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

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PHARMACEUTICAL CHEMISTRY

Section 2.2

(analysis of drugs that affect the afferent nervous system and drugs that improve blood supply to organs and tissues, as well as antihistamines and sulfonamides)

Study Guide

for 3rd year English-speaking students of the specialty "Pharmacy, Industrial Pharmacy"

Zaporizhzhia

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INTRODUCTION

Pharmaceutical chemistry is studied in accordance with the "Model curriculum for the training of 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"б 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 curriculum, pharmaceutical chemistry is taught in the III, IV and V courses. In the III course (V-VI 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.

SPECIFIC GOALS:

Learn the characteristics, classification, connection between structure and pharmacological action, mechanism of action, methods of obtaining, methods of analysis, use in medicine of drugs that affect the afferent nervous system and drugs that improve the blood supply of tissue organs, as well as antihistamine drugs and sulfonamides. Explain the peculiarities of identification of drug products of these groups in accordance with the requirements of the State Pharmacopoeia of Ukraine (SPhU).

Interpret the results of studies on the maximum content of impurities in accordance with the requirements of the SPhU.

Propose and carry out the selection of physical, physico-chemical and chemical methods for determining the good quality of drug products in accordance with the requirements of the SPhU and other regulatory documentation, as well as quality control methods (QCM).

LECTURE PLAN

No.	**Lecture topic**	Number of hours
1.	Antitussives. Characteristics, classification, connection between structure and pharmacological action, mechanism of action, methods of production, methods of analysis. Use in medicine.	3
2.	Nootropic drugs. Characteristics, classification, connection between structure and pharmacological action, mechanism of action, methods of production, methods of analysis. Use in medicine.	3
3.	Nonsteroidal anti-inflammatory drugs. Characteristics, classification, connection between structure and pharmacological action, mechanism of action, methods of production, methods of analysis. Use in medicine.	3
4.	Sleep aids. Characteristics, classification, connection between structure and pharmacological action, mechanism of action, methods of production, methods of analysis. Use in medicine.	3
5.	Control lesson on the section	3

PLAN OF PRACTICAL CLASSES

No.	**Lecture topic**	Number of hours
1.	Antihistamines. Characteristics, classification, relationship between structure and pharmacological action. Mechanism of action, methods of obtaining, methods of analysis. Application in medicine.	3
2.	Agents affecting the afferent nervous system. Means that stimulate receptors of afferent nerve fibers. Characteristics, classification, relationship between structure and pharmacological action. Mechanism of action, methods of preparation, methods of analysis. Application in medicine.	3
3.	Means that improve blood supply to organs and tissues. Characteristics, classification, relationship between structure and pharmacological action. Mechanism of action, methods obtained, methods of analysis. Application in medicine.	3
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5.	**Control lesson on the section**	3

1. ANTIHISTAMINIC DRUGS

Antihistamines completely or partially block the biological action of histamine.

Historically, the term "antihistamines" refers to agents that block H1-histamine receptors, that is, H1-histamine blockers. However, this term is somewhat outdated, as it does not reflect the pharmacodynamics of most new H1-histamine blockers, which are also able to additionally influence the processes allergic inflammation. In addition, new classes of antiallergic drugs have been created that are antagonists not only of histamine, but also of other allergy mediators (serotonin, bradykinin, leukotrienes) - mast cell stabilizers, leukotriene receptor antagonists, 5-lipoxygenase inhibitors, antichemotaxic agents.

Antihistamine drugs that block H1-histamine receptors eliminate or reduce the effects of histamine, such as hypotension caused by it (partially), spasm of smooth muscles (bronchi, intestines), increased tone of the myometrium; an increase in the permeability of the capillary wall with the development of edema, hyperemia, itching and thus prevent the development and facilitate the course of allergic reactions. These agents do not affect the stimulation of gastric gland secretion by histamine.

Almost 20 years after the synthesis of histamine, in 1937, the Swiss-Italian pharmacologist D. Bove synthesized the first antihistamine substance thymoxydiethylamine, and then a number of other compounds from the group of aromatic amines, established their inhibitory effect on the contraction of smooth muscles caused by histamine. In 1957, he was awarded the Nobel Prize for these achievements. However, the first H1-histamine blocker fenbenzamine was used in the clinic only in 1940. Further intensive scientific research was marked by the creation of new H1-histamine blockers, which came to be called "antihistamines" because they effectively inhibited the reactions of organs and tissues to histamine. In 1966, the heterogeneity of histamine receptors in the body was proved, and then the position was formulated about histamine receptors of the 1st and 2nd types (H1- and H2-receptors), which differ in structure, localization, and physiological effects arising from their activation and blockade. It was established that the antihistamines available at that time (suprastin, diphenhydramine, etc.), along with antagonism to H-receptors, block other

receptors (m-cholino-, α-adrenoreceptors, etc.), penetrate through the blood-brain barrier , as a result of which they have various additional pharmacodynamic effects, most of which are considered undesirable in the treatment of allergic reactions (sedative-hypnotic, depressant, constipation, etc.). Therefore, the term "antihistamines" did not fully reflect the spectrum of pharmacological properties of these drugs, and they received the name H1-histamine blockers of the 1st generation (sedative), or classic. As a result, an active period of synthesis and clinical testing of new generations of histamine blockers, which would be devoid of these undesirable effects, begins. The first drug of the II generation was terfenadine (1977). The differences between second-generation histamine blockers are high selective blockade of H-receptors, impossibility of passing through the blood-encephalitis barrier (lack of sedative-hypnotic effect), etc. In the future, drugs of the III generation were created, which are active metabolites of H-antagonists of the II generation, which made it possible to get rid of the cardiotoxic effect characteristic of drugs of the II generation. In the second half of the 1990s, the first such drug was introduced into clinical practice - fexofenadine (an active metabolite of terfenadine). Drugs of the latest generations are able not only to block H-receptors, but also to have an additional effect on the processes of allergic inflammation.

Most H_1-histamine blockers belong to the fat-soluble amines, which have a similar chemical structure, where the nucleus is represented by an aromatic and/or heterocyclic group and is linked by a nitrogen, oxygen or carbon (X) molecule to an amino group.

Thus, in diphenhydramine, the place of fragment X is occupied by oxygen, in suprastin - nitrogen, in diprazine - nitrogen as part of the phenothiazine nucleus, etc. Depending on the X-bond, they are divided into several groups (derivatives of ethanolamine, ethylenediamine, phenothiazine, quinuclidine, tetrahydrocarboline, alkylamine, piperazine, piperidine).

The core determines the severity of antihistamine activity, and the features of the general chemical structure - some properties of the drugs. Most ethanolamine derivatives are characterized by pronounced m-cholinolytic and sedative effects. Most piperazine derivatives have a weak sedative effect. Cholinolytic properties of

phenothiazines are similar to ethanolamine derivatives. Phenothiazine drugs are also used as antiemetics. Derivatives of piperazine and alkylamine are characterized by high selectivity for H_1-receptors in the absence or weak expression of cholinolytic effects.

Classification. In connection with the pharmacodynamic and pharmacokinetic differences of different generations, modern H-histamine blockers are classified according to the time of their creation and chemical structure:

I generation drugs – derivatives:

1) ethanolamine - diphenhydramine hydrochloride (diphenhydramine), clemastine (tavegil), doxylamine, etc.;

2) ethylenediamine - chloropyramine (suprastin), etc.;

3) phenothiazine - promethazine hydrochloride (diprazine, pipolfen);

4) alkylamine - pheniramine;

5) quinuclidine - hifenadine (fenkarol);

6) tetrahydrocardolin - mebhydrolin (diazolin);

7) piperidine - cyproheptadine (peritol).

II generation drugs – derivatives:

1) azatidine - loratadine (Claritin, Rinoral);

2) piperazine - cetirizine (Zyrtek, Cetrin);

3) triprolidine - acrivastine (semprex);

4) oxypiperidine - ebastine (Kestin), levocabastin (Histimet);

5) piperidine - terfenadine (seldan).

III generation drugs (active metabolites of the II generation): fexofenadine (Telfast, Altiva), desloratadine (Aerius), levocetirizine (Xyzal).

Pharmacokinetics. All H-histamine blockers are well absorbed by the oral way. However, the simultaneous intake of food and histamine blockers affects their absorption: the absorption of astemizole decreases by 60%, the absorption of ebastine and loratadine increases, and the absorption of acrivastine, azelastine and cetirizine does not change. First-generation drugs are better absorbed at a pH of 0, so they are prescribed 1 hour before a meal or 2-3 hours after it. Some of them (diprazine,

dimedrol, diazolin, fenkarol) have an irritating effect, so they are recommended after meals.

The antiallergic effect of H-histamine blockers is revealed already 15-30 minutes after ingestion; the maximum concentration in the blood plasma is observed after about 1-3 hours. They are subject to systemic metabolism in the liver, which reduces their bioavailability. Therefore, in extreme cases, their intramuscular and intravenous administration is recommended.

H-histamine blockers are characterized by high affinity to blood proteins (60-90%). This must be taken into account when simultaneously prescribing these drugs with others, as well as hypoproteinemia in patients with burns, cachexia, in the postoperative period, etc. H-histamine blockers of the 1st generation are highly lipophilic substances. Therefore, they easily penetrate the blood-brain barrier, having a sedative-hypnotic effect. Penetrating through the placental barrier, they cause various forms of embryo- and fetotoxic effects, which is why they are not prescribed in the first trimester of pregnancy. H-histamine blockers of other generations practically do not penetrate into the central nervous system.

H1-histamine blockers are rapidly metabolized in the liver by cytochrome P-450 enzymes. Some drugs (diphenhydramine, suprastin) are inducers of microsomal liver enzymes, therefore they accelerate the biotransformation of both their own and other drugs. Most H-histamine blockers of the II generation are transformed into active metabolites with the participation of the CYP 3A4 isoenzyme of the cytochrome P-450B system (terfenadine - into fexofenadine, loratidine - into desloratadine, cetirizine - into levocetirizine, etc.). This prolongs their therapeutic effect. However, some H_1-blockers of the II generation are prolines, that is, their antihistaminic activity is associated with metabolites. Therefore, the variability of the effectiveness of drugs of the II generation in different people is related to the individual characteristics of their metabolism.

The elimination of H_1-histamine blockers and their metabolites is carried out through the kidneys and liver. These agents are excreted in breast milk in lactating women in amounts that may be dangerous for infants.

Due to high affinity to blood proteins, formation of active metabolites, longer connection with receptors, histamine blockers of the II generation have a long duration of action (12-48 hours), which allows them to be prescribed 1-2 times a day. Most drugs of the 1st generation have a short duration of action (4-8 hours), which requires taking them several times a day. Astemizol has the maximum half-life (about 10 days), which suppresses skin reactions to histamine and allergens for 6-8 weeks. The half-life of H-receptor antagonists increases with age, with impaired liver and kidney function.

Pharmacodynamics. The main mechanism of the antiallergic effect of drugs of this class is the ability to reversibly block H-histamine receptors, without exerting a pronounced effect on H_2- and H_3-receptors.

First-generation drugs, having a structure similar to the structure of histamine, block the action of histamine on H-receptors by the mechanism of competitive antagonism, and their affinity for these receptors is much lower than that of histamine. These drugs are not able to displace histamine bound to the receptor, they only block unoccupied receptors or those that are released. In therapeutic doses, they carry out fast, but incomplete (more than 30%) binding of H-receptors. Therefore, H-histamine blockers of the 1st generation are most effective in preventing allergic reactions of the immediate type, and in the case of a developed reaction, they prevent the release of new portions of histamine. Moreover, their long-term use often leads to a weakening of therapeutic effectiveness - the development of tolerance.

In addition to the effect on histamine receptors, drugs of the first generation also block other types of receptors (m-choline, α-adrenergic, serotonin, dopamine). Moreover, penetrating through the blood-brain barrier, they act not only on peripheral but also on central receptors. This is associated with a wide range of their desirable and undesirable pharmacodynamic effects.

Due to the blockade of central H-histamine and m-cholinoreceptors, "classic" histamine blockers have sedative and hypnotic effects. Their antiemetic and antiparkinsonian effects are associated with central cholinolytic activity. Blocking peripheral m-cholinoreceptors, some drugs (mainly derivatives of ethanolamine and ethylenediamine) cause dryness of the mucous membranes, constipation, impaired

urination, vision, etc. their atropine-like effect is generally considered undesirable, but it is used in some diseases (see indications for use).

Some drugs (diphenhydramine, diprazine) have an antitussive effect, which is realized due to direct action on the cough center in the medulla oblongata.

A local anesthetic (cocaine-like) effect is characteristic of most histamine blockers and occurs as a result of sodium channels blockade. Moreover, diphenhydramine and diprazine are stronger local anesthetics than novocaine.

Due to the blockade of histaminergic and serotonergic chains of nociceptive reflexes, some histamine blockers (diphenhydramine, diprazine) have their own analgesic effect and potentiate the action of other analgesics.

Histaminoblockers of the II and III generations have certain advantages over "classical" drugs both in terms of the mechanism of antiallergic action and in terms of the spectrum of additional pharmacodynamic activity. They are characterized by high selectivity of action on H-histamine receptors. They are characterized by a non-competitive and stable connection with H-receptors, which leads to an increase in the duration of the therapeutic effect.

The antiallergic effect of drugs of the II and III generations is explained not only by the blockade of H-receptors. These drugs inhibit the activating flow of Ca2+ into the cell, the release of histamine by basophils of both types (membrane-stabilizing effect), the release of adhesion molecules of various classes, the chemotaxis of eosinophils, the aggregation of platelets, the formation of superoxide anion, and also reduce the permeability of blood vessels. The activity of metabolites can be 2-4 times higher compared to the original compound (for metabolites of acrivastine, ebastine, loratadine) or the same (for metabolites of astemizole), and the duration of the therapeutic effect of some metabolites is much higher than that of the precursor drug (terfenadine and fexofenadine). Metabolites (ie, the latest generation drugs) have some significant additional antiallergic effects. They inhibit the release of mediators of systemic allergic inflammation, including cytokines and chemokines (tryptase, leukotriene C4, prostaglandin D2, IL-3,4, 8, TNF, granulocyte-macrophage colony-stimulating factor, RANTES), reduce the expression of adhesion molecules (P-selectin, ICAM-1), reduce

the severity of allergen-induced bronchospasm, reduce the phenomena of bronchial hyperreactivity. As a result, with long-term use, the drugs do not lose their activity. In addition, they can be used in high doses sufficient to control daytime and nighttime symptoms in patients for a long period of time (for example, flowering).

The advantage of the latest generations is the absence or insignificant influence on other mediator systems. Due to the peculiarities of the structure, they practically do not penetrate through the blood-brain barrier, which minimizes central effects.

In clinical practice, the following classification of histamine receptor blockers is used:

1) with a pronounced sedative effect (diphenhydramine, diprazine, suprastin);

2) with a moderate sedative effect (Tavegil, Diazolin);

3) with a weak sedative effect (fencarol, loratadine, cetirizine);

4) with no sedative effect (fexofenadine).

Indications for the administration of H-histamine blockers are primarily the prevention and weakening of allergic reactions. Due to the peculiarities of pharmacodynamics and pharmacokinetics, H-histamine blockers of different generations have some differences in their use in clinical practice.

First-generation drugs are mainly used to stop acute allergic reactions, especially those where the main mediator is histamine. They are most effective in the early stages of development, when histamine receptors are free, and in situations where the reactions of the early phase of allergic inflammation predominate, and the presence of additional anti-allergic action is not mandatory: urticaria, serum sickness, allergic reactions to food products, drugs (prophylaxis and treatment) etc. In serious life-threatening allergic conditions, such as anaphylactic shock, Quincke's edema, they are used parenterally in complex therapy in combination with functional antagonists. They are effective for episodic symptoms of seasonal allergic rhinitis, when the duration of its exacerbations does not exceed 2 weeks.

In terms of their effectiveness, H_1-blockers are practically the same. Despite the advantages of the latest generations (long duration of action, high selectivity for H_1 receptors, additional antiallergic effect, practical absence of blockade of other receptors

and central effects, tolerance), "classical" drugs are widely used in clinical practice due to the rapid development of the effect, low cost, availability of parenteral forms (necessary in acute situations), rich experience of use.

"Classic" histamine blockers, due to their sedative and hypnotic effects, reduce the period of falling asleep, increase the total duration and quality of sleep, and reduce the level of motor activity during sleep. The only drug from this group, which is allowed to be used for short-term correction of sleep disorders, is doxylamine (Donormil). Other histamine blockers with pronounced hypnotic activity (diprazine, diphenhydramine, etc.) have a large number of side effects and are not used for this purpose today. Compared to modern hypnotics, the disadvantages of doxylamine include a long duration of action (8-10 hours), a decrease or lack of effect after 7-10 days of administration, other manifestations of antihistamine activity, m-cholinergic blocking effect. All this limits its use as a sleeping aid.

The effect of some drugs of this group (diphenhydramine, diprazine) on the central nervous system is sometimes used to treat patients with parkinsonism, seasickness, air sickness, vestibular disorders, vomiting during pregnancy (doxylamine). Peritol is used to stimulate appetite and treat migraines.

To potentiate the effect of analgesics and local anesthetics during premedication, as a component of lytic mixtures, diphenhydramine, diprazine are used.

Side effect. Drugs that have irritating properties (diprazine, diphenhydramine, diazolin, fencarol) can cause gastrointestinal disorders when administered orally (prescribed after meals); with subcutaneous and intramuscular - infiltrates. Some of the drugs (peritol, diprazine, astemizole) increase body weight due to appetite stimulation.

Side effects of drugs of the 1st generation arise from their pharmacodynamic activity associated with the blockade of central and peripheral receptors of various types. As a result of the sedative-hypnotic effect, drowsiness, fatigue, impaired coordination of movement, attention, depressive states, etc. are noted. Therefore, these drugs (diphenhydramine, diprazine, suprastin, etc.) are prescribed in the evening. Their administration is contraindicated for persons whose work requires increased attention (drivers, pilots, operators). The degree of manifestation of the sedative effect varies in

different drugs and in different patients from moderate to pronounced. The sedative effect is enhanced under the influence of alcohol and other CNS depressants (tranquilizers, antipsychotics, etc.). Rarely, psychomotor excitement occurs instead of depression (more often in medium therapeutic doses in children and in adults in high toxic doses).

Due to their anticholinergic activity, ethanolamine and ethylenediamine derivatives cause such negative effects as dry mouth, constipation, urination disorders, visual disturbances, transient tachycardia, etc.

Due to the blockade of sodium and potassium channels, they have a cardiotoxic effect, which is manifested by arrhythmogenicity (quinidine-like effect on the heart): prolongation of the refractory QT phase with the risk of developing severe ventricular tachycardia. Transient hypotension is caused in sensitive individuals.

Another negative property of H_1-blockers of the 1st generation is a gradual decrease in their antiallergic effectiveness with long-term use (tolerance), which requires a change of the drug after 7-12 days of taking it.

In cases of using these products for more than 7-10 days, allergic reactions may develop. Prevention or reduction of many side effects can be achieved by reducing the dose or canceling the drug, sometimes these phenomena pass on their own.

In some cases, N.-histamine blockers of the II generation can cause an atropine-like effect, weakly expressed undesirable effects on the part of the nervous system (insomnia, agitation, apathy, fatigue, lowering of mood, paresthesia, etc.). However, an undesirable effect of the II generation is a cardiotoxic effect, which is manifested by prolongation of the QT interval, the appearance of ventricular extrasystole, atrioventricular blockade, blockade of the branches of His bundles. The probability of an increase in the QT interval when taking these drugs increases with electrolyte disturbances, in people with heart diseases (ischemic heart disease, myocarditis, cardiomyopathy), with an increase in the level of drugs in the blood (with an overdose, liver function disorders, alcohol abuse, interactions with some drugs). Due to the occurrence of fatal arrhythmias, terfenadine and astemizole are prohibited in many

countries. The III generation has no cardiotoxic effect. In connection with the above, drugs of recent generations are divided into:

• potentially sedative - cetirizine, loratadine;

• potentially cardiotoxic - terfenadine, astemizole, ebastine;

• non-sedative and non-cardiotoxic - fexofenadine.

Contraindications: individual increased sensitivity, professional activity that requires a quick mental or motor reaction, with caution - organic lesions of the liver, cardiovascular system, peptic ulcer disease of the stomach and duodenum (especially diazolin), hypotensive conditions (diprazine), asthenodepressive syndrome, glaucoma, prostate adenoma, intestinal and bladder atony, pregnancy, breastfeeding, children under 1 year of age.

Interaction with other drugs. Diphenhydramine, diprazine, suprastin, tavegil potentiate the effect of sleeping pills, neuroleptics, narcotic analgesics and other drugs that depress the central nervous system. Diphenhydramine, diprazine and tavegil (the latter much less) enhance the effects of cholinergic blockers and reduce the motility of the gastrointestinal tract, significantly reduce the absorption of drugs that are simultaneously prescribed to the patient (for example, indirect anticoagulants, paracetamol). When interacting with alcohol, they increase its toxicity. The combination of H-blockers, especially II and III generation, with drugs that inhibit its metabolism to varying degrees is extremely dangerous and even contraindicated.a. These drugs are: macrolide antibiotics, fluoroquinolones, antifungal azoles, HIV protease inhibitors, neuroleptics, antidepressants, diuretics, mineralocorticoids, calcium channel blockers, antiarrhythmic drugs of the 1st and 3rd classes (quinidine, amiodarone), other histamine blockers that prolong QT, grapefruit juice, etc.

H2-histamine blockers are weak alkali in the form of water-soluble hydrochlorides. They differ from H-antagonists by lower lipophilicity. Medicines from the group of H2-antagonists proved to be the most effective and safe as drugs that reduce gastric secretion. Their first generation includes cimetidine (almost not used due to the high risk of side effects), the second and third generations include ranitidine, famotidine, etc.

What is Dimedrol?

According to the accepted medical classification, Dimedrol belongs to blockers of histamine receptors and antiallergic drugs. The active substance of the composition is diphenhydramine hydrochloride, which acts on the central nervous system, suppressing histamine and cholinergic structures with receptors in the brain. Due to this effect, spasm of smooth muscles is removed, the condition of a person with allergies is alleviated.

Composition and form of release

The main forms of drug release are injection solution and tablets. The first can be taken orally or dripped into the eyes. In addition, rectal suppositories are produced based on the active ingredient. The composition and description of the drugs are indicated in the table:

	Solution	Tablet
Description	Transparent colorless	White flat-cylindrical with a chamfer and dash
Diphenhydramine concentration, mg	10 per 1 ml	30, 50 or 100 per 1 pc./ 20 for children
Composition	Purified water for injections	Stearic acid, potato starch, colloidal silicon dioxide, lactose
Packaging	Ampoules of 1 ml, 10 pcs. in a package with instructions for use	Blisters or strips of 6 or 10 pieces, packs of one blister

Physico-chemical properties of Dimedrol

The drug belongs to blockers of brain histamine receptors. Due to this, Diphenhydramine relieves smooth muscle spasm, reduces the permeability of

capillaries, and reduces the intensity of allergic reactions. The active ingredient of the local anesthetic has antiemetic activity, a sedative effect, and a hypnotic effect.

The drug causes local anesthesia, which manifests itself in a short-term sensation of numbness of the oral mucosa, has an antispasmodic effect. Diphenhydramine shows greater effectiveness in bronchospasm caused by histamine liberators (morphine), less in allergic type. The drug is ineffective against bronchial asthma, can be combined with bronchodilators (Theophylline, Ephedrine).

Diphenhydramine antagonizes the effect of histamine, increases blood pressure. In patients with a deficit in the volume of circulating blood, parenteral administration of Diphenhydramine can cause a decrease in pressure and increase hypotension due to the ganglioblocking effect. With local brain damage and epilepsy, the drug can activate epileptic discharges and provoke an epileptic attack.

The drug begins to act in a few minutes, its effect lasts up to 12 hours. Diphenhydramine binds to plasma proteins by 98%, is metabolized in the liver, lungs and kidneys, is excreted by the kidneys, with breast milk in the form of metabolites-conjugates with glucuronic acid. The active substance of the composition penetrates through the blood-brain barrier, a sufficient amount is found in breast milk.

Indications for use

The instructions for use of Diphenhydramine solution and tablets indicate the following indications for use:

- complex therapy of anaphylactic and anaphylactoid reactions;
- Quincke's edema, premedication (preparation for intervention);
- serum sickness;
- acute allergic conditions;
- treatment of urticaria, hay fever, angioedema of tissues;
- allergic conjunctivitis;
- sleep disturbances, chorea, vomiting in pregnant women;
- sea, air sickness, Meniere's syndrome;
- medicinal allergy, treatment of poisoning;

• acute iridocyclitis;

• radiation sickness;

• allergic eye diseases, conjunctivitis.

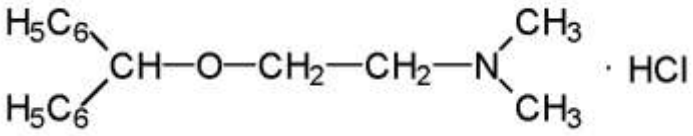
Method of application and dosage

Depending on the form of release of Diphenhydramine, the method of its application and dosage regimen differ. Yes, tablets are taken orally, they have children's and adult dosages, the course of administration depends on the type of disease and the severity of its course. The solution has a wider range of applications - it is administered intramuscularly, intravenously, used in the form of drops and orally.

We will consider the analysis of drugs of this group using an example **Diphenhydramine hydrochloride:**

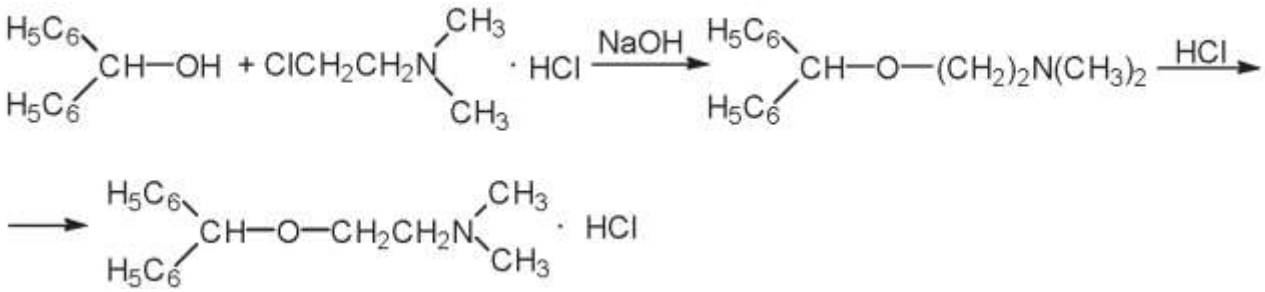
Diphenhydramine hydrochloride (Diphenhydramini hydrochloridum) (SPhU)

Dimedrol (Dimedrolum)



2-(diphenylmethoxy)-N,N-dimethylethanamine hydrochloride

Extraction. By the interaction of benzhydrol and β-dimethylaminoethyl chloride in the presence of sodium hydroxide [10, 170]:

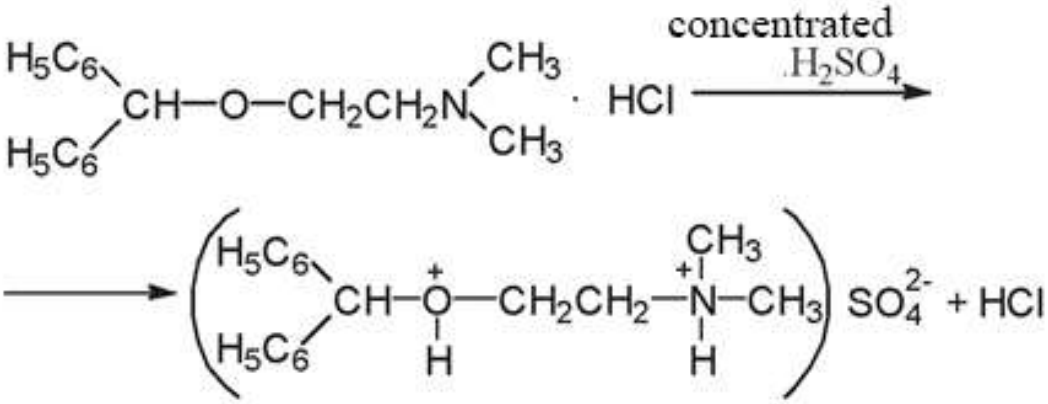


Properties. Crystalline powder of white or almost white color. Very easily soluble in water, easily soluble in 96% alcohol.

Identification:

Physico-chemical methods: melting point, IR spectroscopy, UV spectroscopy.

The reaction of the formation of an oxonium salt when interacting with concentrated sulfuric acid - an intense yellow color appears, which turns red when concentrated nitric acid is added. The resulting solution is diluted with water, cooled and chloroform is added; the chloroform layer turns intense purple[10, 171]:



The substance reacts to chlorides.

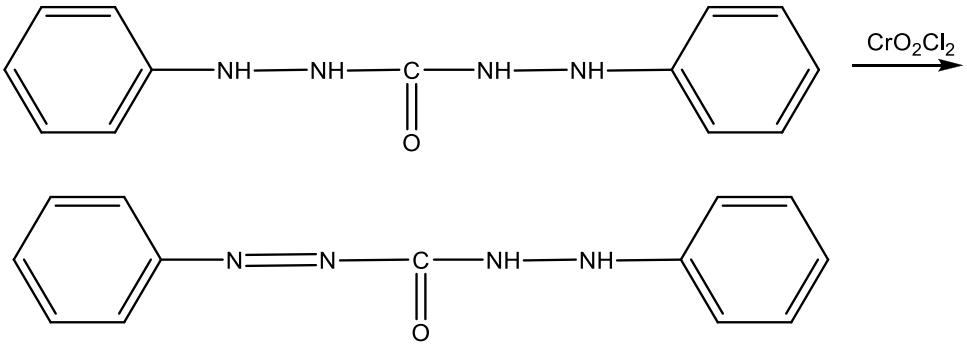
A) Reaction with a solution of silver nitrate in nitric acid medium, a white cheesy precipitate is formed. The precipitate is insoluble in dilute acids, soluble in ammonia solution:

$$Cl^- + Ag^+ \rightarrow AgCl\downarrow;$$

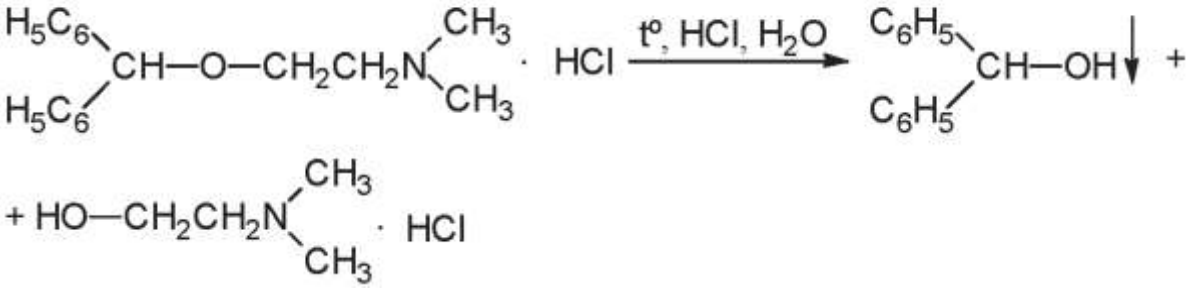
$$AgCl\downarrow + 2NH_4OH \rightarrow [Ag(NH_3)_2]Cl + 2H_2O.$$

B) Reaction with potassium dichromate in a mixture with sulfuric acid: chromyl chloride is formed, the vapors of which are stained with filter paper impregnated with a solution of diphenylcarbazide (colorless), in purple-red color:

$$K_2Cr_2O_7 + 4NaCl + 6H_2SO_4 \rightarrow 2CrO_2Cl_2 + 2KHSO_4 + 2Na_2SO_4 + 3H_2O$$

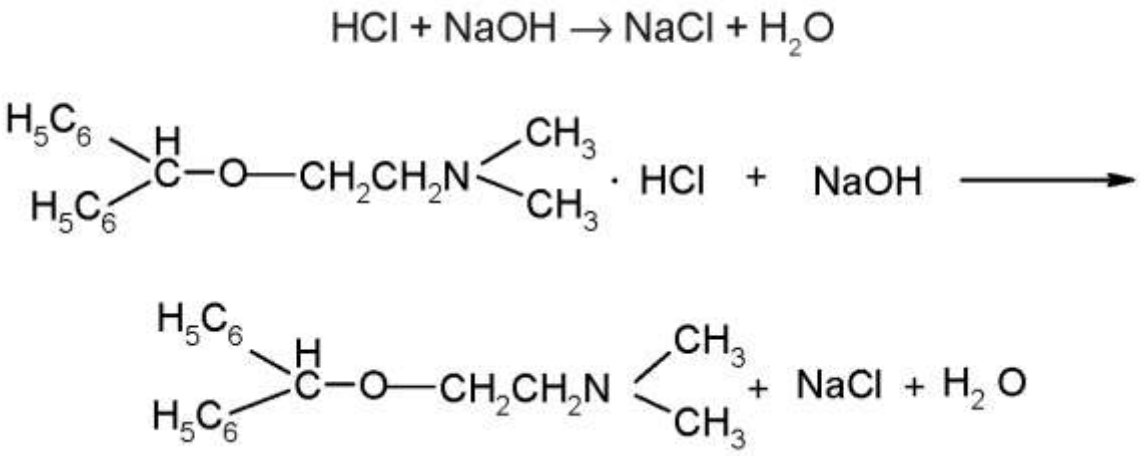


Acid hydrolysis reaction[10, 171]:



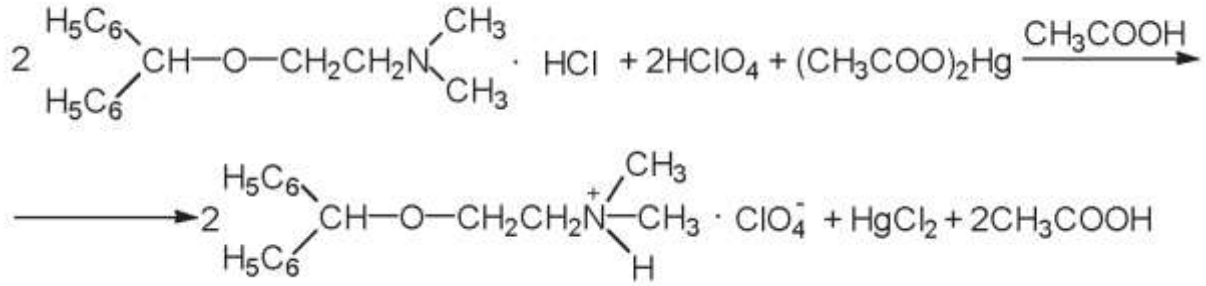
Check the melting point of the formed benzhydrol (62-67 °C).

Quantitative definition. Alkalimetry in a mixture of alcohol and 0.01 M solution of hydrochloric acid, direct titration, potentiometric. The titrant volume between two potential jumps on the titration curve (SPhU) is taken into account [10, 171]:



Acidimetry in a non-aqueous medium. The drug product is dissolved in glacial acetic acid, a solution of mercury (II) acetate is added (to bind hydrogen chloride) and

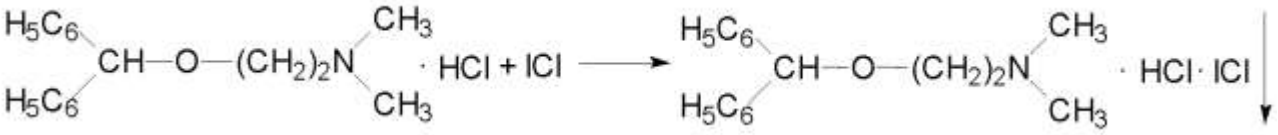
titrated with a solution of perchloric acid in glacial acetic acid to a greenish-blue color, the indicator is crystal violet[10, 171]:



In parallel, a control experiment is conducted.

Iodochlorometry, reverse titration, indicator - starch:

In parallel, a control experiment is conducted[10, 171].



$$ICl + KI \rightarrow I_2 + KCl$$

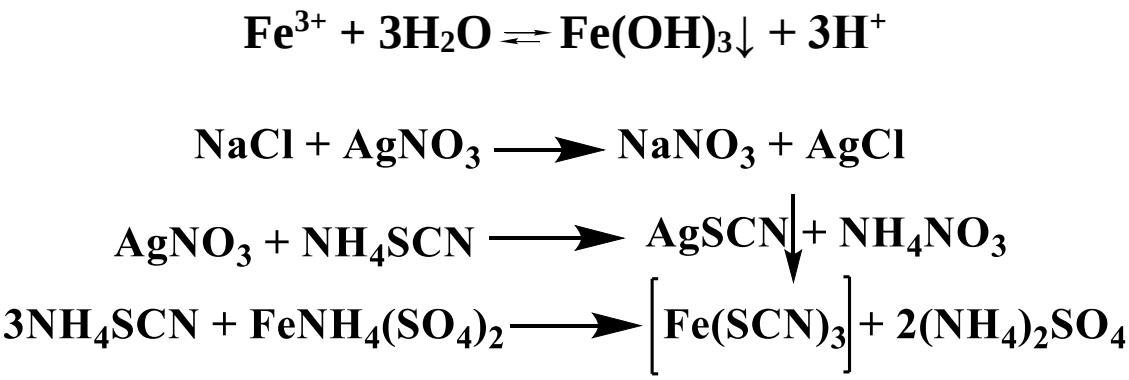
$$I_2 + 2Na_2S_2O_3 \rightarrow 2NaI + Na_2S_4O_6$$

Alkalimetry by bound HCl in the presence of ether, direct titration, indicator - phenolphthalein.

Argentometry by bound HCl according to the Folgard method.

The Folgard method, according to the requirements of the SPU, is used to determine the concentration of chlorides, bromides by back titration. The indicator is a solution of iron (III) ammonium sulfate (solution of iron-ammonium alum). The analysis is carried out in nitric acid. Acidic medium is required for iron (III) ammonium sulfate to be hydrolyzed to form insoluble hydroxides. The product of hydrolysis - iron (III) hydroxide (red-brown) interferes with the exact determination of the equivalence point.

$$\mathbf{FeNH_4(SO_4)_2 \rightleftharpoons NH_4^+ + Fe^{3+} + 2SO_4^{2-}}$$



According to the requirements of the SPU, dibutyl phthalate is used to insulate the surface of silver chloride precipitate.

Storage. In a sealed container that protects against light and moisture, as the drug is hygroscopic and can gradually hydrolyze.

Application (use). Antihistamine (antiallergic) agent.

TEST TASKS ON THE TOPIC «ANTIHISTAMINIC DRUGS»

1. Acid hydrolysis reaction is used to identify:

A) diphenhydramine hydrochloride (diphenhydramine)

B) sodium para-aminosalicylate

C) sodium benzoate

D) sodium salicylate

E) formaldehyde solution

2. A white cheesy precipitate from silver nitrate forms:

A) sodium para-aminosalicylate

B) mefenamic acid

C) phenacetin

D) paracetamol

E) diphenhydramine hydrochloride

3. Dimedrol (diphenhydramine hydrochloride) is an antihistamine (antiallergic) agent, belongs to simple ethers. To confirm high quality, the pharmacist conducts one of the reactions listed below:

A) neutralization

B) acetylation

C) hydrolysis

D) restoration

E) bromination

4. Quantitative determination of diphenhydramine hydrochloride (diphenhydramine) is carried out by the pharmacist by titration method in non-aqueous solvents. For what purpose is the titration carried out in the presence of a solution of mercury (II) acetate?

A) increases the solubility of the substance to be determined

B) strengthens the main properties of the drug under study

C) binds hydrochloric acid in the titration process, which is released

D) inhibits the reaction

E) catalyzes the reaction

5. One of the listed medicines is an antihistamine:

A) diphenhydramine hydrochloride (diphenhydramine)

B) novocaine

C) phenacetin

D) sodium para-aminosalicylate

E) anesthesin

6. For the quantitative determination of diphenhydramine by the acidimetry method in the following solvents, we use its:

A) acidic properties

B) basic properties

C) regenerative properties

D) oxidative properties

E) ability to engage in substitution reactions

7. The laboratory chemist reproduces the method of quantitative determination of the substance diphenhydramine by the acidimetric method in a non-aqueous medium. As a solvent, he/she should use:

A) concentrated nitric acid

B) ethanol

C) glacial acetic acid

D) dioxane

E) diethyl ether

8. Specify a possible method for quantitative determination of diphenhydramine:

A) bromatometry

B) permanganatometry

C) complexonometry

D) nitritometry

E) argentometry

9. What compounds are the starting points for the synthesis of diphenhydramine:

A) benzophenone and β-dimethylaminoethyl chloride

B) benzylic acid and β-dimethylaminoethyl chloride

C) diphenylacetic acid and dimethylaminoethanol

D) solution of phenol and dimethylaminoethanol

E) diphenylpropionic acid and β-dimethylaminoethyl chloride

10. When applying the powder containing diphenhydramine hydrochloride, the pharmacist added 2 drops of concentrated sulfuric acid. The appearance of a yellow color indicates the presence of what in the structure of the diphenhydramine molecule?

A) simple ether communication

B) keto groups

C) phenolic hydroxyl

D) ester group

E) β-lactam cycle

11. Specify the reagent that is used to confirm the corresponding drug products, derivatives of simple ethers, using diphenhydramine as an example:

A) iron (III) chloride

B) the hydroxylamine solution is alkaline

C) concentrated sulfuric and nitric acid

D) sodium hydroxide

E) diluted hydrochloric acid

12. Specify the pharmacopoeial method of quantitative determination of diphenhydramine (diphenhydramine hydrochloride)

A) iodometry

B) nitritometry

C) argentometry

D) iodochlormetry

E) acidimetry

13. During the hydrolysis of diphenhydramine (boiling a solution of the drug with dilute hydrochloric acid), one of the products is formed, which is then identified by its melting point:

A) benzhydrol (diphenylmethanol)

B) dimethylamine

C) diphenylamine

D) phenol

E) dimethylaminoethanol

14. To confirm the presence of a calcium cation in the drug substance "Calcium gluconate", the pharmacy pharmacist uses the following reagents:

A) ammonium acetate solution

B) ammonium chloride solution

C) ammonium oxalate solution

D) ammonium hydroxide solution

E) dilute nitric acid

15. The complexometric method can be used to determine the quantitative content of:

A) calcium lactate

B) sodium citrate

C) potassium iodide

D) sodium thiosulfate

E) potassium chloride

16. The pharmacist of the pharmacy confirms the presence of a calcium ion in the calcium lactate molecule by reaction with ammonium oxalate. The reaction is carried out in the environment of:

A) ammonia

B) acetic acid

C) sodium hydroxide

D) formaldehyde

E) potassium chloride

17. For the quantitative determination of the substance "Calcium lactate" and "Calcium gluconate" in accordance with the requirements of the SPhU, the pharmacist uses the method of:

A) gravimetry

B) permanganatometry

C) dichromatometry

D) ion-exchange chromatography

E) complexonometry

18. For the complexometric determination of calcium gluconate, taking into account the requirements of the SPhU, we use the following indicator:

A) solution of iron (III) ammonium sulfate

B) chalcone carboxylic acid solution

C) methyl red solution

D) phenolphthalein solution

19. A control and analytical laboratory specialist confirms the presence of a calcium cation in calcium gluconate by reaction with a solution of potassium ferrocyanide in the presence of ammonium chloride by the formation of:

A) white precipitate

B) yellow precipitate

C) blue sediment

D) green sediment

E) purple precipitate

20. Quantitative determination of calcium gluconate, in accordance with the requirements of the SPhU, is carried out by the method of:

A) complexonometry

B) gravimetry

C) acidimetry

D) alkalimetry

E) nitritometry

21. Specify the reagent that can be used to identify calcium, zinc, copper, iron (III) ions:

A) potassium iodide

B) potassium ferrocyanide

C) sodium hydroxide

D) silver nitrate

E) magnesium sulfate

22. During the qualitative chemical control of a 10% solution of calcium chloride for injections, a white precipitate was formed in one of the reactions. Such a result is possible when calcium chloride interacts with:

A) ammonium oxalate

B) barium chloride

C) thioacetamide

D) sodium nitrite

E) silver nitrate

23. When identifying the calcium ion in drug products, a red coloration of the chloroform layer is observed. At the same time, the following reagents are used:

A) solution of iron (III) chloride in the presence of chloroform

B) sodium cobalt nitrite solution

C) alcoholic solution of glyoxalhydroxyanil

D) methoxyphenylacetic acid solution

E) sodium sulfide solution

24. The titrant of the "Complexonometric titration" method, in accordance with the requirements of the SPhU, is:

A) sodium edetate solution (disodium salt of ethylenediaminetetraacetic acid)

B) hydrochloric acid solution

C) sodium hydroxide solution

D) potassium permanganate solution

E) sodium thiosulfate solution

25. What causes the change in color of the solution at the equivalence point during direct complexometric titration?

A) by changing the pH of the reaction medium

B) destruction of the complex metal - trilon B (sodium edetate)

C) selection of the free form of the indicator

D) by changing the chemical structure of the indicator

E) decarboxylation of trilon B molecule (sodium edetate)

26. The chemist of the Technical Control Department of the pharmaceutical enterprise fixes the equivalence point in complexonometry using:

A) paper impregnated with lead acetate

B) redox indicators

C) indicatorless method

D) iodine starch paper

E) metal indicators

2. AGENTS AFFECTING AFFERENT INNERVATION: LOCAL ANESTHETICS, ASTRINGENTS, COATING, ADSORBING, IRRITATING AGENTS.

AGENTS AFFECTING AFFERENT INNERVATION

Substances that act in the area of sensitive (afferent) nerve endings include local anesthetics, astringents, coating, adsorbing and irritating agents.

Local anesthetics are substances that, when applied to peripheral nerve tissue, have the ability to reduce or completely suppress the excitability of sensitive nerve endings and inhibit the conduction of impulses along nerve fibers.

Modern local anesthetics can be divided into the following groups:

I. Natural compound - benzoylecgonine ester: cocaine.

II. Synthetic nitrogen compounds:

1. Ester compounds (PABA derivatives)

a) easily soluble in water: novocaine (procaine), dicaine (tetracaine)

b) poorly soluble in water: anesthesin (benzocaine), orthocaine.

2. Amide compounds: lidocaine (Xicaine), trimecaine, etidocaine (Duranest), prilocaine (Citanest), articaine (Ultracaine), pyromecaine (Bumecaine), marcaine (bupivacaine).

Depending on the points of application of local anesthetic agents, the following types of local anesthesia are distinguished: terminal, conduction, and infiltration.

In terminal (surface) anesthesia, local anesthetic is applied to mucous membranes, wounds, ulcers, fresh granulations, etc.

Absorption of drugs when applied to mucous membranes occurs at different speeds, which is of practical importance, since intensive resorption and rapid entry of local anesthetic into the general bloodstream can cause intoxication. The degree of absorption from the mucous membrane of the upper and lower respiratory tract increases in the following order: larynx < trachea < bronchi < alveoli. Local anesthetics are absorbed slowly from the mucous membrane of the urinary bladder, and very quickly from the urethra. The drugs are easily absorbed when applied to wounds and fresh granulations. When applied to intact skin, no local anesthetic penetrates through it

and does not have an anesthetic effect. For terminal analgesia, anesthesin, dicain, xycain, trimecain are used, very rarely - novocaine, because it does not penetrate mucous membranes well.

Conduction (regional) anesthesia involves the introduction of anesthetic in the area of nerve trunks, nodes, sensitive roots of the spinal cord. Its options are: trunk, or actually conductor, anesthesia; plexus, or nerve plexus anesthesia; paravertebral - anesthesia of nerve nodes; spinal and epidural anesthesia.

During stem anesthesia, the drug solution is injected around the nerve. At the same time, the sensitivity of those areas innervated by this nerve is excluded. Novocaine, xycain, and trimecain are used for stem anesthesia.

Infiltration anesthesia is a mixed type of local anesthesia, in which nerve endings and fibers are excluded by layer-by-layer impregnation of tissues with a local anesthetic solution. Novocaine, xycain, and trimecain are used for infiltration anesthesia. In order to prolong the effect of local anesthetics, reduce their absorption and prevent intoxication during stem, epidural and infiltration anesthesia, small amounts of vasoconstrictors are added to anesthetic solutions. For example, 1 drop of 0.1% adrenaline hydrochloride solution is added to 2-10 ml of novocaine solution.

In addition to the local anesthetic effect, drugs of this group during resorption affect other body systems, which in most cases is undesirable. They, with the exception of cocaine, suppress the central nervous system, and in toxic doses cause excitement.

Dikain is a local anesthetic used for terminal anesthesia. It is 8-15 times more powerful than novocaine in terms of its anesthetic effect, but its toxicity is also 10 times higher. It is used in the form of 0.25-1% solutions for anesthesia of the mucous membrane of the eye when removing foreign bodies, before measuring intraocular pressure.

The effect after instillation of the drug develops after 1-2 minutes. Dikain can be used for epidural (extradural, paradural) anesthesia. With epidural anesthesia, it occurs on a limited number of segments necessary for this surgical intervention, develops after 30-40 min. after the introduction of the anesthetic solution and lasts about 4 hours.

Novocaine (Novocainum) is a derivative of paraaminobenzoic acid. During its hydrolysis by tissue esterases, the latter is released. Given that this acid is a bacterial growth factor, novocaine should not be prescribed to patients treated with sulfonamides, as their effectiveness will be reduced with such a combination.

Novocaine is used for infiltration anesthesia in the form of 0.25-0.5% solutions. After a single injection of the drug, anesthesia lasts 30-60 minutes. For stem anesthesia, novocaine is administered in the form of 1-2% solutions, for medical blockades (paranephric, vagosympathetic) - 0.25-0.5% solutions. Blockades are performed to weaken reflex reactions and improve the trophism of the affected organ. For spinal anesthesia, 2-3 ml of 5% novocaine solution is injected into the subarachnoid space at a level not higher than the first lumbar vertebra. The same amount of cerebrospinal fluid must be released beforehand. Anesthesia develops after 3-5 minutes. At the same time, not only the rear (sensitive) roots of the spinal cord are excluded, but also the front (motor) ones. This leads to paralysis of the skeletal muscles, which facilitates surgery. In addition, sympathetic nerve fibers passing through the anterior roots of the spinal cord are blocked. In the last decade, cases of allergic reactions when using novocaine (from skin rashes to anaphylactic shock) have become more frequent. To prevent them, it is necessary to carefully collect anamnesis. In the presence of an allergy to novocaine, the patient, in addition to it, cannot be prescribed any derivatives of para-aminobenzoic acid (dikain, anesthesin, etc.), to which there may be a cross-allergy. To find out possible sensitization to novocaine, it is necessary to conduct an intradermal diagnostic test.

Anesthesin practically does not dissolve in water, so it is used only for terminal anesthesia. In the form of 5-10% powders, ointments, pastes, anesthetics are used for itchy dermatoses, for pain relief of wounds and ulcers. In suppositories, 0.05-0.1 g of anesthetics are used for diseases of the rectum (for fissures, hemorrhoids, itching), in powders and tablets - for spasms and pain in the stomach, for vomiting during pregnancy, sea and air sickness.

Xycain, or lidocaine, is a universal local anesthetic used for all types of local anesthesia. It is 2 times more effective than novocaine with the same toxicity. The

duration of action of the drug does not exceed 1.5-2 hours, after adding adrenaline - up to 4 hours. In the process of its biotransformation, para-aminobenzoic acid is not formed in the body, so it can be used in patients treated with sulfonamide drugs. The drug is used for infiltration anesthesia in the form of 0.25-0.5% solutions, conduction - 0.5-2% solutions, epidural - 0.5% solution, spinal - 5% solution, terminal anesthesia of mucous membranes - 4-10% solution. An important property of xycain is its ability to eliminate cardiac arrhythmias of ventricular origin, for example, extrasystole, ventricular fibrillation in acute myocardial infarction. In such cases, xikain is used intravenously, drop-by-drop or stream slowly in the form of a 0.2% solution. Lidocaine can be used in people who are sensitized to novocaine and other anesthetics from the group of complex ethers (dikaine, anesthesin).

Articaine, or ultracaine, is used for infiltration and conduction anesthesia. The analgesic effect develops after 1-2 minutes. after administration of the drug, lasts 1-3.5 hours. For use in dentistry, a combined preparation containing ultracaine and adrenaline hydrochloride is produced. Local anesthesia is indicated for surgical interventions in weakened, exhausted patients, in elderly and senile persons. It is used in the presence of respiratory and cardiovascular insufficiency, when general anesthesia with the introduction of muscle relaxants and artificial ventilation of the lungs is too risky. Local anesthetics are used during short-term small operations, including in outpatient practice, in cases where the surgeon must also perform the functions of an anesthesiologist.

Contraindications to the use of local anesthesia are surgical interventions in children under 10 years of age, in patients with increased neuropsychological excitability, in the presence of sensitization to drugs of this group, in the presence of pronounced fibrous changes in tissues. It is also not performed during emergency operations that are associated with acute blood loss and are performed to stop bleeding.

In the process of using local anesthetic agents, when the maximum doses are exceeded or when they are administered quickly, the phenomena of intoxication develop. This is manifested by a decrease in blood pressure, heart rhythm disturbances, cardiac arrest, suppression of the central nervous system, dizziness, respiratory depression, convulsions. When they occur, vasoconstrictors (norepinephrine

hydrotartrate, adrenaline hydrochloride), cardiotonics (strophantin, corglycon), anticonvulsants (thiopental sodium, diazepam) are administered to the patient. If necessary, artificial respiration is established, heart massage is performed. In order to prevent intoxication with local anesthetics in all cases of their use, it is necessary to follow the rule: to achieve effective local anesthesia, use the smallest possible amount of the drug in the largest possible dilution.

Agents are called ***astringents***, which, when interacting with proteins, form albuminates and have an astringent, anti-inflammatory, antimicrobial effect.

The drugs of this group include organic and inorganic compounds. Organic astringents of plant origin are tannin, decoction of oak bark, infusions of St. John's wort, chamomile flowers. Inorganic binders are metal compounds, in particular basic bismuth nitrate. When applied to mucous membranes or a wound surface, they cause partial coagulation of mucus or exudate proteins and lead to the formation of a film. The latter protects the nerve endings of tissues from irritation, which is accompanied by a decrease in pain sensations, local narrowing of blood vessels, and restriction of secretion. Consolidation of cell membranes leads to a decrease in the inflammatory reaction. Tannin is halotannic acid (Acidum tannicum), which is obtained from ink nuts (growths on oak leaves), as well as from some plants of the sumac family. A large amount of tannin is contained in freshly brewed tea. The substance is easily soluble in water and alcohol. It is produced in the form of a powder. Tannin is used as an astringent and anti-inflammatory agent in the form of 1-2% aqueous or glycerin solutions for inflammatory processes in the mouth, nose, larynx or pharynx. 3-10% tannin solutions and ointments are used to treat burn surfaces, ulcers, fissures, bedsores. In case of poisoning with salts of heavy metals, with which tannin forms insoluble compounds, the stomach is repeatedly washed with a 0.5% aqueous solution of tannin. The same procedure can be carried out in case of poisoning with alkaloids, which tannin binds. With some alkaloids (morphine, cocaine, atropine, nicotine, physostigmine), the drug forms unstable compounds, so the washing water must be carefully removed from the stomach.

Basic bismuth nitrate is a binder of inorganic origin. Practically insoluble in water and alcohol, easily soluble in hydrochloric acid. Available in powder and tablets of 0.25 and 0.5 g, 10% ointment. It is part of the tablets "Vicalin", "Vikair". Basic bismuth nitrate is used for peptic ulcer disease of the stomach and duodenum, enteritis, colitis (in powders or tablets of 0.25-0.5 g 3-4 times a day 15-30 minutes before meals). In case of inflammatory diseases of the skin and mucous membranes (dermatitis, ulcers, erosion, eczema), the drug is prescribed in the form of 5-10% powders or ointments.

De-nol is a colloidal preparation of bismuth subcitrate. In addition to astringent, it has antacid, coating, antihelicobacter and cytoprotective effects. It is used in the complex therapy of patients with peptic ulcer disease of the stomach and duodenum. Oak bark is used in the form of a decoction (1:10) for rinsing the oral cavity in gingivitis, stomatitis, other inflammatory processes of the oral cavity, pharynx and oral pharynx. For the same purpose, infusions of chamomile flowers, sage leaves, and St. John's wort are used. An infusion of chamomile flowers is also used internally (1-5 tablespoons 2-3 times a day) and in enemas for intestinal spasms, flatulence, and diarrhea.

Coating agents are indifferent substances with a high molecular weight that have the ability to form colloidal solutions that protect tissues from irritation. They include starch (Amylum), which is obtained from potatoes (Amylum Solani), corn (Amylum Maydis), rice (Amylum Oruzae), and wheat (Amylum Tritici). Starch mucus (Mucilago Amyli) is introduced into the composition of mixtures, enemas in the case when they contain substances that irritate mucous membranes. Sometimes it is used to slow down the absorption of poisons that have entered the gastrointestinal tract, to protect the mucous membrane in case of poisoning by cauterizing substances. Unlike binders, coating agents do not have anti -inflammatory effect. Mucilage from flax seeds (Mucilago seminis lini), which is prepared in a ratio of 1:30, is used externally and inside in the same cases as starch mucus. The coating properties have some drugs containing aluminum compounds - aluminum hydroxide, almagel, suracle. When combined with water, they form a gel. In addition, they show adsorbing and, most importantly, antacid properties. They are used in peptic ulcer of the stomach and

duodenum, acute and chronic hyperacid gastritis, esophagitis and other pathology of the digestive tract, where it is necessary to reduce the acidity and proteolytic activity of gastric content.

Adsorbing agents – are indifferent powders that, due to high surface activity, have the ability to absorb various substances.

Activated carbon, or carboline, is black powder, odorless and taste, animal or vegetable. Carbolen has a large active surface, measured by hundreds of square meters per 1 g of substance, which is capable of adsorbing gases, alkaloids, toxins, salts of heavy metals. The gastrointestinal tract is not absorbed. Activated carbon is used 1-2 g 3-4 times a day for flatulence. In acute poisoning, it is prescribed at a dose of 20-50 g in the form of a water suspension inside or through a probe after or during gastric lavage. Nowadays, enterosorbents are widespread - substances that are used to absorb various compounds in the lumen of the intestine._At the same time, they have the ability to excrete poisonous, ballast, biologically active and potentially dangerous substances after their absorption in the digestive canal. Enterosorbents include preparations of different chemical structure: carbon (SKN brands, etc.), silicon (polysorb), derivatives of polyvinylpyrrolidone (enterodesis), vegetable origin (pectins, dietary fiber, polyfepan), etc. Clinical experience shows that enterosorption is effective in food, drug poisoning, diseases of the digestive system, cardiovascular, respiratory, endocrine systems, allergic, skin diseases, in the treatment of pregnancy toxicosis, etc.

Medicines (drugs) that stimulate the end of afferent nerves

Irritative agents are substances that excite the end of the sensitive nerves of the skin and mucous membranes. Due to this, reflex reactions occur. These include solutions of ammonia, menthol, mustard, camphor, other substances of plant origin.

All irritants, except for menthol, when applied to the skin or mucous membranes cause vasodilation (redness), swelling, and local fever. This improves blood supply, increases metabolism, creates favorable conditions for elimination of local pathological processes. With excitation of sensitive receptors of the skin and mucous membranes under the influence of irritating substances increases breathing, increases blood

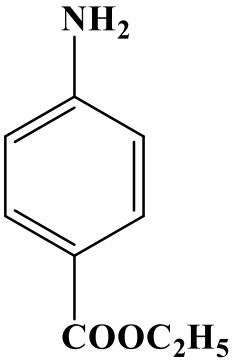
pressure, improves cardiac activity. This is due to the reflex increase in the tone of the respiratory and vascular centers of the medulla oblongata. The stream of impulses, which occurs under the influence of irritants, interacts with those pulses coming from the pathological focus on its way to the brain. The artificially created excitation foci reduces the activity of pulses coming from the diseased organ. This shows the distracting effect of irritating substances, their ability to reduce the intensity of pain in inflammation of the muscles, joints, nerves, heart pain, etc. In addition, the excitation caused by irritant agents captures the centers of sympathetic innervation of the spinal cord, which leads to increased blood supply and trophic of the internal organs. The reflex effect of these substances from the skin on the internal organs is carried out by the law of segmental innervation. It is known that in diseases of the internal organs in the corresponding areas of the skin there are areas of hypersensitivity (Zakharyin-Geda zone). By irritating the corresponding areas of the skin receptors, you can reflexively influence the work of the internal organs (cutaneous-visceral reflexes). In addition, irritation of the receptors of the mucous membranes, skin and subcutaneous structures (including muscle tissue) is accompanied by the stimulation of the formation and isolation of endogenous opioid peptides - endorphins, enkephalins, dinorphins, which play an important role in the regulation of pain. Other physiologically active compounds (histamine, kinins, etc.), which stimulate immune processes, affect blood clotting, etc., are also released. A number of tools in this group can be absorbed and have a resorptive effect, affecting various regulatory reactions (neurotransmitter, immune). In particular, the presence in preparations containing snake or bee poison, hyaluronidase and phospholipase, promotes their penetration through the skin when used topically. This is accompanied by changes in microcirculation, blood coagulation, metabolism. The camphor in subcutaneous administration activates the respiratory and vasomotor centers of the medulla oblongata, stimulates the activity of the heart by enhancing metabolic processes in the myocardium, increasing its sensitivity to sympathetic impulses.

Due to the peculiarities of their pharmacodynamics and scope, drugs of weakening and laxative effects, expectorants of reflex effects, vomiting substances were isolated into separate groups.

In practical classes, drugs that affect afferent innervation: locally anesthetic agents, binders, coating, adsorbing, irritating, we will consider in example: Anasthesin, Novocaine, Dicaine, Nitrate bismuth, hydroxide ammonium, camphor.

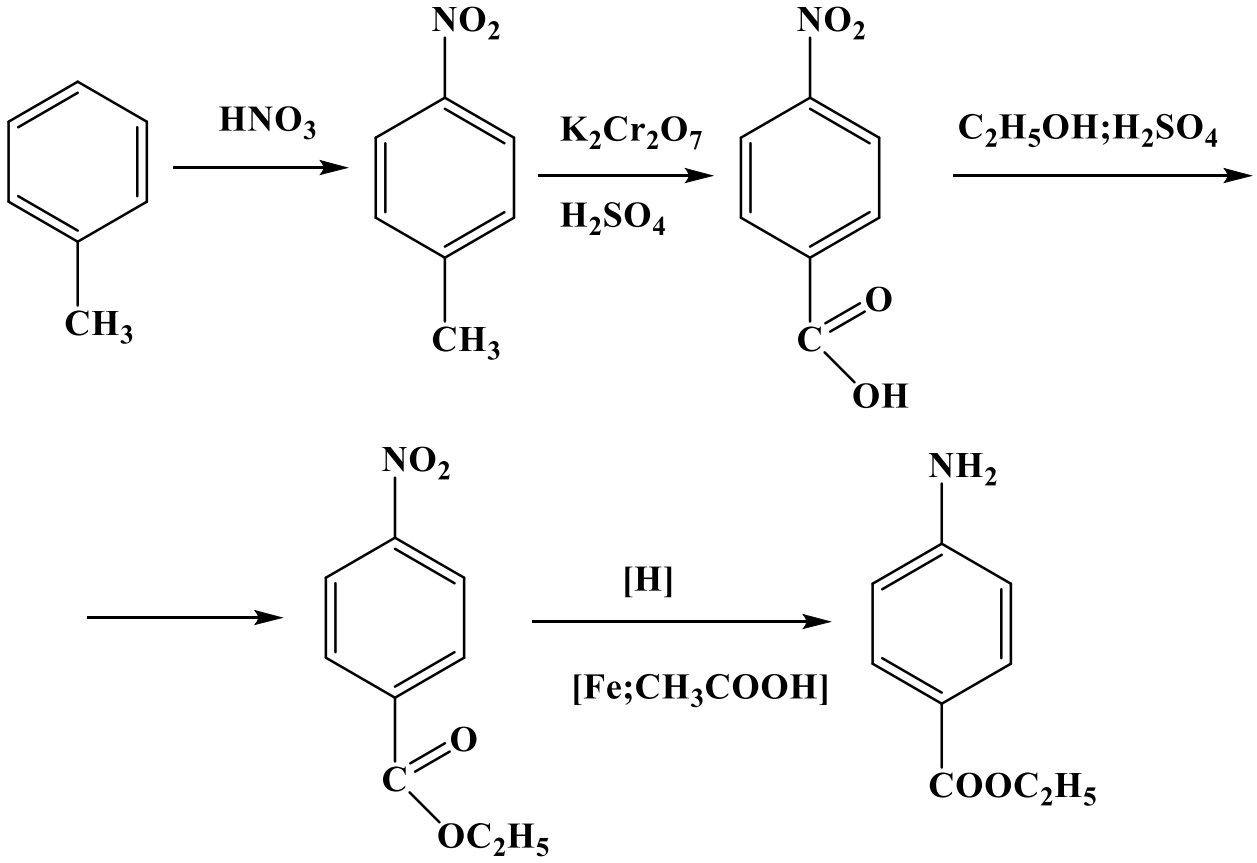
We will consider the analysis of drugs of this group using an example **Anesthesin:**

Anesthesin (Anaesthesinum) Benzocaine



Ethyl ether P-aminobenzoic acid

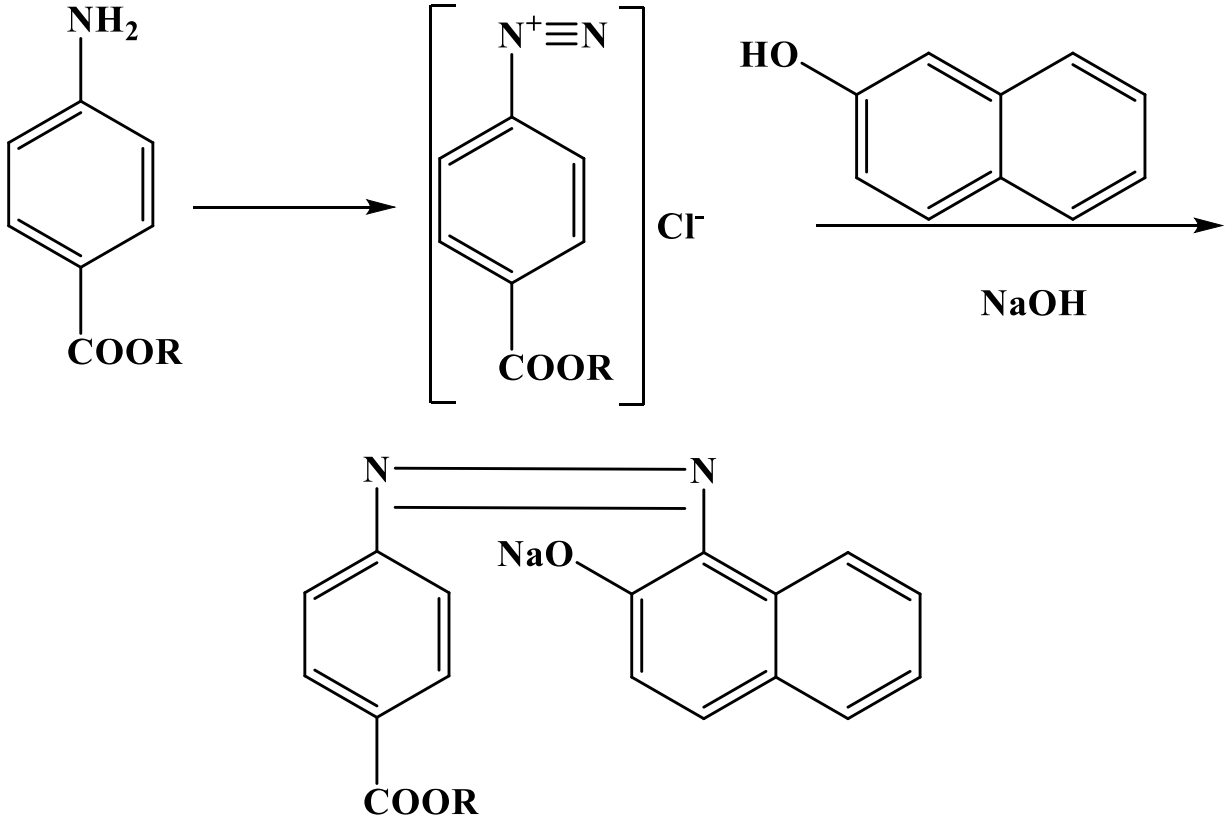
Extraction. The starting substance is toluene:



Properties. White crystalline odorless powder, bitter in taste. It causes a sense of numb on the tongue. Very little soluble in water, easily soluble in alcohol, ether, chloroform, difficult to soluble in fatty oils and diluted chloride acid.

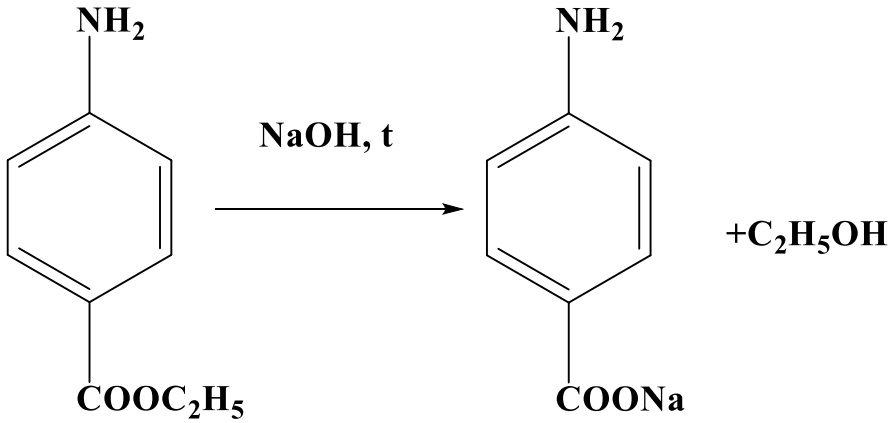
Identification:

Reaction to primary aromatic amino group:



cherry-red azo dye

As a result of alkaline hydrolysis, ethanol is formed, which can be detected by iodoform test:



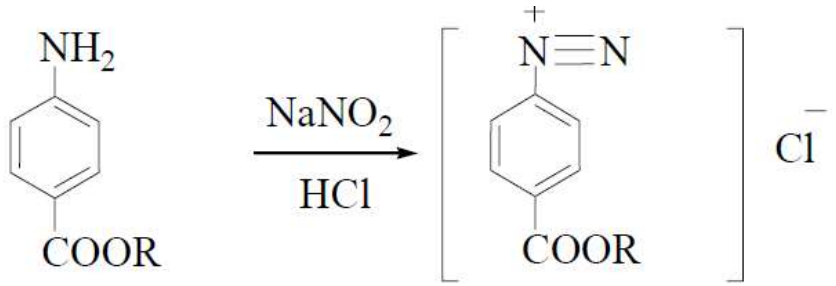
$$C_2H_5OH + 4I_2 + 6NaKOH \rightarrow CHI_3\downarrow + 5NaI + HCOONa + 5H_2O$$

When the medicinal substance is oxidized with a solution of chloramine in the presence of hydrochloric acid and ether - the essential layer is painted in orange.

A reaction with aromatic aldehydes:

Quantitative definition.

Nitritometry, indicator - iodcrohmal paper:



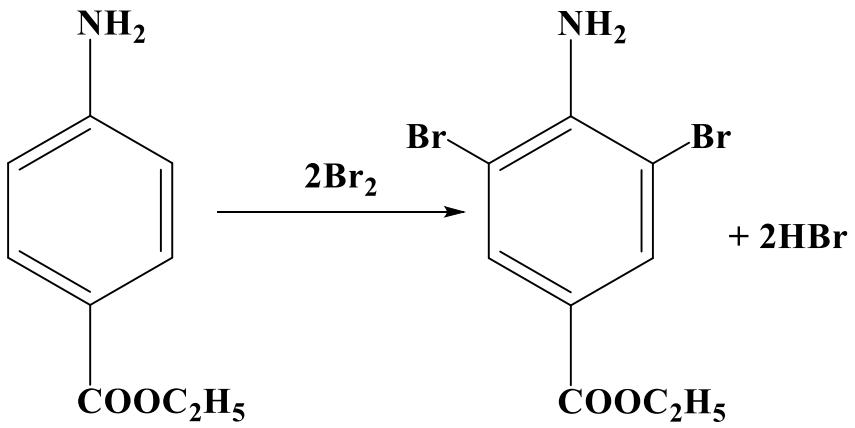
$$2KIO_3 + 5NaNO_2 + 2HCl \rightarrow I_2 + 5NaNO_3 + 2KCl + H_2O$$

In parallel, the control experiment is carried out.

In the case of internal indicators, use neutral red or trapeolin-00 in a mixture with methylene blue.

Bromatometry, reverse titration:

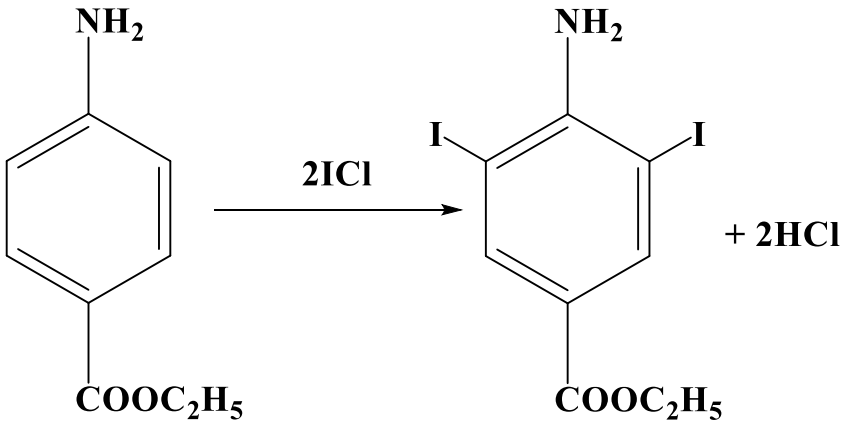
$$KBrO_3 + 5KBr + 6HCl \rightarrow 3Br_2 + 6KCl + 3H_2O$$



$$Br_2 + 2KI \rightarrow I_2 + 2KBr$$

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

Iodochlorometry, reverse titration:



$$ICl + KI \rightarrow I_2 + KCl$$

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

Storage. In a sealed container that protects from light.

Application. It is used in the form of 5-10 % ointment or powders for urticaria or skin diseases, which are accompanied by itching, as well as for anesthesia of wounded and ulcerative surfaces. In diseases of the rectum, suppositories are used. 5-20 %oil solutions are used for anesthesia of the mucous membranes. Orally prescribed in powders, tablets for anesthesia of mucous membranes for spasms and pain in the stomach, hypersensitivity of the esophagus, etc.

TEST TASKS ON THE TOPIC «AGENTS AFFECTING AFFERENT INNERVATION: LOCAL ANESTHETICS, ASTRINGENTS, COATING, ADSORBING, IRRITATING AGENTS. AGENTS AFFECTING AFFERENT INNERVATION»

1. The drug "Novocaine" [Novocainum, Procaine hydrochloride] can be synthesized from:

A) para-Nitrobenzoic acid

B) ortho-Nitrobenzoic acid

C) meta-Nitrobenzoic acid

D) Benzoic acid

E) Salicylic acid

2. During the transportation of the substances novocaine and anesthesin from the manufacturing plant, the labeling on their packaging was damaged. Samples of the substances were sent for analysis to the control and analytical laboratory. One of the reactions that makes it possible to distinguish novocaine from anesthesin is the identification reaction of:

A) Bromides

B) Chlorides

C) Sulfates

D) Tartrates

E) Iodides

3. One of the reactions of novocaine identification is:

A) Phenolic hydroxyl reaction

B) Murexide test

C) Maltol test

D) Reaction to the primary aromatic amino group

E) Reaction to alcohol hydroxyl

4. Specify which method is used in pharmaceutical analysis to quantify novocaine?

A) Nitritometry

B) Permanganatometry

C) Cerimetry

D) Complexonometry

E) Acidimetry

5. The pharmacist determines the quantitative content of the novocaine 1% injection solution made in the pharmacy. Which of the following titrated solutions should he use for this?

A) Sodium thiosulfate

B) Sodium edetate

C) Potassium bromate

D) Sodium nitrite

E) Silver nitrate

6. The drug procaine hydrochloride is a derivative of:

A) p-Aminobenzoic acid

B) Acetylsalicylic acid

C) Sulfanilic acid

D) Benzoic acid

E) Nicotinic acid

7. Indicate which of the following medicines corresponds to the rational chemical name "p-aminobenzoic ether of diethylaminoethanol hydrochloride":

A) Streptocide

B) Diphenhydramine

C) Dikain

D) Streptomycin

E) Novocaine

8. Procaine hydrochloride can be synthesized by transesterification reaction in the presence of sodium alcoholate from:

A) Benzocaine (anesthetic)

B) Resorcinoma

C) Salicylic acid

D) Benzene

E) Trimecaine

9. The pharmacist of the pharmacy conducts internal pharmacy quality control of the procaine hydrochloride substance. Which of the following reagents should be used for its identification?

A) Sodium chloride

B) Silver nitrate

C) Calcium oxalate

D) Potassium bromide

E) Copper(II) sulfate

10. Specify the color of the solution that occurs as a result of the reaction of the formation of an azo dye when identifying procaine hydrochloride:

A) Red

B) Yellow

C) Purple

D) Blue

E) Green

11. The reaction for identifying procaine hydrochloride, in accordance with the requirements of the SPhU, is the interaction of the substance with fuming nitric acid, acetone, and an alcoholic solution of potassium hydroxide. The analytical effect of this reaction is the appearance of such a color:

A) Red-violet

B) Dark red

C) Brownish-red

D) Yellow

E) Emerald green

12. Tetracaine hydrochloride (dicaine) according to its chemical structure belongs to the derivatives of:

A) p-Aminobenzoic acid

B) Salicylic acid

C) Phenol

D) Benzaldehyde

E) Isonicotinic acid

13. Which drug will react with nitric acid to form a nitrosamine?

A) Novocaine

B) Sodium p-aminosalicylate

C) Anesthesin

D) Dikain

E) Novocainamide

14. The reaction product of which drug with nitrite acid does not form an azo dye upon subsequent addition of an alkaline solution of β-naphthol?

A) Anesthesin

B) Novocaine

C) Norsulfasol

D) Streptocide

E) Dikain

15. The pharmacist performs the quantitative determination of the benzocaine substance in accordance with the requirements of the SPhU by the method of:

A) Nitritometry

B) Bromatometry

C) Iodine chlorometry

D) Acidimetry

E) Permanganatometry

16. When analyzing a 10% ammonia solution, its identification is carried out by the formation of white smoke in the presence of:

A) H_2O

B) NaOH

C) H_2SO_4

D) $KMnO_4$

E) HCl

17. The pharmacist determines the admixture of ammonium salts (method A) in sodium tetraborate according to the SPhU using a solution of:

A) Potassium tetraiodomercurate alkaline

B) Potassium ferrocyanide

C) Silver nitrate

D) Sodium tetraphenylborate

E) Barium chloride

18. When heating the studied solution of the drug with sodium hydroxide, a sharp smell is felt, and red litmus paper moistened with water turns blue. What ion is identified in this case?

A) Carbonate ion

B) Nitrate ion

C) Ammonium ion

D) Arsenite ion

E) Acetate ion

19. The pharmacist determines the presence of bismuth ion according to normative and technical documentation. Which of the following reagents does he use?

A) Potassium iodide solution

B) Starch solution

C) Barium chloride solution

D) Phenolphthalein solution

E) Argentum nitrate solution

20. The pharmacist of the laboratory of the State Service of Ukraine on Medicines conducts an analysis of bismoverol. One of the reactions for identification of Bi3+ cations according to the SPhU is the reaction with thiourea. What color is formed in this case?

A) Yellowish-orange color or orange precipitate

B) Yellow color of the solution

C) Red color of the solution or red precipitate

D) Blue color of the solution or blue precipitate

E) Violet color of the solution or violet precipitate

21. The presence of bismuth ions in Dermatol is confirmed by a reaction in an acidic environment with:

A) Ammonium oxalate

B) Barium chloride

C) Argentum nitrate

D) Sodium sulfide

E) Potassium nitrate

22. The pharmacist analyzes the xeroform. Which of the following reagents can he use to identify bismuth in xeroform?

A) Ammonium hydroxide

B) Barium chloride

C) Sodium sulfide

D) Potassium tartrate

E) Copper sulfate

23. What reagent should the pharmacist use to determine bismuth ions when identifying De-nol tablets, the active substance of which is bismuth subcitrate?

A) Silver nitrate

B) Potassium sulphite

C) Sodium sulfide

D) Sodium sulfate

E) Sodium nitrite

24. Quantitative determination of the medicine "Bismuthi subnitras" is carried out by the method of:

A) Complexonometry

B) Alkalimetry

C) Bromatometry

D) Iodometry

E) Permanganatometry

25. Preparations of calcium chloride, magnesium sulfate, zinc sulfate, bismuth nitrate basic can be quantitatively determined:

A) Iodometrically

B) Nitritometrically

C) Acidimetrically

D) Complexometrically

E) Alkalimetrically

26. One of the methods of quantitative determination of aluminum hydroxide in the drug "Almagel" is:

A) Bromatometry

B) Iodochlormetry

C) Complexonometry

D) Argentometry

E) Nitritometry

27. Anesthesin belongs to substances with local anesthetic activity and is a derivative of:

A) p-Aminobenzoic acid

B) p-Chlorobenzoic acid

C) p-Aminophthalic acid

D) p-Aminosalicylic acid

E) p-Aminobenzene sulfonic acids

28. Benzocaine (Anesthesin) is a drug that, according to its chemical structure, belongs to the class of:

A) Aromatic ketones

B) Esters [complex esters] of aromatic amino acids

C) Amides of aromatic amino acids

D) Aromatic aminoaldehydes

E) Amides of aromatic sulfonic acids

29. The presence of an ester group in the structure of benzocaine can be proven by the formation reaction of:

A) Indophenol

B) Diazonium salts

C) Salts of hydroxamatic acids

D) Aurine dye

E) Azomethine dye

30. A pharmacy visitor purchased an ointment whose active ingredient is a derivative of para-aminobenzoic acid with local anesthetic activity, very little soluble in water. Determine the active substance of the specified ointment:

A) Benzocaine

B) Diphenhydramine

C) Dikain

D) Novocaine

E) Novocainamide

31. Which reaction, in accordance with the requirements of the SPhU, is used to identify the substance benzocaine?

A) Diazotization followed by interaction with an alkaline solution of β-naphthol

B) Acid hydrolysis

C) Precipitation by calcium salts

D) Precipitation by heavy metals

E) Interaction with an ammonia solution of silver nitrate

32. The benzocaine identification reaction, as a result of which a cherry-red azo dye is formed, indicates the presence of this drug substance in the structure:

A) Alcoholic hydroxyl

B) Aldehyde group

C) Primary aromatic amino group

D) Phenolic hydroxyl

E) Amide group

33. When identifying the drug substance "Anesthesin", the pharmacist conducts a reaction with iodine in an alkaline medium to determine:

A) Ethanol formed during alkaline hydrolysis

B) Primary aromatic amino group

C) p-Aminobenzoic acid

D) Complex ether group

E) Aldehyde group

3. DRUGS THAT IMPROVE THE BLOOD SUPPLY TO ORGANS AND TISSUES

Today, the need for widespread use of drugs that affect the main links of diseases of the cardiovascular system, including those that reduce myocardial burden, the need for oxygen and improve the course of metabolic processes. Such drugs are called anti - anginal (angina pectoris - stenokardia, breast-pang; angina - shortness of breath).

The most important factors that ensure the normal functioning of the cardiovascular system: blood supply and metabolism in the myocardium. Their disorders lead to coronary heart disease and myocardial infarction (heart attack - the cell of death in the tissues, which is caused by impaired circulation in spasm, thrombus).

Ischemia is a exsanguination that is the result of functional spasm or organic narrowing or overlapping of the vessel through which the blood flow is tolerated. One form of manifestation of coronary heart disease is angina (from the Greek: stenos - narrow, kardia - heart), which is manifested in the attacks of compressive pain in the central or in the left part of the chest. Organic nitrates, nitroglycerin, isosorbide mononitrate, Erynit, are used to relieve angina attacks.

Means that reduce myocardial need for oxygen and improve its blood supply include:

A) organic nitrates;

B) blockers of calcium channels, potassium channels activators and amiodarone.

Nitrates are extremely important in the treatment of angina. There is an opinion that their action is caused by a number of reasons:

- they cause expansion of arterioles, reduce peripheral vascular resistance, make the heart work economical, reduce the need for myocardium in oxygen;

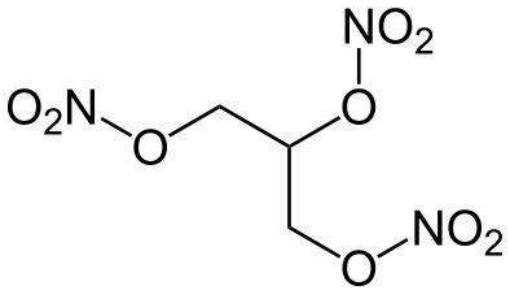
- They lead to the expansion of peripheral vessels, eliminate coronary artery spasm, promote the redistribution of blood in the myocardium, improve blood supply to areas affected by ischemia.

Undoubtedly, the main function of nitrates is that they are donors of nitrogen monoxide in the body. It is quite reasonable to conclude that the spasm of coronary

vessels is caused by a decrease in the release of NO in the endothelium, and organic nitrates are a drug that increases the content of NO in the body. The release of nitric oxide causes the expansion of not only coronary but also other blood vessels (vessels of the brain, peripheral vessels). It should be noted that nitrates are source of nitric oxide. They cause antispasmodic effect in various muscles (gastrointestinal tract, biliary tract, urinary ducts, bronchi). The transformation of nitrates into NO requires the recovery process, which is probably in vitro and in vivo, occurs according to the following general scheme (ē - electron; electron transfer is a mandatory stage of the renewable process):

Considering the problems associated with the use of nitrates in cardiac practice, it is necessary to pay attention to the phenomenon of tolerance that develops when re - prescribed. The appearance of vascular tolerance to nitrates is explained by the fact that the smooth muscle cells of the walls of the vessels stop turning nitrates into NO (the cause of this phenomenon has not yet been established), or there is an accelerated inactivation of nitric oxide vasoconstrictor-endothedin-1 and superoxide-anion.

Nitroglycerin



Nitroglycerin is a representative of the nitrate group (ether of nitric acid and glycerol). The mechanism of its therapeutic action includes a number of components. For a long time, it was believed that its action is the increase in coronary blood flow due to the direct myotropic coronary -spreading action. However, the catheterization of the coronary sinus in patients with angina showed that with sublingual administration nitroglycerin almost does not increase coronary blood flow, although large vessels expand. However, nitroglycerin injected directly into the left coronary artery increased blood flow in the coronary sinus in many patients, but did not prevent an attack of angina pectoris caused by stress. The next injection of nitroglycerin into a vein gave the

desired effect. It follows from these data that the antianginal effect of nitroglycerin is largely related to its extracardiac effect. The main reason for the elimination of an angina attack is the reduction of venous and arterial pressure by nitroglycerin and, accordingly, the reduction of venous return and resistance to blood flow and, as a result, the reduction of pre- and overload on the heart. In turn, this leads to a decrease in the work of the heart and its need for oxygen. Under these conditions, the existing level of blood supply and oxygenation becomes quite adequate and the state of hypoxia is eliminated. According to the sensitivity of blood vessels to nitroglycerin, they are located in the following order: veins > arteries > arterioles and capillary sphincters. Regarding the mechanism of vascular smooth muscle relaxation, it has been shown that nitroglycerin acts similarly to endothelial relaxing factor (NO). Nitric oxide is released from nitroglycerin (and other nitrates) in the body, from which S-nitrosothiols are formed. These compounds activate soluble cytosolic guanylate cyclase. The latter causes a decrease in the content of cytosolic free Ca^{2+} ions, which leads to the relaxation of vascular smooth muscles. It is important that nitroglycerin improves blood supply to the ischemic area of the myocardium. This is due to a number of effects. Thus, reducing the diastolic tension of the ventricular wall improves blood supply to the subendocardial part of the myocardium. A positive role is played by the already mentioned expansion of large coronary vessels. Their expansion at the site of occlusion is especially beneficial. In addition, it was established that nitroglycerin improves collateral blood circulation, and also blocks the central links of reflexes that cause narrowing of coronary vessels. Nitroglycerin also expands the blood vessels of the brain, internal organs, and retina. Being a myotropic antispasmodic, it reduces the tone of smooth muscles of internal organs (digestive tract, bronchioles, etc.).

Among the undesirable effects, it can cause reflex tachycardia (a compensatory reaction associated with a fall in blood pressure), headache, dizziness. These phenomena are especially pronounced after the first doses of the drug. The intensity of the headache subsequently decreases and it ceases to occur. At the same time, the ability to eliminate angina pectoris remains. With the use of nitroglycerin, especially with its overdose, an excessive decrease in blood pressure to the point of collapse is possible.

Addiction to nitroglycerin occurs only in the case of its long-term continuous use (for example, with intravenous infusion, addiction develops within 24 hours). With periodic use of the drug, this is of no practical importance. Fast and short-acting nitroglycerin is intended to stop an attack of angina pectoris that has already occurred. It is usually administered under the tongue in tablets or capsules (the latter contain an oil solution of nitroglycerin; the capsule should be crushed with the teeth), or in the form of an alcohol solution (1-2 drops per piece of sugar). Nitroglycerin is quickly absorbed (its action begins after 2-3 minutes) and eliminates an attack of angina pectoris. The effect is short-lived (up to 30 minutes). There is also a medicinal form of nitroglycerin for intravenous administration, which is used for emergency indications when other drugs are ineffective (as well as for myocardial infarction, if there is no pronounced hypotension). In addition, nitroglycerin is produced in canisters for inhalation.

In order to increase effectiveness, long-acting nitroglycerin dosage forms were created (sustac, trinitrolong, nitrone, etc.). Special microencapsulated and other dosage forms have been created that ensure its gradual absorption. Sustac is one of these drugs.

Sustac - nitroglycerin in the form of tablets that gradually dissolve, and taken orally. The action begins after 10-15 minutes and lasts for several hours (about 4 hours). Side effects are expressed to a lesser extent than when taking nitroglycerin.

Trinitrolong is similar in duration of action (3-4 hours). It is applied in the form of a polymer plate on the gums.

Nitrong has a longer effect (up to 7-8 hours). It is taken orally in tablets.

2% nitroglycerin ointment has a long-lasting effect. The effect occurs after 15-30 minutes and lasts up to 5 hours.

Patches with nitroglycerin are also used. It should be taken into account that when using a patch with nitroglycerin, which provides a constant supply of the drug to the body, addiction develops quickly - within 8-24 hours. Therefore, the patch is left on for no more than 12 hours (usually 8-10 hours), then an interval of 12 hours is made. This ensures the preservation of the effectiveness of nitroglycerin in the indicated dosage form. Addiction, as well as drug dependence, can occur in employees of pharmaceutical and military enterprises working with nitroglycerin.

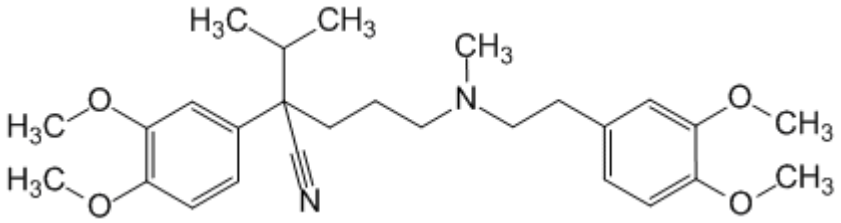
Long-acting nitrates also include nitrosorbide (isosorbide dinitrate), erinite (pentaerythritol tetranitrate, nitropentone) and isosorbide mononitrate. Their effectiveness is somewhat less than prolonged preparations of nitroglycerin. When taken orally, the effect occurs after approximately 30 minutes and lasts 1-4 hours. For nitrosorbide and isosorbide mononitrate, prolonged-acting tablets (6-8 hours) are also available. The drugs bind to blood plasma proteins. They are well tolerated. Side effects are similar to those for nitroglycerin, but expressed to a lesser extent. Possible dyspeptic phenomena. With long-term use, addiction occurs. Cross-addiction to nitrates has been noted. Nitrosorbide (isosorbide dinitrate) is produced in tablets for oral and sublingual use, in an aerosol for inhalation, in transdermal forms (aerosols, cream), transbuccal forms (on a polymer plate), in ampoules and vials for intravenous administration. Heart rate under the influence of calcium channel blockers varies ambiguously. This is due to the fact that the latter have a direct negative chronotropic effect on the heart, which is to one degree or another leveled by reflex tachycardia, which occurs in response to the hypotensive effect of the drugs. The anti-anginal effect of calcium channel blockers is also provided by a pronounced expansion of coronary vessels (as a result of a decrease in the flow of calcium ions into the smooth muscles of the vessels), which increases the delivery of oxygen to the heart. Calcium channel blockers improve subendocardial blood flow and possibly increase collateral circulation. Nifedipine (phenigidine, adalat, corinfar) causes pronounced expansion of coronary vessels, lowers blood pressure. It has a small negative inotropic effect on the heart, but it is compensated by reflex tachycardia and therefore does not manifest itself. As a result, for nifedipine, the basis of the anti-anginal effect is the expansion of coronary vessels. In addition, it is important to reduce the load on the heart, which reduces its need for oxygen. The main use of the drug is the treatment of angina pectoris, as well as arterial hypertension. The antiarrhythmic activity of nifedipine is weak and of no practical interest. The drug is well absorbed from the gastrointestinal tract. The effect develops after 15-20 minutes, reaches a maximum after 1-2 hours and lasts 6-8 hours. Approximately 90% of the drug binds to plasma proteins. Excreted from the body by the kidneys. It is used internally

and sublingually. Side effects: headache, reflex tachycardia, edema, sometimes skin rashes, fever.

Drugs that block calcium channels (calcium antagonists).

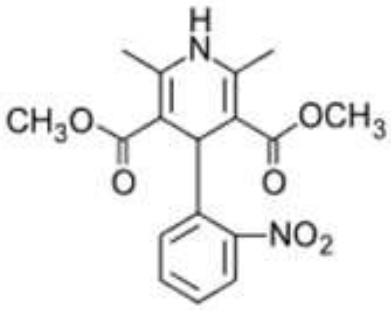
L-type calcium channel blockers used for angina include verapamil, diltiazem, nifedipine (Phenihidin), amlodipine (normodipine), and other drugs. The main principle of their action is that they disrupt the penetration of calcium ions from the extracellular space into the muscle cells of the heart and blood vessels through potential-dependent slow calcium channels (L-channels). The effectiveness of such drugs (for example, verapamil) in angina is explained by the fact that they reduce the work of the heart and expand the coronary vessels, that is, they reduce the heart's need for oxygen and simultaneously increase its delivery. Less influx of calcium ions into the cells of the myocardium leads to a decrease in the use of the energy of phosphate bonds for the mechanical work of the heart. At the same time, the force of heart contractions and the work of the heart decrease. Accordingly, the heart's need for oxygen decreases.

Verapamil



alpha-[3-[[2-(3,4-Dimethoxyphenyl)ethyl]methylamino]propyl]-3,4-dimethoxy-alpha-(1-methylethyl)benzeneacetonitrile (as hydrochloride)

Phenihidin



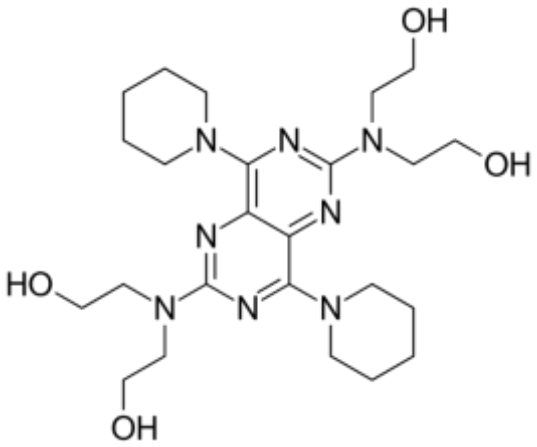
1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridinedicarboxylic acid dimethyl ether

Drugs that increase the delivery of oxygen to the myocardium

This group includes drugs that expand coronary vessels or eliminate coronary spasms. The mechanisms of their action are different. They may be associated with direct effects on vascular smooth muscles or mediated through humoral or neurogenic effects.

a) Coronary dilators of myotropic effect

This group of drugs includes dipyridamole.



Dipyridamole (Curantyl) is a pyrimidine derivative. Its main action consists in reducing the resistance of blood vessels, increasing the volumetric velocity of coronary blood flow and increasing oxygen delivery. The specified changes mainly refer to small resistive vessels of the myocardium. The mechanism of the beneficial effect of dipyridamole on the blood supply of the heart is associated with inhibition of reuptake of adenosine (myocardium, erythrocytes) and inhibition of the enzyme adenosine desamidase. As a result, increased concentrations of adenosine accumulate in the myocardium, which is known to have a pronounced coronary dilating effect and is released during myocardial hypoxia. Dipyridamole has little effect on systemic hemodynamics.

It should be noted that dipyridamole has an inhibitory effect on platelet aggregation, which has a positive effect on microcirculation in the myocardium. The drug is used in angina pectoris without atherosclerosis of the coronary vessels. When a coronary branch is occluded by an atheromatous plaque, dipyridamole not only does not improve the delivery of oxygen to the ischemic zone, but may even worsen its blood

supply. This is explained by the fact that in ischemic myocardium, small coronary vessels are maximally expanded (compensatory reaction to hypoxia). If dipyridamole is introduced, the expansion of arterioles and collaterals in the intact part of the myocardium will occur and this will further reduce the supply of blood and oxygen to the ischemic area (the so-called "robbing syndrome" occurs). Given this feature of dipyridamole's action, it is sometimes used to detect hidden coronary insufficiency.

In general, dipyridamole has low antianginal activity. They take it inside. Side effects include dyspepsia, headache, and hypotension.

Drugs used in case of impaired cerebral blood circulation

Acute and chronic disorders of blood supply to the brain are one of the main causes of mortality and disability of the population.

In cerebrovascular pathology, the main place is occupied by ischemic lesions of the brain, including ischemic stroke. Given that, compared to other tissues, the brain is the most sensitive to ischemia, when it occurs, it is necessary to take emergency measures to eliminate or reduce brain blood supply disorders.

Pathology of cerebral circulation can be associated with functional and organic disorders (vasal spasm, embolism, thrombosis, atherosclerosis of vessels, hemorrhages). In most cases, the cause of ischemic strokes is atherosclerotic vascular damage, especially stenosis of the carotid and vertebral arteries. In such conditions, antiplatelet agents (aspirin, ticlopidine, clopidogrel) are recommended as means of preventing a possible stroke.

Subarachnoid and intracerebral hemorrhages are a frequent form of acute disturbance of cerebral circulation. The causes of hemorrhagic strokes include arterial hypertension, the presence of aneurysms, especially microaneurysms, as well as angiomas. It should be taken into account that vasoconstrictor reactions are also pronounced in hemorrhagic stroke. One of the ways to treat such patients is surgical removal of the hematoma (if it is indicated and possible).

Frequent causes of ischemic stroke are emboli and thrombi, which block individual branches of cerebral vessels. Anticoagulants of direct and indirect action (heparin, LMWH preparations, warfarin, syncoumar, phenylin) are usually used to prevent such conditions and their recurrence.

A transient disturbance of cerebral circulation (transient ischemic attacks) may be associated with spasm of cerebral vessels. And in this case, it is advisable to use antiplatelets and anticoagulants as a preventive measure. However, both groups of drugs are contraindicated in case of hemorrhage or the possibility of their occurrence. In addition, it is advisable to use drugs that reduce the tone of cerebral vessels.

With persistent and pronounced ischemia, necrosis of brain tissue develops. In addition to acute brain damage associated with its ischemia, chronic insufficiency of cerebral blood circulation is often noted. At the same time, memory, intellectual and mental spheres, behavioral and motor reactions are suffering. These adverse manifestations increase gradually and are usually associated with age and accompanying pathological processes (atherosclerosis of blood vessels, arterial hypertension, metabolic disorders, etc.).

One of the main principles of prevention and therapy of cerebral circulation insufficiency is expansion of brain vessels. To obtain such an effect, vasodilators are often used, which reduce the tone of peripheral vessels. But such drugs usually cause general hypotension, which reduces the blood supply to the brain, and the final result can be unfavorable. Therefore, substances are needed that mainly expand cerebral vessels without significantly affecting systemic hemodynamics. However, the creation of such drugs is a rather difficult task. Of the known drugs, only nimodipine, vinpocetine (cavinton) and picamilon have a pronounced tropism for cerebral vessels. Another principle of treatment of vascular pathology of the brain is to increase the resistance of nerve cells to ischemia (hypoxia), that is, we are talking about drugs with a neuroprotective effect.

Means that improve blood circulation in the brain during its ischemia can be represented by the following groups:

I. Agents affecting blood aggregation and coagulation:

• Antiplatelet agents: Acetylsalicylic acid, Ticlopidine, Clopidogrel;

• Anticoagulants: Heparin, low molecular weight heparins, Warfarin, Sinkumar, Phenilin.

II. Agents that increase cerebral blood flow:

• L-type calcium channel blockers: Nimodipine, Cinnarizine, Flunarizine;

1 The advisability of using fibrinolytics in ischemic strokes is questionable because of the high risk of bleeding.

Derivatives of periwinkle plant alkaloids: Vinpocetine (cavinton);

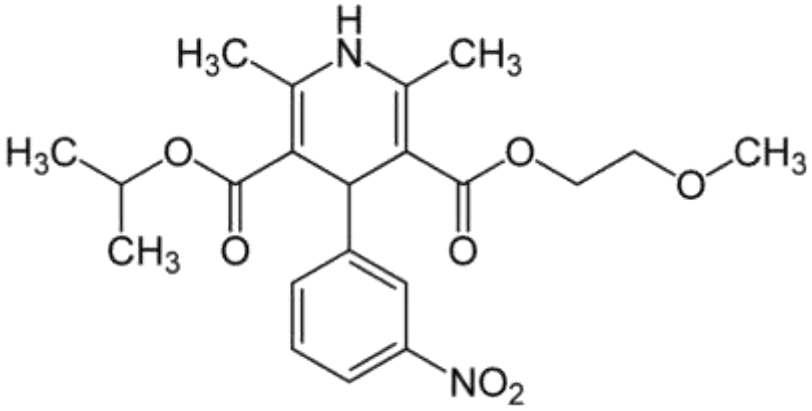
• Derivatives of ergot alkaloids: Nicergoline;

• Derivatives of nicotinic acid: Xanthine nicotinate, GABA and its derivatives: Aminalon, Picamilon.

• Derivatives of purine alkaloids: Pentoxifylline;

• Opium alkaloid of the isoquinoline series: Papaverine hydrochloride;

Blockers of L-type calcium channels with a predominant effect on cerebral circulation include nimodipine.

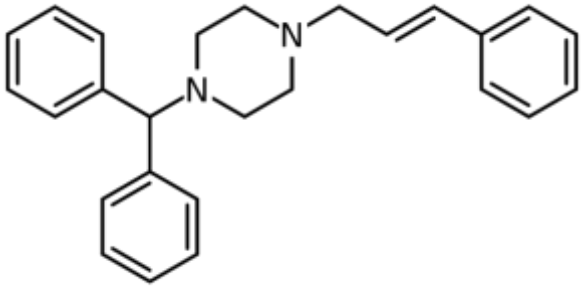


3-(2-Methoxymethyl)5-propan-2-yl-2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate

It is a derivative of 1,4-dihydropyridine. Reduces the tone of brain arterioles. Increases oxygenation of brain tissues. It is used after acute brain ischemia, subarachnoid hemorrhage, chronic brain ischemia. Improves brain activity in the elderly. Among the adverse effects, it can cause headache, dyspeptic disorders, with intravenous administration - hypotension. Some other calcium channel blockers of the

diphenylpiperazine group - cinnarizine (stugeron), flunarizine (sibelium) - have a positive effect on cerebral blood circulation.

Cinnarizine

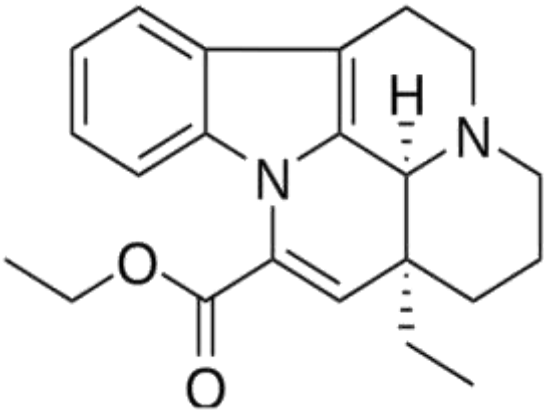


1-(diphenylmethyl)-4-(3-phenyl-2-propenyl)piperazine

They have a minor effect on systemic hemodynamics. They are used for spasms of cerebral vessels, atherosclerosis, vestibular disorders, after a stroke, craniocerebral injuries.

These drugs are well tolerated. Possible drowsiness, sedative effect, dry mouth, dyspeptic disorders. In addition, they enhance the effect of ethyl alcohol.

Vinpocetine (cavinton), a derivative of periwinkle plant alkaloids (Vinca minor L., etc.), is widely used for brain ischemia.



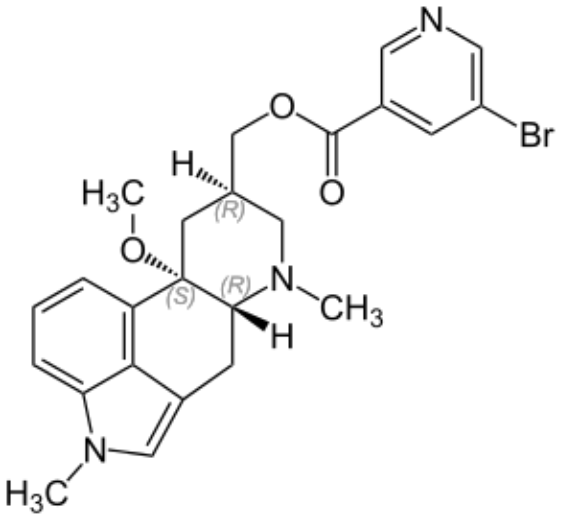
(3α,16α)- Eburnamenine-14-carboxylic acid ethyl ether

It is a semi-synthetic derivative of the devincan alkaloid. Has an antispasmodic effect. Mainly expands brain vessels. The mechanism of the beneficial effect of vinpocetin on cerebral blood circulation has not been finally clarified. A number of authors believe that this is a direct myotropic effect. There is also evidence that the drug

blocks neuronal sodium channels, and this may be important for its anti-ischemic activity. In addition, vinpocetine normalizes metabolism in brain tissues. Reduces platelet aggregation. Reduces pathologically increased blood viscosity. As a result, microcirculation improves.

The drug is well absorbed from the digestive tract. Bioavailability is approximately 57%; ~ 5 h. It is used for disorders of nervous activity after a stroke, for chronic insufficiency of cerebral blood circulation, for ischemia of eye tissues, hearing loss of vascular or toxic origin, memory impairment, dizziness. The drug is well tolerated. With intravenous administration, it can cause hypotension, tachycardia.

Nicergoline (sermion) combines the structures of ergot alkaloids and nicotinic acid.



(8beta)-10-Methoxy-1,6-dimethylergoline-8-methanol 5-bromo-3-pyridine carboxylate (ether)

It has α-adrenoblocking and antispasmodic activity. Expands cerebral and peripheral vessels. It is used for disorders of cerebral blood circulation, for migraine, disorders of peripheral hemodynamics, for ischemia of the optic nerve. Possible side effects: hypotension, dizziness, redness of the skin, itching, dyspeptic disorders.

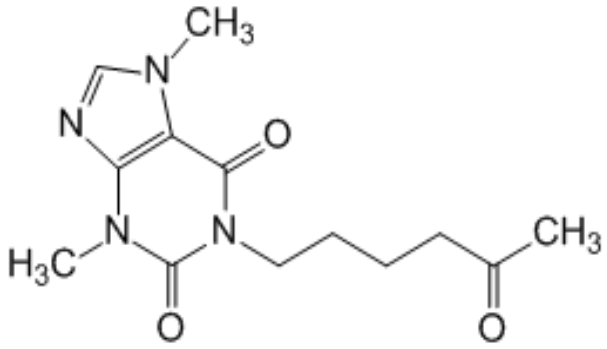
Derivatives of nicotinic acid are also used for cerebral ischemia. The latter is characterized by a pronounced myotropic vasodilator effect on all peripheral vessels and vessels of the brain. However, nicotinic acid causes many adverse effects, therefore, to

eliminate spasm of peripheral and cerebral vessels, it is preferred to use its derivatives, which are safer in terms of side effects.

One of them is xanthinol nicotinate (complamin), the structure of which combines the elements of nicotinic acid and theophylline. It improves peripheral and cerebral blood circulation. Combined drugs containing nicotinic acid and other antispasmodics are also used, for example Nikoverin (nicotinic acid + papaverine), nicospan (nicotinic acid + no-shpa).

Some drugs that belong to the group of GABA and its derivatives (aminalon, picamilon) have a beneficial effect on cerebral blood circulation. Aminalon is GABA, while picamilon combines the structures of GABA and nicotinic acid. Both drugs have a normalizing effect on cerebral blood circulation and metabolic processes occurring in brain tissue. Picamilon clearly expands the blood vessels of the brain.

It has long been noted that purine derivatives (caffeine, theobromine) increase cerebral blood flow. Currently, pentoxifylline (agapurine, trental) is used for disorders of cerebral circulation from this group of substances.



3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)-1H-purine-2,6-dione

It has a moderate vasodilating effect, reduces platelet aggregation, increases the elasticity of the erythrocyte membrane, and improves microcirculation. Vasodilator effect, apparently, is associated with the block of adenosine receptors. In addition, the drug inhibits phosphodiesterase and increases cAMP content in platelets. Pentoxifylline is also used for disorders of peripheral blood circulation, for diabetic angiopathy, and impaired blood supply to the eyes.

Side effects include dyspepsia, dizziness, facial hyperemia. The second direction in the pharmacotherapy of brain ischemia is related to the creation of neuroprotective drugs that increase the resistance of neurons to hypoxia.

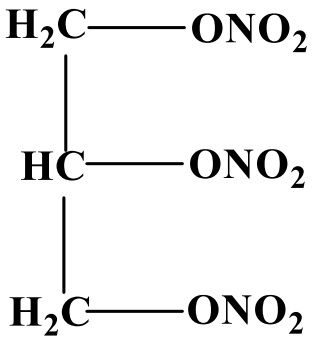
Damage to neurons during brain ischemia is due to many reasons: metabolic disorders, development of acidosis, changes in the release of mediators (glutamate, etc.), rapid entry of excess amounts of calcium ions into cells, release of free radicals, proteolysis, etc. Therefore, the principles of action of neuroprotective agents can be very different.

Substances that suppress metabolism and increase the resistance of brain tissue to hypoxia include barbiturates. Sodium oxybutyrate also has antihypoxic activity. Attention is also drawn to substances that block the effects of excitatory amino acids, for example, NMDA receptor antagonists - dizocilpine (MK 801) and others.

In general, progress in the field of pharmacotherapy of cerebral blood circulation disorders is relatively modest. However, the importance of the problem forces an intensive search for new effective drugs.

We will consider the analysis of drugs that improve the blood supply of organs and tissues using the example of nitroglycerin:

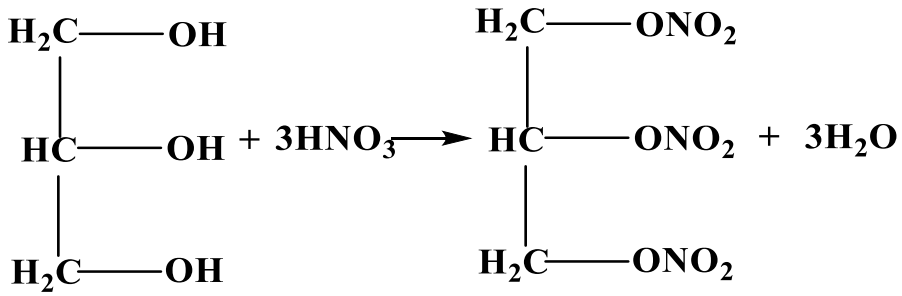
NITROGLYCERIN SOLUTION - SOLUTIO NITROGLYCERINI



Glycerin trinitrate M.m. 227,1

Description: clear, colorless or light yellow liquid. Miscible with acetone and ethanol.

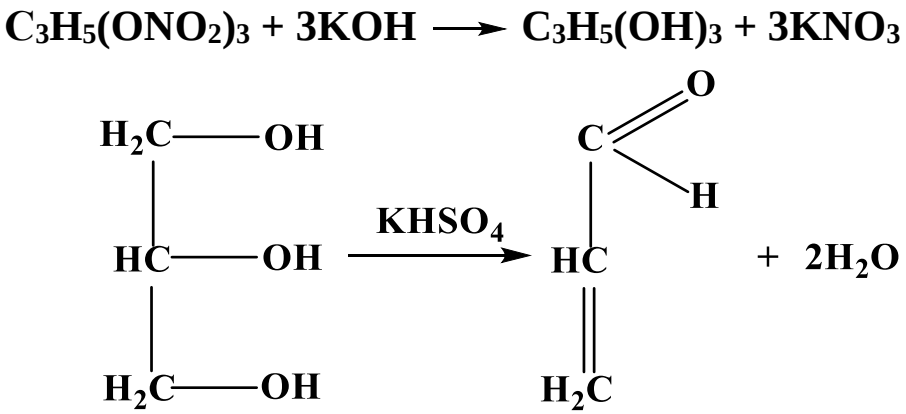
Extraction: Synthesized at a temperature of -150C, passing anhydrous glycerin in a thin stream through a mixture of concentrated sulfuric and nitric acids:



Identification:

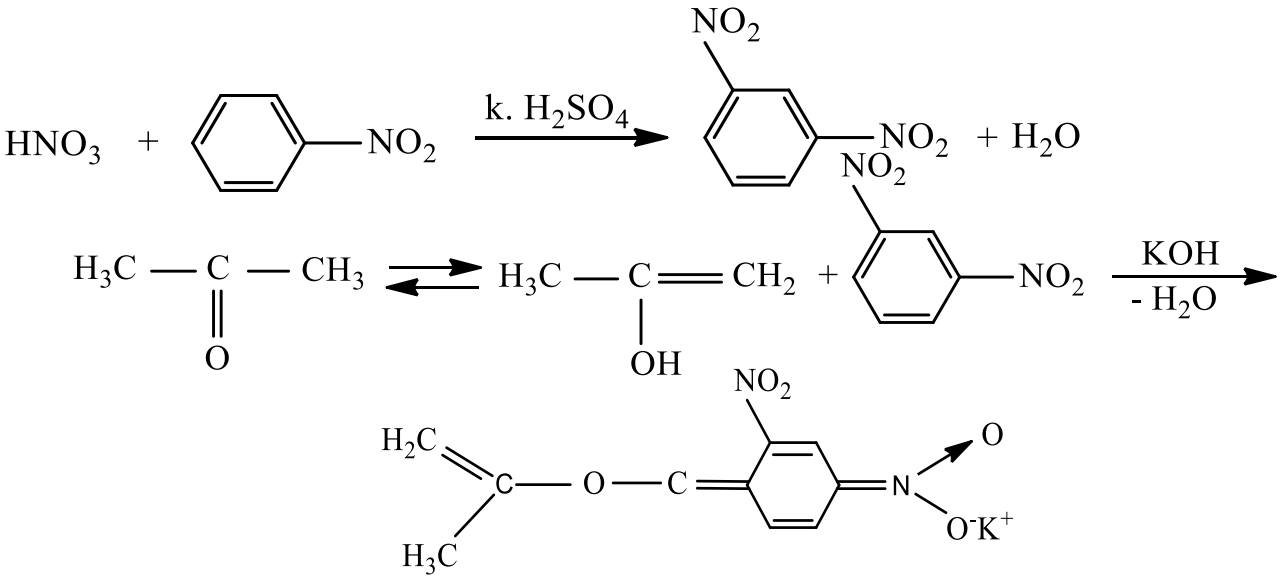
1. According to physical constants: IR spectroscopy, thin-layer chromatography.

2. The substance is saponified by the action of sodium hydroxide solution. Glycerin is formed, then heated with potassium hydrosulfate, acrolein with a characteristic smell is released:

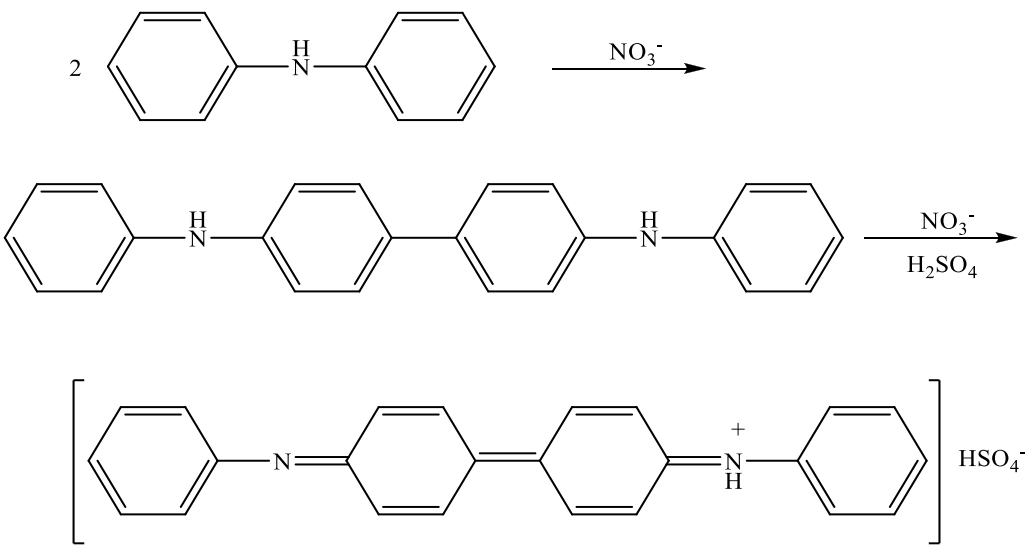


3. After saponification, reaction to nitrates:

After heating with nitrobenzene and concentrated sulfuric acid, a concentrated solution of sodium hydroxide and acetone are added, a purple color appears [7].



4. After hydrolysis, a reaction with diphenylamine is carried out in a strongly acidic environment, an intense blue color appears [7]:



Quantitative definition: method – alkalimetry, titration method – reverse, indicator – phenolphthalein.

An excess of 0.5 M alcoholic solution of potassium hydroxide in the presence of hydrogen peroxide is added to the substance and titrated with a 0.5 M solution of hydrochloric acid:

$$C_3H_5(ONO_2)_3 + 5KOH \xrightarrow{H_2O_2} KNO_3 + 2KNO_2 + CH_3COOK + HCOOK + 3H_2O$$

$$KOH + HCl \rightarrow KCl + H_2O$$

Storage: in a dry place protected from light, away from fire.

TEST TASKS ON THE TOPIC «DRUGS THAT IMPROVE THE BLOOD SUPPLY TO ORGANS AND TISSUES»

1. To what class of compounds according to the chemical structure does the drug nitroglycerin belong?

A) Complex esters

B) Simple ethers

C) Polyhydric alcohols

D) Nitroalkanes

E) Nitroarenes

2. What reaction is carried out to identify nitroglycerin (glycerol trinitrate solution)?

A) Azo dye formation reaction

B) Alkaline hydrolysis reaction

C) Reaction with diphenylamine in the presence of concentrated sulfuric acid

D) Reaction with Nessler's reagent

E) Reaction with potassium permanganate

3. When identifying nitroglycerin, the presence of a glycerol residue in its structure can be confirmed by:

A) Acrolein formation reaction

B) Reaction with iron (III) chloride

C) Reaction of formation of indophenol

D) "silver mirror" reaction

E) Reaction of formation of thiochrome

4. Which of the following drugs does not belong to the group of organic nitrates:

A) Nitroglycerin

B) Metoprolol

C) Isosorbide mononitrate

D) Sustak

E) Trinitrolong

5. Specify an antianginal drug of prolonged action:

A) Phenigidine

B) Sustak

C) Nitroglycerin

D) Nitrosorbide

E) Isosorbide mononitrate

6. The pharmacist identifies sodium nitrite by reacting with a antipyrine in hydrochloric acid. This interaction can be considered positive if:

A) Green colored solution

B) Brown-black sediment

C) Brown vapors of nitrogen oxides

D) Yellow color of the solution

E) Cherry-red color of the solution

7. The reagent for the identification of sodium nitrite, according to the requirements of the SPhU, is:

A) Aniline

B) Resorcinol

C) Phenol

D) Antipyrine

E) β - naphthol

8. Specify a drug that has a vasodilating effect:

A) Sodium nitrite

B) Sodium thiosulfate

C) Magnesium peroxide

D) Hydroperite

E) Perhydrol

9. Suggest reagents for detecting nitrite ions contained in the analyzed pharmaceutical preparation:

A) Iron (III) sulfate (conc.) and potassium bromide

B) Iron (II) sulfate (dissolved) and potassium iodide

C) Antipyrine and hydrochloric acid

D) Iron (II) chloride

E) Iron (III) chloride

10. Indicate which of the reagents is used to confirm the presence of sodium ion in the drug substance:

A) Potassium pyroantimonate (potassium hexahydroxystibiate)

B) Cobalt chloride

C) Copper sulfate

D) Silver nitrate

E) Potassium permanganate

11. Quantitative determination of sodium nitrite, in accordance with the requirements of the SPhU, is carried out by the following method:

A) Argentometry

B) Permanganatometry (reverse method)

C) Iodometry

D) Complexonometry

E) Permanganatometry (direct method)

12. When identifying sodium nitrite [Natrii nitris], a reaction to the nitrite ion is carried out, which is accompanied by the appearance of a blue color. What reagent was used in this test?

A) Diphenylamine

B) Pyridine

C) Sulfuric acid

D) Barium chloride

E) Antipyrine

13. The antispasmodic drug "Erinit" is:

A) Nitroglycerin

B) Pentaerythritol tetranitrate

C) Nitrosorbide

D) Sodium nitrite

E) Potassium nitrate

14. A specialist of the State Inspectorate for Quality Control of Medicines carries out the identification of sodium nitrite by reaction with a antipyrine in an environment of hydrochloric acid. This interaction can be considered positive if:

A) Green colored solution

B) Brown-black sediment

C) Brown vapors of nitrogen oxides

D) Yellow color of the solution

E) Cherry-red color of the solution

4. SULFANILAMIDES. CHARACTERISTICS, CLASSIFICATION, RELATIONSHIP BETWEEN STRUCTURE AND PHARMACOLOGICAL ACTIVITY

Sulfanilamides — Sulfanilamides are antimicrobial drugs, derivatives of sulfanilic acid amide (para-aminobenzosulfonic acids). Sulfanilic acid is a starting material for the production of a large number of drugs, which are combined by chemical structure and pharmacological action into one large group of sulfonamide preparations.

The appearance of sulfonamide drugs dates back to the 1930s. The history of the discovery is connected with the textile industry. In search of better dyes for fabrics, Helmo synthesized p-aminobenzenesulfamide in 1908, which was later named white streptocid. In 1909, chrysoidine dye was obtained. In 1932, a German scientist synthesized the azo dye sulfamidochrysoidine and found that it completely cured white mice infected with a lethal dose of hemolytic streptococcus. This substance was called *prontosil (or red streptocide*), it had high therapeutic activity in streptococcal infections.

Prontosil was the first synthetic antibacterial drug.

In 1934, Domagk first published his research related to prontosil, and in 1939 he was awarded the Nobel Prize in Physiology or Medicine "for the discovery of the antibacterial effect of prontosil."

In 1935, it was established that it is the sulfanilamide part of the prontosil molecule that has the antibacterial effect, and not the structure that gives it color. The active principle of red streptocide is sulfonamide, which was formed during the metabolism of red streptocide. Thus, a large number of derivatives were synthesized on the basis of the streptocide molecule, which are widely used in medicine.

Sulfanilamides were the first synthetic chemotherapeutic compounds that were widely used in practical medicine, but the importance of drugs of this group has not been lost even today. And in some cases, they are successfully prescribed for various infectious diseases.

Relationship between structure and pharmacological action. In order for the compound to have activity, the presence of a sulfonyl radical is necessary:

This part of the sulfonamide molecule is the basis for obtaining a physiological effect.

If the amino group in position 4 or its hydrogen atoms are replaced by such radicals, when a free aromatic amino group cannot be formed again in the body, such a compound is physiologically inactive.

The movement of the amino group from position 4 to position 2 or 3 of the benzene nucleus leads to a complete loss of activity.

The introduction of additional radicals into the benzene nucleus leads to destruction or a significant decrease in activity.

When replacing hydrogen in the sulfamide group with various radicals, depending on the radical, it leads to a decrease or an increase in physiological activity.

Mechanism of action. All modern sulfonamides are similar in spectrum and mechanism of antimicrobial action. Streptococci, staphylococci, pneumococci, gonococci, meningococci, intestinal, dysentery, diphtheria bacilli, as well as cholera vibrios, etc., are sensitive to them.

Sulfonamides have a bacteriostatic effect. Their action is based on the theory of competitive antagonism. This mechanism is mainly related to the violation of the formation of growth factors necessary for the development of microorganisms - folic and dihydrofolic acids and other substances, in the synthesis of which PABA participates. Folic and folinic acids are necessary for microorganisms to synthesize nucleic acids, which are the main factor that ensures the growth and reproduction of microorganismsBy structure, sulfonamide drugs are very similar to PABA, they are used by the microbial cell instead of PABA. Replacing PABA in the process of folic acid synthesis, sulfonamides disrupt the formation of this acid and prevent the formation of nucleic acids, which is accompanied by the retention of the development and reproduction of microorganisms.

Mechanism of action of sulfonamide drugs

Folic acid is also necessary for the development of cells in the human body. However, unlike microorganisms, human cells do not synthesize folic acid themselves, but absorb it from the blood, into which this acid is absorbed from the small intestine. This explains the fact that human cells are practically insensitive to the action of sulfonamides.

The peculiarity of the mechanism of action of sulfonamides is also explained by the fact that in environments with a high content of PABA (blood, manure), the antibacterial activity of sulfonamides is significantly reduced. A similar phenomenon is observed in the case of the use of sulfonamides together with drug substances, the breakdown of which produces PABA (for example, procaine hydrochloride, etc.)

The effect of sulfonamides is also weakened when combined with folic acid or with other substances that participate in its synthesis (for example, with methionine).

Sulfonamides have the same spectrum and mechanism of action, but differ in their ability to be absorbed from the gastrointestinal tract.

According to this feature, sulfonamides can be divided into two groups:

1. Drugs that are well absorbed from the gastrointestinal tract (streptocide, sulfadimezin, etazol, sodium sulfacyl, sulfazine, urosulfan, etc.);

2. Drugs that are poorly absorbed from the gastrointestinal tract (phthalazol, sulgin, phtazin).

Sulfonamide drugs, which are well absorbed from the gastrointestinal tract, are inactivated and excreted from the body at different rates, which depends on the different duration of their action:

The highest concentration in the blood is created by drugs of short and medium duration of action. Metabolized in the liver. Excreted with urine and bile.

Short (<10 h.)	**Average (10 – 24 h.)**	**Long-lasting (24-48 h.)**	**Over-long (> 48 h)**
Sulfanilamide	Sulfazine	Sulfadimethoxine	Sulfalen
Sulfadimezin	Sulfamethoxazole	Sulfapyridazine	Sulfamethoxypyridazine
Urosulfan			
Etazol			
Sodium sulfacetamide			

On the first day of treatment, sulfonamides are prescribed in high (shock) doses, and then proceed to treatment with maintenance doses. The number of doses and the frequency of administration are set depending on the duration of the drug's action.

Sulfanilamides, which are poorly absorbed from the gastrointestinal tract (phthalazole, phtazine, sulgin), do not accumulate in the blood and tissues in bacteriostatic concentrations. After ingestion, they are found in the largest concentrations in the intestines. Therefore, they are used for the treatment of gastrointestinal infections.

Sulfonamide drugs differ from antibiotics in the mechanism of antimicrobial action and can be effective in the treatment of infections caused by antibiotic-resistant microflora.

Drugs containing sulfonamides in combination with trimethoprim (for example, biseptol) are of great importance. Trimethoprim prevents the formation of folinic acid from folic acid. In addition, the simultaneous use of sulfonamides with trimethoprim slows down the development of resistance of microorganisms to sulfonamides.

Trimethoprim inhibits dihydrofolic acid reductase, blocks its transition to active tetrahydrofolic acid. Therefore, with the introduction of combined sulfonamide drugs, not only the synthesis of folic acid is inhibited, but also its transformation into an active coenzyme (tetrahydrofolate). The drugs have bactericidal activity against gram-positive and gram-negative bacteria.

The main route of introduction of sulfonamides is through the mouth. In the small intestine, they are quickly and completely absorbed (except for drugs - phthalazole, phtazine, salazo-sulfanilamides, which are prescribed for intestinal infections), in the blood, they bind to plasma proteins, and then, gradually being released from, begin to show an antimicrobial effect, only the free fraction has antimicrobial activity. Almost all sulfonamides pass well through tissue barriers, including hepatohematous, hematoencephalitic, and placental. They are biotransformed in the liver, part of them is excreted in bile (especially long-acting ones), and therefore they are successfully used for infections of the biliary tract.

The main way of biotransformation of sulfonamides is acetylation. Acetylated metabolites lose their antibacterial activity, dissolve poorly, and in the acidic environment of urine, they can form crystals that damage or block the renal channels. For urinary tract infections, sulfonamides are prescribed, which are not acetylated and are excreted in the urine in free form (urosulfan, etazol).

Another way of biotransformation is glucuronidation. Most long-acting (or ultra-long-acting) drugs (sulfadimethoxine, sulfalen) lose their activity when binding to glucuronic acid. The glucuronides formed are well soluble (there is no danger of crystalluria).

Despite the pronounced selectivity of action, sulfonamide drugs cause numerous complications: allergic reactions, damage to parenchymal organs (kidneys, liver), nervous system, blood and hemopoietic organs. Frequent complications are crystalluria as a result of crystallization of sulfonamides and their acetylated metabolites in the kidneys, ureters, and bladder. Falling into the sediment, they form sand and stones, irritating the kidney tissue, blocking the urinary tract and leading to renal colic. For prevention, plenty of drinking is prescribed, the acidity of urine is reduced (citrates or sodium bicarbonate are prescribed to alkalinize urine). An alkaline environment promotes the transition of sulfonamides to the ionic state, which facilitates the capture and assimilation of drugs by the microbial cell. Very effective use of combinations consisting of 2-3 sulfonamides (probability of crystalluria decreases by 2-3 times).

Comparative characteristics of drugs

Sulfanilamide (streptocide) - is a standard sulfonamide drug, most sulfonamide drugs are derived from its molecule. Active against pneumococci, streptococci, staphylococci, gonococci, etc. It is quickly and completely absorbed from the gastrointestinal tract. C_{max} in the blood is created after 1-2 hours, is evenly distributed throughout the tissues. It is acetylated in the liver with the loss of antibacterial properties. It is mainly excreted by the kidneys (90-95%).

Sulfathiazole (norsulfazole) is easily absorbed from the gastrointestinal tract and is excreted from the body with urine, mainly in non-acetylated form.

Sulfadimezin (sulfadimidine) is quickly absorbed, highly effective and low-toxic. 75-86% binds to plasma proteins. Easily penetrates into tissues, quickly excreted from the body. Biotransformed in the liver (acetylation), acetylated metabolites can be precipitated in acidic urine. The solubility of metabolites improves with urine alkalinization.

Sulfaetidol (ethazol) is little acetylated. Does not change the blood pattern. It is used internally and externally. Ethazol-sodium is an easily soluble drug that can be used parenterally.

Urosulfan (sulfacarbamide) is highly effective against staphylococci and Escherichia coli. Low toxicity, does not acetylate, does not cause crystalluria. Accumulates in urine in high concentration, prescribed for urinary tract infections.

Sulfazine (sulfadiazine) binds less to plasma proteins, is eliminated from the body more slowly than norsulfazole, and ensures a sufficient concentration in tissues and blood. It is often prescribed together with antimalarial drugs.

Silver sulfadiazine is a silver salt of sulfazine. Drug for local use. When using it, as a result of dissociation, silver ions are slowly formed, which have an antimicrobial effect that does not depend on the content of PABA. The concentration of silver ions is toxic to microorganisms but does not destroy human tissues.

Sulfalen has an "ultra-long effect", the half-life from the blood is 65 hours. 60% of the administered dose is excreted within 9 days. It is found in bile in a high

concentration, to a lesser extent than other sulfonamides, binds to proteins, which ensures a high concentration in the blood in a free active form. It circulates in the blood for a long time. Effective for the treatment of chronic diseases of the respiratory organs, urinary and biliary tracts, osteomyelitis, mastitis.

Phthalylsulfathiazole (phthalazole) is slowly absorbed, shows high efficiency in intestinal infections. It is low-toxic, has antibacterial activity after the formation of an amino group, which occurs in the intestines. Under the action of aminopeptidase, sulfathiazole (norsulfazole) is gradually formed, which does not have time to be adsorbed and provides a high antimicrobial effect. It is excreted mainly in feces, and only 5-10% is evenly distributed in the body, acetylated in the liver and excreted in the urine.

Sulgin (sulfaguanidine) is also an effective remedy for intestinal diseases. It is absorbed very slowly and the main amount remains in the intestines.

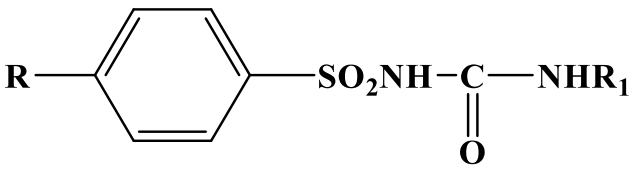
Sulfadimethoxine belongs to long-acting sulfonamides, it is relatively slowly absorbed, it is detected in the blood after 30 minutes, Cmax is reached after 8-12 hours. Compared to other long-acting sulfonamides, it passes through the blood-brain barrier worse.

Phtazine is better absorbed from the intestines than phthalylsulfathiazole and is more effective in the treatment of intestinal infections. Sulfapyridazine is cleaved from the phtazine molecule very slowly and remains in the intestine for a long time.

Salazopyridazine in the body decomposes into sulfapyridazine and 5-aminosalicylic acid, has antibacterial and anti-inflammatory effects.

Analysis of drugs of this group

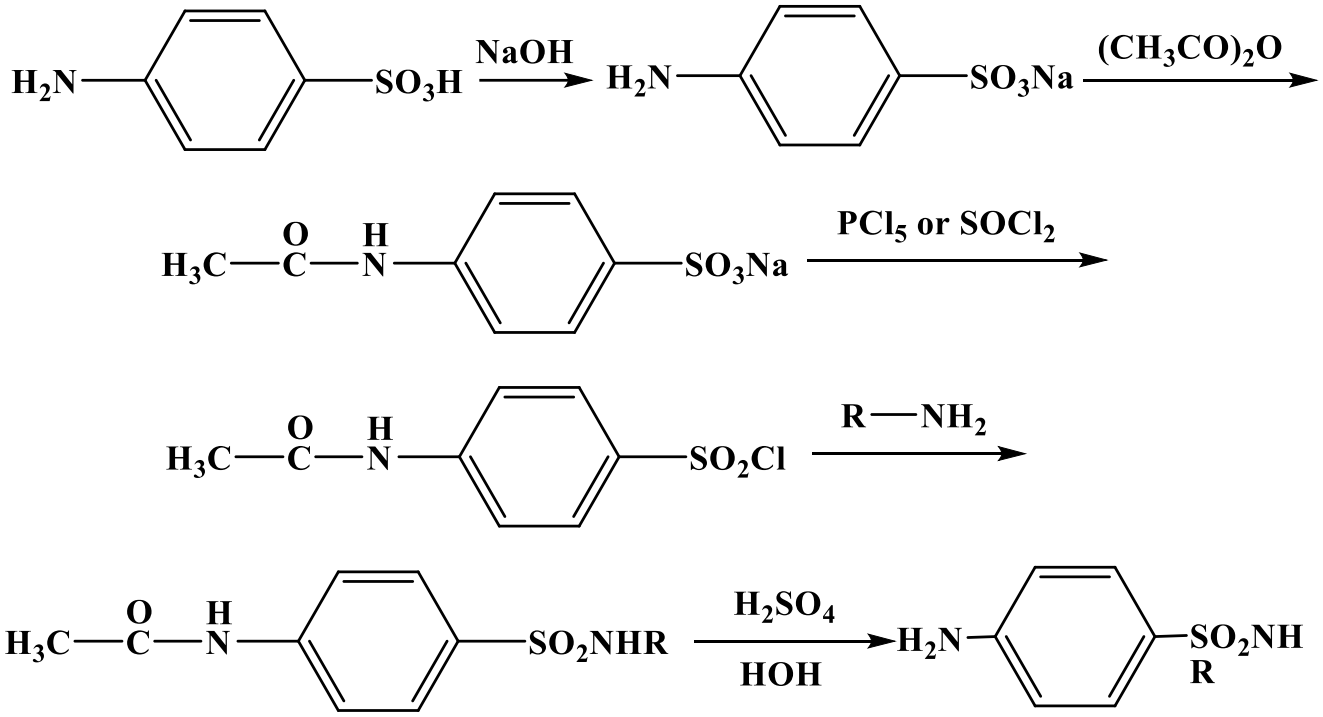
Drug products, derivatives of alkylureides of sulfonic acids:



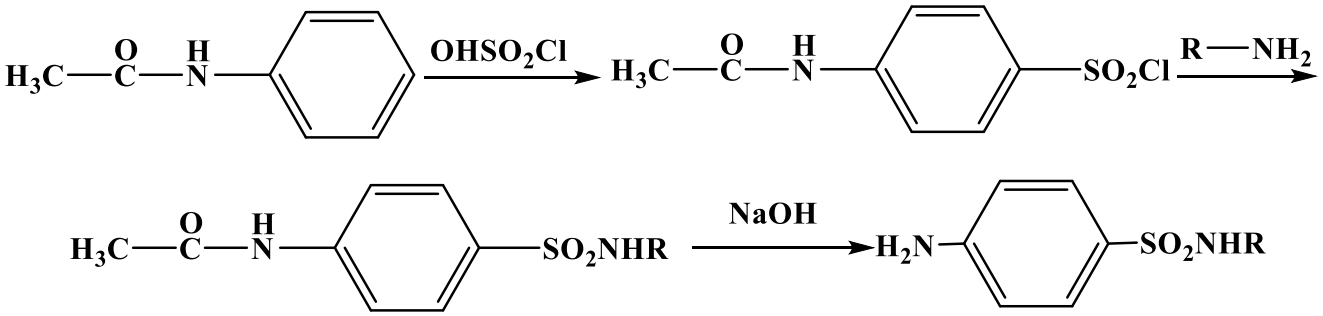
R = -CH_3, - Cl, - NH_2
R_1= -C_4H_9, -C_3H_7

Extraction:

1. The starting substance is sulfanilic acid:



2. The most rational and economical is the synthesis from N-carbomethoxyaniline:

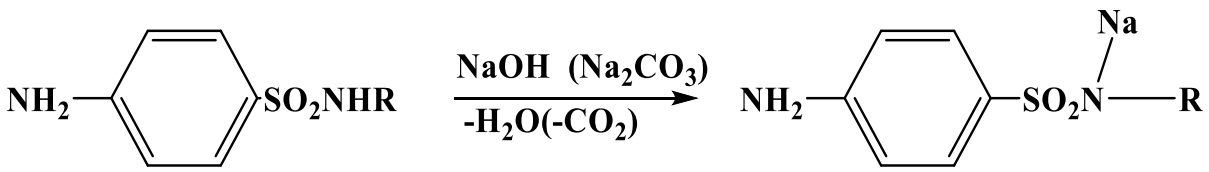


Chemical properties and identification:

1. Most sulfonamide substances are amphoteric compounds. The main properties are due to the presence of an aromatic amino group. As bases, they dissolve in acids, forming salts:

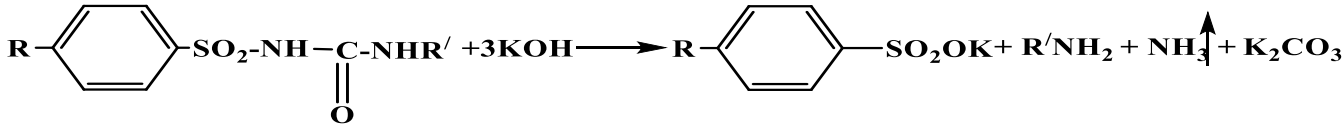
However, salts in water are highly hydrolyzed and practically do not exist.

Acidic properties are due to the presence of mobile hydrogen in the sulfamide group, which can be substituted for metals with the formation of salts. Drug products are easily dissolved in alkalis and carbonates of alkali metals:

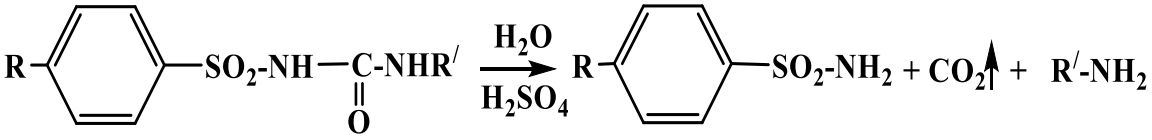


Common identification reactions:

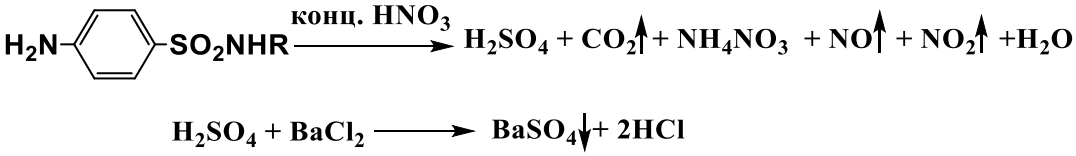
• When the preparations are heated in a 30% solution of potassium hydroxide, hydrolysis occurs with the formation of ammonia, which can be detected by the smell or by the blue color of red litmus paper. The smell of fatty amine appears (fat stains):



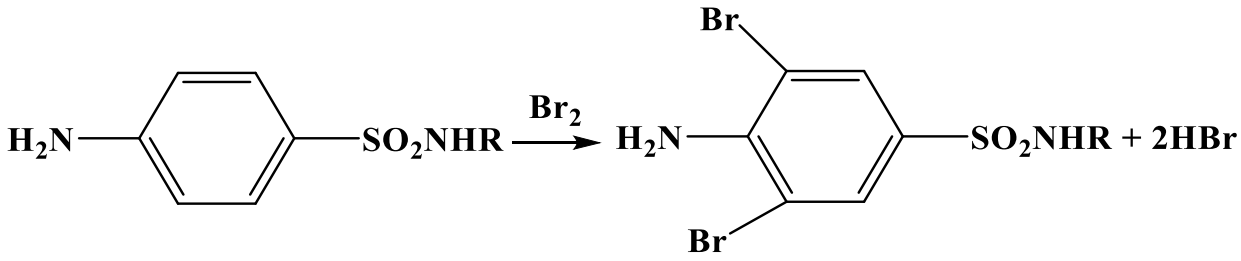
• With long-term heating of the preparations in the presence of 50% sulfuric acid (with a reverse cooler) and subsequent neutralization, a precipitate of the corresponding sulfamide is formed, which is filtered and the melting point is determined.



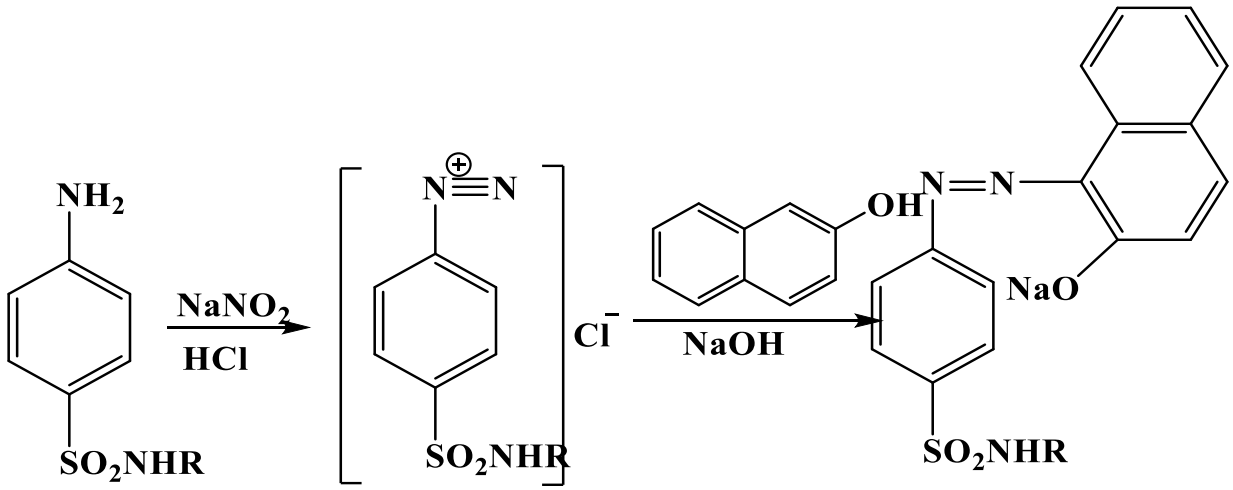
• All sulfonamides have a sulfur atom in the sulfamide group. To detect it, the drug is oxidized with concentrated nitric acid or fused with a 10-fold amount of potassium nitrate. At the same time, sulfur turns into sulfate.



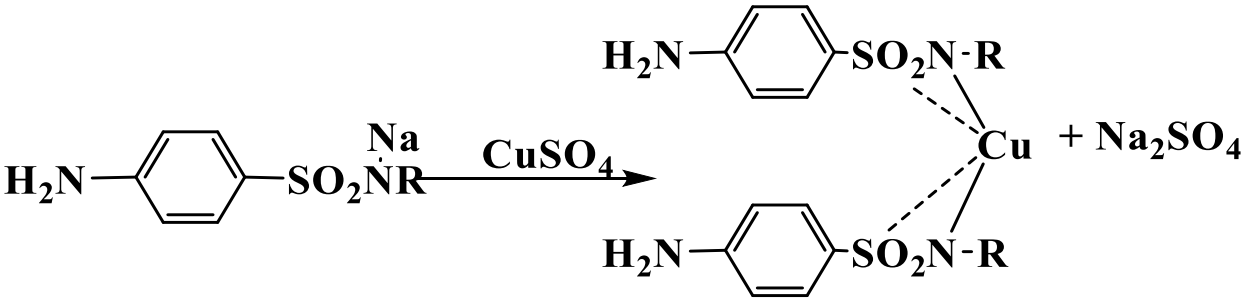
• All sulfonamides can be halogenated, nitrated, and sulfonated along the aromatic ring:



• Due to the presence of a primary aromatic amino group, sulfonamides undergo diazotization reactions followed by azo coupling. As a result of the reaction, a cherry-red color appears or an orange-red precipitate falls out:



• Hydrogen in the imide group determines the possibility of interaction with salts of heavy metals ($CuSO_4$, $CoCl_2$, $FeCl_3$). At the same time, differently colored complexes, soluble and insoluble in water, are formed. This reaction makes it possible to identify sulfonamides. The drug is dissolved in a 0.1 M alkali solution, and then a solution of heavy metal salts is added. There should not be an excess of alkali, because hydroxides of heavy metals may precipitate:



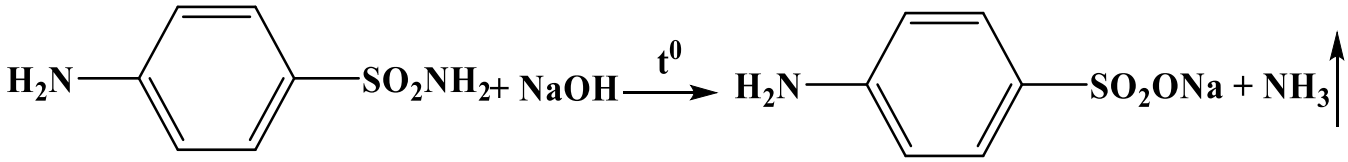
COLOR REACTIONS WITH SALTS OF HEAVY METALS ON SOME SULFONAMIDE DRUGS

Medicine	Color of the precipitate or solution with reagents		
	$FeCl_3$	**$CoCl_2$**	**$CuSO_4$**
Streptocide white not soluble	yellow solution	pink solution	blue solution
Streptocide white soluble	red solution	pink solution	blue precipitate with a greenish tint
Sulfacil	-	-	blue precipitate with a greenish tint
Sulfazole	-	a blue-violet precipitate that turns greenish-gray	unstable greenish precipitate
Norsulfasol	light orange precipitate	lilac precipitate that turns into dirty purple	a dirty purple precipitate that turns dark purple
Sulfazine	-	red precipitate; crimson colored solution	a solution of green color, which turns into dirty purple
Sulfadiazine	-	red precipitate; crimson colored solution	a green precipitate that turns dirty purple
Sulfadimezine	-	lilac precipitate	a yellow-green

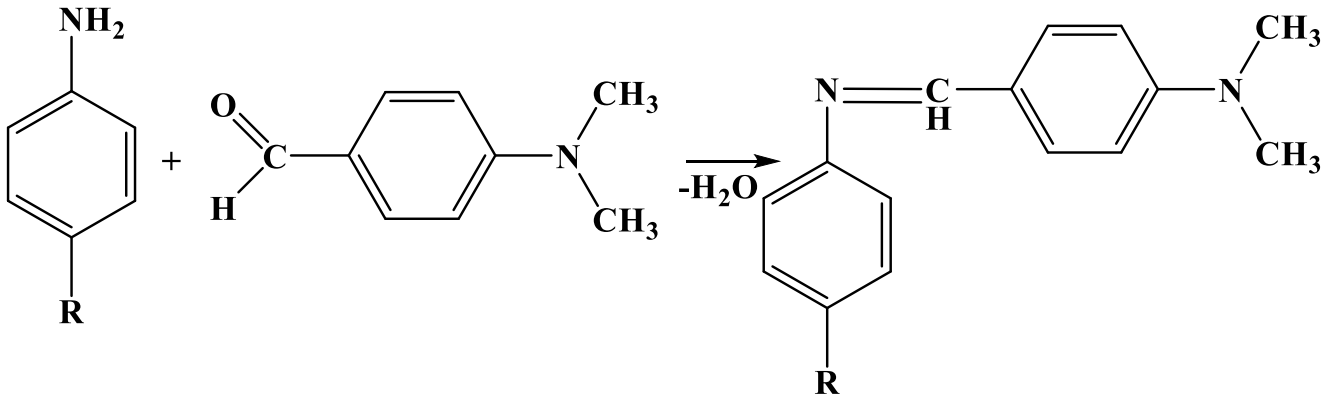
			precipitate that turns red-brown
Sulfamethazine	-	pink precipitate	green precipitate
Sulgin	yellow solution	розчин рожевого кольору	blue solution
Etazol	-	білий осад	grass-green precipitate that turns into dark green
Sulfantrol	-	-	a light green precipitate that turns blue-green

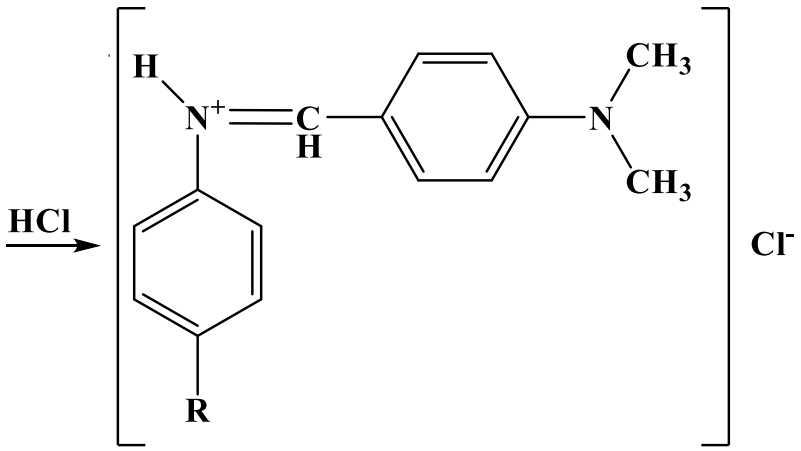
When adding a 1% sodium nitroprusside solution to a sulfonamide solution in the presence of alkali and subsequent acidification, red or red-brown solutions or precipitates are formed.

The ability of substances of this group to oxidize is manifested during pyrolysis. Thus, streptocide forms a blue-violet liquid during pyrolysis, while aniline and ammonia are released. If there is a sulfur heteroatom in the structure, hydrogen sulfide is formed during pyrolysis.



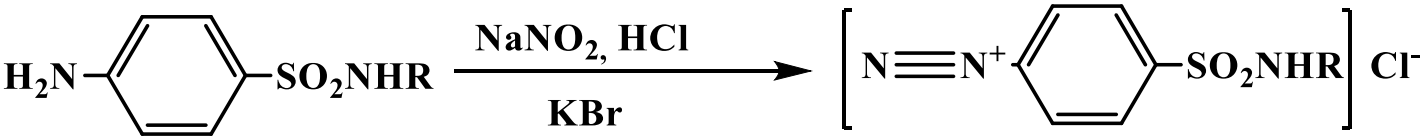
Lignin sample is used for express analysis. A few grains of the medicine and 1 drop of diluted hydrochloric acid are placed on the paper containing lignin. A yellow-orange color appears. (Lignin contains aromatic aldehydes: coniferyl, etc.)





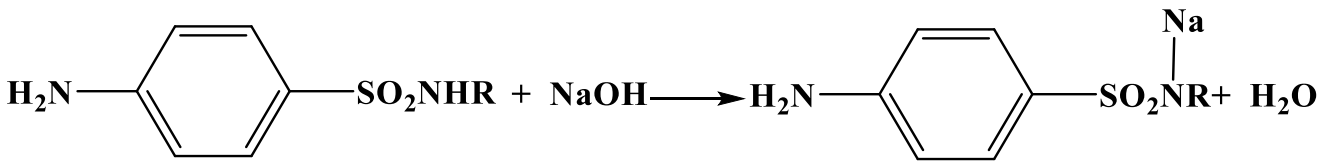
Quantitative definition:

1. Most drugs of this group are determined by the nitritometry method. The substance is titrated with sodium nitrite in an acidic environment in the presence of a potassium bromide catalyst at a temperature not higher than 20 C. Indicators are internal or external.

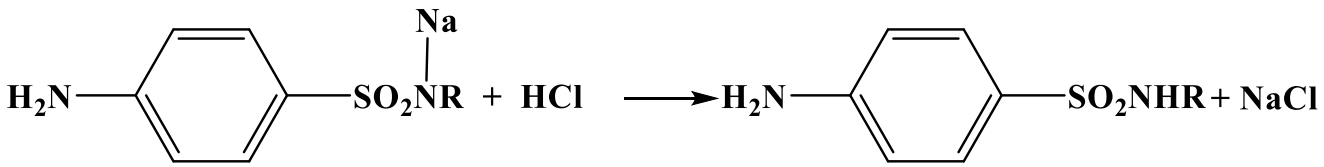


$$2KIO_3 + 5NaNO_2 + 2HCl \rightarrow I_2 + 5NaNO_3 + 2KCl + H_2O$$

2. Alkalimetry. It is based on the acidic properties of the sulfamide group. Acidic forms are titrated with sodium hydroxide solution in the presence of thymolphthalein indicator.

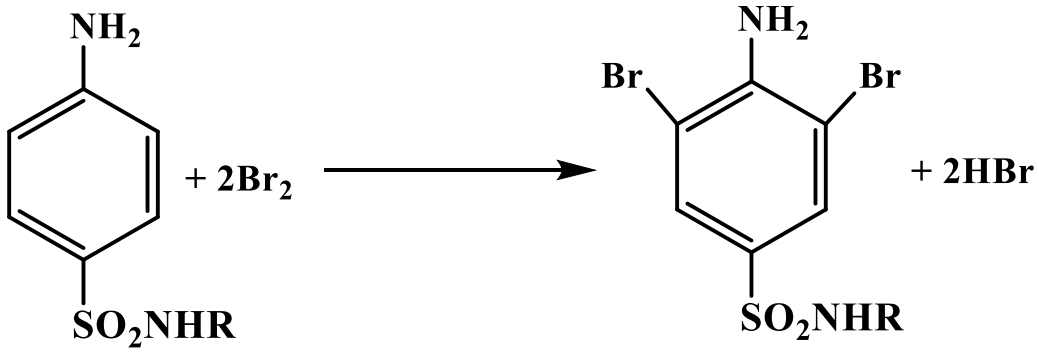


3. Acidimetry. Sodium salts of sulfonamides can be titrated with acid in an alcohol-acetone medium, the indicator is methyl orange.



4. Bromatometry, reverse titration. The method is not based on the halogenation reaction of sulfonamide drug substances. The titrated solution is potassium bromate. The excess of bromine is determined iodometrically, the indicator is starch.

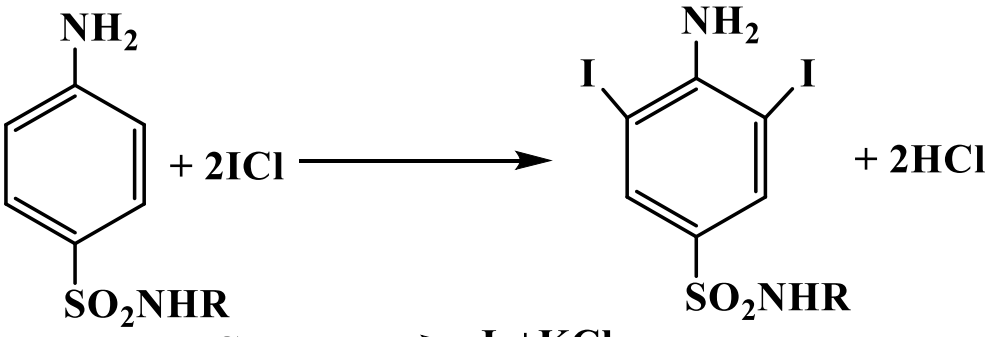
$$KBrO_3+5KBr+3H_2SO_4 \longrightarrow 3Br_2+3K_2SO_4+3H_2O$$



$$Br_2+2KI \longrightarrow I_2+2KBr$$

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

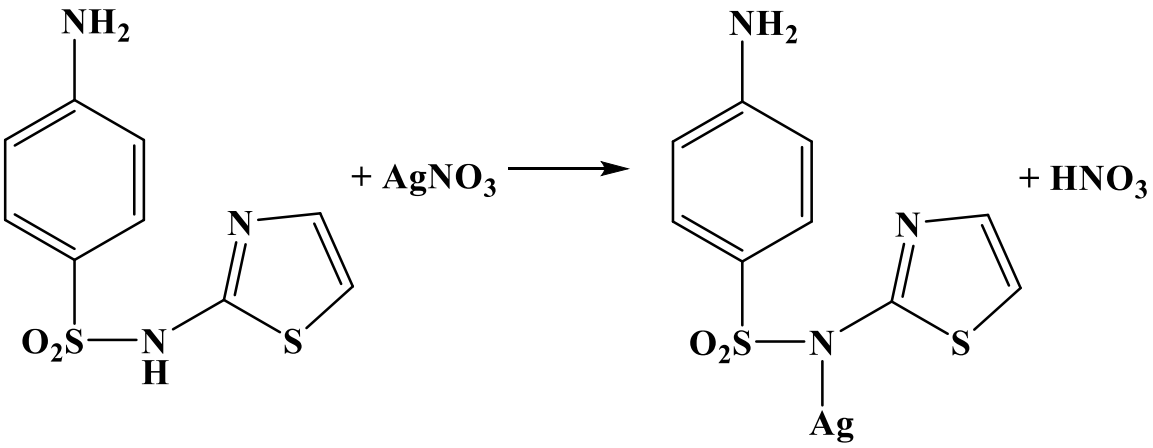
5. Iodochlorometry, reverse titration. It consists in the halogenation of drug substances with a titrated solution of iodine monochloride, the excess of which is determined iodometrically.



$$ICl+KI \longrightarrow I_2+KCl$$

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

6. Argentometry. Some sulfonamides can form salts when interacting with argentum nitrate (for example, norsulfasol) .



$$2HNO_3 + Na_2B_4O_7 + 5H_2O \rightarrow 4H_3BO_3 + 2NaNO_3$$

To reduce the concentration of hydrogen ions, which make the reaction reversible and dissolve the sediment, the titration is carried out in the presence of sodium tetraborate, the indicator is potassium chromate (Mohr's method).

7. Photocolorimetry. It is based on the ability of sulfonamide drugs to form azo dyes.

8. Spectrophotometric methods of quantitative determination.

Application. Chemotherapeutic drugs for the treatment of diseases caused by streptococci, gonococci, meningococci, Escherichia coli.

TEST TASKS ON THE TOPIC «SULFANILAMIDES. CHARACTERISTICS, CLASSIFICATION, RELATIONSHIP BETWEEN STRUCTURE AND PHARMACOLOGICAL ACTIVITY»

1. Salazopyridazine can be distinguished from sulfadimezin by:

A) appearance

B) ninhydrin test

C) oxime formation

D) formation of a complex ester

E) precipitation of silver by nitrate

2. Which of the drug substances after acid hydrolysis decomposes with the release of formaldehyde?

A) chloramine

B) urosulfan

C) butamide

D) streptocide is soluble

E) norsulfasol

3. The reagents that allow you to differentiate sulfadimezin, streptocid, norsulfazole include:

A) sodium nitrite in an acidic environment, an alkaline β-naphthol solution

B) sodium nitrite in an alkaline medium, phenol

C) iron (III) chloride, hydrochloric acid

D) sodium nitrite in an acidic environment

E) sodium nitrite in a neutral environment, cobalt chloride

4. Which of the drug substances does not give a colored product during pyrolysis?

A) streptocide

B) butamide

C) urosulfan

D) norsulfasol

E) sulgin

5. The main properties of sulfonamide drugs are due to:

A) phenolic hydroxyl

B) carboxyl group

C) keto group

D) primary aromatic amino group

E) sulfamide group

6. The acid-base titration method in dimethylformamide is used to assess the quality of which drug substance from the group of sulfonamide drugs?

A) streptocide

B) sulgin

C) urosulfan

D) phthalazole

E) sulfadimezin

7. What process is a substance subjected to detect sulfamide sulfur?

A) mineralization by boiling with concentrated nitric acid

B) alkaline hydrolysis (alloy with alkali)

C) formation of oxonium salts

D) formation of hydroxamates

E) formation of colored complexes with salts of heavy metals

8. To detect the specific admixture of norsulfasol in phthalazole, the following reaction is used:

A) formation of indophenol

B) acid hydrolysis

C) alkaline hydrolysis

D) oxime formation

E) formation of azo dye (azo compound)

9. The solubility of phthalazole in alkali solutions is determined by the presence of:

A) comlex ether group

B) simple ether group

C) carboxyl group

D) imide group

E) amino groups

10. Which of the drug substances during pyrolysis forms a colored product and ammonia?

A) butamide

B) chlorpropamide

C) norsulfasol

D) urosulfan

E) phthalazole

11. For the quantitative determination of sulfonamides, the most appropriate volumetric method is:

A) nitritometry method

B) method of neutralization

C) iodometry method

D) mercurimetry method

E) cerimetry method

12. Quantitative determination of phthalazole is carried out by the method of acid-base titration in the medium of:

A) glacial acetic acid

B) acetic anhydride

C) formic acid

D) diluted sulfuric acid

E) dimethylformamide

13. The following conditions should be observed during nitritometric quantitative determination of streptocide:

A) compliance with the temperature regime

B) preliminary hydrolytic decomposition

C) use of the reverse titration method

D) neutral reaction of the environment

E) use of α-naphthol, phenol

14. The general group reaction for sulfonamide drugs is the reaction:

A) salt and complex formation with salts of heavy metals

B) with solutions of aldehydes in sulfuric acid

C) with phenols

D) with meadows

E) with alkali metals

15. One of the following drug substances does not dissolve in acids:

A) sulfacyl sodium

B) norsulfasol

C) etazol

D) phthalazole

E) streptocide

16. One of the following drug substances does not dissolve in alkalis:

A) sulgin

B) sulfadimezin

C) etazol

D) sulfalene

E) streptocide

17. Among the following drug substances, indicate one that is colored:

A) chloramine

B) salazopyridazine

C) pantocid

D) phthalazole

E) norsulfasol

18. One of the rational names of sulfonamide drug substances belongs to norsulfazole:

A) 2-(p-aminobenzenesulfamido)-5-ethyl-1,3,4-thiadiazole

B) p-aminobenzenesulfamide

C) 2-(p-aminobenzenesulfamido)-thiazole

D) 2-(p-aminobenzenesulfamido)-4,6-dimethylpyrimidine

E) p-aminobenzenesulfamidoguanidine

19. One of the names according to the International Pharmacopoeia is norsulfasol:

A) Sulfathiazolum

B) Phthalylsulfathiazolum

C) Sulfaethiodolum

D) Sulfaguanidinum

E) Phthalazolum

20. All sulfonamide drugs are united by the presence of:

A) sulfanilic acid amide

B) amide of benzene sulfonic acid

C) p-aminobenzoic acid amide

D) p-chlorobenzenesulfonic acids

E) p-aminosalicylic acid

21. One of the drug substances is not a derivative of sulfanilic acid amide:

A) Aethazolum

B) Salasopyridazinum

C) Sulginum

D) Chlorpropamidum

E) Sulfadimezinum

22. The structure of one drug substance is based on the reaction of acylation of norsulfazole with phthalic acid:

A) Sulfanilamide

B) Phthalysulfathiazolum

C) Sulfadimidinum

D) Tolbutamidum

E) Sulfacarbamid

23. What acid is the basis of the structure of the chemotherapeutic substance - streptocide:

A) benzoin

B) salicylic

C) sulfanilic

D) γ-pyridinecarbon

E) nicotine

24. One of the compounds is not a derivative of heterocycles:

A) Phthalysulfathiazolum

B) Sulfaethidolum

C) Sulfadimidinum

D) Sulfanilamide

E) Sulfathiazolum

25. One of the drug substances is a derivative of sulfanilic acid amide:

A) Sulginum

B) Chlorpropamidum

C) Pantocidum

D) Chloraminum B

E) Butamidum

26. The drug substance Phthalazol has a rational name:

A) p-aminobenzenesulfamidoguanidine

B) sodium p-aminobenzenesulfacetamide

C) 2-[p-(o-carboxybenzamido)-benzenesulfamido]-thiazole

D) p-aminobenzenesulfanylurea

E) 2-(p-aminobenzenesulfamido)-thiazole

27. The reaction of the formation of an azo dye makes it possible to identify drugs that have in their structure:

A) sulfamide group

B) primary aromatic amino group

C) aldehyde group

D) simple ether group

E) carboxyl group

28. To identify streptocide, sodium sulfacyl, norsulfazole, sulfadimesin, the reaction should be carried out:

A) formation of azo dye

B) formation of iodoform

C) formation of murexide

D) formation of naphthoquinone

E) formation of fluorescein

29. One of the listed sulfonamide drug substances is fused with resorcinol in concentrated sulfuric acid, the melt is dissolved in sodium hydroxide solution - a bright green fluorescence appears:

A) 2-(p-aminobenzenesulfamido) - 4,6-dimethylpyrimidine (sulfadimezin)

B) 2-[p-(o-carboxybenzamido)-benzenesulfamido]-thiazole (phthalazole)

C) p-aminobenzenesulfamide (streptocide)

D) p-aminobenzenesulfanylurea (urosulfan)

E) 2-(p-aminobenzenesulfamido)-thiazole (norsulfazole)

30. One of the listed drug substances with salicylic acid in concentrated sulfuric acid forms a crimson color:

A) 2-(p-aminobenzenesulfamido)-5-ethyl-1,3,4-thiadiazole (ethazole)

B) sodium p-aminobenzenesulfiminomethanesulfonate (soluble streptocide)

C) p-aminobenzenesulfamide (streptocide)

D) sodium p-aminobenzenesulfacetamide (sodium sulfacyl)

E) 2-(p-aminobenzenesulfamido)-thiazole (norsulfazole)

31. One of the preparations is identified with potassium iodide:

A) Pantocidum

B) Sulfanilamide

C) Sulfacetamidum

D) Sulfaguanidinum

E) Sulfacarbamidum

32. One of the substances during heat treatment forms a dark brown melt and hydrogen sulfide:

A) Sulfacylum soluble

B) Streptocidum

C) Norsulfazolum

D) Chloraminum B

E) Pantocidum

33. Specify a sulfonamide medicinal product, for the identification of which preliminary hydrolysis is necessary for the formation of an azo dye:

A) Sulfaguanidinum (Sulginum)

B) Streptocidum soluble

C) Sulfadimidinum (Sulfadimezinum)

D) Sulfathiazolum (Norsulfazolum)

E) Urosulfanum

34. One of the substances does not form an azo dye without prior acid hydrolysis:

A) Sulfacylum Natrium

B) Phthalazolum

C) Sulfaguanidinum

D) Sulfadimidinum

E) Sulfathiazolum

35. One of the sulfonamide medicinal substances forms a blue-violet alloy, while ammonia and aniline are released:

A) Sulfanilamide

B) Sulfathiadolum

C) Sulfacarbamidum

D) Phthalylsulfathiazolum

E) Sulfacetamidum Natricum

36. Eye drops made at a pharmaceutical enterprise, the composition of which includes sulfacyl sodium (a sulfamide preparation), are subject to control, according to normative and technical documentation. What reaction for the identification of the active substance should the Department of Technical Control Chemist conduct?

A) with ammonium oxalate solution

B) formation of auric dye

C) formation of azo dye

D) with potassium hydroxide solution

E) with sodium citrate solution

37. According to normative and technical documentation, the characteristic reaction of identification for sulfanilic acid amides is the reaction:

A) from silver nitrate

B) with copper sulfate

C) with mercury (II) chloride

D) with barium sulfate

E) with potassium permanganate

38. One of the drugs in the presence of a solution of sodium hydroxide and phenolphthalein forms a red color:

A) Streptocidum

B) Urosulfanum

C) Sulginum

D) Sulfadimezinum

E) Norsulfazolum

39. In which of the drugs listed below does the pharmacist of the control and analytical laboratory determine the admixture of phthalic acid by the acid-base titration method:

A) ftivazide

B) phenyl salicylate

C) phenolphthalein

D) norsulfazol

E) phthalazole

40. The nitritometric method of quantitative determination is used for drug substances having a primary aromatic amino group (sulfanilamide drugs). What kind of environment should be created by the pharmacist-analyst in the already mentioned solution:

A) neutral

B) alkaline

C) hydrochloric acid

D) ammonia

E) phosphoric acid

41. For colorimetric and photocolorimetric determination of drug substances from the group of primary aromatic amines, the following reactions are used:

A) formation of isocyanides

B) deposition

C) neutralization

D) formation of indophenol

E) azo compound

42. A chemist-analyst of a control and analytical laboratory uses the method of fixing the end point of the titration under the nitritometric method of quantitative determination of the Streptocide substance using:

A) adsorption indicator

B) metal indicator

C) external indicator (iodostarch paper)

D) in an indicatorless way

E) starch solution

43. According to the requirements of normative and technical documentation, the pharmacist determines the quantitative content of the substance norsulfazole. He uses the nitritometry method for his work. What indicator should he use?

A) eriochrome T

B) methyl red

C) neutral red

D) iodine-starch paper

E) dimethyl yellow

44. What changes in the structure of sulfonamide drugs do not lead to loss of their activity?

A) transfer of the amino group to another position in the benzene ring

B) introducing other substituents into the benzene cycle

C) amino group is replaced by a radical, which in the body turns into a free amino group

D) replacement of the sulfamide group by a radical

E) transfer of the sulfamide group to another position

45. The mechanism of action of sulfonamide drugs is based on:

A) oxidative phosphorylation

B) inhibition of monoamine oxidase synthesis

C) inhibition of folic acid synthesis ("competitive antagonism" theory)

D) protein denaturation

46. Sulfanilamide drugs show:

A) antacid effect

B) antitumor

C) neurotropic

D) antibacterial

E) painkiller

47. The pharmacist identifies the streptocide. The presence of Sulfur in the drug molecule after oxidation with concentrated nitric acid can be confirmed by reaction with the solution of:

A) barium chloride

B) lead acetate

C) lead sulfide

D) barium sulfate

E) silver nitrate

48. To identify streptocide, sulfacyl-sodium, norsulfazole, sulfadimesin, we should carry out the formation reaction of:

A) azo dye

B) murexide

C) naphthoquinone

D) fluorescein

E) iodoform

49. Streptocide belongs to chemotherapeutic substances. What compound is the basis of the structure of this drug substance?

A) salicylic acid

B) sulfanilic acid

C) γ-pyridinecarboxylic acid

D) nicotinic acid

E) benzoic acid

50. The presence of what in the sulfadimesin molecule is indicated by the formation of a red azo dye?:

A) nitro groups

B) aldehyde group

C) complex ether group

D) keto groups

E) primary aromatic amino group

51. Which of the following drugs is quantified by nitritometry without prior acid hydrolysis?

A) sulfadimezin

B) phthalazole

C) phtazine

D) paracetamol

E) streptocide soluble

52. Sulfadimezin, etazol, urosulfan are used as chemotherapeutic drugs. According to their chemical structure, they are derivatives of:

A) barbituric acid amide

B) benzoic acid amide

C) salicylic acid amide

D) sulfanilic acid amide

E) nicotinic acid amide

53. The structure of which medicinal product includes a thiazole heterocycle:

A) norsulfasol

B) streptocide

C) sulgin

D) etazol

E) sulfadimezin

54. The pharmacist performs a quantitative determination of one of the following drugs by the nitritometry method. Specify this drug:

A) norsulfasol

B) chloramine

C) antipyrine

D) atropine sulfate

E) ftivazide

55. The pharmacist of the pharmacy performs an express analysis of the substance etazol. He confirmed the presence of a primary aromatic amino group using a lignin sample. What reagent did the analyst use for this reaction?

A) acetic anhydride

B) benzene

C) unbleached paper

D) pyridine

E) chloroform

56. Sulfanilamide drugs undergo a diazotization reaction followed by an azo compound. For which drug substance does this study require preliminary hydrolysis?

A) sulfadimethoxine

B) sulfacyl sodium

C) sulgin

D) etazol

E) phthalazole

57. The pharmacist of the laboratory of the State Inspection for Quality Control of Medicines carries out the identification of the substance "Sulfamethoxazole" by adding solutions of hydrochloric acid, sodium nitrite and β-naphthol to the drug. At the same time, an intense red color is formed. Indicate which functional group is being reacted with:

A) primary aromatic amino group

B) complex ether group

C) sulfamide group

D) carboxyl group

E) aldehyde group

58. In which drug can phthalic acid be identified after hydrolysis?

A) sulfapyridazine

B) sulfazine

C) sulfadimethoxine

D) phthalazole

E) phenacetin

59. In which of the following drug can ammonia be identified after heating:

A) sulgin

B) propazine

C) etazol

D) norsulfasol

E) sulfadimezin

Recommended literature

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9. Basic methods of quantitative determination of drugs substances physical and physicochemical methods of drugs substances analysis. Express analysis of drugs: Study guide for 3rd year English-speaking students of the specialty "Pharmacy, Industrial Pharmacy" / L. I. Kucherenko, O. O. Portna, O. V. Khromyleva [et al.]. – Zaporizhzhia: ZSMU, 2022. – 130 p.

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