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CARBOHYDRATES

CARBOHYDRATES-

are among the most important organic compounds in the living organisms;

- is 65-90% of organic substances in plants, and is formed in the process of photosynthesis;
- in animals - 1-5%

THE FUNCTIONS OF CARBOHYDRATES :

- **Energetical function** – source of energy for the cellular reactions; carbohydrates supply energy (glucose) and serve as storage form of energy (starch, glycogen). Oxidation of a 1 g carbohydrate generates 4,5 kcal;
- **Structural function** – cellulose in plant, glycosaminoglycans, glycoproteins in connective tissue and in cell membranes in animals; structural elements of nucleic acids, coenzymes;
- **Informational** – are involved in cellular interactions, molecular recognition (receptors), determines the individual characteristics of the cell (antigens), etc .;
- **protective and mechanical functions;**
- **coenzymatic function;**
- **hydroosmotic, etc.**

In chemical terms carbohydrates are

<u>polyhydroxycarbonylic compounds</u> –

have several hydroxyl groups (-OH) and one carbonyl group (C = O), being

<u>polyhydroxy aldehydes or polyhydroxy ketones;</u>

and their oligo- or polymers

Classification of carbohydrates

- **Monosaccharides – contain a single carbohydrate unit and can't be hydrolyzed into smaller molecules; general formula $C_nH_{2n}O_n$, where $n \geq 3$;**
- **Oligosaccharides and Polysaccharides – can be hydrolyzed, on hydrolysis form the constituent monosaccharides;**
  - **Oligosaccharides** consist of two or more (ten in maximal number) monosaccharide units;
  - **Polysaccharides** consist of hundreds or even thousands of monosaccharide units joined together to form macromolecules, or polymers.

Monosaccharides

is classified :

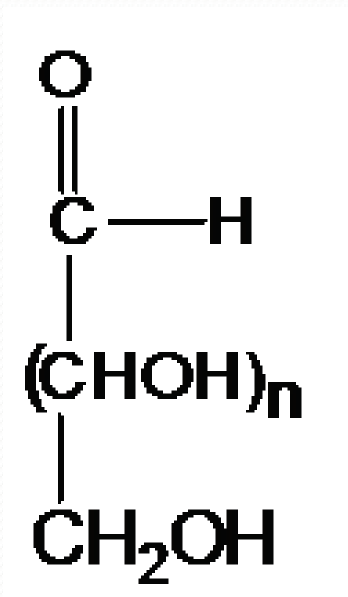
- according to the number of C atoms :

trioses - C_3, tetroses - C_4, pentoses - C_5, hexoses - C_6, heptoses - C_7

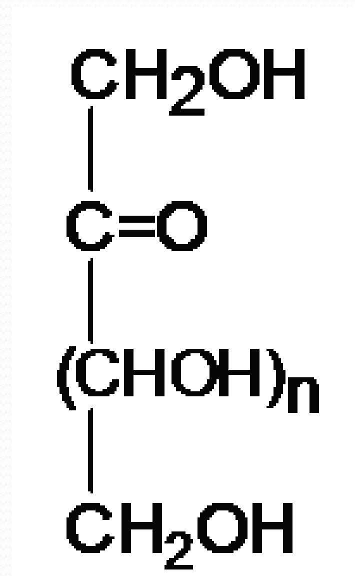
- according to the position of the functional group:
  - ✓ **aldoses - the carbonyl group is at the first carbon atom and the monosaccharide is an aldehyde;**
  - ✓ **ketoses - the carbonyl group is at a different carbon atom and the monosaccharide is a ketone.**

The structure of monosaccharides -

the general formula of polyhydroxy aldehydes (aldoses) and polyhydroxy ketones (ketoses):



Aldoses (n = 1,2,3..)

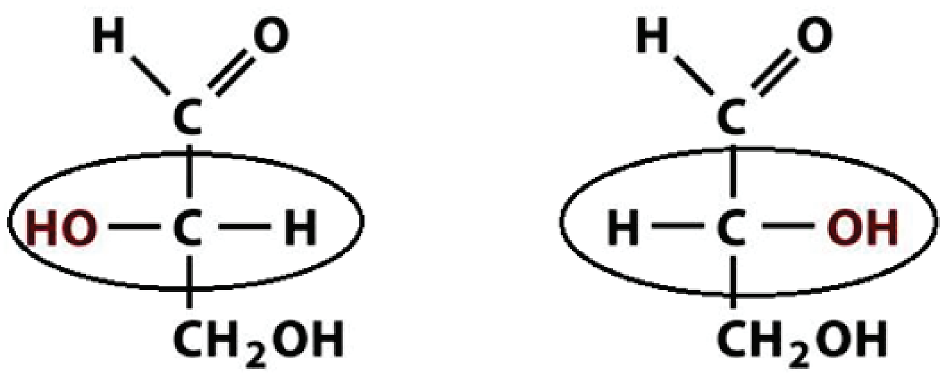


Ketoses (n = 0,1,2,3…)

Stereoisomeria of monosaccharides

Monosaccharides contain one or more **chiral carbon atoms** (exception - the ketose with n=0 – dihydroxyaceton).

The relative configuration of the monosaccharides can be determined using the configuration standard – glyceraldehyde (n=1). Glyceraldehyde has one chiral carbon atom and therefore has two enantiomers (mirror-image isomers)



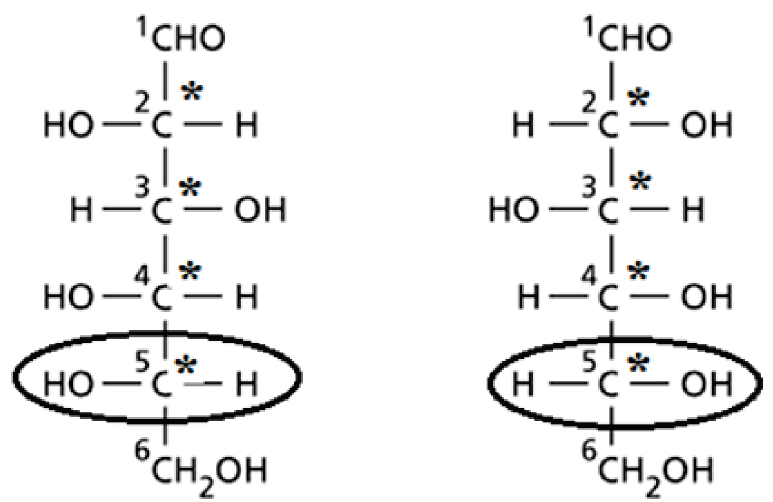
L(-)-glyceraldehyde D(+)-glyceraldehyde

Only the dextrorotary (D(+)) enantiomer occurs naturally.

Stereoisomeria of monosaccharides

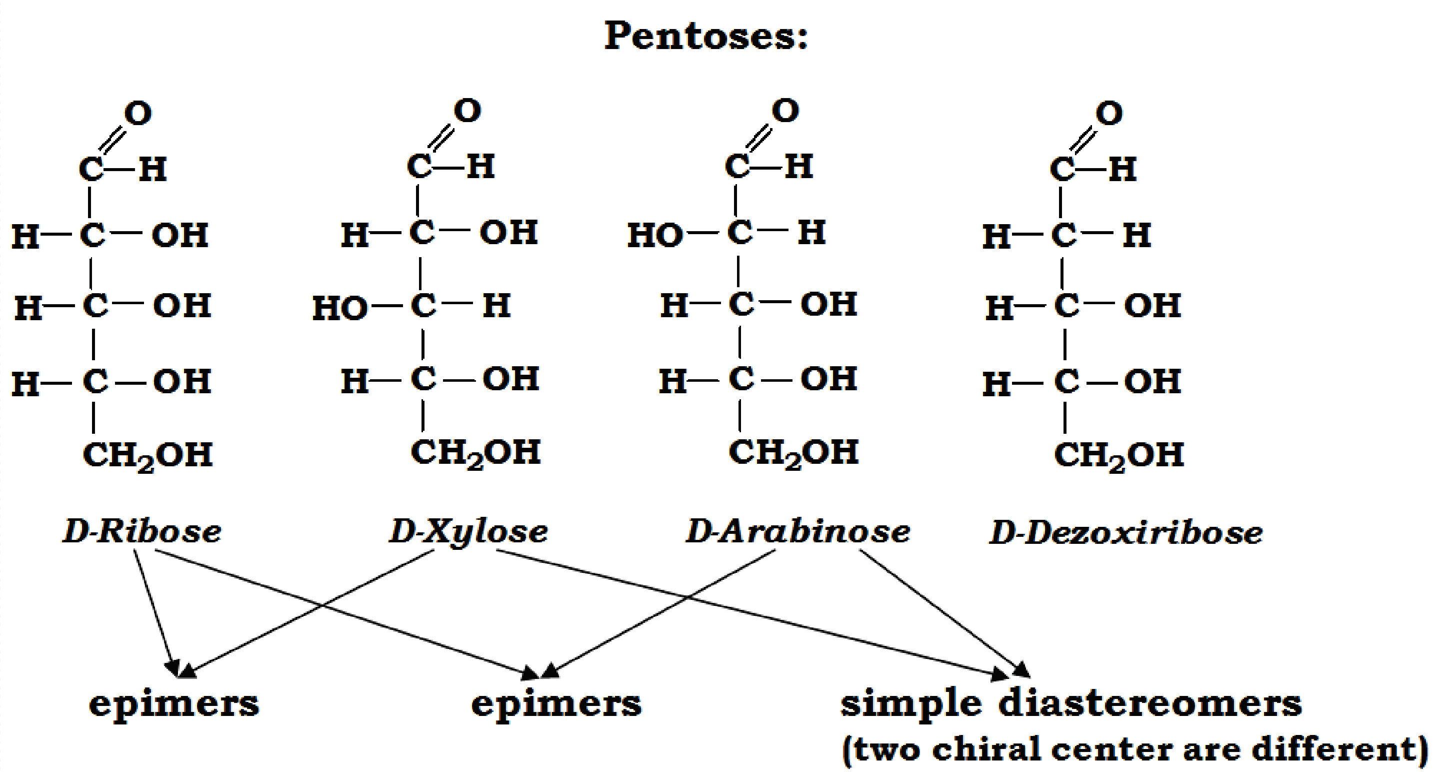
There are a great number of stereoisomers for a monosaccharide having more chiral atoms. For example, aldohexoses ($C_6H_{12}O_6$), that contain 4 chiral atoms, have 16 stereoisimers (N=2n) and 8 pair of enantiomers

To determine the belonging of monosaccharide to L- or D-series we use the configuration at the farthest carbon atom from the carbonyl group.

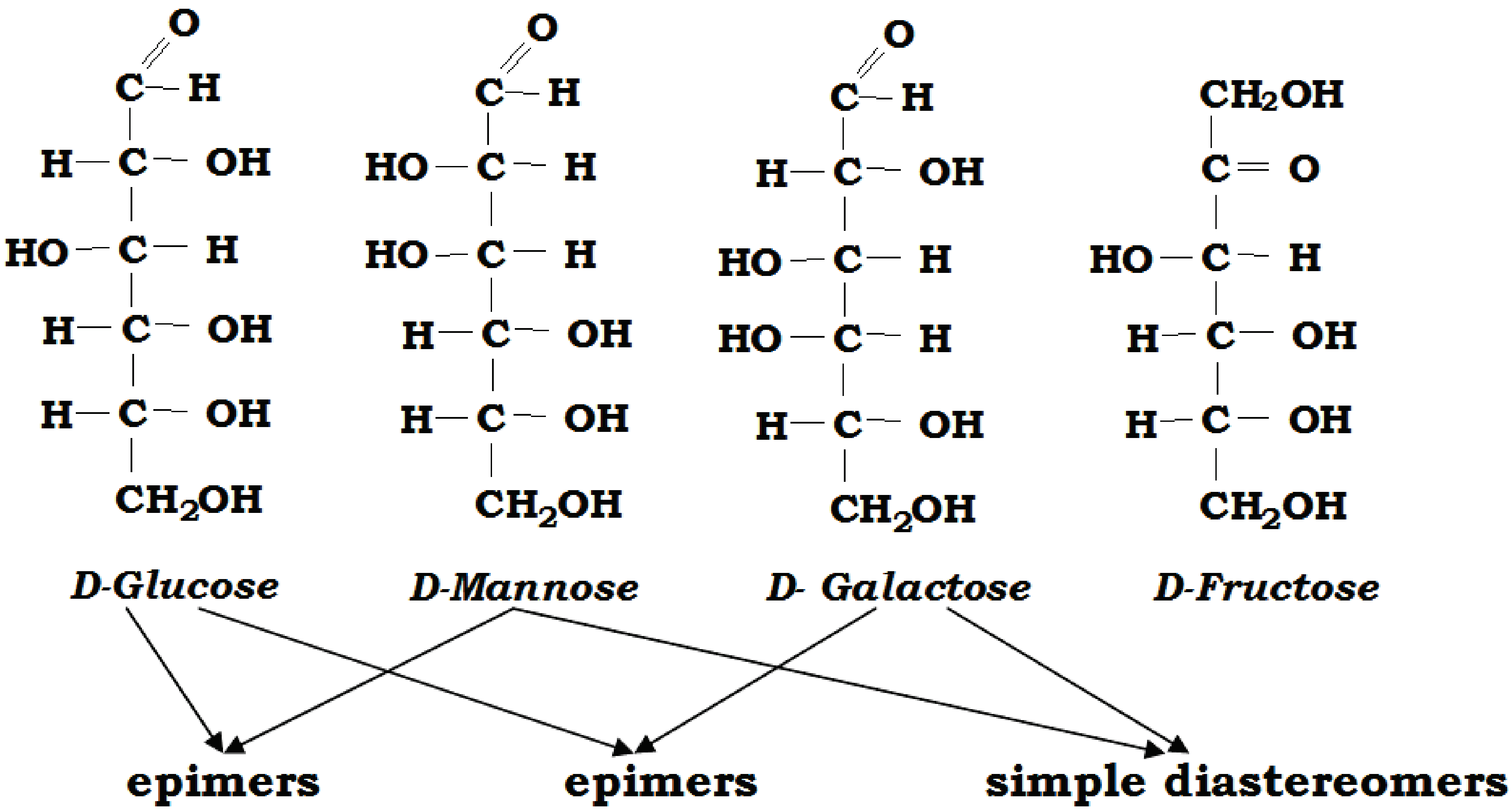


L-glucose D-glucose

- Stereoisomers, which differ by the configuration of one or more chiral atoms, are called **diastereomers**.
- Two diastereomers which differ only by the configuration of one chiral atom are called **epimers**.



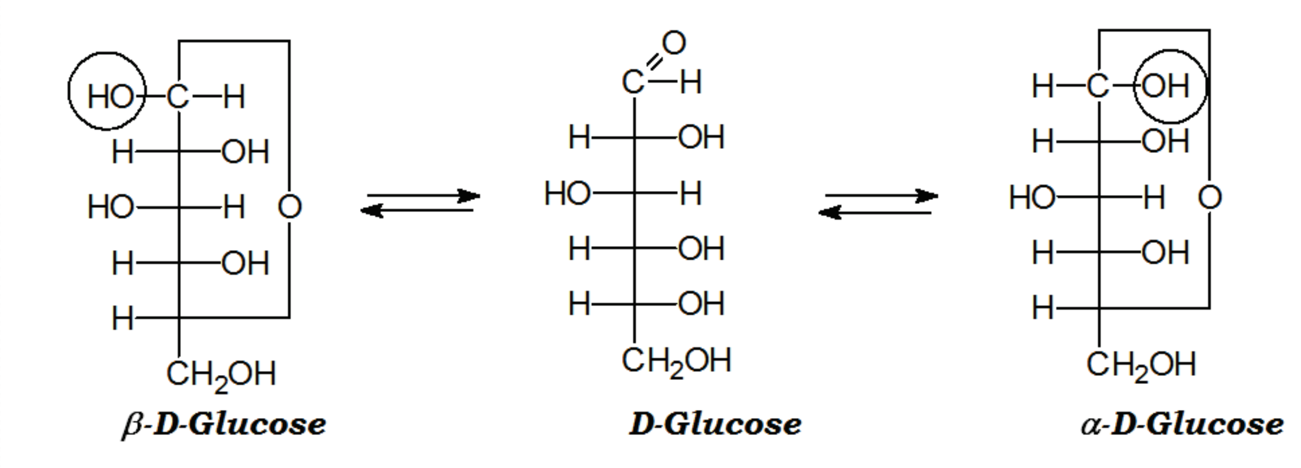
Hexoses:



D-Glucose
D-Mannose
D- Galactose
D-Fructose
epimers
epimers
simple diastereomers

Cyclic structures of monosaccharides: hemiacetal formation

If both the hydroxyl and carbonyl group are present in the same molecule, an intramolecular reaction can take place, leading to the formation of **a cyclic hemiacetal**. In pentoses and hexoses the **C-1 and C-4 or C-5** atoms may be close in space, making possible the interaction of the aldehyde (or ketone) and hydroxyl functional groups, and formation of a cyclic hemiacetal:



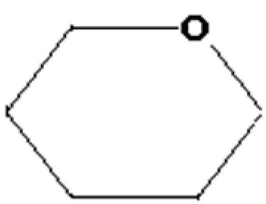
Cyclic hemiacetal formation leads to an additional chiral center, since the first C-1 carbon atom becomes asymmetric. This chiral center C-1 is called **anomeric**, and the two stereoisomers –

α- şi β-anomers.

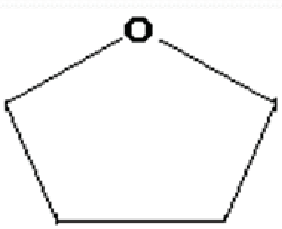
Fischer projection formulas used above do not reflect the steric relations between atoms in the molecule, so do not reflect the real shape of the molecules. A more accurate structure of monosaccharides is achieved by using

Haworth formulas.

Pyranose and furanose rings in Haworth formulas are represented as flat ring systems located perpendicular to the plane of the drawing, and the substituents are below or above the plane of the ring:



Pyranose cycle (six-membered)

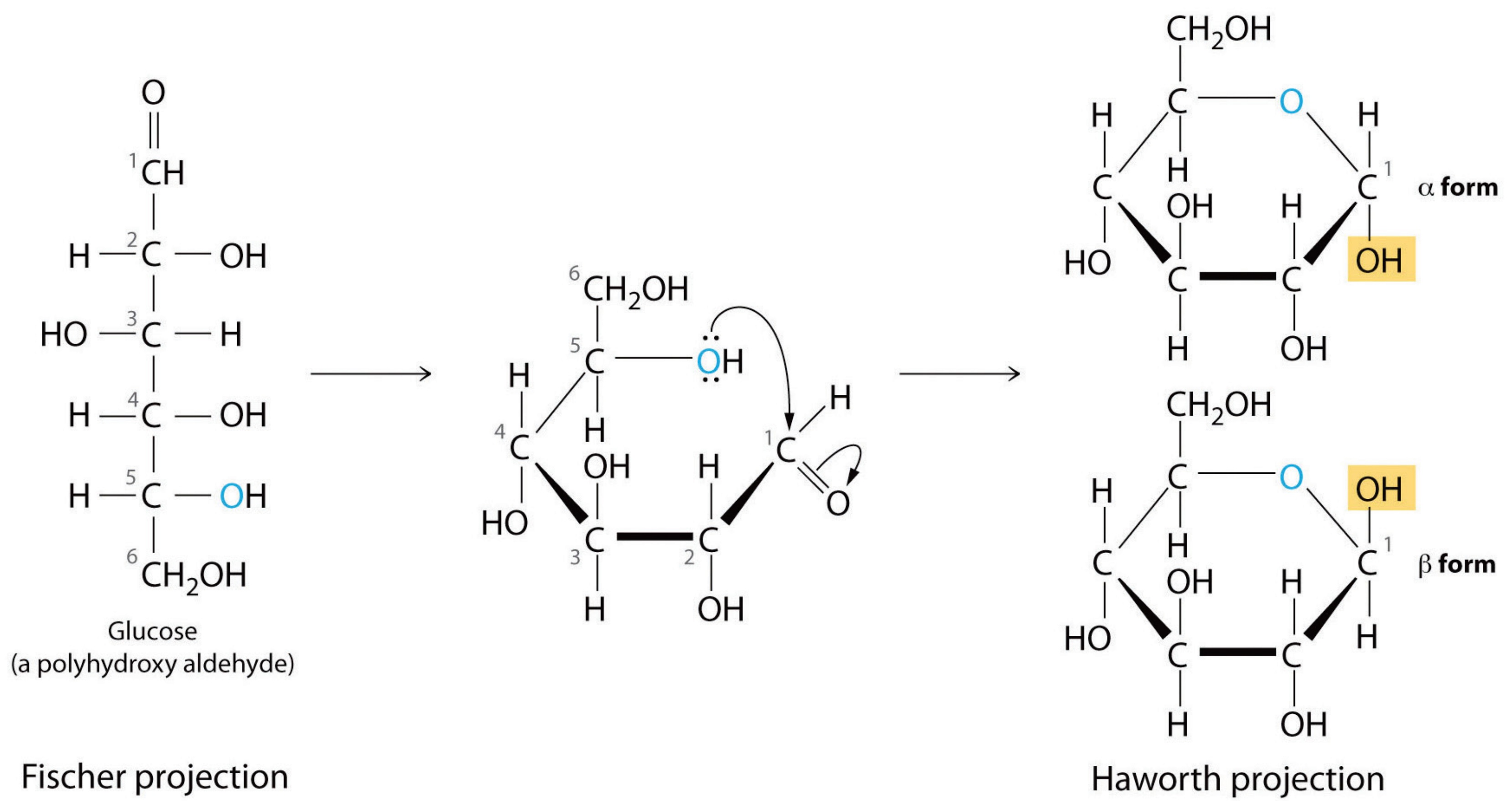


Furanose cycle (five-membered)

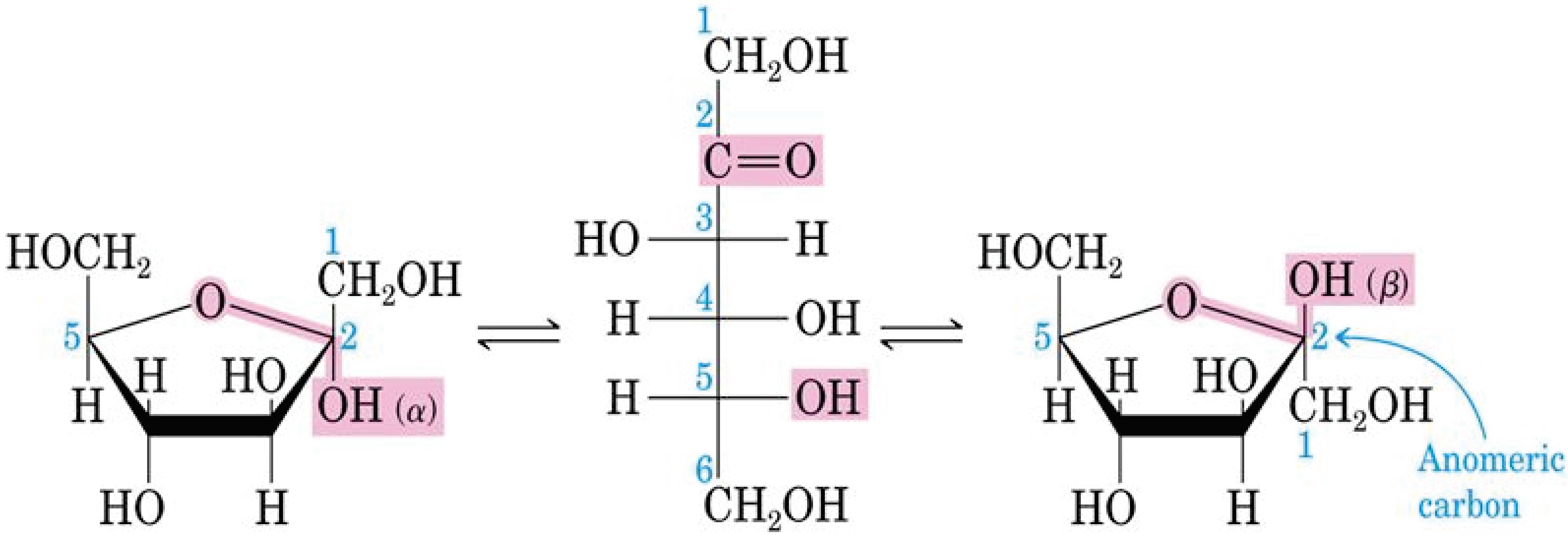
The two anomer forms can pass one to another via acyclic form, thus establishing a dynamic equilibrium called

cyclo-oxo-tautomerism.

For example, D-glucose has several tautomeric forms, including the pyranose form and the open form (oxo) :



D-fructose – a representative of ketohexoses – also exists as several tautomeric forms, but furanose forms predominate:



α-D-Fructofuranose
α-D-Fructose

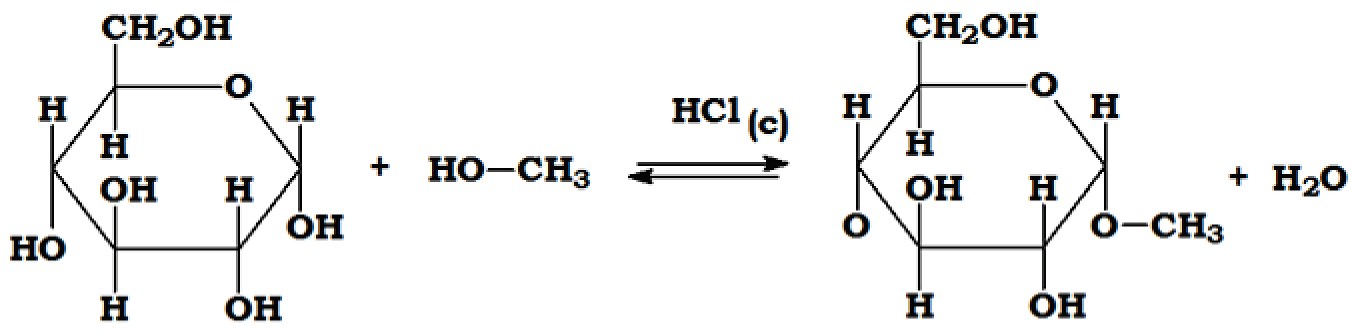
D-Fructose

β-D-Fructofuranose
β-D-Fructose

Chemical properties of monosaccharides

1. Glycoside formation

Monosaccharides as cyclic hemiacetals interact with alcohol under acid catalysis forming acetals called ***glycosides***:



methyl α-D-glucopyranoside

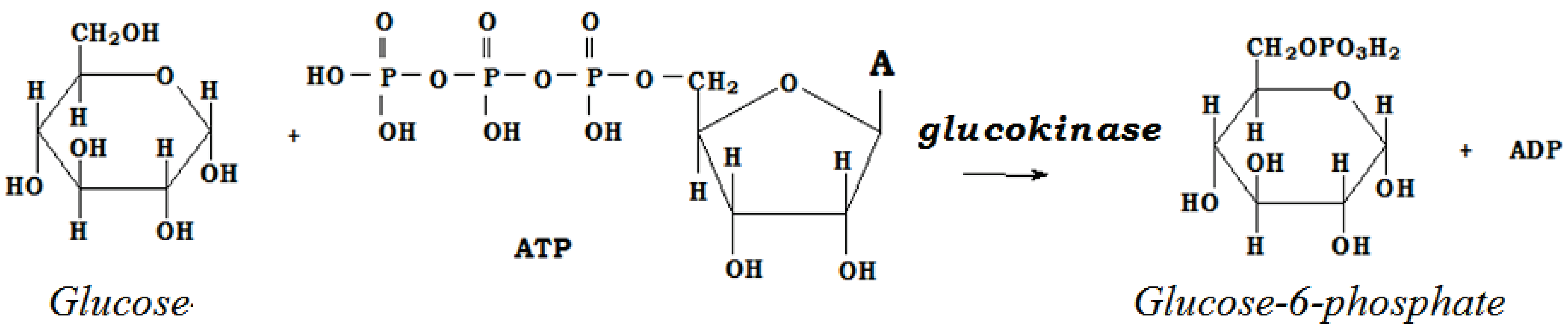
Glycosides are widespread in nature and have a great importance in life processes (polysaccharides, cardiac glycosides, etc.).

There are also **N-glycosides**, for example *nucleosides* as components of nucleic acids.

2. *Phosphate ester formation*

In the living cells the reaction of monosaccharides phosphorylation occurs with the formation of phosphoric acid esters (phosphates).

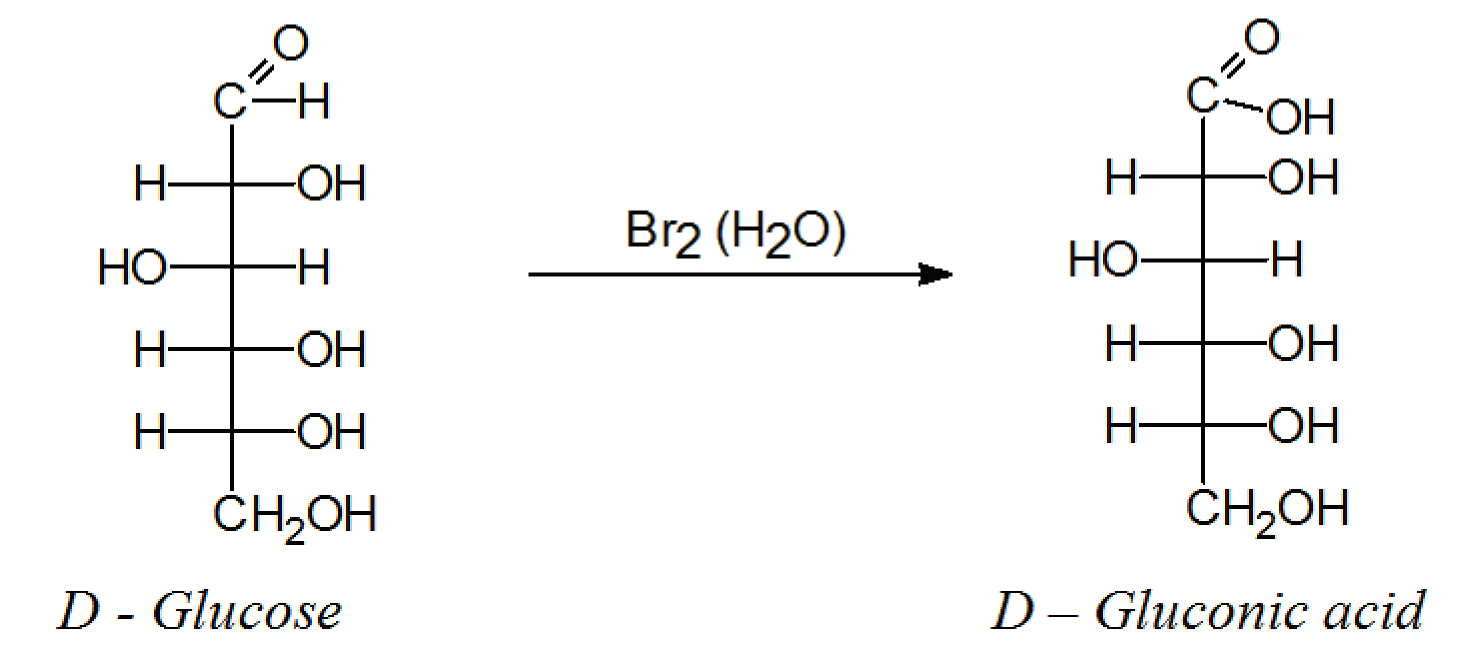
For example, glucose phosphorylation takes place with the participation of ATP and enzyme glucokinase:



3. *Oxidation of monosaccharides*

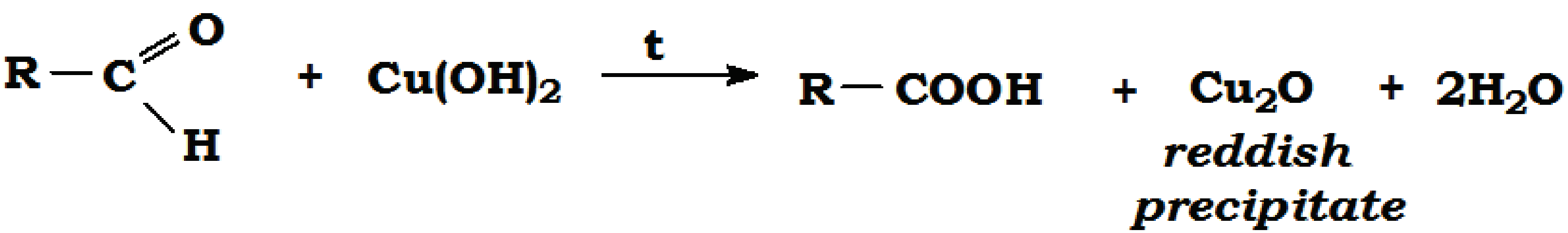
- Like other aldehydes, aldoses are easily oxidized to carboxilic acids. In soft conditions monosaccharides form ***aldonic (gliconic) acids***.

For exemple: glucose oxidation leads to the formation of gluconic acid:

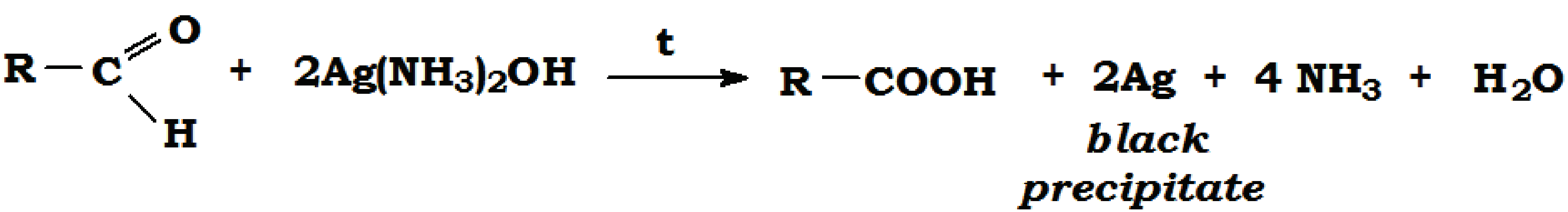


- Aldoses react with Fehling's reagent ($Cu(OH)_2$) and Tollen's reagent (Ag^+ in aqueous ammonia), to form the oxidized sugar and a reduced metal. All these reactions serve as simple chemical tests for **identification of reducing sugars** (reducing because the sugar reduces the metal).

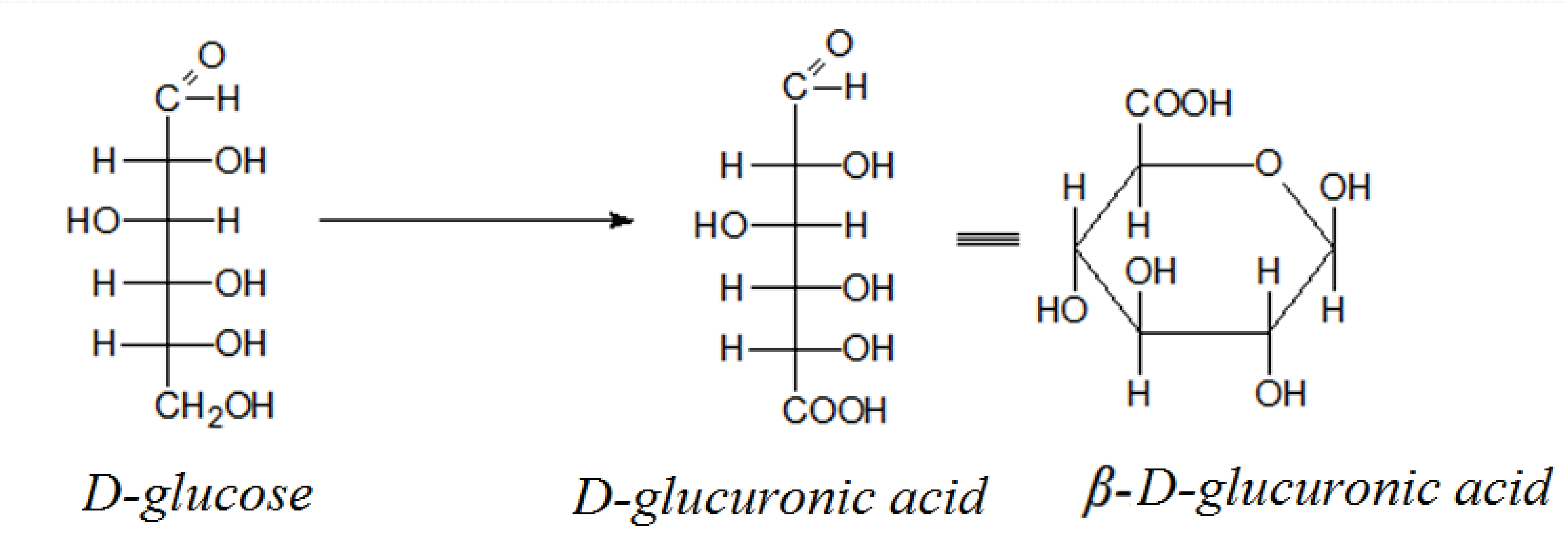
a) With Fehlling reagent:



b) With Tollens reagent:



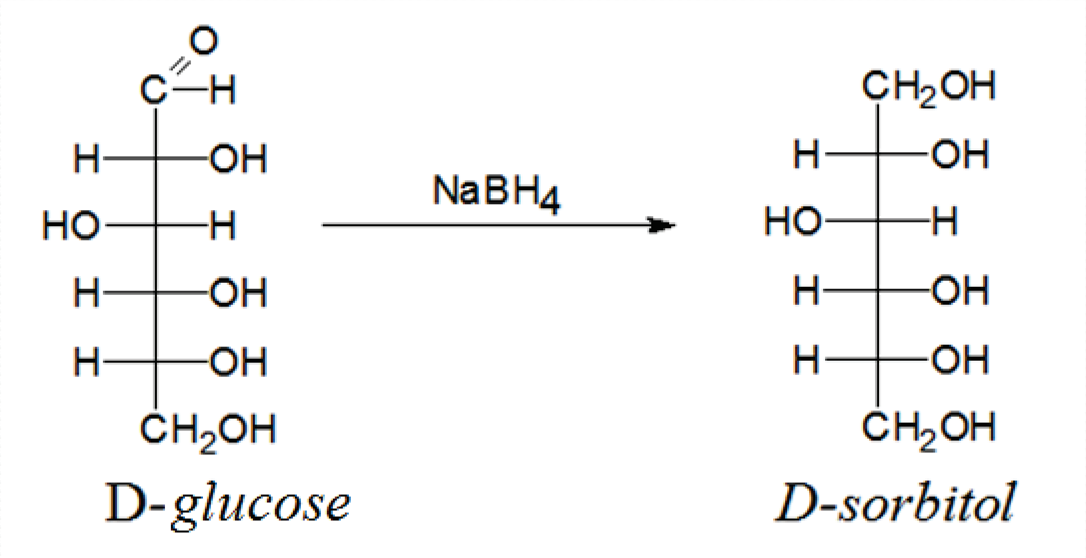
In animal organism (*in vivo*) monosaccharides can be oxidized at the C_6 atom with the participation of enzymes to form **uronic acids**:



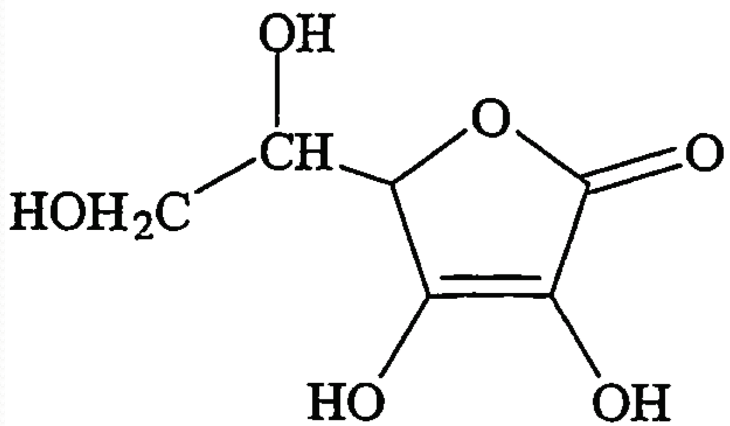
Glucuronic acid occurs in proteoglycans(mucopolysaccharides);
and is important in the reaction of xenobiotics conjugation in liver – an important process of metabolites, poisons and drugs detoxification, transformation and excretion via the liver, intestine, and kidney.

4. Reduction of monosaccharides

Treatment of an aldose or ketose with borohydride reduces it to a polyalcohol called **alditol**. The reduction of glucose leads to the formation of D-sorbitol:



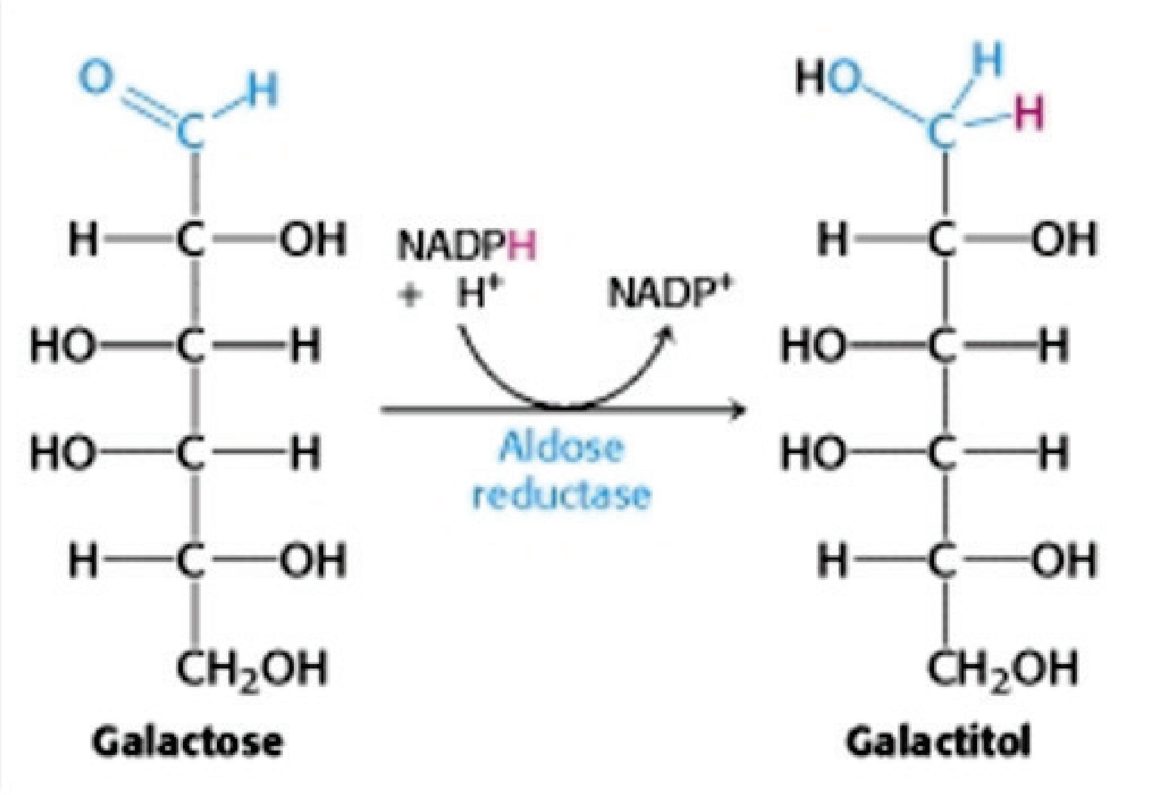
- Reduction of glucose in D-sorbitol is one of reactions to obtain **ascorbic acid (vitamin C):**



Ascorbic Acid

Ascorbic acid plays an essential role in human body - it has potent antioxidant properties, is important in antibacterial protection, detoxification, the synthesis of collagen in connective tissue. It insufficiency in the diet causes scurvy, decreases the body's resistance to infectious diseases etc.

The reductind product of galactose is **galactitol**:

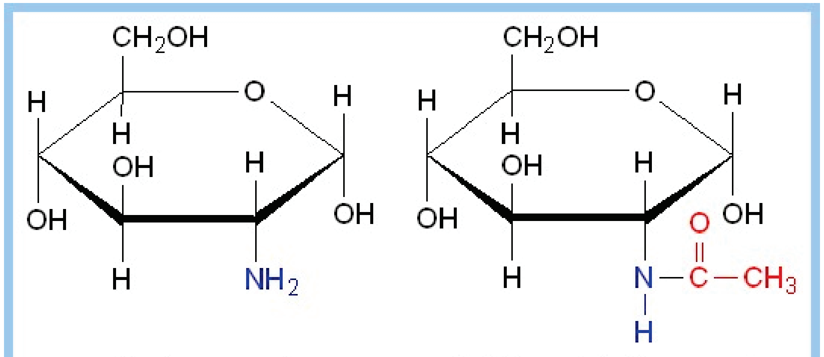


Galactitol is produced from galactose in a reaction catalyzed by the enzyme **aldose reductase**. In people with ***galactosemia*** (an inherited disorder of the galactose metabolism) an excess galactitol forms in the lens of the eye leading to **cataracts**.

Aminosugars

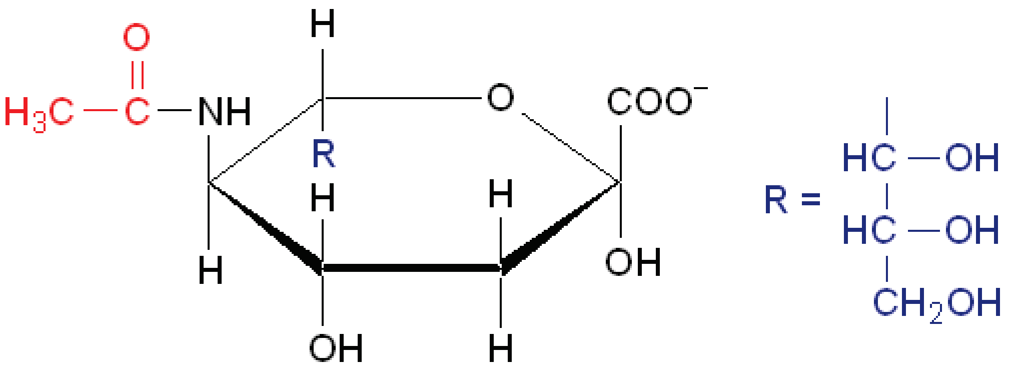
-contain amino groups.

-The main representatives of **aminosugars** are:



α-D-glucosamine α-D-*N*-acetylglucosamine

An important representative of aminosugars is **neuraminic acid** and its derivatives - **sialic acids**. In the free state are found in the spinal fluid, are part of brain gangliosides, are involved in the nerve impulses conducting. For example**, N-acetylneuraminic acid:**



N-acetylneuraminate (sialic acid)

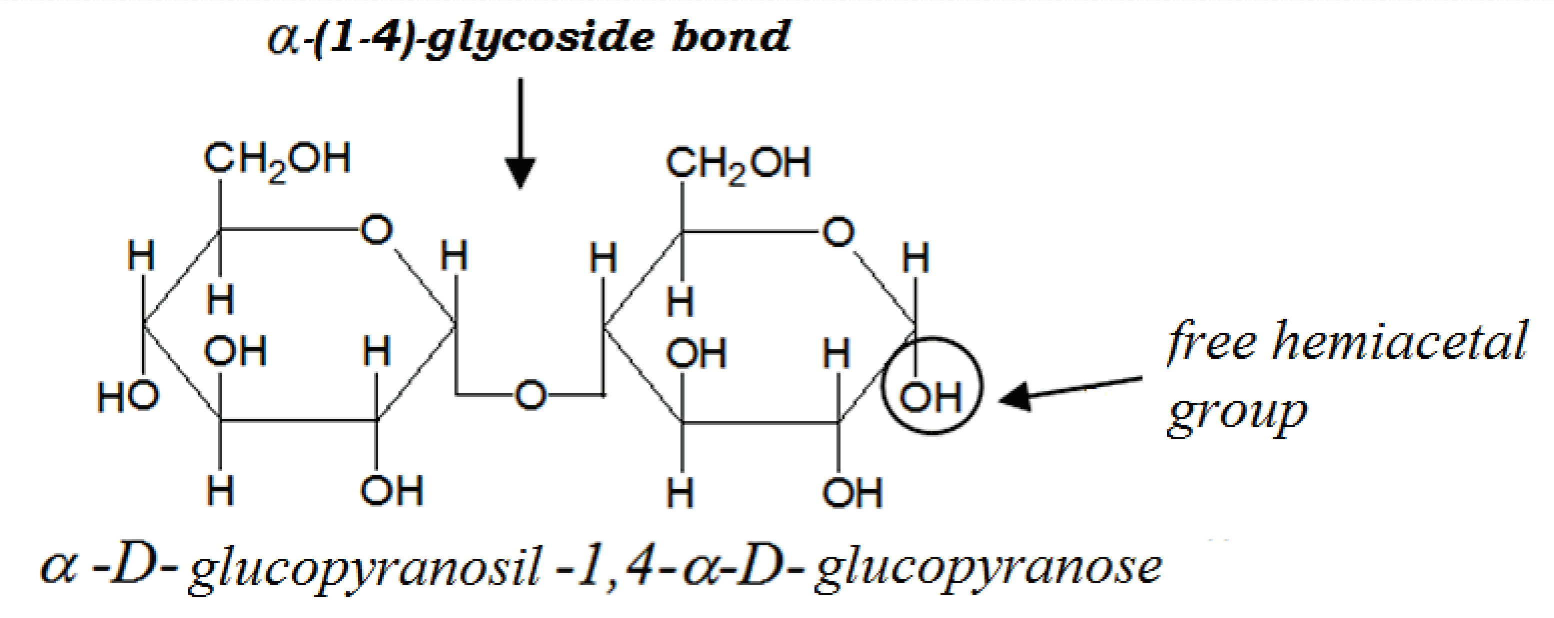
Oligosaccharides

- consist of 2 or more (up to 10-20 monosaccharide units) joined by **glycosidic linkages;**
- are classified as: **di-, tri-, tetra saccharides**;
- are divided into ***reducing and non-reducing***;
- the most important are the disaccharides: **maltose, lactose, sucrose.**

Reducing disaccharides

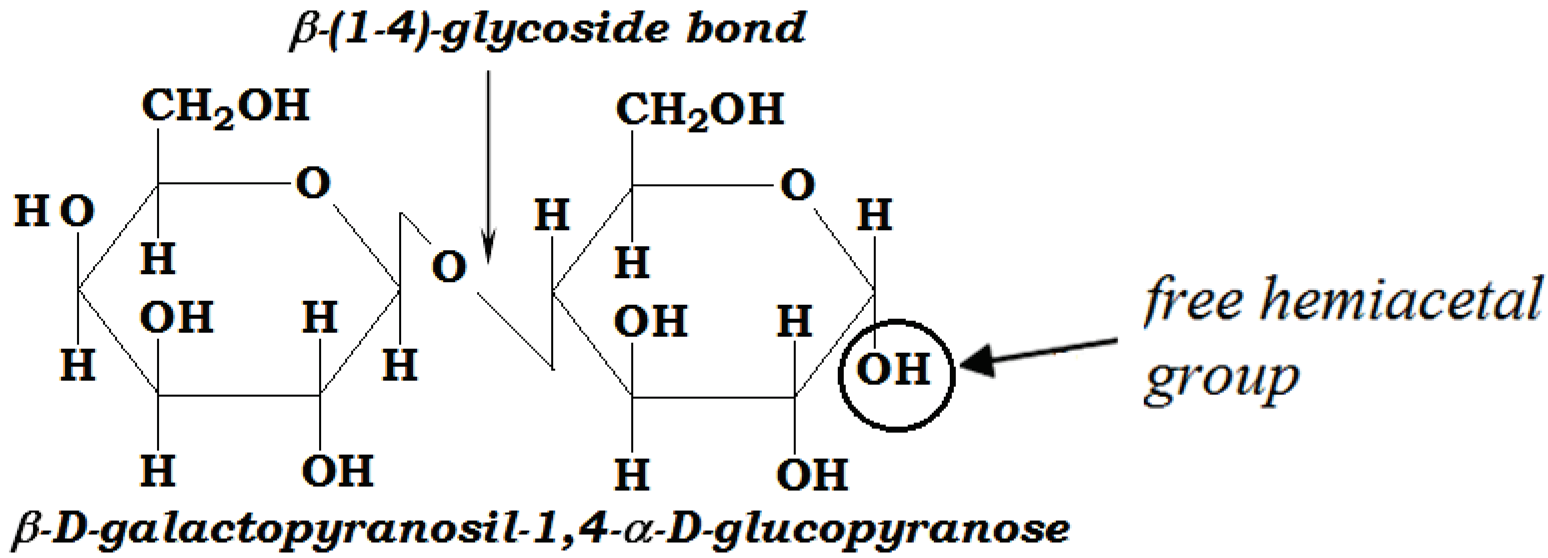
1. Maltose

- consists of two **α-D-glucoses** (α-D-glucopyranoses) joined by a **α(1→4)glycoside bond**
- is the product of starch cleavage in the duodenum
- Maltose is a ***reducing*** sugar because one of the monosaccharide unit has a free hemiacetal group, which can reduce Tollends' or Fehling's reagent:



2. Lactose

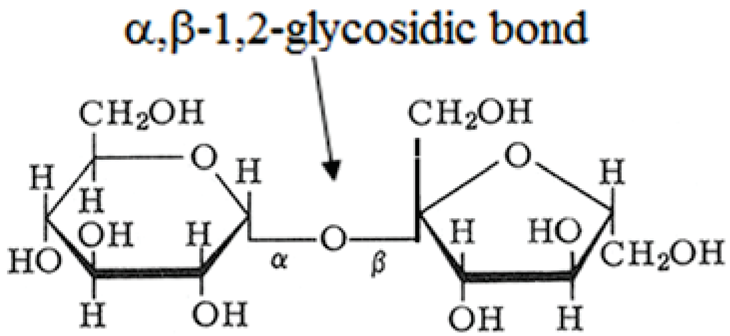
- Consists of **β-D-Galactose** and **α-D-Glucose** joined by a **β (1→4) glycoside bond.**
- lactose is present in the mammalian milk

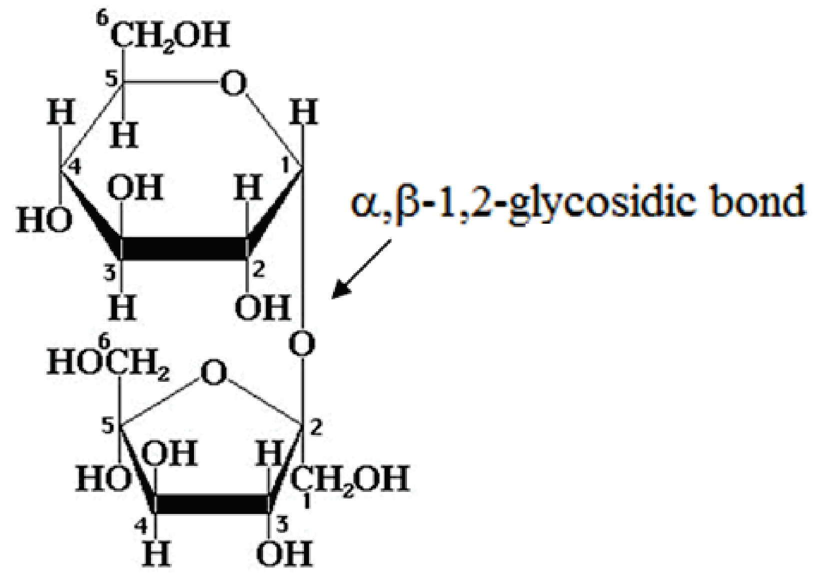


Non-reducing disaccharides

3. Sucrose

- Consists of **α-D-Glucose** and **β-D-fructose** joined by a **α1→β2 glycoside bond.**





Sucrose

α-D-glucopyranosyl-1,2-β-D-fructofuranoside

Polysaccharides

- are natural polymers that consist of hundreds (or even thousands) of monosaccharide units joined through glycoside linkages.
- are divided into 2 groups: **homopolysaccharides and heteropolysaccharides;**
- **homopolysaccharides** are polymers that consist of only one type of monosaccharides – for example starch (the polymer of α-D-glucose);
- **heteropolysaccharides** are polymers that consist of 2 or more different types of monosaccharides or their derivatives.

Homopolysaccharides

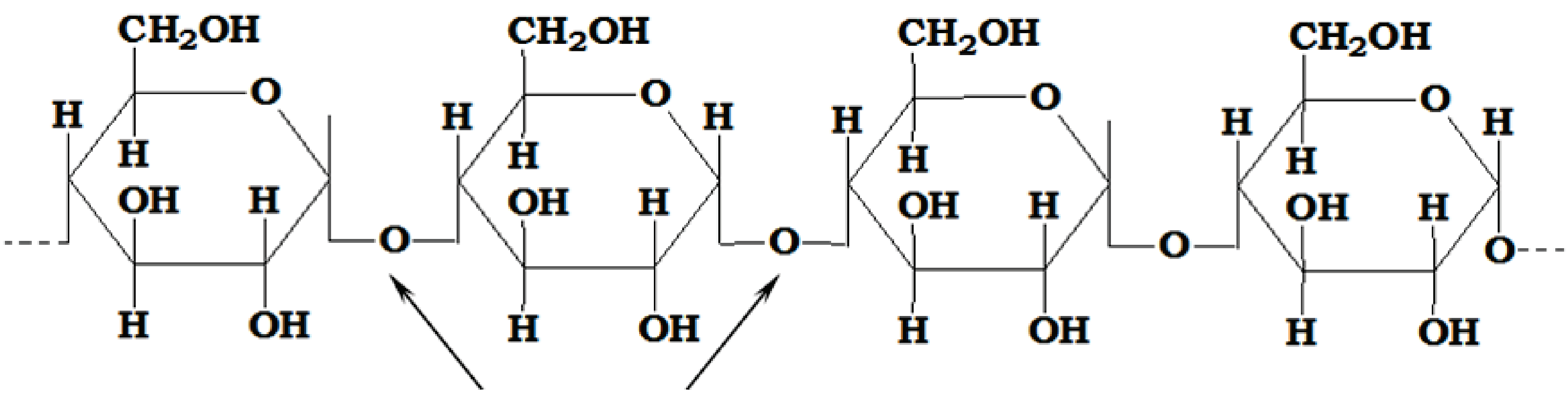
- **Starch**
- **Glycogen**
- **Cellulose**

Starch-

- Reserve polysaccharide in plants, is formed in the process of photosynthesis and is stored;
- Starch is a mixture of two homopolizaharides - ***amylose (20%)*** and ***amylopectin (80%)***. Both components are made of **α-D-glucose** joined by **α(1 →4) glycoside bonds**;

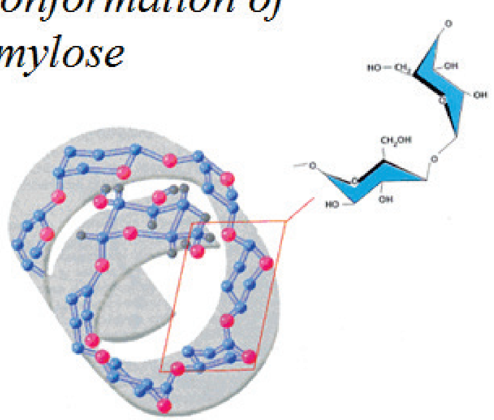
Amylose

has a linear structure, spiral in secondary structure:



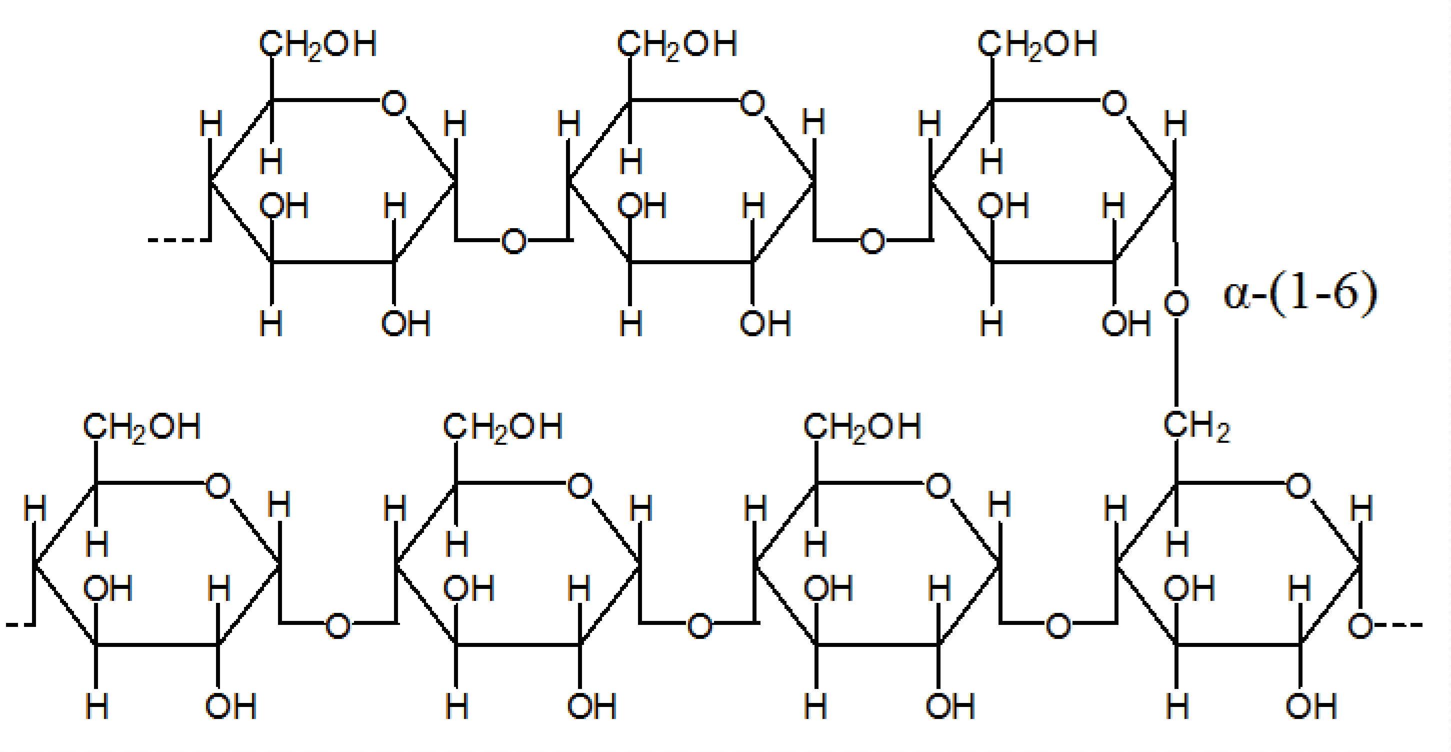
α(1 →4) glycoside bond

Conformation of amylose



Amylopectin

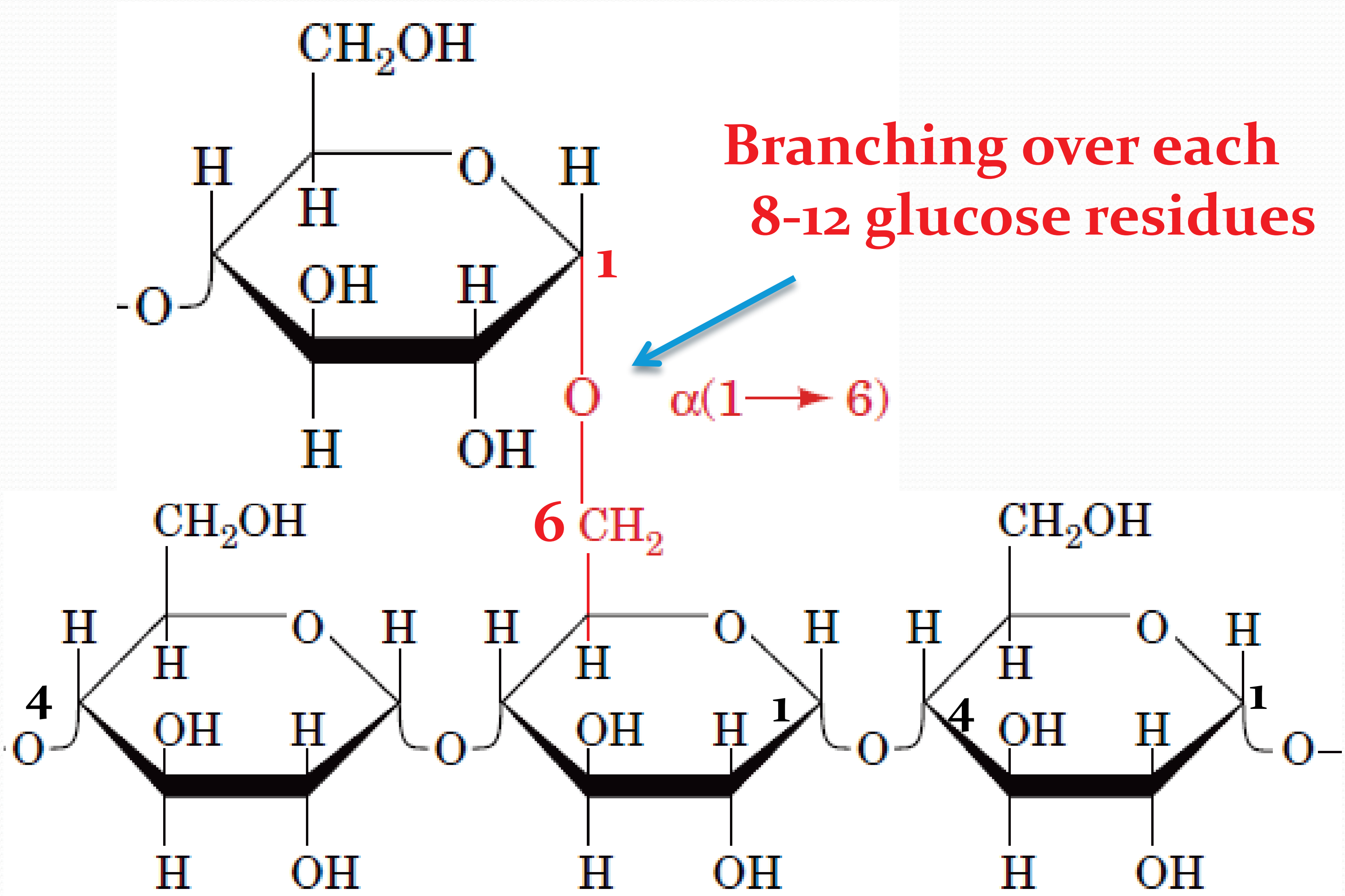
- is a polysaccharide with branched structure - in the main chain the residues of α-D-glucose are connected to each another by α(1-4)-glycosidic bonds, and in the branching point – by α(1-6) glycosidic bonds. A branching occurs every 24 to 30 glucose residues.



Glycogen

- Is a reserve polysaccharide in human and animals;
- Are stored predominantly in muscle (1-2%) and liver (7-10%)
- It serves as a reserve of glucose needed to maintain the blood glucose level and as a source of energy in muscle;
- It consists of thousands of **α-D-glucose** residues joined by two types of **glycosidic linkages: α (1 → 4) and α (1 → 6);**
- In the glycogen macromolecule the branching is repeated over every 8-10 glucose residues in the backbone.

Chemical structure of glycogen



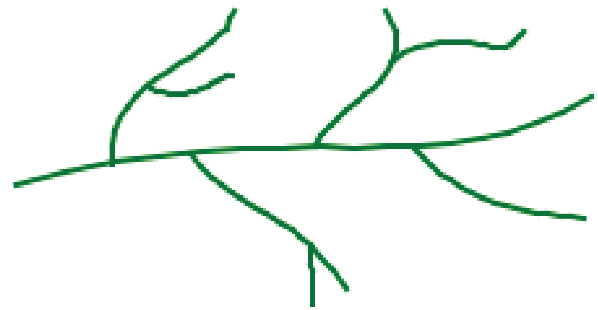
CARBOHYDRATE POLYMER STRUCTURES

glucose homopolymers

AMYLOSE

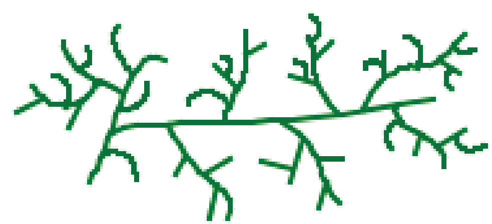
left-handed helix
MW 150 - 600 kD
α 1-4 linkages

AMYLOPECTIN



few thousand to million residues
branch lengths 20-25 residues
α 1-4 & α 1-6 linkages

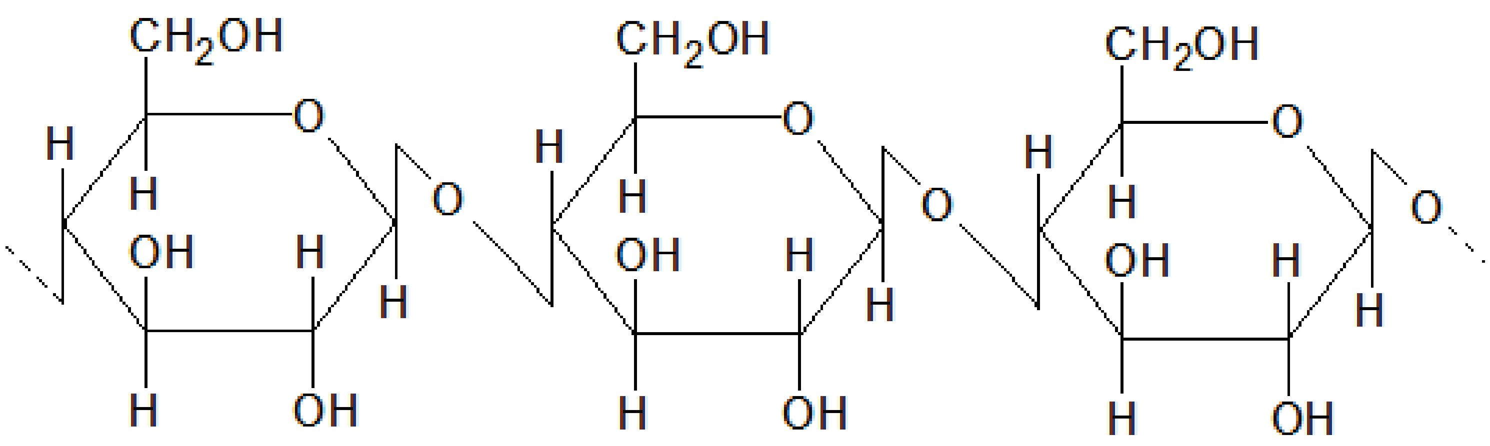
GLYCOGEN



MW up to 20 million
branch lengths 5-10 residues
α 1-4 & α 1-6 linkages

Cellulose

- Is a homopolysaccharide with structural functions in plants;
- The linear molecules are composed of **β-D-glucose** (10000-15000 units) joined by **β(1→4) glycoside bond:**

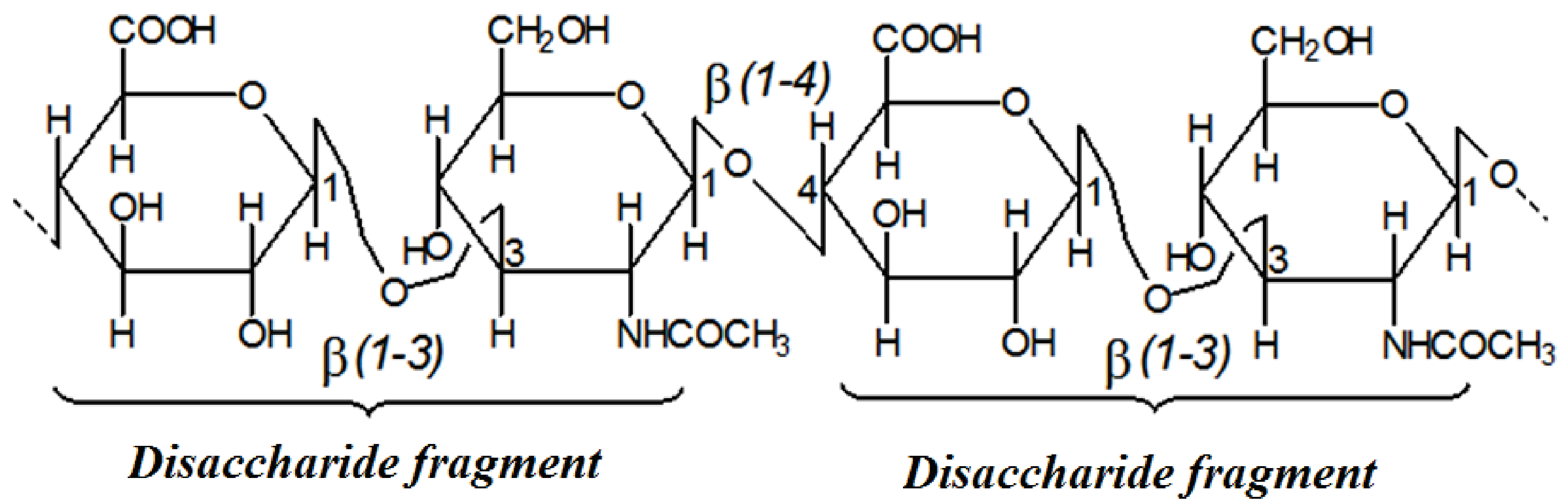


Heteropolysaccharides

- Hyaluronic acid
- Chondroitin sulfates
- Heparin

Hyaluronic Acid

Hyaluronic acid is a linear heteropolysaccharide, unbranched, consisting of disaccharide units joined by **β (1-4)-glycosidic** bonds. Disaccharide fragments consist of **β-D-glucuronic** acid and **N-acetyl-β-D-glucosamine** joined by **β (1-3)-glycosidic bonds:**

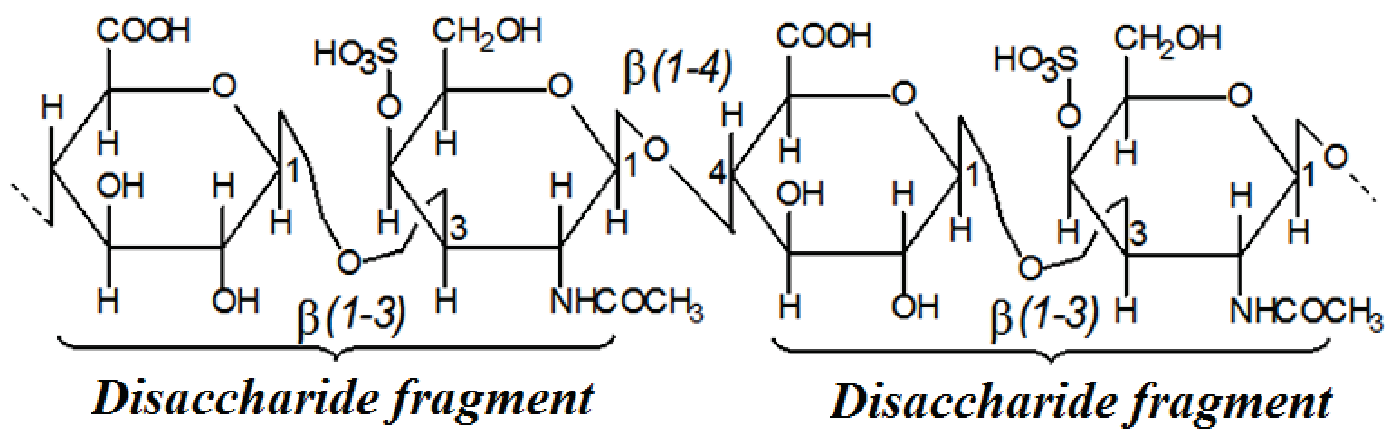


Hyaluronic Acid

- Hyaluronic acid is widely distributed throughout connective, epithelial, and neural tissues. As an extracellular matrix component is contained in the umbilical cord, vitreous humor of the eye, synovial fluid.
- Being a component of the extracellular matrix, hyaluronic acid is involved in multiple important biological processes - migration, proliferation, intercellular adhesion and recognition, invasion and tumor inhibition.

Chondroitin sulfates

Chondroitin sulphates are similar by structure with hyaluronic asid and consist of repeated disaccharided units connected **by β(1-4)-glycoside bonds** and formed of **β-D-glucuronic acid** and **N-acetyl-β-D-galactoseamine**, joined **by β (1-3) glycoside bonds**.

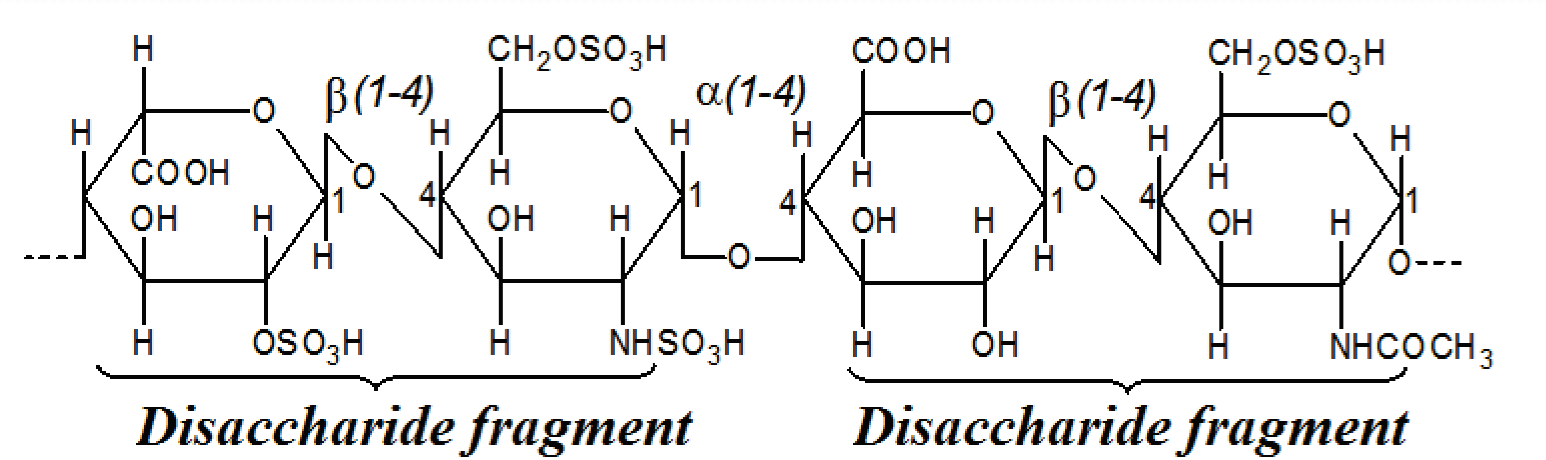


Chondroitin -4-sulphate

Chondroitin sulfates are found in humans in cartilage, bone, cornea, skin, the arterial wall and play an important role in tissue mineralization.

Heparin

consists of the disaccharide repeated units, connected **by β(1-4)-glycosidic** bonds and formed by a **α-D-glucozamine sulphate** residue and two uronic acids - **β-D-glucuronic and β-L-iduronic**, joined **by β(1-4) glycosidic bond**:



Heparin is largely used in practical medicine as an anticoagulant preparation.