Chapter 11

Learning objectives:

Structure and function of

- monosaccharides,
- polysaccharide,
- glycoproteins
- lectins.

Carbohydrates

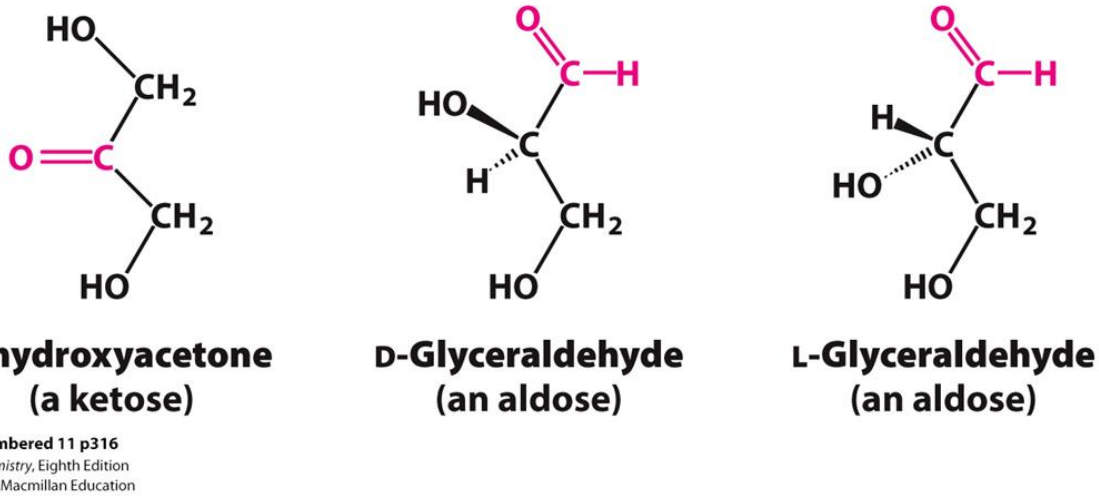
- Fuels
- Structural components
- Coating of cells
- Part of extracellular matrix in multicellular organisms
- Important for cell to cell communication
- Basis for human blood groups

- Carbohydrates are formed by monosacharids (3 to 9 carbon atoms)
- Vary in size and stereo-chemical configurations
- Large variety of polysaccharide structures – information reach molecules
- Glycobiology – study of synthesis and structure of carbohydrates and its interactions with other proteins
- Glycomics study of glycome (all carbohydrates that are produced by the cell at certain time and under certain conditions

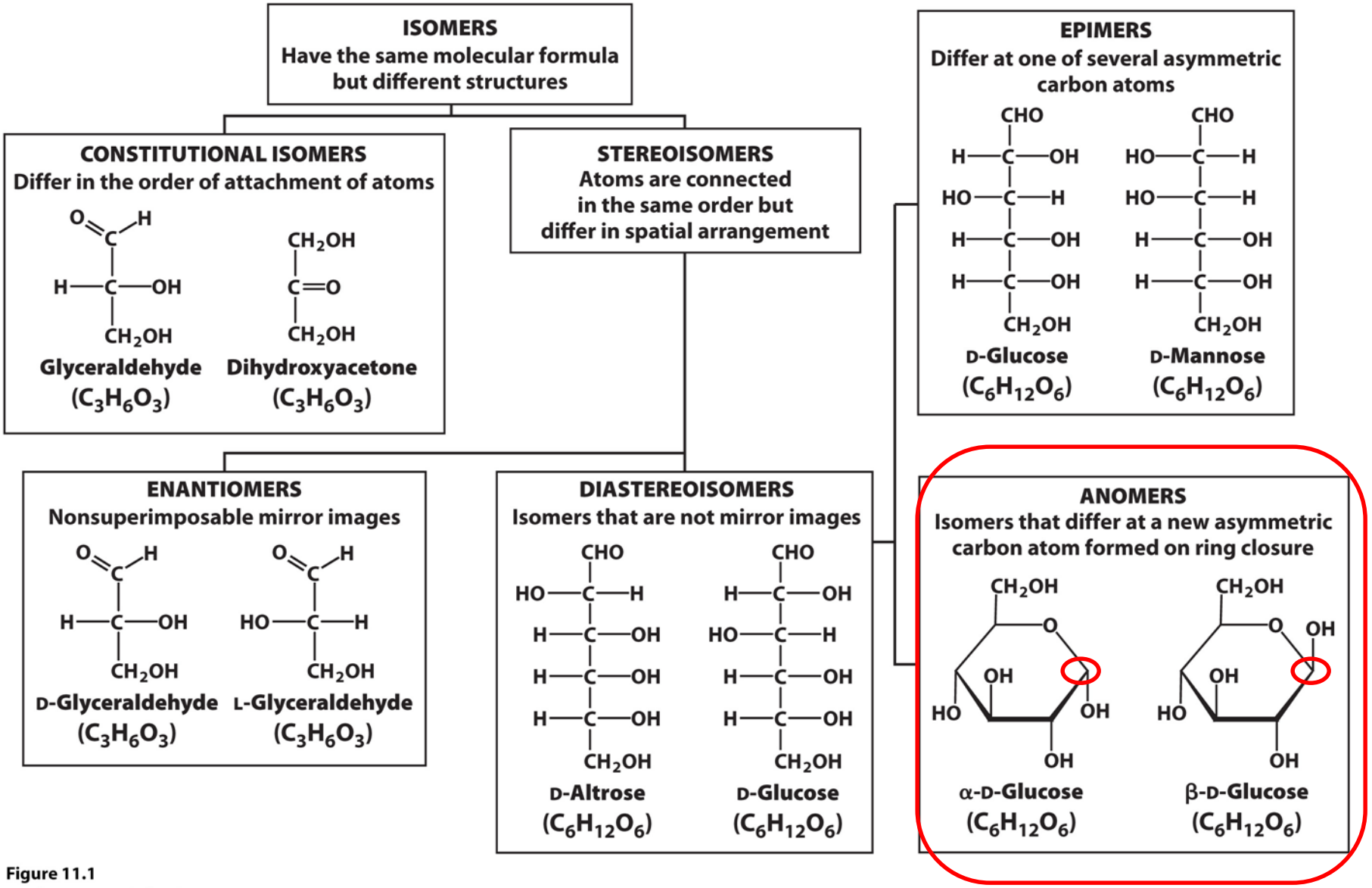
Monosacharids

- Carbohydrates $(CH_2O)_n$ carbon hydrates
- Monosaccharides are <u>aldehydes</u> or <u>ketones</u> that contain two or more hydroxyl groups.

<u>Trioses</u>: three carbon monosaccharids:



Isomeric forms of carbohydrates



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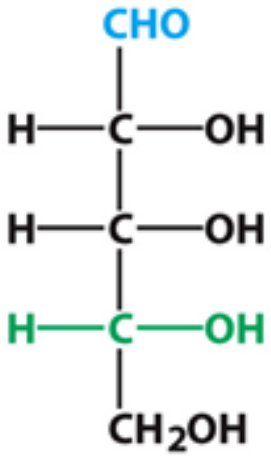
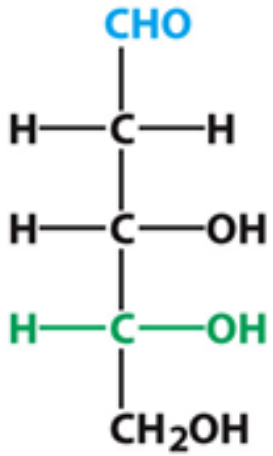
- Tetroses:

- Pentoses

D- Ribose and D-deoxyribose are found in nucleic acids. Both are aldose.

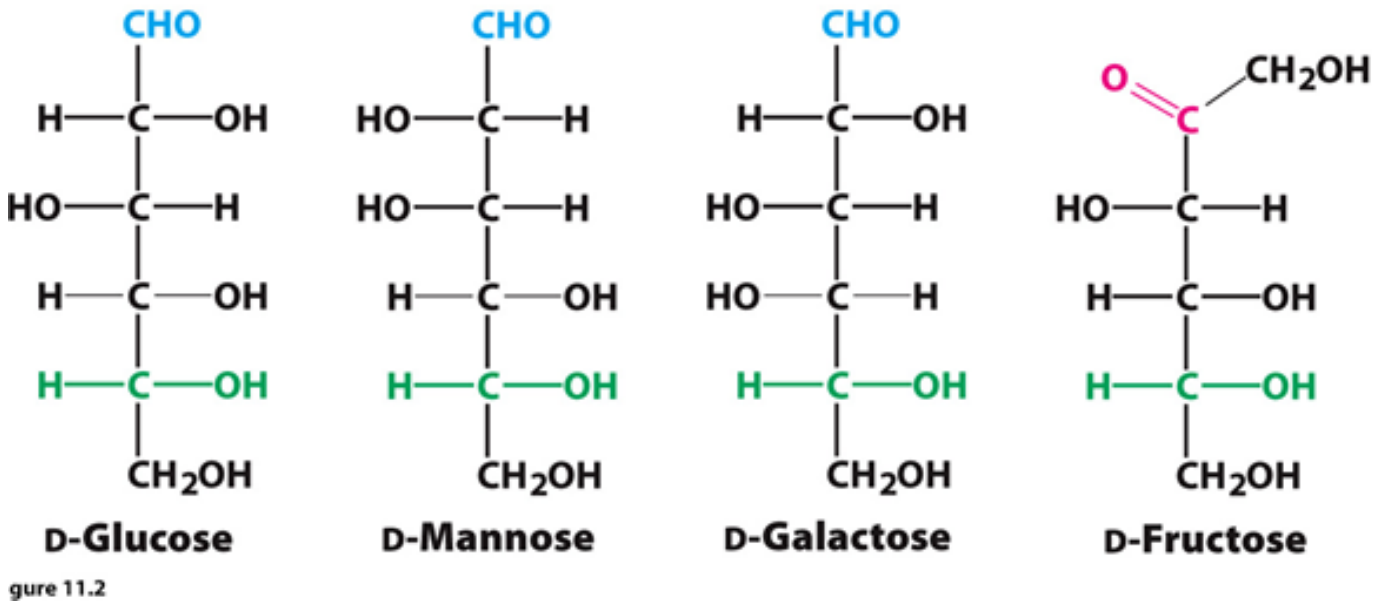


D-Ribose



D-Deoxyribose

- Hexoses
  - D-glucose, D-galactose and D- mannose are abundant aldoses
  - D-fructose is abudant ketose



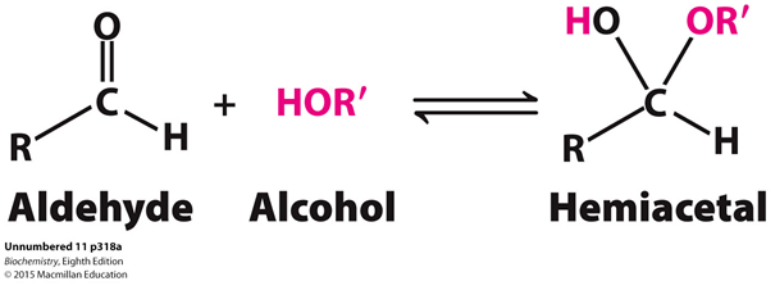
gure 11.2

D-glucose and D-mannose are epimers at carbon 2
D-glucose and D-galactose are epomres at carbon 4

Cyclic form

In vitro and *in vivo* many sugars tends to adopt a cyclic form

Aldehydes reacts with an alcohols to form a hemiacetal
Ketone reacts with an alcohol to form a hemiketal



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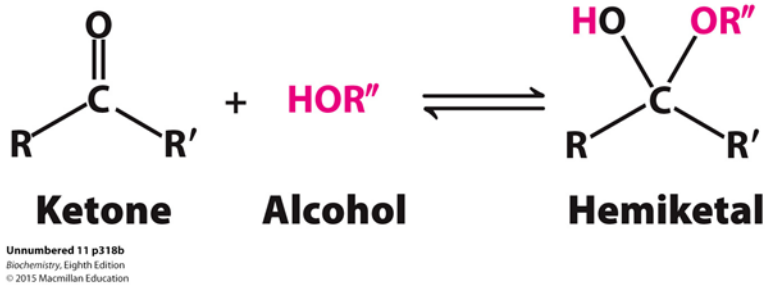

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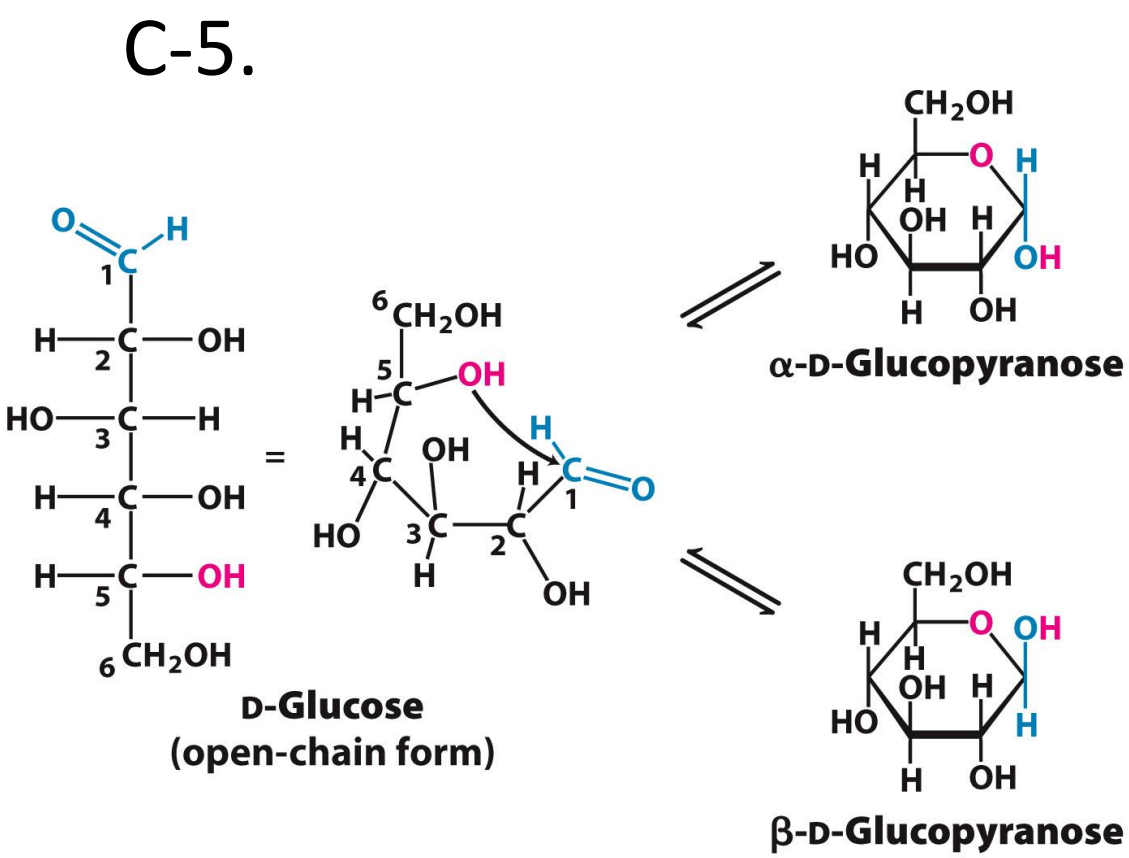
- Aldohexose such as glucose form an intramolecular hemiacetal. The aldehyde group on C-1 reacts with the hydroxy group of C-5.



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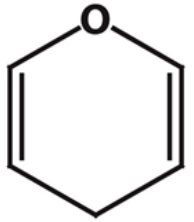
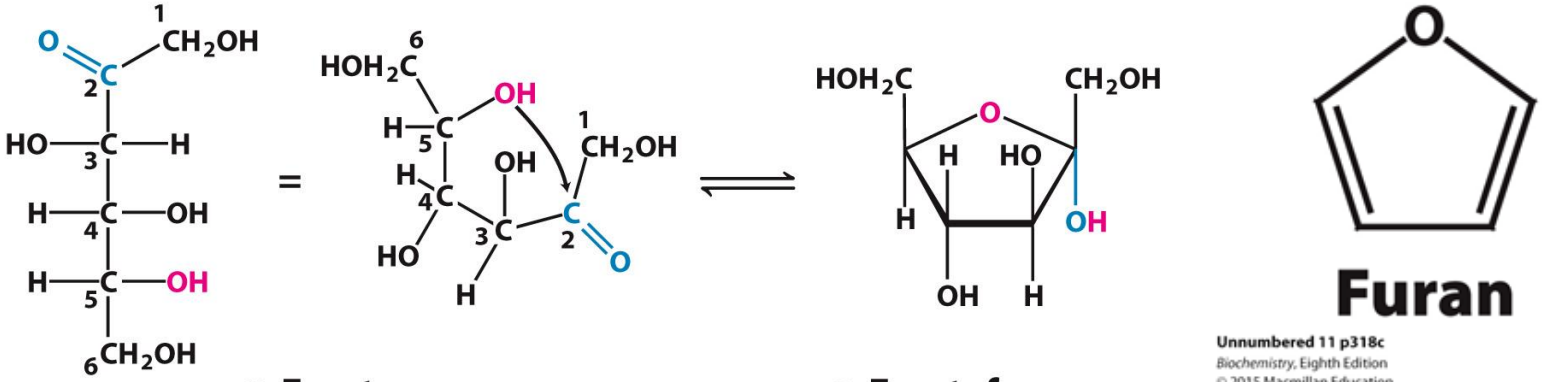


Harword projection

Designation α means that the hydroxy group on C-1 is on the oposite site of the ring as C-6
Designation β means that the hydroxy group on C-1 is on the same site of the ring as C-6

At equilibrium mixture of glucose the cyclic β form is the predominant

- C-2 ketogroup of the ketohexose can react with the C-5 hydroxyl group forming five-membered cyclic hemiketal



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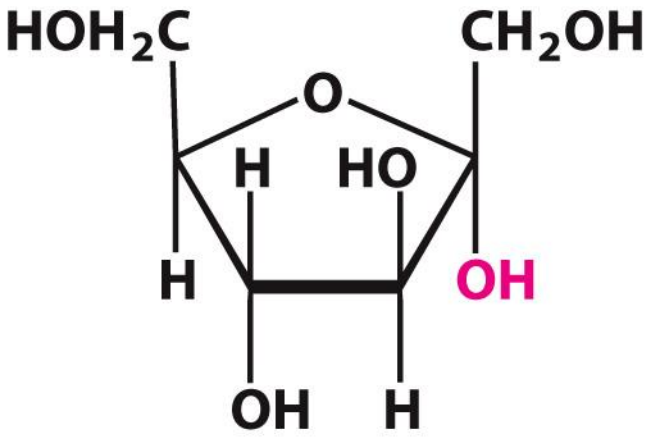
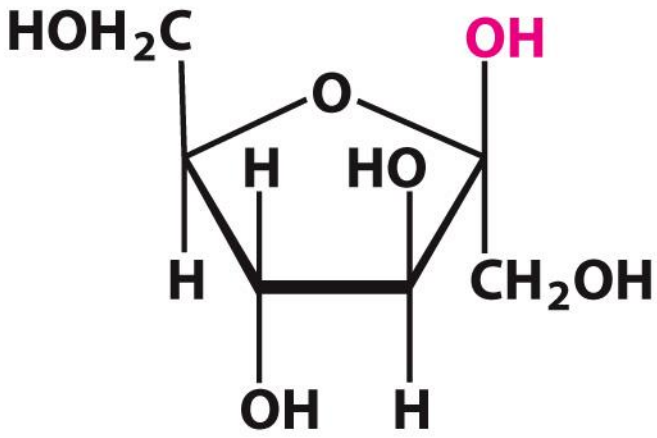
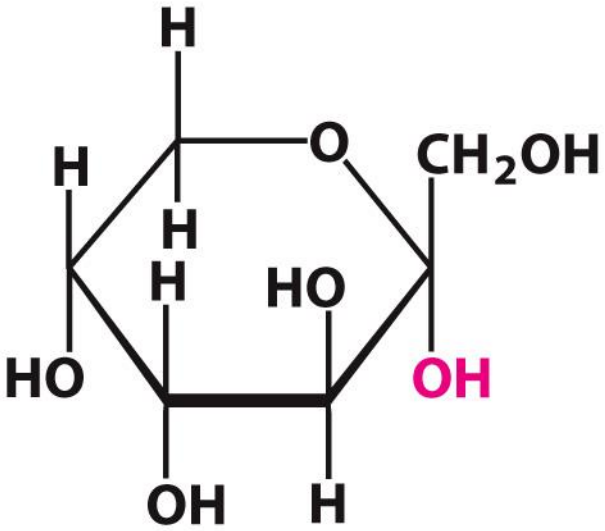
Fructose forms both the pyranose form, which predominates when fructose is free in solution, and a furanose form, commonly seen in fructose derivatives.



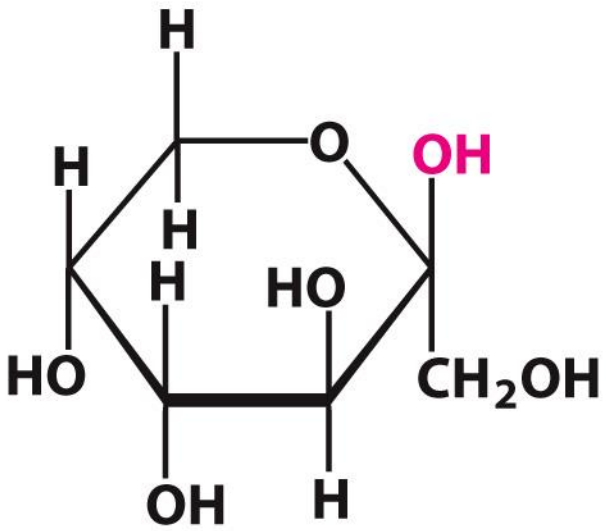
α-D-Fructofuranose



β-D-Fructofuranose



α-D-Fructopyranose



β-D-Fructopyranose

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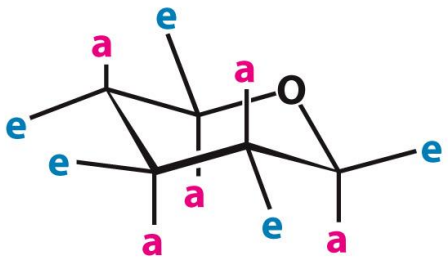
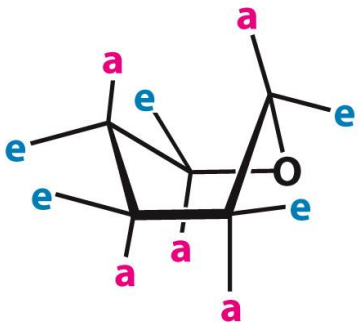
Sweetest chemical known. Found in honey

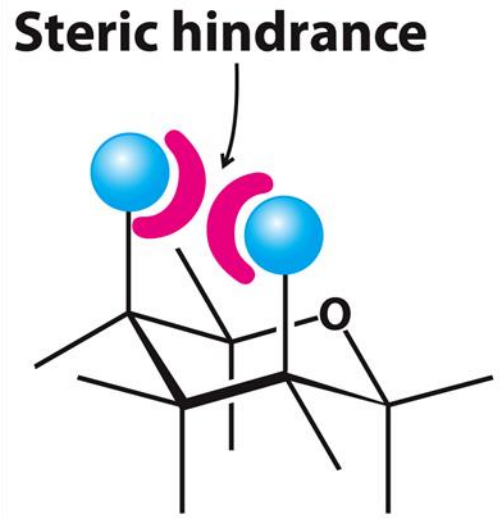
Pyranose rings can adopt two types of conformation, called boat and chair.

In the chair form, substituents on the carbon ring atoms have two orientations: axial and equatorial.

β-D-glucopyranose adopts the chair conformation because the axial positions are occupied by hydrogens, reducing steric hindrance.







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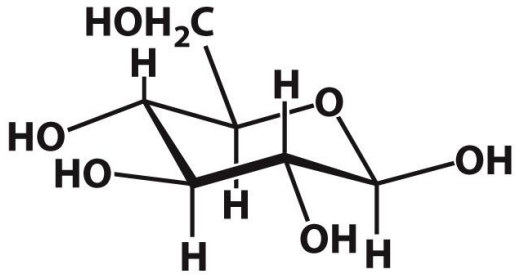
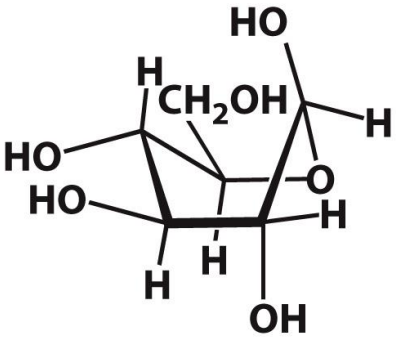
D-glucopyranose



Chair form



Boat form

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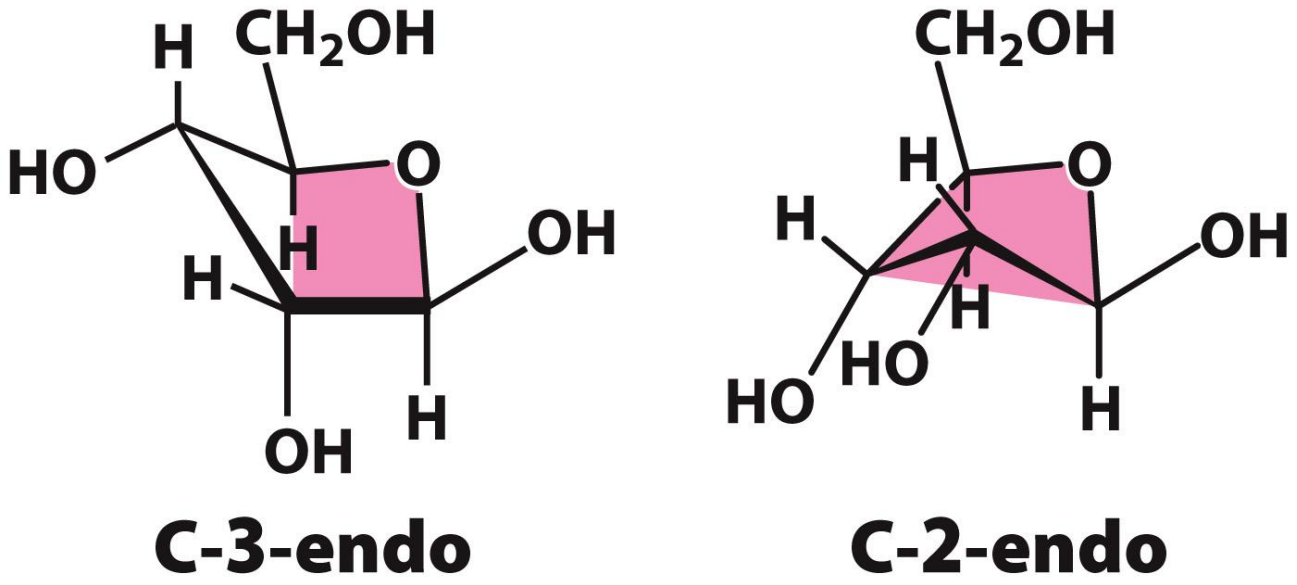
- Conformations of furanose

Furanose rings, like pyranose rings, are not planar and commonly adopt a conformation called the envelope form.

In the ribose component of most biomolecules, two conformations are observed: C-2 is out of the plane on the same side as C-5 (C-2-endo), or C-3 is out of the plane on the same side as C-5 (C-3-endo).



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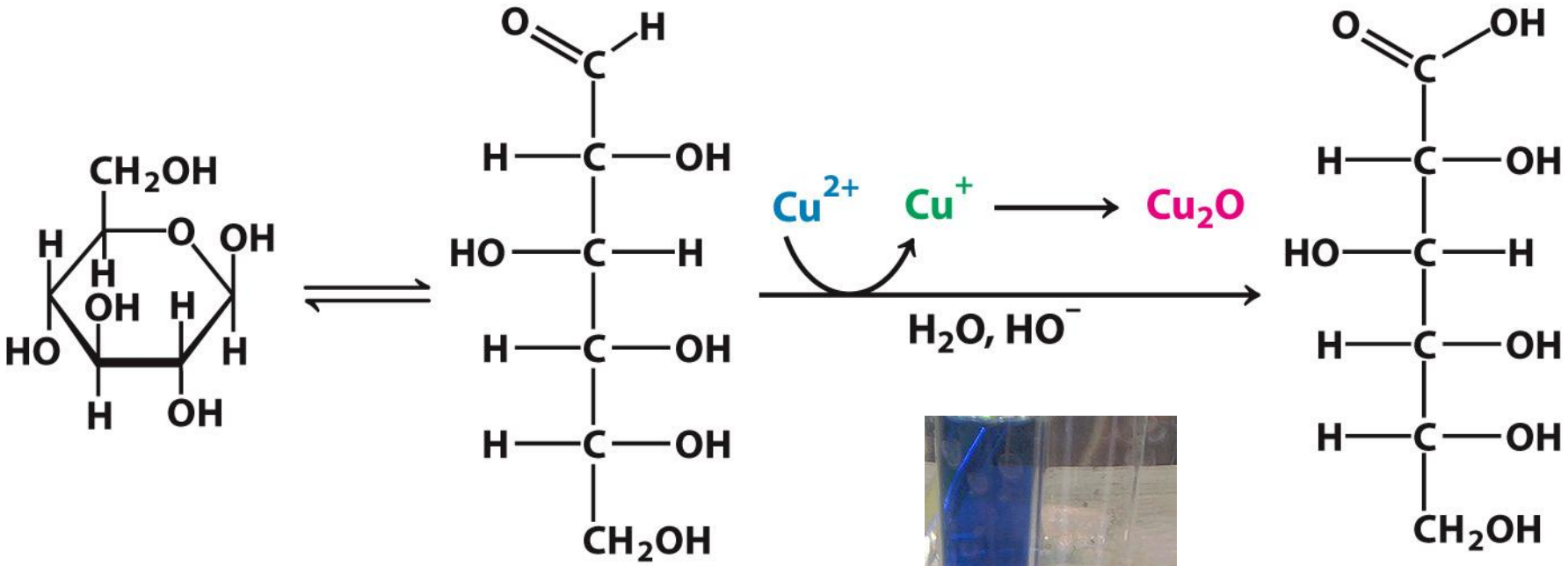
Reducing sugars

- Fehling solutions contains cupric ion
- In the presence of sugars (aldose) such as glucose Cu^{2+} is reduced to cuprous ion



Gluconic acid

As a reducing sugar, glucose can react with hemoglobin, forming glycosylated hemoglobin (hemoglobin A1c), which is fully functional.

Determining the amount of hemoglobin A1c in the blood allows one to monitor the long-term control of blood glucose levels in diabetics.

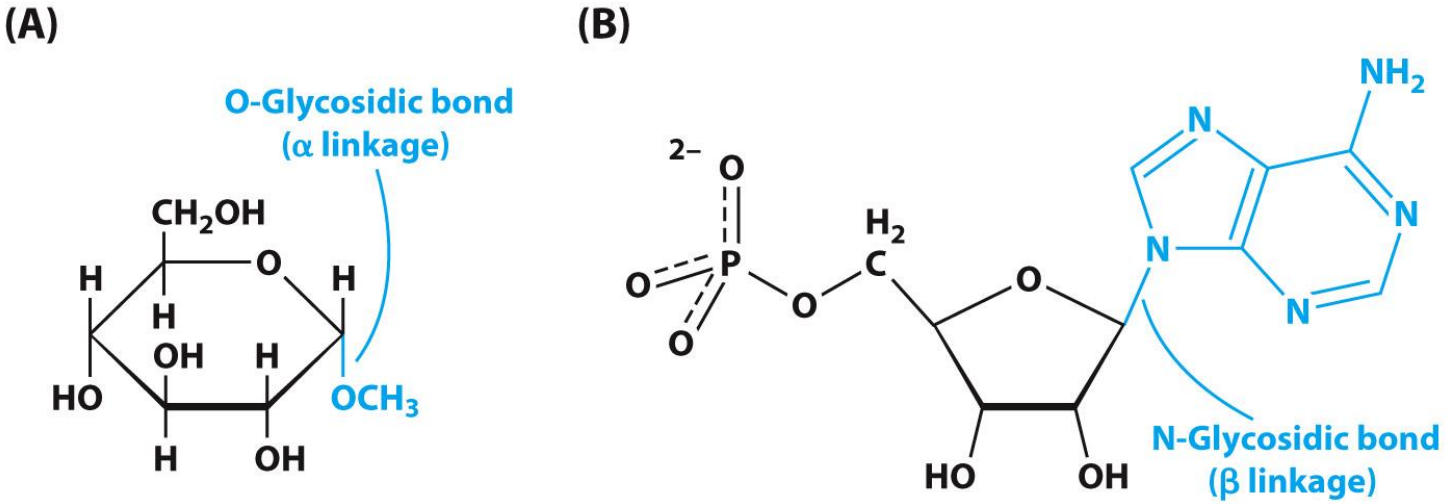
Reactions between carbohydrates and proteins often impair protein function.

Such modifications, called advanced glycation end products, have been implicated in a number of pathological conditions

Monosacharides modifications – glycosidic bond

A bond formed between the anomeric carbon atom and an oxygen atom of an alcohol is called an *O*-glycosidic bond, and the product is called a glycoside.

A bond formed between the anomeric carbon atom and an amine is called an *N*-glycosidic bond.



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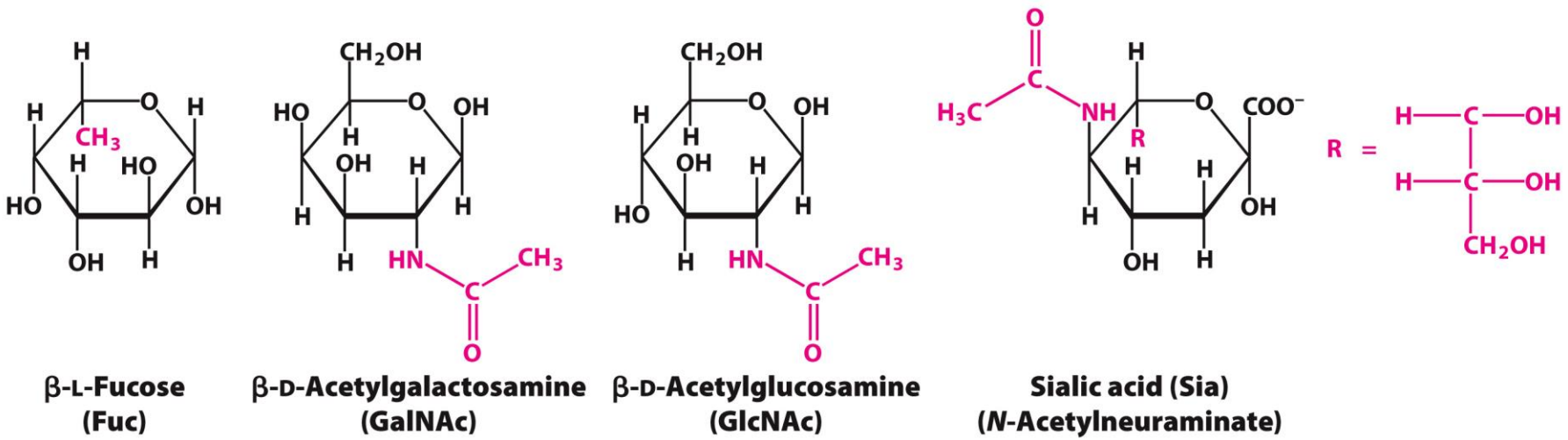

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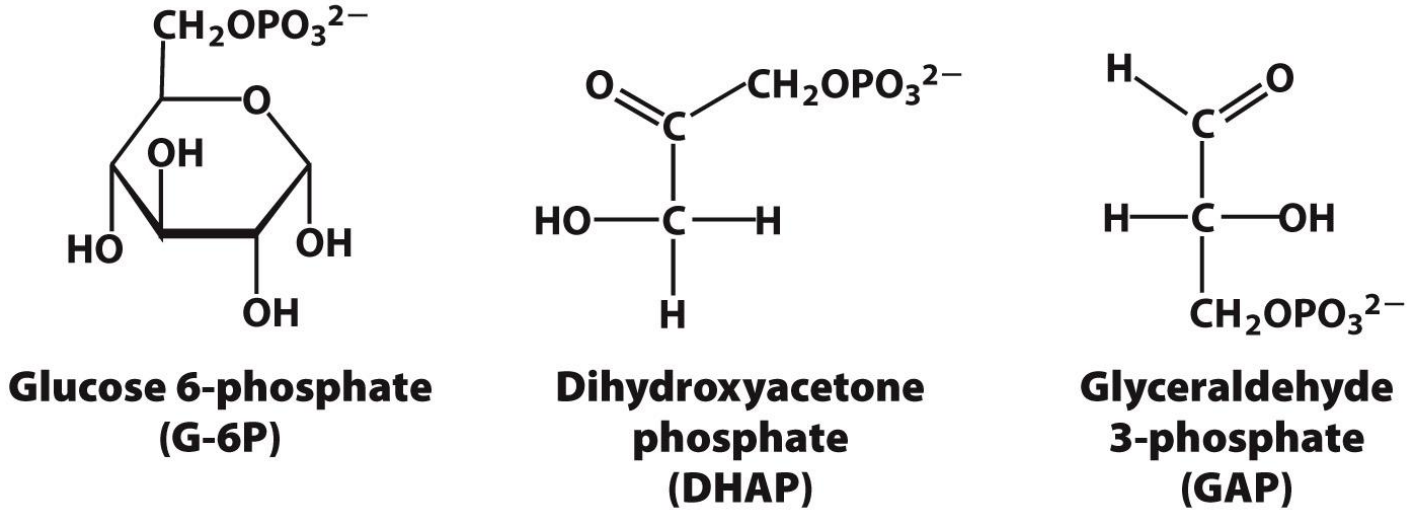
Modifications with alcohols; amines; phosphates
Signaling molecules, sugars expressed on the cell surface

Phosphorylation is a common modification of carbohydrates.

Phosphorylation makes the sugars anionic and prevents them from leaving the cell.

Phosphorylation also facilitates the metabolism of sugars.



Glucose 6-phosphate (G-6P)

Dihydroxyacetone phosphate (DHAP)

Glyceraldehyde 3-phosphate (GAP)

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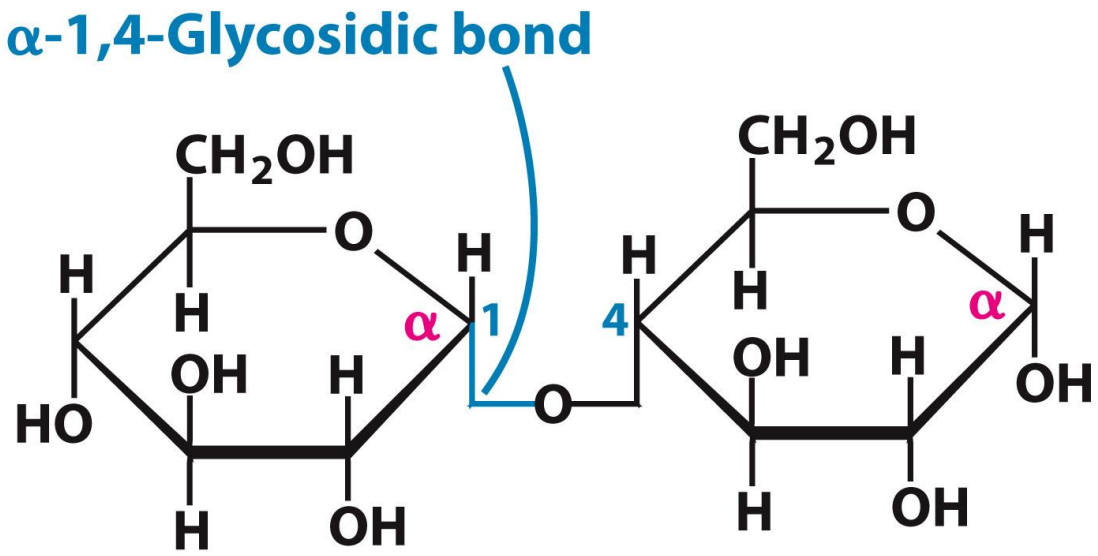
Oligosacharides: complex carbohydrates

Oligosaccharides containing two or more monosaccharides are linked by *O*-glycosidic bonds.

Mannose:



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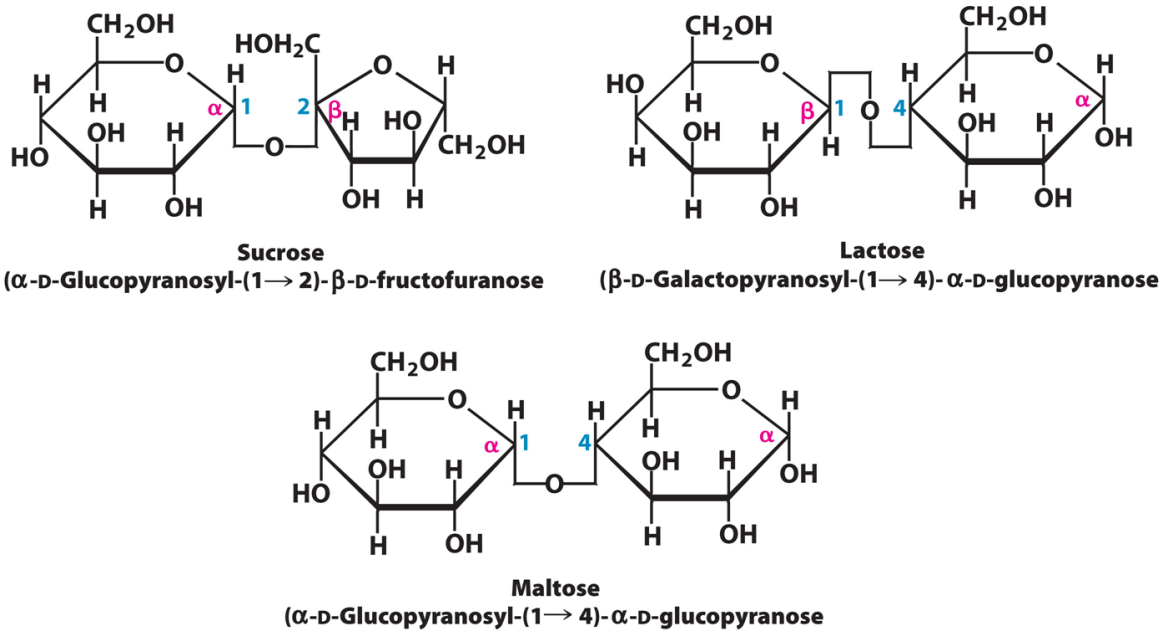
- Common disaccharides

Sucrose is obtained from sugar cane and sugar beets and is composed of a glucose linked to a fructose. The linkage is α for glucose and β for fructose. Sucrose is cleaved by sucrase.

Lactose is the disaccharide of milk that consists of a galactose linked to a glucose by a β-1-4-linkage. Lactase cleaves lactose.

Maltose, a degradation product of large oligosaccharides, is composed of two glucose molecules linked by an α-1-4-linkage. Maltose is hydrolyzed by maltase.



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Large polymeric oligosaccharides are called polysaccharides. If all of the monosaccharides in the polysaccharide are the same, the polysaccharide is called a homopolymer.

The polysaccharide glycogen is the storage form of glucose in animal cells.

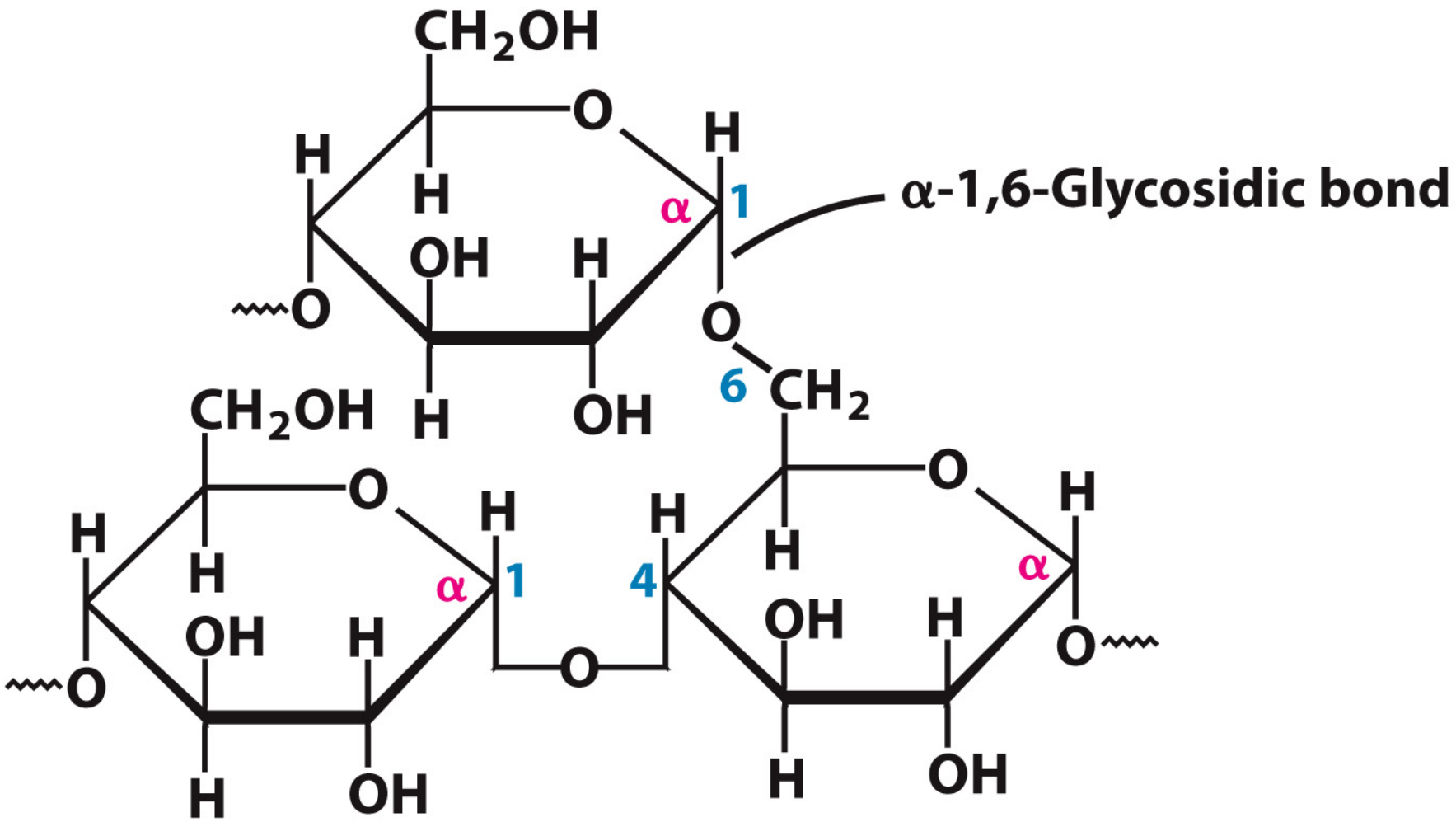
Most glucose units in glycogen are lined by α-1,4-glycosidic bonds, with branches formed by α-1,6-glycosidic bonds every 10 glucose units.

In plants, glucose is stored as starch, of which there are two forms.

Amylose is a linear polymer of glucose units linked by α-1,4-glycosidic bonds.

Amylopectin is a branched polymer, with an α-1,6-glycosidic bond for every 30 α-1,4-glycosidic bonds.

Glycogen



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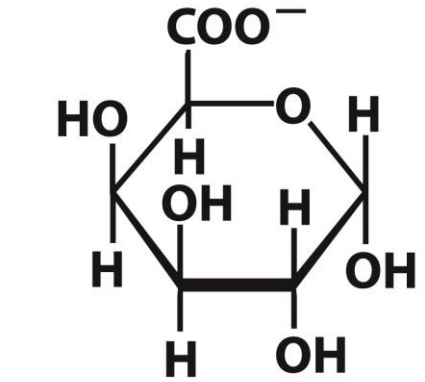
Cellulose: structural component of plants

Cellulose is a homopolymer of glucose units linked by a β-1,4-glycosidic bond.

The β linkage yields a straight chain capable of interacting with other cellulose molecules to form strong fibrils.

The α linkages of starch and glycogen form compact hollow cylinders suitable for accessible storage.

Although mammals cannot digest cellulose and other plant fibers, soluble fibers, such as polygalacturonic acid, aid in digestion.



Galacturonic acid

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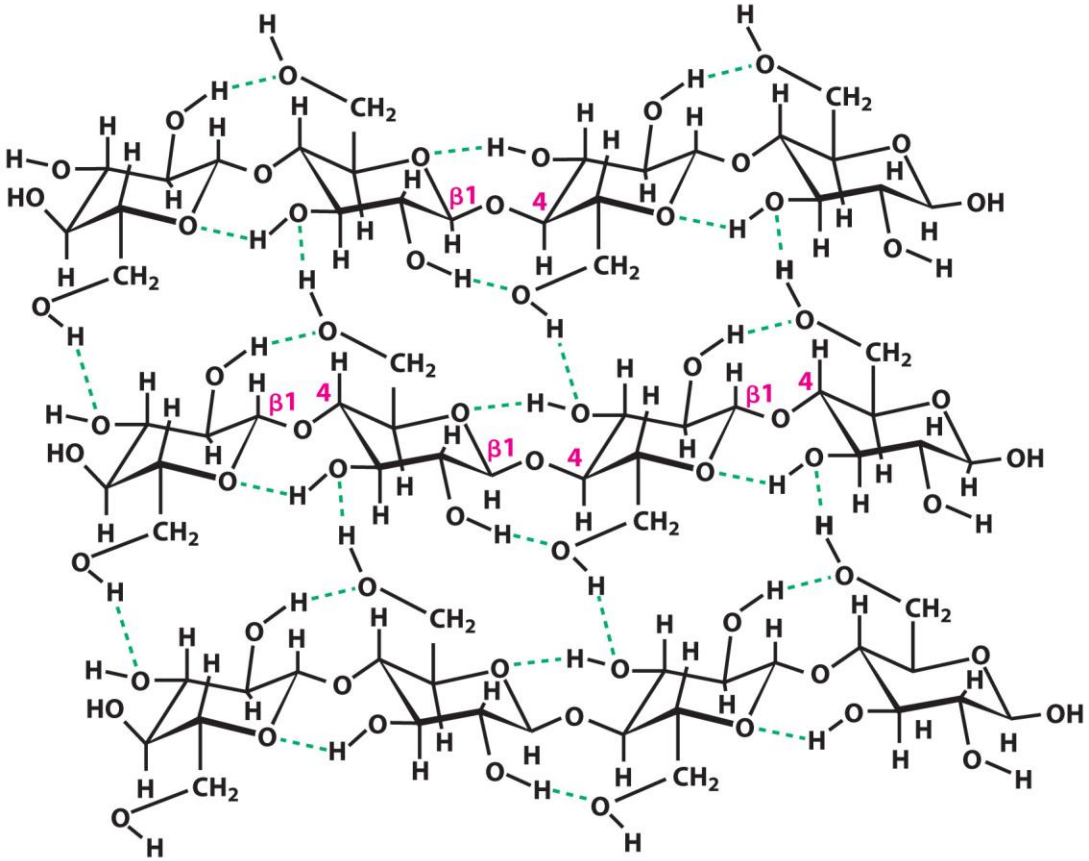

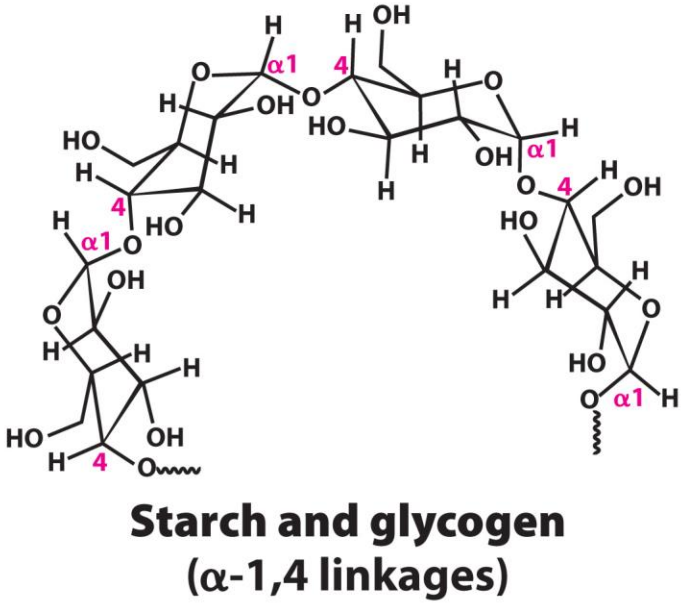

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Cellulose: long straight chains. Fibriles forms by the hydrogen bonding of the long chains generate a rigid structure

Glycoproteins

Proteins with carbohydrates attached are called glycoproteins. There are three main classes of glycoproteins:

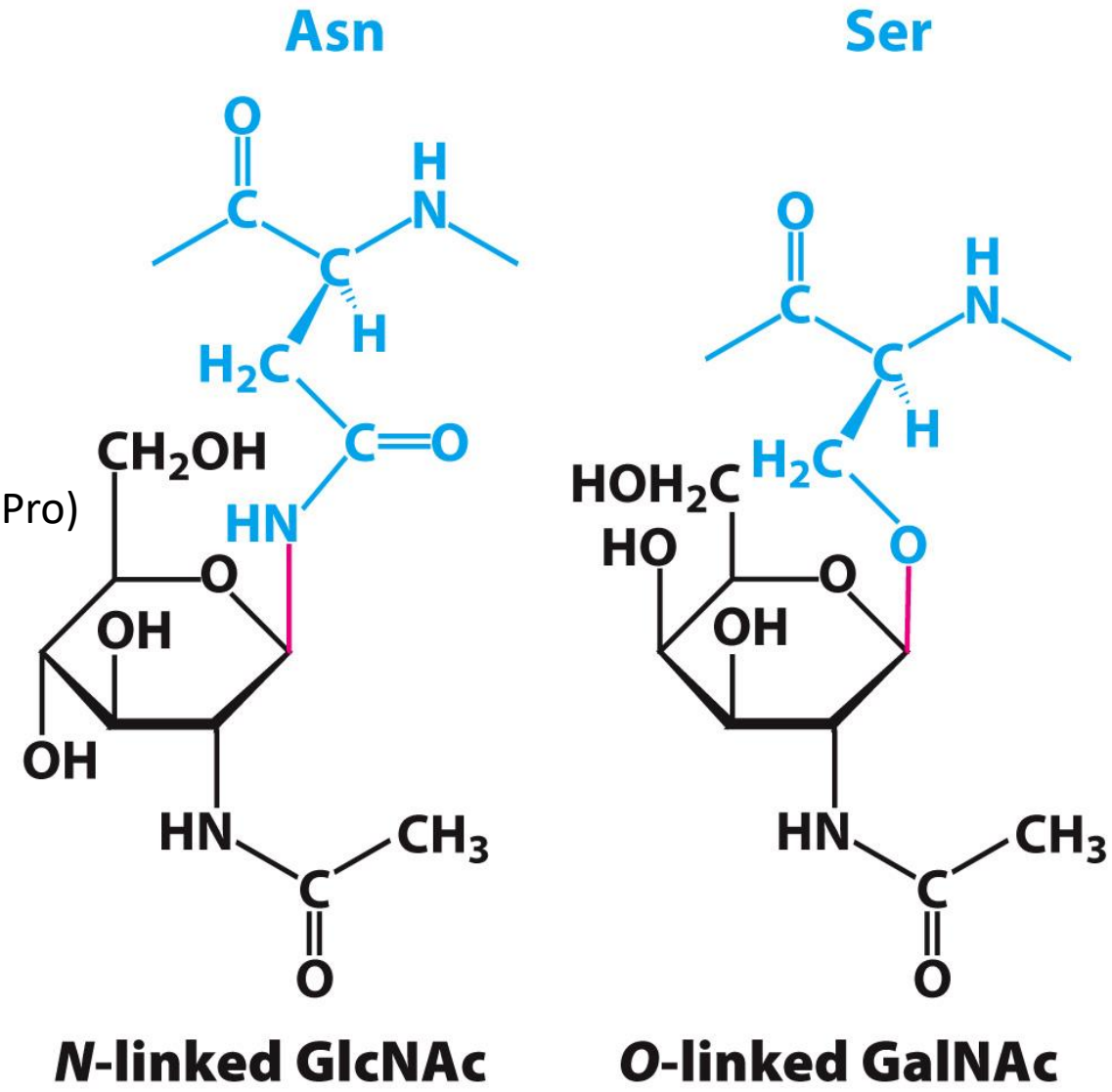
1. Glycoproteins: The protein is the largest component by weight. Glycoproteins play a variety of roles, including as membrane proteins.

2. Proteoglycans: The protein is attached to a particular type of polysaccharide called a glycosaminoglycan. By weight, proteoglycans are mainly carbohydrate. Proteoglycans play structural roles or act as lubricants.

3. Mucins or mucoproteins: Like proteoglycans, mucins are predominantly carbohydrate. The protein is characteristically attached to the carbohydrate by *N*-acetylgalactosamine. Mucins are often lubricants.

Glycoprotein are attached to the sugar part either through ASN (N-linkage) or through Ser or Thr (O-linkage)

In case or N-linkage:
Asn-X-Ser
Asn-X-Thr (X any residue except of Pro)



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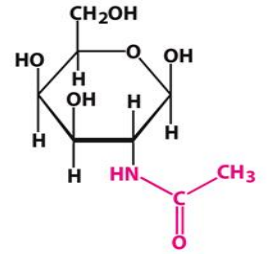
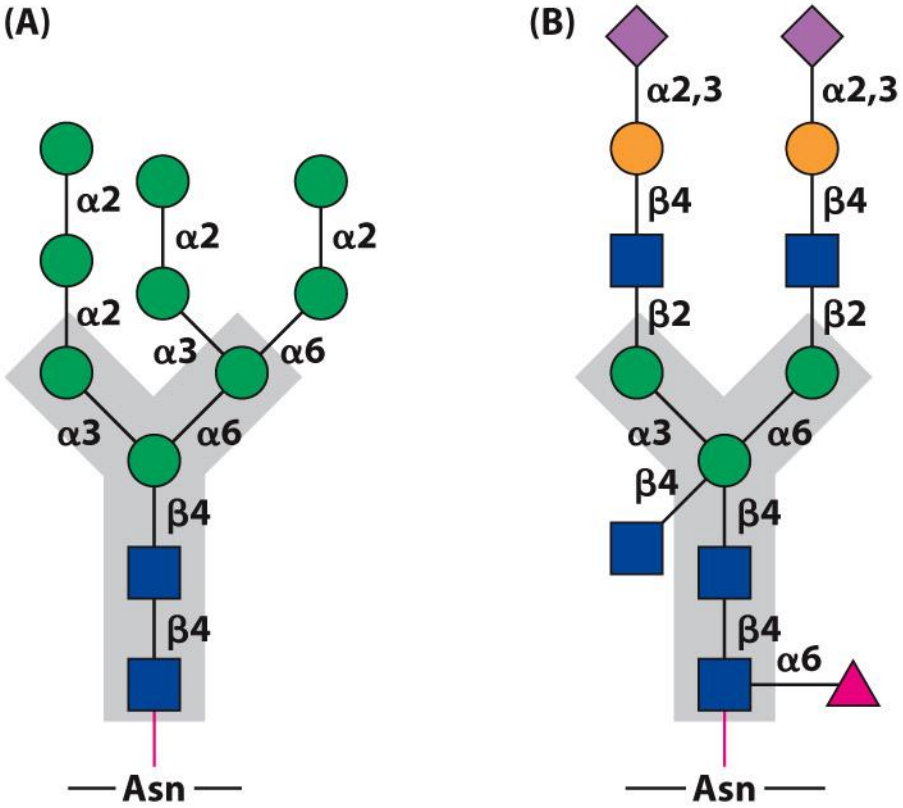
N-linkage oligosacharides: share a common pentasacharide core



Abbreviations for sugars

Fuc	▲	Fucose
Gal	●	Galactose
GalNAc	■	*N*-Acetylgalactosamine
Glc	●	Glucose
GlcNAc	■	*N*-Acetylglucosamine
Man	●	Mannose
Sia	◆	Sialic acid



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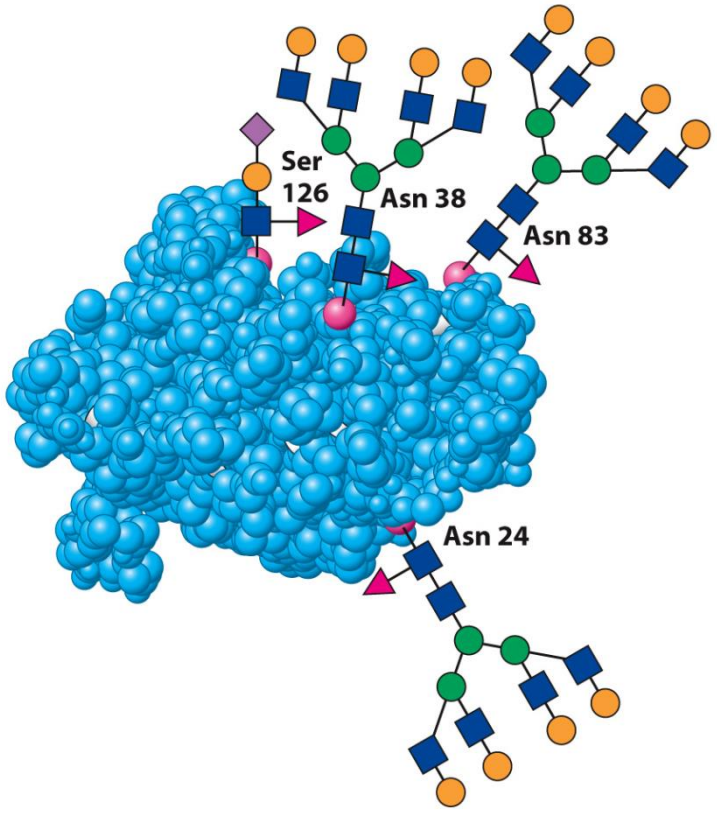
Physiological role of glycoproteins:

Erythropoietin, a glycoprotein 40% carbohydrate by weight,
Hormone that is secreted into the blood by the kidney to stimulate the production of red blood cells.

Glycosylation of erythropoietin enhances the stability of the protein in the blood.



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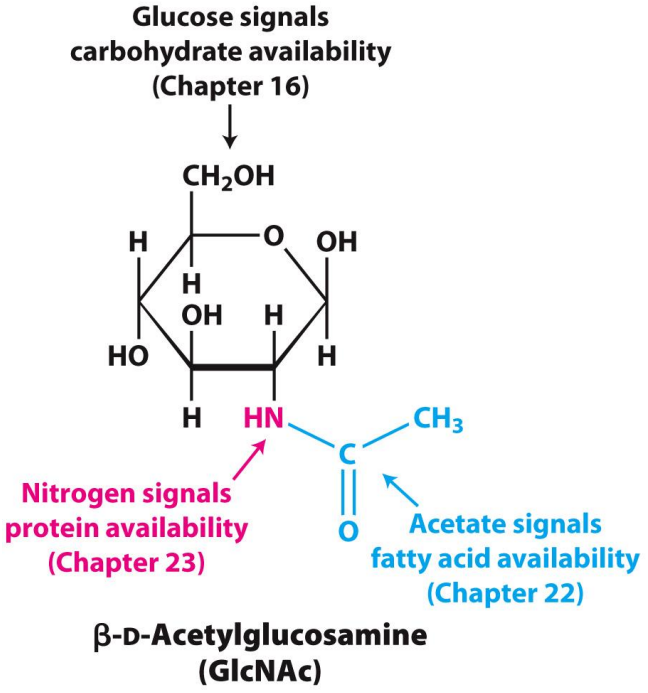
Physiological role of glycoproteins:

Many proteins are modified by the attachment of N-acetylglucosamine (GlcNAc) to serine or threonine residues by GlcNAc transferase. GlcNAc is attached to protein when nutrients are abundant.

[GlcNAc] reflects the active metabolism of sugars, amino acids and fatty acids

The attachment is reversible, with GlcNAcase removing the carbohydrate.

Improper regulation of the transferase has been linked to a number of pathological conditions such as insuline resistance, diabetes, cancer etc.



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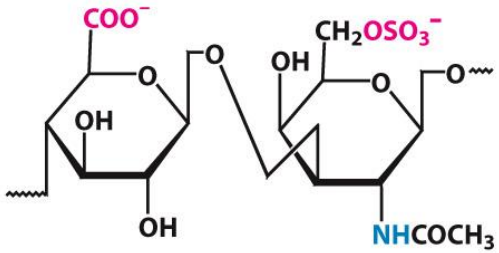
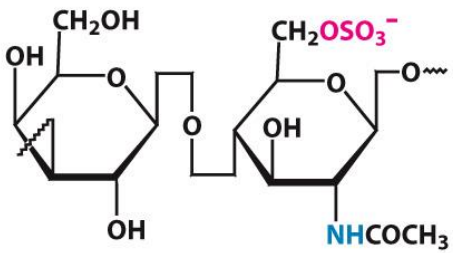
Proteoglycans

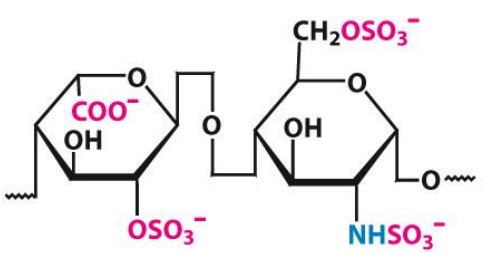
- Proteins attached to glycosaminoglycan
- Glycosaminoglycan make up up to 85% of Mw of proteoglycan
- Properties resemble to oligosaccharides
- Structural components and lubricants
- Properties depend on the oligosaccharide component
- Often includes a repeating units of glycosaminoglycan



Chondroitin 6-sulfate

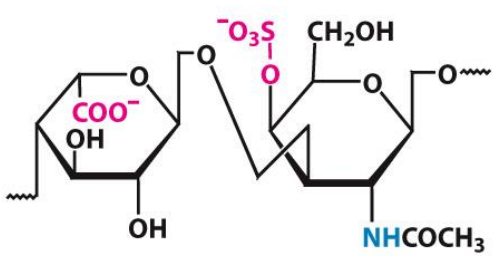


Keratan sulfate

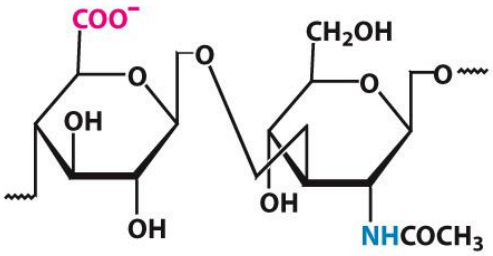


Heparin

Negatively charged carboxy or sulfate group
Heparin is anticoagulant



Dermatan sulfate



Hyaluronate

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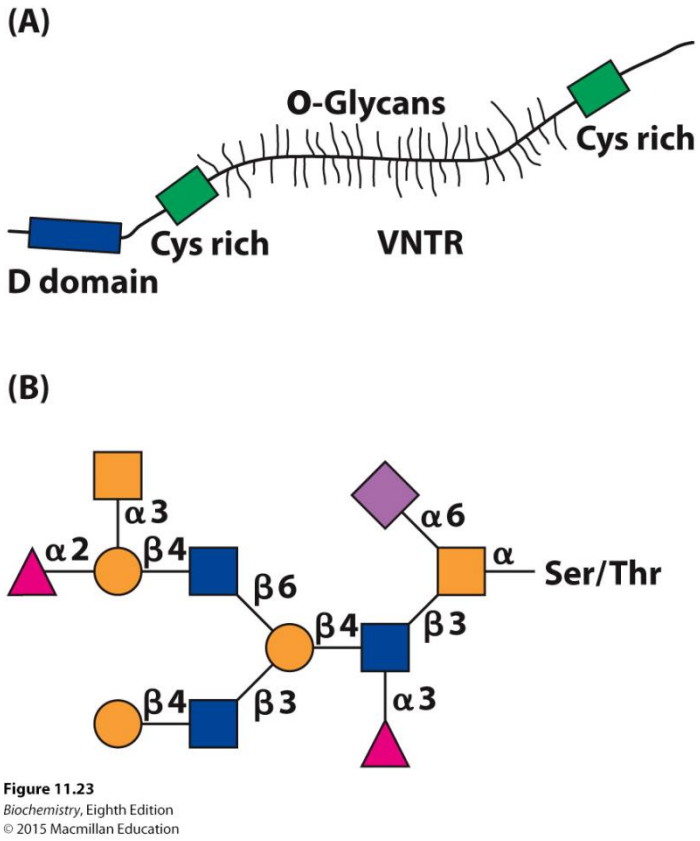
Mucins

- Protein component is heavily glycosylated at Ser or Thr reside
- Mucins form large polymeric structures
- Synthesized by specialized cells in gastrointestinal, genitourinary and tracheobronchial track
- Found in saliva as lubricants
- Protectant role, involved in immune responds, fertilization and cell adhesion.

VNTR – variable number of tandem repeat
Ser Thr reach region that is O-glycosylated



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