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

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PHARMACEUTICAL CHEMISTRY

SECTION 2.1

Study and methodical Guide

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

Zaporizhzhia

2023

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P56

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P56 **Pharmaceutical Chemistry. Section 2.1**: Study and methodical Guide for 3rd year English-speaking students of the specialty "Pharmacy, Industrial Pharmacy" / L.I. Kucherenko, O.O. Portna, O.V. Khromylova [et al.]. – Zaporizhzhia: ZSMU, 2023. – 118 p.

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INTRODUCTION

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

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

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

Block 1 - "Pharmaceutical analysis"

Block 2 - "Special pharmaceutical chemistry"

Block 2 consists of three sections.

SPECIFIC GOALS:

To learn the characteristics, classification, connection between structure and pharmacological action, mechanism of action, methods of production, methods of analysis of the use of antitussive, nootropic, non-steroidal anti-inflammatory, hypnotic drugs in medicine.

To explain the peculiarities of the identification of drugs according to the requirements of the State Pharmacopoeia of Ukraine (SPhU).

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

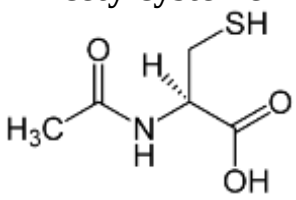
To propose and carry out a selection of physical, physico-chemical and chemical methods for determining the good quality of drugs in accordance with the requirements of the SPhU and other regulatory documentation, as well as Quality Control Methods (QCM).

PLAN OF PRACTICAL CLASSES

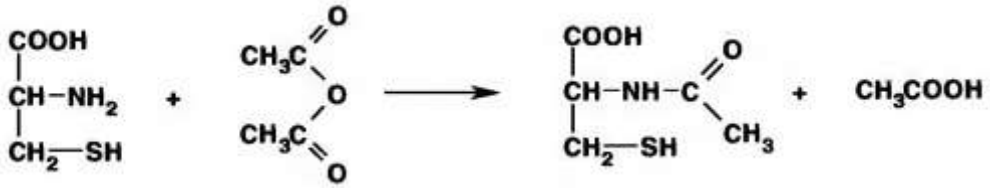
No.	**Lecture topic**	Number of hours
1.	Antitussives. Characteristics, classification, connection between structure and pharmacological action, mechanism of action, methods of production, methods of analysis. Use in medicine.	3
2.	Nootropic drugs. Characteristics, classification, connection between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

I. ANALYSIS OF ANTITUSSIVE DRUGS

Acetylcysteine



The production of acetylcysteine is based on the ability of amino acids to be acetylated by the amino group:



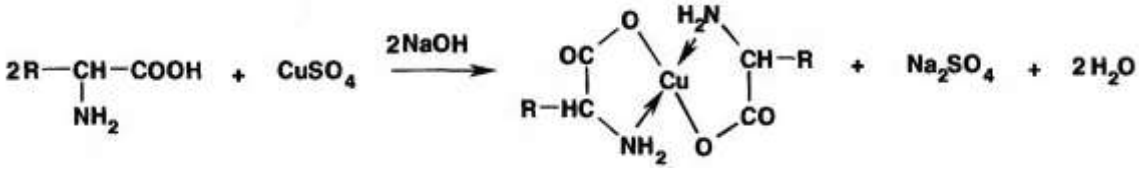
N-acetyl-L-cysteine

Description: White or white with a slightly yellowish tinge crystalline powder with a weak specific smell. Melting point: 106-110°C. Specific rotation from +21 to +26 ° (in sodium hydroxide solution). Acetylcysteine is easily soluble in water.

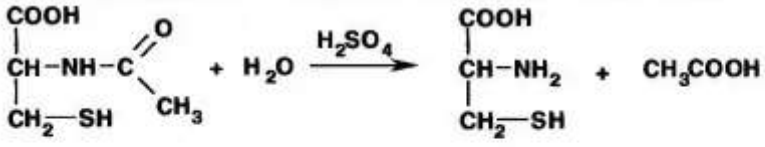
Such physical constants as melting point and specific rotation are used for identification.

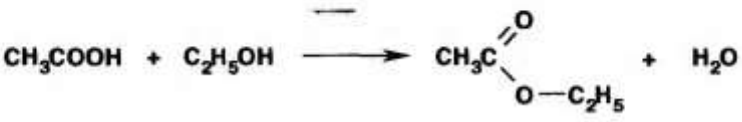
The UV absorption spectrum of acetylcysteine has an absorption maximum at 233 nm (solvent 0.1 M sodium hydroxide solution). The specific absorption index is 353.

A general color reaction with ninhydrin is used to test the authenticity of amino acids. As a result of the reaction, an ammonium salt of the enol form of diketohydrindenketohydrinamine is formed, which has a blue-violet color.



The reaction of the formation of ethyl acetate is used to detect the acetyl group in acetylcysteine. It is pre-boiled with a solution of potassium dichromate in sulfuric acid, and then ethanol is added.

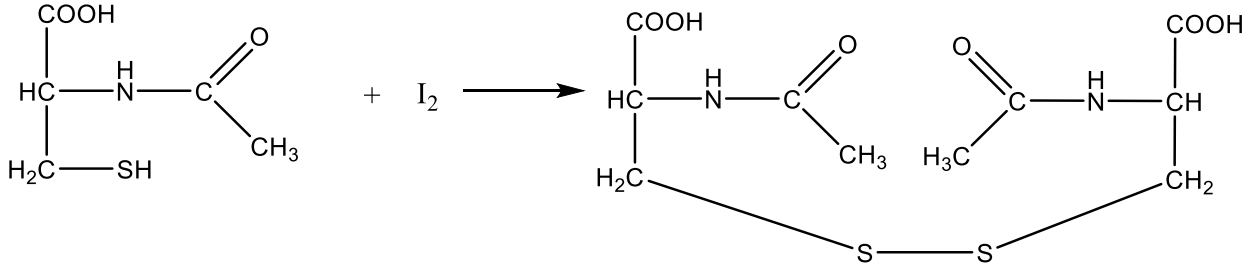




The presence of a thio group in a cysteine molecule can be established by a color reaction in an alkaline environment with sodium nitroprusside (red-violet color).

The thio group in the molecule of cysteine and acetylcysteine is confirmed by a color reaction with iron (III) chloride by the appearance of a rapidly disappearing blue color, or sodium nitrite is used as a reagent in the presence of acetic acid (red color). When cysteine and acetylcysteine solutions are treated with selenium acid, a red precipitate is formed.

Sulfur-containing amino acids are determined by the iodometric method. Cysteine and acetylcysteine are titrated in an acidic environment with a 0.1 M iodine solution. The definition is based on the oxidation of sulfhydryl groups according to the general scheme:

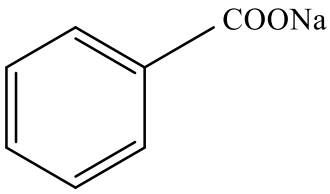


Amino acids are stored in a well-sealed container protected from light in a dry, cool, light-protected place to prevent decomposition.

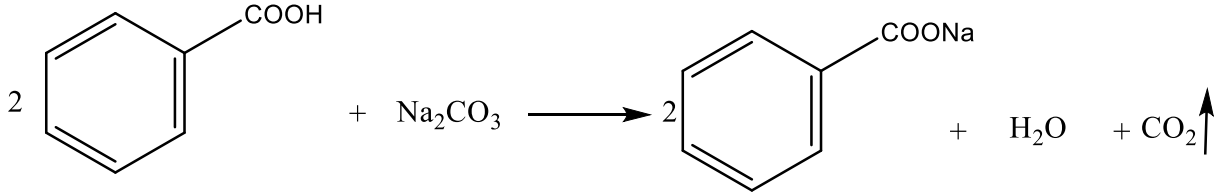
Acetylcysteine belongs to list B.

Acetylcysteine has a mucolytic effect (thins sputum and facilitates its separation). They are used in the form of 20% solutions for inhalation.

NATRII BENZOAS
SODIUM BENZOATE



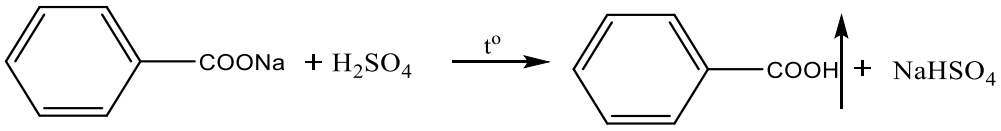
Extraction. By dissolving benzoic acid in a soda solution.



Properties. White crystalline or granular powder or flakes, weakly hygroscopic. Easily soluble in water, moderately soluble in 90% alcohol.

Identification:

The substance gives reactions to ***benzoates.*** 0.2 g of the tested substance, fine-cut if necessary, is placed in a test tube, moistened with 0.2 ml or 0.3 ml of sulfuric acid; carefully heat the bottom of the test tube; a white coating appears on the inner walls of the test tube.



The substance reacts to ***sodium***.

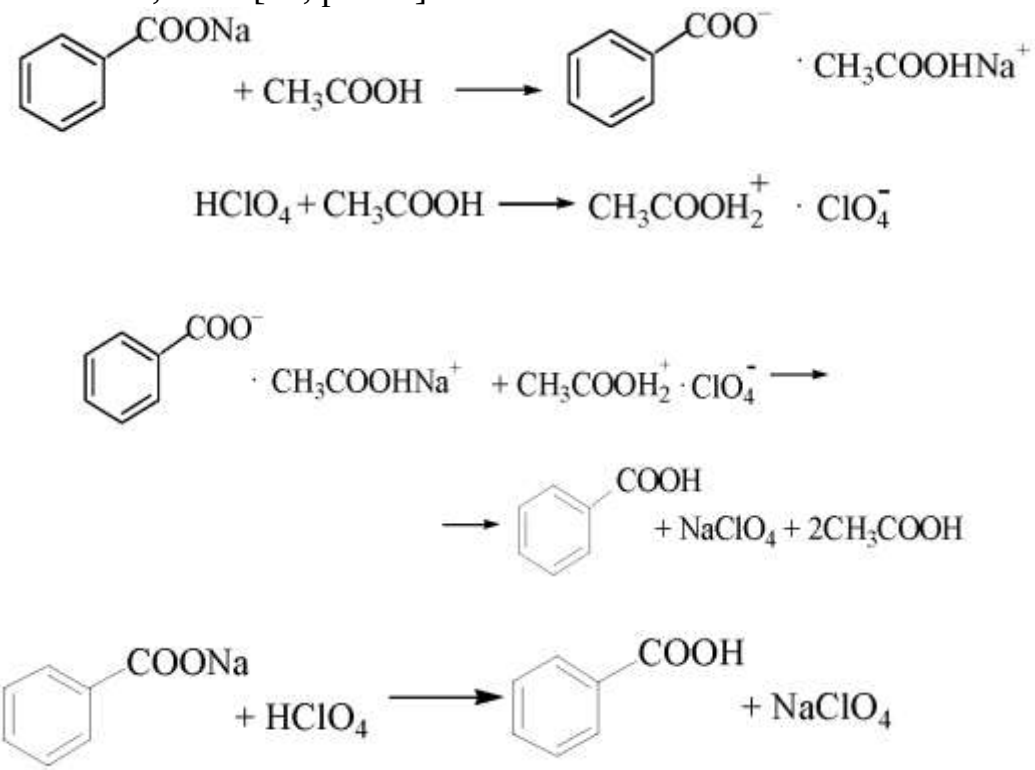
0.1 g of the tested substance is dissolved in 2 ml of water. To the resulting solution or to 2 ml of the solution specified in a separate article, we add 2 ml of a solution of 150 g/l of potassium carbonate and heat to boiling: no precipitate is formed. Add 4 ml of a solution of pyroantimonate R to the solution and heat to boiling, then cool in ice water and, if necessary, rub the inner walls of the test tube with a glass rod; a thick white precipitate is formed.

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

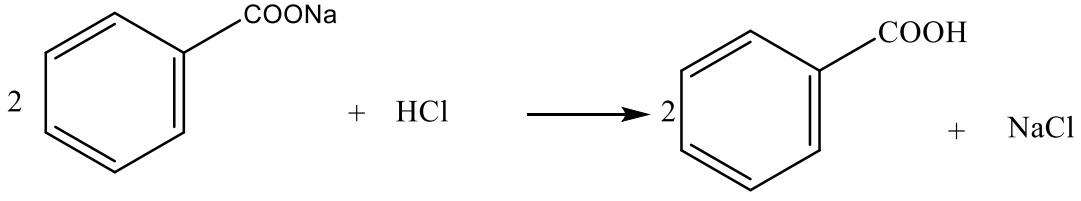
$$K[Sb(OH)_6] + HCl \rightarrow HSbO_3 \cdot 3H_2O\downarrow + KCl$$

Quantitative definition:

Acidimetry in a non-aqueous environment, direct titration, indicator - naphtholbenzene, s = 1 [10, p. 236]:



Acidimetry, direct titration in the presence of ether to extract benzoic acid, which can affect the pH of the solution and change the color of the indicator before the equivalence point, the indicator is a mixture of methyl orange and methylene blue.



Storage. In a tightly closed container.

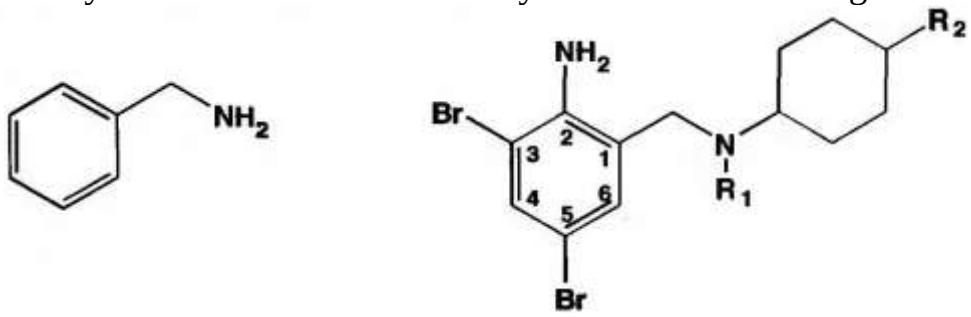
Use. Orally as an expectorant for bronchitis and other diseases of the upper respiratory tract, in powders and mixtures.

It is also administered intravenously (15% solution) for lung abscess, purulent bronchitis.

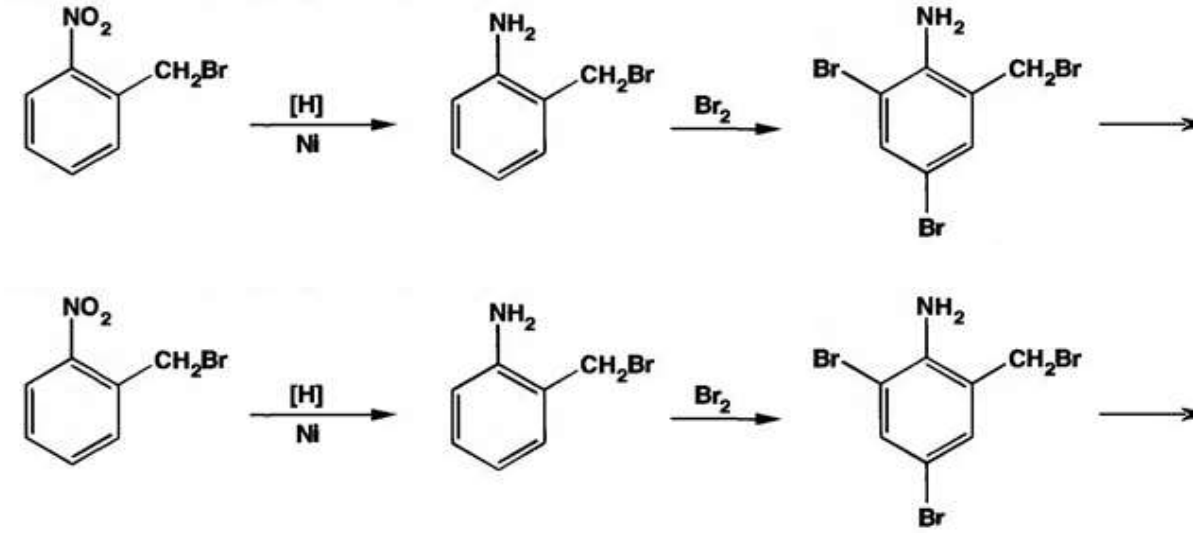
Sodium benzoate is also used to study the antitoxic function of the liver. The essence of the method is that aminoacetic acid (glycine) produced in the liver reacts with benzoic acid introduced into the body, resulting in the formation of hippuric acid. And the functional state of the liver is judged by the amount of hippuric acid released.

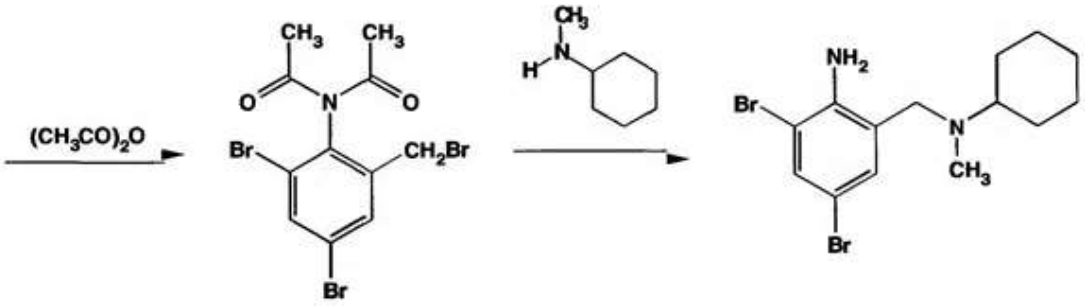
Aminodibromophenylalkylamines

This group includes drug substances, derivatives of phenylalkylamine (I) - bromhexine hydrochloride and ambroxol hydrochloride with the general formula.

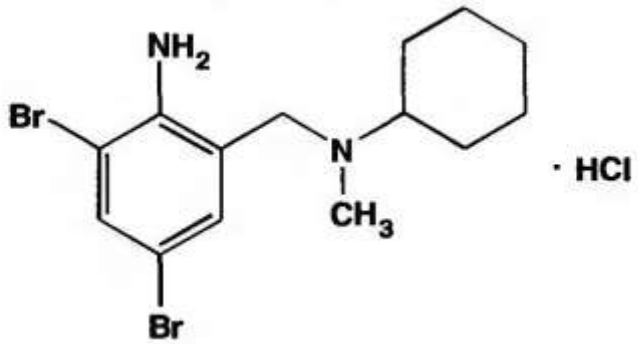


The synthesis of bromhexine is carried out according to the scheme:





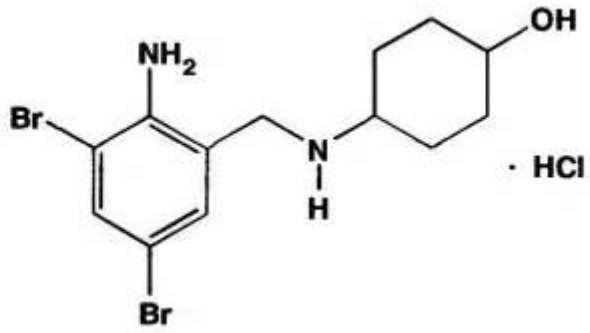
BROMHEXINE HYDROCHLORIDE



N-(2-amino-3,5-dibromobenzyl)-N-methylcyclohexylamine hydrochloride

Description: Odorless white crystalline powder. Melting point 234-239°C

AMBROXOL HYDROCHLORIDE



trans-4-[(2-amino-3,5-dibromobenzyl)amino]cyclohexanol hydrochloride

Description: Odorless white crystalline powder.

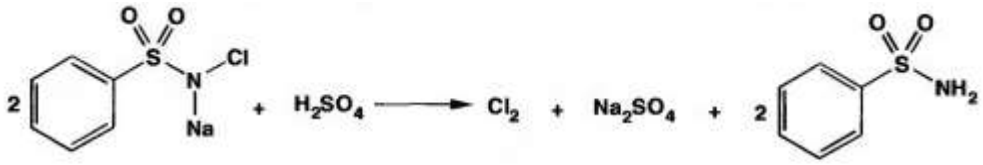
Bromhexine hydrochloride is easily soluble in water, ethanol, chloroform, practically insoluble in ether and acetone. Due to the similarity in the chemical structure of ambroxol hydrochloride, it has a similar solubility in these solvents.

The identity of aminodibromophenylalkylamines is established by UV absorption spectra. Bromhexine hydrochloride has light absorption maxima at 240 and 315 nm (ethanol solvent), and ambroxol hydrochloride at 245 and 307 nm (0.1 M hydrochloric acid solution).

To test the identity of bromhexine hydrochloride, specific absorption indicators and the ratio of optical densities at the first and second maximum, as well as derivative spectrophotometry, are used.

The presence of a bromine atom in bromhexine hydrochloride is established by destroying the organic part of the molecule to sodium bromide by boiling in a 30% solution of sodium hydroxide. After cooling, acidify with dilute sulfuric acid,

add a 5% solution of chloramine and tetrachloromethane, the layer of which turns orange-yellow.



$$2NaBr + Cl_2 \longrightarrow Br_2 + 2NaCl$$

The bromide ion together with SPU is detected by the precipitation of its silver with nitrate. This forms a light yellow precipitate, slowly soluble in ammonia solution:

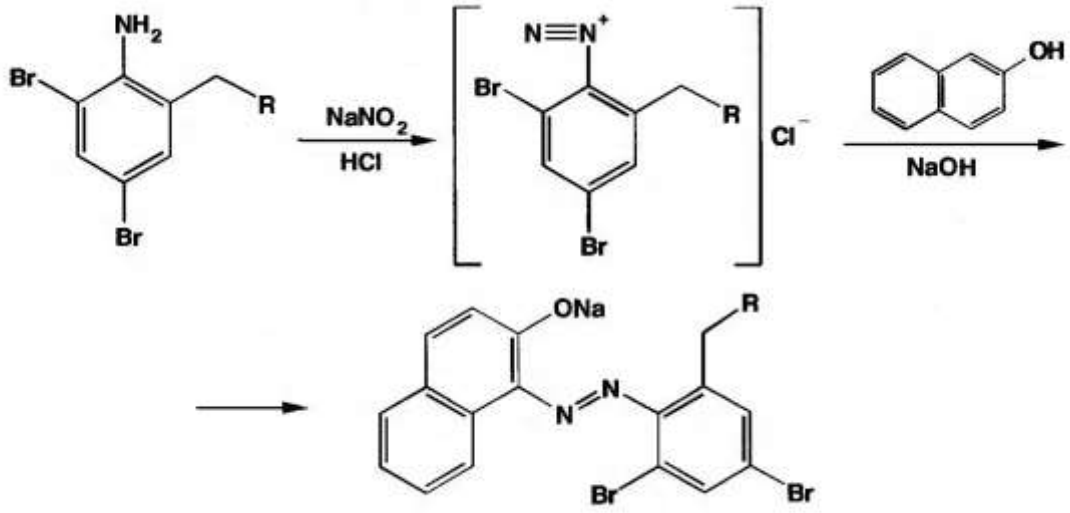
$$\mathbf{Br^- + AgNO_3 \rightarrow AgBr\downarrow + NO_3^-;}$$

$$\mathbf{AgBr + 2NH_4OH \rightarrow [Ag(NH_3)_2]Br + 2H_2O.}$$

With a solution of bromhexine ammonium nitrate, the hydrochloride forms a reaction product colored pink. The presence of a tertiary amino group in the molecules of both drug substances is determined by the appearance of a red-violet color after heating in a water bath with a 2% solution of citric acid in acetic anhydride. The reaction to chloride ions is also carried out.

To confirm the identity of bromhexine and ambroxol hydrochlorides and establish the absence of foreign impurities in them, the TLC method is used. Chromatograms of the tested and standard samples obtained on the Sorbfil plate are compared.

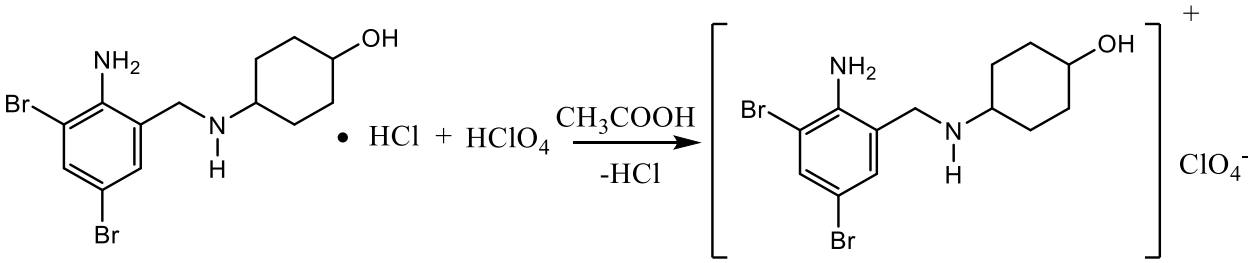
The presence of a primary aromatic amino group in the molecule determines the positive reaction of the formation of an azo dye with the use of various azo components, for example, ß-naphthol:



This reaction is used for identification and photocolorimetric determination of bromhexine hydrochloride. The identity of bromhexine and ambroxol hydrochlorides can be confirmed using general alkaloid reagents. The reaction with Dragendorff's reagent, which forms an orange precipitate, is the most sensitive.

Two color reactions are used for identification and spectrophotometric determination of ambroxol hydrochloride in the visible region. One of them is based on interaction with 3-methyl-2-benzothiazolinone hydrazone and cerium (IV) sulfate. The colored product has an absorption maximum at 545 nm. The second reaction consists in the interaction of ambroxol hydrochloride with a solution of iron (III) chloride and potassium hexacyanoferrate (III) in an acidic environment. Then measure the optical density at 740 nm. Bromhexine hydrochloride gives a similar reaction with extraction of the green-colored reaction product with benzene. It is also identified by an oxidative condensation reaction, for example, with p-dimethylaminobenzaldehyde.

Quantitative determination of bromhexine hydrochloride (BS) is carried out by non-aqueous titration method in a mixture of formic acid and acetic anhydride (2:40). Titrate with a 0.1 M perchloric acid solution, the crystal indicator is crystal violet.



A unified method for determining bromhexine hydrochloride in tablets by reversed-phase HPLC with detection at 307 nm has been developed.

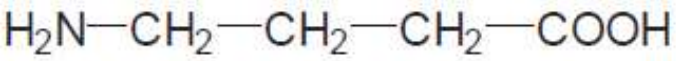
When analyzing tablets, quantitative determination of ambroxol hydrochloride is performed by UV spectrophotometry at a wavelength of 245 nm (solvent 0.1 M solution of hydrochloric acid). The calculation is carried out according to the value of the optical density of Standard Sample Solution. Various variants of spectrophotometry were used for spectrophotometric determination of bromhexine hydrochloride, including additive method and derivative spectrophotometry. Ambroxol hydrochloride in tablets during mass production is determined by the flow-injection method on the Spectrophoresis 100 device with a scanning detector in the UV region at 209 nm.

Store bromhexine and ambroxol hydrochlorides on list B in a dry place protected from light.

Bromhexine hydrochloride and ambroxol hydrochloride are mucolytic agents that stimulate the formation of surfactant (anti-atelectase factor), which facilitates the release of sputum. They have a secretolytic, expectorant and weak antitussive effect. Bromhexine hydrochloride 0.008 g, ambroxol hydrochloride 0.03 g are released in the form of tablets and dragees; syrup, mixture. Ambroxol hydrochloride is also used in the form of a solution for inhalation.

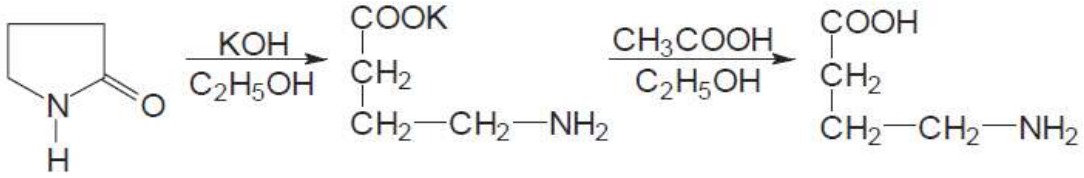
II. ANALYSIS OF DRUGS WITH NOOTROPIC ACTION

Aminalonum
Acidum gamma-aminobutyricum



γ-aminobutyric acid or 4-aminobutanoic acid

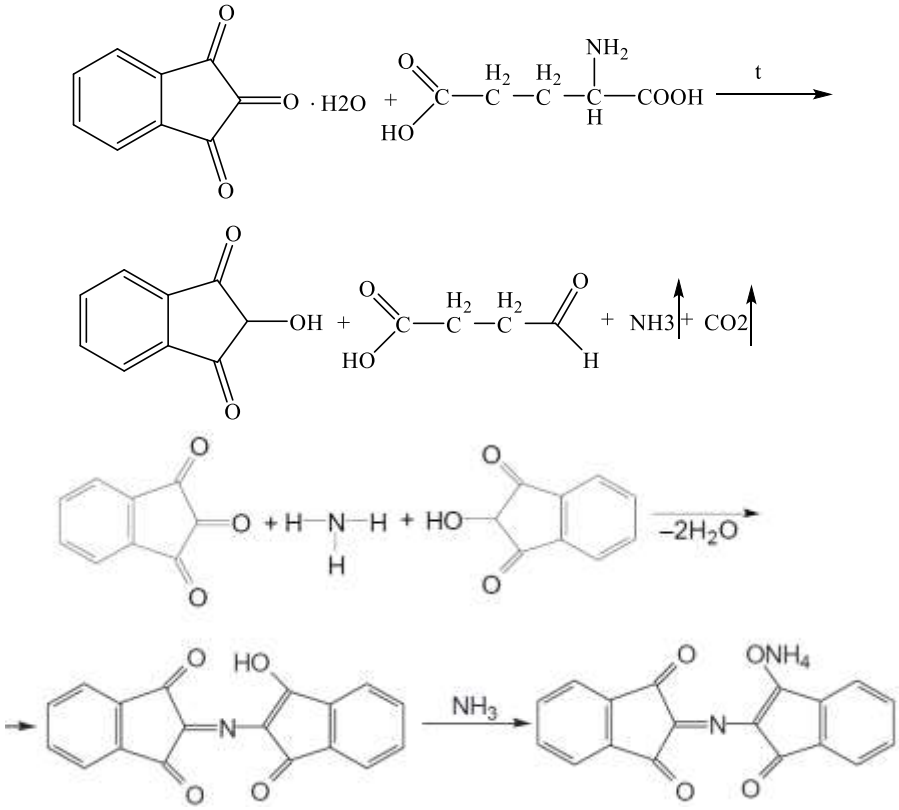
Extraction. Alkaline hydrolysis of pyrrolidone-2 [10, p. 163]:



Properties. White crystalline powder with a weak specific smell, bitter taste. Hygroscopic. Easily soluble in water, very slightly soluble in alcohol, practically insoluble in chloroform, acetone.

Identification: Reaction with ninhydrin.

1. A blue-violet color is formed:

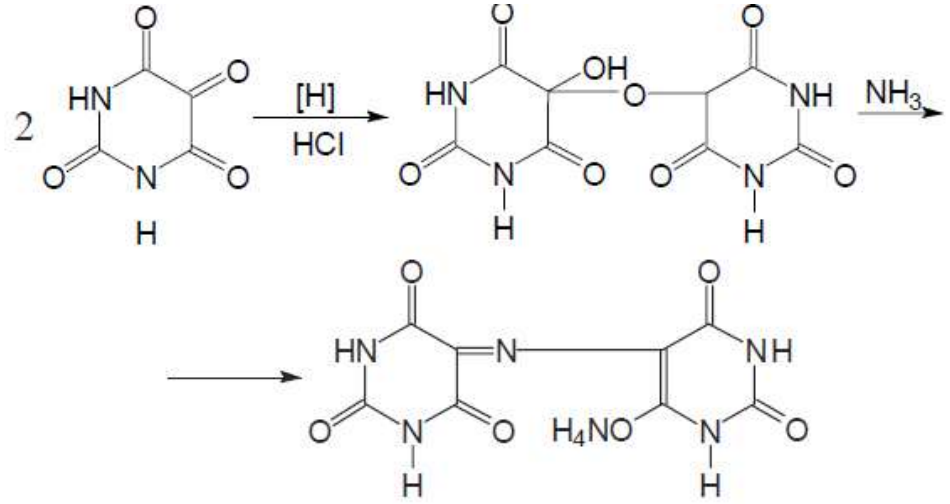


Ammonium salt
Diketohydrindenketohydrinamine

2. When fusing with potassium thiocyanate, hydrogen sulfide is released, which is detected using paper moistened with lead (II) acetate.

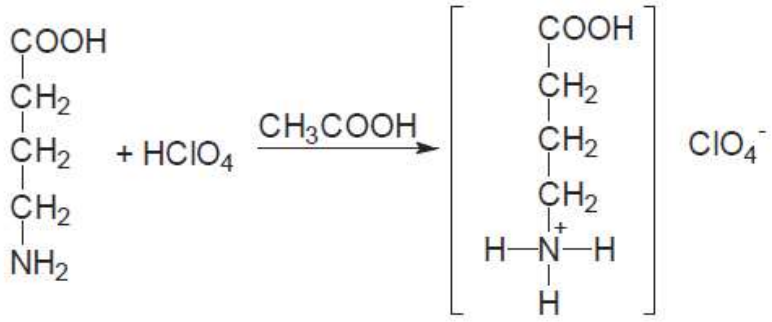
$$H_2S + (CH_3COO)_2Pb \rightarrow PbS\downarrow + 2CH_3COOH$$

3. When a mixture of aminalon and alloxan is heated in an environment of dimethylformamide, a bright crimson color is formed [10, p. 163]:



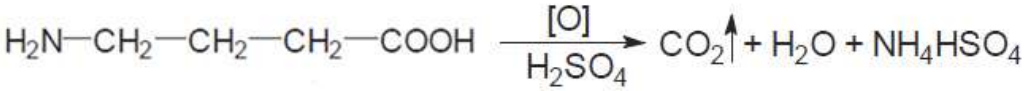
Quantitative determination:

1. Acidimetry in a non-aqueous environment, direct titration, indicator – crystal violet [10, p. 164]:



2. Determination of nitrogen after mineralization with sulfuric acid.

The method includes two stages: mineralization of organic matter (boiled in a special device in the presence of K_2SO_4, $CuSO_4$, concentrated H_2SO_4 and selenium) and acidimetry [10, p. 164]:



Then add a concentrated NaOH solution:

$$NH_4HSO_4 + 2NaOH \xrightarrow{t^\circ} NH_3\uparrow + 2H_2O + Na_2SO_4$$

The released ammonia is distilled into a receiving flask containing a 0.01 M solution of hydrochloric acid:

$$NH_3 + HCl \rightarrow NH_4Cl$$

The excess of hydrochloric acid is titrated with a 0.01 M solution of sodium hydroxide, using a mixed solution of methyl red as an indicator:

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

The test is repeated using glucose instead of the tested substance (control experiment).

The nitrogen content is calculated according to the formula:

$$nitrogen\ content, \% = \frac{0{,}01401 * (n_1 - n_2)}{m_н}$$

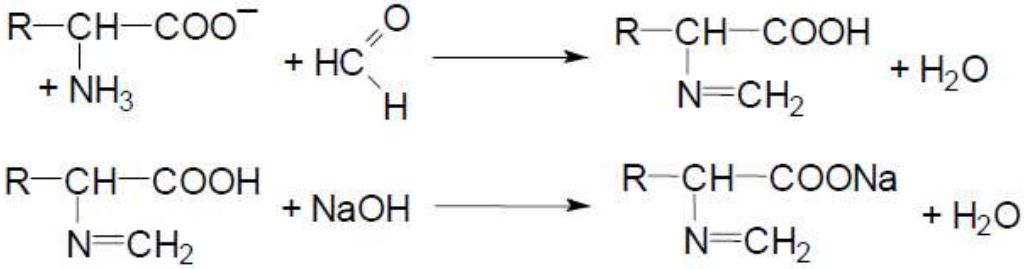
where: n_1 - volume of 0.01 M NaOH in the main experiment, ml;

n_2 - volume of 0.01 M NaOH in the control experiment, ml;

$m_н$ - weight of the tested substance.

3. Alkalimetry according to the Sorensen's method (formal titration).

Titration of amino acids with alkali is difficult because they exist in the form of internal salts, so formalin neutralized by phenolphthalein is added to the solution of amino acids. In this case, an N-methylene derivative is formed, and the liberated carboxyl group can be titrated with sodium hydroxide [10, p. 164]:



Pharmaceutical form. Coated tablets.

Indication. As part of complex treatment of diseases of the central nervous system:

• vascular diseases of the brain (atherosclerosis, damage to cerebral vessels in arterial hypertension);

• chronic insufficiency of cerebral blood circulation with impaired memory, concentration of attention, speech, dizziness, headache;

• encephalopathy (alcoholic, post-stroke, post-traumatic);

• children's cerebral palsy;

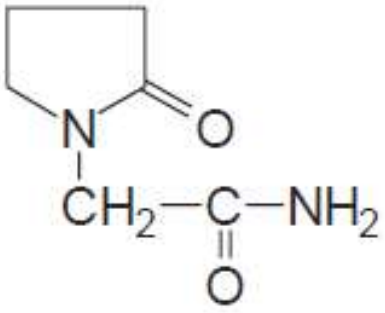
• retardation of mental development in children (aged 5 and over);

• dementia in old age (initial stages of dementia);

• sea and air sickness (for the prevention and treatment of the wavering symptom complex).

Storage conditions. Store in the original packaging at a temperature not higher than 25 ºC. Keep out of the reach of children.

Piracetam (Pyracetamum)
Nootropil



2-(2-Oxopyrrolidin-1-yl)acetamide

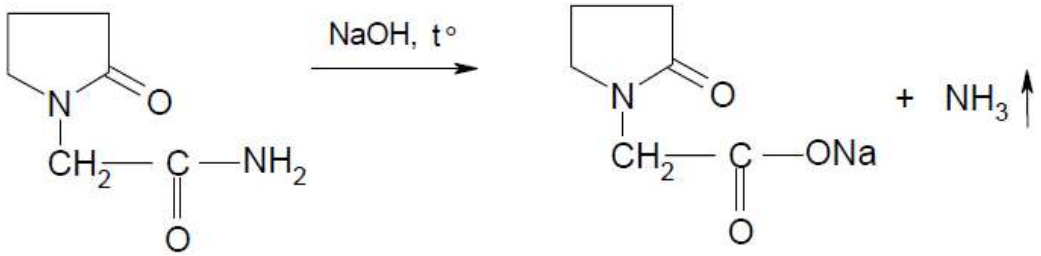
Properties. White crystalline powder, easily soluble in water and ethanol, slightly soluble in chloroform.

Identification:

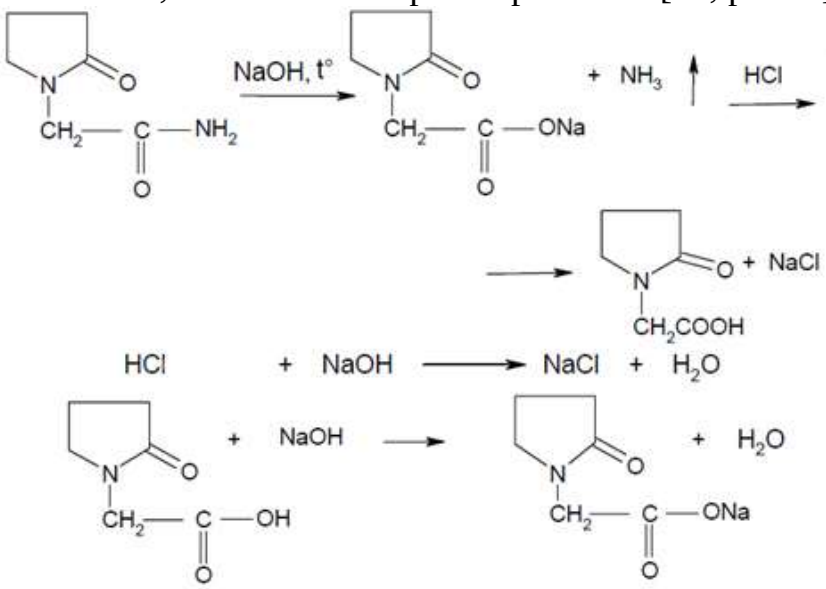
1. IR spectroscopy.

2. Absence of pronounced absorption maxima in the UV spectrum of a 1% aqueous solution in the range of 230–350 nm.

3. Release of ammonia when heated with sodium hydroxide solution [10, p. 306]:



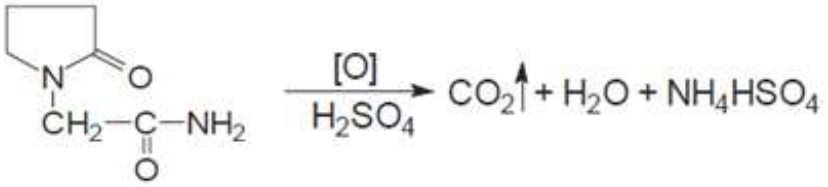
Quantitative determination: according to *Ph. Eur.* alkaline hydrolysis of the substance is carried out beforehand, after which an excess of a titrated solution of hydrochloric acid is added, followed by titration of the reaction mixture with sodium hydroxide solution, the indicator is phenolphthalein [10, p. 306]:



2. Determination of nitrogen in organic compounds.

Determination of nitrogen after mineralization with sulfuric acid.

The method includes two stages: mineralization of organic matter (boiled in a special device in the presence of K_2SO_4, $CuSO_4$, concentrated H_2SO_4 and selenium) and acidimetry [10, p. 306]:



Then add a concentrated NaOH solution:

$$NH_4HSO_4 + 2NaOH \xrightarrow{t^\circ} NH_3 \uparrow + 2H_2O + Na_2SO_4$$

The released ammonia is distilled into a receiving flask containing a 0.01 M solution of hydrochloric acid:

$$NH_3 + HCl \rightarrow NH_4Cl$$

The excess of hydrochloric acid is titrated with a 0.01 M solution of sodium hydroxide, using a mixed solution of methyl red as an indicator:

$$HCl + NaOH \rightarrow NaCl + H_2O$$

The test is repeated using glucose instead of the test substance (control experiment).

The nitrogen content is calculated according to the formula:

$$\text{nitrogen content } \% = \frac{0{,}01401 * (n_1 - n_2)}{m_н}$$

where: n_1 – volume of 0.01 M NaOH in the main experiment, ml;

n_2 – volume of 0.01 M NaOH in the control experiment, ml;

$m_н$ - weight of the tested substance.

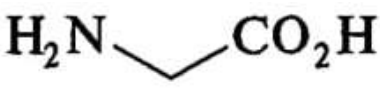
Pharmaceutical form. Film-coated tablets.

Indication. In adults: symptomatic treatment of pathological conditions accompanied by memory impairment, cognitive disorders, with the exception of diagnosed dementia (frailty); treatment of cortical myoclonus: as a monopreparation or as part of complex therapy.

Storage conditions. In the original packaging at a temperature not higher than 25 °C.

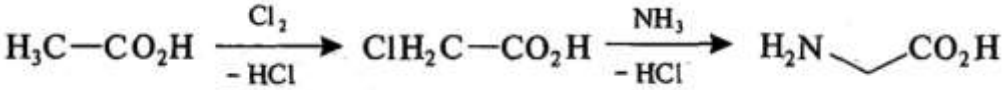
Keep out of the reach of children.

GLYCINE



2-Aminoacetic acid

Extraction. It is obtained by acid hydrolysis of animal glue or by synthesis through halogen acids [10, p. 154]:

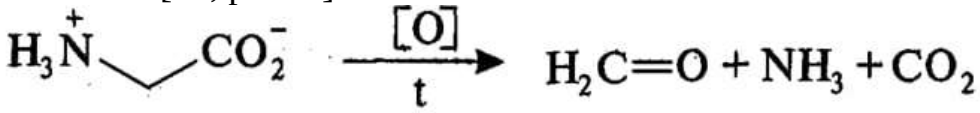


Properties: White crystalline powder, easily soluble in water, poorly soluble in ethanol. Melting point = 232 - 236 °C with decomposition.

Identification: the IR absorption spectrum of the substance must correspond to the IR spectrum of glycine pharmaceutical standard sample.

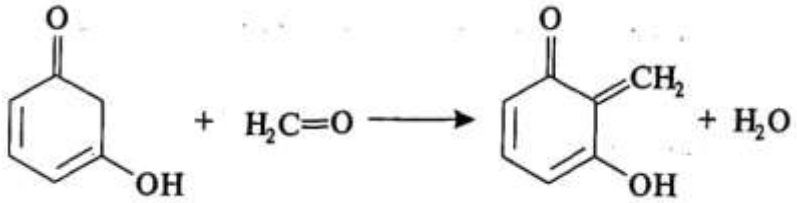
Method of thin-layer chromatography in the solvent system: concentrated ammonia solution - propanol (30:70), detect using a mixture: ninhydrin solution - diluted acetic acid - butanol (1:5:95).

Oxidative decarboxylation of the drug under the action of NaOCl during heating is carried out [10, p. 155]:



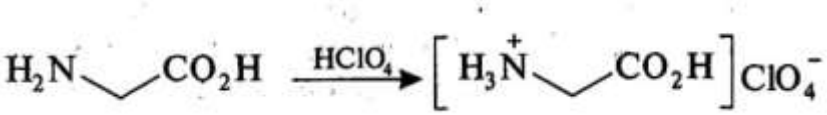
The released formaldehyde reacts in an alkaline environment with the keto-form of resorcinol to form a product that colors the solution purple with a greenish-yellow fluorescence:

After a few minutes, the color changes to orange with yellow fluorescence [10, p. 155].



Purity test: Determine chlorides, heavy metals, loss in mass during drying, sulfated ash.

Quantitative determination: titrate with a 0.1 M perchloric acid solution with potentiometric fixation of the end point of the titration [10, p. 155]:



1 sublingual tablet contains glycine 100 mg;

excipients: povidone, montan glycol wax, ammonium methacrylate copolymer (type A), calcium stearate.

Pharmaceutical form. Sublingual tablets.

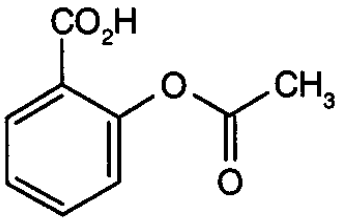
Indication. Decreased mental capacity. In stressful situations and psycho-emotional tension (during exams, in conflict situations). Deviant forms of behavior of children and adults. Functional and organic diseases of the nervous system (neuroses, neurosis-like states, vegetative-vascular dystonias, consequences of neuroinfection and brain injury, perinatal and other forms of encephalopathy, including alcoholic genesis), which are accompanied by increased excitability, emotional instability, decreased mental capacity, sleep disturbance. Ischemic stroke and impaired cerebral circulation.

As an aid in the treatment of alcoholism.

Storage conditions. Store in the original packaging in a place inaccessible to children at a temperature not higher than 25 °C.

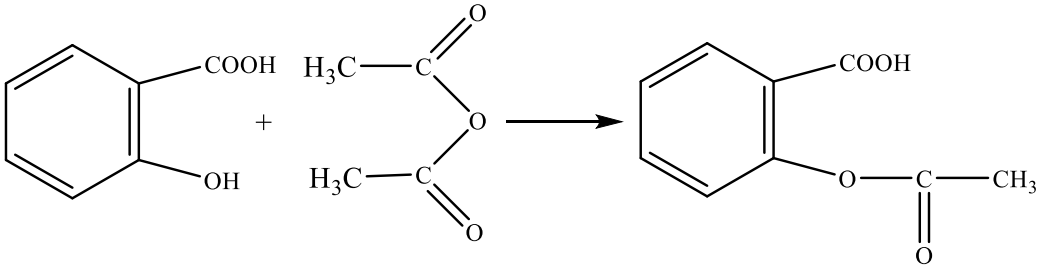
III. ANALYSIS OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS

Acetylsalicylic acid - Acidum acetylsalicylicum (SPhU)

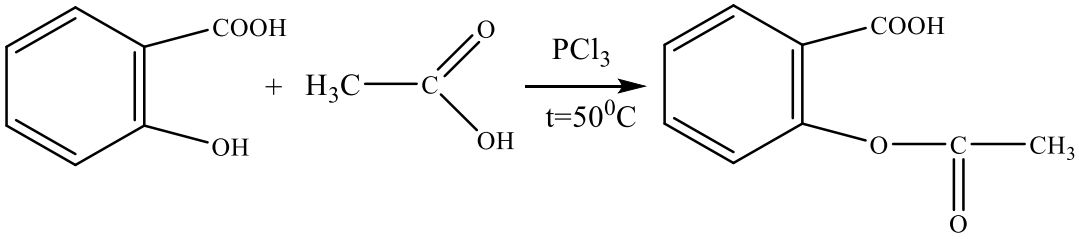


2-(Acetoxy)benzoic acid

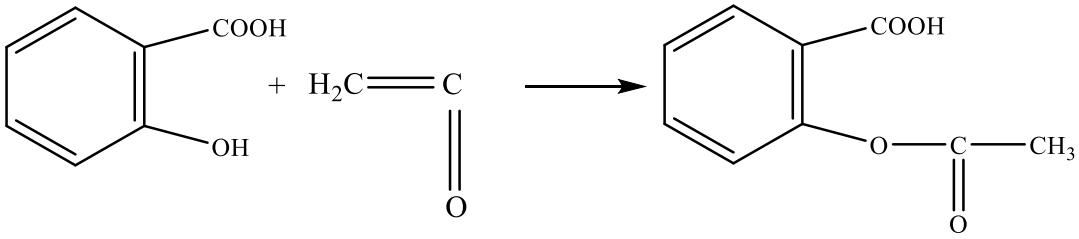
Extraction: Acetylation of salicylic acid with acetic anhydride:



Acetylation of salicylic acid with acetic acid in the presence of phosphorus trichloride:



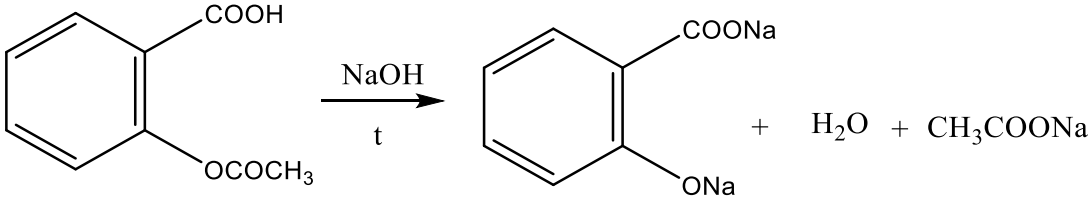
The interaction of salicylic acid with ketene:



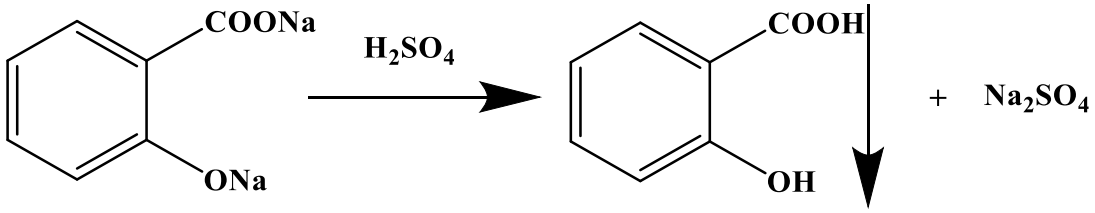
Properties. White crystalline powder or colorless crystals. The drug is stable in dry air, in wet air it is gradually hydrolyzed with the formation of acetic and salicylic acids. Sparingly soluble in water, easily soluble in 96% alcohol, soluble in ether, solutions of alkali metal hydroxides and carbonates.

Identification: IR spectroscopy.

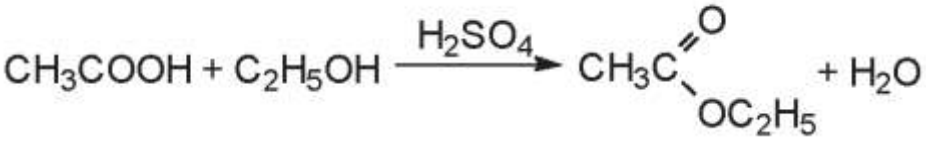
The medicinal product is subjected to alkaline hydrolysis:



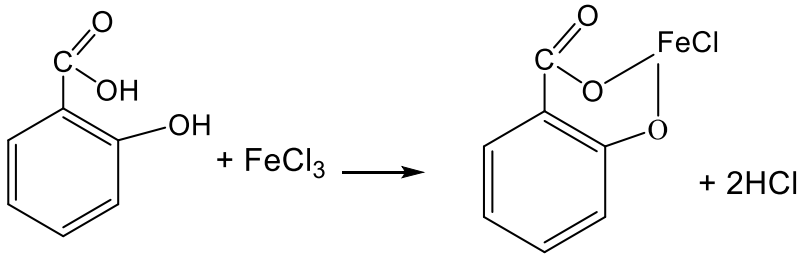
Then it is acidified with dilute sulfuric acid - the formation of a white crystalline precipitate of salicylic acid is observed, which is identified by its melting point (SPhU):



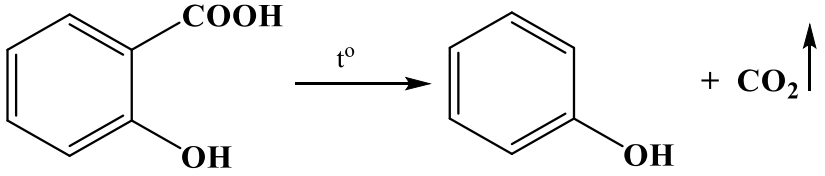
The reaction mixture is filtered, alcohol and concentrated sulfuric acid are added to the filtrate: acetic ethyl ester is formed, which has a characteristic odor (non-pharmacopoeial reaction):



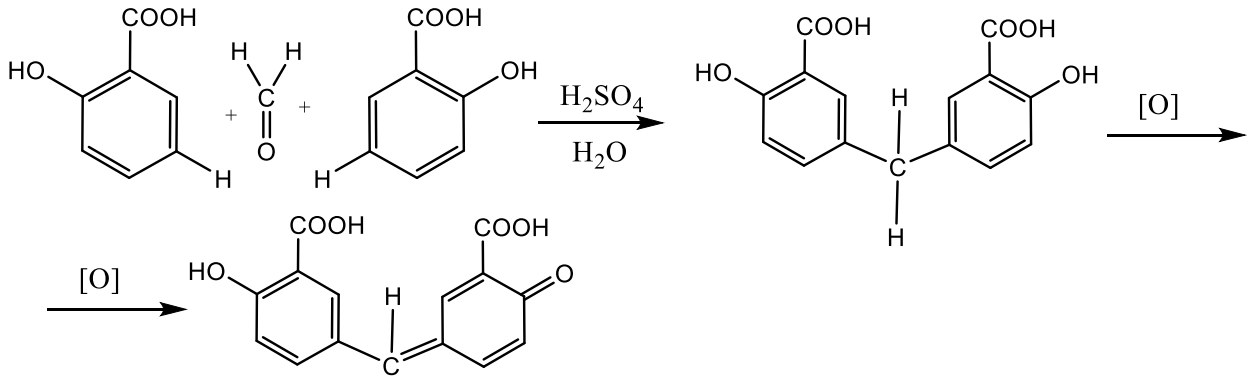
Salicylic acid contained in the precipitate is identified with a solution of ferrum (III) chloride by the appearance of a purple color (SPhU).



When salicylic acid is heated above 160 °C, its decarboxylation occurs with the formation of phenol (smell). To prevent sublimation, the reaction is carried out in the presence of salts of organic acids (sodium citrate):



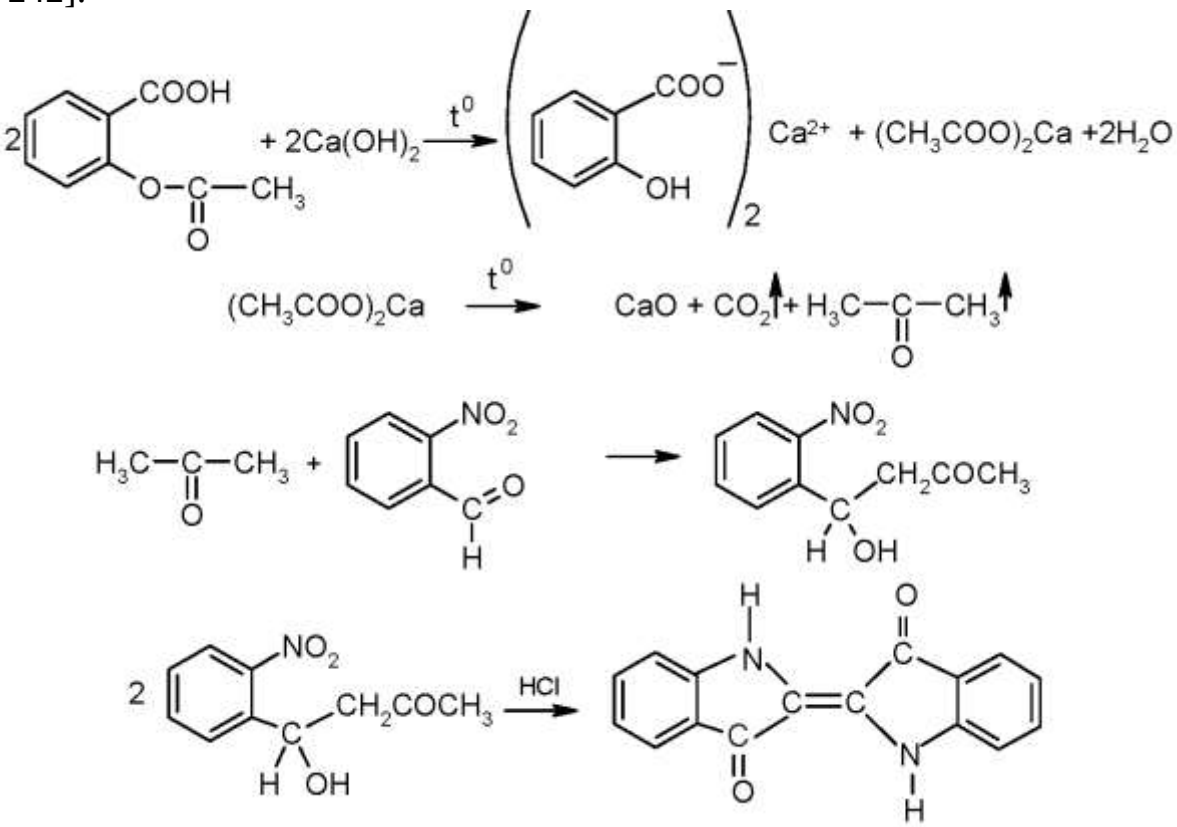
The reaction of the formation of an auric dye with a formaldehyde solution in the presence of concentrated sulfuric acid (Marquis reagent):



Purity test. During the synthesis of salicylic acid, small amounts of oxydiphenyl may be formed:

The drug substance is dissolved in sodium carbonate solution, in which hydroxydiphenyl does not dissolve, it is extracted with ether, the ether layer is separated, evaporated, and the residue is weighed.

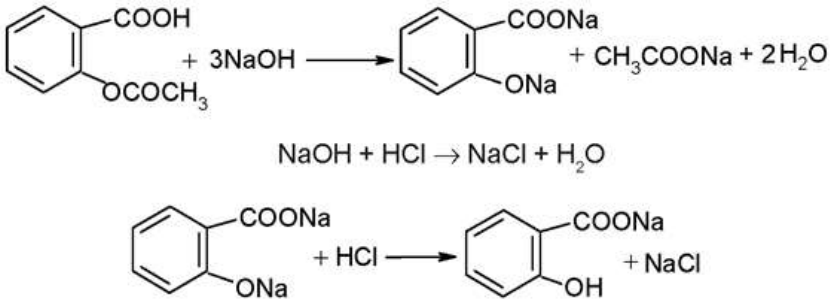
When calcined with calcium hydroxide, acetone is formed, the vapors of which color the filter paper moistened with *o*-nitrobenzaldehyde yellow-green, blue-green, and when moistened with a solution of hydrochloric acid - blue (SPhU) [10, p. 242]:



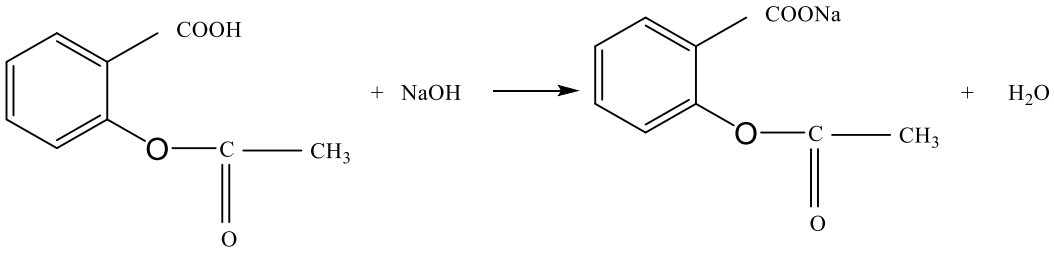
Non-pharmacopoeial reaction: acid hydrolysis. When concentrated sulfuric acid is added, the smell of acetic acid appears. If you then add a formaldehyde solution to the mixture, a pink color (salicylic acid) appears.

Quantitative definition:

Alkalimetry, reverse titration (SPhU). The method is based on the saponification of the substance with a solution of sodium hydroxide, the excess of which is titrated with hydrochloric acid (the indicator is phenolphthalein); s = 1/2. In parallel, a control experiment is conducted [10, p. 243]:



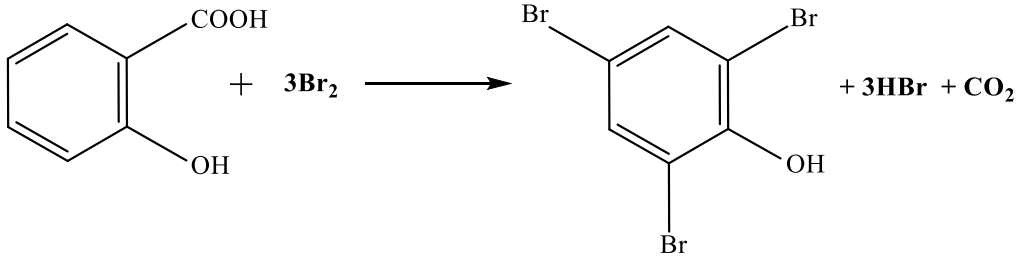
Alkalimetry, direct titration in phenolphthalein-neutralized alcohol:



At a temperature above 20 °C, the drug substance can be partially hydrolyzed.

Bromatometry after hydrolysis.

- **$KBrO_3 + 5KBr + 3H_2S0_4 \rightarrow 3Br_2 + 3H_20 + 3K_2S0_4$**



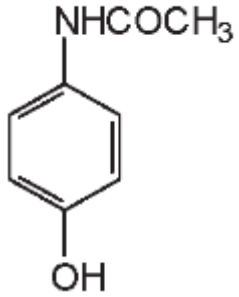
$$Br_2 + 2KI \longrightarrow I_2 + 2KBr$$

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

Storage. In a sealed container.

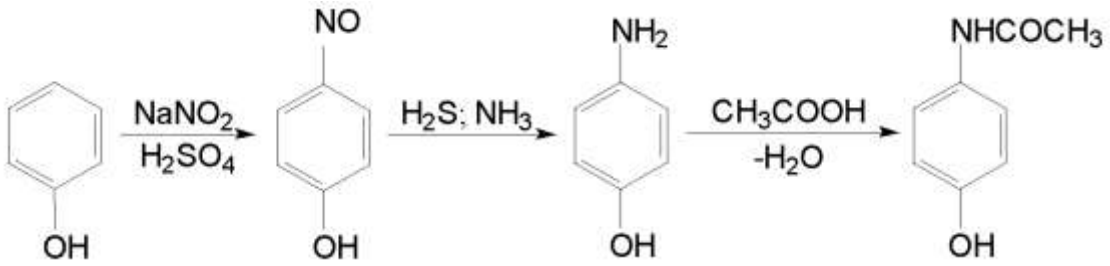
Use. Antirheumatic, anti-inflammatory, antipyretic, pain reliever, as well as to prevent the formation of blood clots, in case of thrombosis of retinal vessels, violation of cerebral blood circulation, to prevent complications and reduce angina attacks in ischemic heart disease.

Paracetamol (Paracetamolum) (SPhU)



N-(4- Hydroxyphenyl)acetamide

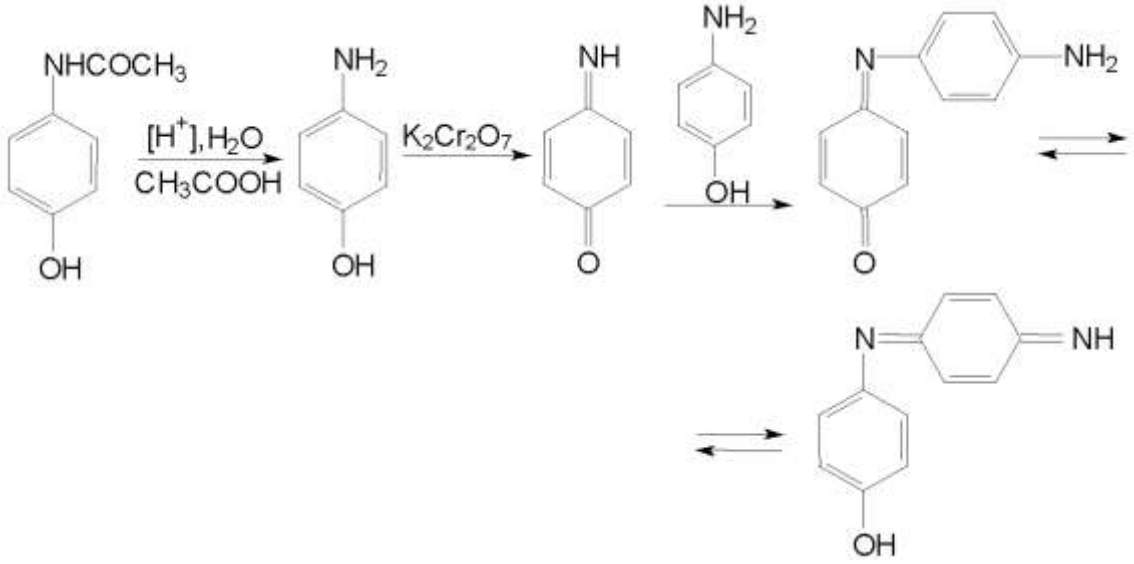
Extraction. Phenol is nitrosated with sodium nitrite in an acidic environment. The formed p-nitrosophenol is reduced with hydrogen sulfide in an ammonia environment to p-aminophenol, which is acetylated [10, p. 227]:



Properties. White crystalline powder. Moderately soluble in water, easily soluble in 96% alcohol, very slightly soluble in methylene chloride. Due to phenolic hydroxyl, it dissolves in alkalis.

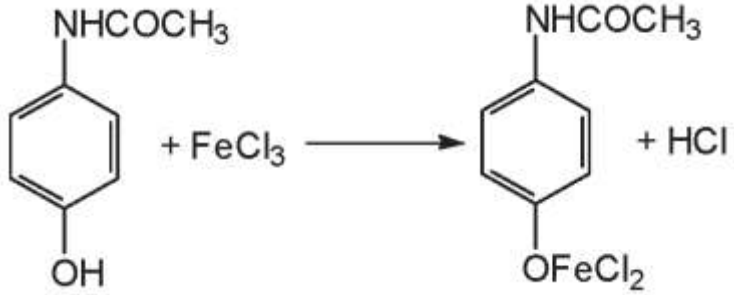
Identification: Physico-chemical methods: melting point, UV and IR spectroscopy.

During acid hydrolysis, *n*-aminophenol is formed, which is oxidized by potassium dichromate to indophenol of violet color, which does not turn red [10, p. 227]:

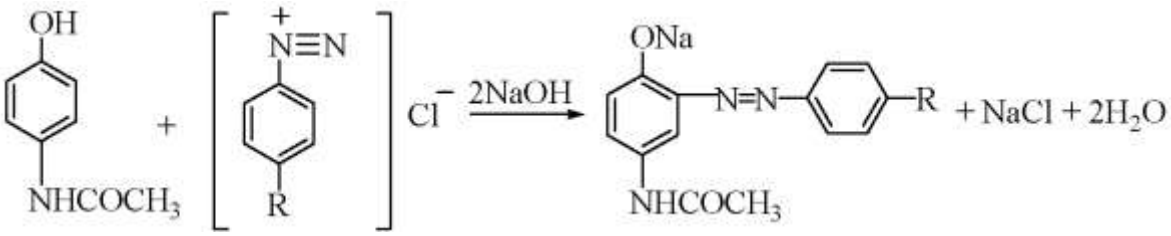


The substance reacts with acetyl. Heating is carried out over an open flame.

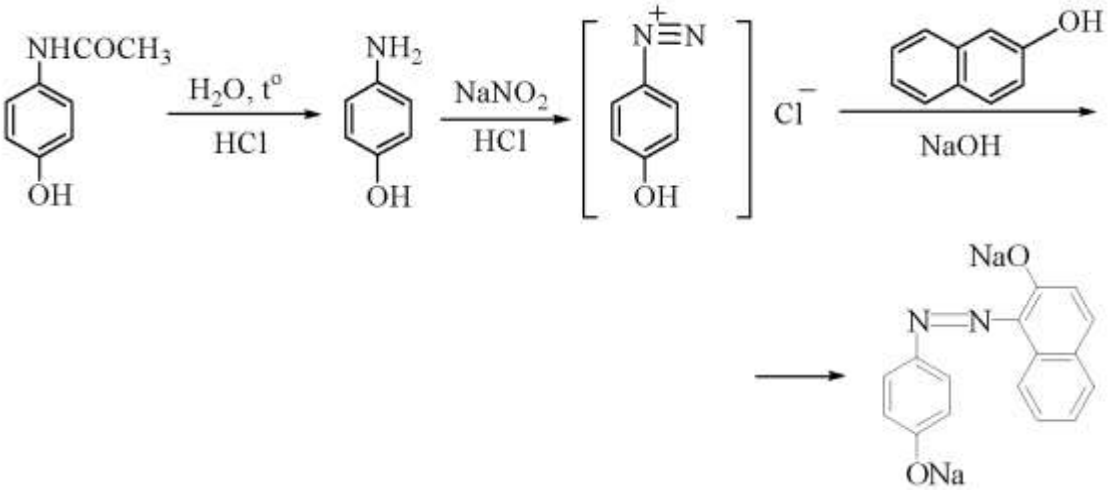
Non-pharmacopoeial reactions: a) with a solution of ferrum (III) chloride, a blue-violet color is formed [10, p. 228]:



b) the presence of phenolic hydroxyl in the molecule causes the reaction of paracetamol with diazonium salts - a red azo dye is formed [10, p. 228]:

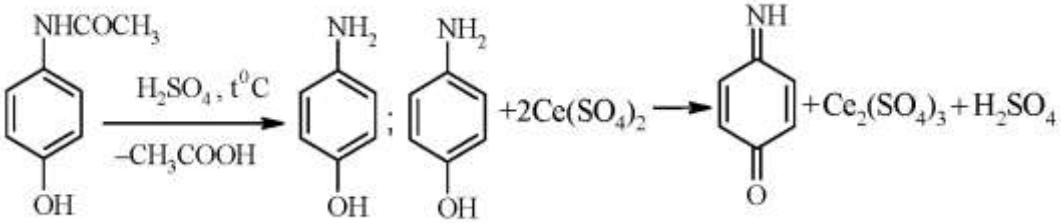


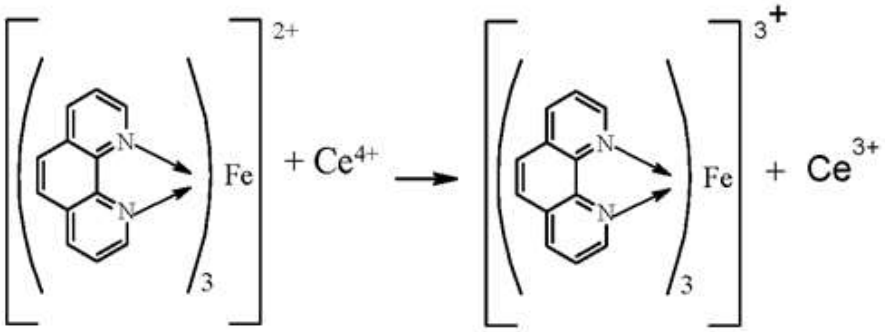
c) after acid hydrolysis, during which the primary aromatic amino group is formed, the drug substance gives a diazotization reaction with the following azo compound [10, p. 228]:



Quantitative definition:

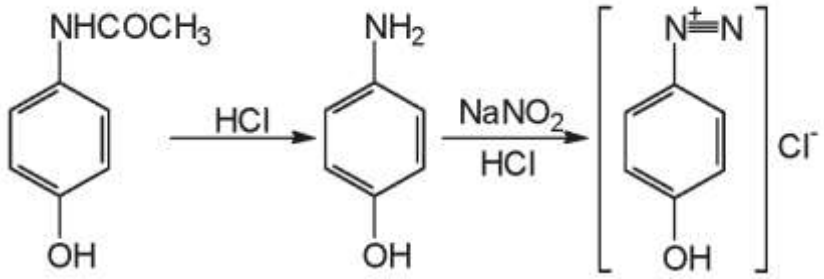
Cerimetry (SPhU) after preliminary hydrolysis of the substance with dilute sulfuric acid. The formed *n*-aminophenol is titrated with a solution of cerium (IV) sulfate, the indicator is ferroin. In parallel, a control experiment is conducted [10, p. 229]:





red coloring blue coloring

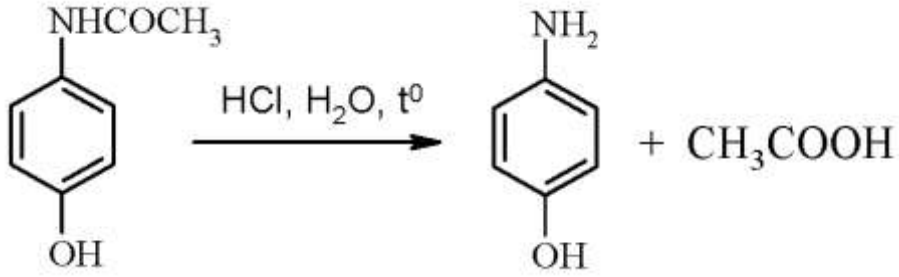
Nitritometry after hydrolysis of the drug substance, direct titration, indicator - iodine-starch paper [10, p. 229]:



The equivalence point is determined by the blue color of iodine-starch paper from an excess drop of titrant:

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

Alkalimetry, direct titration after acid hydrolysis, indicator - phenolphthalein, s = 1. In parallel, a control experiment is carried out [10, p. 229]:



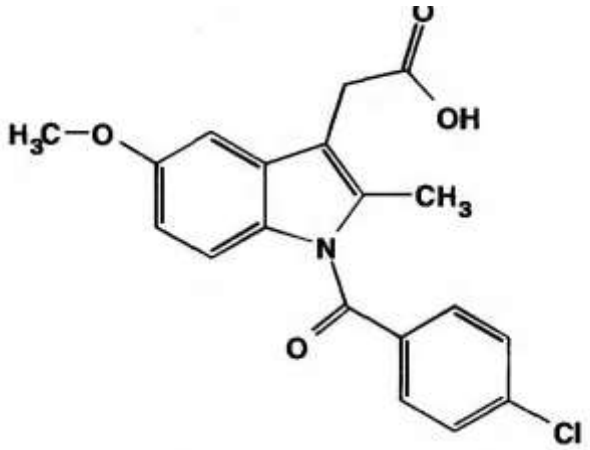
$$CH_3COOH + NaOH \rightarrow CH_3COONa + H_2O$$

$$HCl + NaOH \rightarrow NaCl + H_2O$$

Storage. In a sealed container that protects against light.

Use. Antipyretic and pain reliever.

Indometacin

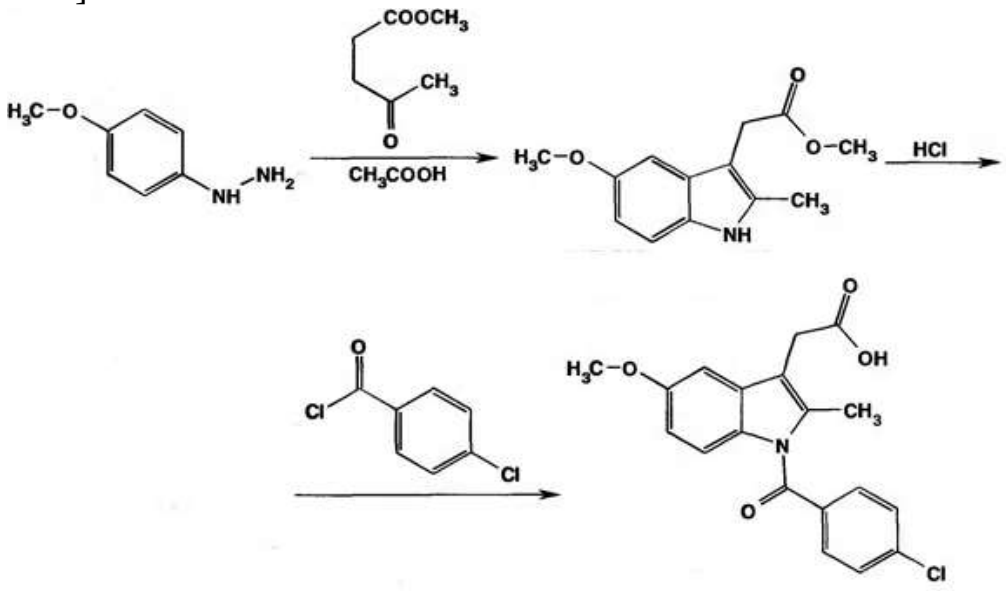


1-(para-chlorobenzoyl)-5-methoxy-2-methylindole-3-acetic acid

Properties. White to yellow crystalline powder. Melting point: 158-162°C. Moderately soluble in chloroform, ether and alkali solutions.

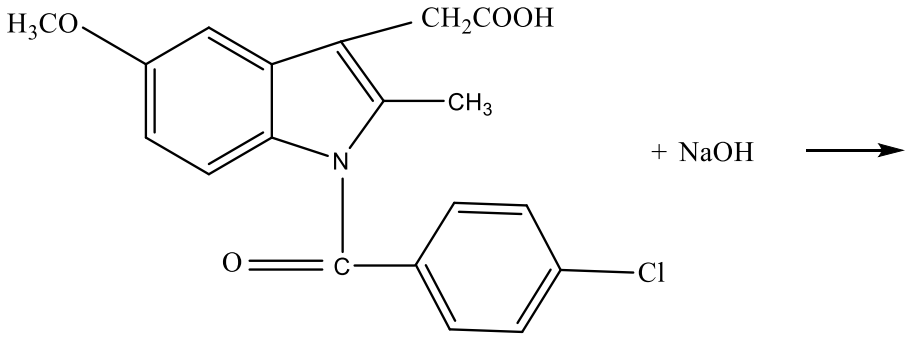
The synthesis of indomethacin is carried out by condensation of i-methoxyphenylhydrazine with methylate of 3-acetylpropionic acid. The resulting

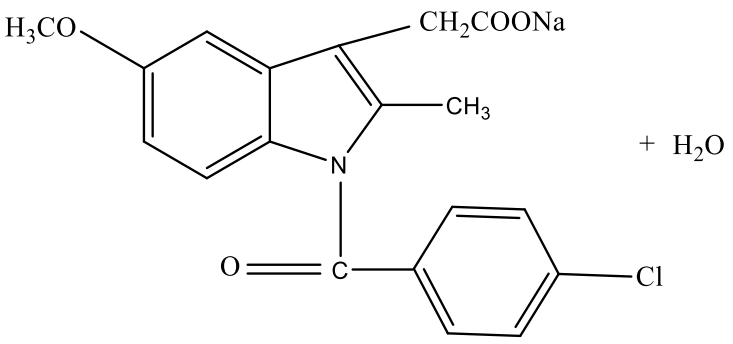
indoleacetic acid ester is hydrolyzed and acylated with p-chlorobenzoyl chloride [10, p. 365]:



IR and UV spectrophotometry are used to test the identity of indolylalkylamines. IR spectra are the most informative. The IR spectrum of indomethacin should match the spectrum of the standard sample or the comparison spectrum of this drug substance. Such tests confirm the presence of the corresponding polymorphic form.

Indomethacin, which is an acid, can be determined by the neutralization method. The sample is dissolved in acetone and titrated with a 0.1 M solution of sodium hydroxide (phenolphthalein indicator). Control titration of solvents is carried out in parallel.





There is a known method for determining indomethacin by HPLC. Chromatographed using a mobile phase of water-a mixture of mono- and disubstituted sodium hydrogen phosphates in acetonitrile (1:1). It is detected at a wavelength of 254 nm. standard solution - Standard sample solution of indomethacin.

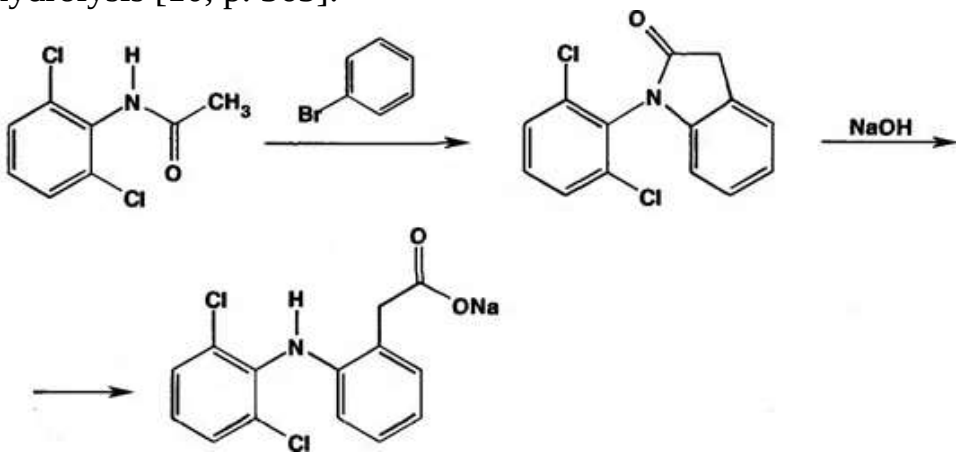
Indomethacin is stored according to list B at room temperature in a place protected from light.

Indomethacin is one of the most active non-steroidal analgesic and anti-inflammatory drugs. It is used to treat diseases associated with inflammatory processes and is prescribed internally in the form of tablets, capsules and dragees of 0.025 g, suppositories of 0.05 g and 10% ointment.

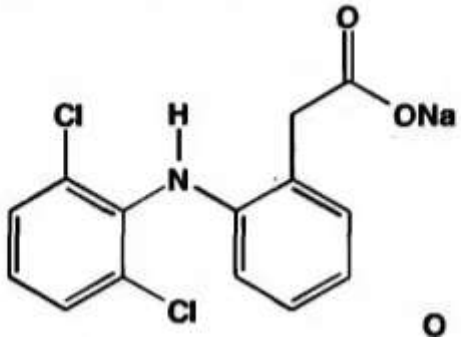
DERIVATIVES OF PHENYLACETIC ACID

Modern nonsteroidal anti-inflammatory drugs include a number of drug substances derived from arylaliphatic acids: phenylacetic acid (I) - diclofenac, which is used in the form of a sodium salt.

Diclofenac sodium is synthesized from 2,6-dichloroacetanilide and bromobenzene. The resulting N-(2,6-dichloro-phenyl)-indolinone-2 is subjected to alkaline hydrolysis [10, p. 365]:



Diclofenac Sodium (Ortofen)



sodium salt of 2-[(2,6-dichlorophenyl)-amino]-phenylacetic acid

Properties. White or almost white crystalline powder. Slightly soluble in water, easily - in ethanol and methanol, practically insoluble in chloroform.

Identification. IR spectra, the absorption bands of the tested solutions should fully correspond to the IR spectra of standard solutions in the region of 4000-400 cm'1.

Identity is established using UV spectra.

Under the action of concentrated sulfuric acid, diclofenac sodium crystals acquire a crimson color (the reaction is carried out on an glass slide). Colored oxidation products are produced by the action of solutions of potassium dichromate, sodium nitrite, potassium permanganate, potassium iodate in the same acid. Marquis reagent forms a green-white ring when layered on a solution of diclofenac sodium in concentrated sulfuric acid.

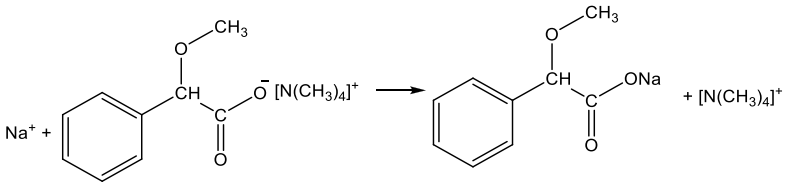
Diclofenac sodium gives a characteristic reaction to sodium ion and to chlorides in the filtrate (after ignition in a crucible and dissolving the contents in water).

1. The sodium cation according to the requirements of SPU is determined using a solution of potassium pyroantimonate (potassium hexahydroxostibiate) resulting in a white precipitate.

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

The reaction should be carried out in a slightly alkaline environment

2. Sodium salts with methoxyphenylacetic acid reagent P in chilled ice water form a white crystalline precipitate that does not disappear at room temperature:



3. The sodium salt is moistened with concentrated hydrochloric acid to form volatile sodium salts, which turn the colorless flame of the burner yellow

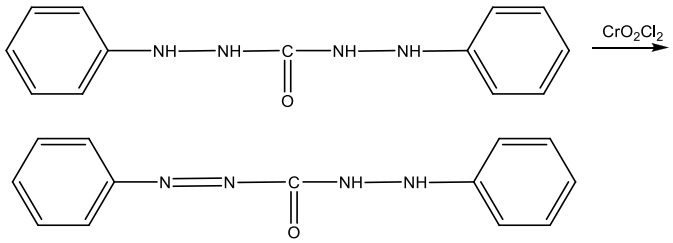
4. Reaction with a solution of silver nitrate in nitric acid medium, a white cheesy precipitate is formed. The precipitate is insoluble in dilute acids, soluble in ammonia solution:

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

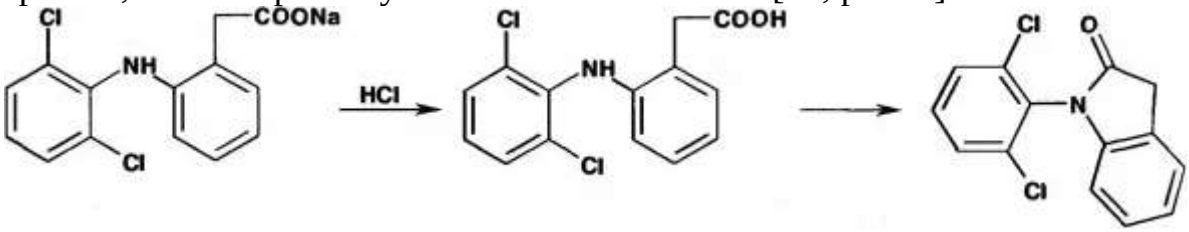
$$AgCl\downarrow + 2NH_4OH \rightarrow [Ag(NH_3)_2]Cl + 2H_2O.$$

5. 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:

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



When dilute hydrochloric acid is added to an aqueous solution of sodium diclofenac, a white precipitate of 2-[2,6-(dichlorophenyl)-amino]-phenylacetic acid is precipitated, which is partially converted to indolinone [10, p. 268]:



When testing for the purity of diclofenac sodium, the presence of impurities of intermediate synthesis products: [2-(2,6-dichlorophenyl)-amino]phenylacetic acid and N-(2,6-dichlorophenyl)indolinone-2 is determined by HPLC. The mobile phase is used: methanol-0.1% solution of orthophosphoric acid (6:4), the detector is a spectrophotometer (wavelength 254 nm).

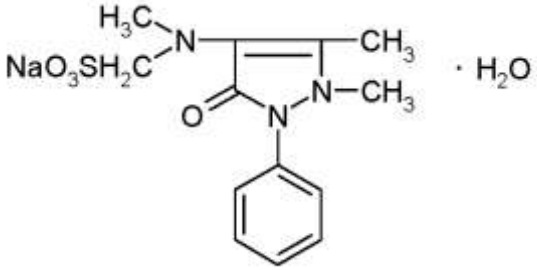
Diclofenac sodium is determined by the method of non-aqueous titration in a glacial acetic acid medium, titrated with a 0.1 M perchloric acid solution (crystal violet indicator). The equivalence point is set potentiometrically.

The drug substance is stored according to list B, in a dry, light-protected place at room temperature, in a well-closed container.

Diclofenac sodium has anti-inflammatory, analgesic, antipyretic activity. It is used for rheumatoid and other arthritis, arthrosis, as well as for pain syndrome (neuralgia, myalgia).

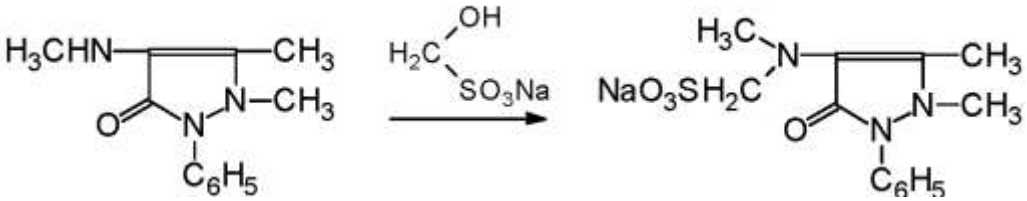
Diclofenac sodium is released in the form of tablets of 0.025 g, retard tablets of 0.1 g; 2.5% solutions in ampoules of 5 ml, gels and ointments for external use.

Metamizole sodium salt (Metamizolum natricum) (SPhU)
Analgin (Analginum) Metamizole Sodium



[(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-N-methylamino]methanesulfonate

Extraction. It is carried out according to the following schemeм [10, p. 313]:



monomethylaminoantipyrine metamizole sodium salt

Properties. Crystalline powder of white or almost white color. Decomposes in the presence of moisture. Aqueous solutions turn yellow on standing. Very easily soluble in water, soluble in 96% alcohol.

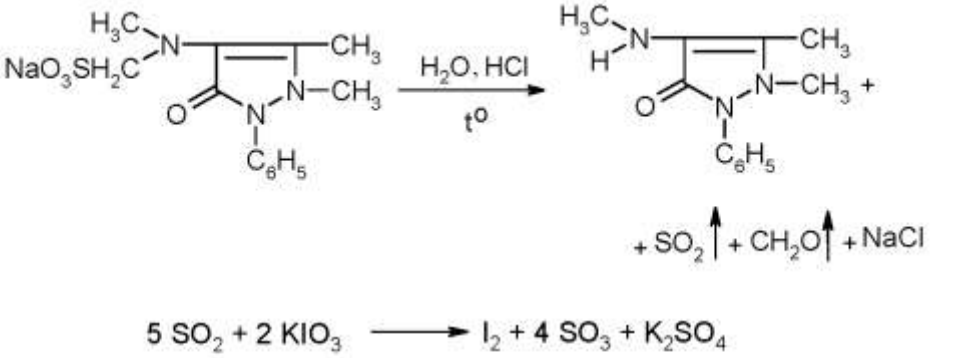
Identification:

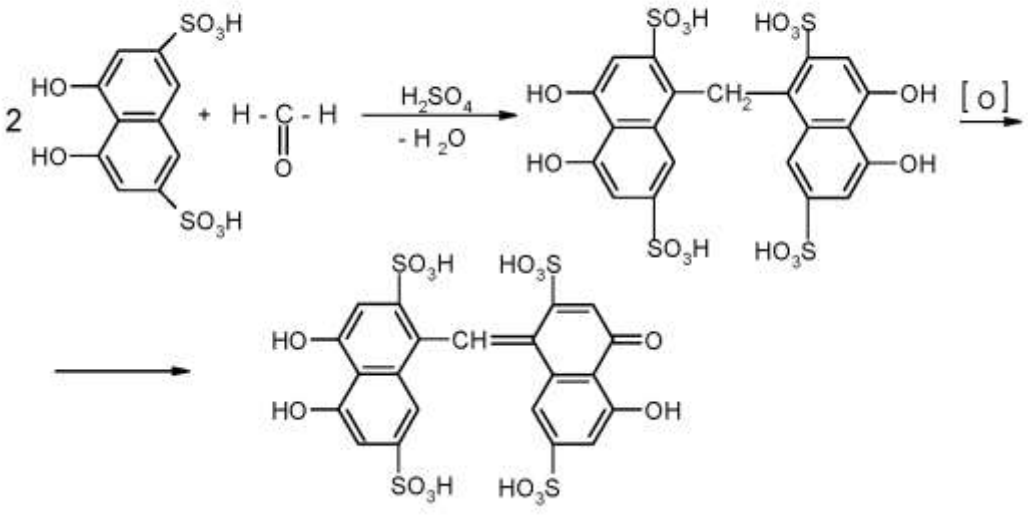
1. IR spectroscopy.

2. The substance with a solution of concentrated hydrogen peroxide gives a blue color, which quickly disappears and turns into intense red after a few minutes.

With other oxidants ($FeCl_3$, chlorinated lime, concentrated HNO_3), analgin also forms colored oxidation products.

3. The acidified solution of the substance is carefully heated. The test tube is covered with filter paper soaked in potassium iodide solution and starch solution. The sulfur (IV) oxide vapors released turn the filter paper blue. Formaldehyde released with a solution of the sodium salt of chromotropic acid in sulfuric acid gives a blue-violet color [10, p. 313]:





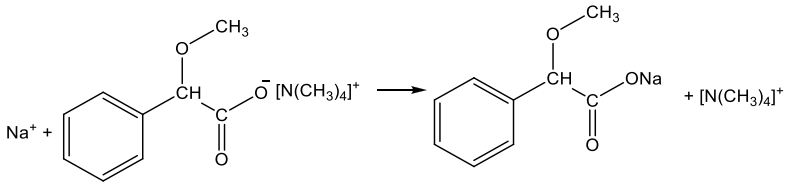
4. The substance reacts to sodium ions.

A) The sodium cation according to the requirements of SPU is determined using a solution of potassium pyroantimonate (potassium hexahydroxostibiate) resulting in a white precipitate.

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

The reaction should be carried out in a slightly alkaline environment

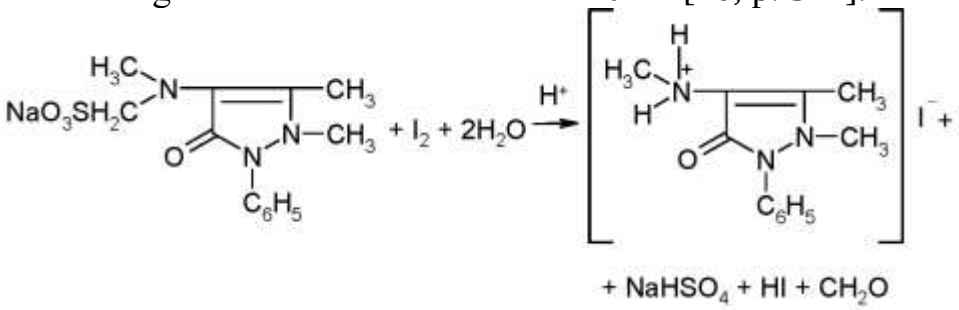
B) Sodium salts with methoxyphenylacetic acid reagent P in chilled ice water form a white crystalline precipitate that does not disappear at room temperature:



C) The sodium salt is moistened with concentrated hydrochloric acid to form volatile sodium salts, which turn the colorless flame of the burner yellow

5. Non-pharmacopoeial reaction. An acidified alcoholic solution of the substance turns crimson (oxidation intermediates) upon addition of a potassium iodate solution, and upon further addition of the reagent, the color intensifies and a brown precipitate of iodine is released.

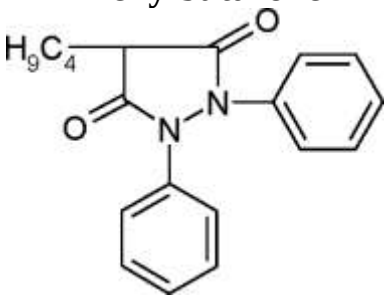
Quantitative definition. Iodometry (SPhU), direct titration, indicator – starch. The acidified solution of the substance is titrated with iodine solution until a blue color appears, which does not disappear within 2 minutes. The temperature of the solution during titration should not exceed 10 °C [10, p. 314]:



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

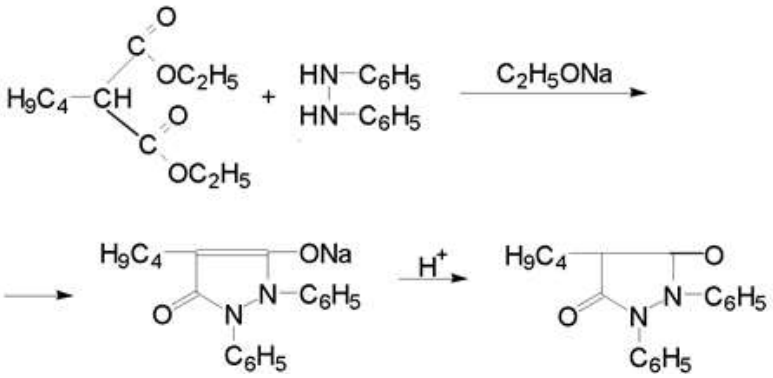
Use. In terms of activity and speed of action, analgin is superior to antipyrine. Its solubility promotes rapid absorption, and also facilitates elimination from the body. It is especially convenient in those cases when it is necessary to urgently create a high concentration of a drug substance in the blood.

Butadione (Butadionum)
Phenylbutazone

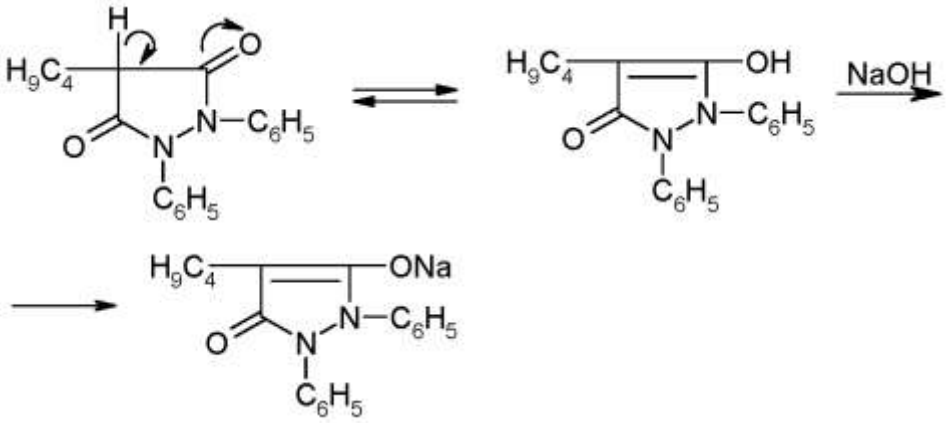


1,2-Diphenyl-4-butylpyrazolidinedione-3,5

Extraction. Condensation of n-butylmalonic ester with hydrazobenzene in the presence of sodium ethylate [10, p. 316]:



Properties. White, sometimes slightly yellowish powder. Practically insoluble in water, sparingly soluble in alcohol, easily soluble in sodium hydroxide solution, chloroform, ether and acetone, practically insoluble in dilute acids. The solubility of butadione in hydroxides of alkali metals is explained by its acidic properties due to the ability to keto-enol tautomerism [10, p. 316]:

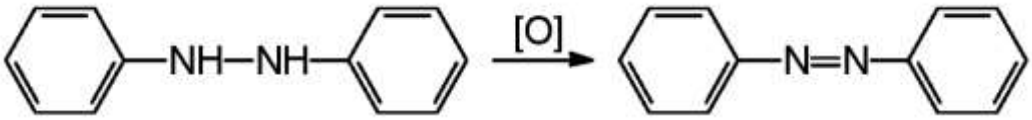


Identification:

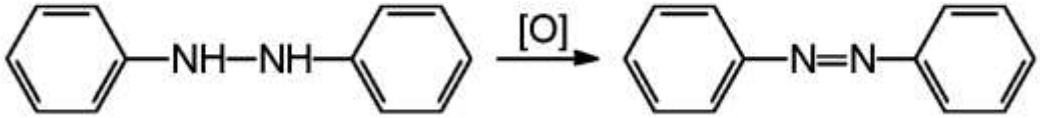
1. Physico-chemical methods: determination of melting point, IR spectroscopy, thin-layer chromatography.

2. After heating the substance with a mixture of concentrated acetic and hydrochloric acids, sodium nitrite is added – a yellow color appears. To the resulting solution, add an alkaline solution of β-Naphthol; a brownish-red precipitate is observed.

3. The orange color, which changes to cherry, appears when oxidized with a solution of sodium nitrite in concentrated sulfuric acid. At the same time, the release of gas bubbles is observed. Under harsh conditions, butadione as a hydrazobenzene derivative is oxidized to azobenzene derivatives [10, p. 317]:

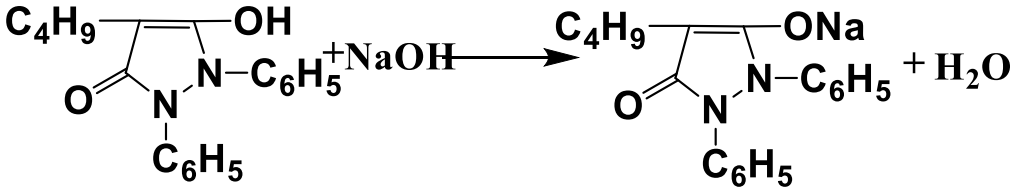


With solutions of salts of heavy metals, the substance forms insoluble colored salts. After neutralization with hydroxides of alkali metals, butadione with a solution of copper (II) sulfate gives a grayish precipitate that turns pale blue [10, p. 317]:



Purity test. Hydrazobenzene is an unacceptable impurity. They are detected by oxidation with a solution of ferrum (III) chloride in concentrated sulfuric acid. A cherry-red color should not appear.

Quantitative definition. Alkalimetry in acetone environment, direct titration, indicator – phenolphthalein.



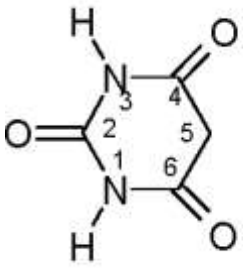
Storage. In a sealed container that protects against light.

Use. Analgesic, anti-inflammatory and antipyretic agent.

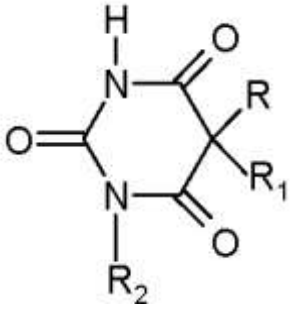
IV. ANALYSIS OF HYPNOTIC DRUGS

Drig substances - derivatives of barbituric acid

The structure of barbituric acid, which can be considered as a cyclic ureide, is based on the pyrimidine cycle. Derivatives of barbituric acid - barbiturates - are used in medicine as hypnotics, sedatives and anticonvulsants.

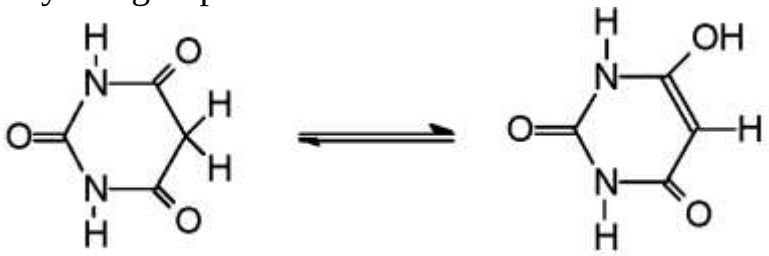


Barbituric acid



Barbiturates (general formula)

The acidic properties of barbituric acid are due to the mobility of hydrogen atoms of methylene and imide groups. In this regard, barbituric acid is characterized by two types of tautomerism: keto-enol, due to the mobility of the hydrogen of the methylene group:



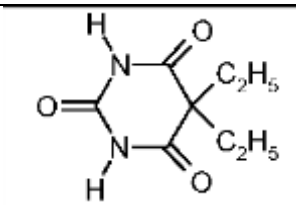
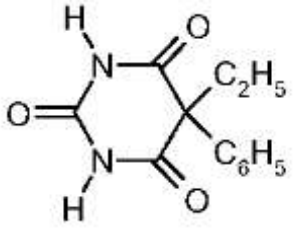
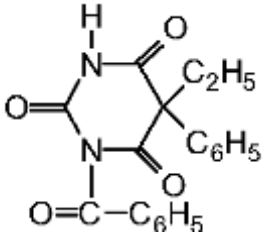
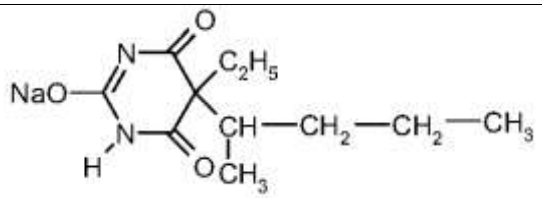
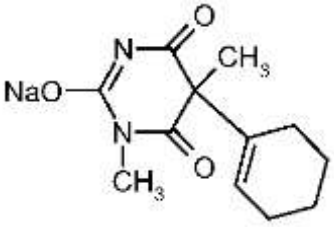
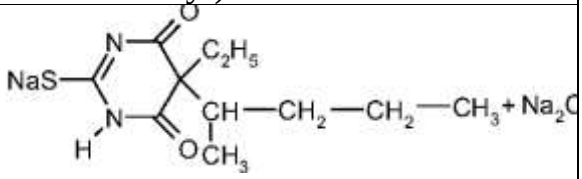
ketone form enol form

lactam-lactim, due to the mobility of the hydrogen of the imide group:

lactam form lactim form

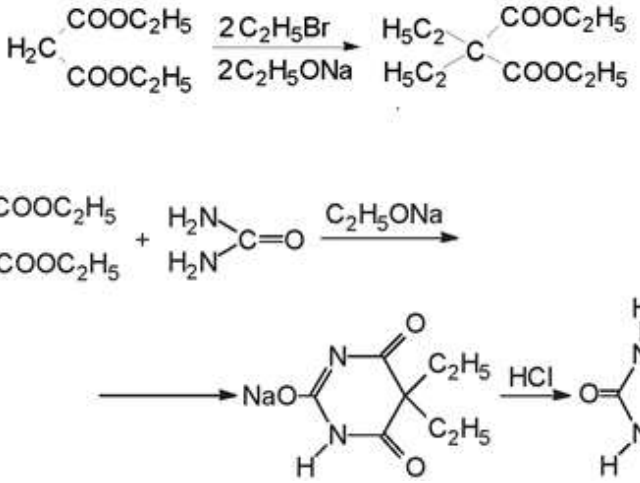
Barbituric acid is 5-6 times stronger than acetic acid. 5-Monosubstituted barbituric acids are also quite strong acids (for example, 5-ethylbarbituric acid), and 5,5-disubstituted (for example, 5,5-diethylbarbituric acid) are very weak acids, weaker than carbonate. The acidic properties of barbiturates make it possible to obtain salt forms that, unlike acid forms, are soluble in water:

Drug substances of the barbiturate group

Drug substance Latin, Ukrainian, international name	Chemical structure, chemical name
Barbitalum Barbital*	 5,5-diethylbarbituric acid
Phenobarbitalum Luminal*	 5-ethyl-5-phenylbarbituric acid
Benzonalum Benzobarbitalum* Benzobarbital*	 1-benzoyl-5-ethyl-5-phenylbarbituric acid
Aethaminalum-natrium Nembutal* Pentobarbitalum Natricum*	 5-ethyl-5-(2'-amyl)-sodium barbiturate
Hexenalum Hexobarbital Sodium* Hexobarbitalum Natricum*	 Sodium 1,5-dimethyl-5-(cyclohexen-1'-yl)-barbiturate
Thiopentalum-natrium Thiopentalum Natricum cum Natrii Carbonate* Thiopental Sodium with Sodium Carbonate*	 mixture of sodium 5-ethyl-5-(2'-amyl)-2-thiobarbiturate with anhydrous sodium carbonate

Extraction. The synthesis of barbituric acid derivatives consists of two stages: obtaining the corresponding malonic acid ester; condensation of the obtained ester with urea in the presence of sodium alkoxide in a solution of absolute alcohol.

As an example, we can cite the barbital synthesis scheme [10, p. 338]:



Properties. White crystalline substances, white foamy mass (hexenal) or dry porous mass of yellowish color with a peculiar smell (thiopental-sodium), bitter to the taste. Acid barbiturates are practically insoluble or very slightly soluble in water, soluble or hardly soluble in alcohol and other organic solvents, easily soluble in alkali solutions. Barbiturates are hygroscopic salts, soluble or easily soluble in water and alcohol, practically insoluble in ether.

Identification:

Physico-chemical methods: determination of the melting point, IR spectroscopy, thin-layer chromatography.

Formation of complex salts with cations of heavy metals:

• argentum nitrate - white precipitate;

• cobalt (II) nitrate in the presence of calcium chloride - blue-violet color and precipitate (group reaction to barbiturates, with the exception of N-substituted ones) (SPhU);

• copper (II) sulfate in the presence of potassium bicarbonate and potassium carbonate (specific reaction):

• barbital - blue color and red-lilac precipitate;

• phenobarbital - a light lilac-colored precipitate that does not change upon standing;

• benzonal - gray-blue color, changing to bright blue, after which a white precipitate falls out;

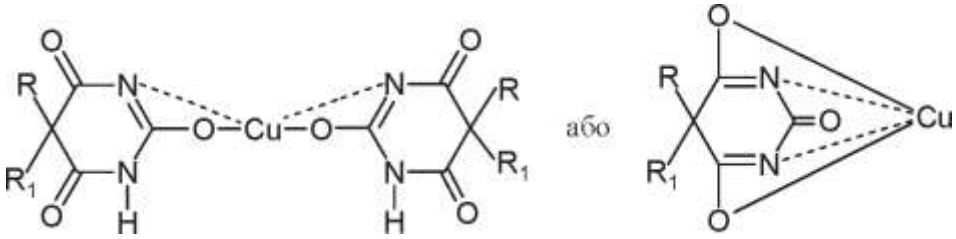
• sodium ethaminal - a blue precipitate;

• hexenal - blue color, changing to bright blue, after which a white precipitate falls out;

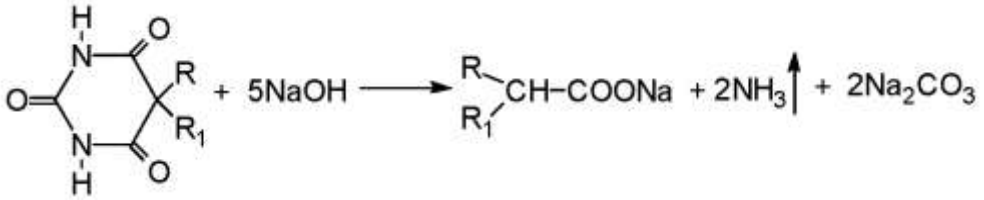
• sodium thiopental - yellow-green color with suspension.

The reactions must be carried out in a neutral environment (to prevent the formation of precipitates of metal hydroxides). Acidic forms are initially neutralized with sodium hydroxide solution.

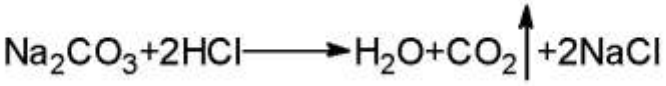
It is assumed that the composition of complexes can be as follows [10, p. 339]:



Fusion reaction with sodium hydroxide with the formation of salts of disubstituted derivatives of acetic acid, ammonia and sodium carbonate [10, p. 339]:



During further acidification, gas bubbles (CO_2) are released and the characteristic smell of acetic acid derivatives is felt [10, p. 339]:

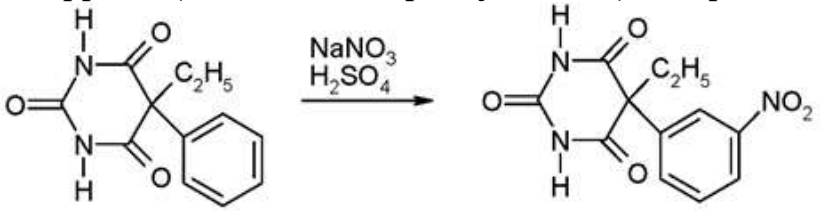


Formation reactions of colored products during condensation: with formaldehyde and concentrated sulfuric acid: phenobarbital, benzonal - pink color; hexenal - dark red with green fluorescence;

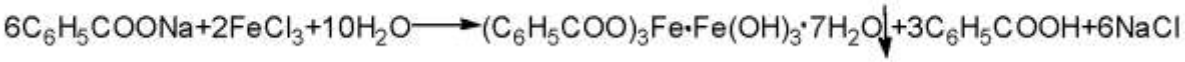
with p-dimethylaminobezaldehyde and concentrated sulfuric acid: ethaminal sodium - cherry-red color; barbital - yellow.

Specific reactions are due to the presence of substituents in positions 1 and 5.

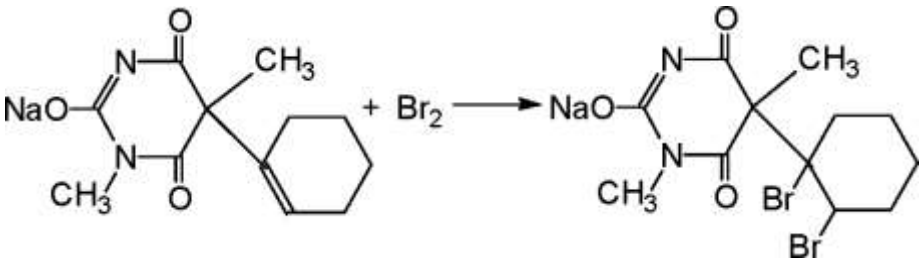
When phenobarbital interacts with sodium nitrate and concentrated sulfuric acid, a yellow color appears (reaction to the phenyl radical) [10, p. 340]:



Benzonal after alkaline hydrolysis gives a reaction to the benzoate ion (from ferrum (III) chloride - a pinkish-yellow precipitate) [10, p. 340].

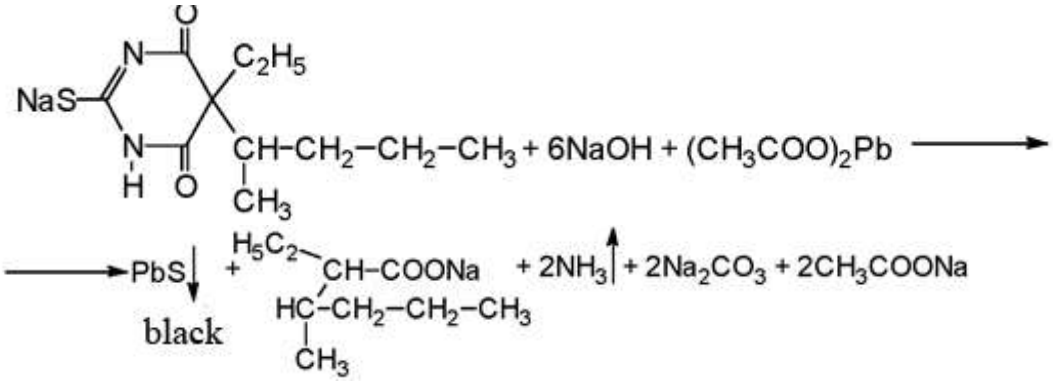


Hexenal decolorizes a solution of potassium permanganate and bromine water (due to the presence of a double bond) [10, p. 340]:



Sulfur in sodium thiopental is detected:

a) when heated with solutions of lead (II) acetate and sodium hydroxide [10, p. 340]:



After acidification, hydrogen sulfide is released:

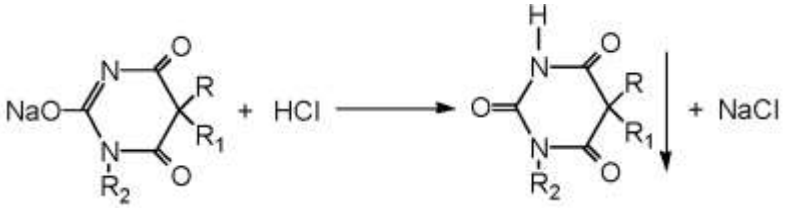
reaction to sulfate ions with barium chloride after dry mineralization with a mixture of sodium carbonate and potassium nitrate, releases a white precipitate of barium sulfate, insoluble in water, mineral acids or alkalis (even when heated).

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

Sodium salts of barbiturates are also identified by:

a) corresponding reactions to sodium;

b) melting point of the acidic form after adding hydrochloric acid [10, p. 341]:



Purity test. In barbital and phenobarbital, in addition to general impurities, an admixture of 5-ethyl- or 5-phenylbarbituric acid, respectively, is determined by acidic properties. Since these acids are stronger than the corresponding barbiturates, when methyl red is added, the solution should be red-orange (but not red).

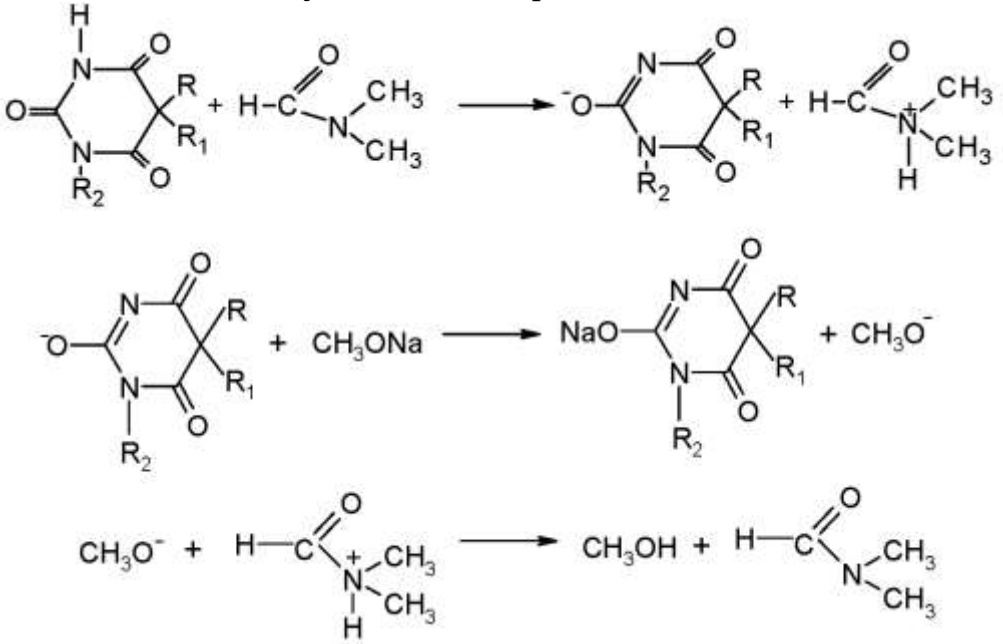
In salt forms of barbiturates, allowable impurities are determined:

free alkali (by titration with hydrochloric acid, indicator - thymolphthalein);

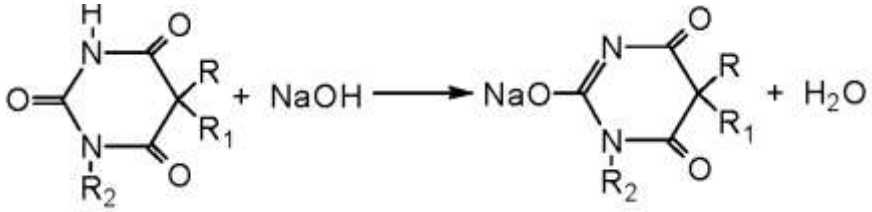
methyl alcohol by reaction with chromotropic acid (see metamizole sodium salt).

Quantitative definition: Acid-base titration:

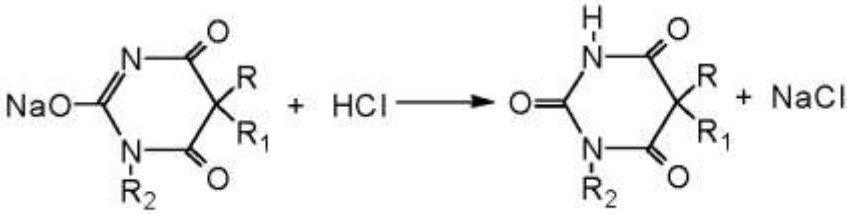
a) alkalimetry in a non-aqueous environment for acid forms of barbiturates. The weight of the substance is dissolved in dimethylformamide (DMF) or a mixture of dimethylformamide and benzene, neutralized by thymol blue (strengthens the acidic properties of barbiturate) and titrated with a solution of sodium methylate or a solution of sodium hydroxide in a mixture of methanol and benzene, the indicator is thymol blue [10, p. 343]:



b) alkalimetry in a water-alcohol environment for acid forms of barbiturates. The sample is dissolved in thymolphthalein-neutralized alcohol to improve the solubility of barbiturates and reduce the hydrolysis of their salts [10, p. 343]:



acidimetry in an aqueous environment for sodium salts of barbiturates, indicator - methyl orange [10, p. 343]:



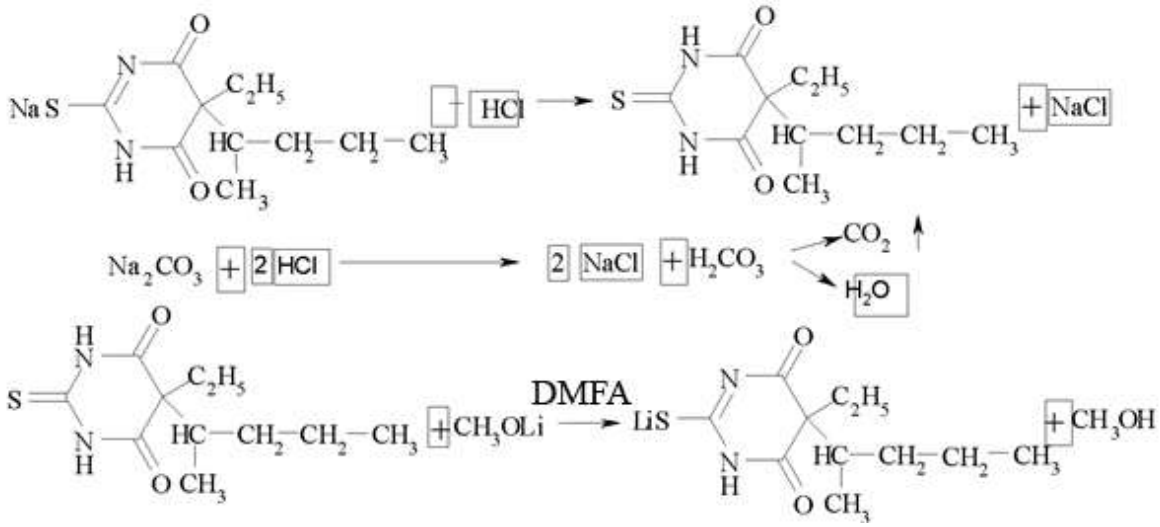
At the same time, the admixture of free alkali is also titrated. The content of barbiturate sodium salt (%) in terms of dry matter is calculated according to the formula [10, p. 343]:

$$\% = \frac{V_{HCl} \cdot KП \cdot T \cdot 100 \cdot 100}{m \cdot (100 - \%_{\text{moisture}})} - \%_{\text{alkali}} \cdot K,$$

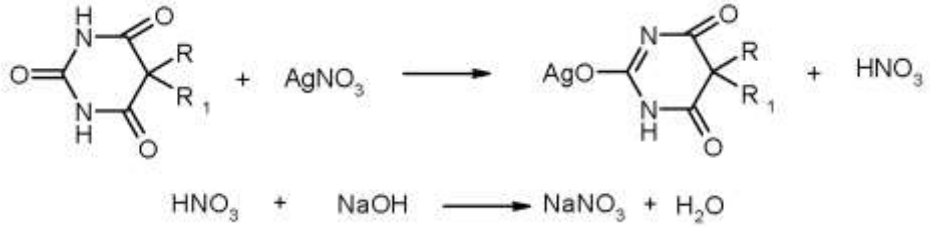
where: % alkali - percentage content of free alkali in the substance;

K - coefficient, which is calculated as a ratio of M.m. salt to M.m. sodium hydroxide.

Sodium thiopental is converted into an acid form and titrated with a solution of lithium methylate [10, p. 344]:

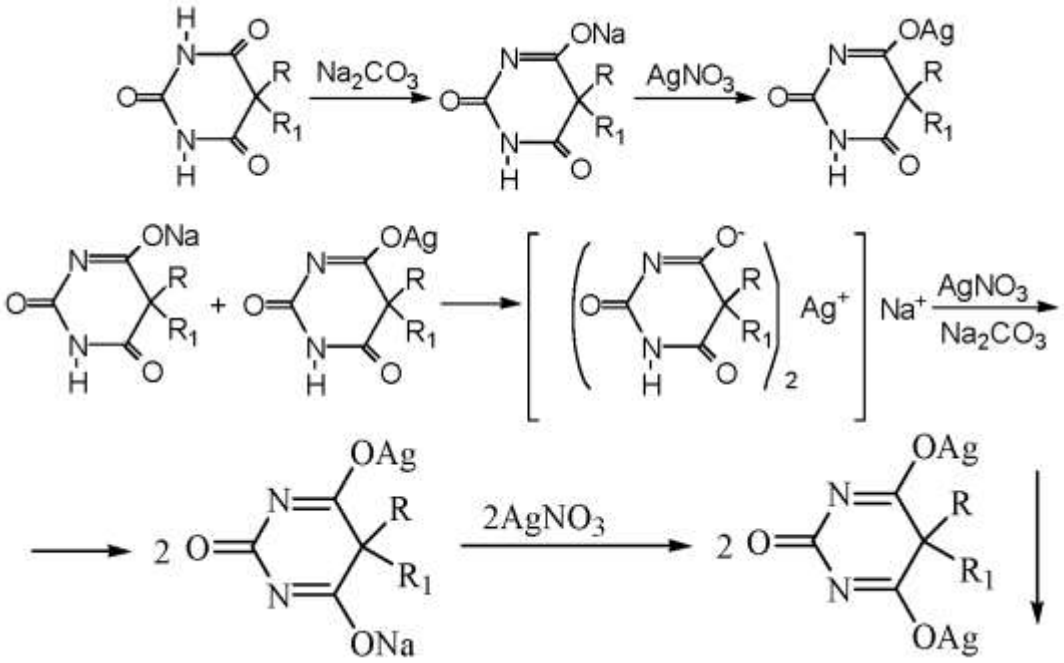


Alkalimetry by substitute. The method is based on the formation of a silver salt during the interaction of a barbiturate with a solution of argentum nitrate in pyridine, as a result of which an equivalent amount of nitric acid is released, which is titrated with an alcoholic solution of sodium hydroxide, the indicator is thymolphthalein. In parallel, a control experiment is carried out [10, p. 344]:



Gravimetry. Acidic forms of barbiturates are extracted with ether from an acidic solution. The ether is distilled off, the residue is dried and weighed. The method is used for the analysis of sodium thiopental.

Argentometry. A weight of acid or salt form is dissolved in a 5% solution of anhydrous sodium carbonate and titrated with a solution of argentum nitrate without an indicator until the appearance of permanent turbidity (disubstituted argentum barbiturate salt) [10, p. 345]:



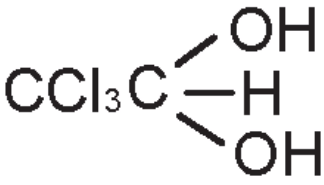
Storage. In well-stoppered glasses. Phenobarbital and benzonal – in glasses made of dark glass in a place protected from light. Hexenal and sodium thiopental – in glass vials of 0.5-1.0 g, hermetically closed with rubber stoppers, crimped with aluminum caps, in a dry, cool, protected from light place.

As a stabilizer, 0.05-0.25% sodium hydroxide is added to hexenal; sodium thiopental – 5-6% of sodium carbonate.

Aqueous solutions of sodium salts of barbiturates are easily hydrolyzed, so their solutions are prepared ex tempore.

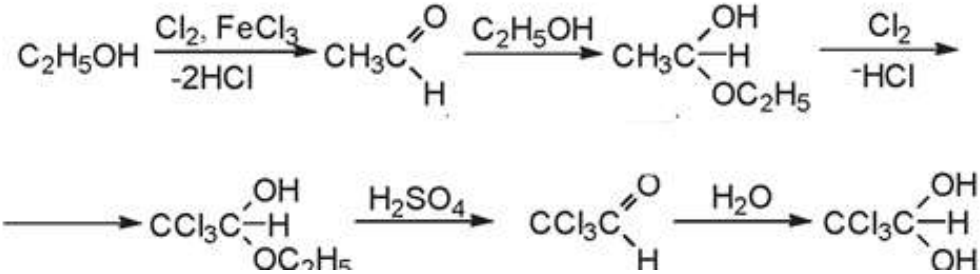
Use. Sedatives and hypnotics. Phenobarbital and benzonal are used as antiepileptic drugs. Hexenal and sodium thiopental solutions are used for intravenous anesthesia.

Chloral hydrate (Chloralum hydratum)



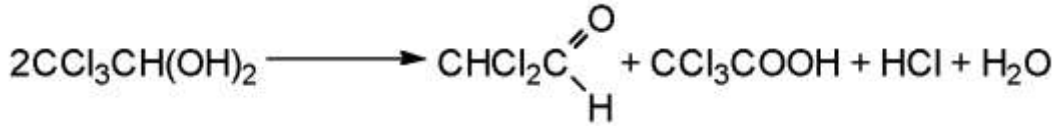
1,1-Dihydroxy-2,2,2-trichloroethane

Extraction. Electrochemical oxidation of ethyl alcohol in the presence of sodium or potassium chlorides [10, p. 147]:



trichlorosemiacetal trichloroacetaldehyde

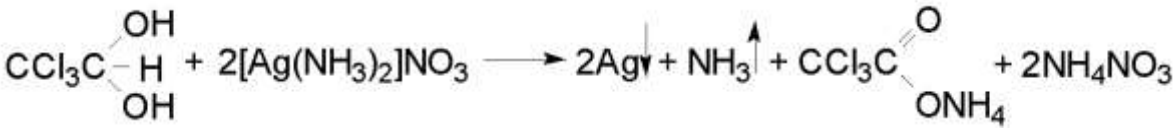
Properties. Colorless transparent crystals or fine crystalline powder with a characteristic pungent smell and slightly bitter peculiar taste. Hygroscopic at high humidity; evaporates slowly in air. Very easily soluble in water, alcohol and ether. Under the influence of light, it slowly decomposes [10, p. 147]:



The absence of decomposition products is controlled by checking the acidity.

Identification:

Reaction of the "silver mirror":



2. Formation of chloroform when interacting with sodium hydroxide [10, p. 148]:

$$CCl_3CH(OH)_2 + NaOH \rightarrow CHCl_3\downarrow + HCOONa + H_2O$$

Purity test. Chloro-Alkoxide (trichlorosemiacetal) - an intermediate product - is determined by the reaction of the formation of iodoform after hydrolysis [10, p. 148]:

$$CCl_3CH(OH)OC_2H_5 + NaOH \rightarrow CHCl_3 + HCOONa + C_2H_5OH$$

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

Quantitative definition:

1. Acid-base reverse titration. A solution of sodium hydroxide is added to the weight of the substance, the excess of which is titrated with a solution of sulfuric acid [10, p. 148]:

$$CCl_3CH(OH)_2 + NaOH \rightarrow CHCl_3 + HCOONa + H_2O$$

$$2NaOH + H_2SO_4 \rightarrow Na_2SO_4 + 2H_2O$$

Chloroform can also react with sodium hydroxide solution to form sodium chloride, which is determined argentometrically by Mohr's method [10, p. 149]:

$$CHCl_3 + 4NaOH \rightarrow 3NaCl + HCOONa + 2H_2O$$

$$NaCl + AgNO_3 \rightarrow AgCl\downarrow + NaNO_3$$

$$2AgNO_3 + K_2CrO_4 \rightarrow Ag_2CrO_4\downarrow + 2KNO_3$$

The volume of the titrant is found by the difference in volumes

$$[(V_{NaOH} \cdot E_{\text{ɛ}\,NaOH} - V_{H_2SO_4} \cdot E_{\text{ɛ}\,H_2SO_4}) - V_{AgNO_3} \cdot E_{\text{ɛ}\,AgNO_3}].$$

Alkalimetry, reverse titration, indicator – phenolphthalein.

$$CCl_3CH(OH)_2 + NaOH \rightarrow CHCl_3 + HCOONa + H_2O$$

$$NaOH + HCl \rightarrow NaCl + H_2O$$

Conducted in parallel: iodometry, reverse titration, indicator – starch [10, p. 149]:

$$2CCl_3CH(OH)_2 + 2I_2 + 3Na_2CO_3 \rightarrow 2CCl_3COONa + 4NaI + 3H_2O + 3CO_2\uparrow$$

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

Storage. In a sealed container that protects from light, in a cool place.

Use. Sedative, hypnotic and analgesic agent; in large doses, close to toxic, has narcotic properties. It is used for mental illnesses and to eliminate seizures.

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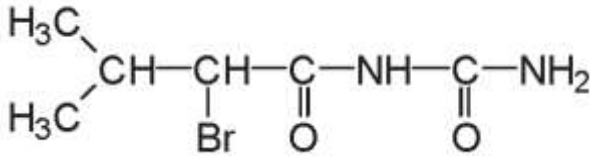
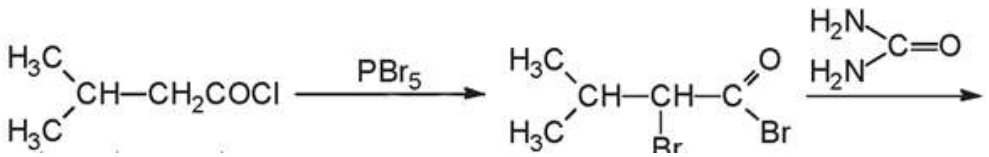
Ureids

Bromisoval (Bromisovalum)

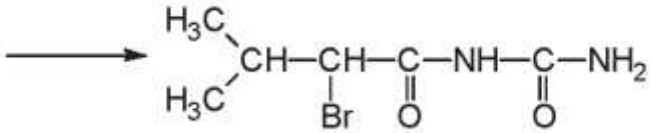


N-(α-Bromisovalerianyl)-urea

Extraction. Acylation of urea with α-bromosovaleric acid bromohydride [10, p. 188]:



isovaleric acid chloride α-bromosovaleric acid bromohydride.

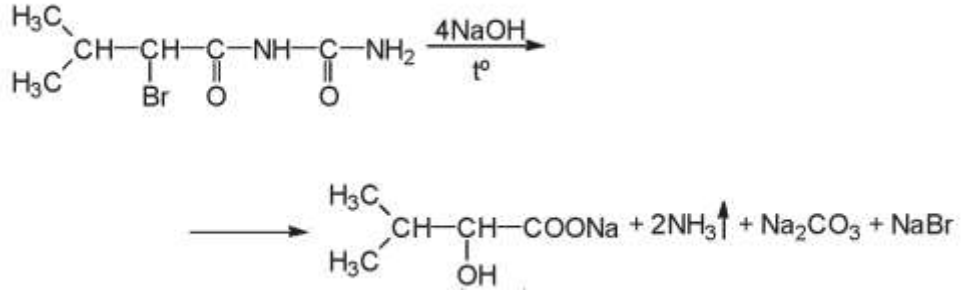


Bromisoval

Properties. White crystalline powder with a weak odor, bitter taste. Very slightly soluble in water, soluble in 96% alcohol.

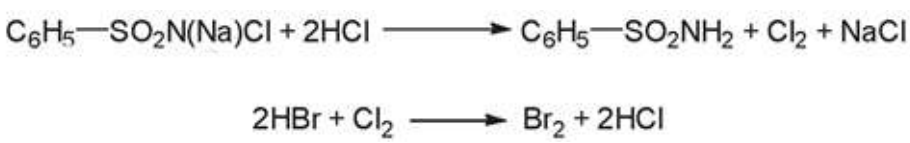
Identification:

When heated with alkali solutions, hydrolysis occurs and ammonia is formed, which is detected by its smell. At the same time, organically bound bromine passes into the ionic state [10, p. 189]:



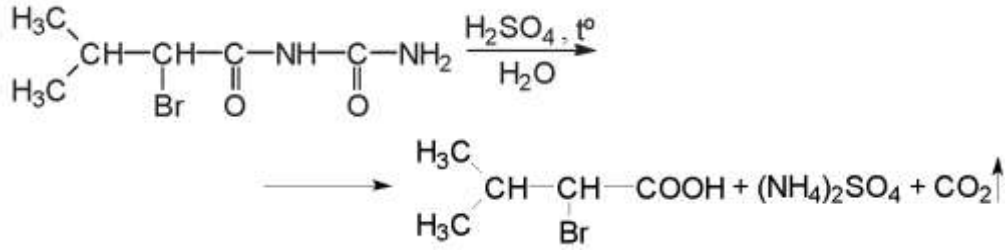
sodium salt of α-hydroxyisovaleric acid

After cooling, dilute hydrochloric acid, chloramine B and chloroform are added [10, p. 189]:



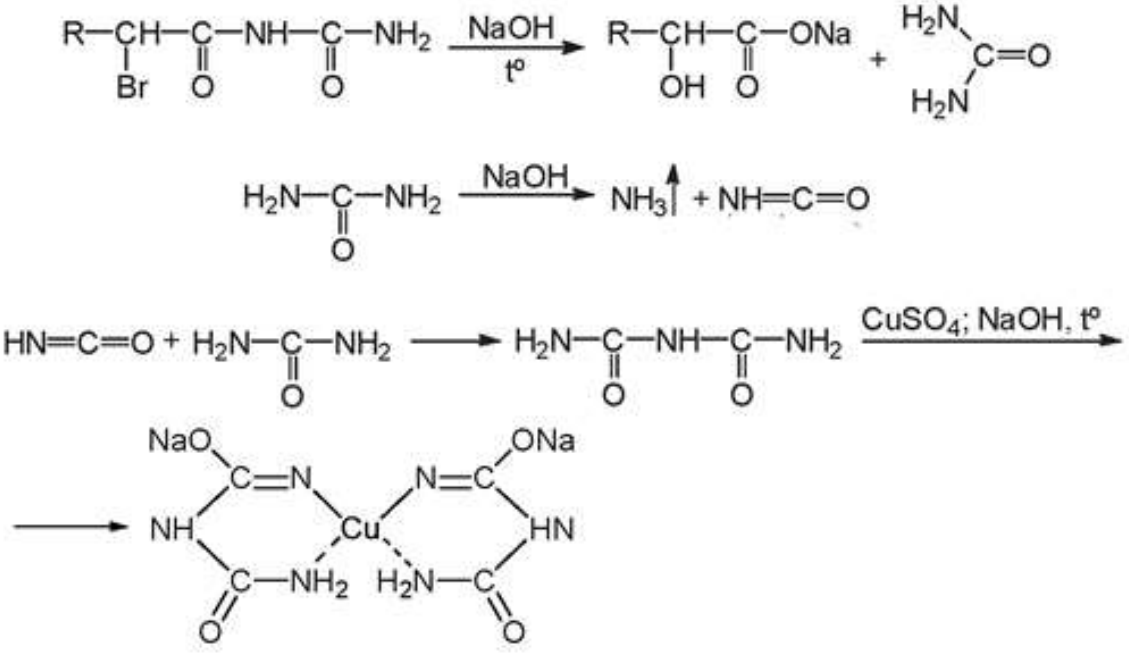
Free bromine colors the chloroform layer yellow.

When the drug substance is heated with a solution of sulfuric acid, a strong smell of a-bromosovaleric acid appears [10, p. 189]:



bromisovaleric acid

3. Biuret reaction to urea. When the drug product is heated with a solution of cuprum (II) sulfate in an alkaline environment, a pink-red or (with an excess of cuprum (II) sulfate) red-violet color appears [10, p. 189]:



Quantitative definition. Argentometry after alkaline hydrolysis, reverse titration according to the Volhard method, indicator – ferrum (III) ammonium sulfate. In parallel, a control experiment is carried out [10, p. 190]:

$$NaBr + AgNO_3 \rightarrow AgBr\downarrow + NaNO_3$$

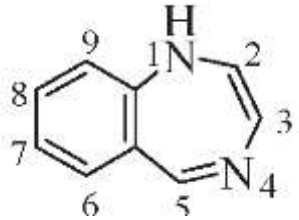
$$AgNO_3 + NH_4SCN \rightarrow AgSCN\downarrow + NH_4NO_3$$

$$3NH_4SCN + NH_4Fe(SO_4)_2 \rightarrow Fe(SCN)_3 + 2(NH_4)_2SO_4$$

Storage. In a sealed dark glass container.
Use. As a sedative and mild hypnotic.

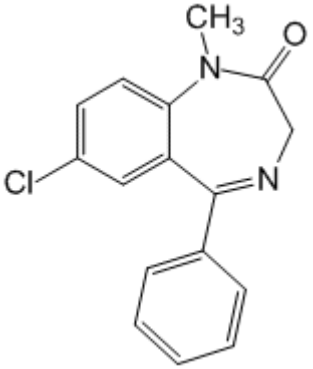
Drugs - benzodiazepine derivatives

Benzodiazepine is a heterocyclic system that includes a benzene core and a seven-membered heterocycle - 1,4-diazepine:



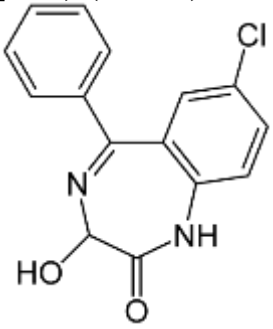
Benzodiazepine derivatives have a tranquilizing (sedating) effect.

Diazepam (Diazepamum) (SPhU) Sibazonum, Seduxen, Valium



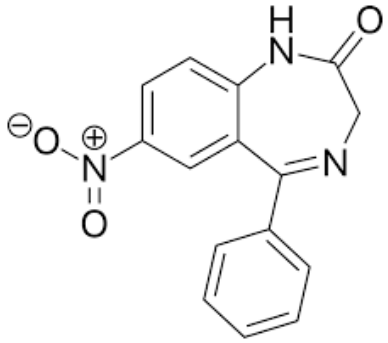
7-Chloro-1-methyl-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-2-one

Oxazepam (Oxazepam) (SPhU) Nozepanum, Tazepam



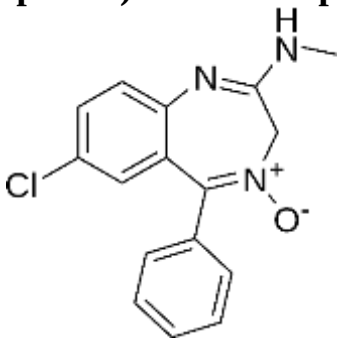
7-Chloro-3-hydroxy-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one

Nitrazepam (Nitrazepamum) (SPhU) Radedorm, Eunoctin



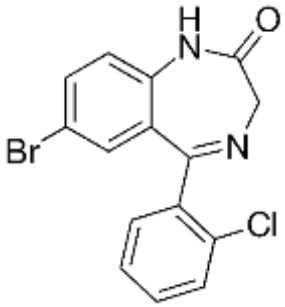
7-Nitro-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one

Chlozepide (Chlozepidum) Chlordiazepoxide* Elenium Librium



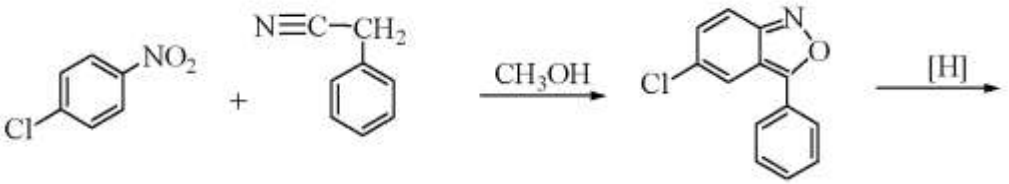
7-Chloro-2-methylamino-5-phenyl-3H-1,4-benzodiazepine-4-oxide

(Phenazepamum) Phenazepam

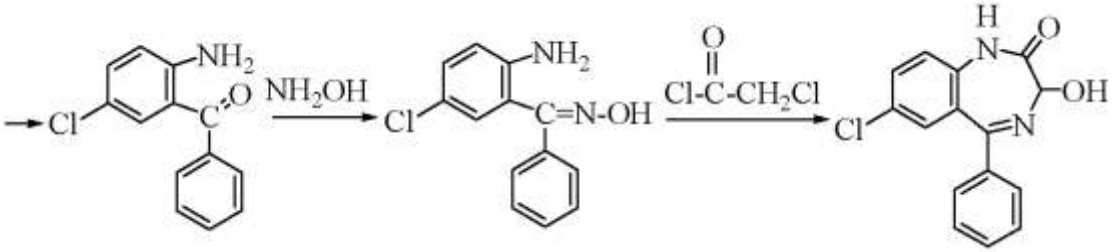


7-Bromo-2,3-dihydro-5-(o-chlorophenyl)-1H-1,4-benzodiazepin-2-one

Extraction. The synthesis of benzodiazepine derivatives can be considered using the example of the industrial production of oxazepam:



p-nitrochlorobenzene benzyl cyanide 5-chloro-3-phenylanthranyl



2-amino-5-chloro-benzophenone oxazepam

Properties. White crystalline powders with a yellowish or cream tint. Nitrazepam has a light-yellow color with a greenish tint. The substances are practically insoluble in water, sparingly soluble in alcohol. When heated in solutions of mineral acids, the drug substances of this series undergo hydrolysis.

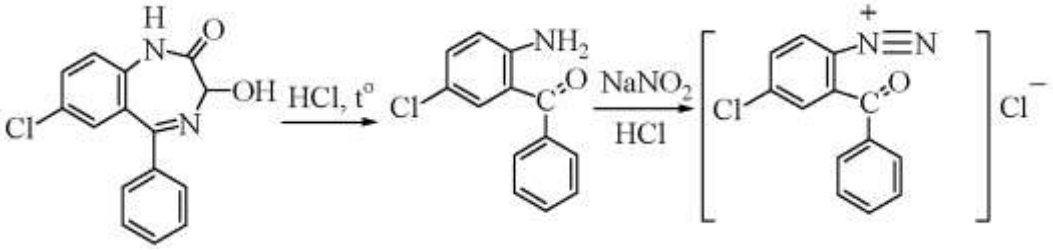
4-benzodiazepines and their dihydro-derivatives exhibit weakly basic properties due to the heterocyclic nitrogen in position 4. Compounds with the lactam group -NH-CO- also exhibit weakly acidic properties, forming salts with alkali metals, that is, they are amphoteric.

Identification:

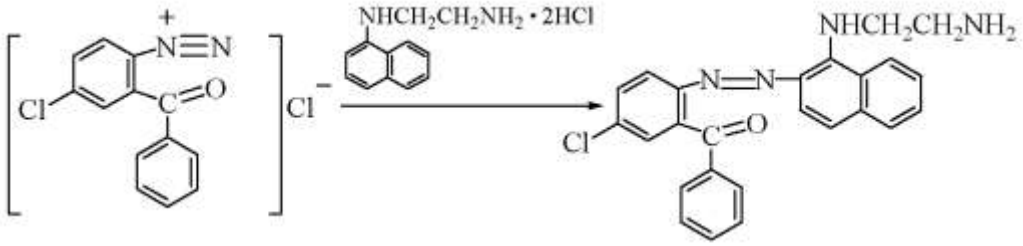
According to physical and chemical indicators: determination of melting point, UV and IR spectroscopy, thin-layer chromatography (TLC).

With concentrated acids (H_2SO_4, HCl, $HClO_4$), benzodiazepine derivatives form colored salts that fluoresce in UV light (SPhU).

The general reaction to benzodiazepine derivatives that do not contain substituents in position 1 is the reaction of the formation of an azo dye after preliminary hydrolysis:



SPhU recommends using naphthylethylenediamine dihydrochloride in the azo compound reaction:



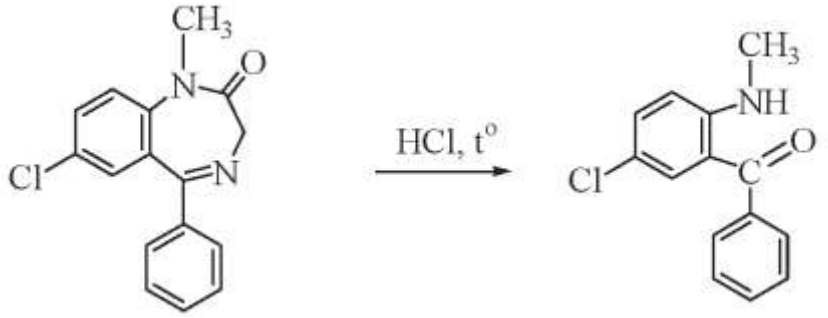
Organically bound chlorine in the diazepam molecule according to SPhU is determined after mineralization of the substance by the action of argentum nitrate.

The presence of heterocyclic nitrogen causes a positive reaction with general alkaloid precipitating reagents.

A specific reaction for benzodiazepine derivatives is the formation of a green-colored melt during pyrolysis.

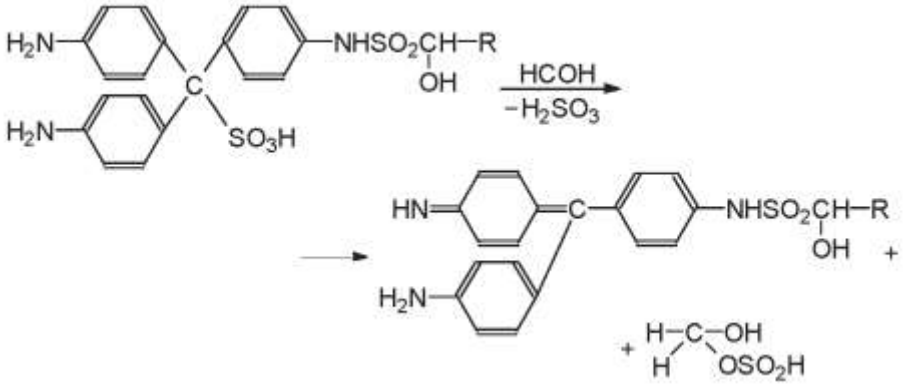
Fusion with sodium hydroxide leads to the destruction of molecules of benzodiazepine derivatives and the release of ammonia or methylamine (diazepam), which are detected by the smell or by the bluing of wet red litmus paper. Under these conditions, oxazepam forms an emerald-green coating on the walls of the test tube.

Compounds with a substituent in position 1 (diazepam) after acid hydrolysis turn into colored benzophenone derivatives:

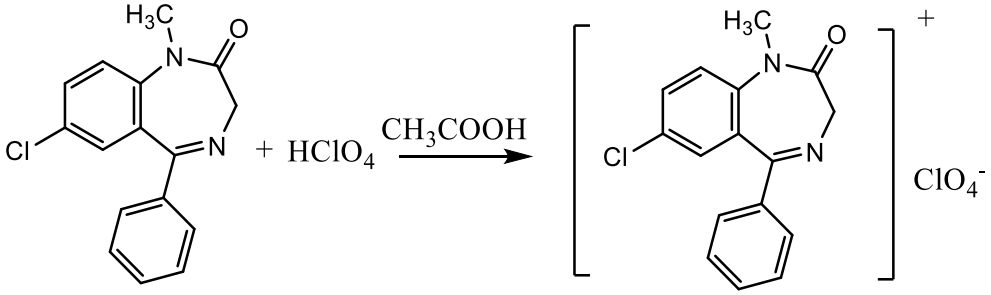


yellow color

Oxazepam, when heated with concentrated phosphoric acid, is hydrolyzed with the formation of formaldehyde, which with fuchsin sulfurous acid gives a purple color:



Quantitative definition. Acidimetry in a non-aqueous environment, direct titration (SPhU).



Spectrophotometric and photocolorimetric methods are also known.

Storage. In a container that protects from light, in a dry place.

Use. Tranquilizers (agents that have a calming effect on the central nervous system and have a hypnotic effect). Nitrazepam, in addition to its hypnotic properties, also has anticonvulsant activity. Long-term use leads to addiction. They are released strictly according to the prescription.

LESSON No. 1

TOPIC: Antitussives. Characteristics, classification, connection between structure and pharmacological action, mechanism of action, methods of production, methods of analysis. Use in medicine.

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

3. TARGETS:

3.1. Know the definition of the concept of "cough", its classification and be able to give an example for each of the sections 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 antitussive drugs.

4. **PLAN AND ORGANIZATIONAL STRUCTURE OF THE LESSON:**

4.1. Organizational questions - 2 minutes.

4.2. Setting the purpose of the lesson and motivation for studying the topic of the lesson (introductory speech by the teacher) - 5 minutes.

4.3. Safety briefing in the chemical laboratory - 10 minutes.

4.4. Control and correction of the initial level of knowledge-skills - 20 minutes.

4.5. Organization of students' independent work (target instructions of the teacher, safety techniques) - 5 minutes.

4.6. Laboratory work and preparation of protocols - 80 minutes.

4.7. Final control: checking the results of laboratory work and protocols - 10 minutes.

4.8. The final word of the teacher, instructions for the next lesson - 3 minutes.

5. 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 quantitative determination of antitussive drugs;

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

EDUCATIONAL QUESTIONS FOR STUDENTS' SELF-PREPARATION:

1. Learn the concept of cough and its characteristics.
2. Study the classification of antitussive drugs, as well as expectorants.
3. Study the mechanism of action of antitussive drugs.

4. 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) on the example of bromhexine, glaucine hydrochloride, ambroxol, acetylcysteine, sodium benzoate.

TEST TASKS

1. A chemist of a pharmaceutical enterprise can confirm the sodium cation in the tested substance, according to the SPhU, with a solution of:

A. Potassium pyroantimonate
B. Potassium ferrocyanide
C. Potassium chloride
D. Potassium hydroxide
E. Potassium nitrate

2. The pharmacist determines the quantitative content of sodium benzoate by the method of acidimetry in a non-aqueous environment in accordance with the requirements of the SPhU. What reagent does he use as a solvent?

A. Concentrated sulfuric acid
B. Pyridine
C. Anhydrous acetic acid
D. Dimethylformamide
E. Sulfanilic acid

3. The reaction of the formation of ethyl acetate is used to detect the acetyl group in Acetylcysteine when adding which reagent:

A. Iron chloride
B. Sodium hydroxide solution
C. 2,4 - dinitrochlorobenzene
D. 96% alcohol
E. Boiling with a solution of potassium dichromate in sulfuric acid and subsequent addition of ethanol.

4. Which reagent should be used to detect the thiogroup in the acetylcysteine molecule:

A. With iron oxide chloride
B. With alkali
C. With alcohol
D. With chloroform
E. With chloramine

5. What reagent must be added to determine the carboxyl group in Acetylcysteine:

A. Concentrated acid
B. Heavy metal salt
S. Dimethylformamide
D. Perhydrol
E. Alkali

6. What method can quantitatively determine acetylcysteine:

A. Iodometric

B. Bromatometric

C. Iodochlormetric

D. Argentometric

E. Complexonometric

7. What is the iodometric titration of acetylcysteine based on:

A. physical and chemical properties

B. presence of a primary amino group in the drug

C. specific rotation index

D. oxidation of sulfhydryl groups

E. pharmacological properties

8. Suggest a reagent for detecting the primary aromatic amino group in the bromhexine molecule:

A. Sodium nitrite, sulfuric acid and β-naphthol

B. Sodium nitrate, hydrochloric acid and β-naphthol

C. Sodium nitrite, hydrochloric acid and β-naphthol

D. Sodium nitrite, hydrochloric acid

E. Hydrochloric acid and β-naphthol

9. The presence of bromine in bromhexine hydrochloride is established after the destruction of the organic part of the molecule to sodium bromide by boiling in a 30% solution of sodium hydroxide and the subsequent addition of:

A. Dilute hydrochloric acid, 5% chloramine and tetrachloromethane

B. Dilute sulfuric acid, 5% chloramine

C. Dilute sulfuric acid, tetrachloromethane

D. Dilute sulfuric acid

E. Tetrachloromethane

10. To confirm the reliability of bromhexine hydrochloride and establish the absence of extraneous impurities, we use the following method:

A. thin-layer chromatography

B. HPLC

C. Photoelectric Colorimetry

D. Refractometry

E. Polarimetry

11. When identifying glaucin hydrochloride, a reagent was added to the preparation, a white curdled precipitate is formed, dissolved in an ammonia solution. What reagent was added:

A. Sodium hydroxide

B. Concentrated sulfuric acid

C. Alkali solution

D. Potassium dichromate

E. Silver nitrate

12. Identification of bromhexine and ambroxol can be carried out with the help of general alkaloid reagents. Which reaction has the most sensitivity with the reagent:

A. Dragendorf
B. Marquis
C. Froehde
D. Bouchard
E. Wagner

13. One of the possible methods of quantitative determination of bromhexine hydrochloride is the method of:

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

14. Bromhexine hydrochloride can be determined quantitatively using non-aqueous titration as a titrant with:

A. Iodine solution
B. Hydrochloric acid solution
C. Potassium permanganate solution
D. Perchloric acid solution
E. Sodium thiosulfate solution

15. Bromhexine hydrochloride can be determined quantitatively using non-aqueous titration as an indicator with:

A. Crystal violet
B. Phenolphthalein
C. Etching black
D. Methyl orange
E. Tropeolin 00

16. Ambroxol hydrochloride belongs to the following group of antitussives according to the mechanism of action:

A. Non-narcotic drugs
B. Narcotic drugs
C. Peripheral-type antitussives
D. Mucolytics
E. Expectorants

17. Bromhexine hydrochloride belongs to the following group of antitussives according to the mechanism of action:

A. Non-narcotic drugs
B. Narcotic drugs
C. Peripheral-type antitussives
D. Expectorants
E. Mucolytics

18. Acetylcysteine belongs to the following group of expectorants according to the mechanism of action:

A. Synthetic mucolytics

B. Surfactant synthesis stimulants

C. Enzyme drugs

D. Drugs of mixed type

E. Drugs of the resorptive type of action

19. When determining the chloride ion from silver with nitrate in Glaucine hydrochloride, a precipitate of what color falls out:

A. White, curdled

B. The solution is white

C. chloroform layer is purple in color

D. Yellow

E. Yellow solution

20. The second phase of drug metabolism (conjugation phase) includes interactions of xenobiotics or their metabolites, which have active functional groups, with hydrophilic endogenous molecules. This phase includes the process of:

A. S-Oxidation

B. Glucuronidation

C. Hydroxylation

D. Recovery

E. Hydrolysis

21. Drugs are metabolized in several stages. Functional groups in the drug substance molecule undergo biochemical transformation during the following phase:

A. Conjugations

B. Secretions

C. Hydration

D. Functionalization

E. Depolarization

22. Drugs are metabolized in several stages. Biochemical conjugation of functional groups of the molecule with acid residues, such as glucuronic and sulfate, or glycine, occurs in the phase of:

A. Functionalization

B. Secretions

C. Hydration

D. Depolarization

E. Conjugations

23. Metabolism of drugs is one of the stages of pharmacokinetics. Agents that are metabolically transformed into biologically active substances are called:

A. Vitamins

B. Prodrugs

C. Hormones

D. Enzymes

E. Conjugates

24. Drugs are able to undergo biotransformation in the body. The metabolic phase of functionalization is aimed at:

A. Binding to endogenous molecules

B. Increase in hydrophilicity

C. Mineralization of matter

D. Formation of polymers

TASKS.

1. Calculate the percentage content of sodium benzoate (M.m. 144.11) in the preparation, if 20.06 ml of a 0.1 M solution of perchloric acid (correction factor= 1.0022) was spent on the titration of a weight of 0.2991 g, and the loss in weight during drying - 2.5%.

2. Calculate the volume of 0.1 M perchloric acid solution that was used for the titration of 0.2991 g of sodium benzoate (M.m. 144.11) (correction factor= 1.0022), and the percentage content of the drug is 100%.

3. Calculate the weight of sodium benzoate (M.m. 144.11), if 20.06 ml of 0.1 M perchloric acid solution (correction factor= 1.0022) was spent on its titration, and the percentage content of the drug is 99.10% .

LABORATORY WORK

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

Each student individually analyzes the dosage form that will include the antitussive drug, and also prepares the protocol according to the requirements.

Medicinal forms:

1. Infusion of thermopsis grass 0.8-200.0

Sodium benzoate

Sodium hydrocaronate

Anise-anise drops 4.0 each

Distilled water 100.0

Identification:

The sodium ion is determined by the yellow color of the flame, and the hydrogen carbonate by the release of carbon dioxide when the solution is acidified. Benzoate - ion for separation from sodium bicarbonate and ammonia is extracted with ether (to 20 drops of the mixture add 1 drop of methyl orange solution, 1-2 ml of ether, dilute hydrochloric acid drop by drop until a pink color appears and shake. The ether layer is separated, the ether is evaporated under a weak heating in a water bath, add 15-20 drops of 10% ammonia solution to the residue and evaporate to dryness again. Dissolve the residue in 3-5 drops of water and carry out a reaction with iron oxide chloride, a pinkish-yellow precipitate is formed). Ammonia-anise drops are determined by smell and with Nessler's reagent (a drop

of the solution is placed on filter paper and a drop of Nessler's reagent is added, a brown precipitate is released).

Quantitative definition:

Sodium benzoate, sodium hydrogen carbonate and ammonia-anise drops are titrated with a total of 0.1 N hydrochloric acid solution in the presence of ether - V ml is spent. Benzoic acid is determined in the separated ether layer by titration with a 0.1 N caustic soda solution. The sodium benzoate content is calculated based on the number of milliliters of caustic soda used for titration; 1 ml of 0.1 N caustic soda solution corresponds to 0.0144 g of sodium benzoate.

For the quantitative determination of ammonia-anise drops, the same volume of the drug mixture that was taken for titration with hydrochloric acid is evaporated until the smell of ammonia is completely removed, and the sum of sodium benzoate and sodium bicarbonate is titrated with a 0.1 N solution of hydrochloric acid in the presence of ether - V_1 ml is spent. Based on the difference between the amount of hydrochloric acid used for the first (V) and second (V_1) titrations, the content of ammonia-anise drops is calculated according to the formula:

$$X = \frac{(\mathrm{V} - V_1) \cdot 0{,}0017 \cdot\ 100\ \cdot \mathrm{B}}{1{,}5 \cdot a}$$

Note: The analysis of ammonia-anise drops is reduced to the quantitative determination of ammonia, which should be 1.42-1.58% in the preparation. The average ammonia content is 1.5%.

The content of sodium hydrogen carbonate is calculated by the difference between the amount of hydrochloric acid (V1) used to titrate the amount of sodium benzoate and sodium hydrogen carbonate, and the amount of caustic soda solution used to titrate benzoic acid; 1 ml of 0.1 N hydrochloric acid solution corresponds to 0.0084 g of sodium bicarbonate.

2. Infusion of Althaea root 200.0
Sodium bicarbonate
Sodium benzoate
4.0 drops of aniseed anise
Codeine phosphate 0.2

Identification:

Phosphate ion gives a characteristic reaction with silver nitrate. Codeine is extracted with chloroform (put 10-15 drops of liquid medicinal form into a test tube, add 2-3 drops of 10% caustic soda or ammonia, 1-2 ml of chloroform and shake, after settling with a pipette lowered to the bottom of the test tube, remove part of the chloroform layer, transfer to a porcelain cup, chloroform is removed by heating and an appropriate reaction is carried out with the residues), 1-2 drops of Marquis reagent are added to the residue, a blue-violet color appears.

Sodium ion is determined by the yellow color of the flame, hydrogen carbonate by the release of carbon dioxide when the solution is acidified. Benzoate - ion for separation from sodium bicarbonate and ammonia is extracted with ether (to 20 drops of the mixture add 1 drop of methyl orange solution, 1-2 ml of ether, dilute hydrochloric acid drop by drop until a pink color appears and shake. The ether layer is separated, the ether is evaporated under a weak heating in a water bath, add 15-20 drops of 10% ammonia solution to the residue and evaporate to dryness again. Dissolve the residue in 3-5 drops of water and carry out a reaction with iron oxide chloride, a pinkish-yellow precipitate is formed). Ammonia-anise drops are determined by smell and with Nessler's reagent (a drop of the solution is placed on filter paper and a drop of Nessler's reagent is added, a brown precipitate is released).

Quantitative definition:

Transfer 10-15 ml of the mixture to a separatory funnel, add 2-3 drops of 10% caustic soda and extract the codeine with chloroform.

Sodium benzoate, sodium hydrogen carbonate and ammonia-anise drops are titrated with a total of 0.1 N hydrochloric acid solution in the presence of ether - V ml is spent. Benzoic acid is determined in the separated ether layer by titration with a 0.1 N caustic soda solution. The sodium benzoate content is calculated based on the number of milliliters of caustic soda used for titration; 1 ml of 0.1 N caustic soda solution corresponds to 0.0144 g of sodium benzoate.

For the quantitative determination of ammonia-anise drops, the same volume of the medicinal mixture that was taken for titration with hydrochloric acid is evaporated until the smell of ammonia is completely removed, and the sum of sodium benzoate and sodium bicarbonate is titrated with a 0.1 N solution of hydrochloric acid in the presence of ether - V_1 ml is spent. Based on the difference between the amount of hydrochloric acid used for the first (V) and second (V_1) titrations, the content of ammonia-anise drops is calculated according to the formula:

$$X = \frac{(\mathrm{V} - V_1) \cdot 0{,}0017 \cdot\ 100\ \cdot \mathrm{B}}{1{,}5 \cdot a}$$

Note: The analysis of ammonia-anise drops is reduced to the quantitative determination of ammonia, which should be 1.42-1.58% in the preparation. The average ammonia content is 1.5%.

The content of sodium hydrogen carbonate is calculated by the difference between the amount of hydrochloric acid (V_1) used to titrate the amount of sodium benzoate and sodium hydrogen carbonate, and the amount of caustic soda solution used to titrate benzoic acid; 1 ml of 0.1 N hydrochloric acid solution corresponds to 0.0084 g of sodium bicarbonate.

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;

b. State Pharmacopoeia of Ukraine;

9.5. Training and control tools:

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

9.7. b. Control questions and tests.

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Additional

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LESSON No. 2

TOPIC: Nootropic drugs. Characteristics, classification, connection between structure and pharmacological action, mechanism of action, methods of production, methods of analysis. Use in medicine.

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

3. TARGETS:

3.1. Study the characteristics and classification of nootropic drugs;
3.2. Study the connection between the structure and pharmacological action of nootropic drugs;
3.3. Study the mechanism of action of nootropic drugs;
3.4. Learn the Latin names, synonyms, structural formulas, chemical names of the investigated drug substances (piracetam, aminalon, glycine, calcium pangamate);
3.5. Study the physical and physico-chemical properties of nootropic drugs;
3.6. Study the structure of normative and technical documentation, quality control methods; and quality indicators that are included in them;
3.7. Determine general and specific impurities;
3.8. Carry out calculations of weight, gram, percentage content;
3.9. Study methods of identification of drug substances of this group based on their physical and chemical properties;
3.10. Study methods of quantitative determination of investigated drug substances;
3.11. Study the application, form of release, storage of drug substances;
3.12. 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. Repeat the theoretical material from the course of organic and analytical chemistry, regarding quantitative determination by various methods: acidimetry, alkalimetry, complexonometry, precipitation, redoxmetry, 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 nootropic drugs.
2. Connection between the structure and pharmacological action of nootropic drugs.
3. Mechanism of action of drugs of this group.
4. Chemical structure, Latin names, synonyms of drugs of this group (piracetam, aminalon, glycine, calcium pangamate).

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. Define general and specific impurities.
9. Calculate weight, gram, and percentage content.
10. Quantitative methods, conditions and chemism of reactions.
11. Use in medicine.
12. Substantiate the conditions of storage of preparations of this group of drugs, based on their physical and chemical properties.
13. Study the use, form of release, storage of drug substances;
14. Give a correct assessment of the obtained results of the analysis and to draw a conclusion about the benign quality of drug substances of this group.

5. TEST TASKS

1. The doctor prescribed piracetam to a patient after a traumatic brain injury. To which pharmacological group does this drug belong?
A. Nootropic drugs
B. Non-narcotic analgesics
C. Tranquilizers
D. Means for anesthesia
E. Neuroleptics
2. When identifying the substance of nootropil (piracetam) by heating with sodium hydroxide solution, ammonia is released. The pharmacist confirms its formation with the help of:
A. Wetted lignin paper
B. Wetted litmus paper
C. Addition of $FeCl_3$ solution
D. Addition of $FeCl_2$ solution
E. Addition of $AgNO_3$ solution
3. The presence of an amide group in the piracetam structure is confirmed by the pharmacist by reaction with sodium hydroxide when heated. What characteristic product is formed as a result of alkaline hydrolysis of piracetam?
A. Ethanol
B. Urea
C. Hydroxylamine
D. Ammonia
E. Sodium acetate
4. To identify piracetam, a reaction is carried out, as a result of which ammonia is released when heated. What reagent is used in this reaction?
A. Sodium hydroxide solution
B. Hydrochloric acid solution

C. Copper (II) sulfate solution
D. Silver nitrate solution
E. Ammonium oxalate solution
5. Indicate which drug substance corresponds to the chemical name "4-aminobutanoic acid"?
A. Methionine
B. Cysteine
C. Alanine
D. Glutamic acid
E. Aminalon
6. Identification of nootropic drugs from the group of amino acids of the aliphatic series is carried out by the appearance of a blue-violet color with:
A. Ninhydrin
B. Aniline
C. Pyridine
D. Methylamine
E. Resorcinoma
7. Specify the reagent that can be used to confirm glycine belonging to amino acids during pharmaceutical analysis:
A. Saturated sodium bicarbonate solution
B. Sulfuric acid solution
C. Sulfosalicylic acid solution
D. Ninhydrin solution
E. Barium hydroxide solution
8. The control and analytical laboratory received the glycine substance. According to the SPhU, its identification involves the determination of substances detected by ninhydrin. This test is carried out by the method of:
A. Thin-layer chromatography
B. Gas chromatography
C. Liquid chromatography
D. Gas-liquid chromatography
E. Ion exchange chromatography
9. A control and analytical laboratory specialist uses formol titration (according to Sorensen) for the quantitative determination of nootropic drugs from the group of amino acids. At the same time, the role of formaldehyde is reduced to:
A. Carboxylation of the amino group
B. Blocking of the amino group
C. Neutralization of the carboxyl group
D. Alkylation of the carboxyl group
E. Formation of betaines
10. The pharmacist of the laboratory of the State Service of Ukraine on Medicines carries out quantitative determination of "Aminolone" in accordance with the requirements of the SPhU. Indicate by what method he should carry out quantitative determination:

A. Nitritometry
B. Acidimetry in a non-aqueous medium
C. Bromatometry
D. Argentometry
E. Complexonometry
11. Aminalon in the environment of dimethylformamide forms a bright crimson color when heated with the reagent of:
A. Formaldehyde solution
B. Sodium nitrite
C. Ninhydrin
D. Alloxon
E. Sulfuric acid
12. With what reagent when aminalon is fused, hydrogen sulfide is released, which is detected using paper impregnated with lead (II) acetate:
A. Sodium nitrite
B. Potassium thiocyanate
C. Ninhydrin
D. Formaldehyde solution
E. Alloxon
13. By what quantitative method is it possible to determine aminolone:
A. Kjeldahl method
B. Nitritometry
C. Acidimetry
D. Complexonometry
E. Iodometry
14. What heterocycle is included in the chemical structure of piracetam:
A. Morpholin
B. Piperazine
C. Pyrimidine
D. Thiazole
E. Pyrrolidine
15. When glycine is identified, oxidative decarboxylation of the drug is carried out under the action of NaOCl during heating. What is formed at the same time?
A. Phenol
B. Acetic acid
C. Formaldehyde
D. Sodium nitrite
E. Alloxon
16. When heating which drug with alloxone, a bright crimson color is formed:
A. Aminalon
B. Glycine
C. Piracetam
D. Acetylsalicylic acid
E. Streptocide

17. Aminalon is identified by reaction with ninhydrin. A positive result of the reaction should be considered:
A. Appearance of red color
B. Release of gas bubbles
C. Appearance of a characteristic smell
D. Appearance of a blue-violet color
E. Precipitation of a white precipitate
18. Drugs containing pyrrolidine in their structure include:
A. Piracetam
B. Phenobarbital
C. Furacilin
D. Isoniazid
E. Analgin
19. For quantitative determination of azote [Nitrogen] in drug substances of organic nature, use:
A. Kjeldahl method
B. Kolthoff method
C. Kolbe-Schmidt method
D. Mohr's method
E. Fajans method

TASKS:

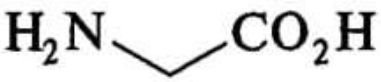
1. Calculate the volume of a 0.1 M solution of perchloric acid (correction factor= 1.0000), which will be spent on the titration of 0.1426 g of glycine (M.m. 75.07) by the non-aqueous titration method, if its percentage content in the substance - 93.37%, and the titrant volume in the control experiment - 0.75 ml.
2. Calculate the concentration of gamma-aminobutyric acid (M.m. 103.12), if 12.65 ml (correction factor= 1.0000) were spent on its titration with a 0.1 M sodium hydroxide solution, and its percentage content in the substance is 99, 78%.
3. Determine the gram content of gamma-aminobutyric acid (M.m. 103.12) in tablets, the average weight of which is 500 mg, if 2.84 ml of 0.1 M perchloric acid was spent on its titration (correction factor= 1.0010), the weight of the sample is 50 mg, the volume of the control experiment is 0.42 ml.

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 researching 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, the students make a conclusion about the

substances included in the composition of 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. After the end of the practical work, each student fills out the protocol according to the requirements listed below.

Glycine



Properties: White crystalline powder, easily soluble in water, poorly soluble in ethanol. Melting point = 232 - 236°C with decomposition.

Identification:

A. 0.02 g of the drug is dissolved when heated in 1 ml of water P, 1 ml of freshly prepared ninhydrin solution is added and heated, observing the formation of a blue-violet image.

B. Method of thin-layer chromatography in the solvent system: concentrated ammonia solution - propanol (30:70), is detected using a mixture: ninhydrin solution - diluted acetic acid - butanol (1: 5: 95).

C. The IR absorption spectrum of the substance must correspond to the IR spectrum of glycine pharmaceutical standard sample.

Purity test:

Solution S. 5.00 g of the substance is dissolved in a 1 M solution of hydrochloric acid under low heating and the volume of the solution is brought to 50.0 ml with the same acid.

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

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

Chlorides (2.4.4). Not more than 0.02% (200 ppm). 0.25 g of the substance is dissolved in 3 ml of diluted nitric acid and the volume of the solution is brought to 15 ml with water. The resulting solution must withstand the test for chlorides, without the further addition of dilute nitric acid.

Sulfates (2.4.13). Not more than 0.03% (300 ppm). 5 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 D). Not more than 0.001% (10 ppm). 2.0 g of the substance must withstand the test for heavy metals. The standard is prepared using 2 ml of standard lead solution (10 ppm Pb).

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 ^{0}C to 105 ^{0}C.

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

Quantitative determination: Dissolve an exact amount of the drug in 10 ml of water, add 10 ml of formalin neutralized with phenolphthalein. In this case, an

N-methylene derivative is formed, which is then titrated with a 0.1 M sodium hydroxide solution, the indicator is neutral red.

1 ml of 0.1 M sodium hydroxide solution corresponds to 0.007507 g of $C_2H_5NO_2$.

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LESSON No. 3

TOPIC: Nonsteroidal anti-inflammatory drugs. Characteristics, classification, connection between structure and pharmacological action, mechanism of action, methods of production, methods of analysis. Use in medicine.

2. PURPOSE: To study the classification, mechanism of action, as well as standardization of nonsteroidal anti-inflammatory drugs.

3. TARGETS:

3.1. Study the characteristics and classification of nonsteroidal anti-inflammatory drugs (NSAIDs);
3.2. Study the connection between the structure and pharmacological action of NSAIDs;
3.3. Study the mechanism of action of NSAIDs;
3.4. Learn the Latin names, synonyms, structural formulas, chemical names of the studied drug substances (acetylsalicylic acid, analgin, butadione paracetamol, indomethacin, mefenamic acid, sodium diclofenac);
3.5. Study the physical and physico-chemical properties of NSAIDs;
3.6. Study the structure of normative and technical documentation, quality control methods and quality indicators that are included in them;
3.7. Determine general and specific impurities;
3.8. Carry out calculations of weight, gram, percentage content;
3.9. Study methods of identification of drug substances of this group based on their physical and chemical properties;
3.10. Study methods of quantitative determination of investigated drug substances;
3.11. Study the use, form of release, storage of drug substances;
3.12. 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 nonsteroidal anti-inflammatory drugs.
2. The connection between the structure and pharmacological action of NSAIDs.
3. Mechanism of action of drugs of this group.
4. Chemical structure, Latin names, synonyms of drugs of this group (acetylsalicylic acid, paracetamol, indomethacin, mefenamic acid, sodium diclofenac, analgin, butadione).
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. Use 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. Specify a drug that exhibits pronounced selectivity in relation to COX-2:
A. Nimesulide
B. Acetylsalicylic acid
C. Celecoxib
D. Ibuprofen
E. Acetoaminophen
2. Choose an international non-proprietary name for aspirin:
A. Diclofenac
B. Phenylbutazone
C. Nimesulide
D. Acetylsalicylic acid
E. Ibuprofen
3. One of the NSAIDs belongs to the group of non-narcotic analgesics:
A. Analgin
B. Ibuprofen
C. Paracetamol
D. Indomethacin
E. Fentanyl
4. One of the NSAIDs belongs to the drugs of the pyrazolone group:
A. Indomethacin
B. Ibuprofen
C. Phenacetin
D. Acetylsalicylic acid
E. Analgin
5. Which NSAID has the weakest anti-inflammatory effect:
A. Diclofenac
B. Piroxicam
C. Paracetamol
D. Celecoxib
E. Indomethacin
6. A patient suffering from a headache, who was prescribed a cyclooxygenase inhibitor - an aminophenol derivative, came to the pharmacy for consultation. What drug was prescribed to the patient?
A. Diclofenac
B. Paracetamol
C. Ketorolac
D. Ibuprofen
E. Acetylsalicylic acid
7. The doctor prescribed an antipyretic drug to the patient. Specify this drug.
A. Ascorbic acid
B. Cyanocobalamin
C. Oxytocin
D. Famotidine

E. Paracetamol
8. The doctor prescribed paracetamol, a cyclooxygenase inhibitor, to a patient with arthritis. The formation of which biologically active compounds is inhibited by this drug?
A. Catecholamines
B. Prostaglandins
C. Cytokines
D. Iodothyronine
E. Interferons
9. What is the mechanism of action of diclofenac sodium?
A. Suppresses cholinesterase
B. Activates the synthesis of phosphodiesterase
C. Blocks cyclooxygenase
D. Activates adenylate cyclase
E. Inhibits phosphodiesterase
10. A patient with osteoarthritis was prescribed a drug that caused a side effect in the form of an ulcer.
A. Meloxicam
B. Diclofenac-Sodium
C. Nimesulid
D. Celecoxib
E. Rofeccoxib
11. To relieve inflammation and pain, the doctor prescribed a drug that belongs to the group of NSAIDs. Specify this drug:
A. Glibenclamide
B. Diclofenac-Sodium
C. Loratadine
D. Prednisolone
E. Calcium chloride
12. The doctor recommended a patient with an acute myocardial infarction to take an antiplatelet drug that blocks platelet cyclooxygenase. What is this drug?
A. Tiklopidine
B. Clopidogrel
C. Dipyridamol
D. Acetylsalicylic acid
E. Abciximab
13. Acetylsalicylic acid is used to treat rheumatism. What process does acetylsalicylic acid affect?
A. Breakdown of glucose
B. Synthesis of glycogen
C. Fat breakdown
D. Synthesis of amino acids
E. Synthesis of prostaglandins

14. What nonsteroidal anti-inflammatory drugs selectively block COX-2?
A. Ortofen, Voltaren
B. Meloxicam, nimesulide
C. Indomethacin, sodium diclofenac
D. Ibuprofen, ketoprofen
E. Mefenamic acid, naproxen
15. Help the doctor choose a drug from the group of nonsteroidal anti-inflammatory drugs, which is a COX-2 inhibitor and does not damage the stomach?
A. Acetylsalicylic acid
B. Paracetamol
C. Celecoxib
D. Indomethacin
E. Diclofenac sodium
16. Acetylsalicylic acid is identified by saponification products. Name the products that come out after its saponification:
A. Phenol and acetic acid
B. Salicylic acid and acetic acid
C. Benzoic acid and acetic acid
D. Ethyl acetate
E. Benzene and phenol
17. Bromatometric determination of drugs, phenol derivatives is based on the reaction:
A. Oxidation
B. Substitution
C. Accession
D. Elimination
E. Recovery
18. The indicator for the inverse bromatometric method of quantitative determination of drugs is:
A. Starch
B. Neutral red
C. Metallic red
D. Methyl orange
E. Thymolphthalein
19. Acetylsalicylic acid belongs to the class of esters. With improper and long-term storage, we felt a smell of:
A. Ammonia
B. Acetic acid
C. Hydrogen sulfide
D. Formaldehyde
E. Alcohol

20. The pharmacist of Control and Analytical Laboratory performs the identification of the drug substance "Acetylsalicylic acid" in accordance with the requirements of the SPhU. What is the result of the reaction with iron (III) chloride?
A. A purple color appears, which does not disappear after the addition of acetic acid
B. A pink solution is formed, which decolorizes after the addition of ammonia solution
C. A white precipitate insoluble in dilute hydrochloric acid is formed
D. Filter paper moistened with a solution of diphenylcarbazide turns purple-red
E. An orange-red precipitate is formed, which dissolves when a solution of diluted sodium hydroxide is added
21. Quantitative determination of acetylsalicylic acid according to normative and technical documentation is carried out by the method of alkalimetry. Titration at a temperature of 8-10 ºC is recommended in order to prevent:
A. A side reaction of esterification
B. Hydrolysis of the ester group
C. Oxidation of drug substance
D. Decarboxylation
E. Precipitation of the formed salt
22. Which of the following compounds is the starting point for the synthesis of the drug paracetamol?
A. *p* -Aminophenol
B. *p* -Nitrotoluene
C. *m*-Aminophenol
D. *o*-Aminophenol
E. *p*-Xylene
23. State which set of reagents is used in pharmaceutical analysis to confirm the presence of a primary aromatic amino group in the structure of sodium p-aminosalicylate:
A. Sodium nitrite, solution of hydrochloric acid, alkaline solution of β-naphthol
B. Sodium chloride, solution of hydrochloric acid, alkaline solution of β-naphthol
C. Copper (II) sulfate, hydrochloric acid solution, phenol solution
D. Sodium nitrate, sodium hydroxide solution, alkaline β-naphthol solution
E. Sodium thiosulfate solution, hydrochloric acid solution, resorcinol solution
24. Which compound is most often used in pharmaceutical analysis as an azo component in azo coupling reactions with aryldiazonium salts?
A. Naphthalene
B. Naphthysin
C. β-Naphthol
D. Ninhydrin
E. Nitrobenzene

25. Paracetamol substance was received for analysis. When it interacts with a solution of iron (III) chloride, a blue-violet color is formed, which indicates the presence in its structure of:
A. Ester group
B. Keto groups
C. Phenolic hydroxyl
D. Aldehyde group
E. Alcoholic hydroxyl
26. Choose the reagent that is most often used in pharmaceutical analysis to confirm the presence of phenolic hydroxyl in the structure of drugs:
A. Potassium iodide solution
B. 2,4-dinitrochlorobenzene solution
C. Hydroxylamine solution
D. Iron (III) chloride solution
E. Sodium bicarbonate solution
27. Checking the good quality of butadione according to normative and technical documentation, the chemist of the Quality Control Department of the pharmaceutical enterprise determines the presence of a specific impurity. Specify which impurity he defines:
A. Hydrazobenzene
B. 4-Aminoantipyrine
C. p-phenetidine
D. p-Aminophenol
E. Vanillin
28. In order to identify acetylsalicylic acid, its hydrolysis is carried out. Which of the reagents is used to identify hydrolysis products?
A. Iron (III) chloride
B. Potassium phosphate
C. Magnesium sulfate
D. Ammonium molybdate
E. Sodium nitrate
29. The pharmacist of Control and Analytical Laboratory conducts the analysis of the drug substance "Acetylsalicylic acid" in accordance with the requirements of the SPhU. The test with iron (III) chloride gives a purple color, since this reaction to:
A. Benzoic acid, which was formed after acid hydrolysis
B. p-Acetaminophenol formed after reduction
C. Salicylic acid, which was formed after alkaline hydrolysis
D. A specific admixture of acetic anhydride
E. A specific admixture of phosphorus trichloride
30. A chemist-analyst of the laboratory of the tablet workshop of a pharmaceutical enterprise analyzes the manufactured tablets of acetylsalicylic acid of 0.5 g. Which of the listed methods does he use to determine the quantitative content of the active substance in these tablets?

A. Alkalimetric
B. Permanganatometric
C. Complexometric
D. Nitritometric
E. Argentometric
31. Name the industrial method of obtaining paracetamol:
A. Interaction of m-cresol and vanillin
B. Interaction of ethylene and cyclohexane
C. Interaction of adamantane and 2-methylbutadiene
D. Acetylation of p-aminophenol
E. Extraction from oil
32. Paracetamol is studied in the control and analytical laboratory. With which reagent does the substance under study form a purple color that does not change to red?
A. Sodium hydroxide
B. Magnesium sulfate
C. Potassium dichromate
D. Sodium chloride
E. Zinc sulfate
33. Specify the product of the interaction of paracetamol with potassium dichromate in an acidic environment:
A. Indophenol dye
B. Aurine dye
C. Schiff base
D. Azo dye
E. Thiochrome
34. Quantitative content of paracetamol in accordance with the requirements of the SPhU is determined by the cerimetry method. As a titrant we use a solution of:
A. Potassium permanganate
B. Iodine monochloride
C. Cerium sulfate
D. Silver nitrate
E. Hydrochloric acids
35. Quantitative determination of the substance "Paracetamolum" according to the SphU is carried out after preliminary acid hydrolysis by the method of:
A. Nitritometric, titrant - sodium nitrite, indicator - tropeolin 00
B. Cerimetric, titrant - cerium sulfate, indicator - ferroin
C. Nitritometric, titrant - sodium nitrate, indicator - methylene blue
D. Nitritometric, titrant - sodium nitrite, indicator - neutral red
E. Nitritometric, titrant - sodium nitrite, external indicator - iodine-starch paper
36. Paracetamol is quantitatively determined by the cerimetric method after preliminary acid hydrolysis, while para-aminophenol is oxidized by cerium (IV) sulfate to:
A. Quinone

B. Hinonymina
C. Hydroquinone
D. Indophenol
E. Resorcinol
37. The pharmacist performs quantitative determination of paracetamol by the cerimetry method. Specify which indicator the SPhU recommends to use for the indicated method:
A. Tropeolin 00
B. Phenolphthalein
C. Methyl orange
D. Ferroin
E. Potassium chromate
38. The quantitative content of which drug substance can be determined by the nitritometry method only after preliminary hydrolysis?
A. Paracetamol
B. Anesthesin
C. Procaine hydrochloride
D. Sodium para-aminosalicylate
E. Dicainum
39. A heterocycle is present in the structure of the drug analgin:
A. Pyridine
B. Pyrazole
C. Pyrimidine
D. Piperidine
E. Pyrrol
40. Analgin substance was received for analysis. Select the method by which you can determine the quantitative content of analgin:
A. Iodometry
B. Alkalimetry
C. Permanganatometry
D. Complexonometry
E. Acidimetry
41. The solubility of butadione (phenylbutazone) in hydroxides of alkali metals is explained by its ability to undergo tautomeric transformations. What type of tautomerism is characteristic of butadione?
A. Amino-imine tautomerism
B. Keto-enol tautomerism
C. Lacto-lactim tautomerism
D. Azole tautomerism
E. aci-Nitrotautomerism
42. Indomethacin belongs to non-steroidal anti-inflammatory drugs. The basis of its structure is a condensed heterocyclic system. What cycles does it consist of?
A. Pyrrole and benzene
B. Benzene and thiazole

C. Benzene and pyridine
D. Two residues of 4-oxycoumarin
E. Pyrimidine, imidazole
43. In the laboratory for quality control of drug products, the benign quality of indomethacin is checked. Its chemical name is as follows:
A. [1-(4-chlorobenzoyl)-5-methoxy-2-methylindol-3-yl]acetic acid
B. Ethyl ester of di-(4-oxycoumarin-3)-acetic acid
C. 5-Nitro-8-hydroxyquinoline
D. 4-chloro-2-(furfurylamino)-5-sulfamoylbenzoic acid
E. 1,2-Diphenyl-4-butylpyrazolide-indione-3,5
44. Indomethacin forms complex compounds with salts of heavy metals (Fe^{3+}, Cu^{2+}) due to the presence in its structure:
A. Methyl group
B. Benzene ring
C. Carboxyl group
D. Covalently bonded chlorine
E. Methoxy groups
45. To identify the sodium salt of mefenamic acid, the pharmacist of the control and analytical laboratory should use the reagent:
A. Sodium nitrite solution
B. Sodium hydroxide solution
C. Lithium carbonate solution
D. Magnesium sulfate solution
E. Ammonium sulfide solution
46. Which of the physicochemical methods is used to establish the equivalence point in nitritometry?
A. Polarimetry
B. Potentiometry
C. Spectrophotometry
D. Refractometry
E. Photoelectrocolorimetry
47. For what purpose is potassium bromide added during nitritometric titration:
A. To raise the temperature of the reaction environment
B. To change the pH of the environment
C. As a buffer solution
D. As a catalyst
E. As a reaction inhibitor
48. Anthranilic acid (ortho-aminobenzoic) preparations include mefenamic acid (N-(2,3-dimethyl) anthranilic acid). Quantitative determination of the indicated drug can be carried out by any method, except:
A. Acid-base titration
B. Bromatometry
C. Complexonometry
D. Nitritometry

E. Iodometry

49. Analgin (sodium 2,5-dimethyl-2-phenyl-3-oxo-2,3-dehydro-1H-pyrazole-4-N-methyl-methanesulfonate) belongs to pyrazole derivatives, when it is heated with mineral acids, it is released:

A. Sulfur gas and ammonia
B. Sulfur gas and carbon dioxide
C. Sulfur gas and formaldehyde
D. Sulfur gas and nitrogen oxide
E. Sulfur gas and nitrous oxide

50. The pharmacist of a pharmaceutical company received the substance metamizole sodium (analgin) for analysis. Quantitative determination of this substance should be carried out by the iodometric method. According to normative and technical documentation, titration is carried out without an indicator until the appearance of:

A. Red color of the solution
B. Green color of the solution
C. Brown color of the solution
D. Black color of the solution
E. Yellow color of the solution

51. When certifying the analgin substance, the analytical chemist must identify the cation:

A. Sodium
B. Iron (III)
C. Iron (II)
D. Calcium
E. Magnesium

52. One of the directions of biotransformation of paracetamol in the liver is oxidation by microsomal enzymes. As a result, a toxic metabolite is formed:

A. phenol
B. o-xylene
C. phthalic anhydride
D. m-dioxybenzene
E. quinonymine

53. Paracetamol belongs to non-steroidal anti-inflammatory drugs and is biotransformed in the body by deacetylation. What metabolite is formed?

A. P-aminophenol
B. Aminobenzene
C. O-xylene
D. Nitrobenzene
E. M-dioxybenzene

54. An acidic environment is optimal for the absorption of the main metabolite of acetylsalicylic acid. Name this metabolite:

A. Barbituric acid
B. Phenylacetic acid

C. Salicylic acid
D. Uric acid
E. Valproic acid

7. TASKS

1. Calculate the sample weight of acetylsalicylic acid (M.m. 180.16), if 12.5 ml of 0.1 M sodium hydroxide solution (correction factor= 1.0023) was spent on its titration, the percentage content in the preparation is 100.02%.
2. Calculate the percentage content of acetylsalicylic acid (M.m. 180.16) in the preparation, if 25.60 ml of a 0.5 M solution of hydrochloric acid is used for titration, by the pharmacopoeial method, weighing 1.0023 g (correction factor= 1.0002); the volume of the titrant in the control experiment is 49.76 ml.
3. Calculate the sample weight of paracetamol (M.m. 151.17) if 10.09 ml of 0.1 M sodium nitrite solution (v = 1.0001) was spent on its titration; and the percentage content of paracetamol in the drug is 100.2.
4. Calculate the sample weight of analgin (M.m. 351.36), if 12.00 ml of 0.05 M iodine solution (correction factor= 1.0003) was spent on its titration, the content of the active substance in the preparation is 99.2%, weight loss during drying - 5.24%.
5. Calculate the percentage content of analgin (M.m. 351.36), if 11.42 ml of 0.05 M iodine solution (correction factor= 0.9999) was spent on the titration of a weight of 0.2015 g.

FORM OF FILLING OUT THE LESSON PROTOCOL

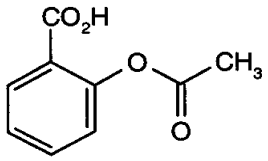
«____» _____20 ____ (Date)

Protocol No. _____

Lesson topic: _____

Lesson purpose: _____

ACIDUM ACETYLSALICYLICUM
ACETYLSALYCILIC ACID



$C_9H_8O_4$ M.M. 180.2

Subject	Methodology, chemism of reaction	Conclusion

8. Laboratory work

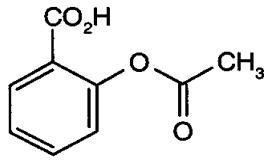
When performing laboratory work, it is necessary to strictly follow the rules of safe work in a chemical laboratory.

Each student individually conducts an analysis of the quality of one of the above drug substances in accordance with the requirements of the State

Pharmacopoeia or other normative and technical documentation using the graphological structure of the analysis.

The student studies the received pharmacopoeial article:

ACIDUM ACETYLSALICYLICUM
ACETYLSALYCILIC ACID



$C_9H_8O_4$ М.м. 180.2

Acetylsalicylic acid contains not less than 99.5% and not more than 101.0% of 2- (acetoxy) benzoic acid, based on dry matter.

Properties

Description. White crystalline powder or colorless crystals.

Solubility. Slightly soluble in water, easily soluble in 96% alcohol, soluble in ether.

(It melts at a temperature of about 143 ^{0}C (instant method).

Identification

First identification: **A, B.**

Second identification: **B, C, D.**

A. The infrared absorption spectrum (2.2.24) of the substance must correspond to the pharmaceutical standard sample spectrum of acetylsalicylic acid.

B. We add 4 ml of diluted sodium hydroxide solution to 0.2 g of the substance, boil for 3 minutes, cool and add 5 ml of diluted sulfuric acid; a crystalline precipitate falls out. The resulting mixture is filtered, the precipitate is washed, then dried at a temperature from 100 ^{0}C to 105 ^{0}C. The melting point (2.2.14) of the obtained residue should be from 156 ^{0}C to 161 ^{0}C.

C. In a test tube, we mix 0.1 g of the substance with 0.5 g of calcium hydroxide. The mixture is heated and a piece of filter paper soaked in 0.05 ml of nitrobenzaldehyde solution is kept in the vapors that appear. The paper gradually turns yellowish-green or blue-green. Then the paper is moistened with hydrochloric acid diluted, the paper turns blue.

D. About 20 mg of the precipitate obtained in test B, in the "Identification" section, when heated, is dissolved in 10 ml of water and cooled.

The resulting solution gives reaction (a) to salicylates (2.3.1).

Purity test

Transparency of the solution (2.2.1). 1.0 g of the substance is dissolved in 9 ml of 96% alcohol. The resulting solution should be transparent.

Color of the solution (2.2.2, method II). The solution prepared as specified in the "Transparency of solution" test should be colorless.

Concomitant impurities. The determination is carried out by the method of liquid chromatography (2.2.29). Solutions are prepared immediately before use.

Heavy metals (2.4.8, method B). no more than 0.002% (20 ppm). 1.0 g of the substance is dissolved in 12 ml of acetone and the volume of the solution is brought to 20 ml with water. 12 ml of the resulting solution must withstand the test for heavy metals. The standard is prepared using a reference solution of lead (1 ppm Pb), obtained by diluting a reference solution of lead (100 ppm Pb) with a mixture of water - acetone (6:9).

Loss in mass during drying (2.2.32). no more than 0.5%. 1,000 g of the substance is dried in a vacuum.

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

Quantitative definition

1.00 g of the substance is placed in a flask with a polished glass stopper, dissolved in 10 ml of 96% alcohol. Then we add 50.0 ml of 0.5 M sodium hydroxide solution. The flask is closed and kept for 1 hour. The resulting solution is titrated with a 0.5 M solution of hydrochloric acid, using 0.2 ml of a phenolphthalein solution as an indicator.

In parallel, a control experiment is conducted.

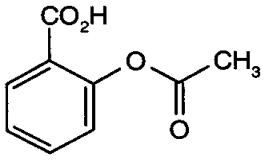
1 ml of 0.5 M sodium hydroxide solution corresponds to 45.04 mg of $C_9H_8O_4$.

Storage

In an airtight container.

PRACTICAL WORK:

ACIDUM ACETYLSALICYLICUM



ACETYLSALYCILIC ACID

$C_9H_8O_4$ М.м. 180.2

Acetylsalicylic acid contains not less than 99.5% and not more than 101.0% of 2-(acetoxy) benzoic acid, based on dry matter.

Properties

Description. White crystalline powder or colorless crystals. (The student conducts an external examination of the received drug product, and draws a conclusion based on the results obtained – it meets or does not meet the SPhU).

Solubility. Slightly soluble in water, easily soluble in 96% alcohol, soluble in

ether.

(It melts at a temperature of about 143 ^{0}C (instant method).

Identification

First identification: A, B.

Second identification: B, C, D.

A. The infrared absorption spectrum (2.2.24) of the substance must correspond to the pharmaceutical standard sample spectrum of acetylsalicylic acid.

B. We add 4 ml of diluted sodium hydroxide solution to 0.2 g of the substance, boil for 3 minutes, cool and add 5 ml of diluted sulfuric acid; a crystalline precipitate falls out. The resulting mixture is filtered, the precipitate is washed, then dried at a temperature from 100 ^{0}C to 105 ^{0}C. The melting point (2.2.14) of the obtained residue should be from 156 ^{0}C to 161 ^{0}C.

(4 ml of diluted sodium hydroxide solution is added to 0.2 g of the substance, taken on hand scales, boil for 3 minutes, cool and add 5 ml of diluted sulfuric acid; observe the precipitation of a white crystalline precipitate).

C. In a test tube, mix 0.1 g of the substance with 0.5 g of calcium hydroxide. The mixture is heated and a piece of filter paper soaked in 0.05 ml of nitrobenzaldehyde solution is kept in the vapors that appear. The paper gradually turns yellowish-green or blue-green. Then the paper is moistened with hydrochloric acid diluted. The paper turns blue.

D. About 20 mg of the precipitate obtained in test B, in the "Identification" section, when heated, is dissolved in 10 ml of water and cooled.

(The precipitate obtained in test B, when heated, is dissolved in 10 ml of water and cooled. To 1 ml of the obtained solution, we add 0.5 ml (10k) of iron trichloride, and observe the appearance of a purple color, which does not disappear after adding 0.1 ml (2k) of acetic acid)

Purity test

Transparency of the solution (2.2.1). 1.0 g of the substance is dissolved in 9 ml of 96% alcohol. The resulting solution should be transparent.

Color of the solution (2.2.2, method II). The solution prepared as specified in the "Transparency of solution" test should be colorless.

Concomitant impurities. The determination is carried out by the method of liquid chromatography (2.2.29). Solutions are prepared immediately before use.

Heavy metals (2.4.8, method B). no more than 0.002% (20 ppm). 1.0 g of the substance is dissolved in 12 ml of acetone and the volume of the solution is brought to 20 ml with water. 12 ml of the resulting solution must withstand the test for heavy metals. The standard is prepared using a reference solution of lead (1 ppm Pb), obtained by diluting a reference solution of lead (100 ppm Pb) with a mixture of water - acetone (6:9).

Loss in mass during drying (2.2.32). no more than 0.5%. 1,000 g of the substance is dried in a vacuum.

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

Quantitative definition

1.00 g of the substance is placed in a flask with a polished glass stopper, dissolved in 10 ml of 96% alcohol. Add 50.0 ml of 0.5 M sodium hydroxide solution. The flask is closed and kept for 1 hour. The resulting solution is titrated with a 0.5 M solution of hydrochloric acid, using 0.2 ml of a phenolphthalein solution as an indicator.

In parallel, a control experiment is conducted.

1 ml of 0.5 M sodium hydroxide solution corresponds to 45.04 mg of $C_9H_8O_4$.

Performance of work:
The student calculates:
1. Titer;
2. Estimated weight per 10 ml of 0.5 M sodium hydroxide solution.

Quantitative definition

About 0.5 g of the substance (precisely weighed) is placed in a flask with a polished glass stopper, dissolved in 10 ml of 96% alcohol. Add 25.0 ml of a 0.5 M sodium hydroxide solution; the flask is closed and kept for 1 hour. The resulting solution is titrated with a 0.5 M solution of hydrochloric acid, using 0.2 ml (4 k) of a phenolphthalein solution as an indicator.

In parallel, a control experiment is conducted.

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

Educational and research work of students: Each student, on the basis of physicochemical properties, solves the question of one of the studied drug substances as unknown. In addition, she/he 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.

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LESSON No. 4

TOPIC: Sleep aids. Characteristics, classification, connection between structure and pharmacological action, mechanism of action, methods of production, methods of analysis. Use in medicine.

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

3. TARGETS:

3.1. Study the characteristics and classification of hypnotic drugs;
3.1. Study the connection between the structure and pharmacological action of hypnotics;
3.2. Study the mechanism of action of hypnotics;
3.3. Learn the Latin names, synonyms, structural formulas, chemical names of the studied drug substances;
3.4. Study the physical and physico-chemical properties of hypnotics;
3.5. Study the structure of normative and technical documentation, quality control methods and quality indicators that are included in them;
3.6. Determine general and specific impurities;
3.7. Carry out calculations of weight, gram, percentage content;
3.8. Study methods of identification of drug substances of this group based on their physical and chemical properties;
3.9. Study methods of quantitative determination of investigated drug substances;
3.10. Study the use, form of release, storage of drug substances;
3.11. 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 hypnotics.
2. Connection between the structure and pharmacological action of hypnotic drugs.
3. Mechanism of action of drugs of this group.
4. Chemical structure, Latin names, synonyms of drugs of this group (barbituric acid derivatives, chloral hydrate, bromisoval, zopiclone, benzodiazepine derivatives).
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. Use 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. A woman turned to a neurologist with complaints of poor sleep, feelings of fear, anxiety. What drug should be prescribed to the patient?
A. Levodopa
B. Diazepam
C. Oxytocin
D. Nitroglycerin
E. Lisinopril
2. A 50-year-old patient was prescribed a benzodiazepine derivative to treat insomnia. Name this drug.
A. Bromizoval
B. Phenobarbital
C. Zolpidem
D. Nitrazepam
E. Donormil
3. Which drug from the group of barbiturates will discolor bromine water?
A. Hexenal
B. Barbital
C. Phenobarbital
D. Benzonal
E. Sodium barbital
4. The introduction of which position of radicals determines the pharmacological effect of barbituric acid derivatives:
A. 5
B. 4
C. 1
D. 2
E. 3
5. Replacing the ethyl radical with a phenyl radical in the 5th position leads to an increase in the pharmacological effect and the appearance of:
A. Soporific effect
B. Local irritant action
C. Aseptic action
D. Exciting action
E. Anticonvulsant action
6. To determine the covalently bound bromine in the bromisoval, we carry out:
A. Reaction with silver nitrate solution without prior mineralization
B. Mineralization of the substance with sodium hydroxide solution followed by reaction with bromides
C. Reaction with silver nitrate solution after destruction of the drug with concentrated nitric acid
D. Reaction with mercury dichloride solution
E. Reaction with a solution of iron (III) chloride

7. Barbiturates according to their chemical structure are:
A. Cyclic ureides
B. Complex esters
C. Lactones
D. Ureids
E. Acyclic ureides
8. The interaction of barbiturates with salts of heavy metals is due to the following properties:
A. Main
B. Acidic
C. Oxidative
D. Restorative
E. Amphoteric
9. The general group reaction for barbiturates is:
A. Salt and complex formation with salts of heavy metals
B. With solutions of aldehydes in concentrated sulfuric acid
C. Formation of azo dye
D. Hydrolytic decomposition
E. Reduction reactions
10. The formation of a precipitate is observed when the following solution is acting on aqueous solutions of salt forms of barbiturates:
A. Sodium hydroxide solution
B. Hydrochloric acid solution
C. Ammonium hydroxide solution
D. Sodium bicarbonate solution
E. Potassium carbonate solution
11. Which of the listed drugs is determined by the argentometric method after preliminary boiling with sodium hydroxide solution:
A. Sodium barbital
B. Bromisoval
C. Sodium thiopental
D. Benzonal
E. Phenobarbital
12. In the control and analytical laboratory, an analysis of barbital is carried out for the presence of chloride impurities. For this, the pharmacist should use as a reagent a solution of:
A. Silver nitrate
B. Acetic acids
C. Barium chloride
D. Sodium sulfide
E. Ammonium oxalate

13. What druf substance is synthesized by the reaction between diethylmalonic ether and urea in the presence of sodium ethylate followed by treatment with hydrochloric acid?
A. Barbital
B. Benzoic acid
C. Benzonal
D. Nicotinic acid
E. Ascorbic acid
14. Which drug substance from the group of barbiturates corresponds to the chemical name 1-benzoyl-5-ethyl-5-phenylbarbituric acid?
A. Barbital
B. Benzonal
C. Phenobarbital
D. Hexenal
E. Benzobamil
15. The hypnotic drug bromisoval contains in its structure:
A. Carbamide group
B. Oxygenated heterocycle
C. Phenolic hydroxyl
D. Complex ether group
E. Nitro- and carboxyl groups
16. Quantitative determination of which of the specified drug substances can be carried out by the Folgard method only after alkaline hydrolysis?
A. Bromisoval
B. Procaine hydrochloride
C. Sulfacyl sodium
D. Phthalazole
E. Drotaverin hydrochloride
17. The reaction of diazotization followed by azo compound is common to substances that contain a primary aromatic amino group. Which of the following drugs does not cause this reaction:
A. Barbital
B. Benzocaine
C. Procaine hydrochloride
D. Procainamide hydrochloride
E. Streptocide
18. The drug phenobarbital has a sedative, hypnotic and antiepileptic effect. Specify its international non-proprietary name:
A. Chloramphenicol
B. Nitrofural
C. Luminal
D. Diazepam
E. Salol

19. The pharmacist performs the identification reaction of barbiturates according to the SPhU. With which reagents do they form a violet-blue color with the formation of a precipitate?
A. Cobalt nitrate, calcium chloride, sodium hydroxide
B. Copper sulfate, potassium bicarbonate, potassium carbonate
C. Iron (III) chloride, potassium bicarbonate, potassium carbonate
D. Lead nitrate, calcium chloride, sodium hydroxide
E. Nickel nitrate, potassium bicarbonate, potassium carbonate
20. Specify the color of the complex salt, which is formed during the identification of phenobarbital by reaction with a solution of cobalt (II) nitrate:
A. Pink-lilac
B. Yellow
C. Blue-violet
D. Orange-red
E. Yellow-green
21. The pharmacist identifies the drug, a derivative of barbituric acid, by reaction with copper (II) sulfate in the presence of potassium bicarbonate and potassium carbonate. At the same time, the appearance of a blue color and the formation of a red-lilac precipitate make it possible to detect:
A. Barbital
B. Phenobarbital
C. Benzonal
D. Ethaminal sodium
E. Hexenal
22. In which drug from the group of barbiturates can a fragment of benzoic acid be identified with a hydroxam test?
A. Sodium barbital
B. Barbital
C. Phenobarbital
D. Hexanal
E. Benzonal
23. The specialist of the Department of Technical Control of the chemical-pharmaceutical enterprise fuses the drug substance with sodium hydroxide. Further acidification of the reaction product leads to the release of gas bubbles (carbon dioxide) and the appearance of the characteristic smell of phenylethylacetic acid. Name the drug substance that can be identified by these tests:
A. Phenobarbital
B. Resorcinol
C. Codeine
D. Streptocide
E. Phenoxymethylpenicillin

24. Drug products from the barbiturate-acid group are quantitatively determined by the method of alkalimetry in a non-aqueous environment. The following should be used as a solvent:
A. Dimethylformamide
B. glacial acetic acid
C. Acetic anhydride
D. Ethyl alcohol
E. Glycerin

7. TASKS:

1. Calculate the sample weight of barbital (M.m 184.20), if 8.14 ml of 0.1 M sodium hydroxide solution (correction factor= 1.0030) was spent on its titration in a non-aqueous environment, and the content of the active substance in the preparation is 99 .2%.
2. Calculate the percentage content of sodium barbital (M.m. 206.18), if 24.27 ml of a 0.1 M solution of hydrochloric acid (correction factor= 0.9984) was spent on the titration of 0.4983 g of the drug, and the content of free alkali is 0.23%.
3. Calculate the volume of 0.1 M sodium hydroxide solution (correction factor= 1.0000), which will be spent on the titration of 0.1984 g of phenobarbital (M.m. 232.24), if the content of the active substance in the preparation is 100, 1%
4. Calculate the sample weight of the hexenal sample (M.m. 258.20), if 18.83 ml of a 0.1 M solution of hydrochloric acid (correction factor= 1.0000) was spent on its titration. The content of the active substance in the preparation is 98.9%, the content of free alkali is 0.21%, and the weight loss during drying is 0.7%.

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, on the basis of physical and chemical properties, solves the question of one of the studied drug substances as unknown. In addition, she/he 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.

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Additional

10. Фармацевтична хімія: підруч. для студ. вищ. фармац. навч. закл. і фармац. ф-тів вищ. мед. навч. закл. III-IV рівнів акредитації / П. О. Безуглий [та ін.]; за ред. П. О. Безуглого. - 3-є вид., випр. и доопрац. - Вінниця: Нова книга, 2017. - 456 с.

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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 good quality of antitussive, nootropic, non-steroidal anti-inflammatory, hypnotic drugs.

3. TARGET TASKS:

3.1. Check and consolidate theoretical knowledge and practical skills regarding the establishment of good quality of antitussive, nootropic, non-steroidal anti-inflammatory, hypnotic drugs;

3.2. Check the protocols of laboratory work and analyze the correctness of the course of analysis according to the requirements of the SPhU and other of Quality Control Methods.

4. CONTROL QUESTIONS OF THE LESSON

4.1. Characteristics and classification of antitussive, nootropic, non-steroidal anti-inflammatory, hypnotic drugs.

4.2. The concept of cough and its characteristics and classification.

4.3. Mechanism of action of antitussive, nootropic, non-steroidal anti-inflammatory, hypnotic drugs.

4.4. The connection (relationship) between the structure and pharmacological action of antitussive, nootropic, non-steroidal anti-inflammatory, hypnotic drugs.

4.5. Analysis of antitussive drugs (Latin, Ukrainian, chemical name; chemical formula; description; extraction method; all possible methods of identification; all possible methods of quantitative determination) on the example of bromhexine, glaucine hydrochloride, ambroxol, acetylcysteine, sodium benzoate.

4.6. Analysis of nootropic 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 piracetam, aminalon, glycine, calcium pantogam.

4.7. Analysis of non-steroidal anti-inflammatory drugs (Latin, Ukrainian, chemical name; chemical formula; description; extraction method; all possible methods of identification; all possible methods of quantitative determination) acetylsalicylic acid, paracetamol, indomethacin, mefenamic acid, diclofenac sodium.

4.8. Analysis of hypnotic 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 barbituric acid derivatives, bromisoval, benzodiazepine derivatives, chloral hydrate.

4.9. Use in medicine.

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

5. TEST TASKS

1. A chemist of a pharmaceutical enterprise can confirm the sodium cation in the tested substance, according to the SPhU, with a solution of:

A. Potassium pyroantimonate
B. Potassium ferrocyanide
C. Potassium chloride
D. Potassium hydroxide
E. Potassium nitrate

2. The pharmacist determines the quantitative content of sodium benzoate by the method of acidimetry in a non-aqueous environment in accordance with the requirements of the SPhU. What reagent does he use as a solvent?

A. Concentrated sulfuric acid
B. Pyridine
C. Anhydrous acetic acid
D. Dimethylformamide
E. Sulfanilic acid

3. The reaction of the formation of ethyl acetate is used to detect the acetyl group in Acetylcysteine when adding which reagent:

A. Iron chloride
B. Sodium hydroxide solution
C. 2,4 - dinitrochlorobenzene
D. 96% alcohol
E. Boiling with a solution of potassium dichromate in sulfuric acid and subsequent addition of ethanol.

4. Which reagent should be used to detect the thiogroup in the acetylcysteine molecule:

A. With iron oxide chloride
B. With alkali
C. With alcohol
D. With chloroform
E. With chloramine

5. What reagent must be added to determine the carboxyl group in Acetylcysteine:

A. Concentrated acid
B. Heavy metal salt
C. Dimethylformamide
D. Perhydrol
E. Alkali

6. What method can quantitatively determine acetylcysteine:

A. Iodometric
B. Bromatometric
C. S. Iodochlormetric
D. Argentometric
E. Complexonometric

7. What is the iodometric titration of acetylcysteine based on:
A. physical and chemical properties
B. presence of a primary amino group in the drug
C. S. specific rotation index
D. oxidation of sulfhydryl groups
E. pharmacological properties
8. Suggest a reagent for detecting the primary aromatic amino group in the bromhexine molecule:
A. Sodium nitrite, sulfuric acid and β-naphthol
B. Sodium nitrate, hydrochloric acid and β-naphthol
C. Sodium nitrite, hydrochloric acid and β-naphthol
D. Sodium nitrite, hydrochloric acid
E. Hydrochloric acid and β-naphthol
9. The presence of bromine in bromhexine hydrochloride is established after the destruction of the organic part of the molecule to sodium bromide by boiling in a 30% solution of sodium hydroxide and the subsequent addition of:
A. Dilute hydrochloric acid, 5% chloramine and tetrachloromethane
B. Dilute sulfuric acid, 5% chloramine
C. Dilute sulfuric acid, tetrachloromethane
D. Dilute sulfuric acid
E. Tetrachloromethane
10. To confirm the reliability of bromhexine hydrochloride and establish the absence of extraneous impurities, we use the following method:
A. thin-layer chromatography
B. HPLC
C. Photoelectric Colorimetry
D. Refractometry
E. Polarimetry
11. When identifying glaucin hydrochloride, a reagent was added to the preparation, a white curdled precipitate is formed, dissolved in an ammonia solution. What reagent was added:
A. Sodium hydroxide
B. Concentrated sulfuric acid

C. Alkali solution
D. Potassium dichromate
E. Silver nitrate

12. Identification of bromhexine and ambroxol can be carried out with the help of general alkaloid reagents. Which reaction has the most sensitivity with the reagent:

A. Dragendorf
B. Marquis
C. Froehde
D. Bouchard
E. Wagner

13. One of the possible methods of quantitative determination of bromhexine hydrochloride is the method of:

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

14. Bromhexine hydrochloride can be determined quantitatively using non-aqueous titration as a titrant with:

A. Iodine solution
B. Hydrochloric acid solution
C. Potassium permanganate solution
D. Perchloric acid solution
E. Sodium thiosulfate solution

15. Bromhexine hydrochloride can be determined quantitatively using non-aqueous titration as an indicator with:

A. Crystal violet
B. Phenolphthalein
C. Etching black
D. Methyl orange
E. Tropeolin 00

16. Ambroxol hydrochloride belongs to the following group of antitussives according to the mechanism of action:

A. Non-narcotic drugs
B. Narcotic drugs
C. Peripheral-type antitussives
D. Mucolytics
E. Expectorants

17. Bromhexine hydrochloride belongs to the following group of antitussives according to the mechanism of action:

A. Non-narcotic drugs
B. Narcotic drugs
C. Peripheral-type antitussives
D. Expectorants
E. Mucolytics

18. Acetylcysteine belongs to the following group of expectorants according to the mechanism of action:

A. Synthetic mucolytics
B. Surfactant synthesis stimulants
C. S. Enzyme drugs
D. Drugs of mixed type
E. Drugs of the resorptive type of action

19. When determining the chloride ion from silver with nitrate in Glaucine hydrochloride, a precipitate of what color falls out:

A. White, curdled
B. The solution is white
C. chloroform layer is purple in color
D. Yellow
E. Yellow solution

20. The second phase of drug metabolism (conjugation phase) includes interactions of xenobiotics or their metabolites, which have active functional groups, with hydrophilic endogenous molecules. This phase includes the process of:

A. S-Oxidation
B. Glucuronidation
C. Hydroxylation
D. Recovery
E. Hydrolysis

21. Drugs are metabolized in several stages. Functional groups in the drug substance molecule undergo biochemical transformation during the following phase:

A. Conjugations
B. Secretions
C. Hydration
D. Functionalization
E. Depolarization

22. Drugs are metabolized in several stages. Biochemical conjugation of functional groups of the molecule with acid residues, such as glucuronic and sulfate, or glycine, occurs in the phase of:

A. Functionalization
B. Secretions
C. Hydration
D. Depolarization
E. Conjugations

23. Metabolism of drugs is one of the stages of pharmacokinetics. Agents that are metabolically transformed into biologically active substances are called:

A. Vitamins
B. Prodrugs
C. Hormones
D. Enzymes
E. Conjugates

24. Drugs are able to undergo biotransformation in the body. The metabolic phase of functionalization is aimed at:

A. Binding to endogenous molecules
B. Increase in hydrophilicity
C. Mineralization of matter
D. Formation of polymers

25. The doctor prescribed piracetam to a patient after a traumatic brain injury. To which pharmacological group does this drug belong?

A. Nootropic drugs
B. Non-narcotic analgesics
C. Tranquilizers
D. Means for anesthesia
E. Neuroleptics

26. When identifying the substance of nootropil (piracetam) by heating with sodium hydroxide solution, ammonia is released. The pharmacist confirms its formation with the help of:

A. Wetted lignin paper
B. Wetted litmus paper
C. Addition of $FeCl_3$ solution
D. Addition of $FeCl_2$ solution
E. Addition of $AgNO_3$ solution

27. The presence of an amide group in the piracetam structure is confirmed by the pharmacist by reaction with sodium hydroxide when heated. What characteristic product is formed as a result of alkaline hydrolysis of piracetam?

A. Ethanol
B. Urea
C. Hydroxylamine
D. Ammonia
E. Sodium acetate

28. To identify piracetam, a reaction is carried out, as a result of which ammonia is released when heated. What reagent is used in this reaction?

A. Sodium hydroxide solution
B. Hydrochloric acid solution
C. Copper (II) sulfate solution
D. Silver nitrate solution
E. Ammonium oxalate solution

29. Indicate which drug substance corresponds to the chemical name "4-aminobutanoic acid"?

A. Methionine
B. Cysteine
C. Alanine
D. Glutamic acid
E. Aminalon

30. Identification of nootropic drugs from the group of amino acids of the aliphatic series is carried out by the appearance of a blue-violet color with:

A. Ninhydrin
B. Aniline
C. Pyridine
D. Methylamine
E. Resorcinoma

31. Specify the reagent that can be used to confirm glycine belonging to amino acids during pharmaceutical analysis:

A. Saturated sodium bicarbonate solution
B. Sulfuric acid solution
C. Sulfosalicylic acid solution
D. Ninhydrin solution
E. Barium hydroxide solution

32. The control and analytical laboratory received the glycine substance. According to the SPhU, its identification involves the determination of substances detected by ninhydrin. This test is carried out by the method of:

A. Thin-layer chromatography
B. Gas chromatography
C. Liquid chromatography
D. Gas-liquid chromatography
E. Ion exchange chromatography

33. A control and analytical laboratory specialist uses formol titration (according to Sorensen) for the quantitative determination of nootropic drugs from the group of amino acids. At the same time, the role of formaldehyde is reduced to:
A. Carboxylation of the amino group
B. Blocking of the amino group
C. Neutralization of the carboxyl group
D. Alkylation of the carboxyl group
E. Formation of betaines

34. The pharmacist of the laboratory of the State Service of Ukraine on Medicines carries out quantitative determination of "Aminolone" in accordance with the requirements of the SPhU. Indicate by what method he should carry out quantitative determination:
A. Nitritometry
B. Acidimetry in a non-aqueous medium
C. Bromatometry
D. Argentometry
E. Complexonometry

35. Aminalon in the environment of dimethylformamide forms a bright crimson color when heated with the reagent of:
A. Formaldehyde solution
B. Sodium nitrite
C. Ninhydrin
D. Alloxon
E. Sulfuric acid

36. With what reagent when aminalon is fused, hydrogen sulfide is released, which is detected using paper impregnated with lead (II) acetate:
A. Sodium nitrite
B. Potassium thiocyanate
C. Ninhydrin
D. Formaldehyde solution
E. Alloxon

37. By what quantitative method is it possible to determine aminolone:
A. Kjeldahl method
B. Nitritometry

C. Acidimetry
D. Complexonometry
E. Iodometry
38. What heterocycle is included in the chemical structure of piracetam:
A. Morpholin
B. Piperazine
C. Pyrimidine
D. Thiazole
E. Pyrrolidine
39. When glycine is identified, oxidative decarboxylation of the drug is carried out under the action of NaOCl during heating. What is formed at the same time?
A. Phenol
B. Acetic acid
C. Formaldehyde
D. Sodium nitrite
E. Alloxon
40. When heating which drug with alloxone, a bright crimson color is formed:
A. Aminalon
B. Glycine
C. Piracetam
D. Acetylsalicylic acid
E. Streptocide
41. Aminalon is identified by reaction with ninhydrin. A positive result of the reaction should be considered:
A. Appearance of red color
B. Release of gas bubbles
C. Appearance of a characteristic smell
D. Appearance of a blue-violet color
E. Precipitation of a white precipitate
42. Drugs containing pyrrolidine in their structure include:
A. Piracetam
B. Phenobarbital
C. Furacilin
D. Isoniazid
E. Analgin
43. For quantitative determination of azote [Nitrogen] in drug substances of organic nature, use:
A. Kjeldahl method
B. Kolthoff method

C. Kolbe-Schmidt method
D. Mohr's method
E. Fajans method
44. Specify a drug that exhibits pronounced selectivity in relation to COX-2:
A. Nimesulide
B. Acetylsalicylic acid
C. Celecoxib
D. Ibuprofen
E. Acetoaminophen
45. Choose an international non-proprietary name for aspirin:
A. Diclofenac
B. Phenylbutazone
C. Nimesulide
D. Acetylsalicylic acid
E. Ibuprofen
46. One of the NSAIDs belongs to the group of non-narcotic analgesics:
A. Analgin
B. Ibuprofen
C. Paracetamol
D. Indomethacin
E. Fentanyl
47. One of the NSAIDs belongs to the drugs of the pyrazolone group:
A. Indomethacin
B. Ibuprofen
C. Phenacetin
D. Acetylsalicylic acid
E. Analgin
48. Which NSAID has the weakest anti-inflammatory effect:
A. Diclofenac
B. Piroxicam
C. Paracetamol
D. Celecoxib
E. Indomethacin
49. A patient suffering from a headache, who was prescribed a cyclooxygenase inhibitor - an aminophenol derivative, came to the pharmacy for consultation. What drug was prescribed to the patient?
A. Diclofenac
B. Paracetamol
C. Ketorolac

D. Ibuprofen
E. Acetylsalicylic acid

50. The doctor prescribed an antipyretic drug to the patient. Specify this drug.
A. Ascorbic acid
B. Cyanocobalamin
C. Oxytocin
D. Famotidine
E. Paracetamol

51. The doctor prescribed paracetamol, a cyclooxygenase inhibitor, to a patient with arthritis. The formation of which biologically active compounds is inhibited by this drug?
A. Catecholamines
B. Prostaglandins
C. Cytokines
D. Iodothyronine
E. Interferons

52. What is the mechanism of action of diclofenac sodium?
A. Suppresses cholinesterase
B. Activates the synthesis of phosphodiesterase
C. Blocks cyclooxygenase
D. Activates adenylate cyclase
E. Inhibits phosphodiesterase

53. A patient with osteoarthritis was prescribed a drug that caused a side effect in the form of an ulcer.
A. Meloxicam
B. Diclofenac-Sodium
C. Nimesulid
D. Celecoxib
E. Rofeccoxib

54. To relieve inflammation and pain, the doctor prescribed a drug that belongs to the group of NSAIDs. Specify this drug:
A. Glibenclamide
B. Diclofenac-Sodium
C. Loratadine
D. Prednisolone
E. Calcium chloride

55. The doctor recommended a patient with an acute myocardial infarction to take an antiplatelet drug that blocks platelet cyclooxygenase. What is this drug?
A. Tiklopidine

B. Clopidogrel
C. Dipyridamol
D. Acetylsalicylic acid
E. Abciximab

56. Acetylsalicylic acid is used to treat rheumatism. What process does acetylsalicylic acid affect?
A. Breakdown of glucose
B. Synthesis of glycogen
C. Fat breakdown
D. Synthesis of amino acids
E. Synthesis of prostaglandins

57. What nonsteroidal anti-inflammatory drugs selectively block COX-2?
A. Ortofen, Voltaren
B. Meloxicam, nimesulide
C. Indomethacin, sodium diclofenac
D. Ibuprofen, ketoprofen
E. Mefenamic acid, naproxen

58. Help the doctor choose a drug from the group of nonsteroidal anti-inflammatory drugs, which is a COX-2 inhibitor and does not damage the stomach?
A. Acetylsalicylic acid
B. Paracetamol
C. Celecoxib
D. Indomethacin
E. Diclofenac sodium

59. Acetylsalicylic acid is identified by saponification products. Name the products that come out after its saponification:
A. Phenol and acetic acid
B. Salicylic acid and acetic acid
C. Benzoic acid and acetic acid
D. Ethyl acetate
E. Benzene and phenol

60. Bromatometric determination of drugs, phenol derivatives is based on the reaction:
A. Oxidation
B. Substitution
C. Accession
D. Elimination
E. Recovery

61. The indicator for the inverse bromatometric method of quantitative determination of drugs is:

A. Starch
B. Neutral red
C. Metallic red
D. Methyl orange
E. Thymolphthalein

62. Acetylsalicylic acid belongs to the class of esters. With improper and long-term storage, we felt a smell of:

A. Ammonia
B. Acetic acid
C. Hydrogen sulfide
D. Formaldehyde
E. Alcohol

63. The pharmacist of Control and Analytical Laboratory performs the identification of the drug substance "Acetylsalicylic acid" in accordance with the requirements of the SPhU. What is the result of the reaction with iron (III) chloride?

A. A purple color appears, which does not disappear after the addition of acetic acid
B. A pink solution is formed, which decolorizes after the addition of ammonia solution
C. A white precipitate insoluble in dilute hydrochloric acid is formed
D. Filter paper moistened with a solution of diphenylcarbazide turns purple-red
E. An orange-red precipitate is formed, which dissolves when a solution of diluted sodium hydroxide is added

64. Quantitative determination of acetylsalicylic acid according to normative and technical documentation is carried out by the method of alkalimetry. Titration at a temperature of 8-10 ºC is recommended in order to prevent:

A. A side reaction of esterification
B. Hydrolysis of the ester group
C. Oxidation of drug substance
D. Decarboxylation
E. Precipitation of the formed salt

65. Which of the following compounds is the starting point for the synthesis of the drug paracetamol?

A. *p* -Aminophenol
B. *p* -Nitrotoluene

C. *m*-Aminophenol

D. *o*-Aminophenol

E. *p*-Xylene

66. State which set of reagents is used in pharmaceutical analysis to confirm the presence of a primary aromatic amino group in the structure of sodium p-aminosalicylate:

A. Sodium nitrite, solution of hydrochloric acid, alkaline solution of β-naphthol

B. Sodium chloride, solution of hydrochloric acid, alkaline solution of β-naphthol

C. Copper (II) sulfate, hydrochloric acid solution, phenol solution

D. Sodium nitrate, sodium hydroxide solution, alkaline β-naphthol solution

E. Sodium thiosulfate solution, hydrochloric acid solution, resorcinol solution

67. Which compound is most often used in pharmaceutical analysis as an azo component in azo coupling reactions with aryldiazonium salts?

A. Naphthalene

B. Naphthysin

C. β-Naphthol

D. Ninhydrin

E. Nitrobenzene

68. Paracetamol substance was received for analysis. When it interacts with a solution of iron (III) chloride, a blue-violet color is formed, which indicates the presence in its structure of:

A. Ester group

B. Keto groups

C. Phenolic hydroxyl

D. Aldehyde group

E. Alcoholic hydroxyl

69. Choose the reagent that is most often used in pharmaceutical analysis to confirm the presence of phenolic hydroxyl in the structure of drugs:

A. Potassium iodide solution

B. 2,4-dinitrochlorobenzene solution

C. Hydroxylamine solution

D. Iron (III) chloride solution

E. Sodium bicarbonate solution

70. Checking the good quality of butadione according to normative and technical documentation, the chemist of the Quality Control Department of the pharmaceutical enterprise determines the presence of a specific impurity. Specify which impurity he defines:

A. Hydrazobenzene

B. 4-Aminoantipyrine
C. p-phenetidine
D. p-Aminophenol
E. Vanillin

71. In order to identify acetylsalicylic acid, its hydrolysis is carried out. Which of the reagents is used to identify hydrolysis products?
A. Iron (III) chloride
B. Potassium phosphate
C. Magnesium sulfate
D. Ammonium molybdate
E. Sodium nitrate

72. The pharmacist of Control and Analytical Laboratory conducts the analysis of the drug substance "Acetylsalicylic acid" in accordance with the requirements of the SPhU. The test with iron (III) chloride gives a purple color, since this reaction to:
A. Benzoic acid, which was formed after acid hydrolysis
B. p-Acetaminophenol formed after reduction
C. Salicylic acid, which was formed after alkaline hydrolysis
D. A specific admixture of acetic anhydride
E. A specific admixture of phosphorus trichloride

73. A chemist-analyst of the laboratory of the tablet workshop of a pharmaceutical enterprise analyzes the manufactured tablets of acetylsalicylic acid of 0.5 g. Which of the listed methods does he use to determine the quantitative content of the active substance in these tablets?
A. Alkalimetric
B. Permanganatometric
C. Complexometric
D. Nitritometric
E. Argentometric

74. Name the industrial method of obtaining paracetamol:
A. Interaction of m-cresol and vanillin
B. Interaction of ethylene and cyclohexane
C. Interaction of adamantane and 2-methylbutadiene
D. Acetylation of p-aminophenol
E. Extraction from oil

75. Paracetamol is studied in the control and analytical laboratory. With which reagent does the substance under study form a purple color that does not change to red?
A. Sodium hydroxide

B. Magnesium sulfate
C. Potassium dichromate
D. Sodium chloride
E. Zinc sulfate

76. Specify the product of the interaction of paracetamol with potassium dichromate in an acidic environment:
A. Indophenol dye
B. Aurine dye
C. Schiff base
D. Azo dye
E. Thiochrome

77. Quantitative content of paracetamol in accordance with the requirements of the SPhU is determined by the cerimetry method. As a titrant we use a solution of:
A. Potassium permanganate
B. Iodine monochloride
C. Cerium sulfate
D. Silver nitrate
E. Hydrochloric acids

78. Quantitative determination of the substance "Paracetamolum" according to the SphU is carried out after preliminary acid hydrolysis by the method of:
A. Nitritometric, titrant - sodium nitrite, indicator - tropeolin 00
B. Cerimetric, titrant - cerium sulfate, indicator - ferroin
C. Nitritometric, titrant - sodium nitrate, indicator - methylene blue
D. Nitritometric, titrant - sodium nitrite, indicator - neutral red
E. Nitritometric, titrant - sodium nitrite, external indicator - iodine-starch paper

79. Paracetamol is quantitatively determined by the cerimetric method after preliminary acid hydrolysis, while para-aminophenol is oxidized by cerium (IV) sulfate to:
A. Quinone
B. Hinonymina
C. Hydroquinone
D. Indophenol
E. Resorcinol

80. The pharmacist performs quantitative determination of paracetamol by the cerimetry method. Specify which indicator the SPhU recommends to use for the indicated method:
A. Tropeolin 00
B. Phenolphthalein
C. Methyl orange

D. Ferroin
E. Potassium chromate

81. The quantitative content of which drug substance can be determined by the nitritometry method only after preliminary hydrolysis?
A. Paracetamol
B. Anesthesin
C. Procaine hydrochloride
D. Sodium para-aminosalicylate
E. Dicainum

82. A heterocycle is present in the structure of the drug analgin:
A. Pyridine
B. Pyrazole
C. Pyrimidine
D. Piperidine
E. Pyrrol

83. Analgin substance was received for analysis. Select the method by which you can determine the quantitative content of analgin:
A. Iodometry
B. Alkalimetry
C. Permanganatometry
D. Complexonometry
E. Acidimetry

84. The solubility of butadione (phenylbutazone) in hydroxides of alkali metals is explained by its ability to undergo tautomeric transformations. What type of tautomerism is characteristic of butadione?
A. Amino-imine tautomerism
B. Keto-enol tautomerism
C. Lacto-lactim tautomerism
D. Azole tautomerism
E. aci-Nitrotautomerism

85. Indomethacin belongs to non-steroidal anti-inflammatory drugs. The basis of its structure is a condensed heterocyclic system. What cycles does it consist of?
A. Pyrrole and benzene
B. Benzene and thiazole
C. Benzene and pyridine
D. Two residues of 4-oxycoumarin
E. Pyrimidine, imidazole

86. In the laboratory for quality control of drug products, the benign quality of indomethacin is checked. Its chemical name is as follows:
A. [1-(4-chlorobenzoyl)-5-methoxy-2-methylindol-3-yl]acetic acid
B. Ethyl ester of di-(4-oxycoumarin-3)-acetic acid
C. 5-Nitro-8-hydroxyquinoline

D. 4-chloro-2-(furfurylamino)-5-sulfamoylbenzoic acid
E. 1,2-Diphenyl-4-butylpyrazolide-indione-3,5

87. Indomethacin forms complex compounds with salts of heavy metals (Fe^{3+}, Cu^{2+}) due to the presence in its structure:
A. Methyl group
B. Benzene ring
C. Carboxyl group
D. Covalently bonded chlorine
E. Methoxy groups

88. To identify the sodium salt of mefenamic acid, the pharmacist of the control and analytical laboratory should use the reagent:
A. Sodium nitrite solution
B. Sodium hydroxide solution
C. Lithium carbonate solution
D. Magnesium sulfate solution
E. Ammonium sulfide solution

89. Which of the physicochemical methods is used to establish the equivalence point in nitritometry?
A. Polarimetry
B. Potentiometry
C. Spectrophotometry
D. Refractometry
E. Photoelectrocolorimetry

90. For what purpose is potassium bromide added during nitritometric titration:
A. To raise the temperature of the reaction environment
B. To change the pH of the environment
C. As a buffer solution
D. As a catalyst
E. As a reaction inhibitor

91. Anthranilic acid (ortho-aminobenzoic) preparations include mefenamic acid (N-(2,3-dimethyl) anthranilic acid). Quantitative determination of the indicated drug can be carried out by any method, except:
A. Acid-base titration
B. Bromatometry
C. Complexonometry
D. Nitritometry
E. Iodometry

92. Analgin (sodium 2,5-dimethyl-2-phenyl-3-oxo-2,3-dehydro-1H-pyrazole-4-N-methyl-methanesulfonate) belongs to pyrazole derivatives, when it is heated with mineral acids, it is released:
A. Sulfur gas and ammonia
B. Sulfur gas and carbon dioxide
C. Sulfur gas and formaldehyde
D. Sulfur gas and nitrogen oxide

E. Sulfur gas and nitrous oxide

93. The pharmacist of a pharmaceutical company received the substance metamizole sodium (analgin) for analysis. Quantitative determination of this substance should be carried out by the iodometric method. According to normative and technical documentation, titration is carried out without an indicator until the appearance of:

A. Red color of the solution
B. Green color of the solution
C. Brown color of the solution
D. Black color of the solution
E. Yellow color of the solution

94. When certifying the analgin substance, the analytical chemist must identify the cation:

A. Sodium
B. Iron (III)
C. Iron (II)
D. Calcium
E. Magnesium

95. One of the directions of biotransformation of paracetamol in the liver is oxidation by microsomal enzymes. As a result, a toxic metabolite is formed:

A. phenol
B. o-xylene
C. phthalic anhydride
D. m-dioxybenzene
E. quinonymine

96. Paracetamol belongs to non-steroidal anti-inflammatory drugs and is biotransformed in the body by deacetylation. What metabolite is formed?

A. *p*-aminophenol
B. Aminobenzene
C. *o*-xylene
D. Nitrobenzene
E. *m*-dioxybenzene

97. An acidic environment is optimal for the absorption of the main metabolite of acetylsalicylic acid. Name this metabolite:

A. Barbituric acid
B. Phenylacetic acid
C. Salicylic acid
D. Uric acid
E. Valproic acid

98. A woman turned to a neurologist with complaints of poor sleep, feelings of fear, anxiety. What drug should be prescribed to the patient?

A. Levodopa
B. Diazepam
C. Oxytocin

D. Nitroglycerin
E. Lisinopril

99. A 50-year-old patient was prescribed a benzodiazepine derivative to treat insomnia. Name this drug.
A. Bromizoval
B. Phenobarbital
C. Zolpidem
D. Nitrazepam
E. Donormil

100. Which drug from the group of barbiturates will discolor bromine water?
A. Hexenal
B. Barbital
C. Phenobarbital
D. Benzonal
E. Sodium barbital

101. The introduction of which position of radicals determines the pharmacological effect of barbituric acid derivatives:
A. 5
B. 4
C. 1
D. 2
E. 3

102. Replacing the ethyl radical with a phenyl radical in the 5th position leads to an increase in the pharmacological effect and the appearance of:
A. Soporific effect
B. Local irritant action
C. Aseptic action
D. Exciting action
E. Anticonvulsant action

103. To determine the covalently bound bromine in the bromisoval, we carry out:
A. Reaction with silver nitrate solution without prior mineralization
B. Mineralization of the substance with sodium hydroxide solution followed by reaction with bromides
C. Reaction with silver nitrate solution after destruction of the drug with concentrated nitric acid
D. Reaction with mercury dichloride solution
E. Reaction with a solution of iron (III) chloride

104. Barbiturates according to their chemical structure are:
A. Cyclic ureides
B. Complex esters
C. Lactones
D. Ureids

E. Acyclic ureides

105. The interaction of barbiturates with salts of heavy metals is due to the following properties:

A. Main
B. Acidic
C. Oxidative
D. Restorative
E. Amphoteric

106. The general group reaction for barbiturates is:

A. Salt and complex formation with salts of heavy metals
B. With solutions of aldehydes in concentrated sulfuric acid
C. Formation of azo dye
D. Hydrolytic decomposition
E. Reduction reactions

107. The formation of a precipitate is observed when the following solution is acting on aqueous solutions of salt forms of barbiturates:

A. Sodium hydroxide solution
B. Hydrochloric acid solution
C. Ammonium hydroxide solution
D. Sodium bicarbonate solution
E. Potassium carbonate solution

108. Which of the listed drugs is determined by the argentometric method after preliminary boiling with sodium hydroxide solution:

A. Sodium barbital
B. Bromisoval
C. Sodium thiopental
D. Benzonal
E. Phenobarbital

109. In the control and analytical laboratory, an analysis of barbital is carried out for the presence of chloride impurities. For this, the pharmacist should use as a reagent a solution of:

A. Silver nitrate
B. Acetic acids
C. Barium chloride
D. Sodium sulfide
E. Ammonium oxalate

110. What druf substance is synthesized by the reaction between diethylmalonic ether and urea in the presence of sodium ethylate followed by treatment with hydrochloric acid?

A. Barbital
B. Benzoic acid
C. Benzonal
D. Nicotinic acid

E. Ascorbic acid

111. Which drug substance from the group of barbiturates corresponds to the chemical name 1-benzoyl-5-ethyl-5-phenylbarbituric acid?

A. Barbital
B. Benzonal
C. Phenobarbital
D. Hexenal
E. Benzobamil

112. The hypnotic drug bromisoval contains in its structure:

A. Carbamide group
B. Oxygenated heterocycle
C. Phenolic hydroxyl
D. Complex ether group
E. Nitro- and carboxyl groups

113. Quantitative determination of which of the specified drug substances can be carried out by the Folgard method only after alkaline hydrolysis?

A. Bromisoval
B. Procaine hydrochloride
C. Sulfacyl sodium
D. Phthalazole
E. Drotaverin hydrochloride

114. The reaction of diazotization followed by azo compound is common to substances that contain a primary aromatic amino group. Which of the following drugs does not cause this reaction:

A. Barbital
B. Benzocaine
C. Procaine hydrochloride
D. Procainamide hydrochloride
E. Streptocide

115. The drug phenobarbital has a sedative, hypnotic and antiepileptic effect. Specify its international non-proprietary name:

A. Chloramphenicol
B. Nitrofural
C. Luminal
D. Diazepam
E. Salol

116. The pharmacist performs the identification reaction of barbiturates according to the SPhU. With which reagents do they form a violet-blue color with the formation of a precipitate?

A. Cobalt nitrate, calcium chloride, sodium hydroxide
B. Copper sulfate, potassium bicarbonate, potassium carbonate
C. Iron (III) chloride, potassium bicarbonate, potassium carbonate
D. Lead nitrate, calcium chloride, sodium hydroxide
E. Nickel nitrate, potassium bicarbonate, potassium carbonate

117. Specify the color of the complex salt, which is formed during the identification of phenobarbital by reaction with a solution of cobalt (II) nitrate:

A. Pink-lilac
B. Yellow
C. Blue-violet
D. Orange-red
E. Yellow-green

118. The pharmacist identifies the drug, a derivative of barbituric acid, by reaction with copper (II) sulfate in the presence of potassium bicarbonate and potassium carbonate. At the same time, the appearance of a blue color and the formation of a red-lilac precipitate make it possible to detect:

A. Barbital
B. Phenobarbital
C. Benzonal
D. Ethaminal sodium
E. Hexenal

119. In which drug from the group of barbiturates can a fragment of benzoic acid be identified with a hydroxam test?

A. Sodium barbital
B. Barbital
C. Phenobarbital
D. Hexanal
E. Benzonal

120. The specialist of the Department of Technical Control of the chemical-pharmaceutical enterprise fuses the drug substance with sodium hydroxide. Further acidification of the reaction product leads to the release of gas bubbles (carbon dioxide) and the appearance of the characteristic smell of phenylethylacetic acid. Name the drug substance that can be identified by these tests:

A. Phenobarbital
B. Resorcinol
C. Codeine
D. Streptocide
E. Phenoxymethylpenicillin

121. Drug products from the barbiturate-acid group are quantitatively determined by the method of alkalimetry in a non-aqueous environment. The following should be used as a solvent:

A. Dimethylformamide
B. glacial acetic acid
C. Acetic anhydride
D. Ethyl alcohol
E. Glycerin

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