

Polysaccharides

From a chemical point of view, sugars are a group of organic compounds with strictly defined properties and biological significance. The most well-known representative of this group is glucose, which chemists describe as a polyhydroxyl alcohol containing an aldehyde group, i.e. it is aldose. The presence of functional groups determines the possibility of sugar to participate in characteristic reactions.

But from a medical and biochemical point of view, glucose is the most important sugar of blood and cells. This glucose during its transformations gives energy necessary for various metabolic pathways. Glucose is a kind of signal molecule. The decrease in blood glucose results in a sense of hunger and an increase in satiety. Due to the key importance of glucose for the proper functioning of cells, its concentration is strictly controlled by the whole set of hormones. But in order to find glucose in blood, glucose from food (mainly in the form of polymolecules) must be digested and absorbed in the gastrointestinal tract (there are species differences in the structure of the gastrointestinal tract and the presence of enzymes). The most important enzyme responsible for the digestion of polysaccharides in the intestine is pancreatic amylase, an enzyme that breaks down 1,4 glycosidic bonds. In the digestive tract, other monosugars are also absorbed which, depending on their chemical properties, may also be further metabolically used. The adult carbohydrate reserve is estimated at approx. 300 g. From the blood glucose goes into the cells, which in part is also hormonally controlled. There, it undergoes transformations enabling not only to stay in the cell but also to enter into anabolic and catabolic pathways. It is worth noting that individual carbon atoms of glucose can be found in other monosugars as well as in fatty molecules or amino acids. What is the biochemical mechanism of "arresting" glucose in cells and how carbon atoms of glucose go to other groups of organic compounds? And how are heteroglycans formed and why do they perform just specific biological functions? Answers to these questions will appear during classes in biochemistry, however, to understand these biochemical mechanisms, basic information about glucose and other sugars, their structure, properties and biological significance must be conveyed and assimilated as part of chemistry classes.



Monosugars are bifunctional compounds defined as polyhydroxylic alcohols containing additionally either aldehyde (at the number 1 - aldose) or ketone (at the number 2 - ketose) functional group and at least one asymmetric carbon atom.

There are many classifications of monosugars taking into account various criteria, for example:

Amount of carbon atoms in the molecule:

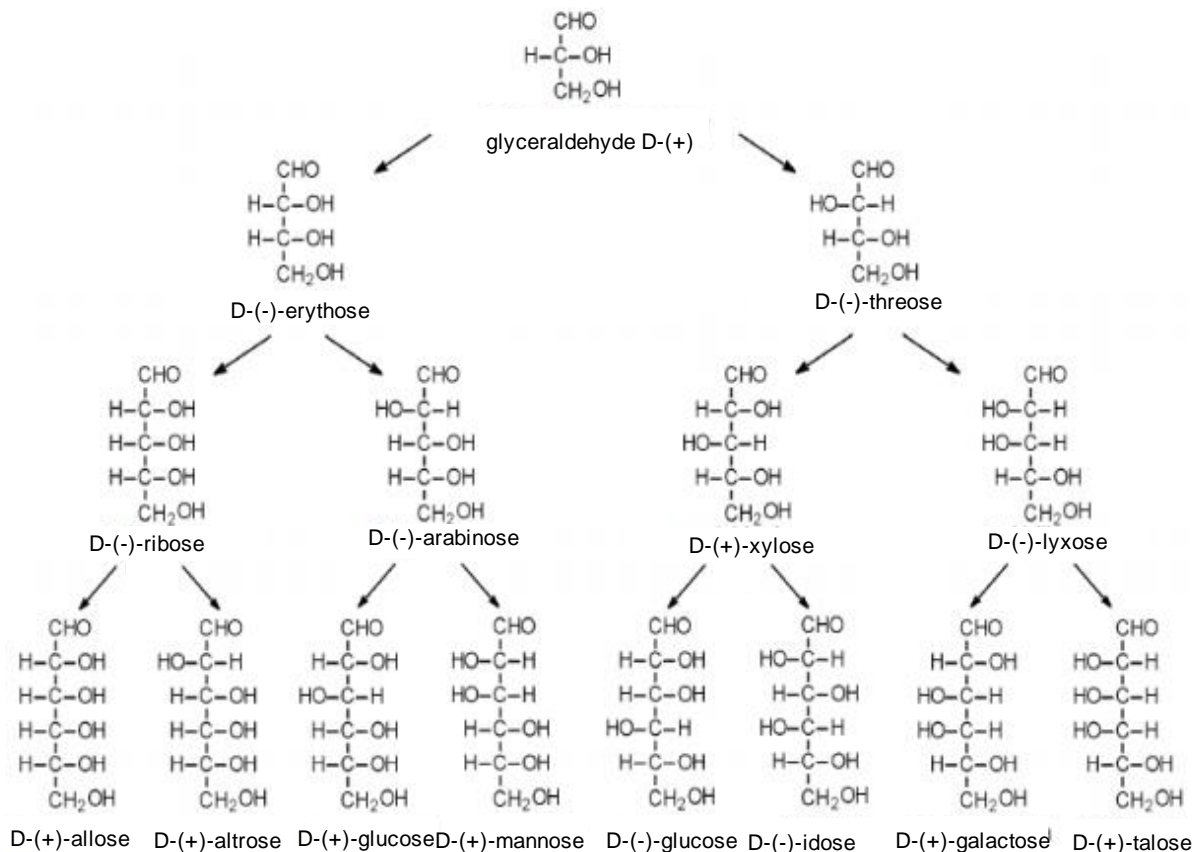
Aldoses:

trioses (glyceraldehyde),

tetroses - (erythrose, threose),

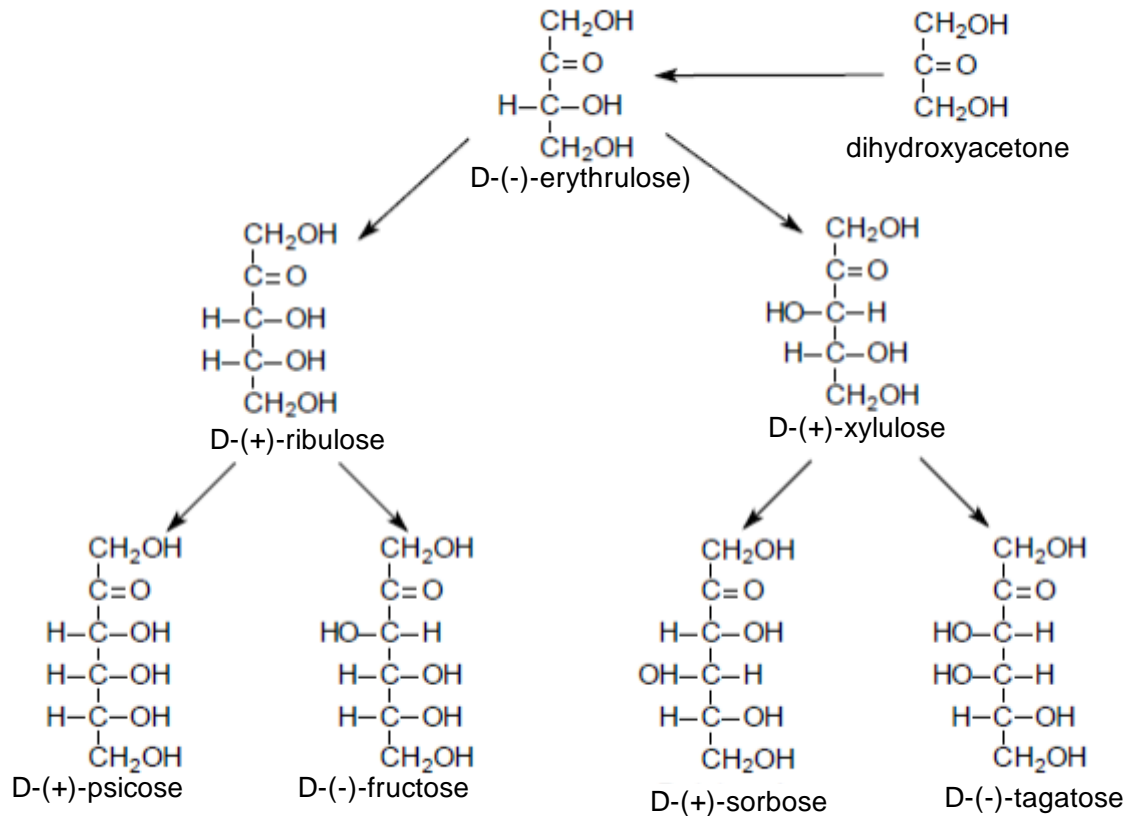
pentoses - (ribose, arabinose, xylose, lyxose),

hexoses - (glucose, galactose, mannose, gulose, allose, altrose, idose, talose)

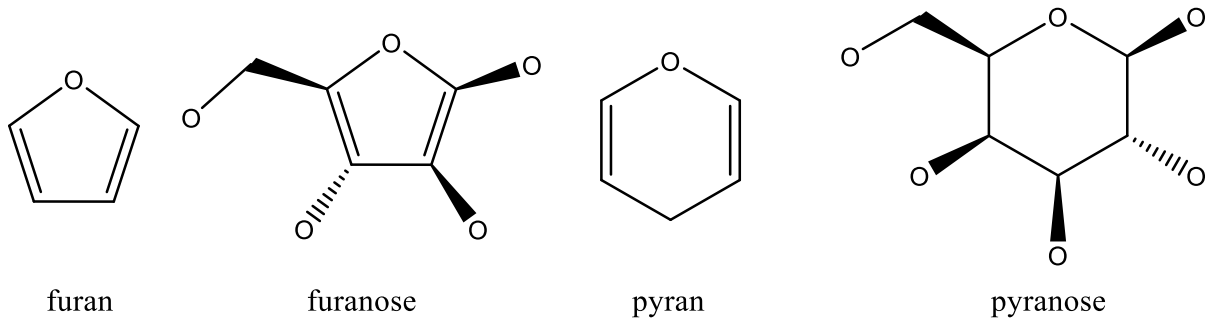


Ketoses - tetrose (erythrulose), pentose (ribose, xylose), hexose (fructose, sorbose, tagatose, psicose), heptulose





Type of rings created: furanose, pyranose

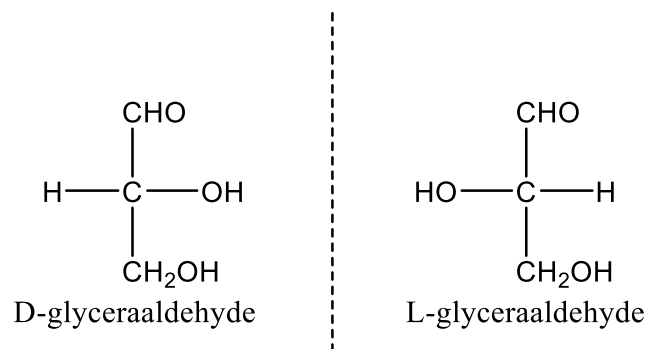


The phenomenon of isomerism concerns chemical compounds of various structure and has many aspects, both cognitive and practical, important for the food, cosmetics, pharmaceutical and, finally, medical industries. This study will deal with the importance of monosugar isomerism for understanding their metabolic changes in living cells that build animal tissues. It should be remembered that while the main metabolic pathways are based on glucose transformation, other sugars are in cells and constitute, for example, components of lactose, nucleotides, glycoproteins, glycolipids or even heteroglycans themselves, so important for the proper functioning of connective tissue.



Knowledge of the mechanisms of mutual transformations between the isomers is knowledge useful in understanding sugar metabolism and the importance of individual sugars in their biological functions. Their biological activity is based on their chemical properties. Knowing the properties is easy to get to know and understand the metabolism.

Configuration: it distinguishes series D and L based on the glyceraldehyde standard (which is also a standard for all monosugars and other optically active compounds). The presence of asymmetric carbon in the glyceraldehyde molecule and other sugars allows to distinguish two enantiomers that differ in the spatial distribution of 4 different substituents around the asymmetric carbon so called differ in configuration.

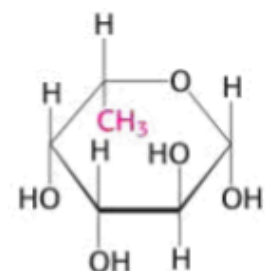


Members of the D or L series of other monosugars are deduced from the position of the OH group with the last asymmetric carbon (with the highest numbering). The presence of the OH group on the right classifies this molecule to the series D and from the left to the L series (not to be confused here with optical rotation!).

Enantiomers with different configurations should have similar physical and chemical properties but may differ in their optical properties and biological activity. The enantiomers twist the polarized light plane to the right (+) or left (-) respectively, regardless of whether they belong to the D or L series. The enantiomeric rotations are determined experimentally.

Racemic mixture - a mixture of equal amounts of the right and left-rotated enantiomer.

Living organisms have the ability to recognize and assimilate optically active compounds of a specific configuration only and can use only them in further reactions in cells. In general, cells use the D-series monosugars (important for drug production!).



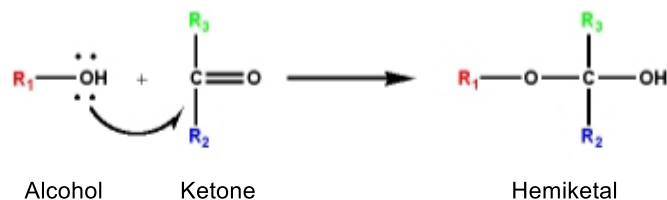
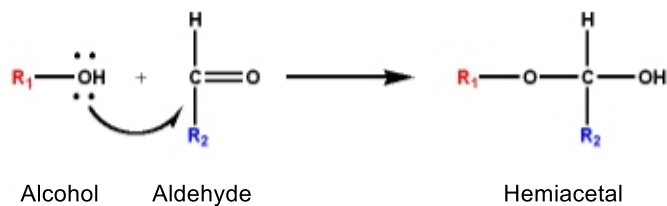
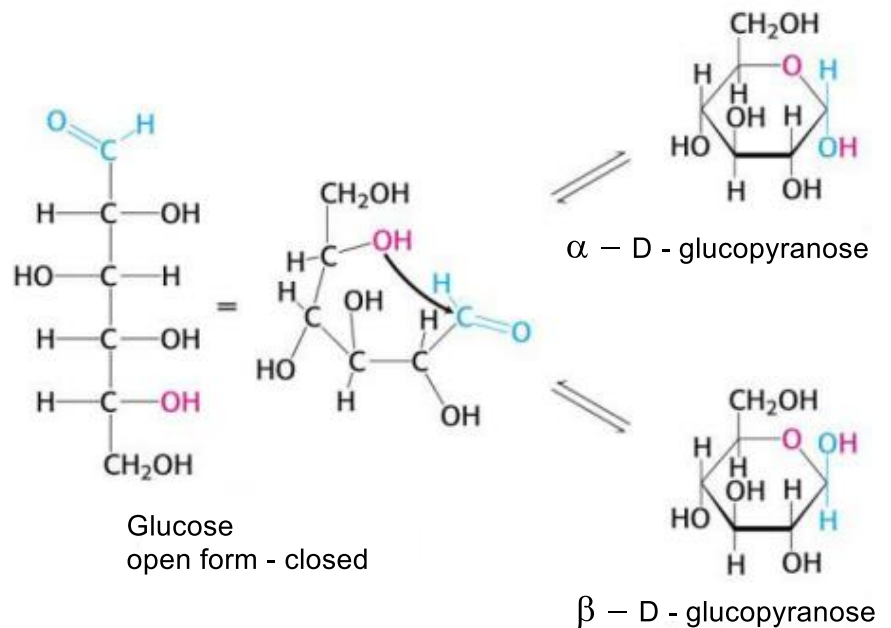
β -L-fucose (Fuc)



There are few exceptions to this rule, so it is worth to remember them. L-fucose and L-iduronate do not exist in the free state, they are components of oligo and polysaccharides in mammalian cells.

Monosaccharides in aqueous solutions occur mainly as ring forms. This is due to the formation of hemiacetal or hemiketal intramolecular bonds.

The hemiacetal bond arises between the OH group at C5 and the aldehyde group at C1 which leads to the formation of a cyclic six-membered system referred to as the pyranose ring. If the hemiacetal bond is formed between the OH group at C4 and the aldehyde group at C1 then a five-membered cyclic system which is called a furanose ring appears. Similarly, hemiketal connections form a pyranose and furanose ring, respectively.

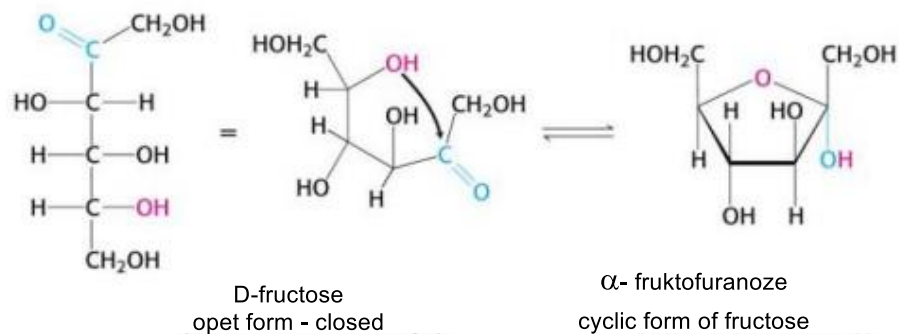


The process of formation of ring forms of monosugars is associated with the appearance of the **phenomenon of anomerism**, which affects the position of OH groups at the anomeric carbon -



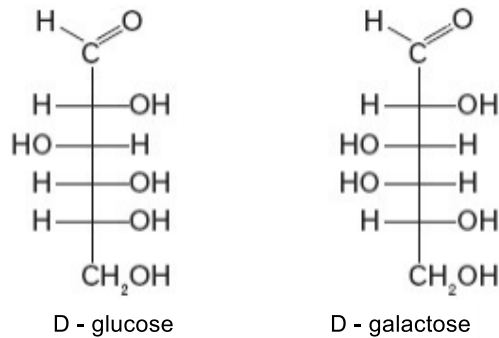
C1 in aldoses and C2 in ketoses.

The anomer α is one in which the OH group at the anomeric carbon in the Haworth formula is below the plane of the ring, i.e. on the opposite side to the last group $-\text{CH}_2\text{OH}$ in the series D. The anomer β is characterized by the position of the OH group of the anomeric carbon over the plane of the ring, i.e. the last $-\text{CH}_2\text{OH}$ group in row D, respectively. The phenomenon of anomerism is closely linked to the **phenomenon of mutarotation** consisting in the transition of one anomer to the other through the chain form shortly after dissolving the crystalline monosaccharide in water. There is a temporary change in the solution rotation until the equilibrium is established. Mutarotation may provide evidence for the ring structure of monosaccharides in solutions.

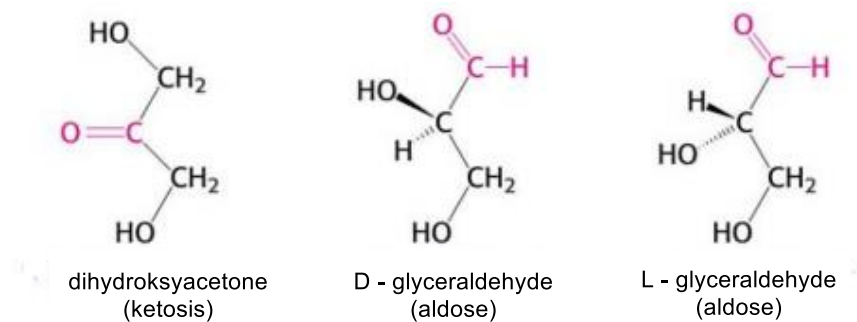


The phenomenon of epimerization allows for the mutual transformation of monosugars by changing the position of substituents at a single asymmetric atom in monosugars. Epimers are those isomers that differ in the location of only one OH group but other than in C1 in aldoses or C2 in ketoses and other than at the last asymmetric carbon. After solubilizing the monosaccharide in the weakly basic solution, the bond in the ring disintegrates, the monosugar passes into the chain form and also the tautomeric rearrangement through the intermediate form so-called endiol to another aldose or ketose. The common form of the endiol possess, for example, glucose, mannose and fructose. Epimerization occurs in cells, it is catalyzed by the enzymes - epimerases and allows, inter alia, the transformation of D-glucose into D-galactose, which is necessary for the synthesis of lactose in the mammary gland during lactation.





Trioses represented by glyceraldehyde and dihydroxyacetone are glycolysis metabolites formed from the decomposition of 1,6-bisphosphofructose.



Erythrose-4-phosphate is biologically important tetrose, a metabolite of the pentose phosphate cycle.

Pentoses that built nucleotides are β -D-ribose and β -D-deoxyribose. Phosphorylated β -D-ribose is a metabolite in the pentose cycle and is involved in the synthesis of 5-phospho- β -D-ribosyl diphosphate (PRPP) - compound necessary for the biosynthesis of pyrimidine and purine nucleotides.

Among biologically important hexoses are glucose, fructose and galactose. Glucose occurs in human plasma at a concentration of approx. 0.1% and in animals (0.03-0.15%). Galactose occurs in cells of living organisms in a bound form in lactose as well as free under pathological conditions of carbohydrate metabolism disorders. Fructose phosphate esters take part in sugar transformation and is also an important component of semen.

Characteristic reactions:

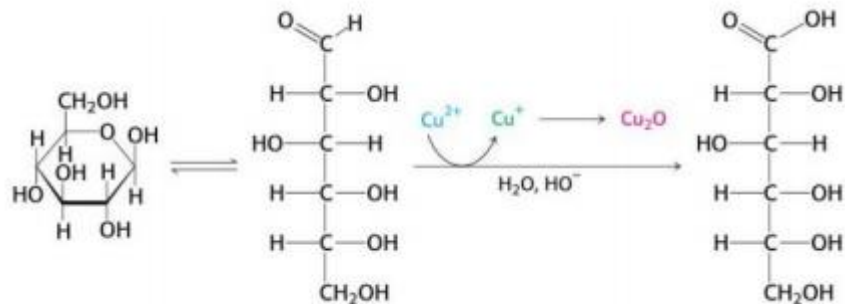
Oxidation and reduction

Aldoses behave like other aldehydes because they have the same

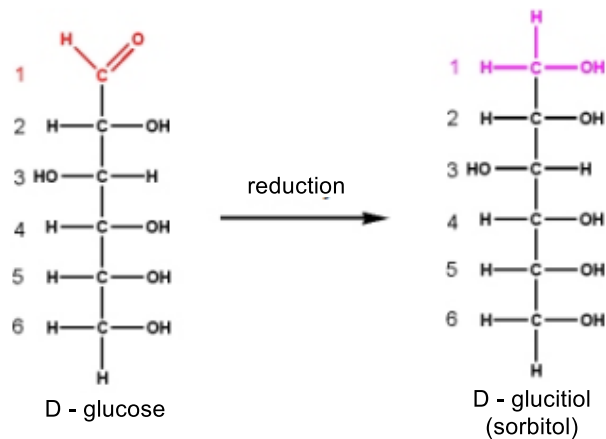


functional group (knowledge of the properties of aldehydes will facilitate the assimilation and understanding of the properties of monosaccharides containing the same group).

The C1 aldehyde group of aldoses, like aldehydes, is readily oxidized to the carboxyl group. The OH group at C6 carbon may be oxidized independently of the C1 carbon or together. The following products are created:



Uronic acids, respectively: C1 - gluconic (aldonic), C6 - glucuronic (uronic), C1 + C6 - glucar (aldar).



D-glucuronic acid is of particular biological importance - it is a component of heteroglycans and it participates in detoxification processes. It undergoes coupling with hydrophobic substances and by this increases their solubility, which leads to easier urinary excretion of toxic compounds. Glucuronic acid, in addition to xenobiotics or drugs, can bind to steroid hormones and bilirubin. As a result of the epimerization of glucuronic acid, it can form the L-iduronic acid mentioned above.

The reduction of monosaccharides leads to the formation of



polyhydroxylic alcohols, the so-called alditols. Such reactions take place also in cells under physiological and pathological conditions. A well-known product of glucose reduction is sorbitol, which is responsible for nerve cell damage and the late consequences of diabetes. Galactitol synthesized from galactose in the course of galactosemia also has adverse effects. By depositing in the lens of the eye, it can lead to cataracts. As a result of the reduction of fructose, sorbitol and mannitol may be synthesized (a diuretic drug that increase the osmotic pressure and cause the shift of fluids from the cells to the lumen of the blood vessels, which leads to reduction, of among others, intracranial pressure and reduction of brain edema; it also accelerates the excretion of toxic substances through the kidneys but together with them also sodium and chloride are removed).

The reduction properties of sugars are used in the reactions of their identification.

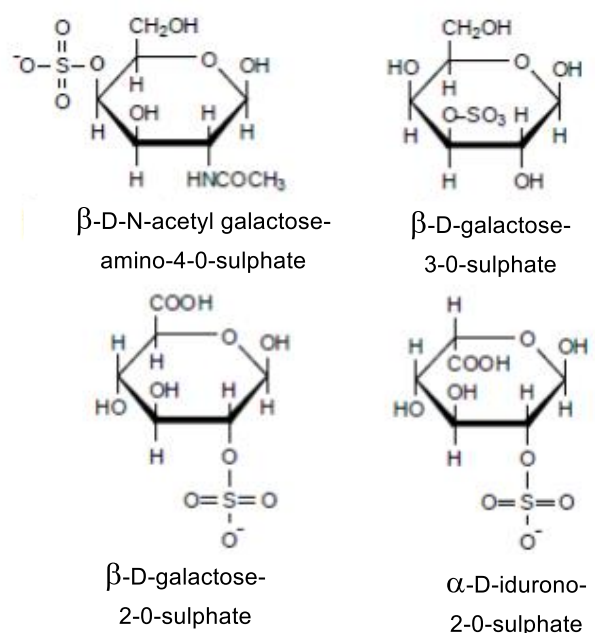
Esterification

Among the esters of monosugars from the biochemical point of view, phosphate esters are important. They are synthesised in living cells in phosphorylation reactions catalyzed by kinases and are substrates in sugar transformation processes. Phosphate esters having a phosphate group at C1 or / and at C6 are known. Phosphorylation of glucose is also necessary for it to be retained in cells - such a reaction prevents phosphorylated glucose crossing the cell membrane due to obtaining a negative charge. Phosphorylation precedes the entry of glucose into the glycogen synthesis or lactose synthesis. It is worth remembering that as a result of phosphorolytic breakdown of glycogen in cells, glucose-1-phosphate is formed. Dephosphorylation is carried out with the participation of phosphatases.

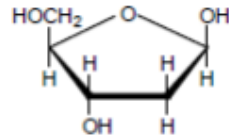
Sulphate esters of monosugars are components of heteroglycans.

Other

Deoxysugars are characterized by the absence of a hydroxyl group. They include deoxyribose that builds DNA nucleotides. The transformation of ribose into deoxyribose takes place in living cells. Mentioned

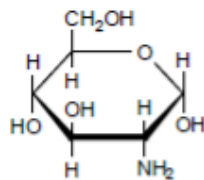


above L-fucose that builds conjugated sugars is also an example of deoxysugar.

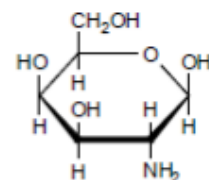


2-deoksy- β -D-ribofuranoze

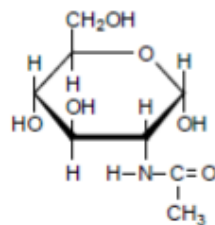
Amino-sugars are formed during the exchange of hydroxyl group at C2 carbon to the amino group. In addition, cells usually undergo acetylation reactions to form acetyl derivatives. They are components of heteroglycans. One of the few aminosugars that are not acetylated in cells is α -D-glucosamine known from drugs used for treatment of joints.



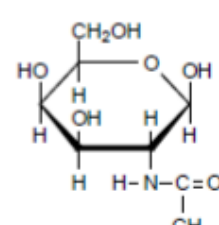
α -D-glucosamine
(GlcN)



β -D-galactosamine
(GalN)



α -D-N-acetylglucosamine
(GlcNAc)

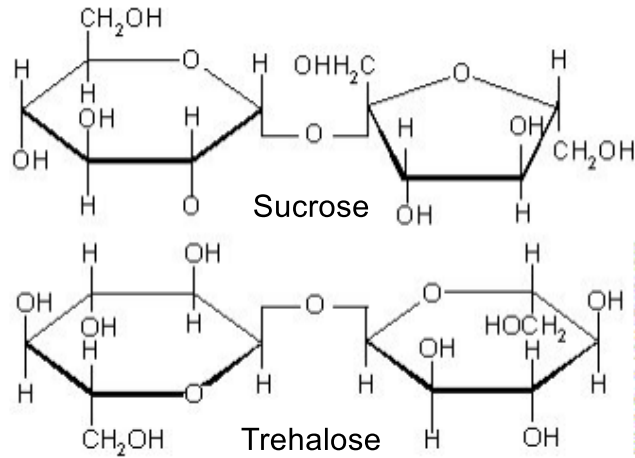


β -D-N-acetylgalactosamine
(GalNAc)

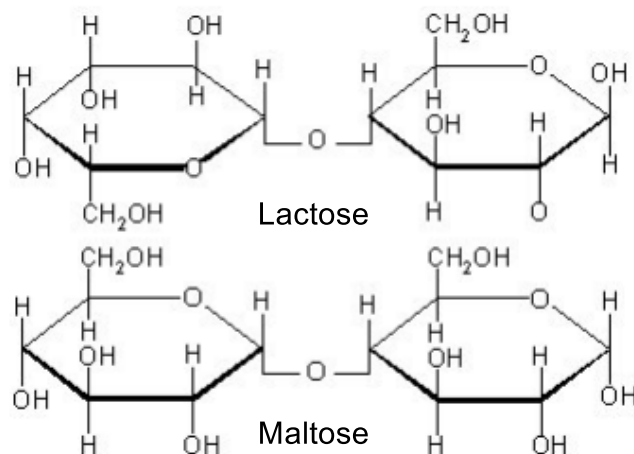
Disaccharides

The two monosugars can react with each other to form a glycosidic bond. However, depending on which functional groups are involved in this bond, disaccharides with different properties will arise. We distinguish non-reducing disaccharides that do not show mutarotation phenomena if the glycosidic linkage connects the hemiacetal and hemiketal group. We include here: trehalose (α -D-glucopyranosyl-1- α -glucopyranoside) and sucrose (α -D-glucopyranosyl-1-2- β -fructofuranoside).

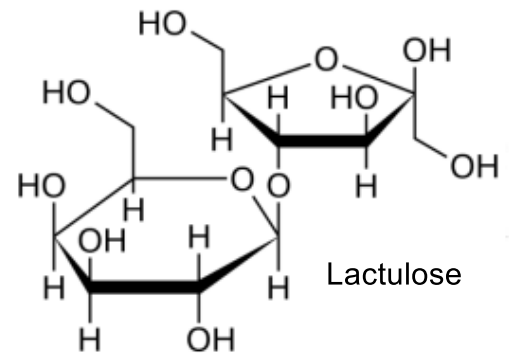




The reducing disaccharides are formed when a glycosidic bond is formed between a hemiacetal group of one monosugar and a non-hemiacetal hydroxyl group in the other monosugar. This will block one hemiacetal group but still the second monosugar will have its free hemiacetal group responsible for demonstrating the reducing properties, oxidation to carboxylic acids, mutarotation and the formation of glycosides with alcohols. It includes: maltose, isomaltose, cellobiose and lactose. The first three do not occur in the free state, they are products of degradation of starch and cellulose, respectively. Lactose is a milk sugar that is broken down in the gastrointestinal tract by β -galactosidase. Lack of this enzyme may cause lactose intolerance. Then, the absorption of water in the large intestine, microbial decomposition and fermentation diarrhea occurs. Lactose is synthesized in living cells.



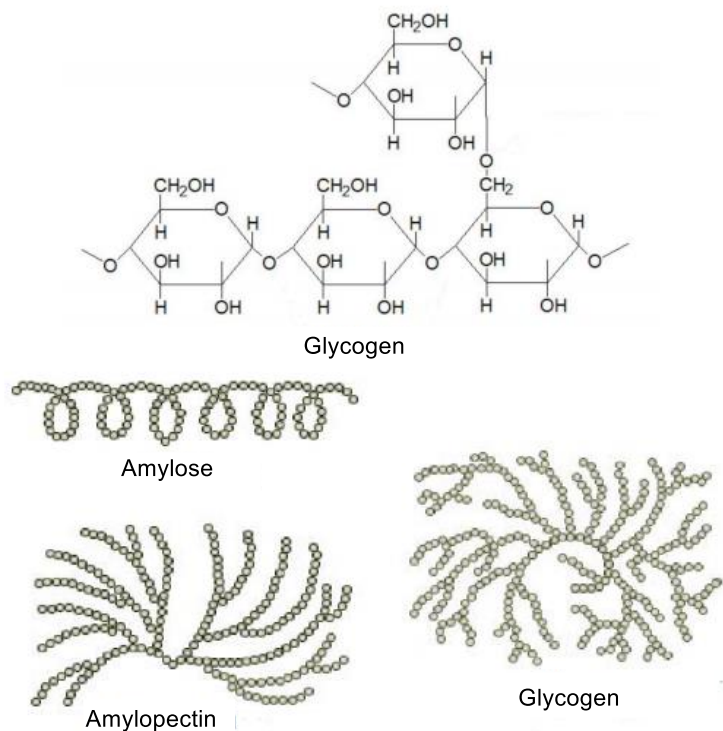
Lactulose is a synthetic disaccharide composed of galactose and fructose connected by 1-4 glycosidic bond. Due to its intestinal water retention properties, it promotes the hydration of fecal masses and is used to treat constipation. In addition, acidifying the intestinal content causes a beneficial change in the composition of the intestinal flora.



Homoglycans

Homoglycans are defined as sugars composed of identical building units. They perform spare and structural functions both in plants and in animals. To what extent animal cells can use them depends on the type of glycosidic bonds present in these compounds and how much the digestive tract of animals is equipped with enzymes digesting these sugars. Hence, knowledge about the properties of homoglycans and the type of bonds that create them allows to predict the use of individual homoglycans by individual animals and humans.

Glycogen is a storage homoglycan in animal cells, composed of glucose molecules connected by α -1,4-glycosidic and α -1,6-glycosidic bonds. This provides a characteristic, highly branched glycogen structure. In the situation of the need of rapid increase in blood glucose concentrations, phospholytic enzymes acting on many non-reducing ends of glycogen molecule release in a relatively short time many molecules of phosphorylated glucose. The content of glycogen in individual tissues is conditioned by the metabolic specifics - in tissues where there is an intense aerobic metabolism the content of glycogen is lower than in tissues with anaerobic metabolism. In the heart and brain



the content of glycogen is lower than in skeletal muscle, and the liver constituting the glycogen storage is not subject to this principle.

Starch is a storage homoglycan in plant cells and is one of the most important nutrients for humans. It is made of glucose molecules connected by glycosidic bonds similar to glycogen, but with a slightly different spatial structure. It consists of linear amylose and branched amylopectin. Starch is digested in the digestive tract of humans and animals with the participation of pancreatic amylase.

Dextrins are a group of products of enzymatic hydrolysis of starch made of simple and complex sugars from 3 to about 12-14 units. They are white crystalline substances, easily soluble in water. A distinction can be made between linear dextrins (with open chains) and cyclic dextrins called cyclodextrins.

During the hydrolysis of starch, consecutively shorter polysaccharide chains are formed, which give a different color with iodine:

- amyloextrin (stained with I_2 in blue),
- erythroextrin (stained with I_2 in red),
- achroekstrins (non-staining with I_2)
- maltose and glucose

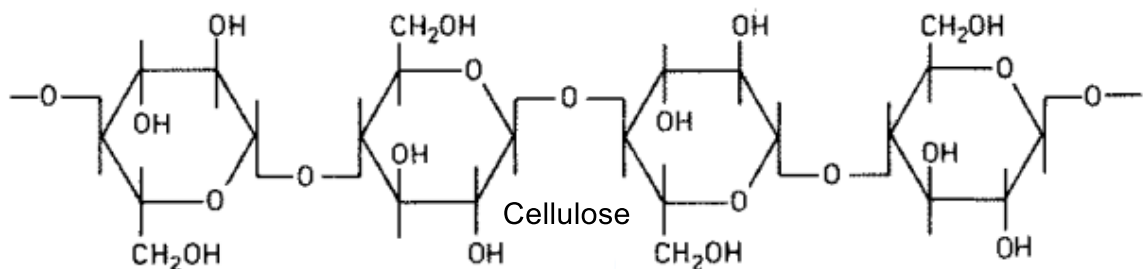
Dextrins have a number of practical applications, due to the ease of their production and low price. In medicine, they are used as tablet masses, tablet coatings and capsule shells that dissolve in the intestinal tract after ingestion. Aqueous solutions of dextrins are used as blood replacement fluids, because it is relatively easy to obtain from the dextrins a solution with a suitable viscosity that allows their intravenous administration in the form of a drip. Cyclodextrins, thanks to their unique structure, are used as molecules capable of transporting drugs to specific tissues. They are also used in the food industry and for the production of disposable dishes.

Dextran is a glucose polymer produced from mucus that covers cells of bacteria *Leuconostoc mesenteroides*. It is characterized by high molecular weight, good solubility in water and is used as a blood replacer. After intravenous administration, it raises the osmotic pressure and increases the volume of plasma (1 g of dextran binds 20 ml of water). It also reduces the blood viscosity which counteracts the aggregation of blood cells. It



should be remembered, however, that dextran has no binding and oxygen transfer properties - therefore it can not be used as a substitute for whole blood. Its half-life is 6-8h, it is mainly excreted by the kidneys (to a lesser extent the lungs). Not excreted dextran is metabolized in the liver to carbon dioxide and water. It does not penetrate the blood-brain barrier.

Cellulose is structural homoglycan in plant cells made of glucose connected by β -1,4-glycosidic bonds. Due to the β form this sugar can not be broken down in the digestive tract of humans and animals. This is done only by microorganisms living in the forestomachs of ruminants producing the necessary enzymes. Despite the lack of digestibility, cellulose is biologically important as a natural intestinal ballast that stimulates peristalsis.



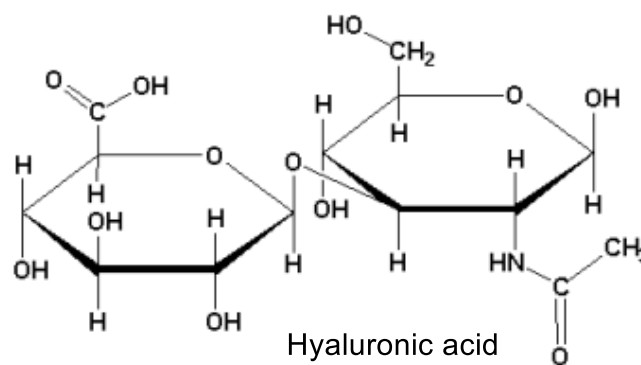
Inulin is a storage plant polysaccharide composed of 30-35 fructofuranose residues linked by β -2,1-glycosidic bonds with one glucose residue. It is used in laboratory diagnostics for testing fluid volumes. Inulin as a natural polysaccharide has the property that it freely permeates in the kidneys, does not reabsorb, and the whole filtered amount of the substance is excreted into the urine. The maintenance of a constant concentration of this polysaccharide in the blood for a period of time as well as the knowledge of its concentration and the amount of secreted inulin to produced at this time urine are necessary to calculate the clearance or level of glomerular filtration according to the general formula for renal clearance.

Heteroglycans are defined as polymers composed of various building units. They are therefore characterized by different chemical properties that reflect their biological properties. For the most part, these are structural compounds that build connective tissue.

- **acidic mucopolysaccharides** (glycosaminoglycans are linear polyanionic long chain polymers, are present as sulphate esters and are covalently linked to the protein (with the exception of hyaluronic acid) We divide them into:



Hyaluronic acid - glucuronic acid conjugated with N-acetylglucosamine with β 1,3 glycosidic bond. The only non-protein-linked glycosaminoglycan and non-sulphated. It is characterized by a high ability to bind water, thereby retaining it in the connective tissue and protecting against injuries. It forms extremely sticky colloidal solutions, making it a biological lubricant in the joints and muscle tissue. It is degraded with the participation of hyaluronidase, an enzyme present in some bacteria, which facilitates their penetration during infection due to the loss of tissue fluid viscosity.



Galactosaminoglycans - chondroitin sulfates (A - glucuronic acid conjugated with N-acetylgalactose-4-sulfate with β 1,3 glycosidic bond and C - glucuronic acid conjugated with N-acetylgalactose-6-sulfate) and dermatan sulfate (iduric acid conjugated with N-acetylgalactosamine). They are building units of connective tissue, they occur in tendons, bones, skin, cartilages and blood vessel walls - mostly in connections with proteins. These compounds are broken down by specific lyases - chondroitinases.

Glucosaminoglycans - heparan sulfate, heparin, keratan sulphate

Heparin (glucose-amino-N-sulfuric acid conjugated with glucuronic acid with 1,4-glycosidic bond) and heparan sulfate are known as anticoagulants. This property is due to the presence of the pentasaccharide sequence that binds antithrombin III. This process inhibits blood coagulation (inhibition of the conversion of prothrombin to thrombin and thrombin to fibrinogen).

- neutral mucopolysaccharides

chitin - N-acetyl-D-glucosamine linked by 1,4-glycosidic bond, a component of the skeleton in invertebrates.

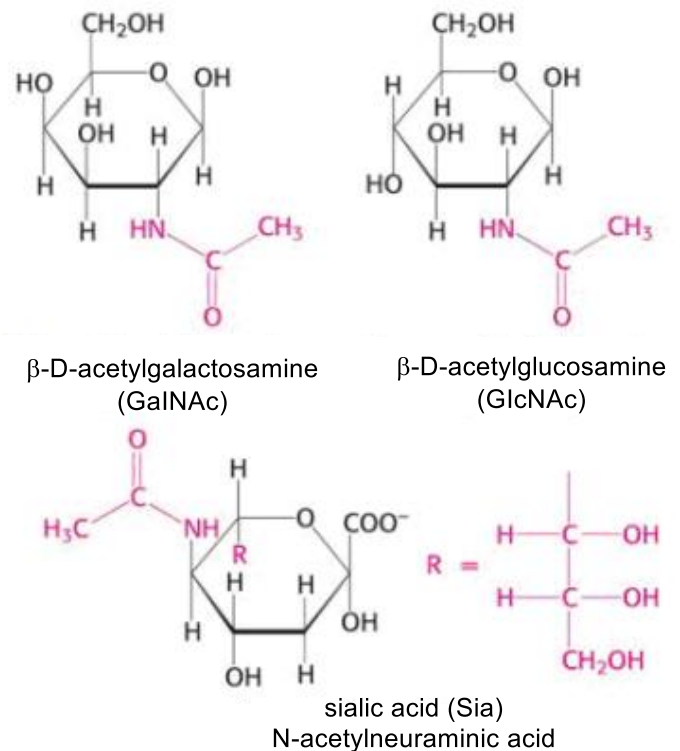


glycoproteins (mucoproteins) - they do not contain uronic acids but polypeptide fragments and most often acetylglucosamine, arabinose, sialic acids (derivatives of phosphorylated aminosugars, eg, N-acetylneuraminic acid). They are components of cellular antigens).

- • plasma glycoprotein
- • mucin - has mucoid properties
- • blood group substances - A, B, 0 agglutinogens in erythrocytes

Blood groups are determined by A, B and 0 agglutinogens which have glycoprotein structure. The protein part and part of the sugar fragment are similar but there are differences in the peripherally localized sugar in individual blood groups. In the blood group A, this sugar is N-acetylgalactosylamine, in group B - galactose and the lack of both sugars characterizes group 0. Serological reaction with isoagglutinins and haemolysis of red blood cells in the incompatible with regard to blood groups transfusions may occur and may result in the destruction of oxygen "transporters" and serious negative consequences for the body. Therefore, it is necessary to know the blood groups before transfusion and if it is impossible to perform appropriate tests confirming antigen compliance. Otherwise, instead of helping you can seriously harm the patient.

In veterinary medicine, blood transfusions are also used and the above rules must be followed. Currently, 3 blood groups have been defined in cats, 12 in dogs, 11 in cattle, 16 in pigs and 34 in horses. In the case of the FIRST transfusion in a dog or horse, checking antigen compliance is not that important because in these species the antibodies appear only after exposure to the antigen. Then the second transfusion in such animals must already be



antigenically compatible.

Glycosides are defined as compounds arising from the conjugation of sugar molecules between themselves or sugar with another non-sugar compound by glycosidic bond. O-glycosides where sugar is conjugated with an alcohol, phenol or carboxylic acid molecule through an oxygen atom are distinguished. Depending on the type of the aglycone part, the following bonds may be formed: with carbon - C-glycosides, with nitrogen - N-glycosides (nucleotides) or with sulfur - S-glycosides. Glycosides are widespread in the plant world and play the role of biologically active substances such as flavonoids with antioxidant activity or cardiac glycosides. Among these compounds are also poisons, for example, solanine or amygdalin. Glycosides of glucuronic acid or steroids are formed in living organisms. It is one of the forms of metabolizing and excretion of unnecessary products of metabolic.

- **phenolic glycosides** (plant flavonoids)
- **steroid glycosides** - cardiac, saponins, steroid glycoalkaloids - mostly poisonous, contain alkaloids (eg tomato - tomatin, potato - solanine)
- **cyanogenic glycosides** - amygdalin in almonds, peach seeds, plums - during the transformation of hydrogen cyanide
- **glucuronic acid glycosides** (glucuronides) - allow the excretion of phenols, steroids or aspirin in the form of conjugate

Sugar metabolism in cells proceeds according to known hormonally controlled pathways. However, there are pathological conditions where these pathways are often disturbed on the genetic background leading to the enzymopathy of enzymes involved in these reactions. Galactosemia is known to block the conversion of galactose and to accumulate it, which consequently causes serious changes in the nervous system. Glycogenoses relate to disorders in glycogen metabolism and the accumulation of this sugar in the liver, which leads to cirrhosis of the liver and changes in the muscles.

Glycated hemoglobin is a diagnostic parameter in disorders of sugar metabolism. It is formed as a result of the glycation process, ie the non-enzymatic association of glucose with proteins, in this case with hemoglobin, in the situation of increased blood glucose concentration. **Fructosamine** (glycated plasma protein) is of similar importance.

Upon suspicion of disturbances of sugar metabolism, the concentration of glucose in plasma is determined, either directly

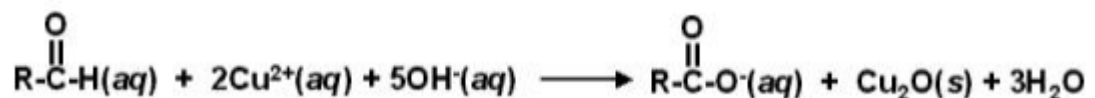


or in various metabolic tests. The selection of these tests, the method of sampling and storage of samples are important for the reliability of obtained results. And this knowledge is closely related to the knowledge of the physicochemical properties of glucose.

Ketosis is a disease that occurs in cows and is associated with impaired glucose metabolism. It leads to increased synthesis of ketone bodies and their accumulation in the blood and excretion in the urine.

Diabetes is a disorder of insulin secretion and activity leading to serious abnormalities in sugar metabolism and, as a consequence, dangerous to health and life clinical symptoms occurring quickly or in the long-term time frame of the disease, so-called acute and chronic consequences. Generally, the background of the disease is the presence and stay of glucose in the peripheral circulation, the lack of transport inside the cells and thus the lack of this sugar inside the cells what may lead to the excretion of glucose in the urine. The biochemical disturbances triggered by this condition lead to dangerous for life clinical symptoms. In large part, these symptoms remain in close relationship with the physicochemical properties of glucose.

The reaction for glucose detection in diabetics is based on the formation of orange copper (I) oxide deposit with the participation of copper sulphate in an alkaline medium and aldehyde groups from sugar.



Descriptions of the reactions of the detection of pentoses, ketoses, reducing disaccharides, non-reducing disaccharides, starch and their results as well as methods for identifying and distinguishing individual sugars are found in lab protocols.

