8

BIOCHEMISTRY

faculty of medicine - JU2017

◉ Sheet ○ Slides

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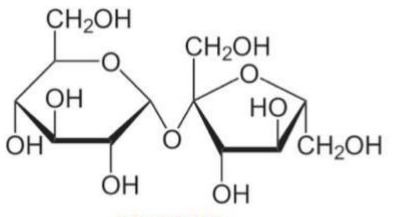
Modified Disaccharides

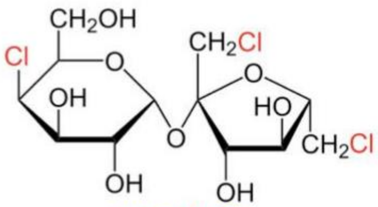
The following compounds are artificial sweeteners:

1. Saccharine. (an old one)
2. Aspartame: an amino acid that also gives a sweet taste.
3. Sucralose (artificial sweetener):
    - It's not a sugar.
    - It's a sugar substitute.
    - Chlorinated Sucrose.
    - Can't be metabolized → No. of calories = Zero (noncaloric).

Some studies say that Saccharine causes cancer in mice, but there is no sufficient evidence to indicate that it causes cancer in humans.



sucrose



sucralose

Milk Problems

Not everyone can drink milk peacefully, some may have:

Lactose Intolerance: A deficiency in the enzyme lactase in the intestinal villi allows lactase of intestinal bacteria to digest it producing hydrogen gas, carbon dioxide, and organic acids and leads to digestive problems (bloating and diarrhea), vomiting and abdominal cramps.

Galactosemia: Missing a galactose-metabolizing enzyme can result in galactosemia where nonmetabolized galactose accumulates within cells and is converted to the hydroxy sugar galactitol, which cannot escape cells. Water is drawn into cells by osmosis and the swelling causes cell damage, particularly in the brain, resulting in severe and irreversible retardation; therefore, it must be detected early in infants . It also causes cataract.

Cataract: a diseased area that can grow on a person's eye and cause difficulty in seeing

Oligosaccharides (Trisaccharides)

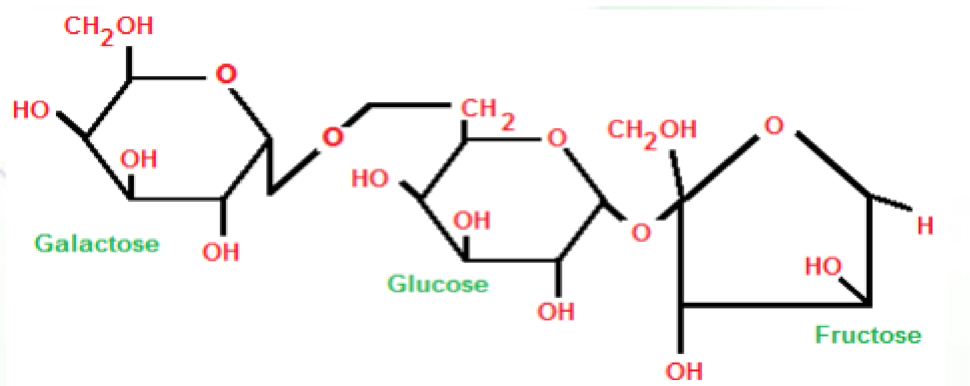
Ex: Raffinose: Its structure may seem like it's composed of a

Disaccharide and a Monosaccharide attached to it

Sucrose (glucose+fructose) ← → Galactose

However, it was originally a galactose molecule to which glucose got added to, then fructose got added as well. It is useful to recognize the sucrose structure in it.

- It's found in beans and vegetables such as cabbage, brussels sprouts, broccoli and asparagus.
- Humans lack the alpha-galactosidase enzyme that is needed to break down raffinose. Intestinal bacteria can ferment it into hydrogen, methane, and other gases which result in bloating.

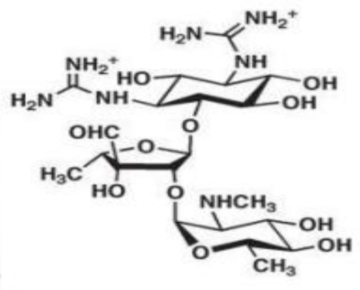


- Glycosidic bond between glucose and galactose is α (1-6) O-glycosidic bond.
- Glycosidic bond between glucose and fructose is α (1-s) O-glycosidic bond

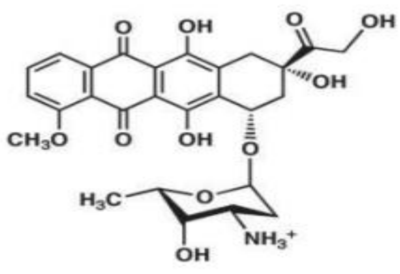
Modified Oligosaccharides can be used in medicine:

1. Streptomycin and erythromycin (antibiotics): used for upper respiratory tract infections that are common during the winter.
2. Doxorubicin (cancer chemotherapy).

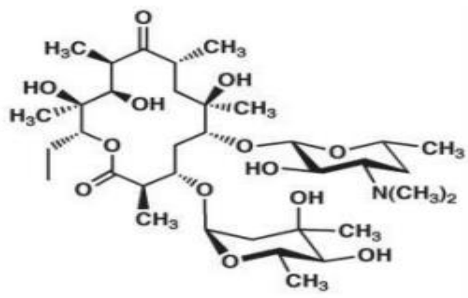
3. Digoxin (cardiovascular diseases).



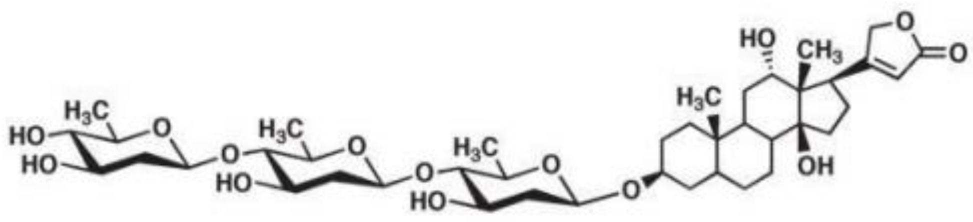
Streptomycin



Doxorubicin



Erythromycin A



Digoxin

Polysaccharides

Polysaccharides can be:

I. Homopolysaccharides (Homoglycan) → repetitive sequence of the same monosaccharide (residue).
II. Heteropolysaccharides → residues are different.

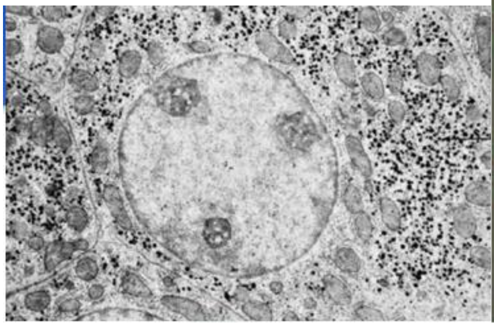
Features of polysaccharides:

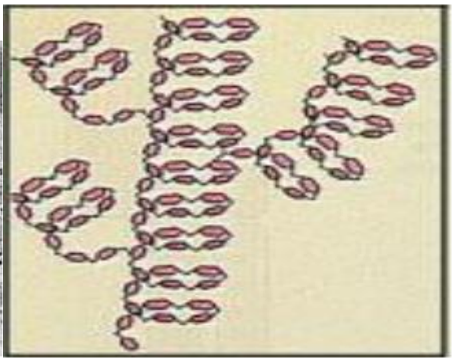
I. Monosaccharides and whether it is α or β.
II. Length.
III. Branching.
IV. The type of the bond (the carbons involved in the glycosidic bond).
V. Purpose:
   - Storage (glycogen, starch, dextran)
   - Structural (cellulose, pectin, chitin)

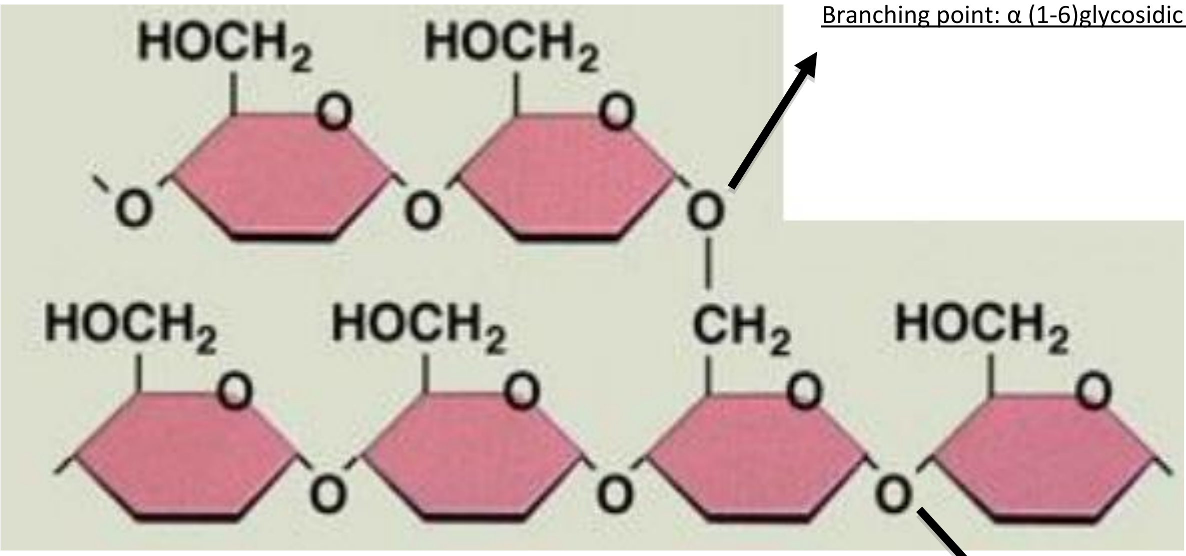
Polysaccharides include the following:

1. Glycogen:

- A storage polysaccharide found in mammalian cells (humans and animals). It doesn't exist in bacteria or plants.
- Homopolysaccharides (glucose residues).
- Mainly used to produce energy.
- 90% of glycogen in our body is stored in liver cells, and 10% in muscle cells.
- Highly branched.
- Glycogen is stored as granules and look like droplets containing excess glucose in our bodies (glucose is stored in the form of glycogen).
- The bond between two residues of glucose within the chain: α (1-4) glycosidic bond.
- Branching occurs every 10 residues, and the bond at branching points: α (1-6) glycosidic bond.

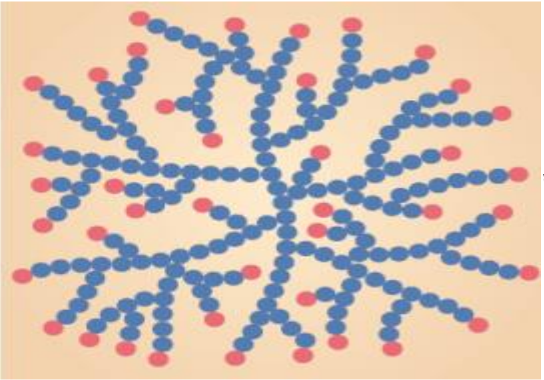






Branching point: α (1-6)glycosidic bond

α (1-4)glycosidic bond

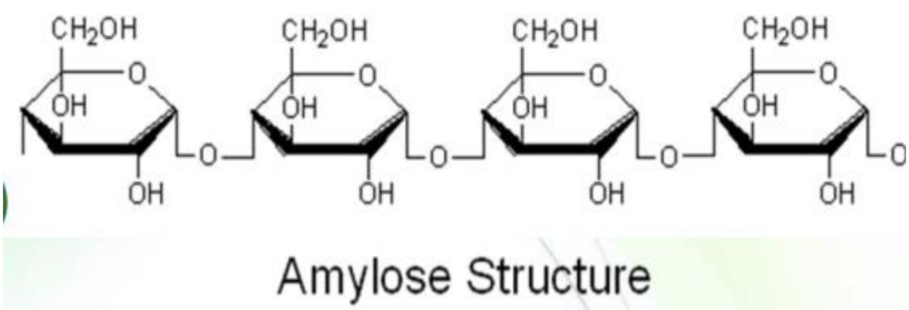


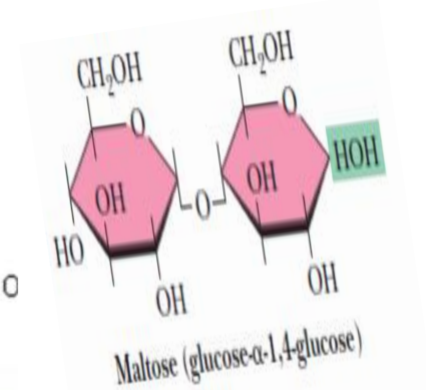
Red points: the terminal glucose residues

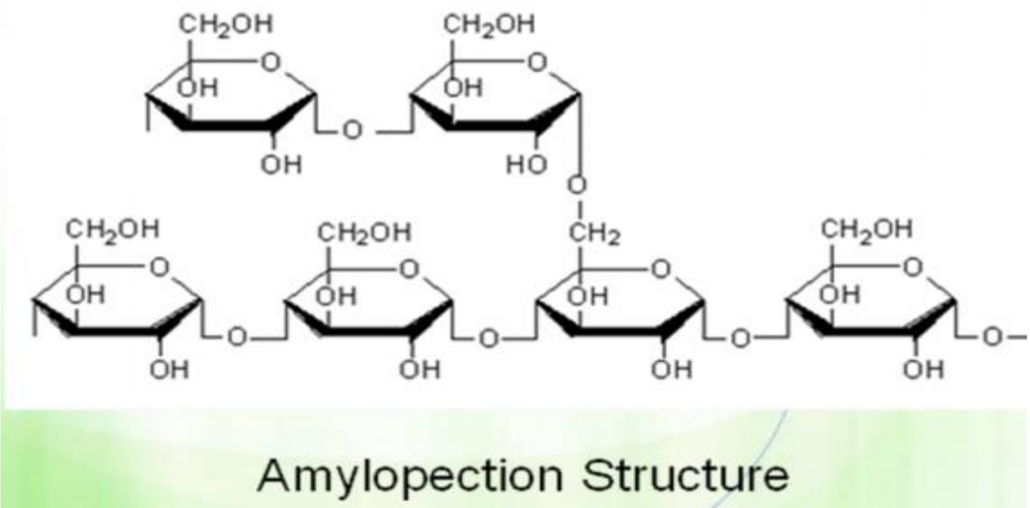
2. Starch:

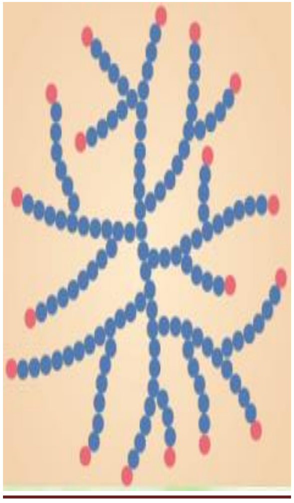
- Found in plants.
- Homopolysaccharides (glucose residues).
- Storage polysaccharides.
- It exists in two forms:
  - ✓ Amylose (10%-20%)
  - ✓ Amylopectin (80-90%)

  ➔ Amylose is unbranched, while Amylopectin is branched.
- Bonds within the chain (Both forms): α (1-4) glycosidic bond.
- The bond at branching points (Amylopectin): α (1-6) glycosidic bond.
- Branching occurs every 25 residues in Amylopectin. Amylopectin is less branched than Glycogen.









<u>What is the importance of α-linkage in these molecules??</u>

α-linkage allows the chain to bend. This bending molecule which stores glucose takes a smaller space in cells. As a result, high amounts of glucose can be stored in a small space).

And that's why glycogen and starch are flexible and can be coiled.

<u>Advantages of branching:</u>

1) More branching means that there are more terminal glucose residues that are easier to be removed by enzymes during metabolism. In contrast, less branches → less terminal residues → less accessible glucose → removal of these terminal glucose residues will be slower.
2) H_2O is required to solubilize glycogen and starch ... as branching increases, less amount of water is needed. Therefore, starch, which is less branched, is found in plants where a high amount of water is present (less water soluble).
   In mammalian cells, branching must be extensive(glycogen) to consume less H_2O (more water soluble).
   **the more terminals there are, the more soluble the polysaccharide is.

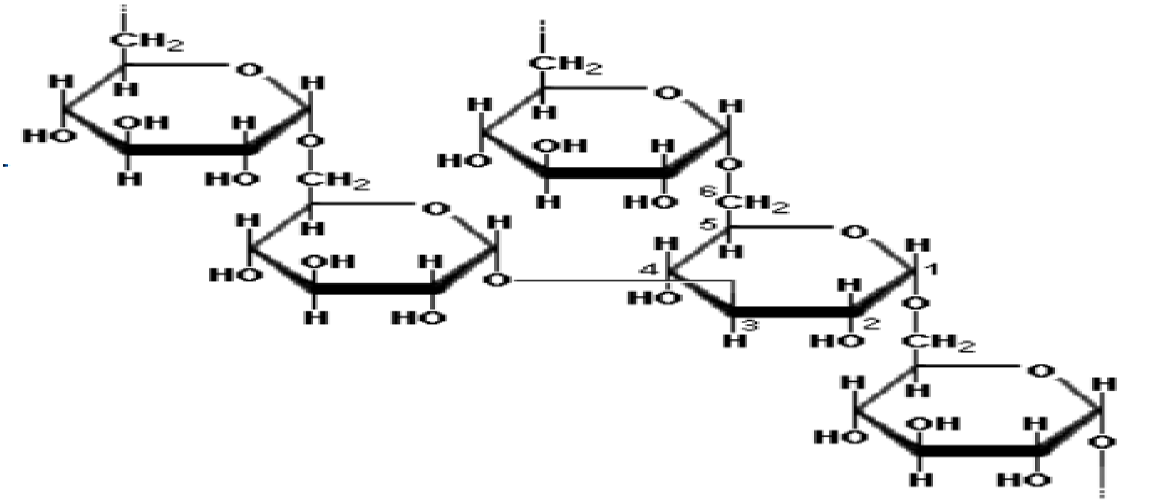
Glycogen vs. amylopectin

- Glycogen and amylopectin have the same monomer, and both are branched.
- Glycogen exists in animals. Amylopectin exists in plants.

- Glycogen is more branched than amylopectin.
- Branch points occur about every 10 residues in glycogen and about every 25 residues in amylopectin.

3. Dextran:

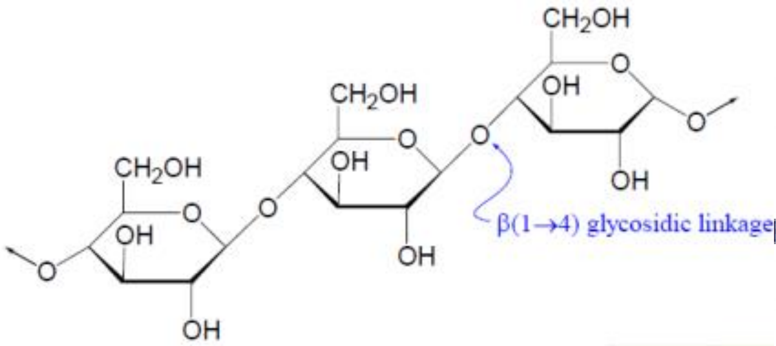
- Storage polysaccharides.
- Homopolysaccharides (glucose residues).
- Present in yeast and bacteria.
- There is a diversity in types of glycosidic bonds in Dextran:
  - α-(1-6)-D-glucose with branched chains.
  - Branches: α (1-2), (1-3), or (1-4).

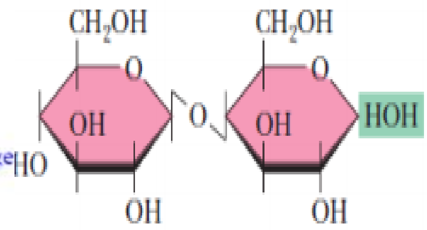


4. Cellulose:

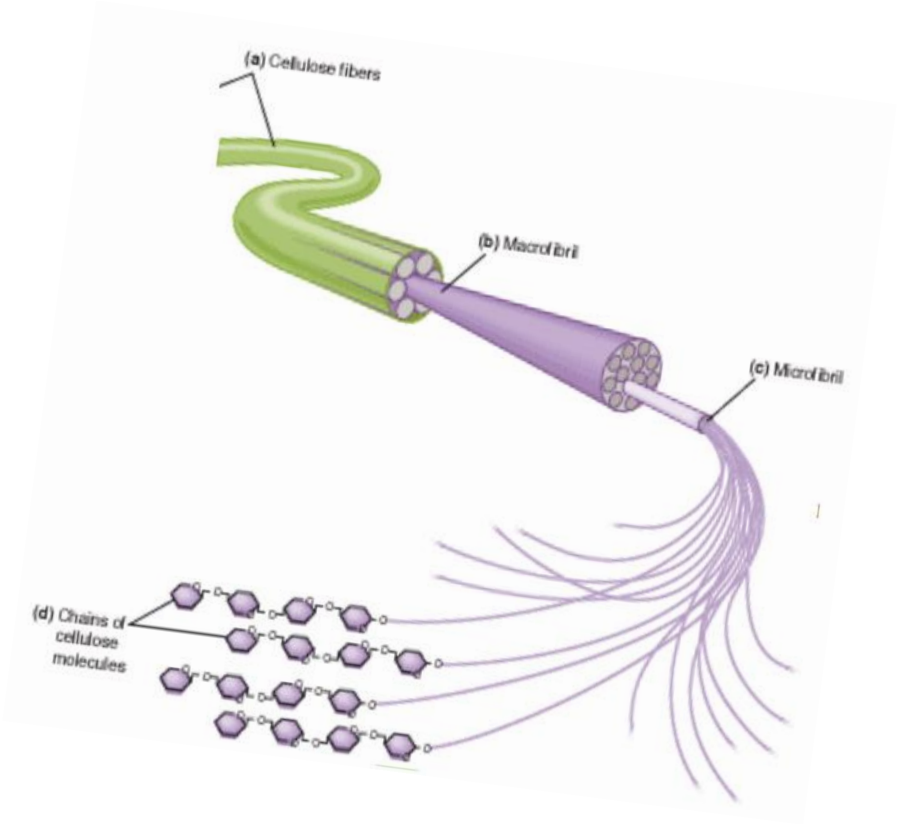
- Found in plants.
- Homopolysaccharides (glucose residues).
- Not branched.
- Not flexible (doesn't bend) due to the β-linkage.
- β -(1-4) glycosidic bond.
- Purpose: structural support (***β***) (no storage or energy purposes).

Ex: stem is rigid, **why**? Because cellulose chains are made of β bonds and these chains are firmly packed together due to hydrogen bonds → they form non-flexible fibers that give support to plants.



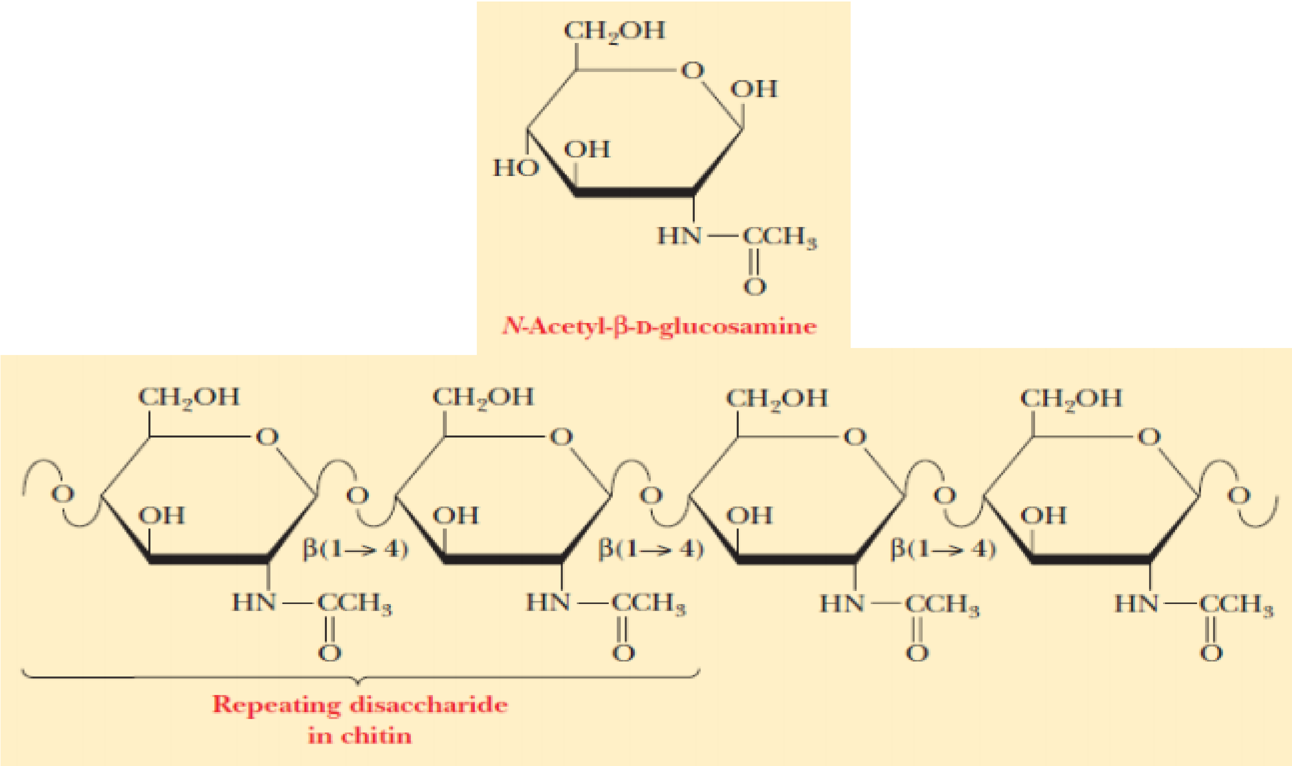


Cellobiose (glucose-β-1,4-glucose)



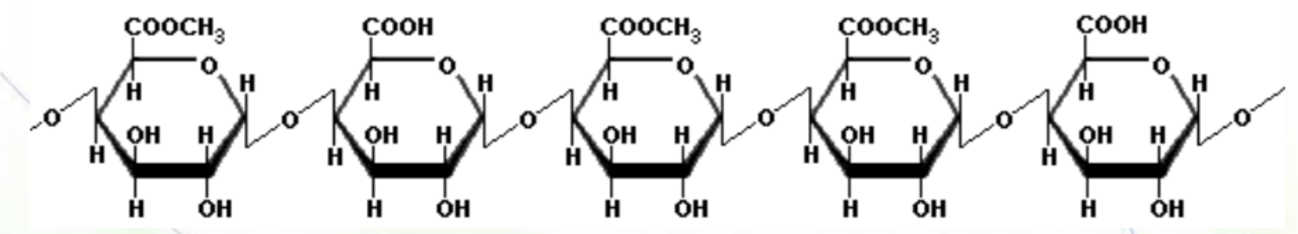
5. Chitin:

- ❖ Homopolysaccharides.
- ❖ Structural support.
- ❖ In crabs, cockroaches, and any insect that has a solid exoskeleton.
- ❖ Not branched.
- ❖ β-(1-4) glycosidic bond.
- ❖ Monomers: N-Acetyl-β-D-glucosamine.



6. <u>Pectin:</u>

- Found in plants, but in less amounts than cellulose.
- It could be heteropolysaccharides (most abundant) or homopolysaccharides.
- It's made of a modified monosaccharide (sugar **<u>acid.)</u>**
- The sugar acid can be modified (methylated).
- Original monosaccharide: **<u>Galactose</u>** (hydroxyl group of the 4th carbon is directed up).
- There is no specific order between methylated and non-methylated sugar acids within the chain.
- Glycosidic bond α-(1-4)
-



<u>Are polysaccharides reducing??</u>

<u>In general **no**:</u>

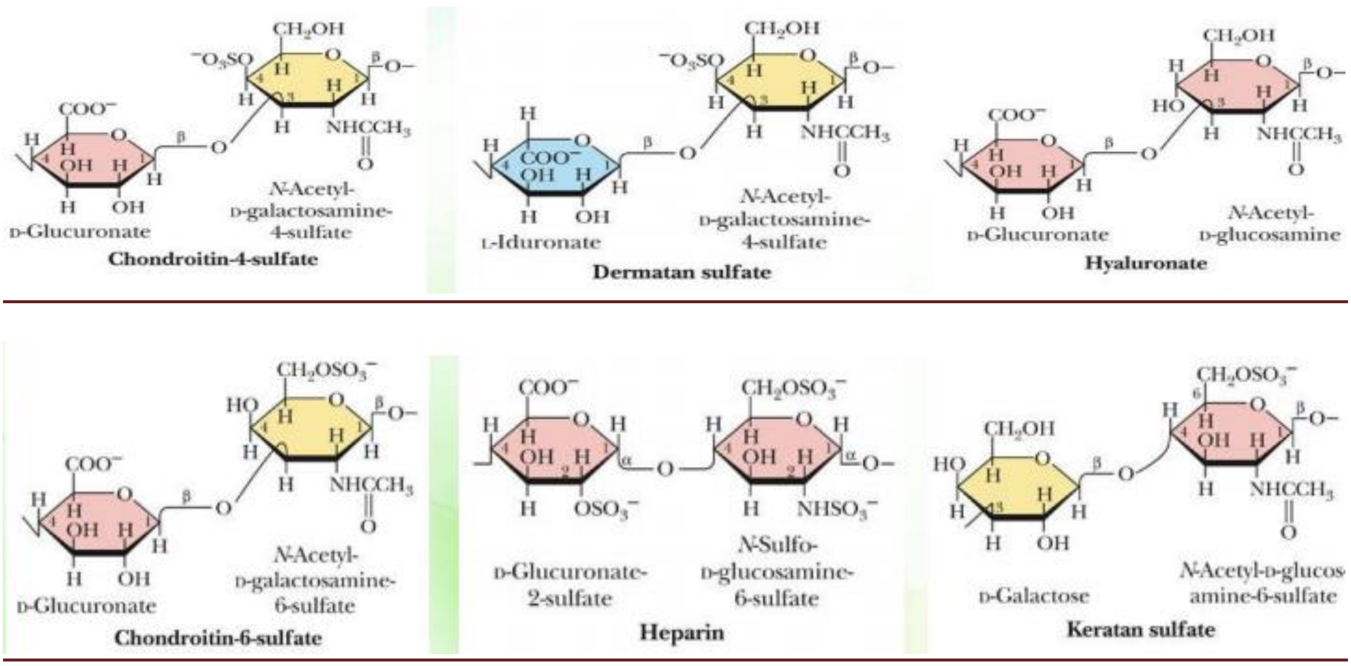
I. The number of residues containing free anomeric carbons is small compared to the molecule, so we can't consider polysaccharides as reducing.

II. A sample that contains only a few molecules of a large polysaccharide, each molecule with a single reducing end, might well produce a negative test because there are not enough reducing ends to detect.

7. Glycosaminoglycans:

- Long unbranched modified polysaccharides consisting of repetitive disaccharide units (heteropolysaccharides).
- They are modified by having Amino groups attached to them.
- They can be further modified by adding sulfate or carboxyl groups: at least one of the sugars in the repeating unit has a negatively charged carboxylate or sulfate group, so they are negatively charged molecules.
- They are all exist extracellularly and form a large structure that is called ***Matrix***.
- Derivatives of an amino sugar, either glucosamine or galactosamine.
- Examples:
    - Heparin (natural anticoagulant in blood).
    - Dermatan Sulfate (in tissues of skin).
    - Keratan Sulfate Hyaluronate.
    - Chondroitin-4-Sulfate.
    - Chondroitin-6-Sulfate.

Dermatology is the branch of medicine dealing with the skin, nails, hair and their diseases.



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

→ You will only be asked about information highlighted in red.

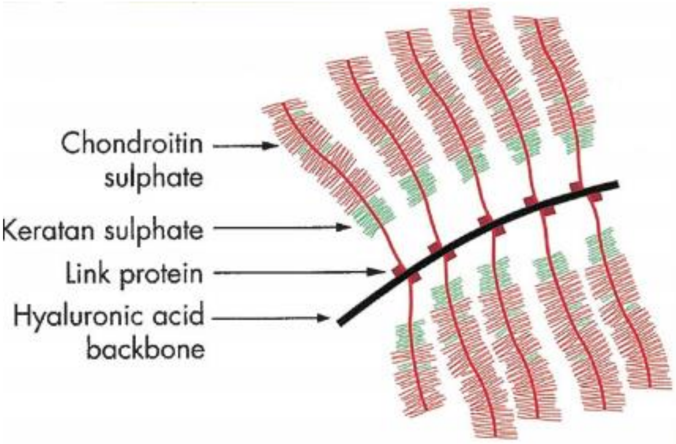
What is the importance of negative charges ofGAGs??

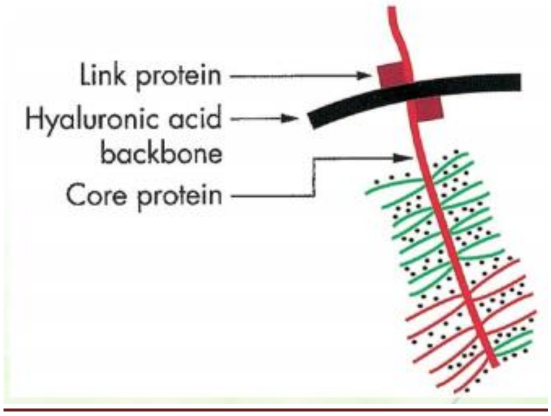
1. Negative charges help in maintaining molecules (Glycosaminoglycans).
2. In cartilage: repulsion force arises between -ve charges after collapse to support joints→ that's why elderly people who have joints' pain are advised to take chondroitin sulfate (glucose amine). However, there is no proof of its usefulness (once it reaches the stomach, it undergoes metabolism).

8. Proteoglycans:

- Glycosaminoglycans can be organized into Proteoglycans.
- Proteoglycans: large sugar molecules with some peptides (GAGs+Peptides).
- Lubricants (minimize friction).
- Structural components in connective tissue.
- Mediate adhesion of cells to the extracellular matrix.
- Bind factors that stimulate cell proliferation.

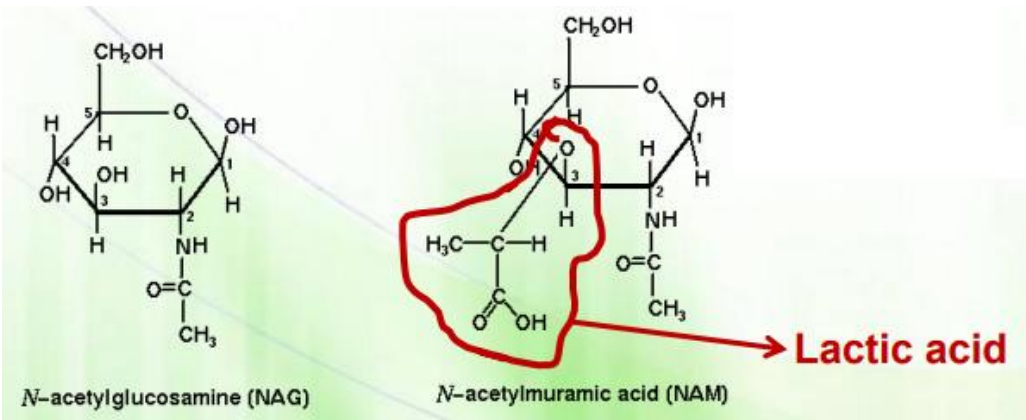
structure as shown in the figures.





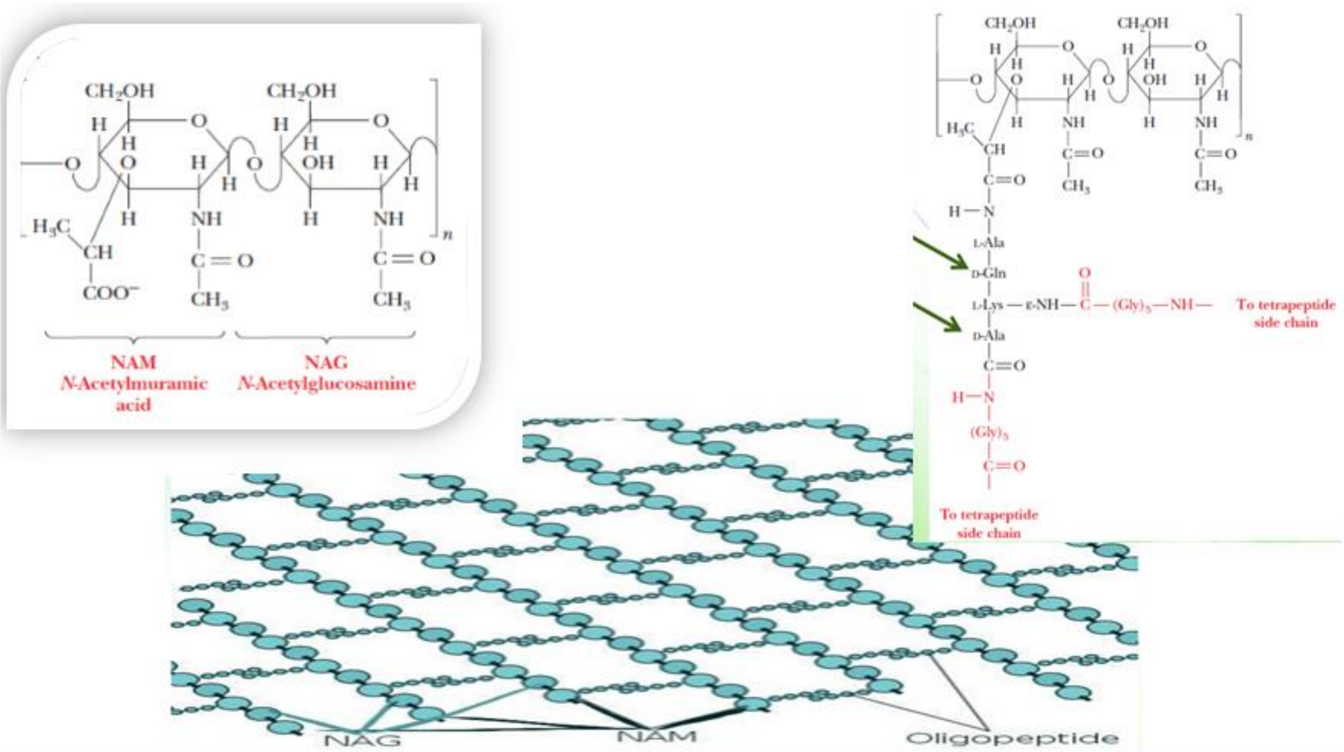
9. Peptidoglycans:

- Modified proteoglycans in Bacterial cell wall.
- Composed of repetitive units of disaccharides (NAM, NAG, NAM, NAG….).
- Oligopeptides: short chains of amino acid that connect long chains of peptidoglycans, also strengthens the structure of bacterial cell wall → cell wall gives strength to bacteria.
- Negatively charged due to the lactic acid.

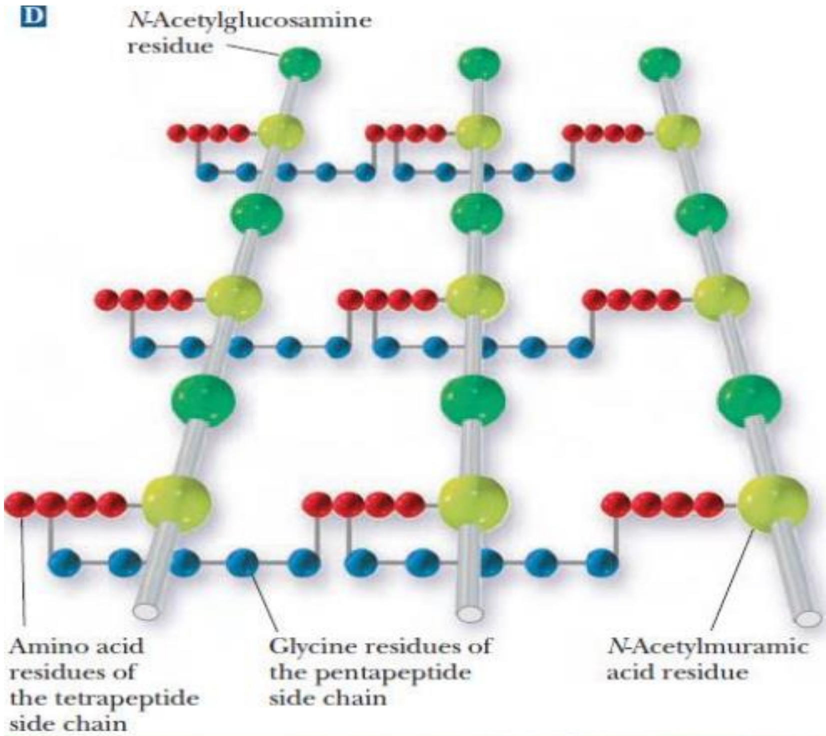


NAG: N-Acetylglucosamine

NAM: N-Acetylmuramic acid = NAG + Lactic Acid



- Structure as shown:



10. Glycoproteins:

- Proteins with little amounts of sugar.

❖ The carbohydrates of glycoproteins are linked to the protein component either by O-glycosidic or N-glycosidic bonds.
❖ The N-glycosidic linkage is through the amide group of asparagine (Asn, N).
❖ The O-glycosidic linkage is to the hydroxyl of serine (Ser, S), threonine (Thr, T) or hydroxylysine (hLys).