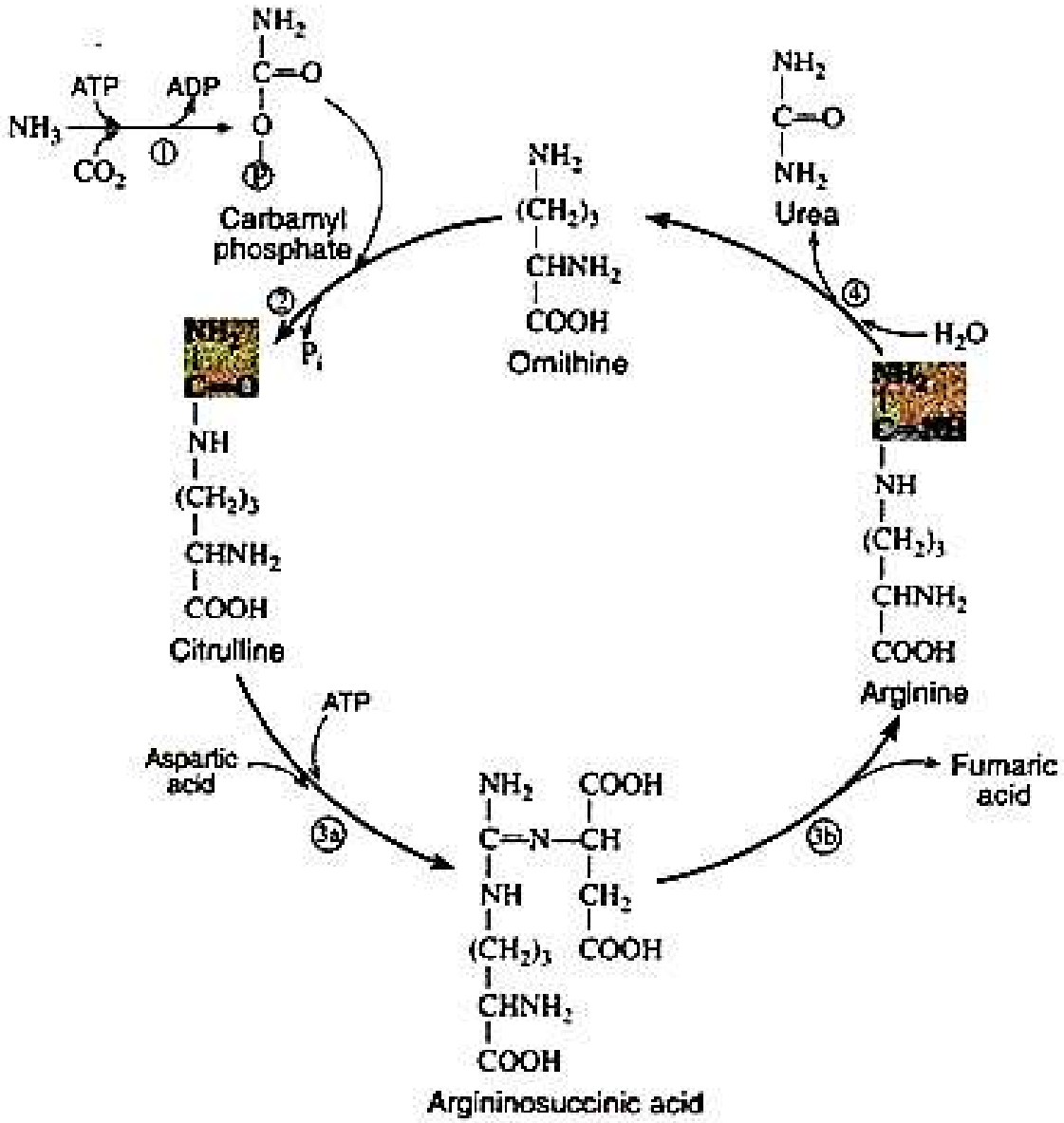
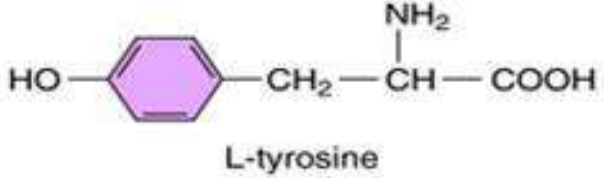


Fig. 8.90 : The Urea cycle

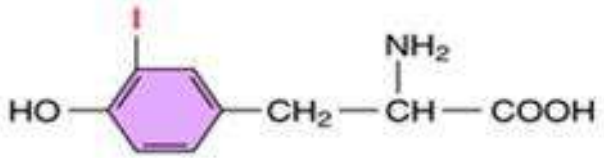
Amino acids containing iodine

- These are precursors of thyroid hormones:

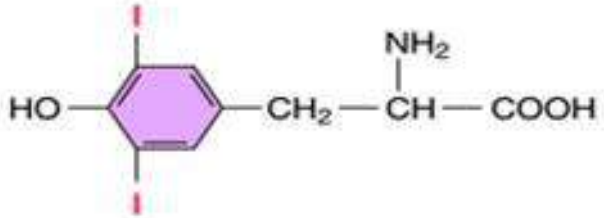
1. Monoiodotyrosine (MIT).
2. Diiodotyrosine (DIT).
3. triiodothyronine (T3).
4. Tetraiodothyronine (T4)



L-tyrosine

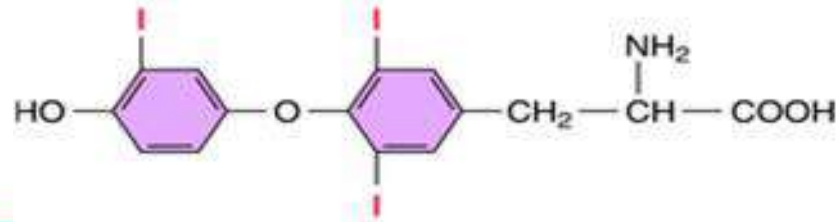


3-monoiodotyrosine (MIT)



3,5-diiodotyrosine (DIT)

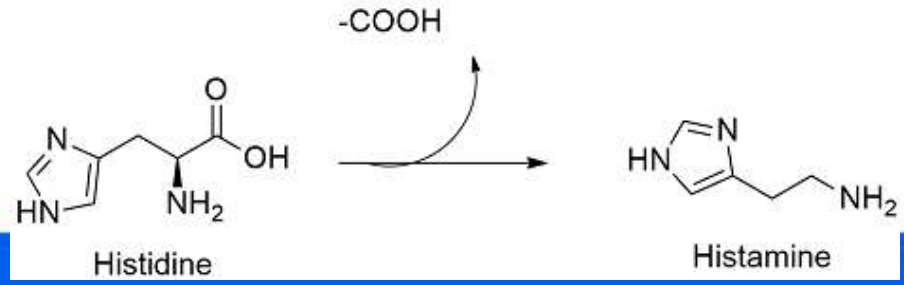
3,5,3′,5′,-tetraiodothyronine (T_4)
(Thyroxine)



3,5,3′-triiodothyronine (T_3)

Function (importance) of amino acids

1. Enter in the structure of plasma proteins, tissue proteins, enzymes, etc.
2. Some hormones are amino acid derivatives e.g. thyroxin.
3. Some amino acid gives corresponding amines by decarboxylation e.g. histidine gives histamine which is vasodilator.
4. Some amino acids as glycine and glutamate act as Neurotransmitters
5. Some amino acids are used in detoxication reactions as glycine binds to drugs to make it soluble in water.



Physical Properties of amino acids

- Solubility: Amino acids may be soluble in water.
- Optical activity: All amino acids - except glycine are optically active because they contain asymmetric carbon atom.
- Melting point: Amino acids are present in crystals and have high melting points above 200°C i.e. they are very stable molecules

Thanks Part 1
Last lecture

Proteins Chemistry

Proteins

Asst. Prof.Mohammed Hasan Eleyan

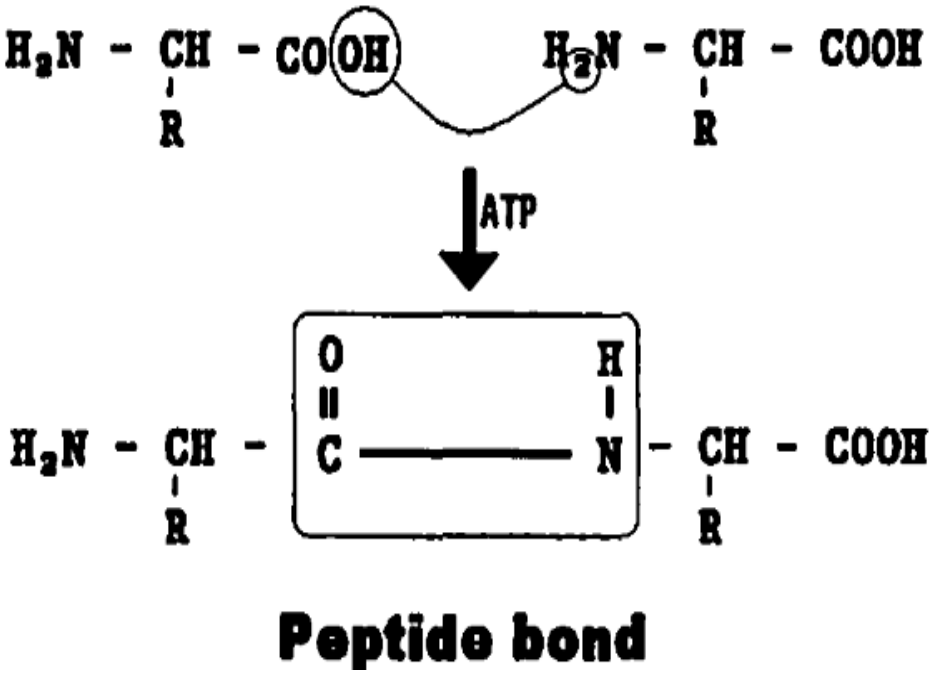
Faculty of Medicine

Al-Azhar University-Gaza

Peptide bond:

- Definition: It is a covalent bond formed between the carboxyl group of one amino acid and the amino group of another.

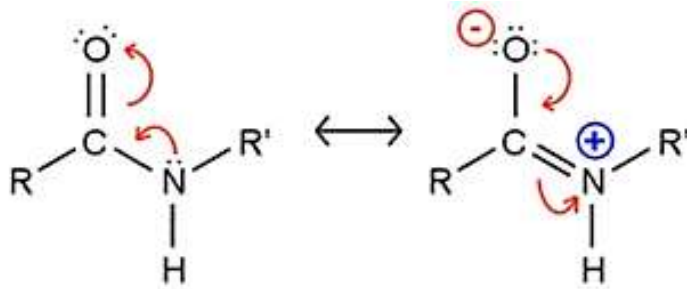
- Mechanism: - it is formed by removal of water.
- Peptide formation needs energy getting from hydrolysis of ATP
- Each individual amino acid in the chain is referred as RESIDUES



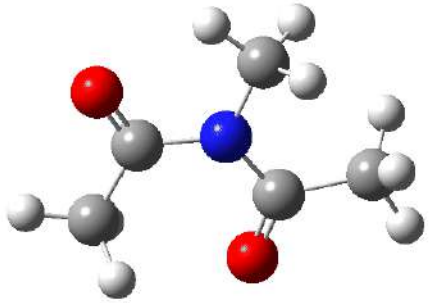
Peptide bond

Peptide bond:

- The peptide bond is almost always is written as a single covalent bond, but it exhibits resonance, where electrons are delocalized between the carbonyl oxygen and the amide nitrogen.

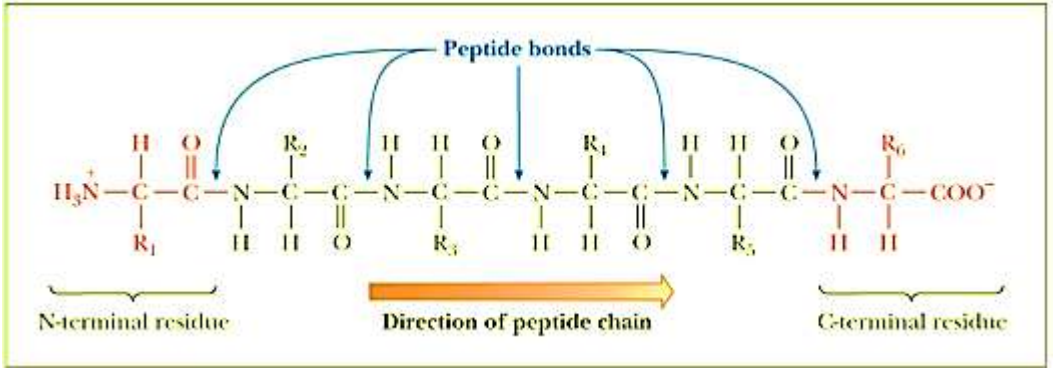


- Peptide bond is semi-rigid bond i.e. no free rotation can occur around bond axis.
- Normally, for single bonds, groups on either side of the bond can spin freely around that bond; but, because of resonance, there is no free rotation around the peptide bond



Peptides

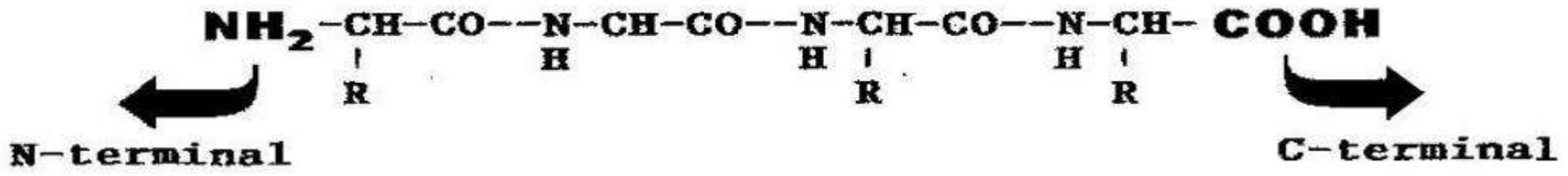
- Definition: Peptides are compounds, formed of less than 50 amino acids linked together by peptide bonds.
- Dipeptide (2 AA. and 1 peptide bond).
- Tripeptide (3 AA. and 2 peptide bond).
- Oligopeptide (3-10 amino acids).
- Polypeptide (10-50 amino acids).



side chains alternating on different sides of the peptide chain—is an important implication of the peptide bond's planarity and resonance.

Structure of peptides:

- In a polypeptide chain:
- The N-terminal amino acid (i.e. the only amino acid that contains free amino group) is always to the left side.
- The C-terminal amino acid (i.e. the only amino acid that contains free carboxyl group) is always to the right.



Biological active peptide

Peptides include many active compounds

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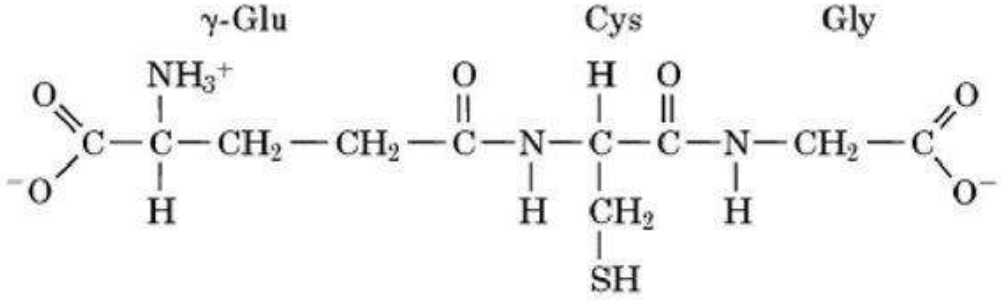
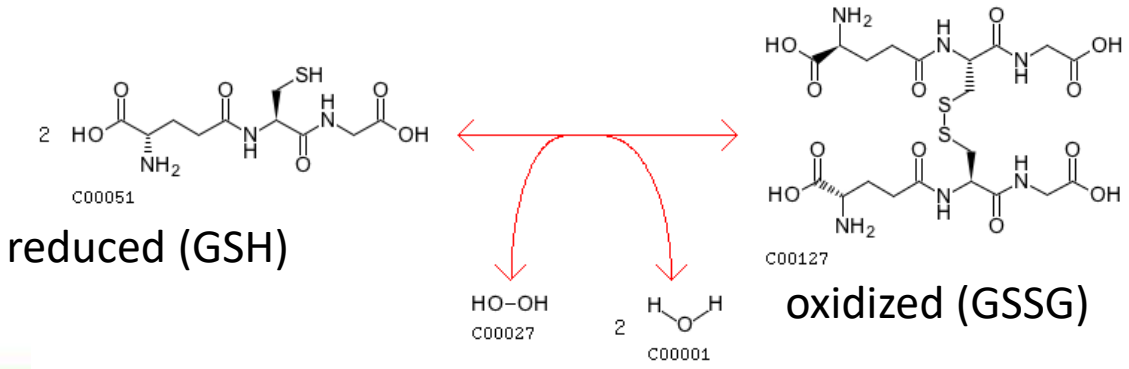
Glutathione:

- It is a Tripeptide formed of three amino acids: glutamate, cysteine and glycine.
- It is also called “glutamyl-cysteinyl-glycine”.
- Glutathione (GSH) where -SH indicates the sulfhydryl group of cysteine and it is the most active part of the molecule.



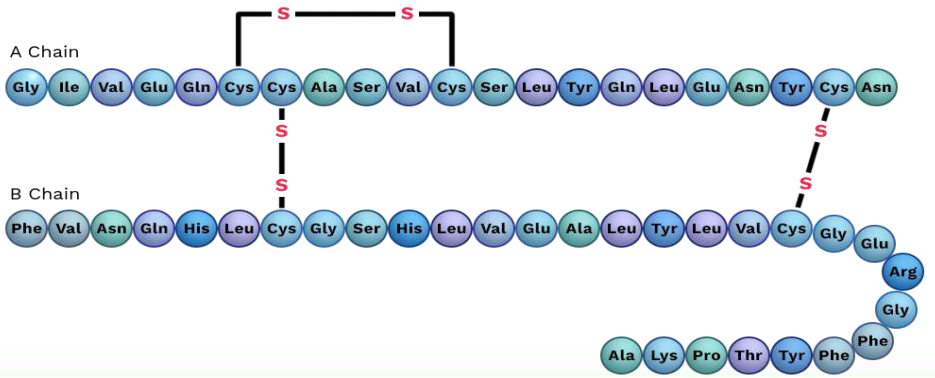
Glutathione:

- Absorption of amino acid: glutathione has a role in transport of amino acids across intestinal cell membrane.
- Protect against cell damage and hemolysis of RBCs: Glutathione breakdown the hydrogen peroxide (H2O2) which causes cell damage and hemolysis.



Glutathione:

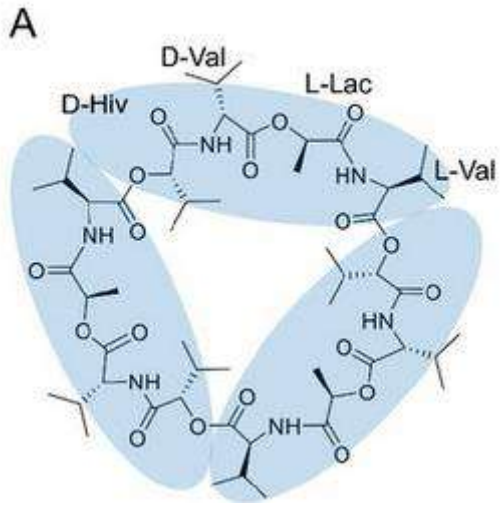
- Participates in the storage and transport of iron by maintaining the reduced form of iron in the cytosol, preventing its precipitation or toxicity.
- Inactivation of insulin hormone.



Hormones

- Insulin (51) and glucagon (29) from Pancreas.
- Vasopressin (ADH) and oxytocin from posterior pituitary gland (9).
- ACTH (39) from anterior pituitary gland.

Other functions



- Antibiotics: e.g. valinomycin (36).
- Antitumor agent: e.g. bleomycin (14).
- Aspartame (2): - It is a dipeptide (aspartic acid and phenylalanine) that serves as sweetening agent. It is used in replacement of cane sugar.

Proteins Chemistry

Nature of proteins: Composition, Size, Functions, and Conformation

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Composition

- Proteins are macromolecules formed of amino acids united together by peptide bonds.
- Amino acids are commonly found in proteins in different proportions.
- Some proteins are formed of 2 or more polypeptide chains.

Size of proteins

- Proteins having a very high molecular weight, ranging from 5,000 to several millions daltons .
- The term protein is applied to describe molecules greater than 50 a.a.
- Molecules contain less than 50 amino acids are termed peptides

Functions of proteins:

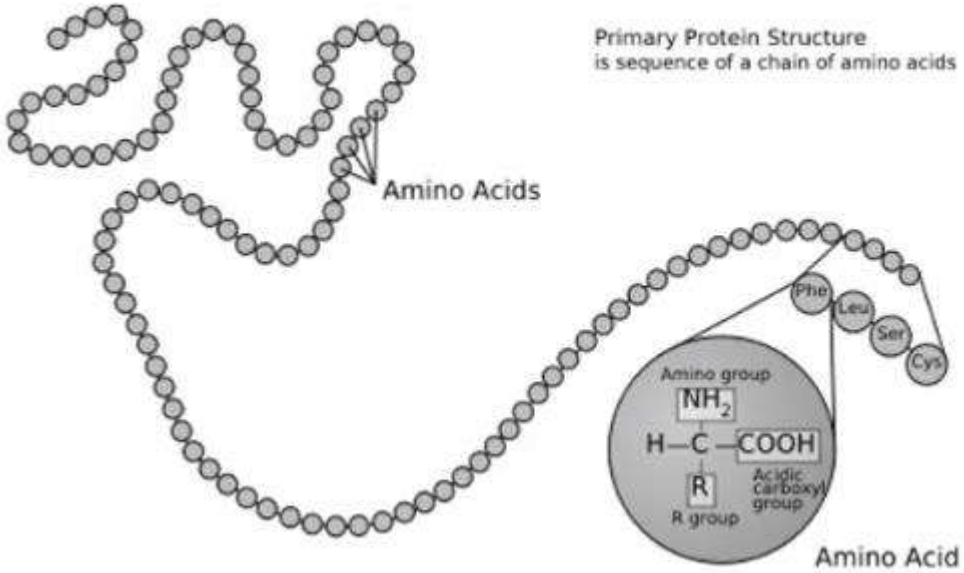
- Enzymes, Hormonal (growth hormone), antibodies (immunoglobulins) and Cellular receptors.
- Transport of small molecules and ions e.g. (Hemoglobin is a carrier for oxygen & Lipids are transported as lipoproteins).
- Cell membrane contains proteins in the form of glycoproteins.
- Skin and bone contains proteins in the form of collagen.
- Control of genetic expression: many regulators of genes are protein in nature.

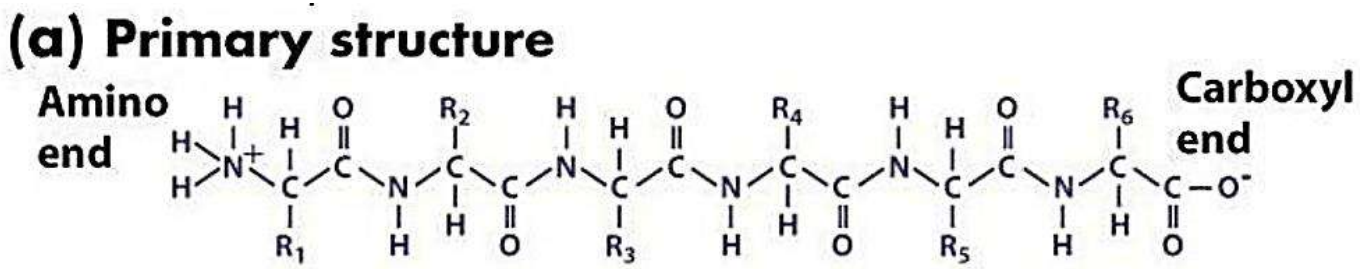
Levels of protein folding

1. Primary structure
2. Secondary structure
3. Tertiary structure
4. Quaternary structure

Primary structure (I°)

- It is the arrangement (sequence) of amino acids in the polypeptide chain.
- Bonds responsible for the primary structure: The peptide bonds "covalent".

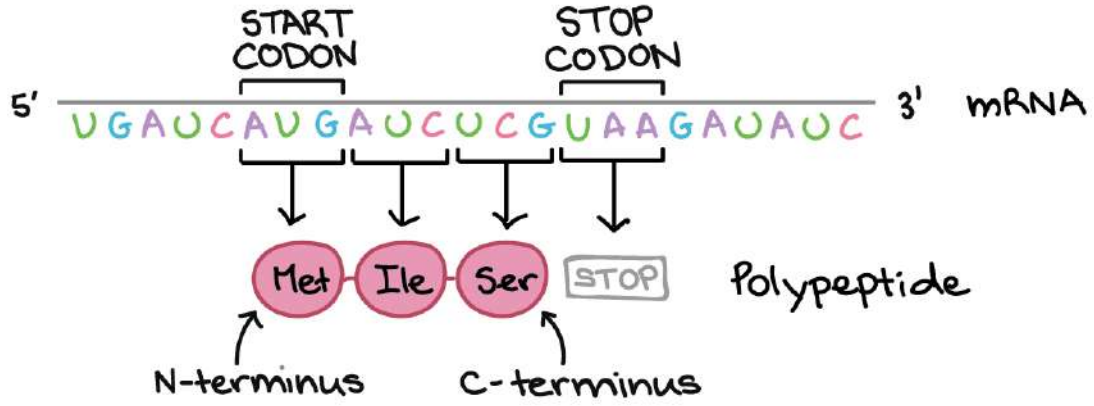




Primary structure (I°)

- I° chain starts on the left side by free amino group of the first amino acid [N-terminal amino acid (or N-terminus)].
- I° ends on the right side by free carboxyl group last amino acid, It is termed C-Terminal amino acid (or C-terminus)].
- The remaining amino acids in the chains are termed: amino acid residues
- The types and arrangement of amino acid in each protein is determined by the genetic information present in DNA.

The types and arrangement of amino acid in each protein is determined by the genetic information present in DNA.

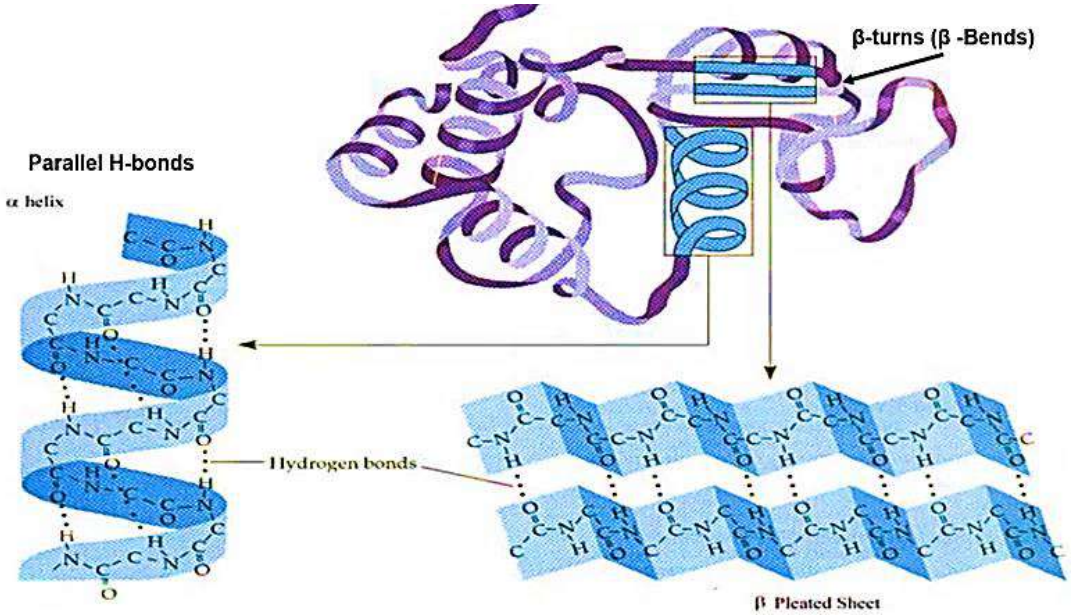


Second letter

First letter	U	C	A	G	Third letter
U	UUU Phe UUC Phe UUA Leu UUG Leu	UCU Ser UCC Ser UCA Ser UCG Ser	UAU Tyr UAC Tyr **UAA Stop** **UAG Stop**	UGU Cys UGC Cys **UGA Stop** UGG Trp	U C A G
C	CUU Leu CUC Leu CUA Leu CUG Leu	CCU Pro CCC Pro CCA Pro CCG Pro	CAU His CAC His CAA Gln CAG Gln	CGU Arg CGC Arg CGA Arg CGG Arg	U C A G
A	AUU Ile AUC Ile AUA Ile **AUG Met**	ACU Thr ACC Thr ACA Thr ACG Thr	AAU Asn AAC Asn AAA Lys AAG Lys	AGU Ser AGC Ser AGA Arg AGG Arg	U C A G
G	GUU Val GUC Val GUA Val GUG Val	GCU Ala GCC Ala GCA Ala GCG Ala	GAU Asp GAC Asp GAA Glu GAG Glu	GGU Gly GGC Gly GGA Gly GGG Gly	U C A G

Secondary structure (2°)

- It is local folding patterns within a protein characterized by the spatial arrangement of **adjacent amino acid residues** in the polypeptide chain.
- Bonds responsible: Hydrogen bond.
  - It is the bond between the hydrogen of -NH group of one amino acid residues and the carbonyl oxygen (C=O) of the fourth one



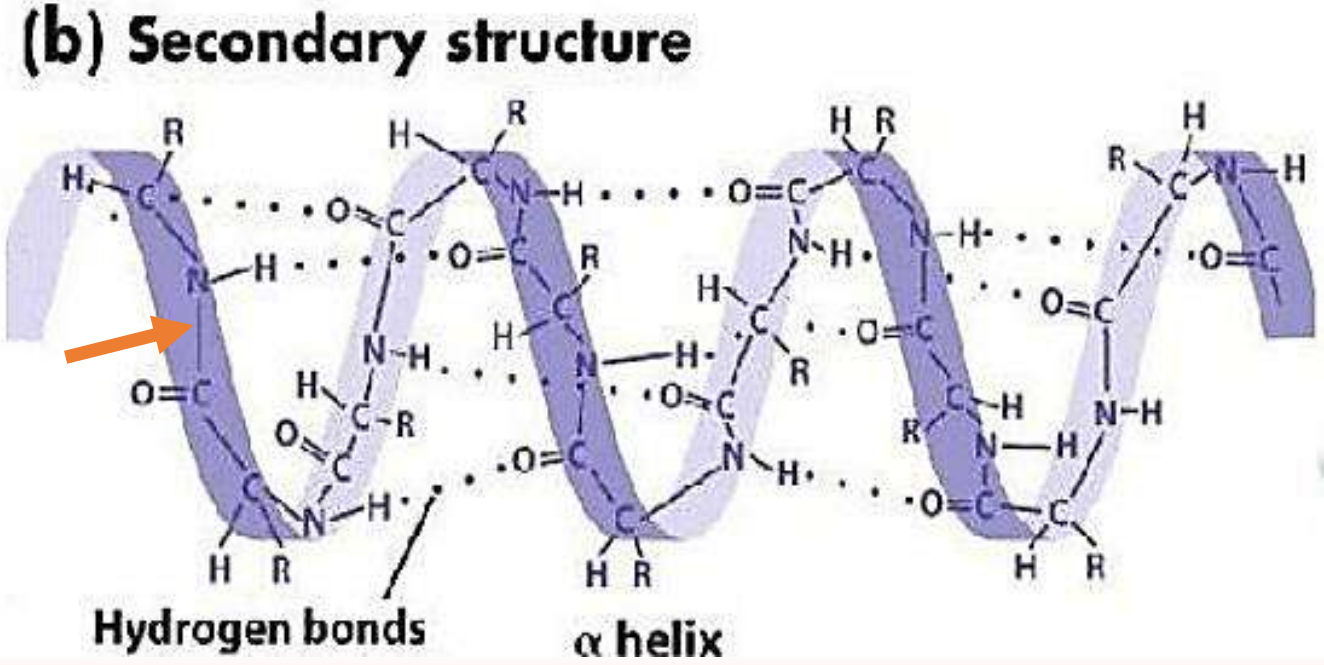
Secondary structure (2°): Mechanism

- Secondary structure results from interaction of adjacent amino acid residues.
- There are 2 main forms of secondary structure:

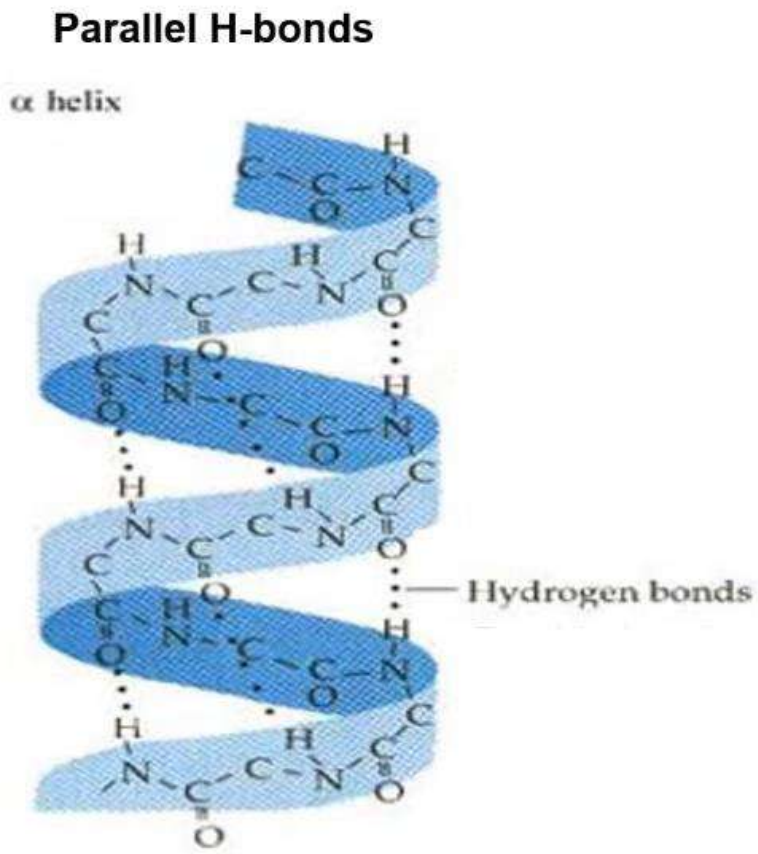
1. α-helix
2. β-pleated sheets.

α-helix

- It is a rod like structure with the peptide bonds coiled tightly inside.
- The side chains of the residues (R) extending outward from the chain.



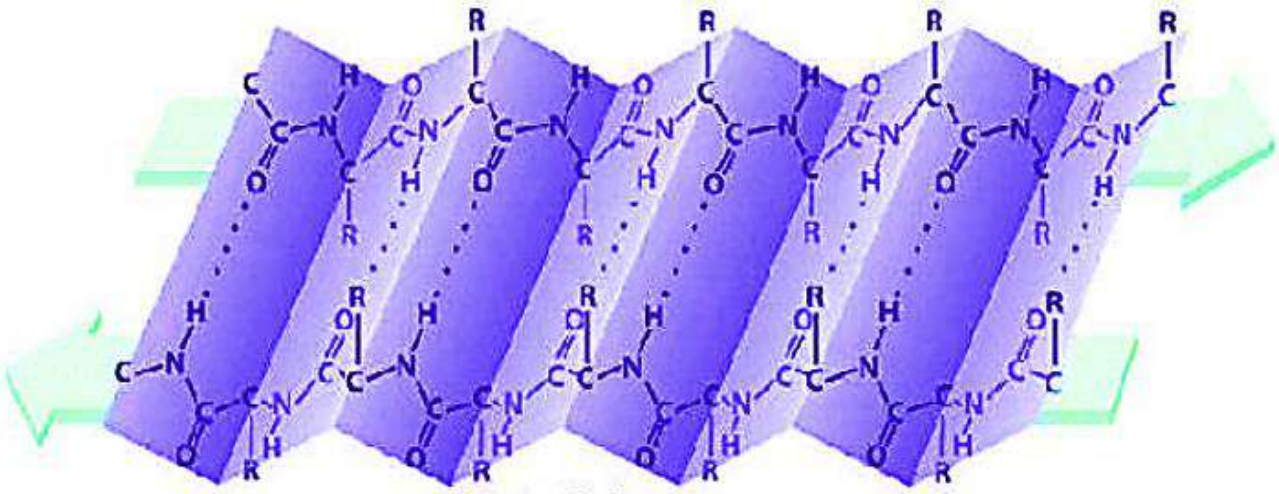
α-helix



- Each (C=O) of one amino acid is hydrogen bonded to the (-NH) of the next fourth amino acid in the chain (1→4)
- The complete turn distance equals 54 nm.
- Each turn contains 3.6 amino acids residues.

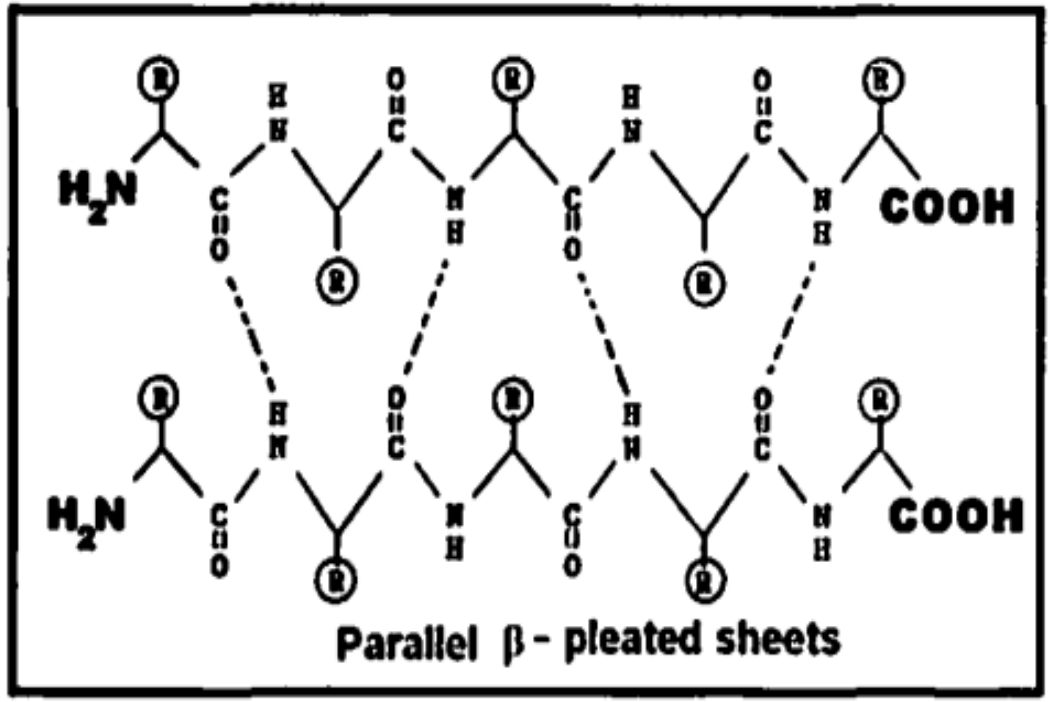
β-pleated sheets

- A 2^{o} structure (sheet-like arrangement) is formed between two or more polypeptide chains.
- Hydrogen bond is also responsible for its formation. It occurs between (-NH) group of one chain (or segment) and (C=O) group of adjacent chain (or segment).

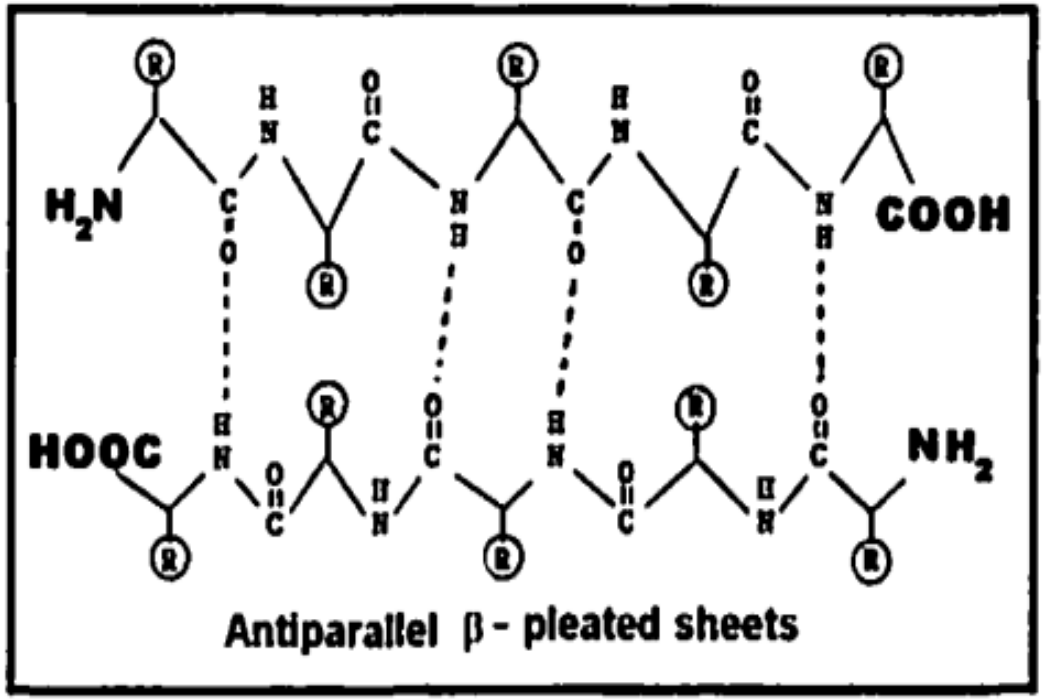


Pleated sheet

- Two types of β-sheets are present:
- Parallel β-sheets: in which the two polypeptide chains run in the same direction.
- Antiparallel β-sheets: in which the two polypeptide chains run in opposite direction.



Parallel β - pleated sheets



Antiparallel β - pleated sheets

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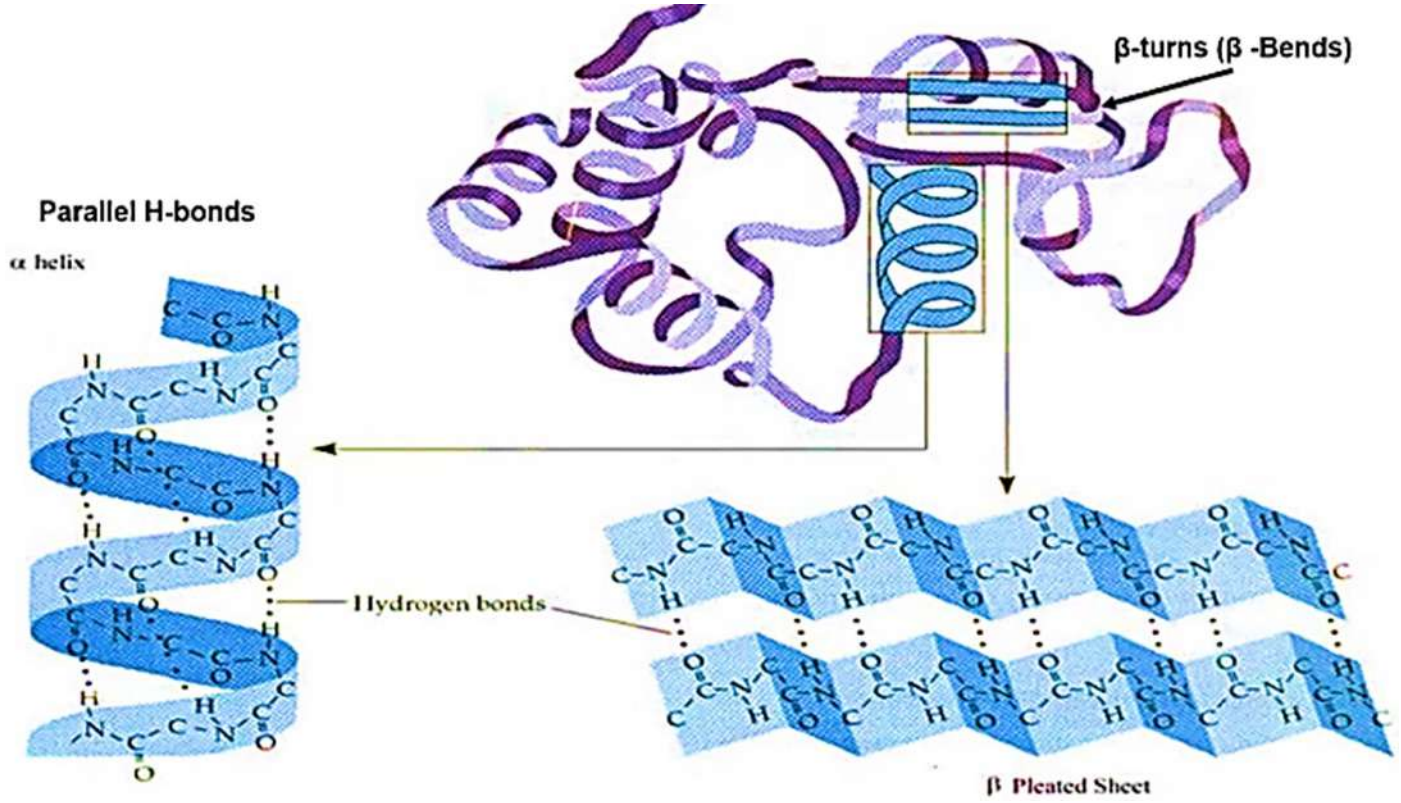
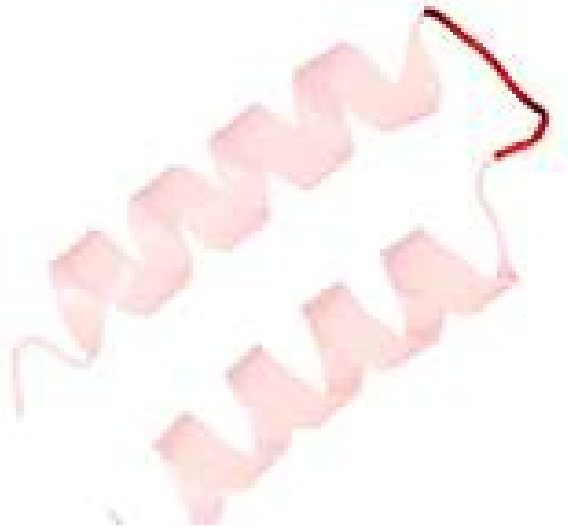
Tertiary structure (3°)

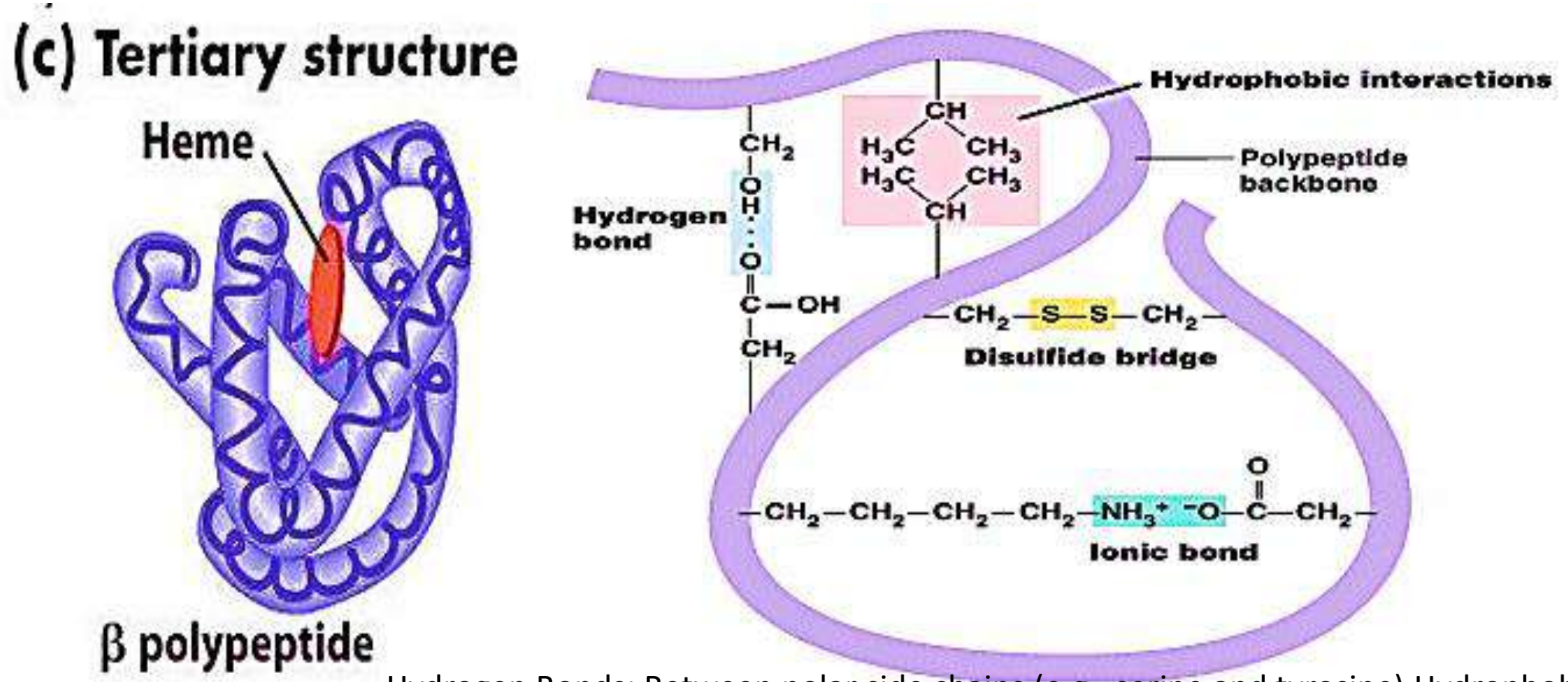
- 3° (functional protein structure) is the 3D conformation of a single polypeptide chain.
- Different parts of the 3° can take on different shapes, including alpha helices, beta sheets, and bends.
- These structural elements contribute to the overall 3D conformation.



Tertiary structure (3°) contains Bends as (2°)

- Bends are regions of a protein where the polypeptide chain changes direction, allowing it to connect alpha helices and beta sheets
- More flexible than regular secondary structures and often play a role in connecting different functional domains of a protein.

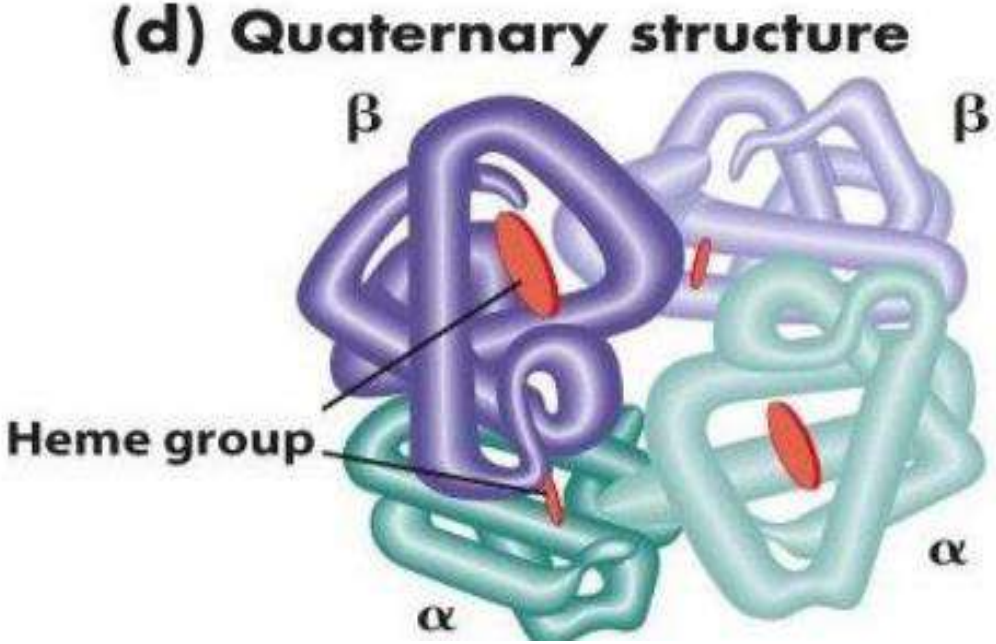




Hydrogen Bonds: Between polar side chains (e.g., serine and tyrosine).Hydrophobic Interactions: Nonpolar side chains (e.g., leucine, isoleucine) aggregate to minimize contact with water.Ionic Bonds (Salt Bridges): Between oppositely charged side chains (e.g., lysine and glutamate).Disulfide Bonds: Covalent bonds between cysteine residues, providing stability in extracellular proteins.

Quaternary Structure (4°)

- 4° involves the arrangement of multiple polypeptide chains (subunits) in a protein complex.
- These subunits may be identical or distinct and are held together by various interactions, including hydrogen bonds and hydrophobic interactions.



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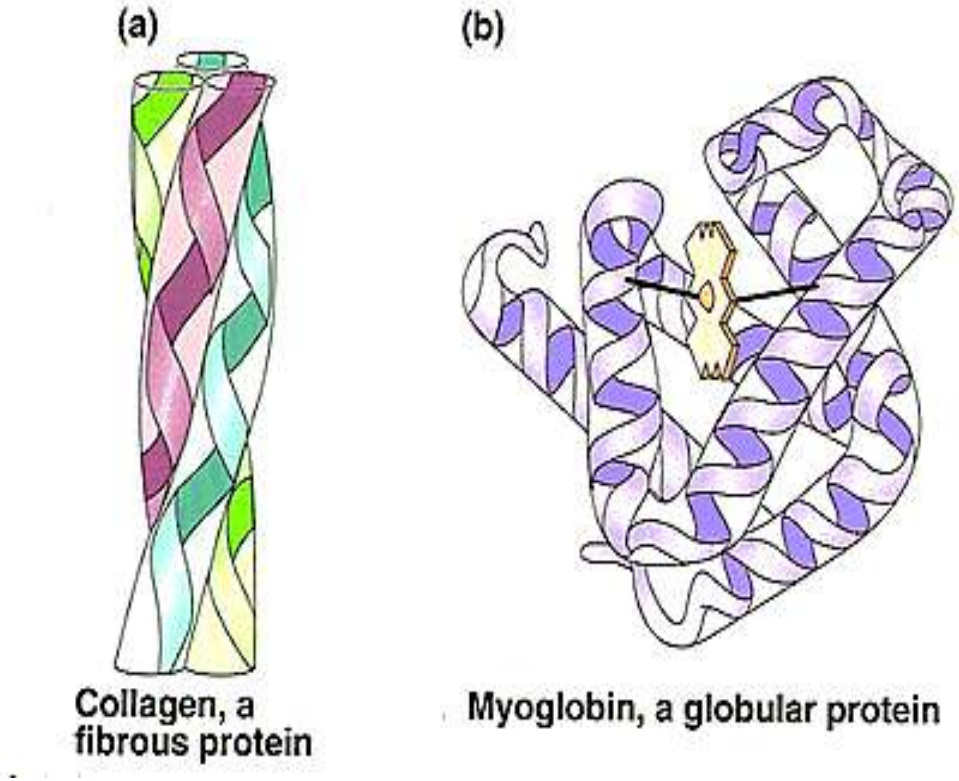
Quaternary Structure (4°)

- The quaternary structure is essential for proteins that require multiple subunits to work together.
- Hemoglobin is a classic example, consisting of four subunits that cooperatively bind oxygen and transport it through the bloodstream.

Protein structure based on their shapes and functions

a) Fibrous: which is an extended form e.g. keratin, collagen and elastin.

b) Globular: which is a compact form and results from folding of polypeptide chain e.g. myoglobin

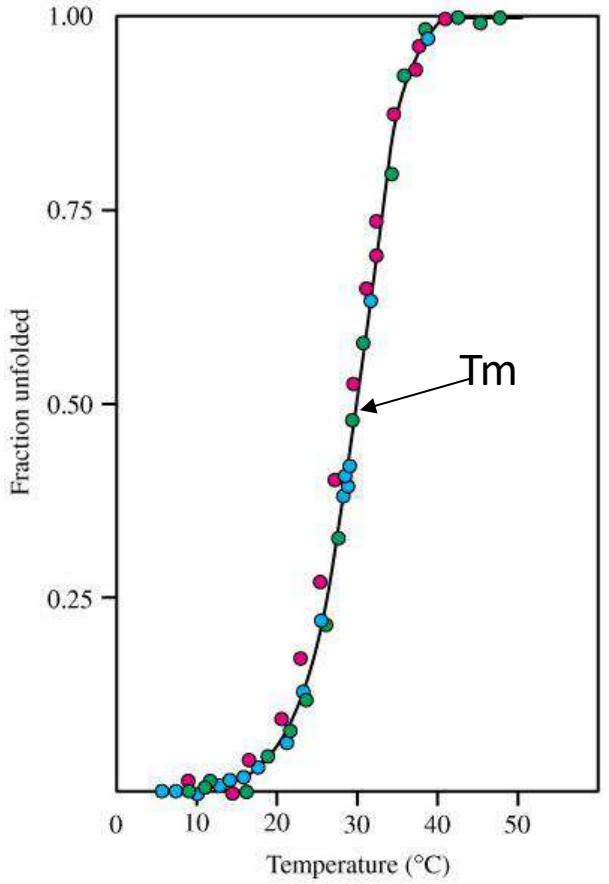


Collagen, a fibrous protein

Myoglobin, a globular protein

Protein denaturation

- Denaturation – disruption of native conformation
- Heat commonly used to denature proteins
- (Melting temperature) Tm = temperature where 50% folded/50% unfolded.
- Typical Tm = 40-60^{o}C
- Tm for thermophiles >100^{o}C (Taq DNA polymerase)
- Chemical denaturants = Urea, Potassium cyanide (KCN)



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Thanks Part 2
Last lecture