MINISTRY OF HEALTH OF UKRAINE

ODESSA NATIONAL MEDICAL UNIVERSITY

Faculty of Pharmacy

Department of Pharmaceutical Chemistry and Drug Technology

APPROVED by

Vice-rector for scientific and pedagogical work

_____Eduard BURYACHKIVSKY

_____, 202_

METHODOLOGICAL DEVELOPMENT
TO THE LECTURES ON THE EDUCATIONAL DISCIPLINE

Faculty, course Pharmaceutical, IV course

Academic discipline Pharmaceutical chemistry

(name of academic discipline)

Approved:

Department meeting Pharmaceutical chemistry and drug technology

Odessa National Medical University

Protocol No. _ dated _____.

Head of Department (_____) Volodymyr GELMBOLDT

(signature) *(First Name Last Name)*

Developers:

Prof. Gelmboldt V.O., senior lecturer Nikitin O.V., Shishkin I.O.

Lecture No. 1

Topic: Agents affecting the afferent nervous system.

Actuality of theme: Pharmaceutical chemistry is a science that studies methods of preparation, structure, physical and chemical properties of medicinal products; relationship between their chemical structure and action on organism; methods of quality control of drugs and changes that occur during their storage, as well as their use in medicine. Therefore, it is urgent to solve the problems facing pharmaceutical chemistry with the help of physical, chemical and physico-chemical methods, which are used both for synthesis, as well as for the analysis of medicinal products.

The purpose:the formation of students' knowledge about the peculiarities of the storage of medicinal products, which affect the afferent nervous system, as well as the characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of obtaining, methods of analysis, application in medicine. As a result of the lecture, students should learn the properties and methods of medical analysis means affecting the afferent nervous system.

Basic concepts:pharmaceutical chemistry, qualitative analysis, quantitative analysis, State Pharmacopoeia of Ukraine, physicochemical methods of analysis, impurities, express analysis.

Plan and organizational structure of the lecture:

1.Preparatory stage

1.1.Determination of educational The purposes.

1.2.Providing positive motivation.

2. The main stage

Presentation of lecture material

Plan:

-Preparations for local anesthesia

- Antacid, enveloping and astringent agents

- Adsorbents

-Peripheral antitussives

- Expectorants

-Irritants

3. The final stage

3.1. Summary of the lecture, general conclusions.

3.2. The lecturer's answers to possible questions

3.3. Tasks for self-training of students.

Content of lecture material (lecture text):

Means that act in the area of the endings of afferent (sensitive) nerves are divided into two groups:

1. Means that reduce the sensitivity of the endings of afferent nerves or protect them from the irritating effect of various agents:

- means for local anesthesia;
- adsorbing;
- enveloping;
- emollients;
- binding

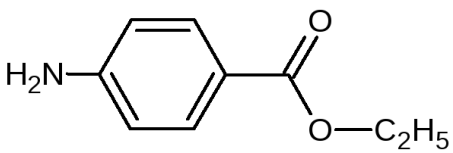
2. Means that stimulate the endings of afferent nerves:

- irritating;
- bitterness;
- vomiting;
- laxatives;
- expectorant

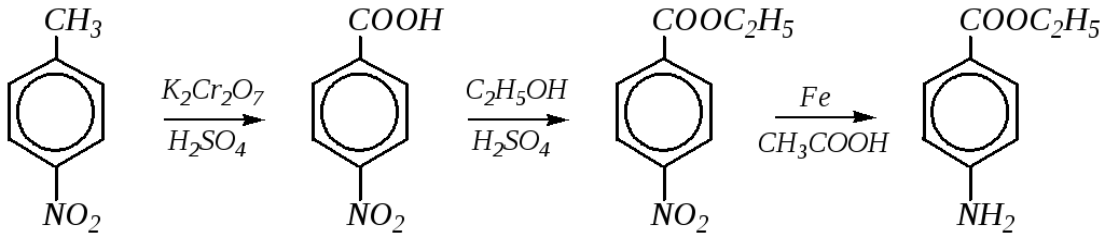
Mechanism of action. It is believed that they act on the membrane of nerve fibers, blocking sodium channels and thus blocking the conduction of impulses. The strength and duration of action of local anesthetics in general depend on the degree of their lipophilicity, since lipophilic compounds easily penetrate into cells.

Esters of p-aminobenzoic acid

Benzocaine (Anesthesin)



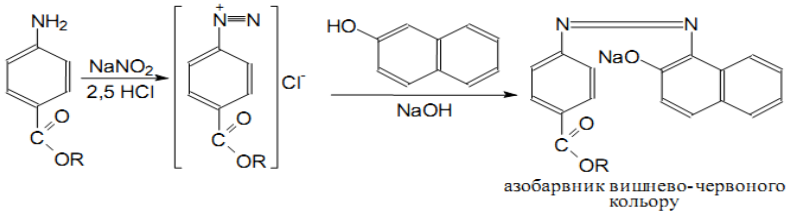
Synthesis.



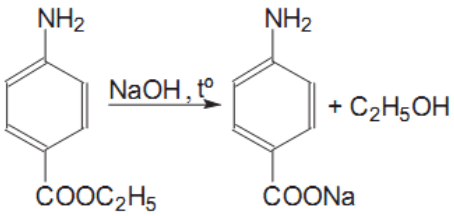
Properties.A white, odorless crystalline powder, slightly bitter in taste, causes a feeling of numbness on the tongue. Very slightly soluble in water, easily soluble in alcohol, ether, chloroform.

Identification.

1. Reaction to the primary aromatic amino group (formation of an azo dye):

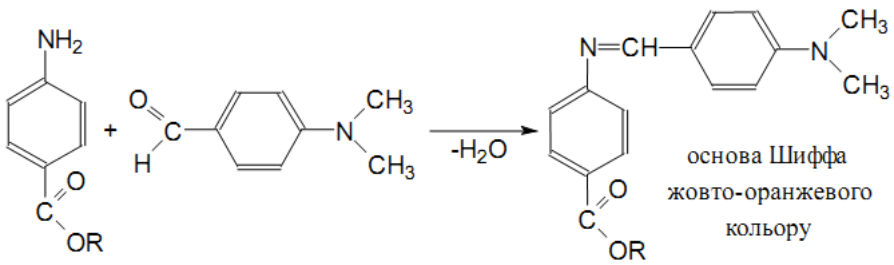


2. Reaction to ethanol residue - iodoform test (after hydrolysis):



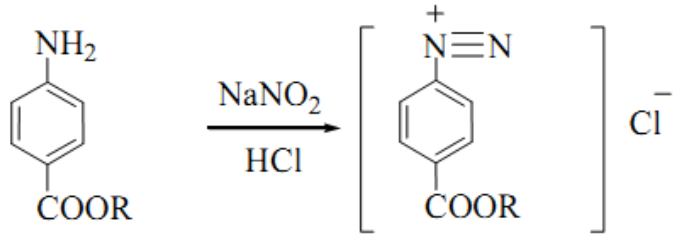
$$C_2H_5OH + 4I_2 + 6NaKOH \rightarrow CHI_3\downarrow + 5NaI + HCOONa + 5H_2O$$

3. The reaction of the formation of a yellow-orange Schiff base:



Quantitative definition.

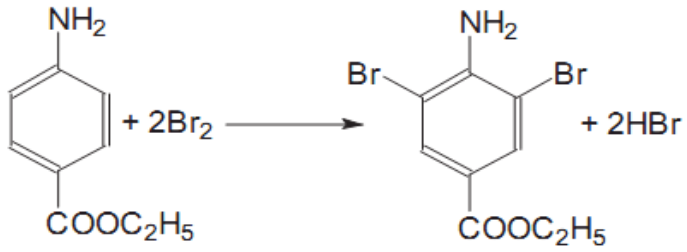
1. Nitritometry, direct titration, indicator – iodine-starch paper, s = 1:



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

2. Bromatometry, reverse titration, s = 1.5:

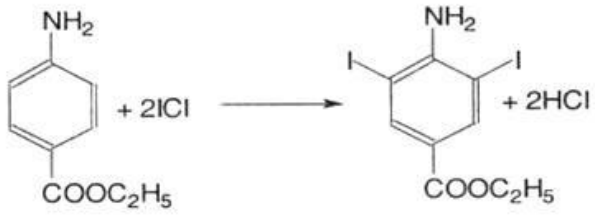
$$KBrO_3 + 5KBr + 6HCl \rightarrow 3Br_2 + 6KCl + 3H_2O$$



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

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

3. Iodochlorimetry, reverse titration, s = 1.5:



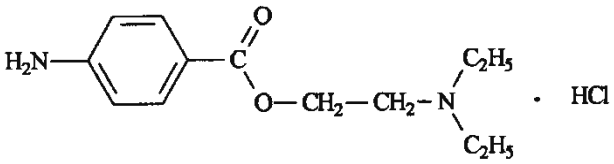
$$ICl + KI \rightarrow I_2 + KCl$$

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

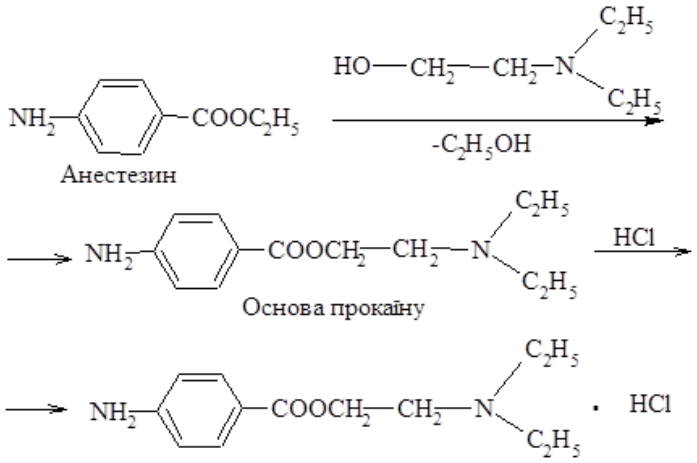
Storage. In a well-closed container that protects from light.

Application. In the form of 5–10% ointment or powder for urticaria or skin diseases accompanied by itching, as well as for pain relief of wounded and ulcerated surfaces. With diseases of the rectum - suppositories. For anesthesia of mucous membranes - 5-20% oil solutions. Orally in powders, tablets for pain relief of mucous membranes for spasms and pains in the stomach, increased sensitivity of the esophagus, etc.

Procaine hydrochloride (Novocaine).



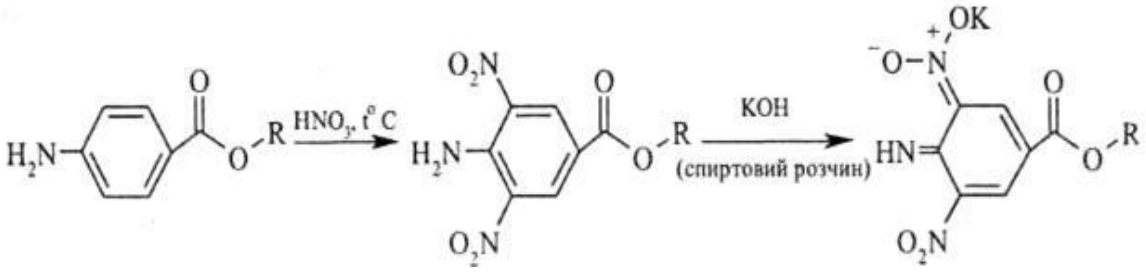
Synthesis.



Properties. White crystalline powder, causes a feeling of numbness on the tongue. Very easily soluble in water, soluble in 96% alcohol, practically insoluble in ether.

Identification.

1. T. pl., IR-, UV-spectroscopy.
2. Reactions to chlorides: Ag+ + Cl—⟶AgCl↓.
3. Reactions on the primary aromatic amino group.
4. LZ + HNO3 (smoke)→evaporate + acetone→brownish-red color:



Quantitative definition.

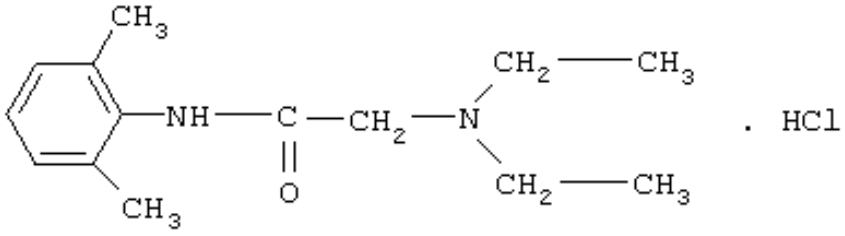
1. Nitritometry, s = 1.
2. Alkalimetry by bound HCl, indicator – phenolphthalein, s = 1.
3. Argentometry by bound HCl, s = 1.

Storage.In well-stoppered dark glass jars.

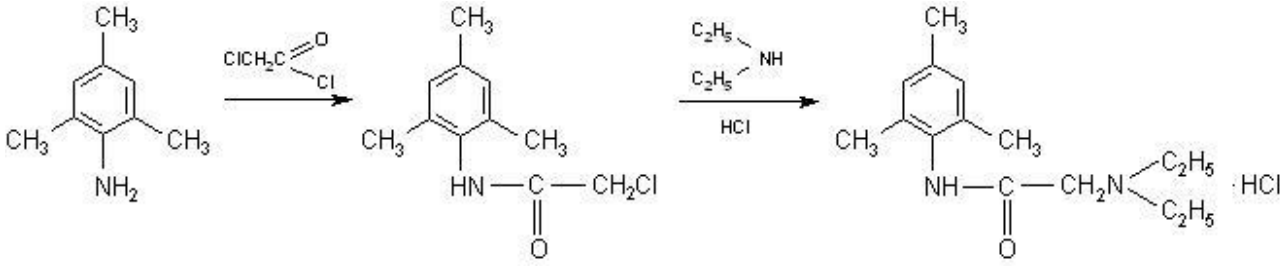
Application. Local anesthetic agent. When absorbed and directly injected into the blood, it affects the entire body as a whole.

Acetanilide derivatives.

Lidocaine hydrochloride.



Synthesis.



Properties. The solution for injection is a clear, colorless or slightly colored liquid.

Application. Local anesthetic agent, with the help of which various types of anesthesia are performed (terminal, infiltration, conduction). Lidocaine hydrochloride also has pronounced antiarrhythmic activity.

Arylamides of piperidinecarboxylic acids

Bupivacaine hydrochloride

Properties. White crystalline powder or colorless crystals, soluble in water, easily soluble in alcohol. T. pl ≈ 254 °C with decomposition.

Identification.

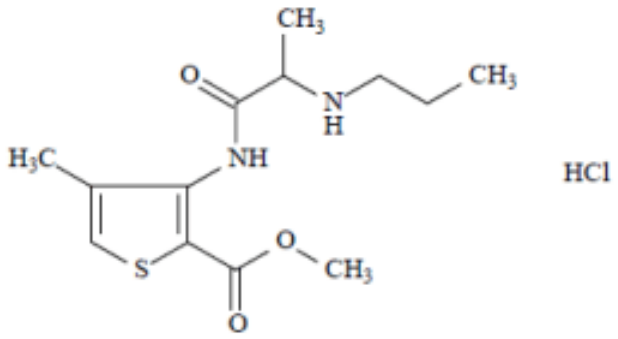
1. T. pl., IR spectroscopy, TLC.

2. Reactions to chlorides: $Ag+ + Cl \longrightarrow AgCl\downarrow$.

Quantitative definition. By the method of alkalimetry in a mixture of ethyl alcohol and a 0.01 M solution of HCl acid potentiometrically.

Application. Local anesthetic, also has an antiarrhythmic effect. Analgesic action continues even after the end of anesthesia, which reduces the need for postoperative analgesia

Articaine hydrochloride (Ultracaine)



Application.A local anesthetic agent, has a rapid and relatively long-lasting effect.

Antacid, enveloping and astringent agents

Magnesium preparations

Magnesium oxide is light, magnesium oxide is heavy

ExtractionBy roasting basic magnesium carbonate at

900 – 1000 °C:

$3MgCO3 \cdot Mg(OH)2 \cdot 3H2O \rightarrow 4MgO + 3CO2\uparrow + 4H2O.$

Properties. Small amorphous white powders. They are practically not soluble in water, in which an alkaline reaction is detected. Dissolve in dilute acids, in most cases with weak release of gas bubbles. In air, absorbing carbon dioxide, turn into magnesium carbonate.

Bulk volume:15.0 g of light MgO→the volume is about 150 ml.

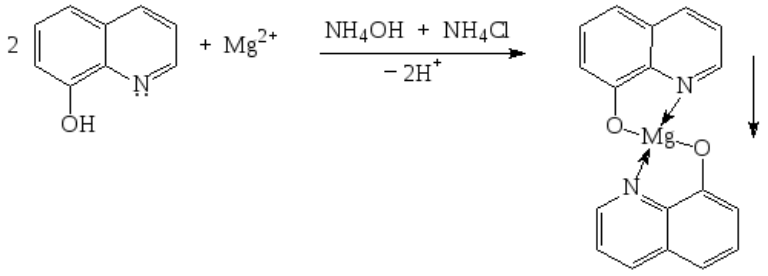
15.0 g of heavy MgO→the volume is about 30 ml.

Identification.

1. Confirmed after dissolving in diluted HNO3:

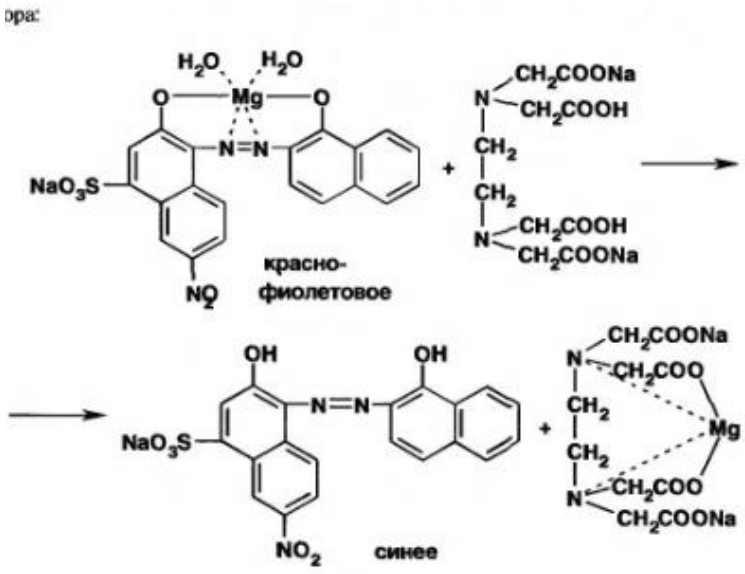
$$MgO + 2HNO3 \rightarrow Mg(NO3)2 + H2O.$$

2. Reaction with 8-oxyquinoline - a yellow-green crystalline precipitate is formed:



Quantitative definition.

1. Complexionometry, direct titration, indicator – mordant black, s = 1, purple color changes to blue:



2. Acidimetry, reverse titration, methyl orange indicator, s = 1/2:

MgO + 2HCl→MgCl2 + H2O,

superintendent HCl + NaOH→NaCl + H2O.

Storage. In a well-sealed container.

Application. An antacid agent for increased acidity of gastric juice, is one of the constituent parts of the drug "Almagel".

Basic light magnesium carbonate

Basic heavy magnesium carbonate

Extraction

4MgSO4 + 4Na2CO3 + 4H2O→3MgCO3·Mg(OH)2·3H2O↓+ 4Na2SO4 + CO2↑

Properties. White powder. Practically not soluble in water, dissolve in dilute acids with violent release of gas bubbles.

Identification.

Bulk volume: 15.0 g of light→volume ~180 ml

15.0 g heavy→volume ~ 30 ml.

Substances give reactions to magnesium and carbonates.

Quantitative definition. Complexonometry, direct titration after alkalinization in HCl acid, s = 1.

The calculation is based on magnesium oxide (40–45%).

Storage. In a well-sealed container.

Application. Astringent and antacid.

Bismuth preparations

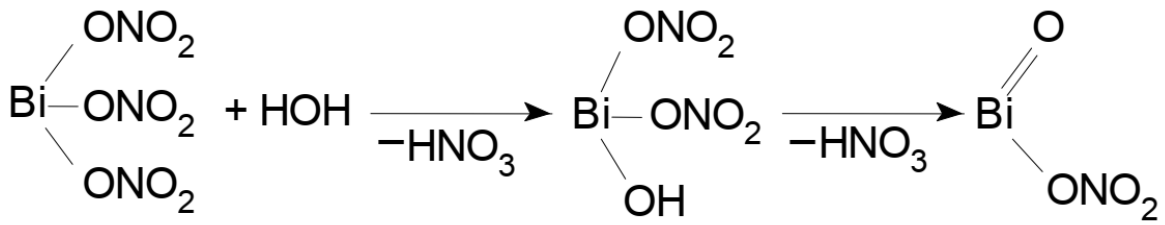
Basic bismuth nitrate

Extraction

$Bi_2O_3 + 3C \rightarrow 2Bi + 3CO\uparrow$,

$Bi + 4HNO_3 \rightarrow Bi(NO_3)_3 + NO\uparrow + 2H_2O$.

Aqueous solutions of bismuth nitrate are hydrolyzed in boiling water to form insoluble basic bismuth nitrate:



Properties. White amorphous or fine crystalline powder, practically insoluble in water, alcohol, soluble in HCl, HNO_3. Soaked in water, blue litmus paper turns red (pH<7).

Identification.

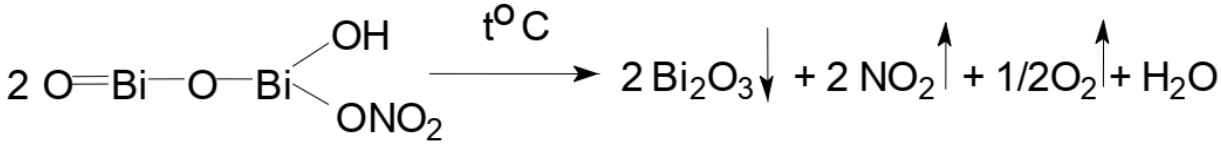
1. The substance gives characteristic reactions to bismuth.

2. With KI solution→black precipitate, soluble in an excess of reagent:

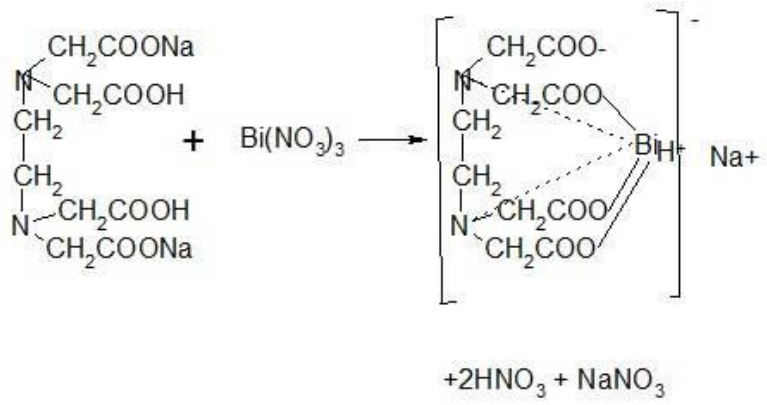
$Bi(NO_3)_3 + 3KI \rightarrow BiI_3\downarrow + 3KNO_3$,

$BiI_3\downarrow + KI \rightarrow K[BiI_4]$.

3. When roasting→yellow-brown vapors and bright yellow residue:



Quantitative definition. Complexonometry, direct titration, indicator – xylenol orange, s = 1:



Storage. In a well-closed container that protects from light.

Application. Astringent, antiseptic agent.

Adsorbing agents

Activated charcoal

ExtractionThey are obtained by pyrolysis of hardwood wood, without access to air. To increase the adsorption capacity, coal is treated with superheated steam at 800 °C, while tarry substances are removed. Then the coal is treated with solutions of zinc chloride, magnesium chloride, sodium hydroxide or phosphoric acid with subsequent heating to 300-400 °C. At the same time, the added substances are decomposed and driven away, loosening the coal and increasing the pore surface. Next, the coal is thoroughly washed with water to remove impurities and dried.

Purity test. Since the LZ is used in large doses, the AND pays great attention to the purity of activated carbon: the content of impurities of chlorides, sulfates, heavy metals, ferrum, and arsenic is regulated. There should be no sulfides or cyanides.

Determine the adsorption capacity of carbon activated with methylene blue and the degree of grinding.

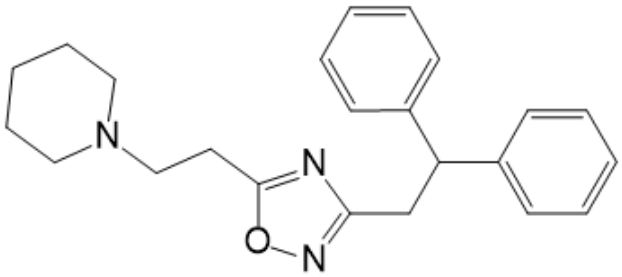
Storage. In a well-closed container, in a dry place.

Application. In case of dyspepsia, food poisoning, poisoning with alkaloids, salts of heavy metals.

Peripheral antitussives

Mechanism of actionantitussives of central action consists in suppressing the cough center. Peripherally acting drugs suppress sensitive receptors and stress receptors of the mucous membrane of the respiratory tract (trachea, bronchi, lung tissue).

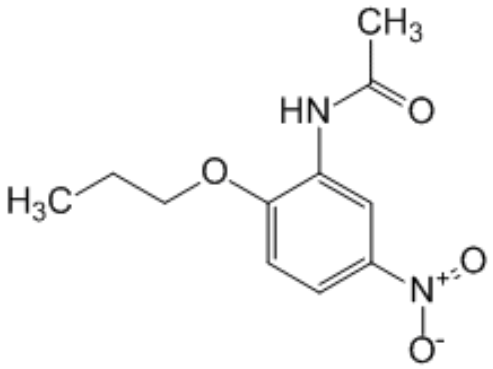
Prenoxdiazine (Libexin)



Properties. White or almost white crystalline powder.

Application. An antitussive agent of peripheral action, the antitussive effect lasts more than 3–4 hours. With catarrh of the upper respiratory tract, acute and chronic bronchitis, bronchopneumonia, bronchial asthma, emphysema, etc.

Acetylaminonitropropoxybenzene



Application. Antitussive, analgesic, deodorizing action; facilitates breathing and stops the development of reflex cough of any nature; leads to liquefaction of mucus, softens pain and has an anti-inflammatory effect.

Expectorants

According to the mechanism of action, expectorants are divided into the following groups:

1. Bronchosecretory or secretomotor agents (rehydrants) that contribute to the removal of liquid sputum (thermopsis grass, althea roots, potassium iodide, sodium hydrogen carbonate, etc.):

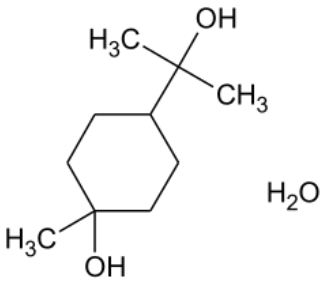
- means of reflex action;
- means of resorptive action.

2. Expectorants of direct action (mucolytics) that contribute to the thinning of sputum (trypsin crystal, acetylcysteine, bromhexine, ambroxol, etc.):

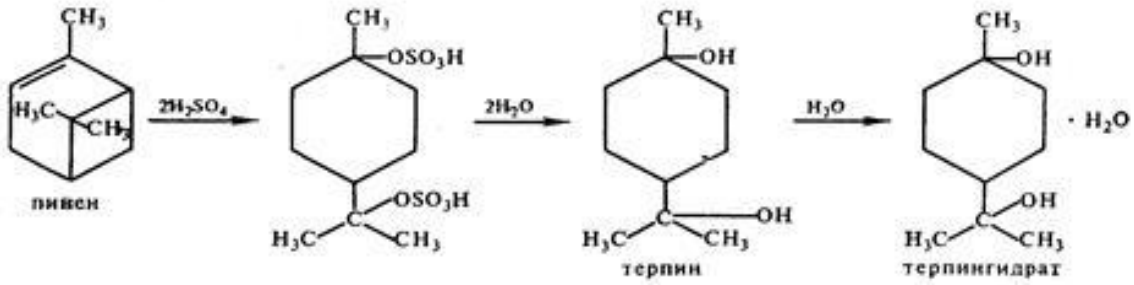
- preparations of proteolytic enzymes, as well as nucleases;
- synthetic mucolytics;
- stimulators of surfactant synthesis (bromhexine, ambroxol - lasolvan);
- surfactant substitutes (Alveofact, Exosurf) - prescribed to infants with disseminated intravascular coagulation syndrome.

Drugs that stimulate expectoration

Terpine hydrate



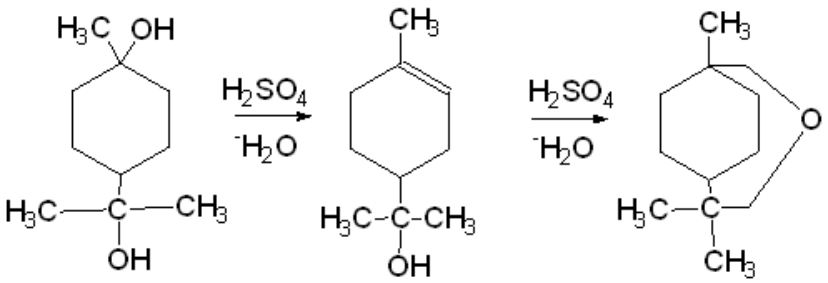
ExtractionHydration of pinene contained in the pinene fraction turpentine:



Properties. Colorless transparent crystals or white crystalline powder without odor, slightly bitter in taste. Slightly soluble in water, chloroform, ether, soluble in alcohol. Sublimes when heated to 100 °C, slowly weathers in dry warm air.

Identification.

1. When adding H2SO4 (conc.) to a hot solution of terpine hydrate (TG), the liquid becomes cloudy and acquires the aromatic smell of terpineol:



2. When TG is evaporated to dryness with an alcoholic solution of FeCl3 in a porcelain cup, a carmine-red, purple, green color appears simultaneously in different places, and when added to the cooled benzene residue, it turns blue.

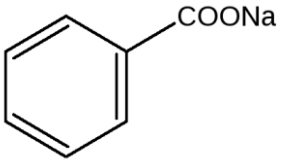
3. T. pl. 115 - 117 °C.

Quantitative definition. For the substance, the AED does not provide for a quantitative determination.

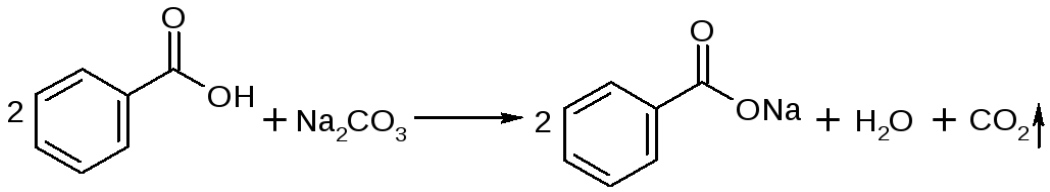
Storage. In a well-sealed container.

Application. With chronic bronchitis as an expectorant.

Sodium benzoate



ExtractionBy dissolving benzoic acid in a soda solution:



Properties. White crystalline powder or flakes, weakly hygroscopic. Easily dissolved in water, sparingly in 90% alcohol.

Identification.

1. The substance reacts to benzoates.

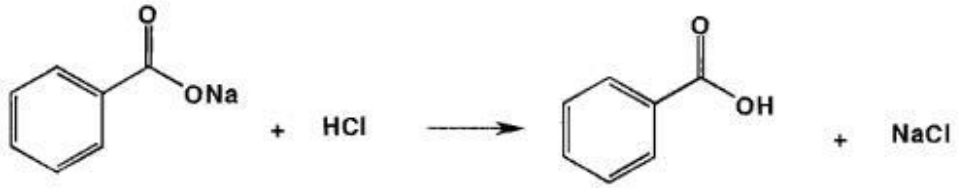
2. The substance reacts with sodium.

Quantitative definition.

1. Acidimetry in a non-aqueous environment, direct titration, indicator – naphtholbenzene, s = 1 (DFU):

C6H5COONa + HClO4→C6H5COOH + NaClO4.

2. Acidimetry, direct titration in the presence of ether, the indicator is a mixture of methyl orange and methylene blue, s = 1:

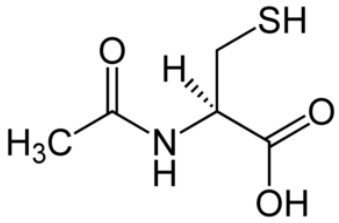


Storage. In a well-sealed container.

Application. Orally as an expectorant for bronchitis and other diseases of the upper respiratory tract in powders and mixtures.

Mucolytic agents

Acetylcysteine

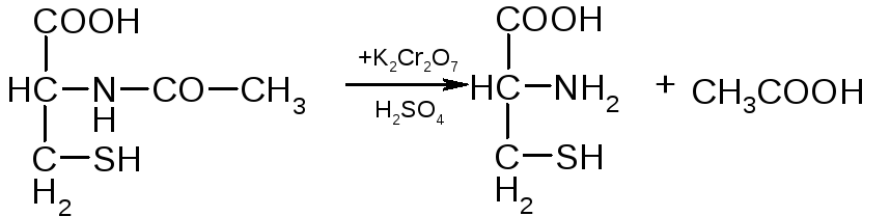


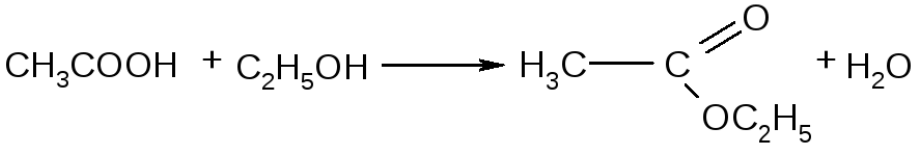
Properties. White or white with a slightly yellowish tinge crystalline powder, with a weak specific smell, easily soluble in water and alcohol, very slightly soluble in ether, in methylene chloride.

Identification.

1. IR spectrum, t.p., method of liquid chromatography.

2. The substance gives characteristic reactions to acetyl:





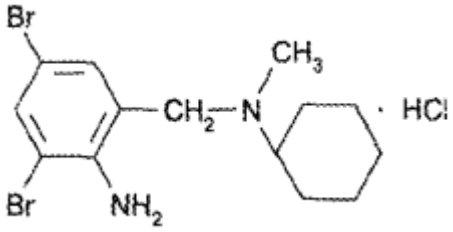
3. With a solution of sodium nitroprusside in the presence of a solution of concentrated ammonia→dark purple color.

Quantitative definition. By the method of iodometry in an acidic medium in the presence of potassium iodide (starch indicator).

Storage. In a well-closed container in a place protected from light.

Application. Expectorant (mucolytic) drug. Thanks to free sulfhydryl groups, it breaks the disulfide bonds of acidic mucopolysaccharides of sputum, which leads to depolymerization of mucoproteins and a decrease in mucus viscosity.

Ambroxol hydrochloride



Properties. White or yellowish crystalline powder, moderately soluble in water, soluble in methanol, practically insoluble in methylene chloride.

Identification.

1. IR spectrum, UV spectrum, TLC method.

2. Reactions to chlorides: $Ag+ + Cl \longrightarrow AgCl\downarrow$.

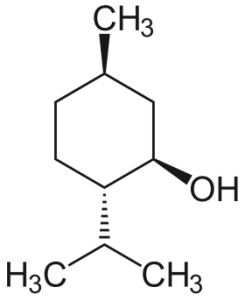
Quantitative definition. By the method of alkalimetry in a mixture of ethyl alcohol and 0.01 M HCl solution potentiometrically.

Storage. In a well-closed container in a place protected from light.

Application. Expectorant (mucolytic) agent. Mucolytic action is based on depolymerization and thinning of mucoprotein and mucopolysaccharide fibers.

Irritants

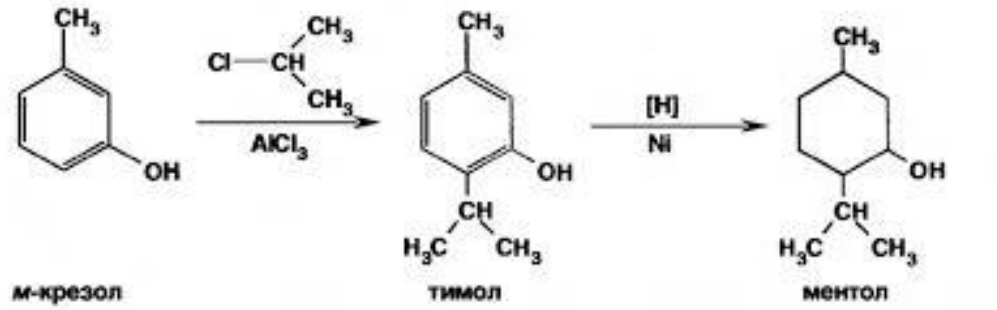
Racemic menthol



Extraction

1. Isolation of menthol from essential peppermint oil.

2. Through the interaction of m-cresol with isopropyl chloride followed by hydrogenation of thymol:



Properties. Crystalline colorless powder with a strong characteristic smell and taste. Volatile at ordinary temperature (t.p.~34 °C). Practically not soluble in water, very easily soluble in 96% alcohols, ethers and petroleum ethers, easily soluble in fatty oils.

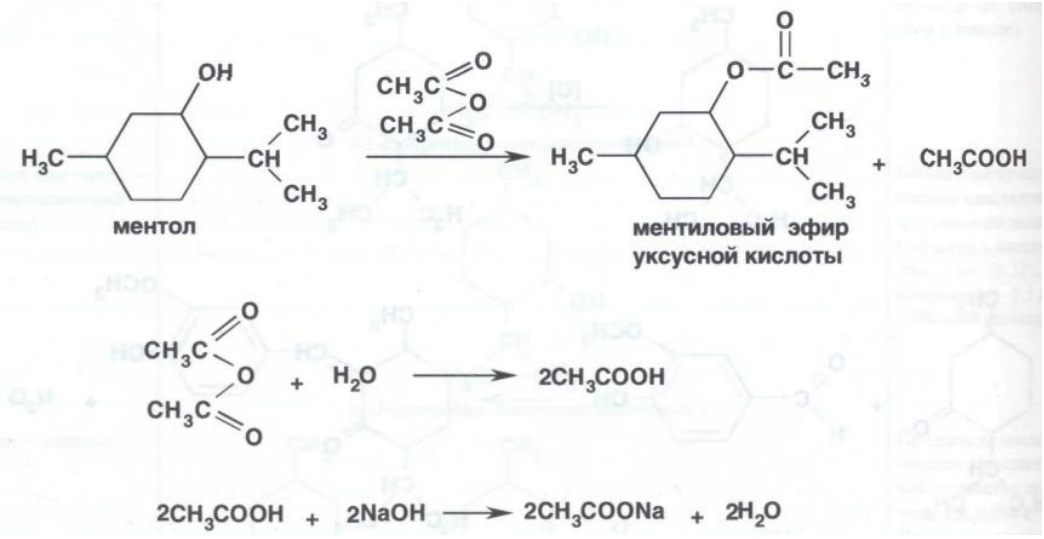
Identification.

1. Specific optical rotation, TLC, gas chromatography.
2. Formation of a complex ether with dinitrobenzoyl chloride (m.p.).

Quantitative definition. The SFU does not require quantitative determination of the substance.

Quantitative menthol content - acetylation method, back titration,

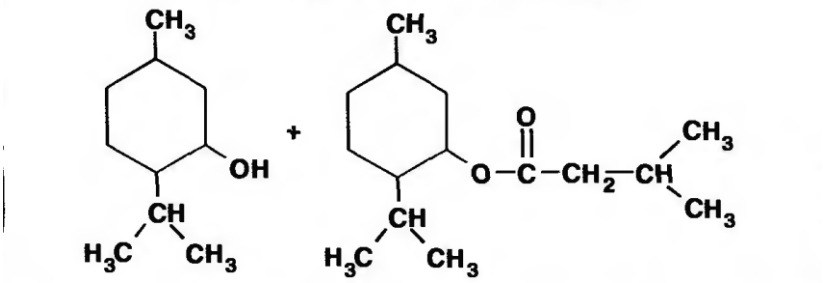
indicator – phenolphthalein, s = 1:



Storage. In a well-closed container, in a cool place.

Application. Externally as an analgesic, weak antiseptic for neuralgia, dermatoses, migraine, inflammatory diseases of the upper respiratory tract; internally as a sedative, vasodilator for mild forms of angina pectoris.

Validol



раствор ментола в ментиловом эфире изовалериановой кислоты (или в смеси ментиловых эфиров изовалериановой и метилэтилуксусной кислот)

ExtractionMenthyl ether of isovaleric acid is obtained, in which menthol is dissolved:

Properties. Transparent oily liquid with the smell of menthol. Practically not soluble in water, easily soluble in alcohol.

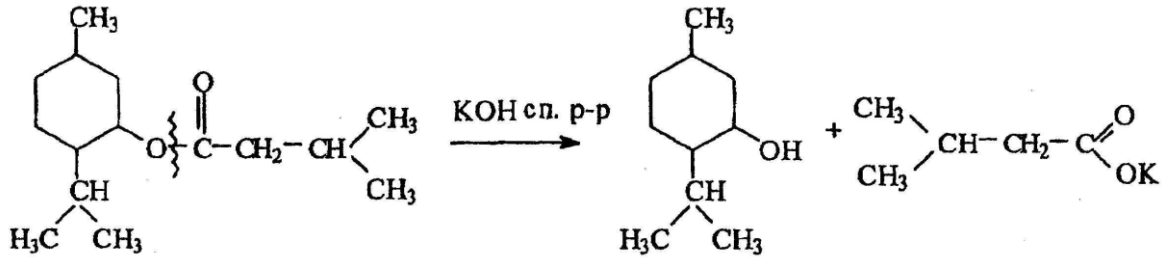
Identification.

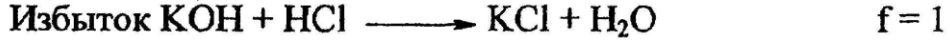
1. The reaction of menthol with a solution of vanillin in H2SO4 (conc.) is a yellow color that changes to crimson-red when water is added.

2. Density 0.894 - 0.907 g/cm3.

Quantitative definition. Alkalimetry, reverse titration,

indicator – phenolphthalein, s = 1:





Storage. In a well-closed container, in a cool place.

Application. As a means that has a calming effect on the central nervous system, it has a moderate reflex vasodilator effect. It is prescribed for angina pectoris, neuroses, sea and air sickness.

General material and bulk-methodological support of the lecture:

- ✓ computer presentation;
- ✓ illustrative materials;
- ✓ examples of solving typical tasks or performing typical tasks;
- ✓ multimedia projector.

Questions for self-control:

1. Preparations for local anesthesia

2.Analysis of antacid, enveloping and astringent agents

3.Adsorbing agents

4.Peripheral antitussives

5.Expectorants

6.Irritants

References:

Main:

1. State Pharmacopoeia of Ukraine: in 3 volumes / Derz. medical service of Ukraine funds, Ukr. of science pharmacopoeia medicine quality center means - 2nd edition. - Kh.: Ukr. of science pharmacopoeia medicine quality center means, 2015. - Vol. 1. - 1128 p.

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4. Pharmaceutical chemistry: Textbook for students. higher pharmacy education closing and pharmacy Faculty of Medical Sciences for students higher pharmacy education closing / In general ed. P.O. Bezuglio - Kind. 3rd edition, revised. – Vinnytsia, NOVA KNYGA, 2017. - 456 p.

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7. Nizhnyk H.P. Pharmaceutical chemistry: a textbook (University I-III years) H.P. Nizhnyk — 2nd ed., ed. - All-Ukrainian specialized publishing house "Medytsyna", 2015. - 352p.

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12. Analytical chemistry and instrumental methods of analysis / A.I. Gab, D.B. Shakhnin, V.V. Malyshev -Ukraine University, 2018- 396 p.

Electronic information resources:

1. Specialized medical online publication for doctors, pharmacists, pharmacists, students of medical and pharmaceutical universities. - [Electronic resource]. - Access mode:http://www.morion.ua.

2. World Health Organization. - [Electronic resource]. - Access mode:http://www.who.int.

3. Pharmaceutical encyclopedia. - [Electronic resource]. – Access mode: http://www.pharmencyclopedia.com.ua.

4. Official website of the International Organization for Standardizationhttp://www.iso.org/iso/home.html

5. Compendium online. [Electronic resource]. - Access mode:https://compendium.com.ua/bad/

6. Medline search database [Electronic resource]. – Access mode: National Library of Medicinehttps://www.nlm.nih.gov/bsd/medline.html

Lecture No. 2

Topic: Means affecting the efferent nervous system.

Actuality of theme: Pharmaceutical chemistry is a science that studies methods of preparation, structure, physical and chemical properties of medicinal products; relationship between their chemical structure and action on organism; methods of quality control of drugs and changes that occur during their storage, as well as their use in medicine. Therefore, it is urgent to solve the problems facing pharmaceutical chemistry with the help of physical, chemical and physico-chemical methods, which are used both for synthesis, as well as for the analysis of medicinal products.

The purpose:the formation of students' knowledge about the peculiarities of the storage of medicinal products, which affect the afferent nervous system, as well as the characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of obtaining, methods of analysis, application in medicine. As a result of the lecture, students should learn the properties and methods of medical analysis means affecting the efferent nervous system.

Basic concepts:pharmaceutical chemistry, qualitative analysis, quantitative analysis, State Pharmacopoeia of Ukraine, physicochemical methods of analysis, impurities, express analysis.

Plan and organizational structure of the lecture:

1.Preparatory stage

1.1.Determination of educational The purposes.

1.2.Providing positive motivation.

2. The main stage

Presentation of lecture material

Plan:

-Classification of drugs affecting efferent innervation

- Agents acting on cholinergic receptors

- Anticholinesterase drugs

-Cholinergic blockers (cholinelytics)

- Means that act on androgen receptors (andrenomimetics)

-Adrenoblockers (adrenolytics)

3. The final stage

3.1. Summary of the lecture, general conclusions.

3.2. The lecturer's answers to possible questions

3.3. Tasks for self-training of students.

Content of lecture material (lecture text):

Efferent nerves include motor (somatic) nerves, which innervate skeletal muscles, and autonomic nerves, which regulate the functions of internal organs.

Vegetative nerves, unlike somatic nerves, terminate in nerve nodes (ganglia) and consist of pre- and postganglionic fibers. Somatic nerves are not interrupted and have one fiber.

Autonomic nerves are divided into sympathetic and parasympathetic. They differ in the place of exit from the CNS, the location of the ganglia (sympathetic - located near the exit from the CNS, and parasympathetic - near the organs). Sympathetic and parasympathetic nerves have opposite effects on the functions of internal organs. This is explained by the fact that neurotransmitters (transmitters) are released from nerve endings - substances that are carriers of nervous excitement. The nerves that release the neurotransmitter acetylcholine are called cholinergic, and the nerves that release norepinephrine are called adrenergic.

Synapseis a place of contact between two neurons or between nerve endings and an effector (executive organ). Synapses in which acetylcholine is released are called cholinergic, and synapses in which noradrenaline are released are called adrenergic.

Classification of drugs that affecton efferent innervation

Cholinergic receptors - special formations on the postsynaptic membrane, differently sensitive to chemicals.

***m*- cholinergic receptors**(muscarine-sensitive) - sensitive to muscarine (alkaloid of amanita mushrooms).

***N*- cholinergic receptors**(nicotine sensitive) – sensitive to nicotine (tobacco alkaloid).

Means that stimulate cholinergic receptors.

- *m-cholinomimetics*: pilocarpine hydrochloride, aceclidine.
- n-cholinomimetics: cititon, lobeline hydrochloride.
- anticholinesterase agents: proserin (neostigmine methyl sulfate), armin.

Means that block cholinergic receptors.

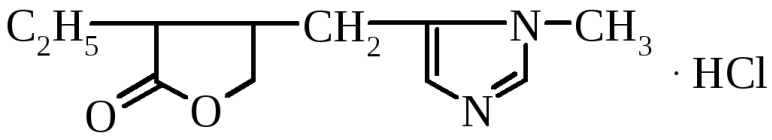
• *m-cholinoblockers*: atropine sulfate, scopolamine hydrobromide, platyphylline hydrotartrate.

• n-choline blockers: pachycarpine hydroiodide.

Means acting on cholinergic receptors

Cholinomimetics

Pilocarpine hydrochloride

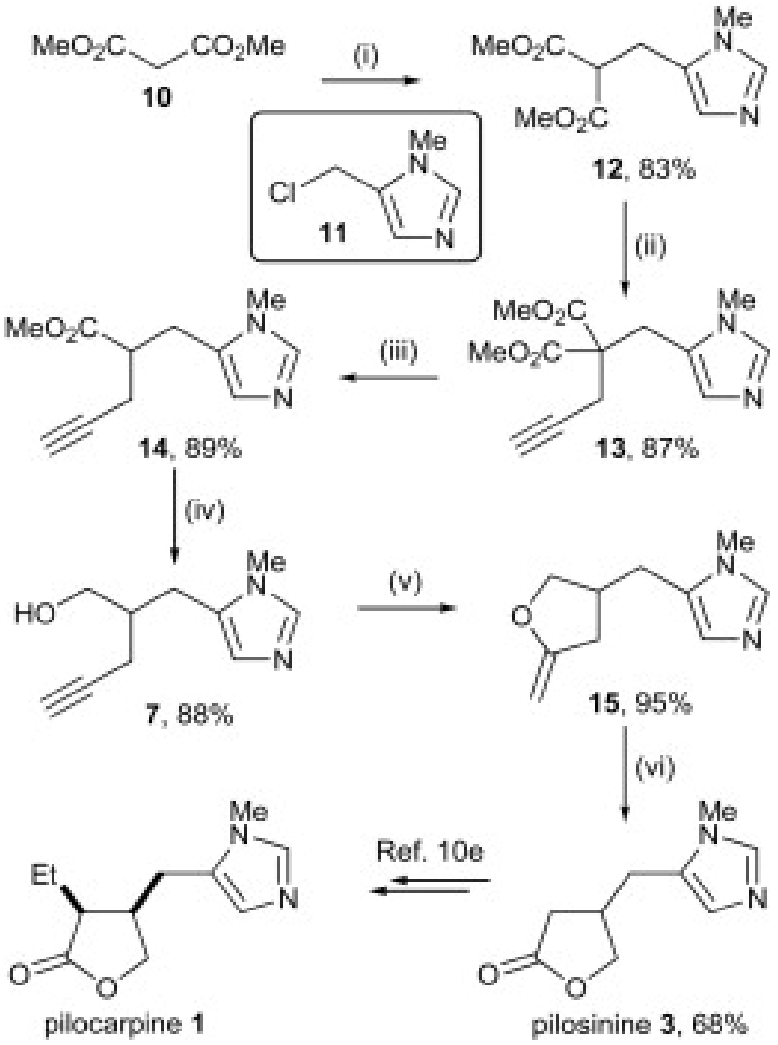


Mechanism of action.*m*-cholinomimetic, the mechanism of action is due to the stimulation of peripheral m-cholinoceptors, which leads to the contraction of the circular muscle of the iris and the ciliary muscle, accompanied by the narrowing of the pupil and the opening of the angle of the anterior chamber of the eye, improving the outflow of intraocular fluid, which generally causes a decrease in intraocular pressure and improves trophic processes in eye tissues.

Properties. Colorless crystals or white, odorless crystalline powder. Hygroscopic, very easily soluble in water, easily soluble in alcohol, practically insoluble in ether and chloroform.

The natural dextrorotatory cis-isomer exhibits activity. Pilocarpine is isolated from the leaves of plants of the genus Pilocarpus, in which its content reaches 0.8% (based on dry matter).

Synthesis.

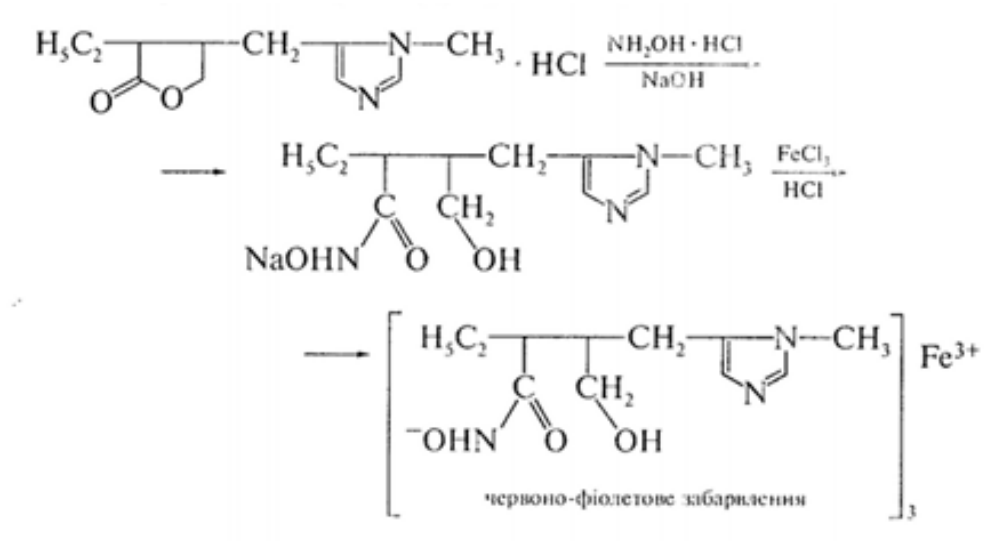


Identification.

1. Reaction to chlorides:
2. The reaction of perchromic acid formation:

(H_2O_2 + conc. H_2SO_4 + $K_2Cr_2O_7$) → in the presence of pilocarpine, they are extracted with chloroform and color the CHCl3 layer in a blue-violet color.

3. Specific rotation from +88.5 ° to +91.0 ° (2% aqueous solution).
4. Hydroxam test (butyrolactone):



Quantitative definition.

1. Acidimetry in a non-aqueous environment in the presence of mercury(II) acetate, s = 1.

2. Alkalimetry in an alcoholic medium, s = 1.

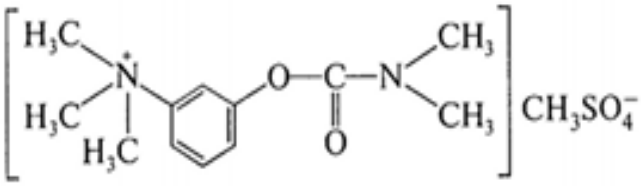
Storage. In a well-closed container that protects against light and moisture.

Application. Cholinolytic (miotic) agent. It is prescribed in the form of eye drops or ointment for the treatment of glaucoma.

Anticholinesterase agents

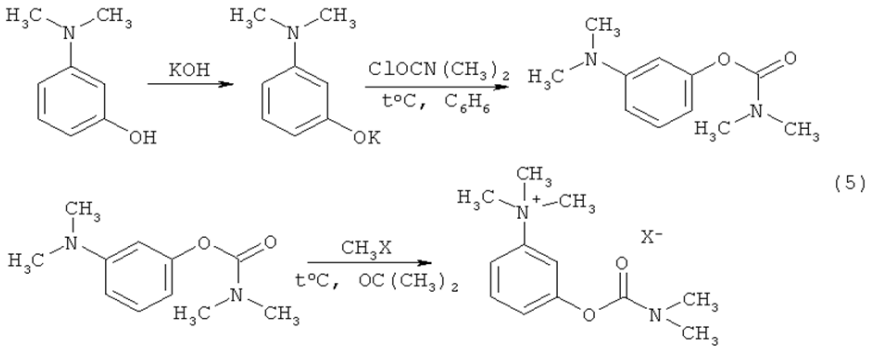
Reversible anticholinesterase drugs

Neostigmine methyl sulfate (Proserin)



Mechanism of action. It reversibly blocks cholinesterase, which leads to the accumulation and strengthening of the action of acetylcholine on organs and tissues and the restoration of neuromuscular conduction.

Synthesis.



(5)

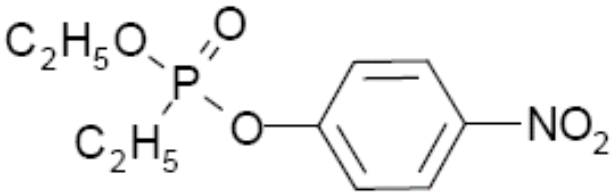
Properties. White crystalline powder without odor, bitter taste. Hygroscopic. It acquires a pinkish hue in the light. Very easily soluble in water (1:10), easily - in alcohol (1:5).

Storage. In well-closed cans made of dark glass that protect against light.

Application. Anticholinesterase, miotic agent for glaucoma. Proserin is also used for myasthenia, movement disorders, and neuritis.

Irreversible anticholinesterase drugs

Armin



Mechanism of action. Irreversible inhibits cholinoesterase, activates the process of synaptic transmission in cholinergic nerve endings. Causes a strong miotic effect, lowers intraocular pressure. It forms a strong complex with cholinesterase, and if special reactivators are not used, the activity of the enzyme is not restored.

Properties. Yellow or dark yellow liquid, odorless. Slightly soluble in water, the 0.01% solution is a colorless transparent liquid, pH 3.5-5.5. Easily soluble in ethanol, ether, benzene.

Storage. In a place protected from light.

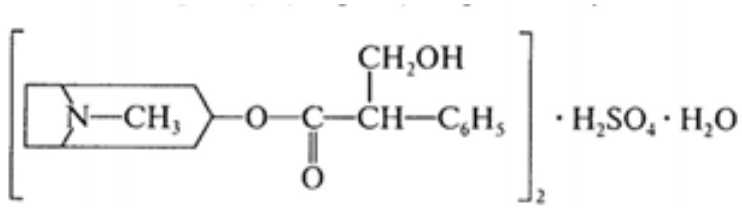
Application. Anticholinesterase, a miotic agent for glaucoma, has a stronger and longer-lasting effect compared to proserin.

Cholinergic blockers (cholinelytics)

m-Cholinoblockers

Mechanism of action. They block m-cholinergic receptors and prevent the interaction of acetylcholine with them. Under their influence, the effects of parasympathetic nerve stimulation are reduced or eliminated.

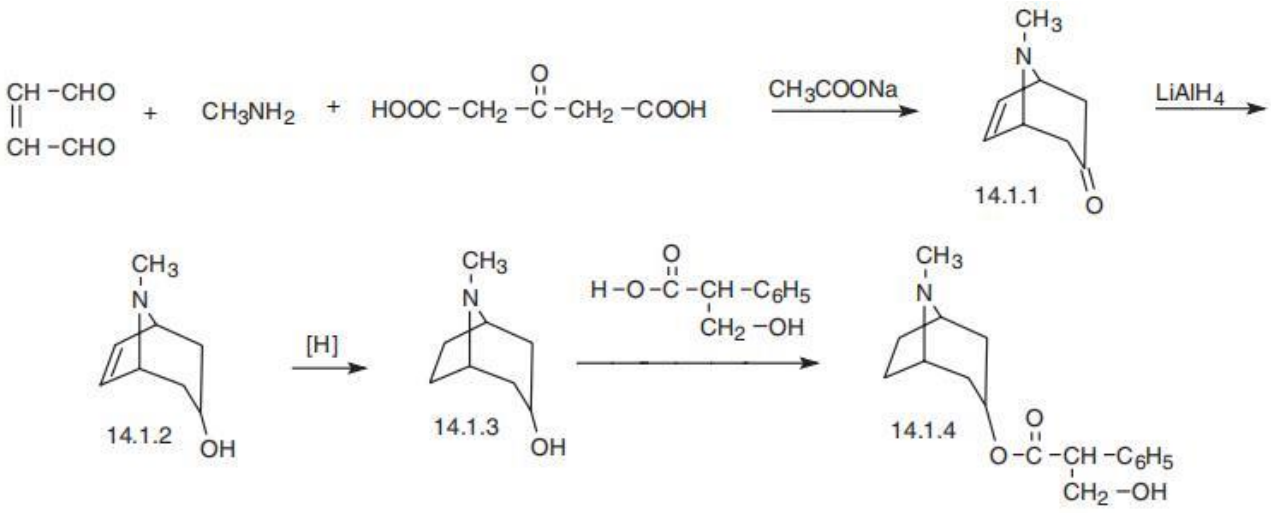
Atropine sulfate



Тропінового ефіру (+),(−)-тропової кислоти сульфат, моногідрат

Atropine was first isolated in 1833 from belladonna. Obtained by racemization of the levorotatory isomer of hyoscyamine with NaOH solution at a temperature of 114-116 °C.

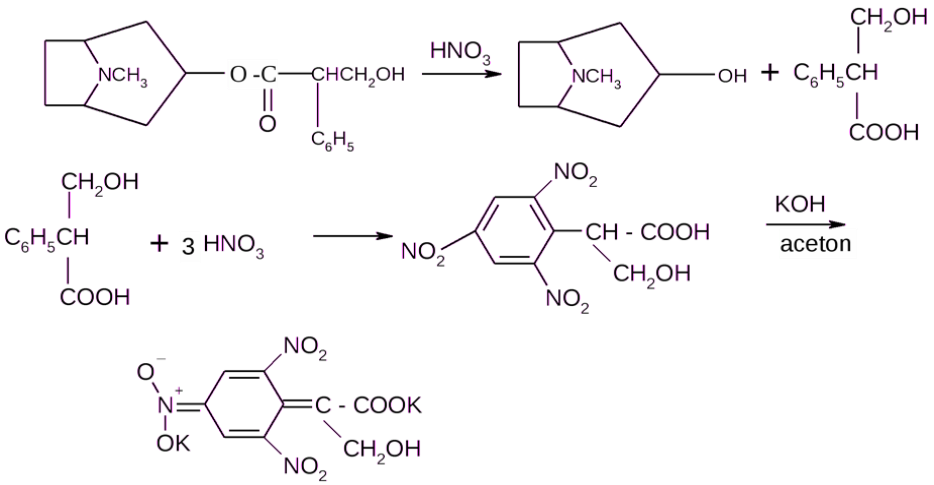
Synthesis.



Properties. White crystalline powder or colorless crystals. Very easily soluble in water, easily soluble in 96% alcohol, practically insoluble in ether. Melts at ~ 190 °C with decomposition.

Identification.

1. IR spectrum, optical rotation.
2. For t. pl. atropine picrate.
3. Vitaly-Moren's reaction to tropic acid:

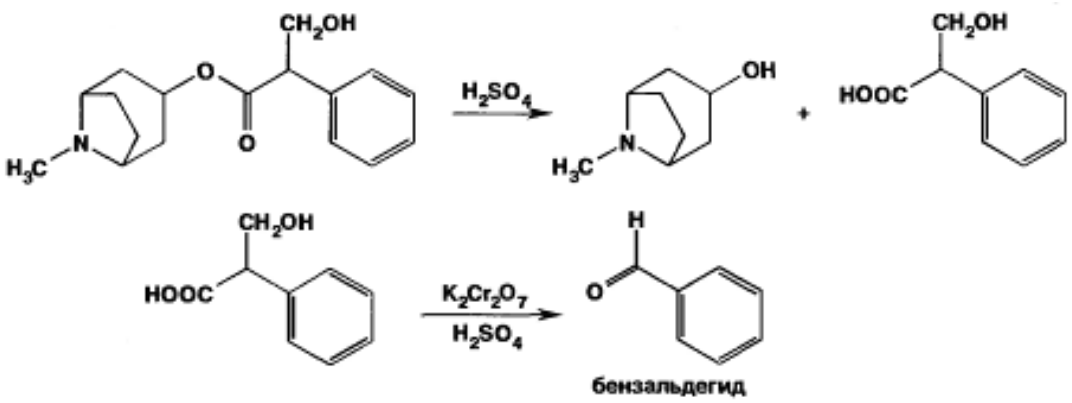


4. Reaction to sulfates: + BaCl2 → BaSO4↓

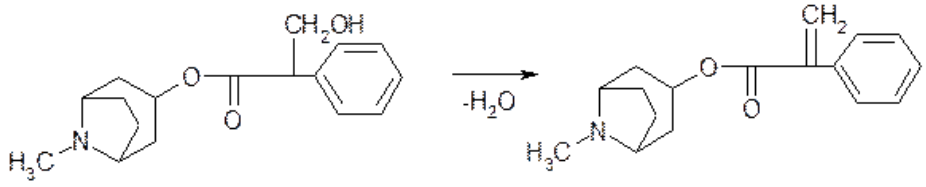
5. General reaction to alkaloids: + K[BiI4] → orange-red precipitate.

6. Non-pharmacopoeial reactions:

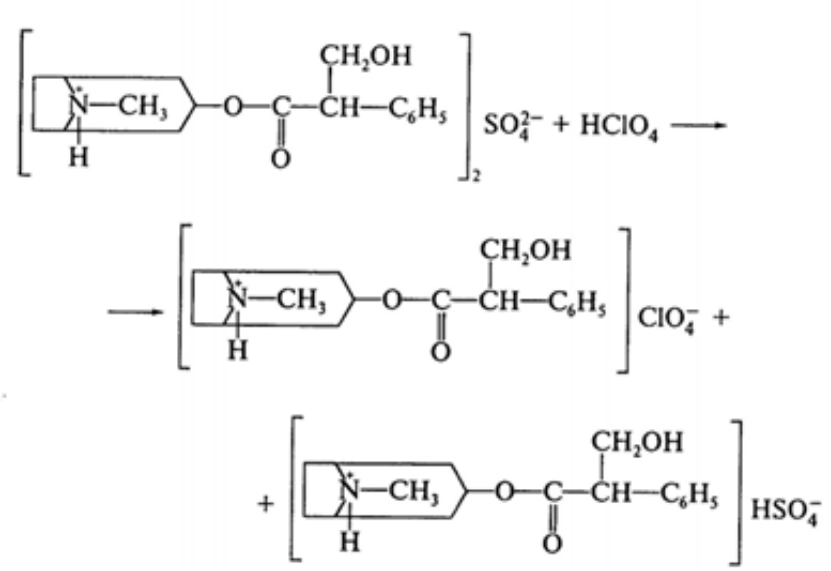
- t. pl. atropine base (115-117 °C) after precipitation with ammonia solution;
- formation of benzaldehyde (smell of bitter almonds) by heating atropine with H2SO4 (conc.) + K2Cr2O7 crystals:



Purity test. An unacceptable admixture in atropine sulfate is apoatropine, which is determined spectrophotometrically:



Quantitative definition.1. Acidimetry in a non-aqueous environment, direct titration with potentiometric fixation of the end point of the titration, s = 1:



2. Alkalimetry in an alcohol-chloroform environment, s = ½.

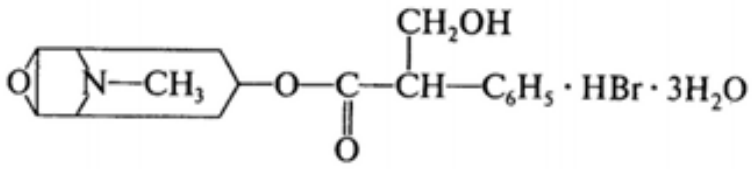
3. Photocolorimetry by reaction with picric acid.

Storage. In a well-sealed container.

Application. Cholinolytic (spasmolytic, mydriatic)

means.

Scopolamine hydrobromide



Скопінового ефіру (−)-тропової кислоти гідробромід, тригідрат

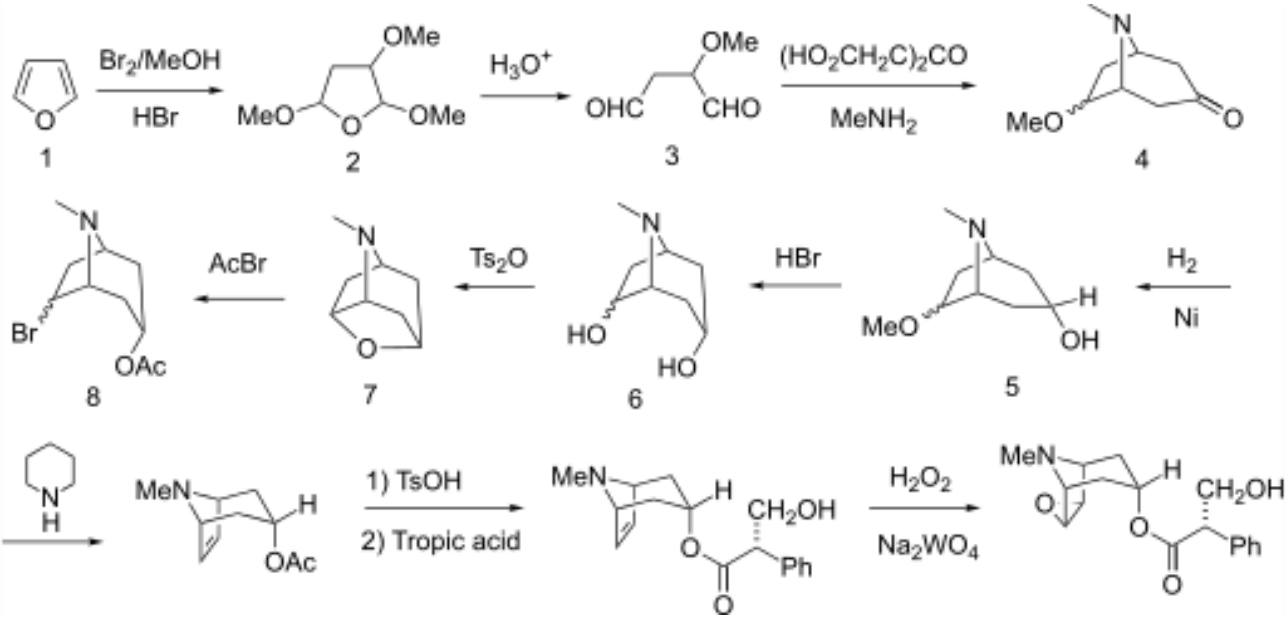
Properties. Colorless transparent crystals or white crystalline powder. Easily soluble in water, soluble in alcohol, very slightly soluble in chloroform.

Identification.

1. Reaction on bromide:+ AgNO3 → AgBr↓.
2. Vitaly-Moren reaction (for tropic acid).
3. T. pl. (192-196 °C) and specific rotation (from –22° to –26°).

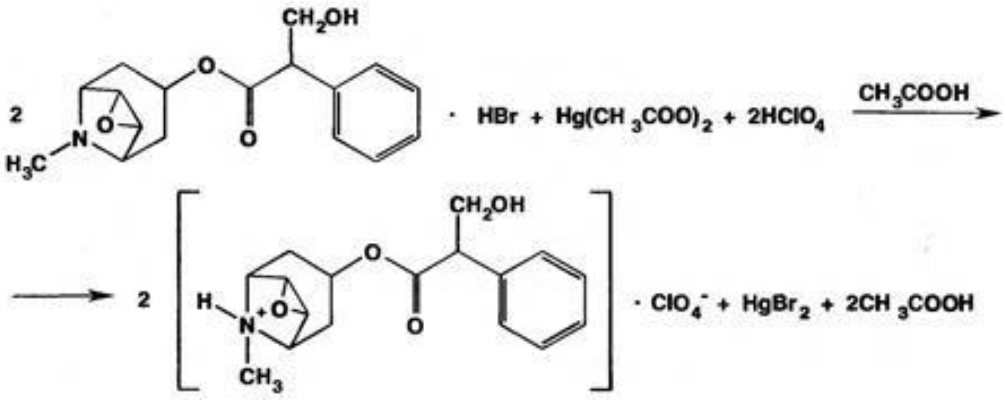
Purity test. Determine apoatropine, aposcopolamine and other reducing substances by reaction with a 0.1 M solution of KMnO4 - the pink color should not disappear within 5 minutes. Extraneous alkaloids are determined by adding ammonia solution - there should be no turbidity.

Synthesis.



Quantitative definition.

1. Acidimetry in a non-aqueous environment, direct titration in the presence of mercury (II) acetate, the indicator is crystal violet, s = 1:

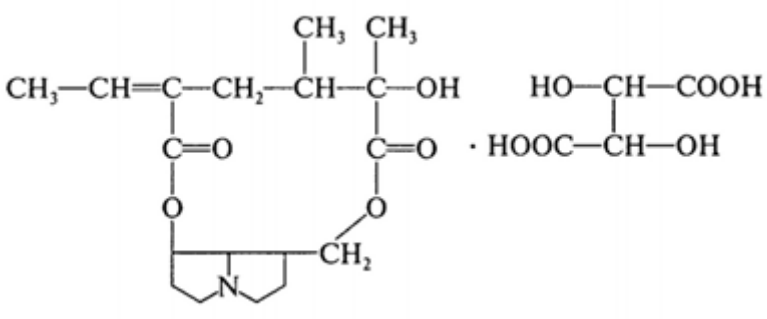


2. Argentometry according to the Fayance method in acetic medium, the indicator is bromophenol blue, s = 1.

Storage. In a well-closed container, in a place protected from light.

Application. Cholinolytic agent, "truth serum".

Platyphyllin hydrotartrate



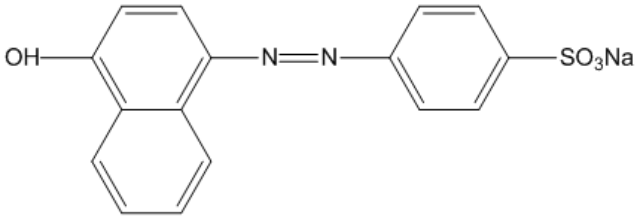
Properties. White crystalline powder without odor or with a weak specific odor, bitter in taste. Easily soluble in water, very slightly soluble in alcohols, practically insoluble in chloroform and ether.

Identification.

1. Reaction of tartrates with potassium salts → white crystalline precipitate.
2. With Mayer's reagent $K_2[HgI_4]$ → white precipitate.
3. With β-naphthol + H_2SO_4 (conc.), heating → green color.
4. Reaction of formation of ferrum (III) hydroxamate → red color.
5. Specific rotation: from –38° to –40° (5% aqueous solution).

Quantitative definition.

1. Acidimetry in a non-aqueous medium, direct titration, indicator – crystal violet, s = 1.
2. Alkalimetry in an alcohol-chloroform environment, s = 1.
3. Photocolorimetry – determination of platyphyllin hydrotartrate in injection solution and tablets by reaction with tropeolin 000-II:

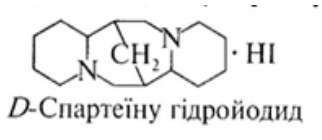


Storage. In a well-sealed container.

Application. Cholinolytic (spasmolytic, mydriatic) agent.

n-Cholinoblockers

Pachycarpine hydroiodide



D-Спартеїну гідройодид

Properties. White crystalline powder. Easily soluble in chloroform, soluble in alcohol and water, difficultly soluble in ether and acetone.

Identification.

1. Reaction to iodides: + $AgNO_3$ → AgI↓.
2. Isolation of the pachycarpine base, which is identified by:

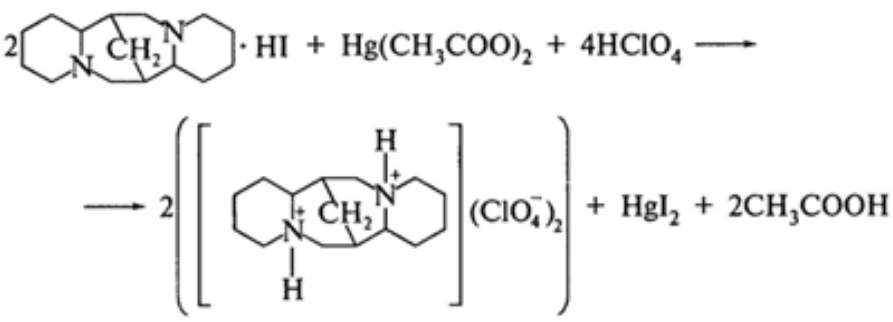
- by the formation of pachycarpine picrate (t. pl.);

- according to the reaction on filter paper with bromine and ammonia vapors - a pink color appears after heating.

3. With an alkaline solution of sodium nitroprusside $Na_2[Fe(CN)_5NO]$ → red-brown precipitate, which dissolves in an excess of HCl.
4. Specific rotation: from +8.6° to +9.6° (7% solution in alcohol).

Quantitative definition.

1. Acidimetry in a non-aqueous environment, direct titration in the presence of mercury (II) acetate, the indicator is crystal violet, s = 1:



2. Argentometry, Fayance method, indicator – sodium sosinate, s = 1.
3. Alkalimetry in an alcoholic medium using thymolphthalein, s = 1.
4. Photocolorimetry.

Storage. In a place protected from light.

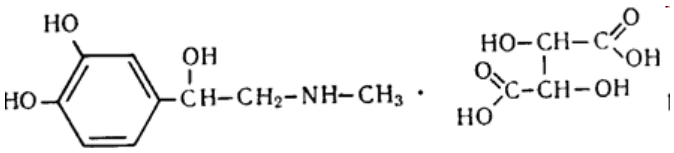
Application. Ganglioblocker; a tool that stimulates the muscles of the uterus.

Means acting on andrenoceptors

Andrenomimetics

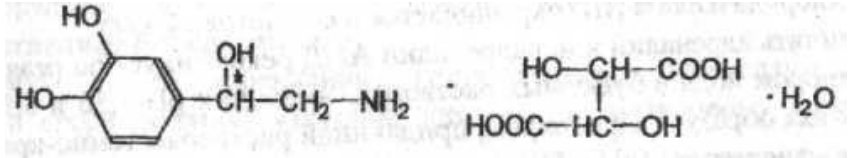
Epinephrine

(Adrenaline hydrotartrate)



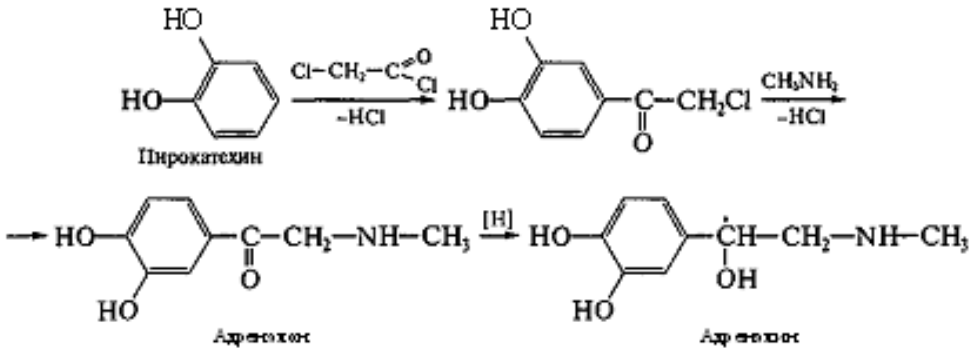
Norepinephrine

(Noradrenaline hydrotartrate)



Mechanism of action. Adrenomimetics have a direct, very strong stimulating effect on α-adrenoceptors and a more moderate effect on β-adrenoceptors.

Synthesis.



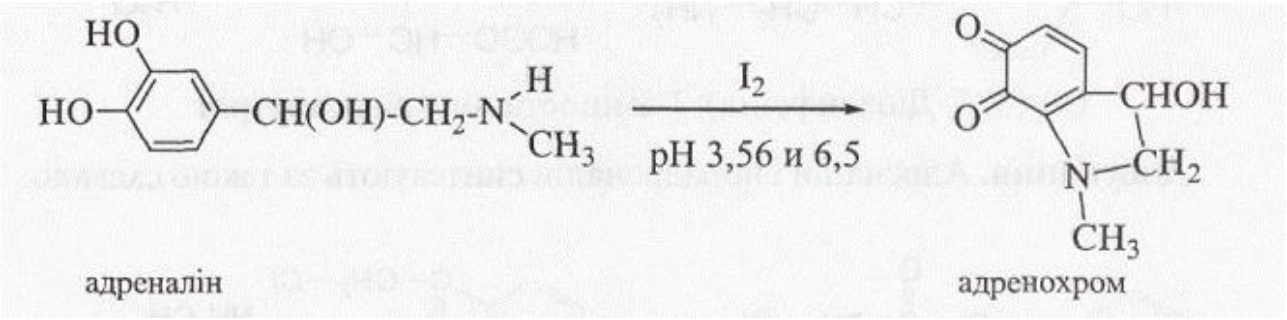
Properties. Epinephrine and norepinephrine are white or white with a yellowish tinge, odorless crystalline substances. Easily soluble in water, practically insoluble in ether and chloroform, sparingly soluble in ethanol. Dissolve in alkali solutions, can be oxidized, under the influence of light and air oxygen form colored oxidation products.

Identification:adrenaline hydrotartrate.

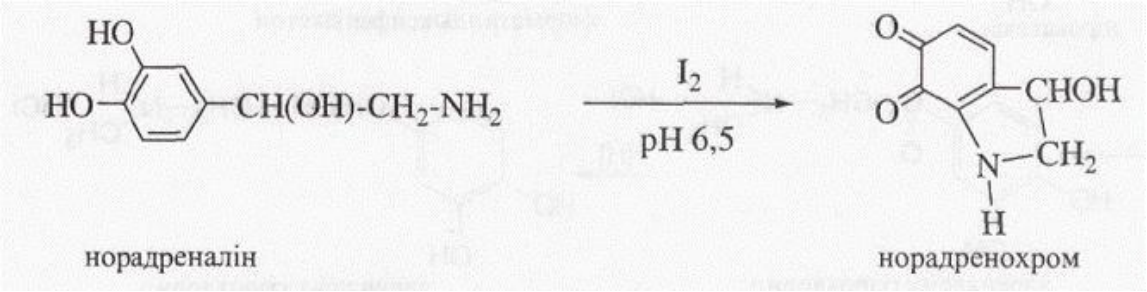
1. Specific rotation, UV and IR spectra.

2. To distinguish between epinephrine and norepinephrine - by the reaction of oxidation with a 0.1 M solution in buffer solutions with a pH of 3.56 and 6.5.

Epinephrine → adrenochrome: dark red (pH 3.56) or red-violet (pH 6.5) color:



Norepinephrine → noradrenochrome: red-violet color (pH 6.5):

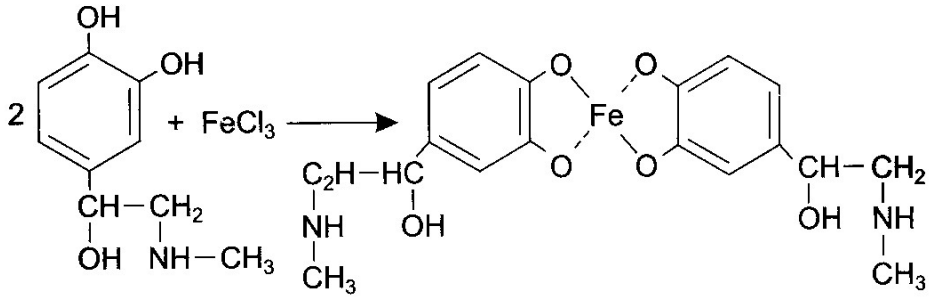


3. Characteristic reaction to tartrates.

4. Non-pharmacopoeial reactions:

- Epinephrine and norepinephrine + FeCl3 → emerald-green color,

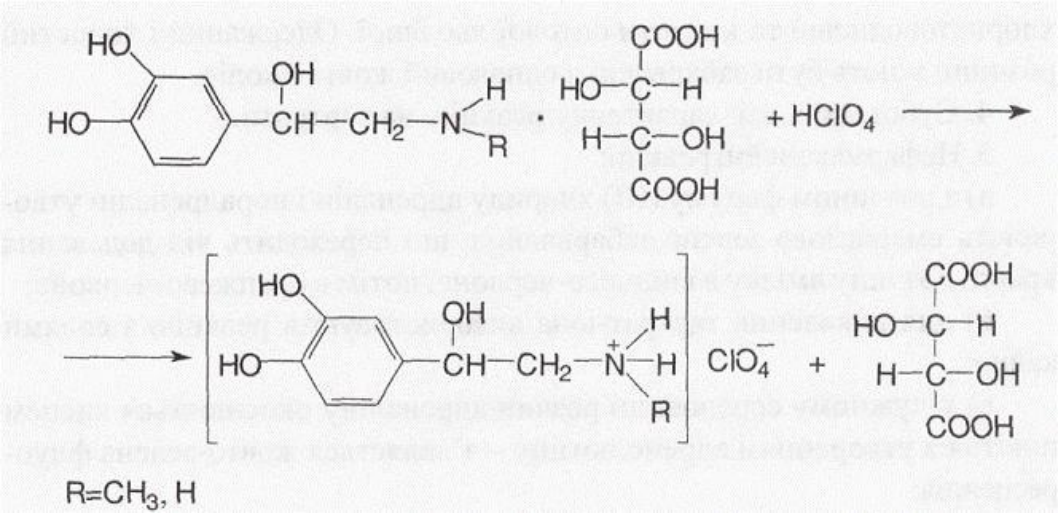
which goes from adding a drop of ammonia to cherry-red, then to orange-red:



- to detect the tartrate ion, a reaction with potassium salts is used.

Quantitative definition.

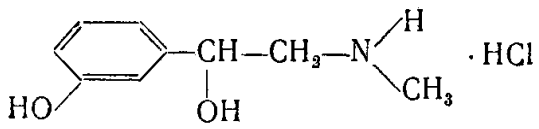
- Acidimetry in a non-aqueous medium, titrate in the medium
- of anhydrous acetic acid, the indicator is crystal violet
- or methyl violet, s = 1:



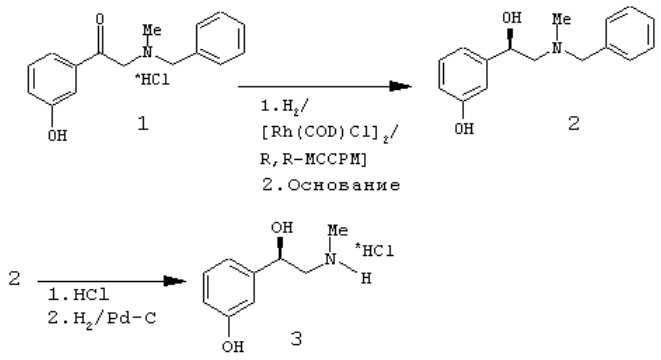
The content of epinephrine and norepinephrine hydrotartrates in solutions for injections is determined by photocolorimetry.

Phenylephrine hydrochloride

(Mesaton)



Synthesis

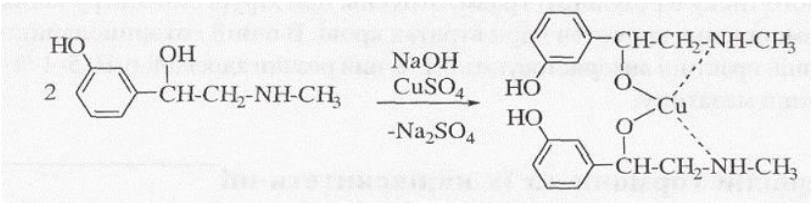


Properties. White or white with a yellowish tinge, odorless crystalline powder. Easily soluble in water, 95% alcohol and practically insoluble in ether.

Identification.

1. Mesaton solution + $FeCl_3$ → purple color.

2. + $CuSO_4$ + NaOH → blue-violet complex, insoluble in ether:

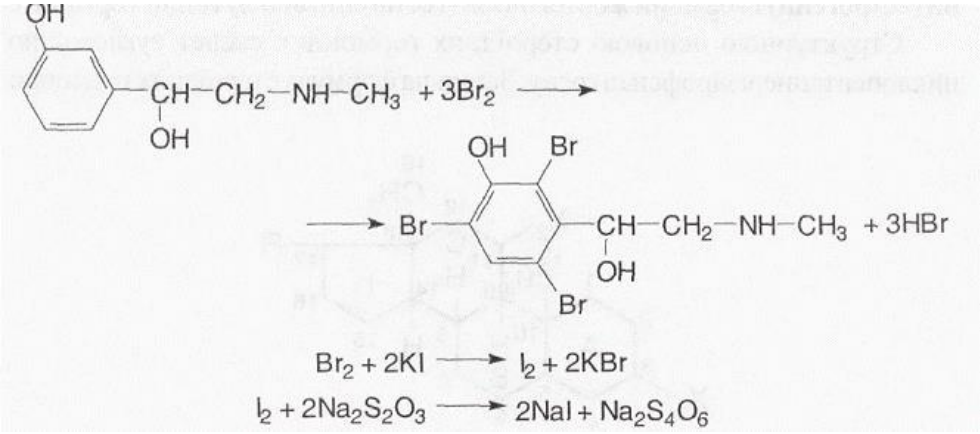


3. Reaction to chlorides: + AgNO3 → AgCl↓.

Quantitative definition.

Bromatometry, reverse titration, indicator - starch, s = 1:

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



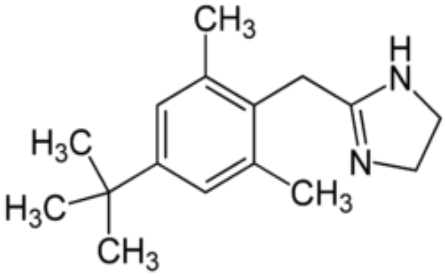
Mesaton can also be quantitatively determined by the methods of acidimetry in a non-aqueous environment in the presence of mercury (II) acetate or by the bound acid HCl by the methods of alkalimetry, argentometry, mercurimetry.

Storage. In a place protected from light, in a hermetically sealed container made of dark glass or in sealed ampoules.

Application. Epinephrine, norepinephrine, and phenylephrine are used as adrenomimetic (vasoconstrictor) agents for collapse, a sharp drop in blood pressure as a result of injuries, poisoning, during surgical interventions, to reduce bleeding and blood loss.

In ophthalmic and otorhinolaryngological practice, a 0.1% solution of epinephrine and 0.5-1% solutions of mesatone are used.

Xylometazoline



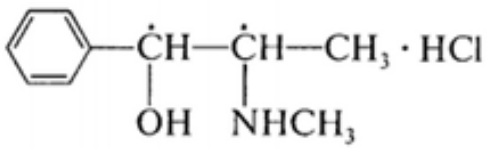
Mechanism of action.α-Adrenostimulator causes the narrowing of blood vessels of the nasal mucosa and adjacent areas of the nasopharynx, thereby eliminating swelling and hyperemia of the nasal mucosa and nasopharynx.

Application. Symptomatic treatment of nasal congestion during colds, hay fever, other allergic rhinitis and sinusitis.

To facilitate the outflow of secretions in diseases of the paranasal sinuses.

Adjunctive therapy in case of otitis media (to eliminate swelling of the mucous membrane).

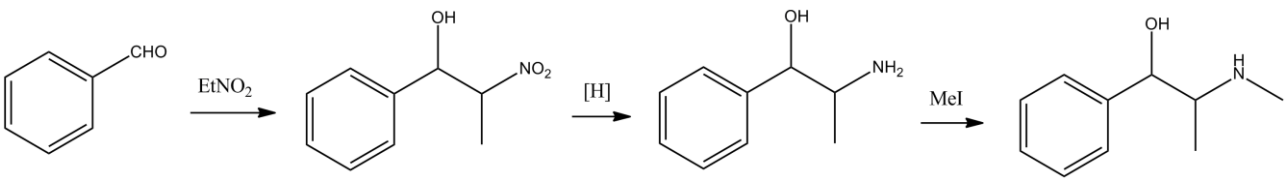
Ephedrine hydrochloride



(−)1-Феніл-2-метиламінопропанолу-1 гідрохлорид

Mechanism of action. Sympathomimetic, stimulates α- and β-adrenoceptors.

Synthesis.

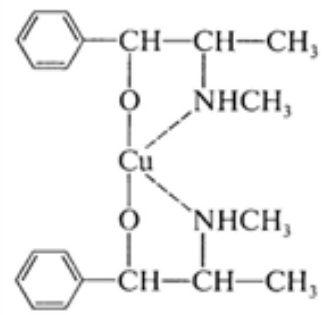


Properties. Colorless needle crystals or white crystalline powder without odor, bitter in taste. Easily soluble in water, soluble in alcohol, practically insoluble in ether. The base of ephedrine is soluble in water, therefore, under the action of alkalis, a solution of its salt does not precipitate.

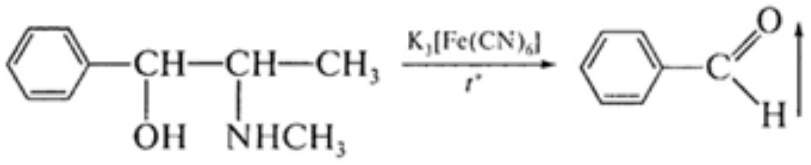
Identification.

1. Reaction on chloride: + $AgNO_3$ → AgCl↓.

2. + $CuSO_4$ + NaOH → blue complex:



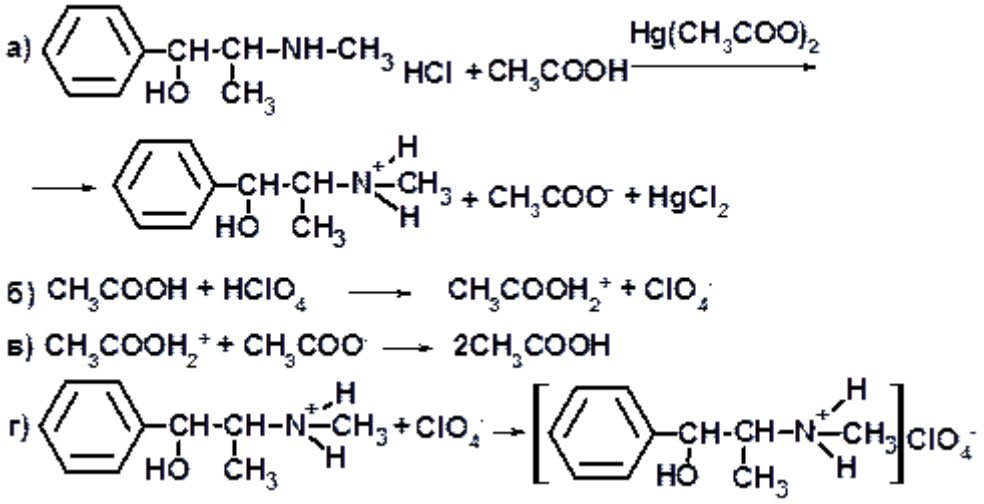
3. When heated with a crystal of potassium ferricyanide (III), the smell of benzaldehyde (bitter almonds) appears:



4. Specific rotation: from –33° to –36° (5% aqueous solution).

Quantitative definition.

1. Acidimetry in a non-aqueous environment in the presence of mercury (II) acetate, s = 1:



2. Alkalimetry in an alcohol-chloroform environment, s = 1.

3. Argentometry by the associated acid HCl, s = 1.

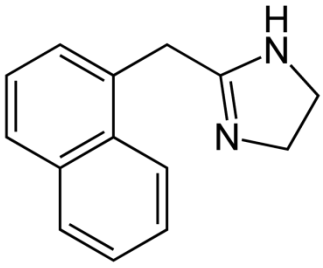
Storage. In a well-closed container that protects from light.

Application.

Sympathomimetic (vasoconstrictor, bronchodilator) agent.

Naphazoline nitrate

(Naphthysine)

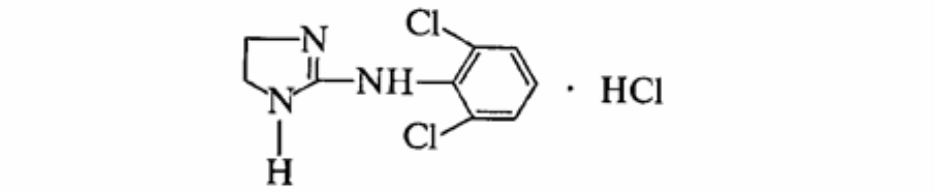


·HNO_3

Mechanism of action. Stimulates the sympathetic nervous system and acts on α-adrenoceptors. As a result of the vasoconstrictor effect, swelling, hyperemia, and exudation are reduced, which facilitates nasal breathing in rhinitis.

Application. Acute rhinitis. As an auxiliary agent for inflammation of the paranasal sinuses and middle ear. To reduce edema of the mucous membrane during diagnostic intervention.

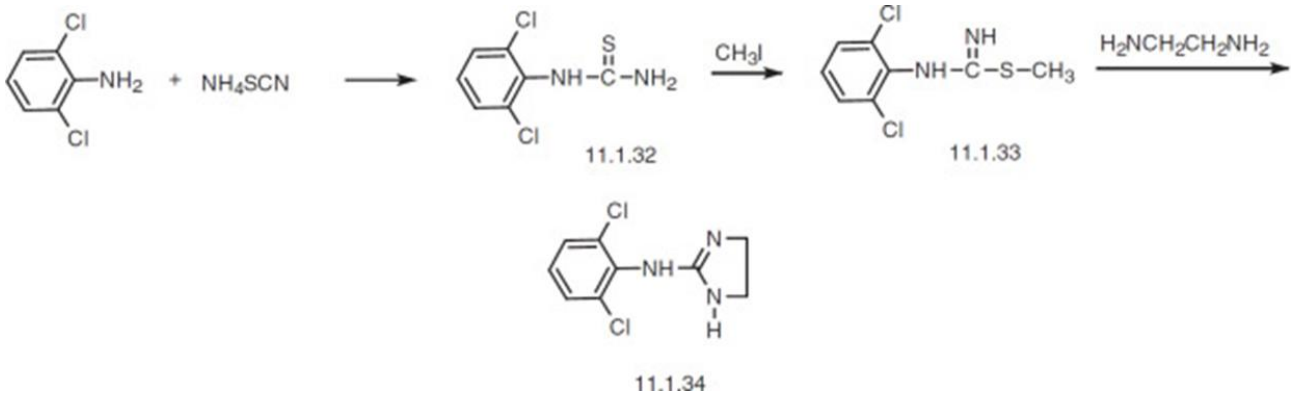
Clonidine hydrochloride (Clofelin)



2-(2', 6'-Дихлорфеніламіно)-імідазоліну гідрохлорид

Mechanism of action. Agonist of α2-adrenergic receptors, imidazoline receptors, hypotensive agent of central action, which acts on various neurohumoral regulation of vascular tone.

Synthesis.



11.1.32 11.1.33 11.1.34

Properties. Crystalline powder of white or almost white color. Soluble in water and 96% ethanol, practically insoluble in chloroform and ether.

Identification.

- IR-, UV-spectra, TLC.
- Reaction to chlorides: + $AgNO_3$ → AgCl↓.

Quantitative definition.

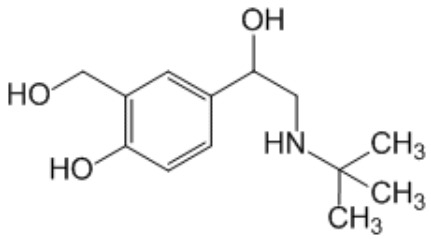
1. Acidimetry in a non-aqueous environment in the presence of mercury (II) acetate, the indicator is crystal violet, s = 1.

2. Alkalimetry in an alcoholic medium, the titrant is an ethanolic NaOH solution, s = 1.

Storage. In a well-closed container that protects from light.

Application. Hypotensive agent.

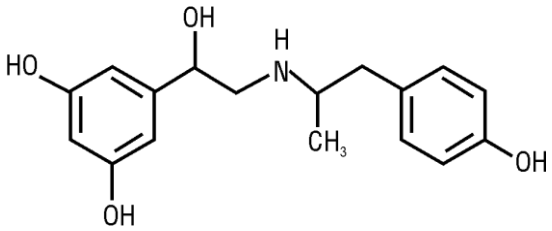
Salbutamol



Mechanism of action.A selective agonist of β2-adrenergic receptors, it has practically no effect on β1-adrenergic receptors of the heart. Short-term (from 4 to 6 hours) bronchodilation with rapid onset (approximately within 5 minutes) with airway obstruction.

Application. With bronchial asthma, chronic obstructive bronchitis, emphysema of the lungs.

Fenoterol

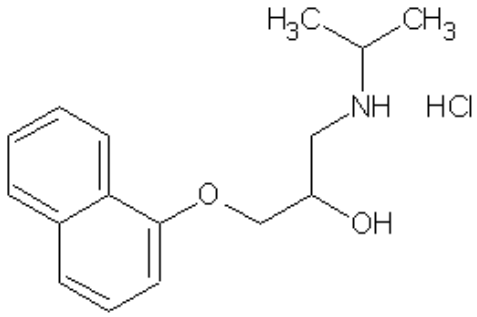


Mechanism of action. Selective β2-adrenoceptor agonist.

Application. Treatment of acute asthma attacks, prevention of exercise-induced asthma, treatment of allergic and non-allergic asthma.

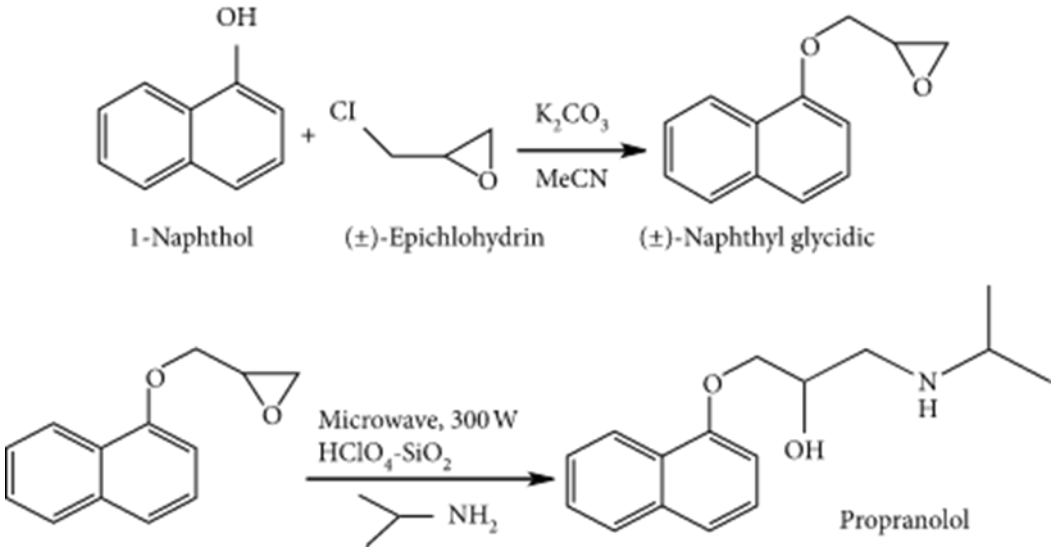
Adrenoblockers(adrenolytics)

Propranolol hydrochloride



Mechanism of action. Non-selective blocker of β-adrenoceptors.

Synthesis.



Properties. White powder, soluble in water, ethyl alcohol,

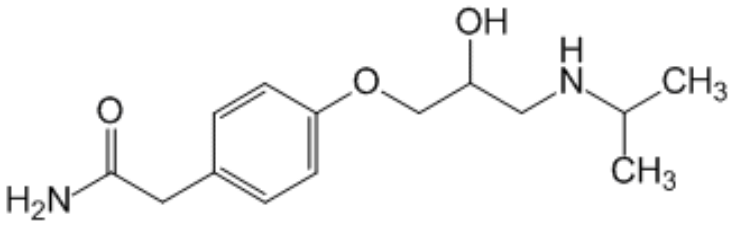
t. pl. = 163–166 °C.

Identification. IR spectrum, mp, TLC on silica gel plates in the ammonia-methanol system.

Quantitative definition. Alkalimetry with potentiometric fixation of the end point of the titration, s = 1.

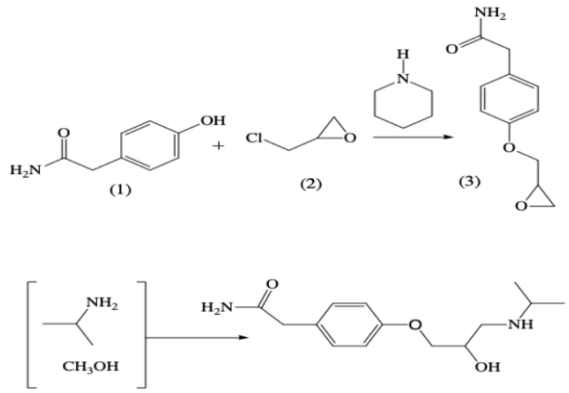
Application. Arterial hypertension, portal hypertension, ischemic heart disease, sinus, supraventricular tachycardia.

Atenolol



Mechanism of action. Cardioselective blocker of β-adrenergic receptors.

Synthesis.



Application. Arterial hypertension, angina pectoris, tachycardia, arrhythmia, myocardial infarction.

General material and bulk-methodological support of the lecture:

- ✓ computer presentation;
- ✓ illustrative materials;
- ✓ examples of solving typical tasks or performing typical tasks;
- ✓ multimedia projector.

Questions for self-control:

1. Classification of drugs that affect efferent innervation

2.Means acting on cholinergic receptors

3.Analysis of anticholinesterase agents

4.Cholinergic blockers (cholinelytics)

5.Means that act on andrenoceptors (andrenomimetics)

6.Adrenoblockers (adrenolytics)

References:

Main:

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2. State Pharmacopoeia of Ukraine: in 3 volumes / Derzh. medical service of Ukraine funds, Ukr. of science pharmacopoeia medicine quality center means - 2nd edition. - Kh.: Ukr. of science pharmacopoeia medicine quality center means, 2014. - Vol. 2. - 724 p.

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11. Pharmaceutical chemistry. General and special pharmaceutical chemistry. Medicines of an inorganic nature: laboratory-practical classes. Study guide / L.G. Mishina - Vinnytsia: PP "TD "Edelweiss and K"", 2010. - 384 p.

12. Analytical chemistry and instrumental methods of analysis / A.I. Gab, D.B. Shakhnin, V.V. Malyshev -Ukraine University, 2018- 396 p.

Electronic information resources:

1. Specialized medical online publication for doctors, pharmacists, pharmacists, students of medical and pharmaceutical universities. - [Electronic resource]. - Access mode:http://www.morion.ua.

2. World Health Organization. - [Electronic resource]. - Access mode:http://www.who.int.

3. Pharmaceutical encyclopedia. - [Electronic resource]. – Access mode: http://www.pharmencyclopedia.com.ua.

4. Official website of the International Organization for Standardizationhttp://www.iso.org/iso/home.html

5. Compendium online. [Electronic resource]. - Access mode:https://compendium.com.ua/bad/

6. Medline search database [Electronic resource]. – Access mode: National Library of Medicinehttps://www.nlm.nih.gov/bsd/medline.html

Lecture No. 3

Topic: Cardiotonic, antiarrhythmic drugs. Means that improve blood supply to organs and tissues. Peripheral vasodilators.

Actuality of theme: Pharmaceutical chemistry is a science that studies methods of preparation, structure, physical and chemical properties of medicinal products; relationship between their chemical structure and action on organism; methods of quality control of drugs and changes that occur during their storage, as well as their use in medicine. Therefore, it is urgent to solve the problems facing pharmaceutical chemistry with the help of physical, chemical and physico-chemical methods, which are used both for synthesis, as well as for the analysis of medicinal products.

The purpose:the formation of students' knowledge about the peculiarities of the storage of medicinal products, which affect the afferent nervous system, as well as the characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of obtaining, methods of analysis, application in medicine. As a result of the lecture, students should learn the properties and methods of medical analysis means affectingon the cardiovascular system.

Basic concepts:pharmaceutical chemistry, qualitative analysis, quantitative analysis, State Pharmacopoeia of Ukraine, physicochemical methods of analysis, impurities, express analysis.

Plan and organizational structure of the lecture:

1.Preparatory stage

1.1.Determination of educational The purposes.

1.2.Providing positive motivation.

2. The main stage

Presentation of lecture material

Plan:

-Classification by pharmacological properties

- Cardiotonic drugs (cardiac glycosides)

- Antiarrhythmic drugs

-Antianginal drugs (nitrovasodilators)

3. The final stage

3.1. Summary of the lecture, general conclusions.

3.2. The lecturer's answers to possible questions

3.3. Tasks for self-training of students.

Content of lecture material (lecture text):

All existing drugs for the treatment of cardiovascular diseases can be combined according to their pharmacological properties into the following main groups:

1. cardiotonic means;

2. antiarrhythmic drugs;

3. means that improve blood supply to organs and tissues, cerebral circulation;

4. hypotensive and hypertensive agents;

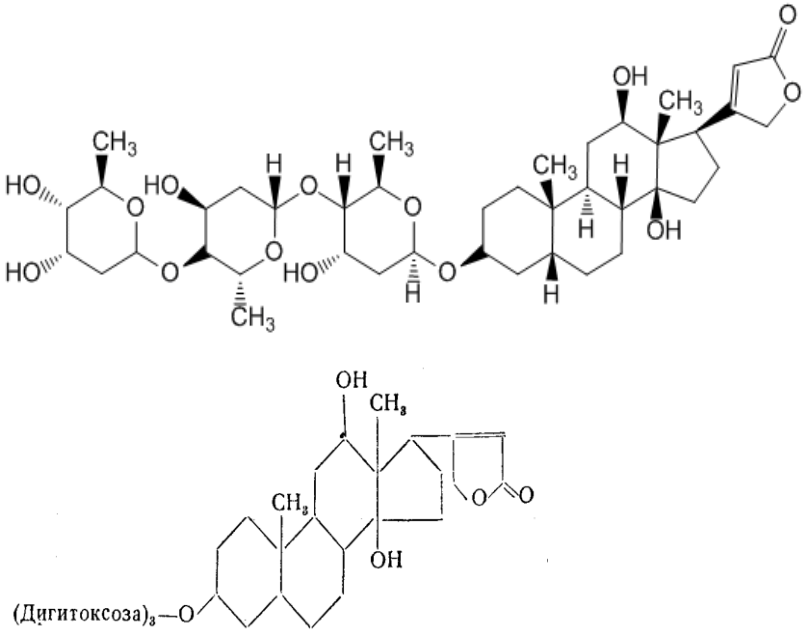
5. angioprotectors and hypolipidemic agents;

6. means that inhibit or stimulate blood coagulation.

Cardiotonic means

(cardiac glycosides)

Digogsin



Mechanism of action. Inhibition of Na+K+ ATPase of cardiomyocyte membranes, increase of calcium ions in SPR of cardiomyocytes.

Properties. White crystalline powder. Practically insoluble in water, easily soluble in a mixture of equal volumes of methanol and methylene chloride, slightly soluble in 96% alcohol.

Identification.

1. IR spectrum, TLC.

2. [α]20D = from +10° to +13° (2% solution in anhydrous pyridine).

3. According to the reaction of an alcoholic solution of the substance with a solution of dinitrobenzoic acid in an alkaline environment, a purple color is obtained.

4. To the acetic acid solution of the substance, add FeCl3 solution and carefully - concentrated H2SO4 - a brown color should appear on the boundary of the separation of the two layers (the upper layer gradually turns green, then blue).

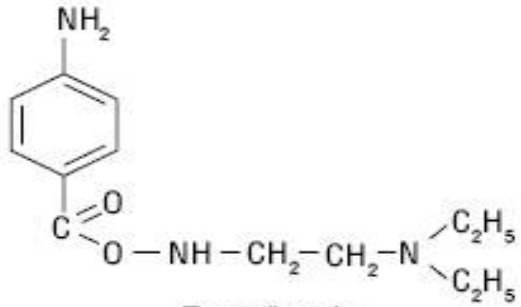
Quantitative definition. The method of spectrophotometry after reaction with a solution of alkaline sodium picrate.

Storage. In a well-closed container that prevents exposure to light.

Application. Chronic heart failure, atrial fibrillation and flutter (to regulate heart rate).

Antiarrhythmic drugs

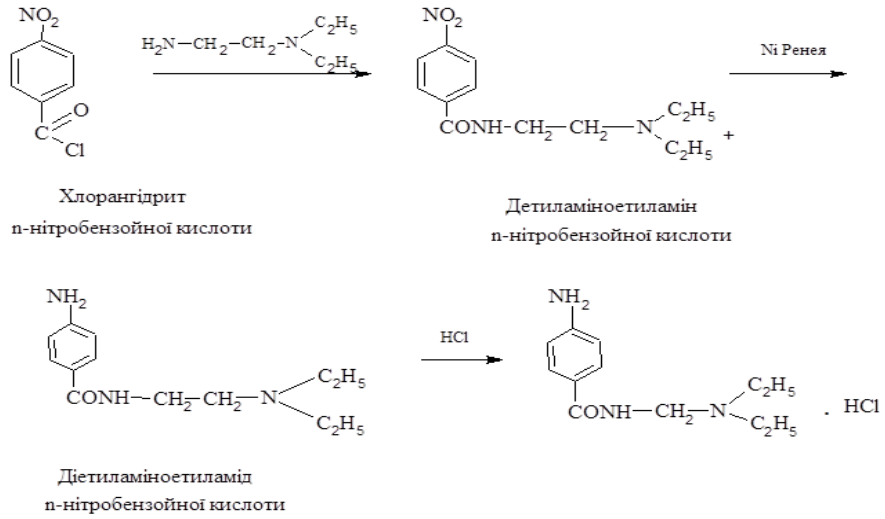
Procainamide hydrochloride



Прокаїнамід

Mechanism of action. Reduces the activity of the sodium-potassium pump, causing a weakening of the flow of Na+ ions into the cell and an increase in the intracellular concentration of K+ ions in the myocardium. Procainamide also has local anesthetic properties.

Synthesis.



Properties. Crystalline powder of white or white with a yellow tinge, hygroscopic, very easily soluble in water, easily soluble in 96% alcohol, sparingly soluble in acetone, practically soluble in ether.

Identification.

1. T. pl., IR spectrum.

2. Reaction to chlorides: AgNO3 + Cl–⟶AgCl↓.

3. Reaction to primary aromatic amines.

4. Non-pharmacopoeial reaction with ammonium vanadate. Ammonium vanadate NH4VO3, concentrated sulfuric acid is added to the drug solution and heated - a cherry-red color appears (unlike procaine hydrochloride).

Quantitative definition.

1. Nitritometry, s = 1.

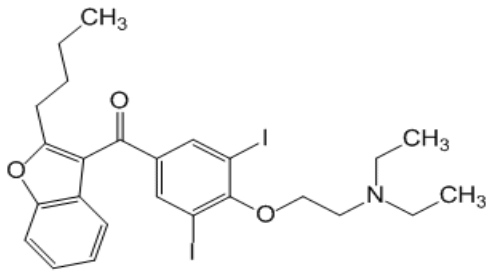
2. Alkalimetry by bound HCl, indicator – phenolphthalein, s = 1.

3. Argentometry by bound HCl, s = 1.

Storage. In well-stoppered dark glass jars.

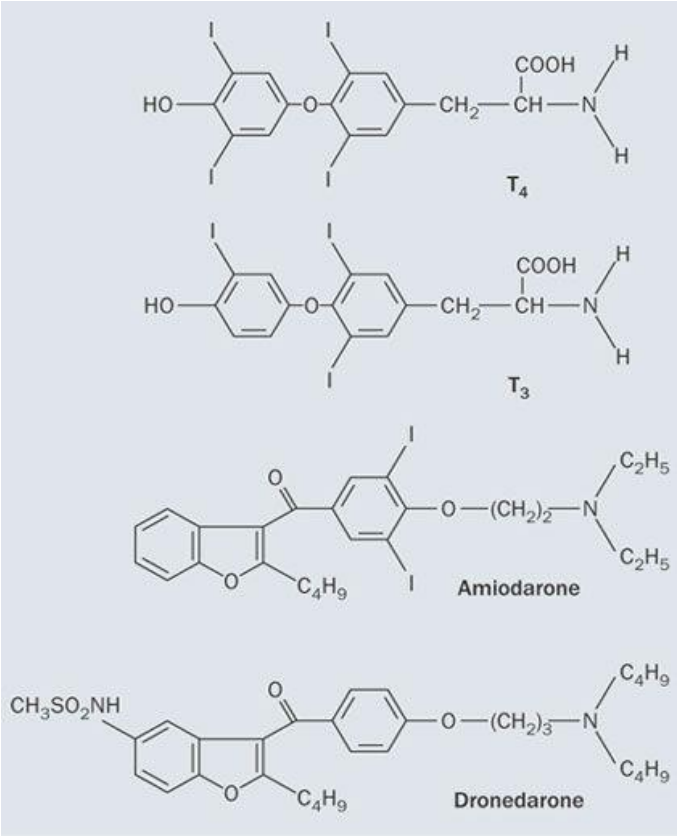
Application. Antiarrhythmic drug. Its chemical structure is similar to procaine hydrochloride, instead of the ether group of procainamide, the hydrochloride contains an amide group. Therefore, procainamide hydrochloride is more stable than procaine, decomposes more slowly by enzymes and is less toxic. It has a slight local anesthetic effect, but the most important pharmacological feature is its ability to reduce the excitability and conductivity of the heart muscle in heart rhythm disorders.

Amiodarone

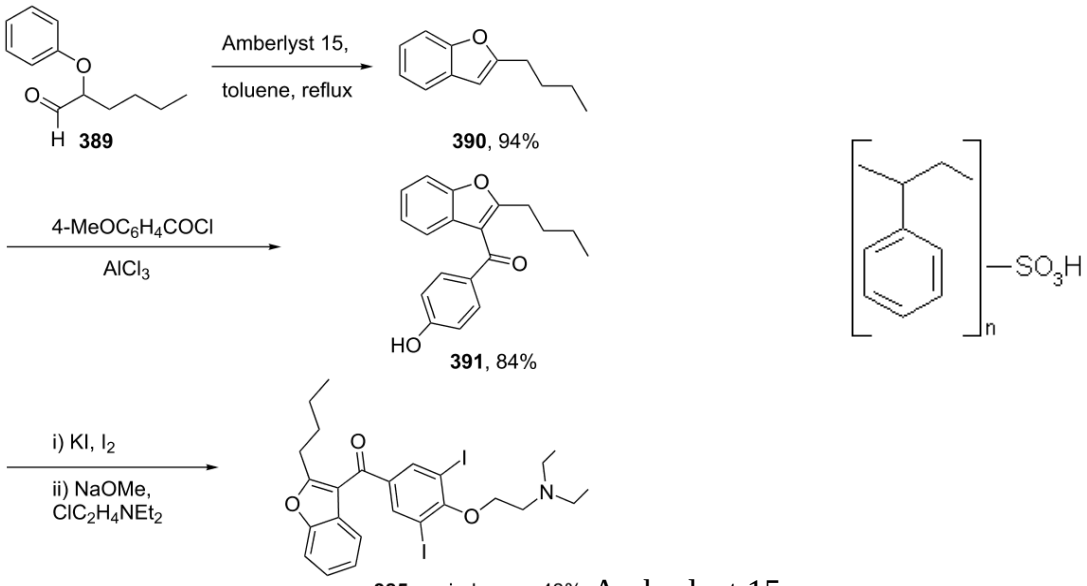


Mechanism of action. Blocks ion channels (mainly potassium, to a lesser extent - calcium and sodium) of cardiomyocyte membranes, inhibits the excitation of alpha- and beta-blockers. Its structure is similar to thyroid hormones, the iodine content is about 37% of its molecular weight. It affects the exchange of thyroid hormones, suppresses the conversion of T4 to T3 (thyroxine-5-deiodinase blockade) and blocks the capture of these hormones by cardiocytes and hepatocytes, which leads to a weakening of the stimulating effect of thyroid hormones on the myocardium.

Similarities in the structure of thyroid hormones and amiodarone



Synthesis.



Amberlyst 15

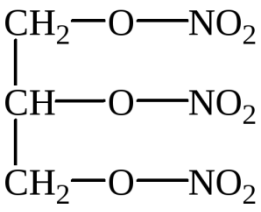
Properties. Crystalline powder of white or cream color. Sparingly soluble in water, soluble in alcohol, well soluble in chloroform.

Application. Severe arrhythmias (as a rule, when other therapy is ineffective or impossible).

Antianginal drugs

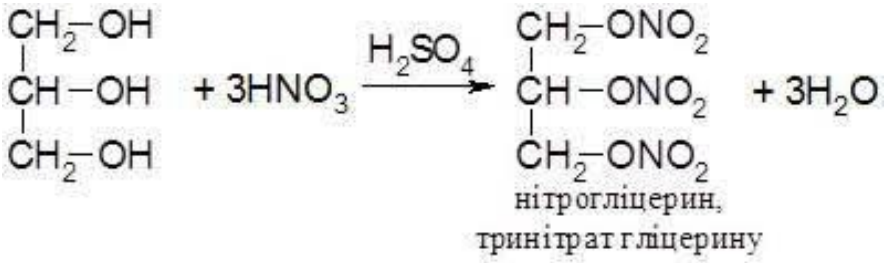
Nitrovasodilators

Glycerin trinitrate solution



Mechanism of action. Associated with the release of the active substance nitric oxide (NO) in vascular smooth muscles. Nitric oxide causes the activation of guanylate cyclase and increases the level of cyclic guanosine monophosphate, which contributes to the relaxation of smooth muscle cells in the vessel walls.

Synthesis.



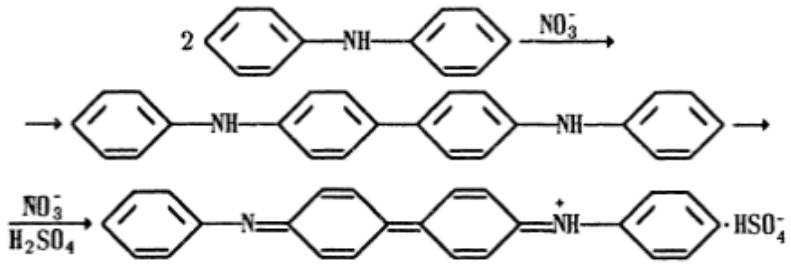
Properties. Ethanol solution of glycerol trinitrate (HTN) is a clear, colorless or light yellow liquid. Miscible with acetone and ethanol. Pure HTN is a colorless liquid, easily soluble in ethanol. Miscible with acetone and immiscible with water.

Identification.

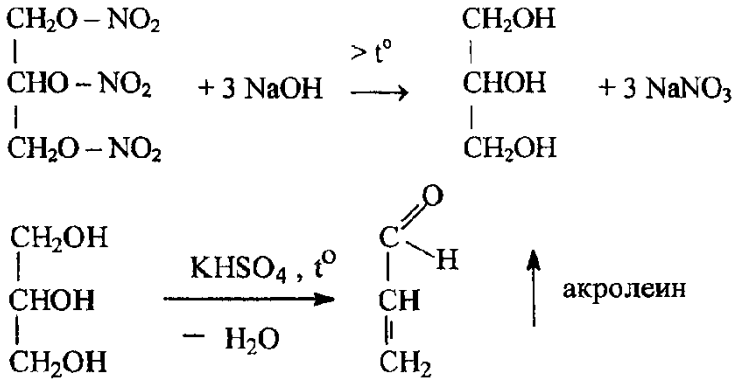
1. IR spectrum, TLC.

2. Non-pharmacopoeial reactions:

- with a solution of diphenylamine in H2SO4 (conc.)→blue color:

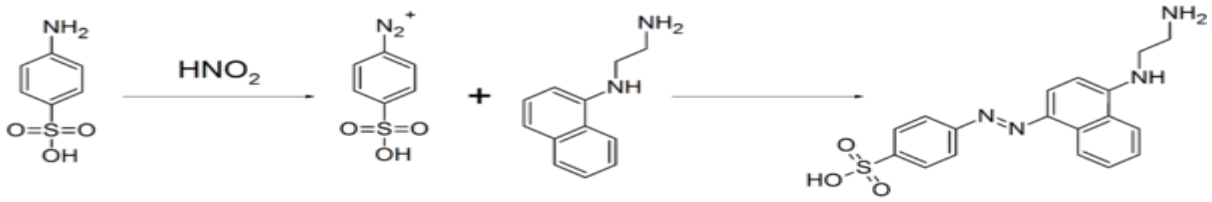


- reaction to the remaining glycerol after alkaline hydrolysis - the smell of acrolein:

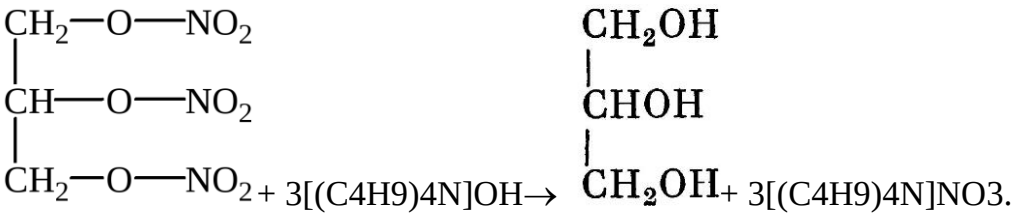


Quantitative definition.

1. Spectrophotometry in the visible region of the spectrum (λ = 540 nm): determination of the optical density of the colored product, which is formed after alkaline hydrolysis of HTN by interaction with a solution of sulfanilic acid in an acidic medium and naphthylenediamine dihydrochloride:



2. Alkalimetry in a non-aqueous environment (in pyridine), the titrant is tetrabutylammonium hydroxide (TFU), s = 1/3:

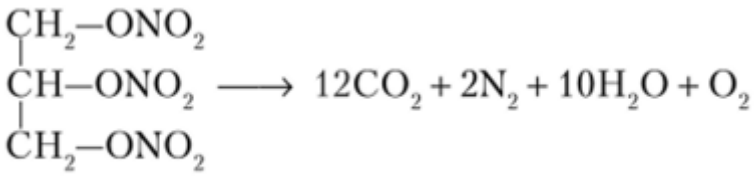


3. Acid-base titration in the presence of H2O2:

$C_3H_5(ONO_2)_3 + 5NaOH \rightarrow NaNO_3 + 2NaNO_2 + CH_3COONa + HCOONa + 3H_2O$.

The excess of NaOH is titrated with a solution of HCl against phenolphthalein, a control experiment is carried out in parallel, s = 1/5.

Storage. Diluted HTN solutions are stored in a place protected from light, at a temperature of 2 to 15 °C. More concentrated solutions are stored in a place protected from light, at a temperature of 15 to 20 °C. Care must be taken when receiving and storing the drug, as it explodes when heated to 180 °C or upon impact:



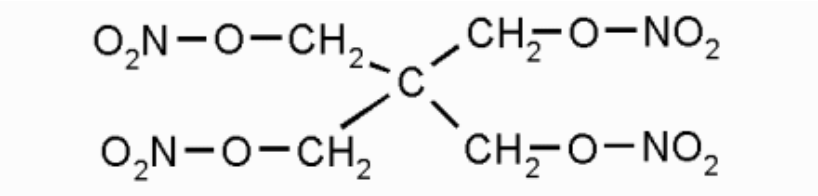
Spilled GNT or its solution must be immediately poured with alkali!

May cause headache in case of skin contact.

Application. Spasmolytic (coronary dilator) agent. Long-acting HTN drugs - Sustak, Nitrong.

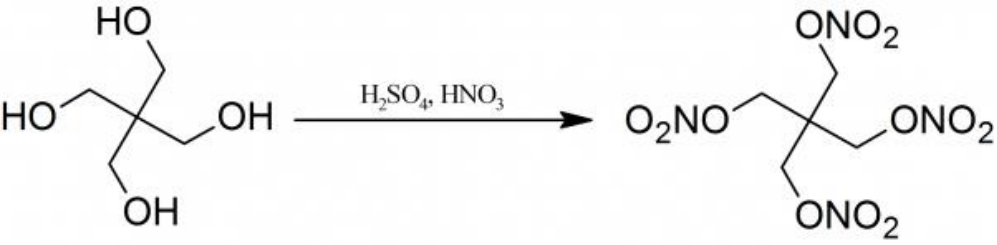
Pentaerythritol tetranitrate

(Erinith)



Mechanism of action. Similar to GNT.

Synthesis.

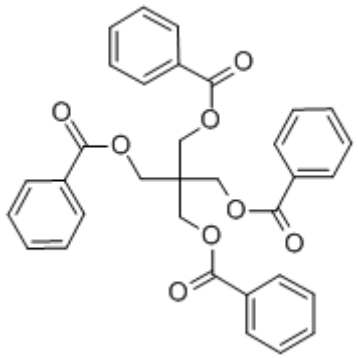


Properties. White crystalline powder. Practically not soluble in water, soluble in ethanol, ether and acetone.

Identification.

1. Reaction after hydrolysis to nitrates with diphenylamine.

2. The alcohol fragment of erinite after hydrolysis is detected by the benzoylation reaction; the product has a t. pl. 99-101 °C:



Quantitative definitionerinite in tablets is carried out gravimetrically after extraction with acetone and evaporation of the solution. The calculation takes into account the content of stearic acid (excipient), which is titrated with NaOH in DMF or acetone.

Storage. In a well-closed container, in a cool place protected from light.

Erinite, like HTN, is an explosive substance.

Application. Spasmolytic (coronary dilator) agent.

General material and bulk-methodological support of the lecture:

- ✓ computer presentation;

- ✓ illustrative materials;
- ✓ examples of solving typical tasks or performing typical tasks;
- ✓ multimedia projector.

Questions for self-control:

1. Classification by pharmacological properties

2.Cardiotonic agents (cardiac glycosides)

3.Antiarrhythmic drugs

4.Antianginal drugs (nitrovasodilators)

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9. Hudoyarova O.S. Pharmaceutical chemistry. - Vinnytsia: "Nilan-LTD" LLC, 2018. - 194 p.

10. Medicinal chemistry: education. manual for students of higher educational institutions / I.S. Hrytsenko, S.G. Taran, L.O. Transition, etc.; for general I.S. Hrytsenko - Kharkiv: NFaU: Golden Pages, 2017. - 552p.

11. Pharmaceutical chemistry. General and special pharmaceutical chemistry. Medicines of an inorganic nature: laboratory-practical classes. Study guide / L.G. Mishina - Vinnytsia: PP "TD "Edelweiss and K"", 2010. - 384 p.

12. Analytical chemistry and instrumental methods of analysis / A.I. Gab, D.B. Shakhnin, V.V. Malyshev -Ukraine University, 2018- 396 p.

Electronic information resources:

1. Specialized medical online publication for doctors, pharmacists, pharmacists, students of medical and pharmaceutical universities. - [Electronic resource]. - Access mode:http://www.morion.ua.

2. World Health Organization. - [Electronic resource]. - Access mode:http://www.who.int.

3. Pharmaceutical encyclopedia. - [Electronic resource]. – Access mode: http://www.pharmencyclopedia.com.ua.

4. Official website of the International Organization for Standardizationhttp://www.iso.org/iso/home.html

5. Compendium online. [Electronic resource]. - Access mode:https://compendium.com.ua/bad/

6. Medline search database [Electronic resource]. – Access mode: National Library of Medicinehttps://www.nlm.nih.gov/bsd/medline.html

Lecture No. 4

Topic: Antagonists of calcium ions. Antioxidants. Agents affecting the renin-angiotensin system.

Hypo- and hypertensive agents.

Actuality of theme: Pharmaceutical chemistry is a science that studies methods of preparation, structure, physical and chemical properties of medicinal products; relationship between their chemical structure and action on organism; methods of quality control of drugs and changes that occur during their storage, as well as their use in medicine. Therefore, it is urgent to solve the problems facing pharmaceutical chemistry with the help of physical, chemical and physico-chemical methods, which are used both for synthesis, as well as for the analysis of medicinal products.

The purpose:the formation of students' knowledge about the peculiarities of the storage of medicinal products, which affect the afferent nervous system, as well as the characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of obtaining, methods of analysis, application in medicine. As a result of the lecture, students should learn the properties and methods of medical analysis means- antagonists of calcium ions, antioxidants, agents affecting the renin-angiotensin system, hypo- and hypertensive agents.

Basic concepts:pharmaceutical chemistry, qualitative analysis, quantitative analysis, State Pharmacopoeia of Ukraine, physicochemical methods of analysis, impurities, express analysis.

Plan and organizational structure of the lecture:

1.Preparatory stage

1.1.Determination of educational The purposes.

1.2.Providing positive motivation.

2. The main stage

Presentation of lecture material

Plan:

-Calcium antagonists

- Antioxidants

- Antihypertensive (hypotensive) drugs

- Antispasmodic agents

3. The final stage

3.1. Summary of the lecture, general conclusions.

3.2. The lecturer's answers to possible questions

3.3. Tasks for self-training of students.

Content of lecture material (lecture text):

*Calcium antagonists*is a group of drugs that block calcium channels.

Classificationby generations

I generation:verapamil, nifedipine, diltiazem.

Characteristics: relatively short duration of action - up to 6.5 hours.

II generation:amlodipine, lercanidipine.

Characteristics: duration of action - up to 36 hours.

Classification by chemical structure

- Derivatives of diphenylalkylamine (verapamil).
- Benzothiazepine derivatives (diltiazem).

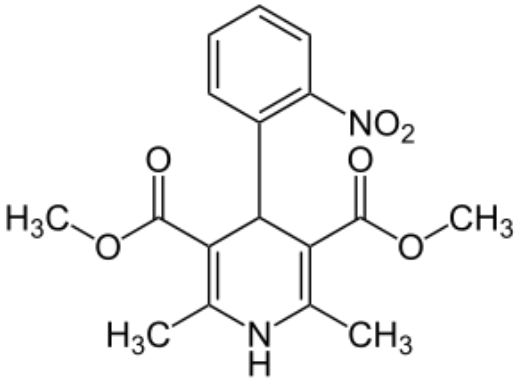
  These first two groups have antianginal, antiarrhythmic, hypotensive effects.
- Dihydropyridine derivatives (nifedipine).

  This group has only antianginal and hypotensive effects.

ClassificationWHO, 1987

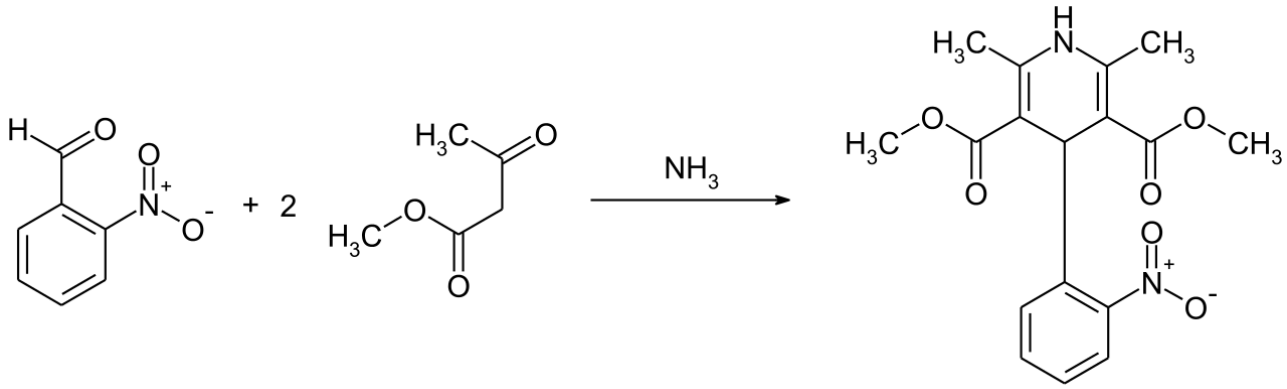
1. Verapamil.
2. Nifedipine.
3. Diltiazem.
4. Flunarizine and its derivatives (affect cerebral circulation).
5. Prenilamine and its derivatives (antianginal drugs).
6. Calcium preparations with a different chemical structure (indomethacin, β-blockers).

Nifedipine



Mechanism of action. Blocking the so-called "slow" calcium channels, slowing down the entry of calcium ions into cells and reducing its concentration in cells.

Synthesis.



Properties. Yellow crystalline powder, practically insoluble in water, well soluble in acetone, sparingly in ethanol.

Identification.

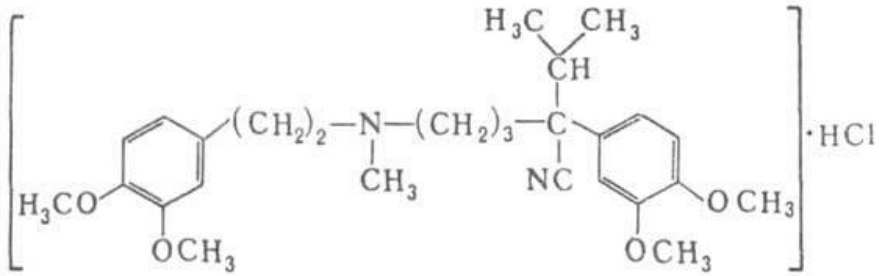
1. T. pl. (171-175 °C), IR spectrum, TLC.

2. With a solution of naphthylethylenediamine hydrochloride - red color.

Quantitative definition. Cerimetry, the indicator is ferroin.

Application. Antianginal, antiarrhythmic, antihypertensive drug.

Verapamil hydrochloride



Mechanism of action. Blocks potential-dependent calcium channels and disrupts the influx of calcium ions into cells, in particular cardiomyocytes and vascular smooth muscle cells, while the concentration of calcium in the blood does not change.

Properties. White crystalline powder, soluble in water, moderately soluble in ethanol, practically insoluble in ether.

Identification.

1. IR spectrum.

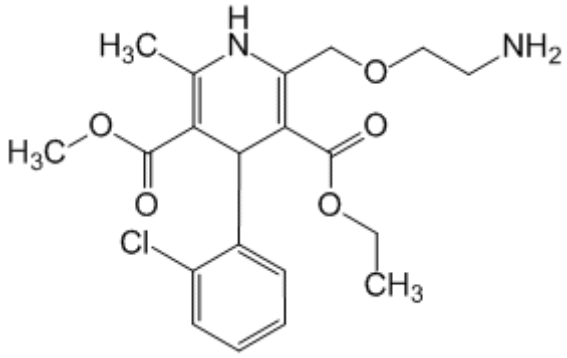
2. Reaction to chlorides: $AgNO_3 + Cl^- \longrightarrow AgCl\downarrow$.

Quantitative definition. By the method of non-aqueous titration in anhydrous acetic acid in the presence of mercury (II) acetate, the equivalence point is determined potentiometrically.

Storage. In a well-sealed container.

Application. Antianginal, antiarrhythmic,
antihypertensive drug.

Amlodipine



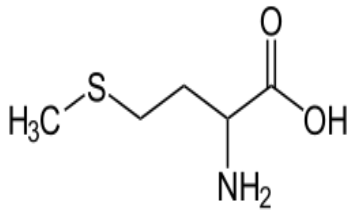
Mechanism of action. Blocker of calcium channels, which inhibits the transmembrane transfer of calcium ions in smooth muscle cells of the myocardium and blood vessels. The mechanism of the antihypertensive effect of the drug is due to the relaxing effect on vascular smooth muscles.

Properties. White crystalline powder, slightly soluble in water, moderately soluble in ethanol.

Application. Antianginal, antihypertensive drug.

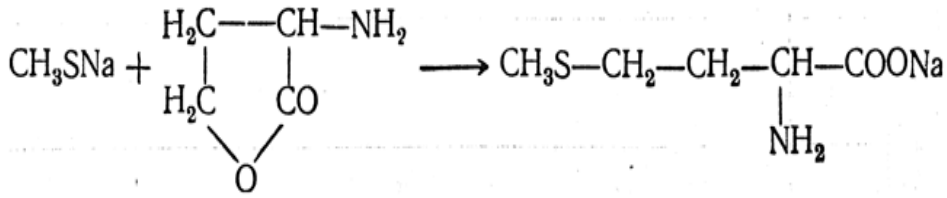
Antioxidants

Methionine



Mechanism of action. Has a lipotropic effect, promotes the synthesis of choline, phospholipids; participates in the synthesis of adrenaline, creatine; activates the action of hormones, vitamins, enzymes.

Synthesis.

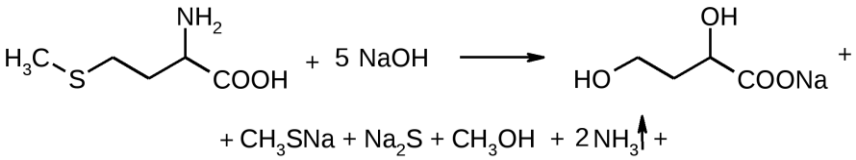


Properties. White or almost white crystalline powder or colorless crystals. Soluble in water, very slightly soluble in 96% alcohol, practically insoluble in ether.

Identification.

1. Specific rotation, IR spectrum, TLC.

2. Reaction with NaOH and sodium nitroprusside in the presence of glycine:



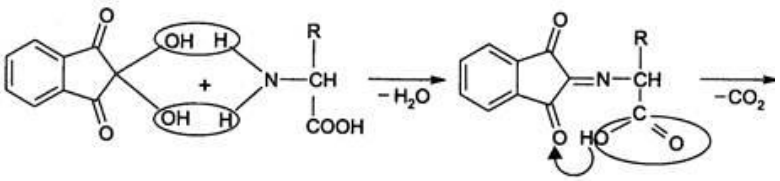
$Na_2S + Na_2[Fe(CN)_5NO] \rightarrow Na_4[Fe(CN)_5NOS]$.

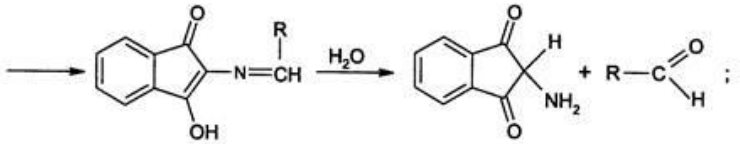
3. Non-pharmacopoeial reactions.

- After alkaline hydrolysis, the mixture is acidified→the smell of hydrogen sulfide and mercaptan:

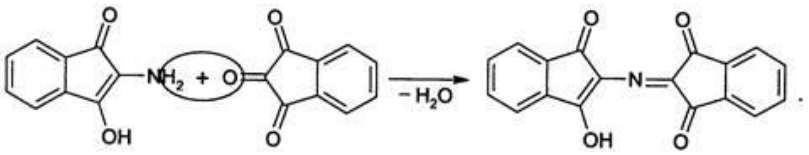
$Na_2S + CH_3SNa + 2H_2SO_4 \rightarrow H_2S\uparrow + CH_3SH\uparrow + Na_2SO_4 + NaHSO_4$.

- When heating the drug with a solution of ninhydrin→blue-violet color:





Основание Шиффа 2-Амино-1,3-диоксоиндан



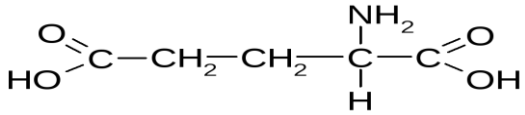
Quantitative definition.

1. Acidimetry in a non-aqueous medium, direct titration, s = 1.
2. Determination of nitrogen after H2SO4 mineralization.
3. Alkalimetry according to the Serensen method (formal titration).
4. Iodometry in a phosphate buffer medium, s = 2.

Storage. In well-stoppered glasses made of dark glass, in a place protected from light.

Application. For the treatment and prevention of diseases and toxic lesions of the liver.

Glutamic acid

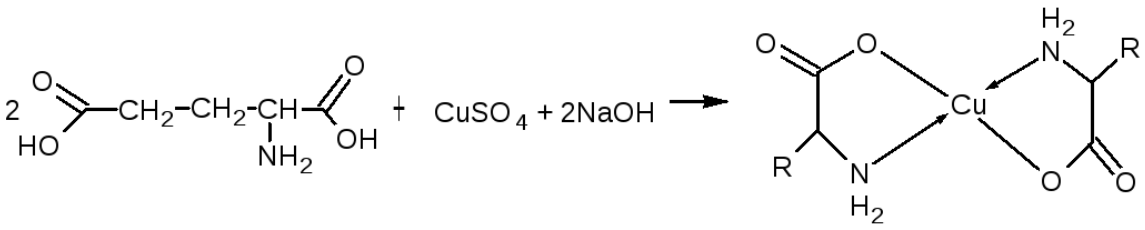


Mechanism of action. Belongs to neurotransmitter amino acids that stimulate the transmission of excitation in the synapses of the central nervous system.

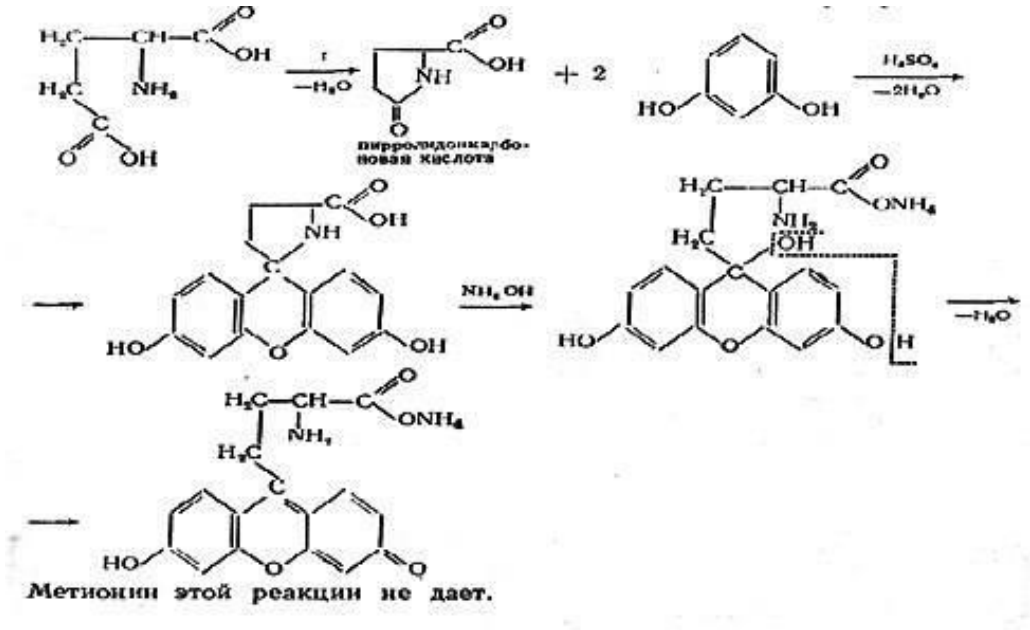
Properties. White crystalline powder or colorless crystals. Easily soluble in boiling water, slightly soluble in cold water, practically insoluble in acetic acid, acetone, 96% alcohol and ether.

Identification.

1. T. pl., specific rotation, IR spectrum, TLC.
2. Reaction with NaOH in the presence of formalin and phenolphthalein.
3. Non-pharmacopoeial reaction with CuSO4:



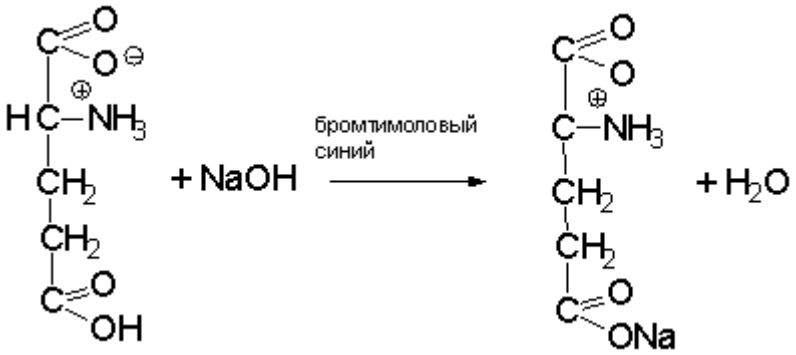
4. Non-pharmacopoeial fusion reaction with resorcinol:



Red-violet color

Quantitative definition.

1. Alkalimetry, direct titration, indicator – bromothymol blue, s = 1:



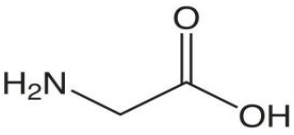
Determination of nitrogen after H2SO4 mineralization.

3. Alkalimetry according to the method of Serensen (formal titration), s = 1/2.

Storage. In a well-closed container that protects against light.

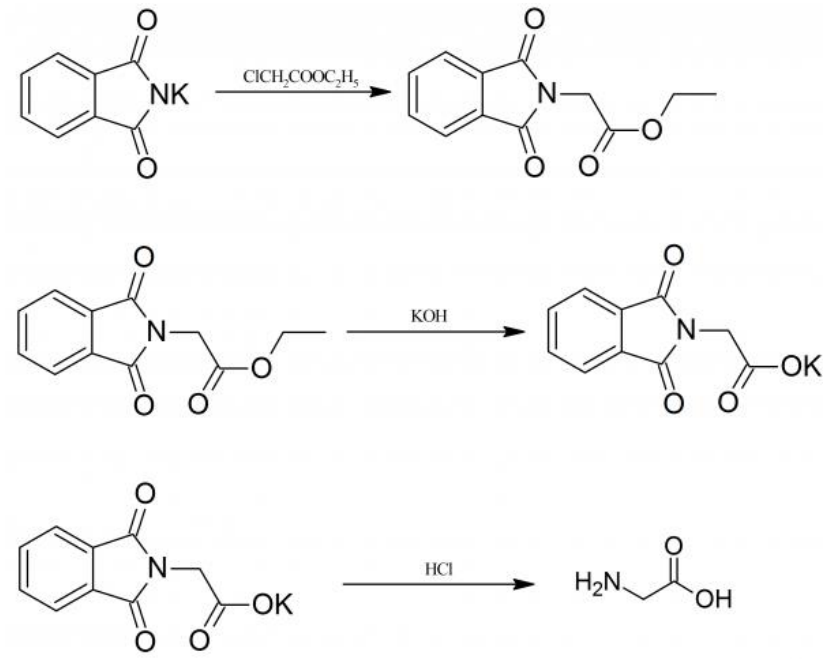
Application. For the treatment of CNS diseases, epilepsy, psychoses, reactive states. In pediatrics - with mental retardation of various etiologies, cerebral palsy, Down's disease.

Glycine



Mechanism of action. It is a neurotransmitter of the inhibitory type of action and a regulator of metabolic processes in the central nervous system.

Synthesis.



Properties. White crystalline powder, easily soluble in water, sparingly soluble in 96% alcohol, practically insoluble in ether.

Identification.

1. IR spectrum, TLC.

2. Reaction with NaClO + HCl + resorcinol→purple color with greenish-yellow fluorescence→orange→yellow

Quantitative definition.

Acidimetry in a non-aqueous medium with potentiometric indication of the equivalence point, s = 1:

$H_2NCH_2COOH + HClO_4 \rightarrow [H_2NCH_2COOH]ClO_4^-$.

Application. Functional and organic diseases of the nervous system, with ischemic stroke and disorders of cerebral circulation, as an aid in the treatment of alcoholism.

Antihypertensive drugs

Angiotensin-converting enzyme inhibitors (APF)

Antihypertensive(hypotensive) agents are more often classified by mechanism of action rather than by chemical structure.

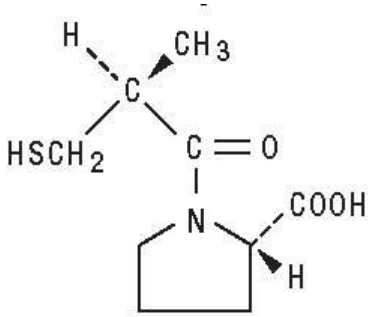
Hypotensive agents lower blood pressure by various mechanisms.

Classification of hypotensive agents

According to the effectiveness and value in the treatment of hypertension, a large number of antihypertensive drugs can be divided into main and auxiliary drugs. The group of basic antihypertensive agents includes:

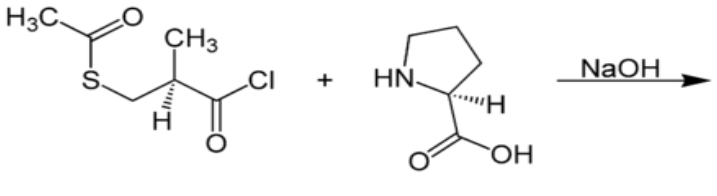
1. β-Adrenoblockers.
2. Blockers of calcium channels.
3. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers.
4. Diuretics.

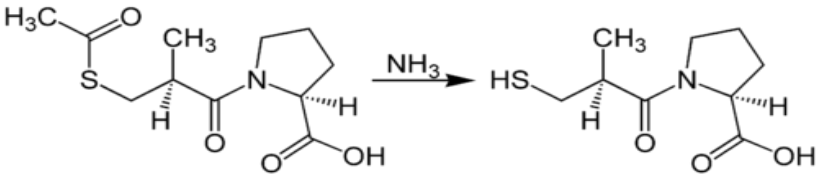
Captopril



Mechanism of action. An ACE inhibitor prevents the conversion of angiotensin I into angiotensin II, which is a powerful vasoconstrictor.

Synthesis.





Properties. White or almost white crystalline powder, easily soluble in water, methylene chloride and methanol.

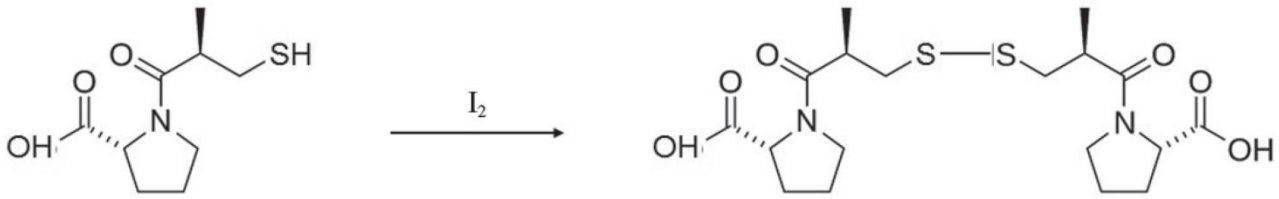
Identification.

1. T. pl., IR spectrum.

2. TLC, based on the discoloration of the iodine solution.

Quantitative definition.

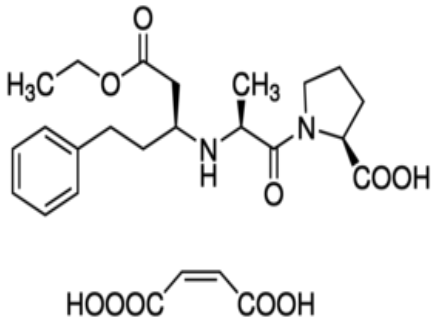
Method of iodometric titration with potentiometric fixation of the equivalence point:



Captopril Captopril dissulfide

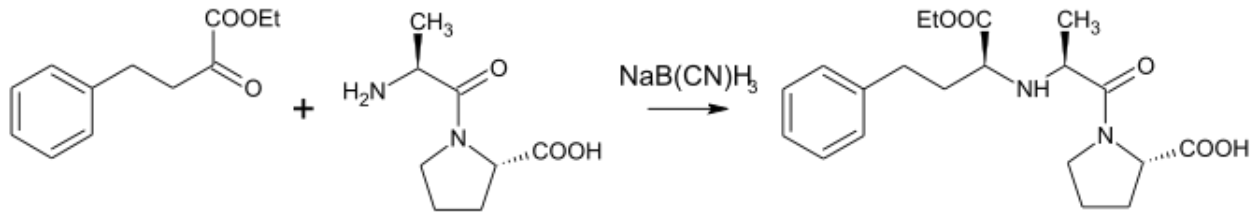
Application. Treatment of all forms of arterial hypertension, congestive heart failure, myocardial infarction and to prevent renal failure in patients with diabetic nephropathy or other chronic kidney diseases (with or without hypertension).

Enalapril maleate



Mechanism of action. After oral administration, the drug is quickly absorbed and transformed (through hydrolysis) into an active metabolite - enalaprilat, which has the properties of a highly specific ACE inhibitor. Enalaprilat inhibits the conversion of angiotensin I to angiotensin II and the breakdown of bradykinin.

Synthesis.

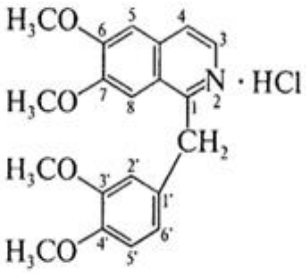


Properties. White or almost white crystalline powder, sparingly soluble in water, soluble in methanol and ethanol.

Application. Treatment of arterial hypertension, heart failure, prevention of clinically pronounced heart failure in patients with asymptomatic left ventricular dysfunction.

Antispasmodic drugs

Papaverine hydrochloride

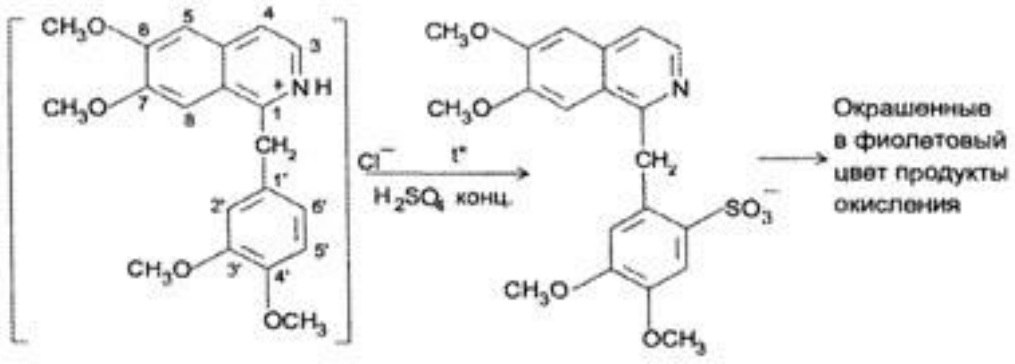


6,7-Диметокси-1-(3',4'-диметоксибензил)-
ізохіноліну гідрохлорид

Mechanism of action. Suppression of the phosphodiesterase enzyme, which contributes to the intracellular accumulation of cyclic 3',5'-adenosine monophosphate, and, as a result, leads to impaired contractility of smooth muscles and their relaxation in spastic conditions.
Properties. White crystalline powder without odor, hygroscopic, slightly bitter taste, moderately soluble in water, soluble in chloroform, sparingly soluble in ethanol, insoluble in ether.

Identification.

1. UV spectrum, t. pl. bases after precipitation of NH_4OH.
2. Chloride reaction: $Cl^- + AgNO_3 \rightarrow AgCl\downarrow$.
3. + HNO_3 (conc.) → yellow color, when heated → orange (in a porcelain cup).
4. Reaction with H_2SO_4 (conc.) upon heating → purple color:



Quantitative definition.

1. Alkalimetry in a mixture of alcohol and 0.01 M HCl solution with potentiometric fixation of the end point of the titration, s = 1.

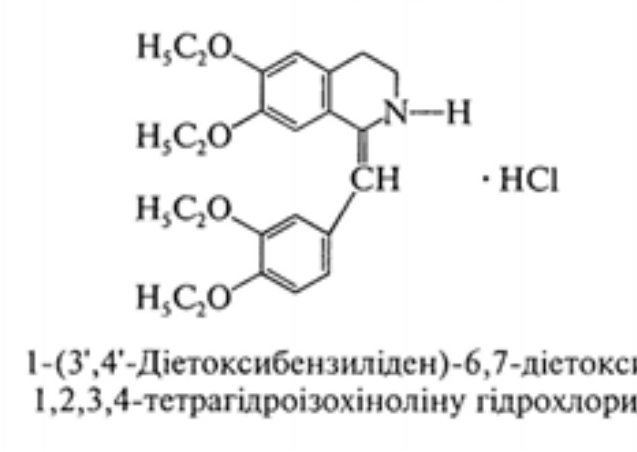
2. Acidimetry in a non-aqueous medium, direct titration in the presence of mercury (II) acetate, s = 1.

3. Spectrophotometry (in medicinal forms).

Storage. In a well-closed container that protects from light.

Application. Antispasmodic agent. Spasms of peripheral vessels, vessels of the brain; endarteritis, spasms of smooth muscles of abdominal organs, bronchi; premedication (as an auxiliary substance).

Drotaverine hydrochloride (HO-ShPA)

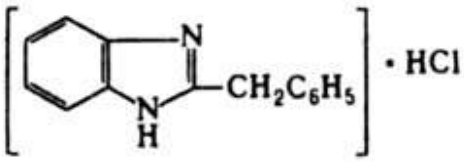


Mechanism of action. Drotaverine hydrochloride is similar in chemical structure and pharmacological action to papaverine, but has stronger and longer antispasmodic activity.

Application. Antispasmodic agent. The action of drotaverine is stronger than the action of papaverine, absorption is faster and more complete, it is less bound to blood plasma

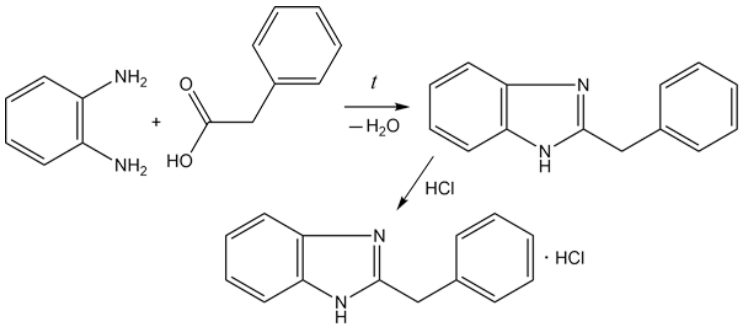
proteins. Another advantage of drotaverine is that, unlike papaverine, after its parenteral administration, such a side effect as respiratory stimulation is not observed.

Bendazol



Mechanism of action. Reduces the content of free calcium in smooth muscles, causing them to relax; increases the synthesis of nucleic acids and proteins, stimulates the immune system (contributes to the formation of antibodies, phagocytosis, synthesis of interferon). Activates interneuron contacts in the spinal cord.

Synthesis.

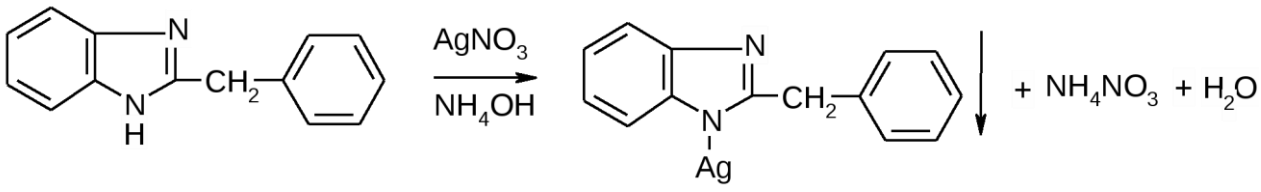


Properties. White, sometimes with a slight grayish or yellowish tinge, crystalline powder, bitter-salty taste. Hygroscopic. Unlike other hydrochlorides, it is difficult to dissolve in water, easily soluble in alcohol and difficult to dissolve in chloroform, slightly soluble in acetone, practically insoluble in ether.

Identification.

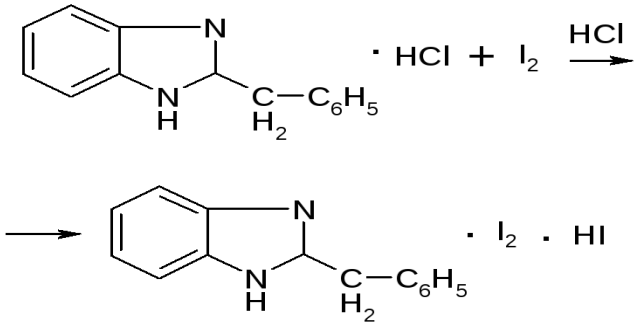
1. UV spectrum.

2. After precipitation of the base with ammonia, chlorides are determined in the filtrate:

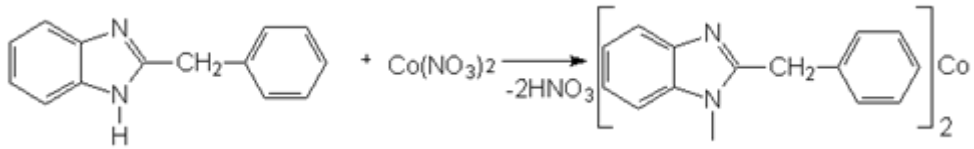


$Cl^- + AgNO_3 \rightarrow AgCl\downarrow$

3. Presence of heterocyclic nitrogen atoms – reaction with I_2 in an acidic environment → reddish-silver precipitate (≤ 25 °C):



4. Reaction with an alcoholic solution of Co(NO3)2 → blue color:



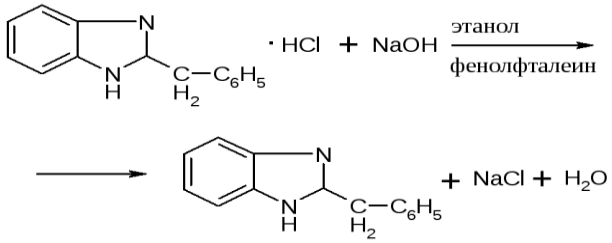
Quantitative definition.

1. Acidimetry in a non-aqueous environment, direct titration in the presence of mercury (II) acetate, s = 1.

2. Thiocyanatometry by substitution, s = 1.

3. Argentometry, direct titration in the presence of acetone and CH_3COONa solution, indicator – potassium chromate, s = ½.

4. Alkalimetry by the bound acid HCl, s = 1:



Storage. In a container that protects from light and moisture.

Application. Antispasmodic agent, with spasms of blood vessels (exacerbation of hypertensive disease, hypertensive crises) and smooth muscles of internal organs (spasms of the pylorus of the stomach, intestines); in the treatment of nervous diseases (mainly, residual effects of poliomyelitis, peripheral paralysis of the facial nerve, polyneuritis).

General material and bulk-methodological support of the lecture:

- ✓ computer presentation;
- ✓ illustrative materials;
- ✓ examples of solving typical tasks or performing typical tasks;

- ✓ multimedia projector.

Questions for self-control:

1. Calcium antagonists

2.Antioxidants

3.Antihypertensive (hypotensive) drugs

4.Spasmolytic agents

References:

Main:

1. State Pharmacopoeia of Ukraine: in 3 volumes / Derz. medical service of Ukraine funds, Ukr. of science pharmacopoeia medicine quality center means - 2nd edition. - Kh.: Ukr. of science pharmacopoeia medicine quality center means, 2015. - Vol. 1. - 1128 p.

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4. Pharmaceutical chemistry: Textbook for students. higher pharmacy education closing and pharmacy Faculty of Medical Sciences for students higher pharmacy education closing / In general ed. P.O. Bezuglio - Kind. 3rd edition, revised. – Vinnytsia, NOVA KNYGA, 2017. - 456 p.

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7. Nizhnyk H.P. Pharmaceutical chemistry: a textbook (University I-III years) H.P. Nizhnyk — 2nd ed., ed. - All-Ukrainian specialized publishing house "Medytsyna", 2015. - 352p.

8. Pharmaceutical chemistry. Analysis of medicinal substances by functional groups: study guide / O.O. Tsurkan, I.V. Nizhenkovska, O.O. Glushachenko. - 3rd edition - All-Ukrainian specialized publishing house "Medytsina", 2019. - 152 p.

9. Hudoyarova O.S. Pharmaceutical chemistry. - Vinnytsia: "Nilan-LTD" LLC, 2018. - 194 p.
10. Medicinal chemistry: education. manual for students of higher educational institutions / I.S. Hrytsenko, S.G. Taran, L.O. Transition, etc.; for general I.S. Hrytsenko - Kharkiv: NFaU: Golden Pages, 2017. - 552p.
11. Pharmaceutical chemistry. General and special pharmaceutical chemistry. Medicines of an inorganic nature: laboratory-practical classes. Study guide / L.G. Mishina - Vinnytsia: PP "TD "Edelweiss and K"", 2010. - 384 p.
12. Analytical chemistry and instrumental methods of analysis / A.I. Gab, D.B. Shakhnin, V.V. Malyshev -Ukraine University, 2018- 396 p.

Electronic information resources:

1. Specialized medical online publication for doctors, pharmacists, pharmacists, students of medical and pharmaceutical universities. - [Electronic resource]. - Access mode:http://www.morion.ua.
2. World Health Organization. - [Electronic resource]. - Access mode:http://www.who.int.
3. Pharmaceutical encyclopedia. - [Electronic resource]. – Access mode: http://www.pharmencyclopedia.com.ua.
4. Official website of the International Organization for Standardizationhttp://www.iso.org/iso/home.html
5. Compendium online. [Electronic resource]. - Access mode:https://compendium.com.ua/bad/
6. Medline search database [Electronic resource]. – Access mode: National Library of Medicinehttps://www.nlm.nih.gov/bsd/medline.html

Lecture No. 5

Topic: Agents affecting the excretory system (diuretics).

Actuality of theme: Pharmaceutical chemistry is a science that studies methods of preparation, structure, physical and chemical properties of medicinal products; relationship between their chemical structure and action on organism; methods of quality control of drugs and changes that occur during their storage, as well as their use in medicine. Therefore, it is urgent to solve the problems facing pharmaceutical chemistry

with the help of physical, chemical and physico-chemical methods, which are used both for synthesis, as well as for the analysis of medicinal products.

The purpose:the formation of students' knowledge about the peculiarities of the storage of medicinal products, which affect the afferent nervous system, as well as the characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of obtaining, methods of analysis, application in medicine. As a result of the lecture, students should learn the properties and methods of medical analysis means,affecting the excretory system.

Basic concepts:pharmaceutical chemistry, qualitative analysis, quantitative analysis, State Pharmacopoeia of Ukraine, physicochemical methods of analysis, impurities, express analysis.

Plan and organizational structure of the lecture:

1.Preparatory stage

1.1.Determination of educational The purposes.

1.2.Providing positive motivation.

2. The main stage

Presentation of lecture material

Plan:

-Classification of diuretics

- Chlorthiazide

- Hydrochlorothiazide

-Furosemide

-Indapamide

-Etacrynic acid

-Spironolactone

-Potassium acetate

-Ammonium chloride

-Aminophylline

-Theophylline

-Theobromine

3. The final stage

3.1. Summary of the lecture, general conclusions.

3.2. The lecturer's answers to possible questions

3.3. Tasks for self-training of students.

Content of lecture material (lecture text):

Diuretics- drugs that increase the formation of urine (diuresis). Diuretics are divided into hydruretics (causing mainly water diuresis) and saluretics.

Saluretics- increase the release of sodium and potassium salts and, due to this, increase diuresis. Diuretics that remove mainly sodium and store potassium in the body are often separated into a separate group and called potassium-sparing diuretics.

Diuretics are divided into the following groups according to their ability to inhibit the reabsorption of Na+ in the renal tubules (therefore, according to their potency):

- strong (inhibit reabsorption by 10-20%) – furosemide, ethacrynic acid, mannitol;
- medium potency (inhibits reabsorption by 5-8%) – dichlothiazid;
- weak diuretics (inhibit reabsorption by no more than 3-5%) - spironolactone, triamterene.

Classification by mechanism of action

1. Petlevy.Suppress the transport of Na^+, K^+, Mg^{2+} and Cl- ions through the apical membrane of epithelial cells in the thick segment of the ascending part of Henle's loop.

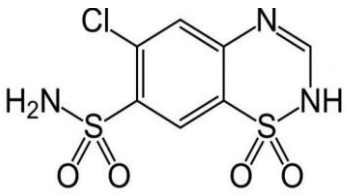
2. Thiazide.Suppress the transport of Na^+, Cl^- ions through the apical membrane in the distal convoluted tubule.

3. Potassium-sparing.It affects the distal renal tubules, in which it either reduces the secretion of potassium, or acts as an antagonist of aldosterone.

4. Osmotic.It increases the osmotic pressure of the blood, which promotes the transfer of fluid from the tissue sector (interstitial) to the lumen of the vessels, the osmotic pressure of the blood increases, the hormonal regulation of urination changes (↓ aldosterone and vasopressin levels), the glomerular filtration increases, and at the same time the reabsorption of water is suppressed, diuresis increases.

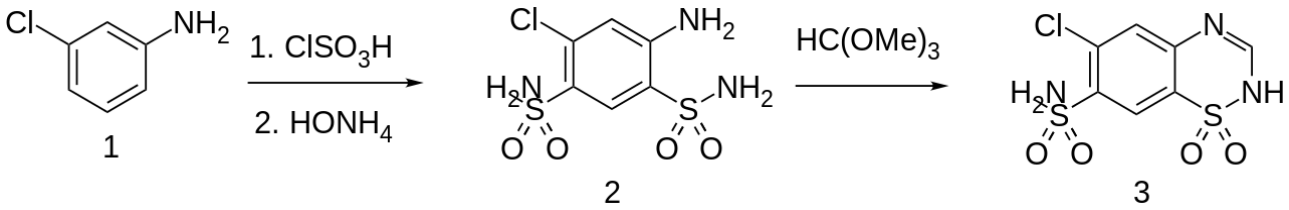
5. Combined.Combined diuretics simultaneously have a diuretic effect and lower blood pressure. The main advantage of these drugs is that the effect occurs 1-3 hours after taking and lasts from 6 to 9 hours.

Chlorthiazide



Mechanism of action. Increasing diuresis by blocking the reabsorption of sodium and chlorine ions at the beginning of the renal tubules. By this, they increase the excretion of sodium and chloride and, therefore, water. Excretion of other electrolytes, namely potassium and magnesium, also increases.

Synthesis.



1 2 3

Properties. White or almost white crystalline powder, very sparingly soluble in water, sparingly soluble in acetone, sparingly soluble in alcohol, soluble in dilute alkali solutions.

Identification.

1. IR-, UV-spectrum, TLC.

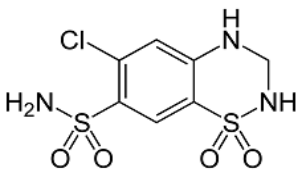
2. By the release of ammonia when heated with crystalline NaOH (blueing of red litmus paper) and the release of hydrogen sulfide during acidification (blackening of lead-acetate paper).

Quantitative definition. Alkalimetry method in alcohol neutralized with phenolphthalein; the indicator is phenolphthalein.

Storage. In a place protected from light.

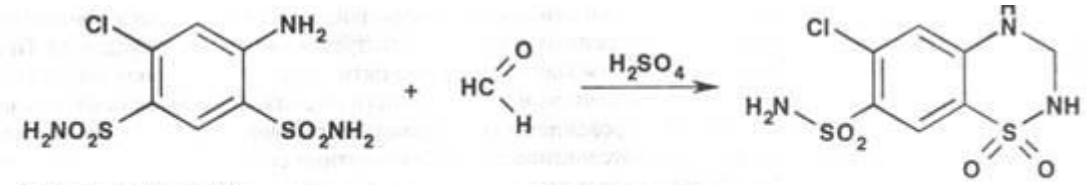
Application. Diuretic agent with hypotensive effect.

Hydrochlorothiazide



Mechanism of action. Increasing diuresis by blocking the reabsorption of sodium and chlorine ions at the beginning of the renal tubules. Increases the excretion of potassium, magnesium, and bicarbonate ions; reduces the excretion of calcium from the urine as a result of a direct effect on the distal tubules, which can prevent the formation of calcium kidney stones.

Synthesis



Properties. White or almost white, odorless crystalline powder. Very difficult to dissolve in water, soluble in acetone, moderately soluble in alcohol. Dissolves in dilute alkali solutions.

Identification.

1. T. pl., IR-, UV-spectrum.

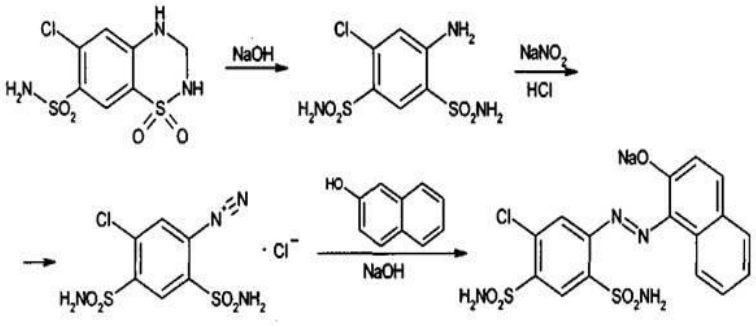
2. After acid hydrolysis, the formaldehyde substance that is released is determined by the reaction with chromotropic acid by the formation of a purple color.

3. The curd atom is determined after mineralization to sulfates by the action of HNO3 (conc.):

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

4. The substance under the influence of H_2SO_4 (concentrate) acquires a purple color.

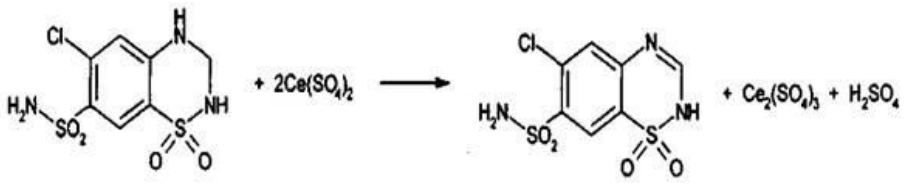
5. After alkaline hydrolysis → reaction to primary aromatic amines:



Quantitative definition.

1. Alkalimetry in a non-aqueous medium, titrant – $[(C_4H_9)_4N]OH$, medium – DMSO, potentiometrically, or CH_3ONa titrant, medium – 1-butylamine, indicator – azo violet solution in benzene.

2. Cerimetry, reverse titration, indicator – starch, s = 1/2:

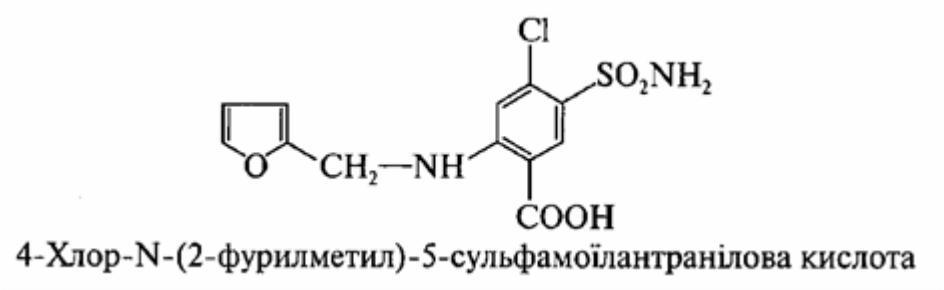


$2Ce(SO_4)_2 + 2KI \longrightarrow I_2 + Ce_2(SO_4)_3 + K_2SO_4$

Storage. In well-stoppered glasses, in a dry place protected from light.

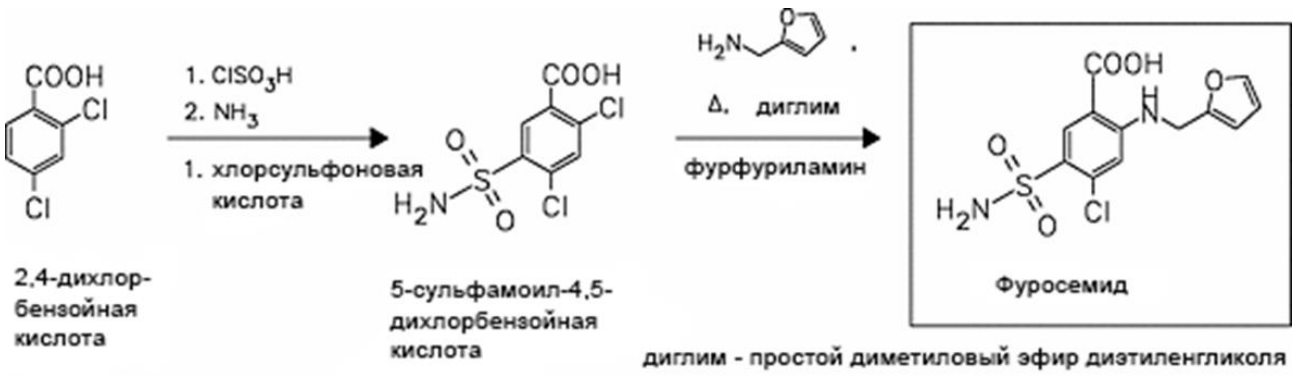
Application. Diuretic agent with hypotensive effect

Furosemide



Mechanism of action. Associated with blockade of reabsorption of sodium and chlorine ions in the ascending part of Henle's loop; also affects convoluted tubules. The drug causes pronounced diuretic, natriuretic, chloruretic effects. It also increases the excretion of potassium, calcium, and magnesium.

Synthesis.



Properties. White or almost white crystalline powder. Practically insoluble in water, soluble in acetone, moderately soluble in ethanol, sparingly soluble in ether.

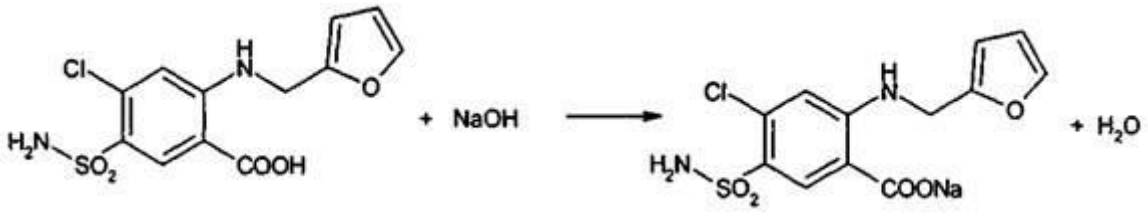
Identification.

1. IR, UV spectrum.

2. Diazotization reaction followed by azo coupling with naphthylenediamine hydrochloride – violet-red coloration.

Quantitative definition.

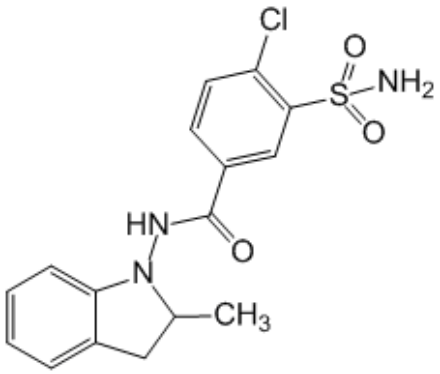
Alkalimetry in a non-aqueous environment (DMF), the indicator is bromothymol blue:



Storage. In a well-closed container that protects against light and moisture.

Application. Loop diuretic, with chronic heart failure, edema of the lungs, brain, hypertension, chronic renal failure, forced diuresis.

Indapamide



Mechanism of action. It is associated with the blockade of reabsorption of sodium, chlorine and water ions in the proximal and distal tubules, as well as in the area of the ascending part of the loop of Henle. The antihypertensive effect does not change and is well preserved in case of impaired kidney function.

Properties. White crystalline powder. Practically insoluble in water, soluble in ethanol, sparingly soluble in ether.

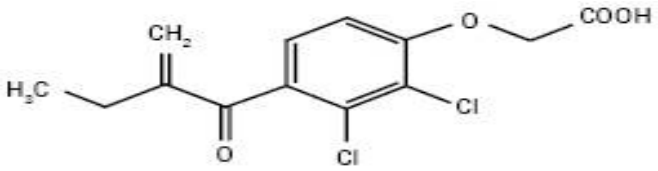
Identification.

IR-, UV-spectrum, TLC.

Quantitative definition. According to the specific absorption coefficient at λmax = 241 nm in ethanol.

Application. Diuretic and hypotensive agent.

Etacrynic acid



Mechanism of action. It has a pronounced diuretic effect, blocking the active reabsorption of ions in the proximal convoluted tubules and at the level of the ascending knee of the loop of Henle. Causes increased urinary excretion of sodium, chlorine, potassium and calcium ions.

Properties. White or almost white crystalline powder, very slightly soluble in water, easily soluble in alcohol and ether, soluble in ammonia, alkali and carbonate solutions.

Identification.

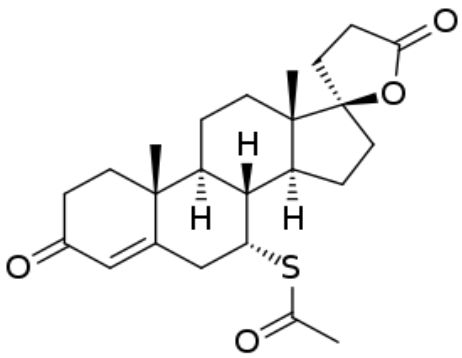
1. IR, UV spectrum.
2. According to the fluorescence reaction at λ = 254 nm after heating in the presence of hydroxylamine hydrochloride, an alcoholic solution of potassium hydroxide and water.
3. By reaction with a solution of the sodium salt of chromotropic acid after heating the substance with a solution of sodium hydroxide (purple auric dye).
4. Beilstein's test for halogen (blue-green color of the flame).

Quantitative definition. The method of alkalimetry in a mixture of methanol and water with potentiometric fixation of the equivalence point.

Application.A strong diuretic. Edema syndrome of various genesis, in particular, with chronic heart failure stage IIB-III, nephrotic syndrome, portal hypertension syndrome. In case of ineffectiveness of other diuretic drugs.

Aldosterone antagonists (potassium sparing)

Spironolactone



Mechanism of action. Competitive inhibition of aldosterone effect.

Properties. Yellowish-white or light yellowish-brown powder, odorless or with a slight characteristic odor. Practically insoluble in water, sparingly soluble in ether, soluble in alcohol, easily soluble in chloroform.

Identification.

1. T. pl., IR-, UV-spectrum, TLC.

2. When shaking with H_2SO_4 (conc.) - the appearance of a yellow-hot color of the solution with yellow-green fluorescence.

3. Characteristic reaction to sulfide ions.

Quantitative definition.

Spectrophotometrically, a 0.1 M solution of the substance in methanol, $\lambda \sim 238$ nm.

Storage. In a tightly closed container, in a place protected from light.

Application. Potassium-sparing diuretic.

Osmotic diuretics

Potassium acetate

CH_3COOK

Mechanism of action. It reduces sodium ion reabsorption, and the amount of water reaching the distal tubules increases.

Synthesis.

$2CH_3COOH + K_2CO_3 \rightarrow 2CH_3COOK + CO_2\uparrow + H_2O$.

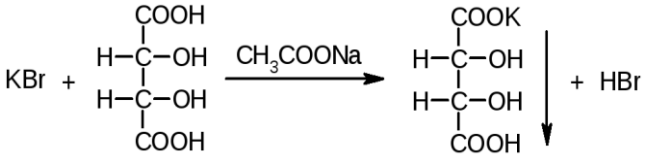
Properties. White or colorless crystalline powder

crystals Dissolves in the air. Very easily soluble in water,

easily soluble in 96% alcohol.

Identification.

1. Reaction to potassium:

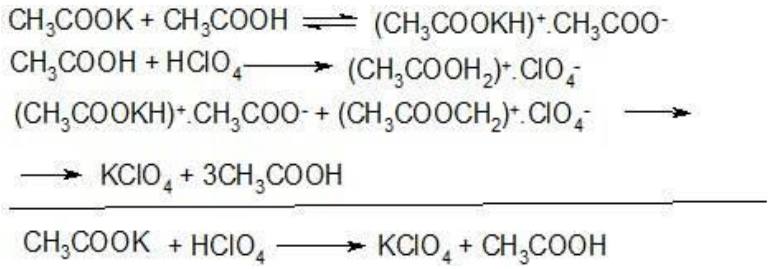


2. Reaction of acetate ion with sulfuric acid:

$CH_3COO– + H+ \rightarrow CH_3COON\uparrow$.

Quantitative definition.

1. Acidimetry in a non-aqueous environment, the indicator is naphtholbenzene, s = 1:



2. Acidimetry, direct titration, indicator – tropeolin-00, s = 1:

$CH_3COOK + HCl \rightarrow CH_3COON + KCl$.

Storage. In a well-sealed container that protects against moisture.

Application. Diuretic agent for edema associated with violation of blood circulation.

Diuretics- xanthine derivatives

Ammonium chloride

NH4Cl

Mechanism of action. It forms ammonium ions, hydrogen and chlorine ions in the blood, as a result of which there is a shift of the acid-alkaline state towards acidosis. Stimulates the glands of the mucous membranes of the respiratory tract, which facilitates the expectoration of bronchial secretions. In a small amount, the release of potassium ions increases, but it has no independent value as a diuretic.

Synthesis.

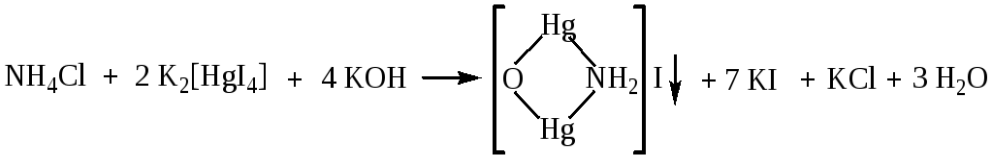
$$NH_3 + HCl \rightarrow NH_4Cl.$$

Properties. White crystalline powder or colorless crystals. Easily soluble in water.

Identification.

1. Reactions on the ammonium cation:

- $NH_4^+ + OH^- \rightarrow NH_3\uparrow + H_2O$.
- Reaction with Nessler's reagent - yellow precipitate:



2. Reaction to chlorides: $AgNO_3 + Cl^- \rightarrow AgCl\downarrow$.

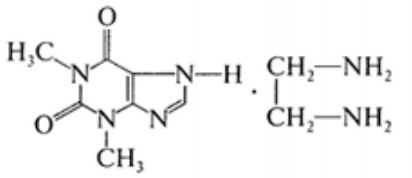
Quantitative definition.

Alkalimetry method by substitute. Formaldehyde solution is added to the substance, and the formed hydrochloric acid is titrated with sodium hydroxide solution (phenolphthalein indicator).

Storage. In a well-sealed container.

Application. Together with diuretics that cause alkalosis, and also as an expectorant for pneumonia, bronchitis, etc.

Aminophylline



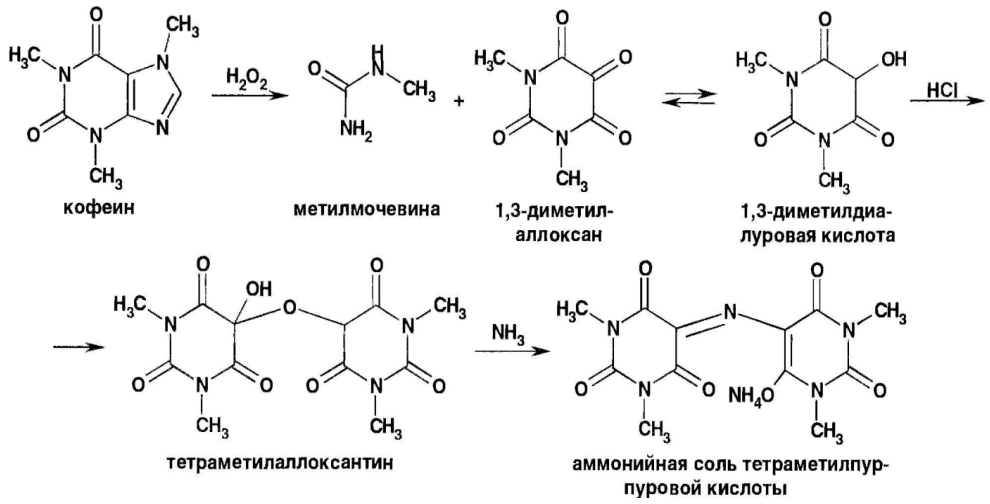
Теофілін з 1,2-етилендіаміном

Mechanism of action. Due to the ability of aminophylline to block adenosine receptors, non-selectively inhibit the enzyme phosphodiesterase and thereby increase the concentration of cyclic 3',5'-adenosine monophosphate (cAMP) in tissues, suppress the transport of calcium ions through "slow" channels of cell membranes and reduce its release from intracellular depots.

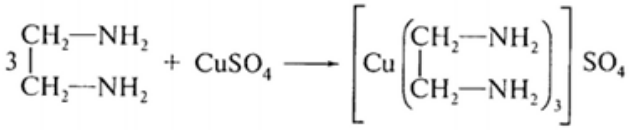
Properties. White, sometimes with a yellowish tinge, crystalline powder with a weak ammonia smell. It absorbs carbon dioxide in the air, while its solubility decreases. Soluble in water, aqueous solutions have an alkaline reaction.

Identification.

1. Murexid sample - purple-red color:

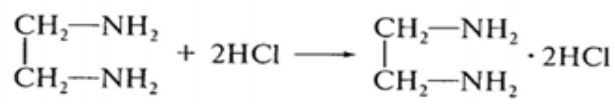


2. Ethylenediamine + CuSO4 → bright purple color:



Quantitative definition.

1. Ethylenediamine is determined acidometrically, the indicator is methyl orange, s=1/2:



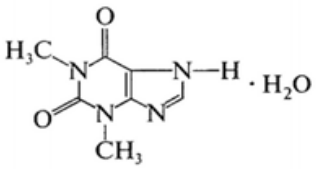
2. Aminophylline is determined by the method of alkalimetry using a substitute after drying the sample in an oven at 125-130 °C until the smell of amines disappears, s = 1.

3. The content of anhydrous theophylline in aminophylline should be 80-85%, in aminophylline for injections - 75-82%.

Storage. In a well-sealed container filled to the top, protecting from light and moisture.

Application. Antispasmodic, bronchodilator, diuretic.

Theophylline



1,3-Диметилксантин

Mechanism of action. Due to the blocking of adenosine receptors, inhibition of phosphodiesterases, increase in the content of intracellular cAMP, decrease in the intracellular concentration of calcium ions.

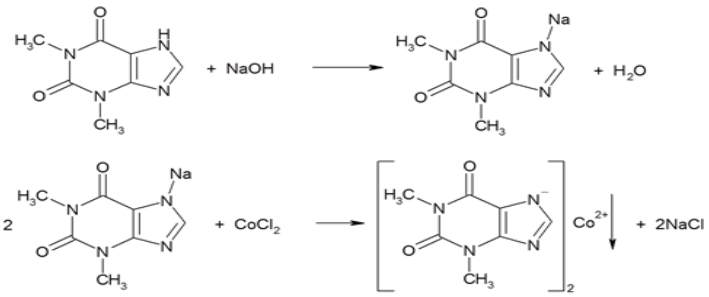
Properties. White crystalline powder, odorless, sparingly soluble in cold water, ethanol, ether, chloroform, soluble in hot water and hot ethanol, in solutions of acids and alkalis.

Identification.

Group reaction - murexide test.

Specific reactions.

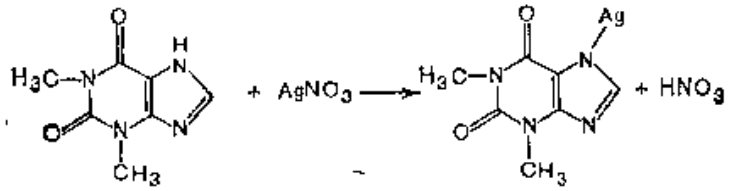
1. The reaction of Na-salt of theophylline with CoCl2 solution - white with a pink tint precipitate:



2. With an alkaline solution of sodium nitroprusside Na2[Fe(CN)5NO] – green color, disappears when an excess of acid is added:

Quantitative definition.

Alkalimetry by substitution, s = 1:

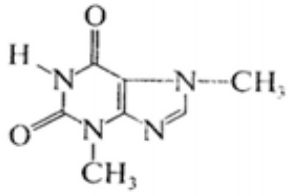


$$HNO_3 + NaOH \longrightarrow NaNO_3 + H_2O$$

Storage. In a well-closed container, protected from light.

Application. Antispasmodic, bronchodilator, diuretic.

Theobromine



3,7-Диметилксантин

Mechanism of action. Due to the blocking of adenosine receptors, inhibition of phosphodiesterases, increase in the content of intracellular cAMP, decrease in the intracellular concentration of calcium ions.

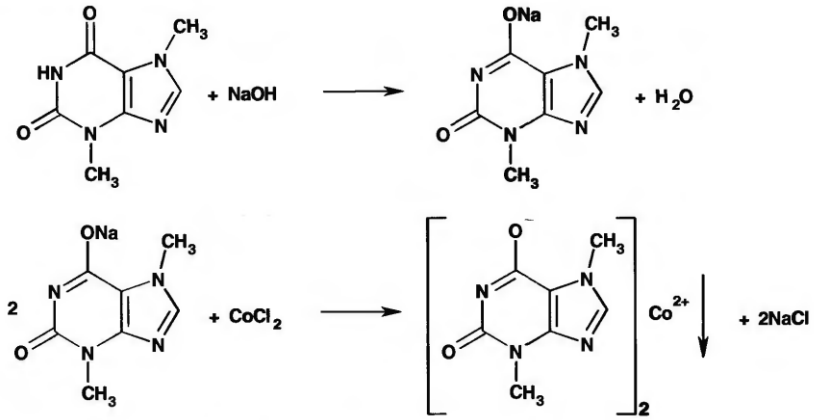
Properties. White crystalline powder, bitter in taste. Very slightly soluble in water, ethanol, ether, chloroform, slightly soluble in hot water, easily soluble in solutions of acids and alkalis.

Identification.

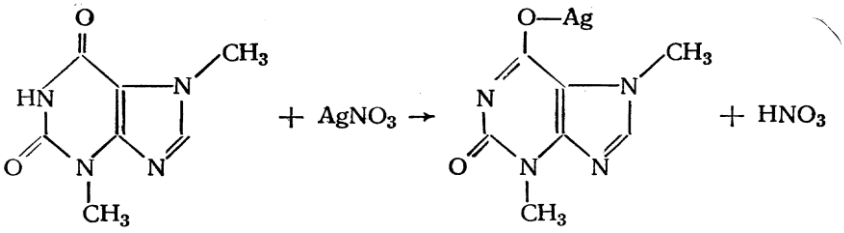
Group reaction - murexide test.

Specific reactions.

1. The reaction of Na-salt of theobromine with $CoCl_2$ solution – an intense purple color, which quickly disappears and a greyish-blue precipitate is formed:

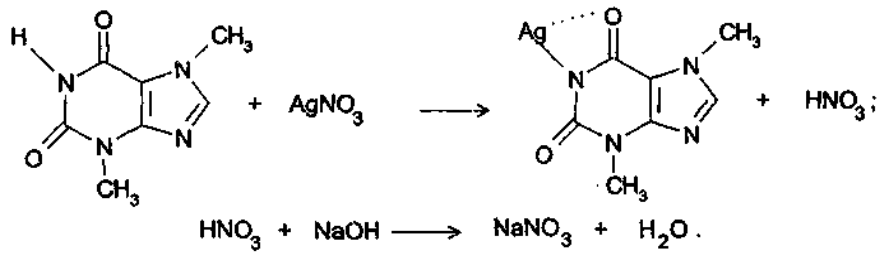


2. The reaction of Na-salt of theobromine with $AgNO_3$ solution is a thick gelatinous mass (Ag-salt), which liquefies when heated to 80 °C and solidifies again when cooled.



Quantitative definition.

Alkalimetry by substitution, s = 1:



Storage. In a well-sealed container.

Application. Antispasmodic, bronchodilator,

diuretic.

General material and bulk-methodological support of the lecture:

- ✓ computer presentation;
- ✓ illustrative materials;
- ✓ examples of solving typical tasks or performing typical tasks;
- ✓ multimedia projector.

Questions for self-control:

1.Classification of diuretics

2.Pharmaceutical analysisChlorthiazide, Hydrochlorothiazide

3.Pharmaceutical analysisFurosemide, Indapamide, Ethacrynic acid,

4.Pharmaceutical analysisSpironolactone, Potassium acetate, Ammonium chloride

5.Pharmaceutical analysisAminophylline, Theophylline, Theobromine

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Main:

1. State Pharmacopoeia of Ukraine: in 3 volumes / Derz. medical service of Ukraine funds, Ukr. of science pharmacopoeia medicine quality center means - 2nd edition. - Kh.: Ukr. of science pharmacopoeia medicine quality center means, 2015. - Vol. 1. - 1128 p.

2. State Pharmacopoeia of Ukraine: in 3 volumes / Derzh. medical service of Ukraine funds, Ukr. of science pharmacopoeia medicine quality center means - 2nd edition. - Kh.: Ukr. of science pharmacopoeia medicine quality center means, 2014. - Vol. 2. - 724 p.

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4. Pharmaceutical chemistry: Textbook for students. higher pharmacy education closing and pharmacy Faculty of Medical Sciences for students higher pharmacy education closing / In general ed. P.O. Bezuglio - Kind. 3rd edition, revised. – Vinnytsia, NOVA KNYGA, 2017. - 456 p.

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6. European Pharmacopoeia. Third Edition. Supplement, 2008. Council of Europe Strasbourg.

7. Nizhnyk H.P. Pharmaceutical chemistry: a textbook (University I-III years) H.P. Nizhnyk — 2nd ed., ed. - All-Ukrainian specialized publishing house "Medytsyna", 2015. - 352p.

8. Pharmaceutical chemistry. Analysis of medicinal substances by functional groups: study guide / O.O. Tsurkan, I.V. Nizhenkovska, O.O. Glushachenko. - 3rd edition - All-Ukrainian specialized publishing house "Medytsina", 2019. - 152 p.

9. Hudoyarova O.S. Pharmaceutical chemistry. - Vinnytsia: "Nilan-LTD" LLC, 2018. - 194 p.

10. Medicinal chemistry: education. manual for students of higher educational institutions / I.S. Hrytsenko, S.G. Taran, L.O. Transition, etc.; for general I.S. Hrytsenko - Kharkiv: NFaU: Golden Pages, 2017. - 552p.

11. Pharmaceutical chemistry. General and special pharmaceutical chemistry. Medicines of an inorganic nature: laboratory-practical classes. Study guide / L.G. Mishina - Vinnytsia: PP "TD "Edelweiss and K"", 2010. - 384 p.

12. Analytical chemistry and instrumental methods of analysis / A.I. Gab, D.B. Shakhnin, V.V. Malyshev -Ukraine University, 2018- 396 p.

Electronic information resources:

1. Specialized medical online publication for doctors, pharmacists, pharmacists, students of medical and pharmaceutical universities. - [Electronic resource]. - Access mode:http://www.morion.ua.

2. World Health Organization. - [Electronic resource]. - Access mode:http://www.who.int.

3. Pharmaceutical encyclopedia. - [Electronic resource]. – Access mode: http://www.pharmencyclopedia.com.ua.

4. Official website of the International Organization for Standardizationhttp://www.iso.org/iso/home.html

5. Compendium online. [Electronic resource]. - Access mode:https://compendium.com.ua/bad/

6. Medline search database [Electronic resource]. – Access mode: National Library of Medicinehttps://www.nlm.nih.gov/bsd/medline.html

Lecture No. 6

Topic: Antibiotics.

Actuality of theme: Pharmaceutical chemistry is a science that studies methods of preparation, structure, physical and chemical properties of medicinal products; relationship between their chemical structure and action on organism; methods of quality control of drugs and changes that occur during their storage, as well as their use in medicine. Therefore, it is urgent to solve the problems facing pharmaceutical chemistry with the help of physical, chemical and physico-chemical methods, which are used both for synthesis, as well as for the analysis of medicinal products.

The purpose:the formation of students' knowledge about the peculiarities of the storage of medicinal products, which affect the afferent nervous system, as well as the characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of obtaining, methods of analysis, application in medicine. As a result of the lecture, students should learn the properties and methods of medical analysis means,relating toantibiotics.

Basic concepts:pharmaceutical chemistry, qualitative analysis, quantitative analysis, State Pharmacopoeia of Ukraine, physicochemical methods of analysis, impurities, express analysis.

Plan and organizational structure of the lecture:

1.Preparatory stage

1.1.Determination of educational The purposes.

1.2.Providing positive motivation.

2. The main stage

Presentation of lecture material

Plan:

-Classification of antibiotics

- Tetracyclines

- Chloramphenicol

-Penicillins

-Cephalosporins

-Carbopenems

-Aminoglycoside antibiotics

-Macrolide antibiotics

-Lincosamides

-Polyene antibiotics of glycoside-like structure

-Anzamycin antibiotics

-Antitumor antibiotics

3. The final stage

3.1. Summary of the lecture, general conclusions.

3.2. The lecturer's answers to possible questions

3.3. Tasks for self-training of students.

Content of lecture material (lecture text):

Antibiotics(Greek anti + bios – life) – products of vital activity (or their synthetic analogues and homologues) of living cells (bacterial, fungal, plant and animal origin), which selectively inhibit the functioning of other cells – microorganisms, tumors, etc.

This group includes hundreds of drugs of different chemical structure, distinguished by spectrum and mechanism of action, side effects and indications for use. The term "Antibiotics" was proposed by Z.A. Waxman (1942).

Classification:

• natural (penicillins, lincomycin, vancomycin, etc.).

• semi-synthetic (products of modification of natural molecules: amoxicillin, clindamycin, cefazolin, etc.).

Classification by mechanism of action:

• inhibitors of the synthesis of the cell wall of microorganisms (β-lactams, vancomycin);

• Antibiotics that disrupt the molecular organization and function of cell membranes (polymyxins, antifungals, aminoglycosides, cyclic lipopeptides);

• Antibiotics that suppress the synthesis of protein and nucleic acids - inhibitors of protein synthesis at the level of ribosomes (chloramphenicols, tetracyclines, macrolides, lincosamides, aminoglycosides, oxazolidinones);

• RNA polymerase inhibitors (ansomacrolides).

Classification by chemical structure:

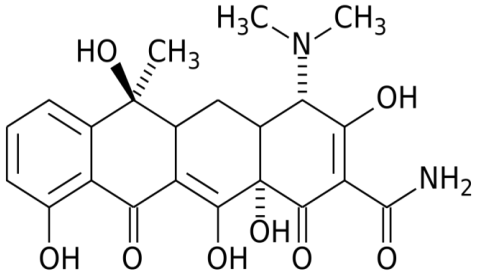
- β-lactams (penicillins, cephalosporins, carbapenems, monobactams);
- aminoglycosides;
- macrolides (erythromycin, clarithromycin, roxithromycin, azithromycin, spiramycin, josamycin, midekamycin);
- chloramphenicol;
- tetracyclines;
- lincosamides (lincomycin, clindamycin);
- fusidic acid;
- ansamacrolides (rifampicin);
- polymyxins;
- polyenes (nystatin, levorin, amphotericin B), etc.

Classificationaccording to the spectrum of antimicrobial activity:

- Antibiotics that act mainly on gram-positive and gram-negative cocci and gram-positive rods - corynebacteria, clostridia;
- Antibiotics active against gram-positive and gram-negative bacteria;
- Antibiotics with predominant activity against gram-negative bacteria;
- anti-tuberculosis antibiotics;
- antifungal antibiotics

Tetracyclines

Tetracycline



In medical practice, it is used in the form of a base or hydrochloride.

Mechanism of action. Associated with a violation of protein synthesis in a bacterial cell. Entering the bacterial cell, the antibiotic prevents the formation of a transport RNA complex with the ribosome, thus protein synthesis stops.

Properties. Yellow crystalline powder, odorless, bitter in taste. Very poorly soluble in water and alcohol. Hygroscopic.

Stable in solutions of weak acids, destroyed in solutions of strong acids and alkalis.

Identification.

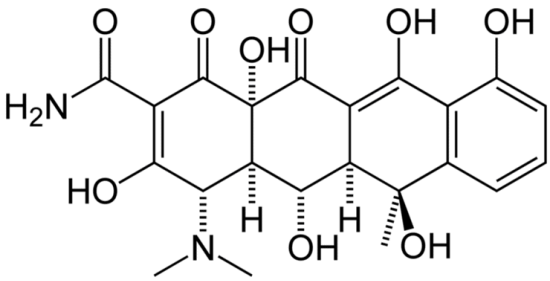
1. TSH
2. When H_2SO_4 is added, the color is purple, which becomes red-brown when $FeCl_3$ is added.

Quantitative definition.HPLC method.

Storage. In a tightly closed container, in a place protected from light at room temperature.

Application. Antibacterial (bacteriostatic) agent, the spectrum of antimicrobial action is wide. Antimicrobial activity of the drug is shown against most gram-positive and gram-negative bacteria, including to leptospira, rickettsiae, as well as to spirochetes and large viruses.

Oxytetracycline



Mechanism of action. Associated with a violation of protein synthesis in a bacterial cell.

Properties. Yellow crystalline powder, easily soluble in water, hardly soluble in ethanol, insoluble in chloroform and ether. Hygroscopic.

Identification.

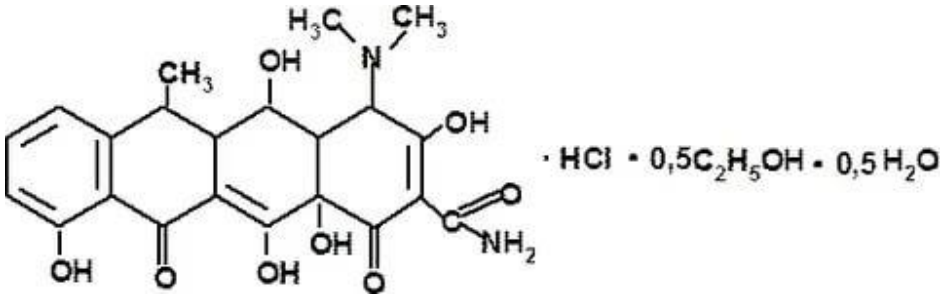
1. IR spectrum, TLC.
2. Reaction with H_2SO_4 (conc.) – purple-red color.
3. Reaction with $FeCl_3$ – brown color.

Quantitative definition.TLC method.

Storage. In a tightly closed container at a temperature of 10-20 °C.

Application. Antibacterial (bacteriostatic) agent.

Doxycycline hydrochloride



Mechanism of action. Associated with a violation of protein synthesis in a bacterial cell.

Properties. Yellow crystalline powder. Hygroscopic. Easily soluble in water, methanol, moderately soluble in 96% ethanol, practically insoluble in ether.

Identification.

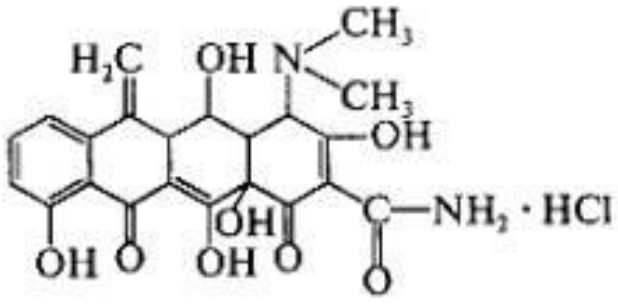
1. TLC.
2. Reaction with H_2SO_4 (conc.) – yellow color.
3. Reaction to chlorides.

Quantitative definition. Method of liquid chromatography.

Storage. In a well-closed container that prevents exposure to light.

Application. Antibacterial (bacteriostatic) agent. Highly effective for upper respiratory tract infections (bronchitis, pleurisy, pneumonia), has a prolonged effect.

Methacycline hydrochloride



Mechanism of action. Associated with a violation of protein synthesis in a bacterial cell.

Properties. Yellow crystalline powder, odorless, bitter in taste. Slowly soluble in water.

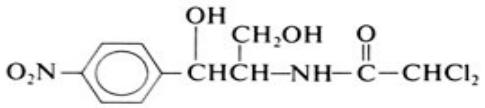
Application. Antibacterial (bacteriostatic) agent.

Treatment of bronchitis, pneumonia, pleurisy, dysentery, whooping cough, tonsillitis, scarlet fever, brucellosis, tularemia, rash and typhus, infectious diseases of the urinary tract, chronic cholecystitis, purulent meningitis, skin and soft tissue infections (phlegmons,

abscesses, furunculosis), prostatitis, syphilis, purulent complications of surgical operations, etc.

Chloramphenicol

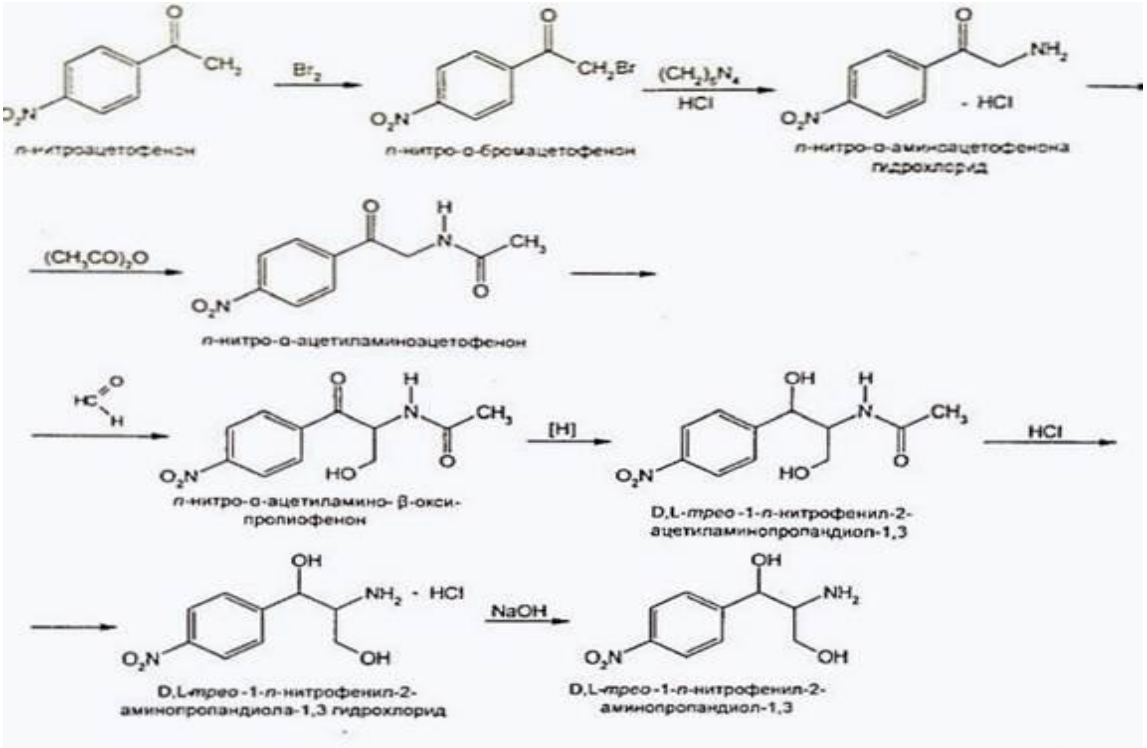
Chloramphenicol



Хлорамфеникол

Mechanism of action. The action is associated with the disruption of the process of protein synthesis in the microbial cell at the stage of transfer of tRNA amino acids to ribosomes.

Synthesis.

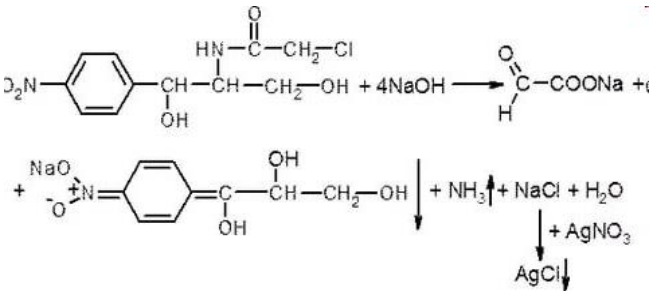


Properties. White crystals with a yellowish tinge, odorless, bitter in taste, sparingly soluble in water, easily soluble in alcohol.

Identification.

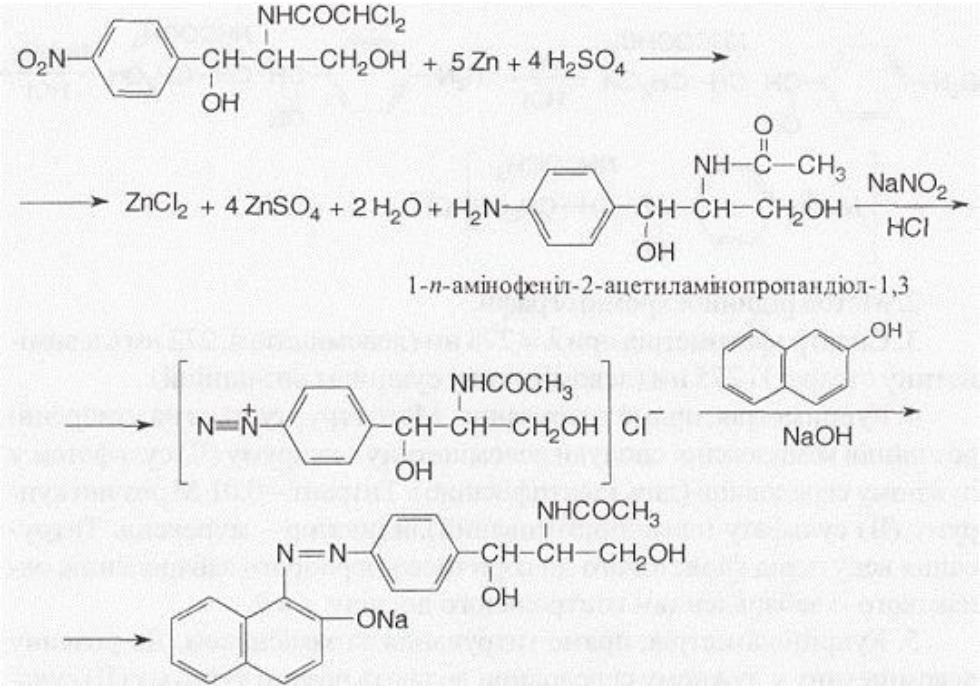
1. T. pl., IR-, UV-spectrum, TLC.

2. Hydrolysis reaction:

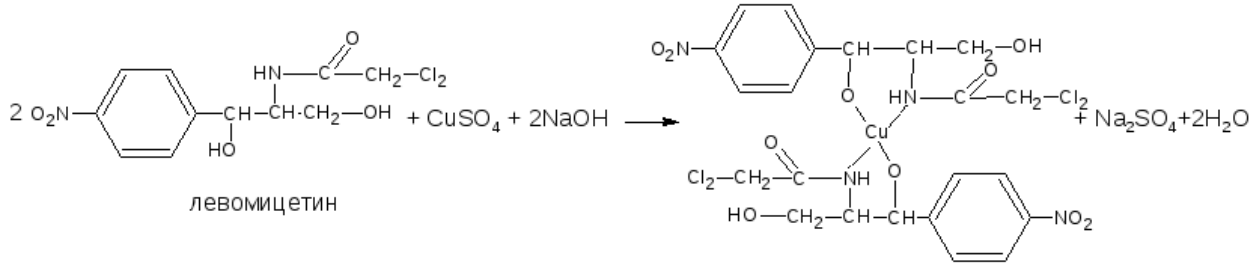


First, a yellow color appears, which turns into red-orange (acinitroform formation). Confirm the presence of chlorides.

3. Reaction of red azo dye formation:

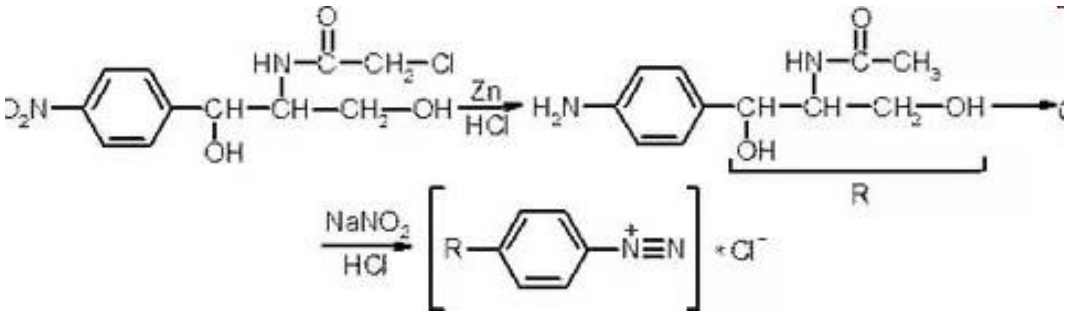


4. In the express analysis – the reaction with $CuSO_4$ in an alkaline environment in the presence of n-butanol:



Quantitative definition.

1. Nitritometry after preliminary reduction of the nitro group, s = 1:



2. Liquid chromatography method.

3. Cupriiodometry, direct titration, indicator – murexide, s = 2.

4. Argentometry or mercurimetry, s = ½.

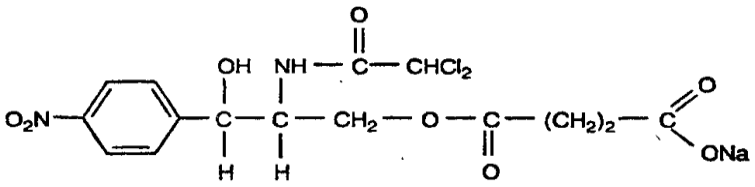
5. Photocolorimetry for the formation of an azo dye after reduction of the nitro group with subsequent diazotization and azo coupling.

6. Iodometry. The method is based on the oxidation of alkaline hydrolysis products of chloramphenicol, s = 1/3.

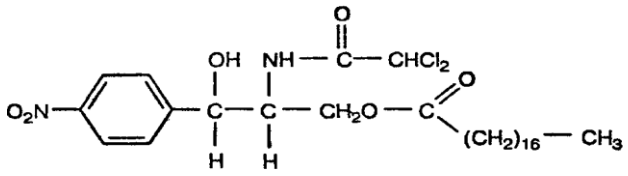
Storage. In a well-closed container, in dark glass glasses.

Application.A broad-spectrum antibiotic, used to treat dysentery, pneumonia, whooping cough, typhoid fever, etc.

Chloramphenicol succinate soluble (HASR)



Chloramphenicol stearate (HAST)



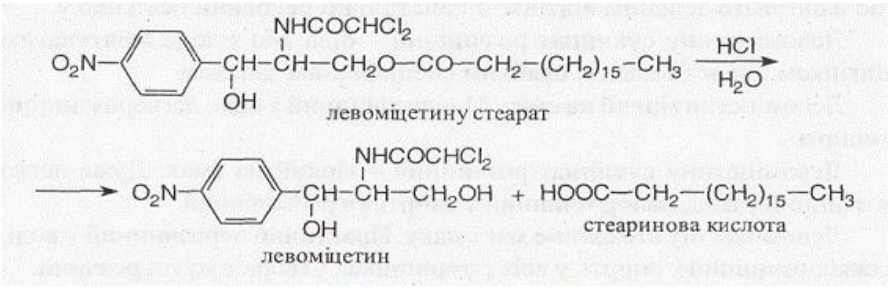
Mechanism of action. The action is associated with the disruption of the process of protein synthesis in the microbial cell.

Properties. KhaSR is a white or slightly yellowish porous mass with a weak specific. Bitter in taste, very easily soluble in water, sparingly soluble in alcohol, hygroscopic.

HAST is a white crystalline substance with a yellowish tinge, odorless, tasteless, practically insoluble in water, forms cloudy solutions in all solvents.

Chloramphenicol stearate is hydrolyzed when heated with HCl acid - stearic acid is formed (oily droplets that solidify when

cooling):



Storage. In a well-closed container, in dark glass glasses.

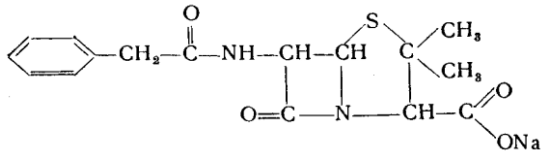
Application. Chloramphenicol stearate is used in children's practice - it does not have a bitter taste.

Side effects. Chloramphenicol disrupts the function of hematopoietic organs, so a blood test is necessary during treatment with these drugs. Can cause dysbacteriosis.

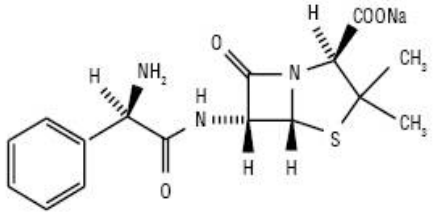
Penicillins

Penicillins

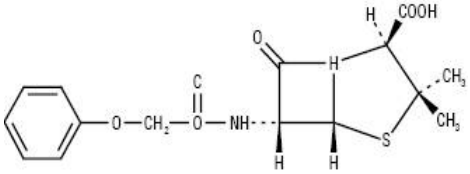
Benzylpenicillin sodium (potassium) salt



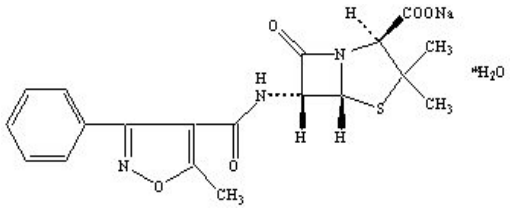
Ampicillin sodium salt



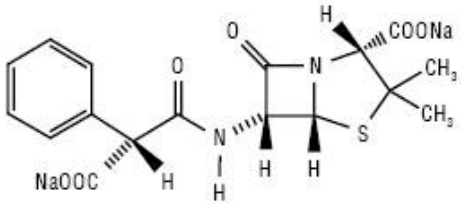
Phenoxymethylpenicillin



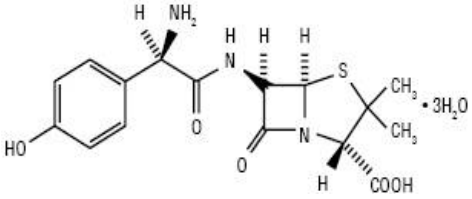
Oxacilin sodium salt



Carbenicillin disodium salt

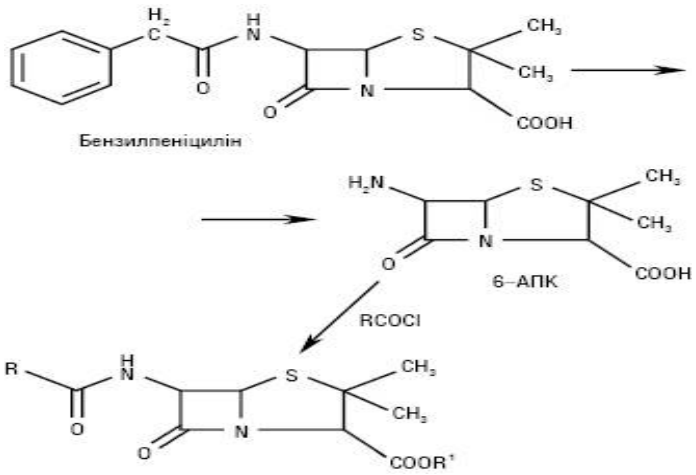


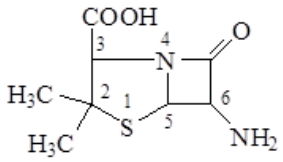
Amoxicillin trihydrate



Mechanism of action. Penicillins block the synthesis of peptidoglycan (a biopolymer that is the main component of the cell wall of bacteria). All P. have a bactericidal effect due to the death of bacteria.

Synthesis.





6-амінопеніцилянатна кислота

Properties. Penicillins are white crystalline substances with a bitter taste. Sodium and potassium salts of P. are easily or very easily soluble in water, difficult in organic solvents, often hygroscopic. Free acids, novocaine salt of benzylpenicillin are sparingly soluble in water and easily soluble in organic solvents.

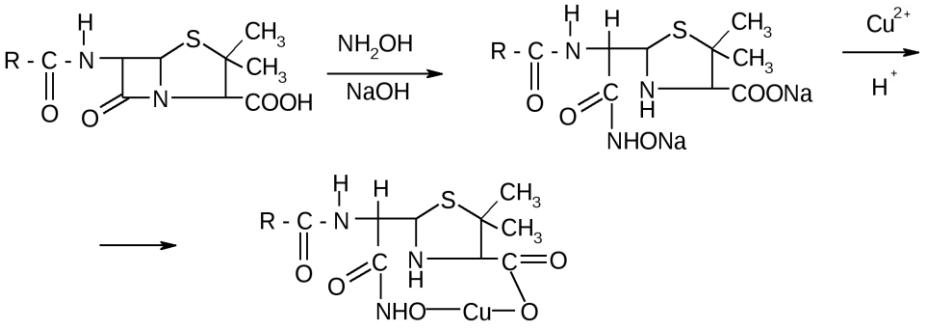
Identification.

1. IR-, UV-spectrum, TLC.

2. Reaction with formaldehyde in the presence of H_2SO_4 (conc.) - characteristic coloration

3. Substances (salts) give reactions to Na^+, K^+, novocaine.

4. Non-pharmacopoeial reactions:



- determination of organically bound sulfur after its transformation into sulfide ion during fusion with alkalis;
- reaction to an aliphatic amino group (ampicillin, amoxicillin) with ninhydrin - purple color

Quantitative definition.

1. Liquid chromatography method.

2. Microbiological method of diffusion in agar.

3. Chemical method in two stages:

- determination of the amount of penicillins;
- determination of the content of the corresponding medicinal substance.

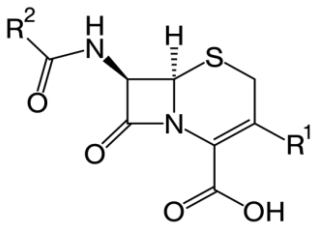
Storage. In a dry place at room temperature.

Application. Natural P. affect gram-positive microorganisms and are used to treat pneumonia, gonorrhea, syphilis, purulent infections, diphtheria, scarlet fever. They cannot

be taken per os, because in an acidic environment - inactivation (phenoxymethylpenicillin and semi-synthetic P. are stable in an acidic environment). Natural P. are destroyed under the action of penicillinase, semi-synthetic analogues are more resistant to it and have a wider spectrum of action.

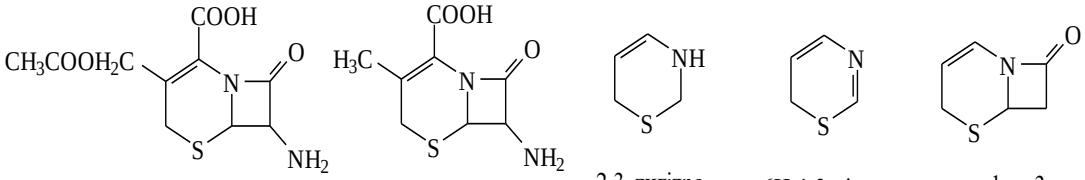
Side effect.P. can cause gastrointestinal disorders. Allergic reactions are very rare.

Cephalosporins



Cephalosporins– beta-lactam antibiotics, whose chemical structure is based on 7-aminocephalosporinic acid (7-ACC).

First isolated in 1948 from the fungus Cephalosporium aeromonium.



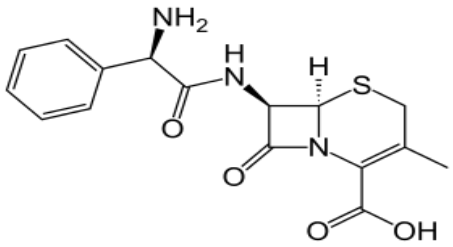
7-АЦК | 7-АДЦК | 2,3-дигідро-1,3,6Н-тіазин | 6Н-1,3-тіазин | цефем-3

Mechanism of action. Associated with damage to the cell membrane of dividing bacteria, which is caused by the specific inhibition of enzymes that are penicillin-binding proteins (PPB).

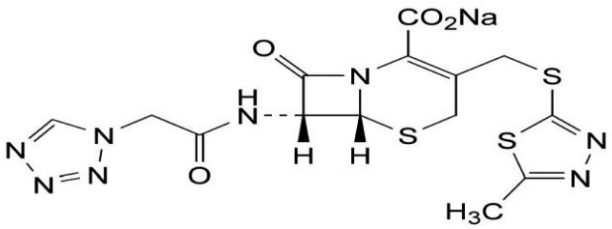
Generation of cephalosporins

Покоління	*Препарати*	*Активність щодо*		*Стійкість до β-лактамаз*	
		грампозитивних бактерій	*грамнегативних бактерій*	*грампозитивних бактерій*	*грамнегативних бактерій*
I	Цефалотин, цефалоридин, цефазолін, цефапірин, цефалексин, цефрадин, цефадроксил, цефтезол, цефацетрил	+++	+/–	+	–
II	Цефуроксим, цефокситин, цефамандол, цефаклор, цефоніцид, цефоранід, цефотетан, цефотіам, цефметазол, цефроксадин, цефминокс, цефузонам, цефтетрам	++	+	+	+/–
III	Цефотаксим, латамоксеф, цефодизим, цефтіолен, цефоперазон, цефпірамід, цефподоксим, цефіксим, цефтибутен, цефтріаксон, цефпімізол, цефзулодин, цефтазидим	+	+++	+/–	+
IV	Цефпіром, цефепім, цефклідин, цефозопран	++	+++	+	++

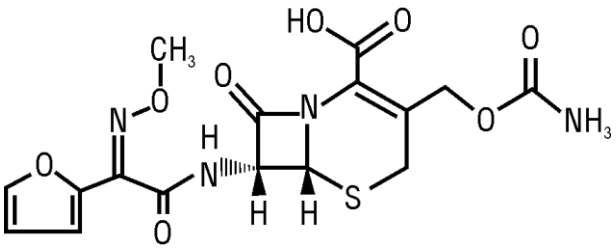
Cephalexin



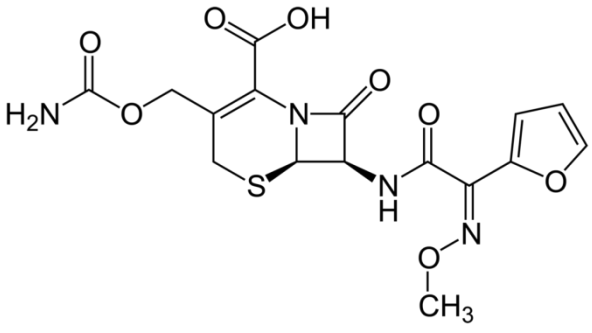
Cefazolin sodium salt



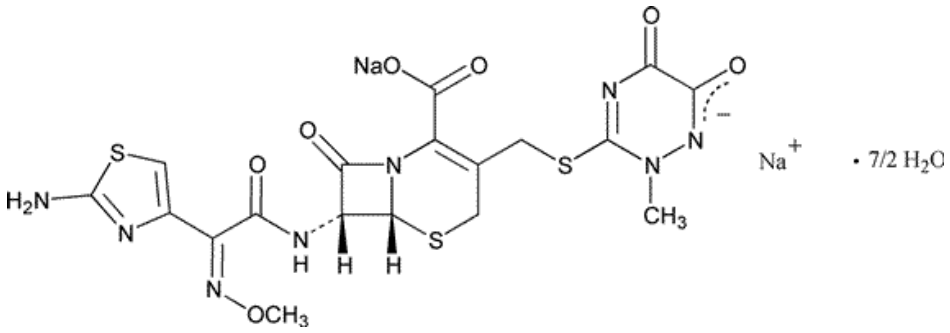
Cefuroxime



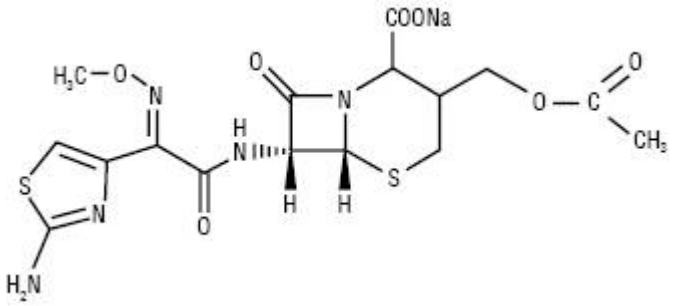
Cefoxitin



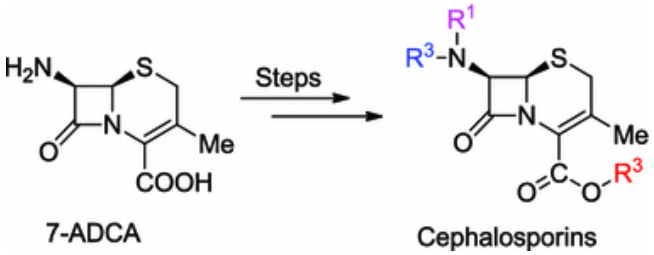
Ceftriaxone sodium salt



Cefotaxime sodium salt



Synthesis.



Properties. White powders, sometimes with a yellowish tinge. Slightly soluble in water (with the exception of Na^+ salts), hardly soluble in alcohol. Some have a characteristic smell and are sensitive to the world.

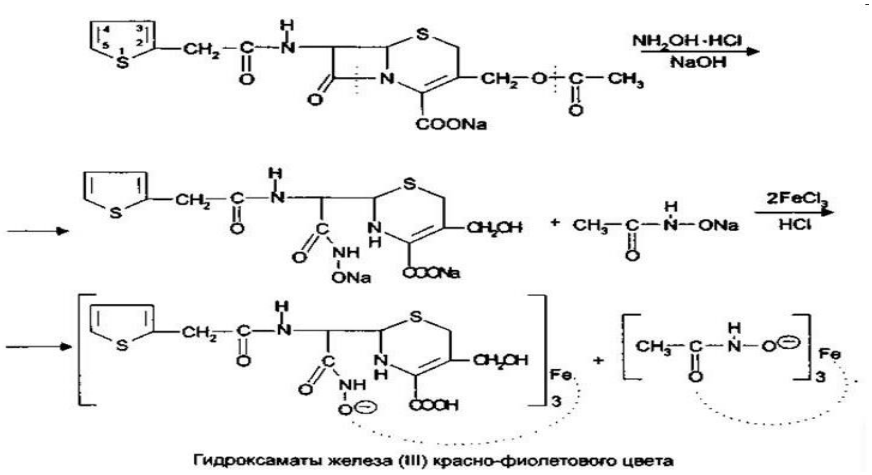
Identification.

1. IR-, UV-spectrum, TLC.

2. Reaction with formaldehyde in the presence of H_2SO_4 (conc.) - characteristic coloration.

3. Na+ salts give corresponding reactions to the sodium cation.

4. The presence of a β-lactam cycle - reactions for the formation of Cu (II) or Fe (III) hydroxamates:



Гидроксаматы железа (III) красно-фиолетового цвета

Quantitative definition.

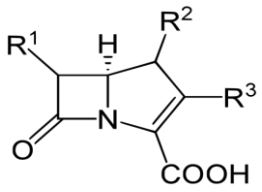
1. Method of liquid chromatography.
2. Chemical methods (analogous to penicillins).
3. Biological methods.
4. Physico-chemical methods (spectrophotometry, photocolorimetry).

Storage. In a dry place protected from light.

Application. Cephalosporins have a wider spectrum of action than penicillins and lower toxicity. The difference in the structure of penicillins and C. determines the resistance of C. to staphylococcal penicillinase and greater resistance to the action of acids. Therefore, Ts. is prescribed for the treatment of penicillin-resistant infections. Ts. is used for acute and chronic diseases of the respiratory organs, urinary tract, and genital organs; with postoperative and other infections.

Carbopenems

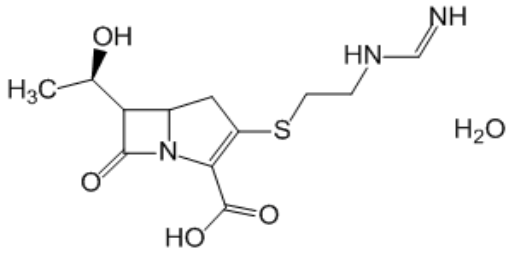
A class of β-lactam antibiotics that have a β-lactam ring in their structure that is not directly connected to a thiazolidine ring:



Mechanism of action. Like all β-lactam antibiotics, it consists in the violation of the synthesis of the microbial cell at the time of mitosis. But at the same time, Carbopenem has certain features. Carbopenems penetrate the microbial cell much better and faster than other β-lactam antibiotics.

Carbopenemshave a wide range of therapeutic effects, are well tolerated, and are low-toxic drugs. The extremely wide range of action of K., the low level of resistance of microorganisms to them make it possible to use them in the mode of antibacterial monotherapy, including for severe infections in intensive care units.

Imipenem



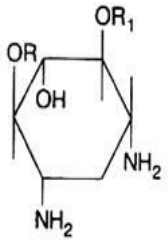
*Imipenem*has been used in clinical practice since 1980 and was developed by the pharmaceutical company Merck Sharp & Dohme, (MSD).

Properties. Powder from white or almost white to light yellow.

Application. Indicated for severe, polyresistant infections (mainly nosocomial) and mixed infections; in cases of primary therapy, preceding the identification of the causative agent; bone and joint infections; infections of the abdominal cavity and gynecological infections, sepsis and septic endocarditis, complicated infections of the genitourinary system, skin and soft tissue infections, lower respiratory tract infections.

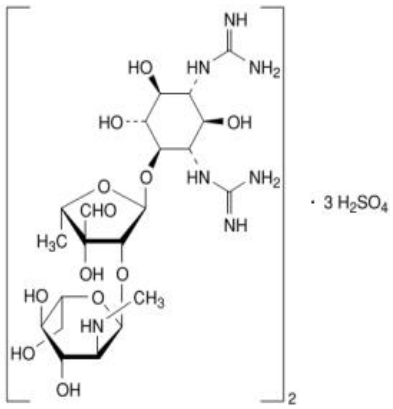
Aminoglycoside antibiotics

Aminoglycosides- a group of natural and semi-synthetic antibiotics, the molecule of which includes aminosaccharides connected by a glycosidic bond with an aglycon fragment - a hexose.



де R, R_1 – аміноцукри

Streptomycin sulfate



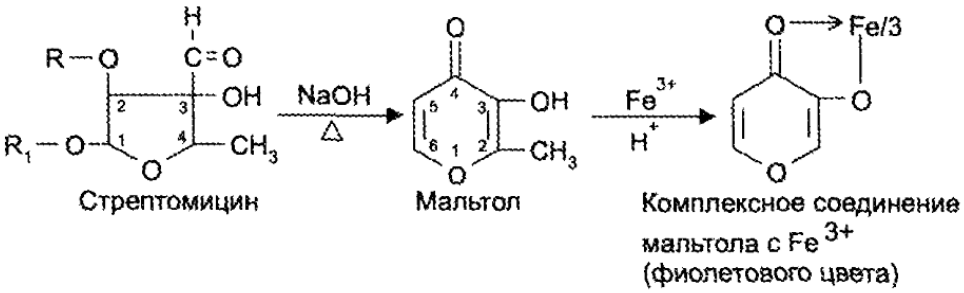
Properties. The powder is white (almost white). Hygroscopic,

very easily soluble in water, practically insoluble in ethanol and ether.

Identification.

1. TSH
2. Maltol test: in an alkaline environment S.→maltol; + $FeCl_3$ –

purple color:



3. Reaction to sulfates:

4. Express methods:

- + NaOH, heating→ammonia;
- + $K_2[HgI_4]$ (alkaline)→brown color;
- + Fehling's reagent→red sediment.

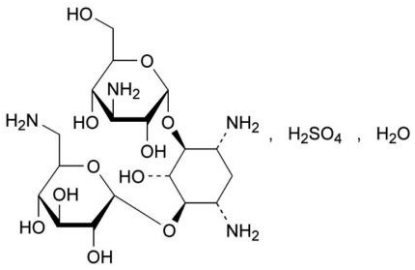
Quantitative definition.

1. Microbiological method.
2. Photocolorimetry using maltol sample.

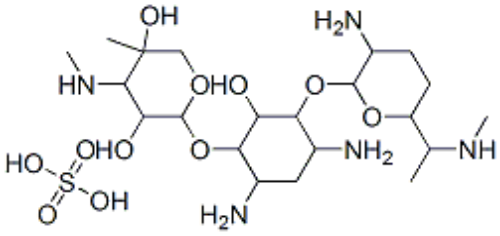
Storage. In a dry place, taking into account hygroscopicity.

Application. In the treatment of tuberculosis, pneumonia, peritonitis, gonorrhea, brucellosis.

Kanamycin monosulfate



Gentamicin sulfate



Properties. Powders of white or almost white color, hygroscopic,
soluble in water.

Identification.

1. TSH
2. Reaction of the aliphatic amino group of kanamycin with ninhydrin.
3. Reaction to sulfates.

Quantitative definition.

1. Microbiological method.
2. Polarimetry (gentamicin sulfate).

Storage. In a sealed package, in a place protected from light.

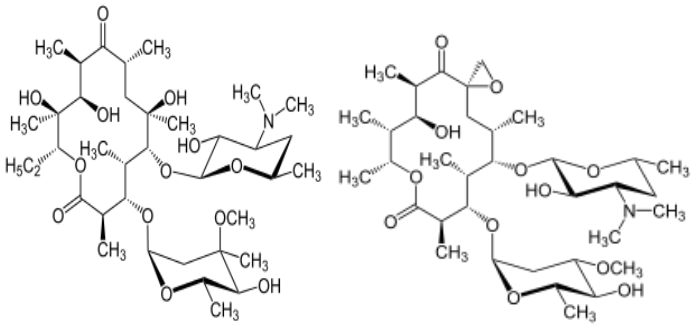
Application.A wider spectrum of antibacterial action than antibiotics of the heterocyclic structure. For the treatment of diseases of the gastrointestinal tract, tuberculosis, infectious diseases of the skin, sepsis, urinary tract.

Macrolide antibiotics

Macrolides(Greek – makros big + lithos – stone) – antibiotics containing in their molecule a macrocyclic lactone ring connected to hydrocarbon residues.

Mechanism of action. They bind to 50S subunits of ribosomes and inhibit RNA synthesis and, accordingly, protein synthesis in the microbial cell.

ErythromycinOleandomycin



Erythromycin. The first antibiotic from the macrolide group, clinical use began in 1952.

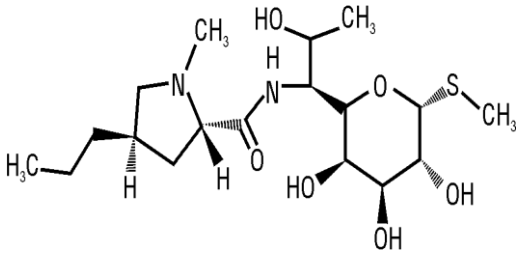
Oleandomycin. First obtained in 1954, Nateper is an outdated antibiotic, not used in clinical practice in most countries of the world.

Application. The spectrum of action is similar to penicillin. For the treatment of diseases of the upper respiratory tract, rheumatic heart disease, diseases of the genitourinary system.

Lincosamides

Lincosamides- a class of antibiotics that includes the natural antibiotic lincomycin and its semi-synthetic analogue clindamycin.

Lincomycin hydrochloride

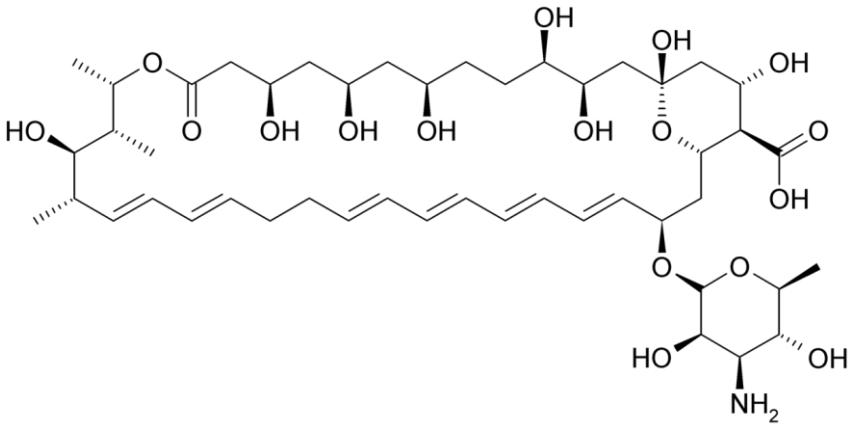


Mechanism of action. Suppress the synthesis of microbial cell proteins by binding 50S subunits of ribosomes, inhibiting the incorporation of transport RNA into ribosome-iRNA complexes. As a result, a bacteriostatic effect develops.

Application. Treatment of severe infections caused by lincomycin-susceptible strains of streptococci, pneumococci, and staphylococci. The use of this drug should be limited to patients allergic to penicillin or other patients for whom, in the opinion of the doctor, the use of penicillin is inappropriate.

Polyene antibiotics of glycosidic structure

Nystatin



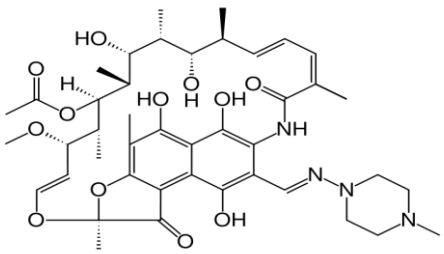
Mechanism of action. It binds to the sterols of the cell membrane of fungi, as a result of which the membrane becomes unable to function as a selective barrier, which leads to the loss of the main components of the cell.

Application. Treatment of diseases caused by fungi of the genus Candida (Candida albicans, etc.), candidiasis of the mucous membranes of the oral cavity, skin and digestive tract.

Anzamycin antibiotics

The basis of the structure is an aromatic core connected to a macrocyclic aliphatic chain called anza-chain. The aliphatic chain does not contain the lactone bonds characteristic of macrolide antibiotics and is attached to the nucleus by an amide N atom.

Rifampicin



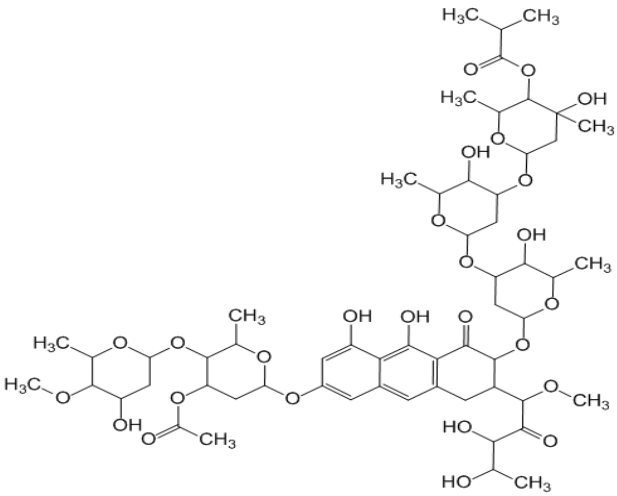
Mechanism of action. It consists in inhibition of DNA-dependent RNA polymerase, which inhibits transcription.

Application.A wide range of action is combined with high efficiency. It is prescribed in cases where other antibiotics are ineffective. For the treatment of all forms of tuberculosis, with lesions of the gastrointestinal tract and purulent infections.

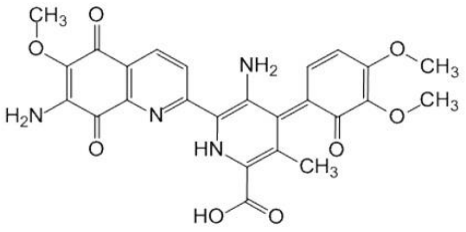
Antitumor antibiotics

Antitumor antibiotics, which are used in medical practice:

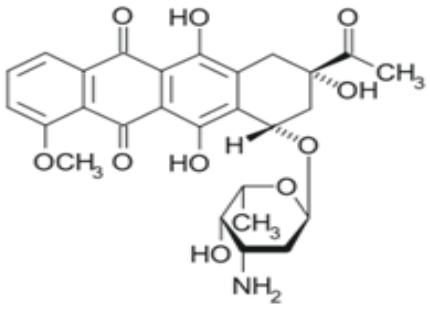
- derivatives of aureolic acid (olivomycin);
- anthracycline derivatives (rubomycin);
- quinoline-3,5-dione derivatives (bruneomycin).



Olivomycin



Bruneomycin



Рубомицин

General material and bulk-methodological support of the lecture:

- ✓ computer presentation;
- ✓ illustrative materials;
- ✓ examples of solving typical tasks or performing typical tasks;
- ✓ multimedia projector.

Questions for self-control:

1.Classification of antibiotics

2.Pharmaceutical analysisTetracyclines

3.Pharmaceutical analysisChloramphenicol

4.Pharmaceutical analysisPenicillins, Cephalosporins

5.Pharmaceutical analysisCarbopenems, aminoglycoside antibiotics,

6.Pharmaceutical analysisMacrolide antibiotics, lincosamides

7. Polyene antibiotics of glycoside-like structure

8.Pharmaceutical analysisAnzamycin antibiotics, Antitumor antibiotics

References:

Main:

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2. World Health Organization. - [Electronic resource]. - Access mode:http://www.who.int.

3. Pharmaceutical encyclopedia. - [Electronic resource]. – Access mode: http://www.pharmencyclopedia.com.ua.

4. Official website of the International Organization for Standardizationhttp://www.iso.org/iso/home.html

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Lecture No. 7

Topic: Antimicrobial drugs. Sulfanilamides. Derivatives of naphthyridine and quinolonecarboxylic acids. Derivatives of 8-oxyquinoline, quinoxaline and nitrofural.

Actuality of theme: Pharmaceutical chemistry is a science that studies methods of preparation, structure, physical and chemical properties of medicinal products; relationship between their chemical structure and action on organism; methods of quality control of drugs and changes that occur during their storage, as well as their use in medicine. Therefore, it is urgent to solve the problems facing pharmaceutical chemistry with the help of physical, chemical and physico-chemical methods, which are used both for synthesis, as well as for the analysis of medicinal products.

The purpose:the formation of students' knowledge about the peculiarities of the storage of medicinal products, which affect the afferent nervous system, as well as the characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of obtaining, methods of analysis, application in medicine. As a result of the lecture, students should learn the properties and methods of analysis of antimicrobial drugs means,sulfonamides, derivatives of 8-oxyquinoline, quinoxaline and nitrofural.

Basic concepts:pharmaceutical chemistry, qualitative analysis, quantitative analysis, State Pharmacopoeia of Ukraine, physicochemical methods of analysis, impurities, express analysis.

Plan and organizational structure of the lecture:

1.Preparatory stage

1.1.Determination of educational The purposes.

1.2.Providing positive motivation.

2. The main stage

Presentation of lecture material

Plan:

-Classification of antimicrobial drugs

- Derivatives of sulfanilic acid amide

- Derivatives of naphthyridine and quinolone carboxylic acids

-Fluoroquinolones

-Derivatives of 8-hydroxyquinoline

-Nitrofuran derivatives

3. The final stage

3.1. Summary of the lecture, general conclusions.

3.2. The lecturer's answers to possible questions

3.3. Tasks for self-training of students.

Content of lecture material (lecture text):

Antimicrobial drugs (Greek anti – against + micros – small + bios – life) – drugs that have a suppressive effect on bacteria.

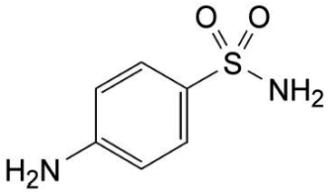
Antimicrobial drugsdivided into two groups:

- drugs of non-selective antimicrobial action, which have a detrimental effect on most microorganisms (antiseptic drugs and disinfectant compounds);
- drugs with a more selective effect on certain types of bacteria and a significant breadth of therapeutic action (chemotherapeutic drugs - antibiotics and synthetic antibacterial drugs: sulfonamides, derivatives of quinolone, naphthyridine, quinoline, nitrofuran, imidazole).

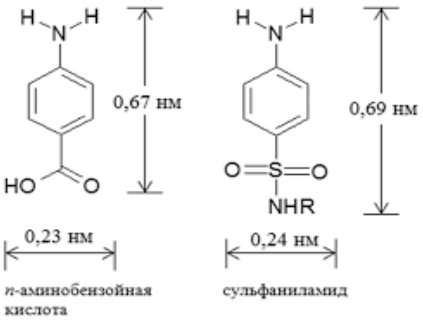
Specific chemotherapeutic (with selective cytotoxicity) antituberculosis drugs are divided into two groups:

- drugs of the first line (main): isonicotinic acid hydrazide (isoniazid) and its derivatives (hydrazones), antibiotics (streptomycin, rifampicin), PASK and its derivatives;
- drugs of the II series: ethionamide, prothionamide, ethambutol, cycloserine, pyrazinamide, thioacetazone, aminoglycosides (kanamycin).

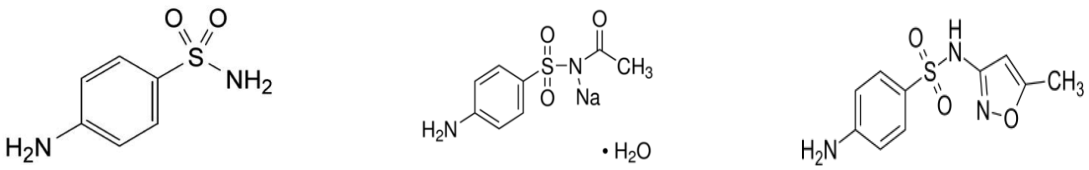
Derivatives of sulfanilic acid amide



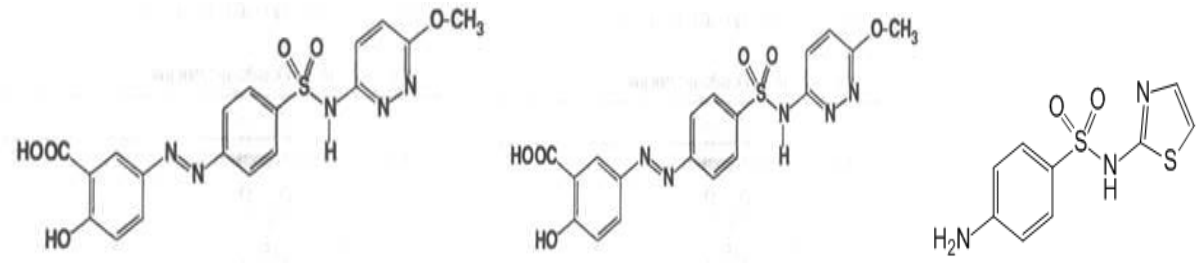
Mechanism of action. It is based on the competitive antagonism of sulfonamides and para-aminobenzoic acid (PABA): PABA is the starting product for the synthesis of folic acid in the microbial cell, without which the growth and reproduction of the microbial cell is impossible. The microbial cell absorbs sulfonamide instead of PABA, thereby blocking the first stage of nucleic acid synthesis.



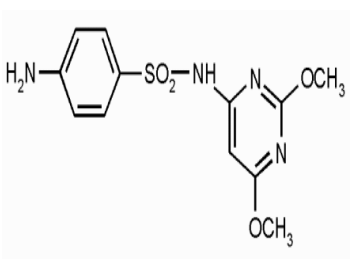
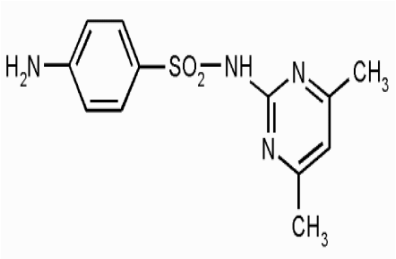
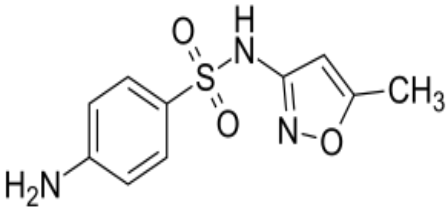
Sulfanilamide Sulfacetamide sodium Cotrimoxazole



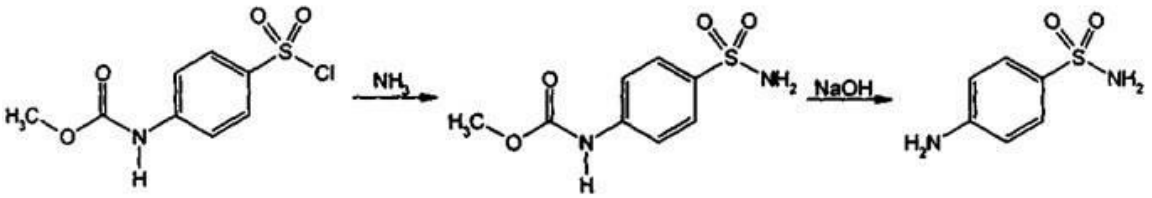
Salazodin Salazopyridazine Sulphathiazole



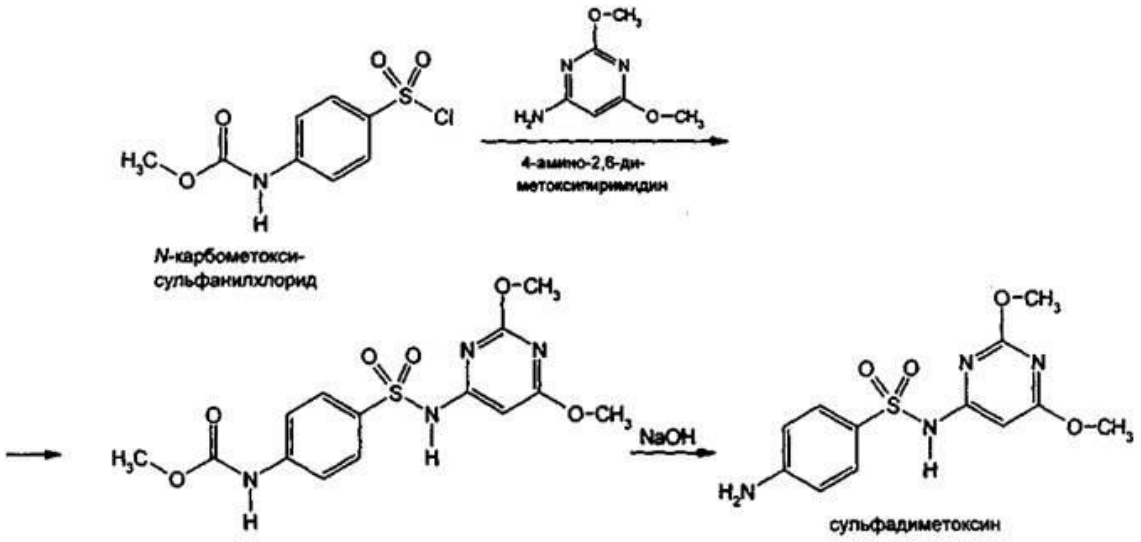
Sulfadimethoxine Sulfadimidine Sulfamethoxazole

Synthesis.

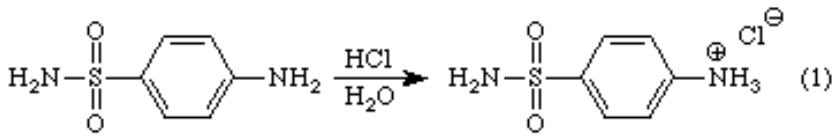


Так получают большинство сульфаниламидов, например сульфадиметоксин:



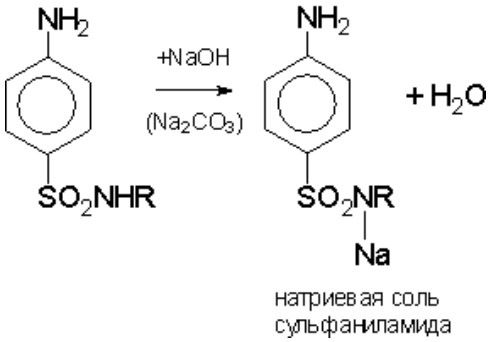
Properties and identification. White, odorless crystalline powders, slightly soluble in water, except for sodium sulfacetamide. Most sulfonamides are amphoteric compounds.

1. How bases dissolve in acids, forming salts that are strongly hydrolyzed in water and practically do not exist.



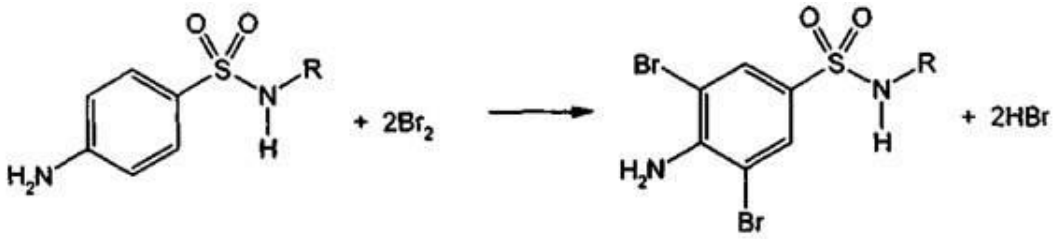
Sulfanilamide Sulfanilamide hydrochloride

Easily dissolve in alkalis and carbonates of alkali metals:

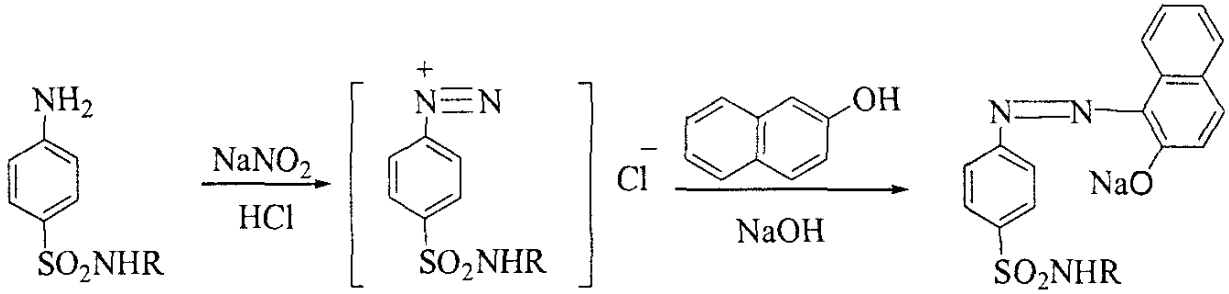


натриевая соль
сульфаниламида

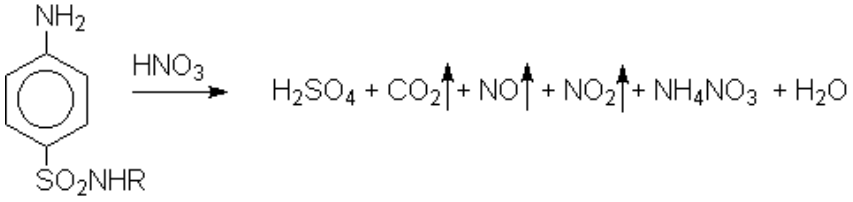
2. All sulfonamides can be halogenated, nitrated, sulfonated:

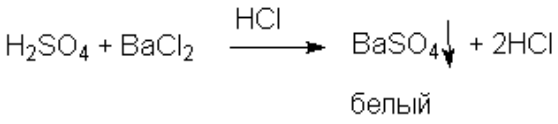


Sulfonamides undergo a diazotization reaction with the following azo compound - a cherry-red color appears:



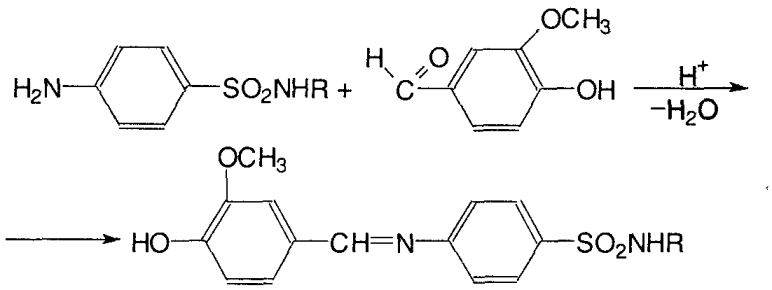
4. To detect the sulfur atom in the sulfamide group - an oxidation reaction; the obtained sulfates are determined by reaction with barium chloride:



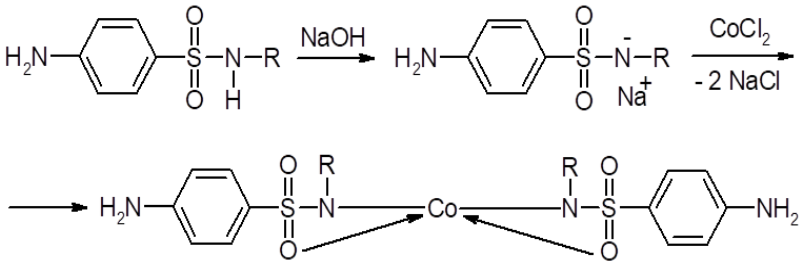


белый

5. Lignin sample – orange-red color

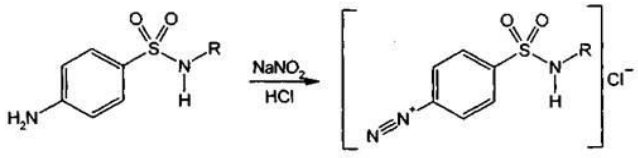


6. Reactions with salts of heavy metals, Cu (II), Fe (III) - colored complexes are formed:

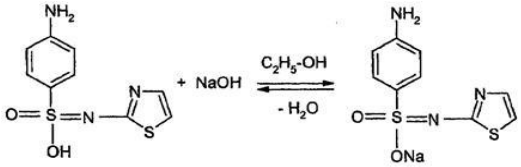


Quantitative definition.

1. Nitritometry method, s = 1:

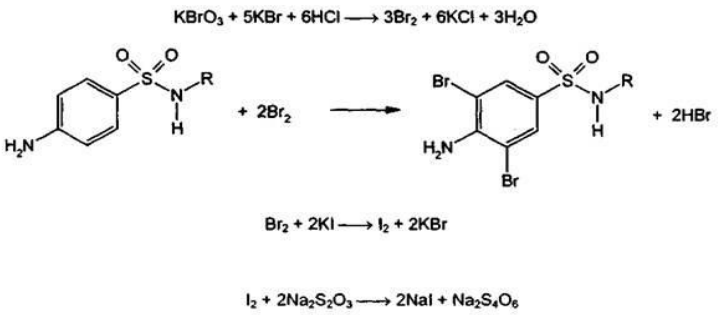


2. Alkalimetry, s = 1:

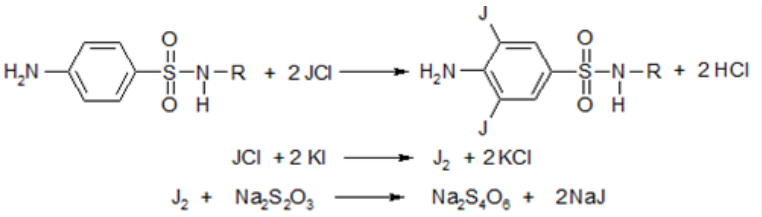


3. Acidimetry, indicator – methyl orange, s = 1:

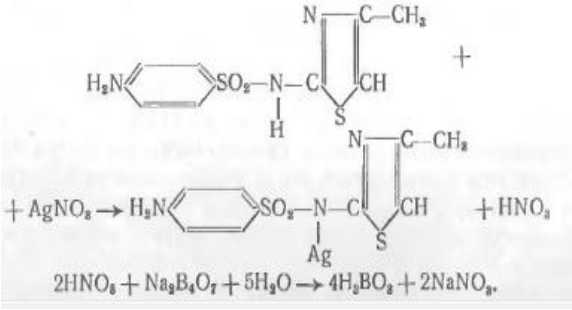
4. Bromatometry, s = 1.5:



5. Iodochlorometry, s = 1/2:



6. Argentometry, titration is carried out in the presence of sodium tetraborate, the indicator is potassium chromate (Mohr's method), s = 1:



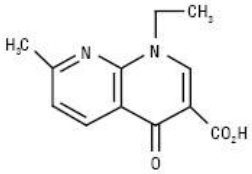
7. Photocolorimetry is based on the ability of sulfonamides to form azo dyes.

8. Spectrophotometric methods of quantitative determination.

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

Derivatives of naphthyridine and quinolonecarboxylic acids

Nalidixic acid



Mechanism of action. Inhibition of DNA synthesis.

Properties. Practically white or pale yellow crystalline powder, practically insoluble in water, soluble in ethanol, chloroform, in methylene chloride and in dilute solutions of alkalis and carbonates.

Identification.

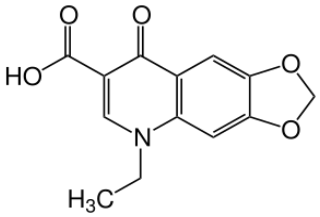
1. IR-, UV-spectrum, TLC.
2. The reaction of the substance in hydrochloric acid with β-naphthol - orange-red color.

Quantitative definition. Alkalimetry in ethanol.

Storage. Store in a tightly closed container, in a place protected from light.

Application. Infectious-inflammatory diseases, mainly of the gastrointestinal tract and genitourinary system, are caused by sensitive microorganisms.

Oxolinic acid



Mechanism of action. Inhibition of DNA synthesis in bacterial cells.

Properties. Almost white or yellowish crystalline powder, practically insoluble in water, alcohol, sparingly soluble in methylene chloride, soluble in dilute alkali solutions.

Identification.

IR-, UV-spectrum, TLC.

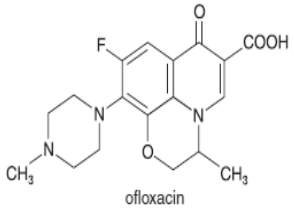
Quantitative definition. Titration of tetrabutylammonium hydroxide in DMF medium with potentiometric fixation of the equivalence point.

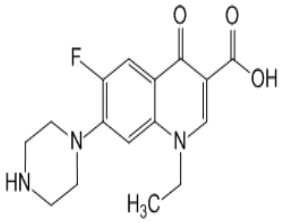
Storage. In a tightly closed container, in a place protected from light.

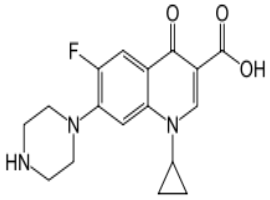
Application. Cystitis, pyelitis, nephritis, prostatitis. Bacteriuria caused by microorganisms sensitive to the drug.

Fluoroquinolones

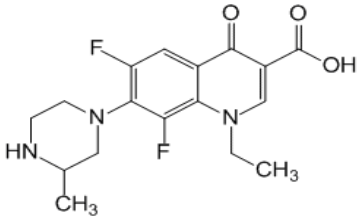
Ofloxacin Norfloxacin Ciprofloxacin hydrochloride

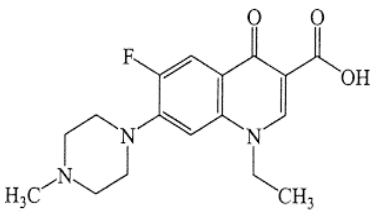






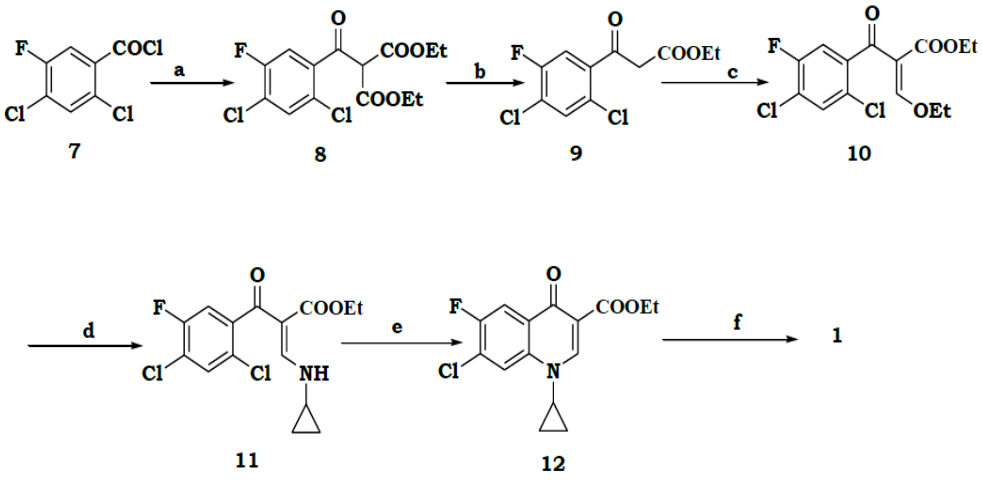
Lomeofloxacin hydrochloride Pefloxacin





Mechanism of action. Act bactericidally, disrupting DNA synthesis in bacterial cells, blocking two vital bacterial enzymes - DNA gyrase and topoisomerase.

Synthesis.



Scheme 2: Bayer's second synthesis of ciprofloxacin
(a) $CH_2(COOEt)_2$/Mg/EtOH; (b) H^+, Δ; (c) $HC(OEt)_3/Ac_2O$; (d) Cyclopropylamine; (e) K_2CO_3, DMF;(f) Piperazine

Properties. Pale yellow crystalline powders, norfloxacin and ciprofloxacin are hygroscopic. Very slightly or practically insoluble in water, slightly soluble in alcohol and acetone. Norfloxacin is photosensitive. The hydrochloride salts of ofloxacin and ciprofloxacin are soluble in water and practically insoluble in alcohol, acetone and methylene chloride.

Identification.

1. IR spectrum.
2. Hydrogen chloride salts - a reaction to chlorides.
3. Reactions on the heterocyclic N-atom of nitrogen with common alkaloid reagents – $K_2[HgI_4]$, picric acid, etc.
4. Fluorine is determined after mineralization.

Quantitative definition.

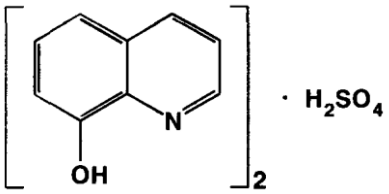
1. Acidimetry in a non-aqueous medium, direct titration, s = 1.
2. Hydrogen chloride salts are determined by liquid chromatography.

Storage. In a well-closed container, in a place protected from light.

Application. All fluoroquinolones are active against most gram-negative microorganisms, many strains of staphylococci, legionella, mycoplasma, and chlamydia. With infections of the respiratory tract, skin and soft tissues, bones
and joints, gastrointestinal tract, postoperative infections.

Derivatives of 8-hydroxyquinoline

Quinozol



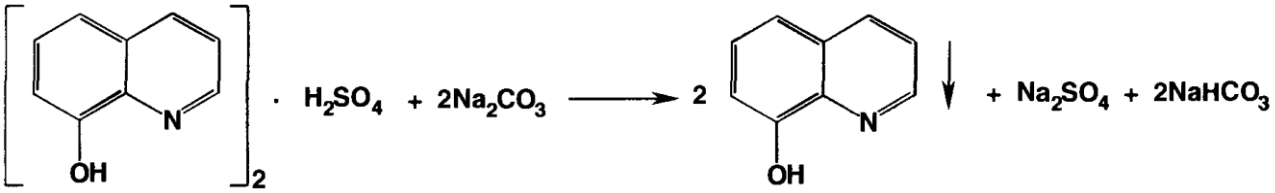
Mechanism of action. Disrupts protein synthesis, forms chelates, the latter intensify oxidative processes in protoplasm.

Synthesis

Properties. Fine-crystalline powder of lemon-yellow color, peculiar smell. Easily soluble in water, slightly soluble in alcohol.

Identification.

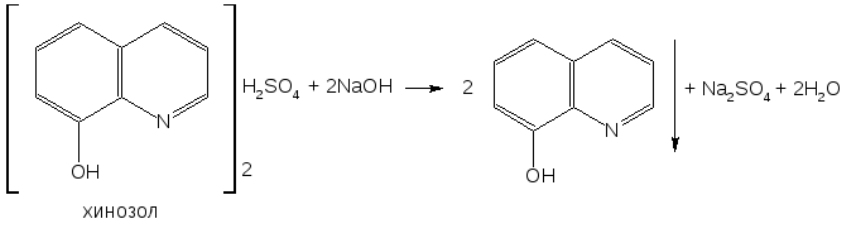
1. Reaction with an aqueous solution of Na2CO3 - a precipitate of 8-oxyquinoline is formed, which dissolves in an excess of the reagent:



2. Complex formation reactions with metal ions (Mg2+, Fe3+, Cu2+).

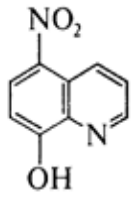
Quantitative definition.

Alkalimetry by the bound acid H2SO4



Application. Antiseptic and spermatocidal drug.

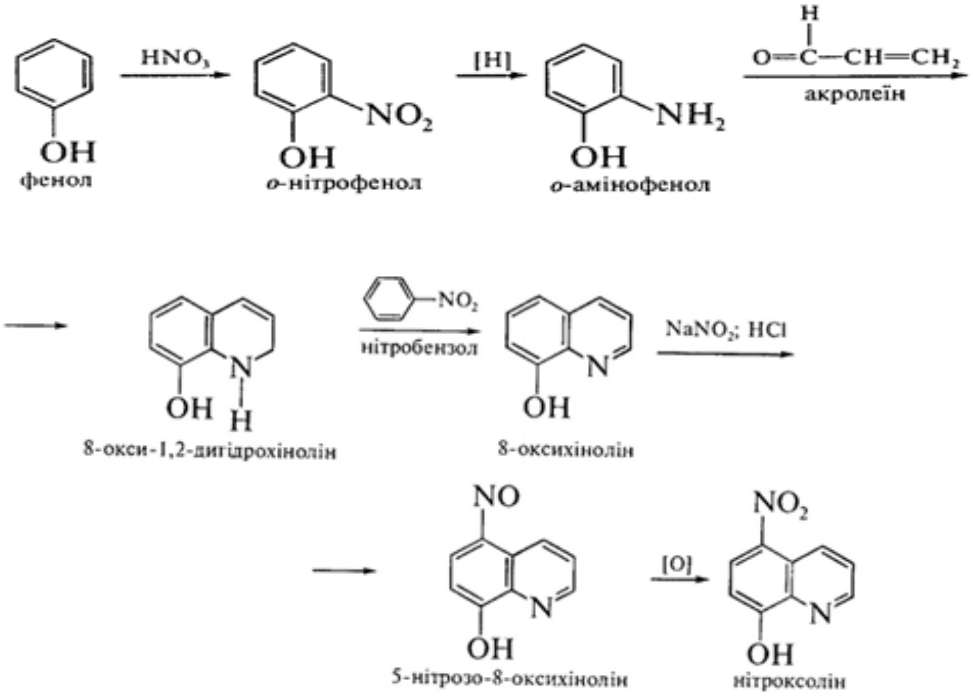
Nitroxoline



5-Нітро-8-оксихінолін

Mechanism of action. Blocks enzyme function by binding metal ions in enzymes of microorganisms, thus preventing these enzymes from binding to a specific substrate.

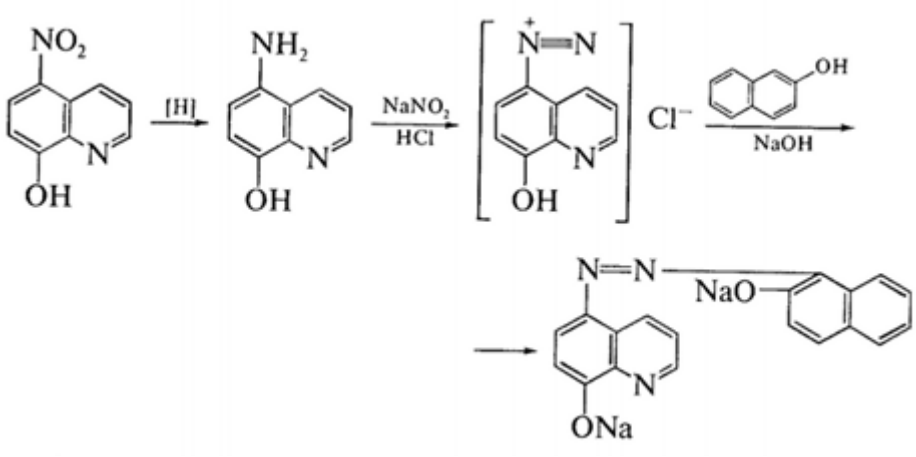
Synthesis.



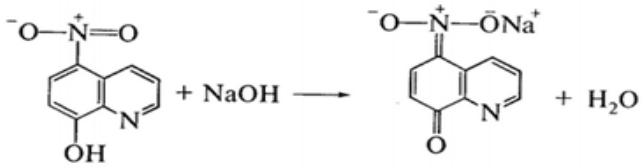
Properties. Fine crystalline powder of yellow or grayish-yellow color. Practically not soluble in water.

Identification.

1. UV spectrum.
2. With $FeCl_3$ solution – black-green color.
3. Reduce $–NO_2$ to $–NH_2$, diazotization reaction and azo compound – orange-red color:

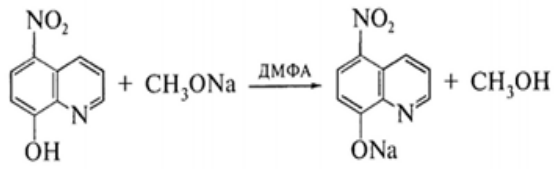


4. Reaction with NaOH solution – red-orange color:

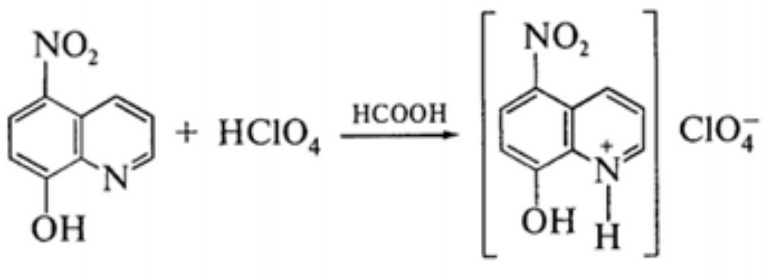


Quantitative definition.

1. Alkalimetry in a non-aqueous environment, direct titration, indicator – thymol blue in DMF, s = 1:



2. Acidimetry in a non-aqueous medium, direct titration, indicator – malachite green, s = 1:



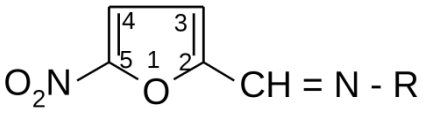
3. Nitritometry after the reduction of the nitro group to the amino group, s = 1.

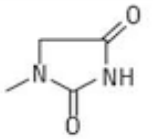
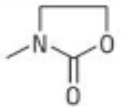
Storage. In a dry place protected from light.

Application. Antibacterial agent for urogenital infections

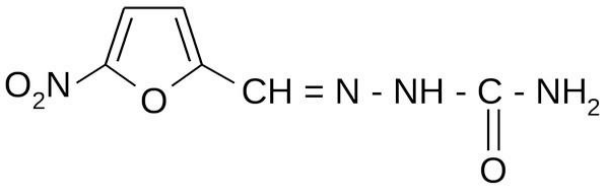
tract (pyelonephritis, cystitis, etc.).

Nitrofuran derivatives



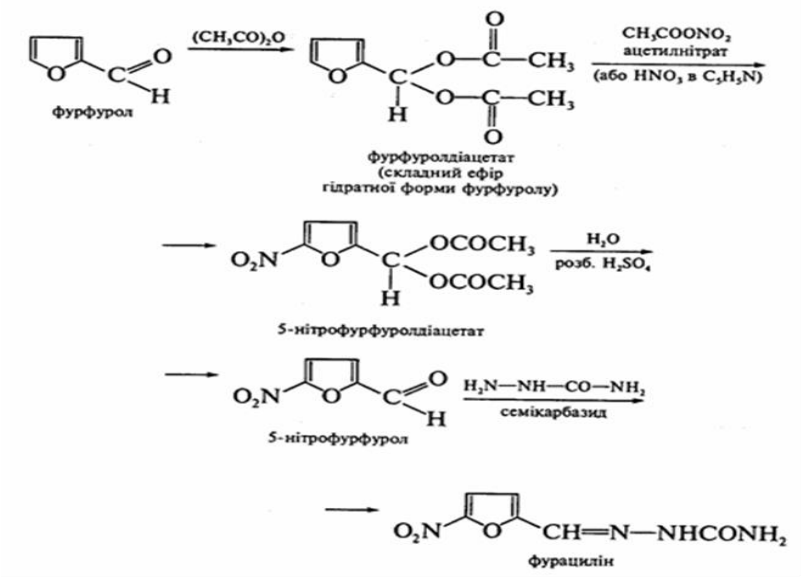
Активна речовина	R
Нітрофурал	–NH–CO–NH$_2$
Нітрофурантоїн	
Фуразолідон	

Nitrofural



Mechanism of action. Associated with the ability to restore a nitro group to an amino group, disrupt DNA function, inhibit cellular respiration of microorganisms

Synthesis.

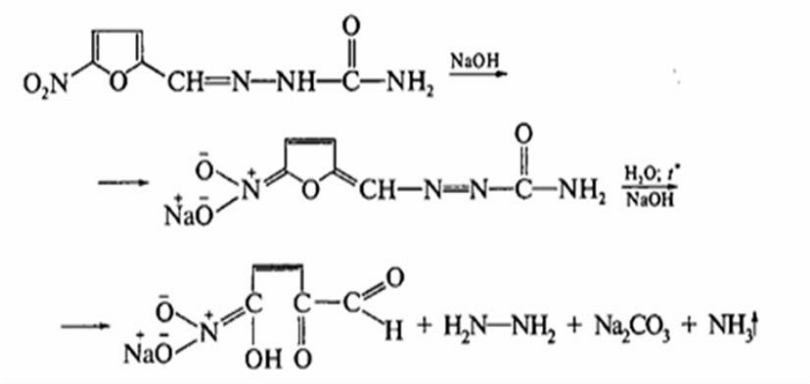


Properties. Yellow or brownish-yellow crystalline powder. Very slightly soluble in water (1:4200, solubility increases in the presence of NaCl), slightly soluble in 96% alcohol, practically insoluble in ether, soluble in alkali solutions.

Identification.

1. IR-, UV-spectrum, TLC.

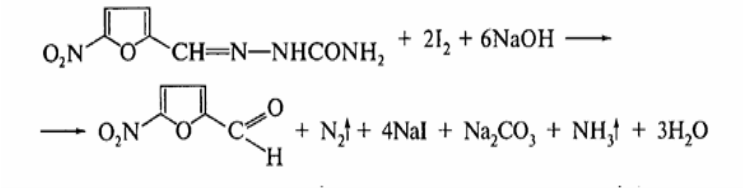
2. + NaOH – orange-red color, heating – release of ammonia:

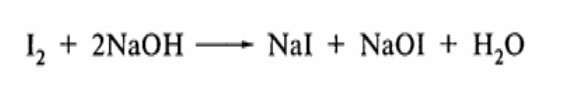


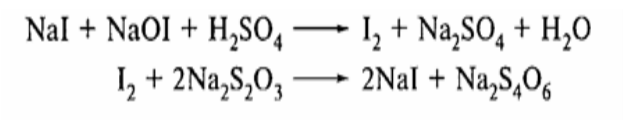
3. Heating in an acidic environment with Zn dust – the solution becomes discolored due to the reduction of $–NO_2$ to $–NH_2$:

Quantitative definition.

1. Iodometry in an alkaline environment, reverse titration, the indicator is starch, s= 1/2:







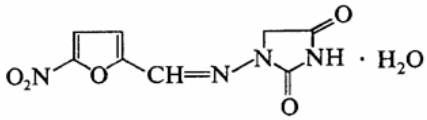
2. Spectrophotometry (standard method at λ = 375 nm).

3. Photocolorimetry (determination of the optical density of an alkaline solution of F.).

Storage. In well-stoppered glasses of dark glass, in a cool place protected from light.

Application. Antibacterial agent, acts on a variety of gram-positive and gram-negative microorganisms. Externally for the treatment and prevention of purulent-inflammatory processes and internally for the treatment of bacterial dysentery.

Nitrofurantoin



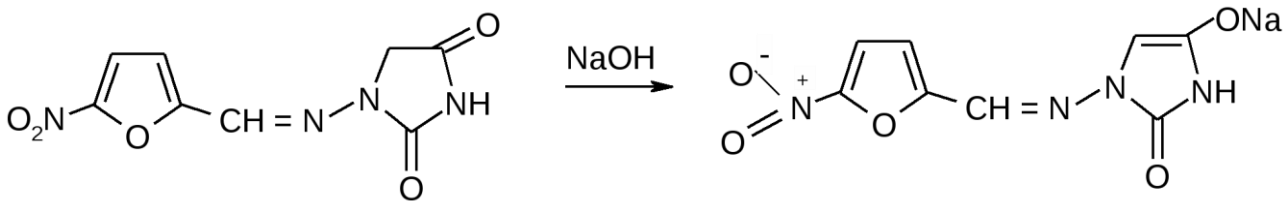
N-(5-Нітро-2-фурфуриліден)-1-аміногідантоїн

Mechanism of action. Associated with the ability to restore a nitro group to an amino group, disrupt DNA function, inhibit cellular respiration of microorganisms.

Properties. Yellow crystalline powder without odor, bitter in taste. Very slightly soluble in water and 96% alcohol, slightly soluble in acetone, soluble in DMF.

Identification.

1. + NaOH – dark red color:



2. Solution of N. in DMF – yellow, + alcoholic KOH – brownish-yellow:

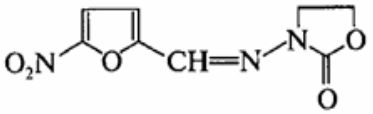
Quantitative definition.

1. UV spectrophotometry.
2. Photocolorimetry by reaction with an aqueous alkali solution.
3. Alkalimetry in a non-aqueous environment, titrant – CH_3ONa, indicator – thymol blue, s = 1.

Storage. In a well-closed container that protects against light and moisture.

Application. Antibacterial agent. Bacterial infections of the urinary tract (pyelitis, pyelonephritis, cystitis, urethritis), including for the treatment of relapses, as well as for the prevention of infection during urological operations, catheterization, cystoscopy.

Furazolidone



N-(5-Нітро-2-фурфуриліден)-3-амінооксазолідон-2

Mechanism of action. Disrupts the process of cellular respiration of bacteria, suppresses the biosynthesis of nucleic acids.

Properties. Yellow or greenish-yellow odorless powder,

bitter to the taste. Practically not soluble in water and ether, very

slightly soluble in 96% alcohol.

Identification.

1. Aqueous solution of F. + NaOH solution, heating - brown color.

2. A solution of F. in DMF is yellow, + a solution of KOH in alcohol is purple:

3. IR spectroscopy.

Quantitative definition.

1. Photocolorimetry by reaction with an alcoholic solution of KOH.

2. UV spectrophotometry (λ = 367 nm).

Storage. In a well-closed container that protects from light.

Application. Antibacterial and antiprotozoal agent. Bacillary dysentery, paratyphoid, food poisoning, enterocolitis, giardiasis, trichomonad colpitis.

General material and bulk-methodological support of the lecture:

- ✓ computer presentation;
- ✓ illustrative materials;
- ✓ examples of solving typical tasks or performing typical tasks;
- ✓ multimedia projector.

Questions for self-control:

1.Classification of antimicrobial drugs

2. Pharmaceutical analysisDerivatives of naphthyridine and quinolonecarboxylic acids

3. Pharmaceutical analysisFluoroquinolones, 8-hydroxyquinoline derivatives

4. Pharmaceutical analysisNitrofuran derivatives

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Main:

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/ In general ed. P.O. Bezuglio - Kind. 3rd edition, revised. – Vinnytsia, NOVA KNYGA, 2017. - 456 p.

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7. Nizhnyk H.P. Pharmaceutical chemistry: a textbook (University I-III years) H.P. Nizhnyk — 2nd ed., ed. - All-Ukrainian specialized publishing house "Medytsyna", 2015. - 352p.

8. Pharmaceutical chemistry. Analysis of medicinal substances by functional groups: study guide / O.O. Tsurkan, I.V. Nizhenkovska, O.O. Glushachenko. - 3rd edition - All-Ukrainian specialized publishing house "Medytsina", 2019. - 152 p.

9. Hudoyarova O.S. Pharmaceutical chemistry. - Vinnytsia: "Nilan-LTD" LLC, 2018. - 194 p.

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11. Pharmaceutical chemistry. General and special pharmaceutical chemistry. Medicines of an inorganic nature: laboratory-practical classes. Study guide / L.G. Mishina - Vinnytsia: PP "TD "Edelweiss and K"", 2010. - 384 p.

12. Analytical chemistry and instrumental methods of analysis / A.I. Gab, D.B. Shakhnin, V.V. Malyshev -Ukraine University, 2018- 396 p.

Electronic information resources:

1. Specialized medical online publication for doctors, pharmacists, pharmacists, students of medical and pharmaceutical universities. - [Electronic resource]. - Access mode:http://www.morion.ua.

2. World Health Organization. - [Electronic resource]. - Access mode:http://www.who.int.

3. Pharmaceutical encyclopedia. - [Electronic resource]. – Access mode: http://www.pharmencyclopedia.com.ua.

4. Official website of the International Organization for Standardizationhttp://www.iso.org/iso/home.html

5. Compendium online. [Electronic resource]. - Access mode:https://compendium.com.ua/bad/

6. Medline search database [Electronic resource]. – Access mode: National Library of Medicinehttps://www.nlm.nih.gov/bsd/medline.html

Lecture No. 8

Topic: Antitubercular drugs. Means for the treatment of oncological diseases. Antiviral and antimalarial agents.

Actuality of theme: Pharmaceutical chemistry is a science that studies methods of preparation, structure, physical and chemical properties of medicinal products; relationship between their chemical structure and action on organism; methods of quality control of drugs and changes that occur during their storage, as well as their use in medicine. Therefore, it is urgent to solve the problems facing pharmaceutical chemistry with the help of physical, chemical and physico-chemical methods, which are used both for synthesis, as well as for the analysis of medicinal products.

The purpose:the formation of students' knowledge about the peculiarities of the storage of medicinal products, which affect the afferent nervous system, as well as the characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of obtaining, methods of analysis, application in medicine. As a result of the lecture, students should learn the properties and methods of analysis of anti-tuberculosis drugs,drugs for the treatment of oncological diseases, antiviral and antimalarial drugs.

Basic concepts:pharmaceutical chemistry, qualitative analysis, quantitative analysis, State Pharmacopoeia of Ukraine, physicochemical methods of analysis, impurities, express analysis.

Plan and organizational structure of the lecture:

1.Preparatory stage

1.1.Determination of educational The purposes.

1.2.Providing positive motivation.

2. The main stage

Presentation of lecture material

Plan:

-Antituberculosis drugs

- Medicinal products for the treatment of oncological diseases

- Antiviral drugs

3. The final stage

3.1. Summary of the lecture, general conclusions.

3.2. The lecturer's answers to possible questions

3.3. Tasks for self-training of students.

Content of lecture material (lecture text):

Classification of anti-tuberculosis drugs according to the strength of their inhibitory effect on mycobacteria, effectiveness and tolerability during long-term use.

Drugs of the first line (basic): isoniazid, rifamlicin, pyrazinamide, ethambutol, streptomycin sulfate (drugs are more active, less toxic).

Second-line drugs (reserve): ethionamide, prothionamide, kanamycin sulfate, cycloserine, sodium paraaminosalicylate (PASK) (less effective, worse tolerated, but can inhibit the growth of mycobacteria, having developed resistance to first-line drugs).

Classificationanti-tuberculosis drugs according to the chemical structure andmechanism of action

Synthetic means: isoniazid, ethambutol, sodium paraaminosalicylate (PASK), ethionamide, pyrazinamide, thioacetazone.

Antibiotics: rifampicin, cycloserine, streptomycin sulfate, kanamycin sulfate, florimycin sulfate.

Classificationantituberculosis drugs on clinical effectiveness

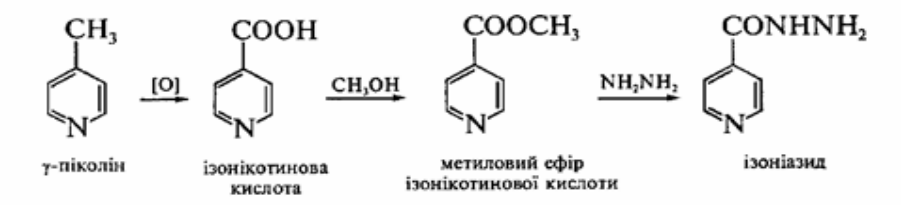
Group A. The most effective drugs: isoniazid, rifampicin.

Group B. Less effective drugs: ethambutol, streptomycin, kanamycin, florimycin, ethionamide, prothionamide, pyrazinamide, cycloserine.

Group C. The least effective drugs: PASK, thioacetazone.

Mechanism of action. Associated with inhibition of the synthesis of mycolic acids with a long chain, which are components of the cell membrane of mycobacteria.

Synthesis.

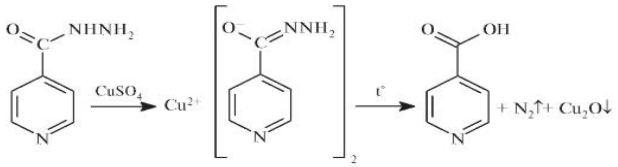


Properties. White crystalline powder, bitter in taste. Easily soluble in water, hardly soluble in alcohol, practically insoluble in ether.

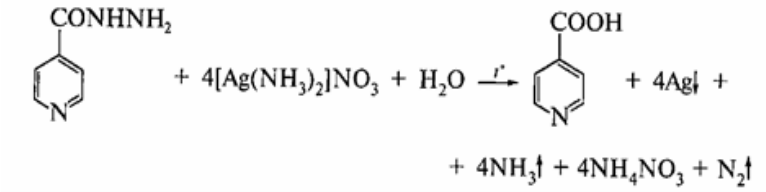
Identification.

1. T. pl., IR spectrum.

2. With $CuSO_4$ solution - blue color and sediment, gas bubbles:



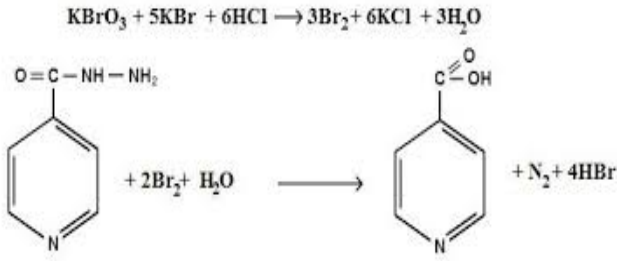
3. + $[Ag(NH_3)_2]NO_3$ solution – yellowish precipitate, then Ag plaque on the walls:



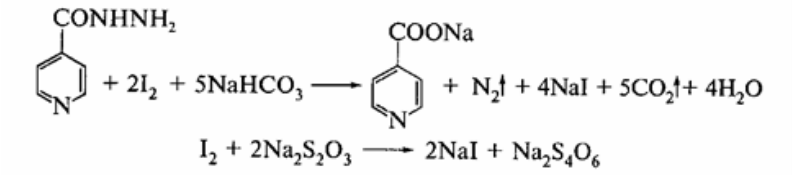
4. Reactions on the pyridine cycle.

Quantitative definition.

1. Bromatometry, direct titration, indicator – methyl red, s = 1.5:



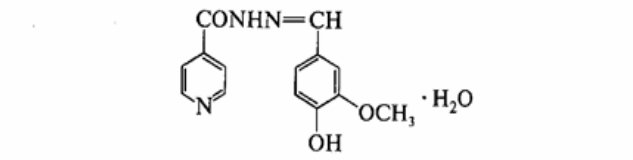
2. Iodometry, reverse titration, indicator - starch, s = 1/2:



Storage. In a well-closed container that protects from light.

Application. Antituberculosis agent.

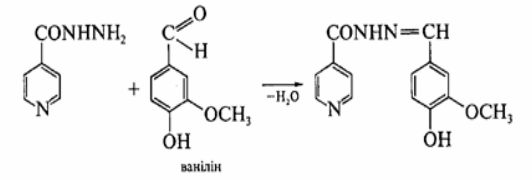
Ftivazid



3-Метокси-4-оксибензиліденгідразид ізонікотинової кислоти, гідрат

Mechanism of action. Associated with inhibition of the synthesis of mycolic acids with a long chain, which are components of the cell membrane of mycobacteria.

Synthesis.

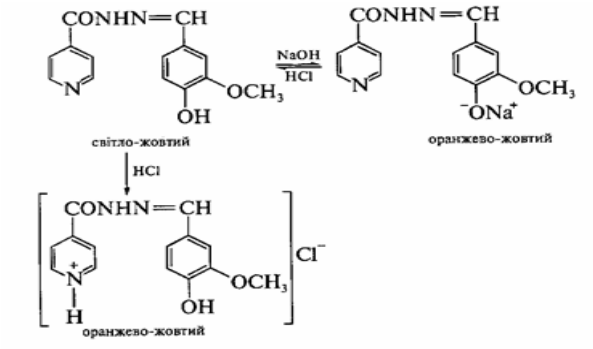


ванілін

Properties. Light yellow or yellow fine crystalline powder with a faint smell of vanillin, tasteless. Very slightly soluble in water, slightly soluble in 96% alcohol, easily soluble in acids and alkali solutions.

Identification.

1. + 2,4-dinitrochlorobenzene, heating + NaOH – yellowish-brown color.
2. + NaOH – light yellow → orange-yellow; + HCl → yellow → orange-yellow:

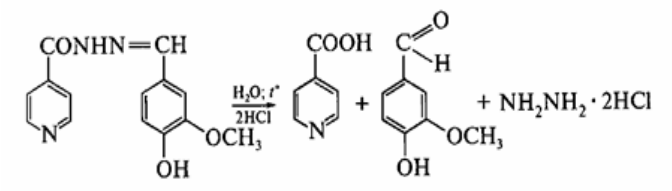


світло-жовтий

оранжево-жовтий

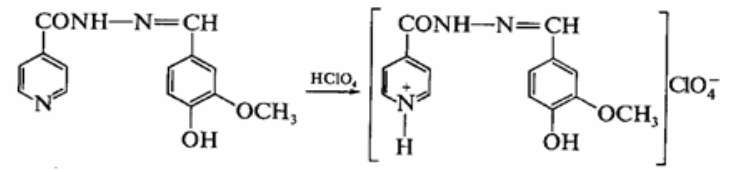
оранжево-жовтий

3. + HCl, heating – smell of vanillin:



Quantitative definition.

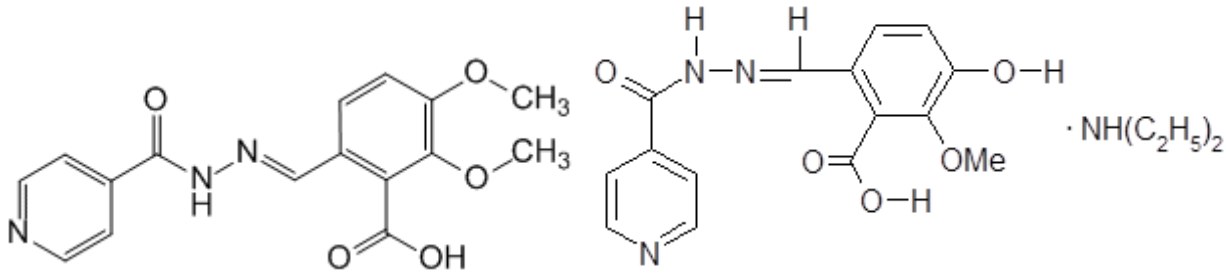
1. Acidimetry in a non-aqueous medium, direct titration, indicator – crystal violet, s = 1:



Storage. In a well-sealed container.

Application. Antituberculosis agent.

Opiniazid Opiniazid is soluble



Mechanism of action. Associated with inhibition of the synthesis of mycolic acids with a long chain, which are components of the cell membrane of mycobacteria.

Properties. Opiniazid is a white or slightly yellowish crystalline powder, slightly soluble in water, practically insoluble in ether, easily soluble in mineral acids and alkaline solutions.

Opiniazid is soluble- white or slightly yellowish crystalline powder, easily soluble in water, slightly soluble in alcohol, practically insoluble in ether.

Identification.

1. O., O.R. + 2,4-dinitrochlorobenzene, heating + NaOH – brown-red color.

*2.*O., O.R. + $CuSO_4$ – green precipitate of copper salt.

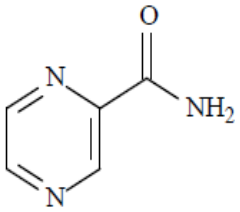
3. O.R. + NaOH, heating - the characteristic smell of diethylamine.

Storage. In a well-closed container that protects from light.

Application. Antitubercular drugs.

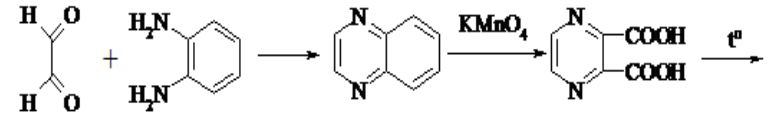
Pyrazine derivatives

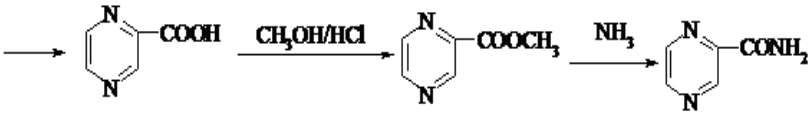
Pyrazinamide



Mechanism of action. It is not precisely established, it is believed that the mechanism is similar to this isoniazid and is associated with a violation of the exchange of mycolic and nucleic acids in mycobacteria.

Synthesis.





Properties. White crystalline powder, odorless, moderately soluble in water and chloroform, sparingly soluble in alcohol, very sparingly soluble in ether.

Identification.

1. T. pl. IR, UV spectrum.
2. + $FeSO_4$ – orange-red color, + NaOH – blue.
3. + NaOH, heating – smell of ammonia.

Quantitative definition.

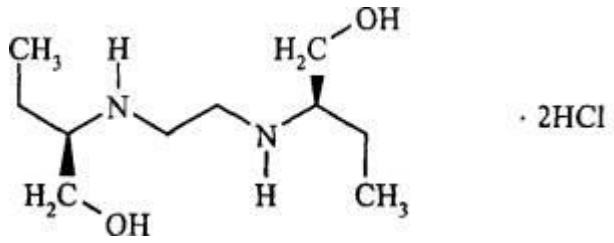
Non-aqueous titration in a mixture of chloroform and acetic anhydride, the indicator is Sudan red.

Storage. In a well-sealed container.

Application. Antituberculosis agent.

Derivatives of aliphatic amines

Ethanbutol hydrochloride



Mechanism of action. It is associated with inhibition of RNA and protein synthesis, ability to interact with ions of divalent biometals (copper, magnesium), disruption of the structure of ribosomes and inhibition of the intensity of lipid metabolism.

Properties. White crystalline powder, easily soluble in water, soluble in alcohol, very slightly soluble in ether.

Identification.

1. IR spectrum.
2. Reaction with $CuSO_4$ in the presence of NaOH – blue color.
3. Reaction to chlorides.

Quantitative definition.

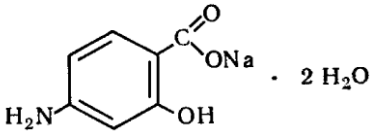
Spectrophotometry.

Storage. In a well-sealed container.

Application. Antituberculosis agent.

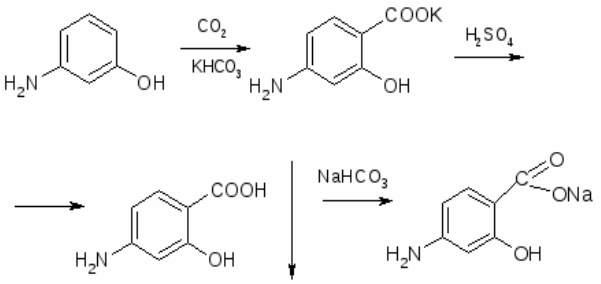
Derivatives of p-aminosalicylic acid

Sodium paraaminosalicylate



Mechanism of action. Associated with inhibition of folic acid synthesis and inhibition of the formation of mycobactin, a component of the mycobacterial wall.

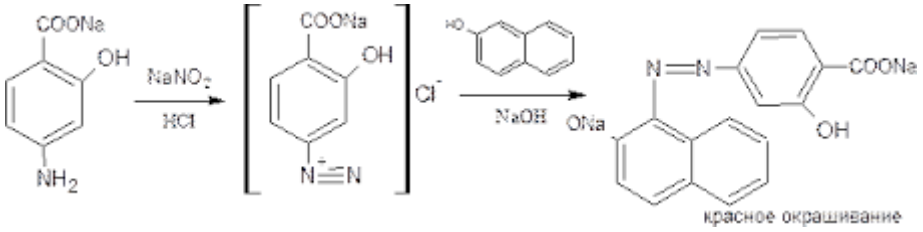
Synthesis.



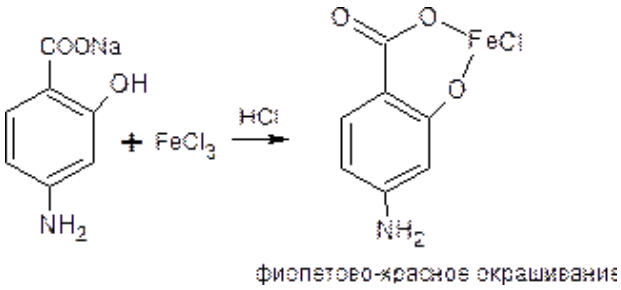
Properties. White, sometimes with a slightly yellowish or pink tint, fine crystalline powder, easily soluble in water, difficult to dissolve in alcohol. Aqueous solutions darken on standing. Na-PASK decomposes at 80 °C, so the solution cannot be sterilized by heating.

Identification.

1. Reaction to the primary aromatic amino group:



2. Reaction with FeCl3 – purple-red color:

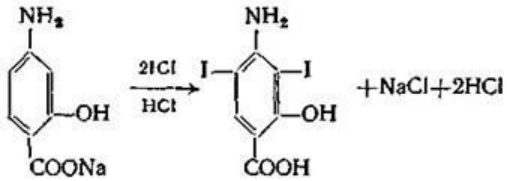


3. Reactions to sodium.

4. UV spectrum.

Quantitative definition.

1. Nitritometry with an external indicator (iodostarch paper), s = 1.
2. Acidimetry, direct titration, s = 1.
3. Bromatometry, s = 1.5.
4. Iodochlorometry, s = ½:

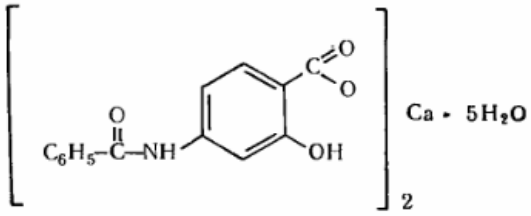


$$ICl + KI = I_2 + KCl$$
$$I_2 + 2Na_2S_2O_3 = 2NaI + Na_2S_4O_6$$

Storage. In a well-closed container that protects from light.

Application. Antituberculosis agent.

Calcium benzamidosalicylate



Mechanism of action. Close to PASK sodium salt.

Properties. White powder, sometimes with a yellowish tint. Practically not soluble in water, difficult and slowly soluble in 95% ethyl alcohol, soluble in methyl alcohol with the formation of slightly cloudy solutions.

Identification.

1. Reaction to Ca^{2+} ions after preliminary heating with HCl.
2. + $FeCl_3$ – purple color.

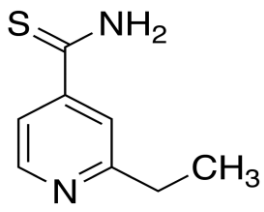
Quantitative definition. Complexonometry, s = 1.

Storage. In a well-closed container that protects from light.

Application. Antituberculosis agent.

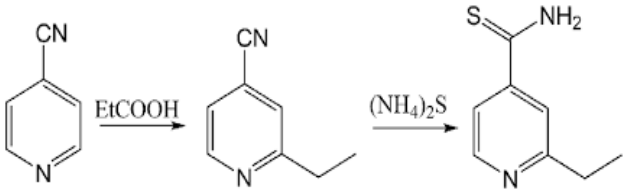
Thioamides of isonicotinic acid

Ethionamide



Mechanism of action. Not fully known today. It is generally known that ethionamide inhibits mycobacterial protein synthesis.

Synthesis.



Properties. Yellow crystalline powder with a weak or moderate sulfur smell. Not hygroscopic, practically not soluble in water and ether, hardly soluble in ethanol and methanol.

Identification.

1. IR, UV spectrum.
2. + NaOH, heating – the smell of ammonia, blue litmus paper.
3. + HCl, heating – release of H_2S vapors, determined by the blackening of filter paper moistened with (CH3COO)2Pb solution:

$$H_2S + (CH_3COO)_2Pb \rightarrow PbS\downarrow + 2CH_3COOH.$$

Quantitative definition.

Acidimetry in a non-aqueous environment (glacial acetic acid), direct titration, indicator – crystal violet, s = 1.

Application. Antituberculosis agent.

DRUGS FOR THE TREATMENT OF ONCOLOGICAL DISEASES

CLASSIFICATION OF ANTI-TUMOR MEDICINES

I. Synthetic means.

1. Alkylating agents.

1.1. Chloroethylamine derivatives.

1.2. Derivatives of ethyleneimine.

1.3. Derivatives of methanesulfonic acid.

1.4. Derivatives of nitrosoureas.

1.5. Platinum compounds.

2. Antimetabolites.

2.1. Antagonists of folic acid.

2.2. Purine antagonists.

2.3. Pyrimidine antagonists.

II. Natural remedies.

1. Antitumor antibiotics.

2. Antitumor agents of plant origin.

3. Enzyme preparations with antitumor activity.

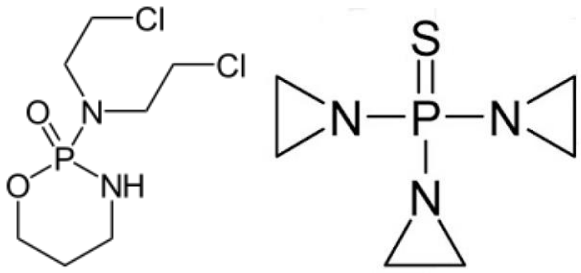
III. Hormonal drugs and their antagonists.

IV. Immunological means.

1. Interferons.

2. Interleukins.

Cyclophosphamide Thiotepa



Mechanism of action. It is based on the interaction between alkylating metabolites of Cyclophosphamide, Thiotepa and DNA. This alkylation leads to the breaking and cross-linking of cross-links of DNA strands and DNA-proteins.

Properties.*Cyclophosphamide*- white or almost white crystalline powder, easily soluble in alcohol, chloroform, poorly soluble in ether, acetone, water.

Identification.

1. T. pl., IR spectrum.
2. +$AgNO_3$, heating - white precipitate, soluble in NH_4OH.
3. + H_2SO_4, + HNO_3, heating, + $(NH_4)_2MoO_4$ – yellow color.

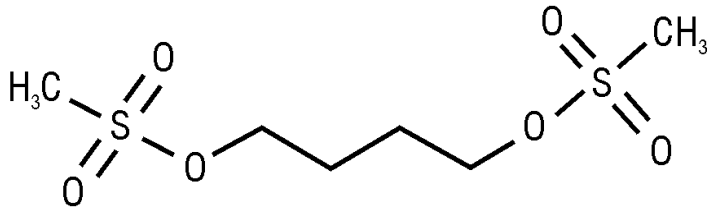
Quantitative definition.

Argentometry (Folgard's method).

Storage. In a well-closed container protected from light, at a temperature not higher than 10 °C.

Application. Antitumor drugs.

Busulfan



Mechanism of action. It consists in the action of active metabolites of B. on tumor cells, as a result of which DNA cross-linking of tumor cells occurs.

Identification.

1. T. pl., IR spectrum, TLC.

2. + NaOH, heating – white gelatinous precipitate:

$CH_3SO_2–O–(CH_2)_4–O–SO_2CH_3 + 2NaOH \rightarrow 2CH_3SO_3Na\downarrow + HO(CH_2)_4OH.$

3. Reaction to sulfates after mineralization: $SO_4^{2-} + Ba^{2+} \rightarrow BaSO_4\downarrow$.

Quantitative definition.

Alkalimetry after hydrolysis, direct titration, indicator – phenolphthalein, s = ½:

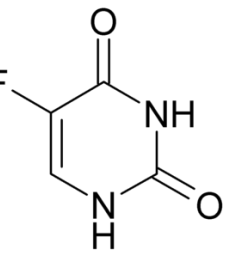
$CH_3SO_2–O–(CH_2)_4–O–SO_2CH_3 + H_2O \rightarrow 2CH_3SO_3H + HO(CH_2)_4OH,$

$CH_3SO_3H + NaOH \rightarrow CH_3SO_3Na + H_2O.$

Storage. In a well-closed container that protects from light.

Application. Antitumor drug.

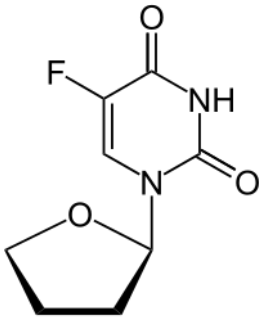
Fluorouracil

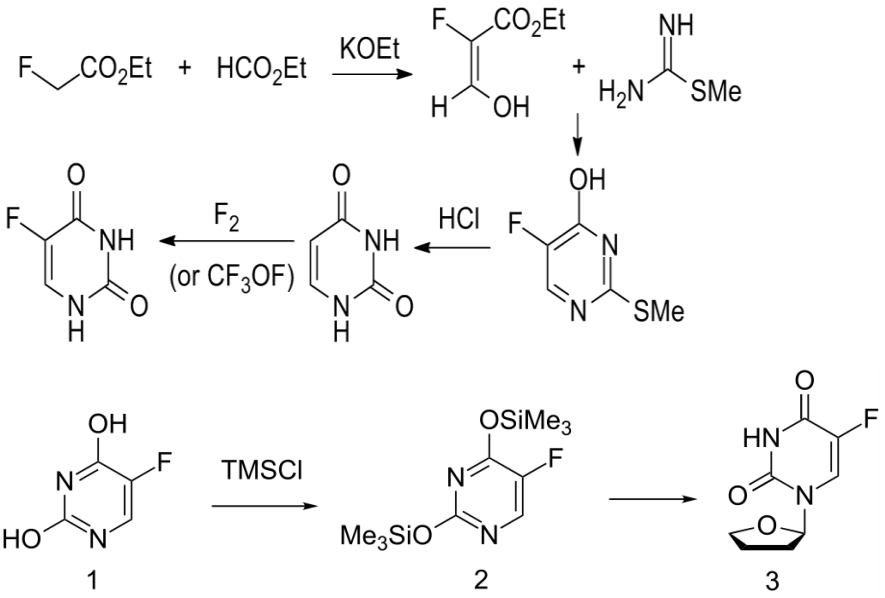


Mechanism of action. It consists in inhibiting the synthesis of purine DNA nucleotides through competitive metabolism after absorption by M., F., and T. cells.

Synthesis.

Tegafur





Properties. White, odorless crystalline substance. Fluorouracil is moderately soluble in water, slightly soluble in 96% ethanol, practically insoluble in ether. Tegafur is hardly soluble in water and ethanol.

Identification.

1. UV, IR spectrum, TLC.

2. Reactions with salts of heavy metals: + $AgNO_3$, $HgCl_2$ – white precipitates, + Co(II) salts – purple color.

3. Fluorine is detected: after preliminary mineralization:

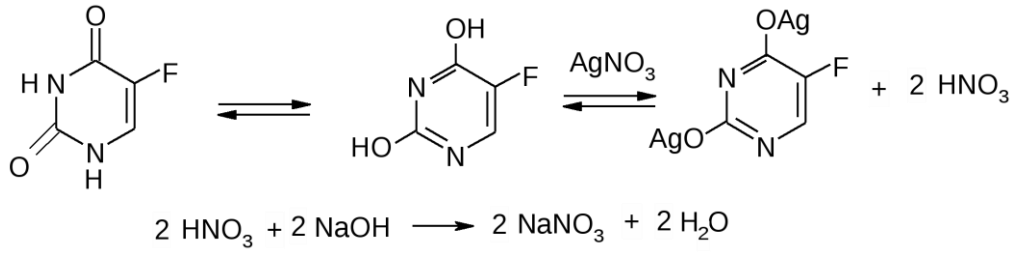
$2F^- + CaCl_2 \rightarrow CaF_2\downarrow + 2Cl^-$ – white opalescence.

4. after burning with oxygen in the presence of hydrogen peroxide:

$Fe(SCN)_3 + 6F^- \rightarrow [FeF_6]^{3-} + 3SCN^-$ – discoloration of $Fe(SCN)_3$ solution.

Quantitative definition. Fluorouracil.

1. Alkalimetry by substitution, the indicator is phenol red, s = ½

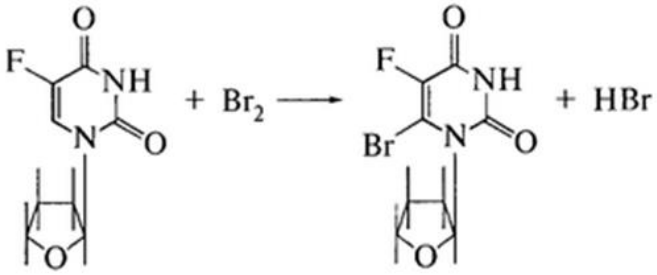


2. Alkalimetry in a non-aqueous medium, direct titration, titrant –[(C4H9)4N]OH in DMF, indicator – thymol blue, s = 1.

Quantitative definition. Tegafur.

Bromatometry, reverse titration, indicator - starch, s = 3:

$KBrO3 + 5KBr + 6HCl \rightarrow 3Br2 + 6KCl + 3H2O$



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

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

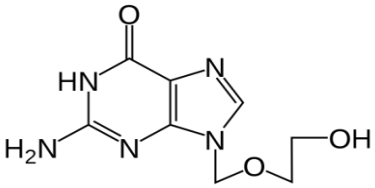
Storage. In a well-closed container that protects from light.

Application. Antitumor drugs.

ANTIVIRAL DRUGS

Analogues of nucleosides

Acyclovir



Mechanism of action. Under the action of an enzyme that is produced only in infected cells, Acyclovir is converted into an active form - acyclovir triphosphate (TPA). TFA penetrates into the infected cell and is incorporated into the process of DNA synthesis of the virus, thereby blocking its reproduction.

Properties. White or almost white crystalline powder, slightly soluble in water, slightly soluble in DMSO, very slightly soluble in alcohol. Soluble in dilute mineral acids and alkali solutions.

Identification.

IR spectrum.

Quantitative definition.

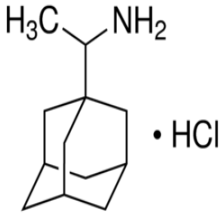
The method of acidimetry in a non-aqueous environment (anhydrous acetic acid).

Storage. In a well-sealed container.

Application. Infections caused by Herpes simplex virus, infant herpes, immunodeficiency states, chicken pox.

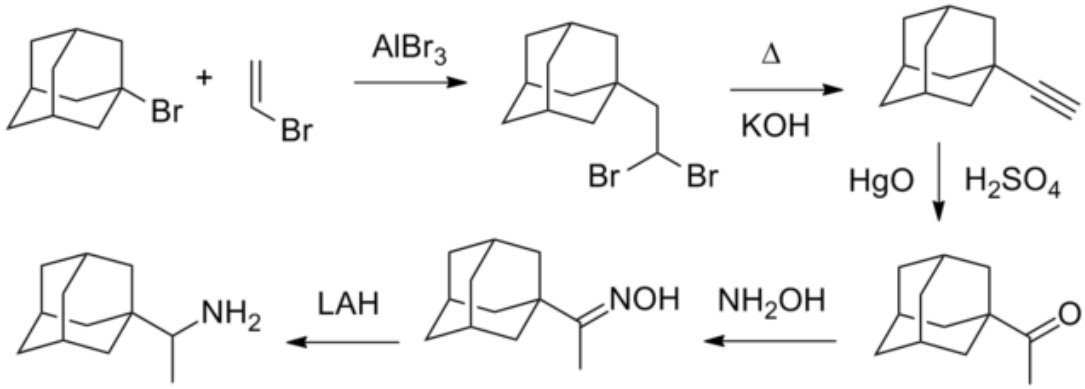
Adamantane derivatives

Rimantadine



Mechanism of action. Rimantadine inhibits virus replication in the early stages of the cycle by disrupting the formation of the viral envelope.

Synthesis.

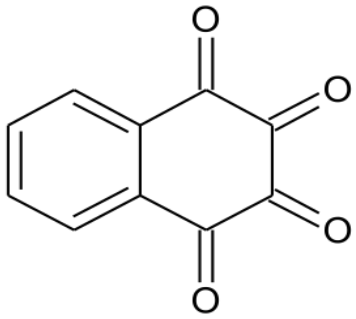


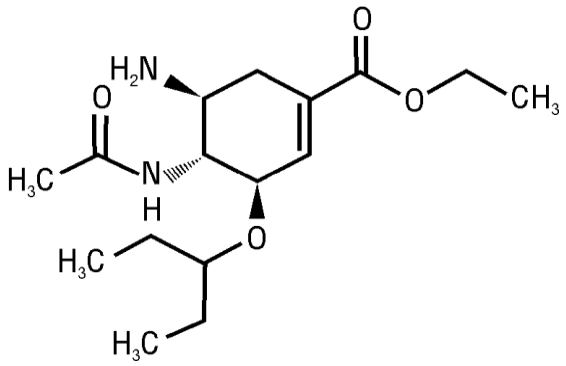
Properties. White crystalline powder, bitter in taste, very slightly soluble in water, slightly soluble in chloroform, slightly soluble in alcohol.

Application. It is effective against various type A influenza viruses, and also has an anti-toxic effect on influenza caused by the type B virus.

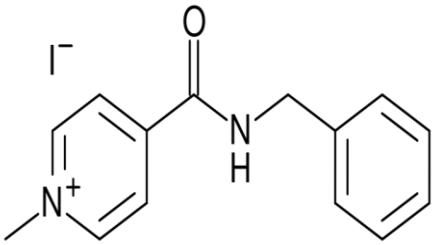
Antiviral drugs of other chemical groups

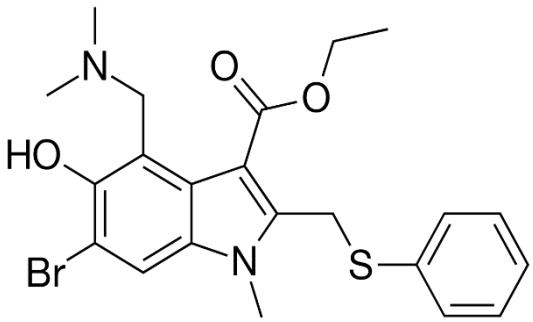
Oxolin Oseltamivir



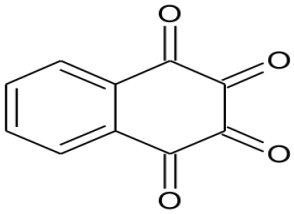


Amazon Amazon





Oxolin



2H2O

Mechanism of action. It has virucidal activity, blocking the binding sites of the influenza virus (mostly type A2) with the surface of the cell membrane, protects cells from the penetration of the virus into them.

Properties. White or white with a cream shade crystalline powder. Easily soluble in water, aqueous solutions are unstable, quickly darken in an alkaline medium.

Identification.

+ 30% NaOH solution – blue color.

Application. With viral diseases of the eyes, skin, with viral diseases

rhinitis and for the prevention of influenza

Antimalarial drugs

The modern classification of antimalarials is based on their chemical structure:

1. Derivatives of 4-methanolquinoline (quinine dihydrochloride, sulfate, hydrochloride; mefloquine).

2. 4-aminoquinoline derivatives (hingamine, hydroxychloroquine).

3. Derivatives of 8-aminoquinoline (primaquine, quinocid).

4. Diaminopyrimidine (chloridine).

5. Biguanide derivatives (bigumal, chlorproguanil).

6. Derivatives of 9-aminoacridine (acrychin)

Antimalarial agents are distinguished from each other by their tropism in relation to certain forms of development of Plasmodium in the human body. In this regard, the following are distinguished:

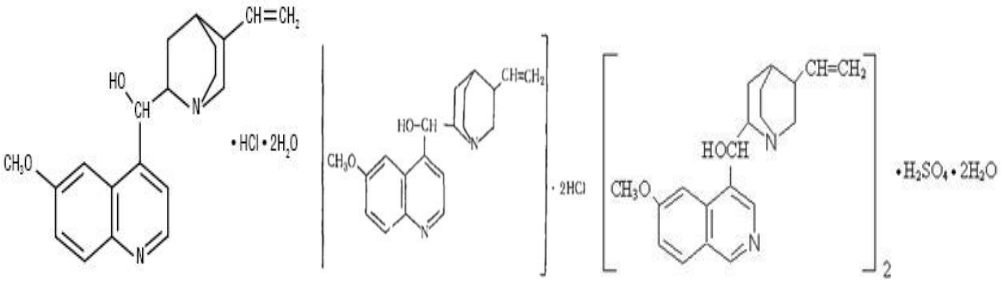
1. gametoschizotropic agents (affect erythrocytic schizonts) – quinine, hingamine, acriquine, bigumal, chloridin;

2. histoshizotropic agents (affect tissue schizonts):

- for pre-erythrocytic forms - bigumal, chloridin;
- for paraerythrocytic forms - chinocid.

3. gamontotropic agents (affecting sexual forms) – chinocid, bigumal, chloridin, hingamine.

Quinine hydrochloride Quinine dihydrochloride Quinine sulfate



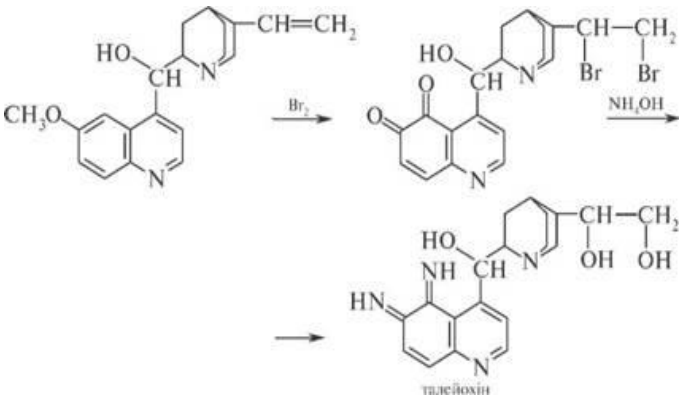
Mechanism of action. May be associated with disruption of lysosome function and docking of nucleic acid synthesis in Plasmodium cells.

Properties. Quinine salts are colorless, odorless, crystalline substances with a very bitter taste. They gradually turn yellow under the influence of light. They are all levorotatory isomers.

Quinine dihydrochloride is very easily soluble, hydrochloride is soluble, sulfate is slightly soluble in water.

Identification.

1. General reaction - thaleochin test:



2. Solutions of all quinine salts + H_2SO_4 (conc.) in UV light - blue fluorescence.

3. Reactions on anion: chlorides or sulfates.

4. Salt solution + H_2SO_4 + alcohol solution I_2 – green crystals of herepatite:

$$(C_{20}H_{24}O_2N_2)_4 \cdot (H_2SO_4)_2 \cdot (HI)_2 \cdot I_4 \cdot 6H_2O.$$

Quantitative definition.

1. Gravimetric method:

$$[C_{20}H_{24}O_2N_2]_2 \cdot H_2SO_4 + 2NaOH \longrightarrow 2C_{20}H_{24}O_2N_2\downarrow + Na_2SO_4 + 2H_2O$$

$$X = \frac{m_{в.ф} \cdot F \cdot 100 \cdot 100}{m_{нав} \cdot (100 - \%_{вол})},$$

2. Alkalimetry, in a mixture of chloroform and alcohol:

$$(C_{20}H_{24}O_2N_2) \cdot HCl + NaOH \longrightarrow C_{20}H_{24}O_2N_2\downarrow + NaCl + H_2O$$

$$E = M.м.$$

$$(C_{20}H_{24}O_2N_2)_2 \cdot H_2SO_4 + 2NaOH \longrightarrow$$

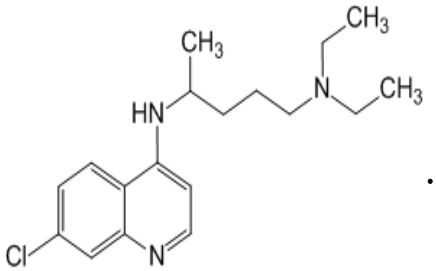
$$\longrightarrow 2C_{20}H_{24}O_2N_2\downarrow + Na_2SO_4 + 2H_2O$$

$$E = 1/2M.м$$

Storage. In a well-closed container that protects from light.

Application. Antimalarial agents that stimulate the muscles of the uterus (quinine sulfate, quinine hydrochloride).

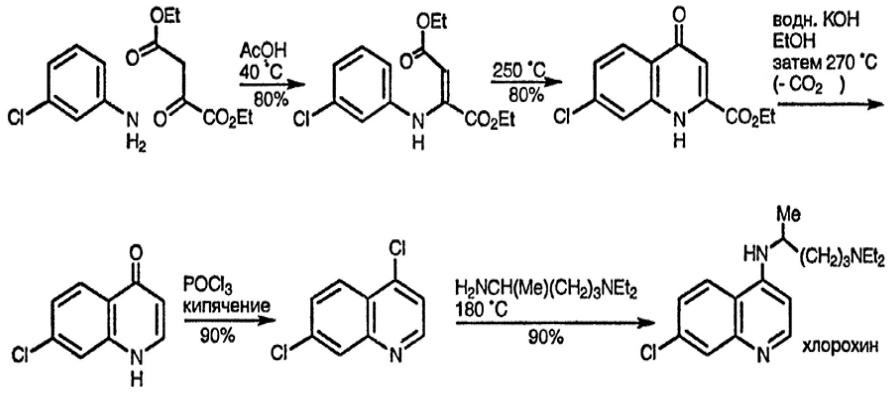
Chloroquine phosphate



·2H3PO4

Mechanism of action. The mechanism of the schizontocidal action of H. in the blood has not been fully elucidated, but in the end it leads to a violation of the parasite's DNA synthesis.

Synthesis.



Properties. White or almost white crystalline powder, hygroscopic, easily soluble in water, very slightly soluble in ethanol, ether and methanol.

Identification.

1. IR, UV spectrum.

2. T. pl. picrate

3. The reaction to phosphates after removing the base of chloroquine with chloroform:

$PO_4^{3-} + AgNO_3 \rightarrow Ag_3PO_4\downarrow$

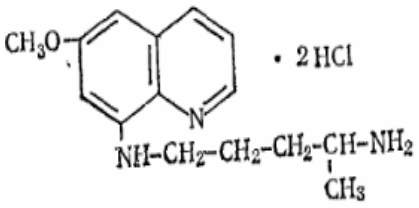
Quantitative definition.

The method of non-aqueous acidimetry with potentiometric fixation of the equivalence point.

Storage. In a well-closed container that protects from light.

Application. Malaria caused by plasmodia susceptible to the drug. Prevention of malaria in persons who have visited endemic areas. Amoebiasis. Diseases of joints, connective tissue and skin.

Quinocide



Mechanism of action. Violation of parasite DNA synthesis.

Properties. Orange-yellow crystalline powder with a bitter taste. Very easily soluble in water, hardly soluble in 95% alcohol, practically insoluble in ether, acetone.

Identification.

1. IR, UV spectrum.

2. Reaction on chloride:

3. Discoloration of bromine water and the formation of a dibromine derivative precipitate.

4. Reactions with general alkaloid reagents: Wagner, Mayer, etc.

5. + NaOH – the formation of a precipitate of quinocid base.

Quantitative definition.

1. Argentometry, s = 1/2.

2. Acidimetry in a non-aqueous medium (glacial acetic acid) in the presence of mercury (II) acetate, direct titration, indicator – crystal violet, s=1/2.

3. Acid-base titration in a two-phase medium (alcohol-chloroform mixture), indicator – phenolphthalein, s = ½:

$C_{15}H_{21}N_3O \cdot 2HCl + 2NaOH \rightarrow C_{15}H_{21}N_3O + 2NaCl + 2H_2O$.

4. Acid-base titration based on quinocide:

$C_{15}H_{21}N_3O \cdot 2HCl + 2NaOH \rightarrow C_{15}H_{21}N_3O + 2NaCl + 2H_2O$,

$C_{15}H_{21}N_3O + 2HCl \rightarrow C_{15}H_{21}N_3O \cdot 2HCl$.

5. UV spectrophotometry.

Storage. In a well-stoppered container of dark glass.

Antimalarial agent. To prevent remote relapses of three-day and four-day malaria.

General material and bulk-methodological support of the lecture:

- ✓ computer presentation;
- ✓ illustrative materials;
- ✓ examples of solving typical tasks or performing typical tasks;

- ✓ multimedia projector.

Questions for self-control:

1. Pharmaceutical analysisAntituberculosis drugs

2.Pharmaceutical analysisdrugs for the treatment of oncological diseases

3.Pharmaceutical analysisAntiviral drugs

References:

Main:

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Lecture No. 9

Topic: Antifungal drugs. Medicines for the treatment of protozoan infections. Anthelmintics.

Actuality of theme: Pharmaceutical chemistry is a science that studies methods of preparation, structure, physical and chemical properties of medicinal products; relationship between their chemical structure and action on organism; methods of quality control of drugs and changes that occur during their storage, as well as their use in medicine. Therefore, it is urgent to solve the problems facing pharmaceutical chemistry with the help of physical, chemical and physico-chemical methods, which are used both for synthesis, as well as for the analysis of medicinal products.

The purpose:the formation of students' knowledge about the peculiarities of the storage of medicinal products, which affect the afferent nervous system, as well as the characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of obtaining, methods of analysis, application in medicine. As a result of the lecture, students should learn the properties and methods of analysis of antifungal drugs,means for the treatment of protozoan infections, anthelmintic means.

Basic concepts:pharmaceutical chemistry, qualitative analysis, quantitative analysis, State Pharmacopoeia of Ukraine, physicochemical methods of analysis, impurities, express analysis.

Plan and organizational structure of the lecture:

1.Preparatory stage

1.1.Determination of educational The purposes.

1.2.Providing positive motivation.

2. The main stage

Presentation of lecture material

Plan:

-Classification of antifungal agents

- Synthetic drugs

- Herbal remedies

-Means for the treatment of protozoan infections

- Anthelmintics

3. The final stage

3.1. Summary of the lecture, general conclusions.

3.2. The lecturer's answers to possible questions

3.3. Tasks for self-training of students.

Content of lecture material (lecture text):

Antifungal drugs(lat. fungcida < fungus + cido kill) are drugs used to treat fungal diseases and have a fungicidal and fungistatic effect.

By origin and chemical structure, drugs are divided into:

1. Antibiotics.

1.1. Polyene series: amphotericin, nystatin, pimafucin.

1.2. Derivatives of benzofurancyclohexane: griseofulvin.

2. Synthetic drugs.

2.1. Azoles.

2.1.1. Imidazoles: ketoconazole (Nizoral, Dermatol), clotrimazole (Kanesten, Candid), etc.

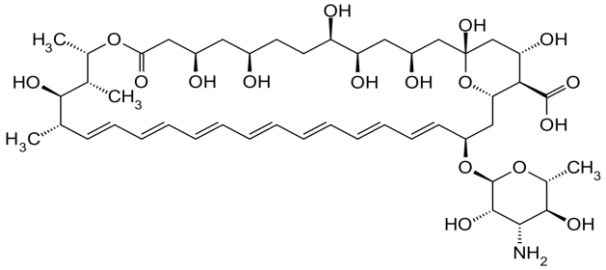
2.1.2. Riazols: fluconazole (diflucan), itraconazole (orungal).

2.2. Allylamines: terbinafine (lamizil).

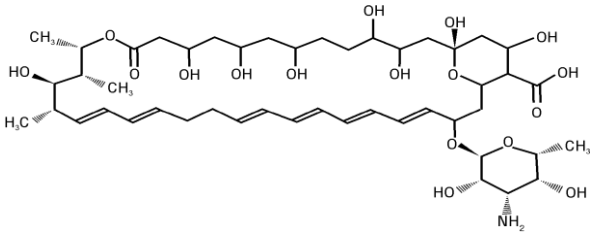
2.3. Others: undecyl acid and its combinations (mycoseptin, thiolac, zincundan), naftifin (exoderil), preparations of iodine, boric acid, sodium hydrogen carbonate, sodium tetraborate, dyes.

3. Herbal remedies: galenic preparations of walnut, elderberry, burdock.

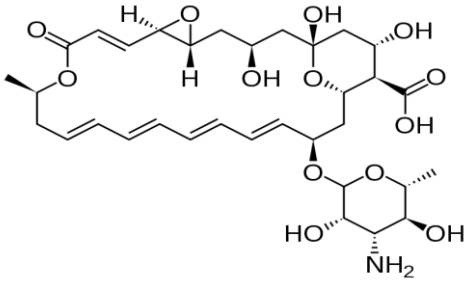
Amphotericin B



Nystatin



Natamycin



Molecules of polyene antibiotics consist of a macrocyclic aglycone (the structure of the aglycone has 6-7 double bonds and 35-40 carbon atoms) and an amino sugar connected to each other by a glycosidic bond.

Mechanism of action. Amphotericin B, Nystatin, Natamycin binds to the sterols of the cell membrane of fungi, as a result of which the membrane becomes unable to function as a selective barrier, which leads to the loss of the main components of the cell.

Properties. *Amphotericin B*– yellow or orange powder, practically insoluble in water, soluble in DMSO and propylene glycol, sparingly soluble in DMF, practically insoluble in alcohol.

Identification.

1. IR spectrum of the substance, UV spectrum of the solution in the DMSO/methanol mixture.

2. Solution A. in DMSO + H_3PO_4 – a blue ring at the boundary of two layers.

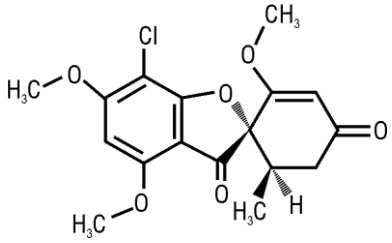
Quantitative definition.

Microbiological method.

Storage. In a well-closed container in a place protected from light at a temperature of 2-8 °C.

Application. In the treatment of potentially life-threatening fungal infections; with systemic mycoses.

Griseofulvin



Mechanism of action. The drug binds to keratin (which is found in nail beds, hair follicles, skin, etc.) and disrupts the synthesis of the fungal cell wall, DNA and protein replication, and also forms a complex with soluble DNA.

Properties. White or yellowish-white very fine

powder, the particles of which generally have a size of 5 μm, sometimes reaching a size of about 30 μm, practically insoluble in water, very easily soluble in DMF, sparingly soluble in ethanol and methanol.

Identification.

1. IR spectrum, t. pl. ~ 220 °C.

2. Reaction with $K_2Cr_2O_7$ + H_2SO_4 (conc.) – dark red color

Quantitative definition.

Spectrophotometry method.

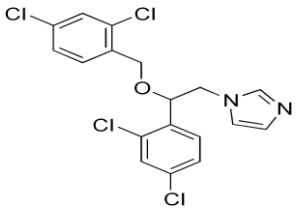
Storage. In a well-closed container that protects from light.

Application. Antifungal agent. Dermatomycosis, skin epidermophytosis, nail lesions caused by pathogenic fungi.

Synthetic drugs

Azoles

Miconazole



Mechanism of action. It consists in damage to the cell membranes of fungi, disruption of lipid metabolism and permeability of the cell wall of fungi.

Properties. White powder, very easily soluble in water and ether, soluble in ethanol, chloroform, methanol, has polymorphism.

Identification.

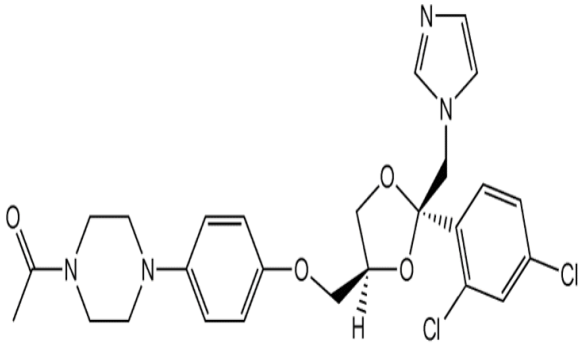
IR spectrum, t.p., TSH.

Quantitative definition. Acidimetry in a non-aqueous medium (acetic acid, methyl ethyl ketone), the indicator is naphtholbenzene, s = 1.

Storage. In a place protected from light.

Application. For fungal and mycobacterial lesions of the skin and nails, candidiasis of the vagina and gastrointestinal tract, oropharyngeal candidiasis.

Ketoconazole



Mechanism of action. It is associated with a violation of the biosynthesis of ergosterol, triglycerides and phospholipids, which are necessary for the formation of the cell membrane of fungi.

Properties. White or almost white crystalline powder, practically insoluble in water, well soluble in methylene chloride, methanol, moderately soluble in ethanol.

Identification.

1. IR spectrum.

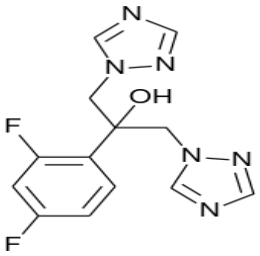
2. Reaction with a solution of n-dimethylaminobenzaldehyde in 1 M HCl solution – purple color.

Quantitative definition. Acidimetry.

Storage. In a well-closed container, in a place protected from light.

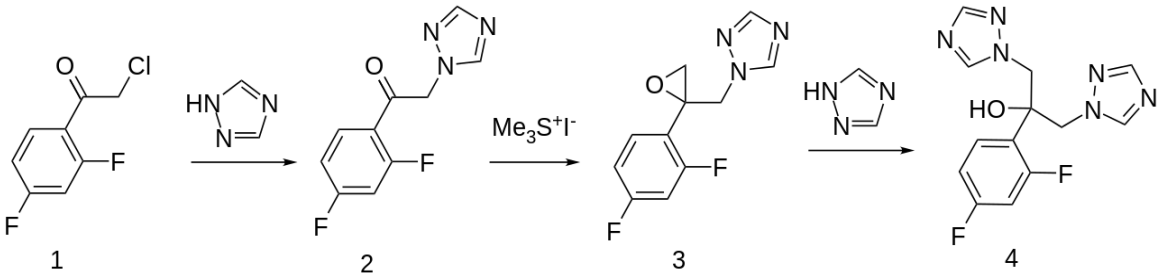
Application. With superficial and systemic mycoses.

Fluconazole



Mechanism of action. It consists in inhibiting the synthesis of sterols in fungal cells, which leads to damage to fungal cell membranes.

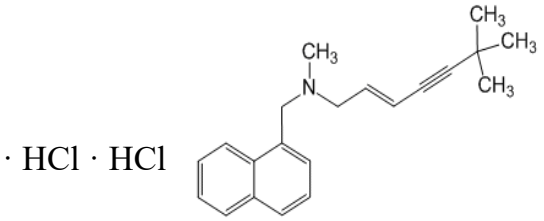
Synthesis



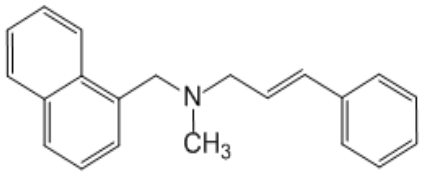
Application. Antifungal agent. Cryptococcal meningitis, candidiasis, dermatomycosis.

Allylamines

Terbinafine Naftifin



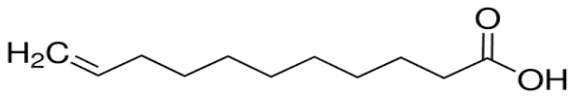
· HCl · HCl



Mechanism of action. It consists in inhibiting the synthesis of sterols in fungal cells by inhibiting the squalene epoxidase enzyme, which leads to damage to fungal cell membranes.

Application. Antifungal drugs. Fungal infections of the skin and nails.

Undecylenic acid



Mechanism of action. Not exactly set.

Properties.A white crystalline substance or a light yellow liquid with a characteristic odor, practically insoluble in water, easily soluble in alcohol, ether, essential oils, benzene.

Identification.

1. According to the refractive index at 25±0.5 °C.
2. Determine the temperature at which the compound crystallizes.
3. When heating K.U. with aniline will form an amide with m.p. 66–68 °C.
4. In a mixture of diluted H2SO4 and glacial acetic acids, the $KMnO_4$ solution becomes discolored.

Quantitative definition. Alkalimetry, indicator – phenolphthalein.

Storage. In a tightly closed non-metallic container, in a cool place protected from light.

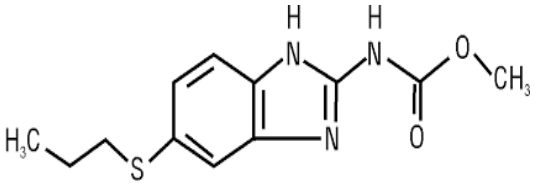
Application. Treatment and prevention of fungal skin diseases.

Means for the treatment of protozoan infections

Protozoan infections, or protozoa (lat. protozooses) – infections caused by parasitic protozoa.

This group includes dangerous diseases: amebiasis, malaria, trypanosomiasis, leishmaniasis.

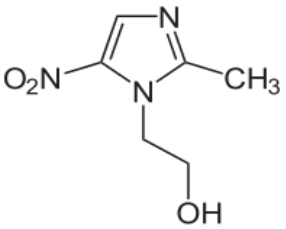
Albendazole



Mechanism of action. The anthelmintic effect of albendazole is due to the inhibition of tubulin polymerization, which leads to a violation of metabolism and the death of helminths.

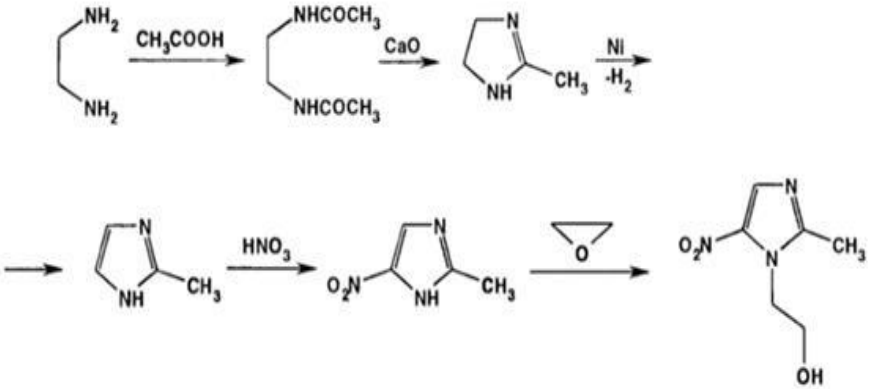
Application. Broad-spectrum antiprotozoal and anthelmintic drug.

Metronidazole



Mechanism of action. It consists in the biochemical reduction of the 5-nitro group of metronidazole. The restored 5-nitro group of metronidazole interacts with the DNA of microorganisms, inhibiting its synthesis, which leads to the death of microorganisms.

Synthesis.



Properties. White or yellowish crystalline powder, slightly soluble in water, acetone, ethanol and methylene chloride, very slightly soluble in ether.

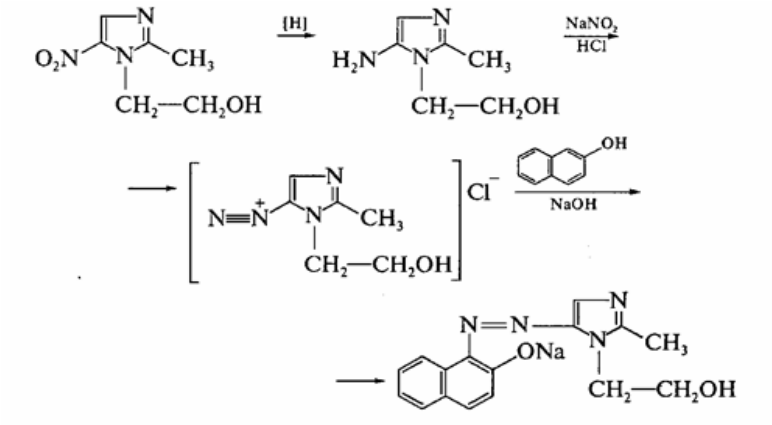
Identification.

1. IR-, UV-spectrum, t. pl.

2. T. pl. picrate: 148-153 °C.

3. Pink color of the solution with β-naphthol.

4. Reaction of formation of azo dye after reduction of $–NO_2$ to $–NH_2$:



Quantitative definition.

1. Acidimetry in a non-aqueous environment, the indicator is crystal violet, s=1.

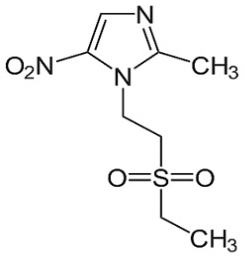
2. UV spectrophotometry.

3. Photocolorimetry.

Storage. In a well-closed container, in a place protected from light.

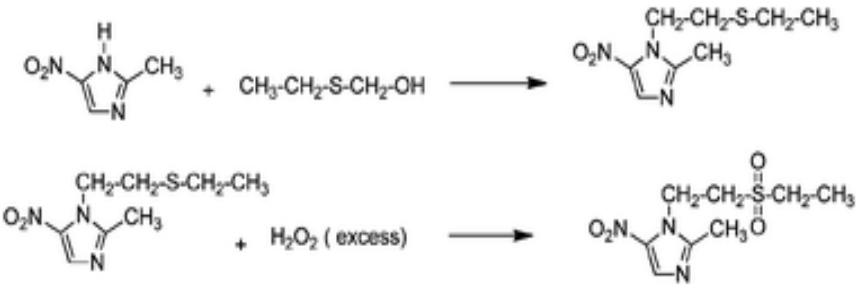
Application.A broad-spectrum antiprotozoal drug. Trichomoniasis, giardiasis, amoebic dysentery, treatment and prevention of anaerobic infections, severe mixed anaerobic and aerobic infections (in combination with an adequately selected antibiotic).

Tinidazole



Mechanism of action. Due to its significant lipophilicity, it easily penetrates inside microorganisms, where it is restored by nitroreductase and destroys bacterial DNA.

Synthesis



Properties. White or bright yellow crystalline powder, insoluble in water, soluble in acetone, dichloromethane, moderately soluble in methanol.

Identification.

1. IR spectrum, t.p., TLC.
2. UV spectrum in methanol in the interval λ = 220–350 nm.
3. Reaction of formation of azo dye after reduction of $–NO_2$ to $–NH_2$.

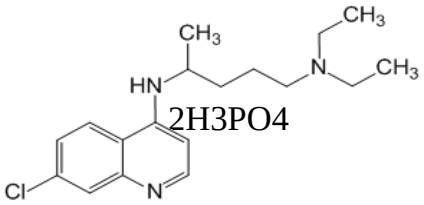
Quantitative definition.

Acidimetry in the medium of glacial acetic acid (the end of the titration is determined potentiometrically).

Storage. In a well-closed container, in a place protected from light.

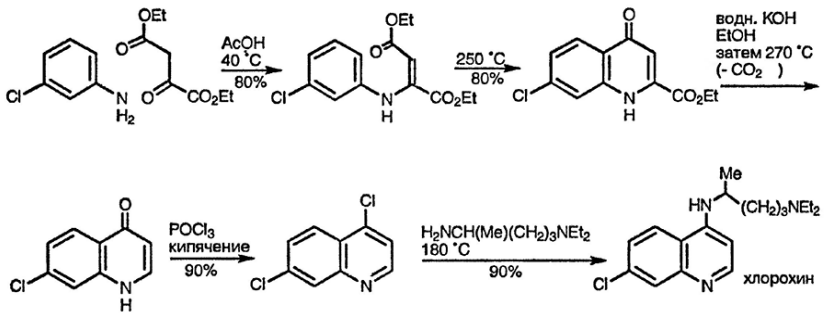
Application. Antiprotozoal drug. Acute and chronic trichomoniasis, giardiasis, amoebic dysentery, cutaneous leishmaniasis; treatment and prevention of anaerobic and mixed infections of any localization.

Chloroquine phosphate



Mechanism of action. Associated with the disruption of DNA replication processes in the cells of malarial plasmodia, the mechanism of action on pathogenic amoebae has not been established.

Synthesis.



Properties. White or almost white crystalline powder, hygroscopic, easily soluble in water, very slightly soluble in ethanol, ether and methanol.

Identification.

1. IR, UV spectrum.

2. T. pl. picrate

3. The reaction to phosphates after removing the chloroquine base $CHCl_3$:

$PO4^{3-} + AgNO3 \rightarrow Ag3PO4\downarrow$.

Quantitative definition.

The method of non-aqueous acidimetry with potentiometric fixation of the equivalence point.

Storage. In a well-closed container that protects from light.

Application. Malaria caused by plasmodia susceptible to the drug. Prevention of malaria in persons who have visited endemic areas. Amoebiasis. Diseases of joints, connective tissue and skin.

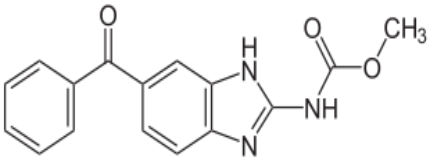
Anthelmintics

Anthelmintics(Greek anti – against + helmis, helminthos – worm, worm) – anthelmintic drugs that are used to treat helminthic infestations.

Anthelminticsclassified by the type of helminths on which the drugs act. According to this classification, three main groups of anthelmintics are distinguished:

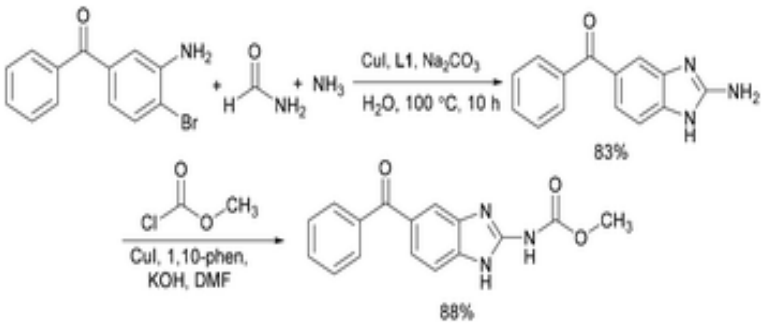
- drugs used for intestinal nematodes - piperazine adipinate, thiabendazole, mebendazole, levamisole, pyrantel;
- drugs that are used for intestinal cestodoses - niclosamide, aminoacrychin, pumpkin seeds;
- drugs that are used for extraintestinal helminthiasis - ditrazine citrate, praziquantel, khloxyl.

Mebendazole



Mechanism of action. It is caused by a selective disruption of the activity of the microtubular system of the cells of the intestinal channel of helminths, which leads to the irreversible death of helminths.

Synthesis.



Properties. White or yellowish powder, practically insoluble in water, ethanol, diethyl ether, soluble in mineral acids, easily soluble in formic acid.

Identification.

IR, UV spectrum.

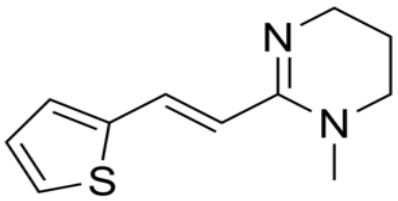
Quantitative definition.

Acidimetry, titration with a 0.1 M perchloric acid solution with potentiometric indication.

Storage. In a well-closed container that protects from light.

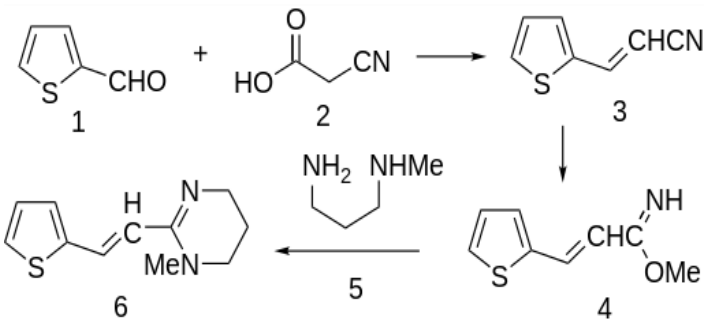
Application. An anthelmintic preparation of a wide spectrum of action. Enterobiosis, ascariasis, hookworm, strongyloidosis, trichocephalosis, trichinellosis, teniosis, echinococcosis, multiple nematodes, alveococcosis, capillariosis, gnathostomosis, mixed helminthiasis.

Pyrantel



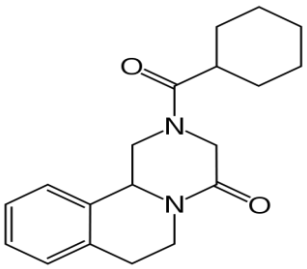
Mechanism of action. Leads to neuro-muscular blockade, paralyzing helminths, as a result of which they are excreted by intestinal peristalsis together with fecal masses.

Synthesis.



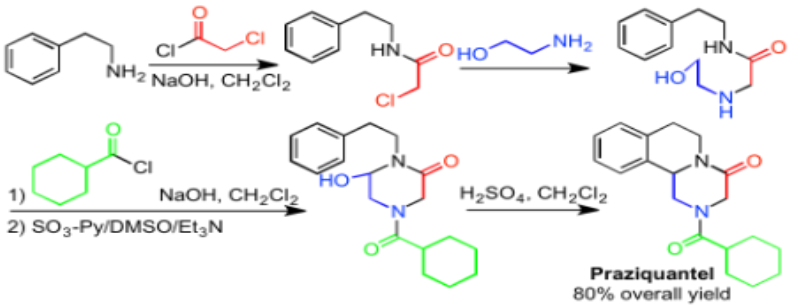
Application. An anthelmintic preparation of a wide spectrum of action.

Praziquantel



Mechanism of action. It is based on the suppression of neuromuscular activity and disruption of the energy exchange of parasites, which causes paralysis and death of helminths, followed by their removal from the gastrointestinal tract.

Synthesis

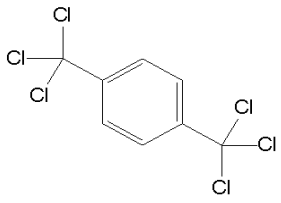


Properties. White crystalline powder, bitter in taste. Hygroscopic, easily soluble in chloroform and DMSO, soluble in ethanol, very slightly soluble in water.

Application. An anthelmintic preparation of a wide spectrum of action.

Treatment of infections caused by schistosomes, liver and lung trematodes.

Khloxyl



Mechanism of action. Contributes to the destruction of covering tissues of helminths.

Properties. White crystalline powder, tasteless and odorless. Practically insoluble in water, hardly soluble in ethanol.

Application. Anthelmintic drug. Helminthiasis of the liver - diseases of the liver caused by parasitic worms: opisthorchosis, fasciolosis, clonorchosis.

General material and bulk-methodological support of the lecture:

- ✓ computer presentation;
- ✓ illustrative materials;
- ✓ examples of solving typical tasks or performing typical tasks;
- ✓ multimedia projector.

Questions for self-control:

1.Classification of antifungal agents

2. Pharmaceutical analysissynthetic drugs of plant origin

3. Pharmaceutical analysismeans for the treatment of protozoan infections

4. Pharmaceutical analysisAnthelmintics

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10. Medicinal chemistry: education. manual for students of higher educational institutions / I.S. Hrytsenko, S.G. Taran, L.O. Transition, etc.; for general I.S. Hrytsenko - Kharkiv: NFaU: Golden Pages, 2017. - 552p.

11. Pharmaceutical chemistry. General and special pharmaceutical chemistry. Medicines of an inorganic nature: laboratory-practical classes. Study guide / L.G. Mishina - Vinnytsia: PP "TD "Edelweiss and K"", 2010. - 384 p.

12. Analytical chemistry and instrumental methods of analysis / A.I. Gab, D.B. Shakhnin, V.V. Malyshev -Ukraine University, 2018- 396 p.

Electronic information resources:

1. Specialized medical online publication for doctors, pharmacists, pharmacists, students of medical and pharmaceutical universities. - [Electronic resource]. - Access mode:http://www.morion.ua.

2. World Health Organization. - [Electronic resource]. - Access mode:http://www.who.int.

3. Pharmaceutical encyclopedia. - [Electronic resource]. – Access mode: http://www.pharmencyclopedia.com.ua.

4. Official website of the International Organization for Standardizationhttp://www.iso.org/iso/home.html

5. Compendium online. [Electronic resource]. - Access mode:https://compendium.com.ua/bad/

6. Medline search database [Electronic resource]. – Access mode: National Library of Medicinehttps://www.nlm.nih.gov/bsd/medline.html

Lecture No. 10

Topic: Antiseptic and disinfectants. Antipediculosis and acaricidal means.

Actuality of theme: Pharmaceutical chemistry is a science that studies methods of preparation, structure, physical and chemical properties of medicinal products; relationship between their chemical structure and action on organism; methods of quality control of drugs and changes that occur during their storage, as well as their use in medicine. Therefore, it is urgent to solve the problems facing pharmaceutical chemistry with the help of physical, chemical and physico-chemical methods, which are used both for synthesis, as well as for the analysis of medicinal products.

The purpose:the formation of students' knowledge about the peculiarities of the storage of medicinal products, which affect the afferent nervous system, as well as the characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of obtaining, methods of analysis, application in medicine. As a result of the lecture, students should learn the properties, methods of analysis of antiseptic and disinfectants, anti-lice and acaricides.

Basic concepts:pharmaceutical chemistry, qualitative analysis, quantitative analysis, State Pharmacopoeia of Ukraine, physicochemical methods of analysis, impurities, express analysis.

Plan and organizational structure of the lecture:

1.Preparatory stage

1.1.Determination of educational The purposes.

1.2.Providing positive motivation.

2. The main stage

Presentation of lecture material

Plan:

-Classificationantiseptic and disinfectants

- Halogens and halogen-containing products

- Oxidizers

- Acids and bases

-Salts of heavy metals

-Aldehydes

-Alcohols

-Phenols

-Dyes

-Detergents

-Sulfur medicinal substances

- Antipediculosis and acaricidal agents

3. The final stage

3.1. Summary of the lecture, general conclusions.

3.2. The lecturer's answers to possible questions

3.3. Tasks for self-training of students.

Content of lecture material (lecture text):

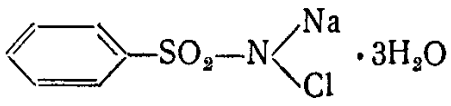
Antiseptic means(Greek anti - against, septicas - putrefaction) are able to lead to the death or stop the growth and development of microorganisms on the surface of the human body. **Disinfectants***(see*- negation, infecere - to infect) neutralize pathogenic microorganisms in the environment. They are used to finish rooms, linens, dishes, medical instruments, equipment, and patient care items.

The classification of antiseptics and disinfectants is based on their chemical structure:

- group of halogens and halogen-containing compounds;
- antiseptics of the aromatic series;
- aliphatic antiseptics;
- group of dyes;
- oxidizers;
- nitrofuran derivatives;
- detergents;
- salts of heavy metals.

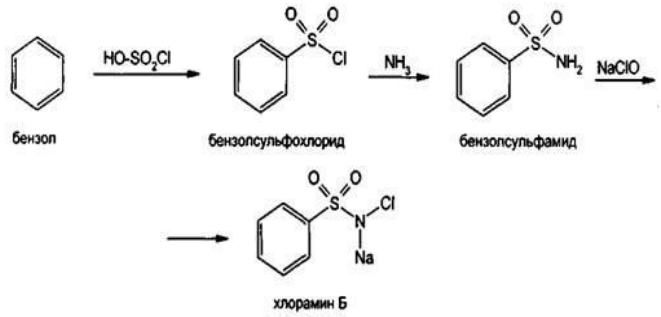
Halogens and halogen-containing products

Chloramine



Mechanism of action. Due to high oxidizing properties and the ability to cause protein denaturation.

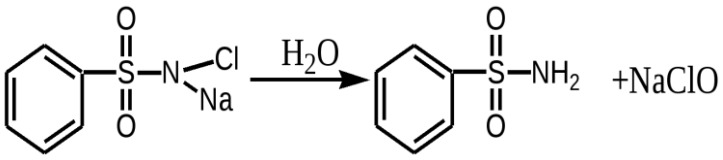
Synthesis.



Properties. Crystalline powder of white or white with a yellowish tinge. Easily soluble in water, soluble in 96% alcohol, practically insoluble in ether.

Identification.

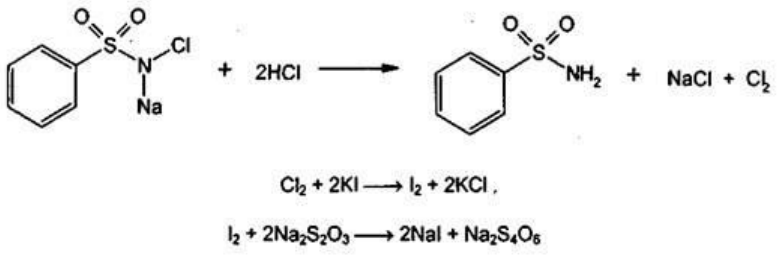
1. When dissolved in water – hydrolysis:



NaClO + H2O→NaOH + HClO,

2HClO→2HCl + O2↑.

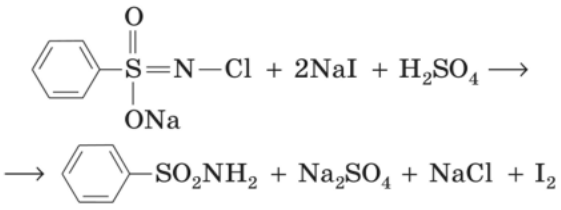
2. Chlorine decomposition reaction:



3. After roasting - reactions to chlorides, sulfates and sodium:

Quantitative definition.

Iodometry, direct titration by substitution, the indicator is starch, s = 1/2:



HOCl + 4KI + H_2SO_4→K_2SO_4 + $2I_2$ + 2KCl + $2H_2O$,

I_2 + $2Na_2S_2O_3$→2NaI + $Na_2S_4O_6$.

Storage. In a well-closed container, in a dark, dry, cool place.

Application. Antiseptic agent. For the treatment of infected wounds, for disinfection of hands (0.25-0.5% solutions), instruments, care items for infectious patients (1-3% solutions).

Iodine, I2

Mechanism of action. It reacts with oxidizing - sulfide (SH) and hydroxyl (OH) groups of amino acids, which are part of enzymes and structural proteins of microorganisms, inactivating or destroying these proteins.

Receiving. Sources are drilling water and seaweed (0.5%).

Properties. Fragile plates or small crystals of grayish-purple color with a metallic luster. Volatile at normal temperature, when heated, sublimes with the formation of purple vapor. Very slightly soluble in water, very easily soluble in aqueous solutions of iodides, soluble in 96% alcohol, ether and chloroform.

Identification.

1. Sublimation.

2. Aqueous solution of iodine + starch - blue color.

Quantitative definition.

A solution of iodine in KI is titrated with sodium thiosulfate, the indicator is starch, s = 1/2:

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

Storage. In glass jars with rubbed corks, in a cool place protected from light.

Application. Antiseptic agent.

Alcohol solution of iodine, 5%

Storage:iodine - 5.0 g; KI – 2.0 g; alcohol 96% – 41.0 g; cleaning water up to 100 ml.

Properties. Transparent red-brown liquid with a characteristic smell.

Identification.

1. + starch solution - blue-blue color.

2. Extraction of iodine with chloroform until the water layer becomes colorless, which is divided into two parts:

- in one, the K+ ion is determined by reaction with tartaric acid;

- in the second - iodide ion according to the reaction:

$$2NaI + 2NaNO_2 + H_2SO_4 \rightarrow I_2 + 2NO\uparrow + 2Na_2SO_4 + 2H_2O.$$

3. Reaction of formation of iodoform:

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

Quantitative definition. Iodine content - titration with sodium thiosulfate until the solution becomes colorless, s = 1/2:

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

The content of potassium iodide - according to the Fayance method:

$$2NaI + KI + 3AgNO_3 \rightarrow 3AgI\downarrow + KNO_3 + 2NaNO_3.$$

The content of potassium iodide is calculated according to the formula:

$$\%KI = \frac{(V_{AgNO_3} \bullet KП - V_{Na_2S_2O_3} \bullet KП) \bullet T \bullet 100}{a}$$

Storage. In glasses made of dark glass, in a place protected from light.

Application. Antiseptic agent.

Triiodomethane, CHI3

Synthesis. Electrolysis of potassium iodide solution in the presence of sodium carbonate and ethanol:

$$C_2H_5OH + 4I_2 + 3Na_2CO_3 \rightarrow CHI_3\downarrow + 5NaI + HCOONa + 2H_2O + 3CO_2\uparrow$$

Properties. Lemon-yellow powder with a sharp specific smell.

First it melts, then it decomposes with the release of violet vapors of iodine. Iodine solutions quickly decompose under the influence of light and air with the release of iodine.

Identification. When heated, violet vapors of iodine are released:

$$CHI_3 + 2O_2 \rightarrow 3I_2 + CO\uparrow + CO_2\uparrow + H_2O.$$

Quantitative definition. Argentometry according to the Folgard method:

$$CHI_3 + 3AgNO_3 + H_2O \xrightarrow{t^o} 3AgI\downarrow + 3HNO_3 + CO\uparrow$$

Э=1/3М.м.

$$AgNO_3 + NH_4SCN \rightarrow AgSCN\downarrow + NH_4NO_3$$

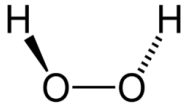
$$Fe^{3+} + 3SCN^- \rightarrow Fe(SCN)_3$$

Storage. In a well-closed container that protects from light, in a cool place.

Application. Antiseptic agent.

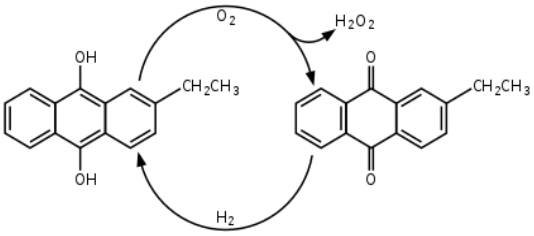
Oxidizers

Hydrogen peroxide solution 3.30%



Mechanism of action. In cells, under the influence of enzymes (peroxidase, catalase), hydrogen peroxide decomposes with the release of atomic oxygen, which exhibits antimicrobial, deodorizing, depigmenting properties.

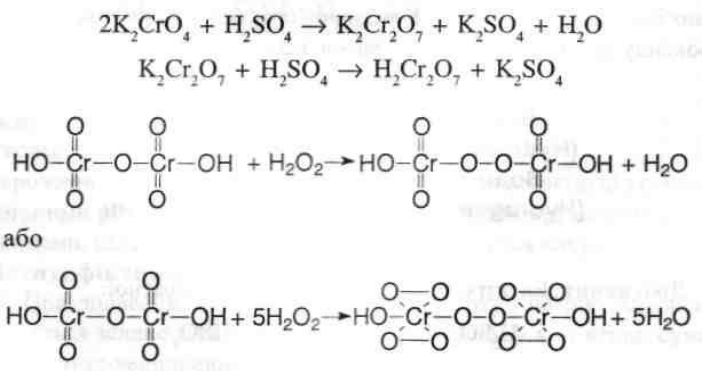
Synthesis. The main industrial method is the oxidation of anthrahydroquinone:



Properties.A colorless, transparent liquid with a slightly acidic reaction. Decomposes in the light, when interacting with oxidizing agents, reducing agents, alkalis, iron, copper, manganese with the formation of oxygen. Miscible in all proportions with water.

Identification.

1. In an acidic environment, the $KMnO_4$ solution becomes discolored.
2. The reaction of the formation of perchromic acids when interacting with K_2CrO4 in an acidic environment in the presence of diethyl ether:



Quantitative definition. Permanganatometry without indicator, s = 2.5:

$5H_2O_2 + 2KMnO_4 + 3H_2SO_4 \rightarrow 2MnSO_4 + K_2SO_4 + 8H_2O + 5O_2\uparrow$.

Storage. In a place protected from light, if the substance does not fit stabilizer, it is stored at t<15 °C.

Application. An antiseptic, also has a hemostatic effect.

Potassium permanganate

KMnO4

Mechanism of action. In the presence of light organic substances that oxidize (tissue components, manure), it easily splits off oxygen and turns into manganese dioxide, which, depending on the concentration of the solution, has an astringent, irritating or caustic effect. The oxygen released has antimicrobial and deodorizing properties.

Synthesis.

$2MnO_2 + 4KOH + O_2 \rightarrow 2K_2MnO_4 + 2H_2O$

$2K_2MnO_4 + Cl_2 \rightarrow 2KMnO_4 + 2KCl.$

Properties. Dark purple or almost black crystals, usually with a metallic luster, soluble in cold water, easily soluble in boiling water. Decomposes when interacting with certain organic substances. When interacting with some organic compounds or substances that are easily oxidized, an explosion may occur.

Identification.

1. + alcohol, NaOH solution – green color:

$4MnO_4^- + 4OH^- \rightarrow MnO_4^{2-} + O_2\uparrow + 2H_2O$

2. Formation of a dark brown precipitate after boiling the solution (1):

$3MnO_4^{2-} + 2H_2O \rightarrow MnO_2 + 2MnO^{4-} + 4OH^-$

3. + hydrogen peroxide, H2SO4 (dil.) – discoloration of the solution:

$2KMnO_4 + 5H_2O_2 + 3H_2SO_4 \rightarrow 2MnSO_4 + K_2SO_4 + 5O_2\uparrow + 8H_2O$

Quantitative definition. Iodometry, titration by substitution, the indicator is starch, s = 1/5:

$2KMnO_4 + 10KI + 8H_2SO4 \rightarrow 2MnSO_4 + 6K_2SO_4 + 5I_2 + 8H_2O$

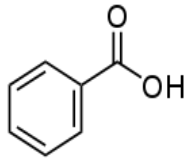
$I_2 + 2Na_2S_2O_3 \rightarrow 2NaI + Na_2S_4O_6$

Storage. In a well-sealed container.

Application. Antiseptic agent.

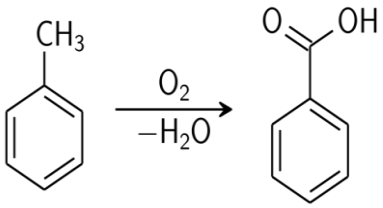
Acids and bases

Benzoic acid



Mechanism of action. It consists in the denaturation of proteins of body cells and microbial cells.

Synthesis.

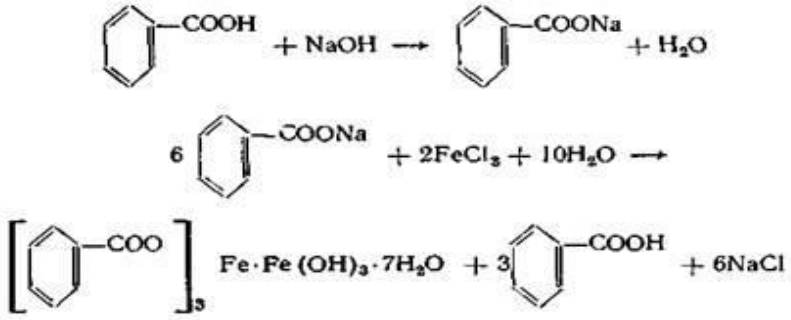


Properties. White crystalline powder. Sublimes when heated. Slightly soluble in water, soluble in boiling water, easily soluble in 96% alcohol, ether and fatty oils.

Identification.

1. T. pl.

2. A characteristic reaction with FeCl3 is a pink-yellow precipitate:



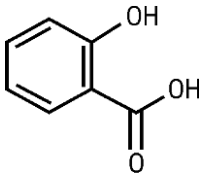
Quantitative definition. Alkalimetry in alcoholic medium, direct titration, indicator – phenol red, s = 1:

$C_6H_5COOH + NaOH \rightarrow C_6H_5COONa + H_2O$.

Storage. In a well-sealed container.

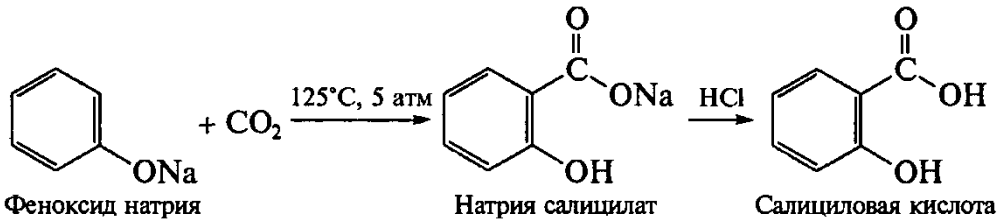
Application. Antiseptic agent.

Salicylic acid



Mechanism of action. It consists in the denaturation of proteins of body cells and microbial cells.

Synthesis

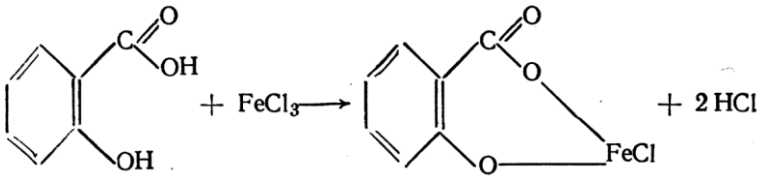


Феноксид натрия Натрия салицилат Салициловая кислота

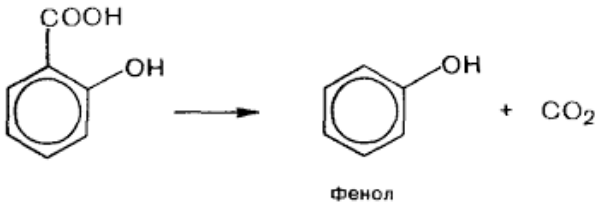
Properties. White small needle crystals or light crystalline powder, sweetish-sour taste. It dissolves poorly in water, easily in alcohol and ether.

Identification.

1. Reaction with FeCl3 – blue-violet color:



2. When heated - decarboxylation with the formation of phenol:



Фенол

3. The reaction of the formation of an auric dye with a solution of HC(O)H and H2SO4 (k.).

Quantitative definition. Alkalimetry in alcoholic medium, direct

titration, the indicator is phenolphthalein, s = 1.

Storage. In a well-sealed container.

Application. Antiseptic agent.

Boric acid

H_3BO_3

Mechanism of action. It coagulates proteins (including enzymes) of the microbial cell, disrupts the permeability of the cell membrane, due to which the growth and development of bacteria is delayed.

Synthesis.

$Na_2B_4O_7 \cdot 10H_2O + 2HCl \rightarrow 4H_3BO_3 + 2NaCl + 5H_2O$,

$B_2O_3 \cdot 2MgO + 2H_2SO_4 \rightarrow 2MgSO_4 + 2H_3BO_3$.

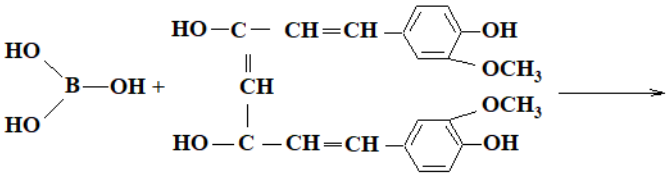
Properties. White crystalline powder, colorless shiny plates or white crystals; hygroscopic.

Identification.

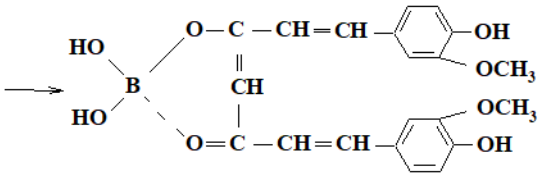
1. A mixture of H_3BO_3 with methanol and H_2SO_4 (conc.) burns with a green flame:

2. An aqueous solution of the substance has an acidic reaction.

3. Turmeric paper turns pink or brownish-red:



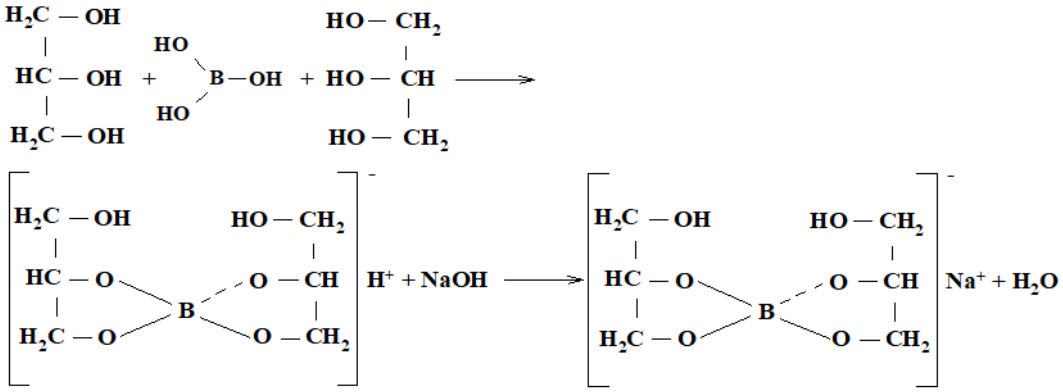
куркумин



розоцианин

Quantitative definition. Alkalimetry, direct titration in medium

mannitol, indicator – phenolphthalein, :



Storage. In a well-sealed container.

Application. An antiseptic agent, externally in the form of aqueous solutions (2-4%) for rinsing the mouth, throat, and eyes, as well as in the form of an ointment (5-10%) and in powders for skin diseases.

Sodium tetraborate, Na2B4O7·10H2O

Mechanism of action. Coagulates proteins (including enzymes) of the microbial cell.

Synthesis.$CaB_4O_7 + Na_2CO_3 \rightarrow Na_2B_4O_7 + CaCO_3\downarrow$ (hot solution).

Properties. White crystalline powder or colorless crystals, weathering, soluble in water, easily soluble in hot water and glycerin.

Identification.

1. A mixture with methanol and H_2SO_4 (conc.) burns with a green flame.

2. Substance + phenolphthalein solution – red color:

$Na_2B_4O_7 + 7H_2O \rightarrow 4H_3BO_3 + 2NaOH$.

Quantitative definition.

1. Alkalimetry of mannitol solutions, the indicator is phenolphthalein, s = 1/2.
2. Acidimetry, indicator – methyl orange, s = ½:
3. $Na_2B_4O_7 + 2HCl + 5H_2O \rightarrow 4H_3BO_3 + 2NaCl$.

Storage. In a well-sealed container.

Application. Externally as an antiseptic. Sometimes orally in the treatment of patients with epilepsy (especially children).

Silver nitrate

AgNO3

Mechanism of action. Provides protein denaturation, blockade of sulfhydryl groups of enzyme systems of the protoplasm of a microbial cell.

Synthesis.

$Ag \cdot Cu + 4HNO_3 \rightarrow AgNO_3 + Cu(NO_3)_2 + NO\uparrow + 2H_2O$.

Properties. White crystalline powder or transparent colorless crystals. Very easily soluble in water, soluble in 96% alcohol.

Identification.

Reactions to silver and nitrates.

Quantitative definition. Thiocyanatometry, direct titration, indicator – ferrum (III) ammonium sulfate, s = 1:

$AgNO_3 + NH4SCN \rightarrow AgSCN\downarrow + NH_4NO_3$,

$3NH_4SCN + FeNH_4(SO_4)_2 \rightarrow Fe(SCN)_3 + 2(NH_4)_2SO_4$

Storage. In a well-closed container, in a place protected from light.

Application. Antiseptic, caustic agent.

Cuprum sulfate pentahydrate

CuSO4·5H2O

Mechanism of action. Provides protein denaturation, blockade of sulfhydryl groups of enzyme systems of the protoplasm of a microbial cell.

Synthesis.

$3Cu + 3H_2SO_4 + 2HNO_3 \rightarrow 3CuSO_4 + 2NO\uparrow + 4H_2O$.

Properties. Blue or transparent blue crystalline powder

crystals Easily soluble in water, practically insoluble in 96% alcohol, aqueous solutions have an acidic reaction (hydrolysis).

Identification.

1. With an ammonia solution, a blue precipitate dissolves in an excess of the reagent:

$2CuSO_4 + NH_4OH \rightarrow Cu_2(OH)_2SO_4\downarrow + (NH_4)_2SO_4$,

$Cu_2(OH)_2SO_4 + 6NH_4OH + (NH_4)_2SO_4 \rightarrow 2[Cu(NH_3)_4]SO_4 + 8H_2O$.

2. Reaction to sulfates: $Ba^{2+} + SO_4^{2-} \rightarrow BaSO_4\downarrow$.

Non-pharmacopoeial reactions:

3. $2CuSO_4 + Fe \rightarrow FeSO_4 + Cu$, (red deposit of copper)

4. $CuSO_4 + Na_2S \rightarrow CuS\downarrow + NaSO_4$, (black precipitate)

$3CuS + 8HNO_3 \rightarrow 3Cu(NO_3)_2 + 3S\downarrow + 2NO\uparrow + 4H_2O$ (yellow precipitate)

5. $2CuSO_4 + K_4[Fe(CN)_6] \rightarrow Cu_2[Fe(CN)_6]\downarrow + 2K_2SO_4$ (red-brown precipitate, soluble in ammonia solutions).

Quantitative definition. Iodometry by substitution, add potassium iodide in the presence of H_2SO_4, titrant – sodium thiosulfate, indicator – starch, s = 1:

$2CuSO_4 + 4KI \rightarrow 2CuI_2\downarrow + 2K_2SO_4$,

$2CuI_2 \rightarrow Cu_2I_2 + I_2$,

$I_2 + 2Na_2S_2O_3 \rightarrow NaI + Na_2S_4O_6$

Storage. In a well-sealed container.

Application. Externally – antiseptic, astringent, caustic, internally – emetic.

Zinc oxide

ZnO

Mechanism of action. Causes denaturation of proteins and the formation of albumins

Synthesis.

1. By roasting zinc spar: $ZnCO_3 \rightarrow ZnO + CO_2\uparrow$

2. By calcination at 250 ºC of freshly precipitated basic zinc carbonate obtained from zinc sulfate according to the reaction:

$5ZnSO_4 + 5Na_2CO_3 + 3H_2O \rightarrow 2ZnCO_3 \cdot 3Zn(OH)_2 + 5Na_2SO_4 + 3CO_2\uparrow$

$2ZnCO_3 \cdot 3Zn(OH)_2 \rightarrow 5ZnO + 2CO_2\uparrow + 3H_2O$

Properties. White or white with a yellowish tinge, amorphous odorless powder, practically insoluble in water and alcohol, soluble in alkali solutions, diluted mineral acids.

Identification.

1. When zinc is fired, the oxide turns yellow, and when it cools, it turns white again.

2. The substance is dissolved in dilute hydrochloric acid:

$ZnO + 2HCl \rightarrow ZnCl_2 + H_2O$

The resulting solution is diluted with water and reactions are carried out for zinc.

3. Non-pharmacopoeial reaction - when zinc oxide is calcined with cobalt(II) nitrate, a characteristic green color (Rinman green) is formed:

$ZnO + Co(NO_3)_2 \rightarrow CoZnO_2 + 2NO_2\uparrow + 1/2O_2\uparrow$

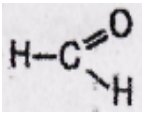
Quantitative definition. Complexionometry, direct titration after dissolving the substance in diluted acetic acid in the presence of HMTA, the indicator is xylenol orange, s = 1.

Storage. In a sealed container.

Application. Externally in the form of powders, ointments, pastes, as an astringent, drying and disinfecting agent for skin diseases.

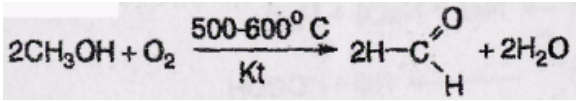
Aldehydes

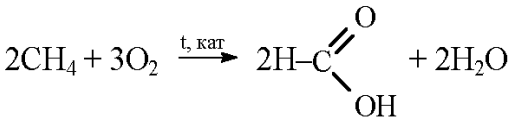
Formaldehyde solution 35%



Mechanism of action. When entering a cell or spore, formaldehyde easily combines with the amino groups of the protein, blocking the reactive groups of the protein molecule.

Synthesis.

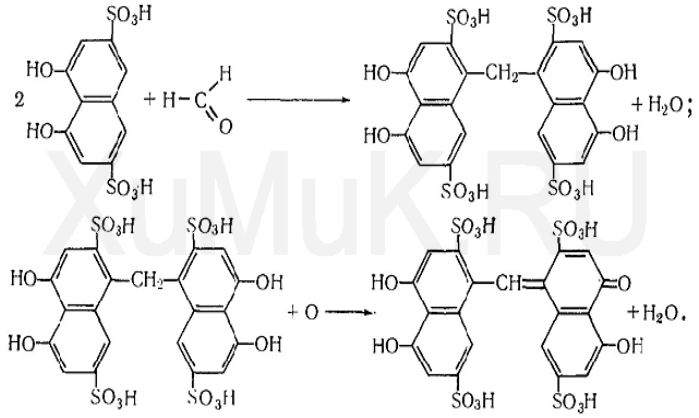




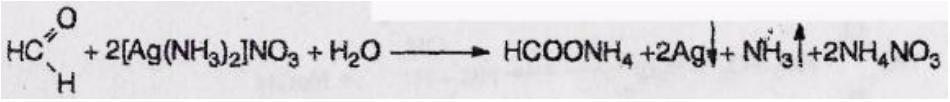
Properties. Transparent colorless liquid. Miscible with water and 96% alcohol. May become cloudy during storage. During storage, it polymerizes with the formation of paraform (white sediment). To prevent polymerization, a stabilizer is added - methyl alcohol (up to 15%).

Identification.

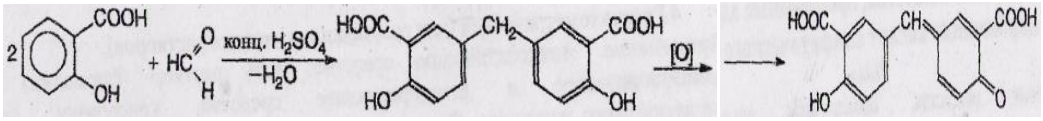
1. When interacting with the sodium salt of chromotropic acid in the presence of concentrated sulfuric acid, a purple-blue or purple-red color is formed:



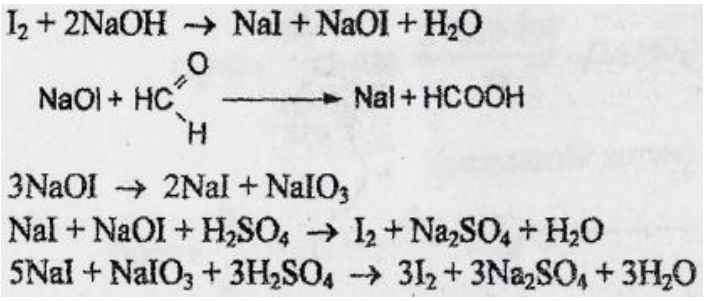
2. The "silver mirror" reaction:



3. Non-pharmacopoeial reaction - with salicylic acid in the presence of concentrated sulfuric acid - red color:



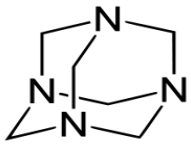
Quantitative definition. Iodometry in an alkaline environment, reverse titration, the indicator is starch, s = 1/2:



Storage. In well-stoppered glasses, in a place protected from light, at a temperature of 15 °C to 25 °C.

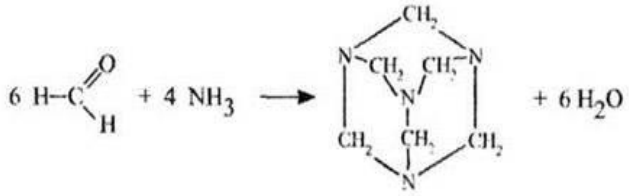
Application. Antiseptic, disinfectant and deodorizing agent, preservative for biological material. Fungicidal properties are used to protect seeds.

Methenamine



Mechanism of action. The mechanism of action consists in cleavage in an acidic environment with the release of formaldehyde, which denatures the protein structures of microbes.

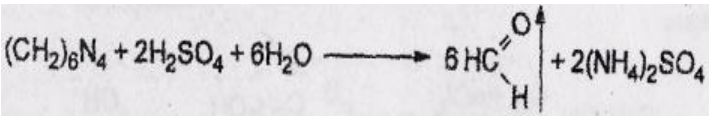
Synthesis.



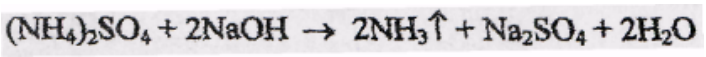
Properties. Colorless crystals or white crystalline powder without odor, burning and sweet, and then bitter taste. When heated, it evaporates without melting. Aqueous solutions have an alkaline reaction. Forms salts with acids. Easily soluble in water and alcohol, soluble in chloroform.

Identification.

Odor of formaldehyde after acid hydrolysis:

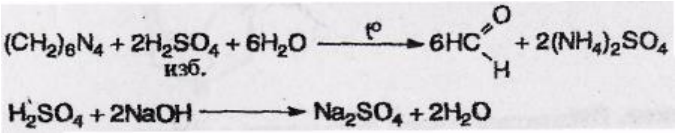


With the following addition of sodium hydroxide, ammonia is released:



Quantitative definition.

1. Acid-base reverse titration, indicator – methyl red, s = 1/2:



2. Acidimetry, direct titration, mixed indicator – methyl orange and methylene blue, s = 1:

$(CH_2)_6N_4 + HCl \rightarrow (CH_2)_6N_4 \cdot HCl$

Storage. In a well-sealed container.

Application. Antiseptic agent, used orally

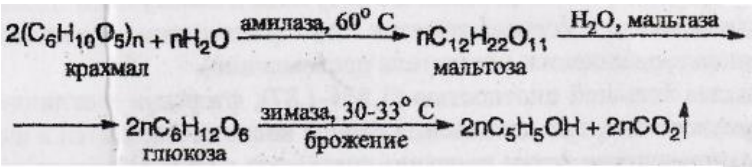
and intravenously for urinary tract infections. Antidote for poisoning by salts of heavy metals.

Alcohols

Ethanol 96%, C_2H_5OH

Mechanism of action. Ethanol coagulates proteins, active against gram-positive and gram-negative bacteria and viruses.

Synthesis.



Properties. Transparent, colorless, volatile, flammable liquid. Hygroscopic, miscible with water, methylene chloride, ether, chloroform, acetone and glycerin. Burn with a pale blue smokeless flame. It boils at a temperature of about 78 ºC.

Identification.

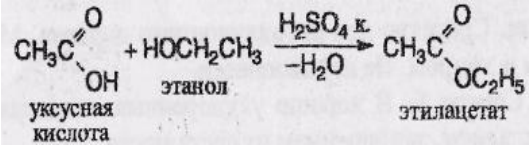
1. Using physical constants (boiling temperature, relative density), IR spectroscopy and the results of chemical reactions.

2. When potassium permanganate is oxidized in the presence of diluted sulfuric acid, acetaldehyde is formed - it has a characteristic smell.

3. Iodoform sample - a yellow precipitate with a characteristic smell is formed:

$C_2H_5OH + 4I_2 + 6KOH \rightarrow CHI_3\downarrow + 5KI + HCOOK + 5H_2O.$

4. Non-pharmacopoeial reaction - formation of ethyl acetate (characteristic smell):



Quantitative definition.DFU does not provide for quantitative determination.

If necessary, for quantitative determination of ethanol can be

used methods:

1. Setting the relative density and determining the concentration of alcohol using alcoholometric tables.

2. Chemical method – dichromatometry.

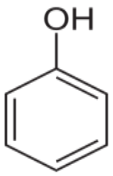
3. In pharmaceuticals, the AN recommends determining the concentration of ethanol by relative density or temperature limits of distillation.

Storage. In a place protected from light.

Application. Externally as an antiseptic and irritant, for rubs and compresses, as well as for making tinctures, extracts and solutions. It is used in the form of 96%, 90%, 70% and 40% aqueous solutions.

Phenols

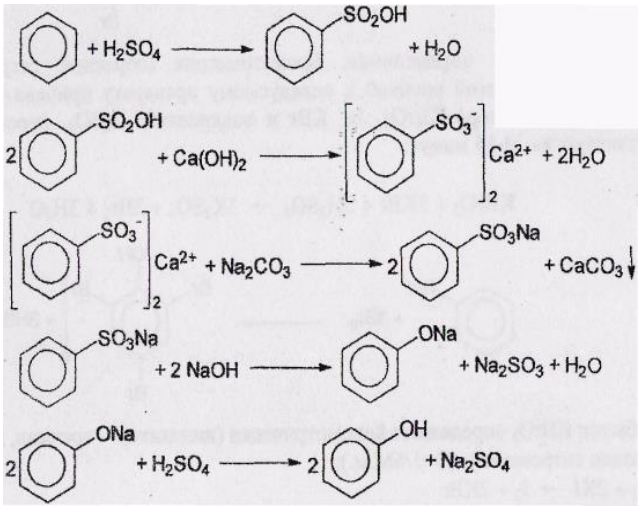
Phenol



Mechanism of action. High concentrations of phenol have a bactericidal effect, leading to the denaturation of the microorganism's proteins. The mechanism of antibacterial activity of phenol is also associated with the inhibitory effect on enzymes, especially dehydrogenase.

Extraction

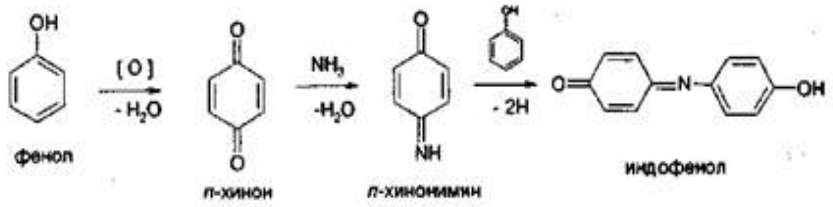
1. From coal tar.
2. Synthetic method:



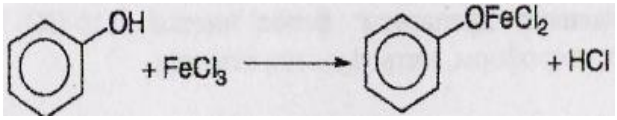
Properties. Colorless, pale pink or pale yellowish crystals that dissolve in the air, with a peculiar smell. Soluble in water, very easily soluble in 96% alcohol, glycerin, methylene chloride and oils. It easily dissolves in alkali and ammonia solutions with the formation of phenolates. The reaction of the aqueous solution is weakly acidic.

Identification.

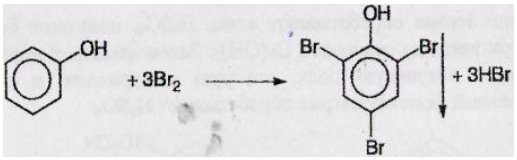
1. Indophenolic reaction - the drug is dissolved in an ammonia solution and a concentrated sodium hypochlorite solution is added - a blue color appears, which later becomes more intense:



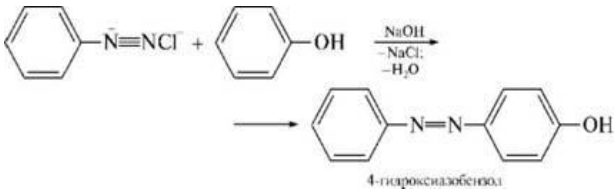
2. Reaction with a solution of ferrum (III) chloride - purple color:



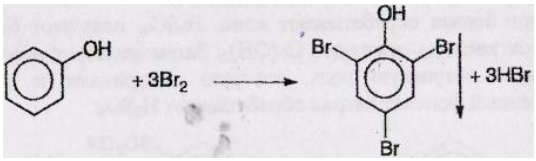
3. With bromine water - pale yellow precipitate of tribromophenol:



4. Non-pharmacopoeial reaction of azo coupling - cherry-red or orange-red azo dyes are formed:



Quantitative definition. Bromatometry, reverse titration, s = 1:



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

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

Storage. In a sealed container that protects from light.

Application. Antiseptic. Pure phenol causes burns, 3-5% solution of phenol in glycerin, 2% phenol ointment, Ferezol (a mixture of cresol and phenol) is used to remove warts and papillomas.

General material and bulk-methodological support of the lecture:

- ✓ computer presentation;
- ✓ illustrative materials;
- ✓ examples of solving typical tasks or performing typical tasks;
- ✓ multimedia projector.

Questions for self-control:

1.Classificationantiseptic and disinfectants

2. Pharmaceutical analysisantiseptic and disinfectants -Halogens and halogen-containing products,Oxidizing agents, acids and bases, salts of heavy metals

3. Pharmaceutical analysisantiseptic and disinfectants -Aldehydes, Alcohols, Phenols

4. Pharmaceutical analysisantiseptic and disinfectants -Dyes, Detergents, Sulfur medicinal substances

5.Pharmaceutical analysisAntipediculosis and acaricidal means

References:

Main:

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2. State Pharmacopoeia of Ukraine: in 3 volumes / Derzh. medical service of Ukraine funds, Ukr. of science pharmacopoeia medicine quality center means - 2nd edition. - Kh.: Ukr. of science pharmacopoeia medicine quality center means, 2014. - Vol. 2. - 724 p.

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4. Pharmaceutical chemistry: Textbook for students. higher pharmacy education closing and pharmacy Faculty of Medical Sciences for students higher pharmacy education closing / In general ed. P.O. Bezuglio - Kind. 3rd edition, revised. – Vinnytsia, NOVA KNYGA, 2017. - 456 p.

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6. European Pharmacopoeia. Third Edition. Supplement, 2008. Council of Europe Strasbourg.

7. Nizhnyk H.P. Pharmaceutical chemistry: a textbook (University I-III years) H.P. Nizhnyk — 2nd ed., ed. - All-Ukrainian specialized publishing house "Medytsyna", 2015. - 352p.

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9. Hudoyarova O.S. Pharmaceutical chemistry. - Vinnytsia: "Nilan-LTD" LLC, 2018. - 194 p.

10. Medicinal chemistry: education. manual for students of higher educational institutions / I.S. Hrytsenko, S.G. Taran, L.O. Transition, etc.; for general I.S. Hrytsenko - Kharkiv: NFaU: Golden Pages, 2017. - 552p.

11. Pharmaceutical chemistry. General and special pharmaceutical chemistry. Medicines of an inorganic nature: laboratory-practical classes. Study guide / L.G. Mishina - Vinnytsia: PP "TD "Edelweiss and K"", 2010. - 384 p.

12. Analytical chemistry and instrumental methods of analysis / A.I. Gab, D.B. Shakhnin, V.V. Malyshev -Ukraine University, 2018- 396 p.

Electronic information resources:

1. Specialized medical online publication for doctors, pharmacists, pharmacists, students of medical and pharmaceutical universities. - [Electronic resource]. - Access mode:http://www.morion.ua.

2. World Health Organization. - [Electronic resource]. - Access mode:http://www.who.int.

3. Pharmaceutical encyclopedia. - [Electronic resource]. – Access mode: http://www.pharmencyclopedia.com.ua.

4. Official website of the International Organization for Standardizationhttp://www.iso.org/iso/home.html

5. Compendium online. [Electronic resource]. - Access mode:https://compendium.com.ua/bad/

6. Medline search database [Electronic resource]. – Access mode: National Library of Medicinehttps://www.nlm.nih.gov/bsd/medline.html