MINISTRY OF HEALTH OF UKRAINE
ZAPORIZHZHIA STATE MEDICAL
AND PHARMACEUTICAL UNIVERSITY
DEPARTMENT OF PHARMACEUTICAL, ORGANIC
AND BIOORGANIC CHEMISTRY

PHARMACEUTICAL CHEMISTRY.

ANALYSIS OF CARDIOTONIC AND ANTIARRHYTHMIC DRUGS

Study Guide

for 4rd year English-speaking students of the specialty

"Pharmacy, Industrial Pharmacy"

Zaporizhzhia
2023

UDC 615.22.074(075.8)
S53

Approved by the meeting of the Central methodological committee of Zaporizhzhia State Medical and Pharmaceutical University and recommended for use in the educational process for foreign students. (Protocol No ___ from 20__)

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S53 **Pharmaceutical chemistry. Analysis of cardiotonic and antiarrhythmic drugs:** Study guide for 4th year English-speaking students of the specialty "Pharmacy, Industrial Pharmacy" / K.P. Shabelnik, N.V. Derevianko, R.R. Akopian. – Zaporizhzhia: ZSMPhU, 2023. – 120 p.

UDC 615.22.074(075.8)

The study guide for students is compiled in accordance with the requirements of the Central Methodical Council of Zaporizhzhia State Medical and Pharmaceutical University. Published for the first time.

Lecture plan

on pharmaceutical chemistry for 4th year students of the Faculty

of Pharmacy (7 semester)

Sl. No.	**Lecture topics**	**Number of hours**
1	Cardiotonic and antiarrhythmic drugs. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine and cosmetology.	2
2	Vitamins of aliphatic and alicyclic structure. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine and cosmetology.	2
3	Vitamins of heterocyclic structure. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine and cosmetology.	2
4	Antibiotics of aromatic and alicyclic structure. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine and cosmetology.	2
5	Heterocyclic antibiotics: penicillins, cephalosporins. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine and cosmetology.	2

PLAN

of laboratory practicals, seminar classes and independent work on pharmaceutical chemistry for 4rd year students of the Faculty of Pharmacy (7th semester)

No. s/p	Lesson topics	**Class type**	Number hours **Lab., semin.**
1.	Analysis of drugs from the group of monosaccharides.	Labor.	3
2.	Analysis of drugs from the group of oligo-, polysaccharides and antiarrhythmic drugs.	Labor.	3
3.	Analysis of cardiotonic drugs. Cardiac glycosides.	Labor.	3
4.	Control lesson from the section.	Seminar	2
5.	Analysis of drugs from the group of vitamins of the aliphatic series.	Labor.	3
6.	Analysis of drugs from the group of vitamins of the heterocyclic series, derivatives of chroman, pyridine.	Labor.	3
7.	Analysis of drugs from the group of heterocyclic vitamins, pyrimidine-thiazole derivatives, pterin, isoalloxazine, corin.	Labor.	3
8.	Analysis of drugs from the group of vitamins of alicyclic and aromatic structure.	Labor.	3
9.	Control lesson from the section.	Seminar	2
10.	Analysis of drugs from the group of antibiotics of the aromatic series.	Labor.	3
11.	Analysis of drugs from the group of alicyclic antibiotics.	Labor.	3
12.	Analysis of drugs from the group of heterocyclic antibiotics.	Labor.	3
13.	Analysis of drugs from the group of glycoside antibiotics.	Labor.	3
14.	Control lesson from the section.	Seminar	3

INTRODUCTION

Pharmaceutical chemistry is studied according to the Model curriculum for training specialists of the second (master's) level of higher education in the field of knowledge 22 "Health Protection" in higher educational institutions of the Ministry of Health of Ukraine in specialty 226 "Pharmacy" educational qualification "Master of Pharmacy" as of 26.07.2016.

According to the order, pharmaceutical chemistry is studied in III, IV and V courses. In the fourth year (VII-VIII semesters) the discipline program is structured into 2 meaningful blocks:

Block 1 - "Pharmaceutical Analysis"

Block 2 - "Special Pharmaceutical Chemistry"

Block 1 consists of three sections:

Section 1 – "Analysis of cardiotonic and antiarrhythmic drugs. General characteristics, classification, relationship of structure with pharmacological action, extraction, methods of analysis, application".

Section 2 - "Analysis of drugs from the group of vitamins. General characteristics, classification, relationship of structure with pharmacological action, extraction, methods of analysis, application".

Section 3 - "Analysis of drugs from the group of antibiotics. General characteristics, classification, relationship of structure with pharmacological action, extraction, methods of analysis, application".

SPECIFIC GOALS:

- Learn the properties of drugs from the group of carbohydrates, cardiotonic and antiarrhythmic drugs.
- Know the main sources and methods of obtaining drugs from the group of carbohydrates, cardiotonic and antiarrhythmic drugs.
- To propose and carry out the selection of physical, physicochemical and chemical methods of quality analysis of drugs from the group of carbohydrates, cardiotonic and antiarrhythmic drugs in accordance with the requirements of the Federal State Medical Institute, analytical regulatory documentation (AND), as well as quality control methods (MQC).
- Explain the peculiarities of the analysis of drugs from the group of carbohydrates, cardiotonic and antiarrhythmic drugs using physical, physicochemical and chemical methods.
- Interpret the results of studies of the proposed drugs from the group of carbohydrates, cardiotonic and antiarrhythmic drugs, obtained using physical, physico-chemical and chemical methods.
- Explain the peculiarities of storage of drugs from the group of carbohydrates, cardiotonic and antiarrhythmic drugs, based on their physical and chemical properties.

LESSON No. 1

1. THEME: Analysis of the quality of medicines from the group of monosaccharides.

2. PURPOSE: Master the methods of analysis of drugs from the group of carbohydrates and their synthetic analogues.

3. OBJECTIVES:

3.1. To study the structure, nomenclature, synonyms, physicochemical properties, sources and methods of obtaining medicines from the group of carbohydrates and their synthetic analogues.

3.2. To study the methods of analysis of the considered group of medicinal products according to the SPU, MQC.

3.3. Propose and justify possible methods of identification and quantification, based on the structure of drugs of the studied group.

3.4. To study specific impurities, as well as testing methods for the purity of this group of substances.

3.5. Consider the peculiarities of the analysis of drugs from the group of carbohydrates and their synthetic analogues using physical, physicochemical and chemical methods.

3.6. To learn how to analyze the quality of the considered group of medicines using physical, physico-chemical and chemical methods.

3.7.Interpret and give a correct assessment of the received analysis results, draw a conclusion about the quality of the analyzed substances.

3.8. Explain the peculiarities of storage of medicines from the group of carbohydrates and their synthetic analogues, based on their physicochemical properties.

3.9.Learn and follow the rules of safe work in a chemical laboratory.

CARBOHYDRATES (glucids, glycides, sugars) are a large group of natural and synthetic compounds that are chemically polyhydroxyl substances containing an aldehyde or ketone group, or form them during hydrolysis.

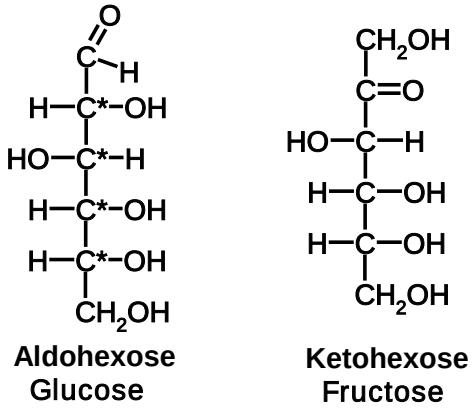
Carbohydrates can be divided into two main groups: monosaccharides and polysaccharides;

- monosaccharides, which are not split during hydrolysis;

polysaccharides are divided into:

- oligosaccharides (contain from 2 to 10 monosaccharides) and
- polysaccharides containing more than 10 monosaccharides, which can be split into monosaccharides during hydrolysis.

Monosaccharides are divided into trioses, tetroses, pentoses, and hexoses according to the number of carbon atoms. The most common and studied are pentoses and hexoses. Depending on the presence of an aldehyde or ketone group, monosaccharides are divided into aldoses and ketoses. For example: glucose is an aldohexose, and fructose is a ketohexose.



Aldohexose Glucose **Ketohexose Fructose**

In addition to carbonyl and hydroxyl, the monosaccharide molecule may also contain other groups, for example, a carboxyl or amino group. Monosaccharides containing amino groups instead of one or more hydroxyl groups are called deoxysugars or simply amino sugars.

Carbohydrates are obtained mainly from plant sources. This is due to the fact that carbohydrates are the primary products of photosynthesis, which is carried out by plants from carbon dioxide and water.

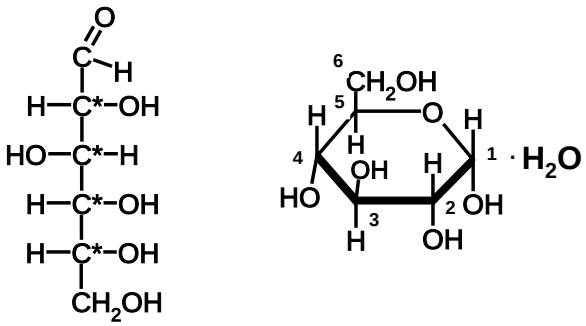
BY PHYSICAL PROPERTIES, they are white, odorless crystalline powders. Monosaccharides are easily soluble in water, slightly soluble or practically insoluble in organic solvents.

The chemical properties of monosaccharides can be divided into three groups:

- properties of alcohols;
- properties of carbonyl compounds (oxidizing and reducing)
- specific reactions associated with the appearance of semiacetal hydroxyl.

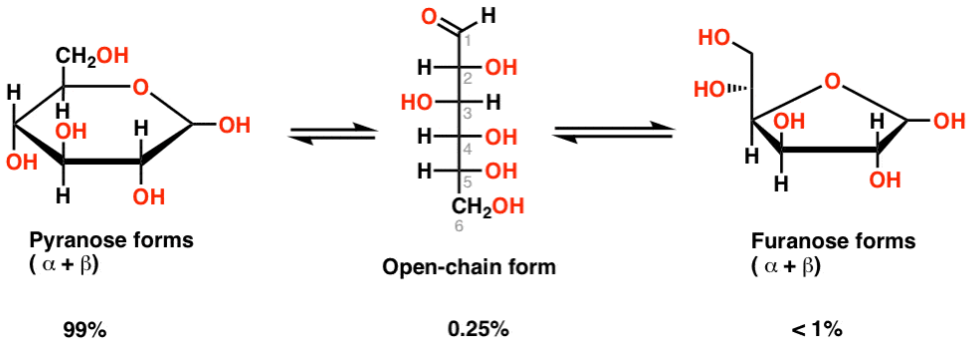
The most significant drug of this group is glucose.

GLUCOSE



D(+)-glucose (aldohexose) α-D(+)- glucopyranose

Glucose has several structures, all in equilibrium with each other: the straight chain form, the pyranose form (alpha and beta), and the furanose form (alpha and beta). In aqueous solution, these five forms are all in equilibrium with each other. When you dissolve glucose in water, here's the distribution you get:



The pyranose forms dominate, with a small amount of the open-chain and furanose forms comprising the rest of the mixture.

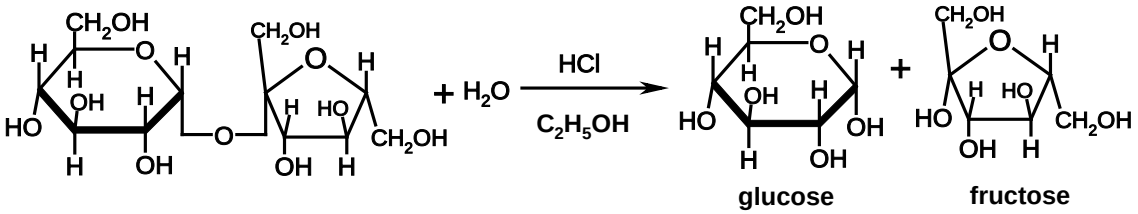
Obtaining methods:

1). Hydrolysis of starch in the presence of mineral acid:

$$(C_6H_{10}O_5)_n + nH_2O \rightarrow nC_6H_{12}O_6$$

Purified by recrystallization from aqueous or alcohol-aqueous solutions.

2). Hydrolysis of sucrose with the participation of an alcoholic solution of hydrochloric acid (HCl):



Glucose is crystallized, and fructose remains in solution.

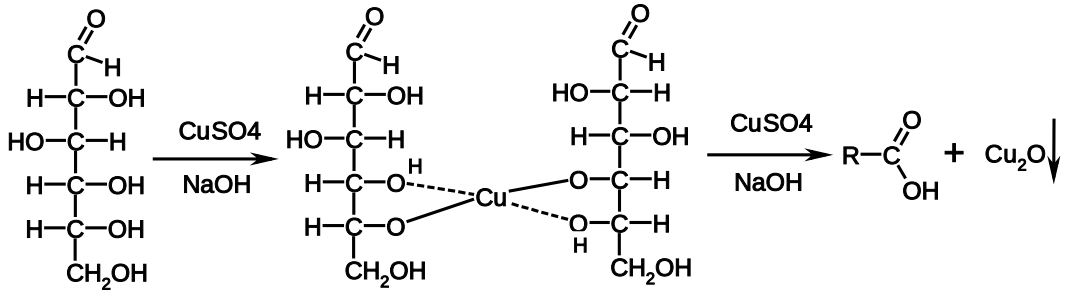
Properties: Colorless crystals or white fine crystalline powder, odorless. Easily (slowly) soluble in water, slightly soluble in 95% alcohol, practically insoluble in ether.

Identification:

Identification reactions must be considered based on the chemical properties of glucose, due to the presence of alcohol hydroxyls and an aldehyde group.

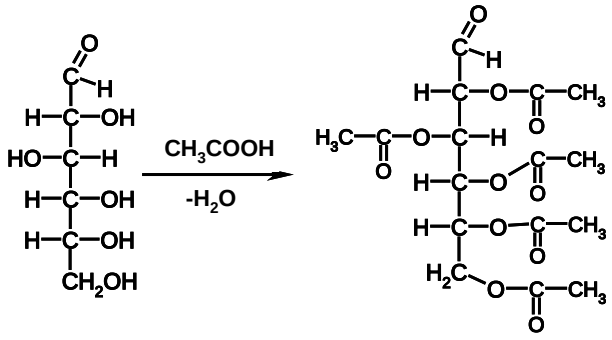
I. Reactions on alcohol hydroxyls

1). Interaction with divalent copper salts: with a solution of divalent copper sulfate in an alkaline medium, a violet-blue complex compound is formed:



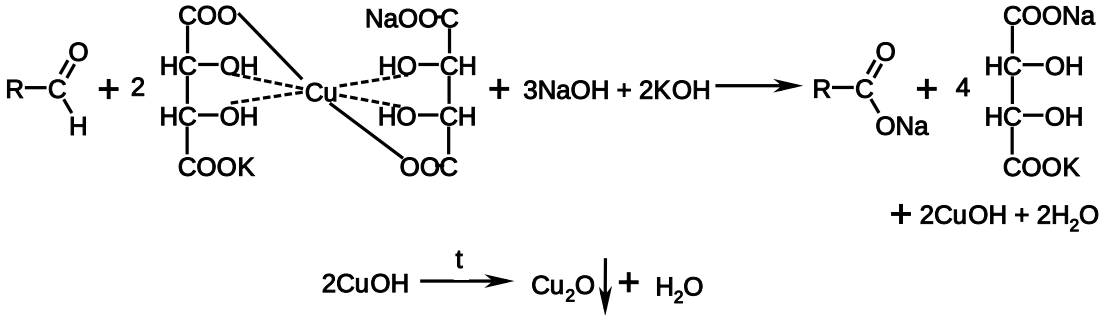
This reaction at the same time proves the presence of both hydroxyl and aldehyde groups, which reduce divalent copper to monovalent copper oxide upon standing.

2). The presence of alcohol hydroxyls can also be proven by the acetylation reaction (the formation of pentaacetates with a stable melting point occurs):



II. Reactions on the aldehyde group.

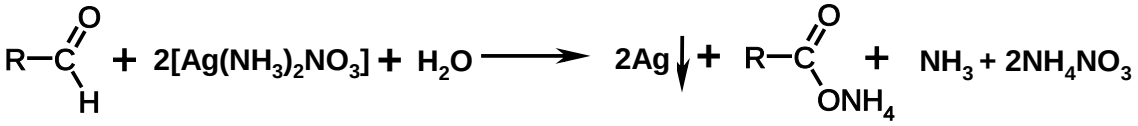
3). In an alkaline or neutral environment, it interacts with weak oxidants (Fehling, Tollens, Nessler reagents):



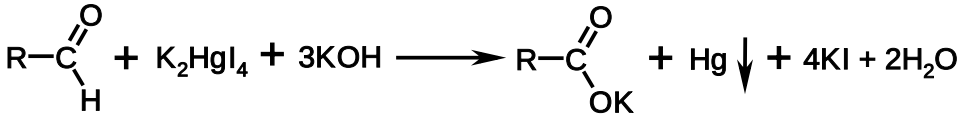
A glucose solution with Fehling's reagent is heated to boiling - a brick-red precipitate of monovalent copper oxide is formed.

Fehling's reagent I - aqueous solution of copper sulfate, Fehling's reagent II - sodium, potassium salt of tartaric acid; when equal amounts of reagents I and II are mixed together, a copper-tartrate reagent potassium, sodium, copper salt of tartaric acid is formed.

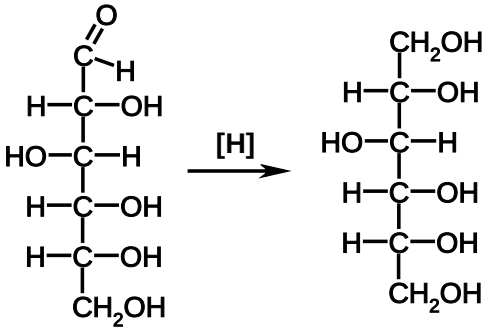
When glucose and fructose are treated with an ammonium solution of silver nitrate (Tollens' reagent), a black precipitate of silver is formed:



With Nessler's reagent, a black precipitate of metallic mercury falls out:



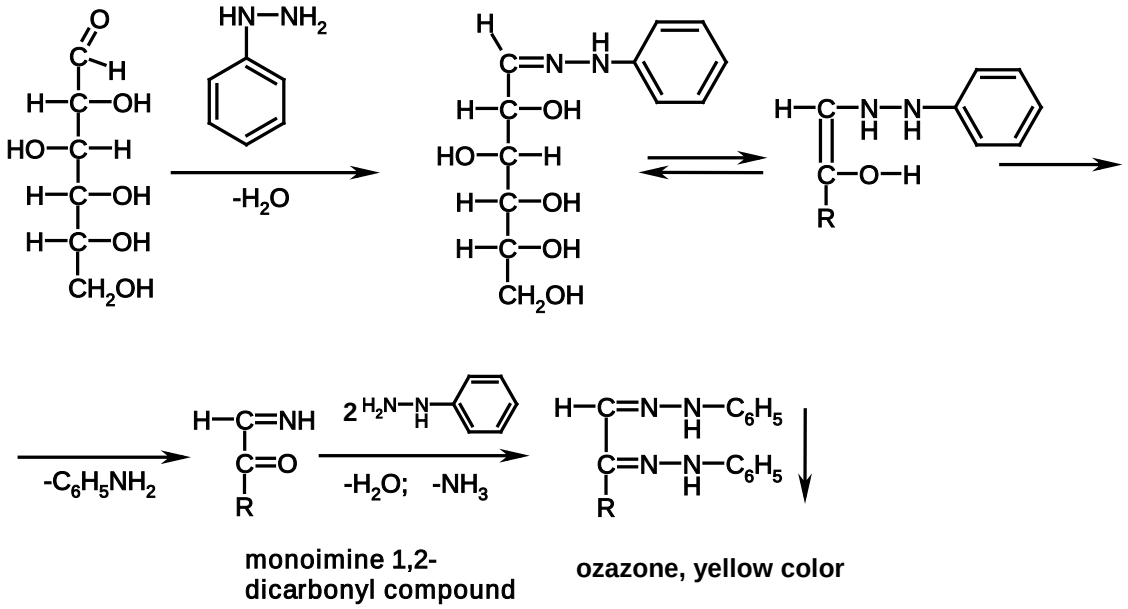
4). The reduction of glucose leads to the formation of sorbitol, which gives classic reactions to polyatomic sugars:



Oxidizing properties of the aldehyde group are not used to identify glucose.

III. Addition reactions (condensation):

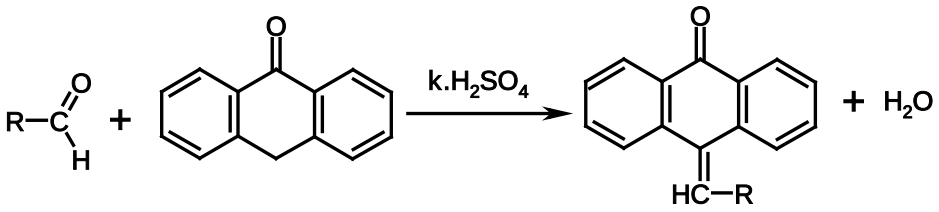
5). Ozazone formation: glucose solutions form phenylhydrazone with phenylhydrazine, which precipitate. Upon further heating in a water bath, ozazones colored in yellow are formed. Ozazones have a characteristic melting point. Glucose interacts with three molecules of phenylhydrazine:



monoimine 1,2-dicarbonyl compound

ozazone, yellow color

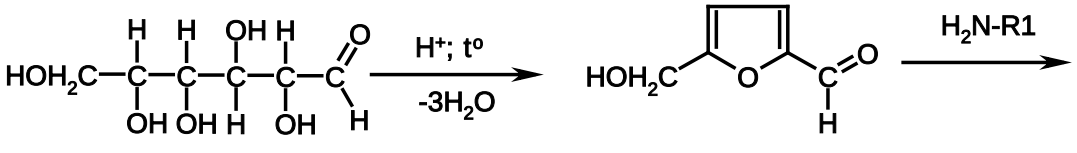
6). Condensation with a solution of anthrone in concentration sulfuric acid (conc. H_2SO_4):



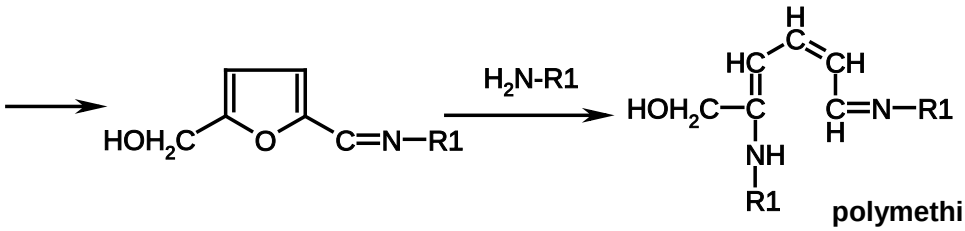
green color changing to blue-green

IV. Reactions to dehydration products:

7). Under the influence of mineral acids or oxalic acid, glucose is transformed when heated in a test tube over a burner flame into hydroxymethylfurfural, which, being a volatile compound, interacts with aniline or procaine applied to the filter paper that covers the test tube. First, Schiff's bases are formed, which have a light yellow color, and then the furan cycle is opened and a polymethine dye is obtained - a derivative of oxyglutacone aldehyde (raspberry-purple color):

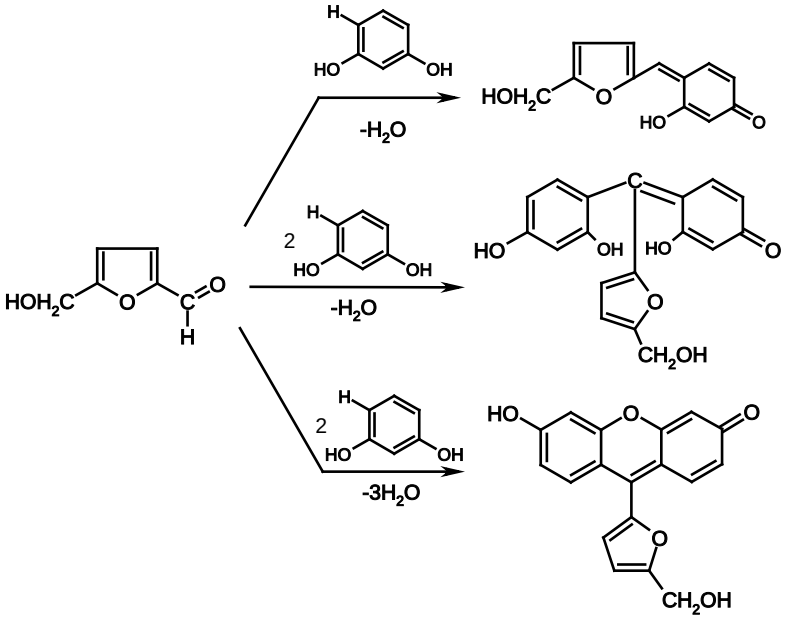


hydroxymethylfurfural



polymethine dye

8). Using the same property of glucose to form hydroxymethylfurfural under the influence of with concentrated sulfuric acid or hydrochloric acid (conc. H_2SO_4 or HCl), based on reactions with phenols (resorcinol, thymol, α-naphthol) - condensation reactions (the product of the reaction is an auric dye, colored red):



V. Instrumental methods.

9). Determination of specific rotation = $+51.5^0$ - 53.0^0 (SPU - State Pharmacopoeia of Ukraine).

10). TLC - Thin Layer Chromatography (SPU - State Pharmacopoeia of Ukraine).

Impurities:

In conditions of thermal sterilization of glucose solutions for injections. Regardless of the presence of a stabilizer, degradation products are formed: deoxyhexazones, organic acids, formaldehyde, 5-oxymethylfurfural.

(**SPU**): 1). Transparency, color, acidity / alkalinity, extraneous sugars (soluble starch, dextrins) - 1.0 g of the substance is dissolved by boiling in 30 ml of alcohol (90%) and cooled - the solution should remain transparent.

2). Sulfites- + water + 0.1 M NaOH solution, bring to 50.0 ml. Up to 10 ml + HCl + colorless fuchsin solution + 0.5% formaldehyde solution, stand for 30 min and determine the optical density at $\lambda = 583$ nm and compare with the standard.

3). Chlorides, Sulphates, Arsenic, Barium, Calcium, Lead, sulphate ash. Pyrogens (for injection solutions).

Quantitative definition:

SPU does not give.

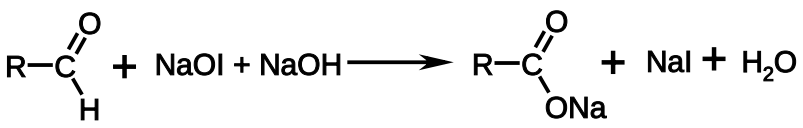
1). Refractometry;

2). The polarimetric method of determining sugars is based on measuring the angle of rotation of polarized light. Knowing the specific rotation, the length of the tube and measuring the angle of rotation, you can calculate the mass fraction in (%) by the formula:

$$C\% = \frac{\alpha * 100\%}{[\alpha]_D^{20} * l_{дм}}$$

3). Iodometry: back titration. It is based on the oxidation of the aldehyde group with alkaline solutions of iodine to form the sodium salt of gluconic acid (f = 1/2, control experiment):

$$I_2 + 2NaOH \rightarrow NaI + NaOI + H_2O$$



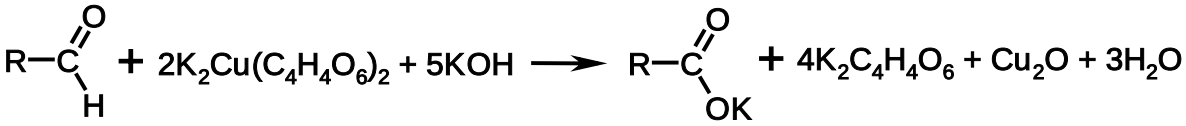
$$NaI + NaOI + H_2SO_4 \rightarrow Na_2SO_4 + I_2 + H_2O$$

$$I_2 + 2Na_2S_2O_3 \rightarrow 2NaI + Na_2S_4O_6$$

$$X=\frac{(V1-V2)*Kn*T*100\%}{a}$$

4). One of the titrimetric methods of monosaccharide analysis is based on the use of Fehling's reagent (2-3 times excess). It is added to the weighing scale in a precisely determined amount, and then the remainder of the divalent copper cation not used for oxidation is determined iodometrically.

The technique is based on carbohydrate reduction of divalent copper to mono-valent copper from the tartrate complex. An excess of Fehling's reagent, containing copper (II) ions, is reduced with iodide in an acidic medium and the released iodine is titrated with sodium thiosulfate (f = 1/2, control experiment).



$$2Cu^{2+} + 5I^- \longrightarrow 2CuI + I_3^-$$

$$I_2 + 2Na_2S_2O_3 \rightarrow 2NaI + Na_2S_4O_6$$

$$X=\frac{(V1-V2)*Kn*T*100\%}{a}$$

5). The gas-liquid chromatography method for determining glucose is used after converting it into volatile compounds (sorbitol acetate or gluconic acid nitrile).

6). A method of permanganatometry with iodometric termination has also been developed.

7). Thin-layer chromatography.

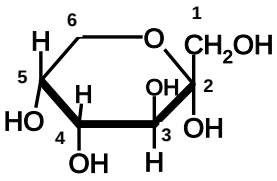
Storage. Store in a well-sealed container at room temperature.

Application. The main function of carbohydrates is the supply of energy necessary for the vital activity of cells. Along with proteins and lipids, carbohydrates are a component of all living organisms. In the course of biochemical oxidation of carbohydrates, the energy necessary for the vital activity of all cells, including skin cells, is released. Carbohydrates enter the skin cells through the blood. Carbohydrates are important for the health and good appearance of the skin.

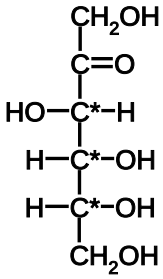
Glucose is used in various diseases of the heart, liver, shock, and collapse as a source of easily digestible food, improves the functions of various organs.

The main ways of glucose metabolism are glycolysis and aerobic oxidation to carbon dioxide, water and ATP (adenosine triphosphate).

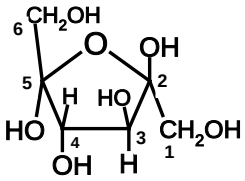
Fructose- Fructosum
(fruit sugar, levulose)



(-)-D-arabinohex-2-ulopyranose
D-fructopyranose



D-fructose



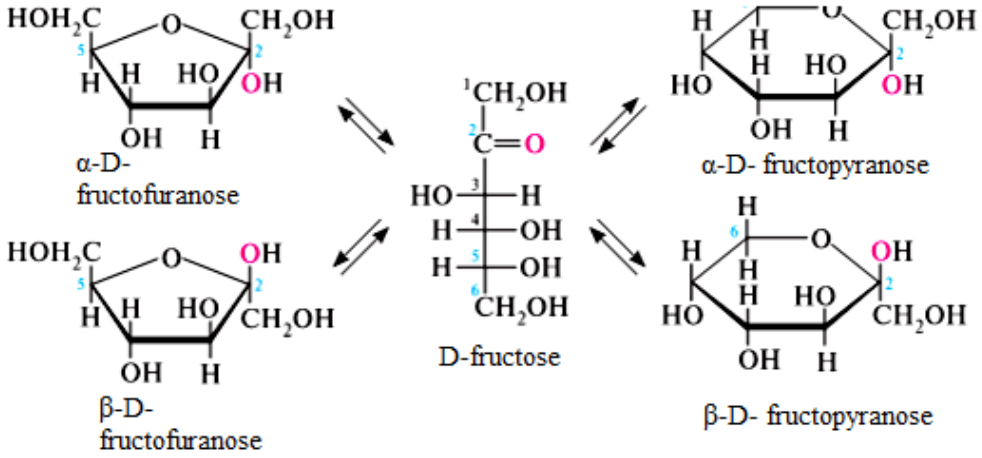
D-fructofuranose

Free fructose is found in fruits and honey. Contains sucrose, raffinose, inulin (contains dahlia tubers, chicory roots.)

Obtaining: from inulin, sucrose, synthetically.

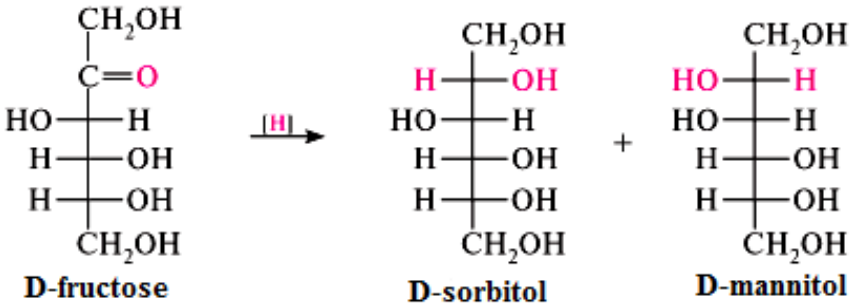
Properties: crystalline powder, sweeter than glucose and sucrose. Soluble in water.

Crystalline represents fructopyranose (melting point of β-anomer 104°C). It is included in oligo- and polysaccharides in furanose form. It has weak reduction properties.



Chemical properties

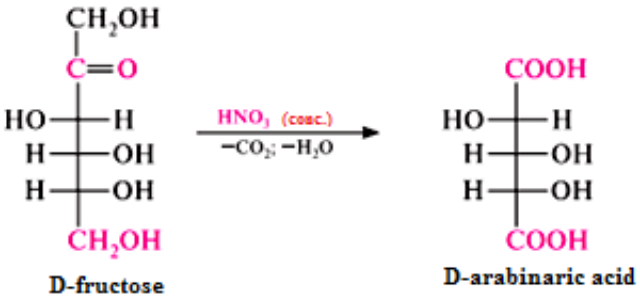
1). Reduction (a mixture of products is formed): reduction of ketones to alcogols.



This reaction is not used in pharmaceuticsl analysis because there is no visible effect.

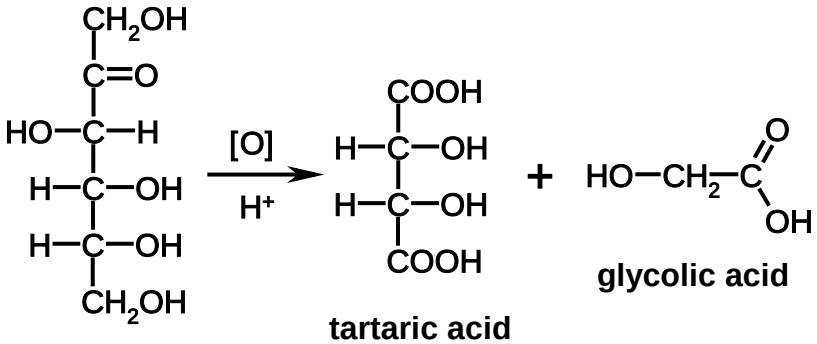
2). Oxidation. Fructose behaves differently when oxidized in acidic / neutral and alkaline environments.

a). In an acidic and neutral environment: it does not interact with weak oxidants (ie, it is not oxidized by bromine water, for example), but strong oxidants oxidize fructose with a break in the carbon chain at the site of the carbonyl group with the formation of dicarboxylic acid:



D-fructose D-arabinaric acid

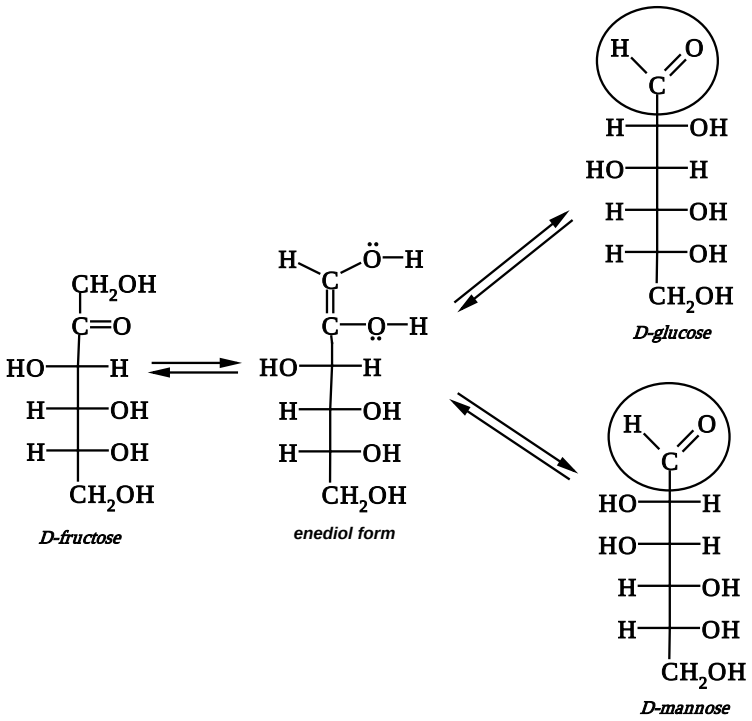
Other authors (Kochetkov) give destruction and oxidation to tartaric and glycolic acids:



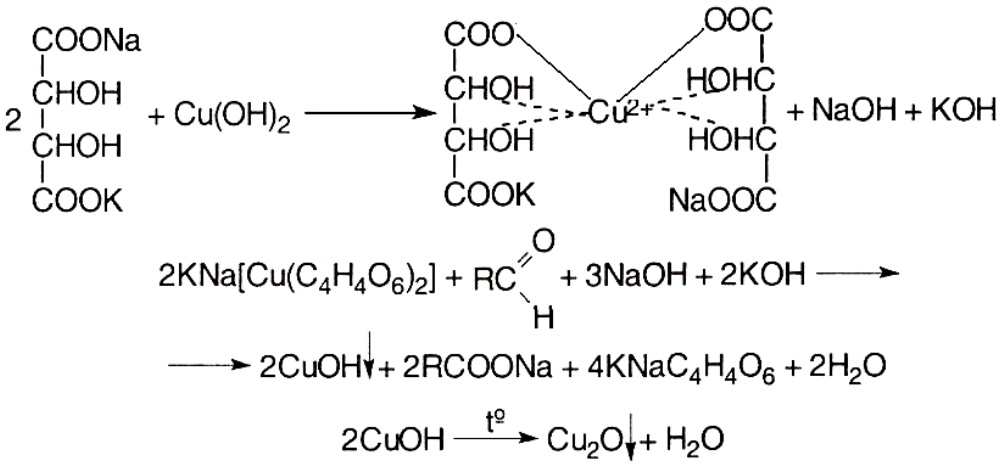
D-fructose tartaric acid glycolic acid

b). In an alkaline environment (even in a weakly alkaline one), interconversions occur through the enediol form, which is formed as a result of migration to the carbonyl group of the mobile hydrogen at the α-carbon atom.

And this reaction can be used to identify fructose (SPU, 1.1. P.475) with Fehling's reagent (as well as Tollens, Nessler).



$$Cu^{2+} + 2OH^- \rightarrow Cu(OH)_2$$

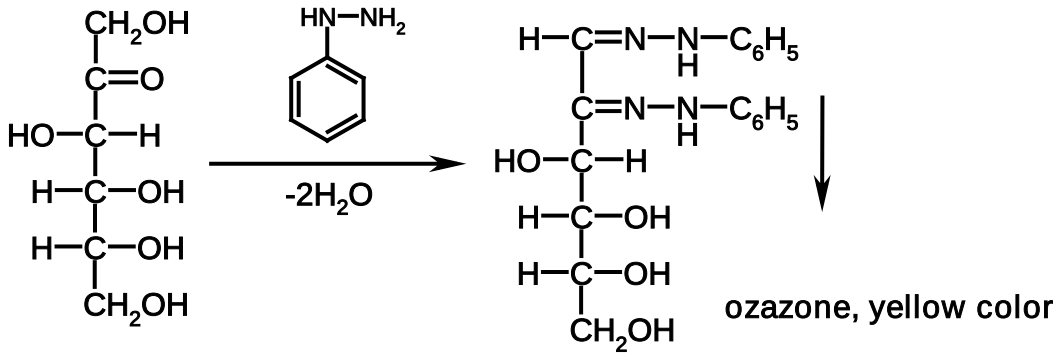


$$2KNa[Cu(C_4H_4O_6)_2] + RC(=O)H + 3NaOH + 2KOH \longrightarrow$$

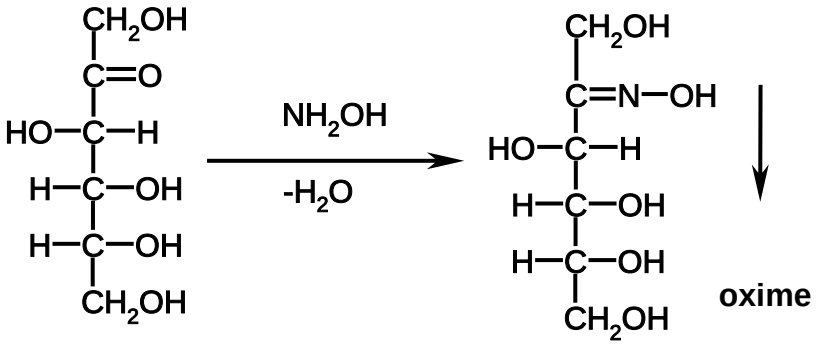
$$\longrightarrow 2CuOH\downarrow + 2RCOONa + 4KNaC_4H_4O_6 + 2H_2O$$

$$2CuOH \xrightarrow{t^\circ} Cu_2O\downarrow + H_2O$$

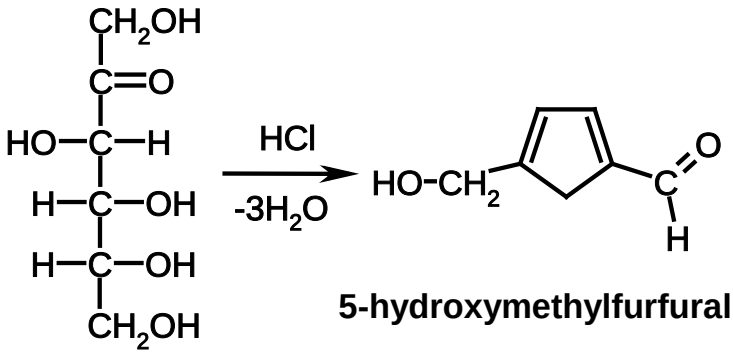
3). Formation of osazone: when heated with phenylhydrazine (1:3), bis-phenylhydrazones are formed - osazones:



4) Interaction with hydroxylamine NH_2OH - oximes are formed:



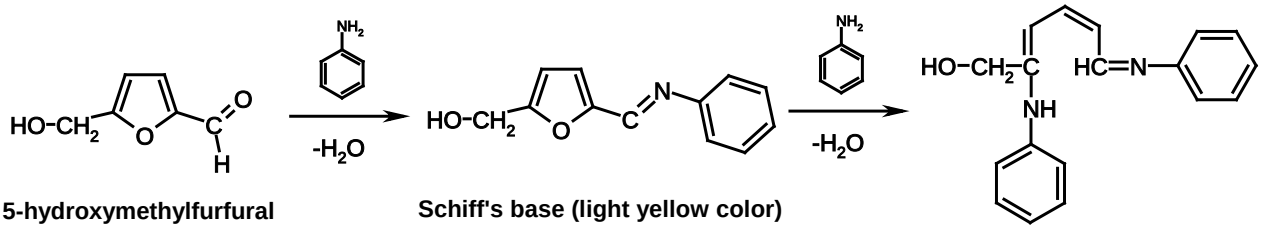
5). Intramolecular dehydration: when heated with mineral acids (hydrochloric or sulfuric acid - HCl, H_2SO_4), 5-hydroxymethylfurfural is formed, which can be confirmed by reaction with aniline:



5-hydroxymethylfurfural

6). Formation of colored Schiff bases. Better with aromatic amines.

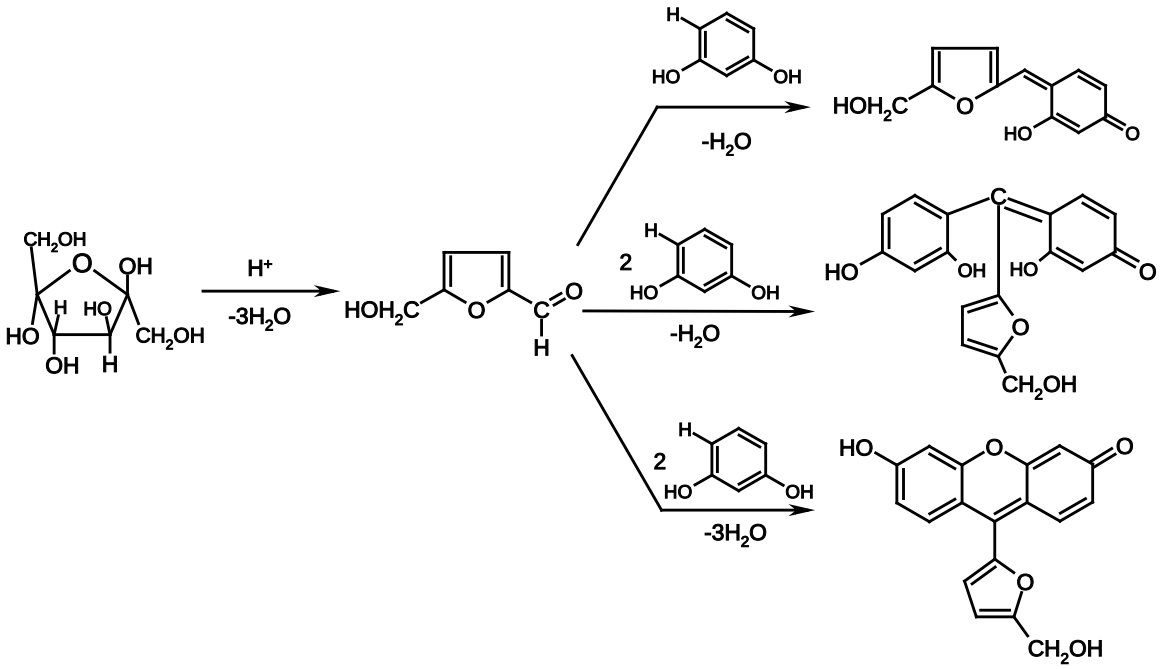
When heated with mineral acids, 5-hydroxymethylfurfural is formed, which then reacts with aniline, forming first a Schiff base, and then a polymethine dye:



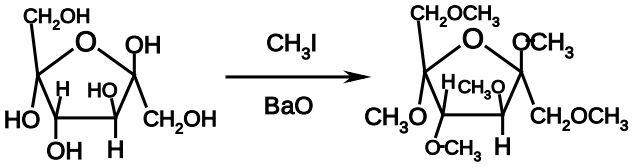
5-hydroxymethylfurfural **Schiff's base (light yellow color)**

polymethine dye
(crimson-violet coloration)

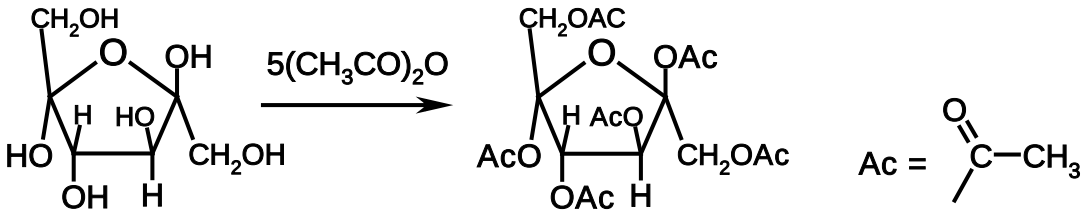
7). Reaction with resorcinol, thymol (after the formation of 5-hydroxymethylfurfural) - a red color appears.



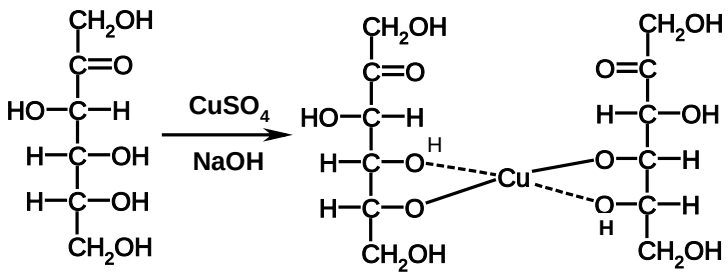
8). Alkylation. Formation of ethers. All hydroxyl groups are capable of alkylation. Including hemiacetal hydroxyl. As a result of the reaction, glycosides are formed, alkylation of all hydroxyl groups. Such compounds in an acidic environment are hydrolyzed only by the glycosidic bond. The simple ethers formed cannot be hydrolyzed by other hydroxyl groups.



9). Acylation. Formation of complex esters with anhydrides of carboxylic acids (formed easily). For example - with acetic anhydride.



10). Interaction with divalent copper (II) salts: with a solution of divalent copper (II) sulfate in an alkaline environment, a violet-blue complex compound is formed:



QUANTITATIVE DETERMINATION

State pharmacopeia of Ukraine (SPU) does not give a quantitative definition. It is enough to identify, determine the specific rotation (-91.0^0 to -93.5^0) and determine the impurities.

Impurities:

- Extraneous sugars: 5 g of substance + water up to 10 ml. To 1 ml of the obtained solution + 9 ml of 96% alcohol. The opalescence should not exceed the opalescence of the original solution + 9 ml of water.
- 5-hydroxymethylfurfural and related impurities: 5 ml of solution S + 5 ml of water. The optical density should not exceed 0.32 at $\lambda = 284$ nm.
- Barium. Up to 10 ml of solution S + 1 ml of sulfuric acid. The opalescence should not exceed the opalescence of a mixture of 1 ml of water and 10 ml of solution S.
- Lead in sugar: no more than 0.00005%.
- And other common impurities.

Application:

Carbohydrates play the role of a source of energy necessary for the most important life processes of the body. They are split into carbon dioxide (CO_2) and water and energy is released. When 1g of carbohydrates is split, 17.6 kJ is released.

In addition to energy, carbohydrates also perform a building function. Insoluble polymers are part of the cell membranes of bacteria and plants, as well as connective tissues and cell membranes of animals, are part of the intercellular substance of the skin, tendons, and cartilage, giving them strength and elasticity.

4. TASKS FOR STUDENT SELF-TRAINING:

4.1. Repeat the theoretical material from organic and analytical chemistry courses on this topic.

4.2. Study the program material on the subject of the lesson according to the questions below.

Educational questions for self-training of students

1. Carbohydrates General characteristics, classification. Distribution in nature. The role of carbohydrates in human life. The concept of deoxy - and amino sugar.
2. Sources of extraction, chemical structure, nomenclature, synonyms of medicinal substances from the group of carbohydrates.
3. To characterize the physicochemical properties of medicinal substances from the group of carbohydrates. Constants of optical activity as indicators of the quality of drugs from the group of carbohydrates.

4. To justify the use of chemical and instrumental methods in the analysis of the quality of medicines from the group of carbohydrates.

5. Monosaccharides. Classification. Stereoisomerism and tautomerism of monosaccharides. Medicines from the group of monosaccharides, sources and methods of extraction.

5.1. Glucose is anhydrous. Glucose monohydrate. Structure, nomenclature, properties, application.

5.2. Using the example of glucose, explain the phenomenon of mutarotation. What is the chemical basis of this phenomenon?

5.3. State the possible methods and reactions for the identification of glucose preparations. Tests for the purity of glucose preparations. Ways of entry and determination of specific impurities (extraneous sugars, soluble starch, dextrins).

5.4. Describe possible methods of quantitative determination of glucose preparations. Give the corresponding reaction equations, calculation formulas.

5.5. Fructose. Structure, nomenclature, properties, analysis, application. Routes of introduction and determination of specific impurities in fructose (extraneous sugars, 5-hydroxymethylfurfural and related compounds).

5.6. Galactose. Structure, nomenclature, properties, analysis, application.

6. Features of storage of drugs from the group of monosaccharides.

4.3. Work out test tasks

1. The pharmacist-analyst of the pharmacy conducts quality control of the 10% glucose solution. What properties of glucose confirm the positive result of the reaction with the copper-tartrate reagent (Fehling's reagent)?

A. Acidic
B. Reduction
C. Amphoteric
D. Oxidizing
E. The main ones

2. The pharmacist-analyst determines the quantitative content of anhydrous glucose by the inverse iodometric method. What indicator should he use for this?

A. Methyl orange
B. Phenolphthalein
C. Starch
D. Potassium chromate
E. Methyl red

3. The pharmacist-analyst conducts tests on the purity of the medicinal product glucose anhydrous according to the SPU. He determines the unacceptable impurity of barium with the help of:

A. Chloric acid
B. Nitric acids
C. Sulfate acids
D. Acetic acid
E. Hydrochloric acids

4. Specify the name of the mirror-symmetric isomers of monosaccharides, the configurations of which are mirror-opposite in the asymmetric centers:

A. Epimers
B. Enantiomers
C. Diastereomers
D. Polymers
E. Anomers

5. State the name of spatial isomers of monosaccharides that differ in the configuration of one or more carbon atoms and are not mirror isomers:

A. Polymers
B. Enantiomers
C. Epimers
D. Anomers
E. Diastereomers

6. The phenomenon is explained by the mutual transformation of tautomeric forms of monosaccharides in solution and the establishment of equilibrium between them:

A. Epimerization
B. Hydrolysis
C. Mutatorations
D. Inversions
E. Heterocyclization

7. Glucose is characterized by the phenomenon of mutarotation. Mutarotation is an involuntary process that is accompanied by:

A. Combining simple carbohydrate molecules into more complex ones
B. Decomposition of complex carbohydrates into simpler components
C. A change over time not only of the angle, but also of the sign of rotation as a result of the hydrolysis of carbohydrates
D. The flow of the ion exchange reaction between various carbohydrates and water

E. Change over time in the angle of rotation of freshly prepared carbohydrate solutions

8. To identify anhydrous glucose by the reaction of ozazone formation, the reagent should be used:

A. Fehling's reagent
B. Phenylhydrazine
C. Phenolphthalein
D. Hydroxylamine
E. Furfural

9. A mixture of equal amounts of enantiomers, which does not have optical activity, is called:

A. Epimeric mixture
B. Invert sugar
C. Grape sugar
D. Anomeric mixture
E. Racemic mixture

10. A pharmacist-analyst analyzes a 10% glucose solution. For quantitative determination, he uses one of the physico-chemical methods, measuring the angle of rotation of the solution, using:

A. Gas chromatograph
B. UV spectrophotometer
C. Potentiometer
D. Polarimeter
E. Refractometer

11. Specify the name of the hydroxyl group formed during the cyclization of monosaccharides:

A. Enolic hydroxyl
B. Phenolic hydroxyl
C. Epimeric hydroxyl
D. Carbonyl hydroxyl
E. Hemiacetal hydroxyl

12. The phenomenon of mutarotation is characteristic of freshly prepared glucose solutions. The chemical basis of this process is:

A. Presence of regenerative properties in glucose
B. Formation of 5-hydroxymethylfurfural
C. Ring-chain tautomerism of glucose
D. Chirality of the glucose molecule
E. Dissociation of glucose in solution

13. The pharmacist-analyst performs quality control of the substance of anhydrous glucose. When testing for purity, in accordance with the requirements of the Federal State Administration of Ukraine, it is assumed that impurities of extraneous sugars, soluble starch and dextrins are determined. To perform this test, the analyst:

A. Concentrated sulfuric acid is added to the solution of the substance in purified water; the opalescence of the obtained solution should not exceed the opalescence of the standard

B. A sample of the substance is dissolved in a mixture of chloroform and dioxane; no red color should appear

C. Measures and compares with pharmacopoeial data the value of the optical density of a 10% solution of the substance in purified water

D. A sample of the substance is dissolved by boiling in ethyl alcohol, cooled; the solution should remain clear

E. Copper-tartrate solution is added to the solution of the substance in purified water and heated; an abundant red precipitate should form

14. In the control and analytical laboratory, the substance of anhydrous glucose is studied by the method of polarimetry. What value is used to identify substances in this method of pharmaceutical analysis?

A. Refractive index

B. Specific optical rotation

C. Molar coefficient of light absorption

D. Angle of rotation

E. Specific refractive index

15. To identify fructose, the analyst of the laboratory of a pharmaceutical company heated a sample of the substance with hydrochloric acid in the presence of resorcinol. In the process of this interaction, substance "X" is formed, which, when condensed with resorcinol, gives a reaction product colored in red. Substance "X" is:

A. 5-Hydroxymethylfurfural

B. Azomethine dye

C. Diazonium salt

D. 2,4,6-Trichlorophenol

E. Glutacon aldehyde

16. To identify glucose monohydrate by the reaction accompanied by the formation of 5-hydroxymethylfurfural, preheating is carried out with:

A. Acetic anhydride

B. Copper-tartrate solution

C. Hydroxylamine

D. Potassium tetraiodomercurate
E. Mineral acids

17. Specify the type of tautomerism characteristic of a glucose molecule:
A. Nitro-acy-nitro tautomerism
B. Lactim-lactam tautomerism
C. Amino-imine tautomerism
D. Cyclo-oxo-tautomerism
E. Keto-enol tautomerism

18. According to the nature of the oxo group, monosaccharides are divided into:
A. Monoses and polyoses
B. *D*- and L-monosaccharides
C. Aldoses and ketoses
D. Epimers and anomers
E. Pentoses and heptoses

19. Not amenable to hydrolysis:
A. Glucose
B. Maltose
C. Starch
D. Sucrose
E. Lactose

20. State the conditions necessary for the identification of glucose monohydrate with a copper-tartrate solution:
A. Addition of HNO_3 (conc.)
B. Cooling
C. Addition of formaldehyde
D. Heating
E. Catalyst (KBr)

21. *D*- Glucose and D-fructose in the crystalline state exist in the form of:
A. Acyclic forms
B. Andiolic forms
C. Linear forms
D. Mixtures of tautomeric forms
E. Cyclic forms

22. Indicate which of the following carbohydrates according to their chemical structure belongs to ketohexoses:
A. Fructose
B. Mannose
C. Glucose
D. Galactose

E. Starch

23. When testing fructose for purity, the pharmacist-analyst, in accordance with the requirements of the State Federal Drug Administration, prepared the initial solution of the substance in purified water in advance. Then, to two equal samples of the original solution, he added the appropriate solvent in equal quantities: to the first sample - 96% ethyl alcohol, and to the second - purified water. Comparing the opalescence of the obtained solutions with each other, the pharmacist-analyst evaluates the content of the impurity:

A. Lead in sugars
B. Third party sugars
C. Formaldehyde
D. Baria
E. 5-Hydroxymethylfurfural and related compounds

24. As a result of the intramolecular interaction of the carbonyl group and the alcohol group spatially close to it, monosaccharides can exist in the form:

A. Cyclic anhydrides
B. Cyclic esters
C. Cyclic hemiacetals
D. Cyclic amides
E. Cyclic carboxylic acids

25. Indicate which physico-chemical method, according to the **SPU**, is used to identify fructose:

A. Refractometry
B. Thin-layer chromatography
C. Photoelectrocolorimetry
D. Potentiometry
E. Polarography

26. The hydroxyl group at the carbon atom is involved in the formation of furanose forms of glucose:

A. C-3
B. C-2
C. C-4
D. C-6
E. C-5

27. Specify a specific admixture for anhydrous glucose:

A. Dextrins
B. Seneciflin
C. Formaldehyde [paraform]
D. Ammonium salts

E. Pantoylactone

28. A positive result of the reaction with a copper-tartrate solution (Fehling's reagent) gives:

A. Polyglukin
B. Starch
C. Dextran 40 for injections
D. Low molecular weight heparin
E. Glucose monohydrate

29. The hydroxyl group at the carbon atom is involved in the formation of pyranose forms of glucose:

A. C-3
B. C-6
C. C-2
D. C-4
E. C-5

30. The pharmacist-analyst identifies the fructose substance. In accordance with the requirements of the **SPU**, during the tests, he performed a reaction that resulted in the formation of a red precipitate. Indicate with which of the reagents this reaction was carried out:

A. Copper-tartrate solution
B. Ammonium silver nitrate solution
C. Potassium tetraiodomercurate solution is alkaline
D. Concentrated formaldehyde solution
E. Potassium pyroantimonate solution

31. The pharmacist-analyst performs the identification of the substance "Glucose anhydrous" with the copper-tartrate reagent. What color precipitate is formed?

A. White
B. Turquoise blue
C. Blue-violet
D. Brick red
E. Emerald green

32. The pharmacist-analyst determines the quantitative content of anhydrous glucose by the inverse iodometric method. At the same time, he should use a standard solution as a titrant:

A. Potassium iodide
B. Potassium iodate
C. Potassium bromate
D. Silver nitrate
E. Sodium thiosulfate

33. According to the SPU, in the fructose substance, it is envisaged to determine the admixture of 5-hydroxymethylfurfural and related compounds by the method of absorption spectrophotometry in the ultraviolet region. At the same time, the following values are measured and compared with pharmacopoeial data:

A. Melting points
B. Optical density
C. pH of the standard solution
D. Specific optical rotation
E. Refractive index

34. Specify the main method of industrial extraction of anhydrous glucose, which is used for medical purposes:

A. Oxidation of glutamic acid
B. Epimerization of fructose
C. Starch hydrolysis
D. Oxidation of glycerol
E. Microbiological synthesis

35. The hemiacetal hydroxyl in the cyclic forms of glucose is located at the carbon atom:

A. C-2
B. C-1
C. C-6
D. C-3
E. C-4

36. The pharmacist-analyst determines the specific optical rotation of anhydrous glucose in accordance with the requirements of the SPU. To accelerate the mutarotation process, the following should be added to the solution of the analyte substance:

A. Sodium hydroxide solution
B. Copper(II) sulfate solution
C. Hydrochloric acid solution
D. Ammonia solution
E. Potassium permanganate solution

37. Indicate which physicochemical method, according to the **SPU**, is used to identify anhydrous glucose:

A. Thin-layer chromatography
B. Polarography
C. Potentiometry
D. Photoelectrocolorimetry
E. Refractometry

4.4. Situational tasks:

1. Describe the properties of drugs from the carbohydrate group based on their structure.
2. Explain how optical activity constants are used in the quality analysis of drugs from the carbohydrate group.
3. Explain the phenomenon of mutarotation using the example of glucose. What is the chemical basis of this phenomenon?
4. Suggest possible reagents that can be used to prove the presence of hemiacetal hydroxyl in the structure of glucose and fructose.
5. How is the correction for the moisture content of the original substance taken into account during the quantitative analysis of dosage forms containing anhydrous glucose?
6. Explain the origin and justify the methods of detecting specific impurities in carbohydrate substances: extraneous sugars, soluble starch, dextrins in anhydrous glucose; extraneous sugars, 5-hydroxymethylfurfural and accompanying impurities in fructose.

4.5. Tasks:

1. Determine the concentration of an anhydrous glucose solution (%), if it is known that the refractive index of this solution is 1.3557, F = 0.00142, and the refractive index of the solvent is 1.3330.
2. Calculate the concentration of anhydrous glucose (%) in the solution, if the refractive index of the solvent is 1.3330, the solution is 1.3450, F = 0.00142.
3. Determine the value of the specific rotation of anhydrous glucose, if it is known that the angle of rotation of a polarized beam of a 35% solution is +18.60° when measuring it in a cuvette 1 dm long.
4. Determine the concentration of an anhydrous glucose solution, if the angle of rotation of this solution is +7.05°, the layer thickness is 1 dm, and the specific rotation of anhydrous glucose is +53.1°.
5. Determine the concentration of an anhydrous glucose solution, if the angle of rotation for this solution is +5.03°, the layer thickness is 1 dm, and the specific rotation of anhydrous glucose is +53.1°.
6. The magnitude of the specific rotation of fructose is -91.90°. The angle of rotation of its aqueous solution, measured in a cuvette with a length of 100 mm, is -45.95°. Determine the concentration of this solution.
7. Calculate what volume of 0.1 M sodium thiosulfate solution (Kp=1.0000) was spent on the titration of 0.0984 g of glucose monohydrate (M. m. 198.2), if 20.2 ml of titrant was spent in the control experiment , and the content of the active substance in the substance was 99.6%.

8. The refractive index of the mixture containing a mixture of sodium bromide, ascorbic acid and glucose is 1.3547 (n0 = 1.3330). The concentrations of sodium bromide and ascorbic acid were determined titrimetrically - 3.96% and 4.10%, respectively. Refractive index factors F(NaBr) = 0.00134, F(asc. k-ty) = 0.00160, F(glucose) = 0.00142. Determine the concentration of glucose in the mixture.

9. The pharmacist-analyst carries out quality control of the dosage form of the following composition:

10% glucose solution - 100 ml

Ascorbic acid 1.0.

Calculate the quantitative content of glucose in the dosage form, using the following data: the refractive index of the mixture is 1.3478, the refractive index of the solvent is 1.3330; the content of ascorbic acid in 100 ml of the dosage form is 0.90 g; refractive index factor of 1% ascorbic acid solution 0.00160; refractive index factor of anhydrous glucose 0.00142; the moisture content of the glucose used to prepare the mixture is 10%.

5. LABORATORY WORK

During laboratory work it is necessary to strictly follow the safety rules in the chemical laboratory.

Each student individually carries out reactions of identification of samples of drug substances under the instruction of the teacher and draws up the test report.

LESSON No. 2

1. SUBJECT: Analysis of drugs from the group of oligo-, polysaccharides and antiarrhythmic drugs.

2. PURPOSE: To master the methods of analysis of drugs from the groupoligo-, polysaccharides and antiarrhythmic drugs.

3. OBJECTIVES:

3.1. To study the structure, nomenclature, synonyms, physico-chemical properties, sources and methods of obtaining medicines from the groupoligo-, polysaccharides and antiarrhythmic drugs.

3.2. To study the methods of analysis of the considered group of medicinal products according to the SPU, MQC.

3.3. Propose and justify possible methods of identification and quantification, based on the structure of drugs of the studied group.

3.4. To study specific impurities, as well as testing methods for the purity of this group of substances.

3.5. Consider the peculiarities of the analysis of drugs from the groupoligo-, polysaccharides and antiarrhythmic drugsusing physical, physicochemical and chemical methods.

3.6. To learn how to analyze the quality of the considered group of medicines using physical, physico-chemical and chemical methods.

3.7.Interpret and give a correct assessment of the received analysis results, draw a conclusion about the quality of the analyzed substances.

3.8. Explain the peculiarities of the storage of medicines from the groupoligo-, polysaccharides and antiarrhythmic drugs, based on their physical and chemical properties.

3.9.Learn and follow the rules of safe work in a chemical laboratory.

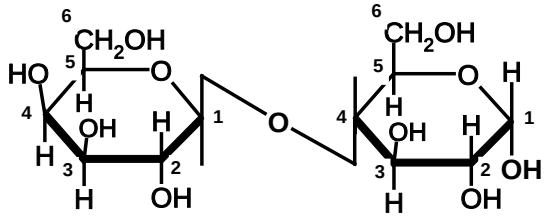
POLYSACCHARIDES,

In addition to monosaccharides, oligosaccharides and polysaccharides are widely used in medicine and cosmetology. Oligosaccharides are called sugar-like complex carbohydrates. Depending on the number of monosaccharide molecules formed during their hydrolysis, oligosaccharides are divided into di-, tri-, tetrasaccharides, etc.

Disaccharides are built as glycosides: (o-glycosides **OLIGOSACCHARIDES**). Compounds of the first type are disaccharides, which are

formed due to the release of water from the semiacetal hydroxyl of one monosaccharide molecule and one of the alcohol hydroxyls of the second (lactose, maltose). Such sugars are called reducing sugars, because they have a free hemiacetal hydroxyl, and therefore are capable of tautomeric transformations (that is, they can be in the solution in both cyclic and acyclic form and, due to the presence of an aldehyde group, enter into an oxidation reaction with Fehling's reagent, the formation of a "silver mirror", etc.).

Lactose(Saccharum lactis, milk sugar)



β-D-galactopyranose α-D-glucopyranose

4-(β-D-galactopyranosido)-α-D-glucopyranose or β-D-galactopyranosyl-(1-4)-α-D-glucopyranose.

Properties: White crystals or white crystalline powder without odor, weak sweet taste. Specific rotation from $+52^0$ to $+ 53.5^0$ (5% aqueous solution). Easily soluble in water, slightly in alcohol, insoluble in ether and chloroform.

Receiving: In industry, it is obtained as a by-product in the production of cheese.

IDENTIFICATION:

1). (**SPU**) According to physicochemical constants: IR spectra (infrared spectrum).

2). (**SPU**) TLC (Thin Layer Chromatography).

3). (**SPU**) with ammonia solution and heated to 80^0C - red color.

4). With Fehling's reagent as glucose.

5). Specific rotation $+54.4^0$ to 55.9^0 (after adding 2 drops of ammonia solution and standing for 30 min - mutarotation - changing the angle of rotation of freshly prepared solutions).

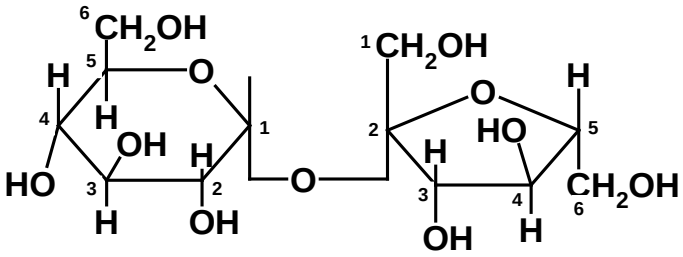
Quantitative definition:

Just like glucose.

Application: non-hygroscopic powder, used for preparation of powders and triturations.

Compounds of the second type are disaccharides, which are formed due to semiacetal hydroxyls of both monosaccharides. Such disaccharides are called non-reducing (sucrose). They are not oxidized by Fehling's reagent, do not give a "silver mirror" reaction under normal conditions.

Sucrose (Saccharum, sugar)



2-α-D-glucopyranosido-β-D-fructofuranoside or α-D-glucopyranosyl (1→2)-O-β-D-fructofuranoside. Cane (beet) sugar.

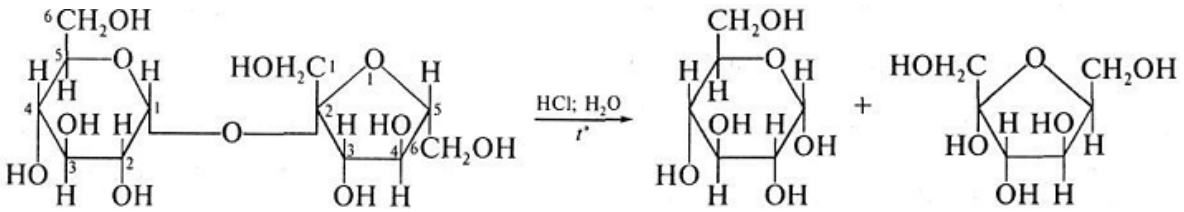
Colorless or white crystals, pieces or white crystalline powder (a blue tint is allowed), odorless, sweet taste. Very easily soluble in water, forming a solution of neutral reaction; almost insoluble in anhydrous alcohol, ether, chloroform. It melts at t = 184-185^{0}C, with further heating it darkens and turns into a brown, bitter-tasting mass (caramel).

IDENTIFICATION

1). The reaction with cobalt nitrate in an alkaline environment - purple color formed (this is reaction to alcohol hydroxyls).

2). In pharmaceutical form, sucrose is identified by its reaction with resorcinol - when heated in the presence of hydrochloric acid HCl - a red color appears. 5-hydroxymethylfurfural is formed, which with resorcin gives color (like glucose and fructose).

3). Formation of invert sugar - when heating acidified aqueous solutions, sucrose is hydrolyzed:



Inversion is a phenomenon when, after hydrolysis, not only the value of the angle of rotation changes, but also the sign.

Specific rotation of sucrose before hydrolysis = +66,0^0 after hydrolysis an equimolar mixture of glucose = + 52,5^0 and fructose = - 93,0^0 is formed.

Total rotation = $40,0^0$.

Quantitative definition:

As glucose: refractometry, polarimetry.

OLIGOSACCHARIDES - high molecular weight carbohydrates containing tens to several thousand monosaccharide residues. Hydrolysis of polysaccharides under the action of acids or enzymes leads to the formation of oligosaccharides and then monosaccharides.

The most important polysaccharides (often used both in medicine and in cosmetology) include: starch, cellulose, chitin and chitosan, hyaluronic acid, pectins, agar-agar, alginic acid, β-1,3-glucan, dextran, etc. .

POLYSACCHARIDE - STARCH - AMYLUM $(C_6H_{10}O_5)n$

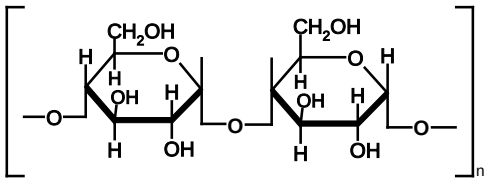
Starch is a mixture of two polysaccharides: 25% amylose and 75% amylopectin. It is obtained from potatoes, wheat, rice, corn.

Starch contains about 25% of the water-soluble fraction called amylose and about 75% of the insoluble fraction called amylopectin. With gradual acid and enzymatic hydrolysis, amylose and amylopectin are split into dextrins (a mixture of polysaccharides with a lower molecular weight), further hydrolysis of which leads to the formation of maltose, and then to D-glucose:

$$\underset{\text{Starch}}{(C_6H_{10}O_5)_n} \longrightarrow \underset{\text{dextrins}}{(C_6H_{10}O_5)_x} \longrightarrow \underset{\text{Maltose}}{C_{12}H_{22}O_{11}} \longrightarrow \underset{\text{D-glucose}}{C_6H_{12}O_6}$$

Amylose is a linear polymer containing more than 1000 monomer units, in which D-glucopyranose residues are connected by an α-1,4-glycosidic bond:

AMYLOSE

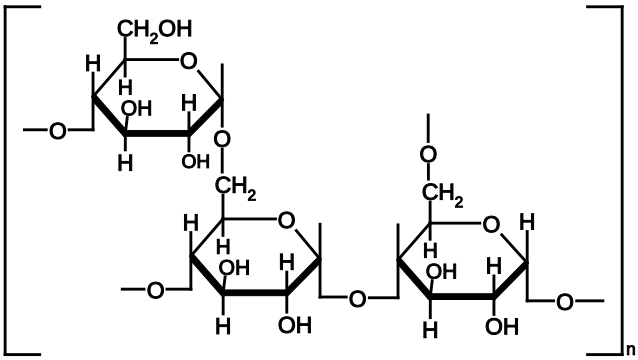


n=50-3000

The molecular weight of amylose is approximately 150,000-600,000. Its molecules are flexible and can take different spatial forms. in the presence of complexing agents, for example, iodine, it can exist in the form of a spiral, each turn of which contains six glucose residues. The size of the inner cavity of the spiral allows the placement of an iodine molecule in it, which leads to the formation of a complex colored in blue.

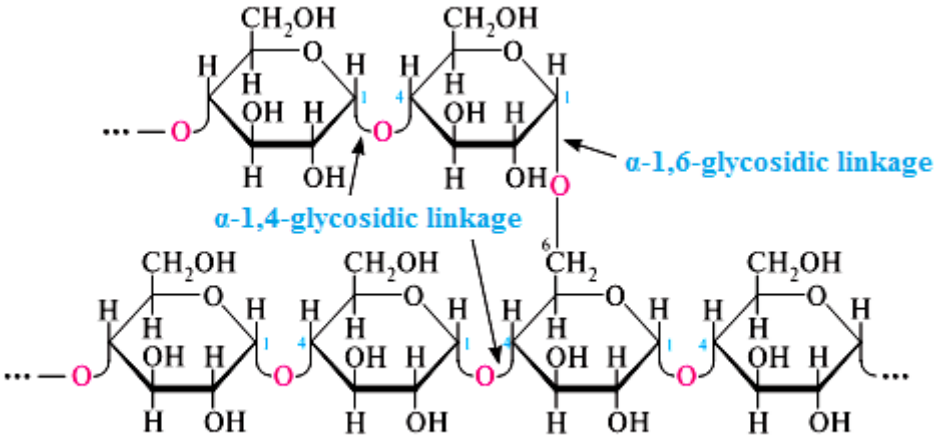
The use of starch as an indicator in pharmaceutical analysis is based on this property.

AMYLOPECTIN



n=3000-4000

Amylopectin is a polymer with a branched structure, which can contain approximately 600-5000 D-glucose residues in a molecule. The molecular weight of amylopectin reaches 1-6 million. All polysaccharide chains - main and side - are built in the same way: glucose residues in them are connected by an α-1,4-glycosidic bond. Side branches are connected to the main chain by an α-1,6-glycosidic bond. Between two adjacent branching points, the main chain contains 20-25 monosaccharide residues:



fragment of amylopectin molecule

Due to the presence of a large number of branches, the amylopectin molecule is unable to adopt a spiral conformation and binds iodine only in a small amount with the formation of a red color.

Identification starch:

1). With iodine solution - blue color.

2). After acid hydrolysis - glucose is formed - all reactions to glucose.

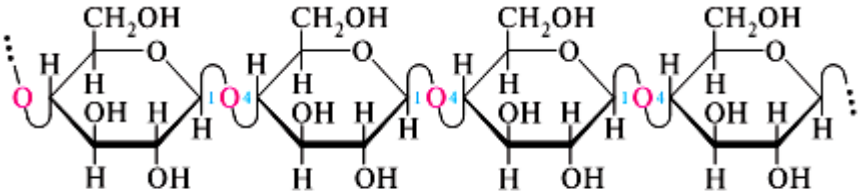
Quantitative definition: not indicated, but after hydrolysis we can use all methods for glucose.

Application: Starch is the main source of carbohydrates in the human diet. The enzyme amylase, contained in saliva, cleaves the α-Glycosidic bond of starch to dextrins and partially to maltose, the further breakdown of which into glucose occurs in the intestines. In pharmacy, starch is used in the production of tablets, as well as for the preparation of powders and pastes. In cosmetology - in decorative cosmetics - because it adsorbs moisture well, has a gentle effect on the skin.

Pasteurized starch - a water-glycerine solution of starch is used in the manufacture of toothpastes. Starch, especially rice starch, is introduced into the composition of powder, dry shadows, and dry deodorants.

CELLULOSE- homopolysaccharide.

Cellulose is a polysaccharide widely distributed in nature, which is a component of plant cell membranes. The composition of wood includes from 50 to 70%, and the composition of cotton - up to 98% cellulose. The cellulose molecule is a linear chain consisting of D-glucopyranose residues connected by a β-1,4-glycosidic bond:



fragment of a cellulose molecule

The molecular weight of cellulose ranges from 250,000 to 1,000,000 (contains at least 1,500 glucose residues).

Cellulose does not dissolve in water and ordinary organic solvents, but dissolves in ammonia solutions of copper (II) hydroxide (Schweizer's reagent) and a concentrated solution of zinc chloride.

Cellulose hydrolysis is carried out by heating in the presence of sulfuric acid:

$$(C_6H_{10}O_5)_n \rightarrow (C_6H_{10}O_5)_x \rightarrow C_{12}H_{22}O_{11} \rightarrow C_6H_{12}O_6$$

cellulose **amyloid** **cellobiose** **D-glucose**

Cellobiose, like maltose, contains 2 D-glucopyranose residues with a 1,4-glycosidic bond, but the hemiacetal hydroxyl has a β-configuration.

Humans and higher animals do not have an enzyme that hydrolyzes the β-glycosidic bond of cellulose, but it is a necessary ballast component of food that improves digestion.

The cellulose molecule has a strictly ordered "rigid rod" conformation in which glucopyranose residues are arranged linearly. This arrangement of residues in space

is due to the fact that the glycosidic oxygen atom and the oxygen atom at C-4 are equatorially connected to the pyranose cycle. The linear conformation of the molecule is fixed by intramolecular hydrogen bonds.

The parallel polysaccharide chains are held together by the formation of hydrogen bonds. Due to this structure, cellulose is chemically relatively inert (insoluble in water, difficult to hydrolyze) and has high mechanical strength.

Cellulose derivatives are of great practical importance. The presence of three free alcohol groups in each glycosidic residue of cellulose makes it possible to obtain its complex esters. Yes, when processing cellulose with a mixture of nitric and sulfuric acids:

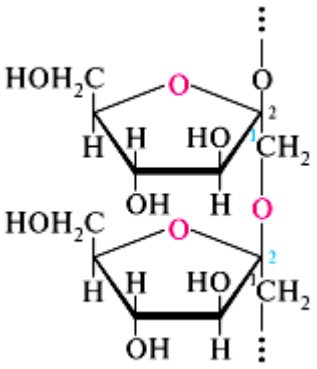
$$[C_6H_7O_2(OH)_3]_n + nHNO_3 \longrightarrow [C_6H_7O_2(OH)_2ONO_2]_n + nH_2O$$
$$[C_6H_7O_2(OH)_3]_n + 2nHNO_3 \longrightarrow [C_6H_7O_2(OH)(ONO_2)_2]_n + 2nH_2O$$
$$[C_6H_7O_2(OH)_3]_n + 3nHNO_3 \longrightarrow [C_6H_7O_2(ONO_2)_3]_n + 3nH_2O$$

cellulose trinitrate

The properties and possibilities of application of these products depend on the degree of nitration. The mixture of mono- and dinitrate is called colloidal cotton, or colloxylin. It is used to make collodion, which is used in medicine to fix bandages. The product of complete nitration of cellulose (cellulose trinitrate, trinitrocellulose, pyroxylin) is an explosive substance used in the production of smokeless gunpowder. Of great national economic importance is cellulose diacetate, which is used in the production of acetate silk, as well as cellulose xanthogenate, which is used to obtain viscose fiber and cellophane. The sodium salt of carboxymethylcellulose is used in the production of medicinal products.

Cellulose and its ethers are also used as an emulsifying, dispersing, thickening, foaming, stabilizing agent and are included in hair styling products, toothpastes, bath and shower preparations, etc.

Inulin. Inulin is a reserve polysaccharide contained in the tubers of complex flowers and other plants.



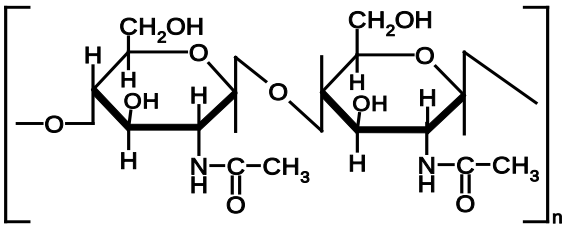
The inulin molecule has a linear structure and consists of β-D-fructofuranose residues connected by a 2,1-glycosidic bond, and ends with an α-D-glucopyranose residue (as in sucrose). The molecular weight is usually no more than 6000.

Inulin is obtained from dahlia tubers by extraction with hot water. It is used to obtain D-fructose.

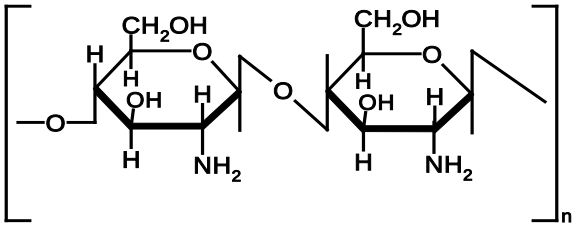
Chitin and chitosan

Chitin is a structural polysaccharide of invertebrates, a component of the cell wall of fungi and some green algae. It is obtained from shells of crustaceans, in which the chitin content reaches 25-50%, by treatment with acids or alkalis. When processing chitin under harsh conditions with alkali, chitosan is formed (deacetylation occurs). Chitin consists of N-acetyl-β-D-glucosamine residues. It has a linear structure, the order of connection is 1-4. Chitosan consists of β-D-glucosamine residues.

Chitin:



Chitosan:



Identification: After hydrolysis, they yield monosaccharides, which can be identified as all monosaccharides.

If aminodesoxysugars are included in the composition, then they give reactions to an aliphatic amino group (release of ammonia, formation of Schiff bases).

There are specific reactions to deoxysugars, such as:

1). Keller-Kiliani reaction: prepare 2 solutions: 1) drug + l. acetic acid and ferrum sulfate(II) solution and 2) conc. sulfuric acid and ferrous sulfate(II) solution. 2 solutions are layered and a colored solution is obtained.

2). Peset reaction (Pezet) - xanthhydrol test (with dibenzo-pyran) in the presence of l. acetic acid, heating and sulfuric or phosphoric acid. A red color is formed. Anthrone reagent can also be used. The reaction is based on the fact that under the action of conc. acids, carbohydrates form furfural, which reacts with anthrone

3). Pezets-Dekvenera - phosphoric acid in acetone - colored solutions are formed.

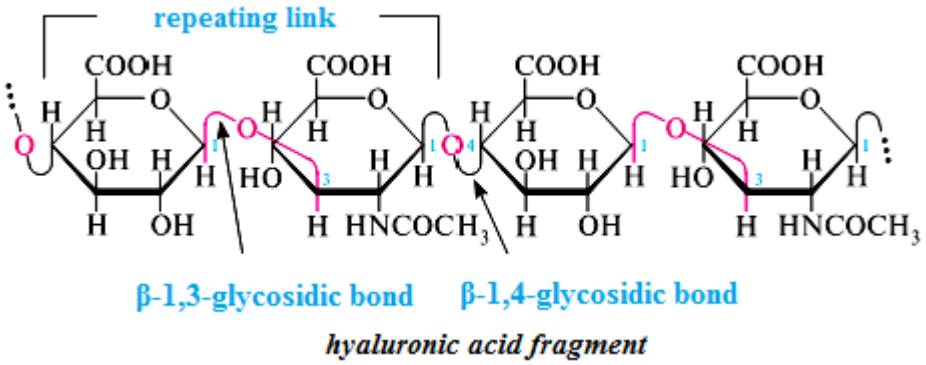
Application: chitin and chitosan, especially chitosan, are used in hair cosmetics, because chitosan is able to form a protective film on the surface of the hair, it also removes the electrical charge. Gives hair shine. Chitosan is non-toxic, used as emulsifiers, film-forming components, has softening, moisturizing, antistatic properties.

HETEROPOLISACCHARIDES

Polysaccharides built from residues of different monosaccharides are called heteropolysaccharides.

Heteropolysaccharides include polysaccharides of connective tissue - chondroitin sulfates, hyaluronic acid, heparin. All of them have a linear carbohydrate chain that is regularly repeated throughout the chain of the disaccharide fragment.

Hyaluronic acid. It is one of the most common polysaccharides of connective tissue. It is contained in cartilage, umbilical cord, joint (synovial) fluid, vitreous body. The repeating unit of hyaluronic acid is D-glucuronic acid and N-acetyl-D-glucosamine, which are connected by a β-1,3-glycosidic bond. Connection between disaccharide fragments - β-1,4:



hyaluronic acid fragment

The molecular weight of hyaluronic acid varies from 1600 to 6400. This polysaccharide has high viscosity, which ensures the impermeability of the connective tissue to bacteria.

In tissues, hyaluronic acid is connected in a complex with protein due to covalent bonds.

Properties: a white powder that is slowly but completely soluble in water, forming a viscous, colorless gel.

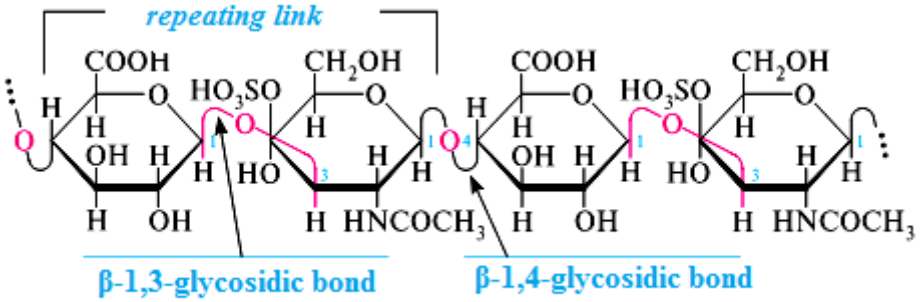
Identification: by functional groups: carboxyl -COOH, hydroxyl -OH, deoxysugar, after hydrolysis - monosugar.

Application: It is perfectly compatible with the skin and never causes irritation or allergic reactions. It has the highest hygroscopicity and retains it even in a dry atmosphere. This valuable quality is used in the treatment of wounds in medicine.

Unlike many biologically active substances, hyaluronic acid shows its valuable qualities at rather low concentrations (0.01-0.1%). It is part of moisturizing creams, lipstick and lip balms, anti-cellulite creams, gels for eyelids. Lotions after tanning, anti-inflammatory lotions, wound-healing and sunscreen lotions.

CHONDROITIN SULFATES- one of the main components of cartilage. They are also found in the skin, tendons, sclera, and bones. The repeating unit of chondroitin sulfates is D-glucuronic acid and N-acetyl-D-galactosamine, which contains a sulfate group. Inside the disaccharide fragment is a β-1,3 bond, and between the fragments - β-1,4. The sulfate group forms an ether bond with the hydroxyl group of N-acetyl-D-galactosamine either in position 4 (chondroitin-4-sulfate) or in position 6 (chondroitin-6-sulfate).

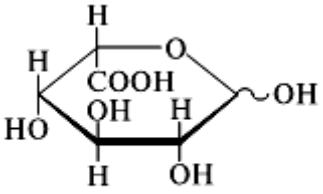
Carbohydrate chains of chondroitin sulfates contain up to 150 disaccharide residues attached in the body by O-glycosidic bonds to hydroxyl groups of amino acid residues included in the protein part of the molecule.



fragment of a chondroitin-4-sulfate molecule

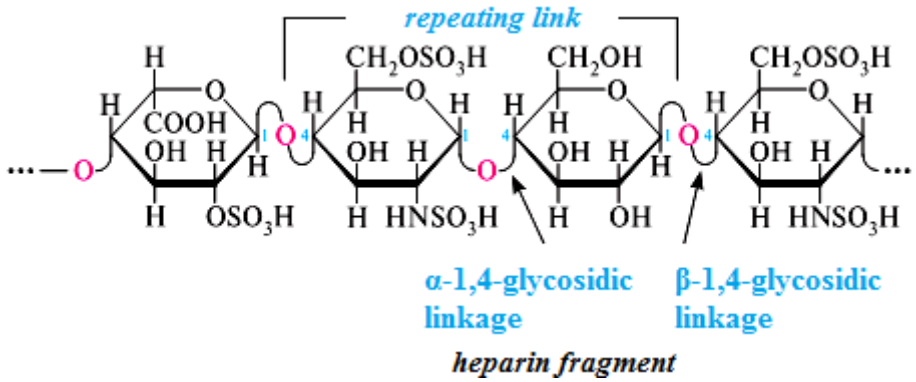
Application: Externally to accelerate the reparative processes in wounds that do not heal for a long time, after injuries and surgical intervention, in trophic ulcers, bedsores.

Heparin. It is produced in the body of humans and animals, it is contained in large quantities in the liver and lungs; in smaller ones - in skeletal muscles, spleen, heart muscle. The periodic link in the structure of heparin consists of D-glucosamine and uronic acid, interconnected by α-1,4-glycosidic bonds. L-iduronic acid and, less often, D-glucuronic acid act as uronic acids.



L-идуроновая кислота

The remains of glucosamine and L-iduronic acid in heparin are partially sulfonated. The molecular weight of heparin is 16,000-20,000. As in hyaluronic acid and chondroitin sulfates, the carbohydrate chains of heparin are connected in tissues with the protein part of the molecule.



heparin fragment

Heparin prevents blood clotting, participates in the exchange of lipids, fats and cholesterol. It is used in medicine as an anticoagulant.

ANTIARRHYTHMIC DRUGS

ANTIARRHYTHMICS are called drugs that normalize heart rhythm disturbances, prevent or eliminate the occurrence of arrhythmias.

Medicines for the pharmacological correction of cardiac arrhythmias are divided into two groups:

I. Means for correction of bradycardia.

1. M-cholinoblockers or the atropine group (atropine sulfate, tincture and dry extract of the beauty, Zelenin drops).
2. Adrenomimetic agents (adrenaline hydrochloride, norepinephrine hydrotartrate, isadrine).
3. Glucagon.

II. Means for correction of tachyarrhythmias:

1. Membrane stabilizers:

a) quinidine, novocainamide, aimalin, ethmosin;

b) lidocaine, trimecaine, difenin;

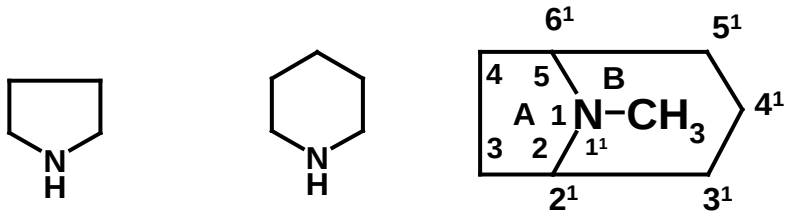
c) etacizin, propafenone, flecainide, etc.

2. Adrenoblockers (anaprilin, atenolol, metoprolol, etc.)
3. Means that slow down repolarization, increase the duration of the action potential, reduce automaticity, increase the effective refractory period (block potassium channels): amiodarone, sotalol, etc.

Blockers of calcium channels (verapamil, halopamil).

Widely distributed in nature. They are found in plants of the nightshade family (Solanaceae), such as belena, belladonna, dahlia, scopolia, etc. (Hyoscyamus niger, Atropa belladonna, Datura stramonium, Scopolia carniolica).

The tropane core is a condensed system consisting of pyrrolidine (A) and piperidine (B).



Pirrolidine Piperidine Tropan

Atropine sulfate (Atropini sulfas, Atropine sulfate)

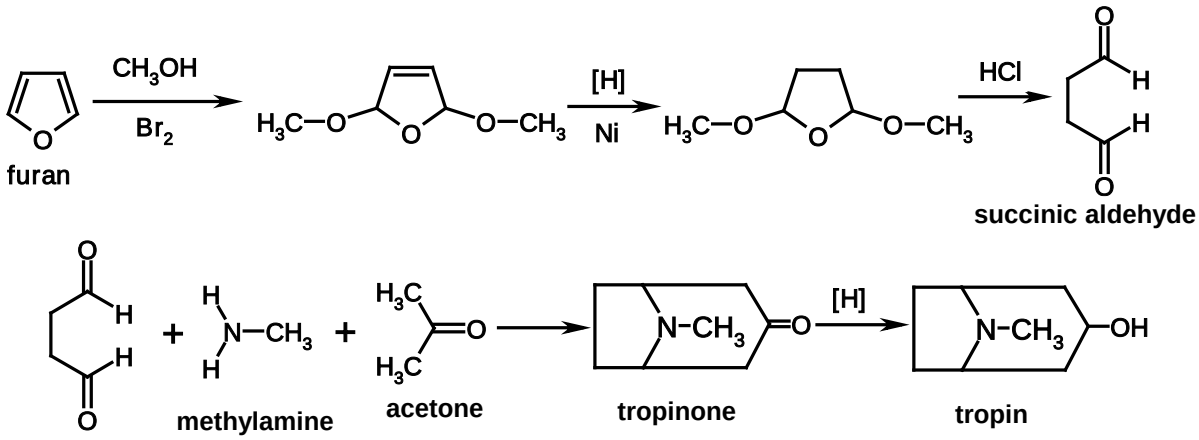
It is a complex ester of d,l (intramolecular racemate)-tropic acid and tropine alcohol.

Receiving. 1). The sources of obtaining these alkaloids are the roots, leaves and seeds of plants of the family nightshades (Solanaceae) - belladonna, dahlia, blekoty. The main alkaloid of this group is atropine, which was first isolated from Belladonna in 1833. However, plants contain only traces of atropine. The main form in which the alkaloid occurs in plants is hyoscyamine (the levorotatory isomer of atropine). Atropine is formed from hyoscyamine as a result of racemization in the process of isolating alkaloids from plants.

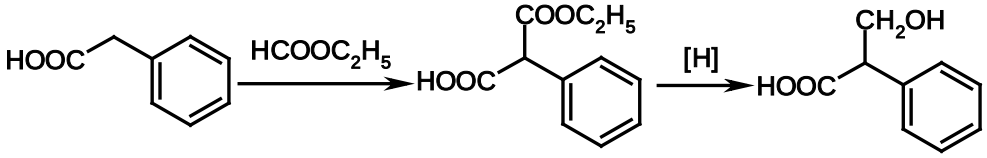
Alkaloids of the atropine group are obtained from belladonna roots and leaves by extraction with water acidified with tartaric acid. The extract is evaporated and diluted with water, while various ballast substances fall out, which, when an organic solvent is added, pass into it. The solution of alkaloids freed from ballast substances is treated with soda or ammonia solution and the bases of alkaloids are extracted with chloroform. The extract is concentrated and heated to 114-116^{o}C. Under these conditions, the levorotatory hyoscyamine is converted to the racemate atropine. In no case should it be allowed to overheat, because in this case apoatropine (atropine anhydride), which does not have a therapeutic effect, may result. Racemization of L-hyoscyamine to atropine can be achieved by treating L-hyoscyamine with alkali. The base of atropine is recrystallized from alcohol with the addition of water.

For the production of atropine, hyoscyamine is also used, which is racemized with an alcoholic solution of NaOH or by heating in a vacuum at T=110-116^{0}C. The resulting atropine base is crystallized from acetone, and then sulfate is obtained.

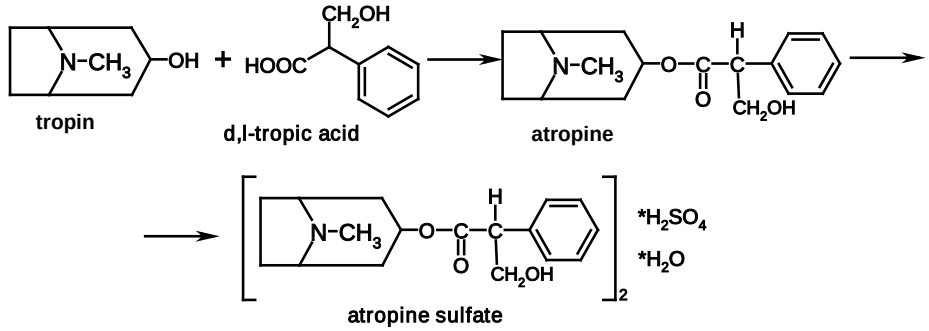
2). Modern industrial synthesis of atropine: The source of obtaining succinic aldehyde is furan, which is successively converted into a dihydro- and then a tetrahydrohydro derivative:



d,l-Tropic acid is obtained by condensation of ethyl formate with phenylacetic acid and subsequent hydrogenation of the obtained ethyl malonate:



Condensation of tropine and d,l-tropic acid:



Properties: white, odorless crystalline powder, easily soluble in water, alcohol, practically insoluble in ether and chloroform.

The optimal pH values at which atropine is stable as an ester are in the range of 3,0-4,0.

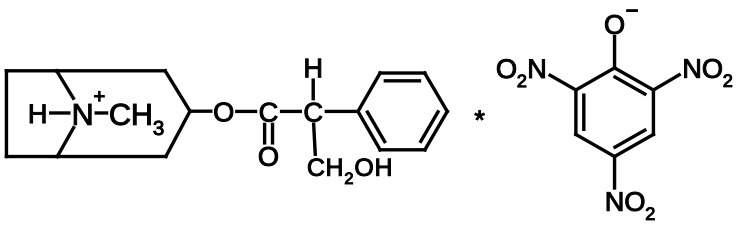
Identification:

Testing of alkaloids, tropane derivatives and their synthetic analogues is carried out using chemical reactions: hydrolysis, nitration, oxidation, detection of anions, neutralization caused by the presence of a tertiary nitrogen atom in molecules, an ester group, a phenyl radical, related inorganic acids, as well as various chemical methods.

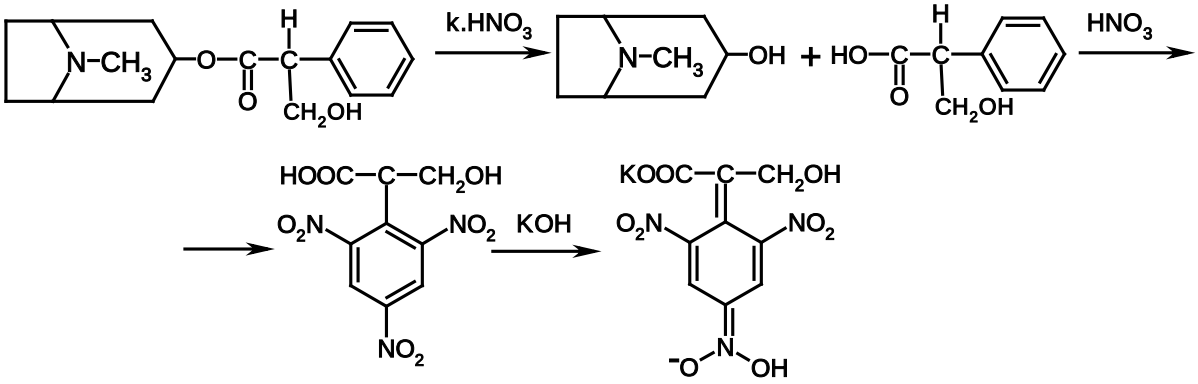
1). The specific rotation should be, because racemate;

2). IR spectroscopy;

3). Picric acid forms a yellow precipitate with a m.p. 174-179^{0}C



4). Vitali-Moren reaction (+HNO3, when heated, + acetone, + KOH in methanol) The reaction is based on their hydrolysis, nitration and oxidation of the acids released (during evaporation with concentrated nitric acid). When acting on the residue after evaporation with an alcoholic solution of potassium hydroxide and acetone, a violet-colored compound of quinoid structure is formed.



The reaction was discovered by Vitali in 1881 and later modified by Moren. Without the addition of acetone, the reaction is less sensitive, but more specific. It should be noted that the reaction involves complex esters, but not acids (tropical, mandelic, etc.).

5). a. On the sulfate ion:

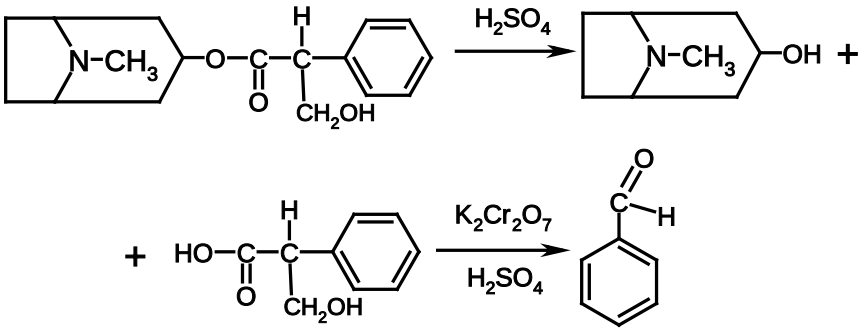
$$SO_4^{2-} + BaCl_2 \rightarrow BaSO_4\downarrow + 2Cl^-$$

b. with 0.05M iodine solution → the yellow color does not disappear, but it becomes discolored if stannous (II) chloride is added dropwise;

6). General alkaloid reagents: Dragendorff's reagent, picric acid, iodine solution, Mark's reagent, etc. With a solution of sulema, a yellow to red precipitate of mercury oxide is formed.

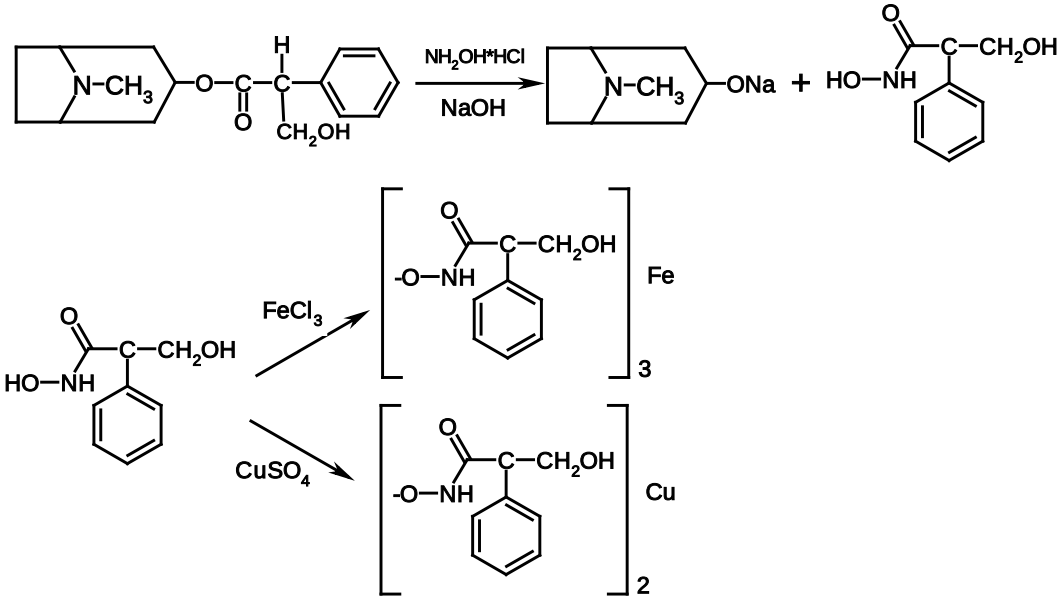
7). With an ammonia solution, a precipitate of atropine base is precipitated from the m.p. 115-1170C.

8). When atropine base is heated with a solution of sulfuric acid in the presence of a potassium dichromate crystal, the smell of bitter almonds is felt due to the formation of benzaldehyde:



benzaldehyde

9). As a complex ether gives a positive hydroxam test: drug + alkaline solution of hydroxylamine hydrochloride $NH_2OH*HCl$; the resulting hydroxamic acid derivative with a solution of $FeCl_3$ or $CuSO_4$ gives colored complexes:



10). UV spectrophotometry.

11). Atropine sulfate, unlike other alkaloids, does not give colored reactions with concentrated sulfuric or nitric acid. However, a solution of p-dimethylaminobenzaldehyde in concentrated sulfuric acid forms a crimson-colored reaction product with it; β-naphthol in the same solvent - green staining and fluorescence; hexamethylenetetramine – pink fluorescence.

12). The GLC method was used to test the authenticity of quantitative determination of tropane derivatives. Qualitative assessment is carried out based on relative retention volumes and Kovach retention indices. An internal standard is used for quantitative determination.

13). Methods of identification and determination of tropane derivatives in medicinal forms have been developed using the HPLC method on the Millichrome liquid chromatograph. A unified methodology based on the use of retention time, capacity factor and other factors is proposed.

Purity:

Extraneous alkaloids and decomposition products: thin-layer chromatography.

Apoatropine (can be obtained by extracting atropine from medicinal herbal raw material at heating more than 116 C): 0.1 is dissolved in 0.01 M HCl solution and the volume is brought up to 100 ml and UV at 245 nm. Absorption rate is just over 4.0. MQS: when adding an ammonia solution to an aqueous solution of the drug, turbidity should not form.

Specific rotation, pH, water, sulfated ash, residual amount of organic solvents.

Quantitative definition:

1. Non-aqueous titration: 0.5 is dissolved in anhydrous acetic acid and titrated potentiometrically with a 0.1M solution of $HClO_4$. Sulfates in anhydrous acetic acid are titrated only to the first degree (that is, dissociates in the medium of a protogenic solvent only to the 1st degree). Fixing the end point of the titration - Potentiometri-tion.

2. Acid-base titration in an alcohol-chloroform medium, because atropine base is strong; by phenolphthalein.

3. Photoelectrocolorimetric regarding the Vitali-Moren reaction, either with picric acid or phospothungstic acid.

Application: has a mydriatic (dilates the pupil) and antispasmodic effect. 0.5-1% solutions are used to dilate the pupil. As an antispasmodic, it is used internally for gastric and duodenal ulcers, cholecystitis, and bronchial asthma. It is also used for poisoning with acetylcholine, carbocholine, morphine, etc.

4. TASKS FOR STUDENT SELF-TRAINING:

4.1. Repeat the theoretical material from organic and analytical chemistry courses on this topic.

4.2. Study the program material on the subject of the lesson according to the questions below.

Educational questions for self-training of students

1. Carbohydrates General characteristics, classification. Distribution in nature. The role of carbohydrates in human life. The concept of deoxy - and amino sugar.
2. Sources of extraction, chemical structure, nomenclature, synonyms of medicinal substances from the group of carbohydrates.
3. To characterize the physicochemical properties of medicinal substances from the group of carbohydrates. Constants of optical activity as indicators of the quality of drugs from the group of carbohydrates.
4. To justify the use of chemical and instrumental methods in the analysis of the quality of medicines from the group of carbohydrates.

5. Oligosaccharides. Classification. Reducing and non-reducing disaccharides. Medicines from the group of oligosaccharides, sources and methods of extraction.

5.1. Sucrose. Structure, nomenclature, properties, application.

5.2. The phenomenon of inversion on the example of sucrose. Determination of impurity of invert sugar in sucrose.

5.3. Identification and methods of quantitative determination of sucrose. Give the corresponding reaction equations, calculation formulas.

5.4. Lactose is anhydrous. Lactose monohydrate. Structure, nomenclature, properties, application.

5.5. Identification and methods of quantitative determination of lactose preparations. Give the corresponding reaction equations, calculation formulas.

6. Polysaccharides. Classification. Homo - and heteropolysaccharides. Medicines from the group of polysaccharides, sources and methods of extraction.

6.1. Starch. Structure, properties, analysis, application.

6.2. Cellulose. Methyl cellulose. Structure, properties, analysis, application.

6.3. Dextrans. Dextran 40 for injections. Polyglukin. Rheopolyglukin. Structure, properties, analysis, application.

6.4. Inulin. Structure, properties, application.

6.5. Hyaluronic acid. Chondroitin sulfate. Structure, properties, analysis, application.

6.6. Heparin. Calcium heparin. Sodium heparin. - Structure, properties, analysis, application.

7. Antiarrhythmic drugs. General characteristics, pharmacological classification.

8. To characterize the physicochemical properties, sources and methods of obtaining drugs from the group of antiarrhythmic drugs.

9. To justify the use of chemical and instrumental methods in the analysis of the quality of antiarrhythmic drugs.

10. Chemical methods of identification of antiarrhythmic drugs. Principles of analysis, reagents used, performance technique and effects of reactions.

11. Methods of quantitative determination of antiarrhythmic drugs.

12. The relationship between the structure and biological action of a number of antiarrhythmic drugs.

13. Atropine sulfate. Structure, nomenclature, obtaining, properties, analysis, application. Determination of apoatropine admixture in atropine sulfate.

14. Quinidine sulfate. Structure, nomenclature, properties, analysis, application.

15. Novocainamide. Structure, properties, analysis, application.

16. Potassium chloride. Obtaining, properties, analysis, application. Determination of impurities of bromides, iodides, barium. Ways of entering the mentioned impuryities into the drug.

17. Amiodarone. Structure, nomenclature, properties, analysis, application.
18. Features of storage of the named group of drugs. Mechanism of action.

4.3. Work out test tasks

1. The chemical structure of sucrose is:
- **A.** Aldohexose
- **B.** Monosaccharide
- **C.** Disaccharide
- **D.** Polysaccharide
- **E.** Ketohexose

2. Indicate which specific impurity in sucrose is determined by reaction with Fehling's reagent:
- **A.** Copper(II) salts
- **B.** Dextrins
- **C.** Ferrum (III) salts
- **D.** Soluble starch
- **E.** Invert sugar

3. According to the chemical structure, starch is:
- **A.** Polysaccharide
- **B.** Monosaccharide
- **C.** Disaccharide
- **D.** Ketohexose
- **E.** Aldohexose

4. Specify the medicinal substance, in the production scheme of which the main stage is the fermentation of sucrose by Leuconostoc mesenteroides bacteria:
- **A.** Low molecular weight heparins
- **B.** Dextran 40 for injections
- **C.** Glucose monohydrate
- **D.** Lactose is anhydrous
- **E.** Methyl cellulose

5. To distinguish between sucrose and anhydrous lactose in pharmaceutical analysis, a reaction with:
- **A.** A solution of bismuth iodide in potassium iodide
- **B.** Ammonium solution of silver nitrate
- **C.** Saturated sodium carbonate solution
- **D.** Sodium hydroxide solution
- **E.** Hydrochloric acid

6. Indicate which of the listed carbohydrates is an intermediate product of starch hydrolysis:

A. Lactose
B. Sucrose
C. Maltose
D. *D*- Galactose
E. *D*-Fructose

7. Indicate which of the listed features is characteristic of non-reducing disaccharides:

A.The reaction with Fehling's reagent gives a positive result
B.The phenomenon of mutarotation is observed in freshly prepared solutions
C.Capable of cyclo-oxo-tautomerism
D.There is no free hemiacetal hydroxyl in the structure
E.The reaction with an ammonia solution of silver nitrate gives a positive result

8. Indicate the correct statement about lactose anhydrous:

A.Easily soluble in water and chloroform
B.Does not interact with Fehling's reagent
C.Aqueous solutions do not mutate
D.Has low hygroscopicity
E.It is a heteropolysaccharide in structure

9. Indicate which of the following carbohydrates is an oligosaccharide according to its chemical structure:

A. Dextrose
B. Galactose
C. Fructose
D. Starch
E. Lactose

10. Indicate which of the medicinal substances is a white crystalline powder without odor, weak sweet taste, easily soluble in water:

A. Lactose monohydrate
B. Methyl cellulose
C. Starch
D. Sucrose
E. Glucose is anhydrous

11. A non-reducing disaccharide is:

A. Maltose
B. Starch
C. Lactose
D. Fructose

E. Sucrose

12. Amylopectin is a starch fraction that:

A. It dissolves well in water

B.It forms a blue complex with iodine

C.Contains branched polymer chains

D. During hydrolysis, it forms a mixture of D-glucose and D-galactose

E.Has a heteropolysaccharide character

13. Name the disaccharide, the molecule of which is formed by the residues of D-glucose and D-galactose:

A. Cellulose

B. Sucrose

C. Lactose

D. Starch

E. Maltose

14. Specify the name of complex carbohydrates that form from two to ten molecules of monosaccharides during hydrolysis:

A. Polysaccharides

B. Oligosaccharides

C. Aldohexoses

D. Ketohexoses

E. Monos

15. The restoring disaccharide is:

A. Sucrose

B. Cellulose

C. Lactose

D. Fructose

E. Starch

16. Plasma substitutes "Polyglukin" and "Reopolyglukin" are obtained by partial hydrolysis and fractionation:

A. Terpenes

B. Proteins

C. Dextrans

D. Heparins

E. Pectins

17. The chemical structure of a heteropolysaccharide is:

A. Dextran 40 for injections

B. Lactose monohydrate

C. Sucrose

D. Chondroitin sulfate

E. Starch

18. The chemical structure of homopolysaccharide is:

A. Lactose monohydrate

B. Sucrose

C. Starch

D. Low molecular weight heparin

E. Chondroitin sulfate

19. The products of incomplete hydrolysis of starch are:

A. Heparins

B. Pectins

C. Ketohexoses

D. Terpenes

E. Dextrins

20. The specialist of the pharmaceutical enterprise needs to confirm the presence of anhydrous lactose as an auxiliary substance in the manufactured tablets. For this he should use:

A. Conc. sulfuric acid

B. Ammonia solution

C. Sodium hydroxide

D. Barium chloride

E. Fehling's reagent

21. Indicate which of the medicinal substances is a white crystalline powder without odor, sweet taste, easily soluble in water, does not reduce Fehling's reagent:

A. Glucose is anhydrous

B. Sucrose

C. Lactose monohydrate

D. Methyl cellulose

E. Starch

22. Name the disaccharide, the molecule of which is formed by the residues of D-glucose and D-fructose:

A. Cellulose

B. Starch

C. Sucrose

D. Lactose

E. Maltose

23. Sucrose is characterized by the phenomenon of inversion. Inversion is a process that is accompanied by:

A.The flow of the ion exchange reaction between various carbohydrates and water

B.Change over time in the angle of rotation of freshly prepared carbohydrate solutions

C.Decomposition of complex carbohydrates into simpler components

D.Combining simple carbohydrate molecules into more complex ones

E.A change over time not only of the angle, but also of the sign of rotation as a result of the hydrolysis of carbohydrates

24. Indicate which monosaccharide is the final product of starch hydrolysis:

A. *D*- Mannose

B. *D*-Xylose

C. *D*- Galactose

D. *D*-Glucose

E. *D*-Fructose

25. Indicate the medicinal product, the complete hydrolysis of which produces D-glucosamine, as well as D-glucuronic, L-iduronic, acetic and sulfuric acids:

A. Methyl cellulose

B. Sodium heparin

C. Polyglukin

D. Dextran 40 for injections

E. Lactose monohydrate

26. Indicate the name of polysaccharides of bacterial origin, built from α-D-glucopyranose residues, which are connected to each other mainly by 1,6-glycosidic bonds:

A. Heparins

B. Terpenes

C. Pectins

D. Dextrans

E. Oligosaccharides

27. Specify the name of complex carbohydrates that form more than 10 monosaccharide molecules during hydrolysis:

A. Ketohexoses

B. Oligosaccharides

C. Monos

D. Aldohexoses

E. Polysaccharides

28. Indicate which of the carbohydrates does not give a positive result when identified with Fehling's reagent:

A. Fructose

B. Glucose is anhydrous

C. Glucose monohydrate

D. Sucrose
E. Lactose

29. Indicate which of the medicinal substances is a white, yellowish-white or grayish-white powder, soluble in cold water with the formation of a colloidal solution, but practically insoluble in hot water:
A. Lactose monohydrate
B. Methyl cellulose
C. Starch
D. Glucose is anhydrous
E. Sucrose

30. Specify the disaccharide in the structure of which the glycosidic bond is formed due to hemiacetal hydroxyls of both monosaccharide units:
A. Lactose is anhydrous
B. Sucrose
C. Maltose
D. Lactose monohydrate
E. Fructose

31. Medicinal substance "Calcium heparin" is obtained:
A. From livestock processing products
B.From plant material (spotted milk thistle)
C.By chemical synthesis (based on n-heptane)
D.Through microbiological synthesis
E.From natural minerals (sylvinite)

32. For the treatment of joint diseases, a substance from the group of polysaccharides, the repeating link of which is formed by D-glucuronic acid and N-acetyl-D-galactosamine containing sulfo groups, is widely used. Enter the name of this substance:
A. Chondroitin sulfate
B. Dextran 40 for injections
C. Starch
D. Methyl cellulose
E. Low molecular weight heparin

33. Amylose is a fraction of starch that:
A.Practically insoluble in water
B.It forms a blue complex with iodine
C.Has a heteropolysaccharide character
D.Contains branched polymer chains
E.During hydrolysis, it forms a mixture of D-glucose and D-galactose

34. Indicate which of the medicinal substances is a white amorphous powder without odor and taste, insoluble in cold water and forms a colloidal solution in hot water:

A. Methyl cellulose
B. Lactose monohydrate
C. Starch
D. Glucose is anhydrous
E. Sucrose

35. Which method of mineralization should be chosen to convert covalently bound iodine into molecular iodine in amiodarone?

A. Reduction mineralization
B. Alkaline hydrolysis
C. Acid hydrolysis
D. Roasting with a mixture of potassium nitrate and sodium carbonate
E. Oxidizing mineralization

36. What identification reaction should be performed to determine the iodide ion obtained after alkaline hydrolysis of amiodarone?

A. With a solution of ferrum (III) chloride
B. With sodium nitrate solution
C. With calcium chloride solution
D. With a solution of ferrum (II) sulfate
E. With potassium chloride solution

37. Indicate which method is used according to the **SPU** for the quantitative determination of amiodarone (2-butyl-3-benzofuranyl-4(2-diethylaminoethoxy)-3,5-diiodophenyl ketone hydrochloride)?

A. Alkalimetry
B. Acidimetry
C. Complexonometry
D. Cerimetry
E. Iodometry

38. The Kjeldahl method is used for the quantitative determination of nitrogen in procainamide (novocainamide). For this purpose, the drug is mineralized:

A. A dilute alkali solution
B. Concentrated sulfuric acid
C. Dilute hydrochloric acid
D. A dilute solution of ammonia
E. With saturated sodium chloride solution

39. What method is used to quantitatively determine procainamide, the structure of which contains a primary aromatic amino group?

A. Complexonometry
B. Nitritometry
C. Permanganatometry
D. Cerimetry
E. Acidometry

40. Quantitative determination of procainamide (novocainamide) is carried out by the nitritometry method. Name which environment you need to create:
A. Alkaline
B. Non-aqueous
C. Neutral
D. Ammonia
E. Sour

41. Indicate which heterocyclic systems are the basis of the structure of tropane alkaloids:
A. Pyridine and pyrazole
B. Pyrrolizidine and imidazole
C. Piperidine and furan
D. Pyrrolidine and piperidine
E. Isoquinoline and pyrrole

42. According to the SPU, fuming nitric acid, acetone and an alcoholic solution of potassium hydroxide are used to identify atropine sulfate. These reagents are used to detect:
A. Remainder of tropic acid
B. Remainder of tropin
C. Sulfate ions
D. Crystallization water
E. Phenolic hydroxyl

43. According to the requirements of the SPU, apoatropin in atropine sulfate is defined as:
A. Interaction with concentrated ammonia solution
B. According to the turbidity of the solution of the substance in chloroform
C. Interaction with concentrated sulfuric acid
D. By the method of thin-layer ascending chromatography
E. By measuring the optical density of the solution and subsequent calculation of the specific absorption index

44. The pharmacist-analyst of the control-analytical laboratory determines the quantitative content of the substance atropine sulfate in accordance with the requirements of the SPU by the method of acid-base titration in non-aqueous media. As a titrated solution, he uses a solution:

A. Chloric acid
B. Sodium hydroxide
C. Sodium methylate
D. Hydrochloric acids
E. Sodium nitrite

45. To identify drugs from the group of alkaloids, tropane derivatives, the Vitali-Morena reaction is used. At the same time, the preparations, after decomposition with nitric acid, are treated with an alcoholic solution of potassium hydroxide in the presence of acetone. The visual effect of this reaction is:
A. The color of the solution is purple
B. Release of gas bubbles
C. The color of the solution is green
D. Fallout of black sediment
E. Precipitation of a white precipitate

46. Specify the characteristic pharmacological action of quinidine sulfate:
A. Antiarrhythmic
B. choleretic
C. Antimalarial
D. Vasodilator
E. Spasmolytic

47. Specify the medicinal product, which is a quinoline derivative according to its chemical structure:
A. Papaverine hydrochloride
B. Akrichin
C. Bigumal
D. Chloridine
E. Quinidine sulfate

48. State the specific reaction used to identify quinidine:
A. Vitaly-Moren's reaction
B. Formation of murexide
C. Thalleiochin test
D. Period formation
E. Picrate formation

49. One of the following methods cannot be used for the quantitative determination of quinidine sulfate. Specify it:
A. Acid-base titration in a two-phase environment
B. Bromatometry
C. Gravimetry
D. Method of acid-base titration in non-aqueous solvents

E. Complexonometry

50. Indicate which heterocyclic systems are part of the quinidine sulfate molecule:

A. Pyridine, piperidine

B. Pyrrolizidine, quinoline

C. Isoquinoline, quinuclidine

D. Pyridine, quinuclidine

E. Quinoline, quinuclidine

51. One of the methods of quantitative determination of quinidine salts involves preliminary precipitation of the quinidine base with sodium hydroxide. Such a procedure is necessary when determining this drug by the method:

A. Acidimetry in a non-aqueous medium

B. Acidimetry in an aqueous environment

C. Alkalimetry

D. Polarimetry

E. Gravimetry

52. The control and analytical laboratory received the substance quinidine sulfate. This medicinal substance can be identified by its formation:

A. Talleiokhina

B. Murexida

C. Iodoform

D. Ferrum (III) hydroxamate

E. Thiochrome

53. The appearance of an emerald-green color when adding bromine water and ammonia solution to the solution of the medicinal substance allows you to identify:

A. Codeine phosphate

B. Quinidine sulfate

C. Caffeine monohydrate

D. Atropine sulfate

E. Pilocarpine hydrochloride

54. A dosage form containing potassium chloride was submitted for analysis. Which reagent can be used to determine the potassium ion in potassium chloride?

A. Tartaric acid

B. Oxalic acid

C. Citric acid

D. Acetic acid

E. Butyric acid

55. Which of the medicinal substances with tartaric acid in the presence of sodium acetate forms a white precipitate, soluble in alkalis and mineral acids?

A. Potassium chloride
B. Sodium chloride
C. Lithium carbonate
D. Sodium iodide
E. Sodium bromide

56. Potassium chloride is identified by the potassium ion by the reaction with:
A. Sodium cobaltinitrite
B. Zincuranyl acetate
C. Silver nitrate
D. Sodium hydroxide
E. Potassium ferricyanide

57. The pharmacopoeial reaction for the identification of potassium ions is the interaction with tartaric acid, as a result of which a precipitate of what color is formed:
A. White
B. Black
C. Gray
D. Blue
E. Green

58. Potassium salts introduced into the colorless flame of a gas burner paint it in color:
A. Violet
B. Red
C. Brick
D. Yellow
E. Green

59. What method is recommended by the SPU for the quantitative determination of the potassium chloride substance?
A. Argentometry
B. Complexonometry
C. Bromatometry
D. Polarimetry
E. Iodometry

60. When carrying out the quantitative determination of potassium chloride by the argentometric method (back titration) according to the SPU, the indicator is used:
A. Ferrum (III) ammonium sulfate
B. Diphenylcarbazone
C. Potassium chromate

D. Phenolphthalein
E. Sodium eosinate

4.4. Situational tasks:

1 Describe the properties of drugs from the carbohydrate group based on their structure.

2 Explain how optical activity constants are used in the quality analysis of drugs from the carbohydrate group.

3 Explain the phenomenon of inversion using the example of sucrose. What is called "invert sugar"? Explain how the presence of an admixture of invert sugar in sucrose is determined.

4 On the example of sucrose and anhydrous lactose, explain the difference between reducing and non-reducing disaccharides.

5 Explain the origin and justify the methods for detecting the specific admixture of invert sugar in the sucrose substance.

6. Suggest ways to convert the covalently bound halogen (iodine) in amiodarone into an ionogenic state.

7. What is the role of alcohol in alkalimetric titration of amiodarone?

8. What argentometric methods can be used to quantitatively determine potassium chloride? Describe the titration conditions and give the corresponding reaction equations.

9. How does apoatropine admixture get into atropine when it is obtained from plant raw materials?

10. Name the differences in the structure of hyoscyamine and atropine, and the peculiarities of the use of the drugs due to this.

11. Specify the method and justify the conditions for quantitative determination of quinidine, taking into account the presence of a double bond in its structure? Write chemistry.

12. Give evidence of the structure of quinidine (the presence of a quinoline cycle, a double bond, a hydroxyl group, a methoxy group), as well as evidence that quinidine contains tertiary nitrogen atoms and is a base.

13. Explain the need to conduct a control experiment when applying the acid-base titration method in the environment of non-aqueous solvents.

14. Calculate the conversion factors for the quantitative determination of quinidine sulfate by weight method.

4.5. Tasks:

1 During chromatography of solutions of anhydrous glucose and anhydrous lactose, the distances from the starting line to the center of the spot of each of the substances were obtained, which were 4.6 cm and 2.3 cm, respectively. At the same time, the distance from the starting line to the front line of the solvent is 10.0 cm. Determine the Rf for each of the carbohydrates.

2 During the chromatography of solutions of fructose and sucrose, the distances from the starting line to the center of the spot of each of the substances were obtained, which were 6.0 cm and 4.3 cm, respectively. At the same time, the distance from the starting line to the front line of the solvent is 12.0 cm. Determine the Rf for each of the carbohydrates.

3 Determine the concentration of the lactose solution, if the angle of rotation for this solution is + 4.12°, the thickness of the layer is 10 cm, and the specific rotation of lactose is +52.5°.

4 Determine the specific rotation of 10% lactose, if the angle of rotation of its aqueous solution, which is measured in a cuvette with a length of 100 mm, is equal to + 5.20°.

5 Calculate what volume of 0.1 M sodium thiosulfate solution (Kp = 1.0000) was spent on the titration of 0.1063 g of lactose (M.m. 360.32), if 19.24 ml of titrant was spent in the control experiment, and the content of the active substance in the substance was 98.84%.

6 Write the reaction equation, calculate the gravimetric factor and the percentage content of quinidine sulfate (M.m. 746.92) in the preparation when determined by the gravimetric method, if it is known that M.m. quinidine base - 324.42, mass of

weighing - 0.4793, mass of weight form - 0.3986 g, loss in mass during drying - 3.8%.

7 Calculate the volume of 0.1 M sodium hydroxide solution (Kp = 1.0000), which is spent on the titration of 0.5018 g of quinidine sulfate (M.m. 746.92), if the content of the active substance in the preparation is 99.2%, and the loss in mass during drying is 4.6%.

8 Calculate the weight of the quinidine sulfate sample (M.m. 746.92), if 12.42 ml of 0.1 M sodium hydroxide solution (Kp = 0.9886) was spent on its titration, and the content of the active substance in the preparation is 99.40% .

9 Calculate the percentage content of atropine sulfate (M.m. 676.8) in the preparation, if the weight of the test piece is 0.4983 g, the volume of a 0.1 M perchloric acid solution (Kp = 0.9892) in the working experiment is 7.42 ml, in the control - 0.21 ml, and the loss in mass during drying - 2.3%.

10 Calculate the weight of atropine sulfate (M.m. 676.8) in the medicinal product, if 6.62 ml of 0.1 M perchloric acid solution (Kp = 0.9982) was spent on the titration. The content of the active substance in the preparation is 98.84%.

11 Determine the mass fraction of atropine sulfate (M.m. 676.8) in the medicinal product, if 7.42 ml of 0.1 M perchloric acid solution (Kp = 0.9892) was spent on the titration of the weight (m = 0.4983 g) .

5. LABORATORY WORK

During laboratory work it is necessary to strictly follow the safety rules in the chemical laboratory.

Each student individually carries out reactions of identification of samples of drug substances under the instruction of the teacher and draws up the test report.

AN EXAMPLE OF FILLING IN THE PROTOCOL IS PRESENTED BELOW:

POTASSIUM CHLORIDE (KALII CHLORIDE, POTASSIUM CHLORIDE)

KCI M.m. 74.6

Potassium chloride contains not less than 99.0% and not more than 100.5% KCI, calculated on a dry basis.

Properties. Description.White crystalline powder or colorless crystals.

Solubility.Easily soluble in water R, almost insoluble in ethanol R.

Identification Solution S. 4.0 g of the substance is dissolved in water free from carbon dioxide, prepared from distilled water R, and the volume of the solution is brought to 40 ml with the same solvent

A.The substance reacts to chlorides (2.3.1). 2-3 drops of nitric acid and 2-3 drops of silver nitrate solution are added to 2 ml of solution S. A white precipitate falls out.

B.To 2 ml of solution S, add 1 ml of tartaric acid solution, 1 ml of sodium acetate solution, shake, cool in ice water. A white precipitate forms.

C. 1 ml of acetic acid and 1 ml of freshly prepared sodium cobaltinitrite solution are added to 2 ml of solution S. A yellow precipitate is formed.

Purity test

Transparency of the solution(2.2.1).Solution S should be clear.

The color of the solution(2.2.2, method II). Solution S should be colorless.

Acidity or alkalinity.0.05 ml (1 drop) of bromothymol blue P1 solution is added to 20 ml of solution S; the color of the solution should change when no more than 0.25 ml (5 drops) of 0.01 M hydrochloric acid solution or 0.01 M sodium hydroxide solution is added.

Sulfates (2.4.13).5 ml of solution S is brought to a volume of 15 ml with distilled water R. The resulting solution must withstand the test for sulfates.

Barium.To 5 ml of solution S, add 5 ml of distilled water P and 1 ml of diluted sulfuric acid R. After 15 minutes, the opalescence of the resulting solution should not exceed the opalescence of a mixture of 5 ml of solution S and 6 ml of distilled water R.

Quantitative definition

1.0.05 g of the substance is dissolved in 20 ml of water R, 3 ml of diluted nitric acid R, 15.0 ml of 0.1 M silver nitrate solution and 1 ml of chloroform are added. The resulting solution is shaken and titrated with a 0.1 M solution of ammonium

thiocyanate, using 1 ml of ferrum (III) ammonium sulfate solution (ferroammonium alum) as an indicator, intensively shaking until the end point of the titration.

1 ml of 0.1 M silver nitrate solution corresponds to 7.46 mg of KSI.

2. Dissolve 0.05 g of the substance in 20 ml of water R, add 2-3 drops of potassium chromate (indicator) and titrate with a 0.1 M solution of silver nitrate to an orange-yellow color.

Titrate with a pipette!

1 ml of 0.1 M silver nitrate solution corresponds to 7.46 mg of potassium chloride.

LESSON No.3

1. SUBJECT: Analysis of cardiotonic drugs. Cardiac glycosides.

2. PURPOSE: Master the methods of analysis of cardiotonic drugs and their synthetic analogues.

3. OBJECTIVES:

3.1. To study the structure, nomenclature, synonyms, physicochemical properties, sources and methods of obtaining cardiotonic drugs.

3.2. To study the methods of analysis of the considered group of medicinal products according to the SPU, QCM.

3.3. Propose and justify possible methods of identification and quantification, based on the structure of drugs of the studied group.

3.4. To study specific impurities, as well as testing methods for the purity of this group of substances.

3.5. To consider the peculiarities of the analysis of cardiotonic drugs using physical, physicochemical and chemical methods.

3.6. To learn how to analyze the quality of the considered group of medicines using physical, physico-chemical and chemical methods.

3.7. Interpret and give a correct assessment of the received analysis results, draw a conclusion about the quality of the analyzed substances.

3.8. Explain the features of storage of cardiotonic drugs based on their physical and chemical properties.

3.9. Learn and follow the rules of safe work in a chemical laboratory.

CARDIOTONIC MEDICINES called drugs that increase the contractile activity of the myocardium and eliminate the symptoms of heart failure. Cardiac glycosides are most widely used in the treatment of heart failure. These are preparations of digitalis, strophanthus, etc. The mechanism of action of cardiac glycosides is related to the effect on the electrolyte balance in the myocardium.

The inotropic effect (strengthening of heart contractions) of these drugs is based on their ability to increase the content of calcium ions in cardiomyocytes. The level of free calcium in the cell determines the contractility of the heart muscle. Calcium binds the modulator protein troponin in the cell, which at the same time changes its spatial configuration and releases the contractile proteins actin and myosin with the formation of actomyosin. This process is accompanied by the contraction of muscle fibers. With heart failure, the rhythmic change in the content of free calcium in the cytoplasm of the cell proceeds sluggishly, the peak increase

of this indicator is not clear, which leads to weakening and disorientation of heart contractions.

Cardiotonic drugs enhance the penetration of calcium ions into cardiomyocytes from the extracellular fluid, and also contribute to its release from the sarcoplasmic reticulum (the sarcoplasmic reticulum is an organelle that captures calcium ions from the cytosol).

Glycosides- complex glycides (carbohydrates) containing organic substances, of plant (rarely animal) origin, the molecules of which consist of a sugary part (glycone) and a non-sugary part (aglycone or genin), or a group of organic compounds, derivatives of monosaccharides, in which hemiacetal hydroxyl substitutted for any functional group.

Classification of glycosides

There are several classifications:

- by pharmacological action;
- botanical classification;
- by the nature of the element that connects sugary and non-sugary parts;
- by the sugary part;
- chemical classification.

Botanical classification:

1. digitalis glycosides [Red digitalis (Digitalis purpurea); Digitalis lanata (Digitalis lanata); Rusty digitalis (Digitalis ferruginae); Ciliated digitalis (Digitalis ciliata);];
2. lily of the valley glycosides;
3. Glycosides of the Greek knotweed;
4. Moringa glycosides;
5. oleander glycosides;
6. strophant glycosides;
7. glycosides of long-fruited jute;
8. yellow sedum and in plants of other families: seven. Cruciferae; family Kutrevykh (Apocynaceae); family Norichnikov (Scrophu-lariaceae) and others.

Chemical classification (O-glycosides, as the most used):

1. phenylglycosides (aglycon – phenyl radical; arbutin – toloknyanki glycoside, salicin);
2. anthraquinone glycosides (aglycon - anthraquinone, for example: chrysophanic acid, frantulaemodin, sennoside, aloeemodin, etc. These are glycosides of shingles, rhubarb, aloe);
3. flavonglycosides (aglycon - derivatives of flavans, for example: rutin, catechin, etc.);
4. nitrogen-containing O-glycosides (cyanoform, for example amygdalin);

5. glycoalkaloids (solasodin, diosgenin);

6. steroid or cardiac glycosides (aglycon - hexadecahydrocyclopenta [a] phenanthrene, digitoxin, strophanthin, etc.);

7. tannins (aglycon - gallic acid, ellagic acid, stilbene derivatives, tannin);

8. saponins (aglycon - sapogenin and terpene derivatives).

The most important of all glycosides are cardiac glycosides is a group of biologically active substances of natural origin that have a specific effect on the heart muscle, while their effect is manifested in relatively small doses.

By their structure, glycosides are simple esters of cyclic forms of sugars, where the sugar part is connected to the aglycon of the steroid structure through the semi-ketal hydroxyl of the glycone and the alcohol hydroxyl of the aglycon. They are also called full acetals.

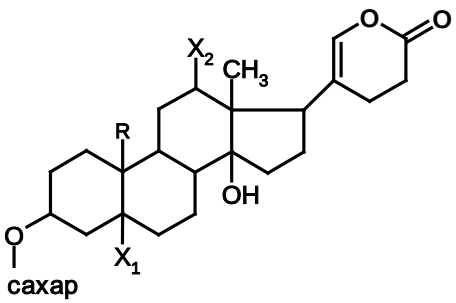
According to the chemical structure, the aglycon is a steroid structure of cyclopentaneperhydrophenanthrene, and depending on the substituent in the 17th position, cardiac glycosides are divided into:

• cardenolides - have a 5-membered lactone ring in the 17th position;

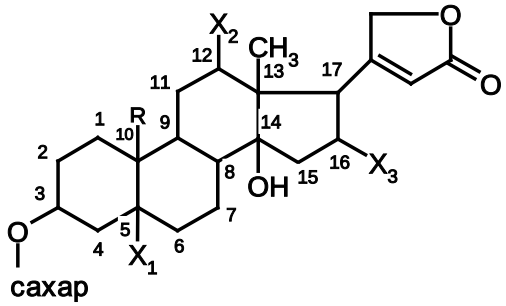
• bufadienolides - have a 6-membered lactone ring in the 17th position.

And depending on the nature of the substituent in the 10th position, cardenolides are divided into the digitalis subgroup (at C10 they contain $-CH_3$) and the strophant subgroup (at C10 they contain $-C(=O)H$). Due to their high toxicity, bufadienolides are not used in medicine.

Based on the above, it is possible to present the general formula of the structure of cardiac glycosides:



Bufadienolides



Cardenolides

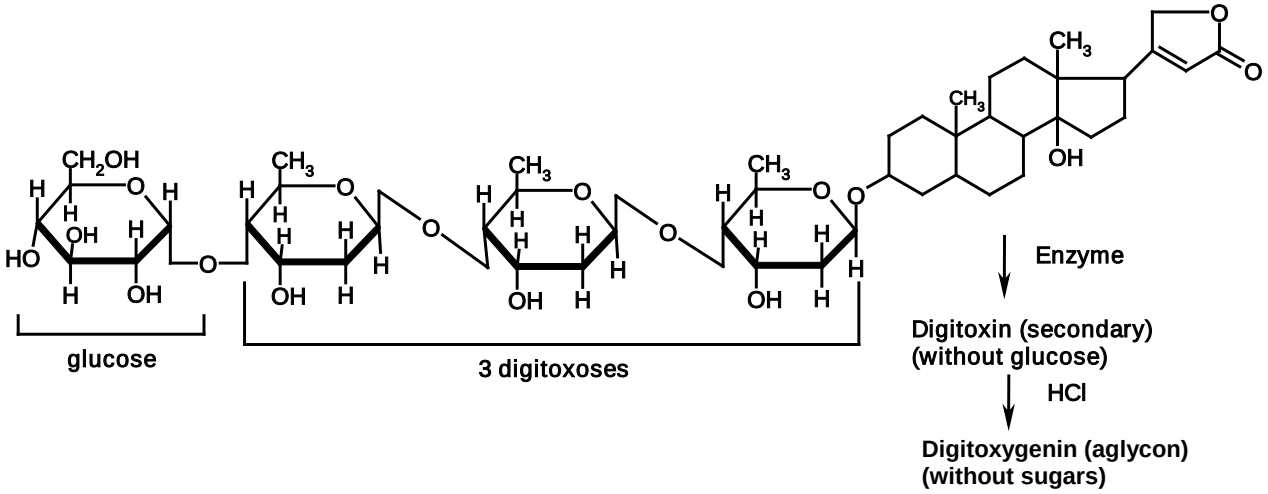
The specific effect of the glycoside on the heart is due to the presence in the structure of the aglycon of the lactone cycle at position 17 and hydroxyl at position 14, and the substituent at position 10 has a great influence on the cardiotonic effect: it is either $-CH_3$ or $-C(=O)H$, or $-CH_2OH$ (ouabain - strophanthin U).

There are also natural glycosides (primary, genins) and secondary ones, which were formed from primary ones and contain 1 or 2 less sugars than primary ones.

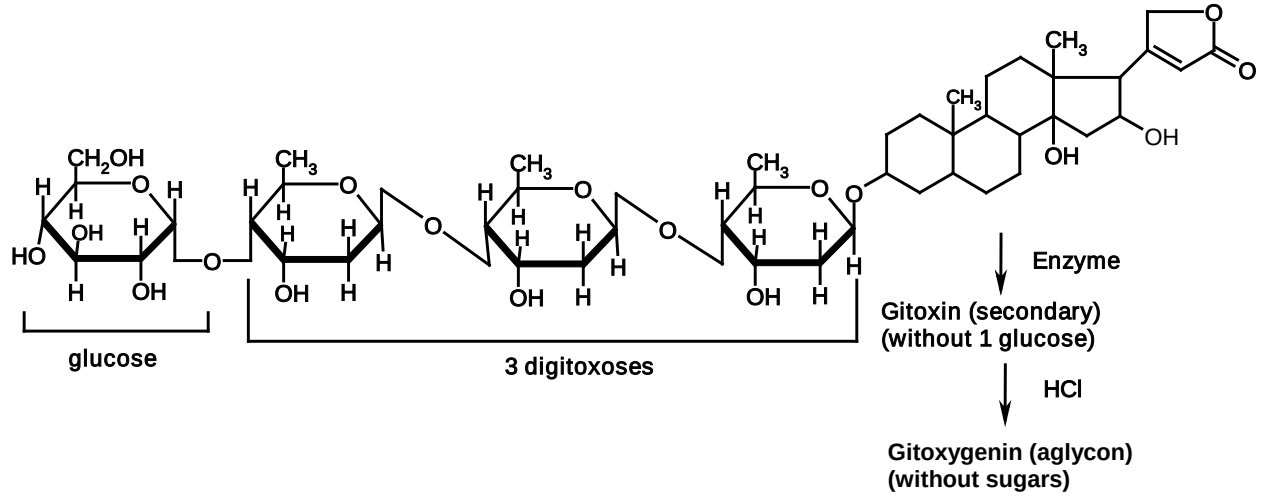
For example, consider the glycosides of digitalis purpurea.

The primary glycosides of digitalis purple are: purpureaglycoside A and purpureaglycoside B. They differ from each other in the number of hydroxyl groups.

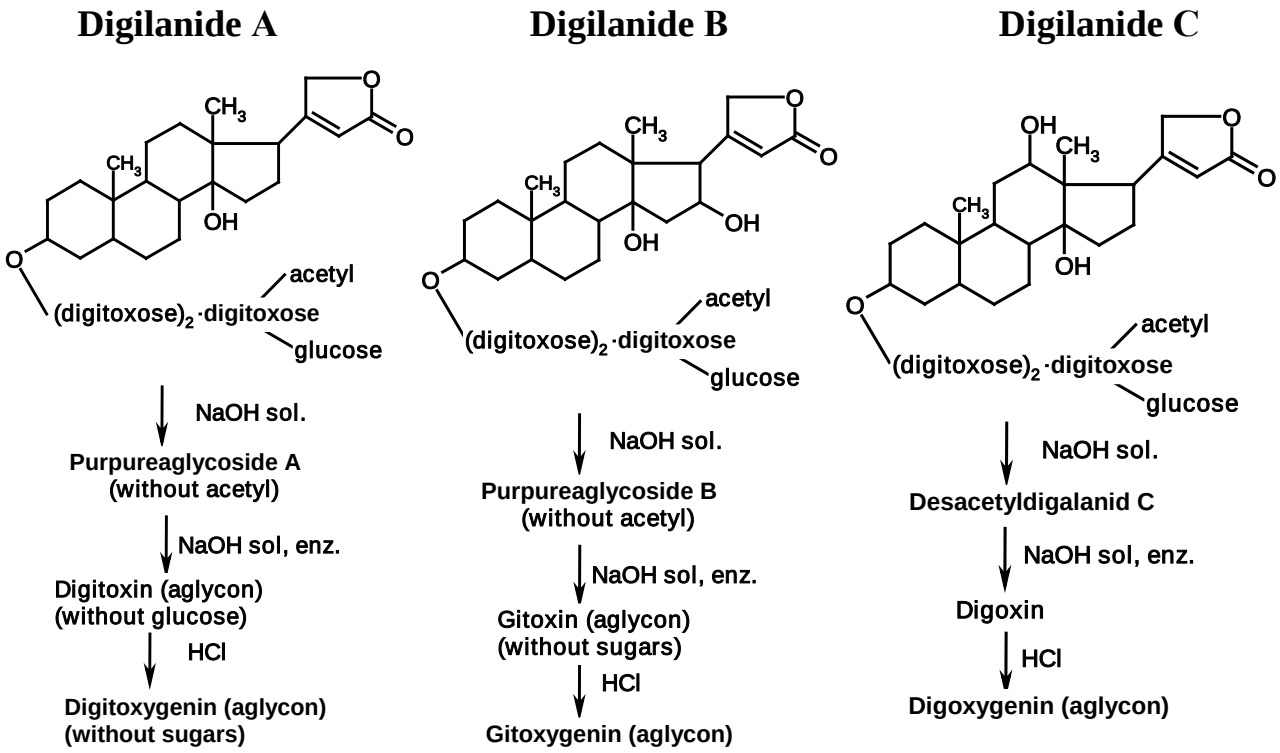
Purpureaglycoside A



Purpureaglycoside B



The primary glycosides of digitalis woolly are: digilanides (lactosides) A, B, C, which differ from each other by a different number of hydroxyl groups, and from glycosides of digitalis purpurea by the presence of 1 acetylated sugar (digitoxose).



As you can see, glycosides, like cyclic acetals, are easily split into their respective parts under the action of acids and enzymes.

Enzymes (or enzymes) act selectively and allow stepwise cleavage of sugar. Enzymes are often found in the same facilities as the glycosides themselves, so care must be taken when isolating glycosides from raw materials. The raw material is dried at 40-600C or placed in a vessel with vapors of alcohol, chloroform - this contributes to the inactivation of enzymes, and the glycosides remain intact.

The quality of glycosides can be judged by the reaction with Fehling's reagent, which is negative if no sugar cleavage has occurred, that is, primary glycosides do not have reducing power, except for those with an aldehyde group.

Physical properties of glycosides

Cardiac glycosides are solid crystalline substances, poorly soluble in water, optically active.

Identification

For cardiac glycosides, there are general, mostly colored reactions due to the aglycone and the sugar component.

We analyzed sugars, both mono- and specific deoxysugars, in the previous lecture. And the reactions that determine the nature of the aglycon can be divided into two groups: reactions characteristic of the steroid cycle, and reactions characteristic of the 5-membered lactone ring, which has a double bond in the α-β position.

I. Analysis of the steroid cycle.

Reactions of the steroid cycle are based on color reactions that take place during interaction with reagents that cause dehydration of hydroxyl groups (especially at C5 and C10) of the steroid skeleton with the formation of anhydro derivatives.

A). Lieberman-Burchard reaction:

A small amount of the drug is dissolved in a few drops of concentrated acetic acid CH_3COOH and mixed with 2 ml of the mixture (50 ml of acetic anhydride and 1 ml of conc. acetic acid), a pink color appears, which turns into green, then into blue.

B). Rosenheim's reaction:

A 96% aqueous solution of trichloroacetic acid is added to the chloroform solution of the substance. The color appears, changing from pink to purple and intense blue.

C). Reichstein's reaction. It is somewhat specific for individual glycosides - gives different colors with concentrated sulfuric acid H_2SO_4. The reaction takes place over time.

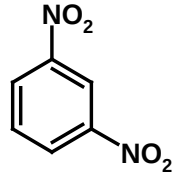
D). Cardenolides are able to give fluorescence in UV light when interacting, for example, with phosphoric acid, or when interacting with a mixture of sulfuric acid H_2SO_4 and phosphoric acid H_3PO_4 and ferric chloride $FeCl_3$; solution of $Fe(ClO_4)_3$ (ferrum perchlorate) in H_2SO_4, etc.

II. Reactions on the β, α-unsaturated lactone ring.

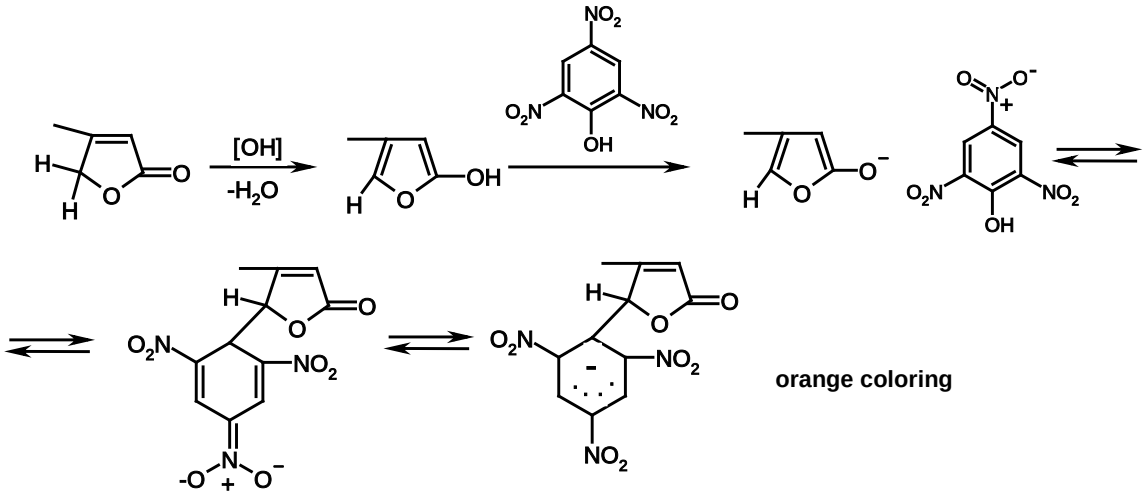
A). Legal's reaction - interaction with an alkaline solution of sodium nitroprusside - a red color appears, which quickly disappears.

Reactions with nitro derivatives:

B). Raymond's reaction - in an alkaline medium with m-dinitrobenzene, a red-violet color is formed.



C). Ballet's reaction (Ballier) - with an alkaline solution of picric acid:



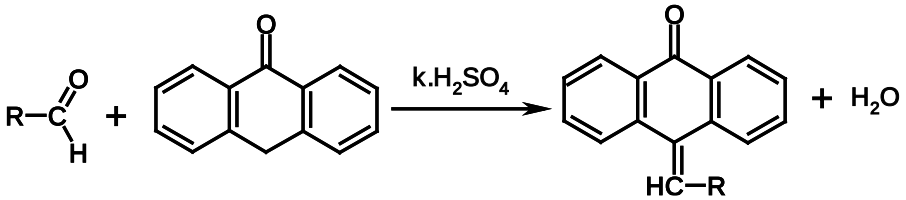
III. Reactions to the sugary part.

Sugars that are part of cardiac glycosides give all the color reactions characteristic of carbohydrates: they reduce Fehling's reagent, ammonia solution of silver nitrate (after hydrolysis), form colored compounds with xanthhydrol, m-dimethylaminobenzaldehyde.

Let's remind that the specific sugars of cardiac glycosides are 2,6-deoxysugars, for their detection, the Keller-Killiani, xanthanhydrol, Pezetz reaction, the reaction with phosphoric acid in acetone (the Pezetz-Dekwecker reaction), etc. are used:

1). Keller-Killiani's reaction: prepare 2 solutions: 1) drug + concentrated acetic acid and a solution of divalent ferrum sulfate (II) and 2) concentrated sulfuric acid and solution of divalent ferrum sulfate (II). 2 solutions are layered and a colored solution is formed.

2). Pesetz's reaction (Pezet) - xanthhydrol test (with dibenzo-γ-pyran) in the presence of concentrated acetic acid, heating and sulfuric or phosphoric acid. A red color is formed. Anthrone reagent can also be used. The reaction is based on the fact that under the action of conc. acids, carbohydrates form furfural, which reacts with anthrone



зеленое окрашивание, переходящее в сине-зеленое

3). Pezets-Dekvener's - phosphoric acid in acetone - colored solutions are formed.

Quantitative definition:

1). To date, the quantification of cardioactive steroids has been carried out mainly using biological methods in animals.

Standardization of cardiac glycosides using a biological method is based on the ability of cardenolides to cause cardiac arrest in animals in the systole stage in toxic doses. Their activity is evaluated in comparison with the activity of standard drugs and is expressed in standard units (SU) - cat's (CSU), frog's (FSU), pigeon's (PSU).

But biological methods are time-consuming, long, poorly reproducible, unreliable (errors within 10-20%). Therefore, many methods are currently known, which are based on titrimetric, photometric, fluorimetric, polarographic determination of cardiac glycosides. And with the help of the HPLC method, not only the main glycosides, but also secondary ones are determined.

Chemical methods

CAT in a non-aquatic environment (strophant subgroup).

Physico-chemical methods

1). UV spectrophotometric method. It is used in the analysis of raw materials and standard substances at λ = 217-219 nm.

2). Photometric method:

- celanide - with xanthhydrol reagent;
- Tatier's reagent (2,4-dinitrophenylsulfone) - recommended for the analysis of raw materials (reaction to a 5-membered lactone ring).

3). Chromatographic methods (HPLC, HLC);

4). Fluorimetric methods based on the ability of glycosides to give fluorescence under the influence of strong acids and oxidants after exposure to UV light.

4. TASKS FOR STUDENT SELF-TRAINING:

4.1. Repeat the theoretical material from organic and analytical chemistry courses on this topic.

4.2. Study the program material on the topic of the lesson according to the questions below.

Educational questions for self-training of students

1. Cardiotonic drugs. General characteristics, classification.

2. Glycosides. General characteristics, structure, classification.

3. Cardiac glycosides. Structural features, classification, distribution in nature.

4. To characterize the physicochemical properties, sources and methods of obtaining drugs from the group of cardiac glycosides.

5. To justify the use of chemical and instrumental methods in the analysis of the quality of drugs from the group of cardiac glycosides.

6. Chemical methods of identification of drugs from the group of cardiac glycosides. Principles of analysis, used reagents, performance technique and effects of reactions.

7. Methods of quantitative determination of drugs from the group of cardiac glycosides.

8. The relationship between the structure and biological action of a number of drugs from the group of cardiac glycosides, the role of steric factors. Accumulation of cardiac glycosides.

9. The concept of biological standardization of drugs from the group of cardiac glycosides. Units of action of cardiac glycosides.

10. Cardenolide cardiac glycosides. Features of the structure, sources and methods of extraction, characteristics of physical and chemical properties, substantiation of methods of identification and quantitative determination.

10.1. Glycosides of the digitalis group. Digitoxin. Digoxin. Celanide. Structure, properties, analysis, application.

10.2. Glycosides of the strophant group. Strophantin K. Structure, properties, analysis, application.

10.3. Glycosides of the ovabagenin group. Ouabain (strophanthin G). Structure, properties, analysis, application.

11. Features of storage of drugs from the group of cardiac glycosides.

4.3. Work out the test tasks:

1. Medicinal substances from the group of cardiac glycosides in chemical terms are:

A. *O*- Glycosides
B. *N*- Glycosides
C. *S*- Glycosides
D. All are listed
E. None of the above

2. To identify the steroid cycle in the structure of ouabain (strophantin G) -medicinal substances from the group of cardiac glycosides - the pharmacist-analyst should use concentrated:

A. Acetic acid
B. Formic acid
C. Picric acid
D. Chromotropic acid
E. Sulfuric acid

3. Specify a characteristic feature of the sugar part of cardiac glycosides of the groupdigitalis:

A. It is represented by a chain of linear forms of carbohydrates
B. Carbohydrate residues are in furanose form
C. Residues of deoxyhexoses and their derivatives are present
D. It is revealed by the Lieberman-Burchardt reaction
E. It is a carrier of pharmacological action

4. A pharmacist-analyst can confirm the presence of a five-membered lactone ring in the structure of medicinal substances from the group of cardiac glycosides by the reaction:

A. With Nessler's reagent (potassium tetraiodomercurate alkaline solution)
B. With concentrated sulfuric acid
C. With a solution of sodium nitroprusside in an alkaline environment
D. With a solution of potassium dichromate in a sulfuric acid medium in the presence of a solution of hydrogen peroxide
E. With Fehling's reagent (copper-tartrate reagent)

5. According to the SPU, the quantitative determination of the digitoxin substance is carried out by the spectrophotometric method. At the same time, measure:

A. pH of the standard solution
B. Refractive index
C. Optical density
D. Specific optical rotation
E. Melting point

6. Legal's reaction is used to identify medicinal substances from the group of cardiac glycosides. What structural fragment allows this reaction to be detected?
A. Lactone cycle
B. Lactam cycle
C. Aldehyde group
D. Remains of 2-deoxysugars
E. Steroid system

7. There is a certain relationship between the structure and pharmacological action of cardiac glycosides. So, the structural fragment that affects the rate of absorption of cardiosteroids is:
A. Alcoholic hydroxyl
B. Lactone cycle
C. Aglycon
D. Sugar component
E. Steroid cycle

8. Indicate which physico-chemical method, according to the SPU, is used to determine concomitant impurities in the digitoxin substance:
A. Polarography
B. Refractometry
C. Photoelectrocolorimetry
D. Thin-layer chromatography
E. Potentiometry

9. The pharmacist-analyst of the pharmaceutical enterprise conducts the analysis of the quality of the strophanthin G substance by the method of polarimetry in accordance with the AN. What value is used to identify substances in this method of pharmaceutical analysis?
A. Angle of rotation
B. Specific absorption index
C. Specific optical rotation
D. Molar coefficient of light absorption
E. Refractive index

10. To identify the steroid cycle in the structure of drugs from the group of cardiac glycosides, the following is carried out:
A. Raymond's reaction

B. Legal's reaction
C. Pezet's reaction
D. Rosenheim's reaction
E. Keller-Kiliani reaction

11. According to the SPU, a reaction with a solution of 1,3-dinitrobenzene in an alkaline medium is used to identify the substance ouabain (strophanthin G). What structural fragment allows this reaction to be detected?
A. Angular methyl group
B. Alcoholic hydroxyl
C. Five-membered lactone cycle
D. Cyclopentaneperhydrophenanthrene cycle
E. Digitoxosis

12. Medicinal substances from the group of cardiac glycosides contain an aglycon in their structure, the basis of which is the following:
A. Steroid system
B. Phenanthrenisoquinoline cycle
C. The sterane system and the lactone ring
D. A chain of monosaccharide residues
E. Saturated Anthrocene cycle

13. A distinctive feature of the chemical structure of cardiac glycosides of the digitalis group is the presence in the 10th position of the steroid cycle:
A. Alcoholic hydroxyl
B. Aldehyde group
C. Methyl group
D. Ethoxy groups
E. Phenolic hydroxyl

14. To detect deoxysugars in cardiac glycosides, the pharmacist-analyst should conduct:
A. Legal's reaction
B. Keller-Kiliani reaction
C. Lieberman-Burchardt reaction
D. Raymond's reaction
E. Vitaly-Moren's reaction

15. In the practice of control and analytical laboratories, the following is used to detect the five-membered lactone cycle in the structure of cardiac glycosides:
A. Vitaly-Moren's reaction
B. Rosenheim's reaction
C. Pezet's reaction
D. Legal's reaction

E. Keller-Kiliani reaction

16. According to the SPU, a reaction with a solution of 3,5-dinitrobenzoic acid in an alkaline medium is used to identify the digitoxin substance. In pharmaceutical analysis, this reaction is known as:

A. Kedde's reaction
B. Legal's reaction
C. Lieberman-Burchardt reaction
D. Keller-Kiliani reaction
E. Pezet's reaction

17. According to the SPU, a reaction with a solution of 1,3-dinitrobenzene in an alkaline medium is used to identify the substance ouabain (strophanthin G). In pharmaceutical analysis, this reaction is known as:

A. Keller-Kiliani reaction
B. Lieberman-Burchardt reaction
C. Raymond's reaction
D. Legal's reaction
E. Kedde's reaction

18. The control and analytical laboratory received the digitoxin substance. Determining its benignity, the pharmacist-analyst used a polarimeter. At the same time, he measured:

A. Optical density
B. Angle of rotation
C. Electromotive force
D. Refractive index
E. Melting point

19. There is a certain relationship between the structure and pharmacological action of cardiac glycosides. So, the carrier of biological activity of cardiosteroids is:

A. Sugar component
B. Steroid cycle
C. Lactone cycle
D. Aglycon
E. Alcoholic hydroxyl

20. A distinctive feature of the chemical structure of cardiac glycosides of the strophant group is the presence in the 10th position of the steroid cycle:

A. Alcoholic hydroxyl
B. Ethoxy groups
C. Aldehyde group
D. Phenolic hydroxyl
E. Methoxy groups

21. The Keller-Kiliani reaction is used to identify drugs from the group of cardiac glycosides. What structural fragment allows this reaction to be detected?

A. Lactam cycle
B. Steroid system
C. Aldehyde group
D. Lactone cycle
E. Remains of 2-deoxysugars

22. To identify which structural fragment in drugs of the group of cardiac glycosides in pharmaceutical analysis, a reaction with a solution of sodium nitroprusside in an alkaline medium is used?

A. Angular methyl group
B. Alcoholic hydroxyl
C. Digitoxosis
D. Cyclopentaneperhydrophenanthrene cycle
E. Five-membered lactone cycle

23. Which physico-chemical method, according to the SPU, is used for the quantitative determination of digoxin?

A. HPLC
B. Potentiometry
C. Mass spectrometry
D. Spectrometry
E. IR spectrometry

24. Digitoxin substance was sent to the control and analytical laboratory for analysis. According to the SPU, one of the reactions for identifying this substance is a reaction with a solution of 3,5-dinitrobenzoic acid in an alkaline medium. What color is observed in this case?

A. Purple
B. green
C. red
D. yellow
E. Pink

25. Cardioactive glycosides of the cardenolide group are characterized by the presence in the 17th position of the steroid cycle:

A. Five-membered lactam cycle
B. Four-membered lactone cycle
C. Four-membered lactam cycle
D. Five-membered lactone cycle
E. Aldehyde group

26. In order to identify a medicinal product from the group of cardiac glycosides, the analyst of the laboratory of the State Inspection for Quality Control of Medicinal Products needs to prove the presence of an unsaturated lactone ring. What reagent should he use for this?

A. Alcoholic solution of potassium tetraiodomercurate
B. Acetic acid solution of ascorbic acid
C. Sodium acetate saturated solution
D. The solution is discolored by fuchsin
E. Picric acid alkaline solution

27. When quantifying the substance ouabain (strophanthin G), according to the SPU, the optical density of the tested and standard solutions is measured after adding one of the reagents. Specify this reagent:

A. Sodium picrate solution is alkaline
B. Sodium nitroprusside solution
C. The sodium acetate solution is saturated
D. Potassium tetraiodomercurate solution is alkaline
E. Fuchsin solution is discolored

28. When testing for the purity of the digoxin substance, it is necessary to determine the specific optical rotation. This research in pharmaceutical analysis is carried out using:

A. Photoelectric colorimeter
B. Refractometer
C. Polarimeter
D. Spectrophotometer
E. Polarograph

29. To detect deoxysugars in the structure of drugs from the group of cardiac glycosides, in the practice of control and analytical laboratories, concentrated sulfuric acid is used together with:

A. A solution of iodine in potassium iodide
B. Hydrogen peroxide with impurities of potassium permanganate
C. Formaldehyde
D. Potassium dichromate in concentrated sulfuric acid
E. Glacial acetic acid in the presence of 0,05% ferrum (III) chloride

30. To identify digitoxin, the pharmacist-analyst prepared glacial acetic acid, a solution of ferrum (III) chloride, as well as concentrated sulfuric acid according to the SPU. This set of reagents is used by the analyst to carry out a reaction known in the pharmaceutical industry
analysis as:

A. Raymond's reaction

B. Keller-Kiliani reaction
C. Lieberman-Burchardt reaction
D. Legal's reaction
E. Kedde's reaction

31. According to the SPU, a reaction with a solution of 3,5-dinitrobenzoic acid in an alkaline medium is used to identify the digitoxin substance. What structural fragment allows this reaction to be detected?
A. Alcoholic hydroxyl
B. Cyclopentaneperhydrophenanthrene cycle
C. Five-membered lactone cycle
D. Digitoxosis
E. Angular methyl group

32. Choose the correct statement about cardiac glycosides from the group of cardenolides:
A.The structure contains a six-membered lactone ring
B.In the steroid cycle, the B and C rings are cis-articulated
C.According to their chemical structure, they are S-glycosides
D.Carbohydrates of sugar parts are in cyclic form
E.The 17α-position of the lactone ring is physiologically active

33. A feature of the chemical structure of cardiac glycosides from the cardenolide group is the presence of the following structural fragment in the 17th position of the steroid cycle:
A. α-Lactone ring
B. Pyridine cycle
C. The pyrrole cycle
D. β-Lactam ring
E. Thiazolidine cycle

34. In the structure of medicinal substances of the group of cardiac glycosides, aglycones are:
A. Derivatives of cyclopentaneperhydrophenanthrene
B. Derivatives of organic acids
C. Nitriles of mandelic acid
D. Derivatives of phenols
E. Oxyderivatives of anthraquinone

35. The Pezetz reaction is used to determine the presence of deoxysugars in the structure of cardiac glycosides. What reagent is used in this reactions?
A. Ninhydrin
B. Alizarin

C. Xanthhydrol
D. Formaldehyde
E. Salicylic acid

36. The Lieberman-Burchardt reaction is used to identify drugs from the group of cardiac glycosides. What structural fragment allows this reaction to be detected?
A. Steroid cycle
B. Lactone cycle
C. Remains of 2-deoxysugars
D. Aldehyde group
E. Lactam cycle

4.4. Situational tasks:

1. Justify the necessity of using special conditions for drying raw materials containing cardiac glycosides.
2. Explain the contribution of structural fragments of cardiac glycosides to their biological activity.
3. Determine which structural fragments allow the identification of drugs from the group of cardiac glycosides by chemical methods.
4. Describe the possible methods of quantitative determination of drugs from the group of cardiac glycosides.
5. Justify the need for biological standardization of cardiac glycosides.
6. Justify the peculiarities of storage of drugs from the group of cardiac glycosides, based on their physicochemical properties.

4.5. Tasks

1. Calculate the specific absorption index and evaluate the quality of digitoxin, if a sample of the substance weighing 0.0201 g was dissolved in 50 ml of ethanol, 5 ml of this solution was transferred to a 50 ml volumetric flask and brought up to the mark with alcohol. 5 ml of sodium picrate was added to 5 ml of the resulting solution. The optical density of the obtained solution at 495 nm was 0.440. The thickness of the used cuvette is 10 mm; the content of digitoxin in the drug is 99.8%. According to MQC, the specific absorption index should be from 215 to 235.

2. Calculate the quantitative content and evaluate the quality of celanide, if a sample of the substance weighing 0.0099 g was dissolved in 50 ml of ethanol, 4.5 ml of water was added to 0.5 ml of the resulting solution and the optical density was measured at 222 nm in a cuvette with a thickness of 10 mm Optical density of the solution equals 0.286, the specific absorption index at this wavelength is 140. According to MQC, the content of celanide should be at least 99.0%.

5. LABORATORY WORK

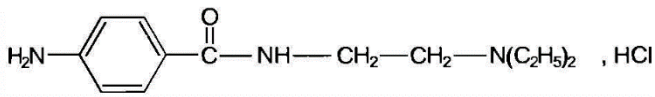
During laboratory work it is necessary to strictly follow the safety rules in the chemical laboratory.

Each student individually carries out reactions of identification of samples of drug substances under the instruction of the teacher and draws up the test report.

AN EXAMPLE OF FILLING IN THE PROTOCOL IS PRESENTED BELOW:

PROCAINAMIDE HYDROCHLORIDE

(Procainamidi hydrochloridum, PROCAINAMlDE HYDROCHLORlDE)



$C_{13}H_{22}ClN_3O$ M.m. 271.8

Procainamide hydrochloride contains not less than 98.0% and not more than 101.0% of 4-amino-N-[2-(diethylamino)ethyl]benzamide hydrochloride, calculated on dry matter:

PROPERTIES

Description. Crystalline powder of white or white with a yellowish tinge; hygroscopic.

Solubility. Very easily soluble in water R, easily soluble in 96% alcohol R, slightly soluble in acetone R, practically insoluble in ether R.

IDENTIFICATION

PREPARATION of solution S: 0.5 g of the substance is dissolved in 5 ml of water.

D. 1 ml of solution S is brought up to 5 ml with water, add 2-3 drops of dilute nitric acid and 2-3 drops of silver nitrate. A white precipitate (chlorides) falls out.

E. 1 ml of solution S is brought to a volume of 2 ml with water, add 3 drops of hydrochloric acid, 2-3 drops of 0.1 M sodium nitrite solution, mix. Add 1 ml of an alkaline β-naphthol solution. An orange or red color appears.

TESTING FOR CLEANLINESS

Transparency of the solution (2.2.1). Solution S should be clear

QUANTITATIVE DETERMINATION

1. NITRITOMETRY. Dissolve 0.1500 g of the substance in 10 ml of diluted hydrochloric acid P, add water to a total volume of 50 ml, 0.5 g of potassium bromide and, with constant stirring, titrate with a 0.1 M solution of sodium nitrite (at the end of the titration, add 0.05 ml titrated solution). Titration is carried out at a temperature of 18-20°C (the titration flask is kept in chilled water). The indicator is tropeolin 00 with methylene blue (4 drops of tropeolin 00 + 2 drops of methylene blue). Titrate to a blue color.

1 ml of 0.1 M sodium nitrite solution corresponds to 0.02718 g of $C_{13}H_{22}ClN_3O$.

2. ACID-BASE TITRATION.

Dissolve about 0.1500 g of the substance in 10 ml of water, add 5 ml of an alcohol-chloroform mixture and titrate with a 0.1 M sodium hydroxide solution to a pink color with the indicator phenolphthalein.

1 ml of 0.1 M sodium hydroxide solution corresponds to 0,02718 g of $C_{13}H_{22}ClN_3O$.

LESSON No.4

1. SUBJECT: Final lesson on theory and practice on the topic: "Drugs from the group of carbohydrates, cardiotonic and antiarrhythmic drugs and their synthetic analogues"

2. PURPOSE: To form systematic knowledge and consolidate practical skills in the analysis of the quality of drugs from the group of carbohydrates, cardiotonic and antiarrhythmic drugs and their synthetic analogues using physical, physico-chemical and chemical methods of analysis.

3. OBJECTIVES:

3.1. Check and consolidate theoretical knowledge and practical skills in the use of physical, physicochemical and chemical methods to analyze the quality of drugs from the group of carbohydrates, cardiotonic and antiarrhythmic drugs and their synthetic analogues.

3.2. Check the protocols of laboratory work and analyze the correctness of the analysis of drugs from the group of carbohydrates, cardiotonic and antiarrhythmic drugs and their synthetic analogues in accordance with the requirements of the State Medical Research Institute, the Ministry of Health.

4. TASK FOR SELF-PREPARATION OF STUDENTS FOR THE FINAL LESSON

4.1. control questions

1. Carbohydrates General characteristics, classification. Distribution in nature. The role of carbohydrates in human life. The concept of deoxy - and amino sugar.
2. Sources of extraction, chemical structure, nomenclature, synonyms of medicinal substances from the group of carbohydrates.
3. To characterize the physicochemical properties of medicinal substances from the group of carbohydrates. Constants of optical activity as indicators of the quality of drugs from the group of carbohydrates.
4. To justify the use of chemical and instrumental methods in the analysis of the quality of medicines from the group of carbohydrates.
5. Monosaccharides. Classification. Stereoisomerism and tautomerism of monosaccharides. Medicines from the group of monosaccharides, sources and methods of extraction.

5.1. Glucose is anhydrous. Glucose monohydrate. Structure, nomenclature, properties, application.

5.2. Using the example of glucose, explain the phenomenon of mutarotation. What is the chemical basis of this phenomenon?

5.3. State the possible methods and reactions for the identification of glucose preparations. Tests for the purity of glucose preparations. Ways of entry and determination of specific impurities (extraneous sugars, soluble starch, dextrins).

5.4. Describe possible methods of quantitative determination of glucose preparations. Give the corresponding reaction equations, calculation formulas.

5.5. Fructose. Structure, nomenclature, properties, analysis, application. Routes of introduction and determination of specific impurities in fructose (extraneous sugars, 5-hydroxymethylfurfural and related compounds).

5.6. Galactose. Structure, nomenclature, properties, analysis, application.

6. Oligosaccharides. Classification. Reducing and non-reducing disaccharides. Medicines from the group of oligosaccharides, sources and methods of extraction.

6.1. Sucrose. Structure, nomenclature, properties, application.

6.2. The phenomenon of inversion on the example of sucrose. Determination of impurity of invert sugar in sucrose.

6.3. Identification and methods of quantitative determination of sucrose. Give the corresponding reaction equations, calculation formulas.

6.4. Lactose is anhydrous. Lactose monohydrate. Structure, nomenclature, properties, application.

6.5. Identification and methods of quantitative determination of lactose preparations. Give the corresponding reaction equations, calculation formulas.

7. Polysaccharides. Classification. Homo - and heteropolysaccharides. Medicines from the group of polysaccharides, sources and methods of extraction.

7.1. Starch. Structure, properties, analysis, application.

7.2. Cellulose. Methyl cellulose. Structure, properties, analysis, application.

7.3. Dextrans. Dextran 40 for injections. Polyglukin. Rheopolyglukin. Structure, properties, analysis, application.

7.4. Inulin. Structure, properties, application.

7.5. Chondroitin sulfate. Structure, properties, analysis, application.

7.6. Heparin. Calcium heparin. Sodium heparin. Structure, properties, analysis, application.

8. Features of storage of drugs from the group of carbohydrates.

9. Antiarrhythmic drugs. General characteristics, pharmacological classification.

10. To characterize the physicochemical properties, sources and methods of obtaining drugs from the group of antiarrhythmic drugs.

11. To justify the use of chemical and instrumental methods in the analysis of the quality of antiarrhythmic drugs.

12. Chemical methods of identification of antiarrhythmic drugs. Principles of analysis, reagents used, performance technique and effects of reactions.

13. Methods of quantitative determination of antiarrhythmic drugs.

14. The relationship between the structure and biological action of a number of antiarrhythmic drugs.

15. Atropine sulfate. Structure, nomenclature, obtaining, properties, analysis, application. Determination of apoatropine admixture in atropine sulfate.

16. Quinidine sulfate. Structure, nomenclature, properties, analysis, application.

17. Novocainamide. Structure, properties, analysis, application.

18. Potassium chloride. Obtaining, properties, analysis, application. Determination of impurities of bromides, iodides, barium. Ways of entering the mentioned impurities into the drug.

19. Amiodarone. Structure, nomenclature, properties, analysis, application.

20. Features of storage of the named group of drugs. Mechanism of action.

21. Cardiotonic drugs. General characteristics, classification.

22. Glycosides. General characteristics, structure, classification.

23. Cardiac glycosides. Structural features, classification, distribution in nature.

24. To characterize the physicochemical properties, sources and methods of obtaining drugs from the group of cardiac glycosides.

25. To justify the use of chemical and instrumental methods in the analysis of the quality of drugs from the group of cardiac glycosides.

26. Chemical methods of identification of drugs from the group of cardiac glycosides. Principles of analysis, used reagents, performance technique and effects of reactions.

27. Methods of quantitative determination of drugs from the group of cardiac glycosides.

28. The relationship between the structure and biological action of a number of drugs from the group of cardiac glycosides, the role of steric factors. Accumulation of cardiac glycosides.

29. The concept of biological standardization of drugs from the group of cardiac glycosides. Units of action of cardiac glycosides.

30. Cardenolide cardiac glycosides. Features of the structure, sources and methods of extraction, characteristics of physical and chemical properties, substantiation of methods of identification and quantitative determination.

30.1. Glycosides of the digitalis group. Digitoxin. Digoxin. Celanide. Structure, properties, analysis, application.

30.2. Glycosides of the strophant group. Strophantin K. Structure, properties, analysis, application.

30.3. Glycosides of the ovabagenin group. Ouabain (strophanthin G). Structure, properties, analysis, application.

31. Features of storage of drugs from the group of cardiac glycosides.

4.2. Test tasks for the final lesson

1. The pharmacist-analyst of the pharmacy conducts quality control of the 10% glucose solution. What properties of glucose confirm the positive result of the reaction with the copper-tartrate reagent (Fehling's reagent)?

A. Acidic
B. Reduction
C. Amphoteric
D. Oxidizing
E. The main ones

2. The pharmacist-analyst determines the quantitative content of anhydrous glucose by the inverse iodometric method. What indicator should he use for this?

A. Methyl orange
B. Phenolphthalein
C. Starch
D. Potassium chromate
E. Methyl red

3. The pharmacist-analyst conducts tests on the purity of the medicinal product glucose anhydrous according to the SPU. He determines the unacceptable impurity of barium with the help of:

A. Chloric acid
B. Nitric acids
C. Sulfate acids
D. Acetic acid
E. Hydrochloric acids

4. Specify the name of the mirror-symmetric isomers of monosaccharides, the configurations of which are mirror-opposite in the asymmetric centers:

A. Epimers
B. Enantiomers
C. Diastereomers
D. Polymers
E. Anomers

5. State the name of spatial isomers of monosaccharides that differ in the configuration of one or more carbon atoms and are not mirror isomers:

A. Polymers

B. Enantiomers
C. Epimers
D. Anomers
E. Diastereomers

6. Glucose is characterized by the phenomenon of mutarotation. Mutarotation is an involuntary process that is accompanied by:
A. Combining simple carbohydrate molecules into more complex ones
B. Decomposition of complex carbohydrates into simpler components
C. A change over time not only of the angle, but also of the sign of rotation as a result of the hydrolysis of carbohydrates
D. The flow of the ion exchange reaction between various carbohydrates and water
E. Change over time in the angle of rotation of freshly prepared carbohydrate solutions

7. To identify anhydrous glucose by the reaction of ozazone formation, the reagent should be used:
A. Fehling's reagent
B. Phenylhydrazine
C. Phenolphthalein
D. Hydroxylamine
E. Furfural

8. A mixture of equal amounts of enantiomers, which does not have optical activity, is called:
A. Epimeric mixture
B. Invert sugar
C. Grape sugar
D. Anomeric mixture
E. Racemic mixture

9. A pharmacist-analyst analyzes a 10% glucose solution. For quantitative determination, he uses one of the physico-chemical methods, measuring the angle of rotation of the solution, using:
A. Gas chromatograph
B. UV spectrophotometer
C. Potentiometer
D. Polarimeter

E. Refractometer

10. Specify the name of the hydroxyl group formed during the cyclization of monosaccharides:

A. Enolic hydroxyl
B. Phenolic hydroxyl
C. Epimeric hydroxyl
D. Carbonyl hydroxyl
E. Hemiacetal hydroxyl

11. The phenomenon of mutarotation is characteristic of freshly prepared glucose solutions. The chemical basis of this process is:

A. Presence of regenerative properties in glucose
B. Formation of 5-hydroxymethylfurfural
C. Ring-chain tautomerism of glucose
D. Chirality of the glucose molecule
E. Dissociation of glucose in solution

12. The pharmacist-analyst performs quality control of the substance of anhydrous glucose. When testing for purity, in accordance with the requirements of the Federal State Administration of Ukraine, it is assumed that impurities of extraneous sugars, soluble starch and dextrins are determined. To perform this test, the analyst:

A.Concentrated sulfuric acid is added to the solution of the substance in purified water; the opalescence of the obtained solution should not exceed the opalescence of the standard
B.A sample of the substance is dissolved in a mixture of chloroform and dioxane; no red color should appear
C.Measures and compares with pharmacopoeial data the value of the optical density of a 10% solution of the substance in purified water
D.A sample of the substance is dissolved by boiling in ethyl alcohol, cooled; the solution should remain clear
E.Copper-tartrate solution is added to the solution of the substance in purified water and heated; an abundant red precipitate should form

13. In the control and analytical laboratory, the substance of anhydrous glucose is studied by the method of polarimetry. What value is used to identify substances in this method of pharmaceutical analysis?

A. Refractive index

B.Specific optical rotation
C.Molar coefficient of light absorption
D.Angle of rotation
E.Specific refractive index

14. To identify fructose, the analyst of the laboratory of a pharmaceutical company heated a sample of the substance with hydrochloric acid in the presence of resorcinol. In the process of this interaction, substance "X" is formed, which, when condensed with resorcinol, gives a reaction product colored in red. Substance "X" is:
A. 5-Hydroxymethylfurfural
B. Azomethine dye
C. Diazonium salt
D. 2,4,6-Trichlorophenol
E. Glutacon aldehyde

15. To identify glucose monohydrate by the reaction accompanied by the formation of 5-hydroxymethylfurfural, preheating is carried out with:
A. Acetic anhydride
B. Copper-tartrate solution
C. Hydroxylamine
D. Potassium tetraiodomercurate
E. Mineral acids

16. Specify the type of tautomerism characteristic of a glucose molecule:
A. Nitro-acy-nitro tautomerism
B. Lactim-lactam tautomerism
C. Amino-imine tautomerism
D. Cyclo-oxo-tautomerism
E. Keto-enol tautomerism

17. According to the nature of the oxo group, monosaccharides are divided into:
A. Monoses and polyoses
B. *D*- and L-monosaccharides
C. Aldoses and ketoses
D. Epimers and anomers
E. Pentoses and heptoses

18. Not amenable to hydrolysis:

A. Glucose
B. Maltose
C. Starch
D. Sucrose
E. Lactose

19. State the conditions necessary for the identification of glucose monohydrate with a copper-tartrate solution:
A. Addition of HNO3 (conc.)
B. Cooling
C. Addition of formaldehyde
D. Heating
E. Catalyst (KBr)

20. *D*- Glucose and D-fructose in the crystalline state exist in the form of:
A. Acyclic forms
B. Andiolic forms
C. Linear forms
D. Mixtures of tautomeric forms
E. Cyclic forms

21. Indicate which of the following carbohydrates according to their chemical structure belongs to ketohexoses:
A. Fructose
B. Mannose
C. Glucose
D. Galactose
E. Starch

22. When testing fructose for purity, the pharmacist-analyst, in accordance with the requirements of the State Federal Drug Administration, prepared the initial solution of the substance in purified water in advance. Then, to two equal samples of the original solution, he added the appropriate solvent in equal quantities: to the first sample - 96% ethyl alcohol, and to the second - purified water. Comparing the opalescence of the obtained solutions with each other, the pharmacist-analyst evaluates the content of the impurity:
A. Lead in sugars
B. Third party sugars
C. Formaldehyde

D. Baria
E. 5-Hydroxymethylfurfural and related compounds

23. As a result of the intramolecular interaction of the carbonyl group and the alcohol group spatially close to it, monosaccharides can exist in the form:
A. Cyclic anhydrides
B. Cyclic esters
C. Cyclic hemiacetals
D. Cyclic amides
E. Cyclic carboxylic acids

24. Indicate which physico-chemical method, according to the SPU, is used to identify fructose:
A. Refractometry
B. Thin-layer chromatography
C. Photoelectrocolorimetry
D. Potentiometry
E. Polarography

25. The hydroxyl group at the carbon atom is involved in the formation of furanose forms of glucose:
A. C-3
B. C-2
C. C-4
D. C-6
E. C-5

26. Specify a specific admixture for anhydrous glucose:
A. Dextrins
B. Seneciflin
C. Formaldehyde [paraform]
D. Ammonium salts
E. Pantoylactone

27. A positive result of the reaction with a copper-tartrate solution (Fehling's reagent) gives:
A. Polyglukin
B. Starch
C. Dextran 40 for injections

D. Low molecular weight heparin
E. Glucose monohydrate

28. The hydroxyl group at the carbon atom is involved in the formation of pyranose forms of glucose:
A. C-3
B. C-6
C. C-2
D. C-4
E. C-5

29. The pharmacist-analyst identifies the fructose substance. In accordance with the requirements of the SPU, during the tests, he performed a reaction that resulted in the formation of a red precipitate. Indicate with which of the reagents this reaction was carried out:
A. Copper-tartrate solution
B. Ammonium silver nitrate solution
C. Potassium tetraiodomercurate solution is alkaline
D. Concentrated formaldehyde solution
E. Potassium pyroantimonate solution

30. The pharmacist-analyst performs the identification of the pharmaceutical substance "Glucose anhydrous" with the copper-tartrate reagent. What color precipitate is formed?
A. White
B. Turquoise blue
C. Blue-violet
D. Brick red
E. Emerald green

31. The pharmacist-analyst determines the quantitative content of anhydrous glucose by the inverse iodometric method. At the same time, he should use a standard solution as a titrant:
A. Potassium iodide
B. Potassium iodate
C. Potassium bromate
D. Silver nitrate
E. Sodium thiosulfate

32. According to the SPU, in the fructose substance, it is envisaged to determine the admixture of 5-hydroxymethylfurfural and related compounds by the method of absorption spectrophotometry in the ultraviolet region. At the same time, the following values are measured and compared with pharmacopoeial data:

A. Melting points
B. Optical density
C. pH of the standard solution
D. Specific optical rotation
E. Refractive index

33. Specify the main method of industrial extraction of anhydrous glucose, which is used for medical purposes:

A. Oxidation of glutamic acid
B. Epimerization of fructose
C. Starch hydrolysis
D. Oxidation of glycerol
E. Microbiological synthesis

34. The hemiacetal hydroxyl in the cyclic forms of glucose is located at the carbon atom:

A. C-2
B. C-1
C. C-6
D. C-3
E. C-4

35. The pharmacist-analyst determines the specific optical rotation of anhydrous glucose in accordance with the requirements of the SPU. To accelerate the mutarotation process, the following should be added to the solution of the analyte substance:

A. Sodium hydroxide solution
B. Copper(II) sulfate solution
C. Hydrochloric acid solution
D. Ammonia solution
E. Potassium permanganate solution

36. Indicate which physicochemical method, according to the SPU, is used to identify anhydrous glucose:

A. Thin-layer chromatography

B. Polarography
C. Potentiometry
D. Photoelectrocolorimetry
E. Refractometry

37. The chemical structure of sucrose is:
A. Aldohexose
B. Monosaccharide
C. Disaccharide
D. Polysaccharide
E. Ketohexose

38. Indicate which specific impurity in sucrose is determined by reaction with Fehling's reagent:
A. Copper(II) salts
B. Dextrins
C. Ferrum (III) salts
D. Soluble starch
E. Invert sugar

39. According to the chemical structure, starch is:
A. Polysaccharide
B. Monosaccharide
C. Disaccharide
D. Ketohexose
E. Aldohexose

40. Specify the medicinal substance, in the production scheme of which the main stage is the fermentation of sucrose by Leuconostoc mesenteroides bacteria:
A. Low molecular weight heparins
B. Dextran 40 for injections
C. Glucose monohydrate
D. Lactose is anhydrous
E. Methyl cellulose

41. To distinguish between sucrose and anhydrous lactose in pharmaceutical analysis, a reaction with:
A. A solution of bismuth iodide in potassium iodide
B. Ammonium solution of silver nitrate

C. Saturated sodium carbonate solution
D. Sodium hydroxide solution
E. Hydrochloric acid

42. Indicate which of the listed carbohydrates is an intermediate product of starch hydrolysis:
A. Lactose
B. Sucrose
C. Maltose
D. *D*- Galactose
E. *D*-Fructose

43. Indicate which of the listed features is characteristic of non-reducinrides disaccharides:
A.The reaction with Fehling's reagent gives a positive result
B.The phenomenon of mutarotation is observed in freshly prepared solutions
C.Capable of cyclo-oxo-tautomerism
D.There is no free hemiacetal hydroxyl in the structure
E.The reaction with an ammonia solution of silver nitrate gives a positive result

44. Indicate the correct statement about lactose anhydrous:
A.Easily soluble in water and chloroform
B.Does not interact with Fehling's reagent
C.Aqueous solutions do not mutate
D.Has low hygroscopicity
E.It is a heteropolysaccharide in structure

45. Indicate which of the following carbohydrates is an oligosaccharide according to its chemical structure:
A. Dextrose
B. Galactose
C. Fructose
D. Starch
E. Lactose

46. Indicate which of the medicinal substances is a white crystalline powder without odor, weak sweet taste, easily soluble in water:

A. Lactose monohydrate
B. Methyl cellulose
C. Starch
D. Sucrose
E. Glucose is anhydrous

47. A non-reducing disaccharide is:
A. Maltose
B. Starch
C. Lactose
D. Fructose
E. Sucrose

48. Amylopectin is a starch fraction that:
A. It dissolves well in water
B.It forms a blue complex with iodine
C.Contains branched polymer chains
D. During hydrolysis, it forms a mixture of D-glucose and D-galactose
E.Has a heteropolysaccharide character

49. Name the disaccharide, the molecule of which is formed by the residues of D-glucose and D-galactose:
A. Cellulose
B. Sucrose
C. Lactose
D. Starch
E. Maltose

50. Specify the name of complex carbohydrates that form from two to ten molecules of monosaccharides during hydrolysis:
A. Polysaccharides
B. Oligosaccharides
C. Aldohexoses
D. Ketohexoses
E. Monos

51. The restoring disaccharide is:
A. Sucrose
B. Cellulose

C. Lactose
D. Fructose
E. Starch

52. Plasma substitutes "polyglukin" and "reopolyglukin" are obtained by partial hydrolysis and fractionation:
A. terpenes
B. Proteins
C. Dextrans
D. Heparins
E. Pectins

53. The chemical structure of a heteropolysaccharide is:
A. Dextran 40 for injections
B. Lactose monohydrate
C. Sucrose
D. Chondroitin sulfate
E. Starch

54. The chemical structure of homopolysaccharide is:
A. Lactose monohydrate
B. Sucrose
C. Starch
D. Low molecular weight heparin
E. Chondroitin sulfate

55. The products of incomplete hydrolysis of starch are:
A. Heparins
B. Pectins
C. Ketohexoses
D. Terpenes
E. Dextrins

56. The specialist of the pharmaceutical enterprise needs to confirm the presence of anhydrous lactose as an auxiliary substance in the manufactured tablets. For this he should use:
A. Conc. sulfuric acid
B. Ammonia solution
C. Sodium hydroxide

D. Barium chloride
E. Fehling's reagent

57. Indicate which of the medicinal substances is a white crystalline powder without odor, sweet taste, easily soluble in water, does not reduce Fehling's reagent:
A. Glucose is anhydrous
B. Sucrose
C. Lactose monohydrate
D. Methyl cellulose
E. Starch

58. Name the disaccharide, the molecule of which is formed by the residues of D-glucose and D-fructose:
A. Cellulose
B. Starch
C. Sucrose
D. Lactose
E. Maltose

59. Sucrose is characterized by the phenomenon of inversion. Inversion is a process that is accompanied by:
A.The flow of the ion exchange reaction between various carbohydrates and water
B.Change over time in the angle of rotation of freshly prepared carbohydrate solutions
C.Decomposition of complex carbohydrates into simpler components
D.Combining simple carbohydrate molecules into more complex ones
E.A change over time not only of the angle, but also of the sign of rotation as a result of the hydrolysis of carbohydrates

60. Indicate which monosaccharide is the final product of starch hydrolysis:
A. *D*- Mannose
B. *D*-Xylose
C. *D*- Galactose
D. *D*-Glucose
E. *D*-Fructose

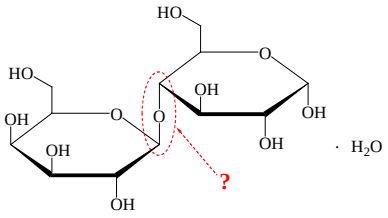
61. Indicate the medicinal product, the complete hydrolysis of which produces D-glucosamine, as well as D-glucuronic, L-iduronic, acetic and sulfuric acids:

A. Methyl cellulose
B. Sodium heparin
C. Polyglukin
D. Dextran 40 for injections
E. Lactose monohydrate

62. Indicate the name of polysaccharides of bacterial origin, built from α-D-glucopyranose residues, which are connected to each other mainly by 1,6-glycosidic bonds:
A. Heparins
B. Terpenes
C. Pectins
D. Dextrans
E. Oligosaccharides

63. Specify the name of complex carbohydrates that form more than 10 monosaccharide molecules during hydrolysis:
A. Ketohexoses
B. Oligosaccharides
C. Monos
D. Aldohexoses
E. Polysaccharides

64. Specify the name of the chemical bond between the monosaccharide units in the structure of this medicinal substance:



A. Glycosidic bond
B. Peptide bond
C. Hydrogen bond
D. Complex ether bond
E. Covalent non-polar bond

65. Indicate which of the carbohydrates does not give a positive result when identified with Fehling's reagent:
A. Fructose
B. Glucose is anhydrous

C. Glucose monohydrate
D. Sucrose
E. Lactose

66. Indicate which of the medicinal substances is a white, yellowish-white or grayish-white powder, soluble in cold water with the formation of a colloidal solution, but practically insoluble in hot water:
A. Lactose monohydrate
B. Methyl cellulose
C. Starch
D. Glucose is anhydrous
E. Sucrose

67. Specify the disaccharide in the structure of which the glycosidic bond is formed due to hemiacetal hydroxyls of both monosaccharide units:
A. Lactose is anhydrous
B. Sucrose
C. Maltose
D. Lactose monohydrate
E. Fructose

68. Medicinal substance "Calcium heparin" is obtained:
A. From livestock processing products
B.From plant material (spotted milk thistle)
C.By chemical synthesis (based on n-heptane)
D.Through microbiological synthesis
E.From natural minerals (sylvinite)

69. For the treatment of joint diseases, a substance from the group of polysaccharides, the repeating link of which is formed by D-glucuronic acid and N-acetyl-D-galactosamine containing sulfo groups, is widely used. Enter the name of this substance:
A. Chondroitin sulfate
B. Dextran 40 for injections
C. Starch
D. Methyl cellulose
E. Low molecular weight heparin

70. Amylose is a fraction of starch that:

A.Practically insoluble in water
B.It forms a blue complex with iodine
C.Has a heteropolysaccharide character
D.Contains branched polymer chains
E.During hydrolysis, it forms a mixture of D-glucose and D-galactose

71. Indicate which of the medicinal substances is a white amorphous powder without odor and taste, insoluble in cold water and forms a colloidal solution in hot water:

A. Methyl cellulose
B. Lactose monohydrate
C. Starch
D. Glucose is anhydrous
E. Sucrose

72. Which method of mineralization should be chosen to convert covalently bound iodine into molecular iodine in amiodarone?

A. Reduction mineralization
B. Alkaline hydrolysis
C. Acid hydrolysis
D. Roasting with a mixture of potassium nitrate and sodium carbonate
E. Oxidizing mineralization

73. What identification reaction should be performed to determine the iodide ion obtained after alkaline hydrolysis of amiodarone?

A. With a solution of ferrum (III) chloride
B. With sodium nitrate solution
C. With calcium chloride solution
D. With a solution of ferrum (II) sulfate
E. With potassium chloride solution

74. Indicate which method is used according to the SPU for the quantitative determination of amiodarone (2-butyl-3-benzofuranyl-4(2-diethylaminoethoxy)-3,5-diiodophenyl ketone hydrochloride)?

A. Alkalimetry
B. Acidimetry
C. Complexonometry
D. Cerimetry
E. Iodometry

75. The Kjeldahl method is used for quantitative determination of nitrogen in procainamide (novocainamide). For this purpose, the drug is mineralized:

A. A dilute alkali solution
B. Concentrated sulfuric acid
C. Dilute hydrochloric acid
D. A dilute solution of ammonia
E. With saturated sodium chloride solution

76. What method is used to quantitatively determine procainamide, the structure of which contains a primary aromatic amino group?

A. Complexonometry
B. Nitritometry
C. Permanganatometry
D. Cerimetry
E. Acidometry

77. Quantitative determination of procainamide (novocainamide) is carried out by the nitritometry method. Name which environment you need to create:

A. Alkaline
B. Non-aqueous
C. Neutral
D. Ammonia
E. Sour

78. Indicate which heterocyclic systems are the basis of the structure of tropane alkaloids:

A. Pyridine and pyrazole
B. Pyrrolizidine and imidazole
C. Piperidine and furan
D. Pyrrolidine and piperidine
E. Isoquinoline and pyrrole

79. According to the SPU, fuming nitric acid, acetone and an alcoholic solution of potassium hydroxide are used to identify atropine sulfate. These reagents are used to detect:

A. Remainder of tropic acid
B. Remainder of tropin
C. Sulfate ions

D. Crystallization water
E. Phenolic hydroxyl

80. According to the requirements of the SPU, apoatropin in atropine sulfate is defined as:
A. Interaction with concentrated ammonia solution
B. According to the turbidity of the solution of the substance in chloroform
C. Interaction with concentrated sulfuric acid
D. By the method of thin-layer ascending chromatography
E. By measuring the optical density of the solution and subsequent calculation of the specific absorption index

81. The pharmacist-analyst of the control-analytical laboratory determines the quantitative content of the substance atropine sulfate in accordance with the requirements of the SPU by the method of acid-base titration in non-aqueous media. As a titrated solution, he uses a solution:
A. Chloric acid
B. Sodium hydroxide
C. Sodium methylate
D. Hydrochloric acids
E. Sodium nitrite

82. To identify drugs from the group of alkaloids, tropane derivatives, the Vitali-Morena reaction is used. At the same time, the preparations, after decomposition with nitric acid, are treated with an alcoholic solution of potassium hydroxide in the presence of acetone. The visual effect of this reaction is:
A. The color of the solution is purple
B. Release of gas bubbles
C. The color of the solution is green
D. Fallout of black sediment
E. Precipitation of a white precipitate

83. Specify the characteristic pharmacological action of quinidine sulfate:
A. Antiarrhythmic
B. choleretic
C. Antimalarial
D. Vasodilator
E. Spasmolytic

84. Specify the medicinal product, which is a quinoline derivative according to its chemical structure:

A. Papaverine hydrochloride
B. Akrichin
C. Bigumal
D. Chloridine
E. Quinidine sulfate

85. State the specific reaction used to identify quinidine:

A. Vitaly-Moren's reaction
B. Formation of murexide
C. Thalleiochin test
D. Period formation
E. Picrate formation

86. One of the following methods cannot be used for the quantitative determination of quinidine sulfate. Specify it:

A. Acid-base titration in a two-phase environment
B. Bromatometry
C. Gravimetry
D. Method of acid-base titration in non-aqueous solvents
E. Complexonometry

87. Indicate which heterocyclic systems are part of the quinidine sulfate molecule:

A. Pyridine, piperidine
B. Pyrrolizidine, quinoline
C. Isoquinoline, quinuclidine
D. Pyridine, quinuclidine
E. Quinoline, quinuclidine

88. One of the methods of quantitative determination of quinidine salts involves preliminary precipitation of the quinidine base with sodium hydroxide. Such a procedure is necessary when determining this drug by the method:

A. Acidimetry in a non-aqueous medium
B. Acidimetry in an aqueous environment
C. Alkalimetry
D. Polarimetry
E. Gravimetry

89. The control and analytical laboratory received the substance quinidine sulfate. This medicinal substance can be identified by its formation:

A. Talleiokhina
B. Murexida
C. Iodoform
D. Ferrum (III) hydroxamate
E. Thiochrome

90. The appearance of an emerald-green color when adding bromine water and ammonia solution to the solution of the medicinal substance allows you to identify:

A. Codeine phosphate
B. Quinidine sulfate
C. Caffeine monohydrate
D. Atropine sulfate
E. Pilocarpine hydrochloride

91. A dosage form containing potassium chloride was submitted for analysis. Which reagent can be used to determine the potassium ion in potassium chloride?

A. Tartaric acid
B. Oxalic acid
C. Citric acid
D. Acetic acid
E. Butyric acid

92. Which of the medicinal substances with tartaric acid in the presence of sodium acetate forms a white precipitate, soluble in alkalis and mineral acids?

A. Potassium chloride
B. Sodium chloride
C. Lithium carbonate
D. Sodium iodide
E. Sodium bromide

93. Potassium chloride is identified by the potassium ion by the reaction with:

A. Sodium cobaltinitrite
B. Zincuranyl acetate
C. Silver nitrate
D. Sodium hydroxide
E. Potassium ferricyanide

94. The pharmacopoeial reaction for the identification of potassium ions is the interaction with tartaric acid, as a result of which a precipitate of what color is formed:

A. White
B. Black
C. Gray
D. Blue
E. Green

95. Potassium salts introduced into the colorless flame of a gas burner paint it in color:

A. Violet
B. Red
C. Brick
D. Yellow
E. Green

96. What method is recommended by the SPU for the quantitative determination of the potassium chloride substance?

A. Argentometry
B. Complexonometry
C. Bromatometry
D. Polarimetry
E. Iodometry

97. When carrying out the quantitative determination of potassium chloride by the argentometric method (back titration) according to the SPU, the indicator is used:

A. Ferrum (III) ammonium sulfate
B. Diphenylcarbazone
C. Potassium chromate
D. Phenolphthalein
E. Sodium eosinate

98. Medicinal substances from the group of cardiac glycosides in chemical terms are:

A. *O*- Glycosides
B. *N*- Glycosides

C. *S*- Glycosides
D. All are listed
E. None of the above

99. To identify the steroid cycle in the structure of ouabain (strophantin G) -medicinal substances from the group of cardiac glycosides - the pharmacist-analyst should use concentrated:
A. Acetic acid
B. Formic acid
C. Picric acid
D. Chromotropic acid
E. Sulfate acid

100. Specify a characteristic feature of the sugar part of cardiac glycosides of the groupdigitalis:
A. It is represented by a chain of linear forms of carbohydrates
B. Carbohydrate residues are in furanose form
C. Residues of deoxyhexoses and their derivatives are present
D. It is revealed by the Lieberman-Burchardt reaction
E. It is a carrier of pharmacological action

101. A pharmacist-analyst can confirm the presence of a five-membered lactone ring in the structure of medicinal substances from the group of cardiac glycosides by the reaction:
A. With Nessler's reagent (potassium tetraiodomercurate alkaline solution)
B. With concentrated sulfuric acid
C. With a solution of sodium nitroprusside in an alkaline environment
D. With a solution of potassium dichromate in a sulfuric acid medium in the presence of a solution of hydrogen peroxide
E. With Fehling's reagent (copper-tartrate reagent)

102. According to the SPU, the quantitative determination of the digitoxin substance is carried out by the spectrophotometric method. At the same time, measure:
A. pH of the standard solution
B. Refractive index
C. Optical density
D. Specific optical rotation
E. Melting point

103. Legal's reaction is used to identify medicinal substances from the group of cardiac glycosides. What structural fragment allows this reaction to be detected?

A. Lactone cycle
B. Lactam cycle
C. Aldehyde group
D. Remains of 2-deoxysugars
E. Steroid system

104. There is a certain relationship between the structure and pharmacological action of cardiac glycosides. So, the structural fragment that affects the rate of absorption of cardiosteroids is:

A. Alcoholic hydroxyl
B. Lactone cycle
C. Aglycon
D. Sugar component
E. Steroid cycle

105. Indicate which physico-chemical method, according to the SPU, is used to determine concomitant impurities in the digitoxin substance:

A. Polarography
B. Refractometry
C. Photoelectrocolorimetry
D. Thin-layer chromatography
E. Potentiometry

106. The pharmacist-analyst of the pharmaceutical enterprise conducts the analysis of the quality of the strophanthin G substance by the method of polarimetry in accordance with the AN. What value is used to identify substances in this method of pharmaceutical analysis?

A. Angle of rotation
B. Specific absorption index
C. Specific optical rotation
D. Molar coefficient of light absorption
E. Refractive index

107. To identify the steroid cycle in the structure of drugs from the group of cardiac glycosides, the following is carried out:

A. Raymond's reaction
B. Legal's reaction

C. Pezet's reaction
D. Rosenheim's reaction
E. Keller-Kiliani reaction

108. According to the SPU, a reaction with a solution of 1,3-dinitrobenzene in an alkaline medium is used to identify the substance ouabain (strophanthin G). What structural fragment allows this reaction to be detected?
A. Angular methyl group
B. Alcoholic hydroxyl
C. Five-membered lactone cycle
D. Cyclopentaneperhydrophenanthrene cycle
E. Digitoxosis

109. Medicinal substances from the group of cardiac glycosides contain an aglycon in their structure, the basis of which is the following:
A. Steroid system and carbohydrate residues
B. Phenanthrenisoquinoline cycle
C. The sterane system and the lactone ring
D. A chain of monosaccharide residues
E. Saturated Anthrocene cycle

110. A distinctive feature of the chemical structure of cardiac glycosides of the digitalis group is the presence in the 10th position of the steroid cycle:
A. Alcoholic hydroxyl
B. Aldehyde group
C. Methyl group
D. Ethoxy groups
E. Phenolic hydroxyl

111. To detect deoxysugars in cardiac glycosides, the pharmacist-analyst should conduct:
A. Legal's reaction
B. Keller-Kiliani reaction
C. Lieberman-Burchardt reaction
D. Raymond's reaction
E. Vitaly-Moren's reaction

112. In the practice of control and analytical laboratories, the following is used to detect the five-membered lactone cycle in the structure of cardiac glycosides:

A. Vitaly-Moren's reaction
B. Rosenheim's reaction
C. Pezet's reaction
D. Legal's reaction
E. Keller-Kiliani reaction

113. According to the SPU, a reaction with a solution of 3,5-dinitrobenzoic acid in an alkaline medium is used to identify the digitoxin substance. In pharmaceutical analysis, this reaction is known as:
A. Kedde's reaction
B. Legal's reaction
C. Lieberman-Burchardt reaction
D. Keller-Kiliani reaction
E. Pezet's reaction

114. According to the SPU, a reaction with a solution of 1,3-dinitrobenzene in an alkaline medium is used to identify the substance ouabain (strophanthin G). In pharmaceutical analysis, this reaction is known as:
A. Keller-Kiliani reaction
B. Lieberman-Burchardt reaction
C. Raymond's reaction
D. Legal's reaction
E. Kedde's reaction

115. The control and analytical laboratory received the digitoxin substance. Determining its benignity, the pharmacist-analyst used a polarimeter. At the same time, he measured:
A. Optical density
B. Angle of rotation
C. Electromotive force
D. Refractive index
E. Melting point

116. There is a certain relationship between the structure and pharmacological action of cardiac glycosides. So, the carrier of biological activity of cardiosteroids is:
A. Sugar component
B. Steroid cycle
C. Lactone cycle
D. Aglycon

E. Alcoholic hydroxyl

117. A distinctive feature of the chemical structure of cardiac glycosides of the strophant group is the presence in the 10th position of the steroid cycle:

A. Alcoholic hydroxyl
B. Ethoxy groups
C. Aldehyde group
D. Phenolic hydroxyl
E. Methoxy groups

118. The Keller-Kiliani reaction is used to identify drugs from the group of cardiac glycosides. What structural fragment allows this reaction to be detected?

A. Lactam cycle
B. Steroid system
C. Aldehyde group
D. Lactone cycle
E. Remains of 2-deoxysugars

119. To identify which structural fragment in drugs of the group of cardiac glycosides in pharmaceutical analysis, a reaction with a solution of sodium nitroprusside in an alkaline medium is used?

A. Angular methyl group
B. Alcoholic hydroxyl
C. Digitoxosis
D. Cyclopentaneperhydrophenanthrene cycle
E. Five-membered lactone cycle

120. Which physico-chemical method, according to the SPU, is used for the quantitative determination of digoxin?

A. ЭЖХ
B. Potentiometry
C. Mass spectrometry
D. Spectrometry
E. IR spectrometry

121. Digitoxin substance was sent to the control and analytical laboratory for analysis. According to the SPU, one of the reactions for identifying this substance is a reaction with a solution of 3,5-dinitrobenzoic acid in an alkaline medium. What color is observed in this case?

A. Purple
B. green
C. red
D. yellow
E. Pink

122. Cardioactive glycosides of the cardenolide group are characterized by the presence in the 17th position of the steroid cycle:
A. Five-membered lactam cycle
B. Four-membered lactone cycle
C. Four-membered lactam cycle
D. Five-membered lactone cycle
E. Aldehyde group

123. In order to identify a medicinal product from the group of cardiac glycosides, the analyst of the laboratory of the State Inspection for Quality Control of Medicinal Products needs to prove the presence of an unsaturated lactone ring. What reagent should he use for this?
A. Alcoholic solution of potassium tetraiodomercurate
B. Acetic acid solution of ascorbic acid
C. Sodium acetate saturated solution
D. The solution is discolored by fuchsin
E. Picric acid alkaline solution

124. When quantifying the substance ouabain (strophanthin G), according to the SPU, the optical density of the tested and standard solutions is measured after adding one of the reagents. Specify this reagent:
A. The solution of sodium picrate is alkaline
B. Sodium nitroprusside solution
C. The sodium acetate solution is saturated
D. Potassium tetraiodomercurate solution is alkaline
E. Fuchsin solution is discolored

125. When testing for the purity of the digoxin substance, it is necessary to determine the specific optical rotation. This research in pharmaceutical analysis is carried out using:
A. Photoelectric colorimeter
B. Refractometer
C. Polarimeter
D. Spectrophotometer

E. Polarograph

126. To detect deoxysugars in the structure of drugs from the group of cardiac glycosides, in the practice of control and analytical laboratories, concentrated sulfuric acid is used together with:

A. A solution of iodine in potassium iodide
B. Hydrogen peroxide with impurities of potassium permanganate
C. Formaldehyde
D. Potassium dichromate in concentrated sulfuric acid
E. Glacial acetic acid in the presence of 0.05% ferrum (III) chloride

127. To identify digitoxin, the pharmacist-analyst prepared glacial acetic acid, a solution of ferrum(III) chloride, as well as concentrated sulfuric acid according to the SPU. This set of reagents is used by the analyst to carry out a reaction known in the pharmaceutical industry
analysis as:

A. Raymond's reaction
B. Keller-Kiliani reaction
C. Lieberman-Burchardt reaction
D. Legal's reaction
E. Kedde's reaction

128. According to the SPU, a reaction with a solution of 3,5-dinitrobenzoic acid in an alkaline medium is used to identify the digitoxin substance. What structural fragment allows this reaction to be detected?

A. Alcoholic hydroxyl
B. Cyclopentaneperhydrophenanthrene cycle
C. Five-membered lactone cycle
D. Digitoxosis
E. Angular methyl group

129. Choose the correct statement about cardiac glycosides from the group of cardenolides:

A. The structure contains a six-membered lactone ring
B. In the steroid cycle, the B and C rings are cis-articulated
C. According to their chemical structure, they are S-glycosides
D. Carbohydrates of sugar parts are in cyclic form
E. The 17α-position of the lactone ring is physiologically active

130. A feature of the chemical structure of cardiac glycosides from the cardenolide group is the presence of the following structural fragment in the 17th position of the steroid cycle:

A. Lactone ring
B. Pyridine cycle
C. The pyrrole cycle
D. β-Lactam ring
E. Thiazolidine cycle

131. In the structure of medicinal substances of the group of cardiac glycosides, aglycones are:

A. Derivatives of cyclopentaneperhydrophenanthrene
B. Derivatives of organic acids
C. Nitriles of mandelic acid
D. Derivatives of phenols
E. Oxyderivatives of anthraquinone

132. The Pezetz reaction is used to determine the presence of deoxysugars in the structure of cardiac glycosides. What reagent is used in this reactions?

A. Ninhydrin
B. Alizarin
C. Xanthhydrol
D. Formaldehyde
E. Salicylic acid

133. The Lieberman-Burchardt reaction is used to identify drugs from the group of cardiac glycosides. What structural fragment allows this reaction to be detected?

A. Steroid cycle
B. Lactone cycle
C. Remains of 2-deoxysugars
D. Aldehyde group
E. Lactam cycle

4.3. Situational tasks:

1. Describe the properties of drugs from the carbohydrate group based on their structure.
2. Explain how optical activity constants are used in the quality analysis of drugs from the carbohydrate group.

3. Explain the phenomenon of mutarotation using the example of glucose. What is the chemical basis of this phenomenon?
4. Suggest possible reagents that can be used to prove the presence of hemiacetal hydroxyl in the structure of glucose and fructose.
5. How is the correction for the moisture content of the original substance taken into account during the quantitative analysis of dosage forms containing anhydrous glucose?
6. Explain the origin and justify the methods of detecting specific impurities in carbohydrate substances: extraneous sugars, soluble starch, dextrins in anhydrous glucose; extraneous sugars, 5-hydroxymethylfurfural and accompanying impurities in fructose.
7. Describe the properties of drugs from the carbohydrate group based on their structure.
8. Explain how optical activity constants are used in the quality analysis of drugs from the carbohydrate group.
9. Explain the phenomenon of inversion using the example of sucrose. What is called "invert sugar"? Explain how the presence of an admixture of invert sugar in sucrose is determined.
10. On the example of sucrose and anhydrous lactose, explain the difference between reducing and non-reducing disaccharides.
11. Explain the origin and justify the methods for detecting the specific admixture of invert sugar in the sucrose substance.
12. Suggest ways to convert the covalently bound halogen (iodine) in amiodarone into an ionogenic state.
13. What is the role of alcohol in alkalimetric titration of amiodarone?
14. What argentometric methods can be used to quantitatively determine potassium chloride? Describe the titration conditions and give the corresponding reaction equations.
15. How does apoatropine admixture get into atropine when it is obtained from plant raw materials?
16. Name the differences in the structure of hyoscyamine and atropine, and the peculiarities of the use of the drugs due to this.
17. Specify the method and justify the conditions for quantitative determination of quinidine, taking into account the presence of a double bond in its structure? Write chemistry.
18. Give evidence of the structure of quinidine (the presence of a quinoline cycle, a double bond, a hydroxyl group, a methoxy group), as well as evidence that quinidine contains tertiary nitrogen atoms and is a base.

19. Explain the need to conduct a control experiment when applying the acid-base titration method in the environment of non-aqueous solvents.
20. Calculate the conversion factors for the quantitative determination of quinidine sulfate by weight method.
21. Justify the necessity of using special conditions for drying raw materials containing cardiac glycosides.
22. Explain the contribution of structural fragments of cardiac glycosides to their biological activity.
23. Determine which structural fragments allow the identification of drugs from the group of cardiac glycosides by chemical methods.
24. Describe the possible methods of quantitative determination of drugs from the group of cardiac glycosides.
25. Justify the need for biological standardization of cardiac glycosides.
26. Justify the peculiarities of storage of drugs from the group of cardiac glycosides, based on their physicochemical properties.

4.4. Tasks:

1. Determine the concentration of an anhydrous glucose solution (%), if it is known that the refractive index of this solution is 1.3557, F = 0.00142, and the refractive index of the solvent is 1.3330.
2. Calculate the concentration of anhydrous glucose (%) in the solution, if the refractive index of the solvent is 1.3330, the solution is 1.3450, F = 0.00142.
3. Determine the value of the specific rotation of anhydrous glucose, if it is known that the angle of rotation of a polarized beam of a 35% solution is +18.60° when measuring it in a cuvette 1 dm long.
4. Determine the concentration of an anhydrous glucose solution, if the angle of rotation of this solution is +7.05°, the layer thickness is 1 dm, and the specific rotation of anhydrous glucose is +53.1°.
5. Determine the concentration of an anhydrous glucose solution, if the angle of rotation for this solution is +5.03°, the layer thickness is 1 dm, and the specific rotation of anhydrous glucose is +53.1°.
6. The magnitude of the specific rotation of fructose is -91.90°. The angle of rotation of its aqueous solution, measured in a cuvette with a length of 100 mm, is -45.95°. Determine the concentration of this solution.
7. Calculate what volume of 0.1 M sodium thiosulfate solution (Kp=1.0000) was spent on the titration of 0.0984 g of glucose monohydrate (M. m. 198.2), if 20.2 ml of titrant was spent in the control experiment , and the content of the active substance in the substance was 99.6%.

8. The refractive index of the mixture containing a mixture of sodium bromide, ascorbic acid and glucose is 1.3547 (n0 = 1.3330). The concentrations of sodium bromide and ascorbic acid were determined titrimetrically - 3.96% and 4.10%, respectively. Refractive index factors F(NaBr) = 0.00134, F(asc. k-ty) = 0.00160, F(glucose) = 0.00142. Determine the concentration of glucose in the mixture.

9. The pharmacist-analyst carries out quality control of the dosage form of the following composition:

10% glucose solution - 100 ml
Ascorbic acid 1.0.

Calculate the quantitative content of glucose in the dosage form, using the following data: the refractive index of the mixture is 1.3478, the refractive index of the solvent is 1.3330; the content of ascorbic acid in 100 ml of the dosage form is 0.90 g; refractive index factor of 1% ascorbic acid solution 0.00160; refractive index factor of anhydrous glucose 0.00142; the moisture content of the glucose used to prepare the mixture is 10%.

10. During chromatography of solutions of anhydrous glucose and anhydrous lactose, the distances from the starting line to the center of the spot of each of the substances were obtained, which were 4.6 cm and 2.3 cm, respectively. At the same time, the distance from the starting line to the front line of the solvent is 10.0 cm. Determine the Rf for each of the carbohydrates.

11. During the chromatography of solutions of fructose and sucrose, the distances from the starting line to the center of the spot of each of the substances were obtained, which were 6.0 cm and 4.3 cm, respectively. At the same time, the distance from the starting line to the front line of the solvent is 12.0 cm. Determine the Rf for each of the carbohydrates.

12. Determine the concentration of the lactose solution, if the angle of rotation for this solution is + 4.12°, the thickness of the layer is 10 cm, and the specific rotation of lactose is +52.5°.

13. Determine the specific rotation of 10% lactose, if the angle of rotation of its aqueous solution, which is measured in a cuvette with a length of 100 mm, is equal to + 5.20°.

14. Calculate what volume of 0.1 M sodium thiosulfate solution (Kp = 1.0000) was spent on the titration of 0.1063 g of lactose (M.m. 360.32), if 19.24 ml of titrant was spent in the control experiment, and the content of the active substance in the substance was 98.84%.

15. Write the reaction equation, calculate the gravimetric factor and the percentage content of quinidine sulfate (M.m. 746.92) in the preparation when determined by the gravimetric method, if it is known that M.m. quinidine base - 324.42,

mass of weighing - 0.4793, mass of weight form - 0.3986 g, loss in mass during drying - 3.8%.

16. Calculate the volume of 0.1 M sodium hydroxide solution (Kp = 1.0000), which is spent on the titration of 0.5018 g of quinidine sulfate (M.m. 746.92), if the content of the active substance in the preparation is 99.2%, and the loss in mass during drying is 4.6%.

17. Calculate the weight of the quinidine sulfate sample (M.m. 746.92), if 12.42 ml of 0.1 M sodium hydroxide solution (Kp = 0.9886) was spent on its titration, and the content of the active substance in the preparation is 99.40% .

18. Calculate the percentage content of atropine sulfate (M.m. 676.8) in the preparation, if the weight of the test piece is 0.4983 g, the volume of a 0.1 M perchloric acid solution (Kp = 0.9892) in the working experiment is 7.42 ml, in the control - 0.21 ml, and the loss in mass during drying - 2.3%.

19. Calculate the weight of atropine sulfate (M.m. 676.8) in the medicinal product, if 6.62 ml of 0.1 M perchloric acid solution (Kp = 0.9982) was spent on the titration. The content of the active substance in the preparation is 98.84%.

20. Determine the mass fraction of atropine sulfate (M.m. 676.8) in the medicinal product, if 7.42 ml of 0.1 M perchloric acid solution (Kp = 0.9892) was spent on the titration of the weight (m = 0.4983 g) .

21. Calculate the specific absorption index and evaluate the quality of digitoxin, if a sample of the substance weighing 0.0201 g was dissolved in 50 ml of ethanol, 5 ml of this solution was transferred to a 50 ml volumetric flask and brought up to the mark with alcohol. 5 ml of sodium picrate was added to 5 ml of the resulting solution. The optical density of the obtained solution at 495 nm was 0.440. The thickness of the used cuvette is 10 mm; the content of digitoxin in the drug is 99.8%. According to AND, the specific absorption index should be from 215 to 235.

22. Calculate the quantitative content and evaluate the quality of celanide, if a sample of the substance weighing 0.0099 g was dissolved in 50 ml of ethanol, 4.5 ml of water was added to 0.5 ml of the resulting solution and the optical density was measured at 222 nm in a cuvette with a thickness of 10 mm Optical density of the solution equals 0.286, the specific absorption index at this wavelength is 140. According to AND, the content of celanide should be at least 99.0%.

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