# MINISTRY OF HEALTH OF UKRAINE ODESSA NATIONAL MEDICAL UNIVERSITY

# **Faculty of Pharmacy**

# **Department of Pharmaceutical Chemistry and Drug Technology**

APPROVED by		
	Vice-rector for scientific and pedagogical work	
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	, 202_	
METHODOLOGICAL DEVELOPMENT		
TO THE INDEPENDENT WORK OF THE STUDENT		
	DUCATIONAL DISCIPLINE	
Faculty, course	Pharmaceutical, III course	
Educational discipline	Pharmaceutical chemistry	

(the name of the educational discipline)

Approved:	
The meeting of the department Pharmaceutical cher	nistry
Odesa National Medical University	
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## **Independent work No. 1**

**Topic:** The subject and tasks of pharmaceutical chemistry. The system of evaluation of the quality of medicinal products. Stability of the composition as a necessary condition for all stages of the existence of the medicinal product. Peculiarities of pharmaceutical analysis are related to the intended use of drugs and the professional responsibility of the pharmacist. Pharmacopoeial analysis.

**Goal:** Acquainted with the peculiarities of pharmaceutical analysis of drugs related to the intended purpose and the professional responsibility of the pharmacist. Pharmacopoeial analysis.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

#### Plan

## 1. Theoretical questions:

- 1) The subject of pharmaceutical chemistry, its importance and connection with pharmacy.
- 2) Ways of formation of pharmaceutical chemistry. Development of theoretical ideas about the structure of organic compounds.
  - 3) Physical properties of medicines.
  - 4) Chemical properties of medicines.
  - 5) Classification of physical and chemical methods of analysis.
  - 6) Principles of selection of methods depending on the structure.

## **Questions for self-control:**

- 1) Methods of quantitative analysis of the content of medicinal products.
- 2) The choice of a method that allows you to evaluate the content of a medicinal substance by functional groups characterizing its properties.
- 3) Peculiarities of quantitative determination of individual substances and dosage forms.

- 4) Relative specificity, sensitivity, correctness (accuracy) and reproducibility of the method.
- 5) The influence of the polyfunctionality of medicinal substances on the choice of the method of quantitative determination.

## **Indicative tasks for processing theoretical material:**

- Compile a dictionary of basic concepts on the topic.

## 2. Practical works (tasks) to be performed:

The task 1. Preparation and establishment of normality of the working solution of potassium rhodanide. Determine the normal concentration of the potassium rhodanide solution and its titer against silver, if 20.00 cm3 of 0.1014 N is used for the titration of 25.00 cm3. AgNO3 solution.

The task 2. Calculate pBr and pAg when titrating 100 cm3 0.1N.of KBr solution 0.1 n. AgNO3 solution if: a) 99 cm3, b) 100 cm3, c) 110 cm3 of titrant are added. PR(AgBr) = 7.7•10-13.

The task 3. How many percent of silver does the alloy contain, if after dissolving a weight of 0.3000 g of this alloy, 23.80 cm<sup>3</sup> of 0.1000 n was spent on the titration of the resulting solution. NH4SCN solution?

- 1) The procedure by which the authorized body confirms that the production of medicinal products meets the established requirements:
  - A. Certification\*;
  - B. Standardization;
  - C. Licensing;
  - D. Quality system;
  - E. Inspection.
- 2) Activities to establish rules, norms and characteristics for general and multiple use in relation to actual or potential tasks in order to achieve the optimal

degree of regulation in the field of creation, production, quality control, registration and sale of medicinal products:

- A. Standardization\*;
- B. Certification;
- C. Quality system;
- D. Licensing;
- E. Inspection.
- 3) A set of rules for the organization of production and quality control, which is an element of the quality assurance system, which ensures the stable production of medicinal products in accordance with the requirements of technical documentation and conducting quality control in accordance with the MKY:
  - A. Good Manufacturing Practice (GMP)\*
  - B. Good Distribution Practice (GDP);
  - C. Good Laboratory Practice (GLP);
  - D. Good Pharmaceutical Practice (GPP);
  - E. Good Regulatory Practice (GRP).
- 4) Principles and rules for the retail sale of medicinal products, their storage, control, manufacturing in the conditions of a pharmacy, dispensing, the observance of which ensures the quality of the medicinal product at the stage of retail trade:
  - A. Good Pharmaceutical Practice (GPP)\*;
  - B. Good Manufacturing Practice (GMP);
  - C. Good Distribution Practice (GDP);
  - D. Good Laboratory Practice (GLP);
  - E. Good Regulatory Practice (GRP).
- 5) Principles and rules regarding distribution, compliance with which ensures the quality of medicinal products in the process of managing and organizing their wholesale trade at all its stages:

- A. Good Distribution Practice (GDP)\*;
- B. Good Laboratory Practice (GLP);
- C. Good Manufacturing Practice (GMP);
- D. Good Pharmaceutical Practice (GPP);
- E. Good Regulatory Practice (GRP).
- 6) An independent scientific institution of the EU for the evaluation of the quality of medicinal products, according to the requirements set out in the European Pharmacopoeia:
  - A. EMEA (European Medicines Agency) \*;
  - B. FDA (Food and Drug Administration);
  - C. EDQM (European Directorate for the Quality of Medicines);
  - D. WHO (World Health Organization);
  - E. CHMP (Committee for Medicinal Products for Human Use).
- 7) Good practice, which is a set of rules for planning, conducting, controlling, evaluating and documenting clinical trials of medicinal products. Compliance with the requirements ensures the accuracy of the received data, the protection of the rights of the persons participating in the tests, the confidentiality of the data about these persons:
  - A. Good Clinical Practice (GCP)\*;
  - B. Good Laboratory Practice (GLP);
  - C. Good Manufacturing Practice (GMP);
  - D. Good Pharmaceutical Practice (GPP);
  - E. Good Distribution Practice (GDP).
- 8) Which of the following items is not one of the main tasks of the European Medicines Agency:
  - A. responsibility for the work of the System of Cooperation of Pharmaceutical Inspections\*;
  - B. creation of a unified system of evaluation of medicinal products with the help of issuing trade licenses;

- C. development of fast and effective procedures for licensing, control and withdrawal of used medicinal products in EU countries;
- D. coordination of checks on compliance by manufacturers and developers of medicinal products with the requirements of good laboratory (GLP), clinical (GCP) and manufacturing practice (GMP);
- E. strengthening control over existing medicinal products by coordinating the activities of national bodies responsible for conducting pharmacological supervision and inspections.
- 9) By which Order of the Ministry of Health of Ukraine was the standard ST of the Ministry of Health 42-1.0:2005 "Pharmaceutical products. Standardization system. Substantive provisions":
  - A. No. 471 dated September 14, 2005\*;
  - B. No. 677 of September 29, 2014;
  - C. No. 584 of December 16, 2003;
  - D. No. 275 dated May 15, 2006;
  - E. No. 360 of July 19, 2005
- 10) The purpose of the International Conference on the Harmonization of Technical Requirements for the Registration of Medicines for Humans is
  - A. harmonization of technical requirements and guidelines for the registration of drugs to eliminate duplication of tests, more economical use of human, animal and material resources, as well as reducing the terms of development and delivery of new medicinal products to the markets while ensuring their quality, safety and effectiveness\*;
  - B. provision of national and all-Union institutions of the EU with scientific advisory assistance on issues of quality, safety and effectiveness of medicinal products;
  - C. creation of a unified system of evaluation of medicinal products with the help of centralized and decentralized MA issuing procedures;

- D. development of fast and effective procedures for licensing, control and, in appropriate cases, withdrawal of used medicinal products in EU countries;
- E. coordination of checks on compliance by manufacturers and developers of medicinal products with the requirements of good laboratory (GLP), clinical (GCP) and manufacturing practice (GMP).

## 4. Individual tasks for students of higher education on the topic:

- 1) The principle of pharmaceutical analysis of monocomponent medicinal products.
- 2) The principle of pharmaceutical analysis of multicomponent medicinal products.
- 3) The structure and difference between the SPHU and the European Pharmacopoeia.

#### 5. References:

#### **Basic:**

- Handbook of pharmaceutical chemictry Vol. 117 / L. Ohannesian, Antony J.
   Streeter. 2016. 582 p.
- 2. Pharmaceutical Chemistry I Laboratory Experiments and Commentary / Attila Almási, Zsuzsanna Rozmer, Pál Perjési. 2014. 179 p.
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- 4. Chemical Analysis Modern Instrumentation Methods and Techniques 2<sup>nd</sup> Edition / F. Rouessac, A. Rouessac. 2007. 599 p.
- 5. Pharmaceutical drug analysis / Addis Ababa. 2005. 554 p.
- 6. Analytical Chemistry Series / John M., Chalmers, Alan J. Handley. 2003. 384 p.
- 7. HANDBOOK OF MODERN PHARMACEUTICAL ANALYSIS Vol. 3 / Satinder Ahuja, Stephen Scypinski. 2001. 587 p.
- 8. Europian Pharmacopoeia 10<sup>th</sup>. 2019. 4255 p.

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#### **Additional:**

- 1. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2015. Т. 1. 1128 с.
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# Independent work No. 2

**Topic:** Analysis of the physicochemical properties of medicinal products as one of the elements of the quality assessment of medicinal products.

**Goal:** Acquainted with the physicochemical properties of medicinal products and their influence on pharmaceutical analysis.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

#### Plan

## 1. Theoretical questions:

- 1) The influence of pharmaceutical factors on the therapeutic effect of drugs.
  - 2) Classification of factors.
  - 3) Physical state of medicinal substances.
  - 4) Simple chemical modification salts, acids, ethers, alkalis.
  - 5) Excipients and their nature.
- 6) Investigation of known cases of therapeutic non-equivalence of medicinal products.

## **Questions for self-control:**

- 1) Medicinal form and ways of its introduction into the body.
- 2) The influence of the preparation technology on the bioavailability of drugs.
  - 3) Homogeneous single-phase ion or molecular dispersion systems.
  - 4) Effect of particle size on therapeutic activity.
  - 5) Polymorphism.

## **Indicative tasks for processing theoretical material:**

- Compile a dictionary of basic concepts on the topic.

## 2. Practical works (tasks) to be performed:

The task 1. Give examples of ways of formation of salts and complexes.

The task 2. Give examples of ways to increase the solubility of poorly soluble substances.

The task 3. The synthetic way is the introduction of hydrophilic groups into the structure of the molecule. Give examples of these modifications.

- 1) The melting point is an important physical constant of medicinal products. In the pharmacopoeial analysis, the determination of the melting point allows the pharmacist-analyst to confirm:
  - A. the authenticity and degree of purity of the medicinal substance
  - B. the amount of volatile substances and water in the preparation
  - C. weight loss during drying of the substance of the medicinal substance
  - D. quantitative content of the medicinal substance
  - E. resistance of the medicinal substance to the influence of external factors
- 2) Determination of the melting point is carried out by various methods depending on the physical properties of medicinal substances. State the method used to determine the melting point of solids that easily turn into powder:
  - A. Capillary
  - B. Racing
  - C. Using a pycnometer
  - D. Potentiometric
  - E. Using a hydrometer
- 3) Medical ether belongs to simple ethers. Before carrying out its identification by boiling point, the pharmacist-analyst must make sure that:
  - A. Peroxide compounds
  - B. Regenerating substances
  - C. Alcohol
  - D. Non-volatile residue
  - E. Carboxylic acids
- 4) The pharmacist-analyst performs the identification of the isoniazid substance in accordance with the requirements of the SPHU by the melting point of the yellow precipitate obtained when interacting with the solution:
  - A. Vanilla
  - B. Hydroxyquinoline

- C. Sodium nitroprusside
- D. Potassium bromide
- E. Ammonium thiocyanate
- 5) Melting point an important physical constant of medicines. In the Pharmacopoeia analysis, the determination of the melting point allows the pharmacist-analyst to confirm:
  - A. Identification and degree of purity of the medicinal substance
  - B. The amount of volatile substances and water in the preparation
  - C. Loss in mass during drying of the substance of the medicinal substance
  - D. Quantitative content of medicinal substance
  - E. E. Resistance of the medicinal substance to the influence of external factors
- 6) The angle of optical rotation of substances, which is determined at a temperature of 20 C, in a layer thickness of 1 decimeter and the wavelength of the D line of the sodium spectrum ( $\lambda$ = 589.3 nm), in terms of the content of 1 g of the substance in 1 ml of solution, is called:
  - A. By specific optical rotation
  - B. Optical density
  - C. Refractive index
  - D. Relative density
  - E. Distribution indicator
- 7) Indicate by what method, according to the SPHU, a control and analytical laboratory specialist determines the melting point of glutamic acid:
  - A. Method 1a is for solid substances that easily turn into powder and are unstable when heated
  - B. Method 1 is for solid substances that easily turn into powder and are resistant to heating
  - C. Method 2—for substances that cannot be ground into powder using a capillary tube
  - D. Method 3 for substances that do not grind into powder using a thermometer of the Ubellode type
  - E. E. All the methods listed above

- 8) In the analysis of the quality of extemporaneous dosage forms, the identification of menthol is carried out:
  - A. By smell
  - B. Acylation followed by determination of the melting point
  - C. With a solution of vanillin in concentrated sulfuric acid
  - D. Steam distillation
  - E. With a solution of iron oxide chloride
- 9) In order to identify the substance "Thymolum" according to SPHU, together with the determination of the melting point and the study of the IR spectrum, the reaction of an alkaline solution of the drug with chloroform with heating on a water heater is used. As a result of the reaction, color appears:
  - A. Purple
  - B. green
  - C. blue
  - D. yellow
  - E. red
- In order to identify the substance "Thymolum" according to SPHU, along with the determination of the melting point, the study of the IR spectrum and the chemical reaction of the alkaline solution of the drug with chloroform, the reaction of the solution of the drug in anhydrous acetic acid with sulfuric and nitric acids is used. As a result of this interaction, color appears:
  - A. Blue-green
  - B. red
  - C. yellow
  - D. Purple
  - E. Yellow-green
  - 4. Individual tasks for students of higher education on the topic:
  - 1) PASS-screening as a way of developing new medicinal substances.

- 2) QSAR analysis as a method of predicting the physicochemical and pharmacological properties of a medicinal substance.
  - 3) Use of programs: ALOGPS, KowWin programs in pharmacy.

#### 5. References:

### **Basic:**

- Handbook of pharmaceutical chemictry Vol. 117 / L. Ohannesian, Antony J. Streeter. 2016. – 582 p.
- Pharmaceutical Chemistry I Laboratory Experiments and Commentary / Attila Almási, Zsuzsanna Rozmer, Pál Perjési. 2014. – 179 p.
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- 8. Europian Pharmacopoeia 10<sup>th</sup>. 2019. 4255 p.

#### **Additional:**

- 1. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2015. Т. 1. 1128 с.
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## Independent work No. 3

**Topic:** The use of spectroscopic and chromatographic methods in the identification of medicinal products; peculiarities of using standard samples of medicinal substances and standard spectra.

**Goal:** Acquainted with the peculiarities of pharmaceutical analysis using spectroscopic and chromatographic methods of analysis.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

#### Plan

# 1. Theoretical questions:

- 1) What is chromatography?
- 2) What is the essence of the chromatographic process?
- 3) Classification and characteristics of the chromatographic method of analysis.
  - 4) Characteristics of partition chromatography.
  - 5) Fields of application of chromatography.
  - 6) Who and when was the chromatographic method of analysis proposed?

## **Questions for self-control:**

- 1) By what factors are chromatographic methods classified?
- 2) What is an eluent?
- 3) In what aggregate state can the stationary and mobile phases, as well as the components of the mixture under analysis, be?
  - 4) Name the main stages of chromatographic analysis.
- 5) What features are the basis for the classification of chromatographic methods.

## **Indicative tasks for processing theoretical material:**

- Compile a dictionary of basic concepts on the topic.

## 2. Practical works (tasks) to be performed:

- The task 1. Formulate the Bouguer-Lambert-Behr law of light absorption.
- The task 2. Explain the scheme of the KFK-2 photocolorimeter.
- The task 3. Methods of atomic spectral analysis. The essence of the method.

- 1) The pharmacist-analyst needs to analyze the concentrate of 10% glucose solution. For this, you can use the method:
  - A. Refractometry
  - B. Complexonometry
  - C. Argentometry
  - D. Thin-layer chromatography
  - E. Acidimetry
- 2) According to SPHU, the quantitative determination of benzylpenicillin is carried out by the method:
  - A. Liquid chromatography
  - B. Gravimetric method
  - C. By the iodometric method

- D. By the method of neutralization
- E. By the method of precipitated titration
- 3) When carrying out purity tests in the substance of atropine sulfate, extraneous alkaloids and decomposition products are determined by the TLC method. At the same time, the chromatographic plate is sprayed with a solution:
  - A. Potassium iodobismuthate
  - B. Ammonia
  - C. Ninhydrin
  - D. Dinitrophenylhydrazine with acetic hydrogen chloride
  - E. Tetrabutylammonium hydroxide
- 4) To identify the "Riboflavinum" substance by SPHU, along with studies of specific optical rotation and chromatographic tests for the presence of lumiflavin, the ability of its aqueous solution to fluorescence with the following coloration is used:
  - A. The aqueous solution in transmitted light has a pale greenish-yellow color, and shows an intense yellowish-green fluorescence in reflected light, which disappears when mineral acids or alkalis are added
  - B. The aqueous solution has a blue color in transmitted light, and in reflected light it exhibits an intense yellow fluorescence, which disappears when mineral acids or alkalis are added
  - C. The aqueous solution has a green color in transmitted light, and a yellow fluorescence in reflected light, which disappears when mineral acids or alkalis are added
  - D. The aqueous solution has a yellow color in transmitted light, and there is no fluorescence in reflected light
  - E. The aqueous solution is colorless, and there is no fluorescence in reflected light
- 5) A physicochemical method is used for the quantitative determination of the folic acid substance according to the SPHU. Name this method.
  - A. Liquid chromatography
  - B. Thin-layer chromatography

- C. Infrared spectroscopy
- D. Refractometry
- E. Nuclear magnetic resonance spectroscopy
- 6) Chromatographic analysis is widely used in the Department of Agriculture of Ukraine to identify plant raw materials and phytopreparations. To identify individual substances in chromatographic analysis, the following value is determined:
  - A. The value of Rf
  - B. Angle of rotation
  - C. Angle of refraction
  - D. Boiling temperature
  - E. Melting point
- 7) Name the main method by which the composition and content of fatty acids will be determined in lipids...
  - A. gas chromatography
  - B. thin layer chromatography
  - C. permanganatometry
  - D. paper chromatography
  - E. polarography
- 8) According to SPHU (Addendum 3), the content of thymol and carvacrol in motherwort grass is determined by gas chromatography. To which class of biologically active substances do they belong?
  - A. Essential oils
  - B. Coumarins
  - C. Flavonoids
  - D. Alkaloids
  - E. Iridoids
- 9) Eucalyptus leaves contain essential oil and are used for the production of phytoremedies with a bactericidal effect. According to the requirements of the

State Pharmacopoeia of Ukraine, identification of raw materials is carried out by the method of thin-layer chromatography. On the chromatographic plate after treatment with the reagent, identify:

- A. cineole
- B. quercetin
- C. scopoletin
- D. apigenin
- E. glaucine
- 10) Motherwort grass is used for the production of phytoremedies. According to the requirements of the State Pharmacopoeia of Ukraine, identification of raw materials involves chromatographic control using thin-layer chromatography. The following substances are identified on the chromatographic plate after treatment with the reagent:
  - A. thymol and carvacrol
  - B. atropine and hyoscyamine
  - C. quercetin and rutin
  - D. apigenin and luteolin
  - E. arbutin and methylarbutin

# 4. Individual tasks for students of higher education on the topic:

- 1) TLC. The essence of the method. Mistakes and shortcomings. Use in pharmaceutical analysis.
- 2) TSH The essence of the method. Mistakes and shortcomings. Use in pharmaceutical analysis.
- 3) IR spectroscopy. The essence of the method. Mistakes and shortcomings. Use in pharmaceutical analysis.

#### 5. References:

#### **Basic:**

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 Streeter. 2016. – 582 p.

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- 2. Pharmaceutical Chemistry I Laboratory Experiments and Commentary / Attila Almási, Zsuzsanna Rozmer, Pál Perjési. 2014. 179 p.
- 3. Introduction to Pharmaceutical Chemical Analysis / S. Hansen, S. Pederson-Bjergaard, K. Rasmussen. 2012. 496 p.
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#### **Additional:**

- 1. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2015. Т. 1. 1128 с.
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- 3. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2014. Т. 3. 732 с.
- 4. Фармацевтична хімія / П.О. Безуглий, В.А. Георгіянц, І.С. Гриценко, І.В. та ін.: за ред. П.О. Безуглого. Вінниця: Нова книга, 2017. 456 с.

 Фармацевтична хімія. Загальна та спеціальна фармацевтична хімія. Лікарські засоби неорганічної природи: лабораторно-практичні заняття. Навчальний посібник / Л.Г. Мішина. – Вінниця: ПП «ТД «Едельвейс і К»», 2010. – 384 с.

## Independent work No. 4

**Topic:** Identification of medicinal substances of inorganic nature.

**Goal:** Acquainted with the features of cationic and anionic analysis in the pharmaceutical analysis of medicinal substances of an inorganic nature.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

#### Plan

## 1. Theoretical questions:

- 1) Give examples of the practical use of outer sphere complexes in qualitative analysis.
  - 2) What role do carbonic acid and its salts play in the human body?
- 3) What factors should be paid attention to when performing qualitative reactions?
  - 4) Ionic strength.
  - 5) Buffer systems. The essence of use in qualitative analysis.
- 6) Peculiarities of determination of fluorine in the medicinal product sodium fluoride.

## **Questions for self-control:**

- 1) What is amphotericity?
- 2) What is the importance of amphotericity in qualitative analysis? The answer will be confirmed by the corresponding reaction equations.
  - 3) What reactions are called redox?
  - 4) What is the role of redox reactions in qualitative analysis?

5) What is the role of argentum, plumbum, hydrargyrum cations in medicine?

## **Indicative tasks for processing theoretical material:**

Compile a dictionary of basic concepts on the topic.

## 2. Practical works (tasks) to be performed:

The task 1. When adding 2N hydrochloric acid to the solution, a white amorphous precipitate was formed, which was dissolved in an excess of ammonium hydroxide. What cation is in the solution?

The task 2. To determine nitrate ions, diphenylamine was added to the test solution. What analytical effect is observed?

The task 3. How can the selectivity of analytical signals be increased?.

- 1) The presence of an iron (II) cation in the dosage form can be confirmed by the pharmacist-analyst of the pharmacy with the help of:
  - A. solution of ammonium sulfide
  - B. sodium chloride solution
  - C. solution of magnesium sulfate
  - D. potassium bromide solution
  - E. sodium phosphate solution
- 2) Choose the name of the reagent that is used during the identification of iron(III) ions according to the requirements of the SPHU.
  - A. potassium thiocyanate solution
  - B. ammonia solution
  - C. potassium chloride solution
  - D. sodium sulfate solution
  - E. silver nitrate solution

- 3) The chemist of the VTK pharmaceutical company can confirm the sodium cation in the substance under study with a solution:
  - A. potassium pyroantimonate
  - B. potassium chloride
  - C. potassium ferrocyanide
  - D. potassium hydroxide
  - E. potassium nitrate
- 4) A pharmacist-analyst examines a dosage form containing magnesium sulfate. With the help of which reagent can he confirm the presence of magnesium cation in the investigated dosage form?
  - A. disodium hydrogen phosphate
  - B. sodium sulfide
  - C. potassium ferrocyanide
  - D. silver nitrate
  - E. sodium tetraphenylborate
- 5) According to SPHU, one of the reactions for identifying mercury (II) salts is the reaction with sodium hydroxide. As a result of the reaction, a precipitate is formed:
  - A. yellow color
  - B. red color
  - C. purple color
  - D. green color
  - E. blue color
- 6) The chemist of the VTK pharmaceutical company can confirm the sodium cation in the substance under study with a solution:
  - A. potassium pyroantimonate
  - B. potassium chloride
  - C. potassium ferrocyanide
  - D. potassium hydroxide

- E. potassium nitrate
- 7) Potassium chloride is identified by the potassium ion by the reaction with:
  - A. tartaric acid
  - B. zincuranyl acetate
  - C. silver nitrate
  - D. sodium hydroxide
  - E. potassium ferricyanide
- 8) Potassium salts added to the colorless flame of a gas burner color it:
  - A. violet
  - B. red
  - C. brick
  - D. yellow
  - E. green
- 9) In medicines, calcium cations can be detected using a solution:
  - A. ammonium oxalate
  - B. silver nitrate
  - C. potassium permanganate
  - D. sodium nitrite
  - E. sodium chloride
- 10) The pharmacist-analyst determines the presence of bismuth ion according to the AED. Indicate which of the following reagents he uses?
  - A. potassium iodide solution
  - B. phenolphthalein solution
  - C. sodium diethyldithiocarbamate solution
  - D. starch solution
  - E. dimethylglyoxime solution
  - 4. Individual tasks for students of higher education on the topic:
- 1) Use of modern methods of qualitative analysis to check the quality of pharmaceuticals.

- 2) Theoretical aspects of the test melting method.
- 3) Buffer action of ampholyte solutions.
- 5. References:

#### Basic:

- Handbook of pharmaceutical chemictry Vol. 117 / L. Ohannesian, Antony J.
   Streeter. 2016. 582 p.
- 2. Pharmaceutical Chemistry I Laboratory Experiments and Commentary / Attila Almási, Zsuzsanna Rozmer, Pál Perjési. 2014. 179 p.
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- 8. Europian Pharmacopoeia 10<sup>th</sup>. 2019. 4255 p.

#### **Additional:**

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- Фармацевтична хімія. Загальна та спеціальна фармацевтична хімія. Лікарські засоби неорганічної природи: лабораторно-практичні заняття. Навчальний посібник / Л.Г. Мішина. – Вінниця: ПП «ТД «Едельвейс і К»», 2010. – 384 с.

## Independent work No. 5

**Topic:** Identification of medicinal substances of organic nature by functional groups (functional analysis).

**Goal:** Acquainted with the features of the functional analysis of medicinal substances of organic nature.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

#### Plan

### 1. Theoretical questions:

- 1) The influence of functional groups on the nature of pharmacological action.
  - 2) Functional analysis methods used in menthol analysis.
  - 3) Functional analysis methods used in validol analysis.
  - 4) Functional analysis methods used in camphor analysis.
  - 5) Functional analysis methods used in bromocamphor analysis.
- 6) Functional analysis methods used in the analysis of sulfocamphoric acid.

## **Questions for self-control:**

- 1) What method of functional analysis is used to identify organic substances that contain the C-Hal bond?
  - 2) What methods of functional analysis are used to identify alcohols?
- 3) What methods of functional analysis are used to identify organic substances that contain a carbonyl group?
- 4) Name the methods of functional analysis used for the identification and quantification of enol derivatives using ascorbic acid as an example.
- 5) Name the functional analysis methods used to identify and quantify carboxylic acid derivatives of the aliphatic series using acetic acid as an example.

## **Indicative tasks for processing theoretical material:**

Compile a dictionary of basic concepts on the topic.

## 2. Practical works (tasks) to be performed:

- The task 1. Functional analysis of bis- $(\beta$ -chloroethyl)-amine derivatives.
- The task 2. Functional analysis methods used for identification and quantification of phenol derivatives.
- The task 3. Functional analysis methods used in the analysis of compounds containing an amide group.

- 1) Bilitrast is a radiopaque agent. Specify the reagent that can be used to confirm the presence of phenolic hydroxyl in its molecule:
  - A. solution of iron (III) chloride
  - B. alcohol solution of iodine
  - C. solution of hydrochloric acid
  - D. solution of iodine in potassium iodide
  - E. silver nitrate solution

- 2) Paracetamol substance was submitted for analysis. When it interacts with a solution of iron (III) chloride, a blue-violet color is formed, which indicates the presence in its structure:
  - A. phenolic hydroxyl
  - B. aldehyde group
  - C. keto groups
  - D. ester group
  - E. alcohol hydroxyl
- 3) When identifying Paracetamol [Paracetamol], the presence of phenolic hydroxyl in its structure is determined by the reaction with:
  - A. FeCl3
  - B. Na2S
  - C. BaCl2
  - D. K4[Fe[CN]6]
  - E. AgNO3
- 4) One of the reactions for the identification of procaine hydrochloride (novocaine) is the reaction:
  - A. on the primary aromatic amino group
  - B. to the aldehyde group
  - C. on sulfate ions
  - D. to phenolic hydroxyl
  - E. to alcohol hydroxyl
- 5) To identify drugs that are benzodiazepine derivatives according to the SPHU, the formation reaction is used (after preliminary acid hydrolysis):
  - A. azo dye
  - B. auric dye
  - C. indophenol dye
  - D. azomethine dye
  - E. polymethine dye

- 6) The morphine substance was submitted for analysis. When it interacts with a solution of iron (III) chloride, a blue-violet color is formed, which indicates the presence in its structure:
  - A. phenolic hydroxyl
  - B. aldehyde group
  - C. alcohol hydroxyl
  - D. ketogroups
  - E. ester group
- 7) The presence of which functional group determines the positive reaction of alcoholic solutions of corticosteroids (prednisone, prednisone) with the copper-tartrate reagent (Fehling's reagent):
  - A. α-ketol group
  - B. pregnane cycle
  - C. optically active carbon atom
  - D. unsaturated carbohydrate bond
  - E. phenolic hydroxyl
- 8) When identifying hormones that contain an ester group, you can use the formation reaction:
  - A. iron(III) hydroxamate
  - B. indophenol
  - C. Berlin blue
  - D. azo dye
  - E. diazonium salts
- 9) When studying the testosterone propionate substance, a hydroxation reaction was carried out, which indicates the presence of a group in the molecule:
  - A. Complex ether
  - B. Hydroxylic
  - C. Carbonyl
  - D. Aldehydic

- E. Aromatic amino group
- 10) The presence of a pyridine ring in the structure of the medicinal product can be confirmed by the reaction with:
  - A. 2,4-dinitrochlorobenzene
  - B. Ninhydrin
  - C. Sodium hydroxide
  - D. 1,3-dinitrobenzene
  - E. 2,4-dinitrophenylhydrazine

## 4. Individual tasks for students of higher education on the topic:

- 1) Elemental and functional analysis.
- 2) Functional analysis methods used for the identification and quantification of  $\alpha$ -hydroxycarboxylic acid derivatives of the aliphatic series.
- 3) Functional analysis methods used in the analysis of compounds containing an ester group.

#### 5. References:

#### **Basic:**

- Handbook of pharmaceutical chemictry Vol. 117 / L. Ohannesian, Antony J.
   Streeter. 2016. 582 p.
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8. Europian Pharmacopoeia 10<sup>th</sup>. 2019. – 4255 p.

#### **Additional:**

- 1. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2015. Т. 1. 1128 с.
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## Independent work No. 6

**Topic:** Reasons for changes in the structure of the medicinal substance (influence of light, moisture, temperature and other factors. Nature and nature of impurities, methods of their detection.

**Goal:** Acquainted with the instability of medicinal substances associated with the influence of external factors: oxidation, hygroscopicity, etc. Analysis of the limit content of impurities.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

#### Plan

## 1. Theoretical questions:

- 1) Permissible and non-permissible impurities in medicinal products.
- 2) Concomitant impurities of natural compounds.
- 3) Technological impurities.
- 4) Impurities affecting the pharmacological effect of the drug.
- 5) Preparation of the reference solution of impurities.
- 6) Determination of impurities by paper chromatography

#### **Questions for self-control:**

- 1) Research on the absence of impurities of arsenic salts.
- 2) Research on the absence of impurities of ammonium salts.
- 3) Research on the absence of nitrite impurities.
- 4) Research on the absence of nitrate impurities.
- 5) Research on the absence of impurities of heavy metals.

# Indicative tasks for processing theoretical material:

Compile a dictionary of basic concepts on the topic.

# 2. Practical works (tasks) to be performed:

The task 1. Specific impurities in sodium and potassium hydroxides.

The task 2. Specific impurities in chloroform, ethyl chloride, fluoroethane, their source and methods of determination.

The task 3. Permissible and non-permissible impurities in purified water within the standard according to FS.

- 1) The pharmacist-analyst carries out a quantitative analysis of isoniazid by direct bromatometry using a titrated solution of potassium bromate, potassium bromide, hydrochloric acid and methyl red indicator. This method is based on the reaction:
  - A. Oxidation of the hydrazine group with bromine
  - B. Reduction of the hydrazine residue with bromine
  - C. Oxidation of the hydrazine residue with potassium bromide
  - D. Opening of the pyridine cycle
  - E. Bromination of the pyridine ring
- 2) Levomycetin can be identified by the reaction of the formation of an azo dye after the previous one:
  - A. Restoration
  - B. Oxidation
  - C. Hydrolysis
  - D. Halogenation
  - E. Alkylation
- 3) Indicate which of the listed drugs requires storage in a well-closed container, protected from light, in a dry place:
  - A. Sodium salicylate
  - B. Calcium chloride
  - C. Benzoic acid
  - D. Resorcinol
  - E. E. Magnesium sulfate
- 4) As a result of improper storage of the substance aminazine, it acquired a dark shade. This is the fault of the employees of the pharmacy warehouse, who did not take into account that under the influence of light, aminazine:
  - A. It oxidizes
  - B. Weathering
  - C. It is distilled

- D. Polymerizes
- E. It is hydrolyzed
- 5) To identify drugs that are benzodiazepine derivatives according to the SPHU, the formation reaction is used (after preliminary acid hydrolysis):
  - A. azo dye
  - B. auric dye
  - C. indophenol dye
  - D. azomethine dye
  - E. polymethine dye
- 6) In order to identify calcium pangamate, its alkaline hydrolysis is carried out in the presence of hydroxylamine. As a result of the reaction, hydroxamic acid is formed, which the pharmacist-analyst must identify with the following reagent:
  - A. iron (III) chloride
  - B. potassium tetraiodomercurate
  - C. silver nitrate
  - D. sodium bicarbonate
  - E. ammonium molybdate
- 7) After hydrolysis of rutin in an acidic medium, the compound can be detected:
  - A. glucose
  - B. starch
  - C. sucrose
  - D. lactose
  - E. dextrin
- 8) For what purpose does a chemist-analyst of the CZL add a solution of mercury (II) acetate during the quantitative determination of diphenhydramine hydrochloride (diphenhydramine) by the method of acidimetry in a non-aqueous environment:
  - A. For binding chloride ions into a slightly dissociated compound

- B. To enhance the hydrolysis of diphenhydramine
- C. To change the density of the solution. To create the optimal pH value of the solution
- D. To accelerate precipitation of the diphenhydramine base
- 9) The pharmacist-analyst of the pharmacy conducts an analysis of purified water. To do this, he brings a certain amount of the studied sample to a boil, adds a 0.02 M solution of potassium permanganate and diluted sulfuric acid. After boiling the resulting solution for 5 minutes, the pink color should remain. What impurity did the pharmacist-analyst determine?
  - A. renewable substances
  - B. nitrates
  - C. carbon dioxide
  - D. sulfates
  - E. heavy metals
- 10) In an alkaline environment, a glucose solution:
  - A. It turns yellow
  - B. Stores well
  - C. A white precipitate falls out
  - D. Turns yellow or brown
  - E. It's storming

# 4. Individual tasks for students of higher education on the topic:

- 1) Sources of impurities in pharmaceuticals and methods of their determination.
- 2) Preparation of reagents and testing for the maximum content of impurities.
  - 3) Physico-chemical methods of determination of impurities.
  - 5. References:

#### **Basic:**

- Handbook of pharmaceutical chemictry Vol. 117 / L. Ohannesian, Antony J.
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- 2. Pharmaceutical Chemistry I Laboratory Experiments and Commentary / Attila Almási, Zsuzsanna Rozmer, Pál Perjési. 2014. 179 p.
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- 8. Europian Pharmacopoeia 10<sup>th</sup>. 2019. 4255 p.

#### **Additional:**

- 1. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2015. Т. 1. 1128 с.
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- 5. Фармацевтична хімія. Загальна та спеціальна фармацевтична хімія. Лікарські засоби неорганічної природи: лабораторно-практичні заняття. Навчальний посібник / Л.Г. Мішина. Вінниця: ПП «ТД «Едельвейс і К»», 2010. 384 с.

## **Independent work No. 7**

**Topic:** Methods of quantitative analysis of the content of medicinal products. Gravimetry.

**Goal:** Acquainted with the methods of gravimetric analysis of medicinal substances.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

### Plan

# 1. Theoretical questions:

- 1) What is the gravimetric method? Name the requirements for precipitation reactions.
- 2) Give the formula for calculating the results of gravimetric analysis. What is the gravimetric factor?
  - 3) Classification of gravimetric methods of analysis.
  - 4) What are ashless filters?
  - 5) What is decantation and why is it performed?
- 6) Why is it impossible to precipitate ferrum(III) hydroxide with alkali solutions in gravimetric analysis when determining ferrum in the form of Fe2O3, but must be precipitated with an ammonia solution?

## **Questions for self-control:**

- 1) Scheme of gravimetric determination of substances by the precipitation method.
- 2) Precipitation and gravimetric forms of sediments and requirements for them.
  - 3) Precipitators in gravimetric analysis.
  - 4) Amorphous and crystalline sediments.
  - 5) Lyophobic and lyophilic deposits.

## **Indicative tasks for processing theoretical material:**

- Compile a dictionary of basic concepts on the topic.

# 2. Practical works (tasks) to be performed:

The task 1. Calculate the conversion factors for determining Mg in the form of Mg2P2O7.

The task 2. Determine the content of chloride ions in the sample, if 0.2040 g of the gravimetric form of AgCI was obtained from a weighing of 1.0000 g.

The task 3. Calculate the volume of 0.5 N sulfuric acid solution required for the quantitative precipitation of Ba2+ ions from a sample of BaCI2•H2O weighing 0.5000 g.

- 1) Dilute hydrochloric acid is used in medical practice. Which of the following methods is used for its quantitative determination?
  - A. Alkalimetry
  - B. Permanganatometry
  - C. Complexonometry
  - D. Acidimetry
  - E. Iodometry

- 2) One of the stages of pharmaceutical analysis is the quantitative determination of the medicinal product. Quantitative determination of hydrochloric acid is carried out by the method:
  - A. Alkalimetry
  - B. Gravimetry
  - C. Acidimetry
  - D. Complexonometry
  - E. Permanganatometry
- 3) Quantitative determination of active chlorine in perchloric lime is carried out by the method?
  - A. iodometry
  - B. alkalimetry
  - C. bromatometry
  - D. cerimetry
  - E. permanganatometry
- 4) Sodium chloride tablets are manufactured at a pharmaceutical enterprise. Specify the method of quantitative determination of the active substance:
  - A. argentometry
  - B. iodometry
  - C. nitritometry
  - D. alkalimetry
  - E. acidimetry
- 5) When carrying out the quantitative determination of potassium chloride by the argentometric method (back titration) according to the SPHU, the following is used as an indicator:
  - A. iron(III) ammonium sulfate
  - B. diphenylcarbazone
  - C. potassium chromate
  - D. phenolphthalein

- E. sodium eosinate
- 6) What method is recommended by the SPHU for the quantitative determination of the potassium chloride substance used in hypokalemia?
  - A. argentometry
  - B. bromatometry
  - C. iodometry
  - D. cerimetry
  - E. polarimetry
- 7) The pharmacist-analyst determines the admixture of chlorides in potassium bromide according to the SPHU method:
  - A. argentometry
  - B. nitritometry
  - C. bromatometry
  - D. alkalimetry
  - E. iodometry
- 8) According to the recommendations of the State Pharmacopoeia of Ukraine, the pharmacist-analyst performs the quantitative determination of potassium iodide by the method:
  - A. iodometry
  - B. argentometry
  - C. alkalimetry
  - D. acidimetry
  - E. mercurimetry
- 9) Identification of iodine preparations in pharmaceutical analysis is carried out with the following reagent:
  - A. starch solution
  - B. lead nitrate solution
  - C. sodium chloride solution
  - D. silver nitrate solution

- E. calcium acetate solution
- 10) The quantitative content of sodium iodide according to the SPHU is determined by the method:
  - A. iodometry
  - B. argentometry
  - C. nitritometry
  - D. permanganatometry
  - E. bromatometry

- 1) Electrogravimetry. The essence of the method and its use in pharmaceutical analysis.
- 2) Chemigravimetry. The essence of the method and its use in pharmaceutical analysis.
- 3) Thermogravimetry. The essence of the method and its use in pharmaceutical analysis.

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# Independent work No. 8

**Topic:** Titrimetric methods of analysis: Mercurimetry, permanganatometry, bromatometry, iodometry, iodatometry, cerimetry, dichromatometry, nitritometry. Potentiometric titration. Determination of nitrogen in organic compounds.

**Goal:** Acquainted with the features of quantitative redox titration of medicinal products.

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**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

### Plan

# 1. Theoretical questions:

- 1) Examples of practical application of permanganatometry.
- 2) Permanganatometry. Characteristics of the method. Methods of fixing the equivalence point.
- 3) Preparation of the titrant working solution and its standardization. How do divalent manganese ions affect the rate of oxidation of oxalates with potassium permanganate?
- 4) Redox titration indicators. Interval of color transition of redox indicators. Selection of indicators.
- 5) What is the basis of iodometric methods? What substances are determined by this method?
  - 6) Iodometric determination of oxidants. Examples.

## **Questions for self-control:**

- 1) What are redox titration methods based on? Classification of methods.
- 2) Construction of a titration curve in permanganatometry and dichromatometry.
- 3) Basic conditions of iodometric determinations. Describe the determination of salts of divalent copper, ferric iron, dissolved oxygen in water, and peroxides by the method of iodometry.
- 4) Working solutions of iodometry, their preparation and standardization. Factors affecting the stability of these solutions.
- 5) Iodometric determination of arsenites, tin, water (determination of reducing agents).

## **Indicative tasks for processing theoretical material:**

Compile a dictionary of basic concepts on the topic.

# 2. Practical works (tasks) to be performed:

The task 1. Calculate the weight of magnesium peroxide (M. MgO2 56.31), if 18.08 ml of 0.1 N potassium permanganate solution (KP = 0.9960) was spent on its titration, and its content in the substance is 25, 2%.

The task 2. Calculate the percentage content of mesatone (M. 203.67) in the substance, if 16.10 ml of 0.1 N sodium thiosulfate solution (n = 1.0000), dry weight - 0.5%, and titrant volume in the control experiment - 48.50 ml.

The task 3. Calculate the volume of 0.1~N sodium thiosulfate solution used for the titration of 38~ml of 0.1~N iodine solution in the quantitative determination of 0.25~g of flame retardant, if the percentage content in the substance is 98%, the mass loss is 1.5%.

- 1) Which method is NOT used for the quantitative determination of thiamine hydrobromide in a substance?
  - A. Bromatometry, reverse titration
  - B. Alkalimetry, direct titration
  - C. Argentometry according to Fayance method
  - D. Argentometry after neutralization with alkali
  - E. Gravimetry
- 2) The Dibazole substance is analyzed for the quantitative content of the active substance by the method of acidimetry in a non-aqueous medium. What titrant and indicator are used in this method?
  - A. Perchloric acid solution, crystal violet
  - B. Sodium methylate solution, thymol blue
  - C. Sulfuric acid solution, naphtholbenzene
  - D. Sodium hydroxide solution, phenolphthalein
  - E. Nitric acid solution, crystal violet

- 3) For the quantitative determination of the fluorouracil substance according to the SPHU, the pharmacist-analyst uses the non-aqueous titration method. What titrated solution should he use?
  - A. Tetrabutylammonium hydroxide
  - B. Sodium nitrite
  - C. Potassium bromate
  - D. Ammonium thiocyanate
  - E. Sodium edetate
- 4) In the control and analytical laboratory, the analysis of the substance of iron sulfate heptahydrate is performed according to the SPHU. The weight of the substance is titrated with a solution:
  - A. Ammonium cerium sulfate
  - B. Argentum nitrate
  - C. Ammonium thiocyanate
  - D. Sodium edetate
  - E. Potassium bromate
- 5) Quantitative content of diphenhydramine hydrochloride in accordance with the requirements of the SPHU is determined by the method of alkalimetry. A solution of the following substance is used as a titrant:
  - A. Sodium hydroxide
  - B. Potassium bromate
  - C. Sodium thiosulfate
  - D. Potassium permanganate
  - E. Hydrochloric acid
- 6) The pharmacist-analyst determines the quantitative content of caffeine in compliance with the requirements of the Federal Drug Administration by the method of acidimetry in non-aqueous media. As a titrated solution, he used the following solution:
  - A. Chloric acid

- B. Sodium edetate
- C. Potassium bromate
- D. Sodium hydroxide
- E. Sodium nitrite
- 7) Quantitative determination of the thymol substance, according to the requirements of the SPHU, is carried out by the method of bromatometry (direct titration). The equivalence point is fixed by:
  - A. Disappearance of pink color
  - B. The appearance of a pink color
  - C. The appearance of blue color
  - D. The transition from pink to purple
  - E. The appearance of a blue precipitate
- 8) In accordance with the requirements of the SPHU, the procurator-analyst conducts a quantitative determination of the substance potassium bromide by the method of reverse argentometric titration (Folgard method) in the presence of dibutyl phthalate. As an indicator, he uses a solution:
  - A. Ferrum (III) ammonium sulfate (iron ammonium alum)
  - B. Potassium chromate
  - C. Tropeolin 00
  - D. Morbid black
  - E. Phenolphthalein
- 9) Quantitative content of the ophylline in accordance with the requirements of the SPHU is determined by the method of alkalimetry by substitute. The titrant in this method is a solution:
  - A. Sodium hydroxide
  - B. Potassium bromide
  - C. Sodium edetate
  - D. Hydrochloric acids
  - E. Ammonium thiocyanate

- 10) For the quantitative determination of medicinal substances from the group of sulfonamides, sodium nitrite titration is used, because their molecules contain:
  - A. Primary aromatic amino group
  - B. Aldehyde group
  - C. Hydroxyl group
  - D. Carboxylic group
  - E. Carbonyl group

- 1) Redox titration indicators. Interval of color transition of redox indicators. Selection of indicators.
- 2) Mercurimetry. The essence of the method and its application in the pharmaceutical analysis of medicinal substances.
- 3) Cerimetry. The essence of the method and its application in the pharmaceutical analysis of medicinal substances.

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# Independent work No. 9

**Topic:** Titrimetric methods of analysis: method of acid-base titration in aqueous and non-aqueous media, argentometry, complexonometry.

**Goal:** Acquainted with the features of acid-base, precipitation and complexonometric methods of analysis of medicinal substances.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

### Plan

# 1. Theoretical questions:

- 1) What titrants are used in complexometric titration?
- 2) What organic reagents are called complexones?
- 3) Titration curves in the complexonometry method. Construction of titration curves.
  - 4) What does the titration jump in the complexometric method depend on?
  - 5) Characteristics of the acid-base titration method.
- 6) Working solutions in acid-base titration, their preparation and standardization.

## **Ouestions for self-control:**

- 1) Peculiarities of reactions of metal cations with complexons.
- 2) What indicators are used in complexonometry? What is their action based on?
  - 3) Primary and secondary standards. They fixed it.
  - 4) Construction of acid-base titration curves for titration cases.
  - 5) Indicators of acid-base titration. Natural and synthetic indicators.

## **Indicative tasks for processing theoretical material:**

- Compile a dictionary of basic concepts on the topic.

# 2. Practical works (tasks) to be performed:

The task 1. Calculate what volume of 0.1 N solution of sodium edetate (KP = 1.0000) will be used for the titration of 0.5145 g of magnesium oxide (M.m. 40.31), if its percentage content in the substance is 96.8%; The volume of the measuring flask is 100 ml, the volume of the pipette is 10 ml.

The task 2. Calculate the mass of glutamic acid (M.m. = 147.13), if 20.06 ml *Methodical development to independent work of the student from educational discipline, EPP* "Pharmacy, Industrial Pharmacy", 3<sup>rd</sup> year, Faculty of Pharmacy, Discipline: "Pharmaceutical Chemistry" p. 49

of 0.1 N sodium hydroxide solution was used for titration by the method of direct alkalimetry. CP = 1.0000. The percentage content in the substance is 99.1%.

The task 3. Calculate the percentage content of diphenhydramine (M.m. = 291.82) in the substance, if 10.49 ml of 0.1N perchloric acid solution was used for the titration of 0.2976 g. PC = 1.0018. The volume of the titrant in the control experiment is 0.36 ml.

- 1) Dilute hydrochloric acid is used in medical practice. Which of the following methods is used for its quantitative determination?
  - A. Alkalimetry
  - B. Permanganatometry
  - C. Complexonometry
  - D. Acidimetry
  - E. Iodometry
- 2) One of the stages of pharmaceutical analysis is the quantitative determination of the medicinal product. Quantitative determination of hydrochloric acid is carried out by the method:
  - A. Alkalimetry
  - B. Gravimetry
  - C. Acidimetry
  - D. Complexonometry
  - E. Permanganatometry
- 3) Quantitative determination of active chlorine in perchloric lime is carried out by the method?
  - A. iodometry
  - B. alkalimetry
  - C. bromatometry
  - D. cerimetry
  - E. permanganatometry

- 4) Sodium chloride tablets are manufactured at a pharmaceutical enterprise. Specify the method of quantitative determination of the active substance:
  - A. argentometry
  - B. iodometry
  - C. nitritometry
  - D. alkalimetry
  - E. acidimetry
- 5) When carrying out the quantitative determination of potassium chloride by the argentometric method (back titration) according to the SPHU, the following is used as an indicator:
  - A. iron(III) ammonium sulfate
  - B. diphenylcarbazone
  - C. potassium chromate
  - D. phenolphthalein
  - E. sodium eosinate
- 6) What method is recommended by the SPHU for the quantitative determination of the potassium chloride substance used in hypokalemia?
  - A. argentometry
  - B. bromatometry
  - C. iodometry
  - D. cerimetry
  - E. polarimetry
- 7) The pharmacist-analyst determines the admixture of chlorides in potassium bromide according to the SPHU method:
  - A. argentometry
  - B. nitritometry
  - C. bromatometry
  - D. alkalimetry
  - E. iodometry

- 8) According to the recommendations of the State Pharmacopoeia of Ukraine, the pharmacist-analyst performs the quantitative determination of potassium iodide by the method:
  - A. iodometry
  - B. argentometry
  - C. alkalimetry
  - D. acidimetry
  - E. mercurimetry
- 9) Identification of iodine preparations in pharmaceutical analysis is carried out with the following reagent:
  - A. starch solution
  - B. lead nitrate solution
  - C. sodium chloride solution
  - D. silver nitrate solution
  - E. calcium acetate solution
- 10) The quantitative content of sodium iodide according to the SPHU is determined by the method:
  - A. iodometry
  - B. argentometry
  - C. nitritometry
  - D. permanganatometry
  - E. bromatometry
  - 4. Individual tasks for students of higher education on the topic:
  - 1) Ionic and chromophoric theories of indicators.
  - 2) Principles of indicator selection.
  - 3) Indicator error of titration.
  - 5. References:

### **Basic:**

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## Independent work No. 10

**Topic:** Optical methods in quantitative analysis: refractometry, polarimetry, UV and IR spectrophotometry, photometry in the visible spectrum.

**Goal:** Acquainted with the peculiarities of pharmaceutical analysis related to the use of optical methods of analysis of medicinal substances.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

### Plan

- 1. Theoretical questions:
- 1) What causes the color of the solution?
- 2) What color is called complementary?
- 3) What is optical density?
- 4) What is light transmission?
- 5) What is the relationship between optical density and light transmission?
- 6) What spectral line is called resonant?

## **Ouestions for self-control:**

- 1) Formulate the Bouguer-Lambert-Behr law of light absorption.
- 2) What is the relationship between optical density and concentration according to the Bouguer-Lambert-Behr law?
  - 3) What is the absorption spectrum of a substance?
  - 4) What is used as a source of radiation in AAS?

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5) In photometry, optical density is measured by comparison with a "zero" solution. What kind of solution is this?

# **Indicative tasks for processing theoretical material:**

Compile a dictionary of basic concepts on the topic.

# 2. Practical works (tasks) to be performed:

The task 1. During the photocolorimetric determination of Fe3+ with sulfosalicylic acid from a standard solution with an iron content of 10 mg/cm3, a number of dilutions were prepared in volumetric flasks with a capacity of 100 cm3, the optical absorption was measured and the following data were obtained:

Vst, cm3 1.0 2.0 3.0 4.0 5.0 6.0

A 0.12 0.25 0.37 0.50 0.62 0.75

Determine the concentration of Fe3+ in the analyzed solutions if their optical absorption is equal to 0.30 and 0.50.

The task 2. Calculate the weight of the powder of crushed tablets of cortisone acetate, taken for quantitative determination by the spectrophotometric method, if the content of cortisone acetate in the tablet is 0.0510 g, the optical density of the tested solution is 0.505, the average weight of the tablet is 0.195 g, the dilution factor is 20, the specific absorption index is 390.

The task 3. When polarizing 5 ml of a saturated solution of lead bromide on an ammonium-ammonia background, the height of the lead wave was 26 mm. The height of the wave obtained during polarography of 0.01 N standard lead solution under similar conditions is 20 mm. Determine the solubility product of lead bromide.

- 1) The pharmacist-analyst needs to determine the refractive index of methyl salicylate. What device should he use for this?
  - A. refractometer
  - B. polarimeter

- C. potentiometer
- D. polarograph
- E. spectrophotometer
- 2) When testing for the purity of the ethylmorphine hydrochloride substance, it is necessary to determine the specific optical rotation. This research is conducted using:
  - A. polarimeter
  - B. spectrophotometer
  - C. photoelectrocolorimeter
  - D. refractometer
  - E. polarograph
- 3) The chemical laboratory analyst received the glucose substance for analysis. To determine its benign quality, he measured the angle of rotation of its aqueous solution. He conducted these studies using:
  - A. polarimeter
  - B. refractometer
  - C. spectrophotometer
  - D. potentiometer
  - E. photoelectrocolorimeter
- 4) The chemical laboratory analyst received the glucose substance for analysis. He used a polarimeter to determine its benignity. At the same time, he measured:
  - A. angle of rotation
  - B. refractive index
  - C. optical density
  - D. melting point
  - E. specific gravity

- 5) The specific optical rotation of 10% glucose solution according to SPHU should be from + 52.5° to 53.3°. To calculate this value, the pharmacist-analyst must measure:
  - A. angle of rotation
  - B. refractive index
  - C. density
  - D. melting point
  - E. viscosity
- 6) The pharmacist-analyst examines the good quality of glycerol in accordance with the requirements of the Federal Drug Administration. Using a refractometer, he measured:
  - A. refractive index
  - B. angle of rotation
  - C. melting point
  - D. density
  - E. viscosity
- 7) A pharmaceutical enterprise produces a solution of cordiamine. During quality control, the analytical chemist determined its quantitative content by refractometry. For this he defined:
  - A. refractive index
  - B. viscosity
  - C. density
  - D. absorption intensity
  - E. angle of rotation
- 8) A pharmacist-analyst analyzes a 10% glucose solution. For quantitative determination, he uses one of the physico-chemical methods, measuring the angle of rotation of the solution, using:
  - A. polarimeter
  - B. potentiometer

- C. gas chromatograph
- D. refractometer
- E. UV spectrophotometer
- 9) Quantitative determination of the riboflavin substance according to the requirements of the SPHU is carried out by the following method:
  - A. Spectrophotometry
  - B. Refractometry
  - C. Thin-layer chromatography
  - D. Column chromatography
  - E. Acidimetry in an aqueous environment
- 10) The presence of which atom in the molecule of an organic compound determines its optical activity?
  - A. asymmetric carbon atom
  - B. hydrogen atom
  - C. nitrogen atom
  - D. oxygen atom
  - E. sulfur atom

- 1) The use of atomic absorption analysis in the pharmaceutical analysis of medicinal substances.
- 2) The use of photoelectrocolorimetric analysis in the pharmaceutical analysis of medicinal substances.
- 3) The use of atomic emission analysis in the pharmaceutical analysis of medicinal substances.

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# Independent work No. 11

**Topic:** Chromatographic methods. Methods based on thermodynamic properties of substances. Combination of extraction, chromatographic and optical methods in the analysis of dosage forms.

**Goal:** Acquainted with the peculiarities of pharmaceutical analysis associated with the use of chromatographic methods for the analysis of medicinal substances.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

### Plan

# 1. Theoretical questions:

- 1) What is the essence of chromatographic separation by the method of gas-solid phase chromatography?
- 2) What is the essence of chromatographic separation by the method of gas-liquid chromatography.
- 3) What is the purpose of stationary phases in gas adsorption and gasliquid chromatography methods?
- 4) What is the nature of the physical and chemical processes occurring in the chromatographic column in gas-solid-phase and gas-liquid chromatography?
- 5) How is the introduction of the sample into the gas chromatograph, if the analyzed sample is gas or liquid?
- 6) What are the areas of application, advantages and disadvantages of gas adsorption chromatography?

## **Questions for self-control:**

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- 1) Name the main components of a gas chromatograph.
- 2) What gases can be used as carriers in gas chromatography?
- 3) What devices are used as dispensers?
- 4) How is a stationary liquid phase applied to a carrier for packed columns?
- 5) In what cases is the temperature programming of the chromatographic column used?

## **Indicative tasks for processing theoretical material:**

- Compile a dictionary of basic concepts on the topic.

# 2. Practical works (tasks) to be performed:

The task 1. Calculate the mass fraction (%) of acetone and ethanol in the sample, if the height and half-width of the peaks of these components on the obtained chromatogram are equal to 60 mm and 2 mm, respectively; 90 mm and 3 mm.

The task 2. Calculate the mass fraction (%) of the components of the studied mixture, if the height and half-width of the chromatographic peaks of ethanol, propanol and butanol are equal to 80 mm and 2 mm, respectively; 60 mm and 3 mm, 100 mm and 3 mm.

The task 3. Determine the mass fraction (%) of the components of the gas mixture, if the areas of the chromatographic peaks of propane, butane and cyclohexane and their correction factors are equal to 175 mm2 and 0.68, respectively; 203 mm2 and 0.68; 35 mm2 and 0.85.

- 1) The method of gas-liquid chromatography is used to identify substances. Identification of substances in the gas-liquid chromatography method is carried out according to:
  - A. retention parameters
  - B. peak width at half its height

- C. peak area
- D. character of the zero line
- E. peak height
- 2) Chromatographic analysis is widely used in the Department of Agriculture of Ukraine for the identification of plant raw materials and phytopreparations. To identify individual substances in chromatographic analysis, the following value is determined:
  - A. value of Rf
  - B. melting point
  - C. boiling point
  - D. angle of refraction
  - E. angle of rotation
- 3) By what method, according to the SPHU, is the admixture of methyl alcohol in ethyl alcohol discovered:
  - A. By the method of gas chromatography
  - B. Redox method
  - C. By the method of neutralization
  - D. By the deposition method
  - E. Complexonometry
- 4) In the control and analytical laboratory, the quantitative content of sodium citrate is determined by the method of ion exchange chromatography using a cationite. What titrated solution should be used for the subsequent titration of citric acid that is formed?
  - A. Sodium hydroxide
  - B. Iodine
  - C. Potassium iodate
  - D. Hydrochloric acids
  - E. Trylon B

- 5) The pharmacist-analyst identifies glutamic acid by thin-layer chromatography. To detect spots on the chromatogram, he must treat it with a solution of the substance:
  - A. ninhydrin
  - B. benzaldehyde
  - C. diphenylamine
  - D. pyridine
  - E. aniline
- 6) The control and analytical laboratory received the drug substance. Its identification, according to the requirements of the SPHU, involves the determination of substances that are detected by ninhydrin and carried out by the method of thin-layer chromatography. Name this medicine.
  - A. glutamic acid
  - B. benzoic acid
  - C. acetylsalicylic acid
  - D. ascorbic acid
  - E. hydrochloric acid
- 7) The amino acid valine is identified by TLC according to the requirements of the SPHU. To develop a chromatogram, a solution of the following reagent is used:
  - A. ninhydrin
  - B. cyanide bromide
  - C. 2,4-dinitrochlorobenzene
  - D. 2,4-dinitrophenylhydrazine
  - E. concentrated ammonia
- 8) The control and analytical laboratory received glutamic acid. Identification in accordance with the Federal Federal Tax Service is carried out by the following method:
  - A. thin layer chromatography

- B. gas chromatography
- C. liquid chromatography
- D. paper chromatography
- E. ion exchange chromatography
- 9) A physicochemical method is used for the quantitative determination of the folic acid substance according to the SPHU. Name this method.
  - A. liquid chromatography
  - B. ion exchange chromatography
  - C. ultraviolet spectrophotometry
  - D. refractometry
  - E. polarimetry
- 10) According to SPHU, the quantitative determination of benzylpenicillin sodium salt is carried out by the method:
  - A. liquid chromatography
  - B. gravimetry
  - C. iodometry
  - D. alkalimetry
  - E. argentometry

- 1) TSH equipment, methodology, determination of system suitability, methods of identification and quantification.
- 2) TOP. equipment, methodology, determination of system suitability, methods of identification and quantification.
- 3) Gas chromatography. Equipment, methodology, determination of system suitability, methods of identification and quantification.

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# Independent work No. 12

**Topic:** Express analysis of medicines. Modern trends in the development of pharmaceutical analysis.

**Goal:** Acquainted with the features of express analysis of medicinal substances.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

#### Plan

## 1. Theoretical questions:

- 1) What indicator is used in refractometric express analysis?
- 2) For an express analysis of a 10% glucose solution, it is necessary to determine its refractive index. What device should the pharmacist-analyst use?
- 3) In the quantitative express analysis of a 2% boric acid solution, is the method used?
- 4) What method of quantitative determination can be used in the express analysis of a sedative mixture with sodium bromide?
- 5) In the express analysis of an extemporaneous mixture, what method can be used to identify the calcium cation?
- 6) What quantitative method can be used in the rapid analysis of eye drops with anti-inflammatory action that contain potassium iodide?

## **Questions for self-control:**

- 1) The concept of express analysis (extemporaneous formulation).
- 2) The main requirement for express analysis.

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- 3) Refractometric express analysis.
- 4) Requirements for high-quality express analysis.
- 5) Requirements for quantitative express analysis.

# **Indicative tasks for processing theoretical material:**

- Compile a dictionary of basic concepts on the topic.

# 2. Practical works (tasks) to be performed:

The task 1. Determine the mass fraction of isoniazid (M.m. 137.14), if an excess of 0.1 N iodine solution (KP = 0.9858) after the reaction with 0.2246 g of isoniazid was titrated with 17.60 ml of 0.1 M of sodium thiosulfate solution (CP = 1.1442), volume of iodine solution - 50.00 ml.

The task 2. Determine the mass of the theobromine test (M.m. 180.17), if 16.50 ml of 0.1 N sodium hydroxide solution (KP=0.9903) was spent on its titration by the method of indirect neutralization. The mass fraction of theobromine in the drug is 99.33%.

The task 3. Determine the mass of sodium bromide test (M.m 102.90), if 19.23 ml of 0.1 N solution of argentum(I) nitrate (KP = 0.9870) was spent on its titration. The mass fraction of sodium bromide in the medicinal product is 99.40%.

- 1) For the express determination of the iron (III) cation, a control and analytical laboratory specialist can use the reaction with:
  - A. with a solution of potassium ferrocyanide Fe (II)
  - B. cobalt nitrate solution
  - C. sodium chloride solution
  - D. calcium chloride solution
  - E. zinc sulfate solution

- 2) A specialist of the control and analytical laboratory performs an express analysis of a complex preparation, which includes amino acids of the aliphatic series. The group reagent for amino acids is:
  - A. ninhydrin
  - B. phenolphthalein
  - C. potassium permanganate
  - D. argentum nitrate
  - E. pyridine
- 3) A specialist of the control and analytical laboratory performs an express analysis of etazol. He confirmed the presence of a primary aromatic amino group using a lignin sample. What reagent can be used in this reaction?
  - A. benzaldehyde
  - B. benzene
  - C. acetic anhydride
  - D. pyridine
  - E. chloroform
- 4) An analyst of the control and analytical laboratory performs an express analysis of morphine hydrochloride. The presence of phenolic hydroxyl is confirmed by the reaction with the solution:
  - A. FeCl3
  - B. NH3
  - C. AgNO3
  - D. K3[Fe(CN)6]
  - E. Concentrated HNO3
- 5) A pharmacist-analyst conducts an express analysis of eye drops containing adrenaline hydrotartrate. After adding a solution of ferric chloride (III), an emerald-green color was formed, which indicates the presence of adrenaline in the molecule:
  - A. phenolic hydroxyl groups

- B. aldehyde groups
- C. aromatic amino groups
- D. ester groups
- E. carboxyl groups
- 6) The pharmacist-analyst determines the quantitative content of the medicinal product by the inverse bromatometric method. Which of the listed titrated solutions should he use:
  - A. Sodium thiosulfate
  - B. Potassium bromate
  - C. Sodium edetate
  - D. Sodium nitrite
  - E. Argentum nitrate
- 7) The pharmacist-analyst performs quantitative express analysis of the liquid dosage form using the titrimetric method. How much of the tested solution can be take for analysis?
  - A. 1-3 ml
  - B. 10-12 ml
  - C. 5-10 ml
  - D. 15-20 ml
  - E. 5-7 ml
- 8) For the express determination of the iron (III) cation, a control and analytical laboratory specialist can use the reaction with:
  - A. A solution of potassium ferrocyanide (II)
  - B. Cobalt nitrate solution
  - C. Sodium chloride solution
  - D. Calcium chloride solution
  - E. Zinc sulfate solution
- 9) Distinguishing reactions to calcium chloride and calcium gluconate in an express analysis can be:
  - A. Reactions to the corresponding anions
  - B. Reactions to the calcium ion

- C. Reactions of obtaining calcium oxalate
- D. Reactions to sulfate ion
- E. Oxidation reactions with K3[Fe(CN)6]
- 10) A specialist of the control and analytical laboratory performs an express analysis of etazol. He confirmed the presence of a primary aromatic amino group using a lignin test. What reagent can be used in this reaction?
  - A. Unbleached paper
  - B. Benzene
  - C. Acetic anhydride
  - D. Pyridine
  - E. Chloroform

- 1) Express analysis in a pharmacy.
- 2) Express analysis of medicinal plant raw materials.
- 3) The difference between the identification of medicinal products by pharmacopoeial and express methods.

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# Independent work No. 13

**Topic:** Modern strategies for creating innovative medicines.

**Goal:** Acquainted with modern methods and strategies for creating new medicines.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

### Plan

# 1. Theoretical questions:

- 1) What is the effect of introducing phenolic hydroxyl into the structure?
- 2) What is the effect of introducing a carboxamide group into the structure?
- 3) What is the effect of introducing a diarylmethane group into the structure?
- 4) What effect do branched alkyl substituents provide in the presence of halogen atoms?
  - 5) What effect does the presence of n-alkyl chains provide?
- 6) Due to what effects do cycloalkyl groups improve binding to the bioreceptor?

# **Questions for self-control:**

- 1) How do ethers and esters change the polarity of molecules and affect bioavailability?
- 2) What bioactivity does the introduction of a bromine atom into the structure provide?
- 3) What bioactivity does the introduction of an isopropion group into the structure provide?
  - 4) Lipophilicity. Characteristic. Examples.
  - 5) Methods of forecasting biological activity.

# Indicative tasks for processing theoretical material:

Compile a dictionary of basic concepts on the topic.

# 2. Practical works (tasks) to be performed:

The task 1. Specify pharmacophoric, chromoform and auxochromic groups:

The task 2. Specify pharmacophoric, chromoform and auxochromic groups:

$$O_2N$$
 $O$ 
 $CH=N-NH-C-NH_2$ 

The task 3. Specify pharmacophoric, chromophoric and auxochromic groups:

### 3. Test tasks for self-control:

- 1) The structural basis of medicinal products of natural and semi-synthetic penicillins is:
  - A. 6-aminopenicillanic acid
  - B. 7-aminocephalosporanic acid
  - C. 7-aminopenicillanic acid
  - D. 8-aminopenicillanic acid
  - E. 7-aminodesacetoxycephalosporanic acid
- 2) Specify the compound that is the starting point for the production of semisynthetic penicillins:
  - A. 6-aminopenicillanic acid
  - B. clavulanic acid
  - C. penicilloic acid
  - D. penaldic acid
  - E. 7-aminocephalosporanic acid

- 3) Which of the following compounds is the starting material for the synthesis of paracetamol?A. n-aminophenol
  - B. n-nitrotoluene
  - C. m-aminophenol
  - D. o-aminophenol
  - E. o-xylene
- 4) Salol (phenyl ester of salicylic acid) is a synthetic antibacterial agent used in intestinal diseases. For its identification, a reagent is used:
  - A. Ferrum (III) chloride
  - B. Ethanol 96%
  - C. Argentum nitrate
  - D. Chloric acid
  - E. Ammonium chloride
- 5) Which of the following compounds is the starting material for the synthesis of anesthesin?
  - A. n-nitrotoluene
  - B. o-nitrotoluene
  - C. m-aminophenol
  - D. o-xylene
  - E. m-cresol
- 6) Procaine hydrochloride (novocaine) can be synthesized from:
  - A. para-nitrobenzoic acid
  - B. ortho-nitrobenzoic acid
  - C. meta-nitrobenzoic acid
  - D. benzoic acid
  - E. salicylic acid
- 7) What compound is synthesized by the reaction between malonic acid diethyl ether and urea?

- A. barbituric acid
- B. benzoic acid
- C. uric acid
- D. nicotinic acid
- E. ascorbic acid
- 8) The pharmacist-analyst performs the identification of the isoniazid substance in accordance with the requirements of the SPHU by the melting point of the yellow precipitate obtained when interacting with the solution:
  - A. Vanilla
  - B. Hydroxyquinoline
  - C. Sodium nitroprusside
  - D. Potassium bromide
  - E. Ammonium thiocyanate
- 9) The chemist of the control and analytical laboratory received the task of preparing turbidity standards according to the requirements of the pharmacopoeia. What substances should he use for this as starting materials?
  - A. Hexamethylenetetramine and hydrazine sulfate
  - B. Calcium sulfate and glycerin
  - C. Sodium chloride and calcium nitrate
  - D. Potassium chloride and barium sulfate
  - E. Furacilin and calcium chloride
- 10) Which of the following compounds are starting substances for the synthesis of sulfonamide preparations?
  - A. Acetanilide
  - B. Naphthalene
  - C. Anthraquinone
  - D. Phenanthrene
  - E. Toluene
  - 4. Individual tasks for students of higher education on the topic:

- 1) Chromophore. Characteristic. Examples.
- 2) Auxochrome. Characteristic. Examples.
- 3) Pharmacophore. Characteristic. Examples.

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- 3. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2014. Т. 3. 732 с.
- 4. Фармацевтична хімія / П.О. Безуглий, В.А. Георгіянц, І.С. Гриценко, І.В. та ін.: за ред. П.О. Безуглого. Вінниця: Нова книга, 2017. 456 с.
- Фармацевтична хімія. Загальна та спеціальна фармацевтична хімія. Лікарські засоби неорганічної природи: лабораторно-практичні заняття. Навчальний посібник / Л.Г. Мішина. – Вінниця: ПП «ТД «Едельвейс і К»», 2010. – 384 с.

## Independent work No. 14

**Topic:** Organic synthesis is the basis for obtaining synthetic small molecules. Combinatorial synthesis and its role in drug design. Strategy for the development and synthesis of libraries of chemical compounds. Prospects for the development of combinatorial synthesis.

**Goal:** Acquainted with the organic synthesis of medicinal substances; combinatorial synthesis; development strategies and synthesis of libraries of chemical compounds.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

#### Plan

## 1. Theoretical questions:

- 1) What is a biologically active substance?
- 2) Give the main strategies of organic synthesis of medicines?
- 3) What is the strategy of prodrugs? Give examples of the application of this strategy.
- 4) What are antimetabolites? The principle of their application in medical practice.

- 5) What is the principle of molecular modeling of medicinal substances?
- 6) Give a schematic diagram of the development of a new medicinal product.

## **Questions for self-control:**

- 1) What is the difference between a medicinal product and a medicinal product?
  - 2) What are the modern requirements for medicinal products?
  - 3) What is a pharmacophore group?
- 4) What is a functional group? What is the role of functional groups in the creation of drugs?
- 5) How does the biological activity of a molecule change when halogen atoms are introduced into it? Describe separately the influence of the fluorine atom.

## **Indicative tasks for processing theoretical material:**

Compile a dictionary of basic concepts on the topic.

# 2. Practical works (tasks) to be performed:

The task 1. Specify the pharmacophore groups and the probable manifestation of biological activity:

The task 2. Specify the pharmacophore groups and the probable manifestation of biological activity:

$$\begin{array}{c|c} \mathbf{H_2N} & \begin{array}{c} \mathbf{O} \\ \mathbf{\parallel} \\ \mathbf{S} \\ \mathbf{O} \end{array} \\ \begin{array}{c} \mathbf{N} \\ \mathbf{O} \\ \end{array} \\ \begin{array}{c} \mathbf{CH_2} \\ \mathbf{CH_2} \\ \end{array}$$

The task 3. Specify the pharmacophore groups and the probable manifestation of biological activity:

$$H_2N$$
  $C$   $O$   $CH_3$ 

### 3. Test tasks for self-control:

- 1) Hexamethylenetetraminewas synthesized in 1980 by A.M. Butler's condensation of formic aldehyde with ammonia in a ratio of 6:4. This compound is used as a medicinal product. What is another name for this compound?
  - A. Urotropin
  - B. Formalin
  - C. Formamide
  - D. urethane
  - E. Fluoroethane
- 2) Phenolphthaleinused as an ind. on an alkaline environment. In what way is it synthesized?
  - A. Condensation of phthalic anhydride with two molecules of phenol.
  - B. Condensation of phthalaldehyde with two molecules of phenol
  - C. Condensation of o-phthalic acid with two molecules of phenol
  - D. Condensation of phenol molecules
  - E. Condensation of formaldehyde with two formaldehyde with three molecules of phenol
- 3) Which of the following compounds is the starting material for the synthesis of paracetamol?
  - A. n aminophenol
  - B. n nitrotoluene
  - C. m- aminophenol
  - D. o-aminophenol
  - E. o-xylene
- 4) Oxaphenamide is obtained from phenyl salicylate by reaction with:

- A. p-aminophenol
- B. benzene
- C. toluene
- D. β-naphthol
- E. anthraquinone
- 5) Pharmaceutical chemistry studies methods of obtaining medicines. When anesthesin interacts with beta-diethylaminoethanol in the presence of sodium ethylate followed by acidification with hydrochloric acid, the following is obtained:
  - A. procaine hydrochloride
  - B. procainamide hydrochloride
  - C. dikain
  - D. xycain
  - E. trimecaine
- 6) Salol (phenyl ester of salicylic acid) is a synthetic antibacterial agent used in intestinal diseases. For its identification, a reagent is used:
  - A. Ferrum (III) chloride
  - B. Ethanol 96%
  - C. Argentum nitrate
  - D. Chloric acid
  - E. Ammonium chloride
- 7) Which of the following compounds is the starting material for the synthesis of anesthesin?
  - A. n-nitrotoluene
  - B. o-nitrotoluene
  - C. m-aminophenol
  - D. o-xylene
  - E. m-cresol
- 8) Procaine hydrochloride (novocaine) can be synthesized from:

- A. para-nitrobenzoic acid
- B. ortho-nitrobenzoic acid
- C. meta-nitrobenzoic acid
- D. benzoic acid
- E. salicylic acid
- 9) What compound is synthesized by the reaction between malonic acid diethyl ether and urea?
  - A. barbituric acid
  - B. benzoic acid
  - C. uric acid
  - D. nicotinic acid
  - E. ascorbic acid
- 10) The pharmacist-analyst performs the identification of the isoniazid substance in accordance with the requirements of the SPHU by the melting point of the yellow precipitate obtained when interacting with the solution:
  - A. Vanilla
  - B. Hydroxyquinoline
  - C. Sodium nitroprusside
  - D. Potassium bromide
  - E. Ammonium thiocyanate
  - 4. Individual tasks for students of higher education on the topic:
  - 1) The influence of unsaturated bonds on biological activity.
  - 2) Effect of optical activity on pharmacological activity.
  - 3) Effect of acidic groups on biological activity.
  - 5. References:

### **Basic:**

1. Handbook of pharmaceutical chemictry Vol. 117 / L. Ohannesian, Antony J. Streeter. 2016. – 582 p.

- 2. Pharmaceutical Chemistry I Laboratory Experiments and Commentary / Attila Almási, Zsuzsanna Rozmer, Pál Perjési. 2014. 179 p.
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- 5. Pharmaceutical drug analysis / Addis Ababa. 2005. 554 p.
- 6. Analytical Chemistry Series / John M., Chalmers, Alan J. Handley. 2003. 384 p.
- 7. HANDBOOK OF MODERN PHARMACEUTICAL ANALYSIS Vol. 3 / Satinder Ahuja, Stephen Scypinski. 2001. 587 p.
- 8. Europian Pharmacopoeia 10<sup>th</sup>. 2019. 4255 p.

### **Additional:**

- 1. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2015. Т. 1. 1128 с.
- 2. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2014. Т. 2. 724 с.
- 3. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2014. Т. 3. 732 с.
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 Фармацевтична хімія. Загальна та спеціальна фармацевтична хімія. Лікарські засоби неорганічної природи: лабораторно-практичні заняття. Навчальний посібник / Л.Г. Мішина. – Вінниця: ПП «ТД «Едельвейс і К»», 2010. – 384 с.

## **Independent work No. 15**

**Topic:** Stages of creation of medicines - "from molecule to drug".

**Goal:** Acquainted with the features of the stages of creation of medicinal products.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

#### Plan

## 1. Theoretical questions:

- 1) Basic mechanisms of action of drugs and biologically active compounds, concepts of molecular/biological targets.
- 2) Characteristics of ligand-oriented and target-oriented design of biologically active compounds, differences.
- 3) Compounds-hits and compounds-leaders, requirements, characteristics, differences. Methods of optimization of leader compounds.
  - 4) Examples of leader compounds. Examples of privileged structures.
- 5) Physicochemical requirements for biologically active compounds as potential medicinal products.
- 6) Functional groups and reactions are involved in metabolic transformations; the concept of pro-drugs, double drugs.

### **Questions for self-control:**

- 1) The use of the achievements of medical and biological research in the creation of medicines on the example of gas transmitters and PPAR receptors.
  - 2) The main stages of drug metabolism. Concept of ADME/Tox.

- 3) Antimetabolites in the creation of medicinal products aspects of chemical modification.
- 4) The relationship between structure and activity is a basic concept of drug chemistry.
  - 5) Pharmacophore groups.

## **Indicative tasks for processing theoretical material:**

Compile a dictionary of basic concepts on the topic.

## 2. Practical works (tasks) to be performed:

The task 1. Aspects of medical chemistry of phenothiazine derivatives. Characteristics of the group, directions of modification, methods of synthesis, peculiarities of the biological effect, metabolism, SAR.

The task 2. Aspects of medical chemistry of barbituric acid derivatives. Characteristics of the group, directions of modification, methods of synthesis, peculiarities of the biological effect, metabolism, SAR.

The task 3.Aspects of medical chemistry of nonsteroidal anti-inflammatory drugs. Characteristics of chemical groups, methods of synthesis, peculiarities of biological effect, metabolism, SAR.

#### 3. Test tasks for self-control:

- 1) The structural basis of medicinal products of natural and semi-synthetic penicillins is:
  - A. 6-aminopenicillanic acid
  - B. 7-aminocephalosporanic acid
  - C. 7-aminopenicillanic acid
  - D. 8-aminopenicillanic acid
  - E. 7-aminodesacetoxycephalosporanic acid
- 2) Specify the compound that is the starting point for the production of semisynthetic penicillins:

- A. 6-aminopenicillanic acid
- B. clavulanic acid
- C. penicilloic acid
- D. penaldic acid
- E. 7-aminocephalosporanic acid
- 3) Which of the following compounds is the starting material for the synthesis of paracetamol?
  - A. n-aminophenol
  - B. n-nitrotoluene
  - C. m-aminophenol
  - D. o-aminophenol
  - E. o-xylene
- 4) Salol (phenyl ester of salicylic acid) is a synthetic antibacterial agent used in intestinal diseases. For its identification, a reagent is used:
  - A. Ferrum (III) chloride
  - B. Ethanol 96%
  - C. Argentum nitrate
  - D. Chloric acid
  - E. Ammonium chloride
- 5) Which of the following compounds is the starting material for the synthesis of anesthesin?
  - A. n-nitrotoluene
  - B. o-nitrotoluene
  - C. m-aminophenol
  - D. o-xylene
  - E. m-cresol
- 6) Procaine hydrochloride (novocaine) can be synthesized from:
  - A. para-nitrobenzoic acid
  - B. ortho-nitrobenzoic acid

- C. meta-nitrobenzoic acid
- D. benzoic acid
- E. salicylic acid
- 7) What compound is synthesized by the reaction between malonic acid diethyl ether and urea?
  - A. barbituric acid
  - B. benzoic acid
  - C. uric acid
  - D. nicotinic acid
  - E. ascorbic acid
- 8) The pharmacist-analyst performs the identification of the isoniazid substance in accordance with the requirements of the SPHU by the melting point of the yellow precipitate obtained when interacting with the solution:
  - A. Vanilla
  - B. Hydroxyquinoline
  - C. Sodium nitroprusside
  - D. Potassium bromide
  - E. Ammonium thiocyanate
- 9) The chemist of the control and analytical laboratory received the task of preparing turbidity standards according to the requirements of the pharmacopoeia. What substances should he use for this as starting materials?
  - A. Hexamethylenetetramine and hydrazine sulfate
  - B. Calcium sulfate and glycerin
  - C. Sodium chloride and calcium nitrate
  - D. Potassium chloride and barium sulfate
  - E. Furacilin and calcium chloride
- 10) Which of the following compounds are starting substances for the synthesis of sulfonamide preparations?
  - A. Acetanilide

- B. Naphthalene
- C. Anthraquinone
- D. Phenanthrene
- E. Toluene

## 4. Individual tasks for students of higher education on the topic:

- 1) The path of the medicinal product "from the molecule to the drug".
- 2) Methods of improving ADME/Tokh parameters of biologically active compounds.
  - 3) Variability of molecules based on bioisosteric substitution.

## 5. References:

#### **Basic:**

- Handbook of pharmaceutical chemictry Vol. 117 / L. Ohannesian, Antony J.
   Streeter. 2016. 582 p.
- 2. Pharmaceutical Chemistry I Laboratory Experiments and Commentary / Attila Almási, Zsuzsanna Rozmer, Pál Perjési. 2014. 179 p.
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- 8. Europian Pharmacopoeia 10<sup>th</sup>. 2019. 4255 p.

### **Additional:**

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- Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2015. Т. 1. 1128 с.
- 2. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2014. Т. 2. 724 с.
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## Independent work No. 16

**Topic:** Principles of classification of medicinal products, their nomenclature. Structure-activity relationship in the creation and analysis of medicinal products.

**Goal:** Acquainted with the peculiarities of the classification of medicinal products. Summarize data on the "structure-activity" relationship.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

#### Plan

## 1. Theoretical questions:

- 1) How are medicines classified?
- 2) Define the international requirements of quality standards.
- 3) Medicinal substance.

- 4) Drug.
- 5) Pharmaceutical product.
- 6) Medicinal product.

### **Questions for self-control:**

- 1) What are the requirements for modern medicines?
- 2) What is the calculation screening method?
- 3) Define the main principles of creating new medicines.
- 4) What are the criteria for determining the purity of drugs?
- 5) Basic mechanisms of action of drugs and biologically active compounds, concepts of molecular/biological targets.

## Indicative tasks for processing theoretical material:

Compile a dictionary of basic concepts on the topic.

## 2. Practical works (tasks) to be performed:

The task 1. Aspects of medical chemistry of antibiotics (on the example of beta-lactams). Characteristics of chemical groups, methods of synthesis, peculiarities of biological effect, metabolism, SAR.

The task 2. Aspects of medical chemistry of nootropic drugs. Characteristics of chemical groups, methods of synthesis, peculiarities of biological effect, metabolism, SAR.

The task 3. Aspects of medical chemistry of antitussive drugs. Characteristics of chemical groups, methods of synthesis, peculiarities of biological effect, metabolism, SAR.

#### 3. Test tasks for self-control:

- 1. The introduction of phenolic hydroxyl into the structure gives the following bioactivity:
  - A. Antiseptic;
  - B. Sleepy;

- C. Tranquilizing; D. Anti-inflammatory; E. Anthelmintic. 2. The introduction of a carboxamide group into the structure gives the following bioactivity: A. Sleepy; B. Antiseptic; C. Tranquilizing; D. Anti-inflammatory; E. Anthelmintic:
- 3. The introduction of a diaryl (aminoalkyl)methane group into the structure gives the following bioactivity:
  - A. Antihistamine;
  - B. Sleepy;
  - C. Tranquilizing;
  - D. Anti-inflammatory;
  - E. Antiseptic.
- 4. Branched alkyl substituents in the presence of halogen atoms provide:
  - A. Difficulty in metabolism;
  - B. Acceleration of metabolism;
  - C. Do not affect metabolism;
  - D. Acceleration of hydrolysis;
  - E. Acceleration of oxidation.
- 5. The presence of n-alkyl chains provides:
  - A. Increase in lipophilicity;
  - B. Decrease in lipophilicity;
  - C. Acceleration of metabolism;
  - D. Difficulty in metabolism;
  - E. Antiseptic effect.

6. Cycloalkyl groups improve binding to the bioreceptor due to: A. van der Waals forces; B. Electrostatics; C. Dragon's topological index; D. Lipophilicity; E. Donor/acceptor of H-bonds. 7. Ethers and esters change the polarity of molecules and affect bioavailability by: A. Slowing down of biodecarboxylation; B. Slowing down biooxidation; C. Acceleration of biodecarboxylation; D. Acceleration of biooxidation; E. Slowing down hydrolysis. 8. Flat organic rings have: A. The same pharmacological effect; B. Heterocyclic rings have a more pronounced pharmacological effect; C. Heterocyclic rings have a more pronounced pharmacological effect; D. Carbocyclic rings have a more pronounced pharmacological effect; E. Carbocyclic rings have a more pronounced pharmacological effect. 9. The introduction of a bromine atom into the structure gives the following bioactivity: A. Sedative; B. Tranquilizing; C. Accelerate metabolism; D. Sleeping pills; E. Anti-inflammatory. 10. The introduction of an isopropion group into the structure gives the following bioactivity: A. Anti-inflammatory; B. Analgesic;

- C. Sleeping pills;
- D. Antiseptic;
- E. Antianginal.
- 4. Individual tasks for students of higher education on the topic:
- 1) Fragment-oriented search for medicinal products. Virtual screening.
- 2) Drug targets. Enzymes are drug targets.
- 3) Drug targets. Receptors are drug targets.
- 5. References:

#### **Basic:**

- Handbook of pharmaceutical chemictry Vol. 117 / L. Ohannesian, Antony J.
   Streeter. 2016. 582 p.
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- 7. HANDBOOK OF MODERN PHARMACEUTICAL ANALYSIS Vol. 3 / Satinder Ahuja, Stephen Scypinski. 2001. 587 p.
- 8. Europian Pharmacopoeia 10<sup>th</sup>. 2019. 4255 p.

### **Additional:**

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- 2. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2014. Т. 2. 724 с.
- 3. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2014. Т. 3. 732 с.
- 4. Фармацевтична хімія / П.О. Безуглий, В.А. Георгіянц, І.С. Гриценко, І.В. та ін.: за ред. П.О. Безуглого. Вінниця: Нова книга, 2017. 456 с.
- 5. Фармацевтична хімія. Загальна та спеціальна фармацевтична хімія. Лікарські засоби неорганічної природи: лабораторно-практичні заняття. Навчальний посібник / Л.Г. Мішина. Вінниця: ПП «ТД «Едельвейс і К»», 2010. 384 с.

## **Independent work No. 17**

**Topic:** The main ways of drug metabolism. Chemical reactions that underlie metabolic transformations. Phases of metabolism. Factors affecting metabolic processes. Prodrugs

**Goal:** Acquainted with the general pathways of drug metabolism.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

#### Plan

# 1. Theoretical questions:

- 1) Chemical reactions that underlie metabolic transformations.
- 2) Phases of metabolism.
- 3) The sequence of phases of the interaction of the medicinal substance with the body.
- 4) The main patterns of drug removal from the body.

  Methodical development to independent work of the student from educational discipline, EPP
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- 5) Stages of the receptor mechanism of action of medicinal substances.
- 6) Modern strategy of finding medicinal substances.

### **Questions for self-control:**

- 1) Pharmacokinetics.
- 2) Therapeutic drug delivery systems.
- 3) Characterization of types of action and routes of administration of medicinal products.
  - 4) Physico-chemical aspects of receptor action of drugs.
  - 5) Basic aspects of the chemical interaction of medicinal products.

## Indicative tasks for processing theoretical material:

Compile a dictionary of basic concepts on the topic.

## 2. Practical works (tasks) to be performed:

The task 1. Aspects of medical chemistry of hypnotic drugs. Characteristics of chemical groups, methods of synthesis, peculiarities of biological effect, metabolism, SAR.

The task 2. Aspects of medical chemistry of antihistamine drugs. Characteristics of chemical groups, methods of synthesis, peculiarities of biological effect, metabolism, SAR.

The task 3. Aspects of medical chemistry of anticonvulsant and antiepileptic drugs. Characteristics of chemical groups, methods of synthesis, peculiarities of biological effect, metabolism, SAR.

#### 3. Test tasks for self-control:

- 1) Which method is NOT used for the quantitative determination of thiamine hydrobromide in a substance?
  - A. Bromatometry, reverse titration
  - B. Alkalimetry, direct titration
  - C. Argentometry according to Fayance method

- D. Argentometry after neutralization with alkali
- E. Gravimetry
- 2) The Dibazole substance is analyzed for the quantitative content of the active substance by the method of acidimetry in a non-aqueous medium. What titrant and indicator are used in this method?
  - A. Perchloric acid solution, crystal violet
  - B. Sodium methylate solution, thymol blue
  - C. Sulfuric acid solution, naphtholbenzene
  - D. Sodium hydroxide solution, phenolphthalein
  - E. Nitric acid solution, crystal violet
- 3) For the quantitative determination of the fluorouracil substance according to the SPHU, the pharmacist-analyst uses the non-aqueous titration method. What titrated solution should he use?
  - A. Tetrabutylammonium hydroxide
  - B. Sodium nitrite
  - C. Potassium bromate
  - D. Ammonium thiocyanate
  - E. Sodium edetate
- 4) In the control and analytical laboratory, the analysis of the substance of iron sulfate heptahydrate is performed according to the SPHU. The weight of the substance is titrated with a solution:
  - A. Ammonium cerium sulfate
  - B. Argentum nitrate
  - C. Ammonium thiocyanate
  - D. Sodium edetate
  - E. Potassium bromate
- 5) Quantitative content of diphenhydramine hydrochloride in accordance with the requirements of the SPHU is determined by the method of alkalimetry. A solution of the following substance is used as a titrant:

- A. Sodium hydroxide
- B. Potassium bromate
- C. Sodium thiosulfate
- D. Potassium permanganate
- E. Hydrochloric acid
- 6) The pharmacist-analyst determines the quantitative content of caffeine in compliance with the requirements of the Federal Drug Administration by the method of acidimetry in non-aqueous media. As a titrated solution, he used the following solution:
  - A. Chloric acid
  - B. Sodium edetate
  - C. Potassium bromate
  - D. Sodium hydroxide
  - E. Sodium nitrite
- 7) Quantitative determination of the thymol substance, according to the requirements of the SPHU, is carried out by the method of bromatometry (direct titration). The equivalence point is fixed by:
  - A. Disappearance of pink color
  - B. The appearance of a pink color
  - C. The appearance of blue color
  - D. The transition from pink to purple
  - E. The appearance of a blue precipitate
- 8) In accordance with the requirements of the SPHU, the procurator-analyst conducts a quantitative determination of the substance potassium bromide by the method of reverse argentometric titration (Folgard method) in the presence of dibutyl phthalate. As an indicator, he uses a solution:
  - A. Ferrum (III) ammonium sulfate (iron ammonium alum)
  - B. Potassium chromate
  - C. Tropeolin 00

- D. Morbid black
- E. Phenolphthalein
- 9) Quantitative content of the ophylline in accordance with the requirements of the SPHU is determined by the method of alkalimetry by substitute. The titrant in this method is a solution:
  - A. Sodium hydroxide
  - B. Potassium bromide
  - C. Sodium edetate
  - D. Hydrochloric acids
  - E. Ammonium thiocyanate
- 10) For the quantitative determination of medicinal substances from the group of sulfonamides, sodium nitrite titration is used, because their molecules contain:
  - A. Primary aromatic amino group
  - B. Aldehyde group
  - C. Hydroxyl group
  - D. Carboxylic group
  - E. Carbonyl group

# 4. Individual tasks for students of higher education on the topic:

- 1) Functional groups and reactions are involved in metabolic transformations; the concept of pro-drugs, double drugs.
  - 2) The main stages of drug metabolism. Concept of ADME/Tox.
- 3) The influence of endogenous factors (genetic, age, and sexual anatomical and physiological characteristics of a person, diseases of individual organs and systems) on the pharmacokinetics and pharmacodynamics (pharmacological and toxicological properties) of drugs.

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- 8. Europian Pharmacopoeia 10<sup>th</sup>. 2019. 4255 p.

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- 1. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2015. Т. 1. 1128 с.
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## Independent work No. 18

**Topic:** Nonsteroidal anti-inflammatory drugs. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of obtaining, methods of analysis, application in medicine.

**Goal:** Acquainted with the peculiarities of pharmaceutical analysis of non-steroidal anti-inflammatory drugs.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

#### Plan

## 1. Theoretical questions:

- 1) Qualitative analysis of diclofenac sodium.
- 2) Quantitative analysis of acetylsalicylic acid.
- 3) Quantitative analysis of paracetamol.
- 4) Qualitative analysis of metamizol sodium salt.
- 5) Pathways of butadione metabolism.
- 6) Metabolic pathways of sodium salicylate.

#### **Ouestions for self-control:**

- 1) Qualitative reactions of sodium cation identification.
- 2) Qualitative reactions for the identification of salicylates.
- 3) Qualitative reactions to the primary aromatic amino group.
- 4) Qualitative reactions to phenyl hydroxyl.

5) Qualitative reactions to acetyl ion.

## **Indicative tasks for processing theoretical material:**

Compile a dictionary of basic concepts on the topic.

## 2. Practical works (tasks) to be performed:

The task 1. Determine the mass fraction (%) of potassium iodide (M.m. 166.01) in a 5% alcoholic solution of iodine, if 8.04 ml of 0.1 N argentum nitrate solution was spent on the titration of 2.00 ml of the drug (KP = 1.0000); volume of 0.1 M sodium thiosulfate solution (CP = 1.0000) used for iodine titration - 5.68 ml.

The task 2. Determine the mass fraction of sodium salicylate (M.m. 160.11) in the medicinal product, if 17.38 ml of 0.5 N hydrochloric acid solution was spent on the titration of 1.5668 g of sodium salicylate (KP = 1.1218).

The task 3. Determine the weight of the weight of sodium salicylate (M.m. 160.11), if 18.52 ml of 0.5 N hydrochloric acid solution (KP = 1.0032) is spent on its titration, and the percentage content of sodium salicylate in the medicinal product is 99.70%.

#### 3. Test tasks for self-control:

- 1. Paracetamol is a drug that has an analgesic, antipyretic and anti-inflammatory effect. When quantifying the active substance by the cerimetric method, the following is used as an indicator:
  - A. Feroin:
  - B. Sodium eosinate;
  - C. Phenolphthalein;
  - D. Starch;
  - E. Potassium chromate.
- 2. Paracetamol is a drug that has an analgesic, antipyretic and anti-inflammatory effect. The identification reaction with a solution of iron (III) chloride is due to the presence in its structure:
  - A. Phenolic hydroxyl;

- B. Aromatic nitro group;
- C. Ester group;
- D. Aldehyde group;
- E. Carboxylic group.
- 3. An express analysis of a liquid dosage form containing sodium salicylate and sodium benzoate is carried out. To detect salicylate and benzoate ions in their simultaneous presence, it is necessary to use a solution:
  - A. Iron (III) chloride;
  - B. Potassium iodide;
  - C. Sodium nitrite:
  - D. Ammonium chloride;
  - E. Aluminum sulfate.
- 4. Acetylsalicylic acid (aspirin) belongs to the group of nonsteroidal antiinflammatory drugs. Its quantitative determination by the method of direct alkalimetry is recommended to be carried out at a temperature not higher than 20 °C in order to prevent:
  - A. Hydrolysis of the ester group;
  - B. Recovery of medicinal substance;
  - C. Oxidation of medicinal substance;
  - D. Decarboxylation of medicinal substance;
  - E. Precipitation of the resulting salt.
- 5. Specify the reaction product of paracetamol with hydrochloric acid and the following addition of potassium dichromate:
  - A. Indophenol dye;
  - B. Aurine dye;
  - C. Triphenylmethane dye;
  - D. Azo dye;
  - E. Schiff base.

6.	Phenylsalicylate (Phenyliisalicilas) can be identified by the smell of phenol,
	which will be released when added to the drug:
	A. H2SO4;
	B. NaCl;
	C. CuSO4;
	D. AgNO3;
	E. CoC12.
7.	A pharmacist-analyst performs an analysis of diclofenac sodium. Indicate the
	method of its quantitative determination in accordance with the requirements
	of the State Federal Office of Ukraine:
	A. Acidimetry in an anhydrous environment;
	B. Alkalimetry in an alcohol-chloroform mixture;
	C. Alkalimetry in the water environment;
	D. Alkalimetry in an anhydrous environment;
	E. Acidimetry in an aqueous medium.
8.	An acidic environment is optimal for the absorption of the main metabolite of
	acetylsalicylic acid. Name this metabolite:
	A. Salicylic acid;
	B. Barbituric acid;
	C. Phenylacetic acid;
	D. Uric acid;
	E. Valproic acid.
9.	One of the directions of biotransformation of paracetamol in the liver is
	oxidation by microsomal enzymes. As a result, a toxic metabolite is formed:
	A. Quinonimine;
	B. Phenol;
	C. o-xylene;
	D. Phthalic anhydride;
	E. m-dioxybenzene.

- 10. The analyst of the control and analytical laboratory performs an express analysis of sodium paraaminosalicylate. The presence of phenolic hydroxyl is confirmed by reaction with the solution:
  - A. FeCl3:
  - B. NH3;
  - C. AgNO3;
  - D. K3[Fe(CN)6];
  - E. Concentrated HNO3.

## 4. Individual tasks for students of higher education on the topic:

- 1) The introduction of pharmacophoric groups ensures the manifestation of anti-inflammatory activity.
- 2) The introduction of pharmacophoric groups ensures the manifestation of antipyretic activity.
- 3) Ibuprofen derivatives. Characteristic. Ways of synthesis. Pharmaceutical analysis.

## 5. References:

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## Independent work No. 19

**Topic:** Narcotic analgesics and their analogues. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of obtaining, methods of analysis, application in medicine.

**Goal:** Acquainted with the peculiarities of pharmaceutical analysis of narcotic analysis and their analogues.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

#### Plan

## 1. Theoretical questions:

- 1) Qualitative analysis of morphine hydrochloride.
- 2) Quantitative analysis of codeine.
- 3) Qualitative analysis of codeine phosphate.
- 4) Quantitative analysis of morphine hydrochloride.
- 5) Metabolism of promedol.
- 6) Metabolism of fentanyl.

### **Questions for self-control:**

- 1) Qualitative reactions to phosphate ions.
- 2) Qualitative reactions to phenolic hydroxyl.
- 3) Oxidation reactions of aromatic compounds.
- 4) Qualitative reactions to chloride ions.
- 5) General precipitation alkaloid reagents.

# Indicative tasks for processing theoretical material:

- Compile a dictionary of basic concepts on the topic.

# 2. Practical works (tasks) to be performed:

The task 1. Determine the volume of a 0.1 N solution of perchloric acid (KP - 0.9985), which will be spent on the titration of a weight of 0.1518 g of morphine hydrochloride M.m. 321.80). The percentage content of morphine hydrochloride in the medicinal product is 99.50%..

The task 2. Determine the volume of 0.1 N perchloric acid solution (KP=0.9835), which will be spent on the titration of 0.1506 g of morphine

hydrochloride (M.m. 321.80), if the quantitative content of morphine hydrochloride in medicinal product -99.00%.

The task 3. Determine the mass fraction of codeine phosphate (M.m. 397.36) in the medicinal product, if 6.19 ml of 0.1 M perchloric acid solution was spent on the titration of a weight of 0.2517 g (KP=0.9916).

### 3. Test tasks for self-control:

- 1. Morphine belongs to the group of narcotic analgesics. According to its chemical structure, it is a derivative:
  - A. Phenantrenisoquinoline;
  - B. Tropan;
  - C. Benzdiazepine;
  - D. Piperidine;
  - E. Furan.
- 2. Codeine is used as an antitussive. The starting material for its synthesis is:
  - A. Morphine;
  - B. Paracetamol;
  - C. Pyrocatechin;
  - D. Nitrofural;
  - E. Caffeine.
- 3. Metabolism of morphine is carried out mainly in the liver. The main way of its metabolism is:
  - A. Glucuronidation;
  - B. Hydrolysis;
  - C. Restoration;
  - D. Halogenation;
  - E. Decarboxylation.
- 4. Due to the presence of a tertiary nitrogen atom, morphine forms sparingly soluble products when interacting with general alkaloid precipitation reagents. With which solution will it form a precipitate:

- A. Potassium tetraiodbismuthate; B. Ammonium oxalate; C. Calcium chloride; D. Formaldehyde; E. Potassium pyroantimonate. 5. A pharmacist-analyst performs the identification of morphine hydrochloride. Due to the presence of phenolic hydroxyl, morphine forms a colored product with a solution: A. Iron (III) chloride; B. Hydrochloric acid; C. Picric acid; D. Formaldehyde; E. Potassium pyroantimonate. 6. Morphine is an optically active substance. With which device does the pharmacist-analyst measure the angle of rotation of the morphine hydrochloride solution? A. Polarimeter: B. Refractometer; C. Potentiometer: D. Areometer: E. Spectrophotometer.
- 7. In medical practice, morphine is used in the form of hydrochloride. What solution is used to identify chlorides:
  - A. Silver nitrate;
  - B. Potassium iodide:
  - C. Sodium chloride;
  - D. Calcium phosphate;
  - E. Magnesium hydroxide.

- 8. Morphine undergoes an azo coupling reaction with the formation of an azo dye. What functional group ensures the course of this reaction?
  - A. Phenolic hydroxyl;
  - B. Aldehyde group;
  - C. Alcoholic hydroxyl;
  - D. Carboxylic group;
  - E. Ester group.
- 9. Quantitative determination of morphine hydrochloride is carried out by the method of acidimetry in a non-aqueous medium in the presence of mercury (II) acetate. How is the solution used as a titrant?
  - A. Chloric acid;
  - B. Sodium hydroxide;
  - C. Potassium permanganate;
  - D. Sodium nitrite:
  - E. Silver nitrate.
- 10. Codeine for medical purposes can be obtained semisynthetically from a plant alkaloid. Choose this alkaloid:
  - A. Morphine;
  - B. Papaverine;
  - C. berberine;
  - D. Protopin;
  - E. Helidonin.
  - 4. Individual tasks for students of higher education on the topic:
- 1) Metabolic transformations of phenanthrene. Activity of metabolites. Dose-effect relationship.
- 2) Ways of improving the pharmaceutical analysis of narcotic analgesics derived from phenanthrenisophenol.
- 3) Metabolic transformations of codeine phosphate. Activity of metabolites. Dose-effect relationship.

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#### **Additional:**

- 1. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2015. Т. 1. 1128 с.
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### Independent work No. 20

**Topic:** Sleep aids. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine.

**Goal:** Acquainted with the peculiarities of the pharmaceutical analysis of hypnotic drugs.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

#### Plan

### 1. Theoretical questions:

- 1) Quantitative analysis of sodium thiopental.
- 2) Quantitative analysis of phenobarbital.
- 3) Qualitative analysis of hexanal.
- 4) Qualitative analysis of ethaminal-sodium.
- 5) Ways of metabolism of bromisoval.
- 6) Ways of metabolism of chloral hydrate.

#### **Questions for self-control:**

- 1) The Kjeldahl method.
- 2) Determination of the melting point of organic bases.

Methodical development to independent work of the student from educational discipline, EPP "Pharmacy, Industrial Pharmacy", 3<sup>rd</sup> year, Faculty of Pharmacy, Discipline: "Pharmaceutical Chemistry" p. 110

- 3) Qualitative reactions to sodium ions.
- 4) General precipitation alkaloid reagents.
- 5) Conditions for the formation of picrates.

### **Indicative tasks for processing theoretical material:**

Compile a dictionary of basic concepts on the topic.

### 2. Practical works (tasks) to be performed:

The task 1. Calculate the barbital content (M. m. 184.20), if 8.0 ml of 0.1 N sodium hydroxide solution was used for the titration of an exact weight of 0.1516 g (CP = 1.0022).

The task 2. Calculate the content of free alkali (m.m. NaOH 40.00) in sodium barbital, if 0.6 ml of a 0.05 N hydrochloric acid solution was used for its determination (KP = 0.9986).

The task 3. Calculate the percentage content of ethaminal-sodium (M, m. 248.26), if 18.4 ml of 0.1 M hydrochloric acid (KP = 1.0012) was used for the titration of an exact measurement of 0.4786 g. The content of free alkali is 0.28%, the loss in mass during drying is 2.3%.

#### 3. Test tasks for self-control:

- 1. Quantitative determination of the substance "Phenobarbital" is carried out by the method of alkalimetry in a non-aqueous environment. What reagent is used as a solvent?
  - A. Dimethylformamide;
  - B. Glacial acetic acid;
  - C. Acetic anhydride;
  - D. Formic acid;
  - E. Ethanol.

- 2. The drug "Phenobarbital" belongs to acid forms of barbiturates. This allows the pharmacist-analyst to carry out its quantitative determination by the method:
  - A. Alkalimetry in a non-aqueous environment;
  - B. Acidimetry in a non-aqueous environment;
  - C. Reverse iodometry;
  - D. Reverse cerimetry;
  - E. Direct bromatometry.
- 3. At a chemical and pharmaceutical enterprise, a drug that depresses the central nervous system is synthesized by condensation of phenylethylmalonic ether with urea. Name this medicine:
  - A. Phenobarbital;
  - B. Triazolam;
  - C. Barbital;
  - D. Nicotinic acid;
  - E. Ascorbic acid.
- 4. A general pharmacopoeial reaction is used to identify hypnotics derived from barbituric acid. For the formation of colored complex compounds, a solution is used:
  - A. Cobalt nitrate:
  - B. Sodium nitrite;
  - C. Potassium iodide;
  - D. Sodium bromide:
  - E. Ammonium chloride.
- 5. The quantitative content of phenobarbital is determined by a chemist-analyst by the method of alkalimetry. What titrated solution does he use?
  - A. sodium hydroxide;
  - B. potassium bromate;
  - C. silver nitrate:

	D. sodium edetate;
	E. cerium sulfate.
6.	A positive "silver mirror" reaction indicates the presence of chloral hydrate in
	the structure:
	A. Aldehyde group;
	B. Complex ester group;
	C. Amide group;
	D. Carboxylic group;
	E. Nitro groups.
7.	What compound is synthesized by the reaction between malonic acid diethyl
	ether and urea?
	A. Barbituric acid;
	B. Benzoic acid;
	C. Uric acid;
	D. Nicotinic acid;
	E. Ascorbic acid.
8.	Which medicinal substance from the group of barbiturates corresponds to the
	chemical name 1-benzoyl-5-ethyl-5-phenylbarbituric acid?
	A. Benzonal;
	B. Barbital;
	C. Phenobarbital;
	D. Hexanal;
	E. Benzobamil.
9.	In which of the barbiturates can the residue of benzoic acid be identified by
	the hydroxam test?
	A. Benzonal;
	B. Barbital;
	C. Phenobarbital;
	D. Hexanal;

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- E. Sodium barbital.
- 10. The drug phenobarbital has a sedative, hypnotic and antiepileptic effect. Name its international non-proprietary name:
  - A. Luminal;
  - B. Nitrofural;
  - C. Chloramphenicol;
  - D. Diazepam;
  - E. Salol.
  - 4. Individual tasks for students of higher education on the topic:
  - 1) Paths of synthesis of hypnotic drugs derived from barbituric acid.
  - 2) Physico-chemical methods of bromisoval and chloral hydrate analysis.
- 3) Metabolic transformations of phenobarbital, barbital and sodium ethaminal. Activity of metabolites.

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# **Independent work No. 21**

**Topic:** Means for anesthesia. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine.

**Goal:** Acquainted with the peculiarities of pharmaceutical analysis of drugs for anesthesia.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

#### Plan

### 1. Theoretical questions:

- 1) Methods of synthesis of sodium thiopental.
- 2) Quantitative analysis of hexenal.
- 3) Qualitative analysis of sodium thiopental.
- 4) Qualitative analysis of hexanal.
- 5) Nitrous oxide metabolism.
- 6) Metabolism of halothane.

### **Questions for self-control:**

- 1) Determination of the melting point of organic acids.
- 2) Synthesis based on malonic ester.
- 3) Qualitative reactions to sodium ions.
- 4) Indicators in argentometry.
- 5) Argentometry. Classification. Conditions for quantitative analysis.

### **Indicative tasks for processing theoretical material:**

Compile a dictionary of basic concepts on the topic.

### 2. Practical works (tasks) to be performed:

The task 1. Determine the mass fraction (%) of phenobarbital (M.m. 232.23) in the medicinal product, if 13.02 ml of 0.1 N solution of argentum (I) nitrate was spent on the titration of a weight of 0.9850 g (KP=1.0100); the volume of the measuring flask is 50.00 ml, the volume of the pipette is 5 ml.

The task 2. Determine the weight of the thiopental sodium sample (M.m 263.32), if 19.23 ml of a 0.1 N solution of argentum (I) nitrate (KP = 0.9870) was spent on its titration. The mass fraction of sodium bromide in the medicinal product is 99.40%.

The task 3. Determine the volume of 0.1 N of argentum (I) nitrate solution (KP = 1.0008), which will be spent on the titration of 0.3145 g of hexenal (M.m 236.27), if its mass fraction in the medicinal product is 99.70%.

#### 3. Test tasks for self-control:

- 1. Barbituric acid is a stronger acid than acetic acid. This is due to:
  - A. Keto-enol tautomerism;
  - B. Lactam-lactim tautomerism;
  - C. Prototropic tautomerism;
  - D. Its cyclical structure;
  - E. The presence of two nitrogen atoms in the molecule.
- 2. The pharmacist-analyst performs the reaction of identification of barbiturates according to the SPHU by the formation of a blue-violet color with the solution:
  - A. Cobalt nitrate;
  - B. Copper sulfate;
  - C. Iron (III) chloride;
  - D. Lead nitrate;
  - E. Nickel nitrate.
- 3. When identifying the medicinal substance by reaction with copper (II) sulfate in the presence of potassium hydrogen carbonate and potassium carbonate, a blue color and a red-lilac precipitate were formed. Name this medicinal substance:
  - A. Barbital;
  - B. Antipyrine;
  - C. Ethacridine lactate;
  - D. Benzocaine:
  - E. Dibazol.
- 4. When barbital is fused with crystalline sodium hydroxide, the following is formed:
  - A. Sodium 2-ethylbutanoate;
  - B. Sodium 2-methylbutanoate;
  - C. Sodium butanoate:

- D. Sodium ethanoate;
- E. Sodium propanoate.
- 5. The chemist of VTK of the pharmaceutical enterprise conducts the alloying of the medicinal substance with sodium hydroxide. Further acidification of the reaction product leads to the release of gas (carbon dioxide) and the appearance of the characteristic smell of phenylethylacetic acid. Name this medicinal substance:
  - A. Phenobarbital;
  - B. Resorcinol;
  - C. Codeine:
  - D. Streptocide;
  - E. Phenoxymethylpenicillin.
- 6. Which of the barbiturates decolorizes bromine water?
  - A. Hexanal:
  - B. Barbital;
  - C. Phenobarbital;
  - D. Benzonal;
  - E. Sodium barbital.
- 7. Hexanal in its structure contains a double bond, which can be determined by the reaction with:
  - A. Bromine water;
  - B. Potassium iodide solution:
  - C. Barite water:
  - D. Calcium hydroxide solution;
  - E. A solution of ammonium thiocinate.
- 8. Which of the following compounds is a specific impurity in the substance sodium ethaninal?
  - A. Free meadow:
  - B. Phenylbarbituric acid;

- C. Ethylbarbituric acid;
- D. Semicarbazide;
- E. Vanillin.
- 9. Indicate which of the following medicinal products corresponds to the chemical name: 5,5-diethylbarbituric acid?
  - A. Barbital;
  - B. Phenobarbital;
  - C. Hexanal;
  - D. Benzonal;
  - E. Methyluracil.
- 10.A student of the Faculty of Pharmacy performs the identification of a medicinal product by the reaction of potassium permanganate discoloration.

  Name the medicine:
  - A. Hexanal;
  - B. Nicotinamide:
  - C. Phenobarbital;
  - D. Cordiamine:
  - E. Nicotinic acid.
  - 4. Individual tasks for students of higher education on the topic:
- 1) Ether for anesthesia. Receiving. Pharmaceutical analysis. Storage conditions and metabolism.
- 2) Metabolic transformations of sodium thiopental and sodium ethaminal. Activity of metabolites.
- 3) The effect of anesthetic agents on the human body. Metabolic transformations of anesthetic agents.

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#### **Basic:**

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- 2. Pharmaceutical Chemistry I Laboratory Experiments and Commentary / Attila Almási, Zsuzsanna Rozmer, Pál Perjési. 2014. 179 p.
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# **Independent work No. 22**

**Topic:** Psychotropic drugs. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine.

**Goal:** Acquainted with the peculiarities of pharmaceutical analysis of psychotropic drugs. Neuroleptics. Antidepressants.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

#### Plan

- 1. Theoretical questions:
- 1) Methods of obtaining chlorpromazine hydrochloride.
- 2) Qualitative analysis of diprazine.
- 3) Quantitative analysis of tryftazine.
- 4) Quantitative determination of propazine.
- 5) Metabolism of stageperazine. Activity of metabolites.
- 6) Ethmosin metabolism. Activity of metabolites.

### **Questions for self-control:**

- 1) Qualitative reactions to chloride ions.
- 2) Qualitative reactions to sulfate ions.
- 3) Mineralization. Methods. Conditions of conduct.
- 4) General precipitation alkaloid reagents.
- 5) Chromatographic methods of analysis.

# **Indicative tasks for processing theoretical material:**

- Compile a dictionary of basic concepts on the topic.

### 2. Practical works (tasks) to be performed:

The task 1. Determine the weight of a sample of chlorprothixene (M.m. 315.96), if 22.42 ml of 0.1 N sodium hydroxide solution (KP = 1.1148) was spent on its titration by the method of direct alkalimetry, and its mass percentage in the medicinal product is 99,70%.

The task 2. Determine the volume of 0.1 N perchloric acid solution (KP=1.0023), which will be spent on the titration of 0.1487 g of stageperazine (M.m. 403.97), if the mass fraction of ftivazide in the medicinal product is 99.15%.

The task 3. Determine the mass fraction of propazine (M.m. 284.42) in the medicinal product, if 7.42 ml of 0.1 N perchloric acid solution was spent on the titration of 0.4990 g of atropine sulfate (KP = 0.9982).

#### 3. Test tasks for self-control:

- 1. Biologically active substances are obtained by chemical synthesis. The reaction of 1-chloro-3-(2-chloro-10H-phenothiazin-10-yl)-propane with dimethylamine gives:
  - A. chlorpromazine;
  - B. Diphenhydramine;
  - C. Aceclidine:
  - D. Phenobarbital;
  - E. Caffeine.
- 2. Phenothiazine derivatives can be oxidized with the formation of colored products. What reagent is used for this reaction?
  - A. bromine water;
  - B. ammonium chloride;
  - C. magnesium sulfate;
  - D. sodium hydroxide;

- E. acetic acid.
- 3. Promethazine hydrochloride belongs to the antihistamines of the first generation. What condensed heterocycle is the basis of the chemical structure of this medicinal substance?
  - A. Phenothiazine;
  - B. Purine;
  - C. Indole;
  - D. Quinoline;
  - E. Acridine.
- 4. A medicinal product, the active ingredient of which has the chemical name 2-chloro-10-(3'-dimethylaminopropyl)-phenothiazine hydrochloride, was sent to a private pharmacy for sale. Specify this medicine:
  - A. Chlorpromazine hydrochloride;
  - B. Promethazine hydrochloride;
  - C. Trifluoroperazine hydrochloride;
  - D. Clonidine hydrochloride;
  - E. Diphenhydramine hydrochloride.
- 5. Which of the following compounds is the starting material for the synthesis of chlorpromazine. hydrochloride?
  - A. 2-chlorophenothiazine;
  - B. 4-chlorophenothiazine;
  - C. 3-chlorophenothiazine;
  - D. 5-chlorophenothiazine;
  - E. 6-chlorophenothiazine.
- 6. The substance chlorpromazine hydrochloride was obtained for analysis. What condensed heterocycle is the basis of the chemical structure of this medicinal substance?
  - A. Phenothiazine;
  - B. Purine:

- C. Acridine;
- D. Indole;
- E. Benzothiazine.
- 7. Due to the presence of a Sulfur atom, phenothiazine derivatives are easily oxidized. What reagent does the SPHU recommend for the identification of the promethazine hydrochloride substance for its oxidation??
  - A. Concentrated nitric acid;
  - B. Hydrogen peroxide;
  - C. Sodium nitrite;
  - D. Iron (III) chloride;
  - E. Potassium permanganate.
- 8. The method of thin-layer chromatography is used to detect aminazine. What reagents do not show aminazine on a chromatogram:
  - A. A solution of diphenylcarbazide in chloroform;
  - B. Ferrum (III) chloride solution;
  - C. Dragendorf's reagent;
  - D. Mark's reagent;
  - E. Iodine vapors.
- 9. The studied extract from biological material contains a substance of a basic nature. For which substance is the Vitaly-Moren reaction not characteristic?
  - A. Aminazine;
  - B. Diprazine;
  - C. Dikain;
  - D. Strychnine;
  - E. Atropine.
- 10. The liver of a corpse with suspicion of aminazine poisoning was submitted for examination. In order to exclude phenothiazine derivatives in the Forensic Toxicological Analysis Plan, it is necessary to conduct a preliminary test that would be positive with:

- A. FNN reagent;
- B. Bromine water;
- C. Nitric acid;
- D. 5% KMnO4 solution;
- E. Bouchard's reagent.

## 4. Individual tasks for students of higher education on the topic:

- 1) Paths of synthesis of phenothiazine derivatives.
- 2) Pharmaceutical analysis and metabolism of haloperidol.
- 3) Metabolic transformations of imizin, nialamide and amitriptyline.
- 5. References:

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## Independent work No. 23

**Topic:** Psychotropic drugs. Part 2. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine.

**Goal:** Acquainted with the peculiarities of the pharmaceutical analysis of tranquilizers.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

### Plan

# 1. Theoretical questions:

- 1) Methods of obtaining phenazepam.
- 2) Qualitative analysis of nitrazepam.

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- 3) Quantitative analysis of clozepd.
- 4) Metabolism of oxazepam.
- 5) Qualitative analysis of diazepam.
- 6) Quantitative analysis of nitrazepam.

### **Questions for self-control:**

- 1) Qualitative analysis for chloride ions.
- 2) General precipitation alkaloid reagents.
- 3) UV spectroscopy of fluorescent compounds.
- 4) Dianitrogenation methods.
- 5) Mineralization by the Kjeldahl method.

## Indicative tasks for processing theoretical material:

- Compile a dictionary of basic concepts on the topic.

### 2. Practical works (tasks) to be performed:

The task 1. Determine the volume of 0.1 N perchloric acid solution (KP = 1.0125), which will be spent on titration of 0.1506 g of nitrazepam (M.m. anhydrous 281.3), if the percent content of ftivazide in the medicinal product is -98, 80%.

The task 2. Determine the weight of the phenazepam sample (M.m. 349.61), if 8.55 ml of 0.1 N perchloric acid solution (KP = 0.9886) was spent on its titration. The percentage content of papaverine hydrochloride in the medicinal product is 99.60%.

The task 3. Determine the mass fraction of diazepam (M.w. 284.7) in the medicinal product, if 7.42 ml of 0.1 N perchloric acid solution was spent on the titration of a weight of 0.4990 g of atropine sulfate (KP = 0.9982).

#### 3. Test tasks for self-control:

1. To identify drugs that are benzodiazepine derivatives according to the SPHU, the formation reaction is used (after preliminary acid hydrolysis):

A. azo dye;

- B. auric dye; C. indophenol dye; D. azomethine dye; E. polymethine dye. 2. The drug sibazon has a tranquilizing (calming) effect. Name its international name: A. diazepam; B. nitrazepam; C. oxazepam; D. nosepam; E. phenazepam 3. To identify diazepam in accordance with the requirements of the SPHU, the pharmacist-analyst uses the following reaction: 80 mg of the substance is placed in a porcelain crucible, 0.3 g of anhydrous sodium carbonate P is added and heated over an open flame for 10 minutes. After cooling, the obtained residue is dissolved in 5 ml of dilute nitric acid P and filtered. 1 ml of water P is added to 1 ml of filtrate, the solution gives a reaction to: A. chlorides; B. sulfates: C. carbonates: D. bromides: E. nitrates 4. Nitrazepam belongs to benzodiazepine derivatives. Identification of A. optical density;
  - nitrazepam is carried out by spectrophotometry. At the same time, measure:
    - B. rotation angle;
    - C. refractive index:
    - D. melting point;
    - E. dynamic viscosity.

- 5. Diazepam belongs to benzodiazepine derivatives with a tranquilizing effect.
  As a result of its biotransformation at the stage of functionalization, an active metabolite is formed:

  A. Oxazepam;
  B. Phenobarbital;
  C. Chlorpromazine;
  D. Paracetamol;
  E. Diphenhydramine.

  6. In the CZL behavetery, when certifying diazeners, the quantitative centent is
- 6. In the CZL laboratory, when certifying diazepam, the quantitative content is determined by the method of acidimetry in a non-aqueous environment. Titration is carried out with a solution:
  - A. perchloric acid;
  - B. potassium bromate;
  - C. silver nitrate;
  - D. sodium edetate;
  - E. cerium sulfate.
- 7. The analytical chemist determines the aromatic nitro group in the studied sample of nitrazepam after preliminary reduction to the amino group. The final product of this reaction is:
  - A. Azo dye;
  - B. Murexid;
  - C. Taleioquinine;
  - D. Indophenol;
  - E. Thiochrome.
- 8. Oxazepam belongs to benzodiazepine derivatives. What method is used for its quantitative determination?
  - A. acidimetry in a non-aqueous medium;
  - B. reverse complexonometry;
  - C. alkalimetry by substitute;

- D. direct bromatometry;
- E. alkalimetry in an aqueous medium.
- 9. 2-Aminobenzophenones are formed in the process of biotransformation:
  - A. 1,4-benzdiazepines;
  - B. Phenothiazines;
  - C. Barbiturates:
  - D. Butyrophenonov;
  - E. Opiates
- 10. When analyzing the chloroform extract obtained after the isolation of 1,4-benzodiazepine derivatives, the reaction with  $\beta$ -naphthol gave an orange coloration. Which compound enters into the reaction of the formation of an azo dye:
  - A. Aminobenzophenone;
  - B. Methylaminobenzophenone;
  - C. Oxazepam;
  - D. Nitrazepam;
  - E. Diazepam.
  - 4. Individual tasks for students of higher education on the topic:
  - 1) Metabolic transformations of benzodiazepines. Activity of metabolites.
  - 2) Paths of synthesis, pharmaceutical analysis and metabolism of amysil.
- 3) Paths of synthesis, pharmaceutical analysis and metabolism of chlordiazepoxide.

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#### **Basic:**

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- 8. Europian Pharmacopoeia 10<sup>th</sup>. 2019. 4255 p.

#### **Additional:**

- 1. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2015. Т. 1. 1128 с.
- 2. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2014. Т. 2. 724 с.
- 3. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2014. Т. 3. 732 с.
- 4. Фармацевтична хімія / П.О. Безуглий, В.А. Георгіянц, І.С. Гриценко, І.В. та ін.: за ред. П.О. Безуглого. Вінниця: Нова книга, 2017. 456 с.
- 5. Фармацевтична хімія. Загальна та спеціальна фармацевтична хімія. Лікарські засоби неорганічної природи: лабораторно-практичні заняття.

Навчальний посібник / Л.Г. Мішина. — Вінниця: ПП «ТД «Едельвейс і К»», 2010. - 384 с.

### Independent work No. 24

**Topic:** Psychotropic drugs. Part 3 Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine.

**Goal:** Acquainted with the peculiarities of pharmaceutical analysis of sedative drugs and psychostimulants.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

#### Plan

### 1. Theoretical questions:

- 1) Quantitative analysis of potassium bromide.
- 2) Methods of extracting sodium caffeine benzoate.
- 3) Quantitative analysis of cocaine.
- 4) Qualitative analysis of sodium bromide.
- 5) Quantitative analysis of phenamine.
- 6) Metabolism of caffeine-sodium benzoate.

### **Questions for self-control:**

- 1) Vitaly-Moren's reaction.
- 2) Qualitative reactions to potassium ions.
- 3) Qualitative reactions to bromide ions.
- 4) Qualitative reactions to sodium ions.
- 5) Murexide test.

### **Indicative tasks for processing theoretical material:**

- Compile a dictionary of basic concepts on the topic.

# 2. Practical works (tasks) to be performed:

The task 1. Determine the mass fraction of sodium benzoate (M.m. 144.11) in caffeine-sodium benzoate, if the weight of the test piece is 1.5114 g, the volume of a 0.5 N solution of hydrochloric acid (KP = 1.0022) is 12.54 ml.

The task 2. Determine the weight of sodium bromide (M.m 102.90), if 19.23 ml of 0.1 N solution of argentum(I) nitrate (KP = 0.9870) was spent on its titration. The mass fraction of sodium bromide in the medicinal product is 99.40%.

The task 3. Determine the volume of 0.1 N solution of argentum (I) nitrate (KP = 0.9968), which will be spent on titration of 10.00 ml of dilution of a mixture of 3% sodium bromide solution (M.m 102.90), volume volumetric flask - 50.00 ml, pipette volume - 5.00 ml.

#### 3. Test tasks for self-control:

- 1. The dry residue obtained after evaporation of the analyzed solution turns the colorless flame of the burner yellow, and when viewed through a blue glass purple. What cations were in the dry residue?
  - A. Na+, K+;
  - B. Na+, Sr2+;
  - C. Ca2+, K+;
  - D. Na+, Ca2+;
  - E. Li+, Ba2+.
- 2. The substance sodium caffeine benzoate is obtained at a chemical and pharmaceutical enterprise. The starting substance in the synthesis of caffeine is:
  - A. dimethylurea;
  - B. diphenylamine;
  - C. ethyl acetate;
  - D. diethyl malonate;
  - E. benzhydrol

- 3. An analytical chemist determines the presence of a sodium cation in the composition of sodium caffeine benzoate. For this, a solution is used: A. potassium pyroantimonate; B. barium chloride: C. sodium sulfate: D. silver nitrate; E. sodium cobalt nitrite. 4. A pharmacist-analyst conducts an express analysis of a sedative mixture with sodium bromide. Quantitative determination of sodium bromide is carried out by the method: A. argentometry; B. complexonometry; C. alkalimetry; D. acidimetry; E. nitritometry. 5. Dosage forms containing potassium bromide are used to treat insomnia. Potassium cation can be identified by reaction with a solution: A. sodium cobaltinitrite; B. potassium pyroantimonate; C. silver nitrate: D. barium chloride; E. potassium ferrocyanide. 6. An express analysis of the mixture containing calcium chloride and sodium bromide is carried out. The summary definition of the ingredients of this dosage form can be determined: A. argentometrically;
- Methodical development to independent work of the student from educational discipline, EPP "Pharmacy, Industrial Pharmacy", 3<sup>rd</sup> year, Faculty of Pharmacy, Discipline: "Pharmaceutical Chemistry" p. 134

B. complexonometrically;

C. alkalimetrically;

D. polarimetrically;

- E. nitritometrically.
- 7. A characteristic feature of purine alkaloids is their instability when heated in an alkaline environment, which leads to the destruction of the heterocycle. In this case, caffeine turns into:
  - A. caffeine;
  - B. ninhydrin;
  - C. theophylidine;
  - D. benzhydrol;
  - E. aminophenol.
- 8. The substance sodium caffeine benzoate is obtained at a chemical and pharmaceutical enterprise. The starting substance in the synthesis of caffeine is:
  - A. dimethylurea;
  - B. diphenylamine;
  - C. ethyl acetate;
  - D. diethyl malonate;
  - E. benzhydrol
- 9. The chemical structure of caffeine is trimethylxanthine. The main way of its metabolism is:
  - A. N-demethylation;
  - B. hydrolysis;
  - C. oxidation;
  - D. restoration:
  - E. acetylation.
- 10.A chemist-analyst performs quantitative determination of caffeine by the method of iodometry. As an indicator, he uses a solution:
  - A. starch;
  - B. murexide:
  - C. phenolphthalein;

- D. ferroin;
- E. tropeolin 00.

## 4. Individual tasks for students of higher education on the topic:

- 1) Paths of synthesis, pharmaceutical analysis and metabolism of phenamine.
  - 2) Paths of synthesis, pharmaceutical analysis and metabolism of pyridrol.
- 3) Synthesis pathways, pharmaceutical analysis and metabolism of cocaine hydrochloride.

### 5. References:

#### **Basic:**

- Handbook of pharmaceutical chemictry Vol. 117 / L. Ohannesian, Antony J.
   Streeter. 2016. 582 p.
- Pharmaceutical Chemistry I Laboratory Experiments and Commentary / Attila Almási, Zsuzsanna Rozmer, Pál Perjési. 2014. – 179 p.
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- 8. Europian Pharmacopoeia 10<sup>th</sup>. 2019. 4255 p.

#### **Additional:**

1. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». — 2-е вид. — X. :

- Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2015. Т. 1. 1128 с.
- 2. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2014. Т. 2. 724 с.
- 3. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2014. Т. 3. 732 с.
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- 5. Фармацевтична хімія. Загальна та спеціальна фармацевтична хімія. Лікарські засоби неорганічної природи: лабораторно-практичні заняття. Навчальний посібник / Л.Г. Мішина. Вінниця: ПП «ТД «Едельвейс і К»», 2010. 384 с.

## Independent work No. 25

**Topic:** Anticonvulsant and antiepileptic drugs. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine.

**Goal:** Acquainted with the peculiarities of pharmaceutical analysis of anticonvulsant and antiepileptic drugs.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

#### Plan

# 1. Theoretical questions:

- 1) Qualitative analysis of sodium valproate.
- 2) Qualitative analysis of hexamidine.

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- 3) Metabolism of phenobarbital.
- 4) Quantitative analysis of clonazepam.
- 5) Qualitative analysis of phenobarbital.
- 6) Metabolism of carbamazepine.

### **Ouestions for self-control:**

- 1) Determination of the melting point of picrates.
- 2) Qualitative reactions to sodium ions.
- 3) Hydraxam test.
- 4) Synthesis based on malonic ester.
- 5) General precipitation alkaloid reagents.

### **Indicative tasks for processing theoretical material:**

Compile a dictionary of basic concepts on the topic.

### 2. Practical works (tasks) to be performed:

The task 1. Determine the volume of 0.1 N perchloric acid solution (KP = 1.0125), which will be spent on the titration of 0.1506 g of clonazepam (M.m. 315.71), if the percent content of ftivazide in the medicinal product is -98.80 %.

The task 2. Determine the weight of papaverine hydrochloride (M.m. 375.86), if 8.55 ml of 0.1 M perchloric acid solution (CP = 0.9886) was spent on its titration. The percentage content of papaverine hydrochloride in the medicinal product is 99.60%.

The task 3. Determine the mass fraction of sodium valproate (M.m. 166.2) in the medicinal product, if 7.42 ml of 0.1 N perchloric acid solution was spent on the titration of 0.4990 g of atropine sulfate (KP = 0.9982).

#### 3. Test tasks for self-control:

1. Quantitative determination of the substance "Phenobarbital" is carried out by the method of alkalimetry in a non-aqueous environment. What reagent is used as a solvent?

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	A. dimethylformamide;
	B. glacial acetic acid;
	C. acetic anhydride;
	D. formic acid;
	E. ethanol.
2.	The drug "Phenobarbital" belongs to acid forms of barbiturates. This allows
	the pharmacist-analyst to carry out its quantitative determination by the
	method:
	A. alkalimetry in a non-aqueous medium;
	B. acidimetry in a non-aqueous medium;
	C. reverse iodometry;
	D. reverse cerimetry;
	E. direct bromatometry.
3.	At a chemical and pharmaceutical enterprise, a drug that depresses the central
	nervous system is synthesized by condensation of phenylethylmalonic ether
	with urea. Name this medicine:
	A. phenobarbital;
	B. triazolam;
	C. barbital;
	D. nicotinic acid;
	E. ascorbic acid.
4.	The quantitative content of phenobarbital is determined by a chemist-analyst
	by the method of alkalimetry. What titrated solution does he use?
	A. sodium hydroxide;
	B. potassium bromate;
	C. silver nitrate;
	D. sodium edetate:

E. cerium sulfate.

5.	Which medicinal substance from the group of barbiturates corresponds to the
	chemical name 1-benzoyl-5-ethyl-5-phenylbarbituric acid:
	A. benzonal;
	B. barbital;
	C. phenobarbital;
	D. hexanal;
	E. benzobamil
6.	The drug phenobarbital has a sedative, hypnotic and antiepileptic effect. Name
	its international non-proprietary name:
	A. luminal;
	B. nitrofural;
	C. chloramphenicol;
	D. diazepam;
	E. salol
7.	In which of the barbiturates can the residue of benzoic acid be identified by
	the hydroxam test?
	A. benzonal;
	B. barbital;
	C. phenobarbital;
	D. hexanal;
	E. sodium barbital.
8.	The chemist of VTK of the pharmaceutical enterprise conducts the alloying
	of the medicinal substance with sodium hydroxide. Further acidification of
	the reaction product leads to the release of gas (carbon dioxide) and the
	appearance of the characteristic smell of phenylethylacetic acid. Name this
	medicinal substance:
	A. phenobarbital;
	B. resorcinol;
	C. codeine;

- D. streptocide;
- E. phenoxymethylpenicillin.
- 9. Which of the barbiturates decolorizes bromine water?
  - A. hexanal:
  - B. barbital;
  - C. phenobarbital;
  - D. benzonal;
  - E. sodium barbital.
- 10.Hexanal in its structure contains a double bond, which can be determined by the reaction with:
  - A. bromine water;
  - B. potassium iodide solution;
  - C. barite water;
  - D. calcium hydroxide solution;
  - E. ammonium thiocinate solution.
  - 4. Individual tasks for students of higher education on the topic:
- 1) Paths of synthesis, pharmaceutical analysis and metabolism of carbamazepine.
- 2) Synthesis pathways, pharmaceutical analysis and metabolism of sodium valproate.
  - 3) The "structure-effect" relationship of the medicinal product Difenin.
  - 5. References:

### **Basic:**

- Handbook of pharmaceutical chemictry Vol. 117 / L. Ohannesian, Antony J.
   Streeter. 2016. 582 p.
- Pharmaceutical Chemistry I Laboratory Experiments and Commentary / Attila Almási, Zsuzsanna Rozmer, Pál Perjési. 2014. – 179 p.
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- 8. Europian Pharmacopoeia 10<sup>th</sup>. 2019. 4255 p.

### **Additional:**

- 1. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2015. Т. 1. 1128 с.
- 2. Державна Фармакопея України : в 3 т. / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. Х. : Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів», 2014. Т. 2. 724 с.
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# Independent work No. 26

**Topic:** Means for the treatment of parkinsonism. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine.

**Goal:** Acquainted with the peculiarities of pharmaceutical analysis of drugs for the treatment of parkinsonism.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

#### Plan

### 1. Theoretical questions:

- 1) Methods of obtaining levodopa.
- 2) Quantitative analysis of cyclodol.
- 3) Qualitative analysis of levodopa.
- 4) Quantitative analysis of selegiline hydrochloride.
- 5) Cyclodol metabolism.
- 6) Bromocriptine metabolism.

## **Questions for self-control:**

- 1) Qualitative reactions to the triple boundary bond.
- 2) Qualitative reactions to phenolic hydroxyl.
- 3) Qualitative reactions to bromide ions.
- 4) Mineralization.
- 5) Chromatographic methods of analysis of medicinal substances.

# Indicative tasks for processing theoretical material:

- Compile a dictionary of basic concepts on the topic.

# 2. Practical works (tasks) to be performed:

The task 1. Determine the mass fraction of cyclodol (M.m. 397.36) in the

medicinal product, if 6.19 ml of 0.1 N perchloric acid solution (KP=0.9916) was spent on the titration of a weight of 0.2517 g.

The task 2. Determine the mass fraction of selegiline hydrochloride (M.m. 287.28), if 7.73 ml of a 0.1 N perchloric acid solution (KP - 1.0165) was spent on the titration of a weight of 0.1536 g of caffeine.

The task 3. Determine the volume of 0.1 N perchloric acid solution (KP = 1.0125), which will be spent on the titration of 0.1506 g of levodopa (M.m. 197.18), if the percent content of ftivazide in the medicinal product is -98.80 %.

#### 3. Test tasks for self-control:

- 1. Quantitative determination of the substance "Phenobarbital" is carried out by the method of alkalimetry in a non-aqueous environment. What reagent is used as a solvent?
  - A. dimethylformamide;
  - B. glacial acetic acid;
  - C. acetic anhydride;
  - D. formic acid;
  - E. ethanol.
- 2. The drug "Phenobarbital" belongs to acid forms of barbiturates. This allows the pharmacist-analyst to carry out its quantitative determination by the method:
  - A. alkalimetry in a non-aqueous medium;
  - B. acidimetry in a non-aqueous medium;
  - C. reverse iodometry;
  - D. reverse cerimetry;
  - E. direct bromatometry.
- 3. At a chemical and pharmaceutical enterprise, a drug that depresses the central nervous system is synthesized by condensation of phenylethylmalonic ether with urea. Name this medicine:

### A. phenobarbital;

	B. triazolam;
	C. barbital;
	D. nicotinic acid;
	E. ascorbic acid.
4.	The quantitative content of phenobarbital is determined by a chemist-analyst
	by the method of alkalimetry. What titrated solution does he use?
	A. sodium hydroxide;
	B. potassium bromate;
	C. silver nitrate;
	D. sodium edetate;
	E. cerium sulfate.
5.	Which medicinal substance from the group of barbiturates corresponds to the
	chemical name 1-benzoyl-5-ethyl-5-phenylbarbituric acid:
	A. benzonal;
	B. barbital;
	C. phenobarbital;
	D. hexanal;
	E. benzobamil
6.	The drug phenobarbital has a sedative, hypnotic and antiepileptic effect. Name
	its international non-proprietary name:
	A. luminal;
	B. nitrofural;
	C. chloramphenicol;
	D. diazepam;
	E. salol
7.	In which of the barbiturates can the residue of benzoic acid be identified by
	the hydroxam test?
	A. benzonal;
	B. barbital;

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- C. phenobarbital;
- D. hexanal;
- E. sodium barbital.
- 8. The chemist of VTK of the pharmaceutical enterprise conducts the alloying of the medicinal substance with sodium hydroxide. Further acidification of the reaction product leads to the release of gas (carbon dioxide) and the appearance of the characteristic smell of phenylethylacetic acid. Name this medicinal substance:
  - A. phenobarbital;
  - B. resorcinol;
  - C. codeine;
  - D. streptocide;
  - E. phenoxymethylpenicillin.
- 9. Which of the barbiturates decolorizes bromine water?
  - A. hexanal;
  - B. barbital;
  - C. phenobarbital;
  - D. benzonal;
  - E. sodium barbital.
- 10.Hexanal in its structure contains a double bond, which can be determined by the reaction with:
  - A. bromine water;
  - B. potassium iodide solution;
  - C. barite water;
  - D. calcium hydroxide solution;
  - E. ammonium thiocinate solution.
  - 4. Individual tasks for students of higher education on the topic:
- 1) Synthesis routes, pharmaceutical analysis and metabolism of bromocriptine.

- 2) The mechanism of receptor action of means for the treatment of parkinsonism.
- 3) "Structure-pharmacological effect" relationship in the medicinal product Tsiklodol.

### 5. References:

### **Basic:**

- 1. Handbook of pharmaceutical chemictry Vol. 117 / L. Ohannesian, Antony J. Streeter. 2016. 582 p.
- 2. Pharmaceutical Chemistry I Laboratory Experiments and Commentary / Attila Almási, Zsuzsanna Rozmer, Pál Perjési. 2014. 179 p.
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## **Additional:**

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## **Independent work No. 27**

**Topic:** Emetics and antiemetics. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine.

**Goal:** Acquainted with the peculiarities of pharmaceutical analysis of emetic and antiemetic medicinal substances.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

### Plan

# 1. Theoretical questions:

- 1) Methods of obtaining tryftazine.
- 2) Quantitative analysis of diprase.
- 3) Qualitative analysis of scopolamine hydrobromide.
- 4) Quantitative analysis of copper sulfate.
- 5) Metabolism of copper sulfate.
- 6) Metabolism of stageperazine.

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# **Questions for self-control:**

- 1) Qualitative reactions to heavy metals.
- 2) Vitaly-Moren's reaction.
- 3) Qualitative reactions to bromide ions.
- 4) Qualitative reactions to sulfate ions.
- 5) Complexometric titration.

## **Indicative tasks for processing theoretical material:**

- Compile a dictionary of basic concepts on the topic.

# 2. Practical works (tasks) to be performed:

The task 1. Determine the volume of 0.05 N of Trilon B solution (CP = 1.1245), which will be spent on the titration of a weight of 0.2152 g of zinc sulfate (M.m. 287.54), if its percentage content in the medicinal product is 99 .85%.

The task 2. Determine the weight of the zinc sulfate test (M.m. 287.54), if 20.72 ml of 0.05 N trilon B solution (KP = 1.0912) was spent on its titration. The mass fraction of zinc sulfate heptahydrate in the medicinal product is 99.85%.

The task 3. Determine the mass fraction (%) of zinc sulfate (M.m. 287.54) in eye drops, if 0.34 ml of 0.05 N Trilon B solution was spent on the titration of 2.00 ml of zinc sulfate heptahydrate solution (KP = 1.0308).

### 3. Test tasks for self-control:

- 1. A pharmacist-analyst performs an express analysis of eye drops containing zinc sulfate. He identifies the zinc cation by reacting it with a solution:
  - A. potassium ferrocyanide;
  - B. sodium chloride;
  - C. potassium permanganate;
  - D. sodium nitrite;
  - E. ammonium oxalate.

- 2. A pharmacist-analyst performs an express analysis of eye drops containing zinc sulfate. He identifies sulfates by reacting with a solution: A. barium chloride; B. ammonium oxalate: C. potassium nitrate; D. sodium nitrite; E. iron (III) chloride. 3. An express analysis of eye drops containing zinc sulfate and boric acid is carried out. The quantitative content of zinc sulfate in this dosage form can be determined by the method: A. complexonometry; B. alkalimetry; C. cerimetry; D. polarimetry; E. nitritometry. 4. The Vitaly-Moren reaction is used for the qualitative detection of some poisonous substances. What substances is this reaction used to detect? A. Strychnine, atropine, scopolamine; B. Morphine, codeine, dionine; C. Pachycarpine, nicotine, anabazin; D. Quinine, quinidine, cinchonine; E. Diprazine, Diazolin, Aminazine. 5. Poisoning with diprazine (a phenothiazine derivative) can be established even 14 days after taking it if its main metabolite is present in the urine: A. Sulfoxide: B. Phenylpropanolamine;
- Methodical development to independent work of the student from educational discipline, EPP "Pharmacy, Industrial Pharmacy", 3<sup>rd</sup> year, Faculty of Pharmacy, Discipline: "Pharmaceutical Chemistry" p. 150

C. Diethylaminoethanol;

D. p-aminobenzoic acid;

E. p-aminophenol.

- 6. When describing the internal organs, a blue-green substance was found in the contents of the stomach. For which substance is it necessary to conduct a chemical-toxicological study?
  - A. Copper salts;
  - B. Barium salts;
  - C. Potassium nitrate;
  - D. Sodium chloride;
  - E. Ammonium oxalate.
- 7. What reaction is used to identify copper ions?
  - A. With ammonium tetrarhodonomercuriate:
  - B. With dithizone;
  - C. With ammonium persulfate;
  - D. With thiourea;
  - E. With 8-oxyquinoline.
- 8. In the chemical and toxicological analysis, the extraction-photocolorimetric method is used for the quantitative determination of copper ions in the mineralization, which is based on the reaction of the ions of this metal with:
  - A. Lead diethyldithiocarbamate;
  - B. Dithizone:
  - C. Potassium hexacyanoferrate (II);
  - D. Ammonium tetrarhodanmercuroate;
  - E. Pyridine-rhodanide reagent.
- 9. Masking must be used during the forensic chemical examination of the mineral. What compound is released by copper ions from the mineral?
  - A. Diethyldithiocarbamate;
  - B. Dithizonate;
  - C. Tetrarhodonomercuriate;
  - D. Hexacyanoferrate;
  - E. Sulfate.

- 10. During preliminary tests, different indicator papers are used. The blue color of the indicator paper (litmus and treated with copper sulfate) indicates the presence in the biological object:
  - A. Ammonium hydroxide;
  - B. Hydrogen chloride;
  - C. Hydrogen sulfide;
  - D. Sulfuric acid;
  - E. Sodium hydroxide.

# 4. Individual tasks for students of higher education on the topic:

- 1) Paths of synthesis, pharmaceutical analysis and metabolism of tryftazine.
  - 2) Mechanism of receptor action of antiemetic drugs.
- 3) "Structure-pharmacological effect" relationship in the medicinal product Scopolamine.

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# Independent work No. 28

**Topic:** Means for the treatment of cough. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine.

Goal: Acquainted with the features of pharmaceutical analysis of antitussives.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

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### Plan

## 1. Theoretical questions:

- 1) Methods of extracting codeine phosphate.
- 2) Qualitative analysis of ethylmorphine hydrochloride.
- 3) Quantitative analysis of ethylmorphine hydrochloride.
- 4) Qualitative analysis of prenoxydiazine hydrochloride.
- 5) Metabolism of prenoxdiazine hydrochloride.
- 6) Metabolism of ethylmorphine hydrochloride.

## **Questions for self-control:**

- 1) Qualitative reactions to chloride ions.
- 2) General precipitation alkaloid reagents.
- 3) Qualitative reactions to fluoride ions.
- 4) Qualitative reactions to phenolic hydroxyl.
- 5) Analytical condensation reactions.

## **Indicative tasks for processing theoretical material:**

Compile a dictionary of basic concepts on the topic.

# 2. Practical works (tasks) to be performed:

The task 1. Determine the mass fraction of codeine phosphate (M.m. 397.36) in the medicinal product, if 6.19 ml of 0.1 N perchloric acid solution was spent on the titration of a weight of 0.2517 g (KP=0.9916).

The task 2. Determine the mass fraction of ethylmorphine hydrochloride (M.m. 313.39) in the medicinal product, if 8.1 ml of 0.1 N perchloric acid solution (KP=1.0000) was spent on the titration of a weight of 0.3110 g.

The task 3. Determine the mass of libexin (M.m. 361.48), if 10.02 ml of hydrochloric acid solution (KP = 0.9678) will be spent on its titration. The percentage content of codeine in the medicinal product is 99.40%.

#### 3. Test tasks for self-control:

1.	Codeine is used as an antitussive. The starting material for its synthesis is:
	A. morphine;
	B. paracetamol;
	C. pyrocatechin;
	D. nitrofural;
	E. caffeine.
2.	Codeine for medical purposes can be obtained semisynthetically from a plant
	alkaloid. Choose this alkaloid:
	A. Morphine;
	B. Papaverine;
	C. berberine;
	D. Protopin;
	E. Helidonin.
3.	Morphine hydrochloride, which contains phenolic hydroxyl, can be
	distinguished from codeine by the action of the reagent:
	A. FeCl3;
	B. BaCl2;
	C. HCl;
	D. NaCl;
	E. CaCl2.
4.	Which of the following reagents allows you to open the phosphate ion:
	A. Molybdenum-vanadium reagent;
	B. Barium chloride in an acidic environment;
	C. 2H solution of nitric acid;
	D. Chlorine water;
	E. Diphenylamine.
5.	In the first phase of biotransformation, xenobiotics can be oxidized, reduced,
	hydrolyzed, dealkylated, deaminated, desulfurized. What is the mechanism by
	which codeine is converted to morphine?

- A. By O-dealkylation;
- B. By N-dealkylation;
- C. By means of S-dealkylation;
- D. By means of demining;
- E. By desulfation.
- 6. A pharmacist-analyst uses a phosphate ion to identify drugs that contain phosphate:
  - A. silver nitrate solution;
  - B. ammonia solution;
  - C. mercury nitrate solution;
  - D. calcium chloride solution;
  - E. sodium hydroxide solution.
- 7. As a result of the metabolism of codeine in the body, morphine is formed. What metabolic process is the basis of this transformation?
  - A. Dealkylation;
  - B. Hydrolysis;
  - C. Oxidation;
  - D. Restoration;
  - E. Conjugation.
- 8. As the main reagent when testing for the limit content of phosphate impurities, the SPHU recommends using it:
  - A. sulfomolybdenum reagent;
  - B. copper-tartrate reagent;
  - C. thioacetamide reagent;
  - D. acetylacetone reagent;
  - E. hypophosphite reagent.
- 9. What color does codeine form when heated with a solution of concentrated sulfuric acid and iron (III) chloride and the subsequent addition of concentrated nitric acid?

- A. blue changing to red;
- B. yellow turning orange;
- C. blue fading to purple;
- D. red turning to green;
- E. green fading to black.
- 10. The pharmacist-analyst performs the analysis of the substance ethylmorphine hydrochloride. To determine water impurity using the semi-micro method in the purity test, he uses the following reagent:
  - A. Sulfuric iodine;
  - B. Biuret:
  - C. Methoxyphenylacetic acid;
  - D. Molybdenum vanadium;
  - E. Hypophosphite.

# 4. Individual tasks for students of higher education on the topic:

- 1) Synthesis pathways, pharmaceutical analysis and metabolism of codeine phosphate.
  - 2) Mechanism of receptor action of antitussives.
- 3) "Structure-pharmacological effect" relationship in the medicinal product Libeksin.

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# Independent work No. 29

**Topic:** Nootropic drugs. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine.

**Goal:** Acquainted with the peculiarities of the pharmaceutical analysis of nootropic drugs.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

## Plan

# 1. Theoretical questions:

- 1) Methods of obtaining picamilon.
- 2) Qualitative analysis of piracetam.
- 3) Quantitative analysis of glycine.
- 4) Qualitative analysis of GABA.
- 5) Metabolism of picamilon.
- 6) Metabolism of glycine.

## **Ouestions for self-control:**

- 1) General precipitation alkaloid reagents.
- 2) Qualitative reactions to sodium ions.
- 3) Qualitative reactions to the carboxyl group.
- 4) Qualitative reactions to chloride ions.
- 5) Ninhydrin test.

# **Indicative tasks for processing theoretical material:**

Compile a dictionary of basic concepts on the topic.

# 2. Practical works (tasks) to be performed:

The task 1. To determine the mass of a sample of picamilon (M.m. 230.19), if 6.62 ml of 0.1 N perchloric acid solution (KP = 0.9769) was spent on its titration.

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The percentage content of papaverine hydrochloride in the medicinal product is 99.60%.

The task 2. Determine the volume of 0.1 N perchloric acid solution (KP=1.0000), which will be spent on the titration of 0.2500 g of glycine (M.m. 70.07), if the mass fraction of ftivazide in the medicinal product 99.15%.

The task 3. Determine the mass fraction of glycine (M.m. 70.07) in the medicinal product, if 7.33 ml of 0.1 N perchloric acid solution was spent on the titration of a weight of 0.5010 g (KP=0.9916).

## 3. Test tasks for self-control:

- 1. Medicines are metabolized in several stages. The phase of drug metabolism, during which the biochemical conjugation of functional groups of the molecule with acid residues, such as glucuronic and sulfate, or glycine, occurs, is called:
  - A. conjugation phase;
  - B. functionalization phase;
  - C. secretion phase;
  - D. mitosis phase;
  - E. depolarization phase.
- 2. In the process of biotransformation in the body, nicotinamide forms a product of interaction with glycine. What type of reaction does this interaction belong to?:
  - A. conjugation;
  - B. restoration;
  - C. oxidation;
  - D. hydrolysis;
  - E. dealkylation.
- 3. A separate group of nootropics is chemically similar to gamma-aminobutyric acid. What drug is its intramolecular amide?
  - A. piracetam;

B. caffeine;
C. camphor;
D. aceclidine;
E. ampicillin
4. To identify the nootropic agent "Piracetam", a reaction is carried out, as a
result of which ammonia is released when heated. What reagent is used in this
reaction?
A. sodium hydroxide solution;
B. magnesium sulfate solution;
C. potassium thiocyanate solution;
D. barium chloride solution;
E. ammonium oxalate solution.
5. When piracetam is heated with a solution of sodium hydroxide, ammonia is
released as a result of the hydrolysis of the amide group. To detect it, use:
A. red litmus paper;
B. iodide starch paper;
C. turmeric paper;
D. mercury bromide paper;
E. silver-manganese paper.
6. Piracetam is a nootropic agent. According to the chemical classification, it belongs
to the derivatives:
A. pyrrolidone;
B. pyridine;
C. benzdiazepine;
D. furan;
E. xanthine
7. A separate group of nootropics is chemically similar to gamma-aminobutyric
acid. What drug is its intramolecular amide?

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A. piracetam;

B. caffeine;
C. camphor;
D. aceclidine;
E. ampicillin
8. When conducting a qualitative chemical analysis of the piracetam substance,
a reaction was carried out, as a result of which ammonia is released when
heated. What reagent was used in this case:
A. Sodium hydroxide solution;
B. Silver nitrate solution;
C. Cobalt nitrate solution;
D. Ammonium oxalate solution;
E. Potassium iodide solution.
9. A substance of alpha-aminobutyric acid was received in the control and
analytical laboratory. What reagent does the pharmacist-analyst use to
identify this substance?
A. ninhydrin;
B. sodium nitrate;
C. Ensol;
D. aniline;
E. calcium bromide.
10.A separate group of nootropics is chemically similar to gamma-aminobutyric
acid. What drug is its intramolecular amide?
A. piracetam;
B. aceclidine;
C. camphor;
D. caffeine;
E. ampicillin
4. Individual tasks for students of higher education on the topic:

- 1) Synthesis routes, pharmaceutical analysis and metabolism of picamilon.
  - 2) Mechanism of receptor action of nootropic drugs.
- 3) "Structure-pharmacological effect" relationship in a medicinal product gamma aminobutyric acid.

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- 8. Europian Pharmacopoeia 10<sup>th</sup>. 2019. 4255 p.

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## Independent work No. 30

**Topic:** Antihistamines. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine.

**Goal:** Acquainted with the peculiarities of the pharmaceutical analysis of antiallergic drugs.

**Basic concepts:** State Pharmacopoeia of Ukraine, qualitative analysis, quantitative analysis, pharmaceutical analysis, express analysis, monograph.

### Plan

# 1. Theoretical questions:

- 1) Why acidimetric determination (not aqueous titration) of diphenhydramine hydrochloride is carried out in the presence of mercury (II) acetate.
  - 2) Methods of obtaining diprazine.
  - 3) Qualitative analysis of chlorpyramine hydrochloride.
- 4) Quantitative analysis of chlorpyramine hydrochloride.

  Methodical development to independent work of the student from educational discipline, EPP
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- 5) Qualitative analysis of mebhydrolin.
- 6) Metabolism of diphenhydramine hydrochloride.

# **Questions for self-control:**

- 1) Conditions for formation of oxonium salts.
- 2) Determination of the melting point of picrates of organic substances.
- 3) Qualitative reactions to chloride ions.
- 4) General precipitation alkaloid reagents.
- 5) Chromatographic methods of analysis. TOP. Advantages of the method when determining medicinal substances.

# Indicative tasks for processing theoretical material:

Compile a dictionary of basic concepts on the topic.

# 2. Practical works (tasks) to be performed:

The task 1. Determine the mass of mebhydrolin (M.m. 279.37), if 10.2 ml of 0.1 N perchloric acid solution (KP = 1.0000) was spent on its titration. The percentage content of papaverine hydrochloride in the medicinal product is 99.60%.

The task 2. Calculate the content of diphenhydramine hydrochloride (M. 291.82) in the substance, if 10.49 ml of 0.1 N perchloric acid solution (KP = 1.0018) was used for the titration of a weight of 0.2976 g.

The task 3. Determine the mass fraction of chlorpyramine hydrochloride (M.m. 289.80) in the medicinal product, if 6.66 ml of 0.1 N perchloric acid solution was spent on the titration of a 0.213 g sample (KP=0.9992).

### 3. Test tasks for self-control:

1. An analytical chemist performs quantitative determination of the antihistamine diphenhydramine hydrochloride by the method of alkalimetry.

A solution is used as a titrant:

- A. sodium hydroxide;
- B. ammonium thiocyanate;

- C. sodium nitrite;
- D. silver nitrate;
- E. potassium bromate.
- 2. The process oficrosomal oxidation in the liver is an important component of drug biotransformation. Which of the following substances is oxidized with the formation of N-oxide:
  - A. diphenhydramine hydrochloride;
  - B. benzoic acid;
  - C. phenol;
  - D. vikasol;
  - E. prednisone
- 3. A VTK analyst of a pharmaceutical enterprise analyzes the substance diphenhydramine hydrochloride. To identify chloride ions, he uses a reaction with a solution:
  - A. silver nitrate;
  - B. ammonium oxalate;
  - C. barium chloride:
  - D. sodium hydroxide;
  - E. potassium iodide.
- 4. The chemical name of the active substance must be given in the registration file for the medicinal product. Enter the chemical name of the antihistamine diphenhydramine hydrochloride:
  - A. 2-(diphenylmethoxy)-N,N-dimethylethanamine hydrochloride;
  - B. (2S)-2-aminopentanedioic acid;
  - C. 5-nitro-2-furaldehyde semicarbazone;
  - D. 4-(2-aminoethyl)benzene-1,2-diol hydrochloride;
  - E. 4-butyl-1,2-diphenylpyrazolidine-3,5-dione.

- 5. A pharmacist-analyst performs a reaction to identify diphenhydramine hydrochloride (diphenhydramine). What compound is formed as a result of adding concentrated sulfuric acid to a medicinal product?
  - A. oxonium salt;
  - B. auric dye;
  - C. azo dye;
  - D. picrate;
  - E. indophenol dye.
- 6. The antihistamine "Diphenhydramine hydrochloride" is an ether. The pharmacist-analyst identifies the compound by the reaction of the formation of an oxonium salt, when adding:
  - A. concentrated sulfuric acid;
  - B. solution of hydroxylamine hydrochloride;
  - C. solution of iron (III) chloride;
  - D. dilute nitric acid;
  - E. potassium pyroantimonate solution.
- 7. The State Inspection for Quality Control of Medicinal Products conducts a quantitative analysis of the substance diphenhydramine hydrochloride. The presence of which functional group determines the possibility of titration with a solution of perchloric acid in a non-aqueous environment?
  - A. tertiary nitrogen;
  - B. phenolic hydroxyl;
  - C. carboxyl group;
  - D. alcohol hydroxyl;
  - E. aromatic amino group.
- 8. The pharmacist-analyst identifies the antihistamine "Diphenhydramine hydrochloride" by the reaction of the formation of an oxonium salt with concentrated sulfuric acid. What functional group determines the possibility of carrying out this reaction?

- A. ethereal;
- B. aldehyde;
- C. sulfamide;
- D. amide;
- E. carboxylic
- 9. The pharmacist-analyst performs the quantitative determination of the antihistamine "Diphenhydramine hydrochloride" by the method of acidimetry in a non-aqueous environment. For what purpose does he add a solution of mercury (II) acetate??
  - A. to bind chloride ions into a slightly dissociated compound;
  - B. to enhance the hydrolysis of diphenhydramine hydrochloride;
  - C. to change the density of the solution;
  - D. to create the optimal pH value of the solution;
  - E. to accelerate precipitation of diphenhydramine base.
- 10. When administered intravenously, it is forbidden to mix medicinal products, as a result of which a precipitate may form and/or bioavailability may change. The solution cannot be mixed with medicinal products that are hydrochlorides (procaine hydrochloride, diphenhydramine hydrochloride, etc.):
  - A. metamizole sodium;
  - B. atropine sulfate;
  - C. calcium chloride;
  - D. ascorbic acid;
  - E. magnesium sulfate.

# 4. Individual tasks for students of higher education on the topic:

- 1) Paths of synthesis, pharmaceutical analysis and metabolism of suprastin.
  - 2) Mechanism of receptor action of antihistamine drugs.
- 3) "Structure-pharmacological effect" relationship in the medicinal product Diprazine.

## 5. References:

## **Basic:**

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- 5. Pharmaceutical drug analysis / Addis Ababa. 2005. 554 p.
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## **Additional:**

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- 5. Фармацевтична хімія. Загальна та спеціальна фармацевтична хімія. Лікарські засоби неорганічної природи: лабораторно-практичні заняття. Навчальний посібник / Л.Г. Мішина. Вінниця: ПП «ТД «Едельвейс і К»», 2010. 384 с.