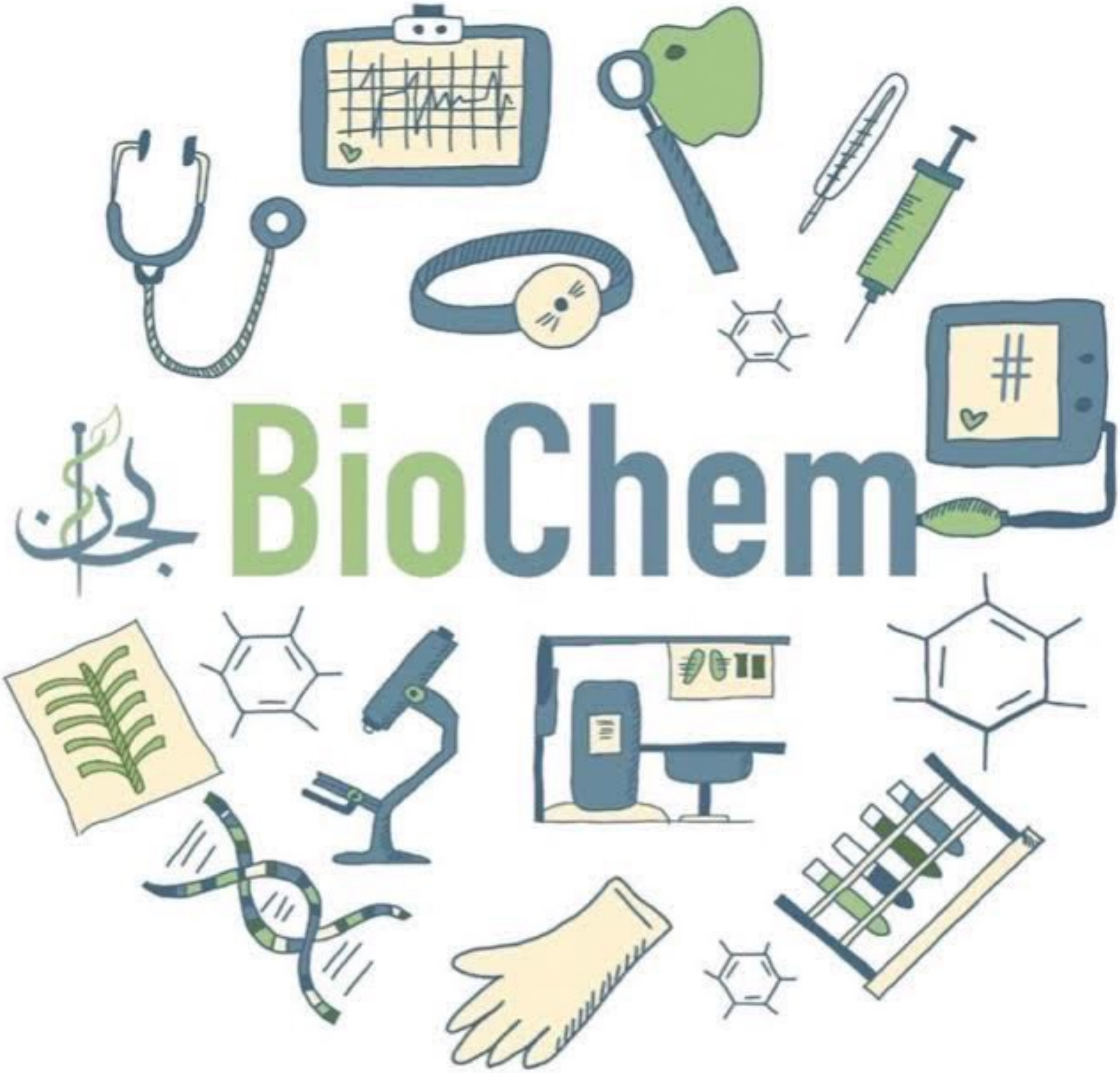

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Final Correction : ________________

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Polysaccharides

Polysaccharides are composed of a very large number of monosaccharides connected with each other.

So, the monomer of a polysaccharide is **monosaccharide**.

Polysaccharides are two types depending on monomers that make up them:

1. **Homopolysaccharides** (homoglycans): Polysaccharides made up of the same monomer type (the same monosaccharide).
2. **Heteropolysaccharides**: Polysaccharides made up of more than one type of monomers (different monosaccharides).

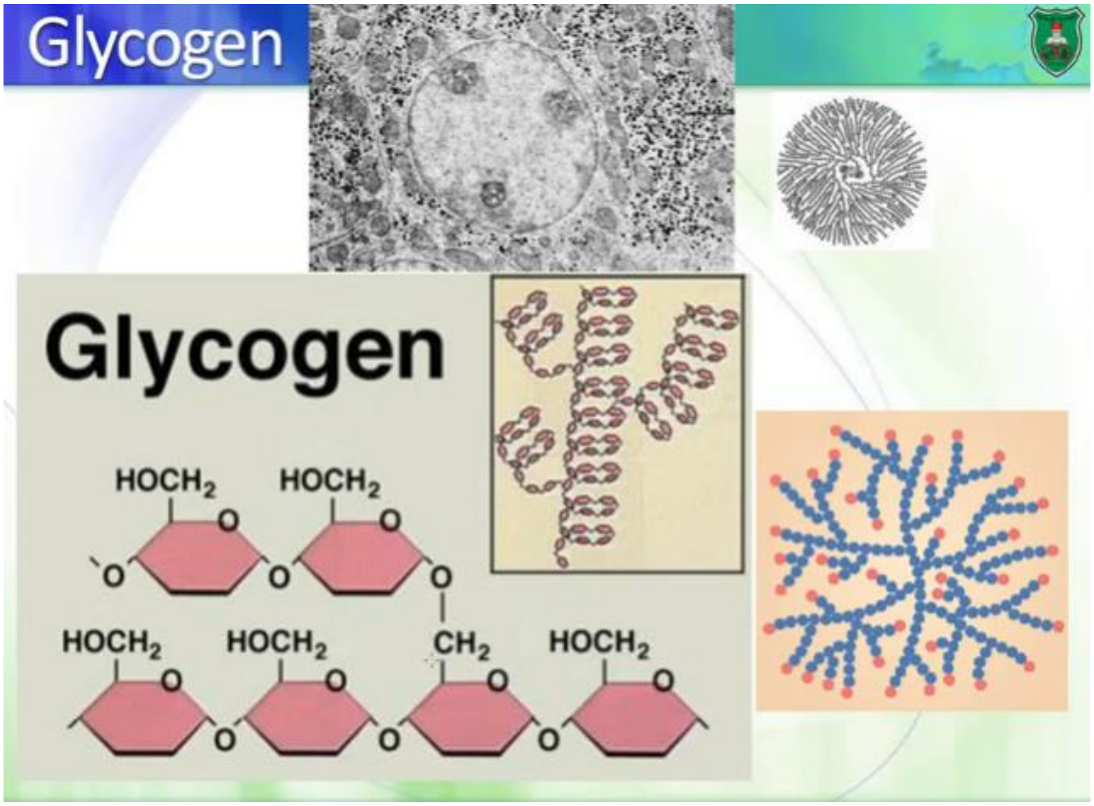
Polysaccharides differ in: (Features of polysaccharides)

- **Monosaccharide** units that are repeated inside them
- **Length**
- **Branching** (Branching type, how often it happens, how many layers of branching we may have, etc…)
- **Purpose** (Polysaccharides have different functions)
  - Storage (glycogen, starch, dextran)
  - Structural (cellulose, pectin, chitin)

We will study six polysaccharides:

1.Glycogen 2.Starch 3.Dextran 4.Cellulose 5.Pectin 6.Chitin

Glycogen (Animal starch)



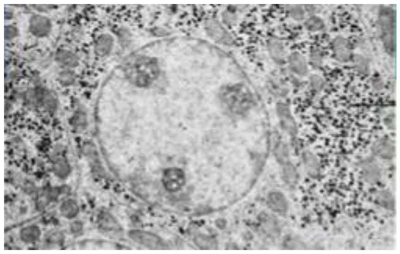
-**Glycogen**: A highly branched storage polysaccharide, made of **glucose** units as monomers, synthesized by **animal cells**.

-As you can see in the picture above, glycogen is **highly branched**

- It has so many layers of branching that it can reach 13 layers.
- Every 10 glucose residues, there is a branching point.

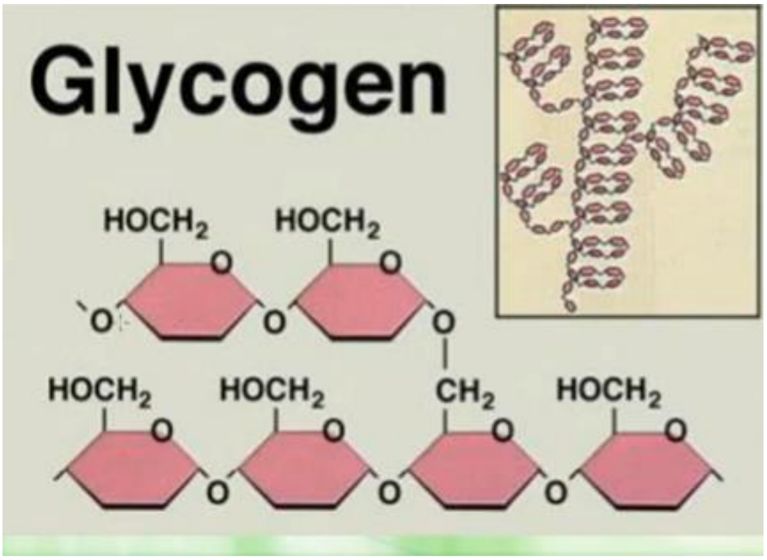
-When we have excess sugar in our bodies, it will be stored as Glycogen, so it is **the storage form of glucose**.

-Glycogen is present in all cells (Glycogen molecules accumulate in glycogen granules in the cytosol of cells), but the main store of glycogen is **Liver** and **Muscles**, since these tissues are very vital and need a large amount of energy.



In the picture, you can see glycogen molecules in cytosol around the nucleus.

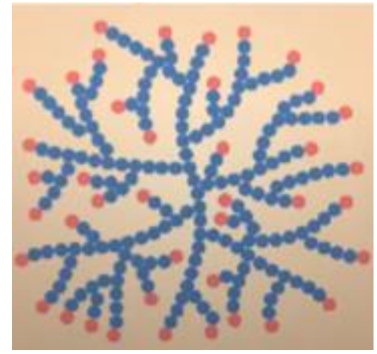
Now, let's study glycogen structure in more details,



-The linkage between two monomers in glycogen is **α(1→4) glycosidic bond**, which is repeated along the main chain and branched chains, but what does it mean? It means that the bond is between carbon no.1 in the first monosaccharide and carbon no.4 in the next monosaccharide. (V-shaped bond also indicates the type)

-The linkage on branching point is **α(1→6) glycosidic bond**, it means that the bond is between carbon no.1 in the first monosaccharide residue of the branch and carbon no.6 in the monosaccharide residue of the main chain, which is outside the ring, thus we avoid steric hindrance.

-The free carbon atom in residues that make glycogen ends (red balls in the picture) is carbon no.4 so they are **non-reducing ends**, which means that they can't be oxidized (carbon no.1 is taken for the bond with the previous residue)



-The free carbon in the residue that makes the free end at the very beginning of the main chain is carbon no.1 (carbon no.1 is the anomeric carbon, so it's important for oxidation reactions), so this end is considered a reducing end, but it's effect is almost negligible, because there is a huge number of non-reducing ends → **Glycogen is a non-reducing sugar**.

Starch

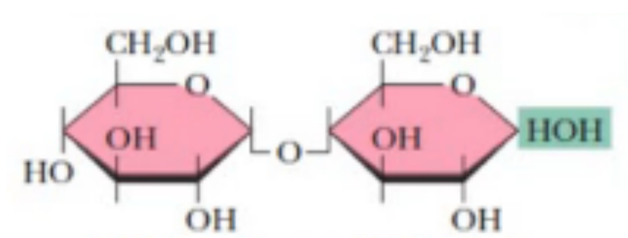
Starch: A **plant** storage polysaccharide, that is made of **glucose** monomers.

-We can't synthesize starch in our cells, but we obtain it from diet (**rice**, **corn**, **potato**)

-Starch is composed of two different forms of molecules:

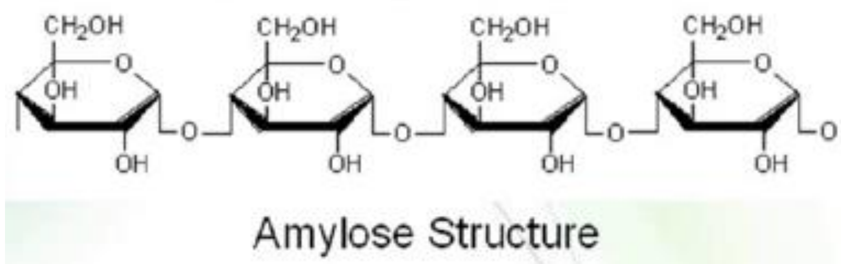
1. **Amylopectin**: it constituets **(80-90) %** of starch composition.
2. **Amylose**: it constituets **(10-20) %** of starch composition.

- **Digestion of starch**: we break up starch units (we cut two residue units), this results in the formation of maltose, which will be broken down into two glucose residues (monosaccharides) for absorption.



Maltose (glucose-α-1,4-glucose)

Amylose

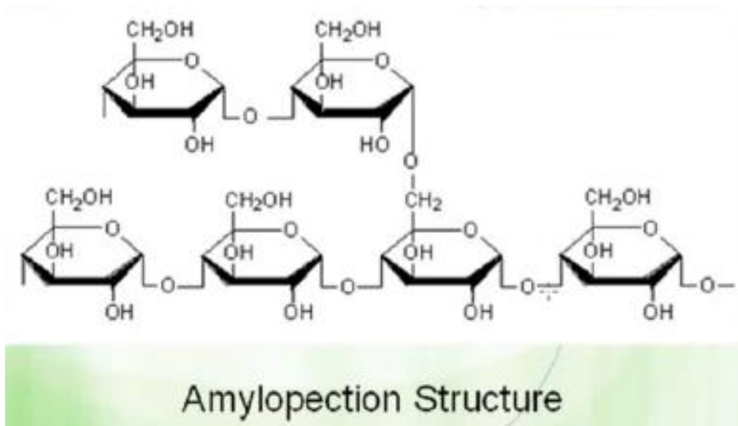


-It's the **unbranched** form of cellulose and it's made of long chains of glucose monomers.

-Amylose chains form helices, similar in shape to α-helix in protein structure.

-The linkage between glucose monomers is **α(1→4) glycosidic bond**.

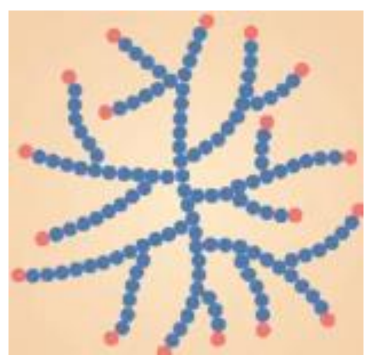
Amylopectin



-It's the **branched** form of cellulose and it's made of long branched chains of glucose monomers.

-Branching of amylopectin isn't as common as glycogen:

- It has less branching layers.
- Every 25 glucose residues, there is a branching point.



-Just like glycogen, amylopectin have non-reducing ends (carbon no.4) except for the very first residue of the main chain (carbon no.1), but it doesn't affect the whole molecule → **Amylopectin is a non-reducing sugar.**

-The linkage between two monomers in amylopectin is **α(1→4) glycosidic bond**.

-The linkage on branching point is **α(1→6) glycosidic bond**

Glycogen vs Amylopectin

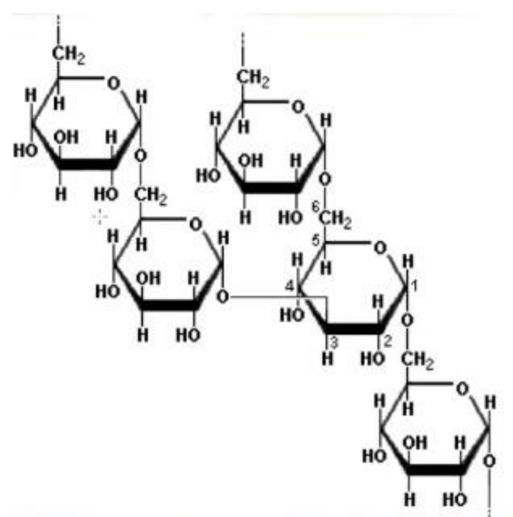
- Both are made from the **same monomer** (glucose monosaccharide)
- Both are **branched**, but glycogen is more branched than amylopectin.
    - In glycogen, every 10 glucose residues, there is a branching point.
    - In amylopectin, every 25 glucose residues, there is a branching point.
- Both have the **same types of bonds**: $\alpha(1\rightarrow4)$ glycosidic linkage and $\alpha(1\rightarrow6)$ glycosidic linkage at branching points.
- They have **different sources**: Glycogen is synthesized by animals, whereas Amylopectin is synthesized by plants.

That's why glycogen is called "Animal starch"

-**What is the importance of branching?**

- For glycogen, the storage form of glucose, when we need glucose as a source of energy we break it down from its free ends and release glucose monomers. Branching **provides more free ends**, so there will be more sites that enzymes can attack and break glycogen down, and this will **increase the efficiency** of breaking down this molecule.
- Branching **increases the solubility** of molecules.

Dextran



Dextran: A **storage** polysaccharide, made of **glucose** residues, synthesized by **bacteria** and **yeast**.

-The linkage between its glucose monomers is

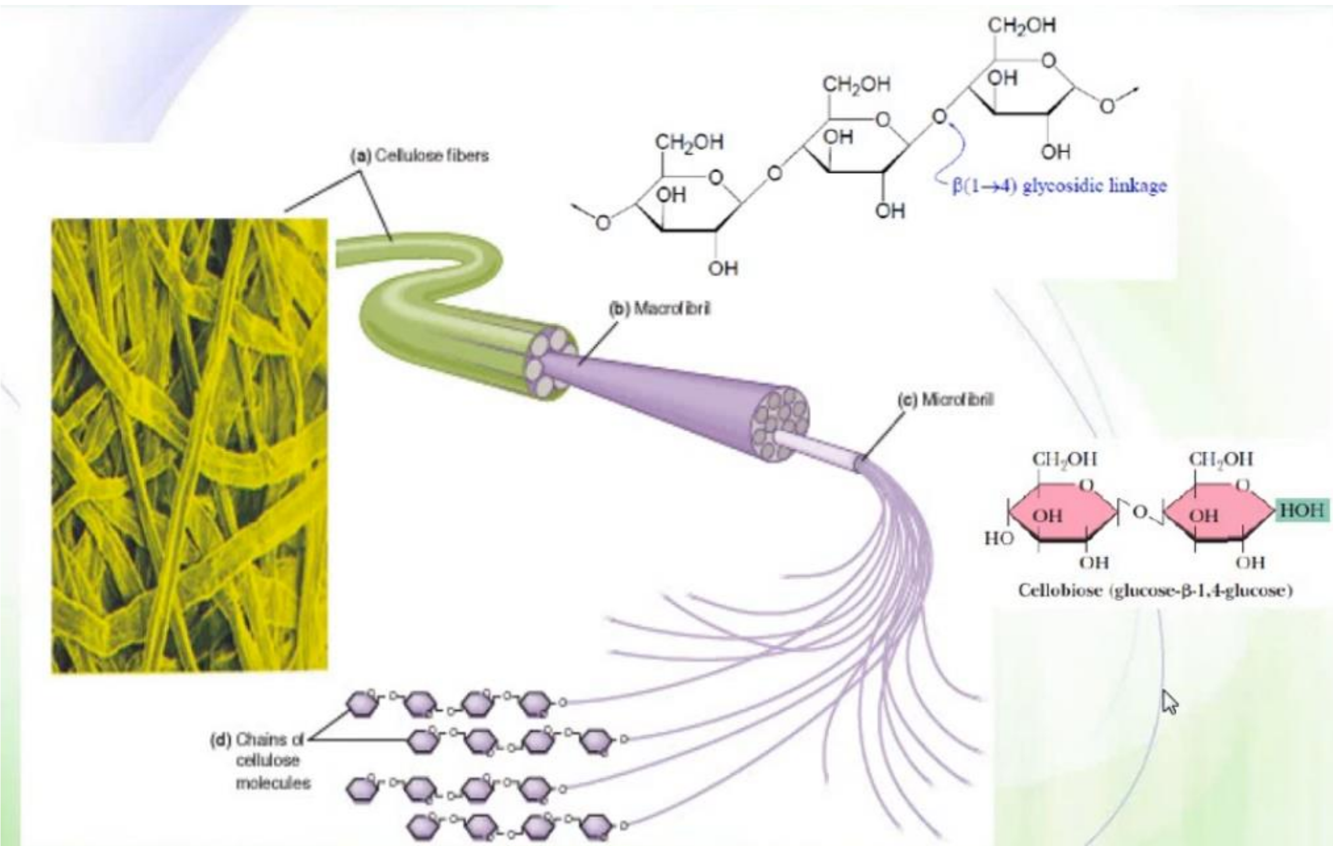
$\alpha(1\rightarrow6)$ glycosidic linkage.

- Branches can be **(1-2)**, **(1-3)** or **(1-4)**, and this creates a very complicated and highly branched polysaccharide.

-Bacteria in the mouth synthesizes dextran and creates a complex network of molecules that can be deposited on tooth surface. Bacteria colonizes these networks of molecules and stay there for a long time, releasing acids and acting on teeth to facilitate destroy and damage making teeth carious and decayed. That's why it's important to maintain oral health.

-البكتيريا الموجودة في الفم بتصنع dextran فبيتجمع على شكل شبكة (لأنه highly branched)، وبتترسب الشبكة على سطح الأسنان، فالبكتيريا بتستعمر هاي الشبكة وبتبقى فيها لمدة طويلة وبتفرز أحماض ومواد بتتسبب بتخريب الأسنان وتسوسها ونخرها.

Cellulose



Cellulose: An **unbranched plant structural** polysaccharide, made of **β-glucose** monomers.

-The linkage between cellulose monomers is **β(1→4) glycosidic linkage**.

-**Cellulose chains** are aligned along each other and they are highly compacted, so there would be more non-covalent interactions between them, specifically **hydrogen bonding**.

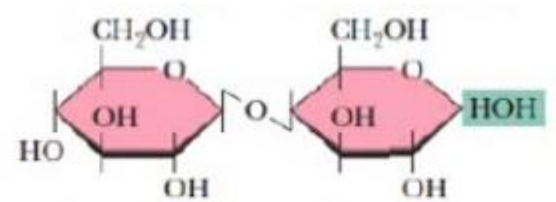
-**Cellulose chains** are parallel to each other and compacted, forming **microfibrils**. Microfibrils are assembled into **macrofibrils**. Macrofibrils are assembled into **cellulose fibers** which make up the structure of trees and plants.

Cellulose chains → Microfibrils → Macrofibrils → Cellulose fibers

-This organization makes cellulose structure **stronger** and better in terms of **mechanical properties**, thus cellulose function as a structural polysaccharide is related to its structure.

-The disaccharide subunit that makes the structure of cellulose is **cellobiose**.

-**Cellobiose**: A disaccharide composed of two glucose residues connected together via **β(1→4) glycosidic linkage**.



Cellobiose (glucose-β-1,4-glucose)

- **β(1→4) glycosidic linkage** is broken down by an enzyme known as **cellulase**, but we humans don't have this enzyme, so we can't digest cellulose, but cellulose is said to be highly beneficial to our bodies!!

- ❖ When we **ingest cellulose fibers**, like in fruits and vegetables, they're going to stay as they are, **not digested**, in the intestinal tract, then they **attract water molecules** toward intestines to maintain osmotic pressure, thus **facilitating getting rid of waste products** (feces). *That's why people with constipation are advised to eat more cellulose fibers*.

- Cellulose (because of its high content of glucose is highly polar molecule) **attracts water molecules**, interacting with them through hydrogen bonds. This will **enlarge the structure**, **filling up the intestines**, what gives you a feeling of **satiety**. *That's why people who want to lose weight are advised to eat fibers*.
- Cellulose acts like a **network** that can **fish cholesterol molecules, toxins, etc.** so **they are not absorbed** by the intestine, rather **we get rid of them into feces**.

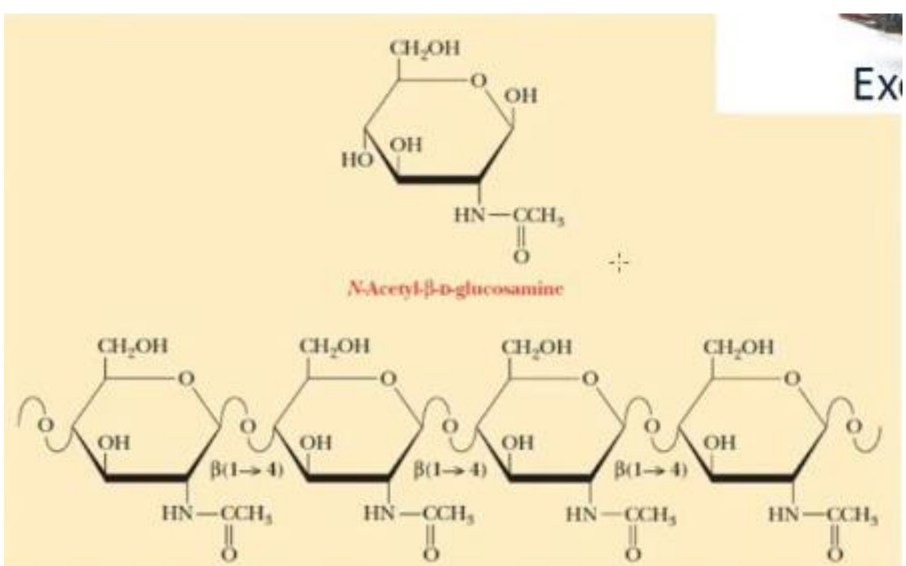
I think that you are now aware why cellulose is beneficial to our bodies.

-The enzyme cellulase is present in the intestines of animals that rely on plants for nutrition like **cows** and **sheeps**, so they can digest cellulose.

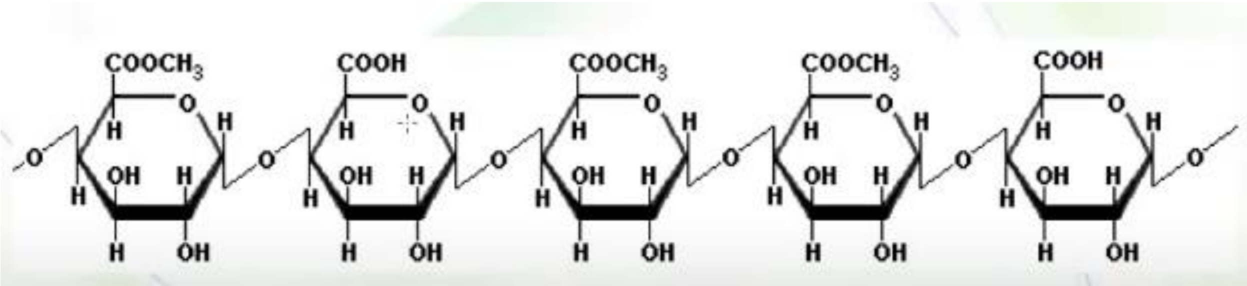
Chitin

Chitin: A structural polysaccharide present in the exoskeleton of different animals.

-Chitin is made of repeated units of **N-Acetyl-β-D-glucosamine** connected with each other via **β(1→4) linkage**.



Pectin



Pectin: A **structural** polysaccharide, composed of **two types of modified galactose** residues, produced by **plant cells** and **bacterial cells**.

-**Pectin** is **heteropolysaccharide**, since it has two different types of monosaccharides.

-The linkage between its monomers is **β(1→4) glycosidic linkage**.

-The monomer that has COOH at carbon no.6 has been **oxidized** and it's called **galacturonic acid**, while the monomer that has $COOCH_3$ has been **esterified**.

-**Pectin** is used as **gelling agent** in plant-based jello (We use it to make a jell-like material)

-In animal-based jello, we use another substance as a gelling material that is called **Gelatin**, it's a different molecule in structure and source. It's source is animals- it comes from **cows** and **pigs**.

Are polysaccharides reducing?

As we learned, the free ends of polysaccharides like glycogen and amylopectin have **carbon no.4 as free carbon** which means they're not going to be reducing sugars. Because they aren't anomeric carbons, they can't get oxidized. **The anomeric carbons are already occupied** and they're bonded through the different types of bonds in different types of polysaccharides. (**The effect of the very first residue which is the only reducing end in a polysaccharide molecule is almost negligible**)

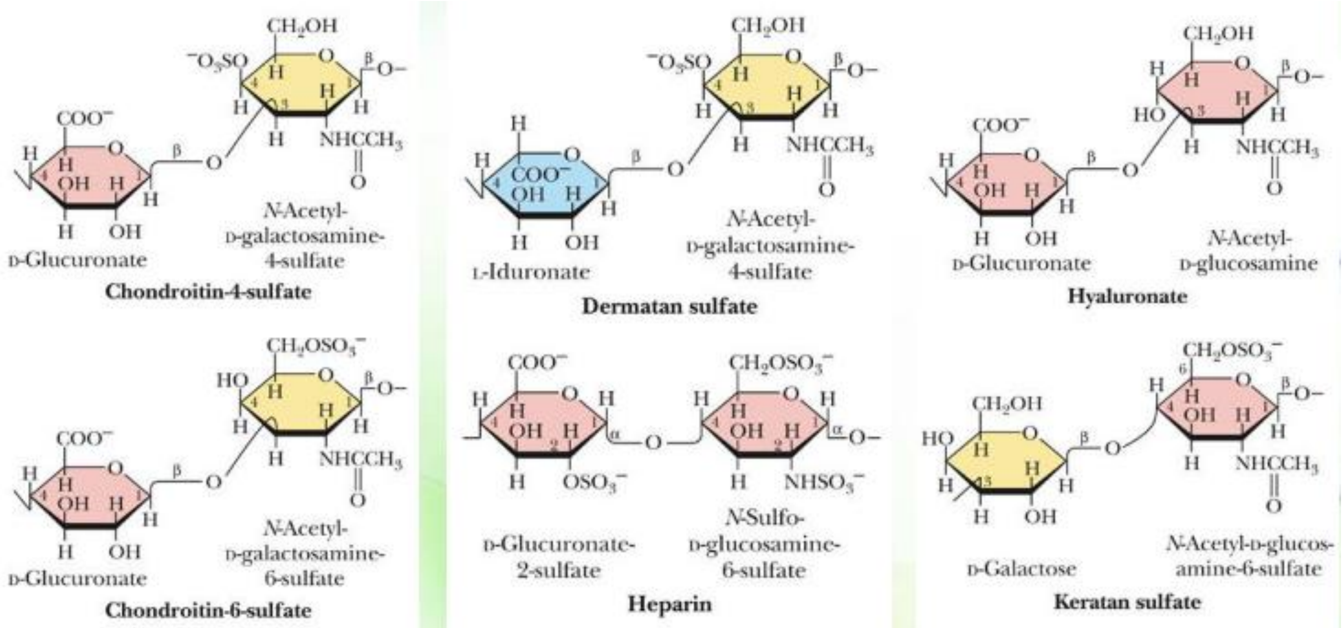
Polysaccharides are non-reducing → They will test negative in oxidation tests.

Glycosaminoglycans (GAGs)

They are different types of polysaccharides found in **ECM** made of repeating units of disaccharides, and they are heteropolysaccharides. The sugars making the disaccharide (repeating unit) has a negatively charged carboxylate (oxidized sugar with carboxyl group that donates the proton and becomes negatively charged).

GAGs are highly polar molecules so they must have a highly polar monomers in their repeating units (negative charge) either by sulfate group which is negatively charged or a carboxyl group, also they may have an amino group (amino sugars: galactosamine, glucosamine..etc) that is highly electronegative and makes polar bonds.

So they are going to attract water molecules towards them--specifically that they are present in the ECM-- and become larger in size and they will act as cushions (shock absorbers) so your cartilage won't be broken easily when it is traumatized.



NOTE: you're not required know the composing monomers of the examples but you have to know the general properties.

To sum up: GAGs are Polysaccharides with disaccharide repeating units these disaccharides are made of monomers and these monomers are modified sugars either with carboxyl group sulfate group in addition to the amino group.

Localization and function of GAG

Hyaluronate: found in synovial fluid (fluid between joints to lubricate them), and in the vitreous humor in the eye (الجسم الزجاجي), it is also present in ECM of loose connective tissue.

Its function is to lubricate the joints and this would make them shock absorbing, and it might be used by dentists for cosmetic reasons.

Chondroitin sulfate: is present in cartilage (chondroitin refers to cartilage), and present also in bones and heart valves. It's the **most abundant** GAG.

Its function to bear load which protects the tissue of being broken; for example heart valves get exposed to pressure that pushes the blood into the body so they need to stay as they are or they may get some distortion but they return to their original position after the pressure is removed.

Heparan sulfate: present in basement membrane of epithelial cells, it's also a component of cell surfaces.

It is a natural anticoagulant (reduce the risk of blood clots), and it is found in mast cells.

Dermatan sulfate: dermatan means skin; so it is present in skin as well as blood vessels and heart valves.

Keratan sulfate: it aggregates with chondroitin sulfate, so where chondroitin sulfate is localized you expect to find keratan sulfate. And its function is like chondroitin sulfate.

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

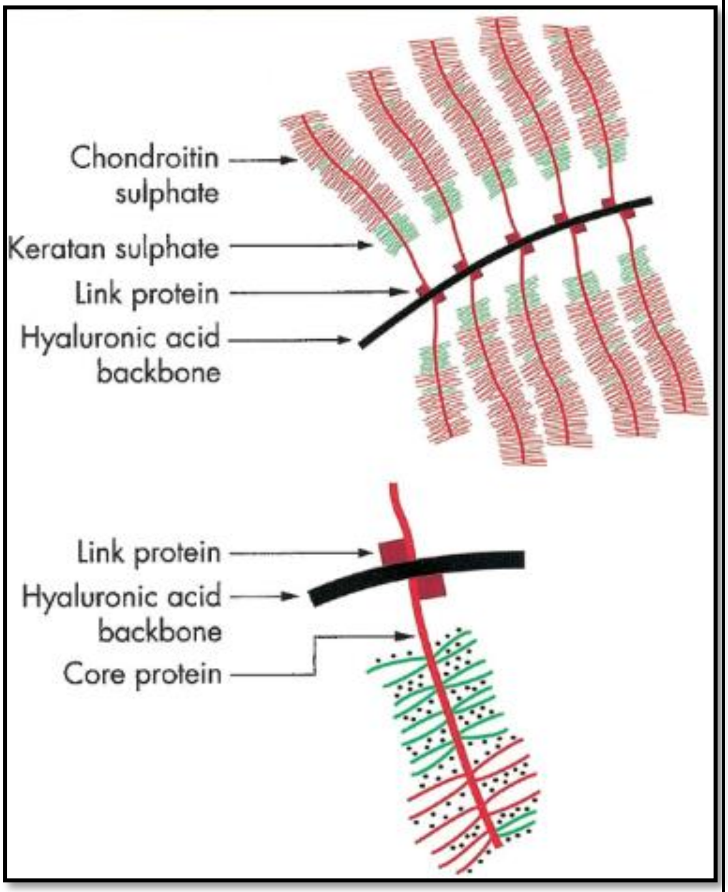
Proteoglycans

It is made of GAGs associated with small protein part.

As the name implies, the major component is the suger, and the minor component is the core protein.

Different types of proteoglycans are different in the ECM as a structural component of distinct examples of connective tissue.

Their main function is to lubricate through their GAG component (suger), they are also essential for adhesion and Interaction between cells, and they also combine and interact with the outer environment surrounding cells, and stimulate cellular proliferation.

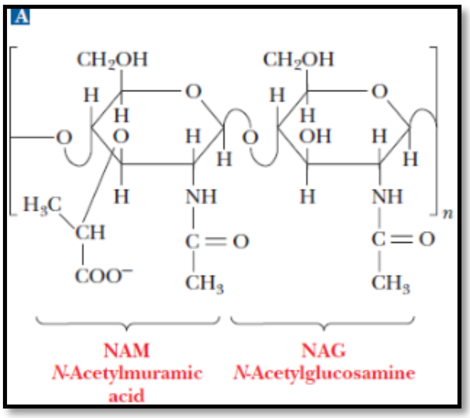


Proteoglycans change a lot with changes in the outer (surrounding) environment around cells; for example the amount of branches (bristles) may change, so whenever we have less bristles, their density will be lower as a result there would be more spaces in the ECM for transport and passage of other molecules, AND VICE VERSA.
So depending on the situation and condition to which the cell is exposed there will be changes in the structure and complexity of proteoglycans as well as ECM.

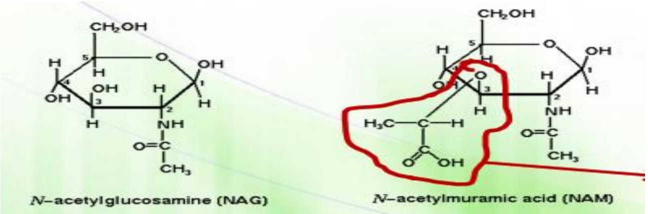
Bacterial cell wall

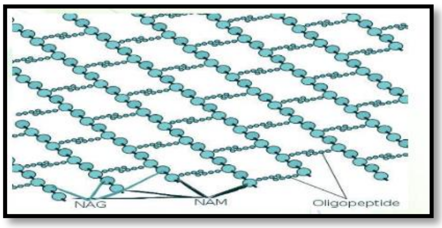
Here the polysaccharides are a structural components of the bacterial cell wall.

The components of the heteropolysaccharide are *N*-Acetylmuramic acid (NAM) and *N*-Acetylglucosamine (NAG)
(NAM) is actually a (NAG) with an addition of an extra Unit to the OH group on C4; so we lost the hydrogen And replaced it with three carbon unit and it has a carboxyl group (lactic acid).



lactic acid

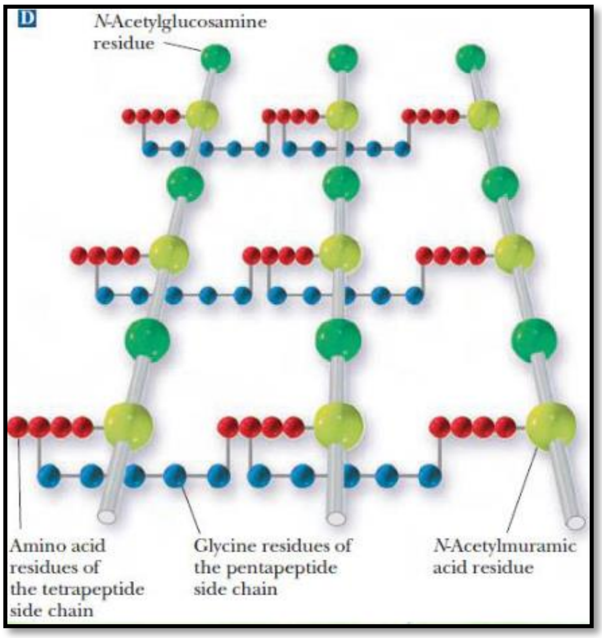




How are polysaccharides organized?

Polysaccharides are alternating and connected by oligopolypeptide for cross linking.

This picture shows how polysaccharides forming bacterial cell wall are organized, so they form long chains that are parallel to each other to strengthen the structure.
And they get cross-linked by using peptides (short chains of amino acids) which is with the Muramic acid named Peptidoglycan.



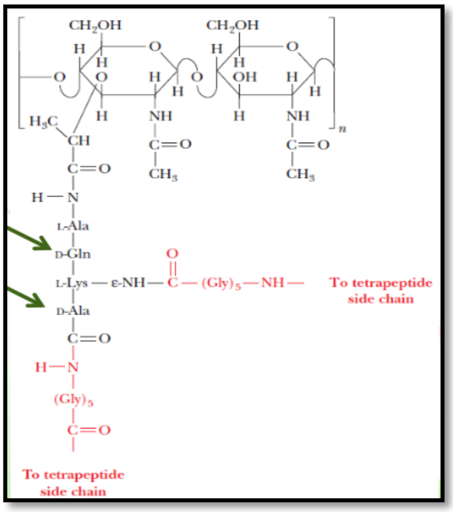
Peptidoglycans

- they contain peptides not long proteins so they are not proteoglycans.

- The main component is sugar and the minor one is peptides (short chains of amino acids).

Peptidoglycans structure: (see picture below)

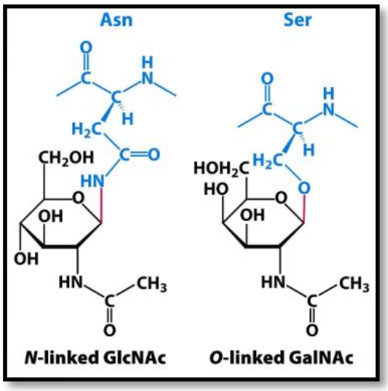
- It is composed of muramic acid extending from it 4 amino acids (alanine, glutamine, lysine, alanine),
- Attached to number 3 (lysine) five glycine residues.
- The last glycine interacts with the last amino acid (alinine) in the adjacent chain which is connected to another muramic acid.



This complicated structure (polysaccharides cross- linked through peptides) make the bacterial cell wall highly rigid.

Glycoproteins

- They are molecules that contain sugar components but they are not polysaccharides, actually they are oligosaccharides connected to a protein component
- The major component is protein while the minor one is sugar (carbohydrate)
- Carbohydrates are linked to the protein via either O-glycosidic (O atom) or N-glycosidic (N atom) bonds.
  - The N-glycosidic linkage is through the amide group asparagine (Asn, N).
  - The O- glycosidic linkage is to the hydroxyl (OH) of serine (Ser, S), threonine (Thr, T) or hydroxylysine (hLys).



Significance of protein-linked sugars (glycoproteins)

Sugars can be added to : soluble proteins (proteins present in the ECM as free proteins, secreted proteins or proteins found in the cytosol or different organelles which are not connected to membranes).
They can also be added to membrane proteins which would support the function of it.

The addition of these sugar components may have different functions such as:

- Protein folding :the presence of the sugar component may guide or facilitate the folding and formation of the final 3D shape of a protein, and if this sugar is removed the protein wont fold properly to its functional 3D shape
- Protein targeting :if a protein is synthesized inside the cell and should go to the cell membrane or lysosomes or any other place, so many of the localization sequences or signals are made of carbohydrates (sugars) coming out from glycoproteins
- Prolonging protein half-life and functionality
- Cell-cell communication: because the interaction between different cells may happen through these sugar components on their surfaces that are part of glycoproteins.
- Cell signaling: means interaction between cells and transporting signals from outside the cell to the inside. Many of the receptors that are present on cell surface are glycoproteins as well as some soluble proteins along the signaling pathways.

Blood typing - ABO System

-As you know there are two ways to classify blood groups:

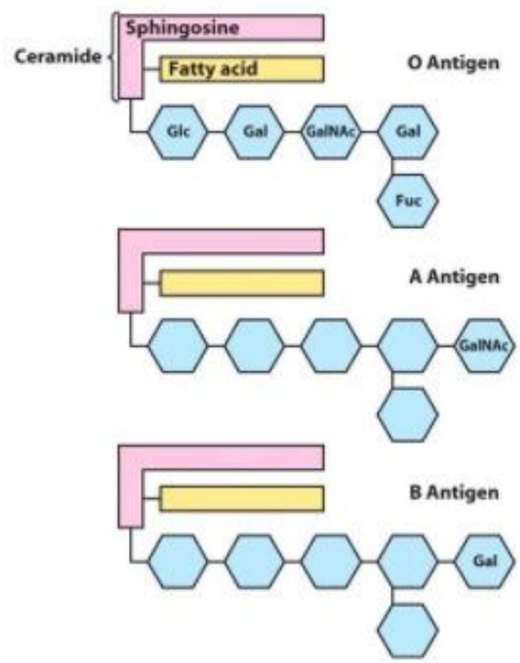
1. **ABO system** (**A**, **B**, **AB**, **O**)

2. **Rh factor** (**Positive +** , **Negative -**)

But here we are concerned with **ABO system**.

-It's an application on the importance of sugars, specifically **glycoproteins** and **glycolipids**.

-In the cell membrane of RBCs, we have glycoproteins and glycolipids which contain a sugar component, specifically an **oligosaccharide**. This oligosaccharide is **variable** among individuals, and actually it's what **determines the blood group**, as in the picture:



-As you can see, **Glc** - **Gal** - **GalNAc** - **Gal** - **Fuc** is found in all blood types, but the difference is:

- **O** blood type → **No** extra monosaccharides.
- **A** blood type → Extra **GalNAc**.
- **B** blood type → Extra **Gal**.
- **AB** blood type → Extra **GalNAc** and **Gal**.

-Person with **O** blood group **can give blood to any blood group** whether it's **O**, **A**, **B** or **AB**. This is because the antigens he has are present in all of them, so they're not recognized as foreign bodies and blood can be accepted by the recipient patient.

Glc = Glucose

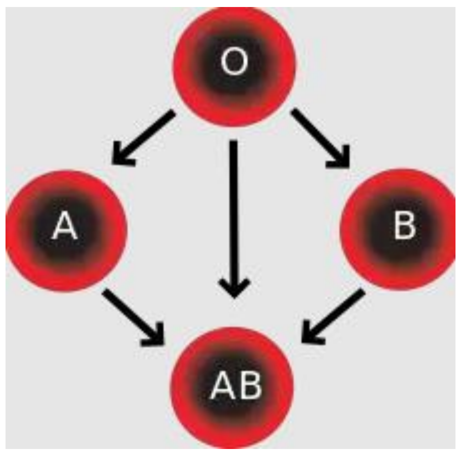
Gal = Galactose

GalNAc = Galactosamine

Fuc = Fucose (Reduced galactose)

-Person with **A** blood group **can donate blood to A and AB** blood groups, because the antigens he has are present in all of them, so they're not recognized as foreign bodies and blood can be accepted by the recipient patient. But he **can't give blood to O or B** blood groups, because his antigens are going to be recognized as foreign bodies and they would be attacked by antibodies.

-This picture summarizes **blood transfusion**:



Short Quiz

1. **The difference/s between glycogen and amylopectin are:**

    a. Bond type
    b. Source and Branching
    c. Source and Bond type
    d. Monomers

2. **One of the following polysaccharides is heteropolysaccharide:**

    a. Chitin
    b. Pectin
    c. Starch
    d. Dextran

3. **Which of the following polysaccharides is related to teeth diseases:**

    a. Dextran
    b. Pectin
    c. Starch
    d. Glycogen

4. **Which is the incorrect blood transfusion process:**

    a. A → AB
    b. O → AB
    c. B → O
    c. O → A

5. **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. They are attached to proteins forming proteoglycans.

Answers:

1. b   2. b   3. a   4. c   5. d