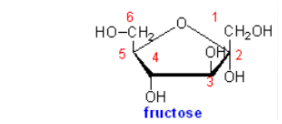
Dr.Ahmad Al-Qawasmi

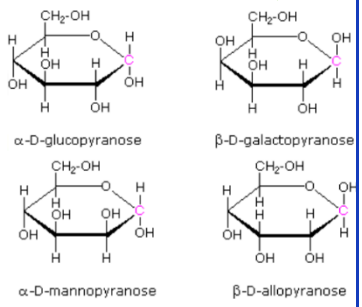
Biochemistry

Carbohydrates 2

❖ Fisher Projections



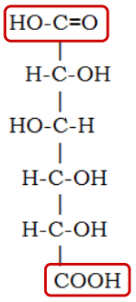
- It is 2-D representation of the 3-D structure of organic molecules
  - OH going to the **left** in the open chain, is actually going **upward** the ring
  - OH going to the **right** in the open chain, is actually going **downward** the ring



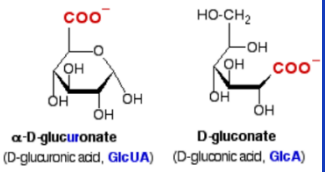
❖ Modified Sugars

♦ Sugar acids (Oxidized)

- The addition of Oxygen to a functional group forming a carboxyl (COOH)
- All monosaccharides can be oxidized

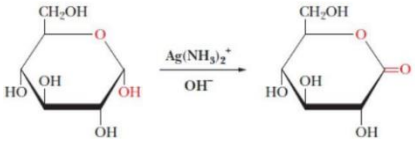


- Oxidation can occur on the **carbonyl** group (**anomeric** carbon) or **hydroxyl** group (mainly on the **last** carbon), depending on the strength of the oxidizing agent:
  - **Weak** oxidizing agents act on the **anomeric** carbon only
  - **Strong** oxidizing agents (such as $KMNO_4$ and Cr_2O_3) act on **both** anomeric and the last carbon
  - Only **enzymes** can oxidize the **last** carbon without oxidizing the anomeric one
- We can know the position of oxidation by the suffix at the end of the molecule's name, If the suffix is:
  - **–onic (-onate):** the anomeric carbon is oxidized
  - **–uronic (-uronate):** the last carbon is oxidized
  - **–aric (-arate):** the both carbons are oxidized (it has 2 carboxyl groups)



- **Notes:**
  - Aldehydes are oxidized directly, but ketones can't be oxidized directly
  - Ketone must be converted into an intermediate (**enediol**) then converted into aldehyde to be oxidized
  - **All monosaccharides** are considered as reducing agents (can be oxidized by a weak oxidizing agent)

- Both forms of monosaccharides can be oxidized (rings and open chains)
- **Oxidation of rings** involves the formation of **lactone**
  - Lactone is a cyclic ester

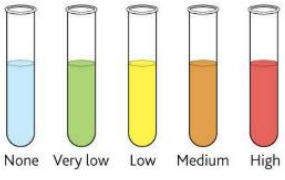


- **Notes:**
  - **Vitamin C (ascorbic acid)** is an unsaturated lactone which can be **oxidized** by air, followed by hydrolysis of the ester bond, leads to **loss of activity** as a vitamin
  - Vitamin C is important for making collagen
  - A lack of fresh food can cause vitamin C deficiencies, which can lead to scurvy

- Many tests can be used to detect the presence of a reducing sugar in the solution, such as:

1) Benedict's Test

- It uses **Benedict's reagent** which is a mixture of Cu^{+2} and NaOH then the solution is heated
- If the oxidation occurred, Cu_2O will precipitate (which is red) and so changing the color of the solution
- The color varies from green to dark red (brick) or rusty-brown according to the **amount of the reducing sugar**



2) Tollen's Test

- It uses $Ag(NH_3)_2^+$ reagent
- It detects reducing sugars (mainly in the ring form)
- It is also called silver-mirror test due to the precipitation of silver on the walls of the tube

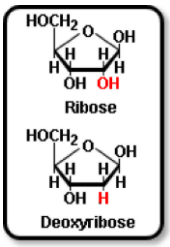
3) Blood Glucose Test

- It is a more recent method for the detection of glucose is based on the use of the enzyme **glucose oxidase**
- This enzyme oxidizes glucose into peroxide and then peroxidase is transformed into a colored substance and the color varies according to the amount of glucose present

♦ Sugar alcohol (reduction)

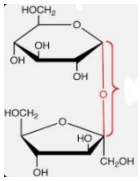
- Formed by the conversion of **carbonyl** group (Ketone, Aldehyde) into hydroxyl (Alcohol)
  - The resulting molecules have the suffix **–itol**
  - Sugar alcohols are used to **sweeten food products** such as Sorbitol, xylitol and mannitol
  - Glycerol is resulted from the reduction of dihydroxyacetone or D-glyceraldehyde
  - D-Sorbitol results from the reduction of C1 of glucose or C2 of fructose or sorbose
  - D-mannitol results from the reduction of C1 of mannose or C2 of fructose
  - D-xylitol results from the reduction of C1 of xylose or C2 of xylulose

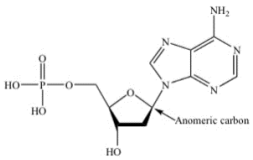
♦ Deoxy-sugars (reduction)



- One or more hydroxyl groups are replaced by hydrogens (reduction of **Hydroxyl**)
- Their names start with the prefix **-deoxy**
- Example: 2-deoxyribose in DNA and Fucose
  - In DNA ribose is deoxy (lost O) on C number 2 making DNA more stable and less reactive and so preventing mutations
  - **Fucose** is also called 6-deoxygalactose and it is used in some **glycoproteins**

♦ Glycosides

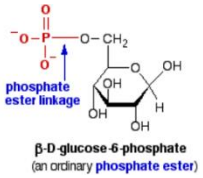


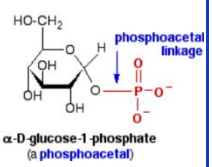


- Sugars forms a glycosidic bond with other molecules on its **anomeric carbon**
  - If this bond links the anomeric carbon to an oxygen, it is called O-glycoside
  - If this bond links the anomeric carbon to a nitrogen, it is called N-glycoside such as the glycosidic bonds between the ribose and the nitrogenous base in the **nucleotides**
  - If this bond links the anomeric carbon to a carbon, it is called C-glycoside such as the bond between **Disaccharides**
- Glycosides derived from furanoses are called furanosides, and those derived from pyranoses are called pyranosides, regardless if they are N- or O- linked

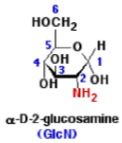
♦ Sugar esters (esterification)

- Esterification is the formation of ester bond by adding molecules into a hydroxyl group, such as **phosphorylation**
  - Phosphorylation is the addition of a phosphate group





♦ Amino sugars



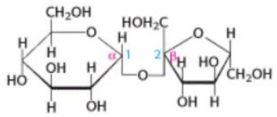
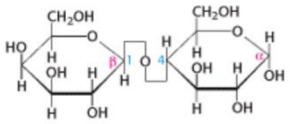
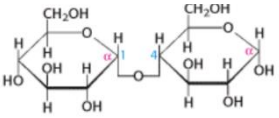
- The OH group in a sugar (on **any C other than the anomeric**) is replaced by an amino group (NH_2)
- It is usually followed by acetylation

- **Notes:**
  - Sugars present mainly in the ring form, but they can also be converted into a linear chain
  - When a sugar forms a **glycosidic** bond, it will **not be able** to reform the linear open chain

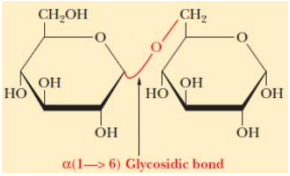
❖ Disaccharids

- Consists of 2 monosaccharides joined by a glycosidic bond
  - Homo-disaccharides: Monomers are similar
  - Hetero-disaccharide: Monomers are different
- Disaccharides are synthesized using the enzyme **glycosyltransferase**
- There are a variety of disaccharides, they differ in:
  - The type of monosaccharides involved and their stereoisomerism (D, L)
  - The carbon involved in the linkage (Carbon number 1, 2, 3, 4 or 5…)
  - The order of the 2 sugar units (monosaccharides)
  - Anomeric configuration of OH on carbon 1 (Alpha and Beta)

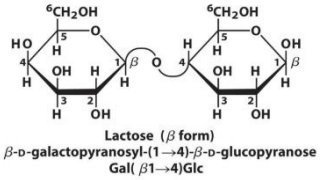
❖ Abundant disaccharides

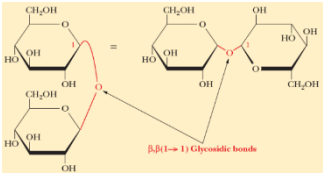
	Sucrose	Lactose	Maltose
Monomers	α-Glucose + β-Fructose	β-Galactose + α-Glucose	α-Glucose + α-Glucose
Bond	1-2	1-4	1-4
Reducing/ non	Non-reducing	Reducing	Reducing
	 Sucrose (α-D-Glucopyranosyl-(1→2)-β-D-fructofuranose	 Lactose (β-D-Galactopyranosyl-(1→4)-α-D-glucopyranose	 Maltose (α-D-Glucopyranosyl-(1→4)-α-D-glucopyranose

- Lactose in the milk sugar
- All disaccharides are formed by dehydration reaction of 2 monomers
- Sucrose, Lactose and Maltose have the same molecular formula: $C_{12}H_{22}O_{11}$

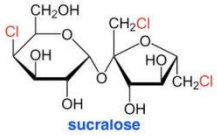


- Disaccharides can have different forms, for example:
  - 2 Glucose monomers can be linked via a 1-6 glycosidic bond rather
  - Lactose has a β form, in which both monomers are in the β configuration
  - We can also find a disaccharide of 2 β-glucose with a 1 → 1 glycosidic bond links them





- **Sucralose** is an artificial sweetener (not natural)
  - Synthesized by replacing OH groups in sucrose by Cl
  - It is associated with some disorders such as increasing Cancer risk and leaky gut because it can damage DNA



- **Lactulose:** It is an isomer of lactose can be produced enzymatically or chemically
  - It is used in treating constipation by increasing water absorption in the colon
  - It promotes the growth of health-promoting gut bacteria
  - It increases the production of small-chain fatty acids and the removal of toxic ammonia
  - It modulates the immune system
- Milk problems due to **lactose intolerance**
  - A deficiency of Lactase enzyme in the intestinal villi allows lactase of intestinal bacteria to digest it producing hydrogen gas, carbon dioxide, and organic acids and leading to digestive problems (bloating and diarrhea)
- **Galactosemia:** A disorder of missing a galactose-metabolizing enzyme
  - Non-metabolized galactose accumulates within cells and is converted to the hydroxy sugar galactitol, which cannot escape cells. Water is drawn into cells and the swelling causes cell damage, particularly in the brain, resulting in severe and irreversible **retardation** and also causes **cataract**

❖ Oligosaccharids

- Consists of a few monosaccharides, such as **Raffinose** it is:
  - It is found in Found in beans and vegetables like cabbage, brussels, sprouts, broccoli and asparagus
  - It is a Tri-saccharide made of α-Galactose + α-Glucose + β-Fructose (Galactose + Sucrose)
  - Humans **lack the alpha-galactosidase enzyme** that is needed to break down raffinose, but intestinal bacteria can ferment it into hydrogen, methane, and other gases
- Some Oligosaccharides are involved in drugs, such as:
  - **Streptomycin & Erythromycin** (antibiotics)
  - **Doxorubicin** (cancer chemotherapy)
  - **Digoxin** (drug for cardiovascular diseases)

❖ Polysaccharides

- Consists of many monosaccharides, which can be similar (Homo-polysaccharide) or different (Hetero)
- What determine the features of a polysaccharide:
  - The type of monosaccharides and their number (length)
  - Branching
  - Purpose (Storage, Structural)

♦ Storage Polysaccharides

	Glycogen	Starch	Dextran
Monomers	**α-Glucose**	**α-Glucose**	**α-Glucose**
Bonds	**α (1-4)**	**α (1-4)**	**α (1-6)**
Branching	**Highly** branched with α (1-6) bonds on the branching points	**Amylose:** Unbranched **Amylopectin:** Slightly branched with α (1-6) bond	Branched with (1-2), (1-3), (1-4) bonds
Location	Animal cells is granules (liver and muscle cells)	Plant cells	Yeast & Bacteria

- Branching is important in making the molecule **water soluble preventing crystallizing** & branching make it easy to **access glucose**
- Glycogen is highly branched where it has a branching point about every 10 residues and about every 25 residues in amylopectin

♦ Structural Polysaccharides

	Chitin	Cellulose	Pectin
Monomers	**N-Acetyl-β-Glucose**	**β-Glucose**	**α-Galacturonic acid**
Bonds	**β (1-4)**	**β (1-4)**	**α (1-4)**
Branching	Unbranched	Unbranched	Unbranched
Location	Exoskeleton of Animal	Plant cells	Plant cells

- Many polysaccharide chains of cellulose present parallel to each other as fibers and these fiber are hydrogen-bonded to each other
- We can't degrade (digest) cellulose, because we **don't have a β-Glycosidase**
- Mostly all polysaccharides are non-reducing the presence of only a single reducing end will not be enough and so the produce a negative test

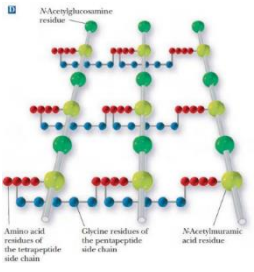
❖ GAGs (Glycosaminoglycans)

- Hetero-polysaccharides composed of repeated units of disaccharides
  - The first monomer is a positively charged amino sugar (glucosamine, galactosamine)
  - The other monomer is a negatively charged sugar with a carboxylate or sulfate group
    - ✓ Mostly their monomers are **β-sugars**
    - ✓ Negative charges produce repulsion aiding their function such as preventing the compactness of the cartilage and prevent coagulation
- GAGs are extracellular charges

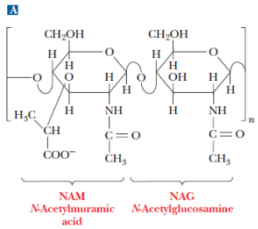
GAG	Localization	Comments
Hyaluronate	synovial fluid, **vitreous humor, ECM of loose connective tissue**	**the lubricant fluid , shock absorbing** As many as 25,000 disaccharide units
Chondroitin sulfate	**cartilage**, bone, heart valves	**most abundant GAG**
Heparan sulfate	basement membranes, components of cell surfaces	contains higher acetylated glucosamine than heparin
Heparin	component of intracellular granules of mast cells lining the arteries of the lungs, liver and skin	**A natural anticoagulant**
Dermatan sulfate	skin, blood vessels, heart valves	
Keratan sulfate	cornea, bone, cartilage aggregated with chondroitin sulfates	Only one not having uronic acid

❖ Proteoglycans & Peptidoglycans

- Consist of sugars (major) with proteins (minor)
- Has many functions and features:
  - Lubricant
  - Structural component of the connective tissue
  - Mediate adhesion and communication of cells to the extracellular matrix
  - Bind factors that stimulate cell proliferation



- Bacterial cell wall consists of proteoglycans, containing a repeating unit of a disaccharide of **NAM** & **NAG** as monomers linked together via **β (1-4)** linkage
  - NAM: N-Acetylmuramic acid which is a **modified glucose** (has lactic acid on its carbon number 3)
  - NAG = N-Acetylglucoseamine



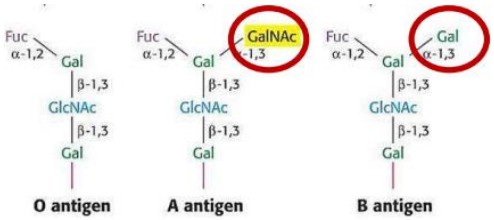
❖ Glycoprotiens

- Proteins (Major) modified by adding sugar (minor) → linked by:
  - **O-Glycosidic bond** → with the hydroxyl of **Serine (Ser)**, **Threonine (Thr)**, **Hydroxylysine (HLys)**
  - **N-Glycosidic bond** → with the amide group of **asparagine (Asn,N)**

- Significance of protein-linked sugars:
  1) Protein **folding**
  2) Protein **targeting**
  3) **Prolonging protein half-life**: More sugar linked to the protein making it harder to be broken
  4) **Cell-Cell communication**
  5) **Signaling**

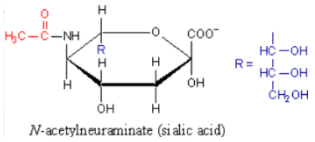
❖ Blood types

- According to the ABO system there are 4 types (A, B, AB, O) differ in the type of the terminal sugar of the oligosaccharide on the surface of RBCs, If this terminal residue is:
  - N-Acetylgalactoseamine (GalNAc) → **A** antigen
  - Galactose (Gal) → **B** antigen
  - None → **O** antigen
  - Gal and GalNAc → **AB** antigen



❖ Sialic acid

- It is also called N- acetylneuraminate
- Precursor: the amino sugar, neuraminic acid
- It is located as a **terminal** residue of oligosaccharide chains of glycoproteins and glycolipids



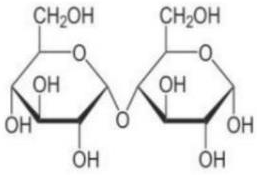
Past papers

1. Blood types differ in their:

A. Sugar content
B. Lipid content
C. Protein content
D. None of the above

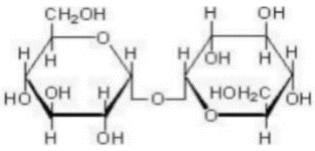
2. Which of the following is not true:

A. The glycosidic bond is Beta (1 – 6)
B. It can be a part of dextran



3. This sugar is a reducing sugar:

A. True
B. False



4. Which of the following sugars has a beta glycosidic linkage

A. Chitin
B. Sucrose
C. Lactose
D. None of the above

5. The polysaccharide in which glucose is stored in animal cells:

A. Stored in melanocytes & Hepatocytes
B. Contain Beta linkages
C. Extremely branched for more efficient energy supply

6. Deoxy sugars produced by:

A. Reduction of a monosaccharide
B. Engaging anomeric carbon in a glycosidic bond
C. Conversion of a sugar to acid
D. Hydrolysis of a disaccharide

7. Oxidation of carbon number 6 of cyclic glucose:

A. Producing fructose
B. Producing glucoronate
C. Stabilizing the anomeric carbon
D. Production of a deoxy-sugar
E. Opening the ring chain

8. Why do some people are lactose-intolerant:

A. The lack of lactase enzyme
B. They can't digest galactose
C. They didn't drink milk when they were children

9. How many chiral centers are in 2-deoxyribose?

A. 1
B. 2
C. 3
D. 4
E. 5

10. What is common between amylose and cellulose?

A. Both are branched
B. Both are unbranched
C. Both have the same branching position
D. Both have the same number of branches
E. Both are synthesized in animals

11. A polysaccharide consisting of glucose and galactose derivatives and at least a sulfur or a carboxylic group and it is highly polar?

A. Glycoaminoglycans (GAGS)
B. Gylcogen
C. Celluose
D. Pectin
E. Dextran

12. Which of the following is an oxidized sugar?

A. Glucuronate
B. Sorbitol
C. Sucrose
D. Fructose
E. Ribose

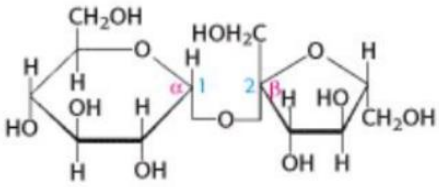
13. Benedict's test is used to?

A. Confirm the presence of cyclic sugars
B. Confirm the presence of reducing sugars
C. Confirm the presence of sucrose
D. Confirm the presence of disacchrides
E. Confirm the presence of sugar acids

14. The polysacchride in a bacterial cell wall has all the following features EXCEPT?

A. is a heteropolysaccharide of NAG and NAM
B. is a homopolysaccharide of sialic acid
C. is a polysaccharide cross-linked by peptides
D. Sugars are connected directly to tetra peptides
E. The strands are connected by Gly pentapeptides

15. One of the following is true about the following structure:



A. Sucrose
B. Lactose
C. Maltose
D. Raffinose

16. Glycosaminoglycans are characterized by all of the following features EXCEPT:

A. The basic unit is a repeated disaccharide
B. At least, one sugar has an amino group
C. At least, one sugar is negatively charged with acidic group
D. The sugars are derived from glucose or fructose
E. It is attached to proteins forming proteoglycans

17. One of the following polysaccharides is heteropoly saccharide:

A. chitin
B. pectin
C. dextran
D. starch

18. one of the following is mismatched:

A. sarbose ——— sorbitiol
B. mannose ——— mannitol
C. xylulose——— xylitol
D. galactose ——— Fucose
E. none of the above

19. You have two pentoses. they are both made of 5 carbons, 10 hydrogens and 5 oxygens. One is an aldose, and the other is a ketose. the aldose has carbon 3 oriented to the right and the ketose has carbon 3 oriented to the left. What is their relationship?

A. They are epimers at carbon 3
B. They are isomers
C. They are enantiomers
D. They are diastereomers
E. They are stereoisomers

20. The following is a non-reducing sugar?

A. cellulose
B. fructose
C. lactose
D. maltose
E. L-glucose

21. The feature of a polysaccharide with a beta-glycosidic bond is?

A. it can be branched
B. it is rigid and straight
C. it is more water-soluble
D. it can be looped taking less space
E. it forms more hydrogen bonds