بسم الله الرحمن الرحيم

BIOCHEMISTRY

Lecture 7

Carbohydrates (pt. 3)

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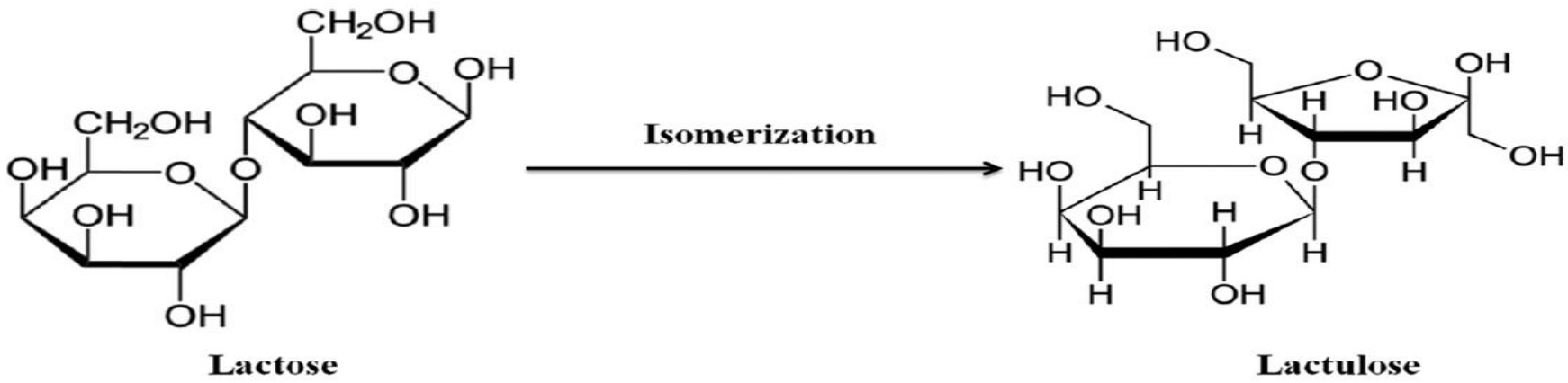
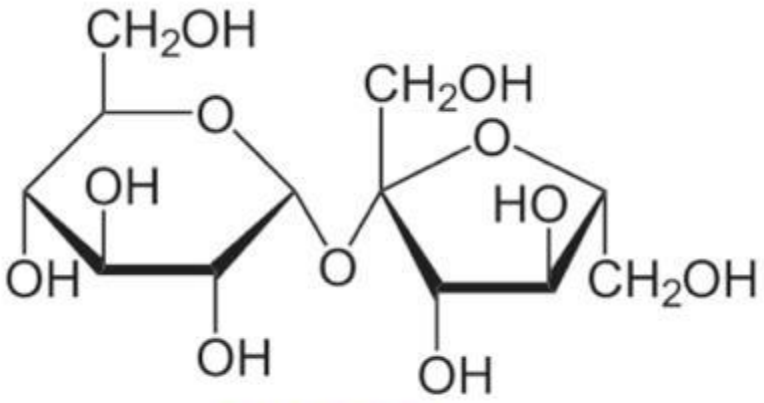
Lactulose

- It is formed by the isomerization of lactose.
- It has health benefits:
  - It is used in treating constipation.
  - It promotes the growth of health-promoting gut bacteria.

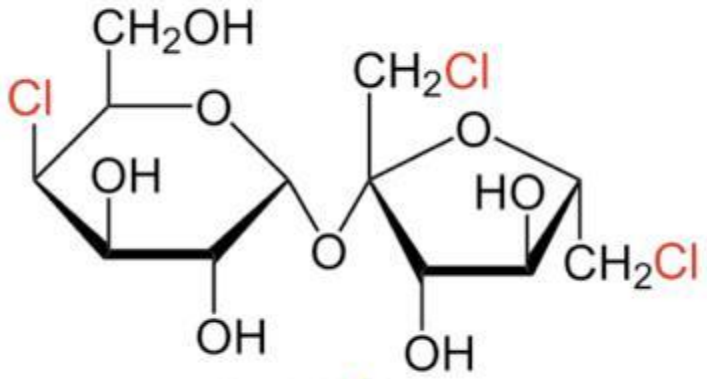
    that bacteria can fix our mood
  - It modulates the immune system.



Sucralose (artificial sweetener)



sucrose



sucralose

News > WebMD Health News

Sucralose Damages DNA, Linked to Leaky Gut: Study

Lisa O'Mary
June 01, 2023

Sucralose, a Common Artificial Sweetener, May Increase Cancer Risk

WebMD

Milk problems

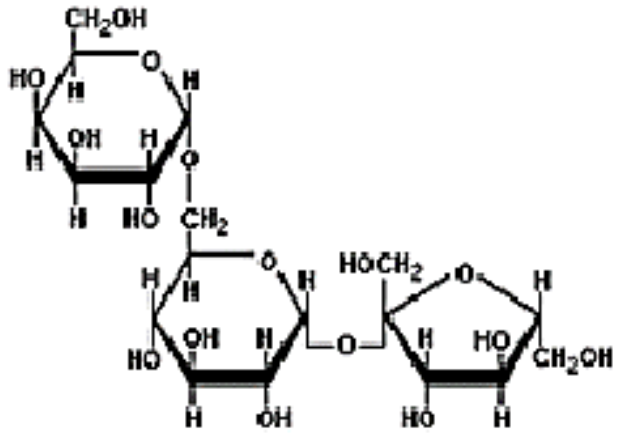
- Lactose Intolerance: A deficiency of the enzyme lactase in the intestinal villi allows lactase of intestinal bacteria to digest it producing hydrogen gas, carbon dioxide, and organic acids and leading to digestive problems (bloating and diarrhea). Some people , especially the elderly, cannot drink milk because they lack the enzyme needed to digest lactose (lactase enzyme). Lactase levels decline with age.
- Consequently, gut bacteria (named Flora), found in Large intestine, digest lactose causing production of gases, may cause muscle cramps and diarrhea for those people.
- Galactosemia: Missing a galactose-metabolizing enzymes 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 and the swelling causes cell damage, particularly in the brain, resulting in severe and irreversible mental retardation.
- It also causes cataract. It can cause blindness.

Raffinose

- What are oligosaccharides? Three to ten contiguous sugars
- Example: raffinose We lack the enzymes responsible for digesting raffinose, so bacteria are the ones that digest it which leads to gas formation

- It is found in beans and vegetables like cabbage, brussels, sprouts, broccoli, and asparagus.

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.

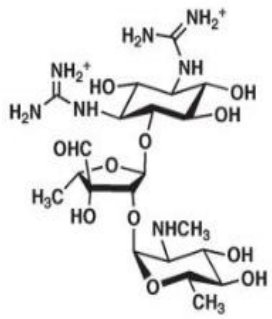


Homework

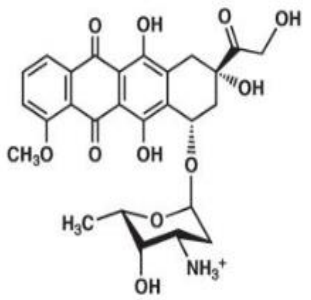
1. Recognize the monosaccharides that make up raffinose.
2. What is the monosaccharide that is attached to *what* disaccharide?

Oligosaccharides as drugs

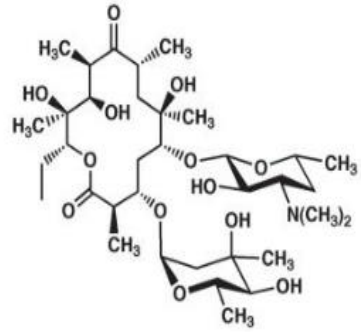
- Streptomycin and erythromycin (antibiotics)
- Doxorubicin (cancer chemotherapy)
- Digoxin (cardiovascular disease)



Streptomycin

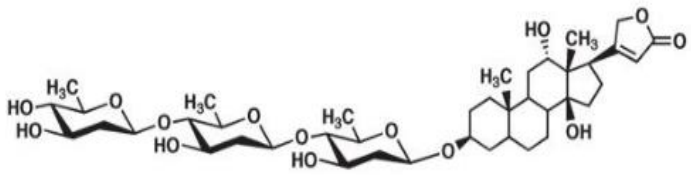


Doxorubicin



Erythromycin A

* Do not memorize the structures



Digoxin

Polysaccharides

- What are polysaccharides?
- Homopolysaccharide (homoglycan) vs. heteropolysaccharides

- Features of polysaccharides:
  - Monosaccharides
  - Length
  - Branching
  - Purpose:
    - Storage (glycogen, starch, dextran)

      For example, when there is an excess amount of glucose in your body, it is stored as polysaccharide (glycogen). When energy is needed, glucose is released from glycogen.

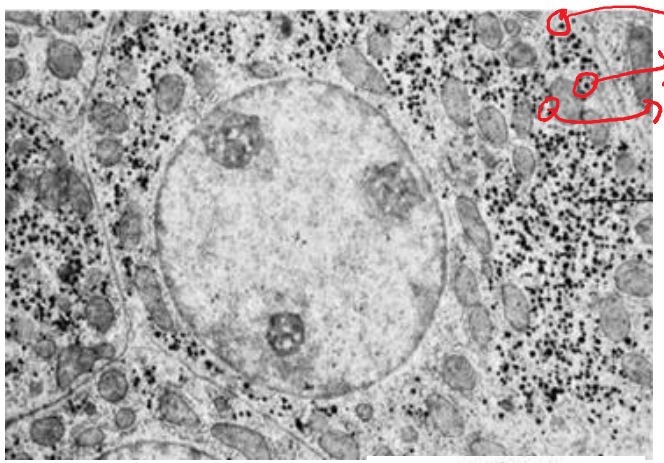
    - Structural (cellulose, pectin, chitin)

Glycogen (exists in animals and humans)

- Glycogen is a storage **homo**polysaccharide, which contains thousands of glucose molecules linked together.

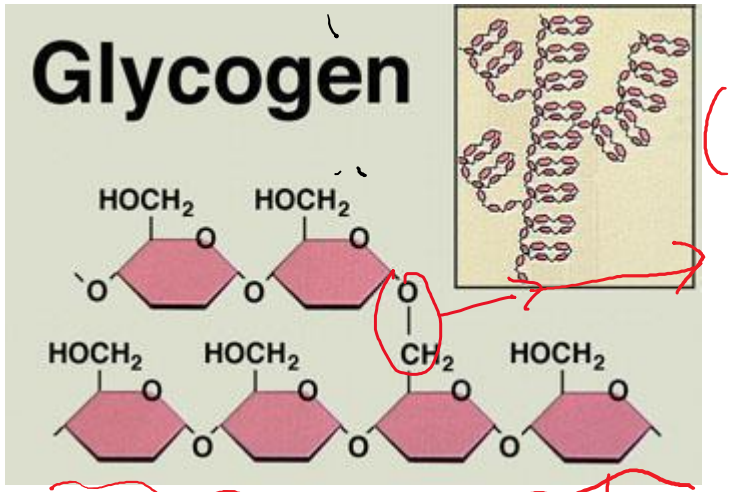
- It's highly branched.

- 90% of glycogen is found in the liver while 10% can be found in skeletal muscles.



Each black dot in this electron microscopic image is a glycogen molecule

Glycogen molecule

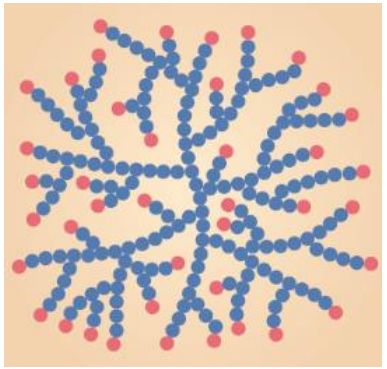


(Branch)

α(1-6)

In the chain ,Glycosidic bonds are Alpha 1- 4 .Bomds in branches are alpha 1-6.

chain α (1-4)



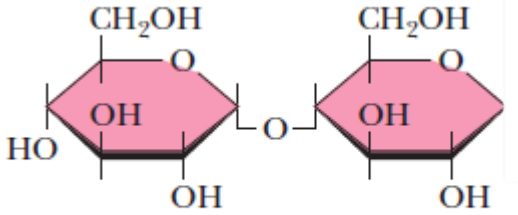
When cells Need glucose, they take it from glycogen one molecule at a time , not In big groups.

The advantage of **Alpha** glycosidic bond is that its flexible. So, the glycogen molecule and the bonds in it can rotate .Consequently, you can store as many glucose residues as possible in as little spaces as possible .

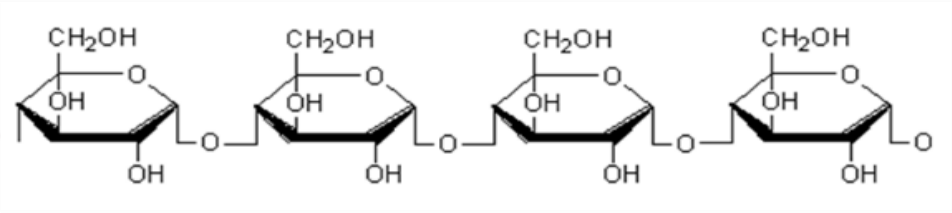
Memorize

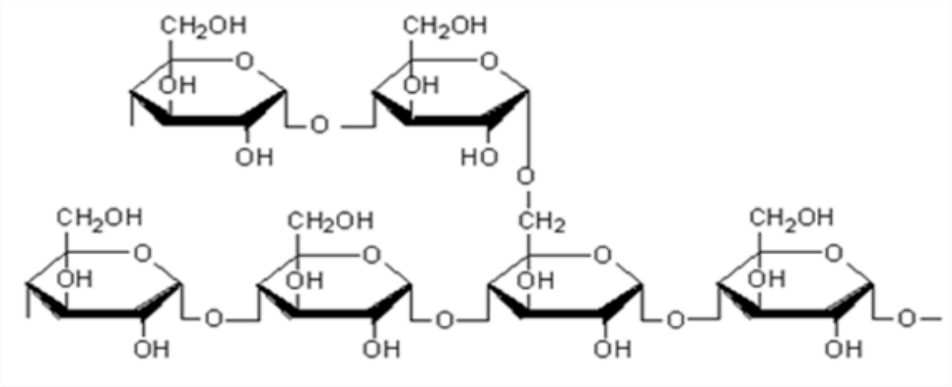
Starch it's a homopolysaccharide found in plants, it's made of glucose residues connected through glycosidic linkages.

- Which organisms?
- Forms:
  - amylose (10-20%) not branched
  - amylopectin (80-90%) branched
  - Most plant cells have 90% amylopectin and 10% amylose

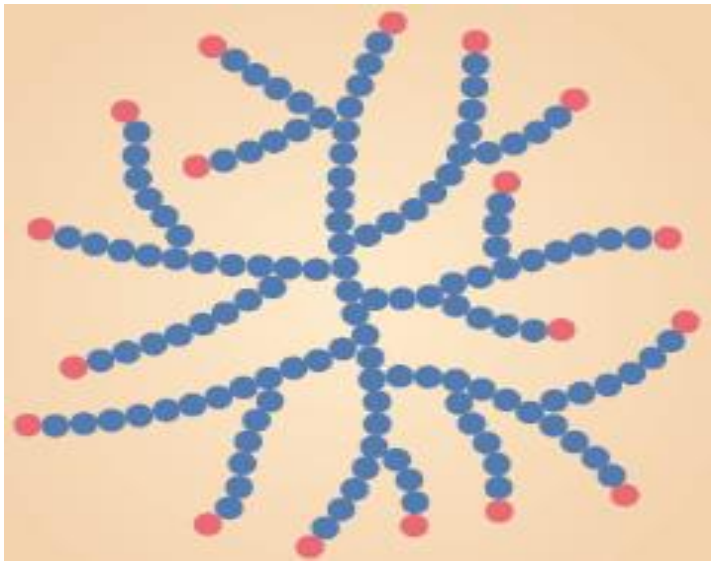


Maltose (glucose-α-1,4-glucose)


Amylose Structure


Amylopection Structure

Memorize



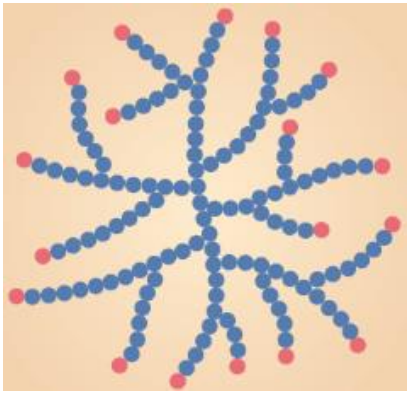
Glycogen vs. amylopectin

- Both are made from the same monomer, and both are branched.
- Glycogen exists in animals and amylopectin in plants.
- Glycogen is more highly branched. Glycogen is more branched than Amylopectin
  - Branch points occur about every 10 residues in glycogen and about every 25 residues in amylopectin.
- Why is branching important?
  - It makes it more water-soluble and does not crystallize.

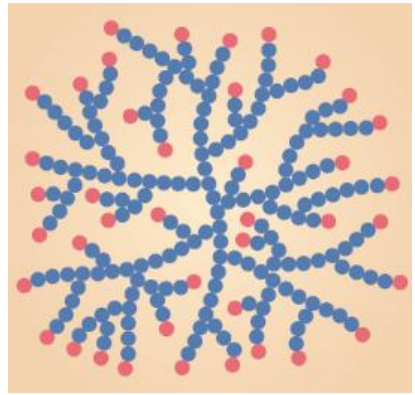
  Plants cells have more water inside them compared to human cells, and since We have less water in our cells , we need the glycogen to be more water soluble, which is achieved by more branching in the glycogen molecule.
  - Easy access to glucose residues.

  More branching means more glucose residues can be removed.

  (Remember that glucose molecules are removed one by one from glycogen)



Starch

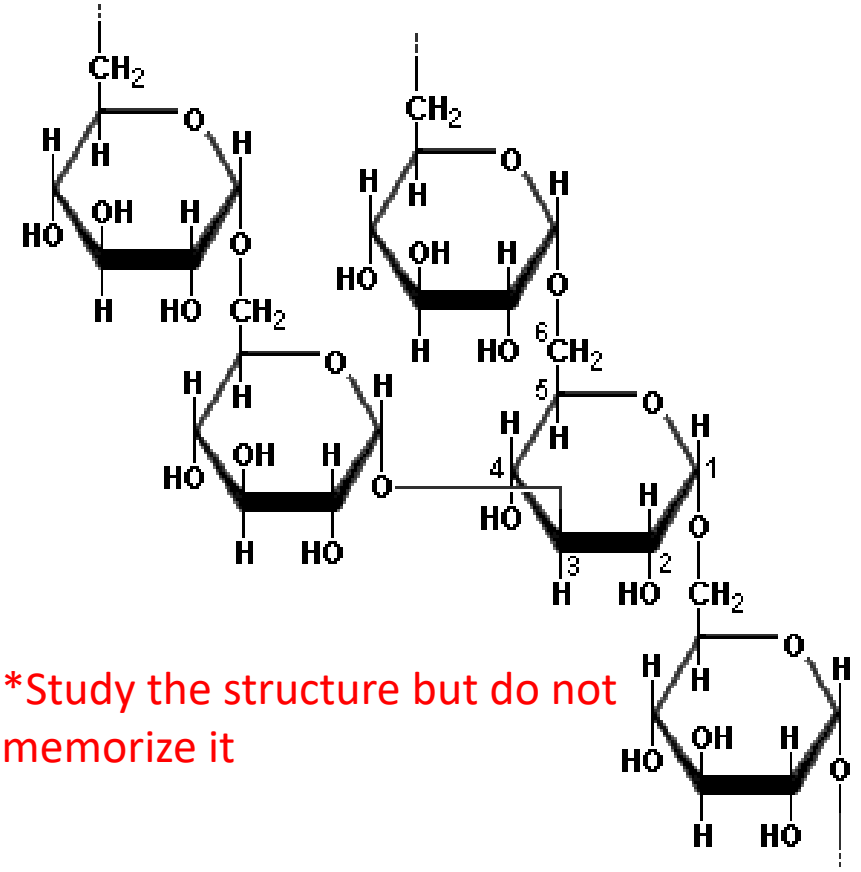


Glycogen

Dextran is a homopolysaccharide made of glucose residues.

- It is a branched molecule
- A storage polysaccharide
- Yeast and bacteria (primitive organisms)
- α-(1-6)-D-glucose with branched chains
- Branches: 1-2, 1-3, or 1-4

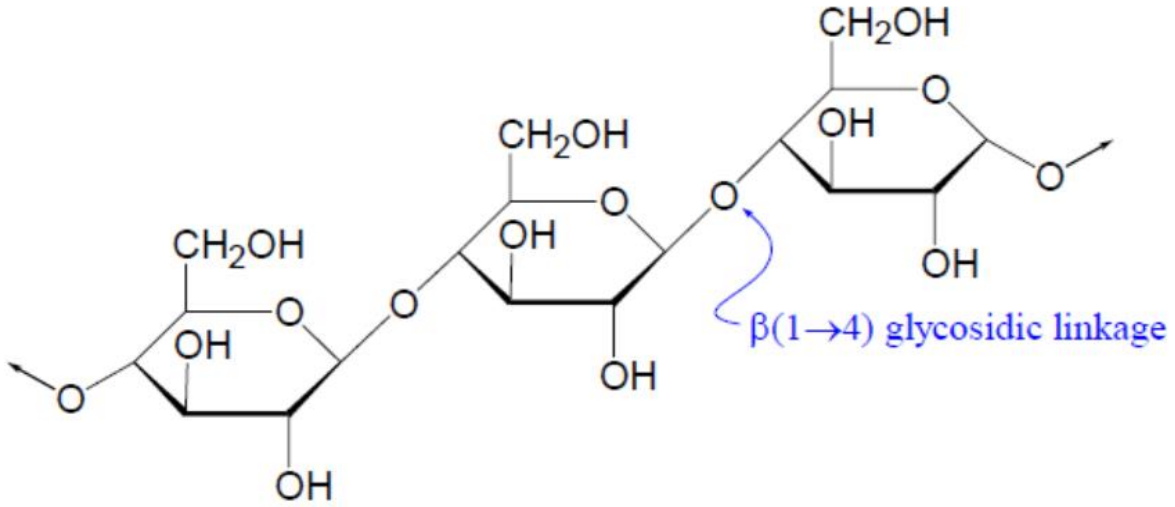
Chain is made of alpha 1-6 residues
While Branches Are variable 1-2/1-3/1-4



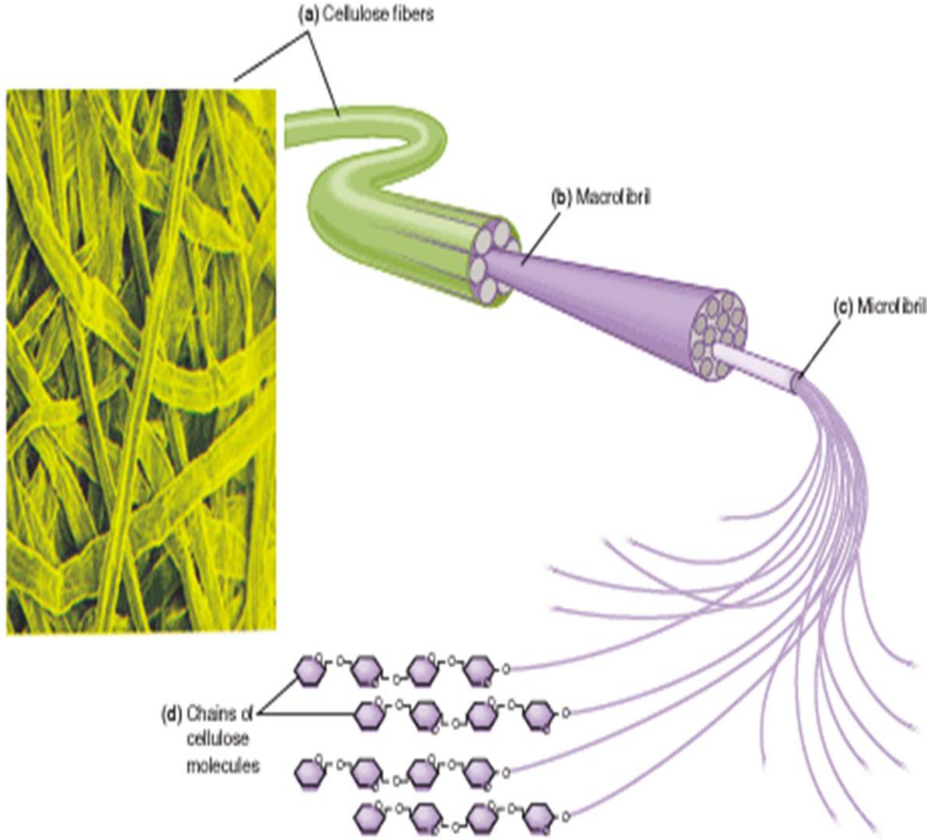
*Study the structure but do not memorize it

Cellulose *is a structural homopolysaccharide made of glucose and found in stems of plants; not branched. We don't have the enzyme that can digest cellulose (cellulase).*

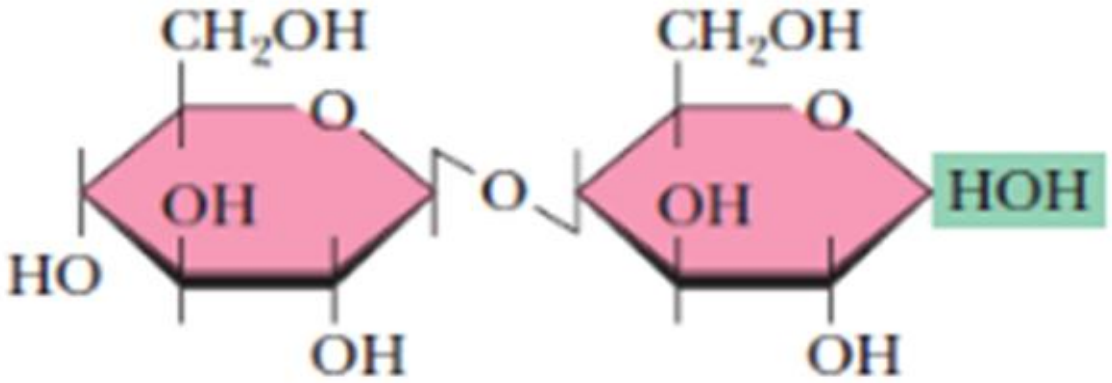
- *Cellulose can treat constipation so its beneficial to our body even if it can't digest it.*



Beta linkage is rigid, so no rotation → straight shape.



Memorize

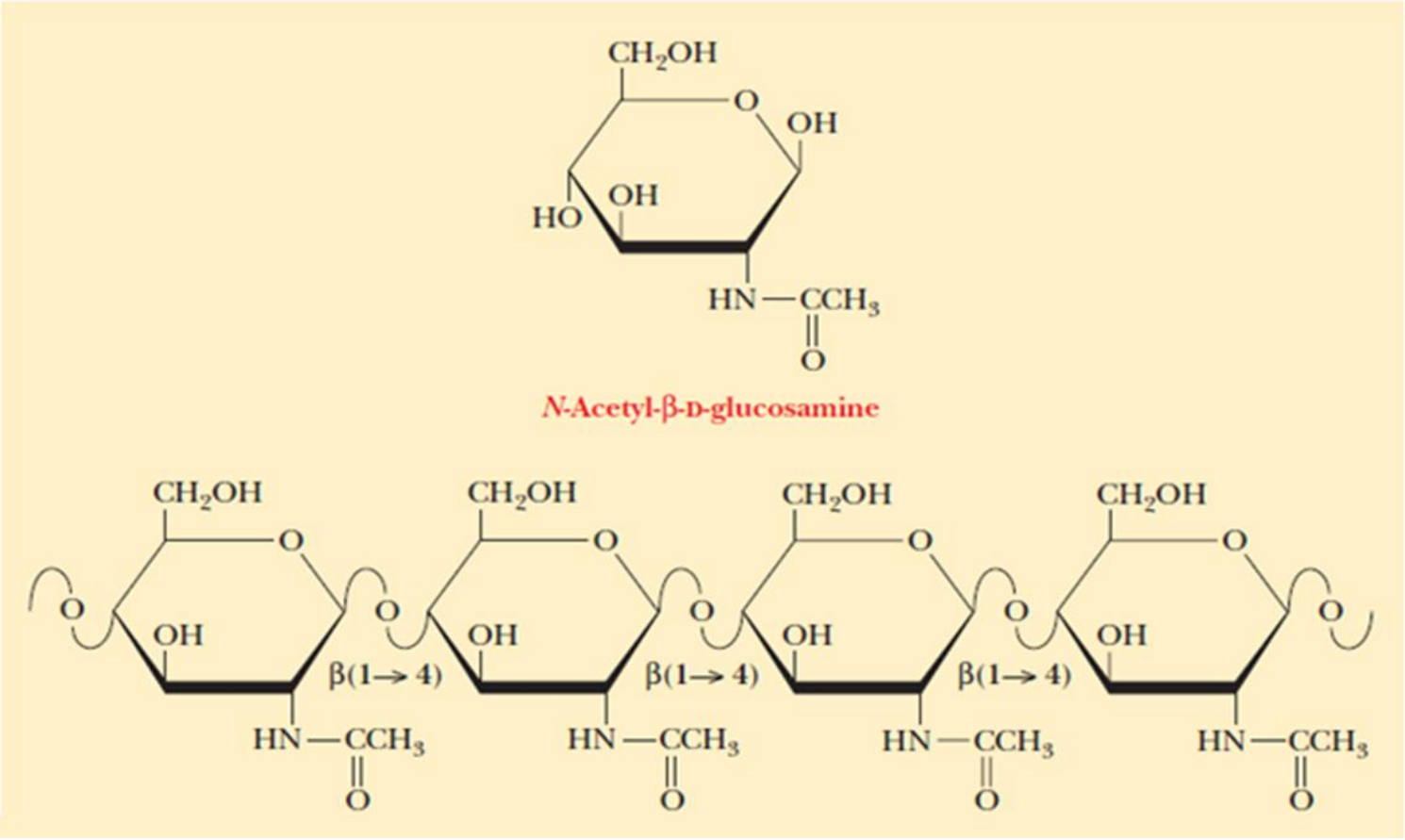


Cellobiose (glucose-β-1,4-glucose)

The chains that lie on top of each other form hydrogen bonds between hydroxyl groups, making the compound more rigid.

Chitin

What is the precursor? Pyranose form…modified sugar.
Where does it exist? In the exoskeleton of the insect.



anomeric configuration: Beta.
Glycosidic bond: 1-4.
Chitin is a rigid molecule, more rigid than cellulose.
The presence of the nitrogen and acetyl group can create a hydrogen bond and that makes it stronger.

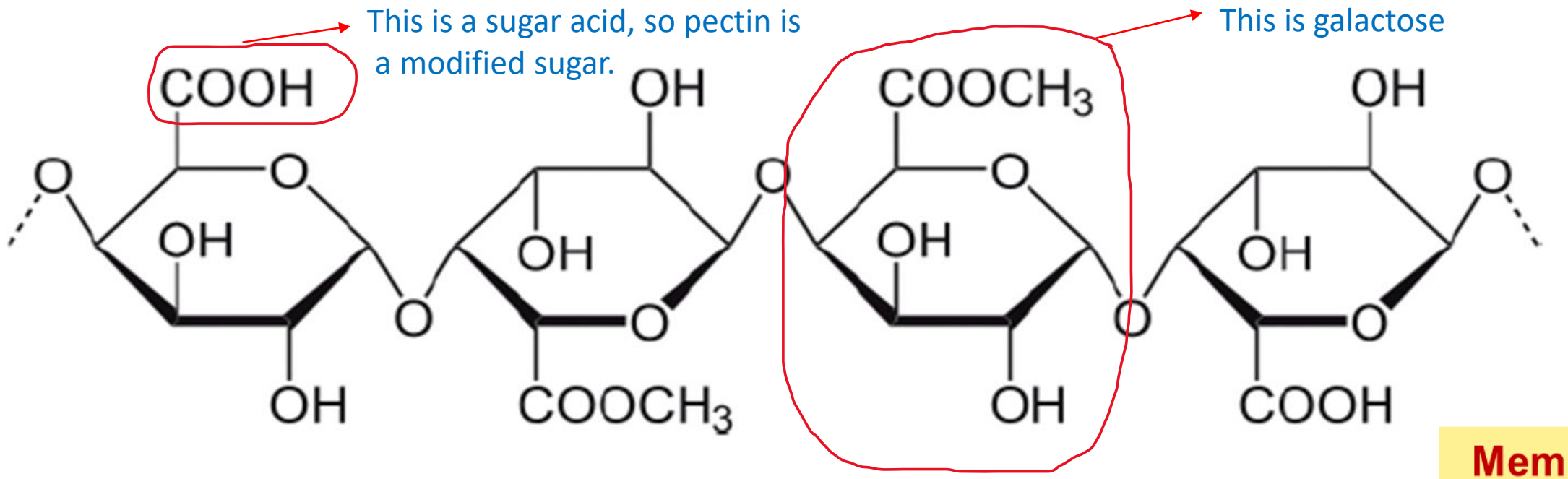
Memorize

Pectin

What is the precursor? **Galactose**

Where does it exist? **In the plants, Which turns into coal.**

Glycosidic bond: alpha(1-4).



Memorize

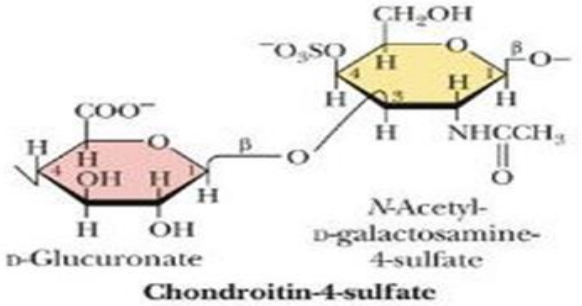
Are polysaccharides reducing?

- Reducing sugars have a free anomeric carbon.
- 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.
- The number of reducing sugars are small compared to the molecule size, so they are considered non-reducing.

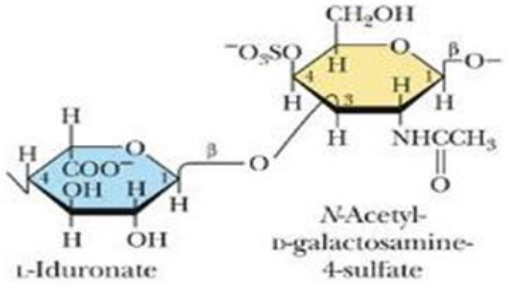
Glycosaminoglycans

- What are they? **They are large molecules, made of repeated disaccharides, and they are heteropolysaccharides.**

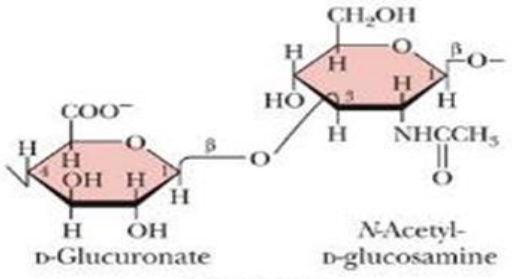
- Where are they located? **Outside the cells**
- Derivatives of an amino sugar, either glucosamine or galactosamine
- At least one of the sugars in the repeating unit has a negatively charged carboxylate or sulfate group



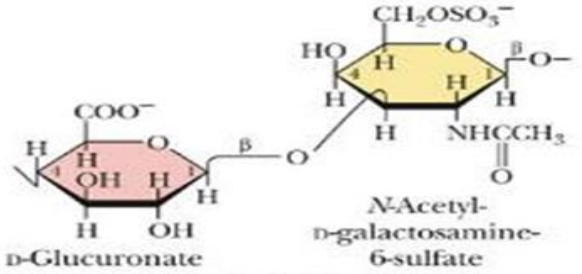
Chondroitin-4-sulfate



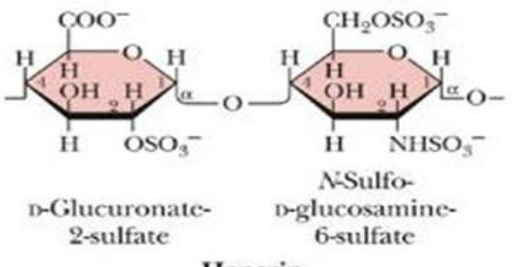
Dermatan sulfate



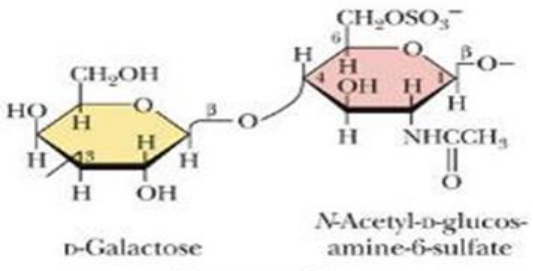
Hyaluronate



Chondroitin-6-sulfate



Heparin



Keratan sulfate

Study the structures but do not memorize them

Localization and function of GAG

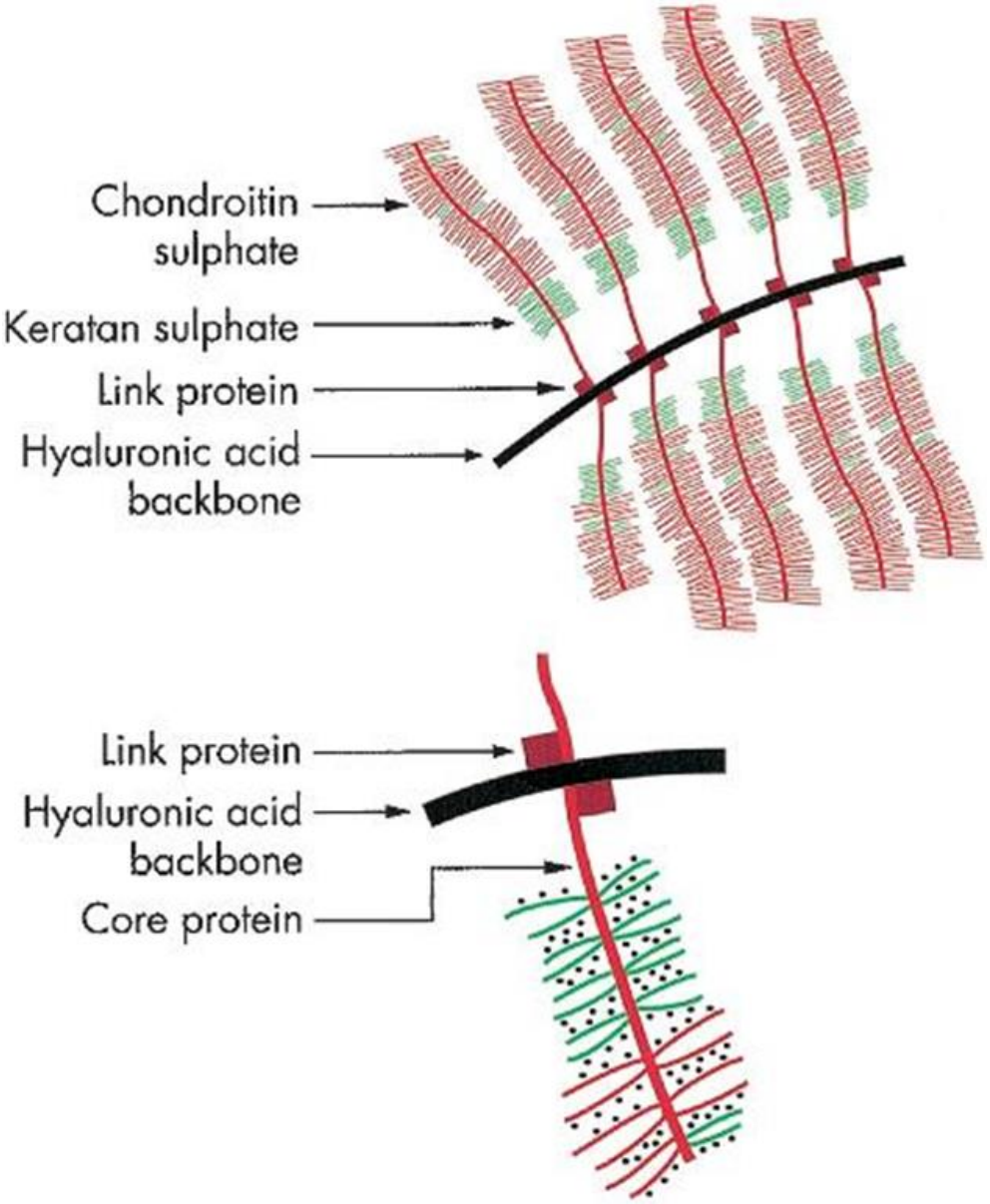
GAG	Localization	Comments
Hyaluronate	synovial fluid, **vitreous humor, ECM of loose connective tissue**	**the lubricant fluid , shock absorbing** As many as 25,000 disaccharide units
Chondroitin sulfate	**cartilage**, bone, heart valves	**most abundant GAG**
Heparan sulfate	basement membranes, components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

The negative charges of the GAGs inside the cartilage, causes repulsion between molecules, It is the reason why cartilage returns to its normal size after external pressure is applied on it.

Proteoglycans

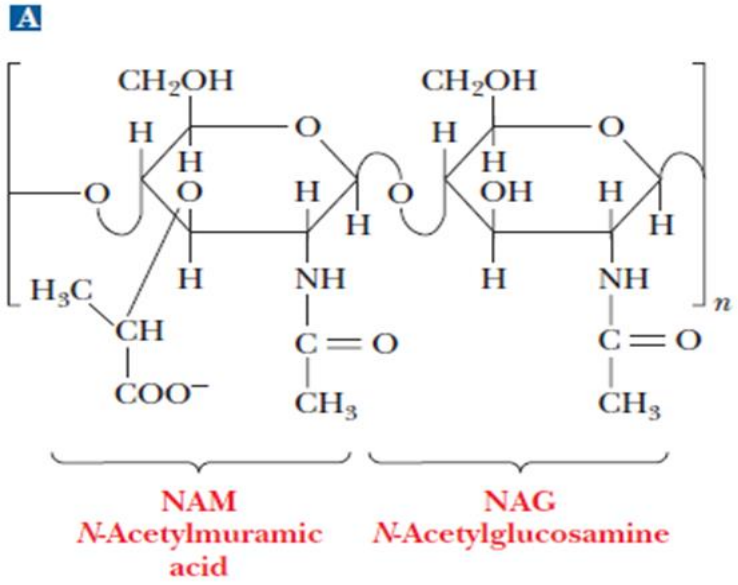
A lot of sugar with some peptides.

- Lubricants.
- Structural components in connective tissue. They exist outside the cells (in the extracellular matrix)
- Mediate adhesion of cells to the extracellular matrix.
- Bind factors that stimulate cell proliferation, such as:- growth factors, cytokines and nutrients.
- Cells can communicate between them by proteoglycans, they connect the cells with each other.



Bacterial cell wall

An example of peptidoglycans (sugar + peptides).



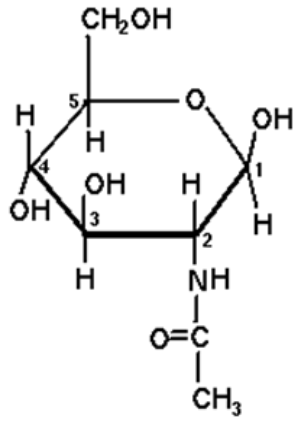
Some bacterial cells have a rigid cell wall in addition to their flexible , fluidic plasma membrane.

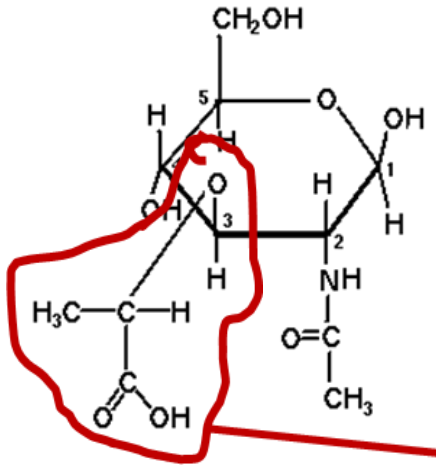
Why it is rigid?

1- because the glycosidic bonds between proteoglycans are Beta.

2- And it isn't branched, so we have many chain of sugar connected by peptide.

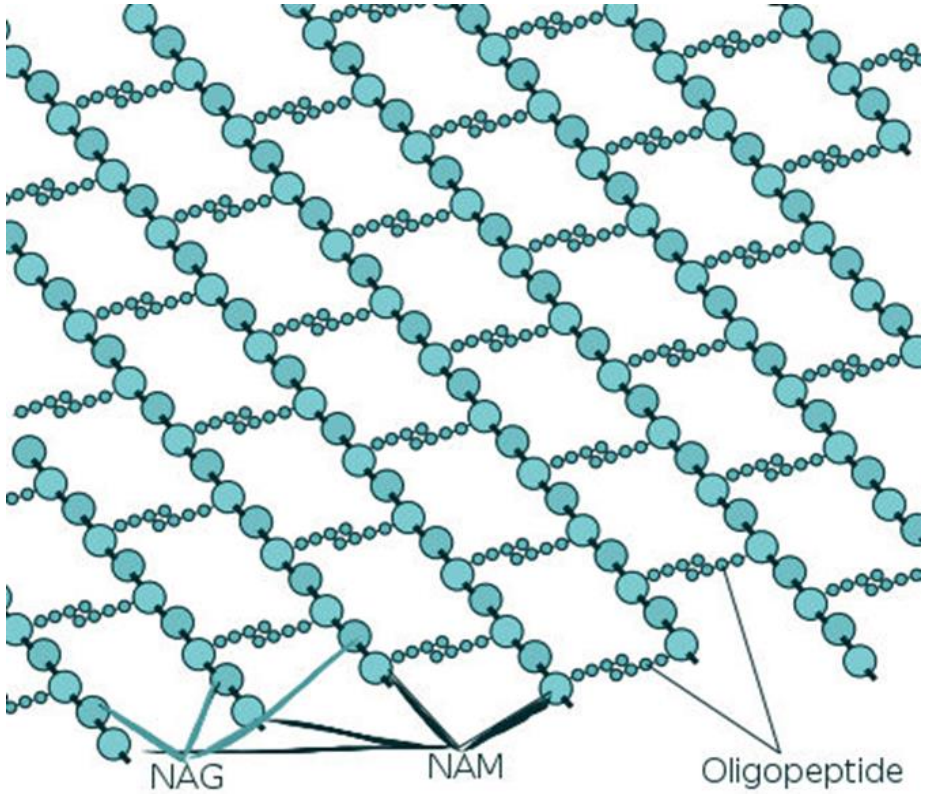
Bacterial cell wall made of two disaccharides.



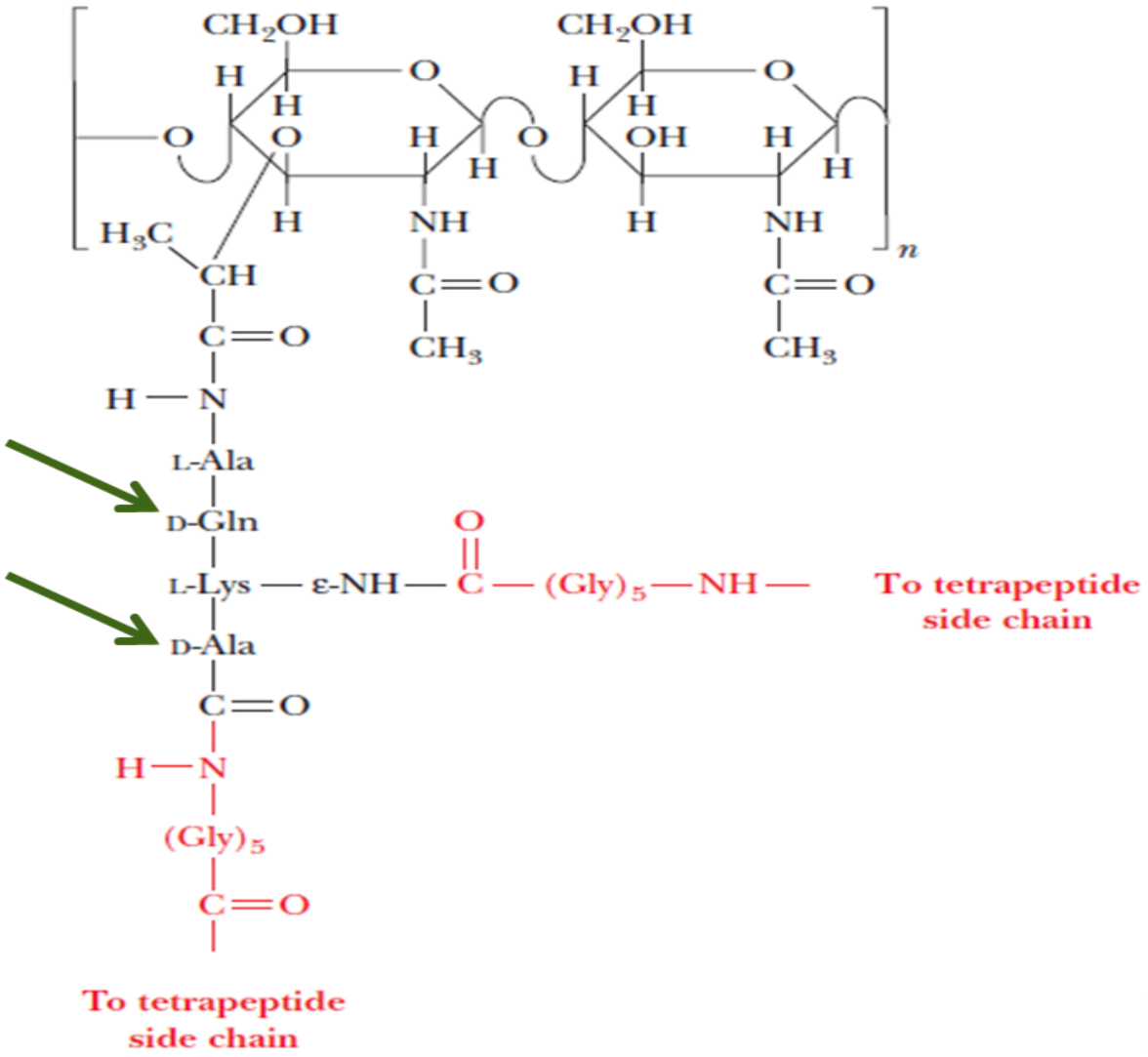


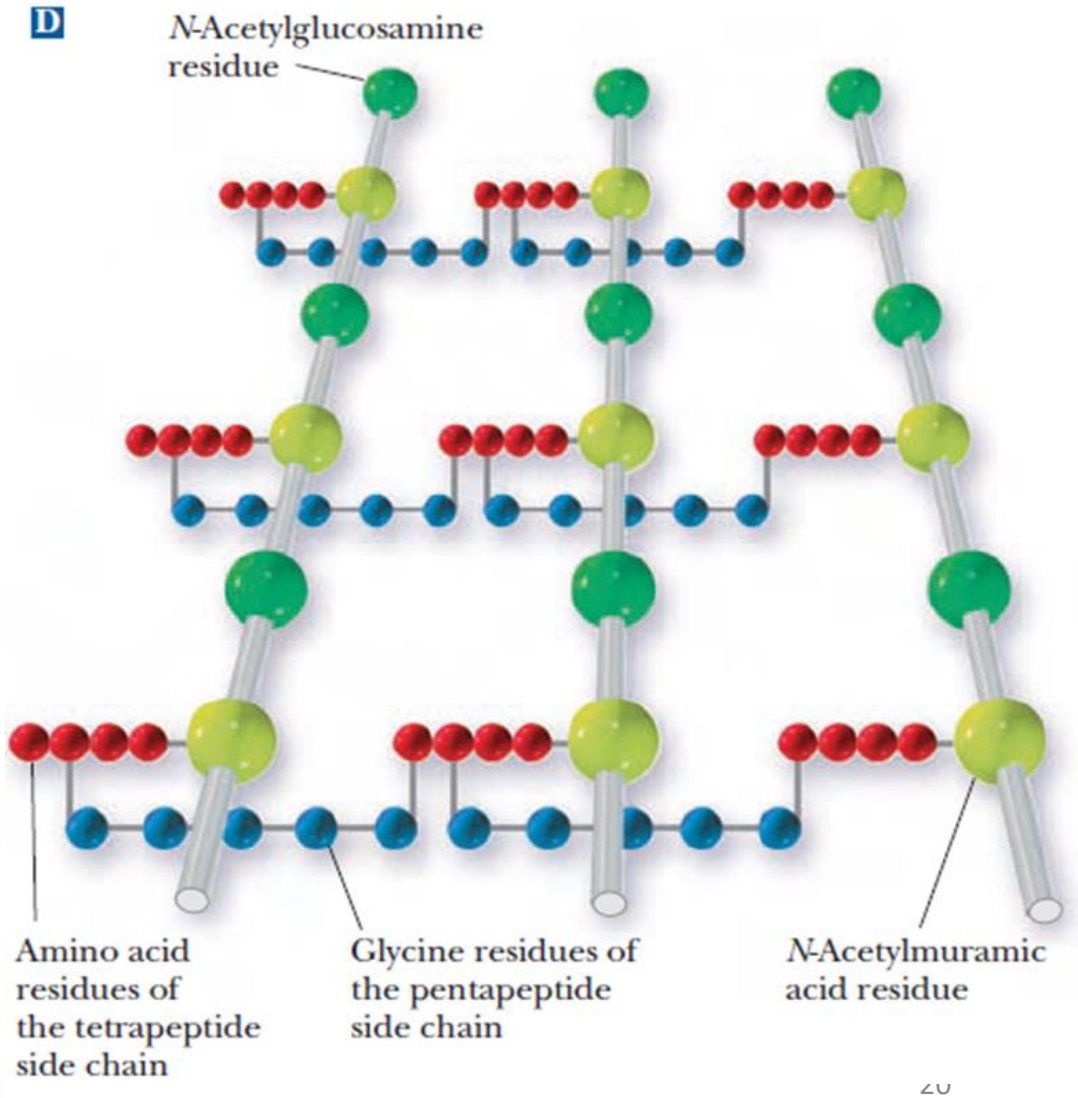
Study the structures but do not memorize them.

Lactic acid



Peptidoglycan





Glycoproteins

Protein with some sugars.

- The carbohydrates of glycoproteins are linked to the protein (amino acids) component through either 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 group of serine (Ser, S), threonine (Thr, T) or hydroxylysine (hLys)

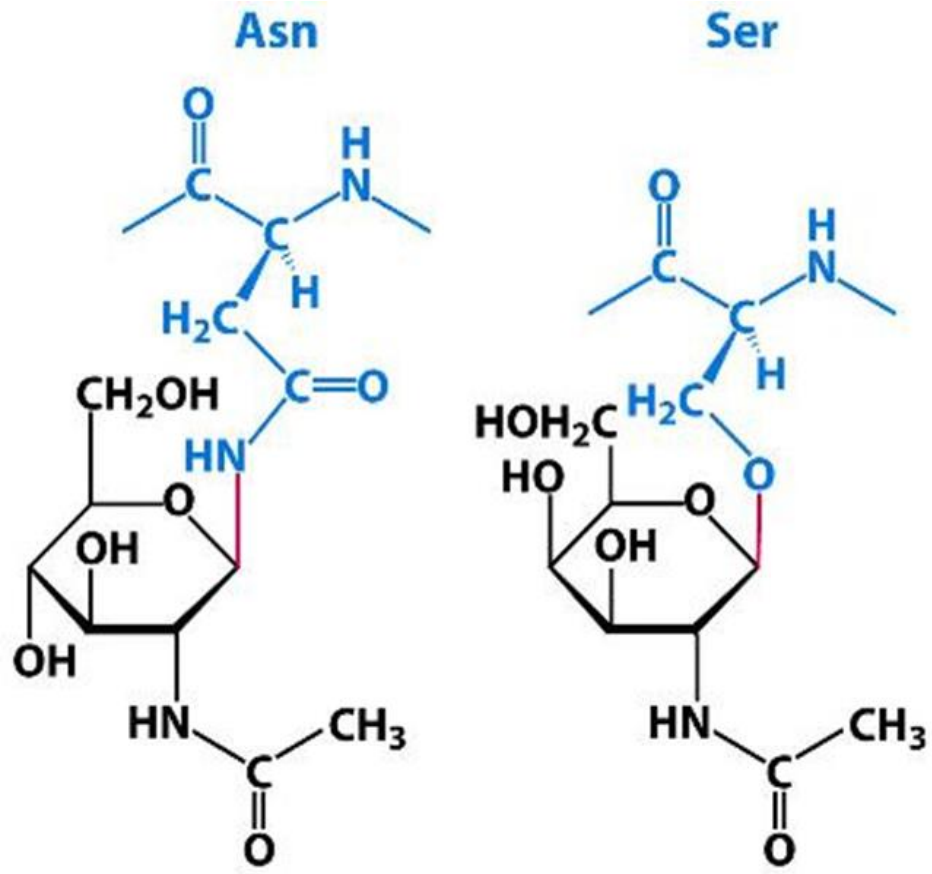


Figure 11.15
Biochemistry, Seventh Edition
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Do not memorize the structures but study them

Significance of protein-linked sugars

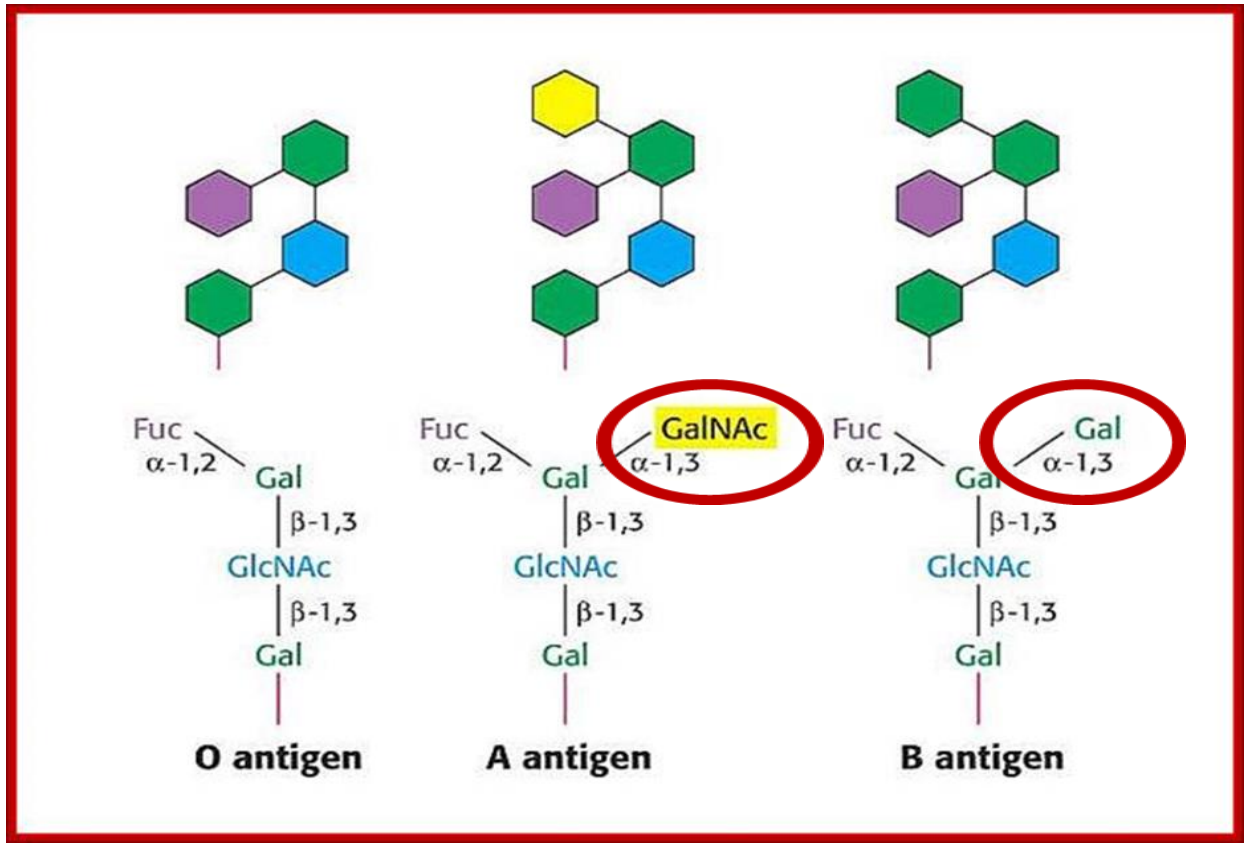
- Soluble proteins as well as membrane proteins
- Purpose:
  - Protein folding Sugar can determine the structure of protein.
  - Protein targeting Acts as a label to differentiation by other cells.
  - Prolonging protein half-life

    protein half-life:- is the time required for half of the amount of protein to be degraded .

    - The stability of protein is controlled by sugar.
  - Cell-cell communication such as immune cells.
  - Signaling signals can be send into the cells by sugar.

Blood typing and glycoproteins

- Three different structures:
  - A, B, and O
- The difference:
  - N-acetylgalactosamine (for A)
  - Galactose (for B)
  - None (for O)



(O) gives all types.

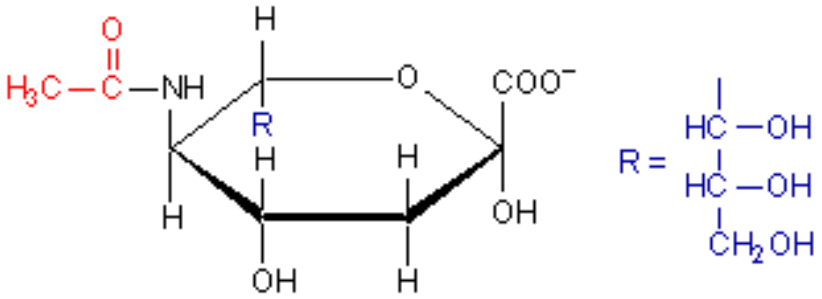
(AB) receives from all types.

(A) gives A & AB.

(B) gives B & AB.

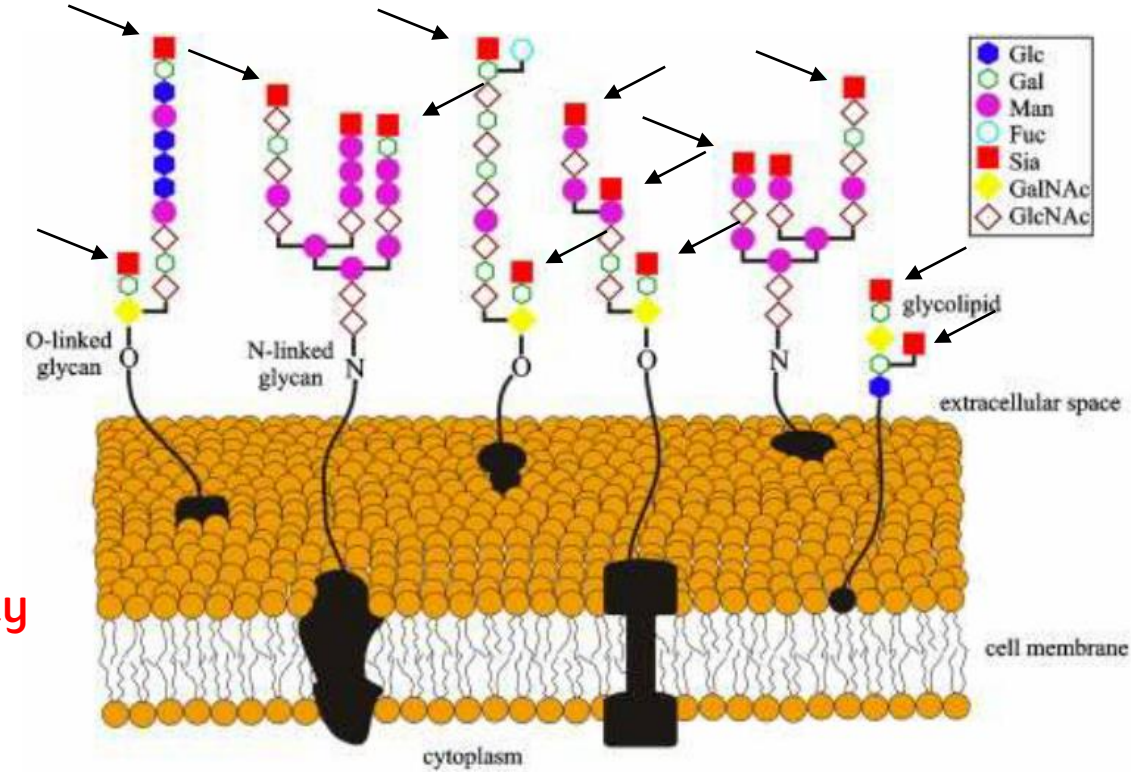
Sialic acid

- N-acetylneuraminate
- Precursor: the amino sugar, neuraminic acid
- Location: a **terminal** residue of oligosaccharide chains of glycoproteins and glycolipids.



N-acetylneuraminate (sialic acid)

Do not memorize the structures but study them



For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V1 → V2	19; top	proteoglycans	peptidoglycans
V2 → V3			

Additional Resources Used:

1. Campbell Textbook:
   sec. 16.3:
   (Some Important Oligosaccharides)
   sec. 16.4:
   (Structures and Functions of Polysaccharides)
   sec. 16.5:
   (Glycoproteins)

رسالة من الفريق العلمي:

شَكَوتُ إِلى وَكِيعٍ سوءَ حِفظي

فَأرشَدني إِلى تَركِ المَعاصي

وأخبرني بِأنَّ العلمَ نورٌ

ونورُ اللهِ لا يُهدى لِعاصي

أبيات الإمام الشافعي رحمه الله