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

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PHARMACEUTICAL CHEMISTRY

Section 2.2

Study and methodical Guide

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

Zaporizhzhia
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CONTENTS

INTRODUCTION

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

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

According to the curriculum, pharmaceutical chemistry is taught in the III, IV and V courses. In the III course (V-VI semesters), the discipline program is structured into 2 meaningful blocks:

Block 1 - "Pharmaceutical analysis"

Block 2 - "Special pharmaceutical chemistry"

Block 2 consists of three sections.

SPECIFIC GOALS:

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

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

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

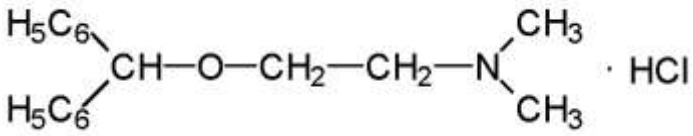
PLAN OF PRACTICAL CLASSES

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

ANALYSIS OF ANTIHISTAMINE DRUGS

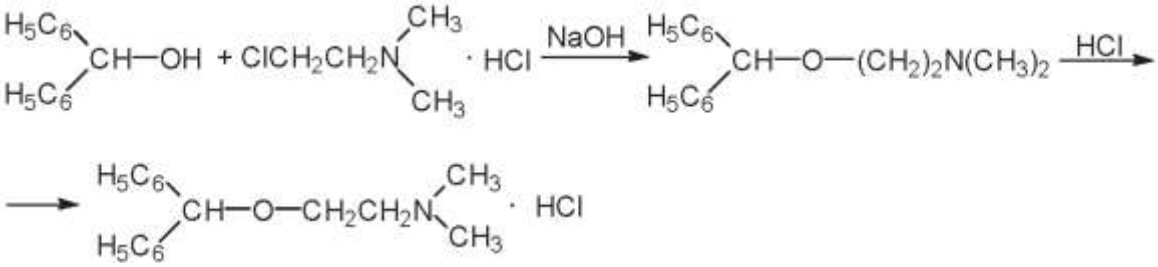
Diphenhydramine hydrochloride (Diphenhydramini hydrochloridum)

(SPhU) Dimedrol (Dimedrolum)



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

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

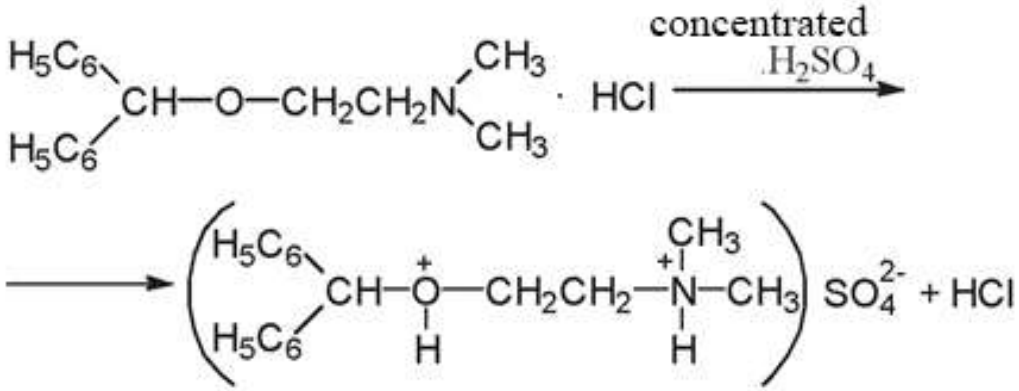


Properties. Crystalline powder of white or almost white color. Very easily soluble in water, easily soluble in 96% alcohol.

Identification:

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

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



The substance reacts to chlorides.

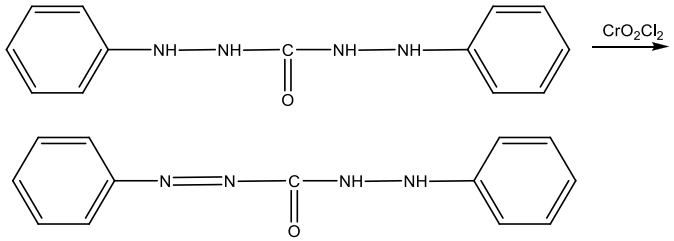
A) Reaction with a solution of silver nitrate in nitric acid medium, a white cheesy precipitate is formed. The precipitate is insoluble in dilute acids, soluble in ammonia solution:

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

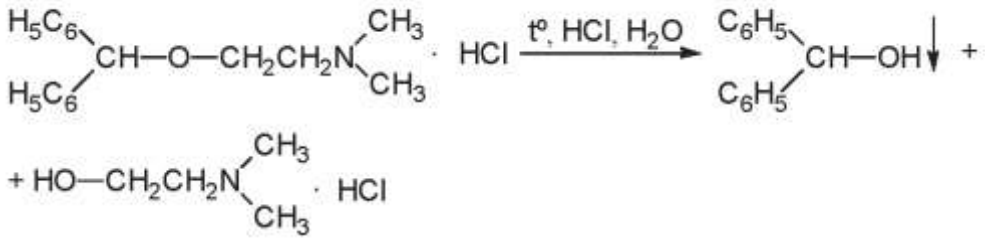
$$AgCl\downarrow + 2NH_4OH \rightarrow [Ag(NH_3)_2]Cl + 2H_2O.$$

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

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

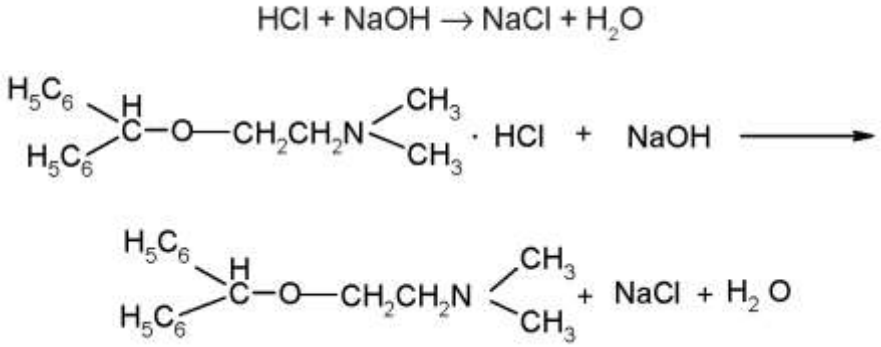


Acid hydrolysis reaction [10, 171]:

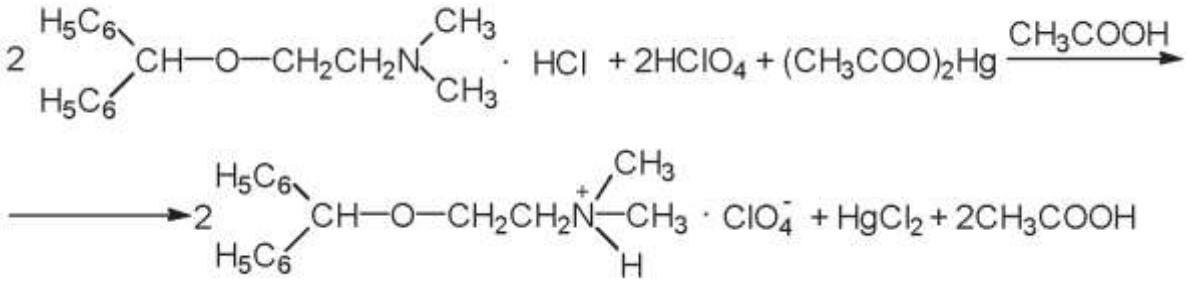


Check the melting point of the formed benzhydrol (62-67 °C).

Quantitative definition. Alkalimetry in a mixture of alcohol and 0.01 M solution of hydrochloric acid, direct titration, potentiometric. The titrant volume between two potential jumps on the titration curve (SPhU) is taken into account [10, 172]:



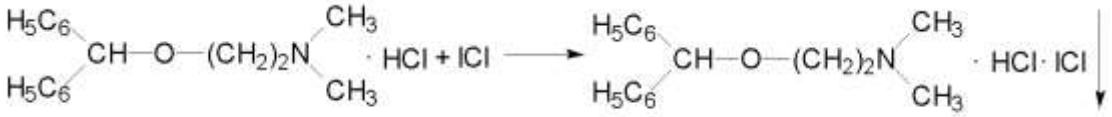
Acidimetry in a non-aqueous medium. The drug product is dissolved in glacial acetic acid, a solution of mercury (II) acetate is added (to bind hydrogen chloride) and titrated with a solution of perchloric acid in glacial acetic acid to a greenish-blue color, the indicator is crystal violet [10, 172]:



In parallel, a control experiment is conducted.

Iodochlorometry, reverse titration, indicator - starch:

In parallel, a control experiment is conducted [10, 172].



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

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

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

Argentometry by bound HCl according to the Folgard method.

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

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

$$Fe^{3+} + 3H_2O \rightleftharpoons Fe(OH)_3\downarrow + 3H^+$$

$$NaCl + AgNO_3 \longrightarrow NaNO_3 + AgCl$$

$$AgNO_3 + NH_4SCN \longrightarrow \downarrow AgSCN + NH_4NO_3$$

$$3NH_4SCN + FeNH_4(SO_4)_2 \longrightarrow \left[Fe(SCN)_3\right] + 2(NH_4)_2SO_4$$

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

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

Application (use). Antihistamine (antiallergic) agent.

Calcium chloride dihydrate (Calcii chloridum dihydricum) (SPhU)

$CaCl_2$ *$2H_2O$

Calcium chloride hexahydrate (Calcii chloridum hexahydricum) (SPhU)

$CaCl_2$ $6H_2O$

Extraction. Dissolving chalk in hydrochloric acid with further purification and concentration [10, 110]:

$$CaCO_3 + 2HCl \rightarrow CaCl_2 + H_2O + CO_2\uparrow$$

Natural minerals contain impurities of magnesium and ferrum ions, which turn into $MgCl_2$ and $FeCl_2$ when treated with hydrochloric acid. The resulting solution is saturated with chlorine ($FeCl_2$ is oxidized to $FeCl_3$), and then an excess of calcium hydroxide is added[10, 110]::

$$2FeCl_3 + 3Ca(OH)_2 \rightarrow 2Fe(OH)_3\downarrow + 3CaCl_2$$

$$MgCl_2 + Ca(OH)_2 \rightarrow Mg(OH)_2\downarrow + CaCl_2$$

The solution is enriched with calcium chloride, and impurities fall into a precipitate that is filtered. Excess calcium hydroxide is converted into calcium chloride by hydrochloric acid[10, 110]::

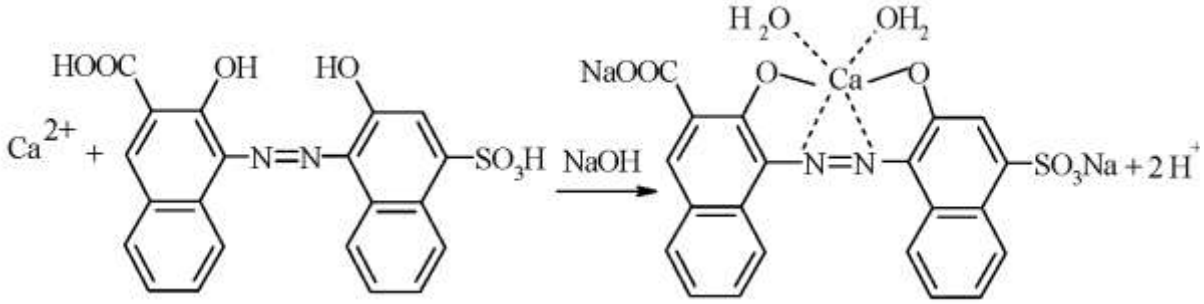
$$Ca(OH)_2 + 2HCl \rightarrow CaCl_2 + 2H_2O$$

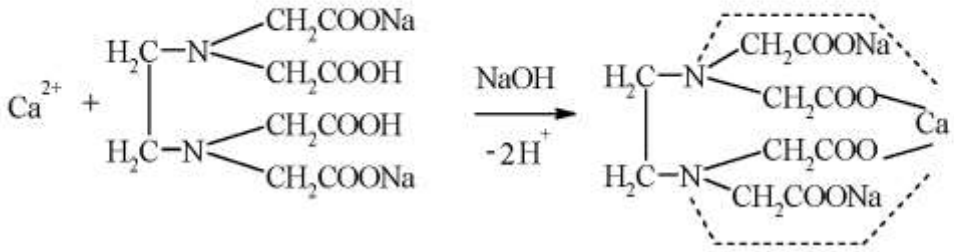
Properties. Calcium chloride dihydrate is a white crystalline powder. Hygroscopic. Easily soluble in water, soluble in 96% alcohol.

Calcium chloride hexahydrate is a white crystalline mass or colorless crystals. Very easily soluble in water, easily soluble in 96% alcohol. The melt freezes at a temperature of about 29 °C.

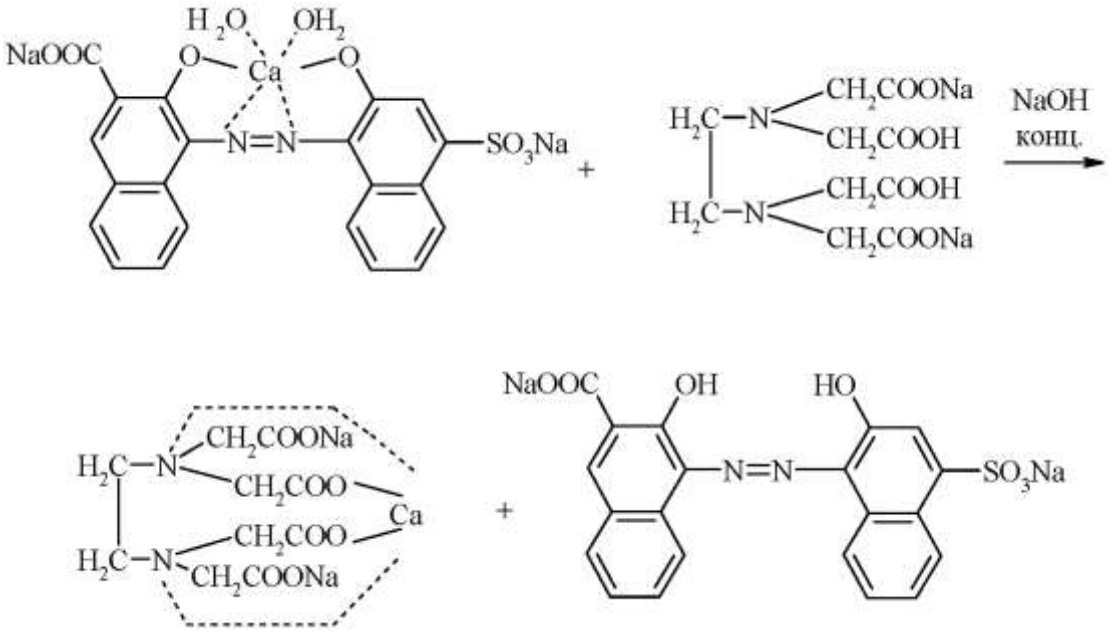
Identification: The substances give reactions to calcium and chlorides.

Quantitative definition. Complexonometry, direct titration in the presence of sodium hydroxide, indicator - chalcone carboxylic acid [10, 110]:





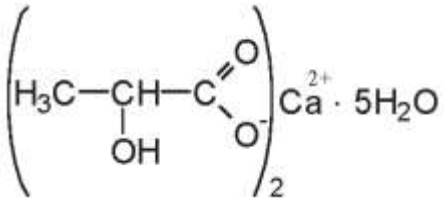
Titrate with sodium edetate until the purple color changes to blue [10, 110]:



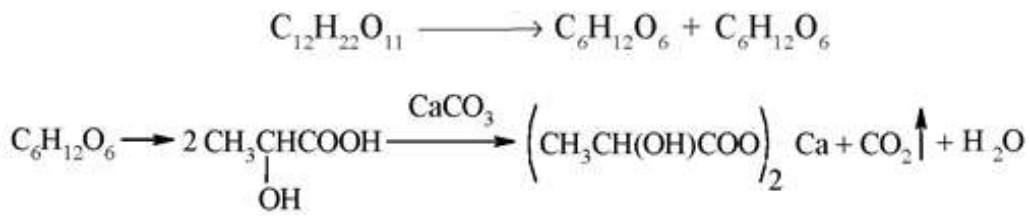
Storage. In a tightly closed container with paraffin plugs in a dry place. Since calcium chloride is extremely hygroscopic and dissolves under the influence of moisture, it is recommended to first prepare a 50% solution and use it to prepare dosage forms.

Application. With increased removal of calcium from the body, with allergic diseases, together with antihistamines, as a means that reduces the permeability of blood vessels, as a hemostatic agent, as an antidote for magnesium salt poisoning.

Calcium lactate pentahydrate
(Calcii lactas pentahydricus) (SPhU)



Extraction Lactic acid fermentation of sugar in the presence of calcium carbonate [10, 150]:



Properties. Crystalline or granular powder of white or almost white color. Slightly weathered. Soluble in water, easily soluble in boiling water, very slightly soluble in 96% alcohol.

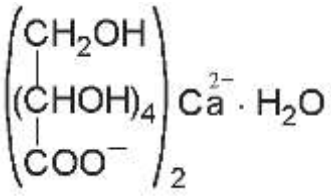
Purity test. Sucrose and reducing sugars are detected using a copper-tartrate reagent solution. A red precipitate should not form.

Quantitative definition. Complexonometry (similar to calcium chloride).

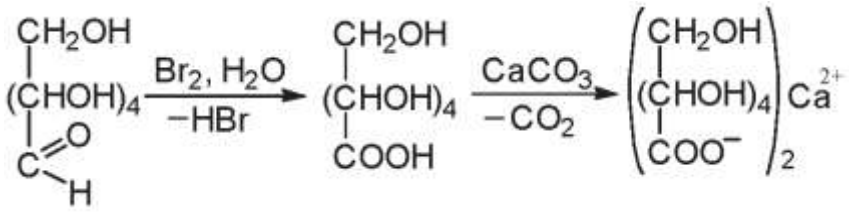
Storage. In a sealed container.

Application. According to its pharmacological properties, it is an analogue of calcium chloride (an anti-allergic and hemostatic agent). Can be used for injections.

Calcium gluconate (Calcii gluconas) (SPhU)



Extraction. Electrochemical oxidation of glucose in the presence of chalk and bromine [10, 151]:



Properties. White crystalline or granular powder. Moderately soluble in water, easily soluble in boiling water.

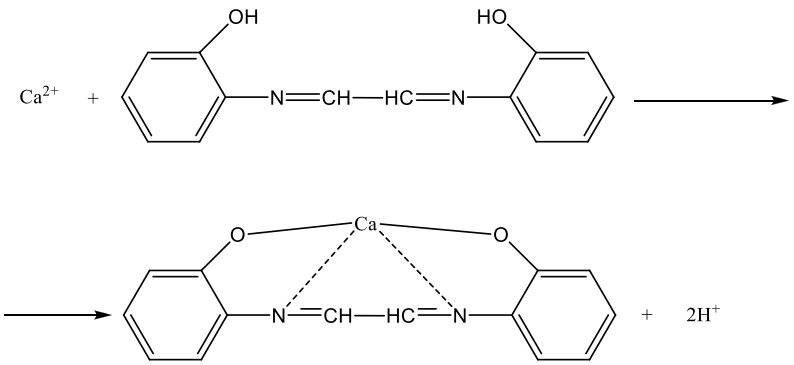
Identification:

By the method of thin-layer chromatography.

The substance reacts to calcium ions.

A) With a solution of glyoxal hydroxyanile.

The reaction is carried out in the presence of a mixture of sodium hydroxide and sodium carbonate, which prevents the formation of complex compounds with other alkaline earth metals, the presence of which interferes with this reaction - there is a red color of the chloroform layer:



B) With a solution of potassium ferrocyanide.

The reaction is carried out at pH ≈ 9:

$$CaCl_2 + K_4[Fe(CN)_6] + NH_4Cl \rightarrow CaNH_4K[Fe(CN)_6]\downarrow + 3KCl$$

NB! The formed white crystalline precipitate of potassium-calcium-ammonium hexacyanoferrate (II) is insoluble in acetic acid. Barium ion (Ba^{2+}) can have a similar effect, so in the presence of Ba^{2+} cations, this reaction should not be used.

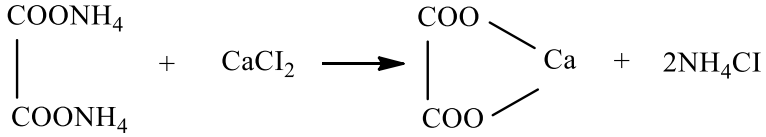
C) With a solution of ammonium oxalate.

The reaction is carried out in acetic acid, a white crystalline precipitate is formed soluble in mineral acids, but not soluble in acetic acid and ammonia solution:

$$Ca^{2+} + C_2O_4^{2-} \rightarrow CaC_2O_4\downarrow$$

$$CaC_2O_4\downarrow + 2HCl \rightarrow CaCl_2 + H_2C_2O_4.$$

or



D) Volatile calcium salts color the colorless flame brick-red.

A non-pharmacopoeial reaction - with a solution of ferrum (III) chloride forms a light green color (reaction to gluconate ions).

Purity test. Sucrose and reducing sugars are detected using a copper-tartrate reagent solution. A red precipitate should not form.

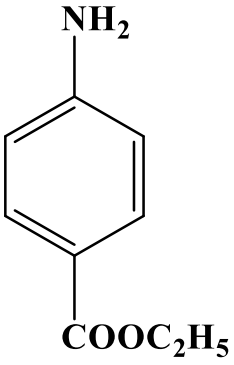
Quantitative definition. Complexonometry (similar to calcium chloride).

Storage. In a sealed container.

Application. According to its pharmacological properties, it is an analogue of calcium chloride (an anti-allergic and hemostatic agent). Can be used for injections.

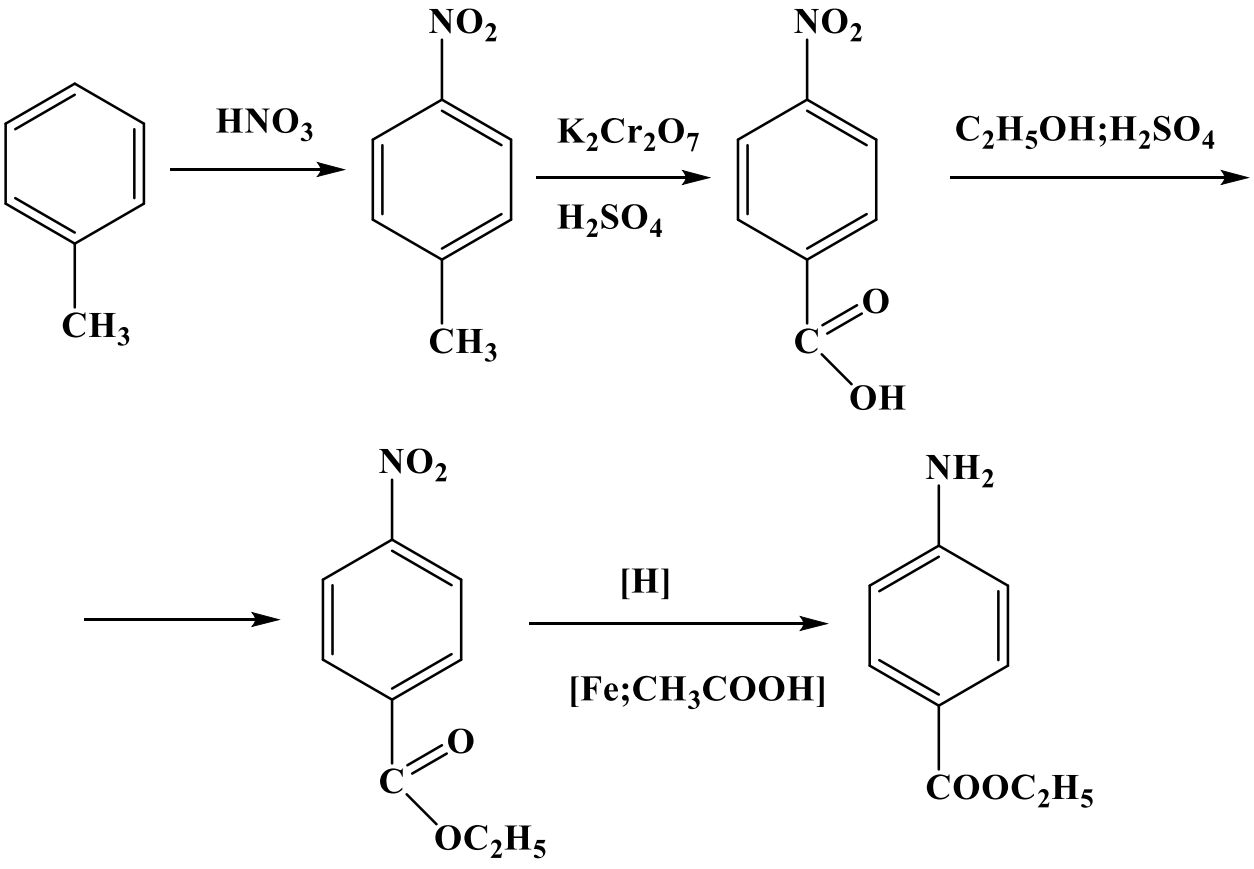
ANALYSIS OF DRUGS AFFECTING AFFERENT INNERVATION

Anesthesin (Anaesthesinum) Benzocaine



Ethyl ether P-aminobenzoic acid

Extraction. The starting substance is toluene:



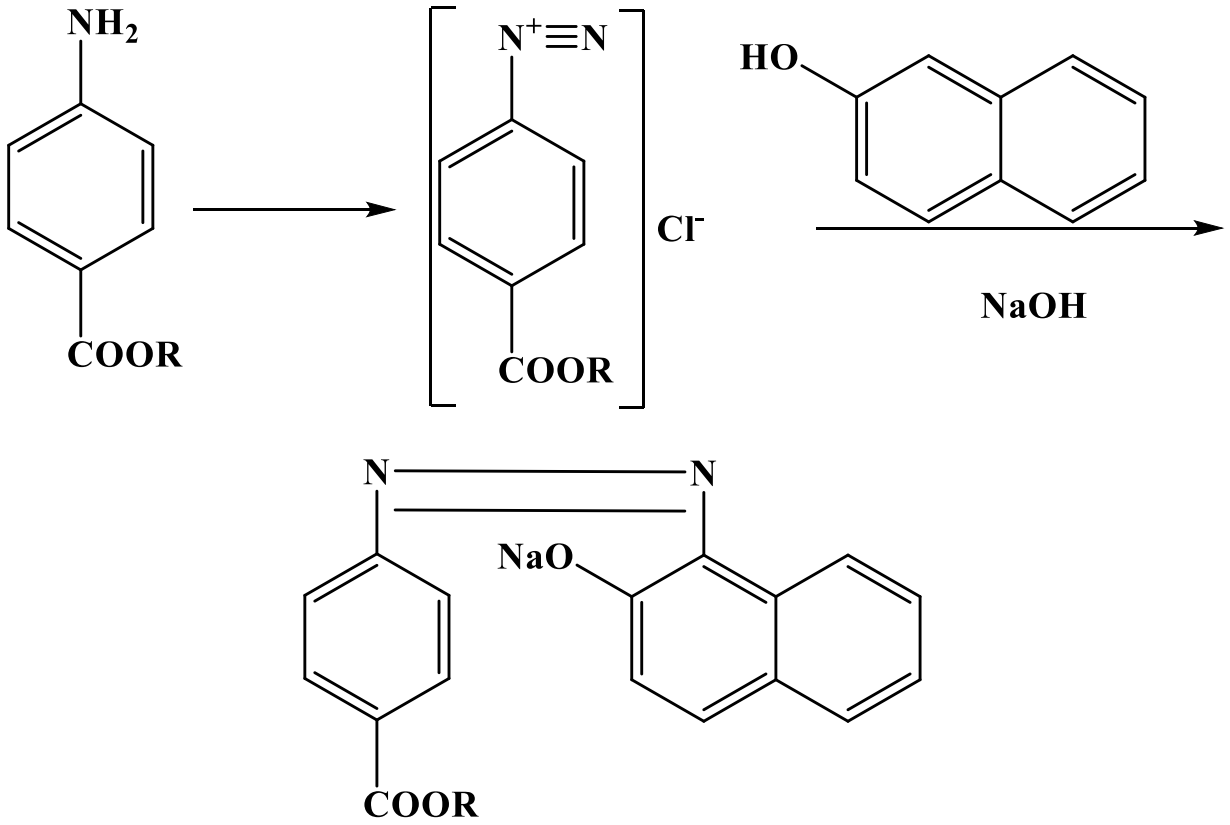
ethyl ether

P-nitrobenzoic acid

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

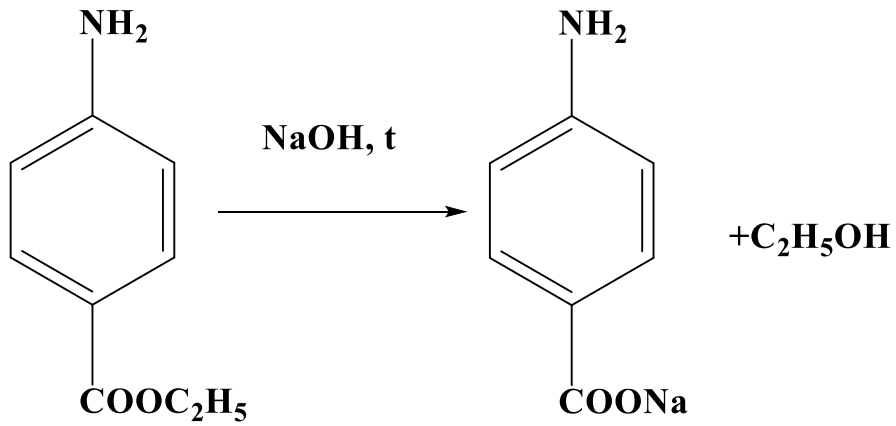
Identification:

Reaction to primary aromatic amino group:



cherry-red azo dye

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



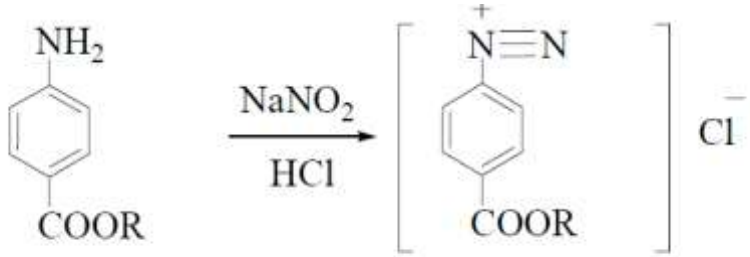
$$C_2H_5OH + 4I_2 + 6NaKOH \rightarrow CHI_3\downarrow + 5NaI + HCOONa + 5H_2O$$

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

A reaction with aromatic aldehydes:

Quantitative definition.

Nitritometry, indicator - iodcrohmal paper:



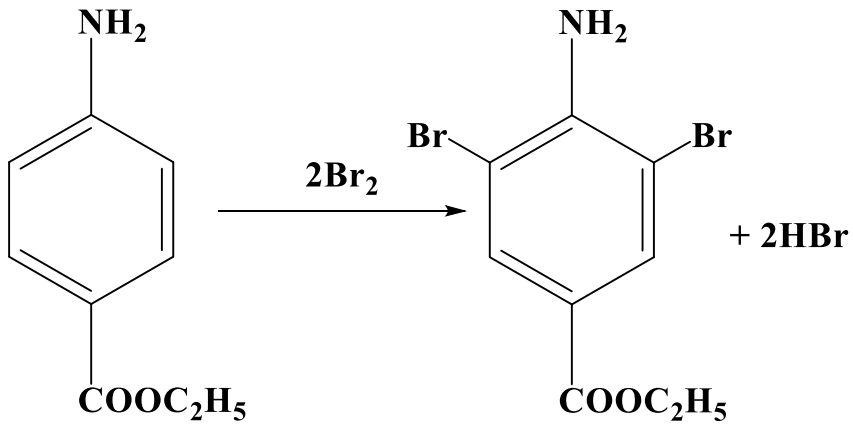
$$2KIO_3 + 5NaNO_2 + 2HCl \rightarrow I_2 + 5NaNO_3 + 2KCl + H_2O$$

In parallel, the control experiment is carried out.

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

Bromatometry, reverse titration:

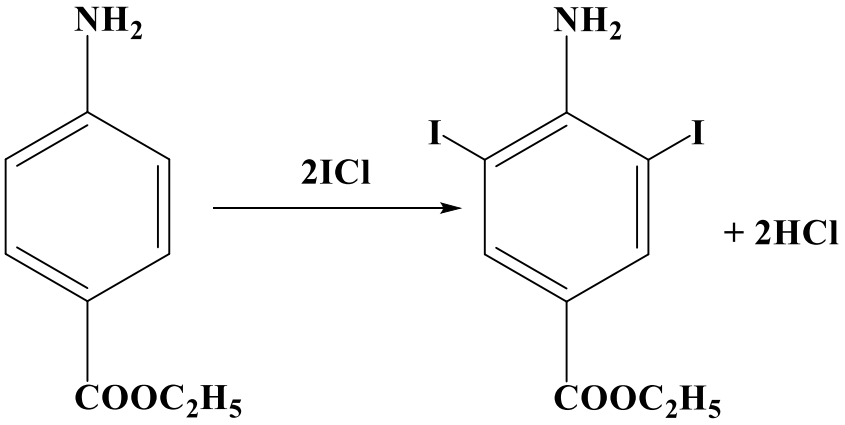
$$KBrO_3 + 5KBr + 6HCl \rightarrow 3Br_2 + 6KCl + 3H_2O$$



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

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

Iodochlorometry, reverse titration:



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

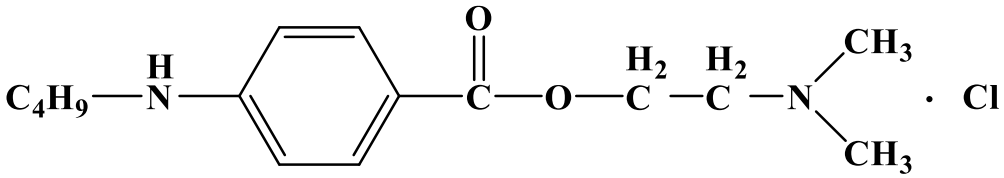
$$I_2 + 2Na_2S_2O_3 \rightarrow 2NaI + Na_2S_4O_6$$

Storage. In a sealed container that protects from light.

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

Dikain - Dicainum

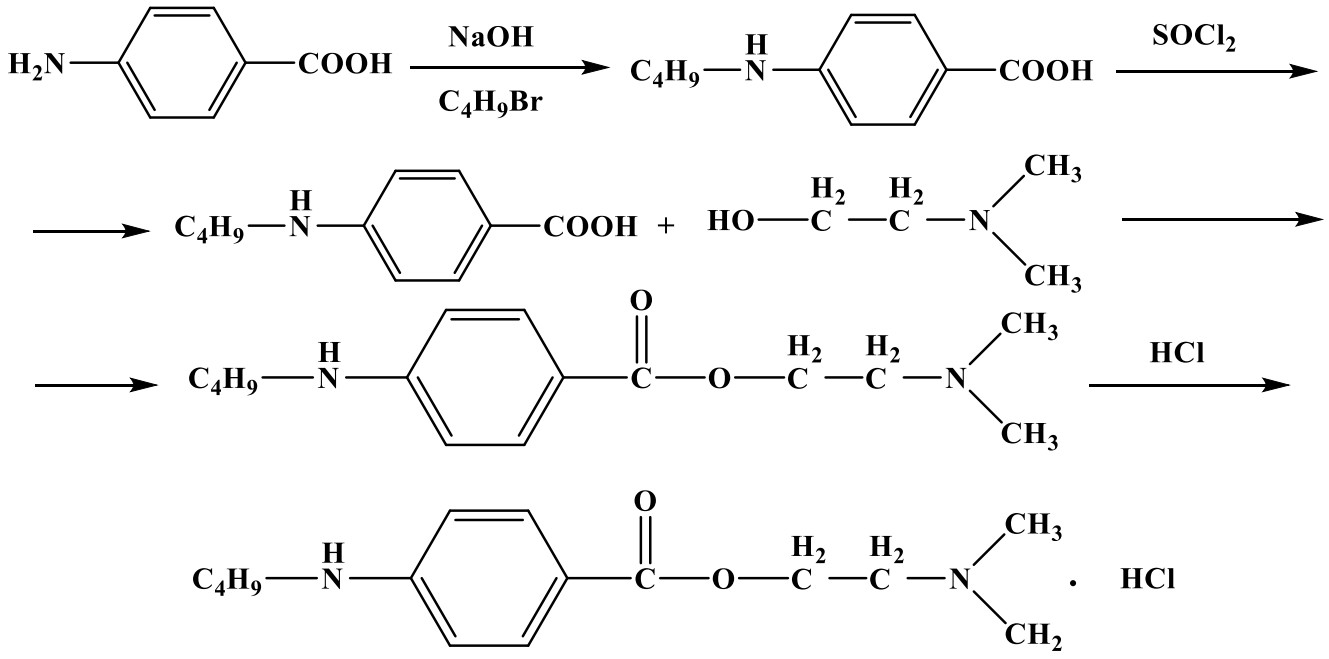
Tetracaini hydrochloridum



β-Dimethylaminoethyl ether

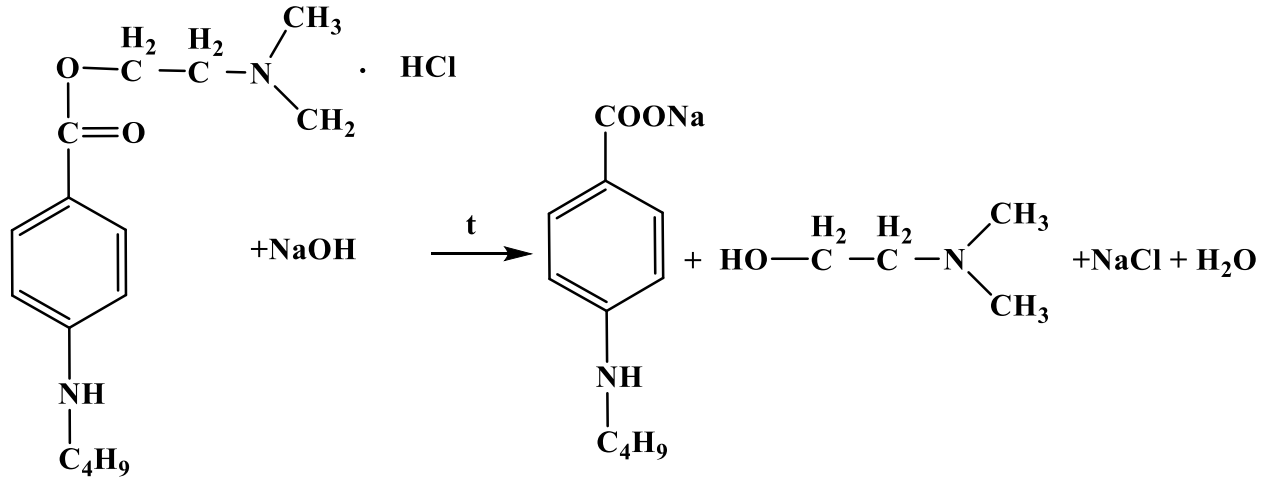
p-butylaminobenzoic acid hydrochloride

Extraction. It is carried out according to the following scheme:

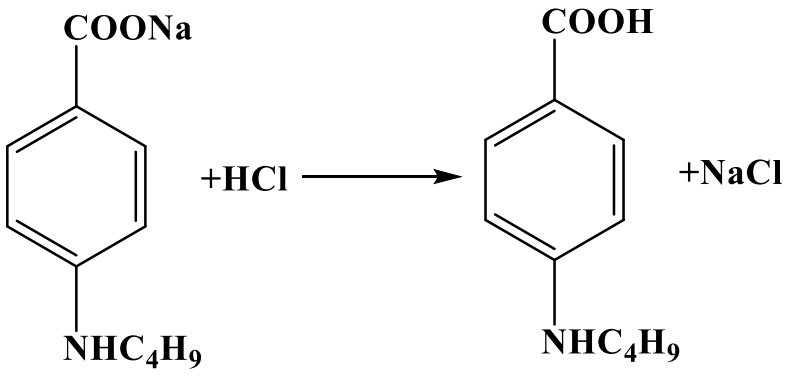


Description. Odorless white crystalline powder. Easily soluble in water and alcohol, sparingly soluble in chloroform, practically insoluble in ether.

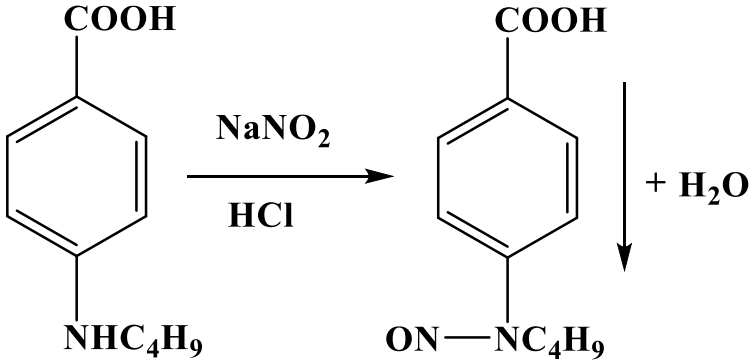
Identification: reaction to the secondary amino group after alkaline hydrolysis:



During acidification, a white precipitate of p-butylaminobenzoic acid falls out, which dissolves in an excess of hydrochloric acid:



Under the action of sodium nitrite, a precipitate of the N-nitroso compound of this acid falls out:



The substance reacts with chlorides (see chlorides).

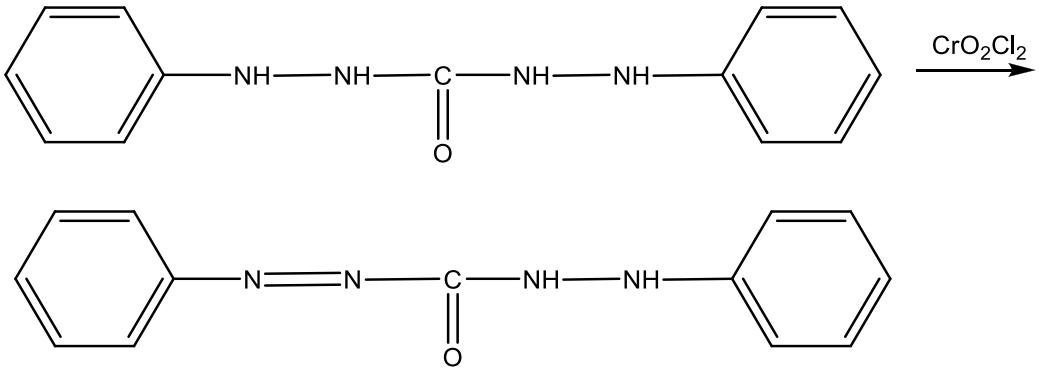
A) Reaction with a solution of silver nitrate in nitric acid medium, a white cheesy precipitate is formed. The precipitate is insoluble in dilute acids, soluble in ammonia solution:

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

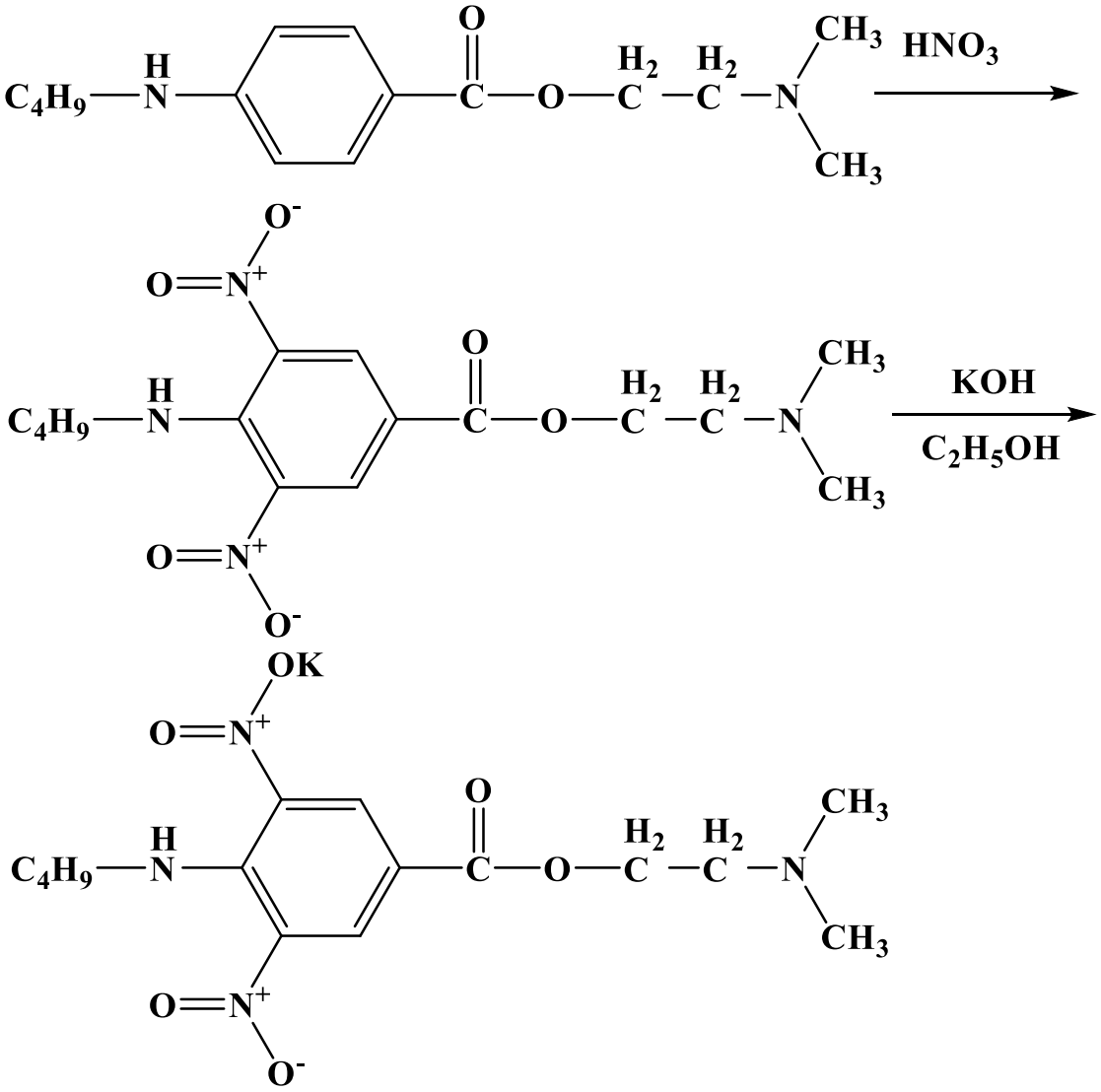
$$AgCl\downarrow + 2NH_4OH \rightarrow [Ag(NH_3)_2]Cl + 2H_2O.$$

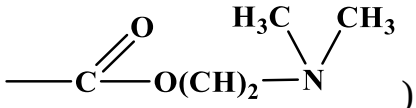
B) Reaction with potassium dichromate in a mixture with sulfuric acid: chromyl chloride is formed, the vapors of which are stained with filter paper impregnated with a solution of diphenylcarbazide (colorless), in purple-red color:

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

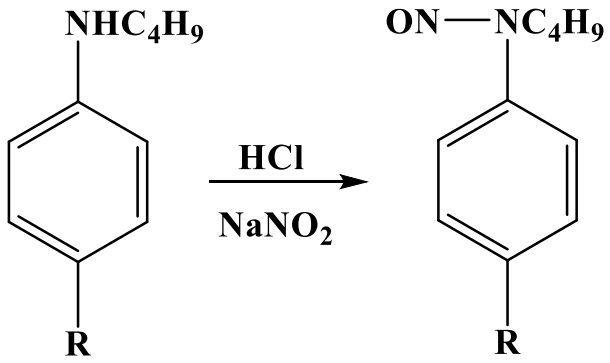


Nitration of dikain with subsequent formation of a potassium salt of acinitroform with an orthoquinoid structure of blood-red color:

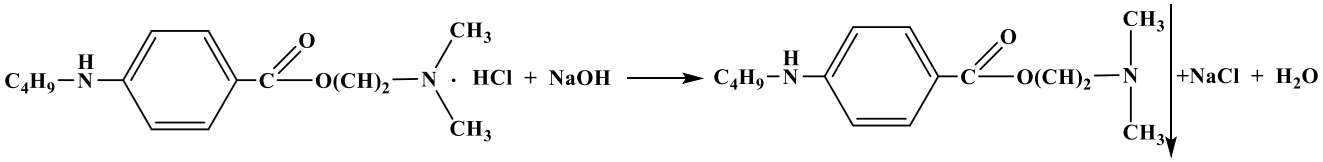


Quantitative definition: nitritometry with external or internal indicator (R = 

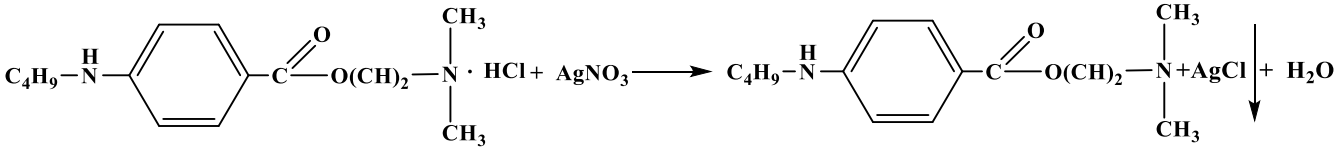
):



Alkalimetry by bound hydrochloric acid. The titration is carried out in the presence of chloroform, which extracts the base that is released, the indicator is phenolphthalein:



Argentometry by bound hydrochloric acid:

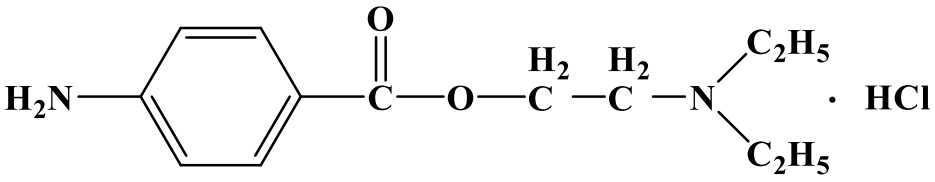


Storage. In a sealed container.

Application. Local anesthetic agent. Dicaine is more potent than procaine hydrochloride, but it is more toxic: 2 times more than cocaine and 10 times more than procaine hydrochloride.

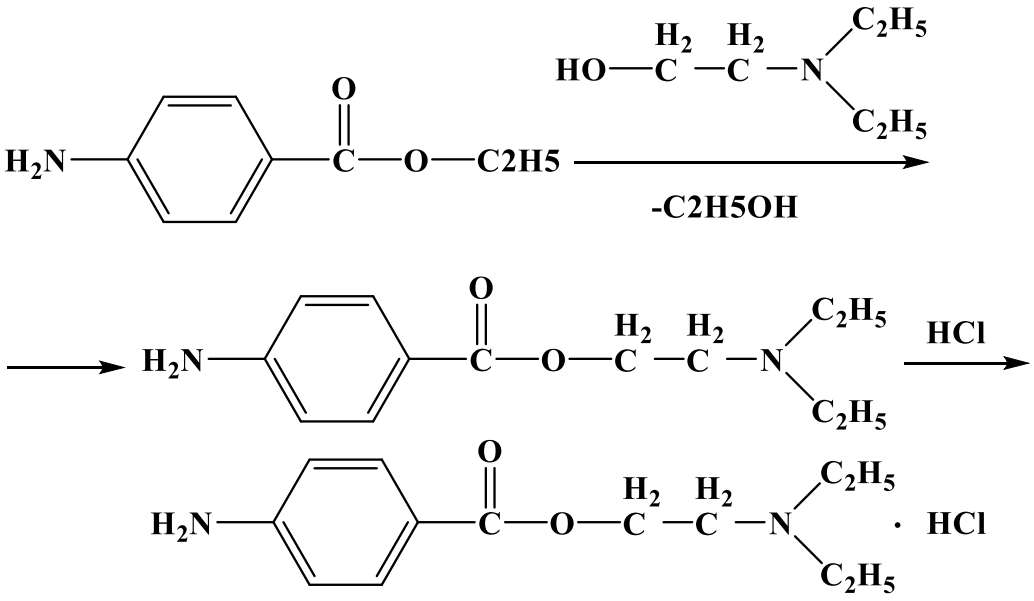
Procaine hydrochloride (Procaini hydrochloridum) (SPhU)

Novocaine (Novocainum)

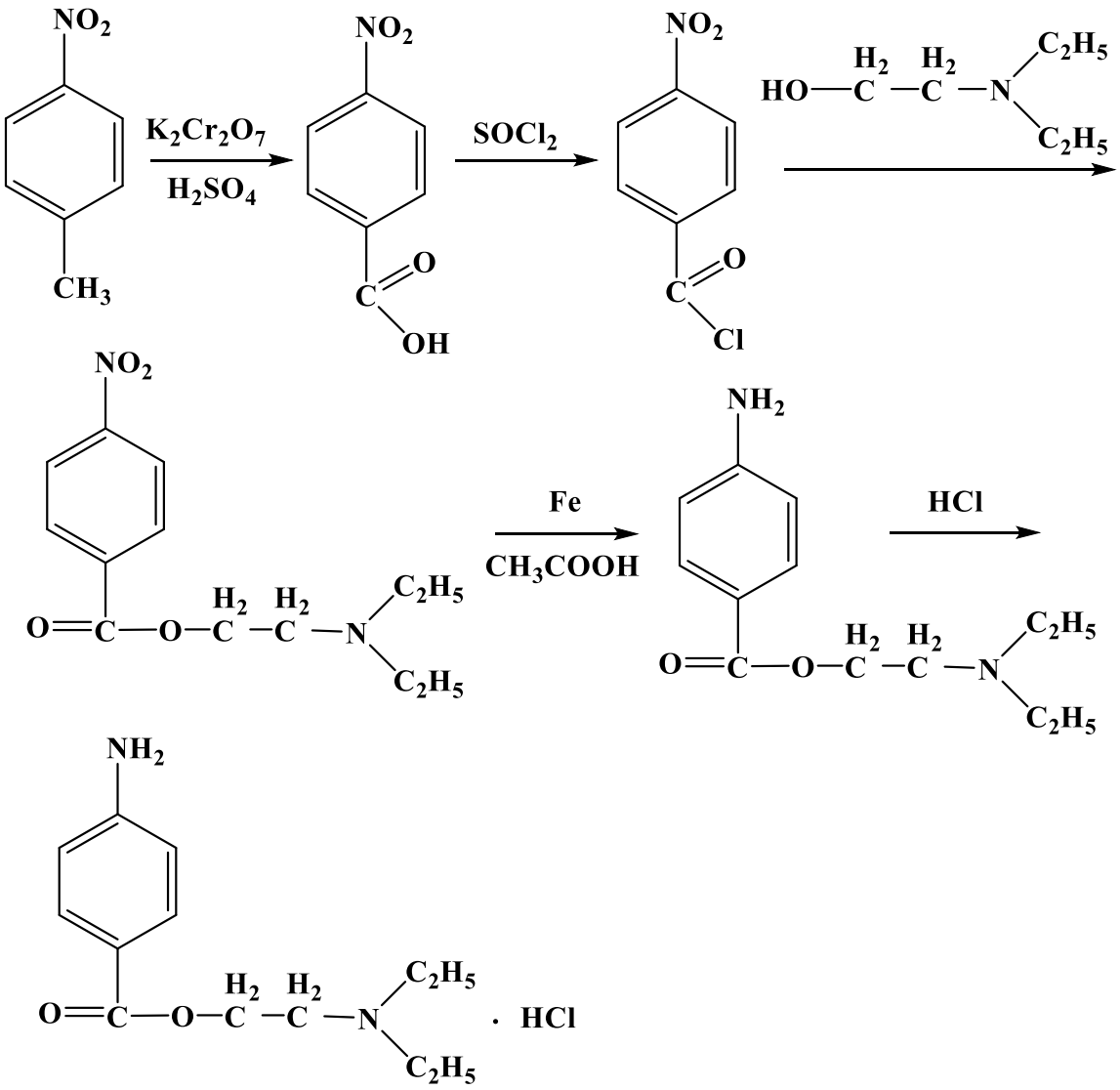


2-Diethylaminoethyl-4-aminobenzoate hydrochloride

Extraction. 1. Procaine hydrochloride is synthesized with anesthesin by the transesterification reaction of β-Diethylaminoethanol in the presence of sodium alcoholate:



2. Procaine hydrochloride can be synthesized in another way, starting from p-nitrotoluenes:

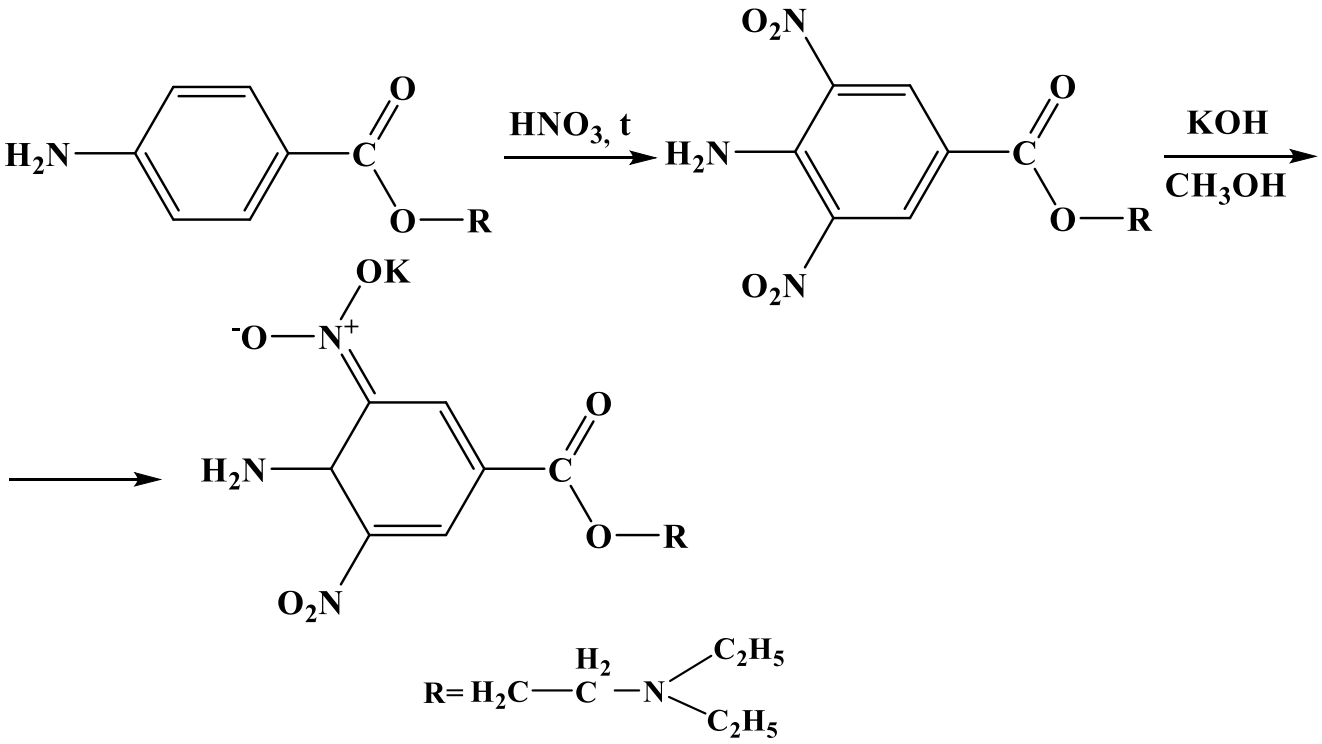


Properties. White crystalline powder or colorless crystals. It causes a feeling of numbness on the tongue. Very easily soluble in water, soluble in 96% alcohol, practically insoluble in ether.

Identification: 1. Physico-chemical methods: melting point, IR spectroscopy.

2. Fuming nitric acid is added to the substance and evaporated to dryness in a water bath, cooled and the residue dissolved in acetone.

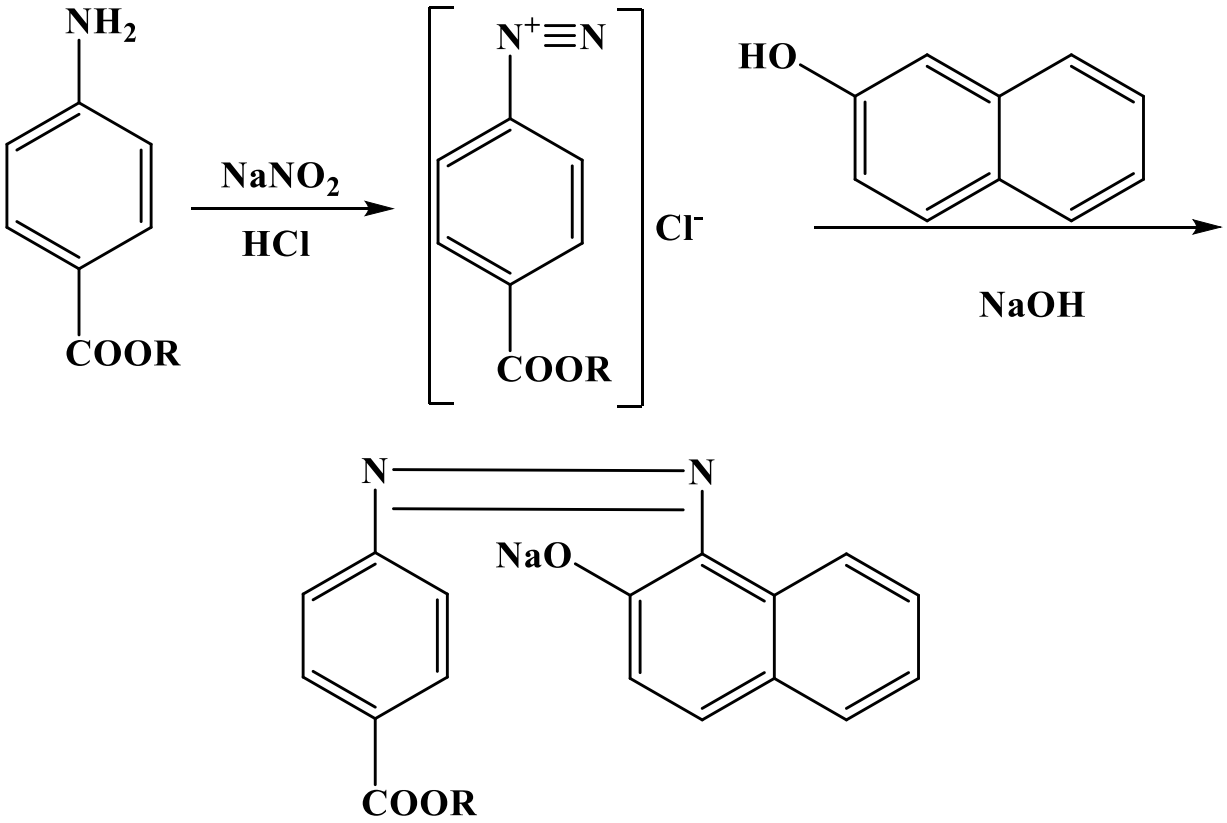
An alcoholic solution of potassium hydroxide is added to the resulting solution; only a brown-red color should appear:



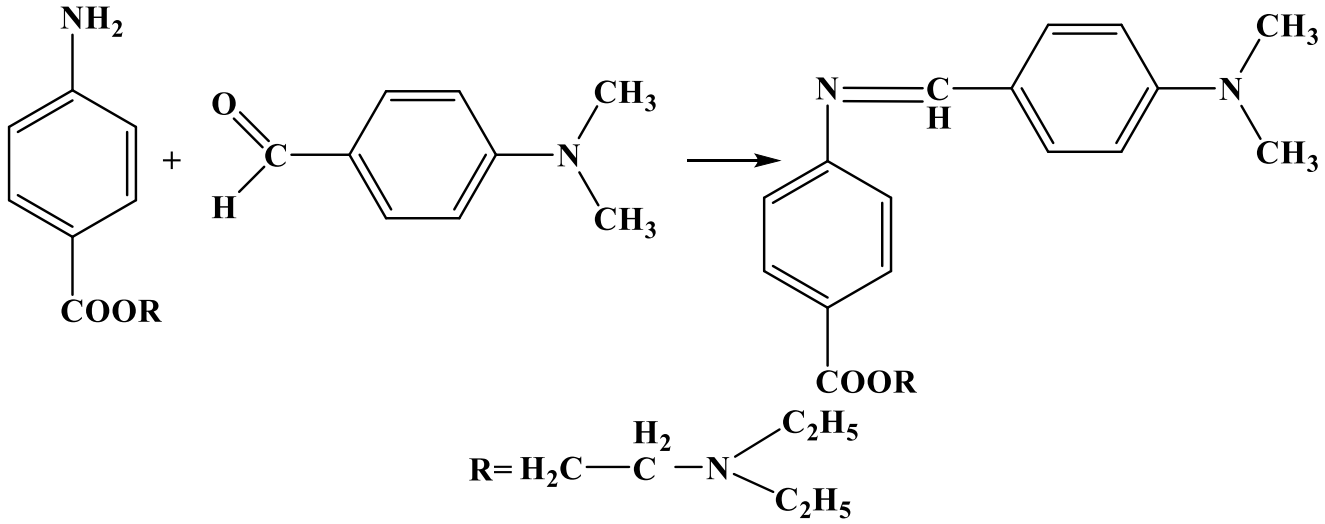
3. Reaction with potassium permanganate. A solution of procaine hydrochloride, acidified with dilute sulfuric acid, quickly decolorizes a 0.1 M solution of potassium permanganate (unlike other anesthetics).

4. The substance reacts with chlorides (see chlorides).

5. The substance reacts with primary aromatic amines:



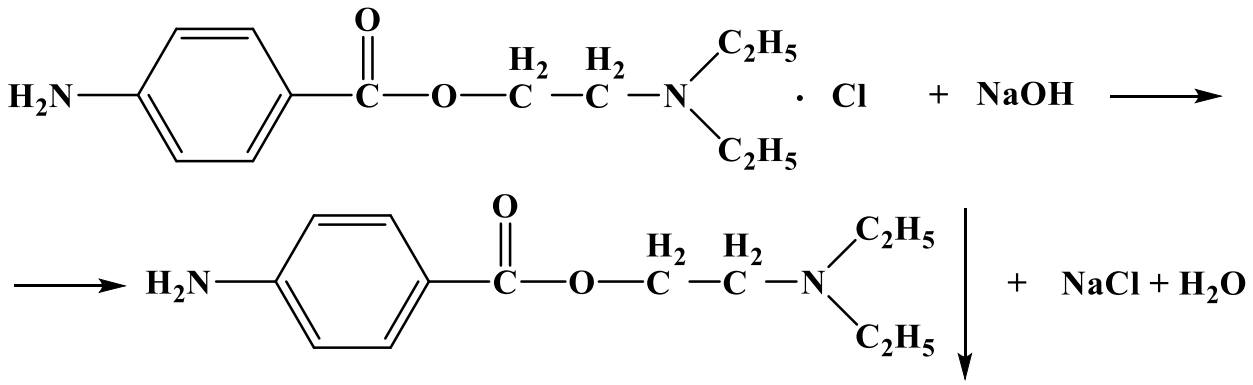
1. Reaction with aromatic aldehydes:



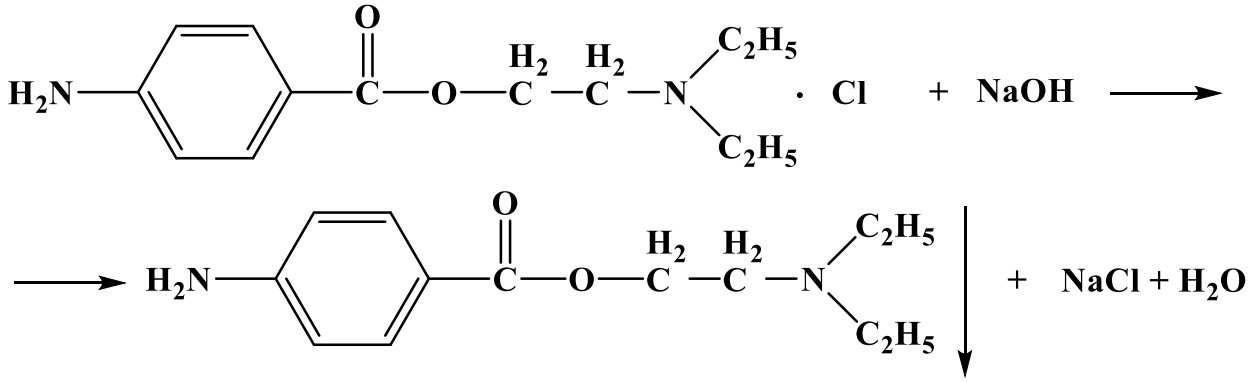
8. Non-pharmacopoeial reactions:

a) reaction with perhydrol. Perhydrol and concentrated sulfuric acid are added to the solution of the substance - a lilac color gradually appears.

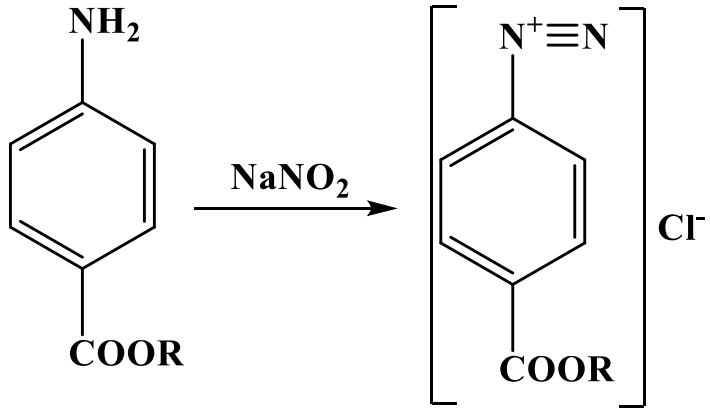
b) When adding a solution of sodium hydroxide, the base of procaine is formed - an oily liquid:



Quantitative determination: Alkalimetry by bound hydrochloric acid. The titration is carried out in the presence of chloroform, which removes the base that is formed, the indicator is phenolphthalein:



Nitritometry, indicator - iodine-starch paper:

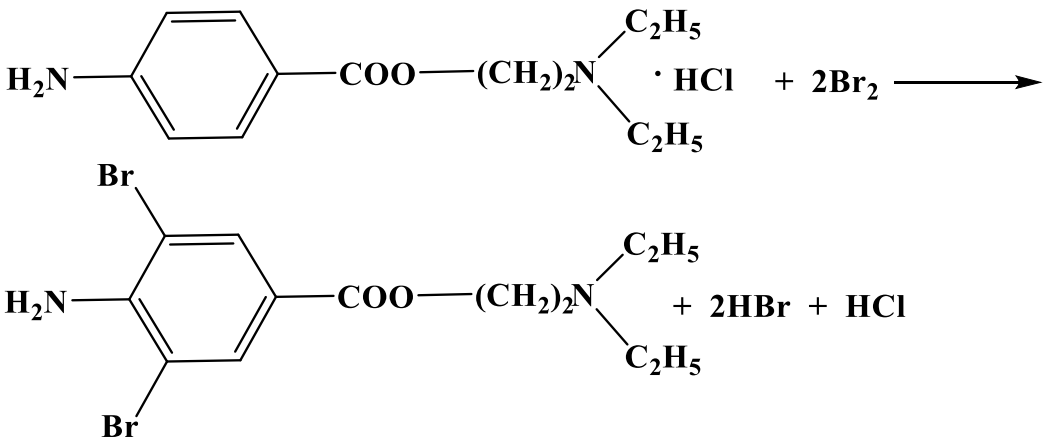


$$2KIO_3 + 5NaNO_2 + 2HCl \rightarrow I_2 + 5NaNO_3 + 2KCl + H_2O$$

In parallel, a control experiment is conducted.

When using internal indicators, use neutral red or tropeolin-00 mixed with methylene blue.

Bromatometry, based on the formation of procaine dibromo derivatives, the indicator is starch:



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.

Reduces the formation of acetylcholine and reduces the excitability of peripheral cholinergic systems. Blocks autonomic ganglia. Reduces spasms of smooth muscles, reduces the excitability of the heart muscle.

In the body, procaine hydrochloride is hydrolyzed relatively quickly, forming p-aminobenzoic acid and diethylaminoethanol. Sulfanilamides are chemically similar to p-aminobenzoic acid (PABA), which, entering into a competitive relationship with them, weakens their antibacterial effect. Novocaine as a derivative of PABA also has an anti-sulfanilamide effect.

Diethylaminoethanol exhibits moderate vasodilating properties. Procaine hydrochloride is used for blockades and anesthesia.

Aluminum hydroxide (Aluminii hydroxydum)

Algeldratum

$Al(OH)_3$

Extraction [10, 103]**:**

$$Al_2(SO_4)_3 + 6NH_4OH \rightarrow 2Al(OH)_3\downarrow + (NH_4)_2SO_4$$

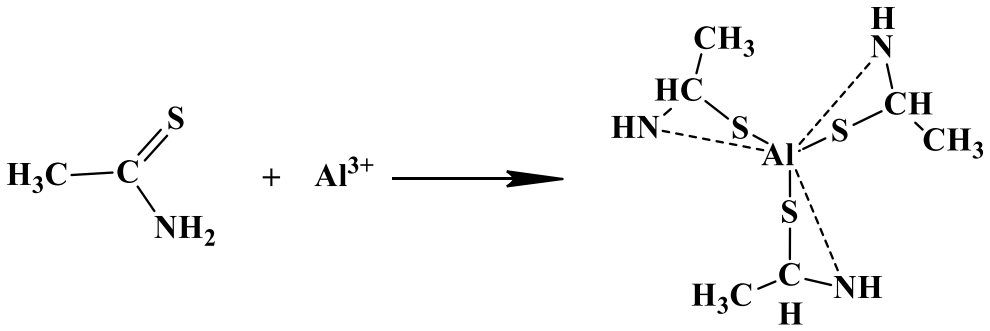
$$2KAl(SO_4)_2 + 6NH_4OH \xrightarrow{60\,^{\circ}C} 2Al(OH)_3\downarrow + K_2SO_4 + 3(NH_4)_2SO_4$$

Properties. White loose amorphous powder. Practically insoluble in water, soluble when heated in dilute acids and alkali solutions with the formation of a transparent or slightly cloudy solution.

Identification:

1. The substance gives characteristic reactions to aluminum.

The identification of the aluminum cation according to the requirements of the SPhU 2nd edition is based on its amphoteric properties. Before carrying out studies on the Al^{3+} cation, diluted hydrochloric acid is added to the solution of the tested substance to form aluminum chloride. Then add thioacetamide reagent:



A precipitate is not formed, since thioacetamide forms a soluble complex with Al^{3+}, unlike insoluble complexes - with Bi^{3+}, Pb^{2+}, Sn^{2+}, Hg^{2+} and others.

Next, a solution of sodium hydroxide diluted to the formation of a gel-like precipitate is added drop by drop (!) to the resulting solution:

$$\mathbf{Al^{3+} + 3OH^{-} \rightarrow Al(OH)_3\downarrow}$$

A further increase in the diluted sodium hydroxide solution leads to the dissolution of the precipitate with the formation of a complex salt - trisodium hexahydroxoaluminate:

$$\mathbf{Al(OH)_3 + 3NaOH \rightarrow Na_3[Al(OH)_6];}$$

Add ammonium chloride solution gradually. A gel-like white precipitate forms again:

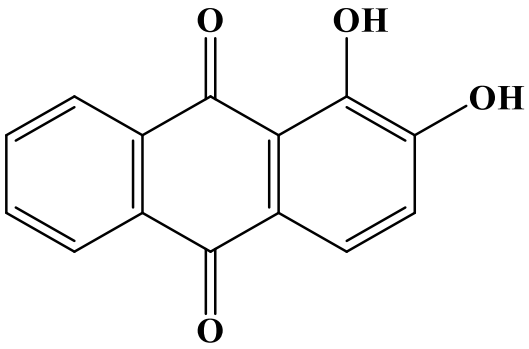
$$\mathbf{Na_3[Al(OH)_6] + 3NH_4Cl \rightarrow Al(OH)_3\downarrow + 3NH_4OH + 3NaCl.}$$

In addition to the method of aluminum identification given in the SPhU, others are also possible:

Reaction with alizarin. Alizarin with aluminum ions forms a red complex compound $AlOH[C_{14}H_6O_3(OH)]_2$, which does not dissolve in acetic acid. It is called "aluminum varnish".

Ions of iron (III), bismuth, copper (II) and some others interfere with the reaction because they form similar colored complexes.

Aluminum is determined by this reaction in a slightly acidic solution (at pH = 4.2-4.6). Under these conditions, alizarin has a yellow color. In an alkaline environment, the reagent has a purple color and therefore affects the results of aluminum detection, masking its red color:



Reaction with sodium thiosulfate. 1. When boiling with solutions of sodium aluminum salts, thiosulfate forms a precipitate of aluminum hydroxide and releases free sulfur:

$$\mathbf{Al_2(SO_4)_3 + 3Na_2S_2O_3 + 3H_2O \rightarrow 2Al(OH)_3\downarrow + 3Na_2SO_4 + 3S\downarrow + 3SO_2\uparrow.}$$

2. When a substance is heated with a solution of cobalt nitrate, cobalt aluminate ("thenar blue") is formed [10, 103]:

$$2Al(OH)_3 \xrightarrow{t^\circ} Al_2O_3 + 3H_2O$$
$$2Co(NO_3)_2 \xrightarrow{t^\circ} 2CoO + 4NO_2 + O_2$$
$$Al_2O_3 + CoO \xrightarrow{t^\circ} Co(AlO_2)_2$$

Quantitative determination: 1. Gravimetry after calcination of the substance in terms of Al_2O_3:

$$\mathbf{2Al(OH)_3 \rightarrow Al_2O_3 + 3H_2O}$$

2. Complexonometry, reverse titration in the presence of solutions of ammonium acetate and dilute acetic acid. The excess of the titrated solution of sodium edetate is titrated with a solution of zinc sulfate, the indicator is dithizone.

1) Al^{3+} + $Na_2H_2TrБ$ → $AlNaTrБ$ + $2H^+$

2) $Na_2H_2TrБ$ + $ZnSO_4$→ $ZnNa_2TrБ$ + $(NH_4)_2SO_4$ + 2 H_2O

At the equivalence point: **$H_3Ind + Al^{3+} \rightarrow AlInd + 3H^+$**

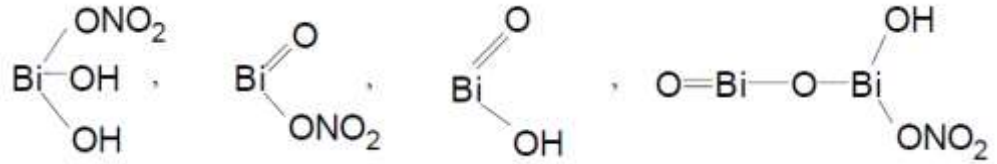
Storage. In a sealed container.

Application. As an adsorbing, enveloping and antacid agent; externally - for powders.

It is one of the components of the drug "Almagel".

Bismuth nitrate basic - Bismuthi subnitras

The chemical composition of basic bismuth nitrate is unstable. This is a mixture of [10, 96]:

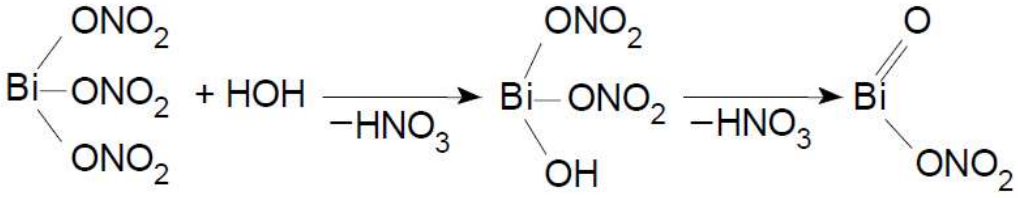


Extraction [10, 96].

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

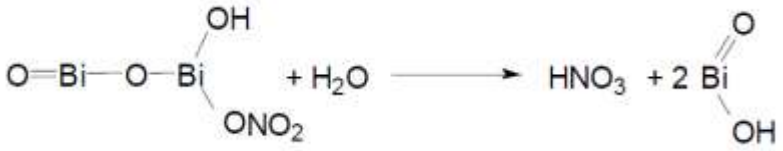
$$Bi + 4HNO_3 \rightarrow Bi(NO_3)_3 + NO\uparrow + 2H_2O$$

Aqueous solutions of bismuth nitrate are hydrolyzed in boiling water with the formation of an insoluble basic salt of bismuth nitrate [10, 97]:



Properties. White amorphous or fine crystalline powder; practically insoluble in water, alcohol, soluble in solutions of hydrochloric and nitric acids.

The powder soaked in water turns blue litmus paper red (pH<7) [10, 97].



Identification:

1. The substance gives characteristic reactions to bismuth.

Bismuth (Bi3+) is determined by separating a brown precipitate of bismuth sulfide from an acidic solution of bismuth salts upon their interaction with sodium sulfide. To carry out this reaction, water-soluble bismuth (III) chloride is obtained when heated. After cooling this solution, hydrolysis of the bismuth chloride salt and precipitation of a white precipitate of basic salts is possible. They are filtered and water is added, a white precipitate of bismuth hydroxide is obtained, which with sodium sulfide gives a brown precipitate:

$$\mathbf{Bi^{3+} + 3HCl \rightarrow BiCl_3 + 3H^+;}$$

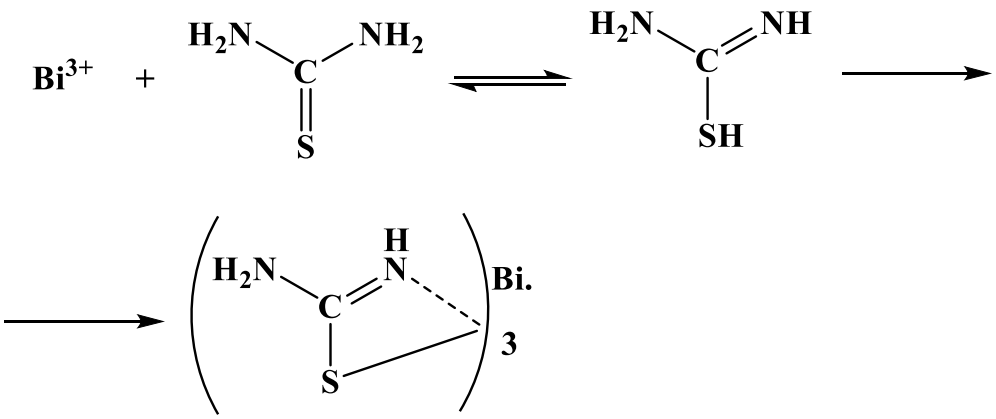
$$\mathbf{BiCl_3 + H_2O \rightarrow BiOCl\downarrow + 2HCl;}$$

$$\mathbf{2BiCl_3 + 3Na_2S \rightarrow Bi_2S_3\downarrow + 6NaCl.}$$

Bismuth (Bi^{3+}) is determined by the formation of a yellowish-orange color or an orange precipitate of a complex salt of bismuth with thiourea.

To carry out this reaction, a water-soluble nitric acid salt of bismuth is obtained upon heating. After cooling the resulting solution, a basic salt may form, which is filtered off, and a solution of thiourea is added to the filtrate. A yellow precipitate or a yellow-orange color of a complex salt that does not react with sodium fluoride should be formed:

$$\mathbf{Bi^{3+} + 3HNO_3 \rightarrow Bi(NO_3)_3 + 3H^+;}$$

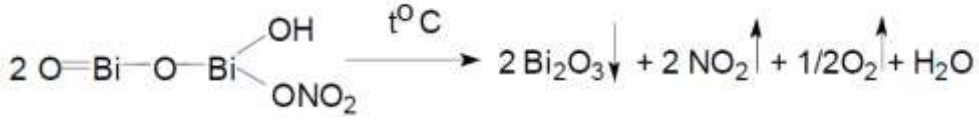


2. With a solution of potassium iodide - a black precipitate is formed, soluble in an excess of the reagent [10, 97]:

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

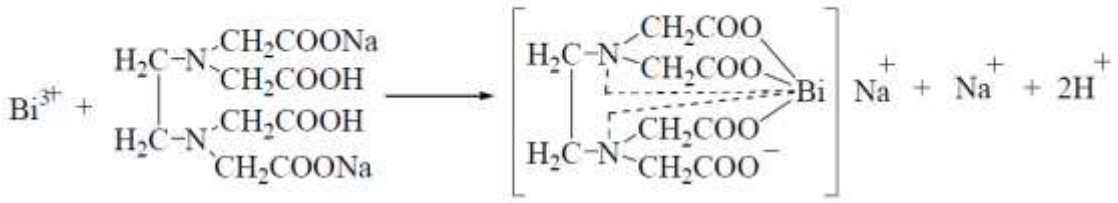
$$\downarrow BiI_3 + KI \rightarrow K[BiI_4]$$

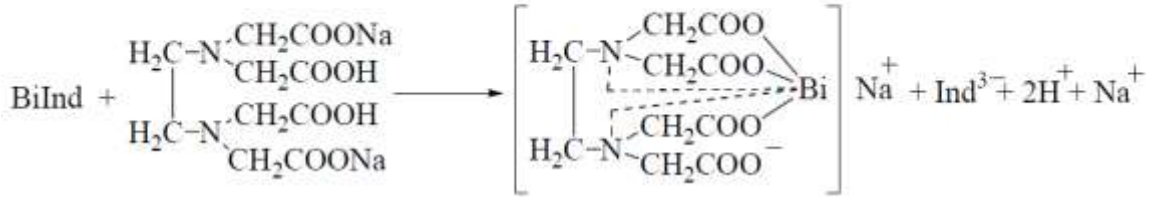
3. Upon calcination of the drug substance, yellow-brown vapors and a bright yellow residue are formed [10, 97]:



Quantitative definition. Complex ionometry, direct titration with sodium edetate solution, indicator – xylenol orange; (s = 1 in terms of bismuth) [10, 98]:

$$H_3Ind + Bi^{3+} \rightarrow BiInd + 3H^+$$





Storage. In a tightly sealed container that protects against light.

Application. Astringent, antiseptic agent.

Concentrated ammonia solution - Ammoniae solutio concentrata

NH_4OH

Extraction. Ammonia is obtained by the interaction of nitrogen with hydrogen at elevated temperature and pressure in the presence of a catalyst:

$$N_2 + 3H_2 \rightarrow 2NH_3$$

The resulting ammonia is dissolved in water.

Description. Transparent colorless liquid with an alkaline reaction of the medium. Mixes with water and 96% alcohol.

Identification: 1. Relative density should be between 0.892 and 0.910.

2. The substance has a strong alkaline reaction.

3. The substance gives a characteristic reaction to ammonium salts.

Ammonium salts are detected by reaction with a solution of sodium cobaltinitrite. Previously, to displace ammonium from its salts, magnesium oxide is added to the tested solution:

$$2NH_4^+ + MgO \rightarrow Mg^{2+} + 2NH_3 + H_2O.$$

A airstream is passed through the liquid, the gas (NH_3) that is formed is directed into a 0.1 M solution of hydrochloric acid with a methyl red indicator. The color of the indicator changes to yellow:

$$NH_3 + HCl \rightarrow NH_4Cl;$$

When adding the reagent, a yellow precipitate falls out:

$$NH_4^+ + Na_3[Co(NO_2)_6] \rightarrow (NH_4)_2Na\,[Co(NO_2)_6]\downarrow.$$

It should be taken into account that the reaction can be carried out in an alkaline environment, since the reagent decomposes with the formation of a dark brown precipitate of $Co(OH)_3$:

$$[Co(NO_2)_6]^{3-} + 3OH^- \rightarrow Co(OH)_3\downarrow + 6NO_2^-.$$

In the presence of strong acids, the complex ion also decomposes:

$$[Co(NO_2)_6]^{3-} + 6H^+ \rightarrow Co^{3+} + 6HNO_2.$$

It is important to use freshly prepared sodium cobalt nitrite solution for the reaction, as it decomposes upon standing, and its brown color changes to crimson (the color of Co^2 ions) and such a reagent is unsuitable for the reaction.

In addition to the method of identification of ammonium salts given in the SPhU, the precipitation reaction with Nessler's reagent is used.

This reaction is used to detect small amounts of ammonia or ammonium ions.

It is based on the interaction of an alkaline solution of a complex salt of potassium tetraiodomercurate ($K_2[HgI_4]$) with ammonia or ammonium salts:

$$\mathbf{NH_4^+ + 2[HgI_4]^{2-} + 2OH^- \rightarrow [NH_2Hg_2I_2]I \downarrow + 5I^- + 2H_2O.}$$

When a glass stick soaked in a solution of hydrochloric acid is raised to the drug product, white smoke is produced:

$$\mathbf{NH_3 + HCl \rightarrow NH_4Cl}$$

Quantitative definition. Reverse acidimetry, indicator - methyl red:

$$\mathbf{NH_4OH + HCl \rightarrow NH_4Cl + H_2O}$$

Excess hydrochloric acid is titrated with sodium hydroxide solution:

$$\mathbf{HCl + NaOH \rightarrow NaCl + H_2O}$$

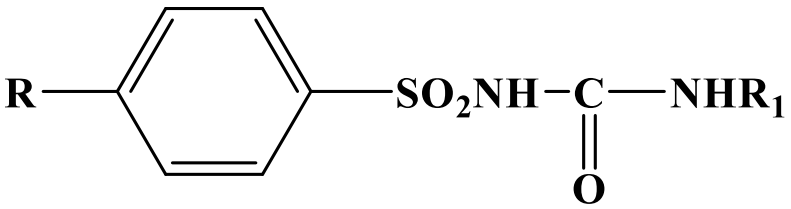
Storage. In a closed container at a temperature not higher than 20 °C.

Application. A 10% solution of ammonia is used as an emergency aid to stimulate breathing and bring the patient out of unconsciousness.

SULFONAMIDES

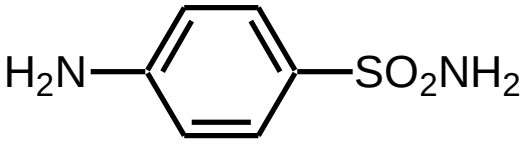
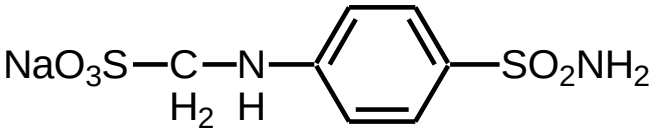
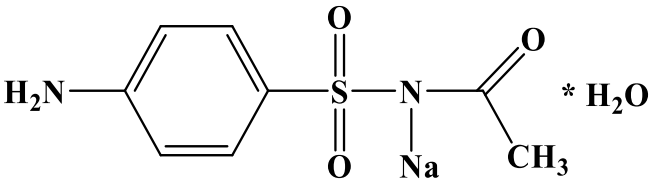
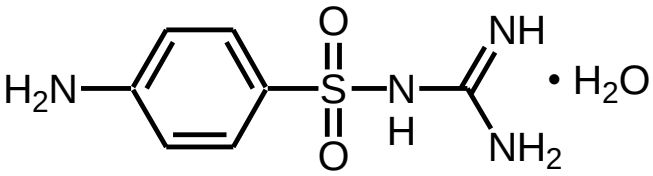
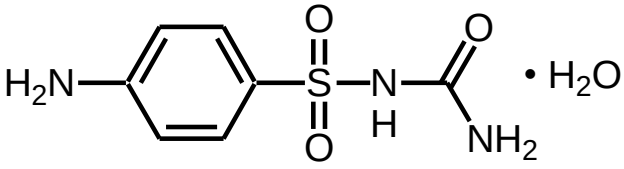
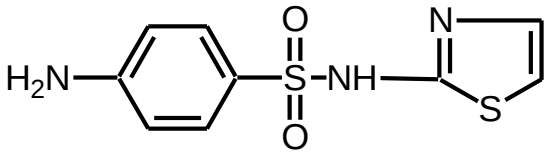
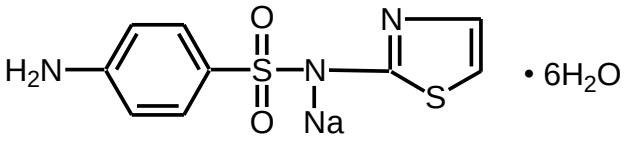
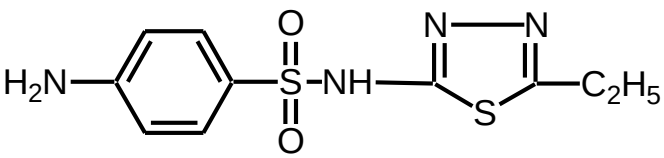
The introduction of a sulfo group into the aromatic core gives the substance acidic properties, promotes its solubility in water, and reduces toxicity. In medical practice, benzenesulfonic acid derivatives are not used, but only benzenesulfonic acid amide derivatives - chloramine, pantocid, chlorpropamide, butamide, cyclamide, etc.

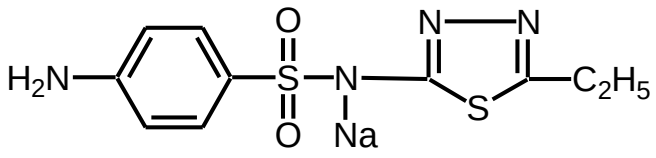
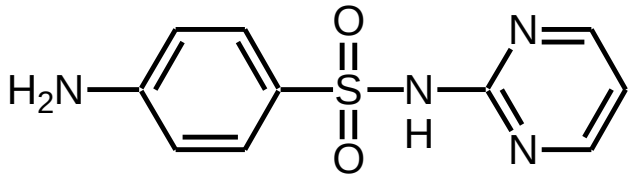
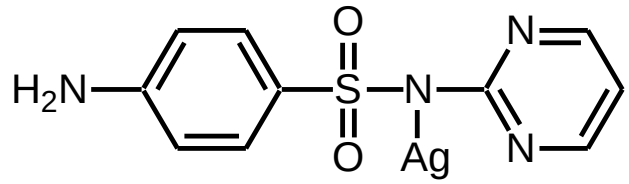
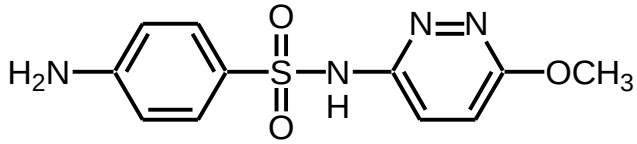
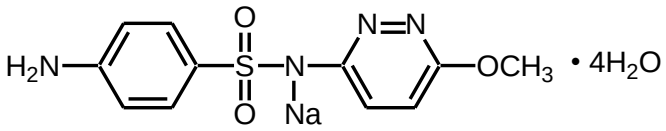
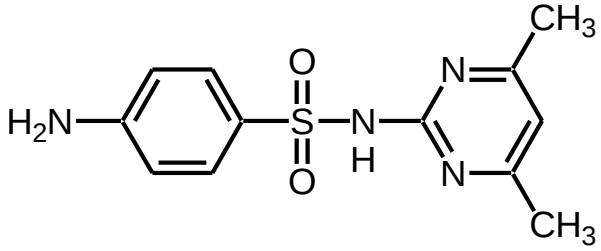
Drug products, derivatives of alkylureides of sulfonic acids:

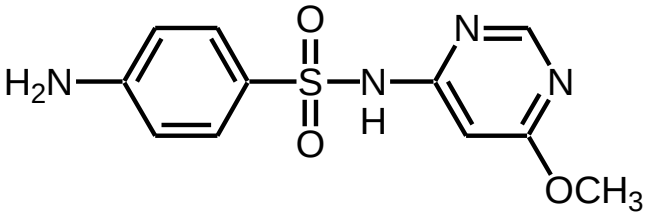
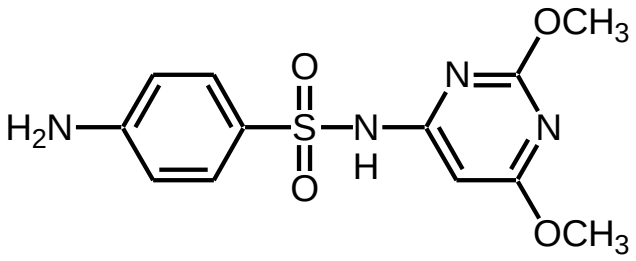
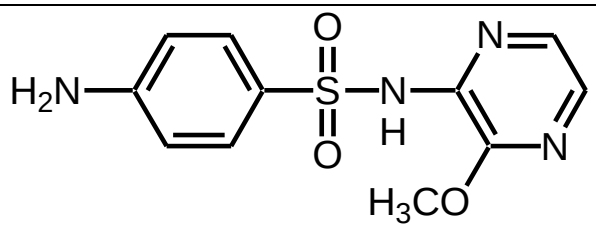
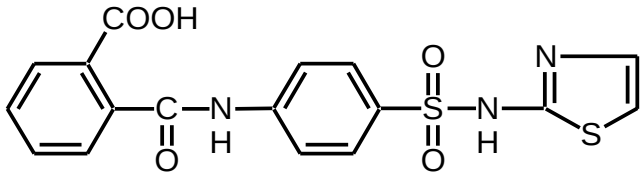
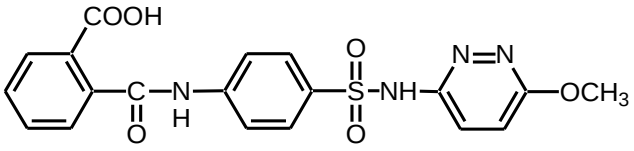
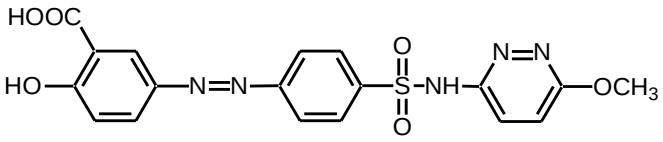
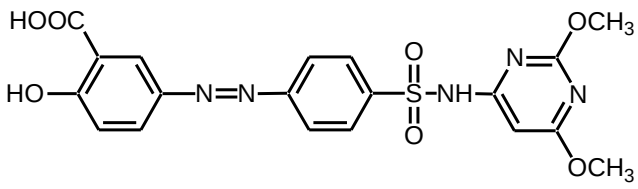


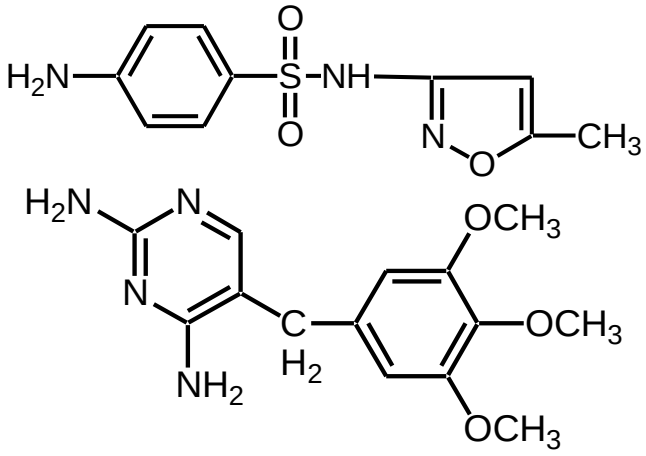
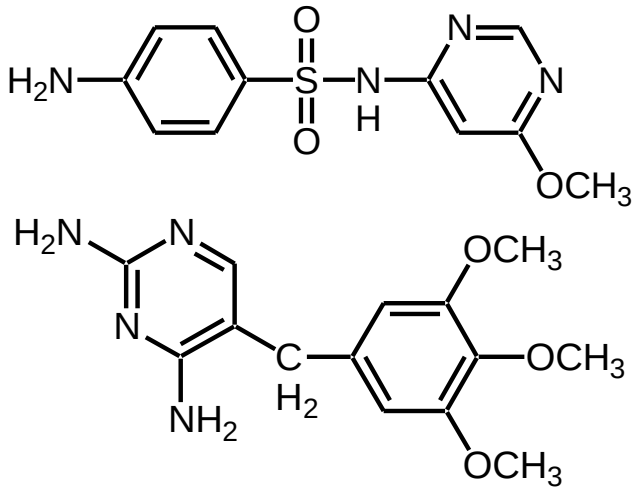
$$\mathbf{R = -CH_3, - Cl, - NH_2}$$
$$\mathbf{R_1 = -C_4H_9, -C_3H_7}$$

Sulfanilamide drugs:

	**Streprocidum.** Sulfanilamide. Streptocide. p-Aminobenzene sulfamide.
	**Streptocidum solubile.** Soluble streptocide. p-Sulfamidobenzene sodium aminomethane sulfate.
	**Sulfacylum-natrium.** Sulfacetamidum natricum. Sulfacyl sodium. p-Aminobenzene-sulfacetamide-sodium.
	**Sulginum.** Sulfaguanidine. Sulgin. p-Aminobenzenesulfoguanidine
	**Ususolfanum.** Sulfacarbamid. Urosulfan. p-Aminobenzenesulfonylurea.
	**Norsulfazolum.** Sulfathiazole. Norsulfasol. 2-(p-Aminobenzene-sulfamido)-thiazole.
	**Norsulfazolum-natrium.** Sulfathiazolum natricum. Norsulfasol-sodium. 2-(p-Amin-obenzenesulfamido)-thiazole-sodium.
	**Aethazolum.** Sulfaethidole. Etazol. 2-(p-Aminobenzenesulfamido)-5-ethyl-1,3,4-thiadiazole.

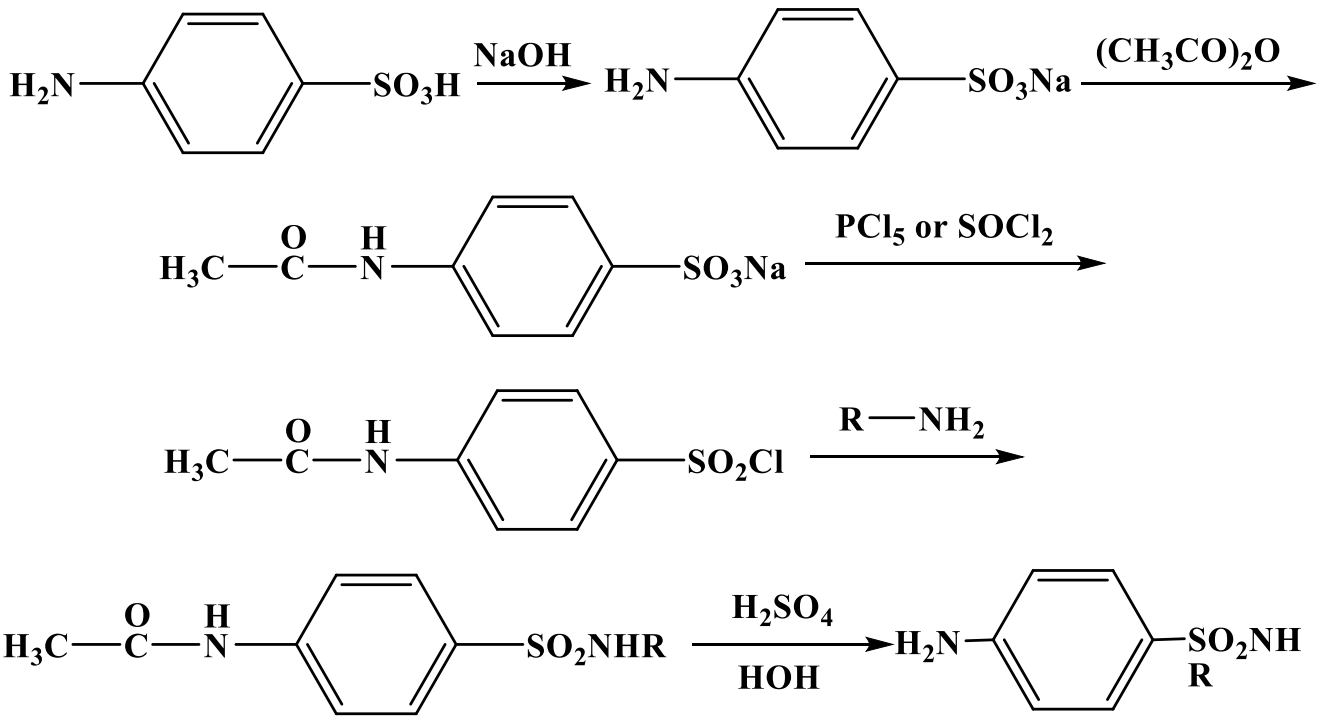
	**Aethazolum-natrium.** Sulfathidolum-natricum. Etazol-sodium. 2-(p-Aminobenzenesulfamido)-5-ethyl-1,3,4-thiadiazole-sodium.
	**Sulfazinum.** Sulfadiazin. Sulfazine. 2-(p-Aminobenzenesulfamido)-pyrimidine.
	**Sulfazini argentum.** Sulfazine silver salt. 2-(p-Amino-benzenesulfamido)-pyrimidine-argentum.
	**Sulfapyridazinum.** Sulfamethoxypyridazine. Sulfapyridazine. 6-(p-Aminobenzenesulfamido)-3-methoxypyridazine.
	**Sulfapyridazinum-natrium.** Sulfamethoxypyridazinum natricum. Sulfapyridazine sodium. 6-(p-Aminobenzenesulfido)-3-methoxypyridazine sodium.
	**Sulfadimezinum.** Sulfadimidine. Sulfadimezin. 2-(p-Aminobenzenesulfamido)-4,6-dimethylpyrimidine.

	**Sulfamonomethoxinum.** Sulfamonomethoxine. Sulfamonomethoxine. 4-(p-Amino-benzenesulfamido)-6-methoxypyrimidine.
	**Sulfadimethoxinum.** Sulfadimethoxine. Sulfadimethoxine. 4-(p-Amino¬benzenesulfamido)-2,6-methoxy¬pyrimidine.
	**Sulfalenum.** Sulfalene. Sulfalen. 2-(p-Aminobenzene-sulfamido)-3-methoxypyrazine.
	**Phthalazolum.** Phthalylsulfathiazole. Phthalazole. 2-(p-Phthalylamino-benzenesulfamido)-thiazole.
	**Phthazinum.** Phthazine. 3-methoxy-6-(N-phthalylsulfanyl-amido)-pyridazine.
	**Salazopyridazinum.** Salazodin. Salazopyridazine. 5-(p-[N-(3-methoxypyridazinyl-6)-sulfamido]-phenylazo)-salicylic acid.
	**Salazodimethoxinum.** Salazodimethoxine. 5-(p-[N-(2,4-dimethoxypyrimidinyl-6)-sulfamido]-phenylazo)-salicylic

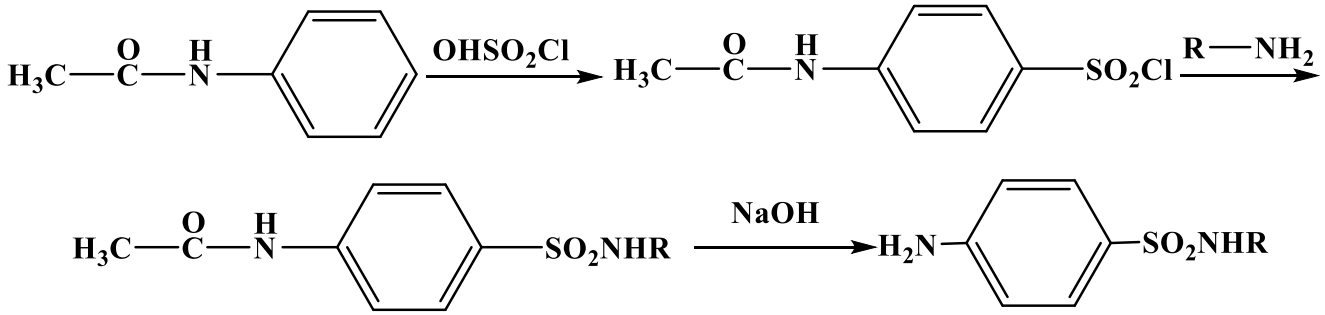
	acid
	**Bactrim.** Bactrim Biseptol. Combined drug: sulfamethoxazole (Sulfamethoxsazolum, 3-(p-amino-benzenesulfamido)-5-methylisoxazole) with trimethoprim – (Trimethoprimum, 2,4-diamino-5-(3,4,5-trimethoxybenzyl)-pyrimidine).
	**Sulfatonum.** Sulphatone. Combined drug (sulfamonomethoxine with trimethoprim)

Extraction:

1. The starting substance is sulfanilic acid:



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

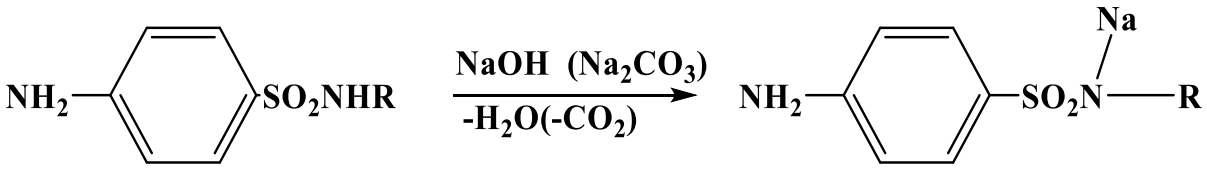


Chemical properties and identification:

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

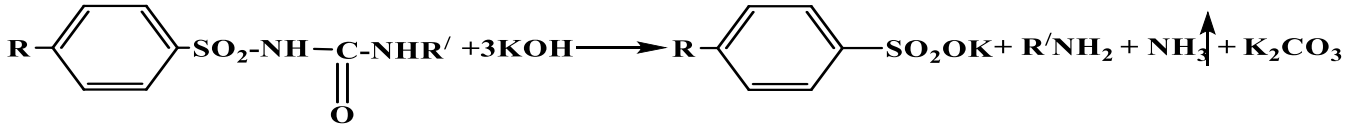
However, salts in water are highly hydrolyzed and practically do not exist.

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

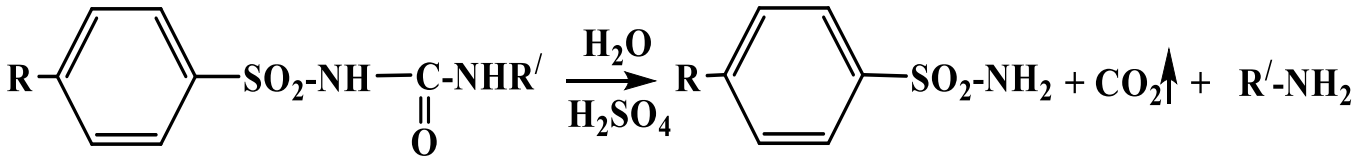


Common identification reactions:

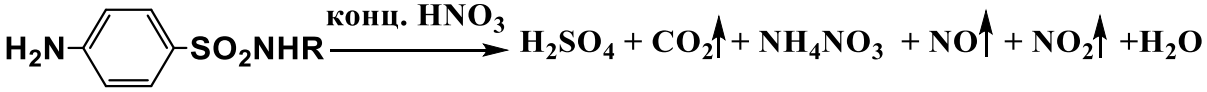
• When the preparations are heated in a 30% solution of potassium hydroxide, hydrolysis occurs with the formation of ammonia, which can be detected by the smell or by the blue color of red litmus paper. The smell of fatty amine appears (fat stains):



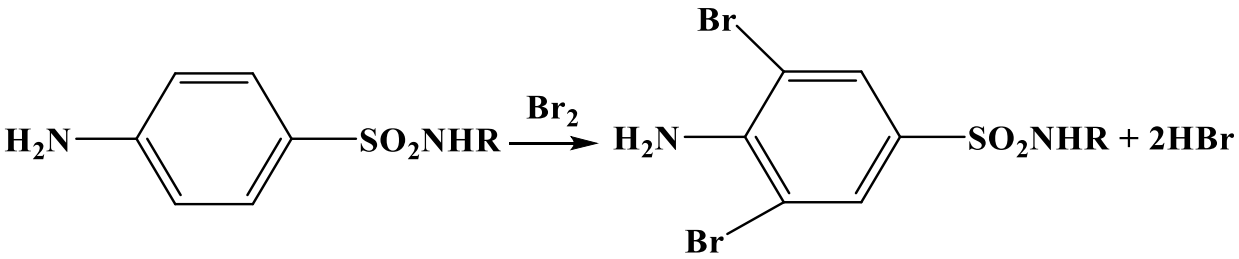
• With long-term heating of the preparations in the presence of 50% sulfuric acid (with a reverse cooler) and subsequent neutralization, a precipitate of the corresponding sulfamide is formed, which is filtered and the melting point is determined.



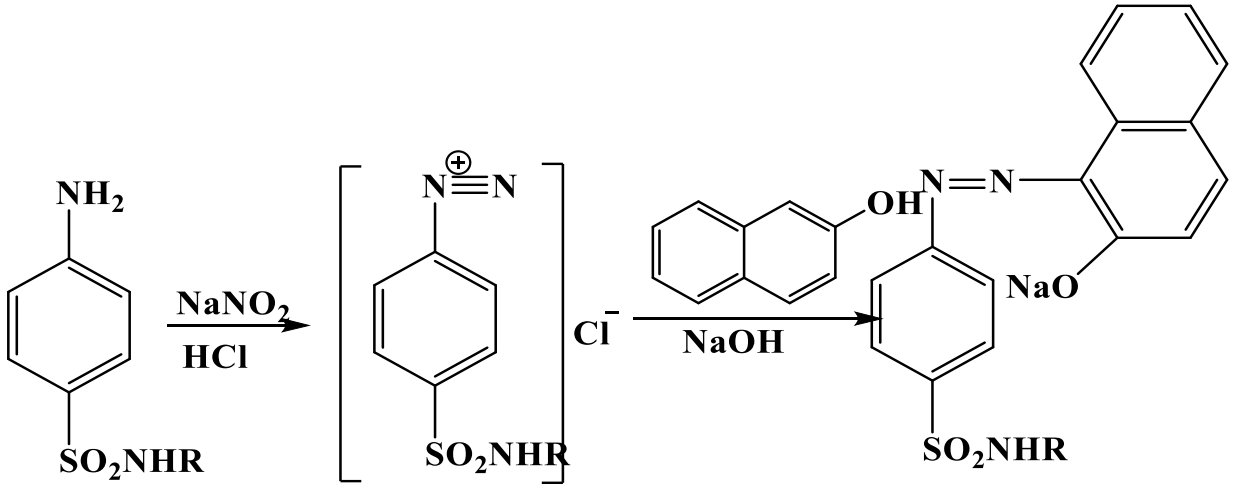
• All sulfonamides have a sulfur atom in the sulfamide group. To detect it, the drug is oxidized with concentrated nitric acid or fused with a 10-fold amount of potassium nitrate. At the same time, sulfur turns into sulfate.



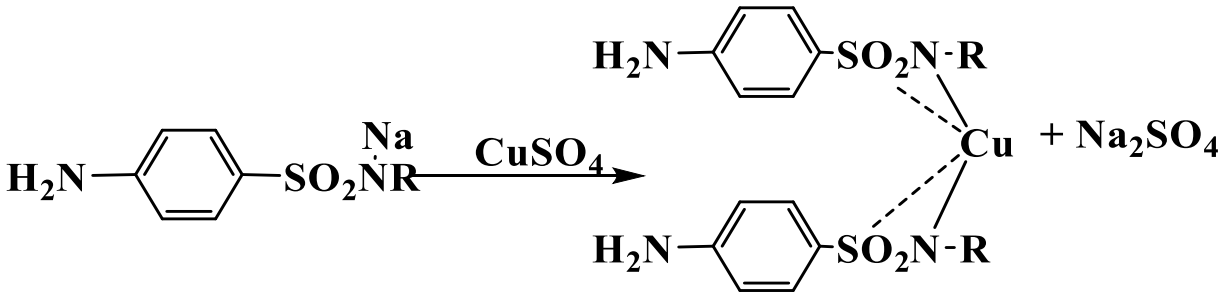
• All sulfonamides can be halogenated, nitrated, and sulfonated along the aromatic ring:



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



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



COLOR REACTIONS WITH SALTS OF HEAVY METALS ON SOME SULFONAMIDE DRUGS

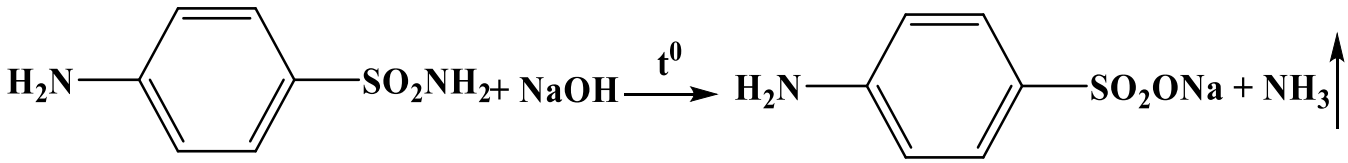
Medicine	Color of the precipitate or solution with reagents		
	$FeCl_3$	$CoCl_2$	$CuSO_4$
Streptocide white	yellow solution	pink solution	blue solution

not soluble			
Streptocide white soluble	red solution	pink solution	blue precipitate with a greenish tint
Sulfacil	-	-	blue precipitate with a greenish tint
Sulfazole	-	a blue-violet precipitate that turns greenish-gray	unstable greenish precipitate
Norsulfasol	light orange precipitate	lilac precipitate that turns into dirty purple	a dirty purple precipitate that turns dark purple
Sulfazine	-	red precipitate; crimson colored solution	a solution of green color, which turns into dirty purple
Sulfadiazine	-	red precipitate; crimson colored solution	a green precipitate that turns dirty purple
Sulfadimezine	-	lilac precipitate	a yellow-green precipitate that turns red-brown
Sulfamethazine	-	pink precipitate	green precipitate
Sulgin	yellow solution	pink solution	blue solution

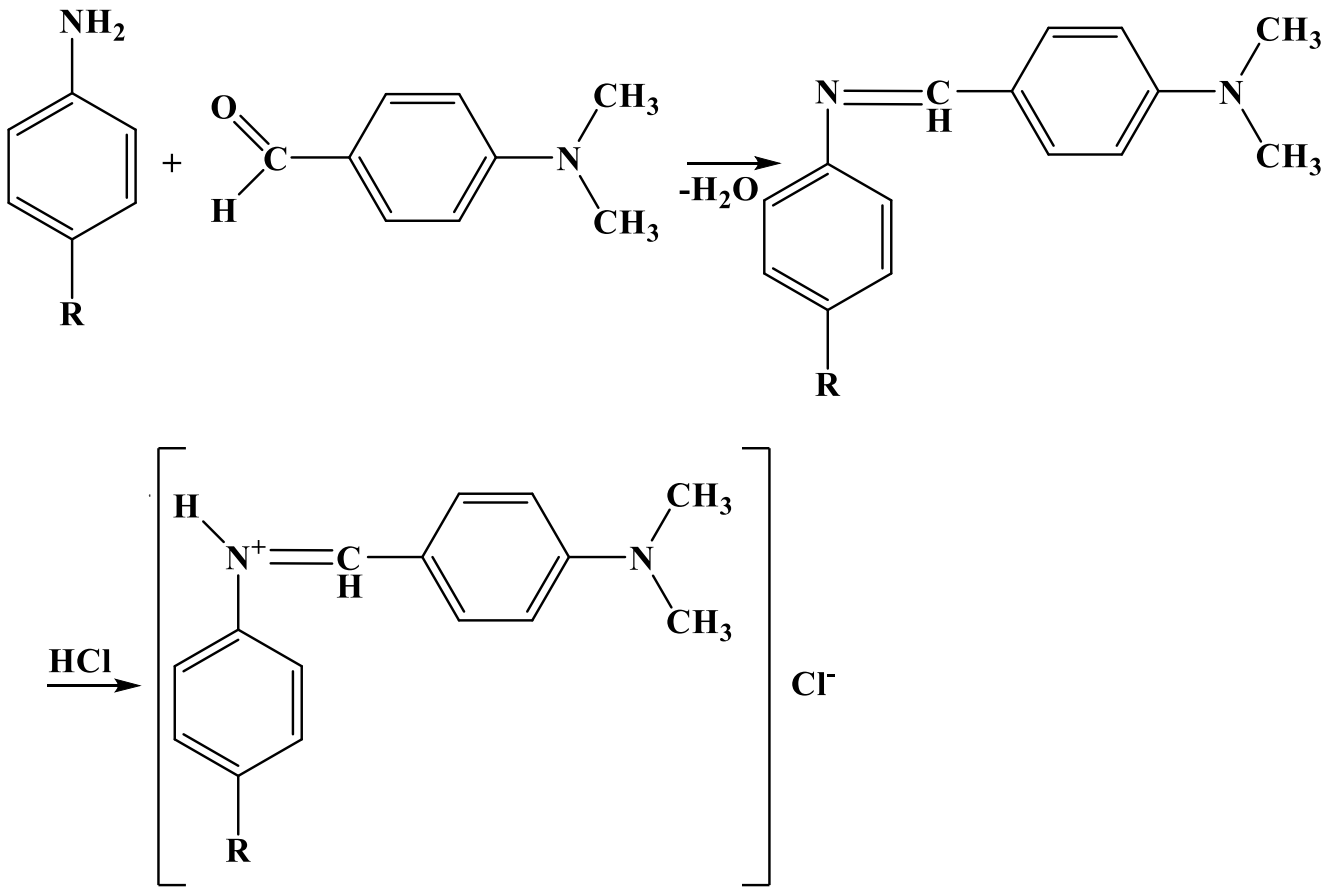
Etazol	-	white precipitate	grass-green precipitate that turns into dark green
Sulfantrol	-	-	a light green precipitate that turns blue-green

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

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

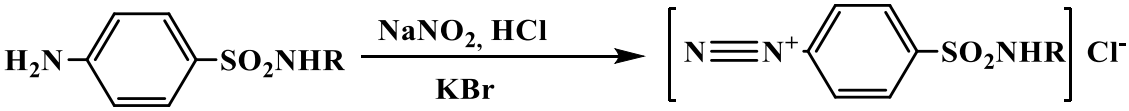


• Lignin sample is used for express analysis. A few grains of the medicine and 1 drop of diluted hydrochloric acid are placed on the paper containing lignin. A yellow-orange color appears. (Lignin contains aromatic aldehydes: coniferyl, etc.)



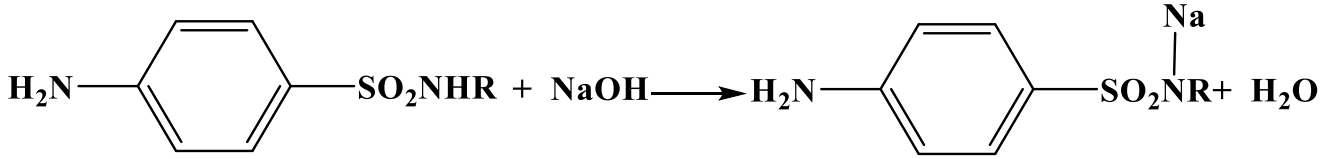
Quantitative definition:

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

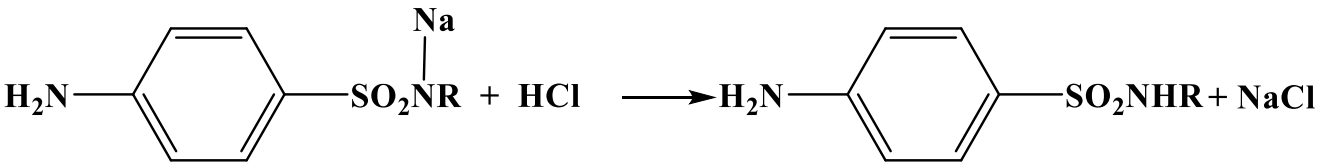


$$2KIO_3 + 5NaNO_2 + 2HCl \rightarrow I_2 + 5NaNO_3 + 2KCl + H_2O$$

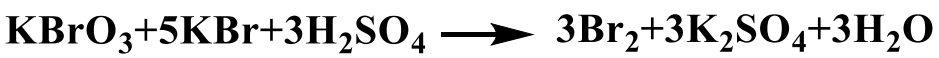
2. Alkalimetry. It is based on the acidic properties of the sulfamide group. Acidic forms are titrated with sodium hydroxide solution in the presence of thymolphthalein indicator.

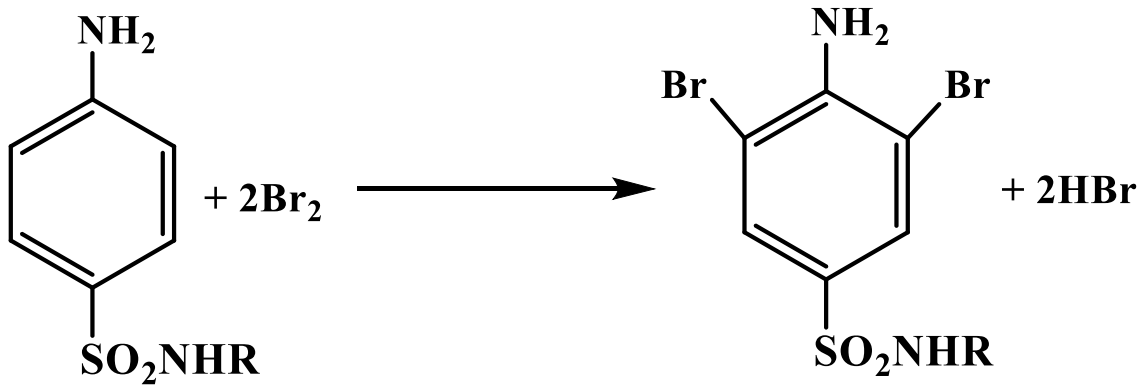


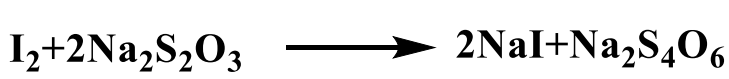
3. Acidimetry. Sodium salts of sulfonamides can be titrated with acid in an alcohol-acetone medium, the indicator is methyl orange.



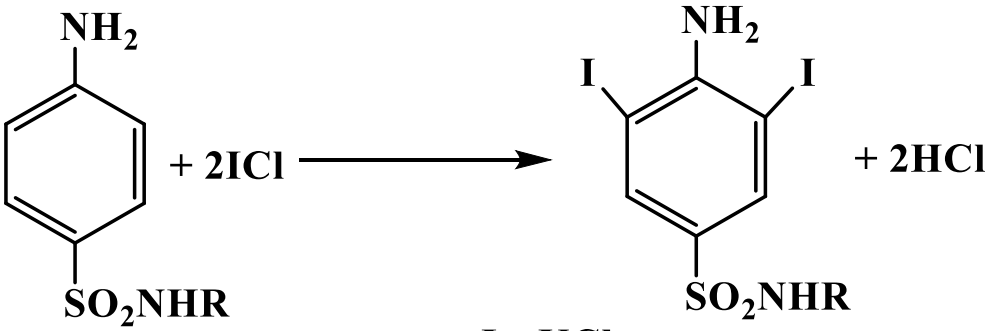
Bromatometry, reverse titration. The method is not based on the halogenation reaction of sulfonamide drug substances. The titrated solution is potassium bromate. The excess of bromine is determined iodometrically, the indicator is starch.

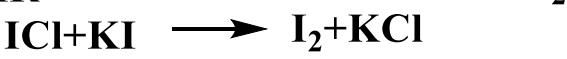


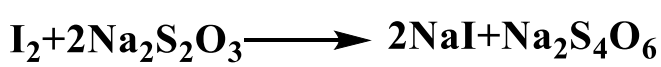




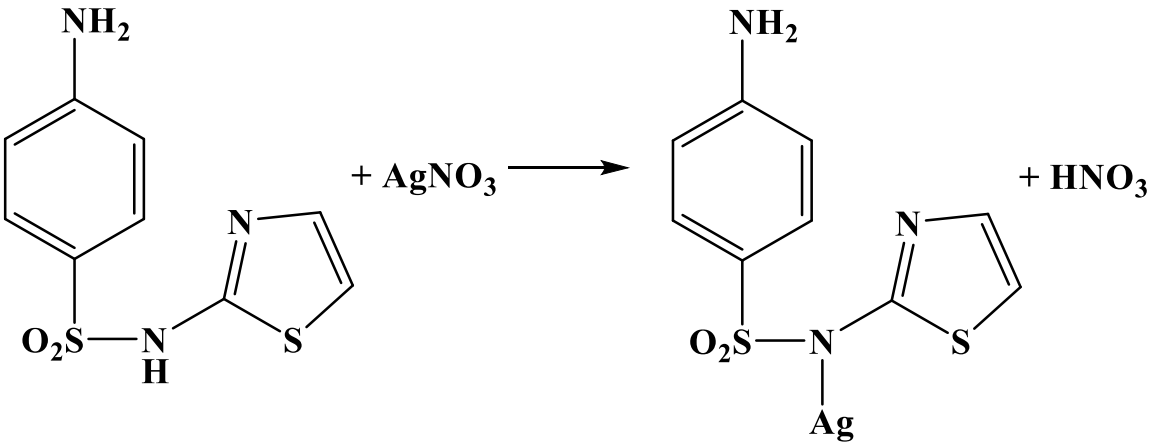
4. Iodochlorometry, reverse titration. It consists in the halogenation of drug substances with a titrated solution of iodine monochloride, the excess of which is determined iodometrically.







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



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

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

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

8. Spectrophotometric methods of quantitative determination.

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

MEDICINES THAT IMPROVE BLOOD SUPPLY

SODIUM NITRITE (NATRII NITRIS)

$NaNO_2$

Extraction:

$$NaNO_3 + Pb \rightarrow PbO + NaNO_2$$

Properties: white, slightly yellowish crystalline powder, hygroscopic. The aqueous solution has a slightly alkaline reaction.

Easily soluble in water, poorly soluble in alcohol.

Identification:

1. The substance gives characteristic reactions to sodium:

A) Sodium cation according to the requirements of SPhU is determined using a solution of potassium pyroantimonate (potassium hexahydroxystibiate), which results in the formation of a white precipitate.

$$Na^+ + K[Sb(OH)_6] \rightarrow Na[Sb(OH)_6]\downarrow + K^+.$$

When heating the investigated solution with potassium pyroantimonate, a supersaturated solution can be obtained, therefore, to create a crystallization center, the solution is cooled in ice water and the walls of the test tube are rubbed with a glass rod.

The reaction should be carried out in a slightly alkaline environment, since in an acidic environment potassium pyroantimonate decomposes with the formation of a white amorphous precipitate of metaantimonic (metaantimony) $HSbO_3$ acid:

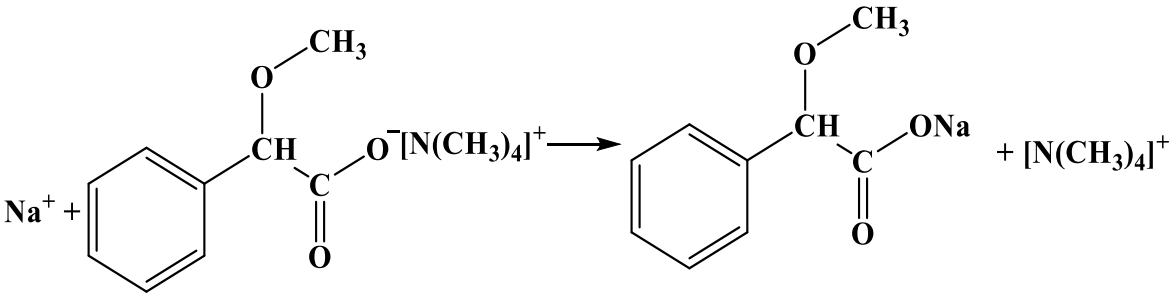
$$K[Sb(OH)_6] + HCl \rightarrow HSbO_3 \cdot 3H_2O\downarrow + KCl$$

To remove NH^{4+} ions, which interfere with the determination, the test solution is preheated with a potassium carbonate solution to boiling (at the same time, an alkaline reaction of the medium is created):

$$2NH_4^+ + K_2CO_3 \rightarrow 2K^+ + (NH_4)_2CO_3\downarrow;$$

B) Sodium salts with the reagent of methoxyphenylacetic acid in chilled ice water form a white crystalline precipitate that does not disappear at room temperature:

Confirmation of the formation of a precipitate of the sodium salt of methoxyphenylacetic acid is its ability to dissolve in a diluted ammonia solution P1.



C) Sodium salt is wetted with concentrated hydrochloric acid to form volatile sodium salts, which color the colorless flame of the burner yellow:

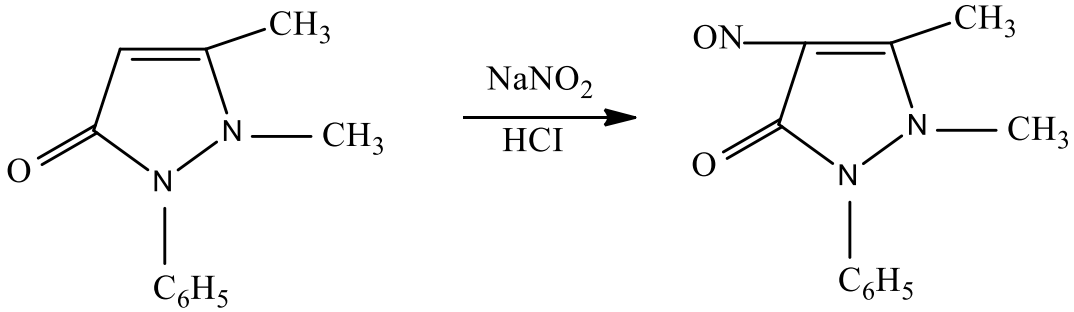
In addition, there is a non-pharmacopoeial reaction with zincuranyl acetate $Zn(UO_2)_3(C_2H_3O_2)_8$ - a greenish-yellow crystalline precipitate is observed that has the shape of tetrahedra or octahedra;

$$\mathbf{Na^+ + Zn(UO_2)_3(C_2H_3O_2)_8 + CH_3COO^- + 9H_2O = NaZn(UO_2)_3(C_2H_3O_2)_9 \cdot 9H_2O}$$

2. Reactions to nitrite ion:

A) Nitrite anion is identified with flame retardant in accordance with the requirements of the SPhU.

The reaction is carried out in the presence of dilute hydrochloric acid. When nitrites interact with hydrochloric acid, they form nitrous acid, which nitrosates antipyrine in the fourth position of the pyrazolone cycle with the formation of 4-nitrosoantipyrine, which has a green color [7]:



B) Reaction with sulfuric acid, yellow-brown vapors are released (difference from nitrates):

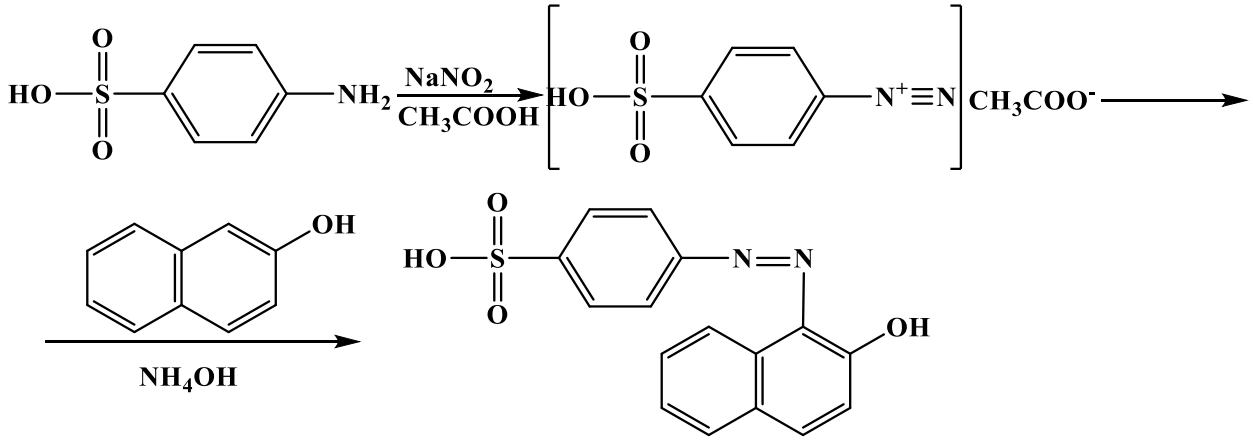
$$\mathbf{2NaNO_2 + H_2SO_4 \rightarrow Na_2SO_4 + 2HNO_2;}$$

$$\mathbf{2HNO_2 \rightarrow NO_2\uparrow + NO\uparrow + H_2O.}$$

C) Nitrite ions decolorize potassium permanganate solution acidified with dilute sulfuric acid.

$$5\ NaNO_2 + 2KMnO_4 + 3H_2SO_4 \rightarrow 2MnSO_4 + 5NaNO_3 + K_2SO_4 + 3H_2O$$

D) Reaction with sulfanilic acid and ß-naphthol. As a result of the reaction, a red color (azo dye) appears.



Quantitative definition. Reverse permanganatometry, excess titrant is determined iodometrically, the indicator is starch.

$$5NaNO_2 + 2KMnO_4 + 3H_2SO_4 \rightarrow 2MnSO_4 + K_2SO_4 + 5NaNO_3 + 3H_2O$$

$$2KMnO_4 + 10KI + 8H_2SO_4 \rightarrow 5I_2 + 6K_2SO_4 + 2MnSO_4 + 8H_2O$$

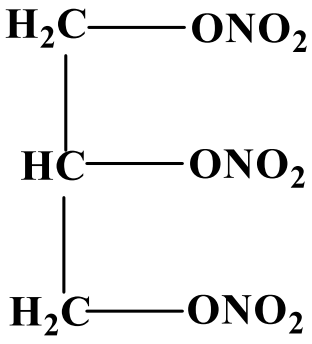
$$I_2 + 2Na_2S_2O_3 \rightarrow 2NaI + Na_2S_4O_6$$

In parallel, a control experiment is conducted.

Storage. In tightly closed glasses of dark glass in a place protected from light.

Application. Antispasmodic agent, antidote for cyanide poisoning.

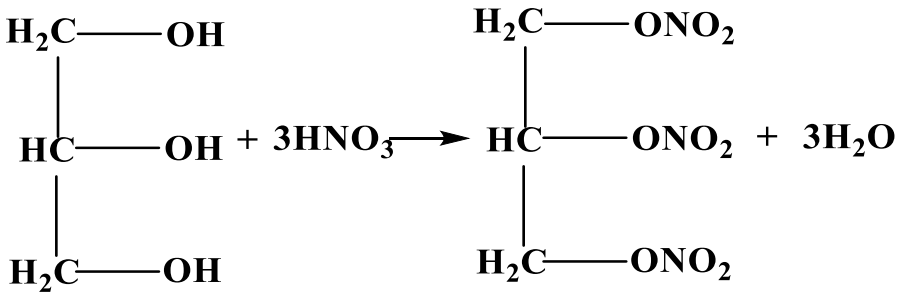
NITROGLYCERIN SOLUTION - SOLUTIO NITROGLYCERINI



Glycerin trinitrate M.m. 227,1

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

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

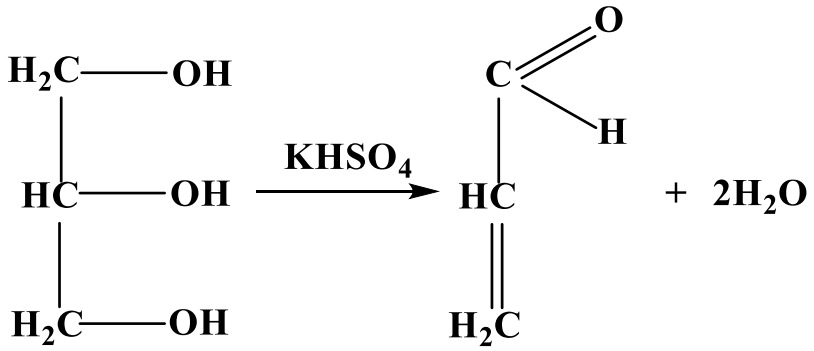


Identification:

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

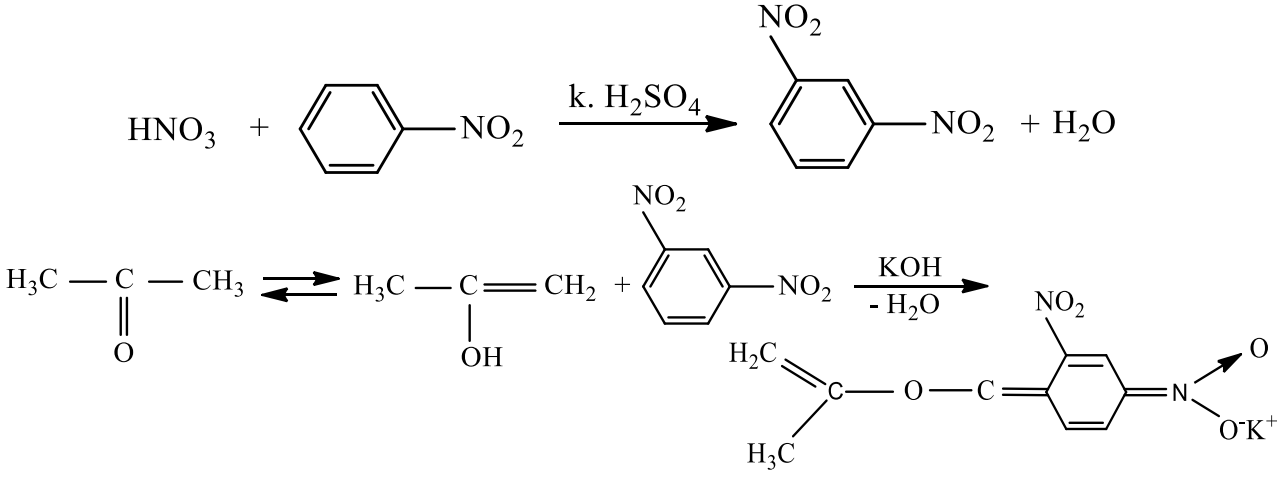
2. The substance is saponified by the action of sodium hydroxide solution. Glycerin is formed, then heated with potassium hydrosulfate, acrolein with a characteristic smell is released:

$$C_3H_5(ONO_2)_3 + 3KOH \longrightarrow C_3H_5(OH)_3 + 3KNO_3$$

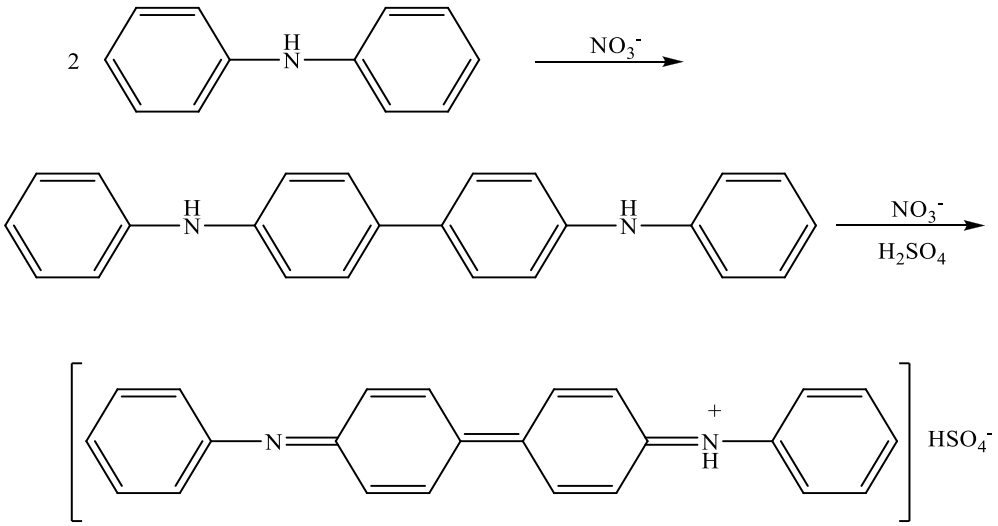


3. After saponification, reaction to nitrates:

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



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



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

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

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

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

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

LESSON NO. 1

TOPIC: «Antihistamines. Characteristics, classification, relationship between structure and pharmacological action. Mechanism of action, methods of obtaining, methods of analysis. Application in medicine.».

PURPOSE: To study the classification, mechanism of action, as well as methods of standardization of antihistamine drugs.

3. TARGETS:

3.1. Know the definition of the term "allergy", the classification of antihistamine drugs and be able to give an example for each section of the classification;

3.2. Know the Latin name, synonyms, structure, chemical name, physicochemical properties of drugs of this group;

3.3. Study all possible identification reactions and methods of quantitative determination of drugs that belong to antitussives;

3.4. Explain the conditions of storage and use in medical practice of antihistamines.

4. TASKS FOR STUDENTS' SELF-PREPARATION:

4.1. Repeat the theoretical material from the course of inorganic, organic and analytical chemistry, regarding all possible methods of identification and quantification of antihistamine drugs;

4.2. Prepare for the lesson according to the questions listed below.

EDUCATIONAL QUESTIONS FOR STUDENTS' SELF-PREPARATION:

1. To study the concept of allergy and its causes.

2. To study the classification of antihistamine drugs.

3. To study the mechanism of action of antihistamine drugs.

4. To be able to analyze drugs of this group (Latin, Ukrainian, chemical name; chemical formula; description; methods of extraction; all possible methods of

identification; all possible methods of quantitative determination) using the example of diphenhydramine, calcium chloride, calcium lactate, calcium gluconate.

TEST TASKS

1. Acid hydrolysis reaction is used to identify:

A) diphenhydramine hydrochloride (diphenhydramine)

B) sodium para-aminosalicylate

C) sodium benzoate

D) sodium salicylate

E) formaldehyde solution

2. A white cheesy precipitate from silver nitrate forms:

A) sodium para-aminosalicylate

B) mefenamic acid

C) phenacetin

D) paracetamol

E) diphenhydramine hydrochloride

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

A) neutralization

B) acetylation

C) hydrolysis

D) restoration

E) bromination

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

A) increases the solubility of the substance to be determined

B) strengthens the main properties of the drug under study

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

D) inhibits the reaction

E) catalyzes the reaction

5. One of the listed medicines is an antihistamine:

A) diphenhydramine hydrochloride (diphenhydramine)

B) novocaine

C) phenacetin

D) sodium para-aminosalicylate

E) anesthesin

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

A) acidic properties

B) basic properties

C) regenerative properties

D) oxidative properties

E) ability to engage in substitution reactions

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

A) concentrated nitric acid

B) ethanol

C) glacial acetic acid

D) dioxane

E) diethyl ether

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

A) bromatometry

B) permanganatometry

C) complexonometry

D) nitritometry

E) argentometry

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

A) benzophenone and β-dimethylaminoethyl chloride

B) benzylic acid and β-dimethylaminoethyl chloride

C) diphenylacetic acid and dimethylaminoethanol

D) solution of phenol and dimethylaminoethanol

E) diphenylpropionic acid and β-dimethylaminoethyl chloride

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

A) simple ether communication

B) keto groups

C) phenolic hydroxyl

D) ester group

E) β-lactam cycle

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

A) iron (III) chloride

B) the hydroxylamine solution is alkaline

C) concentrated sulfuric and nitric acid

D) sodium hydroxide

E) diluted hydrochloric acid

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

A) iodometry

B) nitritometry

C) argentometry

D) iodochlormetry

E) acidimetry

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

A) benzhydrol (diphenylmethanol)

B) dimethylamine

C) diphenylamine

D) phenol

E) dimethylaminoethanol

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

A) ammonium acetate solution

B) ammonium chloride solution

C) ammonium oxalate solution

D) ammonium hydroxide solution

E) dilute nitric acid

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

A) calcium lactate

B) sodium citrate

C) potassium iodide

D) sodium thiosulfate

E) potassium chloride

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

A) ammonia

B) acetic acid

C) sodium hydroxide

D) formaldehyde

E) potassium chloride

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

A) gravimetry

B) permanganatometry

C) dichromatometry

D) ion-exchange chromatography

E) complexonometry

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

A) solution of iron (III) ammonium sulfate

B) chalcone carboxylic acid solution

C) methyl red solution

D) phenolphthalein solution

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

A) white precipitate

B) yellow precipitate

C) blue sediment

D) green sediment

E) purple precipitate

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

A) complexonometry

B) gravimetry

C) acidimetry

D) alkalimetry

E) nitritometry

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

A) potassium iodide

B) potassium ferrocyanide

C) sodium hydroxide

D) silver nitrate

E) magnesium sulfate

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

A) ammonium oxalate

B) barium chloride

C) thioacetamide

D) sodium nitrite

E) silver nitrate

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

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

B) sodium cobalt nitrite solution

C) alcoholic solution of glyoxalhydroxyanil

D) methoxyphenylacetic acid solution

E) sodium sulfide solution

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

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

B) hydrochloric acid solution

C) sodium hydroxide solution

D) potassium permanganate solution

E) sodium thiosulfate solution

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

A) by changing the pH of the reaction medium

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

C) selection of the free form of the indicator

D) by changing the chemical structure of the indicator

E) decarboxylation of trilon B molecule (sodium edetate)

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

A) paper impregnated with lead acetate

B) redox indicators

C) indicatorless method

D) iodine starch paper

E) metal indicators

TASKS.

1. Calculate the percentage content of diphenhydramine (M.m. 291.82) in the drug, if 10.49 ml of 0.1 M perchloric acid solution (correction factor (CF) = 1.0018) was spent on the titration of a 0.2976 g sample; the volume of the titrant in the control experiment is 0.36 ml.

2. Calculate the percentage content of diphenhydramine (M.m. 291.82) in the preparation, if 4.09 ml of 0.1 M sodium hydroxide solution was used for the titration of a 0.1085 g sample in an alcohol-chloroform mixture (CF = 1, 0000); the volume of the titrant in the control experiment is 0.36 ml.

3. Calculate the volume of 0.1 M Trilon B solution (CF = 0.9998) that will be used for the titration of 0.4113 g of calcium gluconate (M.m. 448.4), if its percentage content in the preparation is 99 .7%.

4. Calculate the percentage content of calcium chloride (M.m. 219.08), if 5.08 ml of 0.1 M sodium edetate solution (trilon B CF = 1.0010) was spent on the titration of a weight of 0.1580 g according to the pharmacopoeial method.

5. Calculate the volume of a 0.1 M solution of silver nitrate (CF = 1.0012), which will be spent on the titration of 0.2013 g of calcium chloride (M.m. 219.08), if its percentage content in the preparation is 100 ,90%, indicator - potassium chromate.

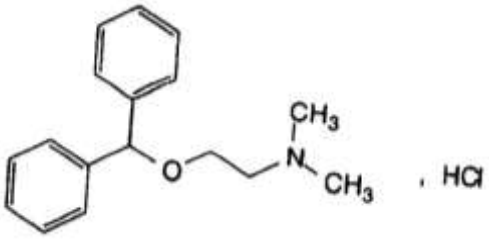
LABORATORY WORK

When performing laboratory work, it is necessary to strictly observe the safety rules of work in a chemical laboratory.

Each student individually conducts an analysis of the dosage form that will include antihistamines, and also prepares a protocol according to the requirements.

DIPHENHYDRAMINE HYDROCHLORIDE

Diphenhydramini Hydrochloridum



$C_{17}H_{22}ClNO$ ***M.m. 291.8***

Diphenhydramine hydrochloride contains not less than 99.0% and not more than 101.0% of 2-(diphenylmethoxy)-N,N-dimethylethanamine hydrochloride, based on dry matter.

Properties

Description. Crystalline powder of white or almost white color.

Solubility. Very easily soluble in water P, easily soluble in 96% alcohol.

Identification

First identification: **A, C, E.**

Second identification: **A, B, D, E**.

A. Melting point (2.2.14). From 168 °C to 172 °C.

B. 50 mg of the substance is dissolved in 96% alcohol and the volume of the solution is brought up to 100.0 ml with the same solvent. The ultraviolet absorption

spectrum (2.2.25) of the obtained solution in the region from 230 nm to 350 nm should have three maxima at the wavelengths of 253 nm, 258 nm, and 264 nm. The specific absorption index at the maxima should be around 12, 15 and 12, respectively.

C. The infrared spectrum (2.2.24) of the substance, obtained in disks with potassium chloride, should correspond to the Pharmacopoeia standard sample spectrum of diphenhydramine hydrochloride.

D. Add 2 ml of sulfuric acid P to 0.05 ml of solution B, prepared as indicated in the section "Purity test"; an intense yellow color gradually appears, which turns into a red color upon addition of 0.5 ml of nitric acid. Add 15 ml of water to the resulting solution, cool, add 5 ml of chloroform and shake; the chloroform layer becomes intensely purple.

E. The substance reacts to chlorides (2.3.1).

Purity test

Solution S. Dissolve 1.0 g of the substance in carbon dioxide-free water, and adjust the volume of the solution to 20 ml with the same solvent.

Transparency of the solution (2.2.1). Solution S and five-fold diluted solution S should be clear.

The color of the solution (2.2.2, method 11). The color of solution S should not be more intense than the standard VU6.

pH (2.2.3). From 4.0 to 6.0. Measure the pH of solution B.

Accompanying impurities. Determination is carried out by the method of thin-layer chromatography (2.2.27), using TLC plates with a layer of silica gel H.

Test solution. 0.2 g of the substance is dissolved in methanol and the volume of the solution is brought up to 10 ml with the same solvent. The solution is prepared immediately before use.

Comparison solution. 1 ml of the test solution is brought to a volume of 100 ml with methanol.

5 μl (100 μg) of the test solution and 5 μl (1 μg) of the comparison solution are applied to the starting line of the chromatographic plate. The plate is placed in a chamber with a mixture of diethylamine - methanol - chloroform (1:20:80) solvents.

When the solvent front passes 10 cm from the start line, the plate is removed from the chamber, dried in air for 5 min, sprayed with sulfuric acid and heated at a temperature of 120 °C for 10 min or until spots appear.

On the chromatogram of the test solution, any spot, except the main one, should not be more intense than the spot on the chromatogram of the comparison solution (1.0%).

Loss in mass during drying (2.2.32). No more than 0.5%. 1,000 g of the substance is dried at a temperature from 100 °C to 105 °C.

Sulfated ash (2.4.14). No more than 0.1%. The determination is carried out with 1.0 g of the substance.

Quantitative definition. Dissolve an exact amount of the drug in 10 ml of water, add 10 ml of a neutralized mixture of alcohol and chloroform (1: 2), 5-6 drops of phenolphthalein and titrate with 0.1 M sodium hydroxide solution while shaking until the aqueous layer turns slightly pink. 1 ml of 0.1 M sodium hydroxide solution corresponds to 0.029180 g of diphenhydramine.

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Additional

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LESSON NO. 2

TOPIC: «Agents affecting the afferent nervous system. Means that stimulate receptors of afferent nerve fibers. Characteristics, classification, relationship between structure and pharmacological action. Mechanism of action, methods of preparation, methods of analysis. Application in medicine».

PURPOSE: To study the classification, mechanism of action, as well as methods of standardization of local anesthetic, astringent, covering, adsorbing drugs.

3. TARGETS:

3.1. To study the characteristics and classification of local anesthetic, astringent, coating, adsorbing drugs;

3.2. To study the connection between the structure and pharmacological action of local anesthetic, astringent, covering, adsorbing drugs;

3.3. To study the mechanism of action of local anesthetic, astringent, covering, adsorbing drugs;

3.4. To learn the Latin names, synonyms, structural formulas, chemical names of the studied drug substances (Anestesin, Dikain, Novocaine, aluminum hydroxide, bismuth nitrate basic, ammonia solution concentrated);

3.5. To study the physical and physico-chemical properties of local anesthetic, astringent, covering, adsorbing preparations;

3.6. To study the structure of normative and technical documentation, quality control methods and quality indicators that are included in them;

3.7. To determine general and specific impurities;

3.8. To carry out calculations of weight, gram, percentage content;

3.9. To study methods of identification of drug substances of this group based on their physical and chemical properties;

3.10. To study methods of quantitative determination of studied drug substances;

3.11. To study the application, form of release, storage of drug substances;

3.12. To give a correct assessment of the obtained results of the analysis and draw a conclusion about the benign quality of drug substances of this group.

EDUCATIONAL QUESTIONS FOR STUDENTS' SELF-PREPARATION

1. Characteristics and classification of local anesthetic, astringent, covering, adsorbing drugs.
2. Connection between the structure and pharmacological action of local anesthetic, astringent, covering, adsorbing drugs.
3. Mechanism of action of drugs of this group.
4. Chemical structure, Latin names, synonyms of drugs of this group (Anesthesin, Dikain, Novocaine, aluminum hydroxide, bismuth nitrate basic, ammonia solution concentrated).
5. Methods of obtaining the researched drugs.
6. Characterize the physical and chemical properties of drugs of this group based on their structure.
7. Identification of drugs in accordance with the requirements of the SPhU. Chemism of reactions, conditions for their implementation.
8. Define general and specific impurities.
9. Calculate weight, gram, and percentage content.
10. Quantitative methods, conditions and chemism of reactions.
11. Application in medicine.
12. Substantiate the conditions of storage of preparations of this group of medicines, based on their physical and chemical properties.
13. Study the application, form of release, storage of drug substances;
14. Give a correct assessment of the obtained results of the analysis and draw a conclusion about the benign quality of drug substances of this group.

5. TEST TASKS

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

A) para-Nitrobenzoic acid

B) ortho-Nitrobenzoic acid

C) meta-Nitrobenzoic acid

D) Benzoic acid

E) Salicylic acid

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

A) Bromides

B) Chlorides

C) Sulfates

D) Tartrates

E) Iodides

3. One of the reactions of novocaine identification is:

A) Phenolic hydroxyl reaction

B) Murexide test

C) Maltol test

D) Reaction to the primary aromatic amino group

E) Reaction to alcohol hydroxyl

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

A) Nitritometry

B) Permanganatometry

C) Cerimetry

D) Complexonometry

E) Acidimetry

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

A) Sodium thiosulfate

B) Sodium edetate

C) Potassium bromate

D) Sodium nitrite

E) Silver nitrate

6. The drug procaine hydrochloride is a derivative of:

A) p-Aminobenzoic acid

B) Acetylsalicylic acid

C) Sulfanilic acid

D) Benzoic acid

E) Nicotinic acid

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

A) Streptocide

B) Diphenhydramine

C) Dikain

D) Streptomycin

E) Novocaine

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

A) Benzocaine (anesthetic)

B) Resorcinoma

C) Salicylic acid

D) Benzene

E) Trimecaine

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

A) Sodium chloride

B) Silver nitrate

C) Calcium oxalate

D) Potassium bromide

E) Copper(II) sulfate

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

A) Red

B) Yellow

C) Purple

D) Blue

E) Green

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

A) Red-violet

B) Dark red

C) Brownish-red

D) Yellow

E) Emerald green

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

A) p-Aminobenzoic acid

B) Salicylic acid

C) Phenol

D) Benzaldehyde

E) Isonicotinic acid

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

A) Novocaine

B) Sodium p-aminosalicylate

C) Anesthesin

D) Dikain

E) Novocainamide

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

A) Anesthesin

B) Novocaine

C) Norsulfasol

D) Streptocide

E) Dikain

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

A) Nitritometry

B) Bromatometry

C) Iodine chlorometry

D) Acidimetry

E) Permanganatometry

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

A) H_2O

B) NaOH

C) H_2SO_4

D) $KMnO_4$

E) HCl

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

A) Potassium tetraiodomercurate alkaline

B) Potassium ferrocyanide

C) Silver nitrate

D) Sodium tetraphenylborate

E) Barium chloride

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

A) Carbonate ion

B) Nitrate ion

C) Ammonium ion

D) Arsenite ion

E) Acetate ion

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

A) Potassium iodide solution

B) Starch solution

C) Barium chloride solution

D) Phenolphthalein solution

E) Argentum nitrate solution

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

A) Yellowish-orange color or orange precipitate

B) Yellow color of the solution

C) Red color of the solution or red precipitate

D) Blue color of the solution or blue precipitate

E) Violet color of the solution or violet precipitate

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

A) Ammonium oxalate

B) Barium chloride

C) Argentum nitrate

D) Sodium sulfide

E) Potassium nitrate

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

A) Ammonium hydroxide

B) Barium chloride

C) Sodium sulfide

D) Potassium tartrate

E) Copper sulfate

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

A) Silver nitrate

B) Potassium sulphite

C) Sodium sulfide

D) Sodium sulfate

E) Sodium nitrite

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

A) Complexonometry

B) Alkalimetry

C) Bromatometry

D) Iodometry

E) Permanganatometry

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

A) Iodometrically

B) Nitritometrically

C) Acidimetrically

D) Complexometrically

E) Alkalimetrically

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

A) Bromatometry

B) Iodochlormetry

C) Complexonometry

D) Argentometry

E) Nitritometry

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

A) p-Aminobenzoic acid

B) p-Chlorobenzoic acid

C) p-Aminophthalic acid

D) p-Aminosalicylic acid

E) p-Aminobenzene sulfonic acids

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

A) Aromatic ketones

B) Esters [complex esters] of aromatic amino acids

C) Amides of aromatic amino acids

D) Aromatic aminoaldehydes

E) Amides of aromatic sulfonic acids

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

A) Indophenol

B) Diazonium salts

C) Salts of hydroxamatic acids

D) Aurine dye

E) Azomethine dye

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

A) Benzocaine

B) Diphenhydramine

C) Dikain

D) Novocaine

E) Novocainamide

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

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

B) Acid hydrolysis

C) Precipitation by calcium salts

D) Precipitation by heavy metals

E) Interaction with an ammonia solution of silver nitrate

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

A) Alcoholic hydroxyl

B) Aldehyde group

C) Primary aromatic amino group

D) Phenolic hydroxyl

E) Amide group

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

A) Ethanol formed during alkaline hydrolysis

B) Primary aromatic amino group

C) p-Aminobenzoic acid

D) Complex ether group

E) Aldehyde group

TASKS:

1. Calculate the percentage content of ammonia solution (M.m. 17.03), which is quantitatively determined by the acidimetry method (reverse method), if 7.3 ml of 0.1 M sodium hydroxide solution was used for the titration of a 2.0000 g sample (CF = 1.0000); volume of 0.1 M solution of hydrochloric acid (CF = 1.0000), taken in excess - 25.0 ml.

2. Calculate the volume of a 0.05 M solution of sulfuric acid (CF = 0.9880), which will be spent on the titration of 2.0045 g of an ammonia solution (M.m. 17.03), if its percentage content is 26.9 %.

3. Calculate the volume of a 0.1 M solution of sodium edetate (trilon B CF = 1.0000), which will be spent on the titration of 0.2230 g of basic bismuth nitrate (M.m. Bi_2O_3 465.66), if its percentage content in the preparation - 80.0%.

4. Calculate the weight of the novocaine test (M.m. 236.31), if 9.55 ml of 0.1 M sodium nitrite solution (CF = 1.0000) was spent on its titration; and the percentage content of novocaine in the drug is 99.8%.

LABORATORY WORK

When performing laboratory work, it is necessary to strictly observe the safety rules of work in a chemical laboratory.

1. Students receive one of the practical sets from the teacher.

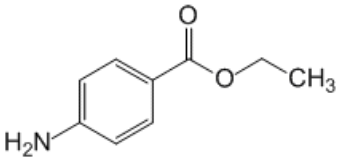
2. The task consists in studying the appearance, solubility of all substances included in the practical set, as well as conducting a functional analysis of each drug.

3. On the basis of the obtained results, students make a conclusion about the substances that make up each test tube, confirming the guess with the conducted reactions for the presence of elemental (presence of nitrogen, sulfur, halogen) and functional composition with the help of qualitative reactions.

4. All the necessary techniques that may be needed to perform practical work are below.

5. In the end of the practical work, each student fills out the protocol according to the requirements listed below.

BENZOCAINE



C_9H11NO_2 M.m. 165,2

Benzocaine contains not less than 99.0% and not more than 101.0% of ethyl 4-aminobenzoate, based on dry matter.

PROPERTIES

Description. White or almost white crystalline powder or colorless crystals.

Solubility. Very slightly soluble in water, easily soluble in 96% alcohol.

IDENTIFICATION

First identification: A. B.

Second identification: A, C, B.

A. Melting point (2.2.4). From 89°C to 92°C.

B. The infrared spectrum (2.2.24) of the substance must correspond to the Pharmacopoeia standard sample spectrum of benzocaine.

C. About 50 mg of the substance is placed in a test tube and we add 500 g/l chromium (VI) oxide to 0.2 ml of a solution. The test tube is covered with filter paper moistened with a freshly prepared mixture of equal volumes of a solution of 50 g/l sodium nitroprusside and a solution of 200 g /l of piperazine hydrate, and carefully boil for at least 30 seconds; the filter paper should turn blue.

D. About 50 mg of the substance is dissolved in 96% alcohol and the volume of the solution is brought up to 100 ml with the same solvent. 2 ml of the resulting solution must pass the test for primary aromatic amines (2.3.1).

PURITY TEST

Transparency of the solution (2.2.1). 1.0 g of the substance is dissolved in 96% alcohol and the volume of the solution is brought up to 20 ml with the same solvent. The resulting solution should be transparent.

The color of the solution (2.2.2, method II). The solution prepared for the "Transparency of solution" test must be colorless.

Acidity or alkalinity. Dissolve 0.5 g of the substance in 10 ml of 96% alcohol, previously neutralized with 0.05 ml of phenolphthalein solution, and add 10 ml of carbon dioxide-free water. The color of the solution should change when no more than 0.5 ml of 0.01 M sodium hydroxide solution is added.

Loss in mass during drying (2.2.32). No more than 0.5%. 1.00 g of the substance is dried in a vacuum.

Sulphated ash (2.4.14) Not more than 0.1%. The determination is carried out with 1.0 g of the substance.

QUANTITATIVE DEFINITION

0.400 g of the substance is dissolved in a mixture of 25 ml of hydrochloric acid and 50 ml of water and the determination is carried out (2.5.8).

1 ml of 0.1 M sodium nitrite solution corresponds to 16.52 mg C9H11NO2

STORAGE

In a place protected from light.

Educational and research work of students.

BENZOCAINE (ANESTHESIN)

1. 0.05 g of the drug is dissolved in 2 ml of water acidified with 3 drops of diluted hydrochloric acid, 3 drops of 0.1 M sodium nitrite solution are added and shaken; the resulting solution is added to 3 ml of an alkaline -naphthol solution; a cherry-red color appears or an orange-red precipitate is formed.

2. 0.05 g of the drug is heated with 5 ml of sodium hydroxide solution and 0.05M iodine solution is added until the yellow color does not disappear; the smell of iodoform appears.

3. 0.05 g of the drug is dissolved in 2 ml of water with 5 drops of diluted hydrochloric acid and 2 ml of chloramine solution is added. After 2 minutes, add 2 ml of ether and shake; the ether layer turns orange.

Quantitative definition. Dissolve about 0.2 g of the drug (precisely weighed) in 10 ml of water and 10 ml of diluted hydrochloric acid, make up to a total volume of 80 ml with water, add 1 g of potassium bromide and, with constant stirring, titrate with a 0.1 M sodium nitrite solution adding it initially at a rate of 2 ml per minute, and at the end

of the titration, 0.05 ml per minute. The indicator is neutral red or tropeolin 00 mixed with methylene blue.

CONCENTRATED AMMONIA SOLUTION

Ammoniae solutio concentrata

NH_4OH

Concentrated ammonia solution contains not less than 25.0% and not more than 30.0% (m/m) of ammonia NH_3; M.m. 17.03).

PROPERTIES

Description. Transparent, colorless, very alkaline liquid.

Solubility. Mixes with water and 96% alcohol.

IDENTIFICATION

A. Relative density (2.2.5). From 0.892 to 0.910.

B. The substance must have a strongly alkaline reaction (2.24).

C. 5 ml of water is added to 0.5 ml of the substance, air is passed through and the resulting gas mixture is directed to the surface of the solution containing 1 ml of 0.1 M hydrochloric acid and 0.05 ml of methyl red solution; the red color of the solution changes to yellow. Add 1 ml of sodium cobaltinitrite solution to the resulting solution; a yellow precipitate is formed.

PURITY TEST

Solution S. Evaporate 220 ml of the substance almost dry in a water bath, cool, add 1 ml of diluted acetic acid, and bring the volume of the solution to 20 ml with distilled water.

Dry residue. 50 ml of the substance is boiled in a water bath and dried at a temperature from 100 °C to 105 °C for 1 hour. The weight of the dry residue should not exceed 1 mg (0.02 g/l).

QUANTITATIVE DEFINITION

Place 50.0 ml of a 1 M solution of hydrochloric acid in a flask with a ground glass stopper, weigh accurately, add 2 ml of the substance and weigh again. The

resulting solution is titrated with 1 M sodium hydroxide solution until the color changes from red to yellow, using 0.1 ml of methyl red solution as an indicator.

1 ml of 1 M solution of hydrochloric acid corresponds to 17.03 mg of NH_3.

Transparency of the solution (2.2.1). Add 8 ml of water to 2 ml of the substance. The resulting solution should be transparent.

The color of the solution (2.2.2, method II). The solution prepared for the "Transparency of the solution" test should be colorless.

Oxidizing substances. 8.8 ml of the substance and 0.75 ml of a 0.002 M solution of potassium permanganate are carefully added to 100 ml of diluted sulfuric acid during cooling. The resulting solution is kept for 5 minutes; the solution should remain slightly pink.

Pyridine and accompanying impurities. The optical density (2.2.25) of the substance, measured at a wavelength of 252 nm, should not be more than 0.06 (0.0002 % (2 ppm), in terms of pyridine). Water is used as a compensation solution.

Carbonates. No more than 0.006% (60 ppm). Place 10 ml of the substation in a test tube with a ground glass stopper, add 10 ml of calcium hydroxide solution. Immediately close with a stopper and mix. The opalescence of the obtained solution should not exceed the opalescence of the standard, prepared similarly to the test solution using 10 ml of a solution of 0.1 g/l sodium carbonate anhydrous.

Chlorides (2.4.4). Not more than 0.0001 % (1 ppm). 5 ml of solution S is brought to a volume of 15 ml with water. The resulting solution must withstand the chloride test.

Sulfates (2.4.73). Not more than 0.0005 % (5 ppm). 3 ml of solution S is brought to a volume of 15 ml with distilled water. The resulting solution must withstand the test for sulfates.

Heavy metals (2.4.8, method A). Not more than 0.0001 % (1 ppm). 4 ml of solution S is brought to a volume of 20 ml with water. 12 ml of the resulting solution must withstand tests for heavy metals. The standard is prepared using a lead standard solution (2 ppm Pb).

Iron (24.9). Not more than 0.000025 % (0.25 ppm). 4 ml of solution S is brought to 10 ml with water. The resulting solution must withstand the iron test.

Storage

In an airtight container, at a temperature not higher than 20 °C.

The student calculates:

Titre;

Estimated weight per 10 ml of titrated solution.

The student makes a conclusion about the qualitative and quantitative content of the drug in accordance with the requirements of the pharmacopoeia.

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LESSON NO. 3

TOPIC: «Means that improve blood supply to organs and tissues. Characteristics, classification, relationship between structure and pharmacological action. Mechanism of action, methods obtained, methods of analysis. Application in medicine».

2. PURPOSE: To study the classification, mechanism of action, as well as standardization of antianginal drugs.

3. TARGETS:

3.1. To study the characteristics and classification of drugs that improve the blood supply to organs and tissues;

3.2. To study the relationship (connection) between the structure and pharmacological action of drugs that improve blood supply to organs and tissues;

3.3. To study the mechanism of action of drugs that improve the blood supply to organs and tissues;

3.4. To learn the Latin names, synonyms, structural formulas, and chemical names of the studied drug substances (nitroglycerin, nifedipine, verapamil, dipyridamole, cinnarizine, nimodipine, vinpocetine, pentoxifylline);

3.5. To study the physical and physico-chemical properties of drugs that improve the blood supply of organs and tissues;

3.6. To study the structure of the normative and technical documentation, quality control methods and the quality indicators that are included in them;

3.7. To determine general and specific impurities;

3.8. To carry out calculations of weight, gram, percentage content;

3.9. To study methods of identification of drug substances of this group based on their physical and chemical properties;

3.10. To study methods of quantitative determination of the studied drug substances;

3.11. To study the application, form of release, storage of drug substances;

3.12. To give a correct assessment of the obtained results of the analysis and draw a conclusion about the benign quality of drug substances of this group.

EDUCATIONAL QUESTIONS FOR STUDENTS' SELF-PREPARATION

1. Characteristics and classification of drugs that improve blood supply to organs and tissues.

2. Connection between the structure and pharmacological effect of drugs that improve blood supply to organs and tissues.

3. Mechanism of action of drugs of this group.

4. Chemical structure, Latin names, synonyms of drugs of this group (nitroglycerin, nifedipine, verapamil, dipyridamole, cinnarizine, nimodipine, vinpocetine, pentoxifylline, sodium nitrite).

5. Methods of obtaining the studied drugs.

6. Characterize the physical and chemical properties of drugs of this group based on their structure.

7. Identification of drugs in accordance with the requirements of the SPhU. Chemism of reactions, conditions for their implementation.

8. Methods of quantitative determination, conditions and chemism of reactions.

9. Application in medicine.

10. Substantiate the conditions of storage of preparations of this group of medicines, based on their physical and chemical properties.

TEST TASKS

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

A) Complex esters

B) Simple ethers

C) Polyhydric alcohols

D) Nitroalkanes

E) Nitroarenes

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

A) Azo dye formation reaction

B) Alkaline hydrolysis reaction

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

D) Reaction with Nessler's reagent

E) Reaction with potassium permanganate

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

A) Acrolein formation reaction

B) Reaction with iron (III) chloride

C) Reaction of formation of indophenol

D) "silver mirror" reaction

E) Reaction of formation of thiochrome

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

A) Nitroglycerin

B) Metoprolol

C) Isosorbide mononitrate

D) Sustak

E) Trinitrolong

5. Specify an antianginal drug of prolonged action:

A) Phenigidine

B) Sustak

C) Nitroglycerin

D) Nitrosorbide

E) Isosorbide mononitrate

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

A) Green colored solution

B) Brown-black sediment

C) Brown vapors of nitrogen oxides

D) Yellow color of the solution

E) Cherry-red color of the solution

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

A) Aniline

B) Resorcinol

C) Phenol

D) Antipyrine

E) β - naphthol

8. Specify a drug that has a vasodilating effect:

A) Sodium nitrite

B) Sodium thiosulfate

C) Magnesium peroxide

D) Hydroperite

E) Perhydrol

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

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

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

C) Antipyrine and hydrochloric acid

D) Iron (II) chloride

E) Iron (III) chloride

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

A) Potassium pyroantimonate (potassium hexahydroxystibiate)

B) Cobalt chloride

C) Copper sulfate

D) Silver nitrate

E) Potassium permanganate

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

A) Argentometry

B) Permanganatometry (reverse method)

C) Iodometry

D) Complexonometry

E) Permanganatometry (direct method)

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

A) Diphenylamine

B) Pyridine

C) Sulfuric acid

D) Barium chloride

E) Antipyrine

13. The antispasmodic drug "Erinit" is:

A) Nitroglycerin

B) Pentaerythritol tetranitrate

C) Nitrosorbide

D) Sodium nitrite

E) Potassium nitrate

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

A) Green colored solution

B) Brown-black sediment

C) Brown vapors of nitrogen oxides

D) Yellow color of the solution

E) Cherry-red color of the solution

7. TASKS

1. Calculate the percentage content of nitroglycerin (M.m. 227.1) in the preparation, weighing 0.2495 g, if 9.46 were spent on the titration of an excess of 20.00

ml of a 0.5 M potassium hydroxide solution (CF = 1.0001) ml of 0.5 M solution of hydrochloric acid (CF = 1.0022).

2. Calculate the volume of hydrochloric acid (CF = 0.9998) that was spent on the titration of 0.2502 g of nitroglycerin (M.m. 227.1), the percentage content of the drug is 99.98%. The volume of 0.5 M potassium hydroxide solution (CF = 1.0001) taken in excess is 20.00 ml.

3. During the quantitative determination of the sodium nitrite substance (M.m. 69.00) weighing 0.6502 g, 20 ml of 0.1 M sodium thiosulfate solution (CF = 1.0000) was used for the titration of the iodine that was released. the titrant volume in the control experiment is 39.05 ml (at the same time, 40 ml of 0.02M potassium permanganate was taken). The volume of the measuring flask is 100.0 ml, the volume of the pipette is 10.0 ml. Does the analyzed drug substance meet the requirements of the SPhU?

4. Calculate the mass of the sodium nitrite sample taken (M.m. 69.00), if 19.98 ml of 0.1 M sodium thiosulfate solution (CF = 1.0000) was used for the titration of the released iodine, the volume titrant in the control experiment - 40.02 ml (at the same time, 40 ml of 0.02M potassium permanganate was taken). The volume of the measuring flask is 100.0 ml, the volume of the pipette is 10.0 ml, and the percentage of the drug is 100.05%.

When performing laboratory work, it is necessary to strictly follow the rules of safe work in a chemical laboratory.

Each student individually conducts an analysis of the quality of one of the above drug substances in accordance with the requirements of the State Pharmacopoeia or other documentation using the graphological structure of the analysis.

The student studies the received pharmacopoeial article:

Sodium nitrite

Natrii nitris

Natrium nitrosum

$NaNO_2$ **M.m. 69,00**

Description: White or white with a slightly yellowish tint crystals. Hygroscopic. The aqueous solution has a slightly alkaline reaction. (The student conducts an external examination of the received drug substance, and draws a conclusion based on the results obtained - it meets or does not meet the SPhU).

Solubility: easily soluble in water, hardly soluble in alcohol. (solubility is determined only in purified water)

Identification: the drug gives characteristic reactions to nitrites with antipyrine and sodium with potassium pyroantimonate.

Quantitative definition

Dissolve 0.3 g of the substance (precisely weighed) in water in a 100 ml volumetric flask, bring it up to the mark with water. 10.0 ml of the received solution is slowly poured into a mixture of 20.0 ml of 0.02 M potassium permanganate solution, 200 ml of water and 10 ml of dilute sulfuric acid. After 20 minutes, 0.5 g of potassium iodide is added and the released iodine is titrated with a 0.1 M sodium thiosulfate solution (starch indicator). In parallel, a control experiment is conducted.

1 ml of 0.1 M sodium thiosulfate solution corresponds to 0.003450 g of sodium nitrite.

Performance of work:

The student calculates:

1. Titre;

2. Estimated weight per 10 ml of titrated solution.

The student makes a conclusion about the qualitative and quantitative content of the drug in accordance with the requirements of the pharmacopoeia.

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LESSON NO. 4

TOPIC: «Sulfanilamides. Characteristics, classification, relationship between structure and pharmacological action. Mechanism of action, methods obtained, methods of analysis. Application in medicine».

2. PURPOSE: to study the classification, mechanism of action, as well as standardization of sulfonamides.

3. TARGETS:

3.1. To study the characteristics and classification of sulfonamide drugs;

3.1. To study the relationship (connection) between the structure and pharmacological action of sulfonamide drugs;

3.2. To study the mechanism of action of sulfonamide agents;

3.3. To learn the Latin names, synonyms, structural formulas, chemical names of the studied drug substances;

3.4. To study the physical and physico-chemical properties of sulfonamide agents;

3.5. To study the structure of normative and technical documentation, quality control methods and quality indicators that are included in them;

3.6. To determine general and specific impurities;

3.7. To carry out calculations of weight, gram, percentage content;

3.8. To study methods of identification of drug substances of this group based on their physical and chemical properties;

3.9. To study methods of quantitative determination of the studied drug substances;

3.10. To study the application, form of release, storage of drug substances;

3.11. To give a correct assessment of the obtained results of the analysis and draw a conclusion about the benign quality of drug substances of this group.

5. TASKS FOR STUDENTS' SELF-PREPARATION:

5.1. Repeat the theoretical material from the course of inorganic, organic and analytical chemistry, regarding the conduct of reactions for the identification of cations, anions, and functional groups.

5.2. To repeat the theoretical material from the course of organic and analytical chemistry, regarding quantitative determination by various methods: acidimetry, alkalimetry, complexonometry, precipitation, redoxmetry, nitritometry, etc.

5.3. Study the program material on this topic according to the questions below.

EDUCATIONAL QUESTIONS FOR STUDENTS' SELF-PREPARATION

1. Characteristics and classification of sulfonamide drugs.

2. Connection between the structure and pharmacological effect of sulfonamide drugs.

3. Mechanism of action of drugs of this group.

4. Chemical structure, Latin names, synonyms of drugs of this group (streptocide, sulfadimezin, norsulfazole, etazol, sulfacyl sodium, phthalazole, urosulfan, sulgin, derivatives of azo compounds: salazopyridazine, salazosulfopyridazine).

5. Methods of obtaining the studied drugs.

6. Characterize the physical and chemical properties of drugs of this group based on their structure.

7. Identification of drugs in accordance with the requirements of the SPhU. Chemism of reactions, conditions for their implementation.

8. Methods of quantitative determination, conditions and chemism of reactions.

9. Application in medicine.

10. Substantiate the conditions of storage of preparations of this group of drugs, based on their physical and chemical properties.

6. TEST TASKS

1. Salazopyridazine can be distinguished from sulfadimezin by:

A) appearance

B) ninhydrin test

C) oxime formation

D) formation of a complex ester

E) precipitation of silver by nitrate

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

A) chloramine

B) urosulfan

C) butamide

D) streptocide is soluble

E) norsulfasol

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

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

B) sodium nitrite in an alkaline medium, phenol

C) iron (III) chloride, hydrochloric acid

D) sodium nitrite in an acidic environment

E) sodium nitrite in a neutral environment, cobalt chloride

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

A) streptocide

B) butamide

C) urosulfan

D) norsulfasol

E) sulgin

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

A) phenolic hydroxyl

B) carboxyl group

C) keto group

D) primary aromatic amino group

E) sulfamide group

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

A) streptocide

B) sulgin

C) urosulfan

D) phthalazole

E) sulfadimezin

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

A) mineralization by boiling with concentrated nitric acid

B) alkaline hydrolysis (alloy with alkali)

C) formation of oxonium salts

D) formation of hydroxamates

E) formation of colored complexes with salts of heavy metals

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

A) formation of indophenol

B) acid hydrolysis

C) alkaline hydrolysis

D) oxime formation

E) formation of azo dye (azo compound)

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

A) comlex ether group

B) simple ether group

C) carboxyl group

D) imide group

E) amino groups

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

A) butamide

B) chlorpropamide

C) norsulfasol

D) urosulfan

E) phthalazole

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

A) nitritometry method

B) method of neutralization

C) iodometry method

D) mercurimetry method

E) cerimetry method

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

A) glacial acetic acid

B) acetic anhydride

C) formic acid

D) diluted sulfuric acid

E) dimethylformamide

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

A) compliance with the temperature regime

B) preliminary hydrolytic decomposition

C) use of the reverse titration method

D) neutral reaction of the environment

E) use of α-naphthol, phenol

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

A) salt and complex formation with salts of heavy metals

B) with solutions of aldehydes in sulfuric acid

C) with phenols

D) with meadows

E) with alkali metals

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

A) sulfacyl sodium

B) norsulfasol

C) etazol

D) phthalazole

E) streptocide

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

A) sulgin

B) sulfadimezin

C) etazol

D) sulfalene

E) streptocide

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

A) chloramine

B) salazopyridazine

C) pantocid

D) phthalazole

E) norsulfasol

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

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

B) p-aminobenzenesulfamide

C) 2-(p-aminobenzenesulfamido)-thiazole

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

E) p-aminobenzenesulfamidoguanidine

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

A) Sulfathiazolum

B) Phthalylsulfathiazolum

C) Sulfaethiodolum

D) Sulfaguanidinum

E) Phthalazolum

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

A) sulfanilic acid amide

B) amide of benzene sulfonic acid

C) p-aminobenzoic acid amide

D) p-chlorobenzenesulfonic acids

E) p-aminosalicylic acid

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

A) Aethazolum

B) Salasopyridazinum

C) Sulginum

D) Chlorpropamidum

E) Sulfadimezinum

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

A) Sulfanilamide

B) Phthalysulfathiazolum

C) Sulfadimidinum

D) Tolbutamidum

E) Sulfacarbamid

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

A) benzoin

B) salicylic

C) sulfanilic

D) γ-pyridinecarbon

E) nicotine

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

A) Phthalysulfathiazolum

B) Sulfaethidolum

C) Sulfadimidinum

D) Sulfanilamide

E) Sulfathiazolum

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

A) Sulginum

B) Chlorpropamidum

C) Pantocidum

D) Chloraminum B

E) Butamidum

26. The drug substance Phthalazol has a rational name:

A) p-aminobenzenesulfamidoguanidine

B) sodium p-aminobenzenesulfacetamide

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

D) p-aminobenzenesulfanylurea

E) 2-(p-aminobenzenesulfamido)-thiazole

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

A) sulfamide group

B) primary aromatic amino group

C) aldehyde group

D) simple ether group

E) carboxyl group

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

A) formation of azo dye

B) formation of iodoform

C) formation of murexide

D) formation of naphthoquinone

E) formation of fluorescein

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

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

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

C) p-aminobenzenesulfamide (streptocide)

D) p-aminobenzenesulfanylurea (urosulfan)

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

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

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

B) sodium p-aminobenzenesulfiminomethanesulfonate (soluble streptocide)

C) p-aminobenzenesulfamide (streptocide)

D) sodium p-aminobenzenesulfacetamide (sodium sulfacyl)

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

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

A) Pantocidum

B) Sulfanilamide

C) Sulfacetamidum

D) Sulfaguanidinum

E) Sulfacarbamidum

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

A) Sulfacylum soluble

B) Streptocidum

C) Norsulfazolum

D) Chloraminum B

E) Pantocidum

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

A) Sulfaguanidinum (Sulginum)

B) Streptocidum soluble

C) Sulfadimidinum (Sulfadimezinum)

D) Sulfathiazolum (Norsulfazolum)

E) Urosulfanum

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

A) Sulfacylum Natrium

B) Phthalazolum

C) Sulfaguanidinum

D) Sulfadimidinum

E) Sulfathiazolum

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

A) Sulfanilamide

B) Sulfathiadolum

C) Sulfacarbamidum

D) Phthalylsulfathiazolum

E) Sulfacetamidum Natricum

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

A) with ammonium oxalate solution

B) formation of auric dye

C) formation of azo dye

D) with potassium hydroxide solution

E) with sodium citrate solution

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

A) from silver nitrate

B) with copper sulfate

C) with mercury (II) chloride

D) with barium sulfate

E) with potassium permanganate

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

A) Streptocidum

B) Urosulfanum

C) Sulginum

D) Sulfadimezinum

E) Norsulfazolum

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

A) ftivazide

B) phenyl salicylate

C) phenolphthalein

D) norsulfazol

E) phthalazole

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

A) neutral

B) alkaline

C) hydrochloric acid

D) ammonia

E) phosphoric acid

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

A) formation of isocyanides

B) deposition

C) neutralization

D) formation of indophenol

E) azo compound

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

A) adsorption indicator

B) metal indicator

C) external indicator (iodostarch paper)

D) in an indicatorless way

E) starch solution

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

A) eriochrome T

B) methyl red

C) neutral red

D) iodine-starch paper

E) dimethyl yellow

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

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

B) introducing other substituents into the benzene cycle

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

D) replacement of the sulfamide group by a radical

E) transfer of the sulfamide group to another position

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

A) oxidative phosphorylation

B) inhibition of monoamine oxidase synthesis

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

D) protein denaturation

46. Sulfanilamide drugs show:

A) antacid effect

B) antitumor

C) neurotropic

D) antibacterial

E) painkiller

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

A) barium chloride

B) lead acetate

C) lead sulfide

D) barium sulfate

E) silver nitrate

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

A) azo dye

B) murexide

C) naphthoquinone

D) fluorescein

E) iodoform

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

A) salicylic acid

B) sulfanilic acid

C) γ-pyridinecarboxylic acid

D) nicotinic acid

E) benzoic acid

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

A) nitro groups

B) aldehyde group

C) complex ether group

D) keto groups

E) primary aromatic amino group

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

A) sulfadimezin

B) phthalazole

C) phtazine

D) paracetamol

E) streptocide soluble

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

A) barbituric acid amide

B) benzoic acid amide

C) salicylic acid amide

D) sulfanilic acid amide

E) nicotinic acid amide

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

A) norsulfasol

B) streptocide

C) sulgin

D) etazol

E) sulfadimezin

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

A) norsulfasol

B) chloramine

C) antipyrine

D) atropine sulfate

E) ftivazide

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

A) acetic anhydride

B) benzene

C) unbleached paper

D) pyridine

E) chloroform

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

A) sulfadimethoxine

B) sulfacyl sodium

C) sulgin

D) etazol

E) phthalazole

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

A) primary aromatic amino group

B) complex ether group

C) sulfamide group

D) carboxyl group

E) aldehyde group

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

A) sulfapyridazine

B) sulfazine

C) sulfadimethoxine

D) phthalazole

E) phenacetin

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

A) sulgin

B) propazine

C) etazol

D) norsulfasol

E) sulfadimezin

7. TASKS:

1. Calculate the weight of sodium sulfacyl weighing (M.m. 254.24), if 17.28 ml of 0.1 M sodium nitrite solution (CF = 0.9995) is spent on its titration, its percentage content in the preparation is 99.48 %, the titrant volume in the control experiment is 0.25 ml.

2. Calculate the volume of 0.1 M sodium nitrite solution (CF = 1.0008) required for the titration of 0.2986 g of Urosulfan (M.m. = 233.25), if its percentage content in the preparation is 99.23% ; the volume of the titrant in the control experiment is 0.40 ml.

3. Calculate the percentage content of sulfadimezin (M.m. 278.33) in the preparation if 10.85 ml of 0.1 M sodium nitrite solution was spent on the titration of 0.3042 g of the sample (CF = 0.9997); the volume of the titrant in the control experiment is 0.35 ml

8. LABORATORY WORK

When performing laboratory work, it is necessary to strictly follow the rules of safe work in a chemical laboratory.

Each student individually conducts an analysis of the quality of one of the above drug substances according to the State Pharmacopoeia or another normative and technical documentation using the graphological structure of the analysis.

Educational and research work of students: Each student solves the question of one of the studied drug substances as an unknown based on physicochemical properties. In addition, he/she carries out quantitative determination of the analyzed drug substances according to the State Pharmacopoeia, as well as by other methods and gives a comparative description of methods of quantitative determination.

9. VISUAL MANUALS, TRAINING AND CONTROL TOOLS:

9.1. Table base on the subject of the lesson;

9.2. Set of samples of drug substances of this group;

9.3. Set of test tubes, devices and measuring utensils, tripods, scales and weights, electric heaters, gas burners;

9.4. Reagents and indicators necessary for conducting tests in accordance with the requirements of the SPhU;

a. Study Guides;

в. State Pharmacopoeia of Ukraine;

9.5. Training and control tools:

a. Cards for finding out the initial level of knowledge and skills;

в. Control questions and tests.

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LESSON NO. 5

TOPIC: “Control lesson on the section”.

PURPOSE: To form systematic knowledge of the theoretical basics and establish the benign quality of drugs that affect the afferent nervous system and drugs that improve the blood supply to organs and tissues, as well as antihistamine drugs and sulfonamides.

3. TARGET TASKS:

3.1. To check and consolidate theoretical knowledge and practical skills in determining the quality of drugs that affect the afferent nervous system and drugs that improve the blood supply to tissue organs, as well as antihistamines and sulfonamides;

3.2. To check the protocols of laboratory work and analyze the correctness of the course of analysis according to the requirements of the SPhU and other quality control methods (QCM).

4. CONTROL QUESTIONS OF THE LESSON

4.1. Characterization and classification of drugs that affect the afferent nervous system and drugs that improve blood supply to organs and tissues, as well as antihistamines and sulfonamides.

4.2. Concepts of allergy, anesthesia, competitive antagonism and their characteristics and classification.

4.3. The mechanism of action of drugs that affect the afferent nervous system and drugs that improve the blood supply to tissue organs, as well as antihistamines and sulfonamides.

4.4. The relationship (connection) between the structure and pharmacological action of drugs that affect the afferent nervous system and drugs that improve the blood supply to tissue organs, as well as antihistamines and sulfonamides.

4.5. Chemical structure, Latin names, synonyms of drugs of this group (streptocide, sulfadimezin, norsulfazole, etazol, sulfacyl sodium, phthalazole, urosulfan, sulgin, derivatives of azo compounds: salazopyridazine, salazosulfopyridazine).

4.6. Analysis of antihistamine drugs (Latin, Ukrainian, chemical name; chemical formula; description; methods of extraction; all possible methods of identification; all possible methods of quantitative determination) on the example of diphenhydramine, calcium chloride, calcium lactate, calcium gluconate.

4.7. Analysis of drugs affecting the afferent nervous system (Latin, Ukrainian, chemical name; chemical formula; description; method of extraction; all possible methods of identification; all possible methods of quantitative determination) on the example of Anesthesin, Dikain, Novocaine, aluminum hydroxide, bismuth nitrate basic, concentrated ammonia solution.

4.8. Analysis of drugs that improve blood supply to organs and tissues (Latin, Ukrainian, chemical name; chemical formula; description; extraction method; all possible methods of identification; all possible methods of quantitative determination) using the example of nitroglycerin, nifedipine, verapamil, dipyridamole, cinnarizine, nimodipine , vinpocetine, pentoxifylline.

4.9. Analysis of sulfonamide drugs (Latin, Ukrainian, chemical name; chemical formula; description; method of extraction; all possible methods of identification; all possible methods of quantitative determination) on the example of streptocide, sulfadimezin, norsulfazole, etazol, sulfacyl sodium, phthalazole, urosulfan, sulgin, derivatives of azo compounds: salazopyridazine, salazosulfopyridazine.

4.10. Application in medicine.

4.11. To substantiate the conditions of storage of preparations of this group of drugs, based on their physical and chemical properties.

TEST TASKS

1. Acid hydrolysis reaction is used to identify:

A) diphenhydramine hydrochloride (diphenhydramine)

B) sodium para-aminosalicylate

C) sodium benzoate

D) sodium salicylate

E) formaldehyde solution

2. A white cheesy precipitate from silver nitrate forms:

A) sodium para-aminosalicylate

B) mefenamic acid

C) phenacetin

D) paracetamol

E) diphenhydramine hydrochloride

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

A) neutralization

B) acetylation

C) hydrolysis

D) restoration

E) bromination

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

A) increases the solubility of the substance to be determined

B) strengthens the main properties of the drug under study

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

D) inhibits the reaction

E) catalyzes the reaction

5. One of the listed medicines is an antihistamine:

A) diphenhydramine hydrochloride (diphenhydramine)

B) novocaine

C) phenacetin

D) sodium para-aminosalicylate

E) anesthesin

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

A) acidic properties

B) basic properties

C) regenerative properties

D) oxidative properties

E) ability to engage in substitution reactions

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

A) concentrated nitric acid

B) ethanol

C) glacial acetic acid

D) dioxane

E) diethyl ether

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

A) bromatometry

B) permanganatometry

C) complexonometry

D) nitritometry

E) argentometry

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

A) benzophenone and β-dimethylaminoethyl chloride

B) benzylic acid and β-dimethylaminoethyl chloride

C) diphenylacetic acid and dimethylaminoethanol

D) solution of phenol and dimethylaminoethanol

E) diphenylpropionic acid and β-dimethylaminoethyl chloride

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

A) simple ether communication

B) keto groups

C) phenolic hydroxyl

D) ester group

E) β-lactam cycle

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

A) iron (III) chloride

B) the hydroxylamine solution is alkaline

C) concentrated sulfuric and nitric acid

D) sodium hydroxide

E) diluted hydrochloric acid

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

A) iodometry

B) nitritometry

C) argentometry

D) iodochlormetry

E) acidimetry

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

A) benzhydrol (diphenylmethanol)

B) dimethylamine

C) diphenylamine

D) phenol

E) dimethylaminoethanol

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

A) ammonium acetate solution

B) ammonium chloride solution

C) ammonium oxalate solution

D) ammonium hydroxide solution

E) dilute nitric acid

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

A) calcium lactate

B) sodium citrate

C) potassium iodide

D) sodium thiosulfate

E) potassium chloride

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

A) ammonia

B) acetic acid

C) sodium hydroxide

D) formaldehyde

E) potassium chloride

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

A) gravimetry

B) permanganatometry

C) dichromatometry

D) ion-exchange chromatography

E) complexonometry

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

A) solution of iron (III) ammonium sulfate

B) chalcone carboxylic acid solution

C) methyl red solution

D) phenolphthalein solution

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

A) white precipitate

B) yellow precipitate

C) blue sediment

D) green sediment

E) purple precipitate

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

A) complexonometry

B) gravimetry

C) acidimetry

D) alkalimetry

E) nitritometry

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

A) potassium iodide

B) potassium ferrocyanide

C) sodium hydroxide

D) silver nitrate

E) magnesium sulfate

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

A) ammonium oxalate

B) barium chloride

C) thioacetamide

D) sodium nitrite

E) silver nitrate

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

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

B) sodium cobalt nitrite solution

C) alcoholic solution of glyoxalhydroxyanil

D) methoxyphenylacetic acid solution

E) sodium sulfide solution

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

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

B) hydrochloric acid solution

C) sodium hydroxide solution

D) potassium permanganate solution

E) sodium thiosulfate solution

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

A) by changing the pH of the reaction medium

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

C) selection of the free form of the indicator

D) by changing the chemical structure of the indicator

E) decarboxylation of trilon B molecule (sodium edetate)

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

A) paper impregnated with lead acetate

B) redox indicators

C) indicatorless method

D) iodine starch paper

E) metal indicators

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

A) para-Nitrobenzoic acid

B) ortho-Nitrobenzoic acid

C) meta-Nitrobenzoic acid

D) Benzoic acid

E) Salicylic acid

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

A) Bromides

B) Chlorides

C) Sulfates

D) Tartrates

E) Iodides

29. One of the reactions of novocaine identification is:

A) Phenolic hydroxyl reaction

B) Murexide test

C) Maltol test

D) Reaction to the primary aromatic amino group

E) Reaction to alcohol hydroxyl

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

A) Nitritometry

B) Permanganatometry

C) Cerimetry

D) Complexonometry

E) Acidimetry

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

A) Sodium thiosulfate

B) Sodium edetate

C) Potassium bromate

D) Sodium nitrite

E) Silver nitrate

32. The drug procaine hydrochloride is a derivative of:

A) p-Aminobenzoic acid

B) Acetylsalicylic acid

C) Sulfanilic acid

D) Benzoic acid

E) Nicotinic acid

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

A) Streptocide

B) Diphenhydramine

C) Dikain

D) Streptomycin

E) Novocaine

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

A) Benzocaine (anesthetic)

B) Resorcinoma

C) Salicylic acid

D) Benzene

E) Trimecaine

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

A) Sodium chloride

B) Silver nitrate

C) Calcium oxalate

D) Potassium bromide

E) Copper(II) sulfate

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

A) Red

B) Yellow

C) Purple

D) Blue

E) Green

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

A) Red-violet

B) Dark red

C) Brownish-red

D) Yellow

E) Emerald green

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

A) p-Aminobenzoic acid

B) Salicylic acid

C) Phenol

D) Benzaldehyde

E) Isonicotinic acid

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

A) Novocaine

B) Sodium p-aminosalicylate

C) Anesthesin

D) Dikain

E) Novocainamide

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

A) Anesthesin

B) Novocaine

C) Norsulfasol

D) Streptocide

E) Dikain

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

A) Nitritometry

B) Bromatometry

C) Iodine chlorometry

D) Acidimetry

E) Permanganatometry

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

A) H_2O

B) NaOH

C) H_2SO_4

D) $KMnO_4$

E) HCl

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

A) Potassium tetraiodomercurate alkaline

B) Potassium ferrocyanide

C) Silver nitrate

D) Sodium tetraphenylborate

E) Barium chloride

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

A) Carbonate ion

B) Nitrate ion

C) Ammonium ion

D) Arsenite ion

E) Acetate ion

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

A) Potassium iodide solution

B) Starch solution

C) Barium chloride solution

D) Phenolphthalein solution

E) Argentum nitrate solution

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

A) Yellowish-orange color or orange precipitate

B) Yellow color of the solution

C) Red color of the solution or red precipitate

D) Blue color of the solution or blue precipitate

E) Violet color of the solution or violet precipitate

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

A) Ammonium oxalate

B) Barium chloride

C) Argentum nitrate

D) Sodium sulfide

E) Potassium nitrate

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

A) Ammonium hydroxide

B) Barium chloride

C) Sodium sulfide

D) Potassium tartrate

E) Copper sulfate

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

A) Silver nitrate

B) Potassium sulphite

C) Sodium sulfide

D) Sodium sulfate

E) Sodium nitrite

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

A) Complexonometry

B) Alkalimetry

C) Bromatometry

D) Iodometry

E) Permanganatometry

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

A) Iodometrically

B) Nitritometrically

C) Acidimetrically

D) Complexometrically

E) Alkalimetrically

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

A) Bromatometry

B) Iodochlormetry

C) Complexonometry

D) Argentometry

E) Nitritometry

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

A) p-Aminobenzoic acid

B) p-Chlorobenzoic acid

C) p-Aminophthalic acid

D) p-Aminosalicylic acid

E) p-Aminobenzene sulfonic acids

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

A) Aromatic ketones

B) Esters [complex esters] of aromatic amino acids

C) Amides of aromatic amino acids

D) Aromatic aminoaldehydes

E) Amides of aromatic sulfonic acids

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

A) Indophenol

B) Diazonium salts

C) Salts of hydroxamatic acids

D) Aurine dye

E) Azomethine dye

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

A) Benzocaine

B) Diphenhydramine

C) Dikain

D) Novocaine

E) Novocainamide

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

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

B) Acid hydrolysis

C) Precipitation by calcium salts

D) Precipitation by heavy metals

E) Interaction with an ammonia solution of silver nitrate

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

A) Alcoholic hydroxyl

B) Aldehyde group

C) Primary aromatic amino group

D) Phenolic hydroxyl

E) Amide group

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

A) Ethanol formed during alkaline hydrolysis

B) Primary aromatic amino group

C) p-Aminobenzoic acid

D) Complex ether group

E) Aldehyde group

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

A) Complex esters

B) Simple ethers

C) Polyhydric alcohols

D) Nitroalkanes

E) Nitroarenes

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

A) Azo dye formation reaction

B) Alkaline hydrolysis reaction

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

D) Reaction with Nessler's reagent

E) Reaction with potassium permanganate

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

A) Acrolein formation reaction

B) Reaction with iron (III) chloride

C) Reaction of formation of indophenol

D) "silver mirror" reaction

E) Reaction of formation of thiochrome

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

A) Nitroglycerin

B) Metoprolol

C) Isosorbide mononitrate

D) Sustak

E) Trinitrolong

64. Specify an antianginal drug of prolonged action:

A) Phenigidine

B) Sustak

C) Nitroglycerin

D) Nitrosorbide

E) Isosorbide mononitrate

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

A) Green colored solution

B) Brown-black sediment

C) Brown vapors of nitrogen oxides

D) Yellow color of the solution

E) Cherry-red color of the solution

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

A) Aniline

B) Resorcinol

C) Phenol

D) Antipyrine

E) β - naphthol

67. Specify a drug that has a vasodilating effect:

A) Sodium nitrite

B) Sodium thiosulfate

C) Magnesium peroxide

D) Hydroperite

E) Perhydrol

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

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

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

C) Antipyrine and hydrochloric acid

D) Iron (II) chloride

E) Iron (III) chloride

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

A) Potassium pyroantimonate (potassium hexahydroxystibiate)

B) Cobalt chloride

C) Copper sulfate

D) Silver nitrate

E) Potassium permanganate

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

A) Argentometry

B) Permanganatometry (reverse method)

C) Iodometry

D) Complexonometry

E) Permanganatometry (direct method)

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

A) Diphenylamine

B) Pyridine

C) Sulfuric acid

D) Barium chloride

E) Antipyrine

72. The antispasmodic drug "Erinit" is:

A) Nitroglycerin

B) Pentaerythritol tetranitrate

C) Nitrosorbide

D) Sodium nitrite

E) Potassium nitrate

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

A) Green colored solution

B) Brown-black sediment

C) Brown vapors of nitrogen oxides

D) Yellow color of the solution

E) Cherry-red color of the solution

74. 1. Salazopyridazine can be distinguished from sulfadimezin by:

A) A) appearance

B) B) ninhydrin test

C) C) oxime formation

D) D) formation of a complex ester

E) E) precipitation of silver by nitrate

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

A) chloramine

B) urosulfan

C) butamide

D) streptocide is soluble

E) norsulfasol

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

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

B) sodium nitrite in an alkaline medium, phenol

C) iron (III) chloride, hydrochloric acid

D) sodium nitrite in an acidic environment

E) sodium nitrite in a neutral environment, cobalt chloride

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

A) streptocide

B) butamide

C) urosulfan

D) norsulfasol

E) sulgin

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

A) phenolic hydroxyl

B) carboxyl group

C) keto group

D) primary aromatic amino group

E) sulfamide group

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

A) streptocide

B) sulgin

C) urosulfan

D) phthalazole

E) sulfadimezin

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

A) mineralization by boiling with concentrated nitric acid

B) alkaline hydrolysis (alloy with alkali)

C) formation of oxonium salts

D) formation of hydroxamates

E) formation of colored complexes with salts of heavy metals

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

A) formation of indophenol

B) acid hydrolysis

C) alkaline hydrolysis

D) oxime formation

E) formation of azo dye (azo compound)

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

A) comlex ether group

B) simple ether group

C) carboxyl group

D) imide group

E) amino groups

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

A) butamide

B) chlorpropamide

C) norsulfasol

D) urosulfan

E) phthalazole

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

A) nitritometry method

B) method of neutralization

C) iodometry method

D) mercurimetry method

E) cerimetry method

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

A) glacial acetic acid

B) acetic anhydride

C) formic acid

D) diluted sulfuric acid

E) dimethylformamide

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

A) compliance with the temperature regime

B) preliminary hydrolytic decomposition

C) use of the reverse titration method

D) neutral reaction of the environment

E) use of α-naphthol, phenol

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

A) salt and complex formation with salts of heavy metals

B) with solutions of aldehydes in sulfuric acid

C) with phenols

D) with meadows

E) with alkali metals

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

A) sulfacyl sodium

B) norsulfasol

C) etazol

D) phthalazole

E) streptocide

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

A) sulgin

B) sulfadimezin

C) etazol

D) sulfalene

E) streptocide

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

A) chloramine

B) salazopyridazine

C) pantocid

D) phthalazole

E) norsulfasol

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

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

B) p-aminobenzenesulfamide

C) 2-(p-aminobenzenesulfamido)-thiazole

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

E) p-aminobenzenesulfamidoguanidine

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

A) Sulfathiazolum

B) Phthalylsulfathiazolum

C) Sulfaethiodolum

D) Sulfaguanidinum

E) Phthalazolum

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

A) sulfanilic acid amide

B) amide of benzene sulfonic acid

C) p-aminobenzoic acid amide

D) p-chlorobenzenesulfonic acids

E) p-aminosalicylic acid

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

A) Aethazolum

B) Salasopyridazinum

C) Sulginum

D) Chlorpropamidum

E) Sulfadimezinum

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

A) Sulfanilamide

B) Phthalysulfathiazolum

C) Sulfadimidinum

D) Tolbutamidum

E) Sulfacarbamid

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

A) benzoin

B) salicylic

C) sulfanilic

D) γ-pyridinecarbon

E) nicotine

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

A) Phthalysulfathiazolum

B) Sulfaethidolum

C) Sulfadimidinum

D) Sulfanilamide

E) Sulfathiazolum

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

A) Sulginum

B) Chlorpropamidum

C) Pantocidum

D) Chloraminum B

E) Butamidum

99. The drug substance Phthalazol has a rational name:

A) p-aminobenzenesulfamidoguanidine

B) sodium p-aminobenzenesulfacetamide

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

D) p-aminobenzenesulfanylurea

E) 2-(p-aminobenzenesulfamido)-thiazole

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

A) sulfamide group

B) primary aromatic amino group

C) aldehyde group

D) simple ether group

E) carboxyl group

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

A) formation of azo dye

B) formation of iodoform

C) formation of murexide

D) formation of naphthoquinone

E) formation of fluorescein

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

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

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

C) p-aminobenzenesulfamide (streptocide)

D) p-aminobenzenesulfanylurea (urosulfan)

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

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

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

B) sodium p-aminobenzenesulfiminomethanesulfonate (soluble streptocide)

C) p-aminobenzenesulfamide (streptocide)

D) sodium p-aminobenzenesulfacetamide (sodium sulfacyl)

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

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

A) Pantocidum

B) Sulfanilamide

C) Sulfacetamidum

D) Sulfaguanidinum

E) Sulfacarbamidum

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

A) Sulfacylum soluble

B) Streptocidum

C) Norsulfazolum

D) Chloraminum B

E) Pantocidum

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

A) Sulfaguanidinum (Sulginum)

B) Streptocidum soluble

C) Sulfadimidinum (Sulfadimezinum)

D) Sulfathiazolum (Norsulfazolum)

E) Urosulfanum

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

A) Sulfacylum Natrium

B) Phthalazolum

C) Sulfaguanidinum

D) Sulfadimidinum

E) Sulfathiazolum

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

A) Sulfanilamide

B) Sulfathiadolum

C) Sulfacarbamidum

D) Phthalylsulfathiazolum

E) Sulfacetamidum Natricum

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

A) with ammonium oxalate solution

B) formation of auric dye

C) formation of azo dye

D) with potassium hydroxide solution

E) with sodium citrate solution

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

A) from silver nitrate

B) with copper sulfate

C) with mercury (II) chloride

D) with barium sulfate

E) with potassium permanganate

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

A) Streptocidum

B) Urosulfanum

C) Sulginum

D) Sulfadimezinum

E) Norsulfazolum

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

A) ftivazide

B) phenyl salicylate

C) phenolphthalein

D) norsulfazol

E) phthalazole

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

A) neutral

B) alkaline

C) hydrochloric acid

D) ammonia

E) phosphoric acid

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

A) formation of isocyanides

B) deposition

C) neutralization

D) formation of indophenol

E) azo compound

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

A) adsorption indicator

B) metal indicator

C) external indicator (iodostarch paper)

D) in an indicatorless way

E) starch solution

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

A) eriochrome T

B) methyl red

C) neutral red

D) iodine-starch paper

E) dimethyl yellow

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

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

B) introducing other substituents into the benzene cycle

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

D) replacement of the sulfamide group by a radical

E) transfer of the sulfamide group to another position

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

A) oxidative phosphorylation

B) inhibition of monoamine oxidase synthesis

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

D) protein denaturation

119. Sulfanilamide drugs show:

A) antacid effect

B) antitumor

C) neurotropic

D) antibacterial

E) painkiller

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

A) barium chloride

B) lead acetate

C) lead sulfide

D) barium sulfate

E) silver nitrate

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

A) azo dye

B) murexide

C) naphthoquinone

D) fluorescein

E) iodoform

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

A) salicylic acid

B) sulfanilic acid

C) γ-pyridinecarboxylic acid

D) nicotinic acid

E) benzoic acid

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

A) nitro groups

B) aldehyde group

C) complex ether group

D) keto groups

E) primary aromatic amino group

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

A) sulfadimezin

B) phthalazole

C) phtazine

D) paracetamol

E) streptocide soluble

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

A) barbituric acid amide

B) benzoic acid amide

C) salicylic acid amide

D) sulfanilic acid amide

E) nicotinic acid amide

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

A) norsulfasol

B) streptocide

C) sulgin

D) etazol

E) sulfadimezin

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

A) norsulfasol

B) chloramine

C) antipyrine

D) atropine sulfate

E) ftivazide

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

A) acetic anhydride

B) benzene

C) unbleached paper

D) pyridine

E) chloroform

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

A) sulfadimethoxine

B) sulfacyl sodium

C) sulgin

D) etazol

E) phthalazole

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

A) primary aromatic amino group

B) complex ether group

C) sulfamide group

D) carboxyl group

E) aldehyde group

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

A) sulfapyridazine

B) sulfazine

C) sulfadimethoxine

D) phthalazole

E) phenacetin

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

A) sulgin

B) propazine

C) etazol

D) norsulfasol

E) sulfadimezin

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