МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ БЕЛАРУСЬ
БЕЛОРУССКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ
КАФЕДРА ФАРМАЦЕВТИЧЕСКОЙ ХИМИИ С КУРСОМ ПОВЫШЕНИЯ КВАЛИФИКАЦИИ И ПЕРЕПОДГОТОВКИ

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ФАРМАЦЕВТИЧЕСКАЯ ХИМИЯ

PHARMACEUTICAL CHEMISTRY

Практикум для студентов 3-го курса медицинского факультета иностранных учащихся, обучающихся по специальности «Фармация»

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Включены методические рекомендации к лабораторным занятиям по фармацевтической химии. Содержатся контрольные вопросы по темам занятий, алгоритмы выполнения лабораторных работ, задания для самостоятельной работы студента, перечни литературы к каждому занятию.

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TRAINING AND RECORD CARD

Student _____ group _____
(Full name)

No.	Laboratory lesson topic	Grade	Teacher's signature
1	Pharmacopoeial analysis of pharmaceutical substances of inorganic nature: p-elements: solutions of hydrogen peroxide, iodine, povidone-iodine, sodium and potassium chlorides, sodium and potassium bromides, sodium and potassium iodides		
2	Pharmacopoeial analysis of pharmaceutical substances of inorganic nature: p-elements: basic heavy bismuth nitrate, sodium bicarbonate, sodium thiosulfate, boric acid, sodium tetraborate, hydrated aluminum oxide, hydrated aluminum phosphate, aluminum chloride, sulfur for external use		
3	Pharmacopoeial analysis of pharmaceutical substances of inorganic nature: d-elements		
4	Pharmacopoeial quality control of pharmaceutical substances of aliphatic nature: alkanes, alcohols, ethers, aldehydes, sulfoxides		
5	Pharmacopoeial quality control of pharmaceutical substances of aliphatic nature: carbohydrates, terpenoids		
6	Pharmacopoeial quality control of pharmaceutical substances of aliphatic nature: carboxylic acids, amino acids		
7	Final lesson «Pharmacopoeial analysis of pharmaceutical substances of inorganic and aliphatic nature»		
8	Pharmacopoeial quality control of pharmaceutical substances of aromatic nature: phenols, aromatic acids		
9	Pharmacopoeial quality control of pharmaceutical substances of aromatic nature: phenylalkylamines, sulfanilic acid		
10	Pharmacopoeial quality control of pharmaceutical substances of heterocyclic nature: nitrofuran and nitroimidazole derivatives		
11	Pharmacopoeial quality control of pharmaceutical substances of heterocyclic nature: derivatives of benzopyran, pyrazole, benzimidazole, pyridine, corrine		
12	Pharmacopoeial quality control of pharmaceutical substances of heterocyclic nature: derivatives of isoquinoline, purine, pteridine, isoalloxazine, pyrimidothiazole		
13	Pharmacopoeial quality control and pharmaceutical chemistry of terpenoids derivatives, chromone, seco derivatives of ergosterol and naphthoquinone, related to fat-soluble vitamins and their derivatives		
14	Pharmacopoeial quality control and pharmaceutical chemistry of aromatic amino acids derivatives related to drugs for local anesthesia		
15	Final lesson «Pharmacopoeial analysis of pharmaceutical substances of aromatic and heterocyclic nature, vitamins, drugs for local anesthesia»		
16	Quality control of pharmaceutically prepared drugs (extemporaneous drugs). Quality control of industrially manufactured medicines		
17	Final lesson on laboratory work		

Lesson 1
PHARMACOPOEIAL ANALYSIS OF PHARMACEUTICAL SUBSTANCES OF INORGANIC NATURE: p-ELEMENTS: SOLUTIONS OF HYDROGEN PEROXIDE, IODINE, POVIDONE-IODINE, SODIUM AND POTASSIUM CHLORIDES, SODIUM AND POTASSIUM BROMIDES, SODIUM AND POTASSIUM IODIDES

Objective: introduce students to methods of preparation, structural formulas, properties, quality control, chemical basis of pharmacological action and storage conditions of pharmaceutical substances — derivatives of p-elements: solutions of hydrogen peroxide, iodine, povidone-iodine, sodium and potassium chlorides, sodium and potassium bromides, sodium and potassium iodides; familiarize students with structural formulas, properties, quality control, chemical bases of pharmacological action and the role of organic and inorganic sodium and potassium salts in water-salt metabolism; develop students' skills in pharmacopoeial quality control of pharmaceutical substances -p-elements derivatives: solutions of hydrogen peroxide, iodine, povidone-iodine, sodium and potassium chlorides, sodium and potassium bromides, sodium and potassium iodides.

Requirements for the initial level of knowledge: repeat features of p-elements– chemical elements of groups IIIA-VIIA in the Periodic Table; general characteristics, physical and chemical properties of groups IIIA-VIIA p-elements.

Problems for discussion:

1. Methods of production, structural formula, properties, quality control, chemical basis of pharmacological action and storage conditions of p-element derivatives: hydrogen peroxide solutions, iodine, povidone-iodine, sodium and potassium chlorides, sodium and potassium bromides, sodium and potassium iodides.
2. Organic and inorganic salts of potassium (acetate, hydroaspartate hemihydrate, sorbate, citrate, lactate, carbonate, stearate, etc.) and sodium (acetate, lactate, citrate, etc.), their role in water-salt metabolism.

Situational tasks

1. A customer came to the pharmacy with a request to sell him a medicinal product with iodine to eliminate pain and redness in the throat, but he has increased dryness of the mucous membranes. Offer the medicinal product to the customer. Explain your answer.

2. When performing quality control of povidone-iodine for iodide content, the following results were obtained: in the quantitative determination section, 10.5 ml of titrant solution were used for titration; when determining iodides, 11.2 ml of titrant solution were used for titration, and in the control experiment — 0.2 ml. Draw a conclusion on the substance's compliance with the requirements of the pharmacopoeial monograph.

3. Fenton's reagent consists of divalent iron salts and hydrogen peroxide in different proportions. This reagent is used for «soft» oxidation of organic substances. Suggest the equations of oxidation reactions of pharmaceutical substances by Fenton's reagent: amoxicillin trihydrate; levofloxacin hemihydrate; metronidazole.

4. Potassium sorbate is used in the pharmaceutical and food industries as a preservative. Explain what properties it is used for? Why is sorbic acid itself not used?

5. Compare bioavailability of the following potassium salts: carbonate, acetate, hydrogen aspartate, citrate and lactate. Why is their bioavailability different? How does the anion affect it?

Algorithm for performing laboratory work
«Quality control of pharmaceutical substances potassium chloride, bromide and iodide»

Goal of the work: develop students' quality control skills for potassium chloride, bromide and iodide.

Quality control of pharmaceutical substance potassium chloride in accordance with the State Pharmacopeia of the Republic of Belarus

IDENTIFICATION

A weighed portion of the test sample containing about 2 mg of chloride ion is dissolved in 2 ml of water R. Resulting solution is acidified with diluted nitric acid R, 0.4 ml of silver nitrate solution R1 is added, mixed and allowed to stand; white cheesy precipitate is formed, which is centrifuged and washed with three portions of water R 1 ml each. This operation is carried out quickly in a place protected from bright light, and it is allowed for liquid above sediment to be not completely transparent. Precipitate is suspended in 2 ml of water R and 1.5 ml of ammonia solution R is added; precipitate dissolves quickly; presence of several large particles that dissolve slowly is allowed.

Reaction equations:
Analytical effect:
Result:

QUANTITATION

Dissolve 0.500 g of the test sample in water R and dilute to a volume of 25.0 ml with the same solvent. To 5.0 ml of the resulting solution add 40 ml of water R and titrate with 0.1 M silver nitrate solution until an orange-yellow color is observed using 0.5 ml of potassium chromate solution R as an indicator.

1 ml of 0.1 M silver nitrate solution corresponds to 7.46 mg KCl.

Content: not less than 99.0 % and not more than 101.0 % (relative to dry substance).

Reaction equations:
Formulas and calculations:
Result:

Conclusion on potassium chloride:

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Quality control of pharmaceutical substance potassium iodide

*Solution S.*1.0 g of the test sample is dissolved in carbon dioxide-free water R prepared from distilled water R and diluted to a volume of 10 ml with the same solvent.

IDENTIFICATION

2 ml of solution S is acidified with dilute nitric acid R, 0.4 ml of silver nitrate solution R1 is added, mixed and left until a light-yellow cheesy precipitate forms. Precipitate is separated by centrifugation and washed with 3 portions of water R 1 ml each. This operation is carried out quickly in a place protected from bright light; it is allowed for liquid above sediment to be not completely transparent. Precipitate is suspended in 2 ml of water R and 1.5 ml of ammonia solution R is added; precipitate does not dissolve.

Reaction equations: *Analytical effect:* *Result:*

QUANTITATION

An accurately weighed sample of potassium iodide (M = 166.0 g/mol) weighing about 0.15 g is dissolved in 10 ml of water, 1 ml of CH3COOH solution (30 %) and 3 drops of 0.1 % sodium eosinate solution are added and is titrated with 0.1 M $AgNO_3$ solution until color of precipitate changes from yellow to pink.

Content: not less than 99.0 % and not more than 100.5 % (relative to dry substance).

Reaction equation: *Formulas and calculations:* *Result:*

Conclusion on potassium iodide:

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Quality control of the pharmaceutical substance potassium bromide in accordance with the State Pharmacopeia of the Republic of Belarus

IDENTIFICATION

A weighed sample of the test sample containing about 3 mg of bromide ion is dissolved in 2 ml of water R. Resulting solution is acidified with diluted nitric acid R, 0.4 ml of silver nitrate solution R1 is added, mixed and left to stand; alight-yellow cheesy precipitate is formed. Precipitate is separated by centrifugation and washed with three portions of water R, 1 ml each. These operations are carried out quickly in a place protected from bright light, and it is allowed for liquid above sediment to be not completely transparent. Resulting precipitate is suspended in 2 ml of water R and 1.5 ml of ammonia solution R is added; precipitate is difficult to dissolve.

Reaction equations: *Analytical effect:* *Conclusion:*

List of literature:

1. *Pharmaceutical* chemistry : textbook / ed. G. V. Ramenskaya. – Moscow : GEOTAR-Media, 2023. – 384 p.

2. *Tsurkan, O. O.* Pharmaceutical chemistry. Analysis of the Medicinal Substances according to Functional Groups: study guide / O. O. Tsurkan. – Kyiv : AUS Medicine Publishing, 2018. – 152 p.

3. *Pharmaceutical* analysis : The study guide for students of higher schools / ed. by V. A. Georgiyants. – Kharkiv : NUPh Golden Pages, 2018. – 494 p.

4. Lecture and information material.

Lesson 2
PHARMACOPOEIAL ANALYSIS OF PHARMACEUTICAL SUBSTANCES OF INORGANIC NATURE: P-ELEMENTS: BASIC HEAVY BISMUTH NITRATE, SODIUM HYDROCARBONATE, SODIUM THIOSULPHATE, BORIC ACID, SODIUM TETRABORATE, HYDRATED ALUMINUM OXIDE, ALUMINUM PHOSPHATE HYDRATED, ALUMINUM CHLORIDE, SULFUR FOR EXTERNAL USE

Objective: introduce students to methods of preparation, structural formulas, properties, quality control, chemical basis of pharmacological action and storage conditions of pharmaceutical substances derived from p-elements: heavy bismuth nitrate, sodium bicarbonate, sodium thiosulfate, boric acid, sodium tetraborate, hydrated aluminum oxide, hydrated aluminum phosphate, aluminum chloride, sulfur for external use; develop students' skills in pharmacopoeial quality control of pharmaceutical substances — p-elements derivatives: heavy bismuth nitrate, sodium bicarbonate, sodium thiosulfate, boric acid, sodium tetraborate, hydrated aluminum oxide, hydrated aluminum phosphate, aluminum chloride, sulfur for external use.

Requirements for the initial level of knowledge: repeat features of p-elements– chemical elements of groups IIIA-VIIA in the Periodic Table; general characteristics, physical and chemical properties of groups IIIA-VIIA p-elements.

Problems for discussion:

1. Methods of preparation, structural formula, properties, quality control, chemical basis of pharmacological action and storage conditions of p-elements derivatives: basic heavy bismuth nitrate, sodium bicarbonate, sodium thiosulfate, boric acid, sodium tetraborate, hydrated aluminum oxide, hydrated aluminum phosphate, aluminum chloride, sulfur for external use. Organic bismuth salts (subgallate, subsalicylate).

Situational tasks

1. Explain ability of its medicinal preparations to have a cytoprotective effect in terms of the chemical properties of bismuth. Which bismuth compounds are preferable for the treatment of erosive lesions of the gastrointestinal tract.

2. Due to what chemical reactions is Demjanovich's solution used to treat scabies? Provide the reaction equations.

3. Compare the safety of antacid drugs with aluminum compounds: oxide and phosphate.

4. What is aluminum chloride used for as a medicine? What chemical properties are its uses based on?

5. Due to what physical and chemical properties do boric acid and sodium bicarbonate have an antimicrobial effect?

Algorithm for performing laboratory work
«Quality control of boric acid and sodium bicarbonate»

Goal of the work: develop students' skills in quality control of boric acid and sodium bicarbonate.

Quantitative determination of a substance boric acid in accordance with the State Pharmacopeia of the Republic of Belarus

Dissolve 0.300 g of the test sample by heating in 50 ml of water R containing 3 g of glycerol R neutralized with phenolphthalein R and titrate with 1 M sodium hydroxide solution until a pink color appears using 0.5 ml of phenolphthalein R solution as an indicator.

1 ml of 1 M sodium hydroxide solution corresponds to 61.8 mg of H_3BO_3.

Content: not less than 99.0 % and not more than 100.5 % (relative to dry substance).

Reaction equations: *Formulas and calculations:* *Conclusion:*

Quality control of pharmaceutical substance sodium bicarbonatein accordance with the State Pharmacopeia of the Republic of Belarus

Solution S. 5.0 g of the test sample is dissolved in 90 ml of carbon dioxide-free water R and diluted to 100.0 ml with the same solvent.

IDENTIFICATION

A. To 5 ml of *solution S add 0.1 ml of phenolphthalein solution R. A pale pink color appears. Then heat it up. Gas bubbles are released and a red color appears.*

Reaction equations: *Analytical effect:* *Result:*

B. Test sample gives reaction (a) to carbonates and bicarbonates (2.3.1). To 2 ml of *solution S add 3 ml of diluted acetic acid R. Test tube is immediately closed with a ground-in stopper with a glass tube bent twice at a right angle; rapid release of bubbles is observed colorless and odorless. Test tube is carefully heated and the evolved gas is passed through 5 ml of barium hydroxide solution R; a white precipitate is formed, which dissolves when adding excess hydrochloric acid P1.*

Reaction equations:

Analytical effect:

Result:

C. Test sample gives *reaction (a) to sodium (2.3.1). To 2 ml of solution S add 2 ml of 150 g/l solution of potassium carbonate R and heat to boiling; no precipitate forms. Add 4 ml of potassium* pyroantimonate *solution R to the solution and heat to boiling, then cool in ice water and, if necessary, rub inner walls of the test tube with a glass rod; a dense white precipitate forms.*

Reaction equations:

Analytical effect:

Result:

QUANTITATION

Dissolve 1,500 g of the test sample in 50 ml of carbon dioxide-free water R and titrate with 1 M hydrochloric acid using 0.2 ml of methyl orange R as indicator.

1 ml of 1 M hydrochloric acid solution corresponds to 84.0 mg of $NaHCO_3$.

Content: not less than 99.0 % and not more than 101.0 % (relative to dry substance).

Reaction equation:

Formulas and calculations:

Result:

Conclusion on sodium bicarbonate:

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List of literature:

1. *Pharmaceutical* chemistry : textbook / ed. G. V. Ramenskaya. – Moscow : GEOTAR-Media, 2023. – 384 p.

2. *Tsurkan, O. O.* Pharmaceutical chemistry. Analysis of the Medicinal Substances according to Functional Groups: study guide / O. O. Tsurkan. – Kyiv : AUS Medicine Publishing, 2018. – 152 p.

3. *Pharmaceutical* analysis : The study guide for students of higher schools / ed. by V. A. Georgiyants. – Kharkiv : NUPh Golden Pages, 2018. – 494 p.

4. Lecture and information material.

Lesson 3
PHARMACOPOEIAL ANALYSIS OF PHARMACEUTICAL SUBSTANCES OF INORGANIC NATURE: d-ELEMENTS

Objective: introduce students to methods of preparation, structural formulas, properties, quality control, chemical basis of pharmacological action and storage conditions of pharmaceutical substances derived from d-elements; develop students' skills in pharmacopoeial quality control of pharmaceutical substances - d-elements derivatives

Requirements for the initial level of knowledge: repeat features of d-elements – elements of groups IB, IIB, VIIIB in the Periodic Table of Chemical Elements; general characteristics, physical and chemical properties of d-elements of groups IB, IIB, VIIIB.

Problems for discussion:

1. Methods of preparation, structural formula, properties, quality control, chemical basis of pharmacological action and storage conditions of d-elements derivatives: zinc oxide, zinc sulfate hexa- and heptahydrate, zinc undecylenate, zinc gluconate, zinc acexamate, iron sulfate heptahydrate and dried, iron chloride hexahydrate, iron fumarate, iron gluconate, copper sulfate pentahydrate and anhydrous, potassium permanganate, silver proteinate, etc.
2. Organic and inorganic salts of zinc, copper and iron. Influence of anion nature on bioavailability of cation. Effect of chemical form and additives on bioavailability of iron. Organic (colloidal) and inorganic (soluble) forms of silver.

Situational tasks

1. Which chemical form of iron is better absorbed and why? Explain the answer based on the characteristics of iron absorption. What substances improve iron absorption?

2. Why do organic forms of iron have greater bioavailability compared to inorganic ones?

3. A customer came to the pharmacy with a request to select a biologically active supplement with zinc. Which supplement can be recommended based on greater bioavailability?

4. Copper-based drugs have antifungal action. What chemical properties enable this action?

5. What is the difference in terms of pharmacological action and safety between organic and inorganic forms of silver?

Algorithm for performing laboratory work
«Quality control of pharmaceutical substances copper sulfate pentahydrate and zinc sulfate hexahydrate»

Goal of the work: develop in students' skills of crystalline hydrates of copper sulfate and zinc sulfate quality control.

Quality control of pharmaceutical substance copper sulfate pentahydrate in accordance with the State Pharmacopeia of the Republic of Belarus

Solution S. Dissolve 5 g of the test sample in water R and dilute to a volume of 100 ml with the same solvent.

IDENTIFICATION

A. To 1 ml of solution S prepared as indicated in the «Tests» section add a few drops of diluted ammonia solution R2. A blue precipitate is formed, which dissolves with further addition of diluted ammonia solution R2, and a dark blue color appears.

Reaction equations:

Analytical effect:

Result:

C. 1 ml of solution S is diluted with water R to a volume of 5 ml. Resulting solution gives reaction (a) to sulfates (2.3.1). 5 ml of solution S add 1 ml of diluted hydrochloric acid R and 1 ml of barium chloride solution R1; a white precipitate forms.

Reaction equations:

Analytical effect:

Result:

QUANTITATION

Dissolve 0.200 g of the test sample in 50 ml of water R, add 2 ml of sulfuric acid R, 3 g of potassium iodide R and titrate with 0.1 M sodium thiosulfate solution, using as an indicator 1 ml of starch solution R, which is added at the end of the titration.

1 ml of 0.1 M sodium thiosulfate solution corresponds to 24.97 mg of $CuSO_4 \times 5H_20$.

Content: not less than 99.0 % and not more than 101.0 %.

Reaction equations:

Formulas and calculations:

Result:

Conclusion on copper sulfate pentahydrate:

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Quality control of the pharmaceutical substance zinc sulfate heptahydrate in accordance with the State Pharmacopeia of the Republic of Belarus

Solution S. Dissolve 2.5 g of the test sample in carbon dioxide-free water R and dilute to a volume of 50 ml with the same solvent.

IDENTIFICATION

A. Solution S gives reactions to sulfates (2.3.1).

a) To 5 ml of solution S add 1 ml of diluted hydrochloric acid R and 1 ml of barium chloride solution R1; a white precipitate forms.

Reaction equations:

Analytical effect:

Result:

b) To the suspension obtained as a result of reaction a) add 0.1 ml of 0.05 M iodine solution; yellow color of iodine does not disappear (unlike sulfites and dithionites), but becomes discolored when a solution of tin chloride R is added dropwise (unlike iodates). Mixture is boiled; precipitate is not colored (unlike selenates and tungstates).

Reaction equations:

Analytical effect:

Result:

B. Solution S gives reactions to zinc (2.3.1).

a) To 5 ml of solution S add 0.2 ml of concentrated sodium hydroxide solution R; a white precipitate forms. Then add another 2 ml of concentrated sodium hydroxide solution R; precipitate dissolves. To the resulting solution add 10 ml of ammonium chloride solution R; solution remains clear. Add 0.1 ml of sodium sulfide solution R to the solution; a white flocculent precipitate forms.

Reaction equations:

Analytical effect:

Result:

b) To 2 ml of solution S add 0.5 ml of potassium ferrocyanide solution R; a white precipitate is formed, insoluble in diluted hydrochloric acid R.

Reaction equations:

Analytical effect:

Result:

C. Test sample meets requirements of the «Quantitative Determination» section.

Result:

QUANTITATION

Dissolve 0.200 g of the test sample in a 500 ml conical flask in 5 ml diluted acetic acid R and dilute with water R to a volume of 200 ml. Add about 50 mg of an indicator mixture of xylenol orange R, and then hexamethylenetetramine R until solution turns purple-pink. After this, an additional 2 g of hexamethylenetetramine R is added and titrated with 0.1 M sodium edetate solution until the violet-pink color changes to yellow.

1 ml of 0.1 M sodium edetate solution corresponds to 28.75 mg of $ZnSO_4 \times 7H_20$.

Content: not less than 99.0 % and not more than 104.0 %.

Reaction equations: *Formulas and calculations:* *Result:*

Conclusion on zinc sulfate heptahydrate:

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List of literature:

1. *Pharmaceutical* chemistry : textbook / ed. G. V. Ramenskaya. – Moscow : GEOTAR-Media, 2023. – 384 p.

2. *Tsurkan, O. O.* Pharmaceutical chemistry. Analysis of the Medicinal Substances according to Functional Groups: study guide / O. O. Tsurkan. – Kyiv : AUS Medicine Publishing, 2018. – 152 p.

3. *Pharmaceutical* analysis : The study guide for students of higher schools / ed. by V. A. Georgiyants. – Kharkiv : NUPh Golden Pages, 2018. – 494 p.

4. Lecture and information material.

Lesson 4
PHARMACOPOEIAL QUALITY CONTROL OF PHARMACEUTICAL SUBSTANCES OF ALIPHATIC NATURE: ALKANES, ALCOHOLS, ETHERS, ALDEHYDES, SULPHOXIDES

Objective: introduce students to methods of preparation, structural formulas, properties, quality control, chemical basis of pharmacological action and storage conditions of pharmaceutical substances of aliphatic nature: alkanes, alcohols, ethers, aldehydes, sulfoxides; develop students' skills in pharmacopoeial quality control of pharmaceutical substances of aliphatic nature: alkanes, alcohols, ethers, aldehydes, sulfoxides.

Requirements for the initial level of knowledge: repeat classification and nomenclature of alkanes; general characteristics, physical and chemical properties of alkanes; general characteristics, physical and chemical properties of alcohols; general characteristics, physical and chemical properties of ethers; general characteristics, physical and chemical properties of aldehydes.

Problems for discussion:

1. Methods of preparation, structural formula, properties, quality control, chemical basis of pharmacological action and storage conditions of alkanes, alcohols, ethers, aldehydes, sulfoxides derivatives: petrolatum, ethyl alcohol 96, 95, 90, 80, 70, 60 and 40 %, glycerin, glycerin 85 %, isopropyl alcohol, anesthetic ether, ether, formaldehyde 35 % solution, chloral hydrate, dimethyl sulfoxide, macrogol.

2. Chemical nature of excipients in soft dosage forms (vaseline oil, petrolatum, ceresin, paraffin, macrogol, etc.).

Situational tasks

1. Compare duration of the laxative effect after taking a solution of magnesium sulfate, glycerin, vaseline oil and macrogol. What is the reason for this difference?

2. Due to what chemical properties do dimethyl sulfoxide and isopropyl alcohol have antimicrobial properties? Why are surfactants added to isopropyl alcohol-based antiseptic drugs?

3. Suggest a method for obtaining dimethyl sulfoxide with the highest yield.

4. When determining the hydroxyl number of macrogol-400, the following results were obtained: 11.3 ml of titrant were used for titration, in the control experiment — 0.3 ml. Draw a conclusion about the compliance of macrogol with the pharmacopoeial monograph.

5. Suggest an excipient to make the ointment hydrophobic so that it does not run off the affected area of skin.

Algorithm for performing laboratory work
«Quality control of glycerin, ethyl alcohol, isopropyl alcohol and dimethyl sulfoxide»

Goal of the work: develop students' skills in quality control of glycerin, ethyl alcohol, isopropyl alcohol and dimethyl sulfoxide.

Determination of ethyl alcohol concentration

Using an alcohol meter (or hydrometer) determine concentration (relative density) of the resulting alcohol solution. If necessary, make appropriate calculations according to alcohol metric tables.

Calculations and results:

Quality control of glycerin according to the «Identification» indicator in accordance with the State Pharmacopeia of the Republic of Belarus

A. Refractive index (2.2.6). From 1.470 to 1.475.

Values: *Result:*

B. 1 ml of the test sample is mixed with 0.5 ml of nitric acid R. 0.5 ml of potassium dichromate solution R is layered on the resulting solution. A blue ring appears at the interface between liquids. Within 10 minutes blue color does not transfer to the lower layer.

Reaction equations: *Analytical effect:* *Result:*

Conclusion on glycerin:

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Quality control of ethyl alcohol according to the «Identification» indicator in accordance with the State Pharmacopeia of the Republic of Belarus

D. To 0.5 ml of the test sample add 5 ml of water R, 2 ml of diluted sodium hydroxide solution R and then slowly 2 ml of 0.05 M iodine solution. After 30 minutes a yellow precipitate forms.

Reaction equation: *Analytical effect:* *Conclusion:*

Quality control of isopropyl alcohol according to the «Test» indicator in accordance with the International Pharmacopeia

Transparency *(2.2.1).* Test sample must be transparent. 1 ml of the test sample is diluted with water R to a volume of 20 ml. Resulting solution should be transparent after 5 minutes.

To determine transparency use identical test tubes made of colorless, transparent and neutral glass with a flat bottom, which have an internal diameter from 15 mm to 25 mm. A 40 mm thick layer of the test liquid is compared with a 40 mm layer of freshly prepared standard I or water R. Comparison of solutions is carried out in diffuse daylight after 5 minutes, viewing objects along the vertical axis of the test tubes against a black background. Liquids are considered transparent if their transparency does not differ from water R, or which do not exceed intensity of turbidity of the reference suspension I.

Observation: *Result:*

Chroma *(2.2.2, method II).* Test sample must be colorless. A solution is considered colorless if it can pass comparison with water R or solvent, or is no more intensely colored than standard B9. A 40 mm layer of the test liquid is compared with a 40 mm layer of water R, solvent or specified reference standard using identical flat-bottomed, clear, neutral glass tubes having an internal diameter of 15 mm to 25 mm. Color comparison is carried out in diffuse daylight, viewing objects along vertical axis of tubes on a white background.

Observation: *Result:*

Acidity or alkalinity. 25 ml of the test sample is carefully boiled for 5 minutes, 25 ml of carbon dioxide-free water R is added, and kept until cooled protecting from air carbon dioxide. Add 0.1 ml of phenolphthalein solution R to the resulting solution. Solution is colorless. When adding no more than 0.6 ml of 0.01 M sodium hydroxide solution, a pale pink color should appear.

Observation: *Result:*

Optical density *(2.2.25).* Not more than 0.30 at a wavelength of 230 nm, not more than 0.10 at a wavelength of 250 nm, not more than 0.03 at a wavelength of 270 nm, not more than 0.02 at a wavelength of 290 nm and not more than 0.01 at wavelength 310 nm.

Optical density is measured in the region from 230 nm to 310 nm using water R as a compensation solution. Spectrum is a falling curve with no visible peaks or shoulders.

Values: *Result:*

Conclusion on isopropyl alcohol:

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Quality control of dimethyl sulfoxide according to the «Test» indicator in accordance with the State Pharmacopeia of the Republic of Belarus

Optical density *(2.2.25).* Nitrogen R is passed through the test sample for 15 minutes. Optical density is measured using water as a compensation solution. Optical density at a wavelength of 275 nm should not exceed 0.30; optical density at wavelengths 285 nm and 295 nm should not exceed 0.20. In the range from 270 to 350 nm, the absorption spectrum of the test sample should not have absorption maxima.

Values: *Result:*

Refractive index *(2.2.6).* From 1.478 to 1.479.

Values: *Result:*

Conclusion on dimethyl sulfoxide:

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List of literature:

1. *Pharmaceutical* chemistry : textbook / ed. G. V. Ramenskaya. – Moscow : GEOTAR-Media, 2023. – 384 p.

2. *Tsurkan, O. O.* Pharmaceutical chemistry. Analysis of the Medicinal Substances according to Functional Groups: study guide / O. O. Tsurkan. – Kyiv : AUS Medicine Publishing, 2018. – 152 p.

3. *Pharmaceutical* analysis : The study guide for students of higher schools / ed. by V. A. Georgiyants. – Kharkiv : NUPh Golden Pages, 2018. – 494 p.

4. Lecture and information material.

Lesson 5
PHARMACOPOEIAL QUALITY CONTROL OF PHARMACEUTICAL SUBSTANCES OF ALIPHATIC NATURE: CARBOHYDRATES, TERPENOIDS

Objective: introduce students to methods of preparation, structural formulas, properties, quality control, chemical basis of pharmacological action and storage conditions of pharmaceutical substances of aliphatic nature: carbohydrates, terpenoids; develop students' skills in pharmacopoeial quality control of pharmaceutical substances of aliphatic nature: carbohydrates, terpenoids.

Requirements for the initial level of knowledge: repeat classification and nomenclature of carbohydrates; general characteristics, physical and chemical properties of carbohydrates; concept of mutarotation; classification and nomenclature of terpenes; differences between terpenes and terpenoids; general characteristics, physical and chemical properties of terpenoids.

Problems for discussion:

Methods of preparation, structural formula, properties, quality control, chemical basis of pharmacological action and storage conditionsof carbohydrates derivatives and terpenoids: glucose monohydrate and anhydrous, lactose monohydrate and anhydrous, sucrose, lactulose, sodium saccharin, levomenthol, racemic menthol, D-camphor, racemic camphor, turpentine oil, etc.

Situational tasks

1. When determining the color value of sucrose, the optical density value was 0.2538; absorption index 1.4145; optical path length 10 cm. Make a conclusion about the compliance of sucrose with the requirements of the pharmacopoeial monograph.

2. When determining associated impurities of camphor, it was found that the peak area on the chromatogram of the reference solution (c) was 1200 units, on the chromatogram of the test solution – 800 units. Calculate percentage content of borneol impurity in camphor.

3. Suggest a method for obtaining sodium saccharin using complete chemical synthesis.

4. A customer came to the pharmacy asking to select an external dosage form with menthol for rubbing after a bruise. Offer the customer options.

5. Why does lactulose have a laxative effect, unlike lactose? Explain your answer.

Algorithm for performing laboratory work
«Quality control of the pharmaceutical substance glucose monohydrate and 5 % glucose solution of pharmaceutical manufacture»

Goal of the work: develop students' glucose quality control skills.

Quality control of the pharmaceutical substance glucose monohydrate in accordance with the State Pharmacopeia of the Republic of Belarus

IDENTIFICATION

A. Specific optical rotation *(2.2.7)*. From +52.5 to +53.3 (relative to anhydrous substance).

Dissolve 5.00 g of the test sample in 40 ml of water R, add 0.1 ml of diluted ammonia solution R1, leave for 30 minutes and dilute with water R to a volume of 50.0 ml.

Values:

Result:

D. Dissolve 0.1 g of the test sample in 10 ml of water R, add 3 ml of copper tartrate solution R and heat. Red precipitate forms.

Reaction equations: *Analytical effect:* *Result:*

TESTS

Electrical conductivity (2.2.38). No more than 20 μS × cm^{-1}.

Dissolve 10.0 g of the test sample in carbon dioxide-free water R prepared from distilled water R and dilute to a volume of 50.0 ml with the same solvent. Electrical conductivity of the resulting solution is measured with gentle stirring on a magnetic stirrer.

Values: *Result:*

Conclusion on glucose monohydrate:

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Quality control of pharmaceutically manufactured medicinal products: glucose 5 % solution by quantitative determination in accordance with the State Pharmacopeia of the Republic of Belarus («Express analysis»)

METHOD 1

1.0 ml of the test sample is placed in a flask with a ground stopper, 10.0 ml of 0.05 M iodine solution, 0.5 ml of sodium hydroxide solution R are added. Flask is closed with a stopper and kept in a place protected from light for 5 minutes. Add 3–5 ml of diluted sulfuric acid R and released iodine is titrated with 0.1 M sodium thiosulfate solution until the solution becomes colorless. At the same time a control experiment is carried out.

1 ml *0.05 M iodine solution corresponds to 9.009 mg* $C_6H_{12}O_6$.

Reaction equations: *Formulas and calculations:* *Result:*

METHOD 2

Determine refractive index (2.2.6). F = 0.00129.

Formulas and calculations: *Result:*

Conclusion on the glucose solution:

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For extemporaneous dosage forms when forming a conclusion about satisfactory manufacturing deviations from the nominal content are calculated and compared with the norms of permissible deviations.

List of literature:

1. *Pharmaceutical* chemistry : textbook / ed. G. V. Ramenskaya. – Moscow : GEOTAR-Media, 2023. – 384 p.

2. *Tsurkan, O. O.* Pharmaceutical chemistry. Analysis of the Medicinal Substances according to Functional Groups: study guide / O. O. Tsurkan. – Kyiv : AUS Medicine Publishing, 2018. – 152 p.

3. *Pharmaceutical* analysis : The study guide for students of higher schools / ed. by V. A. Georgiyants. – Kharkiv : NUPh Golden Pages, 2018. – 494 p.

4. Lecture and information material.

Lesson 6
PHARMACOPOEIAL QUALITY CONTROL OF PHARMACEUTICAL SUBSTANCES OF ALIPHATIC NATURE: CARBOXYLIC ACIDS, AMINO ACIDS

Objective: introduce students to methods of preparation, structural formulas, properties, quality control, chemical basis of pharmacological action and storage conditions of pharmaceutical substances of aliphatic nature: carboxylic acids, amino acids; develop students' skills in pharmacopoeial quality control of pharmaceutical substances of aliphatic nature: carboxylic acids, amino acids.

Requirements for the initial level of knowledge: repeat classification and nomenclature of carboxylic acids; general characteristics, physical and chemical properties of carboxylic acids; classification and nomenclature of amino acids; concept of essential amino acids; general characteristics, physical and chemical properties of amino acids; specific reactions of α-, β-, γ- amino acids.

Problems for discussion:

1. Methods of preparation, structural formula, properties, quality control, chemical basis of pharmacological action and storage conditions of carboxylic acid derivatives, amino acids: magnesium, calcium, manganese, iron and zinc gluconate, glacial acetic acid, lactic acid, S-lactic acid, aminocaproic acid, glycine, glutamic acid, DL-methionine, cysteine hydrochloride.

Situational tasks

1. Predict which of the amino acids after interaction with a concentrated solution of sodium hydroxide will react with lead acetate upon heating to form a brown or black precipitate. Provide possible reaction schemes.

2. How to use a polarimeter to distinguish D,L-methionine from cysteine, aminocaproic acid, glutamic acid and other amino acids?

3. Explain why D,L-methionine logP of which = 0.37 is easily absorbed in the intestine.

4. Explain why glutamic acid, which has two carboxyl groups is titrated with alkali in the presence of bromothymol blue in a 1 : 1 ratio.

5. How can the pharmaceutical substance iron gluconate be distinguished from other gluconates without chemical reactions?

Algorithm for performing laboratory work
«Quality control of glacial acetic acid, cysteine hydrochloride, D,L-methionine and glycine»

Goal of the work: develop students' quality control skills of glacial acetic acid, cysteine hydrochloride, D,L-methionine and glycine.

Quality control of glacial acetic acid in accordance with the State Pharmacopeia of the Republic of Belarus

DESCRIPTION (PROPERTIES)

Crystalline mass or transparent, colorless, volatile liquid.

Miscible with water, 96 % alcohol and methylene chloride.

Observations: *Result:*

IDENTIFICATION

A. A 100 g/l solution of the test sample is strongly acidic (2.2.4). Medium with pH value less than 4 is considered strongly acidic.

Values: *Result:*

TESTS

Solution S. Dilute 20 ml of the test sample with water R to a volume of 100 ml.

Transparency (2.2.1). Test sample must be transparent. To determine transparency use identical test tubes made of colorless, transparent and neutral glass with a flat bottom, which have an internal diameter from 15 mm to 25 mm. A 40 mm thick layer of the test liquid is compared with a 40 mm layer of freshly prepared standard I or water R. Comparison of solutions is carried out in diffuse daylight after 5 minutes, viewing objects along the vertical axis of the test tubes against a black background. Liquids are considered transparent if their transparency does not differ from water R, or do not exceed the intensity of the reference suspension I turbidity.

Observation: *Result:*

Chroma (2.2.2, method II). Test sample must be colorless. Solution is considered colorless if it can withstand comparison with water R or solvent, or is no more intensely colored than standard B9. A 40 mm layer of the test liquid is compared with a 40 mm layer of water R, solvent or specified reference standard, using identical flat-bottomed, clear, neutral glass tubes having an internal diameter of 15 mm to 25 mm. Color comparison is carried out in diffuse daylight, viewing objects along the vertical axis of the tubes on a white background.

Observation: *Result:*

Reducing substances. 2.0 ml of the test sample is brought to a volume of 10.0 ml with water R, 0.1 ml of 0.02 M potassium permanganate solution is added, heated in a water bath for 1 min, a pink color remains.

Analytical effect:
Result:

Quantitation.

Accurately weigh a conical flask with a ground glass stopper containing 25 ml of water R, add 1.0 ml of the test sample and weigh again accurately. Add 0.5 ml of phenolphthalein solution R and titrate with 1 M sodium hydroxide solution.

1 ml of 1 M sodium hydroxide solution corresponds to 60.1 mg $C_2H_4O_2$.

Content: not less than 99.0 % (m/m) and not more than 100.5 (m/m).

Reaction equation:
Formulas and calculations:
Result:

Conclusion on glacial acetic acid:

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Quality control of the pharmaceutical substance cysteine hydrochloride monohydrate in accordance with the State Pharmacopeia of the Republic of Belarus

IDENTIFICATION

Specific optical rotation *(2.2.7).* From +5.5 to +7.0 (relative to dry substance).

1.00 g of the test sample is dissolved in hydrochloric acid R1 and brought to a volume of 12.5 ml with the same solvent.

Values:
Conclusion:

QUANTITATION

0.300 g of the test sample and 4 g of potassium iodide R are placed in a ground flask, dissolved in 20 ml of water R, cooled in an ice bath, 3 ml of diluted hydrochloric acid R1 and 25 ml of 0.05 M iodine solution are added. Flask is capped and kept in a place protected from light for 20 minutes. Titrate with 0.1 M sodium thiosulfate solution using 3 ml of starch solution R as an indicator, which is added at the end of the titration.

At the same time a control experiment is carried out.

1 ml of 0.05 M iodine solution corresponds to 15.76 mg $C_3H_7NO_2S \cdot HCl$.

Content: not less than 98.5 % and not more than 101.0 % (relative to dry substance).

Reaction equation:

Formulas and calculations:

Result:

Conclusion on cysteine hydrochloride monohydrate:

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Quality control of the pharmaceutical substance D,L-methionine in accordance with the State Fund of the Republic of Belarus

IDENTIFICATION

Specific optical rotation (2.2.7). From +5.5 to +7.0 (relative to dry substance).

1.00 g of the test sample is dissolved in hydrochloric acid R1 and brought to a volume of 12.5 ml with the same solvent.

Values:

Result:

Thin layer chromatography (2.2.27). Chromatogram of the test solution (b) shows a main spot corresponding in location, color and size to the main spot in the chromatogram of the reference solution (a).

Test solution (a). Dissolve 0.2 g of the test sample in water R and dilute to a volume of 10 ml with the same solvent.

Test solution (b). 1 ml of the test solution (a) is diluted with water R to a volume of 50 ml.

Reference solution(a). 20 mg of PhSS DL-methionine are dissolved in water R and diluted to a volume of 50 ml with the same solvent.

Reference solution (b). 1 ml of reference solution (a) is diluted with water R to a volume of 10 ml.

Plate: TLC plate with a layer of silica gel GP.

Mobile phase: glacial acetic acid R — water R — butanol R (20:20:60, v/v/v).

Sample volume applied: 5 µl.

Front of eluent: at least 10 cm from the start line.

Drying: on air.

Development: plate is sprayed with ninhydrin R solution and heated at a temperature of 100 °C to 105 °C for 15 minutes.

Chromatographic plates (draw):

Result:

Conclusion on D,L-methionine:

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Quality control of the pharmaceutical substance glycine in accordance with the State Pharmacopeiaof the Republic of Belarus

Solution S. Dissolve 2.0 g of the test sample in carbon dioxide-free water R and dilute to a volume of 20 ml with the same solvent.

TESTS

pH (2.2.3). From 5.9 to 6.4. 20 ml of solution S are diluted with carbon dioxide-free water R to a volume of 40 ml.

Values:

Conclusion:

List of literature:

1. *Pharmaceutical* chemistry : textbook / ed. G. V. Ramenskaya. – Moscow : GEOTAR-Media, 2023. – 384 p.

2. *Tsurkan, O. O.* Pharmaceutical chemistry. Analysis of the Medicinal Substances according to Functional Groups: study guide / O. O. Tsurkan. – Kyiv : AUS Medicine Publishing, 2018. – 152 p.

3. *Pharmaceutical* analysis : The study guide for students of higher schools / ed. by V. A. Georgiyants. – Kharkiv : NUPh Golden Pages, 2018. – 494 p.

4. Lecture and information material.

Lesson 7
FINAL LESSON «PHARMACOPOEIAL ANALYSIS OF PHARMACEUTICAL SUBSTANCES OF INORGANIC AND ALIPHATIC NATURE»

Target: systematize knowledge gained from studying pharmacopoeial quality control of water, inorganic and aliphatic pharmaceutical substances.

Requirements for the initial level of knowledge: repeat pharmacopoeial quality control of water, inorganic and aliphatic pharmaceutical substances.

Test questions on the topic of the lesson:

I. Pharmacopoeial water quality control:

1. Purified water (definition, methods of production, storage);
2. Highly purified water (definition, methods of production, storage);
3. Water for injection (definition, methods of production, storage);
4. Pharmacopoeial tests for water: electrical conductivity for different types of water, chlorides, sulfates, calcium and magnesium, reducing substances, ammonium salts.
5. Pharmacopoeial tests for water: total organic carbon content and reducing substances for different types of water, nitrates, aluminum, heavy metals, acidity and alkalinity, microbiological tests.
6. Main validation characteristics of methods and tests: specificity, correctness, precision, linearity.
7. Main validation characteristics of methods and tests: detection limit, limit of quantification, range of application, stability (robustness).
8. Statistical processing of chemical experiment results: algorithm, calculation formulas.
9. Chemical basis of pharmacological action (medical use) of organic magnesium salts.
10. Chemical basis of pharmacological action (medical use) of organic calcium salts.
11. Bioavailability of organic and inorganic salts of calcium and magnesium.
12. Chemical bases of pharmacological action (medical use) of organic sodium salts. Effect of the anion nature on bioavailability of the cation.
13. Chemical bases of pharmacological action (medical use) of organic potassium salts. Effect of the anion nature on bioavailability of the cation.
14. Chemical basis of pharmacological action (medical use) of organic zinc salts.
15. Chemical basis of pharmacological action (medical use) of organic iron salts.
16. Bioavailability of organic and inorganic salts of zinc and iron. Effect of additives on the bioavailability of iron. Organic (colloidal) and inorganic (soluble) forms of silver.

II. Pharmacopoeial quality control and use of the following pharmaceutical substances:

Barium sulfate, iron chloride hexahydrate.

Light magnesium oxide and heavy magnesium oxide, magnesium hydroxide.

Magnesium sulfate heptahydrate.

Magnesium lactate, magnesium stearate.

Magnesium gluconate, magnesium aspartate dehydrate.

Magnesium acetate tetrahydrate and chloride hexahydrate.

Magnesium carbonate is light and heavy.

Magnesium citrate anhydrous.

Calcium carbonate; calcium glycerophosphate.

Calcium lactate anhydrous, calcium stearate.

Potassium and sodium acetate.

Potassium hydroaspartate hemihydrate and sodium lactate.

Potassium sorbate and carbonate.

Potassium and sodium citrate.

Calcium chloride anhydrous, hexahydrate and dehydrate.

Hydrogen peroxide 3 % (30 %) solution.

Iodine, povidone-iodine.
Sodium chloride and potassium chloride.
Sodium bromide and potassium bromide.
Sodium iodide and potassium iodide.
Sodium bicarbonate.
Bismuth nitrate basic, heavy, subgallate.
Boric acid, sodium tetraborate.
Aluminum oxide hydrated, aluminum phosphate hydrated.
Aluminum chloride, iron fumarate.
Sodium thiosulfate, sulfur for external use.
Potassium permanganate, zinc oxide.
Silver proteinate (protargol), zinc sulfate hexa- and heptahydrate.
Ferrous sulfate heptahydrate and dried.
Copper sulfate pentahydrate and anhydrous.
Iron and calcium gluconate.
Petrolatum, isopropyl alcohol.
Ethyl alcohol 96, 95, 90, 80, 70, 60, 40 %.
Glycerin, glycerin 85 %.
Anesthetic ether, ether.
Formaldehyde 35 % solution.
Chloral hydrate.
Dimethyl sulfoxide, macrogols.
Glucose monohydrate and anhydrous.
Lactose monohydrate and anhydrous.
Sucrose, sodium saccharin.
Lactulose, turpentine oil.
Levomenthol, racemic menthol.
D-camphor, racemic camphor.
Manganese and zinc gluconate.
Acetic glacial acid, aminocaproic acid.
Lactic acid, S-lactic acid.
Glycine, DL-methionine.
Glutamic acid, cysteine hydrochloride.

For pharmacopoeial quality control and use of these pharmaceutical substances pay special attention to the following sections:

− chemical formula, description (properties), solubility, storage;
− identification;
− quantitative determination;
− chemical basis of pharmacological action (medical use).

Ticket includes five basic questions on two substances (one of inorganic nature, second of aliphatic nature):

description (properties), solubility, storage – 1 p (0.5 p + 0.5 p);
identification or water control – 3 p (1.5 p + 1.5 p);
quantitative determination – 2 p (1 m + 1 m);
application – 3 p (1.5 p + 1.5 p);
problem solving – 1 p (0.5 p + 0.5 p).

Literature: see literature for lessons 16–17, 1–7.

Lesson 8
PHARMACOPOEIAL QUALITY CONTROL OF PHARMACEUTICAL SUBSTANCES OF AROMATIC NATURE: PHENOLS, AROMATIC ACIDS

Objective: introduce students to methods of preparation, structural formulas, properties, quality control, chemical basis of pharmacological action and storage conditions of pharmaceutical substances of aromatic nature: phenols, aromatic acids; develop students' skills in pharmacopoeial quality control of pharmaceutical substances of aromatic nature: phenols, aromatic acids.

Requirements for the initial level of knowledge: repeat classification and nomenclature of phenols; general characteristics, physical and chemical properties of phenols and aromatic acids.

Problems for discussion:

1. Methods of preparation, structural formula, properties, quality control, chemical basis of pharmacological action and storage conditions of phenols and aromatic acids derivatives: phenol, resorcinol, benzyl benzoate, benzalkonium chloride, paracetamol, benzoic acid, sodium benzoate, salicylic acid, sodium salicylate, choline salicylate, etc.

Situational tasks

1. Why is glycerin added to Orosept?

2. Why does the S-resorcinol solution need to be heated for 5 minutes when testing color?

3. Write the equation of the reaction that occurs when resorcinol appears in TLC.

4. Analyze routes of impurity entry into the pharmaceutical substance paracetamol.

5. Explain why different indicators are used in the alkalimetric titration of salicylic and benzoic acids.

Algorithm for performing laboratory work
«Quality control of salicylic acid, sodium benzoate, phenol and resorcinol»

Goal of the work: develop students' skills in quality control of phenol, resorcinol, sodium benzoate and salicylic acid.

Quality control of the pharmaceutical substance salicylic acid in accordance with the State Pharmacopeiaof the Republic of Belarus

IDENTIFICATION

A. Melting point (2.2.14): from 158 °C to 161 °C.

Value:
Result:

Quantitation

Dissolve 0.120 g of the test sample in 96 % alcohol R, add 20 ml of water R and titrate with 0.1 M sodium hydroxide solution using 0.1 ml of phenol red R as an indicator.

1 ml of 0.1 M sodium hydroxide solution corresponds to 13.81 mg of salicylic acid.

Content: no less than 99.0 % and no more than 100.5 % (relative to dry substance).

Reaction equation:
Formulas and calculations:
Result:

***Conclusion on salicylic acid*:**

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Quality control of the pharmaceutical substance sodium benzoate in accordance with the State Pharmacopeiaof the Republic of Belarus

DESCRIPTION (PROPERTIES)

White or almost white crystalline or granular powder or flakes. Slightly hygroscopic.

Easily soluble in water, moderately soluble in 90 % (v/v) alcohol.

Dissolution process

Shake vigorously for 1 minute and maintain at a temperature of (25.0±0.5) °C for 15 minutes. If the test sample is not completely dissolved, repeat shaking for 1 minute and maintain at a temperature of (25.0±0.5) °C for 15 minutes.

Methodology

100 mg of finely ground test sample is placed in a test tube (inner diameter — 16 mm, length — 160 mm) with a stopper, 0.1 ml of solvent is added and the dissolution process is carried out as described above. If the test sample has completely dissolved, it is considered very soluble.

If the test sample is not completely dissolved, add 0.9 ml of solvent and carry out the dissolution process as described above. If the test sample has completely dissolved, it is considered readily soluble.

If the test sample is not completely dissolved, add 2.0 ml of solvent and carry out the dissolution process. If the test sample has completely dissolved, it is considered soluble.

If the test sample is not completely dissolved, add 7.0 ml of solvent and carry out the dissolution process as described above. If the test sample has completely dissolved, it is considered moderately soluble.

If the test sample is not completely dissolved, 10 mg of finely ground test sample is placed in a stoppered tube, 10.0 ml of solvent is added and the dissolution process is carried out as described above. If the test sample has completely dissolved, it is considered slightly soluble.

If the test sample is not completely dissolved, 1 mg of finely ground test sample is placed in a stoppered tube, 10.0 ml of solvent is added and the dissolution process is carried out as described above. If the test sample has completely dissolved, it is considered to be very slightly soluble.

Appearance:
Solubility:
Result:

IDENTIFICATION

A. Test sample gives reactions (b) and (c) to benzoates (2.3.1).

b) Place 0.2 g of the test sample in a test tube, moisten it with 0.2 ml or 0.3 ml of sulfuric acid R and gently heat the bottom of the test tube; a white coating appears on the inner walls of the test tube.

Reaction equations:
Analytical effect:
Result:

c) 0.5 g of the test sample is dissolved in 10 ml of water R. To the resulting solution add 0.5 ml of hydrochloric acid R. A precipitate is formed, which, after recrystallization from warm water R and drying under vacuum (2.2.32) has a melting point (2.2.14) from 120 °C to 124 °C.

Reaction equations: *Analytical effect:* *Result:*

B. Test sample gives reaction (a) to sodium (2.3.1). To 2 ml of solution S add 2 ml of 150 g/l solution of potassium carbonate R and heat to boiling; no precipitate forms. Add 4 ml of potassium pyroantimonate solution R to the solution and heat to boiling, then cool in ice water and, if necessary, rub inner walls of the test tube with a glass rod; a dense white precipitate forms.

Reaction equations: *Analytical effect:* *Result:*

TESTS

Acidity or alkalinity. To 10 ml of solution S add 10 ml of water free from carbon dioxide R and 0.2 ml of phenolphthalein solution R. When adding no more than 0.2 ml of 0.1 M sodium hydroxide solution or 0.1 M hydrochloric acid solution the color of solution must change.

Observation: *Result:*

***Conclusion on sodium benzoate*:**

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Quality control of the pharmaceutical substance phenol in accordance with the State Pharmacopeiaof the Republic of Belarus

Solution S. Dissolve 1.0 g of the test sample in water R and dilute to a volume of 15 ml with the same solvent.

IDENTIFICATION

B. To 1 ml of solution S add 10 ml of water R and 0.1 ml of iron (III) chloride solution R1. A violet color appears, which disappears when 5 ml of 2-propanol R is added (DO NOT add 2-propanol!).

Reaction equation:

Analytical effect:

Conclusion:

Quality control of the pharmaceutical substance resorcinol in accordance with the State Pharmacopeiaof the Republic of Belarus

IDENTIFICATION

A. Melting point (2.2.14): from 109 °C to 112 °C.

Values:

Result:

B. Dissolve 0.1 g of the test sample in 1 ml of water R, add 1 ml of concentrated sodium hydroxide solution R, 0.1 ml of chloroform R, heat and cool. An intense dark red color appears. A small excess of hydrochloric acid R is added. A pale yellow color appears.

Reaction equation:

Analytical effect:

Result:

C. 10 mg of finely ground test sample is thoroughly mixed with 10 mg of finely ground potassium hydrophthalate R and heated over an open flame until an orange-yellow color appears. Cool, add 1 ml of diluted sodium hydroxide solution R, 10 ml of water R and shake until dissolved. Resulting solution has intense green fluorescence.

Reaction equations:

Analytical effect:

Result:

Conclusion on resorcinol:

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List of literature:

1. *Pharmaceutical* chemistry : textbook / ed. G. V. Ramenskaya. – Moscow : GEOTAR-Media, 2023. – 384 p.

2. *Tsurkan, O. O.* Pharmaceutical chemistry. Analysis of the Medicinal Substances according to Functional Groups: study guide / O. O. Tsurkan. – Kyiv : AUS Medicine Publishing, 2018. – 152 p.

3. *Pharmaceutical* analysis : The study guide for students of higher schools / ed. by V. A. Georgiyants. – Kharkiv : NUPh Golden Pages, 2018. – 494 p.

4. Lecture and information material.

Lesson 9
PHARMACOPOEIAL QUALITY CONTROL OF PHARMACEUTICAL SUBSTANCES OF AROMATIC NATURE: PHENYLAKYLAMINES, SULPHANYLIC ACID

Objective: introduce students to methods of preparation, structural formulas, properties, quality control, chemical basis of pharmacological action and storage conditions of pharmaceutical substances of aromatic nature: phenylalkylamines, sulfanilic acid; develop students' skills in pharmacopoeial quality control of pharmaceutical substances of aromatic nature: phenylalkylamines, sulfanilic acid.

Requirements for the initial level of knowledge: repeat classification and nomenclature of carboxylic acids; comparative characteristics of aliphatic and aromatic carboxylic acids acidic properties; classification and nomenclature of amines; chemical reactions of aliphatic and aromatic amines; diazotization and nitrogen coupling reactions; concept of antimetabolites.

Problems for discussion:

1. Methods of preparation, structural formula, properties, quality control, chemical basis of pharmacological action and storage conditions of phenylalkylamines and sulfanilic acid derivatives: chloramphenicol and its esters (palmitate, etc.), sulfanilamide, sodium sulfacetamide, sulfomethoxazole, silver sulfadiazine, sulfasalazine. Sulfonamides and trimethoprim, their combinations (co-trimoxazole).

Situational tasks

1. Why is Levomekol used in the first phase of the wound process and syntomycin liniment in the second?

2. In the combined medicinal product Ingalipt one of the components is soluble streptocide. Write its other name and structural formula.

3. Explain the drug incompatibility of sulfasalazine and antibiotics (eg, azithromycin).

4. Explain the advantage of the drug co-trimoxazole compared to sulfamethoxazole.

5. What recommendations regarding the drinking regimen should a pharmacist give to a patient with impaired renal function when selling drugs from the sulfonamide group for systemic use? Why?

Algorithm for performing laboratory work
«Quality control of sulfonamide, sulfomethoxazole, trimethoprim and chloramphenicol»

Goal of the work: develop students' quality control skills for sulfonamide, sulfomethoxazole, trimethoprim and chloramphenicol.

Quality control of the pharmaceutical substance sulfanilamide in accordance with the State Pharmacopeiaof the Republic of Belarus

IDENTIFICATION

A. Melting point (2.2.14): from 164.5 °C to 166.0 °C.

Values:

Result:

QUANTITATION

Dissolve 0.140 g of the test sample in 50 ml of diluted hydrochloric acid R, add 3 g of potassium bromide R. Cool in ice water and then slowly titrate with constant stirring with 0.1 M sodium nitrite solution, maintaining solution temperature at about 15 °C (as an indicator use a solution of tropeolin 00 R mixed with methylene blue R (0.2 ml of a solution of tropeolin 00 R and 0.1 ml of a solution of methylene blue R) — titrate until the color changes from red-violet to blue).

1 ml of 0.1 M sodium nitrite solution corresponds to 17.22 mg of $C_6H_8N_2O_2S$.

Content: not less than 99.0 % and not more than 101.0 % (relative to dry substance).

Reaction equation:
Formulas and calculations:
Result:

Conclusion on sulfanilamide:

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Quality control of the pharmaceutical substance sulfamethoxazole according to the indicator «IDENTIFICATION» in accordance with the State Pharmacopeiaof the Republic of Belarus

Melting point (2.2.14): from 169 °C to 172 °C.

Values:
Conclusion:

Quality control of the pharmaceutical substance trimethoprim according to the indicator «IDENTIFICATION» in accordance with the State Pharmacopeia of the Republic of Belarus

A. Melting point (2.2.14): from 199 °C to 203 °C.

Values:
Result:

B. Ultraviolet-Visible Absorption Spectrophotometry (2.2.25)

Test solution. 20 mg of the test sample is dissolved in 0.1 M sodium hydroxide solution and brought to a volume of 100.0 ml with the same solvent. 1.0 ml of resulting solution is adjusted with 0.1 M sodium hydroxide solution to a volume of 10.0 ml.

Wavelength range: from 230 nm to 350 nm.

Maximum absorption: at 287 nm.

Specific absorption rate at maximum: from 240 to 250.

Absorption maxima of the test solution: *Calculations:* *Result:*

Conclusion on trimethoprim:

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Quality control of the pharmaceutical substance chloramphenicol according to the «TESTS» indicator (associated impurities)

Thin layer chromatography (2.2.27).

Test solution. Dissolve 0.10 g of the test sample in acetone R and dilute to a volume of 10 ml with the same solvent.

Reference solution (a). 0.10 g of chloramphenicol PhSS is dissolved in acetone R and diluted to a volume of 10 ml with the same solvent.

Reference solution (b). 0.5 ml of reference solution (a) is diluted with acetone R to a volume of 100 ml.

Plate: TLC plate with a layer of silica gel GF254 R.

Eluent: water R — methanol R — chloroform R (1:10:90, v/v/v).

Sample volume applied: 1 µl each of the test solution and the reference solution (a) and 20 µl each of the test solution and the reference solution (b).

Eluent front: at least 15 cm from the start line.

Drying: on air.

Development: Viewed under ultraviolet light at a wavelength of 254 nm.

Limit impurity content:

– any impurity (not more than 0.5 %): on the chromatogram with 20 µl of the test solution, any spot other than the main one should be no more intense than the main spot on the chromatogram of the reference solution (b).

Type of chromatographic plates (draw):   *Conclusion:*

Conclusion on chloramphenicol:

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List of literature:

1. *Pharmaceutical* chemistry : textbook / ed. G. V. Ramenskaya. – Moscow : GEOTAR-Media, 2023. – 384 p.

2. *Tsurkan, O. O.* Pharmaceutical chemistry. Analysis of the Medicinal Substances according to Functional Groups: study guide / O. O. Tsurkan. – Kyiv : AUS Medicine Publishing, 2018. – 152 p.

3. *Pharmaceutical* analysis : The study guide for students of higher schools / ed. by V. A. Georgiyants. – Kharkiv : NUPh Golden Pages, 2018. – 494 p.

4. Lecture and information material.

Lesson 10
PHARMACOPOEIAL QUALITY CONTROL OF PHARMACEUTICAL SUBSTANCES OF HETEROCYCLIC NATURE: NITROFURAN AND NITROIMIDAZOLE DERIVATIVES

Objective: introduce students to methods of preparation, structural formulas, properties, quality control, chemical basis of pharmacological action and storage conditions of pharmaceutical substances of heterocyclic nature: furan, nitrofuran and nitroimidazole derivatives; develop students' skills in pharmacopoeial quality control of pharmaceutical substances of heterocyclic nature: derivatives of furan, nitrofuran and nitroimidazole.

Requirements for the initial level of knowledge: review basic heterocycles studied in the organic chemistry course; acidophobicity of pyrrole and furan, features of electrophilic substitution reactions of acidophobic heterocycles; imidazole tautomerism.

Problems for discussion:

1. Methods of preparation, structural formula, properties, quality control, chemical basis of pharmacological action and storage conditions of furan, nitrofuran and nitroimidazole derivatives: ascorbic acid, sodium ascorbate, nitrofural, nitrofurantoin, furazolidone, nifuratel, nifuroxazide; metronidazole and its benzoate, tinidazole, ornidazole and phosphonic acid derivative: phosphomycin.

Situational tasks

1. Why is fosfomycin available only as powders for solutions for internal or intravenous administration? Why can't the powder for intravenous solution be dissolved in saline? What recommendations should be given to the patient in this regard?

2. Analyze routes of impurity entry into the pharmaceutical substance nitrofural.

3. Furacilin solutions manufactured at the pharmacy are quantitatively determined by the method of reverse iodometric titration. Explain why it is important to add a small amount (0.4 ml) of sodium hydroxide solution and to hold the reaction mixture for a short time (2 minutes) before titration? What will happen if the titration conditions are not met?

4. Why can't you drink alcohol while taking metronidazole and tinidazole?

5. Metrogyl Denta gel contains metronidazole benzoate, chlorhexidine digluconate 20 % solution and excipients propylene glycol, carbomer-980, disodium edetate, saccharin, levomenthol, sodium hydroxide and water. Explain why metronidazole ester was chosen in this dosage form and not metronidazole itself.

Algorithm for performing laboratory work
«Quality control of the pharmaceutical substance ascorbic acid, nitrofural and metronidazole tablets»

Goal of the work: develop students' skills in quality control of ascorbic acid, nitrofural and metronidazole.

Quality control of the pharmaceutical substance ascorbic acid in accordance with the State Pharmacopeiaof the Republic of Belarus

IDENTIFICATION

A. Ultraviolet-visible absorption spectrophotometry (2.2.25).

Test solution. Dissolve 0.10 g of the test sample in water R and immediately bring it to a volume of 100.0 ml with the same solvent. To 10 ml of a 0.1 M solution of hydrochloric acid add 1.0 ml of the resulting solution and dilute with water R to a volume of 100.0 ml.

Maximum absorption: at 243 nm; determination is carried out immediately after preparing the test solution.

Specific absorption rate at maximum: from 545 to 585.

Absorption maxima of the test solution: *Calculations:* *Result:*

C. pH (2.2.3): from 2.1 to 2.6. Measure pH of solution S prepared as described in the Test section.

Values: *Result:*

D. To 1 ml of solution S add 0.2 ml of diluted nitric acid R and 0.2 ml of silver nitrate solution R2. A gray precipitate forms.

Reaction equation: *Analytical effect:* *Result:*

TESTS

Solution S. Dissolve 1.0 g of the test sample in carbon dioxide-free water R and dilute to a volume of 20 ml with the same solvent.

Specific optical rotation (2.2.7). From +20.5 to +21.5.

Dissolve 2.50 g of the test sample in water R and dilute to a volume of 25.0 ml with the same solvent.

Values: *Result:*

QUANTITATION

Dissolve 0.150 g of the test sample in a mixture of 10 ml of dilute sulfuric acid R and 80 ml of carbon dioxide-free water R, add 1 ml of starch solution R and titrate with 0.05 M iodine solution until a stable violet-blue color is observed.

1 ml of 0.05 M iodine solution corresponds to 8.81 mg of ascorbic acid.

Content: not less than 99.0 % and not more than 100.5 % (relative to dry substance).

Reaction equation:

Formulas and calculations:

Result:

Conclusion on the pharmaceutical substance of ascorbic acid:

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Quality control of dragees with ascorbic acid

1 dragee of ascorbic acid is dissolved in 5 ml of water R (solution A). To 1 ml of solution A add 0.2 ml of diluted nitric acid R and 0.2 ml of silver nitrate solution R2. A gray precipitate forms

Reaction equation:

Analytical effect:

Result:

Reaction with methylene blue (non-pharmacopoeial)

Add 1 ml of solution A and 0.2 ml of 0.01 % methylene blue solution into a test tube and place in a water bath at 40 °C. Observe gradual discoloration of solution.

Reaction equation:

Analytical effect:

Result:

QUANTITATION

A weighed portion of ground dragees corresponding to 0.10 g of ascorbic acid is dissolved in a mixture of 10 ml of diluted sulfuric acid R and 80 ml of water R, 1 ml of starch solution R is added and titrated with 0.05 M iodine solution until a stable violet-blue color is observed.

1 ml of 0.05 M iodine solution corresponds to 8.81 mg of ascorbic acid.

Deviation of content from the nominal value should not exceed 15 %.

Reaction equation:

Formulas and calculations:

Result:

Conclusion on ascorbic acid tablets:

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Quality control of the pharmaceutical substance nitrofural in accordance with the State Pharmacopeiaof the Republic of Belarus

IDENTIFICATION

A. Ultraviolet-Visible Absorption Spectrophotometry (2.2.25). Test is carried out with protection from bright light.

Test solution. Test solution prepared for quantitative determination.

Wavelength range: 220 nm to 400 nm.

Absorption maxima: at 260 nm and at 375 nm.

Optical Density Ratio: A375/A260 — from 1.15 to 1.30.

Absorption maxima:

Calculations:

Result:

D. 1 mg of the test sample is dissolved in 1 ml of dimethylformamide R and 0.1 ml of potassium hydroxide alcoholic solution R is added. A violet-red color appears.

Reaction equations:

Analytical effect:

Result:

QUANTITATION

Test is carried out with protection from bright light.

Dissolve 60.0 mg of the test sample in 20 ml of dimethylforamide R and dilute with water R to a volume of 500.0 ml. 5.0 ml of the resulting solution is diluted with water R to a volume of 100.0 ml.

A reference solution is prepared similarly using 60.0 mg of PhSS nitrofural (prepared by a laboratory assistant).

Measure optical density (2.2.25) of the resulting solutions at a maximum at a wavelength of 375 nm. Nitrofural content is calculated based on optical densities and concentrations of solutions using the formula:

$$\omega = \frac{A_{as} \times m_{ref}}{A_{ref} \times g_{as}}.$$

Content: not less than 97.0 % and not more than 103.0 % (relative to dry substance).

Calculations: *Result:*

Conclusion on nitrofural:

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Identification of metronidazole in tablets

Test solution. A weighed portion of crushed tablet powder containing about 0.1 g of metronidazole is placed in a 100 ml volumetric flask, 80 ml of a 0.1 M hydrochloric acid solution is added, shaken for 5 minutes, volume of solution is adjusted to the mark with the same solvent and filtered discarding first portions of filtrate. 1.0 ml of the resulting filtrate is placed in a 100 ml volumetric flask and volume of solution is adjusted to the mark with the same solvent.

Compensation solution. 0.1 M hydrochloric acid solution.

Absorption spectrum of the test solution in the wavelength range from 230 to 350 nm should have an absorption maximum at 277 nm.

Maximum absorption: *Conclusion:*

List of literature:

1. *Pharmaceutical* chemistry : textbook / ed. G. V. Ramenskaya. – Moscow : GEOTAR-Media, 2023. – 384 p.

2. *Tsurkan, O. O.* Pharmaceutical chemistry. Analysis of the Medicinal Substances according to Functional Groups: study guide / O. O. Tsurkan. – Kyiv : AUS Medicine Publishing, 2018. – 152 p.

3. *Pharmaceutical* analysis : The study guide for students of higher schools / ed. by V. A. Georgiyants. – Kharkiv : NUPh Golden Pages, 2018. – 494 p.

4. Lecture and information material.

Lesson 11
PHARMACOPEIAL QUALITY CONTROL OF PHARMACEUTICAL SUBSTANCES OF HETEROCYCLIC NATURE: DERIVATIVES OF BENZOPYRANE, PYRAZOLE, BENZIMIDAZOLE, PYRIDINE, CORRINE

Objective: introduce students to methods of preparation, structural formulas, properties, quality control, chemical basis of pharmacological action and storage conditions of pharmaceutical substances — derivatives of benzopyran, pyrazole, benzimidazole, pyridine, corrin; develop students' skills in pharmacopoeial quality control of pharmaceutical substances — derivatives of benzopyran, pyrazole, benzimidazole, pyridine, corrin.

Requirements for the initial level of knowledge: review basic heterocycles studied in the organic chemistry course; reactions of oxidation and reduction, electrophilic and nucleophilic substitution of pyridine, pyrazole and their analogues; electrophilic substitution reactions in imidazole; tautomerism of pyrazolone.

Problems for discussion:

1. Characteristics and classification of vitamins, water-soluble vitamins.
2. Preparation methods, structural formula, properties, quality control, chemical basis of pharmacological action and storage conditions of benzopyran, pyrazole, benzimidazole, pyridinederivatives, corrine: bioflavonoids and their derivatives (rutoside trihydrate, troxerutin), metamizole sodium monohydrate, phenazone, bendazole hydrochloride (dibazole), nicotinic acid, nicotinamide, xanthinol nicotinate, nicketamide, pyridoxine hydrochloride, cyanocobalamin.

Situational tasks

1. Why is it necessary to add formaldehyde solution during iodometric titration of injection solutions of ascorbic acid?

2. Explain the significance of adding ascorbic acid to acetylsalicylic acid in a combination drug.

3. Explain the need to store ascorbic acid and sodium ascorbate in a non-metallic container.

4. What is the role of pyridoxine hydrochloride in combination drugs with magnesium salts?

5. What is metadoxine? Write route of its production. Describe its main use.

6. What is the advantage of phosphate salts and prodrugs over vitamin B1 salts? How does the structure of these compounds affect methods of quantitative determination used? Provide reaction equations. Explain differences in the required storage conditions for salts and prodrugs in terms of their physicochemical properties.

Algorithm for performing laboratory work
«Quality control of pharmaceutical substances of nicotinic acid and troxerutin»

Goal of the work: develop students' skills in quality control of nicotinic acid and troxerutin.

Quality control of the pharmaceutical substance nicotinic acid in accordance with the State Pharmacopeiaof the Republic of Belarus

IDENTIFICATION

A. Melting point (2.2.14): from 234 °C to 240 °C.

Values:

Result:

QUANTITATION

0.250 g of the test sample is dissolved in 50 ml of water R and titrated with 0.1 M sodium hydroxide solution until a pink color appears, using 0.25 ml of phenolphthalein solution R as an indicator. AT THE PARALLEL A CONTROL EXPERIMENT IS CONDUCTED.

1 ml of 0.1 M sodium hydroxide solution corresponds to 12.31 mg of nicotinic acid.

Content: not less than 99.5 % and not more than 100.5 % (relative to dry substance).

Reaction equation: *Formulas and calculations:* *Result:*

Conclusion on nicotinic acid:

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Quality control of troxerutin according to the «IDENTIFICATION» indicator

0.05 g of troxerutin, dissolved in 2 ml of 96 % alcohol R, filtered, add 1 zinc granule and 1 ml of hydrochloric acid R1. A red color appears.

Reaction equation: *Analytical effect:* *Conclusion:*

List of literature:

1. *Pharmaceutical* chemistry : textbook / ed. G. V. Ramenskaya. – Moscow : GEOTAR-Media, 2023. – 384 p.

2. *Tsurkan, O. O.* Pharmaceutical chemistry. Analysis of the Medicinal Substances according to Functional Groups: study guide / O. O. Tsurkan. – Kyiv : AUS Medicine Publishing, 2018. – 152 p.

3. *Pharmaceutical* analysis : The study guide for students of higher schools / ed. by V. A. Georgiyants. – Kharkiv : NUPh Golden Pages, 2018. – 494 p.

4. Lecture and information material.

Lesson 12
PHARMACOPOEIAL QUALITY CONTROL OF PHARMACEUTICAL SUBSTANCES OF HETEROCYCLIC NATURE: DERIVATIVES OF ISOQUINOLINE, PURINE, PTERIDINE, ISOALLOXAZINE, PYRIMIDOTHIAZOLE

Objective: introduce students to methods of preparation, structural formulas, properties, quality control, chemical basis of pharmacological action and storage conditions of pharmaceutical substances of heterocyclic nature: derivatives of isoquinoline, purine, pteridine, isoalloxazine, pyrimidothiazole; develop students' skills in pharmacopoeial quality control of pharmaceutical substances of heterocyclic nature: derivatives of isoquinoline, purine, pteridine, isoalloxazine, pyrimidothiazole.

Requirements for the initial level of knowledge: review basic heterocycles studied in the organic chemistry course; structural features and nomenclature of fused heterocycles; chemical properties (basicity, formation of salts) and general qualitative reactions to alkaloids; structure and chemical properties of quinoline, purine, pterin and isoalloxazine derivatives.

Problems for discussion:

Methods of preparation, structural formula, properties, quality control, chemical basis of pharmacological action and storage conditions of isoquinoline, purine, pteridine, isoalloxazine, pyrimidothiazole derivatives: papaverine hydrochloride, drotaverine hydrochloride, caffeine and its monohydrate, theophylline and its monohydrate, aminophylline (theophylline-ethylenediamine, theophylline-ethylenediamine hydrate and for injection), theobromine, pentoxifylline, folic acid , riboflavin, riboflavin sodium phosphate, thiamine salts and esters (benfotiamine, cocarboxylase, nitrate, hydrochloride).

Situational tasks

1. A patient came to the pharmacy complaining of cold symptoms accompanied by drowsiness. Recommend combination medications in various dosage forms. What common component will they contain based on the request?

2. What chemical reaction is a general group reaction for xanthines? Does it allow identification of caffeine, theophylline and pentoxifylline? Provide reaction equations, indicate the analytical effect.

3. In accordance with the State Pharmacopoeia of the Republic of Belarus thin-layer chromatography is used to identify papaverine hydrochloride, and the zone corresponding to papaverine is detected after viewing the chromatogram in ultraviolet light. Suggest developers capable of visualizing zones corresponding to papaverine in daylight. Write the reaction equations.

4. Conduct a comparative analysis of the indications for use and safety measures of 2 % 2 ml injection solution No. 10 Papaverine hydrochloride and 2 % 2 ml injection solution No. 10 Drotaverine. Justify the differences based on the structural differences of these substances.

Algorithm for performing laboratory work
«Quality control of pharmaceutical substances theophylline-ethylenediamine, caffeine, folic acid, drotaverine hydrochloride, caffeine sodium benzoate injection solution, cyanocobalamin tablets»

Goal of the work: develop in students' skills of theophylline-ethylenediamine, caffeine, caffeine sodium benzoate, folic acid, cyanocabolamin, drotaverine hydrochloridequality control.

Quality control of the pharmaceutical substance theophylline-ethylenediamine in accordance with the State Pharmacopeiaof the Republic of Belarus

QUANTITATION

Ethylenediamine. Dissolve 0.250 g of the test sample in 30 ml of water R, add 0.1 ml of bromocresol green solution R and titrate with 0.1 M hydrochloric acid until a green color appears.

1 ml of 0.1 M hydrochloric acid solution corresponds to 3.005 mg of ethylenediamine.

Ethylenediamine *content*: not less than 13.5 % and not more than 15.0 % (relative to dry substance).

Reaction equation:

Formulas and calculations:

Conclusion:

Quality control of the pharmaceutical substance caffeine in accordance with the State Pharmacopeiaof the Republic of Belarus according to the indicator «IDENTIFICATION»

Melting point: from 234 °C to 239 °C.

Procedure is in accordance with Article 2.2.14 of the State Pharmacopeia of the Republic of Belarus, volume 1

Substance is placed in a capillary tube until a compacted column with a height of 4 mm to 6 mm is obtained. Raise temperature to approximately 10 °C below the expected melting point and then continue heating at a rate of approximately 1 °C per minute. When temperature reaches a value 5 °C below the expected melting point place the capillary tube with substance in the device. Heating is adjusted so that by the time of melting required rate of temperature rise is achieved (from

1.5 to 2 °C/min — when determining the melting temperature above 150 °C). Temperature at which last solid particle passes into the liquid phase is noted.

At least two determinations are made. The average value is taken as the melting temperature. Discrepancy between determinations should not exceed 1 °C.

Values: *Conclusion:*

Quality control of the pharmaceutical substance of folic acid in accordance with the State Pharmacopeiaof the Republic of Belarus

IDENTIFICATION

A. Specific optical rotation (2.2.7): from +18 to +22 (relative to dry substance).

0.25 g of the test sample is dissolved in 0.1 M sodium hydroxide solution and diluted to a volume of 25.0 ml with the same solvent.

Values: *Conclusion:*

Quality control of the pharmaceutical substance drotaverine hydrochloride according to the indicator «IDENTIFICATION» in accordance with the State Pharmacopeiaof the Republic of Belarus

10 mg of the test sample is dissolved in 5 ml of sulfuric acid R, 0.5 ml of a solution of 30 g/l iron (III) *chloride R* is added and heated at a temperature of 100 °C for 3 min. A green color appears. After cooling add 0.5 ml of diluted nitric acid R. A brownish-red color appears.

Reaction equations: *Analytical effect:* *Conclusion:*

Qualitative reactions to caffeine sodium benzoate in solution for injection (SFI)
Qualitative reaction to caffeine (State Pharmacopeia of the Republic of Belarus)

IDENTIFICATION OF CAFFEINE

C. To 0.5 ml (half an ampoule!) of **SFI** add 0.05 ml of iodized potassium iodide solution R. Solution remains clear. Add 0.1 ml of diluted hydrochloric acid R to the resulting solution. A brown precipitate is formed. Neutralize with diluted sodium hydroxide solution R. Precipitate dissolves.

Reaction equations:

Analytical effect:

Result:

Qualitative reactions to benzoate ion (Article 2.3.1 from the State Pharmacopeiaof the Republic of Belarus, Volume 1)

IDENTIFICATION OF BENZOATE

A. To 0.5 ml of **SFI** add 0.5 ml of iron (III) chloride solution R1; a pinkish-yellow precipitate is formed, soluble in ether R.

Reaction is carried out in a neutral environment since in an acidic environment free benzoic acid is released and precipitated.

Selectivity of this test is low — many organic and inorganic substances form complexes with iron chloride.

Reaction equations:

Analytical effect:

Result:

B. Add 0.2 ml of sulfuric acid R to 0.5 ml of **SFI**, carefully heat bottom of the test tube; a white coating appears on the inner walls of the test tube.

When exposed to sulfuric acid, benzoates are released in form of benzoic acid, which, when the bottom of the test tube is heated, sublimes and settles on the cooler walls of the test tube.

Reaction equation: *Analytical effect:* *Result:*

Conclusion on* SFI *of caffeine sodium benzoate:

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Quality control of cyanocobalamin tablets

QUANTITATION

Powder of one crushed pre-weighed tablet is placed in a 100.0 ml volumetric flask, 30 ml of water R is added and shaken for 15 minutes, then adjusted to the mark with water R. Contents of the flask is filtered (triple filter paper), discarding first 10 ml of filtrate. 25.0 ml of filtrate is diluted with water R to 100.0 ml.

Optical density of the final solution is measured using a spectrophotometer at a wavelength of 361 nm in a cuvette with an absorbing layer thickness of 10 mm. Water R is used as a compensation solution. Specific absorption rate of cyanocobalamin is 207.

It is necessary to calculate content of cyanocobalamin in the tablet based on average weight of one tablet.

Deviation of content from the nominal value should not exceed 15 %.

Formulas and calculations: *Conclusion:*

List of literature:

1. *Pharmaceutical* chemistry : textbook / ed. G. V. Ramenskaya. – Moscow : GEOTAR-Media, 2023. – 384 p.

2. *Tsurkan, O. O.* Pharmaceutical chemistry. Analysis of the Medicinal Substances according to Functional Groups: study guide / O. O. Tsurkan. – Kyiv : AUS Medicine Publishing, 2018. – 152 p.

3. *Pharmaceutical* analysis : The study guide for students of higher schools / ed. by V. A. Georgiyants. – Kharkiv : NUPh Golden Pages, 2018. – 494 p.

4. Lecture and information material.

Lesson 13
PHARMACOPOEIAL QUALITY CONTROL AND PHARMACEUTICAL CHEMISTRY OF TERPENOID DERIVATIVES, CHROMONE, SECO DERIVATIVES OF ERGOSTEROL AND NAPHTHOQUINONE, RELATED TO FAT-SOLUTE VITAMINS AND THEIR DERIVATIVES

Objective: introduce students to methods of preparation, structural formulas, properties, quality control, chemical basis of pharmacological action and storage conditions of pharmaceutical substances derived from terpenoids, chromone, ergosterol and naphthoquinone, related to fat-soluble vitamins and their derivatives; develop students' skills in pharmacopoeial quality control of pharmaceutical substances derived from terpenoids, chromone, ergosterol and naphthoquinone, which are fat-soluble vitamins and their derivatives.

Requirements for the initial level of knowledge: repeat structure of fat-soluble vitamins — derivatives of ergosterol and naphthoquinone; chemical properties and structure of terpenoids and chromone derivatives.

Problems for discussion:

1. Characteristics and classification of fat-soluble vitamins. Concept of vitamin-like substances.

2. Methods of preparation, structural formula, properties, quality control, chemical basis of pharmacological action and storage conditions of fat-soluble vitamins: retinol and its esters (acetate, palmitate, etc.), retinoids (tretinoin, isotretinoin, adapalene, etc.), ergocalciferol, cholecalciferol, α-tocopherol, α-tocopheryl acetate and hydrosuccinate, RRR-α-tocopheryl acetate, menadione, phytomenadione, menadione sodium bisulfite.

Situational tasks

1. Why are medications containing retinol (for example, Aevit with retinol palmitate) recommended to be taken in short courses (20–40 days) with intervals of 3–6 months? Describe the process of retinol eliminating from the body.

2. A patient taking cholecalciferol contacted a pharmacy with a request to clarify the meaning of the abbreviation ME near the dosage designation of the drug. What mass of the substance corresponds to 1 ME? What dosage of vitamin D can be recommended as a preventive measure?

3. Due to what structural features is tocopherol effective as an antioxidant? Provide a diagram of the stable free radical's formation.

4. Why was cerimetry chosen as the method for redox titration of menadione sodium bisulfite? What are the advantages of this titration method over others for this substance?

5. Provide pharmaceutical advice when selling a vitamin and mineral complex to a pregnant woman in the 2nd trimester to support body functions.

Algorithm for performing laboratory work
«Quality control of alpha-tocopheryl acetate, menadione sodium bisulfite»

Goal of the work: develop students' skills in quality control of alpha-tocopheryl acetate and menadione sodium bisulfite.

Quality control of the pharmaceutical substance alpha-tocopheryl acetate according to the «DESCRIPTION» indicator in accordance with the State Pharmacopeia of the Republic of Belarus

Transparent colorless or slightly greenish viscous oily liquid.

Observation:

Conclusion:

Quality control of SFI of menadione sodium bisulfite according to the indicator «IDENTIFICATION»

A. UV-visible absorption spectrophotometry (2.2.25)

Test solution (a). Contents of 1 ampoule is dissolved in 100 ml of water R.

Test solution (a) is prepared in advance!

Test solution (b). 2.5 ml of the test solution (a) is diluted with water R to a volume of 10 ml.

Absorption spectrum of the test solution (a) in the region from 280 to 340 nm has a maximum at 305 nm.

Absorption spectrum of the test solution (b) in the region from 220 nm to 280 nm has a maximum at 230 nm and 265 nm and a minimum at 248 nm.

Absorption maxima and minima of the tested solution: *Result:*

B. Test solution gives reaction(a) to sodium (2.3.1)

Reaction equation: *Analytical effect:* *Result:*

Conclusion on the SFI of menadione sodium bisulfite:

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List of literature:

1. *Pharmaceutical* chemistry : textbook / ed. G. V. Ramenskaya. – Moscow : GEOTAR-Media, 2023. – 384 p.

2. *Tsurkan, O. O.* Pharmaceutical chemistry. Analysis of the Medicinal Substances according to Functional Groups: study guide / O. O. Tsurkan. – Kyiv : AUS Medicine Publishing, 2018. – 152 p.

3. *Pharmaceutical* analysis : The study guide for students of higher schools / ed. by V. A. Georgiyants. – Kharkiv : NUPh Golden Pages, 2018. – 494 p.

4. Lecture and information material.

Lesson 14
PHARMACOPOEIAL QUALITY CONTROL AND PHARMACEUTICAL CHEMISTRY OF AROMATIC AMINO ACIDS DERIVATIVES RELATED TO DRUGS FOR LOCAL ANESTHESIA

Objective: introduce students to methods of preparation, structural formulas, properties, quality control, chemical basis of pharmacological action, relationship between structure and action and storage conditions of pharmaceutical substances aromatic amino acid derivatives related to medicinal products for local anesthesia; develop students' skills in pharmacopoeial quality control of pharmaceutical substances aromatic amino acids derivatives related to drugs for local anesthesia.

Requirements for the initial level of knowledge: repeat structure and chemical properties of aromatic amino acids, structure of sodium channels, concept of local anesthetics and local irritants.

Problems for discussion:

1. Characteristics, classification, chemical structure, properties, relationship between structure and action, chemical basis of the mechanism of action and binding on the target, quality control and representatives of drugs for local anesthesia: benzocaine, procaine hydrochloride, tetracaine hydrochloride, lidocaine hydrochloride monohydrate, bupivacaine hydrochloride, articaine hydrochloride, oxybuprocaine hydrochloride, proximetacaine hydrochloride. Local anesthetics as derivatives of aromatic amino acids.
2. Local irritants: capsaicin, etc.

Situational tasks

1. The pK_{BH+} of the local anesthetic bupivacaine is 8.1. Calculate what percentage of the substance will be in molecular and ionized form at a physiological blood pH of 7.4.

2. Compare cocaine, benzocaine, procaine, lidocaine, bupivacaine, oxybuprocaine in terms of chemical stability and duration of action. Specify what type of anesthesia they are used for and why?

3. How is the duration of action of local anesthetics related to the nature of the intermediate chain? Give examples, designate structural fragments.

4. What method is used for quantitative determination of benzocaine? Why should this process occur during cooling? What method of determining the TEP do you consider the most optimal? Justify your answer.

5. Why during alkalimetric titration of procaine hydrochloride is a small amount of hydrochloric acid added before titration? Provide equation of the reaction that occurs.

6. What form is procaine hydrochloride in at physiological pH? (pKa = 7.8–9.0). How will acidity of the environment affect membrane penetration and target binding?

7. Suggest methods for chemical identification of oxybuprocaine hydrochloride.

8. What are the advantages of throat pain relief medications containing oxybuprocoin compared to medications containing lidocaine? Provide trade names.

Algorithm for performing laboratory work
«Quality control of the pharmaceutical substance procaine hydrochloride»

Goal of the work: develop students' skills in quality control of procaine hydrochloride.

Quality control of the pharmaceutical substance procaine hydrochloride in accordance with the State Pharmacopeia of the Republic of Belarus

IDENTIFICATION

A. Melting point (2.2.14): from 154 °C to 158 °C.

Values:
Result:

D. To 0.2 ml of solution S add 2 ml of water R and 0.5 ml of diluted sulfuric acid R and shake. To the resulting solution add 1 ml of of 1 g/l potassium permanganate solution R. Coloring immediately disappears.

Reaction equation:
Analytical effect:
Result:

F. 1 ml of solution S is diluted with water R to a volume of 100 ml. 2 ml of the resulting solution is acidified with diluted hydrochloric acid R and 0.2 ml of sodium nitrite solution R is added. After 1–2 minutes 1 ml of β-naphthol solution R is added; an intense orange or red color appears and, as a rule, a precipitate of the same color is formed.

Reaction equations:
Analytical effect:
Result:

Solution S. Dissolve 1.25 g of the test sample in carbon dioxide-free water R and dilute to a volume of 25.0 ml with the same solvent.

TESTS

pH (2.2.3). From 5.0 to 6.5.

16.0 ml of solution S is diluted with carbon dioxide-free water R to a volume of 40 ml.

Values:
Result:

QUANTITATION

Dissolve 0.400 g of the test sample in 50 ml of dilute hydrochloric acid R, add 3 g of potassium bromide R. Cool in ice water and then slowly titrate with constant stirring with 0.1 M sodium nitrite solution, maintaining temperature at about 15 °C, as an indicator a solution of tropeolin 00 R mixed with methylene blue R is used (0.2 ml of a solution of tropeolin 00 R and 0.1 ml of a solution of methylene blue R) — titrate until color changes from red-violet to blue.

1 ml of 0.1 M sodium nitrite solution corresponds to 27.28 mg of $C_{13}H_{20}N_2O_2$-HCI.

Content: not less than 99.0 % and not more than 101.0 % (relative to dry substance).

Reaction equation:
Formulas and calculations:
Result:

Conclusion on procaine hydrochloride:

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List of literature:

1. *Pharmaceutical* chemistry : textbook / ed. G. V. Ramenskaya. – Moscow : GEOTAR-Media, 2023. – 384 p.
2. *Tsurkan, O. O.* Pharmaceutical chemistry. Analysis of the Medicinal Substances according to Functional Groups: study guide / O. O. Tsurkan. – Kyiv : AUS Medicine Publishing, 2018. – 152 p.
3. *Pharmaceutical* analysis : The study guide for students of higher schools / ed. by V. A. Georgiyants. – Kharkiv : NUPh Golden Pages, 2018. – 494 p.
4. Lecture and information material.

Lesson 15
FINAL LESSON «PHARMACOPOEIAL ANALYSIS OF PHARMACEUTICAL SUBSTANCES OF AROMATIC AND HETEROCYCLIC NATURE, VITAMINS, DRUGS FOR LOCAL ANESTHESIA»

Objective: systematize knowledge gained from study of pharmacopoeial quality control of aromatic and heterocyclic pharmaceutical substances, pharmaceutical chemistry of vitamins and drugs for local anesthesia.

Requirements for the initial level of knowledge: repeat pharmacopoeial quality control of aromatic and heterocyclic pharmaceutical substances, pharmaceutical chemistry of vitamins and drugs for local anesthesia.

Test questions on the topic of the lesson

Pharmacopoeial quality control and use of the following pharmaceutical substances:
phenol, benzyl benzoate;
resorcinol, benzalkonium chloride;
paracetamol;
benzoic acid, sodium benzoate;
salicylic acid, sodium salicylate;
choline salicylate, nifuroxazide;
chloramphenicol and its esters (palmitate, etc.);
sulfonamide, sulfomethoxazole;
sodium sulfacetamide, sulfasalazine;
silver sulfadiazine, trimethoprim;
nitrofural, nitrofurantoin;
furazolidone, nifuratel;
metronidazole and its benzoate;
tinidazole, ornidazole;
ascorbic acid, sodium and calcium ascorbate;
rutoside trihydrate, troxerutin;
metamizole sodium monohydrate;
phenazone, bendazole hydrochloride (dibazole);
nicotinic acid, nicotinamide;
xanthinol nicotinate, niketamide;
pyridoxine hydrochloride, calcium pantothenate;
papaverine hydrochloride, drotaverine hydrochloride;
caffeine and its monohydrate;
theophylline and its monohydrate, cyanocobalamin;
aminophylline (theophylline-ethylenediamine, theophylline-ethylenediamine hydrate and for injection);
theobromine, pentoxifylline;
folic acid, calcium folinate hydrate, calcium levofolinate hydrate;
riboflavin, riboflavin sodium phosphate;
salts and esters of thiamine (benfotiamine, cocarboxylase, nitrate, hydrochloride);
retinol and its esters (acetate, palmitate, etc.);
retinoids (tretinoin, isotretinoin, adapalene, etc.);
ergocalciferol, cholecalciferol;
α-tocopherol, α-tocopheryl acetate and hydrosuccinate, RRR-α-tocopheryl acetate;
menadione, phytomenadione, menadione sodium bisulfite;
benzocaine, proxymetacaine hydrochloride;
procaine hydrochloride, oxybuprocaine hydrochloride;

tetracaine hydrochloride, lidocaine hydrochloride monohydrate;

bupivacaine hydrochloride, articaine hydrochloride.

In pharmacopoeial quality control and medical use of these pharmaceutical substances, pay special attention to the following sections:

− chemical formula, description (properties), solubility, storage;

− authenticity (identification);

− quantitative determination;

− chemical basis of pharmacological action (medical use).

Characteristics, classification, chemical structure and chemical basis of the pharmacological action of the studied groups of drugs:

1. Amphenicols: definition, chemical structure, representatives, chemical mechanism of action. Antimicrobial spectrum. Prodrugs and salts of chloramphenicol.
2. Sulfonamides: definition, classification, chemical structure, representatives, chemical aspects of action mechanism. Sulfonamides and trimethoprim, their combinations (co-trimoxazole). Spectrum of antimicrobial action. Long-acting sulfonamides.
3. Nitrofurans: definition, classification, chemical structure, representatives, chemical aspects of action mechanism. Antimicrobial spectrum. Fosfomycin.
4. Nitroimidazoles: definition, classification, chemical structure, representatives, chemical aspects of action mechanism. Spectrum of antimicrobial activity.
5. Analgesics-antipyretics: definition, classification, chemical structure, chemical aspects of action mechanism. Effect on COX.
6. Xanthine derivatives — phosphodiesterase inhibitors: definition, classification, chemical structure, representatives, features of action based on the chemical structure. Selectivity of action.
7. Isoquinoline derivatives — phosphodiesterase inhibitors: definition, classification, chemical structure, representatives, features of action based on the chemical structure. Selectivity of action.
8. Characteristics and classification of vitamins, water-soluble vitamins.
9. Characteristics, chemical structure, physicochemical properties and chemical basis of the pharmacological action of ascorbic acid.
10. Characteristics, chemical structure, physicochemical properties and chemical basis of the pharmacological action of bioflavonoids and their derivatives.
11. Characteristics, chemical structure, physicochemical properties and chemical basis of the pharmacological action of PP group vitamins.
12. Characteristics, chemical structure, physicochemical properties and chemical basis of the pharmacological action of vitamins B6 and B12.
13. Characteristics, chemical structure, physicochemical properties and chemical basis of the pharmacological action of vitamins B2 and Bc.
14. Characteristics and classification of fat-soluble vitamins. Concept of vitamin-like substances.
15. Characteristics, chemical structure, physicochemical properties and chemical basis of the pharmacological action of retinol and retinoids.
16. Characteristics, chemical structure, physicochemical properties and chemical basis of the pharmacological action of group D vitamins and provitamins.
17. Characteristics, chemical structure, physicochemical properties and chemical basis of the pharmacological action of tocopherols and naphthoquinones.
18. Classification and chemical structure of local anesthetics. Properties of an “ideal” local anesthetic. Chemical structure and duration of local anesthetics action. Local irritants.
19. Relationship between structure and action of ester-type anesthetics. Disadvantages of cocaine as an ester local anesthetic. Hydrolysis of cocaine.

20. Relationship between structure and action of anilide-type anesthetics. Henderson-Hasselbach equation and stages of local anesthetics ionization at physiological pH values as the basis of their actionmechanism.

Ticket includes five main questions on two substances (one of aromatic nature, the second of heterocyclic nature) and a sixth question on general characteristics of the groups of drugs being studied:

description (properties), solubility, storage – 1 p (0.5 p + 0.5 p);
identification – 2 p (1 p + 1 p);
quantitative determination – 2 p (1 p + 1 p);
application – 2 m (1 p + 1 p);
problem solving – 1 m (0.5 p + 0.5 p);
general characteristics – 2 points.

Literature: see the literature for lessons 8–14.

Lesson 16
QUALITY CONTROL OF PHARMACEUTICALLY PREPARED DRUGS (EXTEMPORANEOUS DRUGS). QUALITY CONTROL OF INDUSTRIALLY MANUFACTURED MEDICINES

Objective: familiarize students with approaches to quality control of pharmaceutically produced drugs (extemporaneous drugs) and industrially manufactured drugs; develop students' skills in quality control of pharmaceutically produced drugs (extemporaneous drugs) and industrially manufactured drugs.

Requirements for the initial level of knowledge: repeat basics of pharmaceutical solutions, powders, ointments and other extemporaneous medications preparation.

Problems for discussion

1. Features of pharmaceutically manufactured drugs (extemporaneous drugs) quality control. Legal acts regulating quality control of extemporaneous drugs. In-pharmacy quality control of medicinal products and its types. Article of the State Pharmacopeia of the Republic of Belarus «Express analysis of extemporaneous medicines». Differences between express analysis and pharmacopoeial quality control.
2. Express analysis methods. Quality control of powders, solutions, ointments, suppositories and other pharmaceutical dosage forms. Assessment of extemporaneous drugs quality.
3. Sampling and sample preparation when analyzing various dosage forms.
4. Criteria for selecting identification and quantification methods of industrially manufactured drugs.
5. Pharmaco-technological tests.
6. Methods used in the analysis of industrially manufactured dosage forms. Approaches to quality control of industrial production dosage forms.
7. Features of the multicomponent drugs analysis.
8. Quality control of excipients in dosage forms (preservatives, etc.).

Situational tasks

1. Conduct a comparative analysis of Method 1 and Method 2 for the quantitative determination of extemporaneous preparation Ascorbic acid 2 % solution according to the parameters: titration method, titrant, method for detecting TEP, functional groups involved in the transformations. Provide reaction equations.

2. Suggest methods for determining authenticity of each component of the suppository composition:

Papaverine hydrochloride 0.04 g
Anesthesin 0.3 g
Cocoa butter 1.0 g
Write reaction equations.

3. When conducting a quantitative analysis of the composition formula:
Kalii iodidi 1,5
Purified Aqua 15 ml

The measured refractive index was 1.3501. Calculate concentration of the substance in the solution (F = 0.0013). Find relative and absolute deviation. Taking into account permissible deviation standards draw a conclusion about whether the dosage form has been prepared satisfactorily.

4. A pharmacist at a pharmaceutical company needs to draw up a regulatory document on the quality of a new medicinal product – tablets of substance A. What mandatory sections should be included in this document?

5. Suggest methods/controlled parameters used for folic acid in 0.400 g tablets and folic acid substance in the sections of the pharmacopoeial article «Definition», «Description», «Identity», «Tests», «Quantitative determination», «Storage». Provide your answer in the form of a table.

Algorithm for performing laboratory work
«Express analysis of pharmaceutically produced dosage forms using titrimetric and refractometric methods, quality control of industrially manufactured dosage forms»

Goal of the work: develop students' skills in quality control of pharmaceutical preparations and industrial production.

Quality control of ascorbic acid 2 % solution

DESCRIPTION

Transparent, colorless or slightly yellowish liquid.

Appearance:
Result:

IDENTIFICATION

A. Add 0.5 ml of silver nitrate solution R2 to 1 ml of the test sample. A dark gray precipitate forms.

Reaction equation:
Analytical effect:
Result:

B. To 0.2 ml of the test sample add dropwise a solution of 1 g/l dichlorophenolindophenol sodium salt R in 96 % alcohol R. Blue color of the latter disappears.

Reaction equation:
Analytical effect:
Result:

QUANTITATION

METHOD 1

To 2.0 ml of the test sample add 0.5 ml of potassium iodide solution R1, 2 ml of iodide-free starch solution R, 1 ml of 274 g/l diluted hydrochloric acid solution R and titrate with 0.0167 M potassium iodate solution until faint blue color.

1 ml of 0.0167 M potassium iodate solution corresponds to 8.806 mg of $C_6H_8O_6$.

Reaction equation: *Formulas and calculations:* *Result:*

METHOD 2

To 2.00 ml of the test sample add 2 drops of phenolphthalein R1 solution and titrate with 0.1 M sodium hydroxide solution until a pink color is observed.

1 ml of 0.1 M sodium hydroxide solution corresponds to 17.61 mg $C_6H_8O_6$.

Reaction equation: *Formulas and calculations:* *Result:*

Conclusion on ascorbic acid 2 % solution:

_____

_____

Quality control of potassium iodide 5 % solution

DESCRIPTION

Transparent colorless liquid.

Appearance: *Result:*

IDENTIFICATION

A. Test sample gives reaction(a) to potassium (2.3.1)

Add 1 ml of sodium carbonate solution to 2 ml of solution and heat; no precipitate forms. Add 0.05 ml of sodium sulfide solution to the hot solution; no precipitate forms. Solution is cooled in ice water, 2 ml of a solution of 150 g/l tartaric acid is added and left to settle; a white crystalline precipitate is formed.

Reaction equation:
Analytical effect:
Result:

B. Test sample gives reaction (b) to iodides (2.3.1)

To 0.2 ml of solution add 0.5 ml of diluted sulfuric acid R, 0.1 ml of potassium dichromate solution R, 2 ml of water R, 2 ml of chloroform R, shake for several seconds and leave until separation; the chloroform layer acquires a violet or red-violet color.

Reaction equation:
Analytical effect:
Result:

QUANTITATION

METHOD 1

To 10.0 ml of the test solution add 5 drops of diluted acetic acid R and titrate with a 0.1 M solution of silver nitrate until the precipitate turns pink using a solution of 1 g/l eosin R as an indicator.

1 ml of 0.1 M silver nitrate solution corresponds to 16.6 mg KI.

Reaction equation:
Formulas and calculations:
Result:

METHOD 2
Use only for 5 % potassium iodide solution.
Determine refractive index (2.2.6); F (KI, 5 %) = 0.00130.

Formulas and calculations: *Result:*

Conclusion on potassium iodide 5 % solution:

_____

_____

Quality control of sodium bicarbonate 4 % solution for injection

DESCRIPTION
Transparent, colorless liquid with a pH value from 8.1 to 8.9.

Appearance: *Result:*

IDENTIFICATION
A. 2 ml of the test sample gives reactions (a) and (c) to sodium (2.3.1).

a) To 2 ml of solution *add 2 ml of a solution 150 g/l potassium carbonate R and heat to boiling; no precipitate forms. Add 4 ml of potassium pyroantimonate solution R to the solution and heat to boiling, then cool in ice water and, if necessary, rub inner walls of the test tube with a glass rod; a dense white precipitate forms.*

Reaction equation: *Analytical effect:* *Result:*

c) Sodium salt moistened with *hydrochloric acid and introduced into a colorless flame, colors it yellow*.

Analytical effect: *Result:*

B. Add 2–3 drops of diluted acetic acid R to 3–5 drops of the test sample. Violent release of gas bubbles is observed.

Reaction equation: *Analytical effect:* *Result:*

C. To 4–5 drops of the test sample add 5 drops of a saturated solution of magnesium sulfate R (add 100 ml of water R to 100 g of magnesium sulfate R, shake for 24 hours and filter) and boil. A white precipitate forms.

Reaction equation: *Analytical effect:* *Result:*

QUANTITATION

METHOD 1

Titrate 1.0 ml of the test sample with 0.1 M hydrochloric acid until a pink color appears using methyl orange R as an indicator.

1 ml of 0.1 M hydrochloric acid solution corresponds to 8.40 mg of $NaHCO_3$.

Reaction equation: *Formulas and calculations:* *Result:*

METHOD 2

Determine refractive index (2.2.6); F ($NaHCO_3$, 4 %) = 0.00125.

Formulas and calculations: *Result:*

Conclusion on sodium bicarbonate 4 % solution:

_____

_____

Mass uniformity for unit dosage of medicinal product (2.9.5)

20 units of dosed medicinal product (amlodipine tablets) are selected according to a statistically based scheme, each is weighed separately and the average weight is calculated. The medicinal product is considered to have passed test if no more than two individual masses deviate from the average mass by an amount exceeding value indicated in the table.

Dosage form	Average weight	Permissible deviation, %
Tablets (uncoated and film-coated)	80 mg or less	10
	More than 80 mg but less than 250 mg	7.5
	250 mg or more	5

Results:

m1 =	*m8 =*	*m15 =*
m2 =	*m9 =*	*m16 =*
m3 =	*m10 =*	*m17 =*
m4 =	*m11 =*	*m18 =*
m5 =	*m12 =*	*m19 =*
m6 =	*m13 =*	*m20 =*
m7 =	*m14 =*	

Calculations:

Result:

Conclusion on amlodipine tablets:

_____

_____

List of literature:

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5. Lecture and information material.

Lesson 17
FINAL LESSON ON LABORATORY WORK

Purpose of the lesson: consolidation of practical skills and professional competencies acquired during study of the academic discipline «Pharmaceutical Chemistry» in the 3rd year.

Requirements for the initial level of knowledge: review basics of pharmacopoeial and non-pharmacopoeial methods of drug analysis.

List of practical skills:

1. Acidimetric titration of sodium bicarbonate.
2. Alkalimetric titration of salicylic acid.
3. Alkalimetric titration of benzoic acid.
4. Alkalimetric titration of nicotinic acid.
5. Complexometric titration of zinc sulfate heptahydrate.
6. Determination of the melting point of nicotinic acid.
7. Determination of the melting point of salicylic acid.
8. Determination of the melting point of procaine hydrochloride.
9. Polarimetric determination of ascorbic acid.
10. Polarimetric determination of folic acid.
11. Spectrophotometric determination of nitrofural (authenticity).
12. Spectrophotometric determination of nitrofural (quantitative determination).
13. Spectrophotometric determination of chloramphenicol in capsules.
14. Determination of pH of procaine hydrochloride solution.
15. Refractometric determination of glucose 5 % solution.
16. Refractometric determination of magnesium sulfate 5 % solution.
17. Determination of pH of sodium edetate solution.
18. Identification of medicinal products by structural formulas, their assignment to specific pharmacotherapeutic and chemical groups with an indication of storage conditions.*
19. Calculation of the results of spectrophotometric, titrimetric, polarimetric and refractometric determination, their interpretation and conclusion on the compliance of the medicinal product with the requirements of regulatory documentation.

*The following information is indicated: pharmacopoeial name (indicating the chemical form), what is it a derivative of (according to chemical classification), pharmacologic action / disease for which this drug is used and storage conditions.

QUESTIONS FOR PREPARATION
for the course exam in the academic discipline «Pharmaceutical Chemistry»
for 3rd year students of the Medical Faculty for International Students of the Belarussian State Medical University with English as the language of instruction in the specialty «Pharmacy»

Block 1. General issues of pharmaceutical chemistry and methods of analysis, used in pharmaceutical chemistry

1. Terminology used in pharmaceutical chemistry: medicinal product (MP), medicinal preparation, pharmaceutical substance, excipient, dosage form, original medicinal product, reproduced medicinal product (generic).

2. Terminology used in pharmaceutical chemistry: antiseptic drug, homeopathic drug, biological drug, immunological drug (immunobiological drug), radiopharmaceutical drug, etc.

3. Rules for choosing names of medicinal products. Names of pharmaceutical substances: chemical name, INN, national name. Trade names of medicinal products.

4. Classifications of medicinal substances used in pharmaceutical chemistry: chemical classification, ATX classification.

5. Sources and methods of obtaining medicines: isolation of medicinal substances from natural sources, chemical modification of natural compounds, obtaining medicinal substances by complete chemical synthesis.

6. Modern requirements for medicines: safety, efficacy, quality. Quality assurance system for medicines at all stages of development and use. Standards of good practices: good research practice (GRP), good laboratory practice (GLP), good clinical practice (GCP), good manufacturing practice (GMP), good distribution practice (GDP), good pharmacy practice (GPP), good storage practice (GSP), good pharmacovigilance practice (GVP), etc.

7. Structure of the quality control system for medicines in the Republic of Belarus. Counterfeiting of medicines.

8. Regulatory documentation governing the quality of pharmaceutical substances and medicines. State Pharmacopoeia of the Republic of Belarus: structure, pharmacopoeial monographs. Basic principles of pharmacopoeial analysis. Pharmacopoeia of the Eurasian Economic Union.

9. Stability of medicinal products, its types. Factors affecting stability: physical, microbiological, chemical. Methods of increasing stability: physical, chemical (stabilizers), antimicrobial (preservatives).

10. Stability tests (Decision of the EEC Board of 2018 No. 69 as amended and supplemented): long-term, accelerated, stress, intermediate. Shelf life (Law of the Republic of Belarus of 2006 No. 161-Z as amended and supplemented), expiration date (Decision of the EEC Board of 2018 No. 69 as amended and supplemented).

11. Classification of pharmaceutical substances and medicinal products by storage conditions. Examples of storage of individual groups with indication of storage conditions.

12. Gravimetric method of analysis. Essence of the method. Stages of gravimetric analysis. Application in pharmaceutical analysis.

13. Titrimetric methods of analysis: classification (by type of chemical reaction, by titration method). Titrated solutions, their standardization (establishment of correction factor: k).

14. Determination of nitrogen in organic compounds (Kjeldahl method).

15. Acid-base titration in aqueous media. Essence of the method (titrant, equations of ongoing reactions, establishment of the end point of titration (ETP) (indicators, etc.), conditions of implementation). Application in pharmaceutical analysis.

16. Acid-base titration in aqueous-organic media. Essence of the method. Application in pharmaceutical analysis.

17. Acid-base titration in non-aqueous media. Essence of the method. Application in pharmaceutical analysis.

18. Complexometric titration: complexometry. Essence of the method. Application in pharmaceutical analysis.

19. Precipitation titration: argentometry. Essence of the method. Application in pharmaceutical analysis.

20. Oxidation-reduction titration: iodi(o)metry, chloridometry, iodatometry, bromatometry. Essence of methods. Application in pharmaceutical analysis.

21. Oxidation-reduction titration: nitritometry, permanganatometry, cerimetry. Essence of methods. Application in pharmaceutical analysis.

22. Spectrometric methods: general characteristics and classification.

23. Atomic absorption spectrometry. Basic principles. Device design. Application in pharmaceutical analysis.

24. Molecular absorption spectrometry in the ultraviolet and visible regions. Basic principles. Device design, their differences. Application in pharmaceutical analysis.

25. Infrared spectrometry. Basic principles. Device design. Application in pharmaceutical analysis.

26. Atomic emission spectrometry. Basic principles. Device design. Application in pharmaceutical analysis.

27. Fluorimetry. Basic principles. Device design. Application in pharmaceutical analysis.

28. Spectrometric methods based on the scattering of electromagnetic radiation (nephelometry, turbidimetry). Basic principles. Device design. Application in pharmaceutical analysis.

29. Refractometry. Basic principles. Device design. Application in pharmaceutical analysis.

30. Chiroptic methods of analysis (polarimetry). Basic principles. Device design. Application in pharmaceutical analysis.

31. Chromatographic methods of analysis. General characteristics and classification.

32. Gas chromatography. Basic principles. Classification. Gas chromatograph structure. Detectors. Application in pharmaceutical analysis.

33. TLC. Basic principles. Methods of preparation. Basic chromatographic parameters. Application in pharmaceutical analysis.

34. HPLC. Basic principles. Liquid chromatograph design. Detectors. Application in pharmaceutical analysis.

35. Types of liquid chromatography (size-exclusion chromatography, ion-exchange chromatography). Supercritical fluid chromatography. Basic principles. Application in pharmaceutical analysis.

36. Mass spectrometry. Basic principles and stages. Basic ionization methods. Application in pharmaceutical analysis. Combination of mass spectrometry with chromatographic methods.

37. Thermal methods of analysis: thermogravimetry, differential thermal analysis, differential scanning calorimetry. Basic principles. Application in pharmaceutical analysis.

38. Protein-binding methods of analysis: immunochemical methods. Basic principles. Classification. Application in pharmaceutical analysis.

39. Protein-binding methods of analysis: immunofluorescence and receptor methods. Basic principles. Classification. Application in pharmaceutical analysis.

40. Biological methods of analysis: determination of antibiotic activity. General principles. Methodology. Application in pharmaceutical analysis.

Block 2. Reactions for identification and detection of impurities and pharmacopoeial tests

1. Pharmaceutical analysis: definition, features, types (pharmacopeial, stage-by-stage quality control in industrial production, express analysis of extemporaneous dosage forms, biopharmaceutical analysis).

2. Classification of reagents. Preparation of reagent solutions, standard and buffer solutions. Expiry dates and marking of reagents. Indicators. Features of indicator solutions used in pharmacopoeial analysis preparation.

3.Physical properties of substances: aggregation state, appearance, color, hygroscopicity, crystallinity, polymorphism.

4. Solubility of pharmaceutical substances. Conventional terms denoting solubility. Methodology for determining solubility. Acid-base properties of medicinal substances (basic theories of acids and bases). Henderson-Hasselbalch equation.

5. Authenticity (identification) reactions for inorganic cations: aluminum, calcium, magnesium, zinc.

6. Authenticity (identification) reactions for inorganic cations: ammonium salts, ammonium salts and salts of volatile bases, potassium.

7. Authenticity (identification) reactions for inorganic cations: lead, silver, antimony.

8. Authenticity (identification) reactions for inorganic cations: bismuth, iron, arsenic.

9. Authenticity (identification) reactions for inorganic anions: iodides, chlorides, silicates.

10. Authenticity (identification) reactions for inorganic anions: carbonates and hydrocarbonates, nitrates, nitrites.

11. Authenticity (identification) reactions for inorganic anions: sulfates, sulfites, phosphates.

12. Authenticity (identification) reactions for inorganic ions: sodium, mercury, bromides.

13. Authenticity (identification) reactions for organic substances: acetates, acetyl, benzoates, salicylates.

14. Authenticity (identification) reactions for organic substances: alkaloids, primary aromatic amines.

15. Authenticity (identification) reactions for organic substances: barbiturates, tartrates.

16. Authenticity (identification) reactions for organic substances: xanthines, tartrates.

17. Authenticity (identification) reactions for organic substances: lactates, citrates, esters.

18. General and specific methods for detecting impurities. Tests for maximum impurity content: ammonium salts (A-D), arsenic (A, B).

19. General and specific methods for detecting impurities. Tests for maximum impurity content: calcium, chlorides, fluorides, sulfates.

20. General and specific methods for detecting impurities. Tests for maximum impurity content: magnesium, magnesium and alkaline earth metals, phosphates, potassium.

21. General and specific methods for detecting impurities. Tests for maximum impurity content: heavy metals, iron, aluminum.

22. Determination of melting point (capillary method, open capillary method, instantaneous melting method). Device design.

23. Determination of freezing point, dropping point, distillation temperature limits and boiling point. Device design.

24. Determination of density. Types of density. Devices for determining density.

25. Determination of liquids viscosity. Types of viscosity. Devices for determining viscosity.

26. Nature and character of foreign substances in medicinal products. Impurities: definition, classification (is the structure known, is the maximum permissible level established, by nature, by relative toxicity). Qualification of impurities. Definition of accompanying impurities.

27. Sources of impurities. Methods of determining impurities: chemical, instrumental. Methods of determination: standard, non-standard. Ames test.

28. Determination of transparency and degree of turbidity of liquids. Preparation of standards.

29. Determination of the degree of coloration of liquids. Preparation of standards.

30. Determination of volatile substances and water: micro- and semi-micro-method according to Fischer, distillation method, electrolytic hygrometer.

31. Determination of volatile matter and water: loss on drying. Determination of total ash and sulphate ash.

32. Residual solvents: general concept, classification, toxicity, determination of quantity.

33. Determination of microbiological purity of non-sterile products. General principles. Acceptance criteria. Test methodology. Application in pharmaceutical analysis.

34. Electrochemical methods of analysis. General characteristics and classification. Basic concepts (electrochemical cell, electrodes, electrolytes). Voltammetry (direct voltammetry and amperometric titration). Basic principles. Voltamgram. Application in pharmaceutical analysis.

35. Conductometry (direct conductometry and conductometric titration). Basic principles. Application in pharmaceutical analysis.

36. Potentiometry (ionometry and potentiometric titration). Basic principles. Application in pharmaceutical analysis. Potentiometric determination of pH. Ion-selective electrodes.

37. The main validation characteristics of methods and tests: specificity, correctness, precision, linearity, detection limit, quantification limit, range of application, stability (robustness).

38. Algorithm for statistical processing of chemical experiment results, basic formulas.

39. Purified water, highly purified water, water for injection: definition, methods of production, storage. Pharmacopoeial control of water quality: specific electrical conductivity, chlorides, sulfates, calcium and magnesium, reducing agents, ammonium salts.

Block 3. Pharmacopoeial quality control and medical use of pharmaceutical substances

1. Pharmacopoeial quality control: barium sulfate,magnesium oxide light and magnesium oxide heavy. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

2. Pharmacopoeial quality control: magnesium sulfate heptahydrate, magnesium carbonate basic light and heavy, magnesium citrate. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

3. Pharmacopoeial quality control: calcium chloride anhydrous, hexahydrate and dihydrate, calcium carbonate. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

4. Pharmacopoeial quality control: hydrogen peroxide 3 % (30 %) solution, iodine. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

5. Pharmacopoeial quality control: sodium chloride and potassium chloride. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

6. Pharmacopoeial quality control: sodium bromide and potassium bromide. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

7. Pharmacopoeial quality control: sodium iodide and potassium iodide. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

8. Pharmacopoeial quality control: boric acid, sodium tetraborate. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

9. Pharmacopoeial quality control: hydrated aluminum oxide, hydrated aluminum phosphate, aluminum chloride hexahydrate. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

10. Pharmacopoeial quality control: zinc oxide, zinc sulfate hexa- and heptahydrate. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

11. Pharmacopoeial quality control: silver proteinate (protargol), potassium permanganate, sodium bicarbonate. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

12. Pharmacopoeial quality control: iron sulfate heptahydrate and dried, iron chloride hexahydrate, iron fumarate. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

13. Pharmacopoeial quality control: bismuth nitrate basic, heavy; copper sulfate pentahydrate and anhydrous. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

14. Pharmacopoeial quality control: glycerin, glycerin 85 %, anesthetic ether, ether. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

15. Pharmacopoeial quality control: glucose monohydrate and anhydrous, lactose monohydrate and anhydrous, lactulose. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

16. Pharmacopoeial quality control: sucrose, sodium saccharin. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

17. Pharmacopoeial quality control: D-camphor, racemic camphor, levomenthol, racemic menthol. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

18. Pharmacopoeial quality control: glacial acetic acid, glycine, DL-methionine. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

19. Pharmacopoeial quality control: lactic acid, S-lactic acid, glutamic acid, cysteine hydrochloride. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

20. Pharmacopoeial quality control: phenol, resorcinol. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

21. Pharmacopoeial quality control: benzoic acid, sodium benzoate. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

22. Pharmacopoeial quality control: salicylic acid, sodium salicylate. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

23. Pharmacopoeial quality control: chloramphenicol and its esters (palmitate, etc.). Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

24. Pharmacopoeial quality control: sulfanilamide, sodium sulfacetamide. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

25. Pharmacopoeial quality control: nitrofural, metronidazole and its benzoate. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

26. Pharmacopoeial quality control: ascorbic acid. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

27. Pharmacopoeial quality control: rutoside trihydrate, bendazole hydrochloride (dibazole). Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

28. Pharmacopoeial quality control: nicotinic acid, nicotinamide. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

29. Pharmacopoeial quality control: pyridoxine hydrochloride, silver sulfadiazine. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

30. Pharmacopoeial quality control: papaverine hydrochloride, drotaverine hydrochloride. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

31. Pharmacopoeial quality control: theophylline and its monohydrate, aminophylline (theophylline-ethylenediamine, theophylline-ethylenediamine hydrate and for injection). Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

32. Pharmacopoeial quality control: folic acid, paracetamol. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

33. Pharmacopoeial quality control: riboflavin, riboflavin sodium phosphate. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

34. Pharmacopoeial quality control: salts and esters of thiamine (benfotiamine, cocarboxylase, nitrate, hydrochloride). Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

35. Pharmacopoeial quality control: cyanocobalamin, metamizole sodium monohydrate. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

36. Pharmacopoeial quality control: retinol and its esters (acetate, palmitate, etc.) and the retinoid isotretinoin. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

37. Pharmacopoeial quality control: ergocalciferol, cholecalciferol. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

38. Pharmacopoeial quality control: α-tocopherol, α-tocopheryl acetate, RRR-α-tocopheryl acetate. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

39. Pharmacopoeial quality control: caffeine and its monohydrate, menadione sodium bisulfite. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

40. Pharmacopoeial quality control: benzocaine, proxymetacaine hydrochloride, procaine hydrochloride, oxybuprocaine hydrochloride. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

41. Pharmacopoeial quality control: tetracaine hydrochloride, lidocaine hydrochloride monohydrate, bupivacaine hydrochloride, articaine hydrochloride. Chemical formula, description (properties), solubility, authenticity (identification), quantitative determination, storage, chemical basis of pharmacological action.

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