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DEPARTMENT OF PHARMACEUTICAL, ORGANIC
AND BIOORGANIC CHEMISTRY

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PHARMACEUTICAL CHEMISTRY

ANALYSIS OF MEDICINES THAT AFFECT THE CENTRAL AND PERIPHERAL NERVOUS SYSTEM

Section 2.2

Study and methodical Guide

for 4th year students of the specialty "Pharmacy, Industrial Pharmacy"

Zaporizhzhia
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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.

Most of the drawings were developed by the authors of this study guide.

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 2 consists of three sections:

Section 1 – "Analysis of medicines that affect the central nervous system. General characteristics, classification, relationship of structure with pharmacological action, extraction, methods of analysis, application".

Section 2 - "Analysis of medicines that affect the central and peripheral nervous system. General characteristics, classification, relationship of structure with pharmacological action, extraction, methods of analysis, application".

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

The present Pharmaceutical chemistry guide for 4th year students of the specialty " Pharmacy, Industrial Pharmacy" complies with curriculum and cover most of topics of 8th semester.

Lecture plan

of pharmaceutical chemistry for 4th year students of the Faculty of Pharmacy (8th semester)

No.	Lecture topics	Number of hours
1	Analysis of psychotropic drugs. Medicines for the treatment of parkinsonism. General characteristics, classification, relationship between structure and pharmacological action, methods of preparation, methods of analysis, application in medicine.	**2**
2	Analysis of peripheral vasodilators. General characteristics, classification, relationship between structure and pharmacological action, methods of preparation, methods of analysis, application in medicine.	**2**
3	Analysis of narcotic analgesics. Vomiting and antiemetic drugs. General characteristics, classification, relationship between structure and pharmacological action, methods of preparation, methods of analysis, application in medicine.	**2**
4	Analysis of thyroid hormones, antithyroid drugs. General characteristics, classification, relationship between structure and pharmacological action, methods of preparation, methods of analysis, application in medicine.	**2**
5	Analysis of steroid hormones and their analogues. General characteristics, classification, relationship between structure and pharmacological action, methods of preparation, methods of analysis, application in medicine.	**2**

PLAN

of laboratory practicals and seminar classes on pharmaceutical chemistry for 4th year students of the Faculty of Pharmacy (8th semester)

No.	Lesson topics	Number hours
1.	Analysis of psychotropic drugs: neuroleptics, sedative drugs.	**3**
2.	Analysis of psychotropic drugs: antidepressants, analeptics.	**3**
3.	Analysis of psychotropic drugs: psychostimulants. Medicines for the treatment of parkinsonism.	**3**
4.	**Control lesson from the section.**	**2**
5.	Analysis of peripheral vasodilators.	**3**
6.	Analysis of narcotic analgesics and their analogues. Emetics and antiemetics.	**3**
7.	Analysis of means acting on cholinergic processes. Part 1. Cholinomimetics, anticholinesterase drugs.	**3**
8.	Analysis of means acting on cholinergic processes. Part 2. Cholinergic blockers, ganglioblockers.	**3**
9.	Analysis of agents acting on adrenergic processes: adrenomimetics, adrenoblockers, sympatho mimetics, sympatholytics.	**3**
10.	**Control lesson from the section.**	**2**
11.	Analysis of adrenal medulla hormones (catecholamines), thyroid gland, antithyroid drugs and pancreatic hormones. Synthetic analogues of pharmacological action.	**3**
12.	Analysis of drugs from the steroid hormone group: adrenal cortical hormones (corticosteroids). Synthetic analogues of pharmacological action.	**3**
13.	Analysis of sex hormones: progestogens, estrogens, androgens, anabolic steroids and their analogues. Birth control. Estrogens of nonsteroidal structure.	**3**
14.	**Control lesson from the section.**	**3**

SPECIFIC GOALS:

"Analysis of medicines that affect the central and peripheral nervous system. General characteristics, classification, relationship of structure with pharmacological action, extraction, methods of analysis, application»

- Learn the properties drugs that affect the central and peripheral nervous system.
- Know the main sources and methods of obtaining drugs that affect the central and peripheral nervous system.
- To propose and carry out the selection of physical, physicochemical and chemical methods of quality analysis of drugs that affect the central and peripheral nervous system in accordance with the requirements of the SPhU and other regulatory documentation, as well as Quality Control Methods (QCM).
- Explain the peculiarities of the analysis of drugs that affect the central and peripheral nervous system using physical, physicochemical and chemical methods.
- Interpret the results of studies of the proposed drugs that affect the central and peripheral nervous system, obtained using physical, physico-chemical and chemical methods.
- Explain the peculiarities of storage of drugs that affect the central and peripheral nervous system, based on their physical and chemical properties.

Theoretical material

Antispasmodic drugs(from the Greek spasm - the one that relaxes) are drugs with different chemical structures that cause relaxation of the smooth muscles of internal organs (bronchi, intestines, ureters, ducts of glands) and blood vessels. According to the mechanism of action, they are divided into neurotropic (adrenaline, ephedrine, etc.), the relaxing effect of which is the result of the stimulation of sympathetic nerves, and myotropic (papaverine, no-shpa, euphilin, etc.), which directly affect smooth muscles.

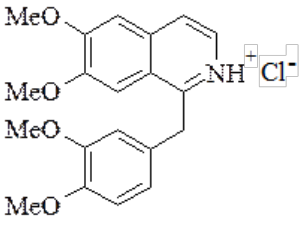
Antispasmodic drugs include peripheral vasodilators.

Peripheral vasodilators are drugs that act on the most distant (distal) areas of the vascular system (arterioles and venules), which determine the stability of peripheral vessels and the deposition of blood in the venous channel. Since the 70s of the last century, the circulatory model has become the main theory of the pathogenesis of chronic heart failure, and peripheral vasodilators have firmly entered the practice of treating patients. The need to act on the vascular bed in chronic heart failure arose from the idea of the integrity of the body's hydrodynamic system: the heart is a pump that "drives" blood through vessels (tubes).

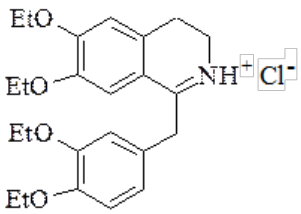
When the heart is damaged and the cardiac output decreases, the perfusion pressure in the vital organs: kidneys, brain, heart drops. In response to this, there is a compensatory "compression" of peripheral arterioles (primarily in the muscles and skin), which allows maintaining the required level of blood supply in the central organs. However, this vascular response increases the "afterload" on the heart (the heart is forced to work against increased peripheral resistance), which contributes to the rapid depletion of its contractile reserve. An increase in the volume of circulating blood, increased blood filling of internal organs and reflex spasm of the venous vascular bed lead to an increase in blood flow to the heart (increased preload), which completes the mechanism of cardiac overload. The use of peripheral vasodilators leads to a significant improvement in the course of heart failure.

Peripheral vasodilators include myotropic antispasmodics.

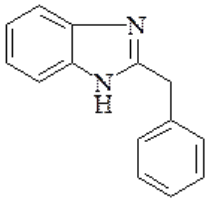
Drugs of this type include papaverine, no-shpa (drotaverine), dibazole, and diprofen. The action of papaverine and no-spi consists in reducing the tone and contractile activity of smooth muscles - hence the vasodilator and antispasmodic effect. These drugs are used for spasms of peripheral vessels, bronchi, brain vessels. For spasms of blood vessels and smooth muscles of internal organs (stomach, intestines, urinary tract, bronchi), Dibazol and Diprofen are also used.



Papaverine

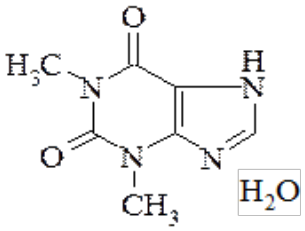


No-shpa (drotaverine)

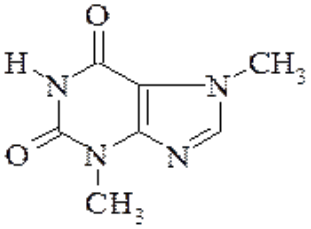


Dibazole

Drugs theobromine, theophylline, euphylline, diprophylline, xanthine nicotinate, pentoxifylline are purine derivatives and have a similar structure. One of the important drugs of this series is theophylline. An important place in the mechanism of action of theophylline is its ability to block adenosine receptors, the stimulation of which in the bronchial muscles can cause bronchospasm. Therefore, the main use of theophylline is as a bronchodilator. The same can be said about euphylline (a drug combining theophylline and ethylenediamine), which is used for bronchial asthma and bronchospasms of various etiologies. Theobromine is used mainly for weak spasms of brain vessels, for edema due to heart or kidney failure.



Theophylline



Theobromine

The above-mentioned myotropic antispasmodics belong to alkaloids and their analogues by action.

ALKALOIDS*–nitrogen-containingorganic bases that are found most often in plants and, as a rule, have an active biological effect.* The main properties characteristic of these compounds determined their name: alkaloid - from the Arabic "like alkali".

Alkaloids are tertiary, rarely secondary amines capable of forming quaternary salts (similar to ammonium salts). Alkaloids are rather weak bases. It should be noted that depending on the structure, alkaloids have different strength of basicity. Thus, codeine exhibits the strongest basic properties ($Kv = 9\times10^{-7}$), the weakest - caffeine ($Kv = 4.1\times10^{-14}$).

The simplest nitrogen-containing compounds (methylamine, trimethylamine and other simple amines), as well as amino acids and their transformation products, although they have a clearly expressed basic character, do not belong to alkaloids. Proteinogenic amines (for example, tyramine) and betaine (stachydrine, trigonelline, etc.) are considered as transitional compounds from simple nitrogen-

containing compounds to alkaloids proper and are sometimes counted among alkaloids.

Physico-chemical properties of alkaloids

The bases of alkaloids are colorless or slightly yellow-brown solid, sometimes liquid (nicotine, anabasine, etc.), bitter-tasting substances. They dissolve in organic solvents (alcohol, ether, benzene, etc.) and, as a rule, are practically insoluble or slightly soluble in water (codeine 1:150, caffeine 1:80, etc.).

Being weak bases, alkaloids form salts, but it is also necessary to pay attention to the fact that alkaloids with weak basicity (Kv = 10^{-10} - 10^{-14}) do not form salts in aqueous solutions (caffeine, theobromine, etc.). Alkaloids of medium basicity (Kv = 10^{-8} - 10^{-10}) do not give salts with organic acids (for example, papaverine with acetic acid). Alkaloids of strong basicity (Kv = 10^{-8} - 10^{-7}) form good salts with acids (atropine, codeine, cocaine, quinine, cytisine, etc.), and their bases in aqueous solutions react with indicators (thymol blue, phenolphthalein, etc.). Salts of alkaloids are easily decomposed under the influence of caustic alkalis, ammonia, and sometimes carbonates and magnesium oxide, while releasing the free bases of alkaloids.

Salts of alkaloids are white crystalline substances, soluble in water, as a rule, practically insoluble or slightly soluble in organic solvents. Some salts of alkaloids (for example, papaverine hydrochloride) are soluble in chloroform, most are soluble in alcohol.

Many alkaloids are optically active substances and have spatial isomers, which affects their biological activity. For example, hyoscyamine (levorotatory) is 2 times more active than atropine (racemate), quinine (left-handed) is an antimalarial drug, quinidine (right-handed) is an antiarrhythmic agent with 50% antimalarial activity.

The physical and chemical properties of alkaloids determine the methods of their extraction from plants, the division of the sum of alkaloids into individual components.

Methods of extracting alkaloids from plant raw materials

Two main methods are used to isolate (extract) alkaloids from pre-dried and crushed plant material:

- allocation of alkaloids in the form of salts;
- allocation of alkaloids in the form of bases.

The steam distillation method is used to isolate liquid and volatile alkaloids (nicotine, pachycarpine).

Methods of separation of alkaloids

It should be taken into account that plants often contain several alkaloids with similar properties, so when they are isolated, a suitable mixture is obtained

("Sum of alkaloids"). Next, it is necessary to separate this mixture - to isolate individual substances from the sum of alkaloids. For this, they use the difference in the physical and chemical properties of the alkaloids themselves or their derivatives.

The following methods are used to separate the amount of alkaloids:

- crushed distillation under vacuum;
- according to the different solubility of alkaloids of bases and salts in organic solvents;
- by different strength of basicity (formation of alkaloid salts);
- according to different adsorption capacity (using different types of chromatography - adsorption, distribution, ion exchange, etc.);
- according to differences in chemical properties (formation of phenolates, nitro derivatives, benzoyl derivatives, ethers, etc.), with subsequent division according to physicochemical properties;
- electrophoresis;
- method of countercurrent distribution and others.

Principles of determining the structure of alkaloids

Establishing the structure of an alkaloid begins with finding out the nature of the carbon skeleton, the presence of functional groups, the nature of the nitrogen atom (aliphatic, heterocyclic, aromatic, primary, secondary, etc.) and oxygen-containing groups. For these purposes, various types of chemical reactions are used, after which the products of cleavage or new compounds are studied, and on the basis of this, assumptions are made about the possible structure of the molecule. Important for determining the structure of alkaloids, namely their heterocyclic part (nitrogen-carbon skeleton), belongs to the "Hoffman" or "Brownian" decay. Currently, various physico-chemical methods (UV, IR, PMR, mass spectroscopy, X-ray structural analysis) are used to determine the structure of substances, which greatly facilitates the task of researchers.

Classification of alkaloids

From the point of view of the chemical structure, alkaloid preparations can be divided into two groups: heterocyclic compounds and substances with an acyclic structure.

I. Acyclic alkaloids and alkaloids with nitrogen in the side chain

1.1. Aliphatic alkaloids

1.2. Aromatic alkaloids

II. Heterocyclic alkaloids

2.1. Pyrrolidine and pyrrolizidine alkaloids.

2.2. Pyridine and piperidine alkaloids.

2.3. Alkaloids with condensed pyrrolidine and piperidine rings.
2.4. Quinolizidine alkaloids.
2.5. Quinoline alkaloids.
2.6. Isoquinoline alkaloids.
2.7. Indole alkaloids.
2.8. Quinazoline alkaloids.
2.9. Purine alkaloids.

III. Diterpene alkaloids.

IV. Steroidal alkaloids (glycoalkaloids).

Alkaloid identification methods

To identify medicinal substances from the group of alkaloids, general (group) reactions are used, which are characteristic of the entire group of substances, and private (specific) reactions are characteristic of this or that individual substance due to the peculiarities of its chemical structure, specific properties, and the presence of certain functional groups.

*General (group) reactions*based on the ability of alkaloids, as bases, to form simple or complex salts with various substances, more often complex acids, salts of heavy metals, complex iodides and others. The products of the interaction of these reagents with alkaloids, as a rule, are insoluble in water, so such reactions are called precipitation reactions, and the reagents are called precipitation reactions.

Of the general alkaloid precipitation reagents, the following are most often used:

1. A solution of bismuth iodide in potassium iodide (Dragendorf's reagent).
2. A solution of iodine in potassium iodide (Wagner, Bouchard, Lugol's reagent). These reagents differ only in the different concentration of iodine in potassium iodide.
3. A solution of mercury iodide in potassium iodide (Mayer's reagent).
4. A solution of cadmium iodide in potassium iodide (Marme's reagent).
5. Phosphoromolybdic acid (Sonnenstein's reagent)
6. Phosphorotungstic acid (Scheibler's reagent).

It should be noted that Dragendorff's reagent is a pharmacopoeial one, because the identification of alkaloids, according to the requirements of the DFU, is carried out by reaction with a solution of potassium iodbismuthate in an acidic medium. At the same time, the appearance of an orange-red precipitate is considered a positive result of the reaction.

In addition to the above-mentioned reagents, picric and picrolic acids, solutions of mercury (II) chloride, tannin, as well as hexachloroplatinic ($H2[PtCl_6]$) and gold chloride ($H[AuCl_4]$) acids, etc., are used for group reactions in

pharmaceutical analysis.

It must be remembered that not all alkaloids form precipitates with the listed reagents, so it is necessary to carry out reactions with at least 4-5 reagents. However, the formation of precipitates does not yet prove the presence of an alkaloid, since in addition to alkaloids, precipitates with precipitation reagents form many other substances containing a tertiary or quaternary nitrogen atom in their structure (most of them are also heterocyclic compounds). Therefore, only the sum of the negative and positive results of the reactions will have an analytical value.

Frequent (specific) reactions are used to detect individual alkaloids. They are due to the peculiarities of the chemical structure and characteristic properties of the analyzed substance. These reactions are based on the processes of dehydration, oxidation, condensation, etc. Most often, the visual effect of such reactions is the appearance of specific staining. Therefore, such reactions are often called staining reactions.

The following reagents are used to perform this group of reactions:

1. Kcenteredsulfuric acid.
2. Aquafortis.
3. A mixture of concentrated sulfuric and nitric acids (Erdman's reagent).
4. A solution of ammonium molybdate in concentrated sulfuric acid (Frede's reagent).
5. A solution of formaldehyde in concentrated sulfuric acid (Markey's reagent).
6. A solution of p-dimethylaminobenzaldehyde in concentrated sulfuric acid (Vazicki reagent) and others.

In addition, specific reactions often include those that are used to detect a group of alkaloids that are close (similar) in structure. For example, the "murexide test" is a reaction specific for alkaloids of the purine group (xanthine); "Taleioquin test" - a reaction characteristic of quinine and its salts; the Vitali-Morena reaction is typical for most alkaloids of the tropane group.

Methods of quantitative determination of alkaloids

Titrimetric (volumetric), gravimetric (weight), as well as physicochemical methods of analysis (photoelectrocolorimetry, spectrophotometry in the visible, UV and IR parts of the spectrum, chromatographic methods) are used for the quantitative determination of alkaloids.

Of the titrimetric (volumetric) methods for determining medicinal preparations from the group of alkaloids, acid-base titration methods are most often used. At the same time, the peculiarities of the analysis of alkaloids-bases and alkaloids-salts should be taken into account.

1. Quantitative determination of medicinal substances from the group of alkaloids-bases. Acidimetry in non-aqueous solvents is most often used for quantitative determination of this group of substances. The main advantage of this method is that the medicinal substance is determined by the physiologically active part of the molecule. For analysis, the alkaloid substance is dissolved in an acidic (protogenic) non-aqueous solvent or a mixture of solvents in which the degree of ionization of the bases increases. In the practice of pharmaceutical analysis, when titrating organic bases, glacial acetic acid (CH_3COOH content of at least 98.0% m/m) is most often used as a solvent, and a standard solution of perchloric acid $HClO_4$ in glacial acetic acid is used as a titrant. The chemical processes taking place during the titration of alkaloids-bases under such conditions can be represented by the following reactions.

1) Dissolving perchloric acid in glacial acetic acid:

$$HClO_4 + CH_3COOH \rightleftharpoons CH_3COOH_2+ + ClO_4^-$$

2) Dissolving the alkaloid base (R_3N) in glacial acetic acid:

$$R_3N + CH_3COOH \rightarrow [R_3NH]^+ + CH_3COO^-$$

3) Interaction of a protonated base with a perchlorate ion:

$$[R_3NH]^+ + ClO_4^- \rightarrow [R_3NH]^+ \cdot ClO4^-$$

4) Interaction of acetonium and acetate ions:

$$CH_3COOH_2^+ + CH_3COO^- \rightarrow 2CH_3COOH$$

Total reaction: $R_3N + HClO_4 \rightarrow [R_3NH]^+ \cdot ClO_4^-$

To fix the end point of the titration of organic bases in non-aqueous media, a crystal violet indicator is usually used or it is set potentiometrically.

Acidimetric titration in aqueous (cytisine) or alcohol-aqueous (codeine) solutions is used for substances that exhibit pronounced basic properties. In this case, there can also be the opposite method of acid-base titration, i.e. adding an excess of a titrated acid solution to the preparation, the excess of which is titrated with an alkali solution.

Theobromine and theophylline are quantitatively determined by the method of alkalimetry by substitute (indirect alkalimetry). This method is based on the acidic properties of these alkaloids and their ability to form insoluble silver salts with the release of equivalent amounts of nitric acid, which is titrated with a standard sodium hydroxide solution using the phenolic red indicator.

2. Quantitative determination of medicinal substances from the group of alkaloids-salts.

For the quantitative determination of alkaloid salts, the method of acidimetry in a non-aqueous medium can be used. Here it is important to note that the dissociation of weak carboxylic acids in glacial acetic acid is completely suppressed. This makes it possible to quantitatively titrate organic salts of alkaloids

based on perchloric acid (platyphyllinum hydrotartrate, spherophysin benzoate, etc.). The dissociation of strong mineral acids is suppressed by acetic acid only partially, therefore, when titrating salts with hydrohalic acids ($R_3N \cdot XX$), a solution of mercury (II) acetate prepared in anhydrous acetic acid is additionally added. This is necessary for the binding of hydrohalic acids into poorly dissociated compounds (HgX_2), which do not interfere with the determination of:

$$2R_3N \cdot HX + (CH_3COO)2Hg \rightarrow HgX_2 + 2[R_3NH]+ \cdot CH_3COO^-$$

Modified alkalimetric titration methods are also used for the quantitative determination of alkaloid salts. For example, if the alkaloid salt is formed by a weak base (papaverine hydrochloride, pilocarpine hydrochloride), the titration is carried out in an aqueous-alcohol medium. At the same time, alcohol contributes to reducing the basicity of the organic base formed in the titration process. If the salt of the alkaloid is formed by a base, the strength of which is sufficient to change the color of the indicator (atropine sulfate, quinine hydrochloride, etc.), then the titration is carried out in the presence of not only alcohol, but also an organic solvent that does not mix with water (chloroform, diethyl ether) . An alkaloid base is formed, which is extracted with an organic solvent and, thus, does not affect the indicator.

To determine the quantitative content of medicinal substances from the group of alkaloid salts, precipitation methods, namely argentometry and mercurimetry, can be used. In addition, other methods have been developed, which are based on precipitation reactions, for example, the iodometric method (based on the reaction of the formation of polyiodides), the complexonometric method (based on the reaction with the Marme precipitating reagent).

*Gravimetric (weight) method*quantitative determination of alkaloids consists most often in the fact that the base of the alkaloid is extracted with an organic solvent, then the solvent is distilled off, the residue is dried to a constant mass, cooled and weighed. The mass of the base of the alkaloid, if necessary, is converted to the mass of the corresponding salt. After that, the content of the analyzed substance is calculated. It should be noted that gravimetric analysis is more accurate than titrimetric analysis. However, due to the duration and complexity of the implementation, it was not widely used for the quantitative determination of alkaloids.

The use of physical and chemical methods (photoelectrocolorimeter, spectrophotometers in the visible, UV and IR parts of the spectrum, chromatography, polarography, polarimetry, etc.) in the analysis of the quality of medicinal substances from the group of alkaloids is characterized by greater expressiveness, sensitivity, selectivity, the possibility of unification and automation, as well as increasing the reliability of the obtained results.

Narcotic analgesics- these are medicinal products of natural (plant and animal), semi-synthetic and synthetic origin, which have a significant pain-relieving effect with a predominant effect on the central nervous system, as well as the ability to cause mental and physical dependence (drug addiction).

The classification of means of this group is determined by the nature of their action. They are divided into agonists, that is, painkillers, their antagonists and synergoantagonists (partial antagonists), they can also be systematized depending on the sources of production: plant, animal, synthetic.

Classification of narcotic analgesics

Agonists

1. Plant origin:
   a) galena preparations (powder and extractopia);
   b) neogalen preparations (omnopon);
   c) alkaloids (morphine hydrochloride, codeine phosphate).
2. Animal origin (derivatives of eikephalins, endorphins).
3. Synthetic and semi-synthetic (ethylmorphine hydrochloride, promedol, fentanyl, tramadol, piritramide).

Synergoantagonists(pentazocine hydrochloride and lactate nalorphine hydrochloride, buprenorphine, butorphanol).

Antagonists(naloxone, naltrexone).

Note. Nalorphine combines the properties of both an agonist (relieving pain) and an antagonist (increasing blood pressure, stimulating breathing, etc.) of narcotic analgesics.

According to the chemical structure, narcotic analgesics can be divided into derivatives:

- phenanthrene (morphine, codeine, omnopon);
- phenylpiperidip (promedol, fentanyl);
- morphine (naloxone);
- benzomorphan (pentazocine).

Morphine is the standard of the group of narcotic analgesics. It is obtained from opium. Therefore, the drugs of this group are also called opiates (contained in opium) and opioids (their synthetic analogues). Narcotic analgesics are sometimes called morphine-like agents.

Opium (Greek *Opos* - juice) is milky juice from unripe capsules of sleeping poppy (Papaver somniferum), dried in the air. Opium can contain up to 10-20% morphine. Some of it is found in poppy straw and possibly in other types of poppy. Opium is one of the oldest medicines. Records of its use were found among the

Egyptians and Sumerians (4000-5000 years ago). Hippocrates and Avicenna talk about this remedy.

Opium is a complex mixture of mineral and organic substances: alkaloids, proteins, mucus, pectins, acids, rubber, dyes. The main compounds of opium are alkaloids. These arc-like substances contain nitrogen and can form salts with acids. More than 20 alkaloids have been obtained from opium. Alkaloids (bases) are non-polar compounds that are not soluble in water; their salts acquire polar properties: they dissolve in water and are used in liquid medicinal form.

New galenic drug opium (purified from ballast substances) - omnopon. It contains all opium alkaloids in the form of chlorides. Its effect, like opium, is due to the content of morphine (about 50%). According to their chemical structure, all opium alkaloids are divided into two groups: derivatives of piperidinephenanthrene (morphine, codeine, thebaine) and benzylisochiioline (papaverine, narcotine, noscapine, etc.).

Phenanthrene derivatives have a clear neurotropic effect, cause a reduction in the feeling of pain, and also lead to drug addiction. Alkaloids of the second group are characterized by antispasmodic activity, the ability to eliminate spasm of the smooth muscles of the intestines, bronchi, and blood vessels, as a result of which they are used in diseases of the digestive system, respiratory system, and circulatory system.

A representative of alkaloids of the phenanthrene series is morphine, a classic narcotic analgesic. For the first time, morphine was isolated from opium in 1803 by the German pharmacist Serturner, who established the hypnotic effect of the drug and named it after the god of sleep, Morpheus.

The synthesis of morphine was carried out only in 1952 p., but this method did not spread due to its complexity and low cost-effectiveness.

According to the chemical structure, morphine consists of several groups. The quaternary carbon atom is connected to the phenyl group and connected to nitrogen by a chain of two carbon atoms. One group near the nitrogen atom is a small alkyl radical. The phenolic hydroxyl contained in the non-hydrogenated ring of the phenanthrene nucleus has a certain influence on the action of morphine. Replacing it with a methoxy (codeine) or ethoxy group (ethylmorphine) leads to a weakening of the analgesic effect.

Ethylmorphine hydrochloride (dionine) is similar in pharmacological properties to codeine. It has a slight pain-relieving effect, does not cause euphoria in therapeutic doses. It is prescribed as an antitussive. The solutions are used in ophthalmology for keratitis, corneal infiltrates, inflammation of the iris, etc.

Among derivatives of phenylpiperidine, promedol (trimeperidine) and fentanyl deserve the most attention.

Promedol is an analogue of meperidine. Its analgesic activity is 5-6 times less than that of morphine. Depresses the respiratory center. Tolerance and dependence develop more slowly than morphine. It has a significant antispasmodic effect. Little toxic for young children, safe for pregnant women, as it almost does not penetrate the placental barrier. A positive property of promedol is a fairly high analgesic efficiency at the initial stages of ontogenetic development, which is possibly due to its effect on subcortical structures.

Fentanyl is a short-acting analgesic. The effect begins 2-3 minutes after intravenous administration and lasts 30-40 minutes. It is 100 times more powerful than morphine in its analgesic effect. Causes significant respiratory depression. It can cause spasm of the bronchial muscles, stiffness of the muscles of the chest and limbs, sinus bradycardia.

It is prescribed for neuroleptanalgesia in combination with droperidol, as well as for premedication, in case of myocardial infarction, injuries.

It is rational to administer fentanyl under the control of an antagonist (naloxone, nalorphine), which eliminates the side effects of the analgesic.

Antagonists of morphine and its analogues - naloxone (Narcan), naltrexone - completely eliminate the side effects of analgesics, are effective antitoxic substances (antidotes).

A group of synergoantagonists, partial antagonists of morphine used in medical practice is of considerable interest.

Nalorphine hydrochloride has a predominant antagonistic effect, but it is also able to increase the threshold of pain sensation. Its negative property is psychotomimetic action - the ability to cause mental disorders, even hallucinations, which limits the use of the drug for analgesia.

Synergoantagonists also include promising drugs such as pentazocine, buprenorphine, nalbuphine, butorphanol.

Pentazocine is a derivative compound of benzomorphan. Acts mainly on k-receptors. In terms of analgesic effect, it is 3-6 times inferior to morphine, it causes respiratory depression similar in strength. It has the ability to increase blood pressure as a result of increasing the tone of the sympathetic nervous system. Causes tachycardia, worsens coronary blood circulation. The advantage of pentazocine is weak penetration through the placenta, which makes it possible to use it in obstetric practice. Has a beneficial effect on the child's body; combines fairly effective analgesia with negligible toxicity.

Tramadol (Tramal) is a phenanthrene derivative. In terms of analgesic effect, it is 5-10 times weaker than morphine, analgesia occurs quickly and lasts about 9 hours. You also have means that increase the excitability of the respiratory center (carbogen inhalation - a mixture of 5-7% carbon dioxide and 93-95% oxygen,

controlled breathing, administration of analeptics). Reflex stimuli that prevent the development of a soporose state (mustards, rubbing, cold dousing) have a positive effect. Atropine sulfate is repeatedly administered to reduce the tone of the parasympathetic nervous system and increase the excitability of the respiratory center. The therapeutic dose does not suppress breathing and does not have a negative effect on blood circulation. Nausea, vomiting, and respiratory depression can be side effects.

Codeine and ethylmorphine hydrochloride are prescribed as antitussives. If the cough is accompanied by bleeding and poses a threat to life, morphine is indicated, which has a strong inhibitory effect on the cough center.

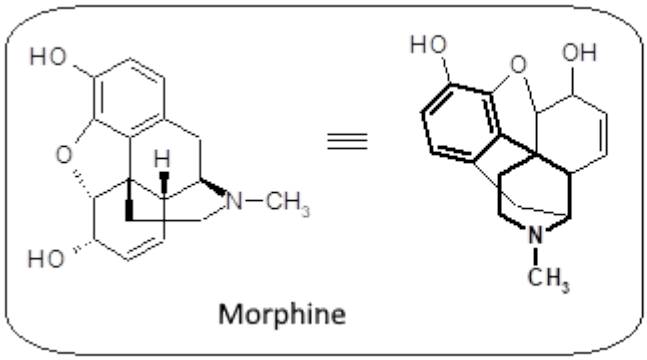
Contraindications: brain injury (increases intracranial pressure); in pediatric practice: high toxicity (promedol, fentanyl, pentazocine are administered).

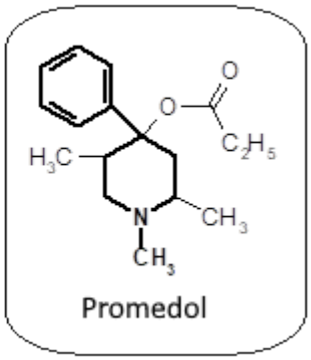
Emergency aid. Administer gastric lavage with a 0.05% solution of potassium permanganate, which oxidizes the alkaloid, inject activated carbon, a sorbent. The most effective means of treatment for acute morphine poisoning are opioid system antagonists naloxone, naltrexone, in particular partial antagonists, such as nalorfip

Aspects of the creation of synthetic drugs based on modifications of the "leader structure" from the group of natural alkaloids

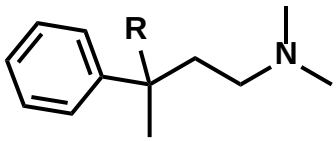
When considering approaches to the creation of medicinal products by modifying the "leader structure" from the group of natural alkaloids, attention is drawn to analgesic preparations obtained on the basis of the morphine alkaloid with the preservation of elements of its structure or its simplification. This principle made it possible to obtain a number of drugs that differ in strength and duration of pain-relieving action, speed and degree of development of addiction, addiction and other side effects.

Thus, the group of the most important analgesics, derivatives of piperidine, dates back to the 1940s, when promedol was synthesized based on the study of the "structure-action" relationship in a number of morphinan alkaloids and the idea of simplifying their structure. According to its chemical structure, this analgesic can be considered as an analogue of the phenyl-N-methylpiperidine part of the morphine molecule, a modified representation of the formula of which is given below for clarity in comparison with the promedol formula (in the form of bases):





Later, the discovery of analgesic activity in a large series of 4-phenylpiperidine derivatives (promedol, fentanyl, prosidol, etc.) led to the formulation of the Beckett-Casey rule, which, despite some simplification, proved to be useful at a certain stage of creating narcotic analgesics. According to this rule, the modeling and construction of a potential narcotic analgesic (interaction with opiate receptors) requires, first, the presence of a quaternary carbon atom and an aromatic ring at this atom. Secondly, it is necessary to have a tertiary nitrogen atom at a distance equivalent to two carbon atoms in sp3 hybridization from the specified quaternary carbon atom:



R=-$COOCH_3$, -$COOC_2H_5$, -$CONH_2$, -$OCOC_3H_7$, -OC_2H_5, H-C_3H_7

According to the latest data, the aromatic ring near the quaternary carbon atom can be replaced by a piperidine ring (pyritramide), a phenylamino group (fentanyl, remifentanil), substituted with benzene, etc. It is also important that the expansion of the six-membered piperidine ring to the seven-membered one (egoheptazine) or the narrowing of the heterocycle to the pyrrolidine ring (prolidin), as well as its replacement with phenyl (estocin) or cyclohexane (tramadol) do not lead to a decrease in analgesic activity. In addition, the above-mentioned rule is observed not only in the case of an oxycarbonyl substituent (see R) at a quaternary carbon atom, but also if this substituent is replaced by hydroxyl, acyloxyl, amide, alkyl and other functional groups.

Many medicines (medical means) provide medical action,influencing specific way on transmission nervous excitation in endings peripheral nerves.WITHandoilandhontransfer excitation in central and peripheral nervous system is carried out by participation endogenous chemical substances–neurotransmitters.To numbers neurotransmitters are relatedacetylcholine, norepinephrine, dopamine, serotonin, etc. The receptors with which they bind are called cholinergic, adrenergic, dopaminergic, etc., respectively.

To cholinergic agentsinclude cholinomimetics and cholinoblockers.

The autonomic nervous system consists of sympathetic and parasympathetic systems. Sympathetic nerve fibers originate from special cells of the thoracic and lumbar regions of the spinal cord. Parasympathetic nerve fibers originate from cells of the brain stem and from cells (segments) of the spinal cord.

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Pharmacological substances that affect efferent innervation (afferent systems process information coming to the brain from receptors, and efferent systems - information that goes from the brain to effectors (muscles, glands), act in the area of contacts between the ends of nerve fibers and cells (nerve cells or tissue cells) on which they end. Such contacts are called the term "synapse" - connection. In all synapses, excitation is transmitted with the help of special substances - mediators.

Mediators are released by nerve fiber endings and affect cell receptors. The action of the mediator is short-lived, the subsequent excitation of nerve fibers causes the release of a new portion of the mediator, etc.

Postganglionic sympathetic fibers secrete noradrenaline as a mediator, with the help of which excitation is transmitted from sympathetic nerve fibers to the cells of organs and tissues. In autonomic ganglia and sympathetic and parasympathetic nervous systems, in synapses formed by the endings of postganglionic fibers of the parasympathetic nervous system and cells of organs and tissues, in neuromuscular synapses (contacts of motor nerves with skeletal muscle cells) the mediator (transmitter of excitation) is acetylcholine.

Nerve fibers that release norepinephrine are called adrenergic, and those that release acetylcholine are called cholinergic. Receptors of the cell membrane, disturbed respectively by acetylcholine and norepinephrine, are also called cholinergic and adrenergic.

Substances that stimulate cholinergic receptors are called cholinomimetics. In addition, anticholinesterase substances are used, which block acetylcholinesterase and thus slow down the breakdown of acetylcholine.

Cholinergic receptors of different synapses show different sensitivity to different pharmacological substances. Postganglionic nerve endings of the parasympathetic nervous system are sensitive to the excitatory effect of muscarine (alkaloid of amanita mushrooms). Such receptors are called M-cholinoceptors (muscarinic-sensitive). The remaining cholinergic receptors of efferent innervation show high sensitivity to nicotine (a tobacco alkaloid), therefore they are called H-cholinergic receptors (nicotine-sensitive).

Cholinomimetics divided into three groups:

1) substances that mainly stimulate M-cholinergic receptors (M-cholinemimetics): pilocarpine;

2) substances that stimulate H-cholinergic receptors (H-cholinemimetics): cytisine;

3) substances that simultaneously excite both receptors (M, H-cholinemimetics): acetylcholine, carbachol.

Pilocarpine is an alkaloid of a plant that grows in South America. Toxic, used only locally in ophthalmic practice - narrows the pupil of the eye (causes the contraction of the circular muscle of the iris), as a result of which the corners of the anterior chamber of the eye open, the outflow of intraocular fluid increases, the intraocular pressure decreases, which is used to treat glaucoma (a disease in which which sharply increases intraocular pressure) in the form of eye ointment or drops. Side effect - spasm of accommodation (setting the eyes for near vision), impaired vision.

Cytisine is an alkaloid of thermopsis grass. As part of Tabex tablets, it is used as an adjunct in the fight against tobacco smoking – it weakens the withdrawal symptoms when smoking is stopped, and smoking becomes unpleasant against its background.

M, H-cholinemimetic of direct action - carbachol ("MIO-COL"), obtained after changing the structure of acetylcholine, works up to 1.5-2 g. In the form of eye drops, it is used for the treatment of glaucoma.

Such drugs as neostigmine ("Proserin"), pyridostigmine bromide ("Kalimin"), distigmine bromide ("Ubretide"), galantamine ("Nivalin", "Reminil"), donepezil ("Narkoz") temporarily block acetylcholinesterase.

Anticholinesterases drugs are used for the treatment of glaucoma (neostigmine, galantamine), treatment of myasthenia gravis (a disease in which muscle weakness develops as a result of impaired transmission of excitation in neuromuscular synapses, - proserin, kalimin). Proserin is used as an antidote for an overdose of muscle relaxants.

M-choline blockers block the influence of the parasympathetic nervous system on internal organs. Thus, their action is the opposite of the effects associated with disruption of the parasympathetic nervous system.

Ganglioblockers are agents that block the transmission of excitation in autonomic ganglia (parasympathetic and sympathetic), as well as H-cholinergic receptors of the cells of the medulla of the adrenal glands. As a result, peripheral vessels expand and blood circulation improves, blood vessels (arterial and venous) expand and blood pressure decreases, the secretory and motor functions of the stomach and intestines deteriorate.

Curare-like drugs, or muscle relaxants, cause relaxation of skeletal muscles.

The transmission of excitement from the postsynaptic nerve endings of the sympathetic nervous system to efferent cells occurs with the help of adrenaline-like substances (adrenaline, norepinephrine, dopamine).

Postganglionic sympathetic fibers secrete noradrenaline as a mediator, with the help of which excitation is transmitted from sympathetic nerve fibers to the cells of organs and tissues. Nerve fibers that release norepinephrine are called adrenergic, and those that release acetylcholine are called cholinergic.

An adrenergic synapse is formed by an adrenergic nerve and a cell (smooth muscle, secretory cells). Similar synapses are located in the central nervous system.

Substances that stimulate adrenoceptors are called adrenomimetics. They are divided into:

a) adrenomimetics of direct action - those that, like norepinephrine, activate adrenoceptors by direct interaction with them;

b) adrenomimetics of indirect action, or sympathomimetics, are those that contribute to the release of norepinephrine from presynaptic endings.

Substances that block adrenoceptors are called adrenoblockers, or adrenolytics.

Substances that reduce the effects of adrenergic innervation by reducing the amount of mediator in the synaptic cleft are called sympatholytics.

Depending on the effect on certain adrenoceptors and the direction of the resulting effects, adrenergic drugs are divided into the following groups:

I. Adrenomimetics

1. α- and β-adrenomimetics (adrenaline hydrochloride, norepinephrine hydrotartrate)
2. dopamine-, α- and β-adrenomimetics (dopamine)
3. α-adrenomimetics (mezaton, naphthyzine, galazolin)
4. β-adrenomimetics (izadrine, salbutamol, fenoterol, terbutaline, dobutamine)

II. Sympathomimetics (ephedrine hydrochloride)

III. Adrenoblockers

1. α-adrenoblockers (phentolamine, tropafen, prazosin, piroxan)
2. β-blockers (anaprilin, atenolol, talinolol, acebutolol)
3. α- and β-blockers (labetalol)

IV. Sympatholytics (reserpine, octadine).

Depending on the chemical structure, adrenomimetic substances can be divided into two groups. The first is substances that have a hydroxyl group in positions 3 and 4 of the benzene ring. They are called catecholamines. These

include norepinephrine, adrenaline, dopamine, isadrin. The second group is non-catecholamine substances (mezatone, ephedrine).

Adrenomimetic substances.

Adrenaline (epinephrine) is an adrenal medulla hormone that is used in the form of adrenaline hydrochloride.

Mesaton (phenylephrine) is a synthetic α1-adrenomimetic agent of direct action.

Naphthysine is an α2-adrenomimetic of direct action. When applied to the mucous membranes, it causes long-term vasoconstriction, which is accompanied by a decrease in edema and an anti-inflammatory effect.

Galazolin, or xylometazolin, is an α2-adrenomimetic that is pharmacodynamically close to naphthyzine. It is used to reduce swelling of mucous membranes in rhinitis, sinusitis, laryngitis of inflammatory and allergic origin.

Izadrin (isoprenaline, novodrin, euspiran) is a synthetic catecholamine that is a strong stimulator of β_1- and β_2-adrenoceptors.

Salbutamol (Ventolin) is a selective β_2-adrenomimetic of direct action.

Sympathomimetics

Ephedrine hydrochloride (Ephedrini hydrochloridum) is an alkaloid of plants of the genus Ephedra, which has indirect α- and β-adrenomimetic (sympathomimetic) activity.

Ephedrine stimulates the central nervous system.

Antiadrenergic substances.

For adrenoblocking, or antiadrenergic, agents, blocking of adrenoceptors with disruption of their interaction with norepinephrine is characteristic. The synthesis of the mediator does not change. As already mentioned, the substances of this group include α- and β-blockers.

α-adrenoblockers include alkaloids of ergot (ergotamine), their dihydrogen derivatives (dihydroergotamine), as well as synthetic drugs (phentolamine, tropafen, prazosin).

β-blockers are a group of drugs that block β-adrenergic receptors, preventing the effect of norepinephrine on them. These drugs include anaprilin (propranolol, obzidan), oxprenolol (trazicor), talinolol (cordanum), atenolol, acebutolol, timolol.

Bisoprolol ("konkor") is a highly effective β_1-AB, characterized by the greatest selectivity and potency.

Sympatholytics

Sympatholytics include reserpine and octadine. These agents act presynaptically, at the level of varicose thickenings of adrenergic nerves, contribute to the depletion of norepinephrine reserves, which leads to the blockade of nerve impulse conduction. They do not affect adrenoceptors.

Reserpine is an alkaloid from the Rauwolfia plant. Blood pressure decreases under the influence of the drug. This happens due to the expansion of blood vessels and a decrease in the frequency and force of heart contractions. The maximum hypotensive effect develops after 5-7 days of regular administration of the drug. After a course of treatment, the effect can last for two weeks.

Reserpine is indicated for the treatment of various forms of hypertension.

LESSON No. 1

1. TOPIC: Analysis of peripheral vasodilators.

2. PURPOSE: To master the methods of analysis of medicinal products from the group of psychotropic drugs such as neuroleptics and sedative drugs.

3. TARGETS:

3.1. To study the structure, nomenclature, synonyms, physicochemical properties, sources and methods of obtaining medicines from the group of peripheral vasodilators.

3.2. To study the methods of analysis of the considered group of medicinal products according to the SPhU, 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. Consider the peculiarities of the analysis of drugs from the group of peripheral vasodilators 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 peripheral vasodilators, based on their physicochemical properties.

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

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. Definition of "peripheral vasodilators", "myotropic antispasmodics".
2. Definition of the term "alkaloids". General characteristics, distribution in nature, principles of classification of alkaloids. Chemical classification of alkaloids.
3. Sources of obtaining alkaloids. General methods of extracting alkaloids from plant raw materials. Methods of dividing the sum of alkaloids.

4. General methods of identification of alkaloids. General alkaloid (precipitating) and special reagents, their composition. Chemical processes underlying the interaction with alkaloids. Reaction performance technique.
5. General methods of quantitative determination of medicinal substances from the group of alkaloids. Peculiarities of quantitative determination of medicinal substances from the group of alkaloids-bases and alkaloids-salts.
6. Sources of production, chemical structure, nomenclature, synonyms, physicochemical properties of medicinal substances from the group of alkaloids, isoquinoline derivatives, purine.
7. To justify the use of chemical and instrumental methods in the analysis of the quality of drugs from the group of alkaloids, isoquinoline derivatives, and purine.
8. Ways of entry and determination of specific impurities in the analysis of the quality of drugs from the group of alkaloids of isoquinoline, purine derivatives.
9. Medicines from the group of alkaloids, Isoquinoline derivatives. Write the structural formula and Latin name of papaverine hydrochloride. Describe the properties of the drug as a nitrogenous base and give reactions confirming these properties. Specify the reactions based on the restorative properties of the drug.
10. Give possible methods for the quantitative determination of papaverine hydrochloride. Explain the role of alcohol in the quantitative determination of papaverine hydrochloride by DFU.
11. Justify the application of the acid-base titration method in the medium of non-aqueous solvents for the determination of papaverine hydrochloride, specify the conditions.
12. Write the structural formulas, Latin names of analogs of papaverine hydrochloride by action: bendazole hydrochloride (dibazole), drotaverine hydrochloride (no-shpa). Describe the properties, analysis. Application.
13. Medicines from the group of alkaloids, purine derivatives. Theobromine. Theophylline. Theophylline monohydrate. Structure, nomenclature, preparation, properties, analysis, application.

    13.1. Describe the relationship between the chemical structure of medicinal substances of this group and their physicochemical properties (solubility in water, in relation to acids and alkalis) and biological activity.

    13.2. Describe the acid-base properties of medicinal substances of the purine group depending on the chemical structure of the molecules. Tautomeric transitions are possible, the preferred state depending on the conditions.

    13.3. Murexide test as a general group reaction to drugs from the group of alkaloids, purine derivatives. Reaction mechanism, its specificity, conditions and performance technique.

13.4. Acid-base properties of purine derivatives and complexation reactions with salts of heavy metals (silver, cobalt, copper). Conditions for carrying out reactions, their importance in the analysis of the quality of drugs from the group of alkaloids, purine derivatives.

14. Identification of drugs from the group of alkaloids, purine derivatives, based on their physicochemical properties and features of the chemical structure.

15. Describe the possible methods of quantitative determination of drugs of this group, the conditions for their implementation. Give the corresponding reaction equations, calculation formulas.

16. Medicines from the group of salt forms of purine alkaloids. Themisal. Theophylline-ethylenediamine (euphylline). Structure, nomenclature, preparation, properties, analysis, application.

17. Medicines from the group of synthetic derivatives of purine alkaloids. Pentoxifylline. Diprofylline. Xanthine nicotinate. Structure, nomenclature, properties, analysis, application.

18. Featuresstorage of medicines from the group of alkaloids, isoquinoline derivatives, purine, as well as their synthetic analogues, based on their physicochemical properties. Factors affecting the stability of preparations of this group of substances and changes occurring under their influence.

19. The main dosage forms, created on the basis of medicinal substances from the group of alkaloids, isoquinoline derivatives, purine. Relationship of structure with biological action.

4.3. Test tasks:

#

1) Choose the correct definition of "alkaloids":

- Carbohydrates of vegetable origin, which are part of various essential oils
- A large group of organic substances, mainly of plant origin (rarely animal), the molecules of which consist of a sugar residue, as well as a residue of one or another organic compound
- Substances of different chemical structure, necessary in small quantities for the normal functioning of the body
- Substances that are produced by microorganisms, higher plants, and animal tissues in the process of their vital activity and are able to exert a selective bactericidal and bacteriostatic effect on microorganisms, viruses, protozoa
- Nitrogen-containing bases, which are found most often in plants and, as a rule, have an active biological effect

#

2) Specify the group reaction for the identification of alkaloids of the purine series:

- Formation of azo dye
- Formation of benzylidene derivatives
- Formation of ammonium salts of purpuric acid derivatives
- The formation of base sediments
- Formation of colored precipitates with copper salts

#

3) Indicate which method is recommended by the DFU for the quantitative determination of theobromine:

- Acidimetry in non-aqueous solvents
- Argentometry
- Substitute acid-base titration
- Iodometry
- Nitritometry

#

4) In the analitycal laboratory of the pharmaceutical enterprise, the quantitative content of theophylline is determined by the method of indirect neutralization. At the same time, alkalimetric titration of nitric acid is carried out, which is quantitatively released as a result of the formation of:

- Potassium salt of theophylline
- Sodium salt of theophylline
- Ammonium salt of theophylline
- Copper salt of theophylline
- Silver salt of theophylline

#

5) Quantitative content of theophylline monohydrate, in accordance with the requirements of the SPhU, is determined by the method of alkalimetry by substitution. The titrant in this method is a standard solution:

- Sodium hydroxide
- Hydrochloric acids
- Potassium bromate
- Sodium edetate
- Ammonium oxalate

#

6) The pharmacist-analyst must confirm the presence of ethylenediamine in the composition of Euphilin. Which of the listed reagents can be used to identify ethylenediamine?

- Sodium hydroxide
- Potassium chloride
- Ammonium oxalate
- Cuprum (II) sulfate
- Glyoxalhydroxyanil

#

7) For the quantitative determination of euphilin by ethylenediamine, a titrated solution is used:
- Sodium hydroxide
- Hydrochloric acid
- Sodium nitrite
- Iodine
- Sodium edetate

#

8) Indicate which of the medicinal products by chemical nature is not a derivative of purine alkaloids:
- Xanthine nicotinate
- Euphilinus
- Ephedrine hydrochloride
- Theobromine
- Themisal

#

9) Indicate which of the following titrimetric methods of analysis is used to quantify theophylline:
- Permanganatometry (direct titration)
- Complexonometry (back titration)
- Alkalimetry (substitute titration)
- Acidimetry (direct titration)
- Nitritometry (direct titration)

#

10) Indicate which of the following reagents cannot be used to identify temisal:
- Iron (III) chloride
- Cobalt (II) chloride
- Concentrated hydrogen peroxide, hydrochloric acid, ammonia solution
- Sodium nitrite
- Silver nitrate

#

11) Indicate which heterocycles the condensed purine system includes:

- Pyridine and pyrazine
- Pyrazole and pyrimidine
- Imidazole and furan
- Pyrimidine and imidazole
- Pyrazine and pyrimidine

#

12) The reaction of an aqueous solution of euphilin:

- Sour
- Neutral
- Alkaline
- Euphilin does not dissolve in water

#

13) Name the reagent that cannot be used to distinguish theophylline from caffeine:

- Ammonia solution
- Marky's reagent
- Cobalt chloride solution
- Silver nitrate solution
- Sodium nitroprusside solution

#

14) Specify the drug that forms a purple color with a solution of cobalt chloride, followed by the formation of a grayish-blue precipitate:

- Caffeine
- Theophylline
- Theobromine
- Euphilinus
- Caffeine monohydrate

#

15) List the reagents necessary for the formation of silver salts of theobromine and theophylline:

- A solution of sodium hydroxide and silver nitrate
- Tannin solution
- A solution of acetic acid and silver nitrate
- Nitric acid and silver nitrate solution
- Perhydrol or bromine water

#

16) The general group reaction to alkaloids, purine derivatives - the murexide test - is based on a chemical process:

- Recovery
- Electrophilic substitution
- Oxidation
- Nucleophilic addition
- Complex formation

#

17) State what Wagner's reagent is:

- A solution of bismuth iodide in potassium iodide
- A solution of mercury (II) iodide in potassium iodide
- A solution of iodine in potassium iodide
- A solution of cadmium chloride in potassium iodide
- Tannin solution 1% in alcohol

#

18) When euphyllin interacts with a solution of copper (II) sulfate, the reaction occurs:

- Esterification
- Oxidation
- Hydrolysis
- Complex formation
- Dianitrogenation

#

19) Specify the composition of the Dragendorff precipitation reagent:

- A solution of iodine in potassium iodide
- A solution of bismuth iodide in potassium iodide
- A solution of mercury iodide in potassium iodide
- A solution of cadmium iodide in potassium iodide
- A solution of lead iodide in potassium iodide

#

20) Specify the composition of Mayer's precipitation reagent:

- A solution of iodine in potassium iodide
- A solution of bismuth iodide in potassium iodide
- A solution of mercury iodide in potassium iodide
- A solution of cadmium iodide in potassium iodide
- A solution of lead iodide in potassium iodide

#

21) Specify the composition of Marki's reagent:

- A mixture of concentrated sulfuric and nitric acids
- Alcohol solution of ammonium molybdate

- A solution of formaldehyde in concentrated sulfuric acid
- A solution of p-dimethylaminobenzaldehyde in chloroform
- A solution of iodine in potassium iodide

#

22) Specify the composition of Bouchard's precipitation reagent:

- A solution of mercury iodide in potassium iodide
- A solution of bismuth iodide in potassium iodide
- Phosphoromolybdenic acid
- Freshly prepared 5% aqueous solution of tannin
- A solution of iodine in potassium iodide

#

23) To identify which of the following drugs is not used reaction with a solution of copper (II) sulfate?

- Caffeine
- Theobromine
- Theophylline
- Euphilinus
- Themisal

#

24) Indicate which of the following reactions cannot be used to identify euphilin:

- Murexide test
- Reaction with 2,4-dinitrochlorobenzene
- Reaction with sodium rhodisonate
- Hydroxam test
- With a solution of copper (II) sulfate

#

25) One of the following drugs, purine derivatives, does not give a positive result (the formation of colored products) in the reaction with a solution of cobalt nitrate. Specify this medicine:

- Theobromine
- Theophylline
- Euphilinus
- Themisal
- Caffeine

#

26) Indicate the pharmacological effect of diprofylline:

- Analgesic

- Anti-inflammatory
- Antipyretic
- Central nervous system stimulant
- Spasmolytic

#

27) Substances of medicinal substances from the group of alkaloids are studied in the control and analytical laboratory. A positive reaction to xanthines is given by substances derived from:

- Purine
- Imidazole
- Hit
- Quinine
- Isoquinoline

#

28) The general reaction for the identification of drugs from the group of purine alkaloids (theobromine, theophylline, etc.) in pharmaceutical analysis is:

- Murexide test
- Reaction with 0.1% tannin solution
- Reaction with silver nitrate solution
- Reaction with cobalt chloride solution
- Interaction with an alkaline solution of sodium nitroprusside

#

29) Specify the name of the medicinal product to which the following systematic name 6,7-dimethoxy-1-(3,4-dimethoxybenzyl) isoquinoline hydrochloride would correspond:

- Tropacin
- Papaverine hydrochloride
- V. Caffeine
- H. Quinidine sulfate
- Dibazol

#

30) What pharmacological effect does papaverine hydrochloride have?

- Antipyretic
- choleretic
- Spasmolytic
- Anti-inflammatory
- Vasoconstrictor

#

31) Specify the method that is the basis for the quantitative determination of papaverine hydrochloride according to the requirements of DFU:

- Acid-base titration in the presence of alcohol and hydrochloric acid with potentiometric termination
- By the method of acid-base titration in non-aqueous solvents
- Acid-base titration in the presence of an alcohol-chloroform mixture
- Argentometry according to Fayance
- Gravimetric

#

32) According to the requirements of the SPhU, concomitant impurities in the papaverine hydrochloride substance are defined as:

- A solution of iodine in potassium iodide
- A solution of mercury iodide in potassium iodide
- A solution of bismuth iodide in potassium iodide
- By the method of ion exchange chromatography
- By the method of liquid chromatography

#

33) Indicate which of the listed drugs is an isoquinoline derivative according to its chemical structure:

- Quinidine sulfate
- Scopolamine hydrobromide
- Pachycarpine hydroiodide
- Papaverine hydrochloride
- Novocaine hydrochloride

#

34) According to the requirements of the SPhU, for the identification of papaverine hydrochlorideprecipitate the base of this alkaloid with ammonia solution; the resulting sediment is washed and dried. Specify the following actions to be performed with the received balance:

- Conduct a reaction on chlorides
- Determine the melting point
- Conduct a reaction with Dragendorff's reagent
- Determine the specific rotation
- Chromatograph (ion exchange chromatography)

#

35) Indicate which of the listed drugs are synthetic analogs of papaverine hydrochloride:

- Bigumal, chloridin

- Tropacin, troventol
- Mesaton, isadrin
- Trimecain, dikain
- Dibazol, no-shpa

#

36) Indicate the pharmacological action of drotaverine hydrochloride (no-shpa):

- Central nervous system stimulant
- Antitussive
- Antimalarial
- Hypertensive
- Spasmolytic

#

37) Enter the name of the alkaloid, the synthetic analogue of which is drotaverine hydrochloride (no-shpa):

- Papaverine
- Pachycarpine
- Quinidine
- Scopolamine
- Morphine

#

38) Specify the reagent with which, during the identification of papaverine hydrochloride, methylene bispapaverine sulfate is formed:

- Sodium metabisulfite
- Dragendorff's reagent
- Ammonium sulfate
- Marky's reagent
- Hydrochloric acid

#

39) Which of the proposed methods cannot quantify dibazole (2-benzylbenzimidazole hydrochloride)?

- Argentometrically
- Acid-base titration (in an alcoholic medium)
- Nitritometrically
- Non-aqueous titration
- Iodometrically

#

40) Indicate by which method you can quantify bendazole hydrochloride (dibazole):

- AND. Acidimetry in non-aqueous environments
- B. Bromatometric
- IN. Gravimetric
- G. Complexometric
- D. Nitritometric

#

41) What pharmacological action does it have?bendazole hydrochloride (Dibazol)?

- Analgesic
- Anti-inflammatory
- Spasmolytic
- Antipyretic
- Antiseptic

#

42) In the control and analytical laboratory, a complete analysis of Dibazol tablets is carried out. To identify these tablets, among other reactions, the analyst conducts a reaction to:

- Sulfates
- Tartrates
- Nitrates
- Nitrite
- Chlorides

#

43) A chemist-technologist of the laboratory of a pharmaceutical enterprise, when determining technological impurities in dibazole, dissolves it in water when heated to 90°C, acidifies it with a solution of hydrochloric acid, adds a solution of iron (III) chloride; after careful mixing, a pink color appeared. What impurity did the technologist chemist determine?

- Hydrazobenzene
- Benzyl chloride
- Benzoyl chloride
- Diphenylacetic acid
- *at*-Phenylenediamine

#

44) What reagent can be used to identify dibazole in a solution for injections?

- Dragendorf's reagent (bismuth periodide solution)
- Nessler's reagent (potassium tetraiodomercurate alkaline solution)
- tannin solution

- A solution of copper sulfate
- A solution of iodine in an acidic medium

#

45) According to SPhU, for the identification of "Papaverini hydrochloridum" a reaction is carried out with acetic anhydride and sulfuric acid when heated in a water bath. As a result of the reaction, the solution is colored in:

- Yellow color with green fluorescence
- Red color with green fluorescence
- Blue color with green fluorescence
- Blue color without fluorescence
- Red color without fluorescence

#

46) Medicinal substances from the group of alkaloids are defined as general alkaloid precipitating reagents. Which of the listed reagents does not belong to them?

- Tollens' reagent
- Dragendorff's reagent
- Mayer's reagent
- Marme's reagent
- Sonnenstein's reagent

1.4. Situational tasks:

1. Explain whether it is possible to establish the authenticity of any alkaloid with the help of precipitation and special reagents without using additional reactions?

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

3. To substantiate the conditions of acid-base titration of bases and salts of alkaloids in an aqueous medium (emphasize the role of alcohol and chloroform).

4. Describe the group reaction used to identify purine alkaloids. Why is this reaction not specific?

5. Explain the conditions for the quantitative determination of theophylline in euphylline. Give the corresponding reaction equations.

6. State the solvents that can be used to conclude that the test drug is theophylline or theobromine.

7. Describe the method of acid-base titration of medicinal substances in non-aqueous media using the example of bendazole hydrochloride (dibazole). Give the reaction equations, the formula for calculating the quantitative content.

8. Describe the substitution titration method using theobromine and theophylline as an example. Give the reaction equations, the formula for calculating the quantitative content.

9. Justify the possibility of using the acid-base titration method in non-aqueous media for the quantitative determination of papaverine hydrochloride. Give the reaction equations, the formula for calculating the quantitative content.

10. Describe the method of substitution titration (thiocyanatometry) using the example of bendazole hydrochloride (dibazole). Give the reaction equations, the formula for calculating the quantitative content.

11. Explain the need to add ammonium hydroxide solution when identifying dibazole (identification of chloride ion). Illustrate the answer with the chemistry of reactions.

4.5. Tasks:

1. Calculate the volume of 0.1 M perchloric acid solution (C_a = 1.0183), which is spent on the titration of 0.1516 g of theobromine (M.w. 180.17), if the titrant volume in the control experiment is 0.15 ml, and the content of the active substance in the preparation is 99.5%.

2. Calculate the percentage content of ethylenediamine (M.w. 60.10) and theophylline (M.w. 180.17) in euphylline, if it is known that 14.85 ml of a 0.1 M solution of hydrochloric acid was spent on the titration of 0.2893 g of the drug (Kn = 1.0133) and 18.33 ml of 0.1 M sodium hydroxide solution (C_a = 0.9925) were spent in the determination of theophylline in 0.3892 g of the drug.

3. Calculate the weight of the theobromine sample (M.w. 180.17), if 16.50 ml of 0.1 M sodium hydroxide solution (C_a = 0.9903) was spent on its titration. The content of the active substance in the preparation is 99.3%, the loss in mass during drying is 0.3%.

4. Calculate the volume of 0.1 M perchloric acid solution (C_a = 0.9865), which is spent on the titration of 0.0977 g of bendazole hydrochloride (M.w. 244.73), if it is known that the content of the active substance is 99.9 %.

5. Calculatevolume0.1 M sodium hydroxide solution (C_a = 0.9886), which was spent during the quantitative determination of 0.4017 g of theophylline (M.w. 180.17) by the method of indirect titration, if the content of the active substance in the pre-dried preparation is 99.4 %.

6. Determine the mass fraction of bendazole hydrochloride (M.w. 244.73) in the medicinal product, if 7.73 ml of 0.1 M sodium hydroxide solution was spent on the titration of 0.1936 g of the substance (C_a = 1.0165). Loss in mass - 0.62%.
7. Calculate the volume of 0.1 M sodium hydroxide solution (C_a = 0.9892), which is spent on the titration of 0.4108 g of theophylline (M.w. (anhydrous) 180,180) by the method of indirect neutralization, if the percentage of theophylline in the medicinal product is 99, 70%.
8. Calculate the weight of papaverine hydrochloride (M.w. 375.86), if 8.33 ml of 0.1 M perchloric acid solution were spent on its titration (C_a = 0.9786). The volume of the titrant in the control experiment is 0.30 ml, the content of the active substance in the preparation is 99.5%.
9. Calculate the percentage content of papaverine hydrochloride (M.w. 375.86), if 5.08 ml of 0.1 M sodium hydroxide solution (C_a = 0.9998) was used for the titration of 0.1879 g of the drug. The loss in mass during drying is 3 , 2%.
10. Calculate the percentage content of dibazole (M.w. 244.73) in the preparation, if 8.42 ml of 0.1 M perchloric acid solution was used for the titration. The weight of the sample is 0.1912 g, and the titrant volume in the control experiment is 0.5 ml.

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. TOPIC: Analysis of narcotic analgesics and their analogues. Emetics and antiemetics.

2. PURPOSE: To master the methods of analysis of medicinal products from the group of narcotic analgesics and their analogues, emetics and antiemetics.

3. TARGETS:

3.1. To study the structure, nomenclature, synonyms, physicochemical properties, sources and methods of obtaining medicines from the group of narcotic analgesics and their analogues, emetics and antiemetics.

3.2. To study the methods of analysis of the considered group of medicinal products according to the SPhU, 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. Consider the peculiarities of the analysis of drugs from the group of narcotic analgesics and their analogues, emetics and antiemetics, 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 narcotic analgesics and their analogues, emetics and antiemetics, based on their physicochemical properties.

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

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. Define the concepts of "narcotic analgesics", "agonists", "antagonists" and "synergoantagonists".

2. Latin names, synonyms, structural formulas and chemical names of drugs derived from morphine (morphine hydrochloride, codeine, codeine phosphate, ethylmorphine hydrochloride, etc.).
3. Use of physico-chemical properties and features of the chemical structure to justify the methods of analysis and storage conditions of the studied drugs.
4. Based on the structure of the studied medicinal substances, justify the identification reactions and methods of quantitative determination, give the chemistry of the corresponding reactions.
5. Write the structural formulas of morphine hydrochloride, codeine, codeine phosphate and ethylmorphine hydrochloride. Specify the physical and physico-chemical properties that allow you to differentiate these medicinal substances.
6. Characterize the functional groups and explain the peculiarities of the reaction of morphine alkaloids (morphine, codeine, ethylmorphine) with a solution of iron (III) chloride.
7. Describe the acid-base and reducing properties of morphine hydrochloride, codeine, ethylmorphine hydrochloride. Give the methods of qualitative and quantitative determination related to them, the conditions in which they are carried out.
8. Synthetic analogues of morphine: promedol, tramadol. Their properties, analysis and application.
9. Synergoantagonists of morphine: nalorphine, pentazocine. Properties, application analysis.
10. Emetic (apomorphine) and antiemetic (ondansetron) drugs. Properties, analysis, application.
11. To substantiate the conditions of acid-base titration of bases and salts of alkaloids in an aqueous medium (emphasize the role of alcohol and chloroform).
12. Justify the storage conditions of the researched medicinal products based on their structure and chemical properties.
13. Release form, dosage and application of the researched means. Relationship between structure and biological action in a number of morphinan derivatives.

4.3. Test tasks:

#

1) Specify a possible method for the quantitative determination of codeine phosphate:
   - Argentometry according to More;
   - Complexonometry;
   - Nitritometry;

- Acid-base titration in non-aqueous solvents;
- Acidimetry

#

2) When adding an ammonia solution to a solution of morphine hydrochloride, the formed morphine base precipitate is dissolved in an excess of sodium hydroxide solution. Specify the reason for its dissolution:
- Morphine base dissolves in water;
- Due to the formation of morphine alcoholate (presence of alcohol hydroxyl);
- Hydrolytic destruction of the morphine base under the action of sodium hydroxide solution;
- Due to the formation of morphine phenolate (the presence of phenolic hydroxyl).
- The presence of a carboxyl group

#

3) Indicate which of the following drugs exhibits pronounced basic properties, which makes it possible to use the method of acid-base titration in an alcohol-water environment:
- Theophylline;
- Caffeine;
- Theobromine;
- Codeine;
- Ethylmorphine

#

4) Indicate which reagent can be used to distinguish morphine hydrochloride from codeine:
- Mayer's reagent;
- Dragendorff's reagent;
- Solution of iron (III) chloride;
- Sodium nitrite solution
- Bouchard, Wagner reagent

#

5) Indicate which reagent can be used to distinguish morphine hydrochloride from codeine:
- Bouchard's, Wagner's reagent;
- Mayer's reagent;
- Marky's reagent;
- Dragendorff's reagent;
- Sodium acetate solution.

#

6) When quantifying which medicinal substance by the acid-base titration method in a glacial acetic acid medium (titrant – 0.1 M perchloric acid solution), you need to add a solution of mercury (II) acetate:

- Quinidine sulfate;
- Theophylline;
- Codeine phosphate;
- Codeine
- Ethylmorphine hydrochloride

#

7) One of the following methods is recommended by the SPhU for the determination of concomitant impurities in codeine. Specify it:

- Polarimetric;
- Ion exchange chromatography;
- Interaction with general alkaloid reagents;
- Determination of the melting point;
- Liquid chromatography.

#

8) Specify the method of quantitative determination recommended by the SPhU for the determination of codeine:

- Ion exchange chromatography;
- Photoelectrocolorimetry;
- Adsorption chromatography;
- Acid-base titration in an alcohol environment;
- Acid-base titration in non-aqueous solvents.

#

9) Specify the specific pharmacological action of codeine:

- Analgesic;
- Central nervous system stimulant;
- Neuroleptic;
- Anti-inflammatory;
- Antitussive.

#

10) One of the listed medicines does not belong to phenanthrenisoquinoline (morphinan) derivatives. Specify it:

- Codeine;
- Ethylmorphine hydrochloride;
- Morphine hydrochloride;

- Codeine phosphate
- Promedol.

#

11) One of the listed drugs gives a positive result of the reaction with iron (III) chloride. Specify it:

- Codeine;
- Promedol;
- Ethylmorphine hydrochloride;
- Papaverine hydrochloride;
- Morphine hydrochloride.

#

12) One of the listed drugs gives a positive result of the reaction with diazonium salts, forming an azo dye. Specify it:

- Platifiline hydrotartrate;
- Papaverine hydrochloride;
- Codeine;
- Ethylmorphine hydrochloride;
- Morphine hydrochloride.

#

13) Indicate which reagents can be used to distinguish morphine hydrochloride from codeine:

- Bouchard's, Wagner's reagent;
- Tannin solution;
- Cobalt nitrate solution;
- Dragendorff's reagent;
- Markie's reagent, iron (III) chloride.

#

14) Indicate the pharmacological action of morphine hydrochloride:

- Antiemetic;
- Anti-inflammatory;
- Antitussive;
- Local anesthetic;
- Analgesic.

#

15) One of the following methods cannot be used for the quantitative determination of morphine hydrochloride. Specify this method:

- Argentometric;

- Photoelectrocolorimetric;
- Acid-base titration;
- Acid-base titration in non-aqueous solvents;
- Complexometric.

#

16) One of the drugs listed below is a synthetic analogue of morphine hydrochloride in action. Specify this analogue:

- Homatropin hydrobromide;
- Proserin;
- Mesaton;
- Promedol;
- Lidocaine.

#

17) Indicate which titrimetric method SPhU recommends to use for the quantitative determination of ethylmorphine hydrochloride:

- Alkalimetry in alcoholic medium;
- Argentometry according to Folgard;
- Faience argentometry;
- Nitritometry;
- Acidimetry in non-aqueous solvents.

#

18) Specify the environment and conditions for the reaction of the identification of ethylmorphine hydrochloride with a solution of iron (III) chloride:

- In an alcoholic environment when boiling the solution;
- In an aqueous solution at a temperature of 5-10°WITH;
- In the presence of nitric acid at room temperature;
- In the presence of sodium hydroxide at a temperature of 40-60°WITH;
- In the presence of sulfuric acid, when heated.

#

19) Ethylmorphine hydrochloride has one of the following pharmacological actions. Specify it:

- Stimulator of breathing;
- Central nervous system stimulant;
- Hypotensive;
- Spasmolytic;
- Anti-inflammatory.

#

20) Indicate which of the following groups of reagents is used to identify promedol:

- Concentrated nitric acid, alcoholic solution of potassium hydroxide;
- Bromine water, ammonia solution;
- Copper sulfate solution, sodium hydroxide solution;
- A solution of hydrogen peroxide, potassium dichromate and sulfuric acid;
- Formaldehyde solution in concentrated sulfuric acid, chloroform

#

21) Specify the name of the synthetic analogue of drugs from the group of alkaloids, to which the chemical name 1,2,5-trimethyl-4-propionyloxy-4-phenylpiperidine hydrochloride would correspond:

- Tropacin
- Drotaverin hydrochloride
- Diprofylline
- Prozerin
- Promedol;

#

22) One of the following titrimetric methods cannot be used to quantify promedol. Specify it:

- Faience argentometry;
- Acid-base titration in a two-phase environment;
- Acid-base titration in a non-aqueous solvent;
- Argentometry according to Folgard;
- Nitritometry.

#

23) Indicate which of the following pharmacological actions promedol has:

- Antipyretic;
- Anti-inflammatory;
- Central nervous system stimulant;
- Hypotensive;
- Analgesic.

#

24) One of the following medicinal plants is the main source of opium. Specify it:

- Rauwolfia snake;
- Scopolia;
- Coffee;
- Sekurinega;
- Poppy is hypnotic.

#

25) One of the below-mentioned pharmacological actions is characteristic of the drug - omnopon. Specify it:

- Antitussive;
- Anti-inflammatory;
- Hypotensive;
- Stimulator of breathing;
- Analgesic.

#

26) One of the alkaloids listed below is a starting substance in the synthesis of apomorphine hydrochloride. Specify it:

- Reserpine;
- Narcotic;
- Anabasin;
- Morphine;
- Solasodin

#

27) One of the alkaloids below is a starting substance in the synthesis of codeine phosphate. Specify it:

- Reserpine;
- Narcotic;
- Anabasin;
- Morphine;
- Solasodin

#

28) One of the below-mentioned pharmacological actions is characteristic of apomorphine hydrochloride. Specify it:

- Analgesic;
- Anti-inflammatory;
- Antiemetic;
- Hypotensive;
- Vomiting, expectorant.

#

29) One of the following pharmacological actions is characteristic of ondansetron. Specify it:

- Analgesic;
- Anti-inflammatory;
- Antiemetic;
- Hypotensive;

- Vomiting, expectorant.

#

30) One of the narcotic analgesics is obtained by modifying the structure of the leader - the natural alkaloid morphine. Specify it:

- Proserin;
- Mesaton;
- Apomorphine hydrochloride;
- Promedol;
- Izadrin.

#

31) A number of drugs from the group of narcotic analgesics (promedol, fentanyl) are synthesized on the basis of studying the relationship between structure and pharmacological action using the leader structure (a natural alkaloid). Specify this alkaloid:

- Atropine;
- Narcotic;
- Morphine;
- Physostigmine;
- Pilocarpine.

#

32) The drug codeine is obtained semi-synthetically - by methylation of a natural alkaloid:

- Morphine
- Papaverin
- Caffeine
- G. Atropine
- Koniine

#

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

- Polarimeter
- Spectrophotometer
- Photoelectrocolorimeter
- Refractometer
- Polarograph

#

34) An analyst of the control and analytical laboratory performs an express analysis of morphine hydrochloride. The presence of phenolic hydroxyl is confirmed by the reaction with the solution:

- $FeCl_3$
- NH_3
- $AgNO_3$
- $K_3[Fe(CN)_6]$
- Concentrated HNO_3

#

35) The substance of morphine hydrochloride was submitted for analysis. When it interacts with a solution of Ferric chloride (III), a blue-violet color is formed. This indicates the presence in the structure of this medicinal substance:

- Phenolic hydroxyl
- Aldehyde group
- Alcoholic hydroxyl
- Ketogroups
- Complex ether groups

#

36) What features of the molecular structure allow us to distinguish between morphine hydrochloride and ethylmorphine hydrochloride by reaction with a solution of iron (III) chloride?

- The presence of phenolhydroxyl
- Presence of alcoholhydroxyl
- Presence of tertiary nitrogen
- The presence of a double bond
- Presence of chloride ions

#

37) The drug codeine is obtained semi-synthetically - by methylation of a natural alkaloid:

- Morphine
- papaverine
- caffeine
- atropine
- Coniine

#

38) Alkylation of the phenolic group in position 3 of the morphine molecule leads to:

- Reduction of analgesic effect and strengthening of antitussive effect

- Reduction of antitussive effect
- Enhancement of analgesic effect
- Appearance of diuretic activity
- It does not affect the pharmacological properties

#

39) Specify the medicinal product, the identification of which, upon reaction with a solution of silver nitrate, produces a yellow precipitate, soluble in dilute nitric acid:

- Codeine phosphate
- Ascorbic acid
- Glucose is anhydrous
- Procaine hydrochloride
- Sodium benzoate

4.4. Situational tasks:

1. Specify the condition under which the reaction of codeine and ethylmorphine hydrochloride with Ferrum (III) chloride is possible.
2. Explain the possibility of creating narcotic analgesics based on the modification of the leader structure (morphine). Beckett-Casey rule.
3. Explain the possibility of quantitative determination of codeine by acidimetry.
4. What is the role of alcohol in the quantification of codeine acidimetrically?
5. Why does morphine hydrochloride dissolve in an excess of sodium hydroxide?
6. Explain why the reaction with iron(III) chloride is different for morphine compared to ethylmorphine and codeine?
7. Explain why nalorphine, having a similar structure to morphine, is its antagonist?
8. Define the term "agonists-antagonists" (synergoantagonists). Give examples.

4.5. Tasks:

1. Calculate the percentage content of codeine phosphate (M.w. 397.36) in the preparation, if the weight of the test piece is 0.2517 g, the volume of a 0.1M solution of perchloric acid (C_a = 0.9916) in the working experiment is 6.19 ml , in the control - 0.18 ml. Weight loss during drying is 6.5%.
2. Determine the volume of a 0.1M solution of perchloric acid (C_a = 0.9985), which was spent on the titration of a weight of 0.1518 g of morphine hydrochloride (M.w. 321.80). The percentage content of morphine hydrochloride in the medicinal product is 99.50%.

3. Determine the weight of codeine test (M.w. 299.39), if 10.02 ml of 0.1M hydrochloric acid solution was spent on its titration (C_a = 0.9678). The percentage content of codeine in the medicinal product is 99.40%.
4. Calculatevolume0.1 M perchloric acid solution (C_a = 0.9835), which was spent on the titration of 0.1506 g of morphine hydrochloride (M.w. 321.80), if the loss in mass during drying is 14.4%, and the content of active substances in the preparation–99.0%.
5. Calculate the weight of the codeine sample (M.w. 299.37), if 9.98 ml of 0.1 M hydrochloric acid solution (C_a = 0.9586) was spent on its titration. The content of the active substance in the preparation – 99.3%, loss in mass during drying– 5.5%.
6. Calculate the percentage content of ethylmorphine hydrochloride (M.w. 385.89) in the preparation, if the mass of the test piece is 0.2042g, the volume of the 0.1M solution of perchloric acid (C_a = 1.0006) in the work experiment is 5.15 ml, in the control - 0.10 ml. Loss in mass during drying is 4.6%.
7. Calculate the percentage content of promedol (M.w. 311.85) in the preparation, if the weight of the test is 0.2577 g, the volume of a 0.1 M perchloric acid solution (C_a = 0.9896) in the working experiment is 8.19 ml , in the control - 0.12 ml. Weight loss during drying is 3.5%.
8. Calculatevolume0.1 M perchloric acid solution (C_a = 0.9995), which was spent on the titration of 0.1802 gpromedol (M.w. 311.85), if the loss in mass during drying is 10.4%, and the content of the active substance in the preparation– 99.8%.
9. Calculate the weight of the weightethylmorphine hydrochloride (M.w. 385.89), if 8.88 ml of 0.1 M perchloric acid solution were spent on its titration (C_a = 0.9886). The content of the active substance in the preparation–99.50%, loss in mass during drying–2.5%.
10. Calculate the percentage content of apomorphine (M.w. 317.30) in the drug, if the weight of the test is 0.3005 g, the volume of a 0.1 M perchloric acid solution (C_a = 0.9902) in the work experiment is 9.52 ml , in the control - 0.10 ml. Weight loss during drying is 1.5%.

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. 3

1. TOPIC: Analysis of means acting on cholinergic processes. Part 1. Cholinomimetics, anticholinesterase drugs.

2. PURPOSE: To master the methods of analysis of medicinal products acting on cholinergic processes: cholinomimetics, anticholinesterase drugs.

3. TARGETS:

3.1. To study the structure, nomenclature, synonyms, physicochemical properties, sources and methods of obtaining medicines acting on cholinergic processes: cholinomimetics, anticholinesterase drugs.

3.2. To study the methods of analysis of the considered group of medicinal products according to the SPhU, 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. Consider the peculiarities of the analysis of drugs acting on cholinergic processes: cholinomimetics, anticholinesterase drugs, using physical, physico-chemical 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 acting on cholinergic processes: cholinomimetics, anticholinesterase drugs, based on their physicochemical properties.

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

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. Give definition concepts: "hallenergeticprocesses", "hallandnoandmetics", "anticholinesterase drugs".
2. Latin names,synonyms,formulas structures and chemical names medical drugs, derivatives imidazole (pilocarpine hydrochloride), indole (physostigmine salicylate), quinolysine (cytisine), quinuclidine (Aceclidine).

3. Using physics-chemical properties,features chemical structures for justification reactions identification, methods quantitative definition and conditions storage investigated drugs
4. Derivativesimidazole –pilocarpine hydrochloride. Medical raw, what contains pilocarpine. Physics-chemical properties pilocarpine hydrochloride.
5. Point reactions on pilocarpine hydrochloride, what confirm structure and authenticity drug. Specify specific reaction identification on pilocarpine hydrochloride and explain her chemical sense.
6. Possible methods quantitative analysis pilocarpine hydrochloride. Explain conditions method acid–base titration in environment non-aqueous solvents. Write chemistry reactions.
7. Synthetic analog pilocarpine hydrochloride – Aceclidine. Him properties, analysis, application.
8. Drugs, derivatives indole (physostigmine salicylate). Sources receiving, physics-chemical properties.
9. Specify, on whose physics-chemical properties physostigmine salicylate founded carrying out identification drug.
10. Point reactions on physostigmine salicylate, what confirm structure and authenticity drug.
11. Possible methods quantitative definition medical drugs, groups indole. Explain value alcohol and chloroform at alkalimetric defined physostigmine salicylate.
12. Synthetic analog physostigmine salicylate – proserin. Properties, analysis, application.
13. Medicinal means with groups alkaloids, derivatives quinolysine. Cytisine. Building, nomenclature, obtaining, properties, analysis, application. Cytitone.
14. Acetylcholine-chloride, carbocholine. Properties, analysis. Application.
15. Justify conditions storage investigated medical means, going out with their structures and chemical properties.
16. The main ones medical forms,created on basis investigated medicalmeans. Form release, dosage.

4.3. Test tasks:

#

1) What is the pharmacological effect of pilocarpine hydrochloride?
   - Anti-inflammatory
   - Antipyretic
   - Reduces intraocular pressure (miotic)
   - choleretic
   - Antihistamine

#

2) Indicate by which method you can quantify pilocarpine hydrochloride:

- Complexometrically
- Iodometrically
- Acid-base titration in non-aqueous solvents
- Nitritometrically
- Acid-base titration in an alcoholic medium

#

3) To identify physostigmine salicylate, a reaction with a solution of Ferrum (III) chloride is used, according to which the structure of the drug reveals:

- Salicylic acid
- The basis of physostigmine
- Lactone cycle
- Aromatic nitro group
- Methyl group

#

4) Specify the pharmacological effect of physostigmine salicylate:

- Diuretic
- Spasmolytic
- Anticholinesterase, miotic
- Mydriatic
- Analgesic

#

5) Indicate which drug corresponds to the chemical name α-ethyl-β-(1-methylimidazole-5-methyl)-γ-butyrolactone hydrochloride:

- Ephedrine hydrochloride
- Pilocarpine hydrochloride
- Morphine hydrochloride
- Quinidine hydrochloride
- Papaverine hydrochloride

#

6) The chemical structure of pilocarpine hydrochloride is a derivative:

А. Indole
Б. Purine
В. Quinoline
Г. Benzylisoquinoline
Д. Imidazole

#

7) Indicate which of the following medicinal preparations is obtained by extraction from Calabar beans:

- Spherophysin benzoate
- Strychnine nitrate
- Euphilinus
- Pilocarpine hydrochloride
- Physostigmine salicylate

#

8) Indicate which of the listed medicines is a synthetic analogue (by action) of physostigmine salicylate:

- Pilocarpine hydrochloride
- Ephedrine hydrochloride
- Mesaton
- Dikain
- Prozerin

#

9) To identify proserin, a reaction is carried out with a solution of sodium hydroxide, after which sulfanilic acid, sodium nitrite and hydrochloric acid are added. The appearance of a red-orange color is due to the formation of:

- Azo dye
- Murexida
- Taleiokhina
- Iodoform
- Fluorescein

#

10) Indicate which of the following reagents are used to identify proserin:

- Hydrochloric acid, sodium nitrite, β-naphthol
- A mixture of concentrated nitric and sulfuric acids
- Solution of copper (II) sulfate
- Silver nitrate solution
- A solution of sodium hydroxide, sulfanilic acid, sodium nitrite, and hydrochloric acid

#

11) List the reagents used to identify pilocarpine hydrochloride:

- Perhydrol, hydrochloric acid, ammonia solution
- A solution of formaldehyde in concentrated sulfuric acid
- Bromine water, ammonia solution
- Concentrated nitric acid, alcoholic solution of potassium hydroxide

- Hydrogen peroxide, potassium dichromate, sulfuric acid, chloroform

#

12) One of the listed methods cannot be used for the quantitative determination of pilocarpine hydrochloride. Specify it:

- Argentometry according to Fayance
- Acid-base titration in a two-phase environment
- Acid-base titration in non-aqueous solvents
- Argentometry according to Folgard
- Argentometry according to More

#

13) The formation of iron (III) hydroxamate during the identification of pilocarpine hydrochloride confirms the presence in its structure:

- Lactone cycle
- Lactam cycle
- Imidazole cycle
- Hydroxyl group
- Double bond

#

14) For quantitative determination of nitrogen in neostigmine methyl sulfate (proserin) use:

- A.The Kjeldahl method
- B. The Kolthoff method
- IN.The Kolbe-Schmidt method
- G. Mohr's method
- D. Fayance method

#

15) To absorb ammonia in the modified Kjeldahl method, use:

- A.Boric acid solution
- B. Saturated NaCl solution
- B. Sodium hydroxide solution
- D. Ethyl alcohol
- D. Acetone

- #

16) Identification of salicylic acid in aceclidine is carried out using a solution:

- Iron (III) chloride
- Sodium hydroxide
- Magnesium sulfate
- Sodium nitrite

- Potassium sulfate

#

17) A pharmacist-analyst identifies salicylic acid in aceclidine by the formation of a red auric dye. What reagent does he use?

- A.Markey's reagent (solution of formaldehyde in concentrated sulfuric acid)
- B. Fisher's reagent
- B. Nessler's reagent (alkaline solution of potassium tetraiodomercurate)
- G. Tollens' reagent
- D. Fehling's reagent

#

18) To quantitatively determine the content of salicylic acid in aceclidine, the following method is used:

- Alkalimetry
- Nitritometry
- Argentometry
- Permanganatometry
- Complexonometry

#

19) The presence of an ester group in the structure of aceclidine can be proven by the formation reaction:

- Salts of hydroxamate [hydroxamic] acids
- Indophenol
- Diazonium salts
- Aurine dye
- Azomethine dye

#

20) Which identification reaction can be used to confirm the presence of a sulfur atom in a molecule of neostigmine methyl sulfate (proserin)?

- Alkaline hydrolysis with subsequent detection of sulfate ion
- With a solution of diphenylcarbazide
- With salts of alkali metals
- With magnesium chloride solution
- With Marki's reagent

#

21) To identify pilocarpine hydrochloride, a reaction with sodium nitroprusside in an alkaline medium (Legal's reaction) is used. At the same time, the appearance of a cherry color confirms the presence of pilocarpine in the structure:

- Lactone ring
- Imidazole cycle
- Methyl groups
- Hchloride ions
- Phenolic hydroxyl

#

22) Enter the name of the medicinal substance, for the identification of which the nitration reaction with subsequent reduction and formation of an azo dye is used:

- Pachycarpine hydroiodide
- Cytisine
- Platyphyllin hydrotartrate
- Caffeine
- Pilocarpine hydrochloride

#

23) Indicate which medicinal plant is the main source of alkaloid cytisine?

- Scopolia
- Rauwolfia snake
- Cocoa beans
- Calabar beans
- Laburnum

#

24) Indicate which of the following reactions is used to identify cytisine:

- Taleiochin test
- With ammonia solution
- Maltol sample
- Formation of murexide
- With cobalt nitrate solution

#

25) Indicate the pharmacological effect of the medicinal product cytiton:

- Spasmolytic
- Analgesic
- Mydriotic
- Stimulator of birth activity
- Stimulator of breathing

#

26) Indicate by which method you can quantitatively determine cytisine:

- Nitritometrically;
- Acid-base titration;
- Argentometrically;
- Complexometrically;
- Mercurimetrically.

#

27) Indicate by which method you can quantitatively determine acetylcholine chloride:

- Alkalimetrically;
- Acidimetric;
- Argentometrically;
- Nitritometrically;
- Complexometrically;

4.4. Situational tasks:

1. Explain the necessity of adding oxymercuric acetate in the quantitative determination of pilocarpine hydrochloride by the non-aqueous titration method.

2. Explain the need to increase the alcohol-chloroform mixture in the quantitative determination of physostigmine salicylate by the method of alkalimetry.

3. Explain due to which functional group pilocarpine hydrochloride gives a hydroxamate test. Write the chemistry of the reactions.

4. Write the specific identification reaction for pilocarpine hydrochloride and explain its chemical meaning.

5. Explain why cytisine is determined acidimetrically in an aqueous environment?

6. Indicate the peculiarities of the structure of cytisine, due to which the formation of picrate with a characteristic melting temperature is possible, as well as the ability to undergo electrophilic substitution reactions (nitration, etc.).

7. Explain why cytitone is not recommended for identification using ferric chloride solution.

4.5. Tasks:

1. Calculate the percentage content of aceclidine (M.w. 307.35) in the preparation, if the weight of the test is 0.2065,the volume of a 0.1 M solution of perchloric acid (C_a = 1.0108) in the working experiment was 6.72 ml, in the control experiment - 0.09 ml.

2. Calculate the weight of pilocarpine hydrochloride (M.w. 244.72), if 8.30 ml of 0.1 M perchloric acid solution (C_a = 1.0108) was spent on its titration. The

content of the active substance in the preparation is 98.9%,volumecontrol experiment–0.21 ml, weight loss during drying 0.4%.

3. Calculate the volume of 0.1 M sodium hydroxide solution (C_a = 1.0022), which will be spent on the titration of 0.1562 g of physostigmine salicylate (M.w. 413.5), if its percentage content in the preparation is 99.8 %, loss in mass during drying - 0.54%.
4. Calculate the percentage content of cytisine (M.w. 190.25), if 9.98 ml of a 0.1 M solution of hydrochloric acid was spent on the titration of 0.1981 g of the drug (C_a = 0.9994).
5. Calculate the volume of 0.1 M perchloric acid solution (C_a = 1.0011), which will be spent on the titration of 0.2421 g of pilocarpine hydrochloride (M.w. 244.72), if its percentage content in the preparation is 99.4 %, the titrant volume in the control experiment is 0.16 ml.
6. Calculate the mass of aceclidine (M.w.307.35), if 10.20 ml of 0.1 M perchloric acid solution was spent on its titration (C_a = 1.0004) The content of the active substance is 98.8%, the loss in mass during drying 0.25%.
7. Calculate the volume of 0.1 M solution of hydrochloric acid (C_a = 0.9888), which will be spent on 0.2103 g of cytisine (M.w. 190.25), if its percentage content in the preparation is 98.86%.
8. Calculate the percentage content of pilocarpine hydrochloride (M.w. 244.72) in the preparation, if the weight of the test piece is 0.2002 g, the volume of 0.1 M sodium hydroxide solution (C_a = 1.0101). Weight loss during drying is 0.23%.
9. Calculate the percentage content of physostigmine salicylate (M.w. 423.5), if 5.08 ml of 0.1 M sodium hydroxide solution (C_a = 0.9978) was spent on the titration of 0.1212 g of the drug, the loss in mass during drying was 0. 45%.
10. Calculate the weight of the weight of physostigmine salicylate (M.w. 413.5), if 6.78 ml of 0.1 M sodium hydroxide solution (C_a = 1.0000) was spent on its titration. The content of the active substance in the preparation is 99.70%.

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. 4

1. TOPIC: Analysis of means acting on cholinergic processes. Part 2. Cholinergic blockers, ganglioblockers.

2. PURPOSE: To master the methods of analysis of medicinal products acting on cholinergic processes: cholinergic blockers, ganglioblockers.

3. TARGETS:

3.1. To study the structure, nomenclature, synonyms, physicochemical properties, sources and methods of obtaining medicines acting on cholinergic processes: cholinergic blockers, ganglioblockers.

3.2. To study the methods of analysis of the considered group of medicinal products according to the SPhU, 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. Consider the peculiarities of the analysis of drugs acting on cholinergic processes: cholinergic blockers, ganglioblockers, 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 acting on cholinergic processes: cholinergic blockers, ganglioblockers, based on their physicochemical properties.

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

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. Define the concepts: "cholinergic processes", "cholinergic blockers", "ganglioblockers".
2. Sources of production, chemical structure, nomenclature, synonyms, physicochemical properties of medicinal substances from the group of

cholinergic agents, diphenylpropionic acid derivatives (aprofen), cholinergic alkaloids, tropane derivatives (atropine sulfate, scopolamine hydrobromide, homatropine hydrobromide), pyrrolizidine (platiphylline hydrotartrate) and ganglioblockers, quinolizidine derivatives (pachicarpine hydroiodide).

3. To substantiate the use of chemical and instrumental methods in the analysis of the quality of drugs from the group of alkaloids, tropane derivatives, pyrrolizidine and quinolizidine and diphenylpropionic acid derivatives.

4. Ways of entry and determination of specific impurities in the analysis of the quality of medicines from the group of alkaloids, tropane derivatives, pyrrolizidine and quinolizidine.

5. Medicines from the group of alkaloids, tropane derivatives.

5.1. Alkaloids of the tropane group. Scopolamine hydrobromide. Structure, nomenclature, preparation, properties, analysis, application.

5.2. Modification of the "leader structure" (atropine, scopolamine) in order to create synthetic analogues by action: homatropine hydrobromide, etc. Structure, nomenclature, properties, analysis, application. Relationship between structure and pharmacological action.

5.3. The Vitali-Morena reaction is a characteristic reaction for medicines from the group of alkaloids, tropane derivatives. The chemical essence of the reaction, its specificity, conditions and execution technique.

5.4. Describe the drugs of the tropane group as ester derivatives. Indicate what reactions the ester group causes for these substances and how these reactions are used in pharmaceutical analysis. Write the appropriate reaction equations, justify the conditions for their implementation.

5.5. Give possible methods of quantitative determination and explain the conditions for their implementation for medicines from the group of alkaloids, tropane derivatives. Write the appropriate reaction equations, calculation formulas.

6. Platyphyllin hydrotartrate. Structure, nomenclature, preparation, properties, application.

6.1. Based on the structure, propose identification reactions. Write the chemistry of reactions.

6.2. Specify the possible methods of quantitative determination of platyphyllin hydrotartrate, justify the conditions for their implementation, write the chemistry of the reactions.

7. Medicines from the group of alkaloids, quinolizidine derivatives. Pachycarpine hydroiodide. Structure, nomenclature, preparation, properties, analysis, application.

8. Medicinal products from the group of cholinergic blockers, derivatives of diphenylpropionic acid. Aprofen. Structure, nomenclature, properties, analysis, application.
9. Featuresstorage of the researched group of medicines based on their physical and chemical properties.
10. The main dosage forms created on the basis of researched medicinal substances from the group of cholinergic blockers and ganglioblockers. Relationship of structure with biological effect.

4.3. Test tasks:

#

1) Indicate which of the listed medicines is a derivative of pyrrolizidine according to its chemical structure?

- Cocaine hydrochloride
- Pilocarpine hydrochloride
- Cytisine
- Reserpine
- Platyphyllin hydrotartrate

#

2) What specific impurity in the medicinal substance "Platyfillin Hydrotartate" is determined by the appearance of turbidity when adding 5% ammonia solution?

- Senecifillin
- Recovery substances
- Apoatropin
- Aposcopolamine
- Foreign alkaloids

#

3) The pharmacist-analyst used a reaction with potassium chloride to identify the drug, which resulted in the formation of a white crystalline precipitate. What drug does the analyst identify?

- Platifylline hydrotartrate
- Caffeine monohydrate
- Atropine sulfate
- G. Pilocarpine hydrochloride
- Scopolamine hydrobromide

#

4) Indicate by which method it is possible to determine the quantitative content of platyphyllin hydrotartrate:

- Argentometry
- Bromatometry
- Acidimeterher
- By the method of acid-base titration in non-aqueous media
- Nitritometry

#

5) Indicate which of the medicinal substances gives a positive result (the formation of a blood-red color) when it is identified by the reaction of the hydroxam test:

- Caffeine monohydrate
- Ephedrine hydrochloride
- Platyphyllin hydrotartrate
- Papaverine hydrochloride
- Euphilinus

#

6) Indicate which plant contains the alkaloid platyphyllin?

- Laburnum
- Rauwolfia
- Scopolia
- Thermopsis
- Crusader

#

7) The formation of iron hydroxamate in platyphyllin hydrotartrate confirms the presence in the structure of this medicinal product:

- Tartaric acid
- Pyrrolizidine cycle
- Hydroxyl group
- Double bond
- Complex ester groups

#

8) Indicate which heterocycle is the basis of the platyphyllin hydrotartrate structure:

- Indole
- Pyrrolizidine
- Piperidine
- Isoquinoline
- Quinoline

#

9) Indicate which of the medicinal substances gives a positive result (the formation of a blood-red color) when identified by the hydroxam test reaction:

- Pachycarpine hydroiodide
- Cytisine
- Papaverine hydrochloride
- Euphilinus
- Homatropin hydrobromide

#

10) Indicate which heterocyclic systems are the basis of the structure of tropane alkaloids:

- Pyridine and pyrazole
- Pyrrolizidine and imidazole
- Piperidine and furan
- Pyrrolidine and piperidine
- Isoquinoline and pyrrole

#

11) For the identification of aprofen, fuming nitric acid, acetone and an alcoholic solution of potassium hydroxide are used. These reagents are used to detect:

- Diphenylpropionic acid residue
- Residue of diethylaminoethanol
- Chloride ion
- Crystallization water
- Phenolic hydroxyl

#

12) Quantitative determination of scopolamine hydrobromide is carried out by the method of acid-base titration in non-aqueous solvents. Indicate how the equivalence point is fixed in the given method?

- Using a crystal violet indicator
- According to the change in the color of the solution due to the increase in the excess titrant drop (indicator-free method)
- Using thymol blue indicator
- Using the phenolphthalein indicator
- Using thymolphthalein indicator

#

13) Specify a medicinal substance from the group of alkaloids, tropane derivatives, in the structure of which is the heterocycle oxirane (ethylene oxide):

- Atropine sulfate

- Scopolamine hydrobromide
- Homatropin hydrobromide
- Tropacin
- Cocaine hydrochloride

#

14) Which of the medicines is a synthetic analogue of alkaloids, tropane derivatives?

- Homatropin hydrobromide
- Atropine sulfate
- Scopolamine hydrobromide
- Papaverine hydrochloride
- Ergometrine maleate

#

15) Specify the medicinal plant from which the alkaloid pachycarpine is obtained:

- Rakitnik
- Cocoa
- Scopolia
- Flat-leaved crucifer
- Sophora is thick-fruited

#

16) Pachycarpine hydroiodide upon interaction with one of the listed reagents gives a yellow precipitate with a characteristic melting point. Specify this reagent:

- Ammonium nitrate solution
- Iodine solution
- Marky's reagent
- A solution of sodium nitrite in an acidic environment
- Picric acid solution

#

17) Which of the listed methods of analysis cannot be used for the quantitative determination of pachycarpine hydroiodide:

- Acid-base titration in non-aqueous solvents
- Argentometry
- Acid-base titration in a two-phase environment
- High performance liquid chromatography
- Nitritometry

#

18) One of the listed medicines does not belong to tropane derivatives. Specify it:

- Atropine sulfate
- Scopolamine hydrobromide
- Homatropin hydrobromide
- Tropacin
- Platyphyllin hydrotartrate

#

19) One of the drugs listed below, derivatives of tropane, does not give the Vitali-Morena reaction. Specify it:

- Atropine sulfate
- Scopolamine hydrobromide
- Tropacin
- Tropafen
- Homatropin hydrobromide

#

20) Which of the following methods cannot be used for the quantitative determination of scopolamine hydrobromide?

- Argentometry according to Fayance
- Mercurimetry
- Acid-base titration in a two-phase environment
- Acid-base titration in non-aqueous solvents
- Argentometry according to More

#

21) Specify which alkaloid camphor salts are part of Aeron tablets?

- Hyoscyamine and scopolamine
- Homatropin
- Tropacin
- Caffeine
- Atropine

#

22) Specify the name of the medicinal substance from the group of alkaloids, the modification of which resulted in a synthetic analogue - homatropine hydrobromide?

- Cytisine
- Themisal
- Pachycarpine hydroiodide
- Physostigmine salicylate

- Atropine sulfate

#

23) The pharmacist-analyst of the control and analytical laboratory determines the quantitative content of the scopolamine hydrobromide substance by the method of acid-base titration in non-aqueous media. What titrated solution does he use:

- Chloric acid
- Sodium hydroxide
- Sodium methylate
- Hydrochloric acids
- Sodium nitrite

#

24) Choose a medicinal substance that belongs to alkaloids, tropane derivatives:

- Scopolamine hydrobromide
- Cytisine
- Strychnine nitrate
- Pachycarpine hydroiodide
- Platyphyllin hydrotartrate

#

25) 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:

- The color of the solution is purple
- Release of gas bubbles
- The color of the solution is green
- Falling of black sediment
- Precipitation of a white precipitate

#

26) Indicate which of the following medicinal products gives a positive reaction to Vitaly-Morena:

- Scopolamine hydrobromide
- Platyphyllin hydrotartrate
- Cytisine
- Papaverine hydrochloride
- Pachycarpine hydroiodide

#

27) What is the pharmacological effect of pachycarpine hydroiodide?

- Central nervous system stimulant;
- Diuretic;
- Bronchodilator;
- Stimulator of breathing;
- Ganglioblockers (with hypertension, increases uterine muscle contraction).

#

28) Indicate the pharmacological action of atropine sulfate:

- Stimulates the muscles of the uterus;
- Reduces intraocular pressure;
- Blocks calcium channels;
- Increases the tone of smooth muscle organs;
- Mydriatic, reduces the tone of smooth muscle organs.

#

29) What is the pharmacological effect of scopolamine hydrobromide?

- Antimalarial;
- Central nervous system stimulant;
- Stimulator of birth activity;
- Antiglaucoma;
- Mydriatic, sedative.

- #

30) What is formed as a result of the interaction of platyphyllin hydrotartrate with β-naphthol in the presence of concentrated sulfuric acid?

- Auric dye.
- Azo dye
- Indophenol dye.
- Azomethine dye

#

31) What test is not performed when identifying Aprophenum [Aprophenum]?

- Iodoform sample
- Hydroxam sample
- Interaction with Markey's reagent
- Vitaly-Moren's reaction
- Interaction with NH_4NO_3 in concentrated H_2SO_4

4.4. Situational tasks:

1. How does the admixture of seneciphyllin get into platyphyllin hydrotartrate when it is obtained from plant raw materials?
2. Why does homatropine hydrobromide not give the Vitali-Morena reaction?
3. What is the role of oxymercury acetate in the quantitative determination of scopolamine hydrobromide by the non-aqueous titration method?
4. Explain why aprofen gives the Vitali-Morena reaction?
5. Explain the essence of the reaction of platyphyllin hydrotartrate with β-naphthol in the presence of conc. sulfuric acid. Write the chemistry of the reaction.
6. Specify the features of the structure of pachycarpine, due to which the formation of picrate with a characteristic melting point is possible.
7. Explain the need to increase the alcohol-chloroform mixture in the quantitative determination of homatropine hydrobromide by the method of alkalimetry.

4.5. Tasks:

1. Calculate the volume of 0.1 M perchloric acid solution (C_a = 1.0000), which was spent on the titration of 0.2014 g of scopolamine hydrobromide (M.w. 384.3), if the volume of the titrant in the control experiment is 0.12 ml, loss in mass when dried - 12.6%, and the content of the active substance in the preparation is 98.7%.
2. Calculate the percentage content of scopolamine hydrobromide (M.w. 384.3) in the preparation, if the weight of the test piece is 0.2383g, volume 0.1 M perchloric acid solution (C_a = 0.9792) in the working experiment – 6.44 ml, in the control–0.18 ml, a loss in mass when drying–1.3%.
3. Calculate the mass of scopolamine hydrobromide measurement (M.w. 384.3), if 6.64 ml of 0.1 M perchloric acid solution (C_a = 1.0001) was spent on its titration,volume titrant in the control experiment – 0.2 ml, and the content of the active substance in the preparation–99.8%.
4. Calculate the mass of a sample of homatropine hydrobromide (M.w. 356.27), if 5.74 ml of a 0.1 M solution of perchloric acid (C_a = 1.0241) was spent on its titration, the volume of the titrant in the control experiment – 0.21 ml, and the content of the active substance in the preparation – 99.4%.
5. Calculate the percentage content of homatropine hydrobromide (M.w. 356.27) in the drug, if the weight of the test is 0.3593 g,volume0.1 M perchloric acid solution (C_a = 1.0009) in the working experiment – 4.53 ml, in the control – 0.16 ml, aloss in masswhen dried is 1.4%.
6. Calculate the volume of a 0.1 M solution of perchloric acid (C_a = 1.0000), which is spent on the titration of 0.1850 g of pachycarpine hydroiodide (M.w. 363.30), if volume titrant in the control experiment – 0.10 ml,loss in mass when

drying – 0.14%, and the content of the active substance in the preparation – 99.0%.

7. Determine the mass fraction of pachycarpine hydroiodide (M.w. 363.30) in the medicinal product, if 6.48 ml of 0.1 M perchloric acid solution was spent on the titration of 0.2302 g of pachycarpine hydroiodide (C_a = 0.9994), ifvolumetitrant in the control experiment – 0.14 ml.
8. Determine the mass fraction of aprofen (M.w. 361.92) in the medicinal product, if 9.42 ml of 0.1 M perchloric acid solution (C_a = 0.9899) was spent on the titration of a weight of 0.3007g, volume titrant in the control experiment – 0.16 ml.
9. Calculate the percentage content of platyphyllin hydrotartrate (M.w. 487.5) in the drug, if the weight of the test is 0.3857g, the volume of a 0.1 M perchloric acid solution (C_a = 1.0208) in the work experiment was 7.82 ml, in the control experiment - 0.09 ml.
10. Calculate the weight of platyfillin hydrotartrate (M.w. 487.5), if 9.70 ml of 0.1 M sodium hydroxide solution (C_a = 1.0198) was spent on its titration. The content of the active substance is 99.2%. Loss in mass upon drying 0.22%.
11. Calculate the volume of 0.1 M perchloric acid solution (C_a = 0.9982), which will be spent on 0.3109 g of platyphyllin hydrotartrate (M.w. 487.5), if its percentage content in the preparation is 98.20% , the titrant volume in the control experiment is 0.12 ml, loss in mass upon drying 0.42%.

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. 5

1. TOPIC: Analysis of agents acting on adrenergic processes: adrenomimetics, adrenoblockers, sympathomimetics, sympatholytics.

2. PURPOSE: To master the methods of analysis of medicinal products acting on adrenergic processes: adrenomimetics, adrenoblockers, sympathomimetics, sympatholytics.

3. TARGETS:

3.1. To study the structure, nomenclature, synonyms, physicochemical properties, sources and methods of obtaining medicines acting on adrenergic processes: adrenomimetics, adrenoblockers, sympathomimetics, sympatholytics.

3.2. To study the methods of analysis of the considered group of medicinal products according to the SPhU, 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. Consider the peculiarities of the analysis of drugs acting on adrenergic processes: adrenomimetics, adrenoblockers, sympathomimetics, sympatholytics, 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 acting on adrenergic processes: adrenomimetics, adrenoblockers, sympathomimetics, sympatholytics, based on their physicochemical properties.

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

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. Define the terms: "adrenergic processes", "adrenomimetics", "adrenoblockers", "sympathomimetics", "sympatholytics".

2. Sources of production, chemical structure, nomenclature, synonyms, physicochemical properties of the investigated medicinal substances.

3. Medicines from the group of alkaloids with an exocyclic atom nitrogen Ephedrine hydrochloride. Structure, nomenclature, preparation, properties, analysis, application.

3.1. Write the structural formula of ephedrine hydrochloride, its chemical and Latin name. Describe the effect of stereoisomerism on pharmacological activity.

3.2. Give schemes of reactions of ephedrine hydrochloride with copper (II) sulfate and hydramine cleavage under different conditions.

3.3. Describe the possible methods of quantitative determination of ephedrine hydrochloride, the conditions for their implementation. Give the corresponding reaction equations, calculation formulas.

4. Mesaton (phenylephrine hydrochloride). Structure, nomenclature, properties, analysis, application.

5. Izadrine (isoprenal hydrochloride). Structure, nomenclature, properties, analysis, application.

6. Anaprilin (propranolol hydrochloride). Structure, nomenclature, properties, analysis, application.

7. Naphthysin (naphazoline nitrate). Structure, nomenclature, properties, analysis, application.

8. Medicinal products derived from tropane (synthetic analogue): tropafen. Structure, nomenclature, properties, analysis, application.

8.1. The Vitali-Morena reaction is a characteristic reaction for drugs that are tropane derivatives. The chemical essence of the reaction, its specificity, conditions and execution technique.

8.2. Describe the drugs of the tropane group as ester derivatives. Indicate what reactions the ester group causes for these substances and how these reactions are used in pharmaceutical analysis. Write the appropriate reaction equations, justify the conditions for their implementation.

8.3. Give the possible methods of quantitative determination and explain the conditions for their implementation for medicinal products, tropane derivatives. Write the appropriate reaction equations, calculation formulas.

9. Drugs, indole derivatives: reserpine. Sources of production, physical and chemical properties.

9.1. Describe the acid-base properties of reserpine and indicate the value of these properties in assessing its quality.

9.2. Explain the essence of the reaction of reserpine (and other indole derivatives) with vanillin in hydrochloric acid. Write the chemistry of the reaction (Van Urck reaction).

9.3. Possible methods of quantitative determination of drugs from the indole group.

10. Peculiarities of storage of researched medicinal products based on their physical and chemical properties.

11. The main dosage forms created on the basis of the investigated medicinal substances. Relationship of structure with biological action.

4.3. Test tasks:

#

1) Indicate which of the listed medicines is a double ester according to its chemical structure:

- Reserpine
- Pilocarpine hydrochloride
- scopolamine hydrobromide
- G. Physostigmine salicylate
- Ephedrine hydrochloride

#

2) One of the alkaloids listed below is isolated from Rauwolfia snake. Specify it:

- Platyphilin
- Caffeine
- Papaverine
- Strychnine
- Reserpine

#

3) Which of the following reagents are specific for the identification of reserpine?

- Cobalt chloride solution
- Iron (III) chloride solution
- A solution of vanillin in hydrochloric acid
- Copper sulfate solution
- Concentrated sulfuric acid

#

4) When ephedrine hydrochloride is heated with a potassium ferricyanide crystal, the smell of bitter almonds appears, which is due to the formation of:

- Benzaldehyde
- Nitrobenz

- Chlorobenzyl
- Aniline
- Toluene

#

5) What reagent should be used to identify ephedrine hydrochloride?

- copper (II) hydroxide
- Bromine water
- Ammonium nitrate
- Hydrochloric acid
- Ammonium chloride

#

6) Identification of ephedrine hydrochloride is carried out by a reaction based on the formation of a blue-violet complex compound. At the same time, a solution is used as the main reagent:

- Copper (II) sulfate
- Potassium ferricyanide
- Sodium edetate
- Hydrochloric acids
- Diethyl ether

#

7) Nitritometry is not used for quantitative determination:

- Ephedrine hydrochloride
- Novocaine
- Streptocide
- Levomycetin
- Sulfazine

#

8) Reserpine gives a positive result of the hydroxam reaction due to the presence in its structure:

- Complex ester groups
- Aromatic core
- Pyrrole nitrogen atom
- Phenolic hydroxyl
- Primary aromatic amino group

#

9) Izadrin, like other catecholamines, is oxidized by iodine solution with the formation of colored products. To create the required pH value, the pharmacist-analyst must add:

- Hydrochloric acid solution
- Acetate buffer solution
- Ammonia buffer solution
- Hydrotartrate buffer solution
- Sodium hydroxide solution

#

10) The pharmacist-analyst carries out the quantitative determination of mesatone, in accordance with the requirements of the SPhU, by the method:

- Nitritometry
- Bromatometry
- Gravimetry
- Alkalimetry in alcoholic medium
- Iodometry

#

11) The drug has an adrenomimetic effect:

- Izadrin
- Procaine hydrochloride
- Dibazol
- Prozerin
- Promedol

#

12) Quantitative analysis of isadrin is carried out in the control and analytical laboratory. For this, the method of quantitative determination is used:

- Acidimetry in a non-aqueous environment
- Acidimetry in an aqueous medium
- Reverse iodometry
- Alkalimetry in a non-aqueous medium
- Nitritometry

#

13) Quantitative analysis of mesatone is carried out in the control and analytical laboratory. For this, the method of quantitative determination is used:

- Acidimetry in an aqueous medium
- Reverse iodometry
- Alkalimetry in a non-aqueous medium
- Nitritometry
- Reverse bromatometry

#

14) A medicinal product characterized by a reaction with Ferrum (III) chloride:

- Procaine hydrochloride
- Magnesium oxide
- Diphenhydramine
- Anesthesin
- Mesaton

#

15) Which of the following drugs are catecholamines?

- Tropafen
- Izadrin
- Naphthysin
- Levomycetin
- Reserpine

#

16) Choose a medicinal substance that belongs to alkaloids, tropane derivatives:

- Tropafen
- Cytisine
- Strychnine nitrate
- Pachycarpine hydroiodide
- Platyphyllin hydrotartrate

#

17) Indicate which of the following medicinal products gives a positive reaction to Vitaly-Morena:

- Tropafen
- Platyphyllin hydrotartrate
- Cytisine
- Papaverine hydrochloride
- Pachycarpine hydroiodide

#

18) To identify medicinal substances, synthetic analogues of atropine: tropafen, tropacin - use the nitration reaction, because they contain:

- Benzene ring
- Aldehyde group
- Carbonyl group
- Merkapogroup
- Carboxylic group

#

19) Specify the reagent used to detect the nitrate ion in naphthizin:

- Silver nitrate solution
- Marky's reagent
- Solution of sulfanilic acid
- Frede's reagent
- Diphenylamine solution

#

20) For the quantitative determination of naphazoline nitrate (naphthyzine), one ofof the following titrimetric methods. Specify it:

- Complexonometry
- Argentometry according to More
- Argentometry according to Fayance
- Nitritometry
- Acid-base titration

#

21) Indicate the derivative of which heterocycle is naphazoline nitrate (naphthyzine):

- Pyrimidine
- Pyrrol
- Imidazoline
- Indole
- Pyrazole

#

22) One of the following titrimetric methods can be used for the quantitative determination of anaprilin (propranolol hydrochloride). Specify it:

- Complexonometry
- Acidimetry
- Nitritometry
- Argentometry according to More
- Iodometry

4.4. Situational tasks:

1. Explain the essence of the reaction of reserpine (and other indole derivatives) with vanillin in hydrochloric acid. Write the chemistry of the reaction (Van Urck reaction).
2. Give examples of chemical reactions confirming that mesatone and isadrin belong to the salts of nitrogenous bases.

3. Justify the possibility of using the acid-base titration method in non-aqueous media for the quantitative determination of ephedrine hydrochloride. Give the reaction equations, the formula for calculating the quantitative content.
4. Explain why it is necessary to add mercury (II) acetate in the quantitative determination of anaprilin by the non-aqueous titration method.
5. Explain why isadrine (isoprenal hydrochloride) and mesatone (phenylephrine hydrochloride) give different colors when interacting with Ferrum (III) chloride.
6. Explain why tropafen gives the Vitali-Morena reaction.

4.5. Tasks:

1. Calculate the percentage content of mesatone (M.w. 203.67) in the preparation, if 16.10 ml of 0.1 M sodium thiosulfate solution (C_a = 1.0000) was spent on the titration of a weight of 0.1120 g, the loss in mass during drying is 0 .5% and the volume of the titrant in the control experiment - 48.50 ml.
2. Calculate the volume of 0.1 M perchloric acid solution (C_a = 0.9865), which is spent on the titration of 0.0977 g of ephedrine hydrochloride (M.w. 201.70), if it is known that the content of the active substance is 99.9 %.
3. Determine the mass fraction of ephedrine hydrochloride (M.w. 201.70), if 4.50 ml of 0.1 M perchloric acid solution was spent on the titration of 0.1035 g of the substance (C_a = 1.1228).
4. Calculate the percentage of reserves on (M.w.608.7) in the preparation, if the weight of the sample is 0.3576 g, the volume of a 0.1 M perchloric acid solution (C_a = 1.0004) in the working experiment is 5.96 ml, in the control - 0.18 ml, and the loss in mass during drying is 0.4%.
5. Calculate the weight of ephedrine hydrochloride (M.w. 201.70), if 5.68 ml of 0.1 M perchloric acid solution (C_a = 1.0041) was spent on its titration, the titrant volume in the control experiment was 0.21 ml, and the content of the active substance in the preparation is 99.4%.
6. Calculate the weight of mesaton weight (M.w. 203.67), if 6.88 ml of 0.1 M perchloric acid solution (C_a = 1.0011) was spent on its titration, the titrant volume in the control experiment was 0.21 ml , and the content of the active substance in the drug is 97.89%.
7. Calculate the volume of 0.1 M perchloric acid solution (C_a = 0.9995), which is spent on the titration of 0.6771 g of reserpine (M.w. 608.70), if it is known that the content of the active substance is 98.5% .
8. Calculate the percentage content of naphazoline hydrochloride (naphthysine) (M.w. 246.7) in the preparation, if the weight of the test is 0.1516 g, the volume

of 0.1 M sodium hydroxide solution (C_a = 1.0015) - 5.96 ml, and the loss in mass during drying is 0.4%.

9. Calculate the volume of 0.1 M perchloric acid solution (C_a = 1.0004), which is spent on the titration of 0.2471naphazoline hydrochloride (naphthysine) (M.w. 246.7),if it is known that the content of the active substance is 99.5%.

10. Calculate the percentage content of anaprilin (propranolol hydrochloride) (M.w. 295.8) in the preparation, if the weight of the test is 0.2374 g, the volume of 0.1 M sodium hydroxide solution (C_a = 1.0025) is 7.96 ml, and the loss in mass during drying is 0.6%.

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. 6

1.THEME: Final lesson on theory and practice on the topic: «Analysis of medicines that affect the central and peripheral nervous system. General characteristics, classification, relationship of structure with pharmacological action, extraction, methods of analysis, application".

2.PURPOSE: To form systematic knowledge and consolidate practical skills in the analysis of the quality of medicines that affect the central and peripheral nervous system and their semi- & synthetic derivatives using physical, physico-chemical and chemical methods of analysis.

3. TARGETS:

3.1. Check and consolidate theoretical knowledge and practical skills in the use of physical, physicochemical and chemical methods to analyze the quality of medicines that affect the central and peripheral nervous system and their semi- & synthetic derivatives.

3.2. Check the protocols of laboratory work and analyze the correctness of the analysis of medicines that affect the central and peripheral nervous system and their semi- & synthetic derivatives 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. Definition of "**peripheral vasodilators**", "**myotropic antispasmodics**".
2. Definition of the term "**alkaloids**". General characteristics, distribution in nature, principles of classification of alkaloids. Chemical classification of alkaloids.
3. Sources of obtaining alkaloids. General methods of extracting alkaloids from plant raw materials. Methods of dividing the sum of alkaloids.
4. General methods of identification of alkaloids. General alkaloid (precipitating) and special reagents, their composition. Chemical processes underlying the interaction with alkaloids. Reaction performance technique.
5. General methods of quantitative determination of medicinal substances from the group of alkaloids. Peculiarities of quantitative determination of medicinal substances from the group of alkaloids-bases and alkaloids-salts.

6. Sources of production, chemical structure, nomenclature, synonyms, physicochemical properties of medicinal substances from the group of alkaloids, isoquinoline derivatives, purine.
7. To justify the use of chemical and instrumental methods in the analysis of the quality of drugs from the group of alkaloids, isoquinoline derivatives, and purine.
8. Ways of entry and determination of specific impurities in the analysis of the quality of drugs from the group of alkaloids of isoquinoline, purine derivatives.
9. Medicines from the group of alkaloids, Isoquinoline derivatives. Write the structural formula and Latin name of papaverine hydrochloride. Describe the properties of the drug as a nitrogenous base and give reactions confirming these properties. Specify the reactions based on the restorative properties of the drug.
10. Give possible methods for the quantitative determination of papaverine hydrochloride. Explain the role of alcohol in the quantitative determination of papaverine hydrochloride by SPhU.
11. Justify the application of the acid-base titration method in the medium of non-aqueous solvents for the determination of papaverine hydrochloride, specify the conditions.
12. Write the structural formulas, Latin names of analogs of papaverine hydrochloride by action: bendazole hydrochloride (dibazole), drotaverine hydrochloride (no-shpa). Describe the properties, analysis. Application.
13. Medicines from the group of alkaloids, purine derivatives. Theobromine. Theophylline. Theophylline monohydrate. Structure, nomenclature, preparation, properties, analysis, application.

    13.1. Describe the relationship between the chemical structure of medicinal substances of this group and their physicochemical properties (solubility in water, in relation to acids and alkalis) and biological activity.

    13.2. Describe the acid-base properties of medicinal substances of the purine group depending on the chemical structure of the molecules. Tautomeric transitions are possible, the preferred state depending on the conditions.

    13.3. Murexide test as a general group reaction to drugs from the group of alkaloids, purine derivatives. Reaction mechanism, its specificity, conditions and performance technique.

    13.4. Acid-base properties of purine derivatives and complexation reactions with salts of heavy metals (silver, cobalt, copper). Conditions for carrying out reactions, their importance in the analysis of the quality of drugs from the group of alkaloids, purine derivatives.
14. Identification of drugs from the group of alkaloids, purine derivatives, based on their physicochemical properties and features of the chemical structure.

15. Describe the possible methods of quantitative determination of drugs of this group, the conditions for their implementation. Give the corresponding reaction equations, calculation formulas.

16. Medicines from the group of salt forms of purine alkaloids. Themisal. Theophylline-ethylenediamine (euphylline). Structure, nomenclature, preparation, properties, analysis, application.

17. Medicines from the group of synthetic derivatives of purine alkaloids. Pentoxifylline. Diprofylline. Xanthine nicotinate. Structure, nomenclature, properties, analysis, application.

18. Features storage of medicines from the group of alkaloids, isoquinoline derivatives, purine, as well as their synthetic analogues, based on their physicochemical properties. Factors affecting the stability of preparations of this group of substances and changes occurring under their influence.

19. The main dosage forms, created on the basis of medicinal substances from the group of alkaloids, isoquinoline derivatives, purine. Relationship of structure with biological action.

20. Define the concepts of "**narcotic analgesics**", "agonists", "antagonists" and "synergoantagonists".

21. Latin names, synonyms, structural formulas and chemical names of drugs derived from morphine (morphine hydrochloride, codeine, codeine phosphate, ethylmorphine hydrochloride, etc.).

22. Use of physico-chemical properties and features of the chemical structure to justify the methods of analysis and storage conditions of the studied drugs.

23. Based on the structure of the studied medicinal substances, justify the identification reactions and methods of quantitative determination, give the chemistry of the corresponding reactions.

24. Write the structural formulas of morphine hydrochloride, codeine, codeine phosphate and ethylmorphine hydrochloride. Specify the physical and physico-chemical properties that allow you to differentiate these medicinal substances.

25. Characterize the functional groups and explain the peculiarities of the reaction of morphine alkaloids (morphine, codeine, ethylmorphine) with a solution of Ferrum (III) chloride.

26. Describe the acid-base and reducing properties of morphine hydrochloride, codeine, ethylmorphine hydrochloride. Give the methods of qualitative and quantitative determination related to them, the conditions in which they are carried out.

27. Synthetic analogues of morphine: promedol, tramadol. Their properties, analysis and application.

28. Synergoantagonists of morphine: nalorphine, pentazocine. Properties, application analysis.
29. Vomiting (apomorphine) and nausea (ondansetron) drugs. Properties, analysis, application.
30. To substantiate the conditions of acid-base titration of bases and salts of alkaloids in an aqueous medium (emphasize the role of alcohol and chloroform).
31. Justify the storage conditions of the researched medicinal products based on their structure and chemical properties.
32. Release form, dosage and application of the researched means. Relationship between structure and biological action in a number of morphinan derivatives.
33. Give definition concepts: "**hallenergeticprocesses**", "**hallandnoandmetic**s", "**anticholinesterase drugs**".
34. Latin names,synonyms,formulas structures and chemical names medical drugs,derivatives imidazole (pilocarpine hydrochloride), indole (physostigmine salicylate), quinolysine (cytisine), quinuclidine (Aceclidine).
35. Using physics-chemical properties,features chemical structures for justification reactions identification,methods quantitative definition and conditions storage investigated drugs
36. Derivatives imidazole –pilocarpine hydrochloride. Medical raw,what contains pilocarpine. Physics-chemical properties pilocarpine hydrochloride.
37. Point reactions on pilocarpine hydrochloride, what confirms structure and authenticity drug. Specify specific reaction identification on pilocarpine hydrochloride and explain her chemical sense.
38. Possible methods quantitative analysis pilocarpine hydrochloride. Explain conditions method acidic-the main titration in environment non-aqueous solvents. Write chemistry reactions.
39. Synthetic analog pilocarpine hydrochloride – Aceclidine. Him properties, analysis, application.
40. Drugs,derivatives indole(physostigmine salicylate). Sources receiving, physics-chemical properties.
41. Specify,on whose physics-chemical properties physostigmine salicylate started carrying out identification drug.
42. Point reactions on physostigmine salicylate, what confirms structure and authenticity drug.
43. Possible methods quantitative definition medical drugs, groups indole. Explain value alcohol and chloroform at alkalimetrichdefined physostigmine salicylate
44. Synthetic analog physostigmine salicylate – proserin. Properties, analysis, application.

45. Medicinal means with groups alkaloids, derivatives quinolysine. Cytisine. Building, nomenclature, obtaining, properties, analysis, application.

46. Acetylcholine-chloride, carbocholine. Properties, analysis. Application.

47. Justify conditions storage investigated medical means, going out with their structures and chemical properties.

48. The main ones medical forms, created on basis investigated medical means. Form release, dosage.

49. Define the concepts: "**cholinergic processes**", "**cholinergic blockers**", "**ganglioblockers**".

50. Sources of production, chemical structure, nomenclature, synonyms, physicochemical properties of medicinal substances from the group of cholinergic agents, diphenylpropionic acid derivatives (aprofen), cholinergic alkaloids, tropane derivatives (atropine sulfate, scopolamine hydrobromide, homatropine hydrobromide), pyrrolizidine (platyphyllin hydrotartrate) and ganglioblockers, quinolizidine derivatives (pachicarpine hydroiodide).

51. To substantiate the use of chemical and instrumental methods in the analysis of the quality of drugs from the group of alkaloids, tropane derivatives, pyrrolizidine and quinolizidine and diphenylpropionic acid derivatives.

52. Ways of entry and determination of specific impurities in the analysis of the quality of medicines from the group of alkaloids, tropane derivatives, pyrrolizidine and quinolizidine.

53. Medicines from the group of alkaloids, tropane derivatives.

53.1. Alkaloids of the tropane group. Scopolamine hydrobromide. Structure, nomenclature, preparation, properties, analysis, application.

53.2. Modification of the "leader structure" (atropine, scopolamine) in order to create synthetic analogues by action: homatropine hydrobromide, etc. Structure, nomenclature, properties, analysis, application. Relationship between structure and pharmacological action.

53.3. The Vitali-Morena reaction is a characteristic reaction for medicines from the group of alkaloids, tropane derivatives. The chemical essence of the reaction, its specificity, conditions and execution technique.

53.4. Describe the drugs of the tropane group as ester derivatives. Indicate what reactions the ester group causes for these substances and how these reactions are used in pharmaceutical analysis. Write the appropriate reaction equations, justify the conditions for their implementation.

53.5. Give possible methods of quantitative determination and explain the conditions for their implementation for medicines from the group of alkaloids, tropane derivatives. Write the appropriate reaction equations, calculation formulas.

54. Platyphyllin hydrotartrate. Structure, nomenclature, preparation, properties, application.

54.1. Based on the structure, propose identification reactions. Write the chemistry of reactions.

54.2. Specify the possible methods of quantitative determination of platyphyllin hydrotartrate, justify the conditions for their implementation, write the chemistry of the reactions.

55. Medicines from the group of alkaloids, quinolizidine derivatives. Pachycarpine hydroiodide. Structure, nomenclature, preparation, properties, analysis, application.

56. Medicinal products from the group of cholinergic blockers, derivatives of diphenylpropionic acid. Aprofen. Structure, nomenclature, properties, analysis, application.

57. Features storage of the researched group of medicines based on their physical and chemical properties.

58. The main dosage forms created on the basis of researched medicinal substances from the group of cholinergic blockers and ganglioblockers. Relationship of structure with biological effect.

58.1. Define the terms: "adrenergic processes", "adrenomimetics", "adrenoblockers", "sympathomimetics", "sympatholytics".

58.2. Sources of obtaining, chemical structure, nomenclature, synonyms, physicochemical properties of the investigated medicinal substances.

58.3. Medicines from the group of alkaloids with an exocyclic atom nitrogen Ephedrine hydrochloride. Structure, nomenclature, preparation, properties, analysis, application.

58.4. Write the structural formula of ephedrine hydrochloride, its chemical and Latin name. Describe the effect of stereo isomer on pharmacological activity.

58.5. Give schemes of reactions of ephedrine hydrochloride with copper (II) sulfate and hydramine cleavage under different conditions.

58.6. Describe the possible methods of quantitative determination of ephedrine hydrochloride, the conditions for their implementation. Give the corresponding reaction equations, calculation formulas.

59. Mesaton (phenylephrine hydrochloride). Structure, nomenclature, properties, analysis, application.

60. Izadrine (isoprenal hydrochloride). Structure, nomenclature, properties, analysis, application.

61. Anaprilin (propranolol hydrochloride). Structure, nomenclature, properties, analysis, application.

62. Naphthysin (naphazoline nitrate). Structure, nomenclature, properties, analysis, application.

63. Medicinal products derived from tropane (synthetic analogue): tropafen. Structure, nomenclature, properties, analysis, application.

63.1. The Vitali-Morena reaction is a characteristic reaction for drugs that are tropane derivatives. The chemical essence of the reaction, its specificity, conditions and execution technique.

63.2. Describe the drugs of the tropane group as ester derivatives. Indicate what reactions the ester group causes for these substances and how these reactions are used in pharmaceutical analysis. Write the appropriate reaction equations, justify the conditions for their implementation.

63.3. Give the possible methods of quantitative determination and explain the conditions for their implementation for medicinal products, tropane derivatives. Write the appropriate reaction equations, calculation formulas.

64. Drugs, indole derivatives: reserpine. Sources of production, physical and chemical properties.

64.1. Describe the acid-base properties of reserpine and indicate the value of these properties in assessing its quality.

64.2. Explain the essence of the reaction of reserpine (and other indole derivatives) with vanillin in hydrochloric acid. Write the chemistry of the reaction (Van Urck reaction).

64.3. Possible methods of quantitative determination of drugs, indole group.

64.4. Peculiarities of storage of researched medicinal products based on their physical and chemical properties.

65. The main dosage forms created on the basis of the investigated medicinal substances. Relationship of structure with biological action.

4.2. Test tasks for the final lesson

#

1) Choose the correct definition of "alkaloids":

- Carbohydrates of vegetable origin, which are part of various essential oils
- A large group of organic substances, mainly of plant origin (rarely animal), the molecules of which consist of a sugar residue, as well as a residue of one or another organic compound
- Substances of different chemical structure, necessary in small quantities for the normal functioning of the body

- Substances that are produced by microorganisms, higher plants, and animal tissues in the process of their vital activity and are able to exert a selective bactericidal and bacteriostatic effect on microorganisms, viruses, protozoa
- Nitrogen-containing bases, which are found most often in plants and, as a rule, have an active biological effect

#

2) Specify the group reaction for the identification of alkaloids of the purine series:

- Formation of azo dye
- Formation of benzylidene derivatives
- Formation of ammonium salts of purpuric acid derivatives
- The formation of base sediments
- Formation of colored precipitates with copper salts

#

3) Indicate which method is recommended by the DFU for the quantitative determination of theobromine:

- Acidimetry in non-aqueous solvents
- Argentometry
- Substitute acid-base titration
- Iodometry
- Nitritometry

#

4) In the analitycal laboratory of the pharmaceutical enterprise, the quantitative content of theophylline is determined by the method of indirect neutralization. At the same time, alkalimetric titration of nitric acid is carried out, which is quantitatively released as a result of the formation of:

- Potassium salt of theophylline
- Sodium salt of theophylline
- Ammonium salt of theophylline
- Copper salt of theophylline
- Silver salt of theophylline

#

5) Quantitative content of theophylline monohydrate, in accordance with the requirements of the SPhU, is determined by the method of alkalimetry by substitution. The titrant in this method is a standard solution:

- Sodium hydroxide
- Hydrochloric acids
- Potassium bromate

- Sodium edetate
- Ammonium oxalate

#

6) The pharmacist-analyst must confirm the presence of ethylenediamine in the composition of Euphilin. Which of the listed reagents can be used to identify ethylenediamine?
- Sodium hydroxide
- Potassium chloride
- Ammonium oxalate
- Cuprum (II) sulfate
- Glyoxalhydroxyanil

#

7) For the quantitative determination of euphilin by ethylenediamine, a titrated solution is used:
- Sodium hydroxide
- Hydrochloric acid
- Sodium nitrite
- Iodine
- Sodium edetate

#

8) Indicate which of the medicinal products by chemical nature is not a derivative of purine alkaloids:
- Xanthine nicotinate
- Euphilinus
- Ephedrine hydrochloride
- Theobromine
- Themisal

#

9) Indicate which of the following titrimetric methods of analysis is used to quantify theophylline:
- Permanganatometry (direct titration)
- Complexonometry (back titration)
- Alkalimetry (substitute titration)
- Acidimetry (direct titration)
- Nitritometry (direct titration)

#

10) Indicate which of the following reagents cannot be used to identify temisal:
- Iron (III) chloride

- Cobalt (II) chloride
- Concentrated hydrogen peroxide, hydrochloric acid, ammonia solution
- Sodium nitrite
- Silver nitrate

#

11) Indicate which heterocycles the condensed purine system includes:

- Pyridine and pyrazine
- Pyrazole and pyrimidine
- Imidazole and furan
- Pyrimidine and imidazole
- Pyrazine and pyrimidine

#

12) The reaction of an aqueous solution of euphilin:

- Sour
- Neutral
- Alkaline
- Euphilin does not dissolve in water

#

13) Name the reagent that cannot be used to distinguish theophylline from caffeine:

- Ammonia solution
- Marky's reagent
- Cobalt chloride solution
- Silver nitrate solution
- Sodium nitroprusside solution

#

14) Specify the drug that forms a purple color with a solution of cobalt chloride, followed by the formation of a grayish-blue precipitate:

- Caffeine
- Theophylline
- Theobromine
- Euphilinus
- Caffeine monohydrate

#

15) List the reagents necessary for the formation of silver salts of theobromine and theophylline:

- A solution of sodium hydroxide and silver nitrate
- Tannin solution

- A solution of acetic acid and silver nitrate
- Nitric acid and silver nitrate solution
- Perhydrol or bromine water

#

16) The general group reaction to alkaloids, purine derivatives - the murexide test - is based on a chemical process:

- Recovery
- Electrophilic substitution
- Oxidation
- Nucleophilic addition
- Complex formation

#

17) State what Wagner's reagent is:

- A solution of bismuth iodide in potassium iodide
- A solution of mercury (II) iodide in potassium iodide
- A solution of iodine in potassium iodide
- A solution of cadmium chloride in potassium iodide
- Tannin solution 1% in alcohol

#

18) When euphyllin interacts with a solution of copper (II) sulfate, the reaction occurs:

- Esterification
- Oxidation
- Hydrolysis
- Complex formation
- Dianitrogenation

#

19) Specify the composition of the Dragendorff precipitation reagent:

- A solution of iodine in potassium iodide
- A solution of bismuth iodide in potassium iodide
- A solution of mercury iodide in potassium iodide
- A solution of cadmium iodide in potassium iodide
- A solution of lead iodide in potassium iodide

#

20) Specify the composition of Mayer's precipitation reagent:

- A solution of iodine in potassium iodide
- A solution of bismuth iodide in potassium iodide
- A solution of mercury iodide in potassium iodide

- A solution of cadmium iodide in potassium iodide
- A solution of lead iodide in potassium iodide

#

21) Specify the composition of Marki's reagent:

- A mixture of concentrated sulfuric and nitric acids
- Alcohol solution of ammonium molybdate
- A solution of formaldehyde in concentrated sulfuric acid
- A solution of p-dimethylaminobenzaldehyde in chloroform
- A solution of iodine in potassium iodide

#

22) Specify the composition of Bouchard's precipitation reagent:

- A solution of mercury iodide in potassium iodide
- A solution of bismuth iodide in potassium iodide
- Phosphoromolybdenic acid
- Freshly prepared 5% aqueous solution of tannin
- A solution of iodine in potassium iodide

#

23) To identify which of the following drugs is not used reaction with a solution of copper (II) sulfate?

- Caffeine
- Theobromine
- Theophylline
- Euphilinus
- Themisal

#

24) Indicate which of the following reactions cannot be used to identify euphilin:

- Murexide test
- Reaction with 2,4-dinitrochlorobenzene
- Reaction with sodium rhodisonate
- Hydroxam test
- With a solution of copper (II) sulfate

#

25) One of the following drugs, purine derivatives, does not give a positive result (the formation of colored products) in the reaction with a solution of cobalt nitrate. Specify this medicine:

- Theobromine
- Theophylline

- Euphilinus
- Themisal
- Caffeine

#

26) Indicate the pharmacological effect of diprofylline:

- Analgesic
- Anti-inflammatory
- Antipyretic
- Central nervous system stimulant
- Spasmolytic

#

27) Substances of medicinal substances from the group of alkaloids are studied in the control and analytical laboratory. A positive reaction to xanthines is given by substances derived from:

- Purine
- Imidazole
- Hit
- Quinine
- Isoquinoline

#

28) The general reaction for the identification of drugs from the group of purine alkaloids (theobromine, theophylline, etc.) in pharmaceutical analysis is:

- Murexide test
- Reaction with 0.1% tannin solution
- Reaction with silver nitrate solution
- Reaction with cobalt chloride solution
- Interaction with an alkaline solution of sodium nitroprusside

#

29) Specify the name of the medicinal product to which the following systematic name 6,7-dimethoxy-1-(3,4-dimethoxybenzyl) isoquinoline hydrochloride would correspond:

- Tropacin
- Papaverine hydrochloride
- V. Caffeine
- H. Quinidine sulfate
- Dibazol

#

30) What pharmacological effect does papaverine hydrochloride have?

- Antipyretic
- choleretic
- Spasmolytic
- Anti-inflammatory
- Vasoconstrictor

#

31) Specify the method that is the basis for the quantitative determination of papaverine hydrochloride according to the requirements of DFU:

- Acid-base titration in the presence of alcohol and hydrochloric acid with potentiometric termination
- By the method of acid-base titration in non-aqueous solvents
- Acid-base titration in the presence of an alcohol-chloroform mixture
- Argentometry according to Fayance
- Gravimetric

#

32) According to the requirements of the SPhU, concomitant impurities in the papaverine hydrochloride substance are defined as:

- A solution of iodine in potassium iodide
- A solution of mercury iodide in potassium iodide
- A solution of bismuth iodide in potassium iodide
- By the method of ion exchange chromatography
- By the method of liquid chromatography

#

33) Indicate which of the listed drugs is an isoquinoline derivative according to its chemical structure:

- Quinidine sulfate
- Scopolamine hydrobromide
- Pachycarpine hydroiodide
- Papaverine hydrochloride
- Novocaine hydrochloride

#

34) According to the requirements of the SPhU, for the identification of papaverine hydrochlorideprecipitate the base of this alkaloid with ammonia solution; the resulting sediment is washed and dried. Specify the following actions to be performed with the received balance:

- Conduct a reaction on chlorides
- Determine the melting point
- Conduct a reaction with Dragendorff's reagent

- Determine the specific rotation
- Chromatograph (ion exchange chromatography)

#

35) Indicate which of the listed drugs are synthetic analogs of papaverine hydrochloride:

- Bigumal, chloridin
- Tropacin, troventol
- Mesaton, isadrin
- Trimecain, dikain
- Dibazol, no-shpa

#

36) Indicate the pharmacological action of drotaverine hydrochloride (no-shpa):

- Central nervous system stimulant
- Antitussive
- Antimalarial
- Hypertensive
- Spasmolytic

#

37) Enter the name of the alkaloid, the synthetic analogue of which is drotaverine hydrochloride (no-shpa):

- Papaverine
- Pachycarpine
- Quinidine
- Scopolamine
- Morphine

#

38) Specify the reagent with which, during the identification of papaverine hydrochloride, methylene bispapaverine sulfate is formed:

- Sodium metabisulfite
- Dragendorff's reagent
- Ammonium sulfate
- Marky's reagent
- Hydrochloric acid

#

39) Which of the proposed methods cannot quantify dibazole (2-benzylbenzimidazole hydrochloride)?

- Argentometrically
- Acid-base titration (in an alcoholic medium)

- Nitritometrically
- Non-aqueous titration
- Iodometrically

#

40) Indicate by which method you can quantify bendazole hydrochloride (dibazole):

- AND. Acidimetry in non-aqueous environments
- B. Bromatometric
- IN. Gravimetric
- G. Complexometric
- D. Nitritometric

#

41) What pharmacological action does it have?bendazole hydrochloride (Dibazol)?

- Analgesic
- Anti-inflammatory
- Spasmolytic
- Antipyretic
- Antiseptic

#

42) In the control and analytical laboratory, a complete analysis of Dibazol tablets is carried out. To identify these tablets, among other reactions, the analyst conducts a reaction to:

- Sulfates
- Tartrates
- Nitrates
- Nitrite
- Chlorides

#

43) A chemist-technologist of the laboratory of a pharmaceutical enterprise, when determining technological impurities in dibazole, dissolves it in water when heated to 90°C, acidifies it with a solution of hydrochloric acid, adds a solution of iron (III) chloride; after careful mixing, a pink color appeared. What impurity did the technologist chemist determine?

- Hydrazobenzene
- Benzyl chloride
- Benzoyl chloride
- Diphenylacetic acid

- *at*-Phenylenediamine

#

44) What reagent can be used to identify dibazole in a solution for injections?

- Dragendorf's reagent (bismuth periodide solution)
- Nessler's reagent (potassium tetraiodomercurate alkaline solution)
- tannin solution
- A solution of copper sulfate
- A solution of iodine in an acidic medium

#

45) According to SPhU, for the identification of "Papaverini hydrochloridum" a reaction is carried out with acetic anhydride and sulfuric acid when heated in a water bath. As a result of the reaction, the solution is colored in:

- Yellow color with green fluorescence
- Red color with green fluorescence
- Blue color with green fluorescence
- Blue color without fluorescence
- Red color without fluorescence

#

46) Medicinal substances from the group of alkaloids are defined as general alkaloid precipitating reagents. Which of the listed reagents does not belong to them?

- Tollens' reagent
- Dragendorff's reagent
- Mayer's reagent
- Marme's reagent
- Sonnenstein's reagent

#

47) Specify a possible method for the quantitative determination of codeine phosphate:

- Argentometry according to More;
- Complexonometry;
- Nitritometry;
- Acid-base titration in non-aqueous solvents;
- Acidimetry

#

48) When adding an ammonia solution to a solution of morphine hydrochloride, the formed morphine base precipitate is dissolved in an excess of sodium hydroxide solution. Specify the reason for its dissolution:

- Morphine base dissolves in water;
- Due to the formation of morphine alcoholate (presence of alcohol hydroxyl);
- Hydrolytic destruction of the morphine base under the action of sodium hydroxide solution;
- Due to the formation of morphine phenolate (the presence of phenolic hydroxyl).
- The presence of a carboxyl group

#

49) Indicate which of the following drugs exhibits pronounced basic properties, which makes it possible to use the method of acid-base titration in an alcohol-water environment:

- Theophylline;
- Caffeine;
- Theobromine;
- Codeine;
- Ethylmorphine

#

50) Indicate which reagent can be used to distinguish morphine hydrochloride from codeine:

- Mayer's reagent;
- Dragendorff's reagent;
- Solution of iron (III) chloride;
- Sodium nitrite solution
- Bouchard, Wagner reagent

#

51) Indicate which reagent can be used to distinguish morphine hydrochloride from codeine:

- Bouchard's, Wagner's reagent;
- Mayer's reagent;
- Marky's reagent;
- Dragendorff's reagent;
- Sodium acetate solution.

#

52) When quantifying which medicinal substance by the acid-base titration method in a glacial acetic acid medium (titrant – 0.1 M perchloric acid solution), you need to add a solution of mercury (II) acetate:

- Quinidine sulfate;
- Theophylline;

- Codeine phosphate;
- Codeine
- Ethylmorphine hydrochloride

#

53) One of the following methods is recommended by the SPhU for the determination of concomitant impurities in codeine. Specify it:

- Polarimetric;
- Ion exchange chromatography;
- Interaction with general alkaloid reagents;
- Determination of the melting point;
- Liquid chromatography.

#

54) Specify the method of quantitative determination recommended by the SPhU for the determination of codeine:

- Ion exchange chromatography;
- Photoelectrocolorimetry;
- Adsorption chromatography;
- Acid-base titration in an alcohol environment;
- Acid-base titration in non-aqueous solvents.

#

55) Specify the specific pharmacological action of codeine:

- Analgesic;
- Central nervous system stimulant;
- Neuroleptic;
- Anti-inflammatory;
- Antitussive.

#

56) One of the listed medicines does not belong to phenanthrenisoquinoline (morphinan) derivatives. Specify it:

- Codeine;
- Ethylmorphine hydrochloride;
- Morphine hydrochloride;
- Codeine phosphate
- Promedol.

#

57) One of the listed drugs gives a positive result of the reaction with iron (III) chloride. Specify it:

- Codeine;

- Promedol;
- Ethylmorphine hydrochloride;
- Papaverine hydrochloride;
- Morphine hydrochloride.

#

58) One of the listed drugs gives a positive result of the reaction with diazonium salts, forming an azo dye. Specify it:

- Platifiline hydrotartrate;
- Papaverine hydrochloride;
- Codeine;
- Ethylmorphine hydrochloride;
- Morphine hydrochloride.

#

59) Indicate which reagents can be used to distinguish morphine hydrochloride from codeine:

- Bouchard's, Wagner's reagent;
- Tannin solution;
- Cobalt nitrate solution;
- Dragendorff's reagent;
- Markie's reagent, iron (III) chloride.

#

60) Indicate the pharmacological action of morphine hydrochloride:

- Antiemetic;
- Anti-inflammatory;
- Antitussive;
- Local anesthetic;
- Analgesic.

#

61) One of the following methods cannot be used for the quantitative determination of morphine hydrochloride. Specify this method:

- Argentometric;
- Photoelectrocolorimetric;
- Acid-base titration;
- Acid-base titration in non-aqueous solvents;
- Complexometric.

#

62) One of the drugs listed below is a synthetic analogue of morphine hydrochloride in action. Specify this analogue:

- Homatropin hydrobromide;
- Proserin;
- Mesaton;
- Promedol;
- Lidocaine.

#

63) Indicate which titrimetric method SPhU recommends to use for the quantitative determination of ethylmorphine hydrochloride:

- Alkalimetry in alcoholic medium;
- Argentometry according to Folgard;
- Faience argentometry;
- Nitritometry;
- Acidimetry in non-aqueous solvents.

#

64) Specify the environment and conditions for the reaction of the identification of ethylmorphine hydrochloride with a solution of iron (III) chloride:

- In an alcoholic environment when boiling the solution;
- In an aqueous solution at a temperature of 5-10°WITH;
- In the presence of nitric acid at room temperature;
- In the presence of sodium hydroxide at a temperature of 40-60°WITH;
- In the presence of sulfuric acid, when heated.

#

65) Ethylmorphine hydrochloride has one of the following pharmacological actions. Specify it:

- Stimulator of breathing;
- Central nervous system stimulant;
- Hypotensive;
- Spasmolytic;
- Anti-inflammatory.

#

66) Indicate which of the following groups of reagents is used to identify promedol:

- Concentrated nitric acid, alcoholic solution of potassium hydroxide;
- Bromine water, ammonia solution;
- Copper sulfate solution, sodium hydroxide solution;
- A solution of hydrogen peroxide, potassium dichromate and sulfuric acid;
- Formaldehyde solution in concentrated sulfuric acid, chloroform

#

67) Specify the name of the synthetic analogue of drugs from the group of alkaloids, to which the chemical name 1,2,5-trimethyl-4-propionyloxy-4-phenylpiperidine hydrochloride would correspond:

- Tropacin
- Drotaverin hydrochloride
- Diprofylline
- Prozerin
- Promedol;

#

68) One of the following titrimetric methods cannot be used to quantify promedol. Specify it:

- Faience argentometry;
- Acid-base titration in a two-phase environment;
- Acid-base titration in a non-aqueous solvent;
- Argentometry according to Folgard;
- Nitritometry.

#

69) Indicate which of the following pharmacological actions promedol has:

- Antipyretic;
- Anti-inflammatory;
- Central nervous system stimulant;
- Hypotensive;
- Analgesic.

#

70) One of the following medicinal plants is the main source of opium. Specify it:

- Rauwolfia snake;
- Scopolia;
- Coffee;
- Sekurinega;
- Poppy is hypnotic.

#

71) One of the below-mentioned pharmacological actions is characteristic of the drug - omnopon. Specify it:

- Antitussive;
- Anti-inflammatory;
- Hypotensive;

- Stimulator of breathing;
- Analgesic.

#

72) One of the alkaloids listed below is a starting substance in the synthesis of apomorphine hydrochloride. Specify it:

- Reserpine;
- Narcotic;
- Anabasin;
- Morphine;
- Solasodin

#

73) One of the alkaloids below is a starting substance in the synthesis of codeine phosphate. Specify it:

- Reserpine;
- Narcotic;
- Anabasin;
- Morphine;
- Solasodin

#

74) One of the below-mentioned pharmacological actions is characteristic of apomorphine hydrochloride. Specify it:

- Analgesic;
- Anti-inflammatory;
- Antiemetic;
- Hypotensive;
- Vomiting, expectorant.

#

75) One of the following pharmacological actions is characteristic of ondansetron. Specify it:

- Analgesic;
- Anti-inflammatory;
- Antiemetic;
- Hypotensive;
- Vomiting, expectorant.

#

76) One of the narcotic analgesics is obtained by modifying the structure of the leader - the natural alkaloid morphine. Specify it:

- Proserin;

- Mesaton;
- Apomorphine hydrochloride;
- Promedol;
- Izadrin.

#

77) A number of drugs from the group of narcotic analgesics (promedol, fentanyl) are synthesized on the basis of studying the relationship between structure and pharmacological action using the leader structure (a natural alkaloid). Specify this alkaloid:

- Atropine;
- Narcotic;
- Morphine;
- Physostigmine;
- Pilocarpine.

#

78) The drug codeine is obtained semi-synthetically - by methylation of a natural alkaloid:

- Morphine
- Papaverin
- Caffeine
- G. Atropine
- Koniine

#

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

- Polarimeter
- Spectrophotometer
- Photoelectrocolorimeter
- G. Refractometer
- D.Polarograph

#

80) An analyst of the control and analytical laboratory performs an express analysis of morphine hydrochloride. The presence of phenolic hydroxyl is confirmed by the reaction with the solution:

- $FeCl_3$
- NH_3
- $AgNO_3$

- G. $K_3[Fe(CN)_6]$
- D. Concentrated HNO_3

#

81) The substance of morphine hydrochloride was submitted for analysis. When it interacts with a solution of Ferric chloride (III), a blue-violet color is formed. This indicates the presence in the structure of this medicinal substance:

- Phenolic hydroxyl
- Aldehyde group
- Alcoholic hydroxyl
- S. Ketogroups
- Complex ether groups

#

82) What features of the molecular structure allow us to distinguish between morphine hydrochloride and ethylmorphine hydrochloride by reaction with a solution of iron (III) chloride?

- The presence of phenolhydroxyl
- Presence of alcoholhydroxyl
- Presence of tertiary nitrogen
- The presence of a double bond
- D.Presence of chloride ions

#

83) The drug codeine is obtained semi-synthetically - by methylation of a natural alkaloid:

- Morphine
- papaverine
- caffeine
- atropine
- Coniine

#

84) Alkylation of the phenolic group in position 3 of the morphine molecule leads to:

- Reduction of analgesic effect and strengthening of antitussive effect
- Reduction of antitussive effect
- Enhancement of analgesic effect
- Appearance of diuretic activity
- It does not affect the pharmacological properties

#

85) Specify the medicinal product, the identification of which, upon reaction with a solution of silver nitrate, produces a yellow precipitate, soluble in dilute nitric acid:

- Codeine phosphate
- Ascorbic acid
- Glucose is anhydrous
- Procaine hydrochloride
- Sodium benzoate

#

86) What is the pharmacological effect of pilocarpine hydrochloride?

- Anti-inflammatory
- Antipyretic
- Reduces intraocular pressure (miotic)
- choleretic
- Antihistamine

#

87) Indicate by which method you can quantify pilocarpine hydrochloride:

- Complexometrically
- Iodometrically
- Acid-base titration in non-aqueous solvents
- Nitritometrically
- Acid-base titration in an alcoholic medium

#

88) To identify physostigmine salicylate, a reaction with a solution of Ferrum (III) chloride is used, according to which the structure of the drug reveals:

- Salicylic acid
- The basis of physostigmine
- Lactone cycle
- Aromatic nitro group
- Methyl group

#

89) Specify the pharmacological effect of physostigmine salicylate:

- Diuretic
- Spasmolytic
- Anticholinesterase, miotic
- Mydriatic
- Analgesic

#

90) Indicate which drug corresponds to the chemical name α-ethyl-β-(1-methylimidazole-5-methyl)-γ-butyrolactone hydrochloride:

- Ephedrine hydrochloride
- Pilocarpine hydrochloride
- Morphine hydrochloride
- Quinidine hydrochloride
- Papaverine hydrochloride

#

91) The chemical structure of pilocarpine hydrochloride is a derivative:

Е. Indole
Ж. Purine
З. Quinoline
И. Benzylisoquinoline
К. Imidazole

#

92) Indicate which of the following medicinal preparations is obtained by extraction from Calabar beans:

- Spherophysin benzoate
- Strychnine nitrate
- Euphilinus
- Pilocarpine hydrochloride
- Physostigmine salicylate

#

93) Indicate which of the listed medicines is a synthetic analogue (by action) of physostigmine salicylate:

- Pilocarpine hydrochloride
- Ephedrine hydrochloride
- Mesaton
- Dikain
- Prozerin

#

94) To identify proserin, a reaction is carried out with a solution of sodium hydroxide, after which sulfanilic acid, sodium nitrite and hydrochloric acid are added. The appearance of a red-orange color is due to the formation of:

- Azo dye
- Murexida
- Taleiokhina

- Iodoform
- Fluorescein

#

95) Indicate which of the following reagents are used to identify proserin:

- Hydrochloric acid, sodium nitrite, β-naphthol
- A mixture of concentrated nitric and sulfuric acids
- Solution of copper (II) sulfate
- Silver nitrate solution
- A solution of sodium hydroxide, sulfanilic acid, sodium nitrite, and hydrochloric acid

#

96) List the reagents used to identify pilocarpine hydrochloride:

- Perhydrol, hydrochloric acid, ammonia solution
- A solution of formaldehyde in concentrated sulfuric acid
- Bromine water, ammonia solution
- Concentrated nitric acid, alcoholic solution of potassium hydroxide
- Hydrogen peroxide, potassium dichromate, sulfuric acid, chloroform

#

97) One of the listed methods cannot be used for the quantitative determination of pilocarpine hydrochloride. Specify it:

- Argentometry according to Fayance
- Acid-base titration in a two-phase environment
- Acid-base titration in non-aqueous solvents
- Argentometry according to Folgard
- Argentometry according to More

#

98) The formation of iron (III) hydroxamate during the identification of pilocarpine hydrochloride confirms the presence in its structure:

- Lactone cycle
- Lactam cycle
- Imidazole cycle
- Hydroxyl group
- Double bond

#

99) For quantitative determination of nitrogen in neostigmine methyl sulfate (proserin) use:

- A.The Kjeldahl method
- B. The Kolthoff method

- IN.The Kolbe-Schmidt method
- G. Mohr's method
- D. Fayance method

#

100) To absorb ammonia in the modified Kjeldahl method, use:

- A.Boric acid solution
- B. Saturated NaCl solution
- B. Sodium hydroxide solution
- D. Ethyl alcohol
- D. Acetone

- #

101) Identification of salicylic acid in aceclidine is carried out using a solution:

- Iron (III) chloride
- Sodium hydroxide
- Magnesium sulfate
- Sodium nitrite
- Potassium sulfate

#

102) A pharmacist-analyst identifies salicylic acid in aceclidine by the formation of a red auric dye. What reagent does he use?

- A.Markey's reagent (solution of formaldehyde in concentrated sulfuric acid)
- B. Fisher's reagent
- B. Nessler's reagent (alkaline solution of potassium tetraiodomercurate)
- G. Tollens' reagent
- D. Fehling's reagent

#

103) To quantitatively determine the content of salicylic acid in aceclidine, the following method is used:

- Alkalimetry
- Nitritometry
- Argentometry
- Permanganatometry
- Complexonometry

#

104) The presence of an ester group in the structure of aceclidine can be proven by the formation reaction:

- Salts of hydroxamate [hydroxamic] acids
- Indophenol

- Diazonium salts
- Aurine dye
- Azomethine dye

#

105) Which identification reaction can be used to confirm the presence of a sulfur atom in a molecule of neostigmine methyl sulfate (proserin)?

- Alkaline hydrolysis with subsequent detection of sulfate ion
- With a solution of diphenylcarbazide
- With salts of alkali metals
- With magnesium chloride solution
- With Marki's reagent

#

106) To identify pilocarpine hydrochloride, a reaction with sodium nitroprusside in an alkaline medium (Legal's reaction) is used. At the same time, the appearance of a cherry color confirms the presence of pilocarpine in the structure:

- Lactone ring
- Imidazole cycle
- Methyl groups
- Hchloride ions
- Phenolic hydroxyl

#

107) Enter the name of the medicinal substance, for the identification of which the nitration reaction with subsequent reduction and formation of an azo dye is used:

- Pachycarpine hydroiodide
- Cytisine
- Platyphyllin hydrotartrate
- Caffeine
- Pilocarpine hydrochloride

#

108) Indicate which medicinal plant is the main source of alkaloid cytisine?

- Scopolia
- Rauwolfia snake
- Cocoa beans
- Calabar beans
- Laburnum

#

109) Indicate which of the following reactions is used to identify cytisine:

- Taleiochin test
- With ammonia solution
- Maltol sample
- Formation of murexide
- With cobalt nitrate solution

#

110) Indicate the pharmacological effect of the medicinal product cytiton:

- Spasmolytic
- Analgesic
- Mydriotic
- Stimulator of birth activity
- Stimulator of breathing

#

111) Indicate by which method you can quantitatively determine cytisine:

- Nitritometrically;
- Acid-base titration;
- Argentometrically;
- Complexometrically;
- Mercurimetrically.

#

112) Indicate by which method you can quantitatively determine acetylcholine chloride:

- Alkalimetrically;
- Acidimetric;
- Argentometrically;
- Nitritometrically;
- Complexometrically;

#

113) Indicate which of the listed medicines is a derivative of pyrrolizidine according to its chemical structure?

- Cocaine hydrochloride
- Pilocarpine hydrochloride
- Cytisine
- Reserpine
- Platyphyllin hydrotartrate

#

114) What specific impurity in the medicinal substance "Platyfillin Hydrotartate" is determined by the appearance of turbidity when adding 5% ammonia solution?

- Senecifillin
- Recovery substances
- Apoatropin
- Aposcopolamine
- Foreign alkaloids

#

115) The pharmacist-analyst used a reaction with potassium chloride to identify the drug, which resulted in the formation of a white crystalline precipitate. What drug does the analyst identify?

- Platifylline hydrotartrate
- Caffeine monohydrate
- Atropine sulfate
- G. Pilocarpine hydrochloride
- Scopolamine hydrobromide

#

116) Indicate by which method it is possible to determine the quantitative content of platyphyllin hydrotartrate:

- Argentometry
- Bromatometry
- Acidimeterher
- By the method of acid-base titration in non-aqueous media
- Nitritometry

#

117) Indicate which of the medicinal substances gives a positive result (the formation of a blood-red color) when it is identified by the reaction of the hydroxam test:

- Caffeine monohydrate
- Ephedrine hydrochloride
- Platyphyllin hydrotartrate
- Papaverine hydrochloride
- Euphilinus

#

118) Indicate which plant contains the alkaloid platyphyllin?

- Laburnum
- Rauwolfia

- Scopolia
- Thermopsis
- Crusader

#

119) The formation of iron hydroxamate in platyphyllin hydrotartrate confirms the presence in the structure of this medicinal product:

- Tartaric acid
- Pyrrolizidine cycle
- Hydroxyl group
- Double bond
- Complex ester groups

#

120) Indicate which heterocycle is the basis of the platyphyllin hydrotartrate structure:

- Indole
- Pyrrolizidine
- Piperidine
- Isoquinoline
- Quinoline

#

121) Indicate which of the medicinal substances gives a positive result (the formation of a blood-red color) when identified by the hydroxam test reaction:

- Pachycarpine hydroiodide
- Cytisine
- Papaverine hydrochloride
- Euphilinus
- Homatropin hydrobromide

#

122) Indicate which heterocyclic systems are the basis of the structure of tropane alkaloids:

- Pyridine and pyrazole
- Pyrrolizidine and imidazole
- Piperidine and furan
- Pyrrolidine and piperidine
- Isoquinoline and pyrrole

#

123) For the identification of aprofen, fuming nitric acid, acetone and an alcoholic solution of potassium hydroxide are used. These reagents are used to detect:

- Diphenylpropionic acid residue
- Residue of diethylaminoethanol
- Chloride ion
- Crystallization water
- Phenolic hydroxyl

#

124) Quantitative determination of scopolamine hydrobromide is carried out by the method of acid-base titration in non-aqueous solvents. Indicate how the equivalence point is fixed in the given method?

- Using a crystal violet indicator
- According to the change in the color of the solution due to the increase in the excess titrant drop (indicator-free method)
- Using thymol blue indicator
- Using the phenolphthalein indicator
- Using thymolphthalein indicator

#

125) Specify a medicinal substance from the group of alkaloids, tropane derivatives, in the structure of which is the heterocycle oxirane (ethylene oxide):

- Atropine sulfate
- Scopolamine hydrobromide
- Homatropin hydrobromide
- Tropacin
- Cocaine hydrochloride

#

126) Which of the medicines is a synthetic analogue of alkaloids, tropane derivatives?

- Homatropin hydrobromide
- Atropine sulfate
- Scopolamine hydrobromide
- Papaverine hydrochloride
- Ergometrine maleate

#

127) Specify the medicinal plant from which the alkaloid pachycarpine is obtained:

- Rakitnik
- Cocoa
- Scopolia

- Flat-leaved crucifer
- Sophora is thick-fruited

#

128) Pachycarpine hydroiodide upon interaction with one of the listed reagents gives a yellow precipitate with a characteristic melting point. Specify this reagent:

- Ammonium nitrate solution
- Iodine solution
- Marky's reagent
- A solution of sodium nitrite in an acidic environment
- Picric acid solution

#

129) Which of the listed methods of analysis cannot be used for the quantitative determination of pachycarpine hydroiodide:

- Acid-base titration in non-aqueous solvents
- Argentometry
- Acid-base titration in a two-phase environment
- High performance liquid chromatography
- Nitritometry

#

130) One of the listed medicines does not belong to tropane derivatives. Specify it:

- Atropine sulfate
- Scopolamine hydrobromide
- Homatropin hydrobromide
- Tropacin
- Platyphyllin hydrotartrate

#

131) One of the drugs listed below, derivatives of tropane, does not give the Vitali-Morena reaction. Specify it:

- Atropine sulfate
- Scopolamine hydrobromide
- Tropacin
- Tropafen
- Homatropin hydrobromide

#

132) Which of the following methods cannot be used for the quantitative determination of scopolamine hydrobromide?

- Argentometry according to Fayance
- Mercurimetry
- Acid-base titration in a two-phase environment
- Acid-base titration in non-aqueous solvents
- Argentometry according to More

#

133) Specify which alkaloid camphor salts are part of Aeron tablets?

- Hyoscyamine and scopolamine
- Homatropin
- Tropacin
- Caffeine
- Atropine

#

134) Specify the name of the medicinal substance from the group of alkaloids, the modification of which resulted in a synthetic analogue - homatropine hydrobromide?

- Cytisine
- Themisal
- Pachycarpine hydroiodide
- Physostigmine salicylate
- Atropine sulfate

#

135) The pharmacist-analyst of the control and analytical laboratory determines the quantitative content of the scopolamine hydrobromide substance by the method of acid-base titration in non-aqueous media. What titrated solution does he use:

- Chloric acid
- Sodium hydroxide
- Sodium methylate
- Hydrochloric acids
- Sodium nitrite

#

136) Choose a medicinal substance that belongs to alkaloids, tropane derivatives:

- Scopolamine hydrobromide
- Cytisine
- Strychnine nitrate

- Pachycarpine hydroiodide
- Platyphyllin hydrotartrate

#

137) 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:

- The color of the solution is purple
- Release of gas bubbles
- The color of the solution is green
- Falling of black sediment
- Precipitation of a white precipitate

#

138) Indicate which of the following medicinal products gives a positive reaction to Vitaly-Morena:

- Scopolamine hydrobromide
- Platyphyllin hydrotartrate
- Cytisine
- Papaverine hydrochloride
- Pachycarpine hydroiodide

#

139) What is the pharmacological effect of pachycarpine hydroiodide?

- Central nervous system stimulant;
- Diuretic;
- Bronchodilator;
- Stimulator of breathing;
- Ganglioblockers (with hypertension, increases uterine muscle contraction).

#

140) Indicate the pharmacological action of atropine sulfate:

- Stimulates the muscles of the uterus;
- Reduces intraocular pressure;
- Blocks calcium channels;
- Increases the tone of smooth muscle organs;
- Mydriatic, reduces the tone of smooth muscle organs.

#

141) What is the pharmacological effect of scopolamine hydrobromide?

- Antimalarial;
- Central nervous system stimulant;
- Stimulator of birth activity;
- Antiglaucoma;
- Mydriatic, sedative.

- #

142) What is formed as a result of the interaction of platyphyllin hydrotartrate with β-naphthol in the presence of concentrated sulfuric acid?

- Auric dye.
- Azo dye
- Indophenol dye.
- Azomethine dye

#

143) What test is not performed when identifying Aprophenum [Aprophenum]?

- Iodoform sample
- Hydroxam sample
- Interaction with Markey's reagent
- Vitaly-Moren's reaction
- Interaction with NH_4NO_3 in concentrated H_2SO_4

#

144) Indicate which of the listed medicines is a double ester according to its chemical structure:

- Reserpine
- Pilocarpine hydrochloride
- scopolamine hydrobromide
- G. Physostigmine salicylate
- Ephedrine hydrochloride

#

145) One of the alkaloids listed below is isolated from Rauwolfia snake. Specify it:

- Platyphilin
- Caffeine
- Papaverine
- Strychnine
- Reserpine

#

146) Which of the following reagents are specific for the identification of reserpine?

- Cobalt chloride solution
- Iron (III) chloride solution
- A solution of vanillin in hydrochloric acid
- Copper sulfate solution
- Concentrated sulfuric acid

#

147) When ephedrine hydrochloride is heated with a potassium ferricyanide crystal, the smell of bitter almonds appears, which is due to the formation of:

- Benzaldehyde
- Nitrobenz
- Chlorobenzyl
- Aniline
- Toluene

#

148) What reagent should be used to identify ephedrine hydrochloride?

- copper (II) hydroxide
- Bromine water
- Ammonium nitrate
- Hydrochloric acid
- Ammonium chloride

#

149) Identification of ephedrine hydrochloride is carried out by a reaction based on the formation of a blue-violet complex compound. At the same time, a solution is used as the main reagent:

- Copper (II) sulfate
- Potassium ferricyanide
- Sodium edetate
- Hydrochloric acids
- Diethyl ether

#

150) Nitritometry is not used for quantitative determination:

- Ephedrine hydrochloride
- Novocaine
- Streptocide
- Levomycetin
- Sulfazine

#

151) Reserpine gives a positive result of the hydroxam reaction due to the presence in its structure:

- Complex ester groups
- Aromatic core
- Pyrrole nitrogen atom
- Phenolic hydroxyl
- Primary aromatic amino group

#

152) Izadrin, like other catecholamines, is oxidized by iodine solution with the formation of colored products. To create the required pH value, the pharmacist-analyst must add:

- Hydrochloric acid solution
- Acetate buffer solution
- Ammonia buffer solution
- Hydrotartrate buffer solution
- Sodium hydroxide solution

#

153) The pharmacist-analyst carries out the quantitative determination of mesatone, in accordance with the requirements of the SPhU, by the method:

- Nitritometry
- Bromatometry
- Gravimetry
- Alkalimetry in alcoholic medium
- Iodometry

#

154) The drug has an adrenomimetic effect:

- Izadrin
- Procaine hydrochloride
- Dibazol
- Prozerin
- Promedol

#

155) Quantitative analysis of isadrin is carried out in the control and analytical laboratory. For this, the method of quantitative determination is used:

- Acidimetry in a non-aqueous environment
- Acidimetry in an aqueous medium
- Reverse iodometry

- Alkalimetry in a non-aqueous medium
- Nitritometry

#

156) Quantitative analysis of mesatone is carried out in the control and analytical laboratory. For this, the method of quantitative determination is used:
- Acidimetry in an aqueous medium
- Reverse iodometry
- Alkalimetry in a non-aqueous medium
- Nitritometry
- Reverse bromatometry

#

157) A medicinal product characterized by a reaction with Ferrum (III) chloride:
- Procaine hydrochloride
- Magnesium oxide
- Diphenhydramine
- Anesthesin
- Mesaton

#

158) Which of the following drugs are catecholamines?
- Tropafen
- Izadrin
- Naphthysin
- Levomycetin
- Reserpine

#

159) Choose a medicinal substance that belongs to alkaloids, tropane derivatives:
- Tropafen
- Cytisine
- Strychnine nitrate
- Pachycarpine hydroiodide
- Platyphyllin hydrotartrate

#

160) Indicate which of the following medicinal products gives a positive reaction to Vitaly-Morena:
- Tropafen
- Platyphyllin hydrotartrate
- Cytisine
- Papaverine hydrochloride

- Pachycarpine hydroiodide

#

161) To identify medicinal substances, synthetic analogues of atropine: tropafen, tropacin - use the nitration reaction, because they contain:

- Benzene ring
- Aldehyde group
- Carbonyl group
- Merkapogroup
- Carboxylic group

#

162) Specify the reagent used to detect the nitrate ion in naphthizin:

- Silver nitrate solution
- Marky's reagent
- Solution of sulfanilic acid
- Frede's reagent
- Diphenylamine solution

#

163) For the quantitative determination of naphazoline nitrate (naphthyzine), one ofof the following titrimetric methods. Specify it:

- Complexonometry
- Argentometry according to More
- Argentometry according to Fayance
- Nitritometry
- Acid-base titration

#

164) Indicate the derivative of which heterocycle is naphazoline nitrate (naphthyzine):

- Pyrimidine
- Pyrrol
- Imidazoline
- Indole
- Pyrazole

#

165) One of the following titrimetric methods can be used for the quantitative determination of anaprilin (propranolol hydrochloride). Specify it:

- Complexonometry
- Acidimetry

- Nitritometry
- Argentometry according to More
- Iodometry

4.3. Situational tasks:

1. Explain whether it is possible to establish the authenticity of any alkaloid with the help of precipitation and special reagents without using additional reactions?

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

3. To substantiate the conditions of acid-base titration of bases and salts of alkaloids in an aqueous medium (emphasize the role of alcohol and chloroform).

4. Describe the group reaction used to identify purine alkaloids. Why is this reaction not specific?

5. Explain the conditions for the quantitative determination of theophylline in euphylline. Give the corresponding reaction equations.

6. State the solvents that can be used to conclude that the test drug is theophylline or theobromine.

7. Describe the method of acid-base titration of medicinal substances in non-aqueous media using the example of bendazole hydrochloride (dibazole). Give the reaction equations, the formula for calculating the quantitative content.

8. Describe the substitution titration method using theobromine and theophylline as an example. Give the reaction equations, the formula for calculating the quantitative content.

9. Justify the possibility of using the acid-base titration method in non-aqueous media for the quantitative determination of papaverine hydrochloride. Give the reaction equations, the formula for calculating the quantitative content.

10. Describe the method of substitution titration (thiocyanatometry) using the example of bendazole hydrochloride (dibazole). Give the reaction equations, the formula for calculating the quantitative content.

11. Explain the need to add ammonium hydroxide solution when identifying dibazole (identification of chloride ion). Illustrate the answer with the chemistry of reactions.

12. Specify the condition under which the reaction of codeine and ethylmorphine hydrochloride with Ferrum (III) chloride is possible.

13. Explain the possibility of creating narcotic analgesics based on the modification of the leader structure (morphine). Beckett-Casey rule.

14. Explain the possibility of quantitative determination of codeine by acidimetry.

15. What is the role of alcohol in the quantification of codeine acidimetrically?
16. Why does morphine hydrochloride dissolve in an excess of sodium hydroxide?
17. Explain why the reaction with iron(III) chloride is different for morphine compared to ethylmorphine and codeine?
18. Explain why nalorphine, having a similar structure to morphine, is its antagonist?
19. Define the term "agonists-antagonists" (synergoantagonists). Give examples.
20. Explain the necessity of adding oxymercuric acetate in the quantitative determination of pilocarpine hydrochloride by the non-aqueous titration method.
21. Explain the need to increase the alcohol-chloroform mixture in the quantitative determination of physostigmine salicylate by the method of alkalimetry.
22. Explain due to which functional group pilocarpine hydrochloride gives a hydroxamate test. Write the chemistry of the reactions.
23. Write the specific identification reaction for pilocarpine hydrochloride and explain its chemical meaning.
24. Explain why cytisine is determined acidimetrically in an aqueous environment?
25. Indicate the peculiarities of the structure of cytisine, due to which the formation of picrate with a characteristic melting temperature is possible, as well as the ability to undergo electrophilic substitution reactions (nitration, etc.).
26. Explain why cytitone is not recommended for identification using ferric chloride solution.
27. How does the admixture of seneciphyllin get into platyphyllin hydrotartrate when it is obtained from plant raw materials?
28. Why does homatropine hydrobromide not give the Vitali-Morena reaction?
29. What is the role of oxymercury acetate in the quantitative determination of scopolamine hydrobromide by the non-aqueous titration method?
30. Explain why aprofen gives the Vitali-Morena reaction?
31. Explain the essence of the reaction of platyphyllin hydrotartrate with β-naphthol in the presence of conc. sulfuric acid. Write the chemistry of the reaction.
32. Specify the features of the structure of pachycarpine, due to which the formation of picrate with a characteristic melting point is possible.
33. Explain the need to increase the alcohol-chloroform mixture in the quantitative determination of homatropine hydrobromide by the method of alkalimetry.
34. Explain the essence of the reaction of reserpine (and other indole derivatives) with vanillin in hydrochloric acid. Write the chemistry of the reaction (Van Urck reaction).

35. Give examples of chemical reactions confirming that mesatone and isadrin belong to the salts of nitrogenous bases.

36. Justify the possibility of using the acid-base titration method in non-aqueous media for the quantitative determination of ephedrine hydrochloride. Give the reaction equations, the formula for calculating the quantitative content.

37. Explain why it is necessary to add mercury (II) acetate in the quantitative determination of anaprilin by the non-aqueous titration method.

38. Explain why isadrine (isoprenal hydrochloride) and mesatone (phenylephrine hydrochloride) give different colors when interacting with Ferrum (III) chloride.

39. Explain why tropafen gives the Vitali-Morena reaction.

4.4. Tasks:

1. Calculate the volume of 0.1 M perchloric acid solution (C_a = 1.0183), which is spent on the titration of 0.1516 g of theobromine (M.w. 180.17), if the titrant volume in the control experiment is 0.15 ml, and the content of the active substance in the preparation is 99.5%.

2. Calculate the percentage content of ethylenediamine (M.w. 60.10) and theophylline (M.w. 180.17) in euphylline, if it is known that 14.85 ml of a 0.1 M solution of hydrochloric acid was spent on the titration of 0.2893 g of the drug (Kn = 1.0133) and 18.33 ml of 0.1 M sodium hydroxide solution (C_a = 0.9925) were spent in the determination of theophylline in 0.3892 g of the drug.

3. Calculate the weight of the theobromine sample (M.w. 180.17), if 16.50 ml of 0.1 M sodium hydroxide solution (C_a = 0.9903) was spent on its titration. The content of the active substance in the preparation is 99.3%, the loss in mass during drying is 0.3%.

4. Calculate the volume of 0.1 M perchloric acid solution (C_a = 0.9865), which is spent on the titration of 0.0977 g of bendazole hydrochloride (M.w. 244.73), if it is known that the content of the active substance is 99.9 %.

5. Calculatevolume0.1 M sodium hydroxide solution (C_a = 0.9886), which was spent during the quantitative determination of 0.4017 g of theophylline (M.w. 180.17) by the method of indirect titration, if the content of the active substance in the pre-dried preparation is 99.4 %.

6. Determine the mass fraction of bendazole hydrochloride (M.w. 244.73) in the medicinal product, if 7.73 ml of 0.1 M sodium hydroxide solution was spent on the titration of 0.1936 g of the substance (C_a = 1.0165). Loss in mass - 0.62%.

7. Calculate the volume of 0.1 M sodium hydroxide solution (C_a = 0.9892), which is spent on the titration of 0.4108 g of theophylline (M.w. (anhydrous) 180,180)

by the method of indirect neutralization, if the percentage of theophylline in the medicinal product is 99, 70%.

8. Calculate the weight of papaverine hydrochloride (M.w. 375.86), if 8.33 ml of 0.1 M perchloric acid solution were spent on its titration (C_a = 0.9786). The volume of the titrant in the control experiment is 0.30 ml, the content of the active substance in the preparation is 99.5%.

9. Calculate the percentage content of papaverine hydrochloride (M.w. 375.86), if 5.08 ml of 0.1 M sodium hydroxide solution (C_a = 0.9998) was used for the titration of 0.1879 g of the drug. The loss in mass during drying is 3 , 2%.

10. Calculate the percentage content of dibazole (M.w. 244.73) in the preparation, if 8.42 ml of 0.1 M perchloric acid solution was used for the titration. The weight of the sample is 0.1912 g, and the titrant volume in the control experiment is 0.5 ml.

11. Calculate the percentage content of codeine phosphate (M.w. 397.36) in the preparation, if the weight of the test piece is 0.2517 g, the volume of a 0.1M solution of perchloric acid (C_a = 0.9916) in the working experiment is 6.19 ml , in the control - 0.18 ml. Weight loss during drying is 6.5%.

12. Determine the volume of a 0.1M solution of perchloric acid (C_a = 0.9985), which was spent on the titration of a weight of 0.1518 g of morphine hydrochloride (M.w. 321.80). The percentage content of morphine hydrochloride in the medicinal product is 99.50%.

13. Determine the weight of codeine test (M.w. 299.39), if 10.02 ml of 0.1M hydrochloric acid solution was spent on its titration (C_a = 0.9678). The percentage content of codeine in the medicinal product is 99.40%.

14. Calculatevolume0.1 M perchloric acid solution (C_a = 0.9835), which was spent on the titration of 0.1506 g of morphine hydrochloride (M.w. 321.80), if the loss in mass during drying is 14.4%, and the content of active substances in the preparation–99.0%.

15. Calculate the weight of the codeine sample (M.w. 299.37), if 9.98 ml of 0.1 M hydrochloric acid solution (C_a = 0.9586) was spent on its titration. The content of the active substance in the preparation – 99.3%, loss in mass during drying– 5.5%.

16. Calculate the percentage content of ethylmorphine hydrochloride (M.w. 385.89) in the preparation, if the mass of the test piece is 0.2042g, the volume of the 0.1M solution of perchloric acid (C_a = 1.0006) in the work experiment is 5.15 ml, in the control - 0.10 ml. Loss in mass during drying is 4.6%.

17. Calculate the percentage content of promedol (M.w. 311.85) in the preparation, if the weight of the test is 0.2577 g, the volume of a 0.1 M perchloric acid

solution (C_a = 0.9896) in the working experiment is 8.19 ml , in the control - 0.12 ml. Weight loss during drying is 3.5%.

18. Calculatevolume0.1 M perchloric acid solution (C_a = 0.9995), which was spent on the titration of 0.1802 gpromedol (M.w. 311.85), if the loss in mass during drying is 10.4%, and the content of the active substance in the preparation– 99.8%.

19. Calculate the weight of the weightethylmorphine hydrochloride (M.w. 385.89), if 8.88 ml of 0.1 M perchloric acid solution were spent on its titration (C_a = 0.9886). The content of the active substance in the preparation–99.50%, loss in mass during drying–2.5%.

20. Calculate the percentage content of apomorphine (M.w. 317.30) in the drug, if the weight of the test is 0.3005 g, the volume of a 0.1 M perchloric acid solution (C_a = 0.9902) in the work experiment is 9.52 ml , in the control - 0.10 ml. Weight loss during drying is 1.5%.

21. Calculate the percentage content of aceclidine (M.w. 307.35) in the preparation, if the weight of the test is 0.2065,the volume of a 0.1 M solution of perchloric acid (C_a = 1.0108) in the working experiment was 6.72 ml, in the control experiment - 0.09 ml.

22. Calculate the weight of pilocarpine hydrochloride (M.w. 244.72), if 8.30 ml of 0.1 M perchloric acid solution (C_a = 1.0108) was spent on its titration. The content of the active substance in the preparation is 98.9%,volumecontrol experiment–0.21 ml, weight loss during drying 0.4%.

23. Calculate the volume of 0.1 M sodium hydroxide solution (C_a = 1.0022), which will be spent on the titration of 0.1562 g of physostigmine salicylate (M.w. 413.5), if its percentage content in the preparation is 99.8 %, loss in mass during drying - 0.54%.

24. Calculate the percentage content of cytisine (M.w. 190.25), if 9.98 ml of a 0.1 M solution of hydrochloric acid was spent on the titration of 0.1981 g of the drug (C_a = 0.9994).

25. Calculate the volume of 0.1 M perchloric acid solution (C_a = 1.0011), which will be spent on the titration of 0.2421 g of pilocarpine hydrochloride (M.w. 244.72), if its percentage content in the preparation is 99.4 %, the titrant volume in the control experiment is 0.16 ml.

26. Calculate the mass of aceclidine (M.w.307.35), if 10.20 ml of 0.1 M perchloric acid solution was spent on its titration (C_a = 1.0004) The content of the active substance is 98.8%, the loss in mass during drying 0.25%.

27. Calculate the volume of 0.1 M solution of hydrochloric acid (C_a = 0.9888), which will be spent on 0.2103 g of cytisine (M.w. 190.25), if its percentage content in the preparation is 98.86%.

28. Calculate the percentage content of pilocarpine hydrochloride (M.w. 244.72) in the preparation, if the weight of the test piece is 0.2002 g, the volume of 0.1 M sodium hydroxide solution (C_a = 1.0101). Weight loss during drying is 0.23%.

29. Calculate the percentage content of physostigmine salicylate (M.w. 423.5), if 5.08 ml of 0.1 M sodium hydroxide solution (C_a = 0.9978) was spent on the titration of 0.1212 g of the drug, the loss in mass during drying was 0. 45%.

30. Calculate the weight of the weight of physostigmine salicylate (M.w. 413.5), if 6.78 ml of 0.1 M sodium hydroxide solution (C_a = 1.0000) was spent on its titration. The content of the active substance in the preparation is 99.70%.

31. Calculate the volume of 0.1 M perchloric acid solution (C_a = 1.0000), which was spent on the titration of 0.2014 g of scopolamine hydrobromide (M.w. 384.3), if the volume of the titrant in the control experiment is 0.12 ml, loss in mass when dried - 12.6%, and the content of the active substance in the preparation is 98.7%.

32. Calculate the percentage content of scopolamine hydrobromide (M.w. 384.3) in the preparation, if the weight of the test piece is 0.2383g, volume 0.1 M perchloric acid solution (C_a = 0.9792) in the working experiment – 6.44 ml, in the control–0.18 ml, a loss in mass when drying–1.3%.

33. Calculate the mass of scopolamine hydrobromide measurement (M.w. 384.3), if 6.64 ml of 0.1 M perchloric acid solution (C_a = 1.0001) was spent on its titration,volume titrant in the control experiment – 0.2 ml, and the content of the active substance in the preparation – 99.8%.

34. Calculate the mass of a sample of homatropine hydrobromide (M.w. 356.27), if 5.74 ml of a 0.1 M solution of perchloric acid (C_a = 1.0241) was spent on its titration, the volume of the titrant in the control experiment – 0.21 ml, and the content of the active substance in the preparation – 99.4%.

35. Calculate the percentage content of homatropine hydrobromide (M.w. 356.27) in the drug, if the weight of the test is 0.3593 g,volume0.1 M perchloric acid solution (C_a = 1.0009) in the working experiment – 4.53 ml, in the control – 0.16 ml, aloss in masswhen dried is 1.4%.

36. Calculate the volume of a 0.1 M solution of perchloric acid (C_a = 1.0000), which is spent on the titration of 0.1850 g of pachycarpine hydroiodide (M.w. 363.30), if volume titrant in the control experiment – 0.10 ml,loss in mass when drying – 0.14%, and the content of the active substance in the preparation – 99.0%.

37. Determine the mass fraction of pachycarpine hydroiodide (M.w. 363.30) in the medicinal product, if 6.48 ml of 0.1 M perchloric acid solution was spent on

the titration of 0.2302 g of pachycarpine hydroiodide (C_a = 0.9994), ifvolumetitrant in the control experiment – 0.14 ml.

38. Determine the mass fraction of aprofen (M.w. 361.92) in the medicinal product, if 9.42 ml of 0.1 M perchloric acid solution (C_a = 0.9899) was spent on the titration of a weight of 0.3007g, volume titrant in the control experiment – 0.16 ml.

39. Calculate the percentage content of platyphyllin hydrotartrate (M.w. 487.5) in the drug, if the weight of the test is 0.3857g, the volume of a 0.1 M perchloric acid solution (C_a = 1.0208) in the work experiment was 7.82 ml, in the control experiment - 0.09 ml.

40. Calculate the weight of platyfillin hydrotartrate (M.w. 487.5), if 9.70 ml of 0.1 M sodium hydroxide solution (C_a = 1.0198) was spent on its titration. The content of the active substance is 99.2%. Loss in mass upon drying 0.22%.

41. Calculate the volume of 0.1 M perchloric acid solution (C_a = 0.9982), which will be spent on 0.3109 g of platyphyllin hydrotartrate (M.w. 487.5), if its percentage content in the preparation is 98.20% , the titrant volume in the control experiment is 0.12 ml, loss in mass upon drying 0.42%.

42. Calculate the percentage content of mesatone (M.w. 203.67) in the preparation, if 16.10 ml of 0.1 M sodium thiosulfate solution (C_a = 1.0000) was spent on the titration of a weight of 0.1120 g, the loss in mass during drying is 0 .5% and the volume of the titrant in the control experiment - 48.50 ml.

43. Calculate the volume of 0.1 M perchloric acid solution (C_a = 0.9865), which is spent on the titration of 0.0977 g of ephedrine hydrochloride (M.w. 201.70), if it is known that the content of the active substance is 99.9 %.

44. Determine the mass fraction of ephedrine hydrochloride (M.w. 201.70), if 4.50 ml of 0.1 M perchloric acid solution was spent on the titration of 0.1035 g of the substance (C_a = 1.1228).

45. Calculate the percentage of reserves on (M.w.608.7) in the preparation, if the weight of the sample is 0.3576 g, the volume of a 0.1 M perchloric acid solution (C_a = 1.0004) in the working experiment is 5.96 ml, in the control - 0.18 ml, and the loss in mass during drying is 0.4%.

46. Calculate the weight of ephedrine hydrochloride (M.w. 201.70), if 5.68 ml of 0.1 M perchloric acid solution (C_a = 1.0041) was spent on its titration, the titrant volume in the control experiment was 0.21 ml, and the content of the active substance in the preparation is 99.4%.

47. Calculate the weight of mesaton weight (M.w. 203.67), if 6.88 ml of 0.1 M perchloric acid solution (C_a = 1.0011) was spent on its titration, the titrant volume in the control experiment was 0.21 ml , and the content of the active substance in the drug is 97.89%.

48. Calculate the volume of 0.1 M perchloric acid solution (C_a = 0.9995), which is spent on the titration of 0.6771 g of reserpine (M.w. 608.70), if it is known that the content of the active substance is 98.5% .

49. Calculate the percentage content of naphazoline hydrochloride (naphthysine) (M.w. 246.7) in the preparation, if the weight of the test is 0.1516 g, the volume of 0.1 M sodium hydroxide solution (C_a = 1.0015) - 5.96 ml, and the loss in mass during drying is 0.4%.

50. Calculate the volume of 0.1 M perchloric acid solution (C_a = 1.0004), which is spent on the titration of 0.2471naphazoline hydrochloride (naphthysine) (M.w. 246.7),if it is known that the content of the active substance is 99.5%.

51. Calculate the percentage content of anaprilin (propranolol hydrochloride) (M.w. 295.8) in the preparation, if the weight of the test is 0.2374 g, the volume of 0.1 M sodium hydroxide solution (C_a = 1.0025) is 7.96 ml, and the loss in mass during drying is 0.6%.

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