НФаУ

STANDARDIZATION OF MEDICINES

METHODOLOGICAL GUIDELINES

MINISTRY OF HEALTH OF UKRAINE
NATIONAL UNIVERSITY OF PHARMACY

STANDARDIZATION OF MEDICINES

METHODOLOGICAL GUIDELINES

for students of the educational program Pharmacy

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Methodological guidelines are created for students of the educational and professional program Pharmacy.

Methodological guidelines contain information about the subject and objectives of the educational component “Standardization of medicines”; information about the rules of work in the laboratory; a list of safety measures when working in the laboratory and methods of providing primary medical care; topic, goal, theoretical questions and questions for independent study, tasks for practical work, methodological instructions for completing the tasks, tasks for independent work and questions for self-control.

Methodological guidelines will help students in preparing for and conducting classes on the educational component “Standardization of medicines”.

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CONTENTS

List of abbreviations

API – active pharmaceutical ingredient

BAS – biologically active substances

GMP (Good manufacturing practice) – Good manufacturing practice

QCM – Quality Control Methods

SPU – State Pharmacopoeia of Ukraine

The purpose and objectives of the educational component "Standardization of medicines", its place in the educational process

Standardization covers almost all areas of the national economy and is the norm of socially necessary requirements for the quality of all types of products. It is of particular importance in relation to pharmaceutical products, since the latter are designed to guarantee the safety and effectiveness of medicines for human health. The standardization of all processes and methods guarantees the receipt of a medicinal product with standard properties, and as a result with the expected pharmacological effects and bioavailability.

"Standardization of medicines" as an educational component will provide students with systemic knowledge of the standardization of pharmaceutical processes, maintaining relevant documentation and knowledge of regulatory acts of the pharmaceutical industry and will provide practical skills in analytical support of pharmaceutical development, selection of parameters for standardization of APIs and dosage forms, as well as experimental support of standardization.

According to the program and curriculum, the educational component "Standardization of medicines" consists of one module.

General theoretical issues of the educational component "Standardization of medicines" are presented in lectures, which also consider the issue of general principles of approach to the features of standardization of pharmaceutical products and methods of their application to solve theoretical and practical problems at pharmaceutical enterprises of any subordination.

Conducting classes is provided with appropriate devices, equipment, reagents, tables, slides, etc. For each class, an appropriate methodological guidance (laboratory workshop) is provided.

The laboratory class begins with a review of theoretical material on the topic to determine the readiness of students to perform laboratory tasks, which is carried out after a conversation between the teacher and the students or a written survey. The practical part of the laboratory session involves performing laboratory experiments on

the development of methods and various tests provided for by the State Pharmacopoeia of Ukraine.

At the end of studying the course on the educational component "Standardization of medicines", students pass a semester control on the module.

These methodological guidelines are compiled with a single methodological system to assist students in preparing for laboratory classes and conducting semester control on the module.

The educational component "Standardization of medicines" should ensure that students acquire the following *general competencies*:

- the ability to apply knowledge in practical situations, make informed decisions;
- knowledge and understanding of the subject area and understanding of professional activity;
- the ability to evaluate and ensure the quality of work performed;
- the ability to conduct research at the appropriate level;

and *professional competencies*:

- the ability to use knowledge of regulatory legal acts, legislative acts of Ukraine and recommendations of good pharmaceutical practices in professional activities.
- the ability to organize and carry out quality control of medicines in accordance with the requirements of the State Pharmacopoeia of Ukraine and good practices, to determine methods of sampling for the control of medicines and to carry out their standardization in accordance with current requirements, to prevent the spread of falsified medicines;
- the ability to develop methods for quality control of medicines, including active pharmaceutical ingredients, medicinal plant raw materials and excipients using physical, chemical, physicochemical, biological, microbiological, pharmacotechnological and organoleptic control methods.

As a result of studying the educational component "Standardization of medicines", the graduate must know:

- the functioning of the standardization system for pharmaceutical products;
- state standardization of the quality of pharmaceutical preparations;
- basic principles of standardization of pharmaceutical preparations;
- use of GMP systems and the National Standard of Ukraine “Medicines. Good Manufacturing Practice for Human Medicines”;
- structure of monographs for active pharmaceutical ingredients; pharmaceutical preparations of industrial production and pharmacy production; medicinal plant raw materials and medicinal plant preparations;
- requirements of the State Pharmacopoeia of Ukraine for the development of monographs and individual tests, general requirements for the development of an analytical document for pharmaceutical preparations;
- use of physical constants, physicochemical and chemical methods in the development of standards by which the quality of pharmaceutical products is assessed;
- determination of pharmaco-technological parameters necessary for inclusion in analytical documentation depending on the dosage form;
- regulatory analytical documentation regulating the quality of medicinal preparations of industrial production and pharmacy production;
- features of standardization of medicinal preparations containing active pharmaceutical ingredients and biologically active substances of natural origin;
- methods of express-in determination of the stability of pharmaceutical preparations.

During the laboratory practicum, the graduate must be able to:

- use analytical documentation that regulates the quality of pharmaceutical preparations (State Pharmacopoeia, International Pharmacopoeia, national and regional pharmacopoeias, analytical documentation, relevant orders and instructions);
- use industry standards, methodological guidelines when developing monographs for pharmaceutical preparations of industrial production and pharmacy manufacture;
- use chemical, physical, physicochemical (instrumental) methods when developing quality indicators of pharmaceutical preparations;

• justify and select methods for analyzing pharmaceutical products when creating quality control methods;

• develop express methods for qualitative and quantitative analysis of active substances in pharmaceutical dosage forms;

• provide a qualified assessment of the quality of pharmaceutical products according to the results of the analysis.

After studying the educational component “Standardization of medicines, a student must have:

• theoretical knowledge and practical skills in the standardization of pharmaceutical products, necessary for the activities of a pharmacist in the field of standardization and quality control of pharmaceutical products;

• skills in the application of physical, physicochemical and chemical methods for the standardization of active pharmaceutical ingredients in substances and pharmaceutical products of both industrial production and pharmacy production.

Interdisciplinary knowledge necessary for mastering the educational component

Physics: understanding the physical properties of substances, methods of their measurement and analysis.

Chemistry: knowledge of the basics of general, organic and analytical chemistry, methods of identification and quantitative determination of substances.

Physical and colloidal chemistry: mastery of methods of analysis of phase equilibria, properties of solutions and mass transfer processes.

Pharmacology and pharmacotherapy: understanding of the properties of drugs, their effect on the body and the principles of interaction of active pharmaceutical ingredients.

Mathematics and statistics: skills in mathematical modeling, analysis and processing of data necessary for standardization.

Drug technology: knowledge of production processes, quality control and storage conditions of pharmaceuticals.

Law: knowledge of regulatory requirements, national and international standards in the pharmaceutical industry.

Laboratory rules of the Department of Pharmaceutical Chemistry

1. Before starting laboratory tasks, students must familiarize themselves with the rules of work in the laboratory, instructions on occupational safety and health, and the fire prevention plan.

2. Before starting the class, students on duty receive the equipment and reagents necessary for the class in the laboratory, which they are obliged to return after the end of the laboratory work.

3. Students must maintain cleanliness and order in the laboratory. Work is allowed only in a medical gown and a special hat. Only items necessary for conducting research should be on the workplace.

4. Laboratory tasks are allowed after preliminary preparation. The teacher monitors the readiness of students to perform laboratory work.

5. Spent solutions containing concentrated acids, alkalis, organic solvents, reagents with toxic substances and precious metals are poured into specially marked glasses for draining.

6. It is not allowed to take any reagents out of the laboratory and conduct additional experiments without the consent of the teacher.

7. After finishing work, it is necessary to thoroughly wash the used dishes, tidy up the workplace, turn off the water and electrical appliances.

It is necessary to remember that cleanliness, accuracy and painstaking work are the key to the successful completion of the laboratory task.

Laboratory safety precautions and first aid methods

1. When working in the laboratory, it is necessary to strictly observe all safety measures in accordance with the rules and instructions.

2. Work with concentrated acids and other substances that emit corrosive or toxic vapors, as well as with substances and solutions that have a strong unpleasant odor, is carried out under a hood.

3. All operations with diethyl ether and other flammable substances must be carried out with extreme caution away from open fire, hot surfaces, electrical and electrostatic sparks.

4. When working with harmful and toxic substances (salts of barium, mercury, lead, arsenic, copper, metallic mercury, cyanide compounds, hydrogen sulfide, etc.), it is necessary to work carefully so that they do not enter the human body. Eating food in a chemical laboratory is prohibited.

5. In case of cuts, make sure that there are no glass fragments left in the wound, treat it with iodine solution and bandage it.

6. In case of burns, it is necessary to make a compress with a tannin solution.

7. In case of skin contact with concentrated sulfuric acid, it is necessary to first wipe the affected area with a dry cotton swab or napkin. Then, rinse with plenty of water. In case of burns of the skin, mucous membranes or eyes with acids, first rinse the affected area well with water, and then with a 2% solution of sodium bicarbonate.

8. In case of burns with caustic alkalis, rinse the affected area well with water, and then with a 1% solution of acetic or citric acid.

9. In case of skin burns with phenol, bromine and similar substances, rinse the affected area with plenty of alcohol and lubricate with ointment from burns.

10. In case of poisoning with chlorine, bromine, nitrogen oxides and other similar substances, the victim must be given a swab soaked in ammonia solution to sniff, and then taken to fresh air and given milk to drink.

11. In case of severe burns, injuries and poisoning, after providing first aid, the victim must be immediately sent to the hospital.

12. The first aid kit should always contain dressings, solutions and medicines necessary for first aid.

13. In case of danger of fire, it is necessary to immediately turn off the exhaust ventilation and the power switch, warn the teacher or laboratory assistant, and take measures to eliminate the fire.

14. Small fires are covered with sand, with a fire blanket or extinguished with a fire extinguisher.

15. In the event of a fire, it is necessary to quickly and in an organized manner leave the laboratory, evacuate the victims and provide them with first aid.

In the event of an accident, contact the teacher immediately!

Laboratory journal

The results of completed laboratory tasks and theoretical study of the material are entered into the laboratory journal.

The title page of the laboratory journal should indicate: *the name of the educational component; name and surname of the student; group number, course, specialty.*

The journal should indicate the date and topic of the lesson, the purpose of the study, and calculation tasks, materials in the form of diagrams and tables for independent filling should also be provided.

For each topic, laboratory work is offered to master practical skills, which includes:

- *the name of the analysis (description of the research object);*
- *the type of control that is being carried out (qualitative, quantitative, etc.);*
- *regulatory documentation according to which the study is being conducted;*
- *research methods, reaction chemistry, calculations, observations;*
- *conclusions obtained during the study, their compliance with the specified requirements.*

TOPIC 1. Standardization in the quality assurance system of medicines. SPU as the main standard of pharmacy. The concept of validation and verification of analytical methods. Problems of quality and falsification of pharmaceuticals in Ukraine

Objective: To determine the place and role of standardization of processes, substances and analytical methods for ensuring the quality of pharmaceutical products and combating the spread of substandard and falsified products; to master modern requirements and approaches to standardization of medicines. **To get acquainted with** the current editions of the Guidelines for ensuring the quality of medicines, the SPU, the rules for establishing the quality parameters of pharmaceutical products and criteria for them, the development of methods for analytical purposes and the formation of a monograph or the International Quality Standard. **To know** the main documents regulating the procedure for standardization and quality control of pharmaceutical products, the stages of quality assurance during production, the main approaches and parameters for validating analytical methods in the process of their development, the main principles of preventing the spread of falsified products. **To be able to use** regulatory documents when planning work on standardization of medicines, to choose adequate tests for analytical support of pharmaceutical development and product standardization; to determine quality parameters, to justify and perform express analysis methods to detect potentially substandard/falsified products.

List of questions from other educational components necessary for mastering the proposed topic

1. The role of good practices in ensuring the quality of medicines.
2. The impact of GMP standards on the production processes and quality control of medicines.

Theoretical questions

1. Principles and main tasks of standardization of pharmaceutical products.
2. System of standardization of pharmaceutical products in Ukraine.
3. Main approaches and principles of modern standardization of pharmaceuticals.
4. Structure and content of the State Pharmacopoeia of Ukraine (SPU). The need to harmonize the requirements of the State Pharmacopoeia with the requirements of the European Pharmacopoeia, the US Pharmacopoeia, the British Pharmacopoeia, etc. International standards regulating the quality of medicines.
5. Development of quality standards for pharmaceutical products (monograph, quality control methods, specifications). Conclusions on the quality of a batch of a pharmaceutical product, a quality certificate for active pharmaceutical ingredients (APIs, substances), their structure, content.
6. The concept of validation and verification of analytical methods in accordance with the requirements of the State Pharmacopoeia: approaches to implementation; characteristics of the main parameters; analytical procedures subject to validation/verification, their characteristics. Statistical processing of analysis results.
7. Problems of quality and falsification of pharmaceuticals in Ukraine. Definition of the concepts of falsified pharmaceuticals, counterfeit, substandard products. National and international programs to combat the production, import, distribution and sale of falsified pharmaceuticals. Methods of detecting substandard drugs. System of organization of certification, quality control in Ukraine.

Theoretical questions for self-study

1. Requirements for the production of pharmaceuticals in Ukraine and the European Union.
2. Principles of approaches to the development of the main sections of monographs on APIs (European, American, national) and their functions.

3. Principles of the approach to the development of methods for quality control of pharmaceutical products depending on the physicochemical properties of APIs.

4. Use of information technologies in the standardization of medicines (electronic pharmacopoeias, databases, software validation, etc.).

5. Requirements for environmental safety during the production and standardization of medicines. The concept of “green chemistry”.

6. The impact of modern technologies on the processes of standardization and quality control (application of automated systems and artificial intelligence).

Tasks for practical work

For better understanding, it is recommended to conduct experimental studies:

1. For the methods of titrimetric quantitative determination of APIs proposed by the teacher, conduct statistical processing of the results of quantitative determination of the two methods to compare the results obtained. Based on them, draw a conclusion about the advantages (disadvantages) of the quantitative determination method. Calculate the uncertainty of volumetric methods and draw a conclusion about the correctness of the analytical method.

2. According to 5.3.N.2. Validation of analytical methods and tests (Appendix 2.7, vol. 2, pp. 126-241) analyze the ICH requirements for terminology and definition of validation characteristics, recommendations of the European Pharmacopoeia, technical guidance for the validation of analytical methods, recommendations of the State Pharmacopoeia of Ukraine for a standardized procedure for the validation of quantitative methods for the quality control of medicinal products.

3. For the measuring vessel proposed by the teacher, check for compliance with the maximum permissible deviation of the actual volume (5.3.N.3. Quality assurance (clause 6 Qualification of measuring vessels).

Methodological guidelines for completing the tasks

To master the methods and learn the material, the relevant articles of the SPU are offered:

- 5.3.N.1. Statistical analysis of the results of a chemical experiment (Appendix 2.7, vol. 2, pp. 35-125),
- 5.3.N.2. Validation of analytical methods and tests (Appendix 2.7, vol. 2, pp. 126-241),
- 5.3.N.3. Quality assurance (Appendix 2.7, vol. 2, pp. 242-261),
- DSTU 1.5:2015 “National standardization. Rules for the development, teaching and registration of national regulatory documents”,
- ST-N MOHU 42-3.4:2020 “Medicines. Instructions for the production of finished medicines”.

Tasks for independent work

Complete the topic “Standardization in the quality assurance system of medicines. SPU as the main standard of pharmacy. The concept of validation and verification of analytical methods. Problems of quality and falsification of pharmaceuticals in Ukraine” in the laboratory journal, complete the practical task, perform the appropriate processing of the results of the statistical experiment and draw a conclusion.

Questions for self-control

1. Normative documents of standardization depending on the object and business entity.
2. Pharmacopoeial model of standardization of requirements for pharmaceuticals.
3. Standardization of the procedure for conducting pharmacopoeial quality control of medicines.

4. Compare the requirements for standardization of pharmaceuticals in the State Pharmacopoeia of Ukraine and the European Pharmacopoeia.

5. The relationship between the State Pharmacopoeia of Ukraine and other structures regulating the quality of medicines.

6. Pharmacopoeial concept of ensuring the quality of medicines.

7. Main validation characteristics and features of their determination when conducting identification, purity tests and quantitative determination.

8. What is the difference between validation and verification of analytical methods?

9. Classification of standard samples and their role in the standardization of pharmaceutical products.

10. Develop an algorithm for checking the quality of medicines in accordance with GMP requirements.

11. Suggest approaches to detect substandard or falsified medicines.

12. What new approaches can be proposed to combat falsification of medicines?

TOPIC 2. Standardization of active pharmaceutical ingredients (substances) for pharmaceutical use

Objective: Learn to determine the list of parameters and develop methods for assessing the quality of APIs and excipients using the approaches of the SPU and ICH Guidelines. **Get acquainted with** the factors affecting the quality of substances during their production and storage, approaches to selecting methods and developing research methods used to confirm the identity, purity and quantitative determination of compounds. **Know** the basic physicochemical properties of substances and their corresponding quality parameters and tests; procedures for determining physical and physicochemical constants to confirm the identity of a compound; methods of volumetric analysis. **Be able to use** regulatory documents when standardizing substances for pharmaceutical use.

List of questions from other educational components necessary for mastering the proposed topic

1. Basic methods of synthesis of organic compounds. Reactivity of substances.
2. Establishing the dependence of the properties of organic compounds on their structure.
3. Features of identification of compounds of inorganic and organic structure.
4. Pharmacopoeial reactions of identification of cations, anions and functional groups.
5. Selection of analysis methods (chemical, physical, physicochemical, etc.) depending on the features of the structure of the substance.
6. Classification of volumetric methods of quantitative determination of a substance.
7. Classification of titrimetric methods by type of chemical reactions and by titration method.

Theoretical questions

1. Main stages of the API standardization process.
2. Requirements of the general article of the SPU “Substances for pharmaceutical use” and international standards for API standardization.
3. Modern principles and approaches (European, American, British, national) to the development of the main sections of monographs on a substance.
4. API quality specification. Certificate of conformity and its role in API standardization.
5. Selection and justification of analysis methods for standardization of pharmaceutical substances (depending on the nature and structure of the substance). Features of standardization of synthetic, biotechnological and natural APIs. Assessment of the “greenness” of the analytical methodology.

6. Use of physical, chemical and physicochemical methods of analysis for the development of tests Identification, Testing, Quantitative determination of substances for pharmaceutical use.

7. Approaches to validation of non-instrumental tests for purity and permissible limits of impurity content, identification tests.

8. Features of validation of physico-chemical methods of identification, determination of impurities and quantitative determination.

Theoretical questions for self-study

1. List of quality parameters determined by the SPU for a substance for pharmaceutical use.

2. Influence of the synthesis method, purification process and storage conditions on the quality of substances.

3. Parameters on which the choice of tests for the purity of a medicinal product depends.

4. Procedure for developing the “Accompanying impurities” test.

5. Selection of titrimetric analysis methods depending on the chemical structure of the compound.

6. Provide a general description of the physicochemical analysis methods used to determine the purity of a substance.

7. Differences between pharmacopoeial and non-pharmacopoeial substances in the context of standardization.

Tasks for practical work

For better learning of the material, it is recommended to conduct experimental studies:

1. Using the synthesis method of the compound (suggested by the teacher): substantiate its possible impurities and propose chemical and physicochemical

methods for their determination; identify residual solvents, propose methods for their determination.

2. For the API proposed by the teacher, taking into account the chemical structure, propose, substantiate and develop methods for identification and quantitative determination.

3. Determine the solubility and hygroscopicity of the API (proposed by the teacher) in accordance with the procedure given in the SPU, 5.11. Section Properties in monographs, and draw a conclusion about its quality, comparing the obtained values with the requirements of the corresponding monograph.

4. Determine the melting point of the API (suggested by the teacher) according to the procedure given in the SPU, 2.2.15 Melting point - open capillary method, and draw a conclusion about its quality, comparing the obtained values with the requirements of the relevant monograph.

5. Analyze the API (suggested by the teacher) according to the procedure given in the SPU, 2.2.1 Determination of transparency and degree of opalescence of liquids and 2.2.2 Degree of color of liquids, and draw a conclusion about its quality, comparing the obtained values with the requirements of the relevant monograph.

Methodological guidelines for completing the tasks

The following regulatory documentation is offered for the assimilation of the material:

- SPU, General monographs Substances for pharmaceutical use;
- SPU, 5.11 Section Properties in monographs;
- SPU, 2.2.1 Determination of transparency and degree of opalescence of liquids;
- SPU, 2.2.2 Degree of color of liquids;
- SPU, 2.2.15 Melting point - open capillary method;
- SPU, 2.4.24. Identification of residual solvents and control of their quantities.

Tasks for independent work

Complete the topic “Methodology of standardization of active pharmaceutical ingredients (substances) for pharmaceutical use” in the laboratory journal “Standardization of medicines”, complete the practical task.

Calculate the total uncertainty of the quantitative determination method developed in the class, carry out statistical processing of the analysis results.

Calculate the environmental friendliness indicators of the proposed methods using AGREE and GAPI software.

Questions for self-control

1. Structure of a monograph for a substance and stages of its development.
2. Melting point, distillation temperature limits, relative density as an indicator of the identity and purity of a medicinal substance.
3. Features of the structure and methods of standardization of optically active compounds.
4. Methods of determining pH and their use in the standardization of compounds.
5. The essence and advantages of volumetric methods of analysis.
6. The use of physicochemical methods in the development of quality standards for medicinal products.

TOPIC 3. Analytical support of pharmaceutical development. Modern approaches to standardization of industrially produced pharmaceuticals. Features of standardization of solid dosage forms of industrial production

Objective: To study the approaches of the SPU and the ICH and ISO Guidelines regarding the features of standardization of industrially produced pharmaceuticals. **To become familiar with** the procedure and stages of standardization of solid dosage forms of industrially produced pharmaceuticals according to the dosage form. **To know** the methods and equipment used in the standardization of industrially produced pharmaceuticals.

List of questions from other educational components necessary for mastering the proposed topic

1. Classification of solid dosage forms of industrial production.
2. Features of the technology of manufacturing solid pharmaceuticals.
3. The influence of excipients on the technology of manufacturing tablets, capsules, granules, etc.
4. List of pharmaco-technological tests necessary to substantiate the quality of the dosage form.
5. Factors affecting the bioavailability of APIs in solid dosage forms.

Theoretical questions

1. Features and general principles of pharmaceutical development of pharmaceutical products. International recommendations ICH and ISO.
2. Main stages of preparation of Module 3 Quality of the registration dossier. Main symbols for pharmaceutical development.
3. Modern approaches to standardization of finished medicines: the concept of pharmaceutical quality by design, the role of standards and regulatory documentation in the standardization of industrially produced pharmaceutical products.

4. Peculiarities of choosing physical, chemical and physicochemical methods of analysis depending on the nature and structure of APIs included in finished medicines.

5. SPU requirements for pharmaco-technological testing of solid dosage pharmaceutical products.

6. Validation and verification of methods for analyzing solid dosage forms: Quantitative determination, accompanying impurities, dissolution test.

7. SPU requirements for standardization and quality control of solid dosage forms of industrial production (tablets, granules, capsules, powders for oral and cutaneous use, powders for injections, solid vaginal and rectal medicines, solid ear medicines, medicinal chewing gums, sticks, solid nasal and oromucosal medicines).

8. Features of standardization of tablets (uncoated, coated, enteric-coated, modified-release, effervescent, soluble, dispersible tablets, orodispersible tablets; chewable tablets, oral lyophilisates), capsules (hard, soft, modified-release, enteric-coated, wafers), powders for oral and cutaneous use, granules (effervescent, coated, modified-release, enteric-coated), vaginal (pessaries, vaginal tablets, vaginal capsules, medical vaginal tampons) and rectal medicines (suppositories, capsules, powders and tablets for rectal solutions and suspensions, rectal tampons), oromucosal medicines (lozenges, pressed lozenges, sublingual tablets and buccal tablets, mucoadhesive preparations, films that disperse in the oral cavity), sticks, chewing gums (effervescent, coated, modified release, enteric), ear medicines (ear powders, ear swabs) by indicators: description, properties, tests (homogeneity of dosage units, homogeneity of content, homogeneity of mass, dissolution, disintegration, degree of dispersion, water, grinding, homogeneity of mass of doses extracted from multi-dose containers, Dissolution test for solid dosage forms or Dissolution test for solid lipophilic dosage forms, sterility, homogeneity of the delivered dose within one container, number of doses in the container), accompanying impurities, quantitative determination.

Theoretical questions for self-study

1. Justification of the choice of analysis methods for studying the pharmaco-technological parameters of solid dosage forms.

2. Pharmaco-technological parameters that are studied depending on the classification of finished solid dosage forms.

3. Analysis methods used for identification, purity testing and quantitative determination of APIs in pharmaceutical preparations.

4. Analysis methods used for pharmaco-technological testing of industrially manufactured solid pharmaceuticals.

5. Possibilities of using absorption infrared spectroscopy in the standardization of APIs in monocomponent and multicomponent pharmaceuticals. The role of near-IR spectroscopy in preventing the spread of counterfeit medicines.

Tasks for practical work

For better understanding of the material, it is recommended to conduct experimental studies:

1. For the solid dosage form proposed by the teacher (depending on its composition and purpose), substantiate the quality indicators for its standardization.

2. For the solid dosage form proposed by the teacher, determine the mass uniformity in accordance with the requirements of the SPU, 2.9.5. Mass uniformity for a dosage form of a medicinal product, calculate the average mass and calculate the deviation from the obtained value.

3. Calculate the uniformity of dosage units (DU) for tablets or capsules proposed by the teacher using the direct determination method, in accordance with the requirements of the SPU, 2.9.40. Homogeneity of dosage units. From the results obtained, determine the acceptance number and draw a conclusion about the quality of the pharmaceutical product.

4. Propose the conditions for conducting the Dissolution test of a solid dosage form of industrial manufacture: environment, time of testing and justify the method for quantitative determination of the API. Conduct the test in accordance with the SPU 2.9.3. Dissolution Test for Solid Dosage Forms using a suitable method, determine the percentage of API release and draw a conclusion about the quality of the dosage form.

Methodological guidelines for completing the tasks

The following regulatory documentation is offered for the assimilation of the material:

- SPU Tablets;
- SPU Capsules;
- SPU Powders for oral use;
- SPU Powders for cutaneous use;
- SPU Preparations for rectal use;
- SPU Preparations for vaginal use;
- SPU Oromucous preparations;
- SPU Sticks;
- SPU Medical chewing gums;
- SPU Ear preparations;
- SPU, 2.5.12 Determination of water by semi-micro method;
- SPU, 2.9.2 Disintegration of suppositories and pessaries;
- SPU, 2.9.3 Dissolution test for solid dosage forms;
- SPU, 2.9.5 Mass uniformity for a unit dose of a medicinal product;
- SPU, 2.9.6 Uniformity of the content of single-dose preparations;
- SPU, 2.9.40 Uniformity of dosage units;
- SPU, 2.9.42 Dissolution test for solid lipophilic dosage forms;
- SPU, 5.1.3 Effectiveness of antimicrobial preservatives;
- SPU, 5.1.4 Microbiological purity of non-sterile pharmaceutical preparations and substances for pharmaceutical use;
- SPU, 5.3.N.2 Validation of analytical methods and tests (Appendix 2.7, Vol. 2, pp. 126-241);
- SPU, 2.2.40 Near-infrared spectrometry.

Tasks for independent work

Complete the practical task in the laboratory journal “Pharmaceutical development. Modern approaches to standardization of industrially produced pharmaceuticals. Features of standardization of solid dosage forms of industrial production”.

Calculate the total uncertainty of the method for quantitative determination of APIs when conducting the Dissolution test, which was developed in the class, and perform statistical processing of the analysis results.

Calculate the environmental friendliness indicators of the proposed methods using AGREE and GAPI software.

Questions for self-control

1. What quality control methods are most often used to determine the pharmacotechnological parameters of solid dosage forms of industrial production?
2. What is the purpose and sections of pharmaceutical development?
3. What are the main requirements for the components of a medicine, taking into account stability, bioavailability, and compatibility?
4. Main approaches to analytical support of pharmaceutical development.
5. What is the purpose of the quality control strategy in the development of a new medicine?

TOPIC 4. Features of standardization of liquid dosage forms of industrial production

Objective: To study the SPU approaches, as well as the ICH and ISO Guidelines regarding the features of standardization of liquid pharmaceuticals. **To get acquainted with** the role of excipients, the features of the production process and storage conditions of liquid dosage forms. **To know** the classification of liquid dosage forms according to the SPU, their main physicochemical properties, the requirements of regulatory documentation for the standardization of different types of liquid medicinal products, the differences between sterile and non-sterile forms.

List of questions from other educational components necessary for mastering the proposed topic

1. Dispersological classification of liquid dosage forms (homogeneous, heterogeneous and combined systems).
2. Classification of liquid drugs depending on the route of administration (form of application).
3. Chemical classification and properties of solvents used in the manufacture of liquid pharmaceuticals.
4. Use of the dissolution process in the manufacture of liquid dosage forms.
5. Features of the technology of liquid dosage forms of industrial production.

Theoretical questions

1. Features and requirements of regulatory documentation (SPU, ICH and ISO Guidelines) for the standardization of liquid dosage forms of industrial production: ophthalmic, aural and nasal medicines, liquid medicines for oral and cutaneous use, parenteral pharmaceuticals.
2. Features of standardization of sterile liquid dosage forms.

3. Development of methods for quality control of liquid dosage forms by indicators: description, identification, solution transparency, solution color, pH, accompanying impurities, component composition, quantitative determination.

4. Use of pharmaco-technological and biological tests (homogeneity of dosage units, homogeneity of content, mechanical inclusions, sterility, microbiological purity; homogeneity of mass of doses extracted from multi-dose containers, bacterial endotoxins, etc.).

5. Development of methods for standardizing excipients (preservatives, stabilizers, antioxidants, acidity regulators, flavor enhancers, etc.) in liquid dosage forms depending on their purpose.

Theoretical questions for self-study

1. Basic physicochemical properties of liquid dosage forms.
2. Features of the production process for manufacturing liquid dosage forms.
3. The role of excipients in the composition of liquid dosage forms.
4. Determination of pharmaco-technological parameters depending on the liquid dosage form and the route of its administration.
5. Features of storage of liquid dosage forms.

Tasks for practical work

For the liquid dosage form proposed by the teacher (depending on its composition and purpose), substantiate the quality indicators for standardization:

- Determine the pH of the liquid dosage form in accordance with the procedure given in the SPU, 2.2.3 Potentiometric determination of pH and draw a conclusion about its quality, comparing the obtained values with the requirements of the relevant monograph;
- Analyze the liquid dosage form (proposed by the teacher) in accordance with the procedure given in the SPU, 2.2.1 Determination of transparency and degree of

opalescence of liquids and 2.2.2 Degree of color of liquids, and draw a conclusion about its quality, comparing the obtained values with the requirements of the relevant monograph;

- Determine the shape and size of particles by analyzing the liquid dosage form in the form of a suspension (proposed by the teacher) under a microscope;
- Visually assess the quality of liquid parenteral medicines for the presence of mechanical inclusions.

Methodological guidelines for completing the tasks

To master the techniques and assimilate the material, the relevant monographs and articles of the SPU are offered:

- SPU, 2.2.3 Potentiometric determination of pH;
- SPU, 2.2.1 Determination of transparency and degree of opalescence of liquids;
- SPU, 2.2.2 Degree of color of liquids;
- SPU, 2.9.17. The volume of drugs for parenteral use that is extracted;
- SPU, 2.9.19. Mechanical inclusions: invisible particles;
- SPU, 2.9.20. Mechanical inclusions: visible particles;
- SPU, 2.6.1 Sterility.

Tasks for independent work

Complete the topic “Features of standardization of liquid dosage forms of industrial production” in the laboratory journal “Standardization of medicines”, complete the practical task.

For the chromatographic method of quantitative determination of the active substance in a liquid dosage form proposed by the teacher, calculate the uncertainty of the analytical method, perform statistical processing of the analysis results.

Calculate the environmental friendliness indicators of the proposed methods using the AGREE and GAPI software.

Questions for self-control

1. What are the advantages and disadvantages of liquid dosage forms compared to solid ones?
2. What methods are used to analyze the pH, viscosity, and density of liquid dosage forms?
3. How to determine the shelf life of liquid dosage forms in the standardization process?
4. How does the standardization of solutions differ from the standardization of suspensions and emulsions?
5. What are the features of the standardization of liquid dosage forms for injections?
6. How do storage conditions affect the quality of liquid dosage forms?
7. Describe the features of the validation of quality control methods for liquid dosage forms.

TOPIC 5. Features of standardization of soft dosage forms of industrial production [1]*

Objective: To study and master the basic principles of standardization of soft dosage forms and their quality indicators. **To be able to** assess the compliance of the quality of soft medicines with the requirements of regulatory documentation, to develop and adapt methods for quality control of soft dosage forms, to identify and quantify APIs using chemical and instrumental methods. **To understand** the role and importance of excipients in the composition of soft dosage forms, their classification and influence on the properties of medicines; basic approaches to extracting active components from the base and their importance for ensuring bioavailability;

[1] Note: * - refers to mild preparations for cutaneous use and preparations applied to certain body surfaces or mucous membranes (Ear preparations, Eye preparations, Nasal preparations, Preparations for rectal use and Preparations for vaginal use)

differences between chemical and physicochemical methods of identification and quantification of APIs; specifics of standardization of different types of soft dosage forms depending on their purpose and conditions of use.

List of questions from other educational components necessary for mastering the proposed topic

1. Existing classifications of soft dosage forms (by type of dosage form, by type of dispersion systems, by affinity for water, etc.).
2. Bases and excipients used in the manufacture of soft dosage forms: classification, requirements.
3. Features of the technology for manufacturing various soft dosage forms depending on the physicochemical properties of API and excipients.
4. Chemical and physicochemical (instrumental) methods for quality control of APIs included in soft dosage forms of industrial production.
5. Classification and characterization of ointments according to the SPU by type of base (hydrophobic, hydrophilic, or water-emulsion).
6. Classification and characterization of creams and gels according to the SPU by type of base (lipophilic, hydrophilic).

Theoretical questions

1. Classification and general characteristics of soft medicines for cutaneous application according to the requirements of the SPU.
2. Basic methods and approaches to the extraction of API from the base.
3. Features of standardization of soft preparations for cutaneous use (ointments, creams, gels, pastes, poultices), ear soft preparations (ointments), soft nasal preparations (ointments, creams, gels), soft preparations for rectal use (creams, gels, ointments), preparations for vaginal use, ophthalmic soft preparations (ointments, inserts) by indicators: description, identification (antimicrobial preservatives of other active substances if necessary), testing (accompanying impurities, component

composition, pH, uniformity of dosage units (for nasal, rectal, vaginal dosage forms), uniformity of content (for nasal, rectal, vaginal dosage forms), uniformity of mass (for rectal, vaginal dosage forms), dissolution (for rectal, vaginal dosage forms), sterility (for sterile and ophthalmic soft dosage forms), particle size and water (for ophthalmic dosage forms), microbiological purity), quantitative determination.

4. For which soft preparations for cutaneous use are the tests Uniformity of the delivered dose, Uniformity of the delivered mass, Number of doses in the container carried out during standardization?

5. Features of validation and verification of methods for quantitative determination of active components of soft dosage forms of industrial production.

Theoretical questions for self-study

Quantitative determination of antibiotics by microbiological method (using the diffusion method as an example).

Tasks for practical work

For better understanding of the material, it is recommended to conduct experimental studies:

1. For the soft dosage form proposed by the teacher (depending on its composition and purpose), propose and justify quality control indicators for standardization. Argue ways to extract active substances from the base (sample preparation) for testing.

2. According to the monograph or MCQ for the soft dosage form provided by the teacher, conduct quality control of the proposed pharmaceutical.

Methodological guidelines for completing the tasks

To master the techniques and learn the material, the relevant monographs and articles of the SPU are offered:

- SPU Soft preparations for cutaneous use;
- SPU Ear preparations;
- SPU Eye preparations;
- SPU Nasal preparations;
- SPU Preparations for rectal use;
- SPU Preparations for vaginal use;
- SPU, 2.2.3 Potentiometric determination of pH;
- SPU, 2.5.12 Determination of water by semi-micro method;
- SPU, 2.6.1 Sterility;
- SPU, 2.7.2 Quantitative determination of antibiotics by microbiological method (method A);
- SPU, 2.9.5. Uniformity of mass of single-dose preparations;
- SPU, 2.9.6. Uniformity of content of single-dose preparations;
- SPU, 2.9.40 Uniformity of dosage units;
- SPU, 2.9.42 Dissolution test for solid lipophilic dosage forms;
- SPU, 5.1.1 Methods of production of sterile medicinal products;
- SPU, 5.1.3 Effectiveness of antimicrobial preservative action;
- SPU, 5.1.4 Microbiological purity of non-sterile pharmaceutical preparations and substances for pharmaceutical use.

Tasks for independent work

Complete the section Features of standardization of soft dosage forms of industrial production in the laboratory journal “Standardization of medicines”.

For the proposed method of quantitative determination of the active substance in the composition of a soft dosage form, calculate the uncertainty of sample preparation and analytical methods, perform a statistical analysis of the results obtained, calculate the uncertainty and conclude on its correctness.

Questions for self-control

1. What are the main requirements of the SPU for the quality of soft dosage forms?

3. What indicators are mandatory for quality control of soft dosage forms of industrial production?

4. In what cases is additional control applied, for example, for sterility, acid number?

5. How is the identification of API in the composition of soft dosage forms carried out?

6. What methods are used to control impurities in soft dosage forms?

7. How is the microbiological purity of soft dosage forms checked?

8. What bases and excipients are used for the manufacture of soft dosage forms? How are the methods for extracting active components from the base of a soft dosage form classified?

9. What instrumental methods are used for the quantitative determination of API in the composition of soft dosage forms?

10. What are the main methods used to extract API from the base of soft dosage forms?

11. In what cases are tests for mass uniformity, content uniformity, and dose uniformity performed for soft dosage forms?

12. What methods are used to assess the sterility of ophthalmic and other sterile soft dosage forms?

13. What are the features of standardization of water-emulsion, hydrophobic, and hydrophilic ointments?

TOPIC 6. Features of standardization of pharmaceuticals manufactured in pharmacies

Objective: To study and master the main features of standardization of pharmaceuticals manufactured in a pharmacy. **To study** the range of modern pharmaceuticals manufactured in pharmacies in Ukraine. **To understand** the choice of methods for standardization of APIs in monocomponent and multicomponent extemporaneous dosage forms.

List of questions from other educational components necessary for mastering the proposed topic

1. Classification of pharmaceuticals manufactured in pharmacies.
2. Features of incoming control in a pharmacy.
3. Types of intra-pharmacy control.
4. Features of manufacturing pharmaceuticals in pharmacies.
5. Incompatible combinations of medicinal substances.

Theoretical questions

1. Features of standardization of pharmaceuticals manufactured in pharmacies.
2. Requirements of the SPU for the analysis of extemporaneous medicinal products. Express analysis of extemporaneous medicinal forms.
3. Application of physical, chemical and physico-chemical methods of analysis for the standardization of pharmaceuticals manufactured in a pharmacy.
4. Features of standardization of multicomponent pharmaceutical preparations of pharmacy manufacture.
6. Ensuring the quality of pharmaceuticals of pharmacy manufacture as an integral part of the Good Pharmaceutical Practice system.
7. Features of studying the validation characteristics of methods for the analysis of pharmaceuticals of pharmacy manufacture.

Theoretical questions for self-study

1. Requirements of monographs of the SPU for concentrated solutions prepared in a pharmacy.
2. Requirements for the analysis of non-sterile pharmaceuticals prepared in a pharmacy.
3. Requirements for the analysis of soft pharmaceuticals prepared in a pharmacy.

Tasks for practical work

For better understanding of the material, it is recommended to conduct experimental studies:

1. For the monocomponent pharmaceutical of pharmacy production proposed by the teacher, propose and justify quality control indicators and methods. Make a conclusion on the compliance of the manufacture of the dosage form with the Order of the Ministry of Health of Ukraine No. 812.
2. For the multicomponent pharmaceutical proposed by the teacher, manufactured in a pharmacy, propose and justify quality control indicators and methods. Make a conclusion on the compliance of the manufacture of the dosage form with the Order of the Ministry of Health of Ukraine No. 812.
3. Carry out quantitative determination of API in a concentrated solution according to the methods of the SPU and make a conclusion on the compliance of the monograph.

Methodological guidelines for completing the tasks

To master the techniques and learn the material, the following articles are offered:

- SPU Pharmaceuticals manufactured in pharmacies;
- SPU Calculations in the manufacture of medicines in pharmacies;

- SPU Non-sterile pharmaceuticals manufactured in pharmacies;
- SPU Soft medicines manufactured in pharmacies;
- SPU Suppositories and pessaries manufactured in pharmacies;
- SPU Powders manufactured in pharmacies;
- Order of the Ministry of Health of Ukraine No. 812.

Tasks for independent work

Complete the section “Features of standardization of pharmaceutical preparations manufactured in pharmacies” in the laboratory journal “Standardization of medicines” and perform practical research.

Questions for self-control

1. Categories of pharmaceuticals that are not subject to state registration.
2. Requirements of the SPU for the standardization of extemporaneous formulations.
3. Application of express analysis in the standardization of pharmaceuticals manufactured in pharmacies.
4. Physico-chemical methods that are most often used for the analysis of pharmaceutical dosage forms manufactured in pharmacies.
5. Features of calculating the quantitative content of active pharmaceutical ingredients in extemporaneous dosage forms.

TOPIC 7. Basics of standardization of medicinal plant raw materials and extracts

Objective: To study and master the classification of medicinal plant raw materials of extracts according to the requirements of the SPU, the features of standardization of types of extracts (liquid, soft, and solid). **To know** the requirements for the production, storage, labeling of extracts, the features of standardization of extracts according to quality indicators. **To understand** the approaches and principles of using modern analytical methods for standardization of extracts.

List of questions from other educational components necessary for mastering the proposed topic

1. Features and approaches to the standardization of medicinal plant raw materials according to the requirements of the SPU.
2. What are the main features and differences in the technologies for the production of tinctures by maceration and percolation methods?
3. What is an extractant and an extract (miscella)? What types of extractants are used to produce extracts?
4. Classification of medicinal plant raw materials by chemical groups of BAS, their physicochemical properties.

Theoretical questions

1. Classification and general characteristics of medicinal plant raw materials of extracts according to the requirements of the SPU depending on: the approach to standardization, determination or correction of the content of quantified components (standardized, quantified, other); aggregate state and method of production (liquid, soft, solid).
2. Requirements and standardization for quantified components or regulated content (regulated content limits) for standardized, quantified and other extracts.

3. Features of standardization of liquid extraction medicinal products (liquid extracts, tinctures) by indicators: description, properties, tests (relative density, ethanol and methanol content, dry residue), quantitative determination.

4. Features of standardization of soft extraction medicinal products (thick extracts, resins) by indicators: description, properties, tests (dry residue for thick extracts and water for resins, residual amounts of solvents), quantitative determination.

5. Features of standardization of solid extraction medicinal products (dry extracts) by indicators: description, properties, tests (loss in mass upon drying, water, residual amounts of solvents, total ash), quantitative determination.

6. Features of the procedure for identifying marker substances by thin-layer and high-performance thin-layer chromatography methods.

7. How is the selection of component(s) for quantitative determination of medicinal plant raw materials of extracts carried out? What is a marker substance, what is it used for? What is the difference between an active and an analytical marker?

8. Features of conducting tests of microbiological purity of medicinal plant raw materials extracts used in the manufacture of herbal medicines for oral use according to the SPU requirements.

9. General provisions on the development of monographs on medicinal plant raw materials extracts according to the SPU requirements.

Theoretical questions for self-study

1. What is a natural extract of medicinal plant raw materials?

2. Requirements for the production, storage and labeling of different types of extracts.

3. What is the difference between the concepts of ratio of medicinal plant raw materials to extract, ratio of medicinal plant raw materials to solvent, and ratio of medicinal plant raw materials to natural extract? Their practical application?

4. SPU requirements for water for the preparation of extracts.

5. Differences between thin-layer and high-performance thin-layer chromatography methods in the standardization of extracts.

6. Features of the use of standard and specific absorption index methods in the quantitative determination of BAS in extracts by absorption spectrophotometry in the ultraviolet and visible range.

7. Possibilities and practical application of the KNOWLEDGE database of the EDQM website in the standardization of medicinal plant raw materials of extracts.

8. Modern methods of optimizing and intensifying the extraction of plant BAS (ultrasound, co-extraction, etc.).

Tasks for practical work

For better understanding of the material, it is recommended to conduct experimental studies:

1. For the extract of medicinal plant raw materials proposed by the teacher, substantiate the quality indicators for standardization.

2. Identify the marker substances for the extract of medicinal plant raw materials (proposed by the teacher) by thin-layer chromatography according to the procedure given in the SPU, 2.2.27 Thin-layer chromatography, compare the obtained chromatographic zones with the zones of standard substances, draw a conclusion about the quality of the extract, comparing the obtained values with the requirements of regulatory documentation.

3. Determine the loss in mass upon drying or water for the dry extract (suggested by the teacher) according to the procedure given in the SPU, 2.8.17 Determination of loss in mass upon drying of extracts or 2.2.32 Loss in mass upon drying or 2.5.12 Water: justify the choice of the approach to the determination, calculate the average value of the indicator and the error of the determination, draw a conclusion about the quality of the extract, comparing the obtained values with the requirements of the regulatory documentation.

4. Determine the total ash for the dry extract (suggested by the teacher) according to the procedure given in the SPU, 2.4.16 Total ash, calculate the average value of the indicator and the error of the determination, draw a conclusion about the

quality of the extract, comparing the obtained values with the requirements of the regulatory documentation.

5. Determine the dry residue for a liquid or thick extract (suggested by the teacher) according to the procedure given in the SPU, 2.8.16 Determination of the dry residue of extracts, calculate the average value of the indicator and the error of determination, draw a conclusion about the quality of the extract, comparing the obtained values with the requirements of regulatory documentation.

6. Determine the quantitative content of biologically active substances in the extract of medicinal plant raw materials (suggested by the teacher): argue the method of quantitative determination, conduct a statistical analysis of the results obtained, calculate the uncertainty of the method, compare the obtained values with the requirements of regulatory documentation and draw a conclusion about the correctness of the analytical method.

Methodological guidelines for completing the tasks

The following regulatory documentation is offered for the assimilation of the material: SPU, 5.23 Monographs on medicinal plant extracts (information article); SPU, General monograph Medicinal plant extracts; SPU, Monographs on the substance Water for the preparation of extracts; SPU, 2.2.5 Relative density; SPU, 2.2.13 Determination of water by distillation method; SPU, 2.2.27 Thin layer chromatography; SPU, 2.2.32 Loss in mass during drying; SPU, 2.5.12 Determination of water by semi-micro method; SPU, 2.6.31 Testing of microbiological purity of herbal medicinal products for oral use and extracts used in their manufacture; SPU, 2.8.16 Determination of dry residue of extracts; SPU, 2.8.17 Determination of mass loss during drying of extracts; SPU, 2.8.25 High-performance thin-layer chromatography of medicinal plant raw materials and medicinal plant preparations; SPU, 2.9.10 Ethanol content and alcoholometric tables; SPU, 2.9.11 Determination of methanol and 2-propanol content; SPU, 5.4 Residual solvents.

Tasks for independent work

Complete the topic “Fundamentals of standardization of medicinal plant raw materials and extracts” in the laboratory journal.

Questions for self-control

1. What is a natural extract of medicinal plant raw materials?
2. How are medicinal plant raw materials extracts classified according to the requirements of the SPU?
3. What is the difference between standardized, quantified and other extracts?
4. How are extracts classified by aggregate state and method of production?
5. What requirements and regulated limits are set for quantified components in standardized extracts?
7. What are the features of the standardization of liquid extraction medicinal products (liquid extracts, tinctures)?
8. What indicators are analyzed for thick extracts and resins within the framework of their standardization?
9. What parameters are taken into account when standardizing dry extracts?
10. What methods are used to identify marker substances in medicinal plant extracts?
11. What is a marker substance, and what role does it play in standardization? What is the difference between an active and an analytical marker?
12. How is the component or components selected for quantification in medicinal plant extracts?
13. What are the features of microbiological testing of medicinal plant extracts for oral use?
14. What are the general requirements for the development of monographs for medicinal plant extracts?
15. What is the possible ratio and their practical application?
16. What are the requirements of the SPU for water used for the preparation of extracts?

17. What are the differences between thin-layer and high-performance thin-layer chromatography methods in the standardization of extracts?

18. How are the methods of standard and specific absorption index used in the quantification of biologically active substances in extracts?

19. What opportunities does the KNOWLEDGE database of the EDQM website provide in the standardization of medicinal plant extracts?

TOPIC 8. Determination of stability of pharmaceuticals

Objective: To know the basic concepts of stability of pharmaceuticals; factors affecting stability; regulatory requirements (ICH, SPU, international pharmacopoeias); types and mechanisms of degradation; modern methods for determining stability. **To understand** the role of stability in ensuring the quality of pharmaceuticals; principles of stability studies (long-term, accelerated, stress); the importance of storage, transportation and packaging conditions for stability. **To study** the features of stability for different dosage forms; programming of study conditions; criteria for sample selection; methods for assessing shelf life; validation of methods for analyzing stability.

List of questions from other educational components necessary for mastering the proposed topic

1. The influence of physicochemical properties of substances on stability.
2. Physical factors affecting the stability of compounds.
3. The choice of packaging materials depending on the physicochemical properties of active pharmaceutical ingredients.

Theoretical questions

1. Basic concepts of drug stability. Factors affecting stability (temperature, humidity, light, pH, oxygen, etc.). Types and mechanisms of drug degradation: hydrolysis, oxidation, photolysis, and thermal degradation.

2. Requirements for drug stability studies in accordance with current regulatory documentation (ICH Q1A–Q1E, SPU, European Pharmacopoeia, US Pharmacopoeia). Features of national requirements for determining stability.

4. Main types of stability studies: long-term, accelerated and stress tests.

5. Programming stability study conditions (temperature regime, humidity, etc.).

6. Differences in the study of the stability of APIs and finished pharmaceuticals. Criteria for sample selection.

7. Calculation of shelf life and storage conditions.

8. Features of stability studies for different dosage forms.

9. Features of storage and transportation of pharmaceuticals: the impact of transportation on stability, monitoring systems during storage.

Theoretical questions for self-study

1. What is the chemical stability of medicines?

2. What is the impact of manufacturing processes on the stability of pharmaceuticals?

3. What are the concepts of expiration date and shelf life?

4. What physical and chemical changes may indicate the instability of pharmaceuticals?

5. Problems associated with the stability of biological medicines: features of the stability of proteins, peptides and vaccines, methods for assessing degradation.

6. The role of packaging in maintaining stability. Research on the compatibility of a pharmaceutical with packaging.

Tasks for practical work

For better understanding of the material, it is recommended to conduct experimental studies to study the effect of storage temperature on the quality and stability of the pharmaceutical:

1. Conduct accelerated stability tests of the pharmaceutical from the Vitamins group by heating the samples at different temperatures (for example, 25 °C, 40 °C, 60 °C). According to the results of the analysis, describe the change in color, odor, consistency and calculate the content of the active substance using the appropriate quantitative determination method, draw conclusions.

Methodological guidelines for completing the tasks

For mastering the techniques and learn the material, relevant articles of the SPU are offered.

Guideline ST-N MOZU 42-3.3:2004 Medicinal products. Guideline on quality. Stability testing.

Tasks for independent work

Fill in the topic “Determination of the stability of pharmaceuticals” in the laboratory journal “Standardization of medicines”, complete the practical task.

Questions for self-control

1. What is the stability of pharmaceuticals and why is it important? What are the main factors affecting stability?
2. What types of degradation of pharmaceuticals do you know, and what mechanisms determine them?

3. What regulatory documents regulate the requirements for the stability of pharmaceuticals?

4. What is the difference between long-term, accelerated and stress stability tests?

5. How are the stability study conditions programmed (temperature, humidity, etc.)?

6. What are the differences between the study of the stability of APIs and finished pharmaceuticals?

7. How is the shelf life of pharmaceuticals calculated?

8. What modern methods are used to determine stability?

9. How does packaging affect the stability of pharmaceuticals, and how is their compatibility with packaging studied?

10. What are the problems associated with the stability of biological products, such as proteins, peptides and vaccines?

11. What is the validation of stability analysis methods, and what acceptance criteria are used?

12. How does transportation affect the stability of medicinal products, and what monitoring systems are used?

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Навчально-методичне видання

Георгіянц Вікторія Акопівна

Бевз Наталія Юріївна

Смєлова Наталія Миколаївна

Сидоренко Людмила Василівна

Северіна Ганна Іванівна

Головченко Ольга Сергіївна

Григорів Галина Валеріївна

СТАНДАРТИЗАЦІЯ ЛІКАРСЬКИХ ЗАСОБІВ

Методичні рекомендації

для здобувачів вищої освіти освітньо-професійної програми “Фармація”

Видається в авторській редакції

Електронне видання

Англійською мовою

Методичні рекомендації призначено для здобувачів вищої освіти освітньо-професійної програми “Фармація”.

Методичні рекомендації містять відомості про предмет і завдання освітнього компонента “Стандартизація лікарських засобів”; інформацію щодо правил роботи у лабораторії; перелік заходів безпеки під час роботи в лабораторії та способів надання первинної медичної допомоги; тему, мету, теоретичні питання та питання для самостійного вивчення, завдання для практичної роботи, методичні вказівки для виконання поставлених завдань, завдання для самостійної роботи та запитання до самоконтролю.

Методичні рекомендації допоможуть здобувачам вищої освіти при підготовці та під час проведення занять із освітнього компонента “Стандартизація лікарських засобів”.

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