MINISTRY OF HEALTH PROTECTION OF UKRAINE
ODESSA NATIONAL MEDICAL UNIVERSITY

Faculty Pharmaceutical
(faculty name)
Department Pharmaceutical chemistry and drug technology
(name of department)

I APPROVE
Vice-rector for scientific and pedagogical work
_____ Eduard BURYACHKIVSKY
" 01 " September 2024

METHODOLOGICAL DEVELOPMENT TO PRACTICAL CLASSES FROM THE ACADEMIC DISCIPLINE (7th SEMESTER)

Faculty, course Pharmaceutical, course 4

Academic discipline Drug technology
(name of academic discipline)

Approved:
Meeting of the Department of Pharmaceutical Chemistry and Drug Technology
Odessa National Medical University

Protocol No. 1 dated August 28, 2024 .

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Developers:
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Practical lesson No. 1

Topic: " Regulatory documentation in the production of GLS "

Purpose: to get acquainted with the terminology used in the production of finished medicinal products, with the structure of state bodies, standardization services, with the requirements for NTDs for medicinal products, as well as with the rules for their packaging and labeling

Basic concepts: ***Technological regulation*** is a regulatory document that defines technological methods, technical means, norms and standards for the manufacture of medicinal products or auxiliary substances, and which ensures optimum technical and economic indicators. That is, it is a document in which, for a specific set of technological equipment, conditions are laid down that ensure the release of high-quality medicinal products in a certain medicinal form or intermediate products.

The technological process of the production of medicinal products consists of separate production stages that follow one another.

The technological stage is a set of operations that lead to the production of an intermediate semi-finished product (at the final stage of the finished product), which can be determined quantitatively and characterized qualitatively. For example, the process of obtaining powders includes the following stages: mixing, dosing, packaging. Each stage consists of a number of consecutive technological operations.

A technological scheme is a graphic representation of a set of interconnected technological nodes in which chemical and physical-mechanical processes for the production of a finished product take place.

Technological operation - a part of the technological process related to the maintenance of one of the main types of equipment. For example, in the production of tablets, such operations are: grinding of ingredients, weighing, sieving, moistening of the mixture to be granulated, etc.

A technological operation is depicted separately with an indication of belonging to a certain stage. Each stage and operation must be characterized by a name and denoted by an index consisting of a conventional designation and a serial number. The numbering of the stages is carried out in the order of their execution in the course of the technological process, starting with the receipt and preparation of raw materials and ending with the shipment of finished products.

Equipment: visual material, multimedia projector, presentation.

Plan:

1. Organizational activities (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).
2. Control of the reference level of knowledge (written work, written test, frontal

survey, etc.) (if necessary):

— requirements for students' theoretical readiness to perform practical classes.

Knowledge requirements.

A student of higher education should know:

- rules of work at a pharmaceutical enterprise and safety rules;
- subject and tasks of drug technology;
- basic concepts of drug technology;
- basic requirements for the drug manufacturing process.

A student of higher education must be able to:

- apply work and safety rules during the manufacture of medicinal products;
- to formulate the basic concepts of drug technology;
- formulate and explain the technological aspects of drug production;
- apply basic calculations during preparatory work for the manufacture of medicinal products.

List of didactic units:

- the text of textbooks;
- a bank of test tasks.

— questions (test tasks, tasks, clinical situations) to check basic knowledge on the subject of the lesson:

1. What is a technological regulation?
2. What is a technological scheme?
3. What is an industrial regulation ?
4. What is the material balance?
5. Name the main provisions of GMP?

3. Formation of professional abilities and skills (mastering the skills of calculating the material balance , drawing up a technological block diagram for the industrial production of medicinal products:

— task content:

1. List the terms and concepts of the industrial technology of drugs ?
2. Define which documents make up regulatory and technical documentation in the industrial production of drugs ?
3. Define the main provisions of GMP.
4. Qualitative and quantitative information contained in a chemical formula and chemical equation.
5. Define the term industrial regulation.
6. Make a material balance sheet: .

— recommendations (instructions) for performing tasks (professional algorithms, orientation maps for the formation of practical skills and abilities, etc.):

Orientation map for independent work with literature on the subject

of the lesson.

№№p.p.	Main tasks	Instructions	Answers
1	2	3	4
1.	RM.	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. – P. 15-20.
2.	Principles of organization of industrial production of medicines.	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. – P. 21-25.

— requirements for the results of the work, including the registration: to state the basic concepts and rules of the pharmaceutical enterprise and safety rules, the concept of proper practice, technological block diagrams, to draw up a material balance.

— control materials for the final stage of the lesson: tasks, tasks, tests, etc. (if necessary):

Task:

Lesson content.

The pharmaceutical industry in the European Union operates according to standards containing high requirements for ensuring the quality of medicinal products during their development, production and control. The system of issuing trade licenses (marketing authorization) provides for all medicinal products to be examined by a competent authorized body to ensure their compliance with modern requirements for safety, quality and effectiveness. Production licensing system (manufacturing authorization) ensures that all products authorized for sale on the European market are manufactured only by manufacturers who have the appropriate license, whose activities are regularly inspected by the competent authorities. Production licenses are mandatory for all pharmaceutical manufacturers in the European Community, regardless of where the products are sold - on the territory of the Community or outside of it.

The Commission adopted two directives establishing the principles and rules of Good Manufacturing Practice (GMP) for medicinal products. Directive 2003/94/EC concerns medicinal products for human use, and Directive 91/412/EEC – medicinal products for veterinary use. Detailed rules (requirements) that are consistent with the

principles of these directives are set out in the guidelines on good manufacturing practices, which are used to evaluate applications for production licenses and on the basis of which drug manufacturers are inspected.

GMP principles and detailed rules apply to all processes requiring licensing under Article 40 of Directive 2001/83/EC and Article 44 of Directive 2001/82/EC, as amended by Directives 2004/27/EC and 2004/28/EC respectively . In addition, they apply to all serial production of medicinal products, in particular to production in hospitals and the manufacture of medicinal products for clinical trials.

All EU countries and industry representatives have agreed that the requirements of good manufacturing practice for medicinal products for veterinary use should be the same as for medicinal products for human use. Some more detailed GMP rules specific to the manufacture of veterinary medicinal products and immunobiological veterinary medicinal products are set out in two annexes.

This Guide consists of two parts, basic requirements and special annexes. Part I contains the principles of GMP for the manufacture of medicinal products. Part II covers GMP principles for the production of active substances used as starting materials.

The chapters of Part I on "essential requirements" start with the principles defined in Directive 2003/94/EC and Directive 91/412/EEC. Chapter 1 "Quality Management" outlines the fundamental concept of quality assurance in the production of medicinal products. According to it, in each of the chapters, a principle is formulated in general terms, aimed at ensuring the aspect of quality to which this chapter is dedicated, and the text of the rules is given, set out in such detail that manufacturers can understand their essence and comply with the implementation of this principle.

Part II was recently created based on guidance developed by ICH and published as ICH document Q7a on "active pharmaceutical ingredients", which was incorporated into the GMP Guidelines as Annex 18 for voluntary application in 2001. Pursuant to the revised Article 47 and Article 51 of Directive 2001/83/EC and Directive 2001/82/EC respectively, as amended, the Commission adopts and publishes detailed rules for GMP principles for active substances used as starting materials. The former Annex 18 has been replaced by the new Part II of the GMP Guidelines, which covers medicinal products for both human and veterinary use.

In addition to the basic principles and rules of good industrial practice set out in parts I and II, the guidance includes a number of annexes containing more detailed rules for specific fields of activity. For some production processes, it is necessary to apply several applications at the same time (for example: applications for the production of sterile medicinal products, radiopharmaceuticals and/or biological medicinal products).

Following the appendices is a glossary of some of the special terms used in this manual.

The instruction does not apply to the safety of personnel employed in production. These issues can be very important in the production of certain drugs, such as potent, biological and radioactive. They are regulated by other Community regulations or national legislation.

The guideline stipulates that the holder of a production license systematically includes the requirements of the trade license regarding the safety, quality, and effectiveness of the drugs in all measures related to production, control, and issuance of release permits.

For many years, the production of medicinal products has been carried out in accordance with the rules of good manufacturing practice; the production of medicinal products is not regulated by CEN/ISO standards. Harmonized CEN/ISO standards adopted by the European Organization for Standardization can be used at the discretion of industrialists as a tool for implementing quality systems in the pharmaceutical sector. In this third edition of the guideline, the CEN/ISO standards were taken into account, but the terminology of these standards was not used.

It is recognized that there are other acceptable methods, other than those described in this guideline, by which the principles of quality assurance can be met. The Guideline is not intended to limit in any way the development of any new concepts or new technologies that have been validated and guarantee a level of quality assurance at least equivalent to that established in this Guideline. This guideline will be regularly revised.

The industrial production of medicines is regulated by the relevant regulatory and technical documentation (NTD), approved in accordance with the established procedure.

The NTD should ensure the improvement of the quality and effectiveness of medicinal products, be constantly improved based on the achievements of science and technology, and be revised in a timely manner with the aim of replacing outdated indicators in accordance with the needs of public health, national defense and export.

Normative documents are documents that establish rules, general principles or characteristics relating to various activities or their results.

NTDs for medicinal products, medicinal plant raw materials and medical equipment products are divided into the following categories:

1. Technological and technical regulations.
2. State Pharmacopoeia (SPh).
3. Analytical regulatory documentation.
4. State standards (GOST, DST U).
5. Industry Standards (OST), Industry Standard of Ukraine (GST U).
6. Technical conditions (TU U).

7. Governing normative document (KD) — instructions, methodological guidelines, etc.

8. Production technological instructions.

The technological regulation is a regulatory document that outlines the technological methods, technical means, standards and regulations for the manufacture of a medicinal product.

On the basis of technological regulations, serial production of chemical and pharmaceutical products is carried out.

The technological process of the production of medicinal products consists of separate production stages that follow one after the other.

The production stage is a set of technological operations that lead to the production of an intermediate product (at the final stage - the finished product). For example, the process of obtaining tablets includes the following production stages: mixing, granulation, pressing. Each stage, in turn, represents a combination of a number of consecutive technological operations.

The technological scheme of the production should visually (graphically in the form of a block diagram) reflect the sequence of work in this production with their subdivision by stages and operations of the technological process, indicating the main material and energy communications (raw material supply, steam, water supply, places of waste generation, sewage water, emissions into the atmosphere).

Technological operation - a part of the technological process related to the maintenance of one of the main types of equipment. For example, in the production of tablets, such operations are: grinding of ingredients, weighing, sieving, moistening of the mixture to be granulated, etc.

A technological operation is depicted separately with an indication of belonging to a certain stage. Each stage and operation must be characterized by a name and denoted by an index consisting of a conventional designation and a serial number. The numbering of the stages is carried out in the order of their execution in the course of the technological process, starting with the receipt and preparation of raw materials and ending with the shipment of finished products.

In the technological scheme, the following designations of stages are used:

"VR" - stages of auxiliary works

"TP" - stages of the main technological process

"VO" - stages of processing of used waste

"OBO" - stages of waste disposal

"OBV" - stages of neutralization of technological and ventilation emissions into the atmosphere

"UMO" - stages of packaging, labeling and shipment of the finished product

If auxiliary works (dissolving and drying raw materials, preparation of solutions of a given concentration) are carried out in separate equipment for one stage of the main technological process, then such auxiliary works are included in this stage of the main technological process.

Auxiliary work carried out in separate equipment for several stages of one or more productions is separated into independent stages of auxiliary work (for example, preparation of purified water, solutions of acids or alkalis with a given concentration for the entire workshop).

If waste processing or their disposal is carried out as independent work, they may not be included in the technological scheme of production. In this case, on the technological diagram, an arrow indicates where the waste goes for processing (disposal).

Analytical normative documentation (AND) — pharmacopoeial articles, documents on methods of analysis, as well as other analytical documentation that allows to control the quality of the medicinal product. ADS is an integral part of registration documents — a set of materials for a medicinal product, the specialized assessment of which makes it possible to draw conclusions about the possibility of its state registration, the need for conducting pre-registration studies or quality control of medicinal product samples.

A standard is a normative document in which rules, requirements, general principles or characteristics relating to various types of activities or their results are established for general and repeated use in order to achieve the optimal degree of orderliness in the specified field.

Technical conditions are a normative document that establishes requirements for specific products or services and regulates relations between the supplier and the consumer of products.

The technological regulation is a regulatory document that outlines the technological methods, technical means, standards and regulations for the manufacture of a medicinal product.

The technical regulation is a regulatory document that, for a specific complex of technological equipment, sets out the conditions that ensure the release of semi-finished products or medicinal products of a separate dosage form of a given quality.

Material balance is the ratio between the amount of raw materials, materials, semi-finished products and intermediate products (C1) used in production, and the amount of finished products actually obtained (C2), by-products (C3), waste or refuse (C4) and losses (C-), i.e. the ratio of theoretically possible and practically obtained yield of finished products. If there are no production by-products, the material balance equation is simplified:

$$C1=C2+C6.$$

Material losses in the production of medicinal products are of various origins, so they are divided into several

groups:

* mechanical, which occur mostly in the absence or insufficient mechanization of the movement of materials during processing (liquid spillage, spraying, shaking, fighting, etc.);

* physico-chemical, which are observed in the case of carrying out a technological process without taking into account the physico-chemical properties of medicinal substances (incomplete extraction of active substances from medicinal plant raw materials, loss of volatile solvents during filtration, essential oil during evaporation, etc.);

* chemical, which are possible due to non-observance or incorrect selection of the parameters of chemical reactions (synthesis).

The material balance is of great practical importance, because it determines the degree of perfection of the technological process. The more complete it is, the more detailed the technology of this drug is studied. The smaller the balance of various types of losses, the more correctly the production process is carried out. Conversely, the more material losses in the balance sheet, the less perfect the technology of this drug is considered.

4. List of recommended literature (main, additional, electronic information resources) :

Main:

- A.G. Bashura, O.S. Shpichak, E.E. Bogutska; under the editorship A.I. Tikhonov and S.A. Tikhonova - Kh.: Original, 2016. - 462 p.
- Vishnevska, N.P. Polovka, R.S. Korytniuk et al. - Kh.: National Academy of Sciences: Original, 2016. - 378p.
- Workshop on industrial technology of medicinal products: teaching. manual for students higher education institutions with the specialty "Pharmacy" / O.A. Ruban, D.I. Dmytrievskyi, L.M. Khokhlova [and others]; under the editorship O.A. Ruban. – Kh.: National Institute of Medical Sciences; Original, 2015. – 320 p.
- Industrial technology of medicines : education. manual for students' independent work / O.A. Ruban , V.D. Rybachuk , L.M. X ohlova etc. - KH.: NPHAU, 2015. - 120 p.
- Study guide for preparation for the final modular control and State certification in the Industrial Technology of Medicines for full-time and part-time students of the "Pharmacy" specialty / Ed. O.A. Ruban. - Kh.: National Academy of Sciences, 2016 . - 80 p.

- Study guide for independent preparation of students of the Faculty of Pharmacy for the licensing integrated exam "Step 2. Pharmacy" / O.A. Ruban, V.D. Rybachuk, L.M. Khokhlova, D.S. Pulyaev - KH.: NPHAU, 2016. - 63 p.
- Auxiliary substances in the production of medicines: training. manual for students higher pharmacy education closing / O.A. Ruban, I.M. _ Pertsev, S.A. Kutsenko, Yu.S. Oily; under the editorship I.M. Pepper - Kh.: Golden Pages, 2016. - 720 p.
- Technology of drugs for industrial production: tutorial. for university students education class: in 2 h. / V.I. Chuyeshov, E.V. Gladukh, I.V. Saiko et al. – 2nd ed., revision. and additional - Kh.: NPhaU: Original, 2012. - Part 1. - 694 p.
- Technology of drugs for industrial production: tutorial. for university students education class: in 2 h. / V.I. Chuyeshov, E.V. Gladukh, I.V. Saiko et al. – 2nd ed., revision. and additional - Kh.: NPhaU: Original, 2013. - Part 2. - 638 p.
- Modern pharmaceutical technologies: education. manual to laboratory classes of full-time, evening and part-time master's students of the specialty 8.110201 "Pharmacy" / under the editorship. O.A. Ruban. - Kh.: Publishing House of the National Academy of Sciences, 2016. - 256 p.

Auxiliary :

- Mathematical planning of an experiment when conducting scientific research in pharmacy / T.A. Groshovyi, V.P. Martsenyuk, L.I. Kucherenko and others. – Ternopil: TDMU Ukrmedknyga, 2008. – 367 p.
- Regulatory and technical documentation and production validation. Material balance: Educational method. river for audit. and external audit. student work special "Pharmacy" of full-time and part-time education / D.I. Dmytrievskyi, G.D. Slipchenko, I.M. Hrubnyk, D.V. Rybachuk . - Kh.: Publishing House of the National Academy of Sciences, 2008. - 45 p.
- Technology of medicinal products of industrial production: training. manual/ edited by Prof. D.I. Dmitrievsky. – Vinnytsia: Nova kniga, 2008. – 280 p.
- Drug technology. Educational and methodological guide: Education. manual for students higher education hall. / O.I. Tikhonov, P.A. Logvin, S.O. Tikhonova, O.V. Bazulin, T.G. Yarnykh, O.S. Shpychak, O.M. Kotenko; under the editorship O.I. Tikhonova, Kh.: Original, 2009. - 432 p.
- C pyrotometry. Recovery and rectification of ethanol: Textbook. help / D.I. Dmytryevsky, L.I. Boguslavskaya, L.N. Khokhlova and others; Ed. Prof. D.I. Dmitrievsky - Kh.: Izd-vo NPhaU, 2006. - 100 p.
- Pharmaceutical encyclopedia / Chief editor. council and the author of the foreword V.P. Black people - 3rd ed., revised. and additional - K.: "MORION", 2016. - 1952 p.

- Encyclopedia of Pharmaceutical Technology: 3-d Ed. / ed. by J. Swarbrick. – New York; London: Informa Healthcare, 2007. - 4128 p.
- European Pharmacopoeia 8.0 [8th edition] / European Directorate for the Quality of Medicines & Healthcare. - Strasbourg, 2013. - 3638 p.
- Handbook of Pharmaceutical Excipients, 6th edition / RC Rowe, PJ Sheskey, ME Quinn. - Pharmaceutical Press and American Pharmacists Association, 2009. - 521 p.
- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeial Center for the Quality of Medicines", 2015. - Vol. 1. - 1128 p.
- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicines", 2014. - Vol. 2. - 724 p.
- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products", 2015. - Vol. 3. - 732 p.
- Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of non-sterile medicinal products in pharmacies" ST-N of the Ministry of Health of Ukraine 42 – 4.5: 2015 // Edited by Prof. O. I. Tikhonov and Prof. T.G. Jarnih - Kyiv, 2015. - 109 p. (Approved by the order of the Ministry of Health of Ukraine No. 398 of 01.07.2015).
- Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of sterile and aseptic medicinal products in pharmacies" ST-N of the Ministry of Health of Ukraine 42 – 4.6: 2015 // Edited by. Prof. O.I. Tikhonov and Prof. T.G. Jarnih - Kyiv, 2015. - 76 p. (Approved by order of the Ministry of Health of Ukraine No. 398 dated 07/01/2015).
- Production technology of extemporaneous medicinal apipreparations and their use in pharmacy, medicine and cosmetology: methodical recommendations / O.I. Tikhonov, T.G. Yarnykh, S.O. Tikhonova, O.G. Bashura, O.S. Shpychak, L.O. Bondarenko, P.S. Sirota, B.T. Kudryk, R.I. Skrypnyk-Tikhonov, N.S. Bohdan, S.G. Bobro, L.V. Kanoshevich, O.E. Bogutska; under the editorship O.I. Tikhonov. - Kh.: Izd-vo NPhaU, 2016. - 75 p.
- Powder manufacturing technology: teaching. manual / L.L. Davtyan, R.S. Korytniuk, A.O. Drozdova, I.O. Vlasenko, Z.V. Malenka, V.P. Popovych, V.V. Gladyshev, S.M. Musoev, T.F. Olifirova, L.I. Vishnevska, O.M. Hlushchenko,

O.O. Khomich; under the editorship L.L. Davtyan, R.S. Korytnyuk - K.: "Education of Ukraine", 2016. - 141 p.

- Pharmacotherapy of mastopathy. Extemporaneous prescriptions. Phytopreparations and homeopathic medicines: methodical recommendations / L.I. Vishnevska,
- S.S. Zuykin. –Kharkiv.: Publishing House of IFNMU-NPhaU, 2017. – 44 p.
- Zujkina SS The pharmacotechnological studies of the phytospecies composition for the complex therapy of mastopathy / SS Zujkina, LI Vishnevska // Herald of pharmacy. – 2017. – No. 2 (90). - P. 43-47.
- Bogutska O.E. The main directions of solving the problem of pharmaceutical incompatibilities / O.E. Bogutska // Modern achievements of pharmaceutical technology and biotechnology: collection of scientific papers. – issue 2. – Kharkiv.: Publishing House of the National Academy of Sciences, 2017. – pp. 29–31.
- Polovko N.P. Assessment of biopharmaceutical factors in the development and production of new medicines / N.P. Polovko, L.I. Vishnevska, O.S. Shpychak // Modern achievements of pharmaceutical technology and biotechnology: collection of scientific works, issue 2. – X.: NPhaU Publishing House, 2017. – P. 155-160.
- Prospects for the creation of new original drugs based on substances of plant origin / O.A. Ruban, S.A. Malinovska, Murad Al-Tawaiti, S.I. Mazurets // Phytotherapy. – 2012. – No. 2. - pp. 63–65.
- The current state of creation, production and quality control of capsules / M.B. Chubka, L.V. Vronska, N.O. Zarivna et al. // Pharmaceutical journal. - 2012. - No. 2. - P. 165-168.
- Murachanian D. Two-Piece Hard Capsules for Pharmaceutical Formulations / D. Murachanian // Journal of GXP Compliance. - 2010. - Vol. 14. - P. 31-42.
- Patel H. New pharmaceutical excipients in solid dosage forms – A review / H. Patel, V. Shah, U. Upadhyay // Int. J. of Pharm. & Life Sci. - 2011. - Vol. 2. – P. 1006–1019.
- Recent trends of treatment and medication peptic ulcerative disorder / D. Bhowmik, Chiranjib, KK Tripathi [et al.] // International Journal of PharmTech Research. - 2010. - Vol. 2. – P. 970–980.
- The effects of powder compressibility, speed of capsule filling and pre-compression on plug densification / M. Llusa , E. Faulhammer , S. Biserni [et al.] // Int. J. Pharm. – 2014. – Vol. 471. – P. 182–188.

Electronic resources:

- www.moz.gov.ua is the official website of the Ministry of Health of Ukraine
- fp.com.ua - website of the magazine "Pharmacist Praktik"
- www.provisor.com.ua – the official website of the magazine "Provisor"
- Compendium: drugs. - [Electronic resource]. - Access mode: http://compendium.com.ua/ - as of October 10, 2016.
- State Register of Medicinal Products of Ukraine. - [Electronic resource]. - Access mode: http://www.drlz.com.ua/ - as of January 10, 2017.
- Database "Equalizer" LLC "Business Credit" - [Electronic resource]. - Access mode: http://eq.bck.com.ua/ - as of September 20, 2016.

Practical lesson No. 2

Topic: " Requirements for sterile products. Determination of the main indicators of the quality of ampoule glass »

Goal: ampoule glass. »

Purpose: to study the peculiarities of the technology of industrial production of sterile products, to study the main technological operations and equipment necessary for the production of sterile products in production conditions

Basic concepts: ***Technological regulation*** — *Sterility* - complete absence of living microorganisms and their spores.

Thermal stability is the ability of glass products not to be destroyed by sharp temperature fluctuations.

Chemical resistance - guarantees the preservation of medicinal substances and other components of the drug, determines the properties of glass before leaching.

Mechanical strength - to withstand loads during the processing of ampoules in the process of production, transportation, storage.

Ampoule glass is a solid amorphous material transparent in one or another part of the optical range (depending on the composition) obtained by solidification of a melt containing glass-forming components (oxides of silicon, boron, aluminum, phosphorus, etc.) and metal oxides (lithium, potassium, magnesium) , lead, etc.).

Equipment: visual material, multimedia projector, presentation, ampoules, sterilizers, dispenser (for example, auger), packaging container, examples of packaging .

Plan:

5. Organizational activities (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).
6. Control of the reference level of knowledge (written work, written test, frontal survey, etc.) (if necessary):

— requirements for students' theoretical readiness to perform practical classes.

Knowledge requirements.

A student of higher education should know:

- rules of work at a pharmaceutical enterprise and safety rules;
- ampoule glass composition;
- ampule manufacturing technology;
- basic quality requirements of ampoule glass.

A student of higher education must be able to:

- apply work and safety rules when working with ampoule glass;
- to formulate basic concepts regarding sterile products;
- formulate and explain the technological block diagram for the production of sterile ampoules;

List of didactic units:

- the text of textbooks;
- a bank of test tasks.

— questions (test tasks, tasks, clinical situations) to check basic knowledge on the subject of the lesson:

1. Requirements for sterile products.

2. Glass for making ampoules and vials, its classes and brands. Basic requirements and quality indicators of ampoule glass. Preparation of glass wire, methods of washing ampoules, study of stability of ampoules.

3. Basic requirements and quality indicators of ampoule glass.

4. Preparation of glass wire, methods of washing ampoules, study of stability of ampoules.

5. GMP requirements for the production of sterile products (preparation of the air environment, personnel, clothing, equipment, premises).

6. Procedure for controlling the temperature regimes of sterilizers

7. Formation of professional abilities and skills (mastering the skills of calculating the material balance, drawing up a technological block diagram for the industrial production of ampoules:

task content:

— 1. Methods of obtaining injection solutions. The equipment used to obtain them in factory conditions?

— 2. Ways of filling ampoules with injection solutions?

— 3. Method of sealing ampoules. Determination of tightness of ampoules?

— 4. The concept of "grade for injections". Additional cleaning during the production of injection solutions.

— 5. Special cleaning of injection solutions of magnesium suMFate, calcium chloride, glucose from chemical impurities.

— 6. Methods of depyrogenization of injection solutions?

— 7. Sterilization of injection solutions in ampoules, vials.

— 8. Chemical and physical methods of sterilization?

— 9. Control of sterility. Step-by-step quality control of injection solutions.

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— 1. At what dilution should the ampoules with a capacity of 2 ml of 2.15 ml be filled, if at a dilution of 400 mm Hg. an ampoule filled with water weighs 4.04 g; at 600 mm Hg - 4.64 g, and empty - 2.10 m?

— 2. When checking the thermal stability of 1,000 ampoules of one series, 125 burst, which explains the low strength of the ampoules and is it possible to increase it?

— 3. After sterilization of ampoules filled with freshly obtained purified water, the pH shift of the water was 1.2. What class does this ampoule glass belong to?

— 4. During the analysis, the glass ampoule placed in the polariscope caused a suitable coloration. What should be done in this case?

— 5. AB-1 ampoules were used in the production of novocaine injection solution. Evaluate the technologist's actions.

— 6. There is 10.7 ml of a 10% glucose solution in an ampoule with a capacity of 10 ml. Does this amount meet regulatory requirements? Justify the answer.

— 7. Ampoules with a capacity of 1 ml contain 1.15 ml of a 20% injection solution of camphor in oil. Does this amount meet regulatory requirements? Justify the answer.

— 8. 6,048 microorganisms were found in the production room of the ampoule shop 4 meters long, 6 m wide and 3.5 m high.

Medicinal products for parenteral use are sterile preparations intended for administration by injection, iNPhaUsion or implantation into the human or animal body. These include aqueous and non-aqueous solutions, emulsions, suspensions, powders and tablets for obtaining solutions and implantation, lyophilized drugs that are administered parenterally (subcutaneously, intramuscularly, intravenously, retrobulbarly or subconjunctivally, in various cavities, etc.).

Introduction of PLZ is carried out by means of injections (injection of a small volume), iNPhaUsions (iNPhaUsion of more than 100 ml at the same time by drop or jet) or implantations with the help of special devices with a violation of the integrity of

the skin or mucous membranes. This application is quite paiNPhaUl, so recently, less paiNPhaUl methods of needle-free introduction of injection solutions have been used in the form of the thinnest (about 0.1-0.12 mm in diameter) jet under high pressure, which is ejected from the hole of a special injector at a speed of 300 m /s and penetrates through the skin to a depth of 3 cm. For this, manual injectors such as "Bee", "Hynospray", "Jetinjection" are used.

According to the SPHU, medicinal products for parenteral use are classified according to the following groups:

1) injectable drugs;

2) intravenous iNPhaUsion drugs;

3) concentrates for injection or intravenous infusion drugs;

4 powders for injection or intravenous infusion drugs;

5) implants.

The requirements of this article do not apply to preparations made from human blood, immunological and radiopharmaceutical preparations, implantable prostheses.

Injectable drugs are sterile solutions, emulsions or suspensions. Solutions for injections should be clear and free of particles. Emulsions for injections should not show signs of delamination. In suspensions for injections, a sediment may be observed, but it should disperse instantly when shaken, forming a suspension. The resulting suspension should be stable enough to provide the required dose when administered.

Intravenous infusion drugs are sterile aqueous solutions or emulsions (water as a dispersion medium) that must be free of pyrogens and usually isotonic with blood. They are intended for use in large doses, so they should not contain any antimicrobial preservatives . ,

Concentrates for injection or intravenous infusion medicinal products are sterile solutions intended for injections or infusions after dilution. Before use, the concentrates are diluted to the indicated volume with the appropriate liquid. After dilution, the resulting solution must meet the requirements for injection or infusion drugs.

Powders for injection or intravenous infusion of drugs are solid sterile substances placed in a sterile container. When shaken with the indicated volume of the appropriate sterile liquid, they should quickly form either a clear, particle-free solution or a homogeneous suspension. After dissolution or suspension, they must meet the requirements set forth for injection or infusion medicinal products.

Implants are sterile solid medicinal products with sizes and forms suitable for parenteral implantation and active substances that are released over a long period . They should be packed in individual sterile containers

Parenteral use of drugs involves a violation of the skin, which is associated with possible infection by pathogenic microorganisms and the introduction of mechanical inclusions. Therefore, sterile production, in comparison with other branches of industry, has specific features dictated by the requirements for injectable dosage forms.

The main ones are the absence of mechanical impurities, sterility, stability, pyrogenicity, etc., and for some drugs, isotonicity, osmolality or osmolarity, isoionicity, isohydricity, viscosity, which is indicated in the relevant regulatory and technical documentation.

Sterile products are produced in special primary packaging (vessels) made of fiberglass (ampoules, vials) or polymer materials (vials, flexible containers, syringe ampoules).

Vessels for injection drugs are divided into 2 groups:

• disposable, containing a certain amount of the drug, intended for a single injection;

• multi-dose, providing the possibility of repeated selection of a certain amount of the drug from the vessel without violating sterility.

The volume of the injectable drug in a single-dose container should be sufficient for the selection and administration of the nominal dose when using the usual method of administration.

Multi-dose aqueous injectable medicinal products contain an appropriate antimicrobial preservative in the required concentration, with the exception of drugs with appropriate antimicrobial properties. When releasing a drug for parenteral administration in a multi-dose container, it is necessary to indicate safety measures for its administration and especially for storage between doses.

The most widespread representative of a disposable vessel is an ampoule. Ampoules are glass vessels of various capacities and shapes, which consist of an expanded part - a body (bulk) and a capillary (stem). In the pharmaceutical industry, ampoules with a capacity of 1, 2, 3, 5 and 10 ml are most common; 20 and 50 ml - typical for veterinary medicine. The capillaries of ampoules can be straight or pinched. The most rational are ampoules with a clamp, so the liquid from the ampoule cannot get into the capillary, which is important when opening the ampoules. Notification 0712.1-98 on the change of TU 480945-005-96 introduced new ampoules with a colored break ring.

In our country, ampoules of syringe and vacuum filling with appropriate labeling are produced:

Ampoules of vacuum filling: VPO - vacuum filling with an open clamp; VO - vacuum filling without squeezing is open;

Syringe filling ampoules: IP-B - syringe filling is open; IP-C - syringe filling with an open bell;

C - paired;

G - for glycerin

Along with the letter designation, the capacity of the ampoules, the brand of glass and the number of regulatory and technical documentation (standard) are indicated.

The quality and size of ampoules must meet the requirements of TU U 480945-005-96 (Appendix D, fig. 1-5) or OST 64-2-485-85.

An example of the designation of an ampoule of the IP type with a nominal capacity of 1.0 ml of the B form without a colored fracture ring made of glass of the USP-1 brand:

Ampoule IP-1B USP-1 TU U 480945-005-96.

An example of the designation of an ampoule of the IP type with a nominal capacity of 1.0 ml, form B , with a colored break ring made of glass of the USP-1 brand:

Ampoule IP-1B KI USP-1 TU U 480945-005-96.

One-time use vessels include a syringe ampoule. These are tubes made of polymer materials with an injection needle protected by a cap. As a rule, they have a special purpose and different names in different countries - citolem, Maiola, Ampigni, etc.

An example of multi-dose containers are vials for infusion solutions with a capacity of 50, 100, 250, 500 ml, made of glass or polymer materials. Promising vessels for iNPhaUsion solutions are flexible containers made of polyvinyl chloride (PVC).

Glass vessels for injection solutions are made of medical glass, which is a solid solution (alloy) of silicates, metal oxides and some salts. By changing the composition of components and their concentration, it is possible to obtain glass with specified properties.

Depending on the qualitative and quantitative content of additives, as well as on the obtained properties, there are 2 classes and several brands of glass used in the production of ampoules.

Since 1996, ampoules made of glass of the medical grade - USP-1 (TU U 480945-002), corresponding to water resistance class 1/121, have been produced in Ukraine. Internal residual inclusions are not allowed in the ampoules, which create a specific difference in the course of the rays of more than 8 million "1, since pollution and glass dust are not washed away. USP-1 ampoules must be thermally stable and withstand a temperature difference of at least 130 °C; chemically stable - the change in pH of the water after processing the ampoules in the sterilizer should not exceed 0.8.

It is allowed to make ampoules from other brands of medical glass that do not impair the quality of products. The first class includes glass brands: HC-3, HC-1, and the second - HC-2, АБ-1.

Production of ampoules is carried out at glass plants from glass tubes (glass wire) of the above-listed classes and brands of glass. Glass wire is a tube 1 to 1.5 meters long with varying internal and external diameters. Wire calibration is very important to obtain ampoules uniform in size, given capacity and the same for the entire series. The quality of the wire is strictly regulated according to the following indicators: taper, difference, straightness, ovality, bending, washing from contamination.

In addition, there must be no mechanical inclusions, air bubbles and other glass defects.

After production and sorting, the wire is washed. Several methods of washing are known:

1. Chamber
2. Ultrasonic
3. Contact-ultrasonic

Glass wire is dried with hot filtered air or using the tunnel method.

All types of ampoules are made of glass wire on rotary glass forming machines or semi-automatic machines of different companies IO-8 "TUNGSRAM" (Hungary), "AMBEG", "MATVER" (Germany). The disadvantage of this method of manufacturing ampoules is the formation of internal stresses when there is a redistribution of bond lengths between the molecules of the glass composition, which can lead to the mechanical destruction of the product or the appearance of microcracks under adverse factors (high temperature, sudden temperature changes, vibration, etc.) . Therefore, after manufacturing, residual stresses are removed by annealing ampoules in special furnaces. The annealing process consists in heating ampoules or vials to a temperature close to the softening temperature of glass, holding them at this temperature for 7-10 minutes and gradually cooling.

The American company "Corning-GLASS" has developed a new method of manufacturing ampoules without the intermediate use of wire. The process of forming glass products on these machines is a jet-blowing method that ensures a high degree of uniformity in the distribution of glass mass in the walls of the finished products.

The following requirements are imposed on glass for ampoules:

• transparency - for visual and optical control for the absence of mechanical inclusions;

• colorless - allows to detect, in addition to mechanical inclusions, a change in the color of the solution;

• low melting point - necessary for high-quality sealing of ampoules at a relatively low temperature to avoid heating the solution;

• thermal stability - the ability of glass products not to be destroyed by sharp temperature fluctuations;

• chemical resistance, which guarantees the preservation of medicinal substances and other components of the drug, which shows the ability of glass to leach;

• mechanical strength - to withstand loads during processing of ampoules during production, transportation and storage. This requirement must be combined with the necessary fragility for easy dissection of the ampoule capillary.

• the specific contact surface of the solution with the glass, because the larger this value is, the higher the chemical resistance of the glass should be.

Preparation of ampoules for filling includes the following operations: dissection of capillaries, determination of the quality of ampoules, washing, drying and (or) sterilization of ampoules.

The quality of ampoule glass and ampoules is evaluated according to the following parameters:

1. Water resistance
2. Alkali resistance
3. Residual stresses
4. Thermal stability
5. Chemical resistance
6. Light-shielding properties (for SNS-1 glass)
7. Visual control of ampoules
8. Radial beating of the ampoule stem relative to the body
9. Deviation from roundness of ampoules
10. For ampoules of vacuum filling, the depth of rarefaction is determined in order to accurately fill the ampoules with the help of a vacuum.
11. For ampoules with a colored fracture ring, the fracture strength is determined.

Table 1.2 shows the comparative characteristics of different brands of ampoule glass.

TABLE 1.2 comparative physical and chemical properties of glasses

Indexes	USP-1	NS-1	ns-z	NS-2
Thermal stability, °C not less	170	150	150	145
Temperature coefficient of linear expansion in the temperature range of 20-400°C, L • 1 07 degrees'1	60-65	68-72	63-67	78-82
Density, g/cm3	2.4-2.5	2.44-2.46	2.42-2.44	2.44-2.46
Water resistance. mg of Na2O per 1 g of glass	0.02-0.062	0.06	0.05	0.15
Resistance to bases, mg/dm2	75-140	85	100	85

The radial runout of the ampoule stem relative to the axis of the body and the radial runout of the conical end relative to the axis of the cylindrical part of the type G ampoule is checked using a universal stand of the ST type according to GOST 10197 or TU 2-034-623, a test prism according to TU 2-034-439 or TU 2- 034-812 and a clock-type indicator according to GOST 577.

The ampoule is placed on the prism, the tip of the indicator is brought to the capillary of the ampoule, and for ampoules of type G - to the conical end, and the ampoule is rotated 360 °. The radial stroke of the stem of ampoules should not exceed:

1.0 mm - for IP-type ampoules with a capacity of 1-2 ml;
1.2 mm - for IP-type ampoules with a capacity of 3 ml;
1.5 mm - for IP-type ampoules with a capacity of 5, 10, 20 ml;
1.5 mm - for type G ampoules with a capacity of 0.3 ml;
1.7 mm - for ampoules of type VO and C with a capacity of 1, 2, 3 ml;
2.0 mm - for ampoules of type VO and C with a capacity of 5 ml;
2.0 mm - for ampoules of the VPO type with a capacity of 10 ml.

The deviation from the roundness of the ampoules, which is determined by the difference between two mutually perpendicular diameters, should not exceed the limit deviations per diameter.

The bottom of ampoules, except for type G ampoules, should ensure the stability of an empty ampoule with a cut stem on a horizontal plane. Concavity of the bottom of VPO-10 ampoules is allowed no more than 2.0 mm.

The breaking strength of ampoules with a colored ring is determined on the installation, the scheme of which is shown in fig. 1, with the following characteristics:

Test speed - 10 mm / min; force measurement limit - 200 N; the temperature of the tested ampoule is 20 ± 5 °C.

Depending on the tested ampoules, the distance between the prisms is set.

The ampoule is placed on the prisms so that the force acts at an angle of 90 ° to the axis of the ampoule at the location of the colored fracture ring. The force continues until the ampoule stem breaks off. At the moment of fracture, the numerical value of the fracture force is determined, which must correspond to the following values:

Nominal capacity	Length L = her + b, mm	The power of breaking, N
1	36=18+18	From 30 to 70 inclusive.
2	36=18 + 18	From 3 to 70 incl.
10	60 = 22 + 38	From 30 to 90 inclusive.

The number of ampoules with a colored fracture ring to determine the fracture force should be at least 0.01% of the batch. A lot is considered to be the number of ampoules of the same type, of the same capacity and brand of glass, issued by one document.

The accuracy of vacuum filling depends on the pressure difference between the rarefaction inside the ampoule, created with the help of the device, and the pressure of the surrounding air. Atmospheric pressure often changes and ampoules of the same nominal volume have different sizes, therefore chemical and pharmaceutical factories compile tables of the required degree of dilution depending on atmospheric pressure, ampoule sizes and the required volume of filling.

In those cases when there are no such tables, the ampoules are filled at the working dilution, which gives the filling volume slightly less and (or) more than the required one, and its desired depth is calculated by the interpolation method. When the value is found, control fillings are made and the correctness of the calculations is checked by the difference in the mass of the ampoules followed by its conversion to the volume before and after filling, or the volume is measured using a calibration syringe.

Light-protective properties are tested in ampoules made of light-protective glass by measuring light transmittance in the range of the spectrum from 290 to 450 nm.

Methods of determining other qualitative characteristics of ampoules are given in the laboratory work.

After determining the quality of the glass, the ampoules are subjected to external and internal washing. External washing is more often carried out by the method of internal washing. The following methods are used for internal washing: syringe, vacuum (turbovacuum, vortex, vapor condensation), vibration, thermal, ultrasonic (vibro-ultrasonic, contact-ultrasonic). After washing the ampoules, in the shortest way and quickly enough to prevent contamination, they are transferred to drying or sterilization, depending on the conditions of the ampoules. Washed, dried or sterilized ampoules and vials are transferred to the ampoule stage.

10. General characteristics. Classification. Requirements

recommendations (instructions) for performing tasks (professional algorithms, orientation maps for the formation of practical skills and abilities, etc.):

Orientation map for independent work with literature on the subject of the lesson.

№№p.p.	Main tasks	Instructions	Answers
1	2	3	4
1.	Preparation of glass ampoules.	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. - P. 475-477.
2.	Preparation of glass vials and stoppers.	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. - P. 475-477.
3.	Polymeric materials for packaging of parenteral medicinal	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. –

	products.		Kh.: NPhaU: Original, 2016. – P. 21-25.

— requirements for the results of the work, including the registration: to state the basic concepts and rules of the pharmaceutical enterprise and safety rules, the concept of proper practice, technological block diagrams, to draw up a material balance.

— control materials for the final stage of the lesson: tasks, tasks, tests, etc. (if necessary):

Task:

8. List of recommended literature (main, additional, electronic information resources) :

Main:

- A.G. Bashura, O.S. Shpichak, E.E. Bogutska; under the editorship A.I. Tikhonov and S.A. Tikhonova - Kh.: Original, 2016. - 462 p.
- Vishnevska, N.P. Polovka, R.S. Korytniuk et al. - Kh.: National Academy of Sciences: Original, 2016. - 378p.
- Workshop on industrial technology of medicinal products: teaching. manual for students higher education institutions with the specialty "Pharmacy" / O.A. Ruban, D.I. Dmytrievskyi, L.M. Khokhlova [and others]; under the editorship O.A. Ruban. – Kh.: National Institute of Medical Sciences; Original, 2015. – 320 p.
- Industrial technology of medicines : education. manual for students' independent work / O.A. Ruban , V.D. Rybachuk , L.M. X ohlova etc. - KH.: NPHAU, 2015. - 120 p.
- Study guide for preparation for the final modular control and State certification in the Industrial Technology of Medicines for full-time and part-time students of the "Pharmacy" specialty / Ed. O.A. Ruban. - Kh.: National Academy of Sciences, 2016 . - 80 p.
- Study guide for independent preparation of students of the Faculty of Pharmacy for the licensing integrated exam "Step 2. Pharmacy" / O.A. Ruban, V.D. Rybachuk, L.M. Khokhlova, D.S. Pulyaev - KH.: NPHAU, 2016. - 63 p.
- Auxiliary substances in the production of medicines: training. manual for students higher pharmacy education closing / O.A. Ruban , I.M. _ Pertsev, S.A. Kutsenko, Yu.S. Oily; under the editorship I.M. Pepper - Kh.: Golden Pages, 2016. - 720 p.

- Technology of drugs for industrial production: tutorial. for university students education class: in 2 h. / V.I. Chuyeshov, E.V. Gladukh, I.V. Saiko et al. – 2nd ed., revision. and additional - Kh.: NPhaU: Original, 2012. - Part 1. - 694 p.
- Technology of drugs for industrial production: tutorial. for university students education class: in 2 h. / V.I. Chuyeshov, E.V. Gladukh, I.V. Saiko et al. – 2nd ed., revision. and additional - Kh.: NPhaU: Original, 2013. - Part 2. - 638 p.
- Modern pharmaceutical technologies: education. manual to laboratory classes of full-time, evening and part-time master's students of the specialty 8.110201 "Pharmacy" / under the editorship. O.A. Ruban. - Kh.: Publishing House of the National Academy of Sciences, 2016. - 256 p.

Auxiliary :

- Mathematical planning of an experiment when conducting scientific research in pharmacy / T.A. Groshovyi, V.P. Martsenyuk, L.I. Kucherenko and others. – Ternopil: TDMU Ukrmedknyga, 2008. – 367 p.
- Regulatory and technical documentation and production validation. Material balance: Educational method. river for audit. and external audit. student work special "Pharmacy" of full-time and part-time education / D.I. Dmytrievskyi, G.D. Slipchenko, I.M. Hrubnyk, D.V. Rybachuk . - Kh.: Publishing House of the National Academy of Sciences, 2008. - 45 p.
- Technology of medicinal products of industrial production: training. manual/ edited by Prof. D.I. Dmitrievsky. – Vinnytsia: Nova kniga, 2008. – 280 p.
- Drug technology. Educational and methodological guide: Education. manual for students higher education hall. / O.I. Tikhonov, P.A. Logvin, S.O. Tikhonova, O.V. Bazulin, T.G. Yarnykh, O.S. Shpychak, O.M. Kotenko; under the editorship O.I. Tikhonova, Kh.: Original, 2009. - 432 p.
- C pyrotometry. Recovery and rectification of ethanol: Textbook. help / D.I. Dmytryevsky, L.I. Boguslavskaya, L.N. Khokhlova and others; Ed. Prof. D.I. Dmitrievsky - Kh.: Izd-vo NPhaU, 2006. - 100 p.
- Pharmaceutical encyclopedia / Chief editor. council and the author of the foreword V.P. Black people - 3rd ed., revised. and additional - K.: "MORION", 2016. - 1952 p.
- Encyclopedia of Pharmaceutical Technology: 3-d Ed. / ed. by J. Swarbrick. – New York; London: Informa Healthcare, 2007. - 4128 p.
- European Pharmacopoeia 8.0 [8th edition] / European Directorate for the Quality of Medicines & Healthcare. - Strasbourg, 2013. - 3638 p.
- Handbook of Pharmaceutical Excipients, 6th edition / RC Rowe, PJ Sheskey, ME Quinn. - Pharmaceutical Press and American Pharmacists Association, 2009. - 521 p.

- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeial Center for the Quality of Medicines", 2015. - Vol. 1. - 1128 p.
- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicines", 2014. - Vol. 2. - 724 p.
- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products", 2015. - Vol. 3. - 732 p.
- Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of non-sterile medicinal products in pharmacies" ST-N of the Ministry of Health of Ukraine 42 – 4.5: 2015 // Edited by Prof. O. I. Tikhonov and Prof. T.G. Jarnih - Kyiv, 2015. - 109 p. (Approved by the order of the Ministry of Health of Ukraine No. 398 of 01.07.2015).
- Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of sterile and aseptic medicinal products in pharmacies" ST-N of the Ministry of Health of Ukraine 42 – 4.6: 2015 // Edited by. Prof. O.I. Tikhonov and Prof. T.G. Jarnih - Kyiv, 2015. - 76 p. (Approved by order of the Ministry of Health of Ukraine No. 398 dated 07/01/2015).
- Production technology of extemporaneous medicinal apipreparations and their use in pharmacy, medicine and cosmetology: methodical recommendations / O.I. Tikhonov, T.G. Yarnykh, S.O. Tikhonova, O.G. Bashura, O.S. Shpychak, L.O. Bondarenko, P.S. Sirota, B.T. Kudryk, R.I. Skrypnyk-Tikhonov, N.S. Bohdan, S.G. Bobro, L.V. Kanoshevich, O.E. Bogutska; under the editorship O.I. Tikhonov. - Kh.: Izd-vo NPhaU, 2016. - 75 p.
- Powder manufacturing technology: teaching. manual / L.L. Davtyan, R.S. Korytniuk, A.O. Drozdova, I.O. Vlasenko, Z.V. Malenka, V.P. Popovych, V.V. Gladyshev, S.M. Musoev, T.F. Olifirova, L.I. Vishnevska, O.M. Hlushchenko, O.O. Khomich; under the editorship L.L. Davtyan, R.S. Korytnyuk - K.: "Education of Ukraine", 2016. - 141 p.
- Pharmacotherapy of mastopathy. Extemporaneous prescriptions. Phytopreparations and homeopathic medicines: methodical recommendations / L.I. Vishnevska,
- S.S. Zuykin. –Kharkiv.: Publishing House of IFNMU-NPhaU, 2017. – 44 p.

- Zujkina SS The pharmacotechnological studies of the phytospecies composition for the complex therapy of mastopathy / SS Zujkina, LI Vishnevska // Herald of pharmacy. – 2017. – No. 2 (90). - P. 43-47.
- Bogutska O.E. The main directions of solving the problem of pharmaceutical incompatibilities / O.E. Bogutska // Modern achievements of pharmaceutical technology and biotechnology: collection of scientific papers. – issue 2. – Kharkiv.: Publishing House of the National Academy of Sciences, 2017. – pp. 29–31.
- Polovko N.P. Assessment of biopharmaceutical factors in the development and production of new medicines / N.P. Polovko, L.I. Vishnevska, O.S. Shpychak // Modern achievements of pharmaceutical technology and biotechnology: collection of scientific works, issue 2. – X.: NPhaU Publishing House, 2017. – P. 155-160.
- Prospects for the creation of new original drugs based on substances of plant origin / O.A. Ruban, S.A. Malinovska, Murad Al-Tawaiti, S.I. Mazurets // Phytotherapy. – 2012. – No. 2. - pp. 63–65.
- The current state of creation, production and quality control of capsules / M.B. Chubka, L.V. Vronska, N.O. Zarivna et al. // Pharmaceutical journal. - 2012. - No. 2. - P. 165-168.
- Murachanian D. Two-Piece Hard Capsules for Pharmaceutical Formulations / D. Murachanian // Journal of GXP Compliance. - 2010. - Vol. 14. - P. 31-42.
- Patel H. New pharmaceutical excipients in solid dosage forms – A review / H. Patel, V. Shah, U. Upadhyay // Int. J. of Pharm. & Life Sci. - 2011. - Vol. 2. – P. 1006–1019.
- Recent trends of treatment and medication peptic ulcerative disorder / D. Bhowmik, Chiranjib, KK Tripathi [et al.] // International Journal of PharmTech Research. - 2010. - Vol. 2. – P. 970–980.
- The effects of powder compressibility, speed of capsule filling and pre-compression on plug densification / M. Llusa , E. Faulhammer , S. Biserni [et al.] // Int. J. Pharm. – 2014. – Vol. 471. – P. 182–188.

Electronic resources:

- www.moz.gov.ua is the official website of the Ministry of Health of Ukraine
- fp.com.ua - website of the magazine "Pharmacist Praktik"
- www.provisor.com.ua – the official website of the magazine "Provisor"
- Compendium: drugs. - [Electronic resource]. - Access mode: http://compendium.com.ua/ - as of October 10, 2016.

- State Register of Medicinal Products of Ukraine. - [Electronic resource]. - Access mode: http://www.drlz.com.ua/ - as of January 10, 2017.
- Database "Equalizer" LLC "Business Credit" - [Electronic resource]. - Access mode: http://eq.bck.com.ua/ - as of September 20, 2016.

Practical lesson No. 3

Topic: " Industrial production of injection solutions "

Goal: to study the peculiarities of the technology of industrial production of injection solutions, to study the main technological operations and equipment necessary for the production of injection solutions in production conditions

Basic concepts: *Sterility* - the absence of viable microorganisms and their spores in the environment, organism, any material or product.

Pyrogenicity - the absence of pyrogenic substances, or pyrogens, in medicines for parenteral use.

Stabilization - is the ability to preserve the properties that characterize the quality of products in accordance with the requirements of regulatory documentation or a technological process aimed at creating a pharmaceutical dispersed system capable of maintaining a stable state, despite physical, chemical and biological processes aimed at changing the phase state (evaporation, melting, sublimation , delamination, agglomeration of particles, etc.), chemical (reactions of hydrolysis, oxidation, reduction, polymerization, racemization, etc.) or biological changes under the influence of microbiological contamination.

Mechanical inclusions are one of the indicators of the quality of sterile substances used for the preparation of parenteral and eye drops. Mechanical inclusions of injection, IV infusion and eye solutions are secondary mobile insoluble particles, excluding gas bubbles accidentally present in the solutions.

Equipment: visual material, multimedia projector, presentation, ampoules, sterilizers, dispenser (for example, auger), packaging container, examples of packaging.

Plan:

9. Organizational activities (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).

10. Control of the reference level of knowledge (written work, written test, frontal survey, etc.) (if necessary):

— requirements for students' theoretical readiness to perform practical classes.

Knowledge requirements.

A student of higher education should know:

- rules of work at a pharmaceutical enterprise and safety rules;

- subject and tasks of drug technology;
- basic concepts of drug technology;
- basic requirements for the drug manufacturing process.

A student of higher education must be able to:

- apply work and safety rules during the manufacture of medicinal products;
- to formulate the basic concepts of drug technology;
- formulate and explain the technological aspects of drug production;
- apply basic calculations during preparatory work for the manufacture of medicinal products.

List of didactic units:

- the text of textbooks;
- a bank of test tasks.

questions (test tasks, tasks, clinical situations) to check basic knowledge on the subject of the lesson:

1. The basic principles of good manufacturing practice for medicinal products (GMP), requirements for the production of sterile products.
2. Classification of clean rooms, cleanliness classes. Water for injections, requirements, equipment, control.
3. Production of injectable drugs without and with stabilizers, aseptically produced using non-aqueous solvents, etc.
4. Methods of stabilization, isotonization, purification of solutions, types of filters.
5. Methods of filling ampoules, modern methods of sealing ampoules and determining their tightness.
6. Sterilization of injection solutions, control of their sterility. Controls the quality of injection solutions.
7. Technological scheme of production; the equipment used.
8. Methods of obtaining injection solutions. The equipment used for their production in factory conditions.
9. Methods of filling ampoules with injection solutions.
10. Method of sealing ampoules. Determination of the tightness of ampoules.
11. The concept of "grade for injections". Additional cleaning during the production of injection solutions.
12. Special cleaning of injection solutions of magnesium sulfate, calcium chloride, glucose from chemical impurities.
13 Methods of depyrogenation of injection solutions.
14. Sterilization of injection solutions in ampoules , vials.
15. Chemical and physical methods of sterilization.
16 . Control of sterility. Step-by-step quality control of injection solutions.
1 7 . Concept of stability of medicines. The basic principle of stabilization.
1 8 . Factors affecting the stability of injection solutions.

1 9 . Stabilization of solutions of salts of weak bases and strong acids.

20 . Stabilization of solutions of salts of strong bases and weak acids.

21 . Stabilization of glucose solutions for injections.

22 . Stabilization of solutions of easily oxidizing substances.

23 . Use of preservatives.

24. Features of the production technology of oil solutions for injections

Lesson content

Medicinal products for parenteral use are sterile preparations intended for administration by injection, infusion or implantation into the human or animal body. These include aqueous and non-aqueous solutions, emulsions, suspensions, powders and tablets for obtaining solutions and implantation, lyophilized drugs that are administered parenterally (subcutaneously, intramuscularly, intravenously, retrobulbarly or subconjunctivally, in various cavities, etc.).

Today, parenteral drugs account for almost 30% of all ready-made medicinal products produced by the domestic pharmaceutical industry. Injectable dosage forms occupy a prominent place in the nomenclature of medicinal products. Injectable drugs account for 10% to 15% of articles in various pharmacopoeias of the world.

Parenteral medicinal products (PLZ) are a relatively young medicinal form.

The parenteral route of drug administration has a number of advantages over other methods:

— rapid action and complete bioavailability of the medicinal substance;

— accuracy and convenience of dosing;

— the possibility of administering a medicinal substance to a patient who is in an unconscious state, or when the medicine cannot be administered orally;

— lack of influence of gastrointestinal tract secretions and liver enzymes, which occurs when drugs are taken internally;

— the possibility of creating large stocks of sterile drugs, which facilitates and accelerates their release from pharmacies.

Along with the advantages, the parenteral route of administration has some disadvantages:

— when liquids are injected through the damaged skin, pathogenic microorganisms can easily enter the blood;

— together with the drug for injections, air may be introduced into the body, which will cause vascular embolism or heart failure;

— even a small amount of extraneous impurities can have a negative effect on the patient's body;

— the psycho-emotional aspect associated with the painfulness of the injection route;

— administration of sterile drugs should be carried out only by qualified specialists.

Introduction of PLZ is carried out by means of injections (injection of a small volume), infusions (infusion of more than 100 ml at the same time by drop or jet) or implantations with the help of special devices with a violation of the integrity of the skin or mucous membranes. This application is quite paiNnful, so recently, less painful methods of needle-free introduction of injection solutions have been used in the form of the thinnest (about 0.1-0.12 mm in diameter) jet under high pressure, which is ejected from the hole of a special injector at a speed of 300 m /s and penetrates through the skin to a depth of 3 cm. For this, manual injectors such as "Bee", "Hynospray", "Jetinjection" are used.

According to the SPHU, medicinal products for parenteral use are classified according to the following groups:

1) injectable drugs;

2) intravenous infusion drugs;

3) concentrates for injection or intravenous infusion medicinal products;

4) powders for injection or intravenous infusion drugs;

5) implants.

The requirements of this article do not apply to preparations made from human blood, immunological and radiopharmaceutical preparations, implantable prostheses.

Injectable drugs are sterile solutions, emulsions or suspensions. Solutions for injections should be clear and free of particles. Emulsions for injections should not show signs of delamination. In suspensions for injections, a sediment may be observed, but it should disperse instantly when shaken, forming a suspension. The resulting suspension should be stable enough to provide the required dose when administered.

Intravenous infusion drugs are sterile aqueous solutions or emulsions (water as a dispersion medium) that must be free of pyrogens and usually isotonic with blood. They are intended for use in large doses, so they should not contain any antimicrobial preservatives.

Concentrates for injection or intravenous infusion medicinal products are sterile solutions intended for injections or infusions after dilution. Before use, the concentrates are diluted to the indicated volume with the appropriate liquid. After dilution, the resulting solution must meet the requirements for injection or infusion drugs.

Powders for injection or intravenous infusion of drugs are solid sterile substances placed in a sterile container. When shaken with the indicated volume of the appropriate sterile liquid, they should quickly form either a transparent, particle-free solution or a homogeneous suspension. After dissolution or suspension, they must meet the requirements set forth for injection or infusion medicinal products.

Implants are sterile solid medicinal products with sizes and forms suitable for parenteral implantation and active substances that are released over a long period. They should be packed in individual sterile containers

Parenteral use of drugs involves a violation of the skin, which is associated with possible infection by pathogenic microorganisms and the introduction of mechanical inclusions. Therefore, sterile production, in comparison with other branches of industry, has specific features dictated by the requirements for injectable dosage forms. The main ones are the absence of mechanical impurities, sterility, stability, pyrogenicity, etc., and for some drugs, isotonicity, osmolality or osmolarity, isoionicity, isohydricity, viscosity, which is indicated in the relevant regulatory and technical documentation.

Solutions for injections are made in special facilities in A or C cleanliness class premises in compliance with all rules asepsis Preparation of aqueous or non-viscous solutions for injections is carried out by the mass-volume method, using hermetically sealed reactors equipped with a shell and a stirring device. In those cases where the density of the solvent is significantly different from the density of water, mass is used a method in which both the medicinal substance and the solvent are taken for by mass Dissolution of slowly or poorly soluble medicinal substances is carried out by heating and stirring.

The stage of preparation of the solution includes the following operations: dissolution, isotonization, stabilization, introduction of preservatives, filtering.

Depending on the properties of medicinal substances, some of the operations may be excluded, for example, isotonization, stabilization, administration of preservatives. Among injection solutions, a special group is isotonic, which means solutions with an osmotic pressure equal to the osmotic pressure of body fluids (blood plasma, lymph, cerebrospinal fluid, etc.).

Isotonic concentrations of medicinal substances in solutions can be calculated by the following methods:

* a method based on Van't-Hoff's law;

* cryoscopic method based on Raoult's law;

* method of equivalents of medicinal substances according to sodium chloride.

Abroad, they also use a graphical method of calculating isotonic concentrations, which allow to quickly, but with some approximation, determine the amount of sodium chloride required for isotonization of a solution of a medicinal substance based on the developed nomograms.

During the manufacture and storage of some medicinal products, a change in their properties is often observed, which occurs with different speed and degree of manifestation. This is due to a decrease in the content of medicinal substances or a decrease in their pharmacological activity, a change in the properties of medicinal forms, etc. Such changes affect the shelf life (storage) of drugs, which can range from

a few hours (antibiotic solutions) or days (enzyme solutions) to several years. Today, special attention is paid to the task of increasing the stability of medicinal products.

Processes occurring in drugs can be conditionally classified into physical, chemical and biological. The convention lies in their relationship: chemical transformations can cause changes in physical properties, while physical changes cause unwanted chemical processes. Biological processes are accompanied by both chemical and physical transformations.

The physical processes that occur mainly during storage include agglomeration of particles of the dispersed phase, delamination, change in consistency, evaporation, sublimation, etc.

Chemical processes often take place during the preparation of the drug, especially during thermal sterilization, and are accompanied by various chemical reactions - hydrolysis, saponification, redox processes, photochemical and enzymatic transformations, polymerization and isomerization, etc. are less often observed.

Biological processes caused by the vital activity of microorganisms, often lead to undesirable chemical transformations of active substances, sometimes to changes in the appearance of the dosage form.

Direct antioxidants:

1) Substances that prevent the formation of active radicals from hydroperoxides : Phenols, naphthols, aromatic amines, molecular iodine

indirect antioxidants; polybasic carboxylic acids; oxyacids (citric, salicylic, tartaric acid); ethylenediaminetetraacetic acid (Trilon B); calcium soltrilone B (tetacin); unitiol; amino acids, thiourea, etc.

Stabilization of substances: apomorphine hydrochloride, ascorbic acid, sodium aminosalicylate, streptocide, etazol sodium stabilizer analgin, sodium sulfite; vikasol sodium salicylate, ascorb stabilizer: sodium meta bisulfite;
novocaine stabilizer: sodium bisulfite; vikasol dicain novocaine streptocide - stabilizer: sodium thiosulfate; Stable substance: thiamine bromide thiamine chloride stab: unitiol; apomorphine hydrochloride - stab: cysteine

The choice of preservative is determined by the composition of the medicinal product; pH of the environment; regime

Requirements: pharmacological indifference to vykonkin (absence of general toxic allergens and irritating effects)

Broad spectrum antimicrobial action at the low end.

Good solubility in the dispersion medium

The chemical is indifferent to drugs, packaging and auxiliary materials

Stable in a wide interval of pH and temperature for a period of 1 hour

There are no effects on organoleptics

Maintain sterility

lack of ability to develop resistance of microorganisms

Application of the drug. Medicines for intracavitary, intraocular, and cerebrospinal fluids , as well as for a single dose of more than 15 ml, should not contain preservatives.

The list of preservatives by type of effect on micro- organisms:
1 Bacteriostatic Nipagin Nipazole Butaben Benzoic and sorbic acids Chlorbutanol hydrate Merthiolate Cefiran Cephyrol Phenylethyl alcohol
2 Bactericidal effect Phenol Tricresol Cresol Chlorcresol

Chemical classification
1 Inorganic - silver water 1-10 mg/l
2 Organic alcohols: ethyl phenylethyl 0.3-0.5% benzyl 2%
Phenols phenol 0253-0.3% chlorocresol 0.05-0.1%
Complex esters of n-hydroxybenzoic acid (Nipagin Nipazole) up to 0.5%
Organic types of benzoin sorbine) 0.1-0.2%
Essential oils laurel, lavender, anise, pink, lemon
Quaternary ammonium salts of benzalkonium chloride
dimethyldodecylbenzylammonium 0.01%
Organometallic merthiolate 0.005%
0.02% 0.1% salts of phenylmercury acetate or nitrate up to 0.2% and 0.001-0.004%

11. Formation of professional abilities and skills (mastering the skills of calculating the material balance , drawing up a technological block diagram for the industrial production of medicinal products:

— task content:

1. Compile a working prescription for obtaining 1000 ampoules of 1 ml of 20% sodium caffeine-benzoate solution (ρ 20% 1.073, KZO=0.65, Krash=1.2).
2. Make a working prescription for obtaining 1000 ampoules of 10 ml of 40% glucose solution (KZO=0.69 at 10% humidity, 40%=1.1498, Krash=1.1).
3. Make a working prescription for obtaining 20 ampoules of 1 ml of a 20% solution of camphor in oil (20%=0.926).
4. Prepared 250 ml of caffeine-sodium benzoate solution. The analysis showed that the solution contains 21% of the drug. How much water is needed to obtain a 20% solution?
5. Prepared 250 ml of caffeine-sodium benzoate solution. The analysis showed that the solution contains 19% of the drug. How much should be added to caffeine sodium benzoate to make a 20% solution?
6. Compile the material balance of the production of 1,000 ampoules of euphilin 2.4%. The cost factor is 1.12.

— recommendations (instructions) for performing tasks (professional

algorithms, orientation maps for the formation of practical skills and abilities, etc.):

Orientation map for independent work with literature on the subject of the lesson.

№№p.p.	Main tasks	Instructions	Answers
1	2	3	4
1.	Requirements for starting substances and solvents	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. – P. 481 – 494.
2.	Preparation of parenteral solutions.	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. – P. 495 – 512.
3.	Filtration of parenteral solutions	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. – P. 513 – 534.
4.	Methods of sterilization of parenteral solutions	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. – P. 535 – 566.

— requirements for the results of the work, including the registration: to state the basic concepts and rules of the pharmaceutical enterprise and safety rules, the concept of proper practice, technological block diagrams, to draw up a material balance.

— control materials for the final stage of the lesson: tasks, tasks, tests, etc. (if necessary):

Task:

1. Draw up a working prescription for obtaining +1000 ampoules of 1 ml of 20% caffeine-sodium benzoate solution (ρ 20% 1.073, KZO = 0.65, Krash = 1.2).

2. Make a working prescription for obtaining +1000 ampoules of 10 ml of 40% glucose solution (KZO = 0.69 at 10% humidity, ρ 40% = 1.1498, Krash = 1.1).

3. Make a working prescription for obtaining 20 ampoules of 1 ml of a 20% solution of camphor in oil (ρ 20% = 0.926).

12. List of recommended literature (main, additional, electronic information resources) :

Main:

- A.G. Bashura, O.S. Shpichak, E.E. Bogutska; under the editorship A.I. Tikhonov and S.A. Tikhonova - Kh.: Original, 2016. - 462 p.
- Vishnevska, N.P. Polovka, R.S. Korytniuk et al. - Kh.: National Academy of Sciences: Original, 2016. - 378p.
- Workshop on industrial technology of medicinal products: teaching. manual for students higher education institutions with the specialty "Pharmacy" / O.A. Ruban, D.I. Dmytrievskyi, L.M. Khokhlova [and others]; under the editorship O.A. Ruban. – Kh.: National Institute of Medical Sciences; Original, 2015. – 320 p.
- Industrial technology of medicines : education. manual for students' independent work / O.A. Ruban , V.D. Rybachuk , L.M. X ohlova etc. - KH.: NPHAU, 2015. - 120 p.
- Study guide for preparation for the final modular control and State certification in the Industrial Technology of Medicines for full-time and part-time students of the "Pharmacy" specialty / Ed. O.A. Ruban. - Kh.: National Academy of Sciences, 2016 . - 80 p.
- Study guide for independent preparation of students of the Faculty of Pharmacy for the licensing integrated exam "Step 2. Pharmacy" / O.A. Ruban, V.D. Rybachuk, L.M. Khokhlova, D.S. Pulyaev - KH.: NPHAU, 2016. - 63 p.
- Auxiliary substances in the production of medicines: training. manual for students higher pharmacy education closing / O.A. Ruban , I.M. _ Pertsev, S.A. Kutsenko, Yu.S. Oily; under the editorship I.M. Pepper - Kh.: Golden Pages, 2016. - 720 p.
- Technology of drugs for industrial production: tutorial. for university students education class: in 2 h. / V.I. Chuyeshov, E.V. Gladukh, I.V. Saiko et al. – 2nd ed., revision. and additional - Kh.: NPhaU: Original, 2012. - Part 1. - 694 p.
- Technology of drugs for industrial production: tutorial. for university students education class: in 2 h. / V.I. Chuyeshov, E.V. Gladukh, I.V. Saiko et al. – 2nd ed., revision. and additional - Kh.: NPhaU: Original, 2013. - Part 2. - 638 p.
- Modern pharmaceutical technologies: education. manual to laboratory classes of full-time, evening and part-time master's students of the specialty 8.110201 "Pharmacy" / under the editorship. O.A. Ruban. - Kh.: Publishing House of the National Academy of Sciences, 2016. - 256 p.

Auxiliary :

- Mathematical planning of an experiment when conducting scientific research in pharmacy / T.A. Groshovyi, V.P. Martsenyuk, L.I. Kucherenko and others. – Ternopil: TDMU Ukrmedknyga, 2008. – 367 p.
- Regulatory and technical documentation and production validation. Material balance: Educational method. river for audit. and external audit. student work special "Pharmacy" of full-time and part-time education / D.I. Dmytrievskyi, G.D. Slipchenko, I.M. Hrubnyk, D.V. Rybachuk . - Kh.: Publishing House of the National Academy of Sciences, 2008. - 45 p.
- Technology of medicinal products of industrial production: training. manual/ edited by Prof. D.I. Dmitrievsky. – Vinnytsia: Nova kniga, 2008. – 280 p.
- Drug technology. Educational and methodological guide: Education. manual for students higher education hall. / O.I. Tikhonov, P.A. Logvin, S.O. Tikhonova, O.V. Bazulin, T.G. Yarnykh, O.S. Shpychak, O.M. Kotenko; under the editorship O.I. Tikhonova, Kh.: Original, 2009. - 432 p.
- C pyrotometry. Recovery and rectification of ethanol: Textbook. help / D.I. Dmytryevsky, L.I. Boguslavskaya, L.N. Khokhlova and others; Ed. Prof. D.I. Dmitrievsky - Kh.: Izd-vo NPhaU, 2006. - 100 p.
- Pharmaceutical encyclopedia / Chief editor. council and the author of the foreword V.P. Black people - 3rd ed., revised. and additional - K.: "MORION", 2016. - 1952 p.
- Encyclopedia of Pharmaceutical Technology: 3-d Ed. / ed. by J. Swarbrick. – New York; London: Informa Healthcare, 2007. - 4128 p.
- European Pharmacopoeia 8.0 [8th edition] / European Directorate for the Quality of Medicines & Healthcare. - Strasbourg, 2013. - 3638 p.
- Handbook of Pharmaceutical Excipients, 6th edition / R.C. Rowe, P.J. Sheskey, M.E. Quinn. - Pharmaceutical Press and American Pharmacists Association, 2009. - 521 p.
- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeial Center for the Quality of Medicines", 2015. - Vol. 1. - 1128 p.
- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicines", 2014. - Vol. 2. - 724 p.
- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products", 2015. - Vol. 3. - 732 p.

- Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of non-sterile medicinal products in pharmacies" ST-N of the Ministry of Health of Ukraine 42 – 4.5: 2015 // Edited by Prof. O. I. Tikhonov and Prof. T.G. Jarnih - Kyiv, 2015. - 109 p. (Approved by the order of the Ministry of Health of Ukraine No. 398 of 01.07.2015).
- Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of sterile and aseptic medicinal products in pharmacies" ST-N of the Ministry of Health of Ukraine 42 – 4.6: 2015 // Edited by. Prof. O.I. Tikhonov and Prof. T.G. Jarnih - Kyiv, 2015. - 76 p. (Approved by order of the Ministry of Health of Ukraine No. 398 dated 07/01/2015).
- Production technology of extemporaneous medicinal apipreparations and their use in pharmacy, medicine and cosmetology: methodical recommendations / O.I. Tikhonov, T.G. Yarnykh, S.O. Tikhonova, O.G. Bashura, O.S. Shpychak, L.O. Bondarenko, P.S. Sirota, B.T. Kudryk, R.I. Skrypnyk-Tikhonov, N.S. Bohdan, S.G. Bobro, L.V. Kanoshevich, O.E. Bogutska; under the editorship O.I. Tikhonov. - Kh.: Izd-vo NPhaU, 2016. - 75 p.
- Powder manufacturing technology: teaching. manual / L.L. Davtyan, R.S. Korytniuk, A.O. Drozdova, I.O. Vlasenko, Z.V. Malenka, V.P. Popovych, V.V. Gladyshev, S.M. Musoev, T.F. Olifirova, L.I. Vishnevska, O.M. Hlushchenko, O.O. Khomich; under the editorship L.L. Davtyan, R.S. Korytnyuk - K.: "Education of Ukraine", 2016. - 141 p.
- Pharmacotherapy of mastopathy. Extemporaneous prescriptions. Phytopreparations and homeopathic medicines: methodical recommendations / L.I. Vishnevska,
- S.S. Zuykin. –Kharkiv.: Publishing House of IFNMU-NPhaU, 2017. – 44 p.
- Zujkina S.S. The pharmacotechnological studies of the phytospecies composition for the complex therapy of mastopathy / S.S. Zujkina, L.I. Vishnevska // Herald of pharmacy. – 2017. – No. 2 (90). - P. 43-47.
- Bogutska O.E. The main directions of solving the problem of pharmaceutical incompatibilities / O.E. Bogutska // Modern achievements of pharmaceutical technology and biotechnology: collection of scientific papers. – issue 2. – Kharkiv.: Publishing House of the National Academy of Sciences, 2017. – pp. 29–31.
- Polovko N.P. Assessment of biopharmaceutical factors in the development and production of new medicines / N.P. Polovko, L.I. Vishnevska, O.S. Shpychak // Modern achievements of pharmaceutical technology and biotechnology: collection of scientific works, issue 2. – X.: NPhaU Publishing House, 2017. – P. 155-160.

- Prospects for the creation of new original drugs based on substances of plant origin / O.A. Ruban, S.A. Malinovska, Murad Al-Tawaiti, S.I. Mazurets // Phytotherapy. – 2012. – No. 2. - pp. 63–65.
- The current state of creation, production and quality control of capsules / M.B. Chubka, L.V. Vronska, N.O. Zarivna et al. // Pharmaceutical journal. - 2012. - No. 2. - P. 165-168.
- Murachanian D. Two-Piece Hard Capsules for Pharmaceutical Formulations / D. Murachanian // Journal of GXP Compliance. - 2010. - Vol. 14. - P. 31-42.
- Patel H. New pharmaceutical excipients in solid dosage forms – A review / H. Patel, V. Shah, U. Upadhyay // Int. J. of Pharm. & Life Sci. - 2011. - Vol. 2. – P. 1006–1019.
- Recent trends of treatment and medication peptic ulcerative disorder / D. Bhowmik, Chiranjib, KK Tripathi [et al.] // International Journal of PharmTech Research. - 2010. - Vol. 2. – P. 970–980.
- The effects of powder compressibility, speed of capsule filling and pre-compression on plug densification / M. Llusa , E. Faulhammer , S. Biserni [et al.] // Int. J. Pharm. – 2014. – Vol. 471. – P. 182–188.

Electronic resources:

- www.moz.gov.ua is the official website of the Ministry of Health of Ukraine
- fp.com.ua - website of the magazine "Pharmacist Praktik"
- www.provisor.com.ua – the official website of the magazine "Provisor"
- Compendium: drugs. - [Electronic resource]. - Access mode: http://compendium.com.ua/ - as of October 10, 2016.
- State Register of Medicinal Products of Ukraine. - [Electronic resource]. - Access mode: http://www.drlz.com.ua/ - as of January 10, 2017.
- Database "Equalizer" LLC "Business Credit" - [Electronic resource]. - Access mode: http://eq.bck.com.ua/ - as of September 20, 2016.

Practical lesson No. 4

Topic: " Industrial production of iNPhaUsion solutions"

Purpose: to study the peculiarities of the technology of industrial production of infusion solutions, to study the main technological operations and equipment necessary for the production of infusion solutions in production conditions

Basic concepts: *Sterility* is the complete absence of living microorganisms and their spores.

Isotonic solutions are solutions that have an osmotic pressure equal to the osmotic pressure of physiological body fluids (blood, plasma, lymph, tear fluid, etc.).

Plasma substitute solutions - solutions that, based on the composition of dissolved substances, osmotic pressure, viscosity and pH value compared to blood plasma, are able to support the vital activity of cells and organs and do not cause significant changes in the physiological balance in the body.

Isohydria is the correspondence of the pH of the solution to the pH of the blood.

Isoviscosity is the correspondence between the viscosity of the solution and the viscosity of blood

Equipment: visual material, multimedia projector, presentation.

Plan:

13. Organizational activities (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).

14. Control of the reference level of knowledge (written work, written test, frontal survey, etc.) (if necessary):

— requirements for students' theoretical readiness to perform practical classes.

Knowledge requirements.

A student of higher education should know:

General characteristics of infusion solutions. Their use in practical medicine.

2. Classification of infusion dosage forms.

3. Requirements for infusion drugs.

4. Prospects for the development of technology for the production of infusion dosage forms.

5 . Concept of stability of medicines. The basic principle of stabilization.

6 . Factors affecting the stability of injection solutions.

7 . Chemical methods of stabilization.

8 . Stabilizers used in the production of injection solutions.

9 . The influence of surfactants on the kinetics of chemical reactions.

10 . Physical methods of stabilization

11. General characteristics. Classification. Requirements .

List of didactic units:

- the text of textbooks;
- a bank of test tasks.

— questions (test tasks, tasks, clinical situations) to check basic knowledge on the subject of the lesson:

1. Characteristics of iNPhaUsion solutions, use.

2. Classification and requirements for infusion solutions.

3. Prospects for the development of infusion solutions, an assortment of

domestic and foreign medicines.

4. Production of infusion solutions. Their quality control.

Lesson content

The purpose of aseptic manufacturing is to preserve the sterility of a product made from components that have each been previously sterilized by one of the methods described above. This is achieved by using the conditions and equipment above and designed to prevent microbial contamination.

Under aseptic conditions, such stages of the production process as filling of containers and sealing, mixing of ingredients with subsequent aseptic filling and. clogging

Prior to the release of each batch of any medicinal product sterilized by filtration or manufactured under aseptic conditions, sterility tests on an appropriate number of samples must be carried out.

Preparation of parenteral solutions that are not subject to thermal sterilization. Observance of all aseptic conditions is especially important in the production of medicinal preparations for injections, which are not subject to heat sterilization in the final packaging. This refers to the preparation of injection solutions from thermolabile substances (barbamil, adrenaline hydrochloride, euphilin) or substances with pronounced bactericidal activity (amino-zine, diprazine, hexam ethyl entetramin, etc.)

Solutions of hexamethylenetetramine at normal temperature are relatively stable and have a bactericidal effect. As the temperature rises, hydrolysis of hexamethylenetetramine occurs with the formation of formaldehyde and ammonia, therefore, the preparation of its 40% solution is carried out in aseptic conditions (purity class A) without heat sterilization. The medicinal substance used to prepare the injection solution should be of higher quality than the pharmacopoeia. It should not contain amines, ammonium salts and paraform. If there is no grade "for injections", then hexa methyl entetramine is subjected to special purification.

To obtain stable solutions of euphilin, use the grade "for injections" with an increased content of ethylenediamine (18-22% instead of 14-18%). Water for injections intended for the preparation of Euphilin solutions is decarbonized. These measures serve to prevent the hydrolysis of euphilin. 12-24% solutions of euphilin for injections are prepared in aseptic conditions, without stabilizers, ampoules are poured and sealed in a stream of nitrogen (gas protection).

Aqueous solutions of aminazine and diprazine are easily oxidized even under short-term exposure to light with the formation of red-colored decomposition products. To obtain a stable preparation, add antioxidants and sodium chloride to isotonize the solution. It is produced in strictly aseptic conditions without thermal sterilization.

The process of filtering through bacterial filters, which removes microorganisms from the solution, thus ensuring its sterility and pyrogenicity, plays an important role

in the technology of preparation of injection solutions that are not subject to heat sterilization. Sterile filtration is achieved using depth and membrane filters.

Infusion medicinal forms. Infusion drugs are the most complex group of parenteral dosage forms. These include the so-called physiological solutions, which, based on the composition of dissolved substances, are able to support the vital activity of cells and organs, without causing significant shifts in the physiological balance in the body. Solutions that are as close as possible to human blood plasma in terms of their properties are called blood substitute fluids. With various pathological conditions accompanied by blood loss, shock, violation of the water-electrolyte and acid-alkaline state of the body, there is a need to introduce significant volumes of iNPhaUsion solutions into the bloodstream. INPhaUsion therapy is based on the long-term parenteral administration of large volumes of drugs into the body, which are sterile, pyrogen-free aqueous solutions or emulsions, usually isotonic blood plasma, showing selectivity and multifunctional effects on the body. Depending on the function performed when administered to the body, iNPhaUsion solutions are divided into six groups:

1. Hemodynamic or anti-shock drugs. Intended for the treatment of shock of various origins, replenishment of circulating blood volume, and restoration of hemodynamic disorders. This group includes: polyglukin, rheopolyglucin, gelatinol, rheo-glumac, etc. Ethanol, bromides, barbiturates, narcotic substances are often added to anti-shock solutions, which normalize disturbances and inhibition of the central nervous system; glucose, which activates redox processes in the body.

2. Deintoxication solutions. Many diseases and pathological conditions are accompanied by intoxication of the body (infectious diseases, large burns, kidney and liver failure, poisoning by various toxic substances, etc.). For their treatment, targeted detoxification solutions are needed, the components of which must bind to toxins and be quickly removed from the body. Such compounds include polyvinylpyrrolidone, polyvinyl alcohol, hemodeze, polydeze neohemodeze, gluco-neodeze, enterodeze, etc.

3. Regulators of water-salt balance and acid-base balance. Such solutions correct the composition of the blood in cases of dehydration caused by diarrhea, brain edema, toxicosis, etc. These include saline injection 0.9% and 10% solutions of sodium chloride, Ringer's and Ringer-Locke's solutions, Petrov's liquid, 4.5-8.4% solutions of sodium hydrogen carbonate, 0.3-0, 6% solution of potassium chloride, etc.

4. Preparations for parenteral feeding. They serve to provide energy resources of the body, deliver nutrients to organs and tissues, especially after surgical interventions, in comatose states of the patient, when he cannot consume food naturally, etc. Representatives of this group are 40% glucose solution, casein hydrolyzate, aminopeptide, amino blood, fibrinosol, lipostabil, lipid, lipofundin, introlipid, aminophosphatide, etc.

5. Solutions with the function of oxygen transfer. They are designed to restore the respiratory function of the blood, they include perfluorocarbon compounds. This group of infusion drugs is in the testing and development stage.

6. Solutions of complex action, or polyfunctional. These drugs, which have a wide range of action, can combine several of the functions listed above.

In addition to the general requirements for solutions for injections (apyrogenicity, sterility, stability, absence of mechanical inclusions), specific requirements are also made for plasma substitute drugs. When introduced into the bloodstream, infusion solutions must fulfill their functional purpose, while being completely excreted from the body without accumulating. They should not damage tissues or disrupt the functions of individual organs. Due to the large volumes administered, blood substitutes should not be toxic, should not cause sensitization of the body after three repeated administrations, should not irritate the vascular wall and should not cause embolism. their physical and chemical properties must be stable. Many infusion solutions must be isotonic, isoionic, isohydric. their viscosity must correspond to the viscosity of blood plasma.

Isotonicity is the ability of solutions to have an osmotic pressure equal to the osmotic pressure of body fluids (blood plasma, tear fluid, lymph, etc.).

Isoionicity is the property of injection solutions to contain certain ions in the ratio and quantities typical for blood serum. Therefore, infusion solutions include ions K+, Ca2+, Mg2+, Na+ C1, SO, PO, and others. Currently, plasma replacement solutions are manufactured, which contain up to 40 trace elements that play an important physiological role.

An important requirement for injection solutions is their stability during a certain storage time. The stability of the drug is the ability of the medicinal substance to preserve its physicochemical properties and pharmacological activity during the time provided by the NTD.

Some medicinal substances are unstable during production or storage, cannot withstand the conditions of thermal sterilization, etc. and can undergo various chemical transformations in solution. At the same time, such chemical reactions as hydrolysis, oxidation-reduction and photochemical processes, isomerization, etc. take place. Various reactions are initiated under the influence of light, air oxygen, elevated temperature during sterilization, changes in the pH value of the solution, chemical impurities in the raw material, and the release of catalysts due to glass leaching.

The stability of injection solutions, first of all, depends on the quality of the original solvents and medicinal substances, the class and brand of glass of ampoules and vials, the presence of oxygen in water and solutions, the pH of solutions, the temperature and time of sterilization, the presence of heavy metal ions, production conditions and storage of drugs, etc.

The mechanism of the oxidation-reduction process was revealed in the peroxic theory of A. N. Bach and I. O. Engler and the theory of branched chains by N. N. Semenov.

Stabilization of solutions is carried out by physical and chemical methods. Physical methods include: separation of ampoules of medicinal substance and solvent, selection of ampoules from chemically resistant material, coating of the inner surface of ampoules with special films, replacement of glass with polymer, compliance with the principle of gas protection.

Chemical methods are based on the addition of stabilizers or antioxidants. Stabilizers can slow down or eliminate unwanted body chemical reactions, create a certain pH value of solutions, increase the solubility of medicinal substances or keep them in a suspended state. The choice of stabilizer depends, first of all, on the nature of medicinal substances.

Despite the variety and extreme complexity of the processes occurring in solutions, medicinal substances that require stabilization can be conditionally divided into three groups:

1) Solutions of salts formed by weak and strong bases
acids (salts of alkaloids, nitrogenous and synthetic nitrogenous salts
grounds, etc.),

2) Solutions of salts formed by strong and weak bases
acids (sodium thiosuMFate, theophylline, sodium caffeine benzoate, etc.),

3) Solutions of easily oxidizing substances (ascorbic acid, etc.)

To stabilize substances of the first group, a 0.1 M solution of hydrochloric acid is used, for substances of the second group - a 0.1 M solution of sodium hydroxide or sodium bicarbonate.

In order to stabilize solutions of easily oxidized substances, direct and indirect antioxidants are used.

Direct antioxidants have a higher ability to oxidize, binding oxygen, thereby preventing unwanted processes in solutions. Indirect antioxidants or negative catalysts are substances that form complex compounds with heavy metal ions that inhibit oxidation-reduction processes.

The possibility of oxidation of medicinal substances decreases with a decrease in the concentration of oxygen in the solvent and above the solution. Therefore, the solvents used for the preparation of injection solutions must be freed from oxygen by boiling, saturated with carbon dioxide or nitrogen and other methods. In the conditions of industrial production of injection solutions, the initial binding of oxygen in the solvent is irrational, therefore, at the post-blowing technological stages of the production of solutions in ampoules, its saturation occurs again. Therefore, it is more appropriate to remove it immediately before filling the ampoules. One of the ways to remove oxygen and stabilize some injection solutions is gas protection.

Another method of stabilizing easily oxidizable substances can be the use of high-molecular or surface-active substances (propylene glycol, low molecular weight polyethylene oxide, etc.). The use of preservatives also increases the stability of many drugs in ampoules.

Solutions of a number of unstable substances cannot acquire the necessary stability when using any one form of stabilization. In this case, it is necessary to use a combination of stabilizing factors of combined protection.

In each specific case, the use of stabilizing substances requires careful study when introducing them into the composition of injection solutions.

Among the diverse range of medicinal products used by modern scientific medicine, dosage forms for the eyes occupy a special place, and their production is the subject of a separate section of pharmaceutical technology. This is explained both by the unique features of the human eye organ (uniqueness of structure and properties), and by the specific mechanisms of absorption, distribution and interaction of medicinal substances with various tissues and fluids of the eye.

The vulnerability of eye tissues, a large number of diseases of the human visual organs (abscesses of the eyelid and eye socket, anioma, blepharitis, glaucoma, trachoma, cataracts and a whole series of other diseases) necessitated the creation and constant improvement of drugs used in ophthalmological practice.

Equally important is the task of creating a simple, convenient, aesthetic, informative, and cost-effective packaging of ophthalmic drugs, which will allow for a long time to store them in a sterile and chemically unchanged state, and at the time of use, ensure speed and ease of administration.

3 . Materials on methodical provision of classes.

3.1 . Control materials for the preparatory stage of the lesson:

1. Concept of stability of medicines. The basic principle of stabilization.
2. Factors affecting the stability of injection solutions.
3. Theories of oxidation-reduction processes by A.N. Bach and I.O. Engler.
4. The theory of branched chains by N. N. Semenov.
5. Chemical methods of stabilization.
6. Stabilizers used in the production of injection solutions.
7. Influence of surfactants on the kinetics of chemical reactions.
8. Physical methods of stabilization.
9. Gas protection of injection solutions.
10. Effect of glass quality on the stability of substances.
11. Characteristics of the group of substances that require chemical stabilization.
12. Mechanisms of action of stabilizers:

    12.1. Stabilization of solutions of salts of weak bases and strong acids.

12.2. Stabilization of solutions of salts of strong bases and weak acids.

12.3. Stabilization of glucose solutions for injections.

13. Stabilization of solutions of easily oxidizing substances.

13.1. Mechanisms of action of direct antioxidants.

13.2. Mechanisms of action of indirect antioxidants.

13.3. Use of VMC for stabilization of injection solutions.

14. The effect of pH and the presence of heavy metals on the rate of oxidation reactions.

15. Methods of removing oxygen from solvents used in the manufacture of injection solutions.

16. Use of preservatives.

17. Technological methods of stabilization of ampoule solutions.

3.2 . Methodological support materials for the main stage of the lesson:

Task No. 1. Preparation of a 0.25% or 0.5% novocaine solution for injection in ampoules of 2 ml

(solutio novocaini 0.25% aut 0.5% pro injectionibus)

composition: (cf. x, art. 468)

Novocaine 2.5 or 5.0 g (fs 42-2709-90)

Hydrochloric acid solution 0.1 N to pH 3.8 - 4.5 (guest 3118-77)

Water for injections up to 1 liter (fs 42-2620-89)

Description. Transparent colorless liquid. pH of the solution, the content of novocaine in 1 ml of the solution should be 0.00235 - 0.00265 g or 0.00485 - 0.00515 g, respectively

Preparation. The technological process begins with dissection, washing and drying of 10 ampoules of neutral glass. The internal washing of ampoules is carried out with the help of laboratory vacuum or syringe washing machines. Drying of ampoules is carried out in a drying cabinet at a temperature of 180 °C. According to the working instructions, the required amount of analgin is weighed and dissolved in a 50 ml volumetric flask in a small amount (20 - 25 ml) of water for injections while stirring. After dissolving novocaine, the solution is brought up to the mark with water for injections, first acidified with the calculated amount of a sterile solution of hydrochloric acid. The solution is thoroughly mixed.

After bringing to the standard concentration, the solution is filtered through a sterile glass filter No. 3 and the ampoules are filled with the syringe method, taking into account the filling norms.

Ampoules are sealed with a heating device or a capillary puller, after which they are sterilized with saturated steam at a temperature of 120 ° C (0.1 MPa) for 8 minutes.

The quality control of the solution in the ampoules is carried out according to the following technological parameters: determination of ampoule filling norms,

determination of pH of the solution, determination of the tightness of the ampoules, control of the presence of mechanical inclusions, determination of the transparency of the solution.

After obtaining satisfactory results of the analysis, labeling and packaging of finished products are carried out.

Task #2. Preparation of sodium solution

Caffeine-benzoate 10% or 20% for injections in ampoules of 2 ml (solutio coffeini-natrii benzoatis 10% aut 20% pro injection1bus)

Composition: (gf x, art. 174)

Caffeine sodium benzoate 100.0 g or 200.0 g

4 ml of 0.1 N sodium hydroxide solution

Water for injections up to 1 l

Description. A colorless, transparent liquid, the pH of the solution should be 6.8 - 8.5.

The content of caffeine-sodium benzoate in 1 ml of solution should be 0.097 - 0.103 or 0.194 - 0.206 m

Preparation. The technological process begins with dissection, washing and drying of 10 ampoules of neutral glass. The internal washing of ampoules is carried out with the help of laboratory vacuum or syringe washing machines. Drying of ampoules is carried out in a drying cabinet at a temperature of 180 °C.

According to the working instructions, the required amount of caffeine-sodium benzoate is weighed, dissolved in a sterile measuring flask with a capacity of 50 ml in haMF the amount of water for injections, to which the calculated amount of sterile 0.1 N sodium hydroxide solution is added. Dissolution is carried out with stirring and gentle heating in a water bath. The volume of the solution is brought up to the mark with water for injections and mixed thoroughly.

After bringing to the standard concentration, the solution is filtered through a sterile glass filter No. 3 and the ampoules are filled with the syringe method, taking into account the filling norms.

Ampoules are sealed with a heating device or a capillary puller, after which they are sterilized with saturated steam at a temperature of 120 °C (0.11 MPa) for 8 minutes.

The quality control of the solution in the ampoules is carried out according to the following technological parameters: determination of ampoule filling norms, determination of pH of the solution, determination of the tightness of the ampoules, control of the presence of mechanical inclusions, determination of the transparency of the solution.

After obtaining satisfactory results of the analysis, labeling and packaging of finished products are carried out.

15. Formation of professional abilities and skills (mastering the skills of calculating the material balance, drawing up a technological block diagram for the industrial production of medicinal products:

— task content:

Task No. 1 . Preparation of the solution

Novocainamide 10% for injections in ampoules of 1 or 2 ml (solutio novocainamide 10% pro injection ibus)

Composition: (gf x art. 465)

Novocainamide 100.0 g

Sodium metabisuMFite 5.0 g

Water for injections up to 1 l

Description. Transparent colorless liquid. The pH of the solution is 3.8-5.0.

The content of novocainamide in 1 ml of solution should be 0.097-0.103 g

Preparation .

Task No. 2 . Preparation of a 5% ascorbic acid solution for injection in ampoules of 5 ml (solut1o acidi ascorb1nici 5% pro injectionibus)

Composition: (df x art. 7)

Ascorbic acid 50.0 g (fs 42-2668-89)

Sodium hydrogen carbonate 23.85 g (df x art. 430 or guest 4201-79)

Sodium suMFite anhydrous 2.0 g (guest 11683-76)

Water for injections, saturated

Carbon dioxide up to 1 liter (fs 42-2620-89)

Description. Transparent, colorless or yellowish solution. The pH of the solution is 6.0 - 7.0.

The amount of ascorbic acid in 1 ml of solution should be 0.0475 - 0.0525 g

— *Preparation* .

— recommendations (instructions) for performing tasks (professional algorithms, orientation maps for the formation of practical skills and abilities, etc.):

Orientation map for independent work with literature on the subject of the lesson.

№№p.p.	Main tasks	Instructions	Answers
1	2	3	4
1.	Requirements for starting substances and solvents	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016.

			– P. 481 – 494.
2.	Preparation of parenteral solutions.	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. – P. 495 – 512.
3.	Filtration of parenteral solutions	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. – P. 513 – 534.
4.	Methods of sterilization of parenteral solutions	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. – P. 535 – 566.

— requirements for the results of the work, including the registration: to state the basic concepts and rules of the pharmaceutical enterprise and safety rules, the concept of proper practice, technological block diagrams, to draw up a material balance.

— control materials for the final stage of the lesson: tasks, tasks, tests, etc. (if necessary):

Task:

16. List of recommended literature (main, additional, electronic information resources) :

Main:

- A.G. Bashura, O.S. Shpichak, E.E. Bogutska; under the editorship A.I. Tikhonov and S.A. Tikhonova - Kh.: Original, 2016. - 462 p.
- Vishnevska, N.P. Polovka, R.S. Korytniuk et al. - Kh.: National Academy of Sciences: Original, 2016. - 378p.
- Workshop on industrial technology of medicinal products: teaching. manual for students higher education institutions with the specialty "Pharmacy" / O.A. Ruban, D.I. Dmytrievskyi, L.M. Khokhlova [and others]; under the editorship O.A. Ruban. – Kh.: National Institute of Medical Sciences; Original, 2015. – 320 p.

- Industrial technology of medicines : education. manual for students' independent work / O.A. Ruban , V.D. Rybachuk , L.M. X ohlova etc. - KH.: NPHAU, 2015. - 120 p.
- Study guide for preparation for the final modular control and State certification in the Industrial Technology of Medicines for full-time and part-time students of the "Pharmacy" specialty / Ed. O.A. Ruban. - Kh.: National Academy of Sciences, 2016 . - 80 p.
- Study guide for independent preparation of students of the Faculty of Pharmacy for the licensing integrated exam "Step 2. Pharmacy" / O.A. Ruban, V.D. Rybachuk, L.M. Khokhlova, D.S. Pulyaev - KH.: NPHAU, 2016. - 63 p.
- Auxiliary substances in the production of medicines: training. manual for students higher pharmacy education closing / O.A. Ruban , I.M. _ Pertsev, S.A. Kutsenko, Yu.S. Oily; under the editorship I.M. Pepper - Kh.: Golden Pages, 2016. - 720 p.
- Technology of drugs for industrial production: tutorial. for university students education class: in 2 h. / V.I. Chuyeshov, E.V. Gladukh, I.V. Saiko et al. – 2nd ed., revision. and additional - Kh.: NPhaU: Original, 2012. - Part 1. - 694 p.
- Technology of drugs for industrial production: tutorial. for university students education class: in 2 h. / V.I. Chuyeshov, E.V. Gladukh, I.V. Saiko et al. – 2nd ed., revision. and additional - Kh.: NPhaU: Original, 2013. - Part 2. - 638 p.
- Modern pharmaceutical technologies: education. manual to laboratory classes of full-time, evening and part-time master's students of the specialty 8.110201 "Pharmacy" / under the editorship. O.A. Ruban. - Kh.: Publishing House of the National Academy of Sciences, 2016. - 256 p.

Auxiliary :

- Mathematical planning of an experiment when conducting scientific research in pharmacy / T.A. Groshovyi, V.P. Martsenyuk, L.I. Kucherenko and others. – Ternopil: TDMU Ukrmedknyga, 2008. – 367 p.
- Regulatory and technical documentation and production validation. Material balance: Educational method. river for audit. and external audit. student work special "Pharmacy" of full-time and part-time education / D.I. Dmytrievskyi, G.D. Slipchenko, I.M. Hrubnyk, D.V. Rybachuk . - Kh.: Publishing House of the National Academy of Sciences, 2008. - 45 p.
- Technology of medicinal products of industrial production: training. manual/ edited by Prof. D.I. Dmitrievsky. – Vinnytsia: Nova kniga, 2008. – 280 p.
- Drug technology. Educational and methodological guide: Education. manual for students higher education hall. / O.I. Tikhonov, P.A. Logvin, S.O. Tikhonova, O.V. Bazulin, T.G. Yarnykh, O.S. Shpychak, O.M. Kotenko; under the editorship O.I. Tikhonova, Kh.: Original, 2009. - 432 p.

- C pyrotometry. Recovery and rectification of ethanol: Textbook. help / D.I. Dmytryevsky, L.I. Boguslavskaya, L.N. Khokhlova and others; Ed. Prof. D.I. Dmitrievsky - Kh.: Izd-vo NPhaU, 2006. - 100 p.
- Pharmaceutical encyclopedia / Chief editor. council and the author of the foreword V.P. Black people - 3rd ed., revised. and additional - K.: "MORION", 2016. - 1952 p.
- Encyclopedia of Pharmaceutical Technology: 3-d Ed. / ed. by J. Swarbrick. – New York; London: Informa Healthcare, 2007. - 4128 p.
- European Pharmacopoeia 8.0 [8th edition] / European Directorate for the Quality of Medicines & Healthcare. - Strasbourg, 2013. - 3638 p.
- Handbook of Pharmaceutical Excipients, 6th edition / R.C. Rowe, P.J. Sheskey, M.E. Quinn. - Pharmaceutical Press and American Pharmacists Association, 2009. - 521 p.
- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeial Center for the Quality of Medicines", 2015. - Vol. 1. - 1128 p.
- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicines", 2014. - Vol. 2. - 724 p.
- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products", 2015. - Vol. 3. - 732 p.
- Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of non-sterile medicinal products in pharmacies" ST-N of the Ministry of Health of Ukraine 42 – 4.5: 2015 // Edited by Prof. O. I. Tikhonov and Prof. T.G. Jarnih - Kyiv, 2015. - 109 p. (Approved by the order of the Ministry of Health of Ukraine No. 398 of 01.07.2015).
- Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of sterile and aseptic medicinal products in pharmacies" ST-N of the Ministry of Health of Ukraine 42 – 4.6: 2015 // Edited by. Prof. O.I. Tikhonov and Prof. T.G. Jarnih - Kyiv, 2015. - 76 p. (Approved by order of the Ministry of Health of Ukraine No. 398 dated 07/01/2015).
- Production technology of extemporaneous medicinal apipreparations and their use in pharmacy, medicine and cosmetology: methodical recommendations / O.I. Tikhonov, T.G. Yarnykh, S.O. Tikhonova, O.G. Bashura, O.S. Shpychak, L.O. Bondarenko, P.S. Sirota, B.T. Kudryk, R.I. Skrypnyk-Tikhonov, N.S. Bohdan, S.G.

Bobro, L.V. Kanoshevich, O.E. Bogutska; under the editorship O.I. Tikhonov. - Kh.: Izd-vo NPhaU, 2016. - 75 p.

- Powder manufacturing technology: teaching. manual / L.L. Davtyan, R.S. Korytniuk, A.O. Drozdova, I.O. Vlasenko, Z.V. Malenka, V.P. Popovych, V.V. Gladyshev, S.M. Musoev, T.F. Olifirova, L.I. Vishnevska, O.M. Hlushchenko, O.O. Khomich; under the editorship L.L. Davtyan, R.S. Korytnyuk - K.: "Education of Ukraine", 2016. - 141 p.
- Pharmacotherapy of mastopathy. Extemporaneous prescriptions. Phytopreparations and homeopathic medicines: methodical recommendations / L.I. Vishnevska,
- S.S. Zuykin. –Kharkiv.: Publishing House of IFNMU-NPhaU, 2017. – 44 p.
- Zujkina S.S. The pharmacotechnological studies of the phytospecies composition for the complex therapy of mastopathy / S.S. Zujkina, L.I. Vishnevska // Herald of pharmacy. – 2017. – No. 2 (90). - P. 43-47.
- Bogutska O.E. The main directions of solving the problem of pharmaceutical incompatibilities / O.E. Bogutska // Modern achievements of pharmaceutical technology and biotechnology: collection of scientific papers. – issue 2. – Kharkiv.: Publishing House of the National Academy of Sciences, 2017. – pp. 29–31.
- Polovko N.P. Assessment of biopharmaceutical factors in the development and production of new medicines / N.P. Polovko, L.I. Vishnevska, O.S. Shpychak // Modern achievements of pharmaceutical technology and biotechnology: collection of scientific works, issue 2. – X.: NPhaU Publishing House, 2017. – P. 155-160.
- Prospects for the creation of new original drugs based on substances of plant origin / O.A. Ruban, S.A. Malinovska, Murad Al-Tawaiti, S.I. Mazurets // Phytotherapy. – 2012. – No. 2. - pp. 63–65.
- The current state of creation, production and quality control of capsules / M.B. Chubka, L.V. Vronska, N.O. Zarivna et al. // Pharmaceutical journal. - 2012. - No. 2. - P. 165-168.
- Murachanian D. Two-Piece Hard Capsules for Pharmaceutical Formulations / D. Murachanian // Journal of GXP Compliance. - 2010. - Vol. 14. - P. 31-42.
- Patel H. New pharmaceutical excipients in solid dosage forms – A review / H. Patel, V. Shah, U. Upadhyay // Int. J. of Pharm. & Life Sci. - 2011. - Vol. 2. – P. 1006–1019.

- Recent trends of treatment and medication peptic ulcerative disorder / D. Bhowmik, Chiranjib, KK Tripathi [et al.] // International Journal of PharmTech Research. - 2010. - Vol. 2. – P. 970–980.
- The effects of powder compressibility, speed of capsule filling and pre-compression on plug densification / M. Llusa , E. Faulhammer , S. Biserni [et al.] // Int. J. Pharm. – 2014. – Vol. 471. – P. 182–188.

Electronic resources:

- www.moz.gov.ua is the official website of the Ministry of Health of Ukraine
- fp.com.ua - website of the magazine "Pharmacist Praktik"
- www.provisor.com.ua – the official website of the magazine "Provisor"
- Compendium: drugs. - [Electronic resource]. - Access mode: http://compendium.com.ua/ - as of October 10, 2016.
- State Register of Medicinal Products of Ukraine. - [Electronic resource]. - Access mode: http://www.drlz.com.ua/ - as of January 10, 2017.
- Database "Equalizer" LLC "Business Credit" - [Electronic resource]. - Access mode: http://eq.bck.com.ua/ - as of September 20, 2016.

Practical lesson No. 5

Topic: " Industrial production of eye, ear and nasal dosage forms"

Purpose: to study the peculiarities of the technology of industrial production of eye, ear and nasal dosage forms, to study the main technological operations and equipment necessary for the production of eye, ear and nasal dosage forms in production conditions

Basic concepts: *Sterility* is the complete absence of living microorganisms and their spores.

Isotonic solutions are solutions that have an osmotic pressure equal to the osmotic pressure of physiological body fluids (blood, plasma, lymph, etc.).

Isoionicity is the property of other injection solutions to contain certain ions in the ratio and quantities typical for blood serum.

Prolongation – extension of the duration of action of drugs after their single use or an increase in the concentration of API in the body for a significant period of time.

Equipment: visual material, multimedia projector, presentation, packaging container .

Plan:

Organizational activities (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).

Control of the reference level of knowledge (written work, written test, frontal survey, etc.) (if necessary):

— requirements for students' theoretical readiness to perform practical classes.

Knowledge requirements.

A student of higher education should know:

- rules of work at a pharmaceutical enterprise and safety rules;
- subject and tasks of the production technology of eye, ear and nasal dosage forms;
- basic concepts of the technology of industrial production of eye, ear and nasal dosage forms;
- basic requirements for the process of industrial production of eye, ear and nasal dosage forms .

A student of higher education must be able to:

- apply work and safety rules during the manufacture of medicinal products;
- to formulate the basic concepts of drug technology;
- formulate and explain the technological aspects of drug production;
- apply basic calculations during preparatory work for the manufacture of medicinal products.

List of didactic units:

- the text of textbooks;
- a bank of test tasks.

— questions (test tasks, tasks, clinical situations) to check basic knowledge on the subject of the lesson:

1. Main characteristics of eye, ear and nasal dosage forms.
2. Methods of their production, the equipment used.
3. Physico-chemical and biological features of creation, prolongation. Quality control.
4. Technological schemes for the production of eye, ear and nasal medicines.
5. Requirements for ophthalmic dosage forms.
6. General technological scheme of production of eye drops.
7. General characteristics of medicated eye films. Excipients used in LPG production.
8. Types of eye drops packaging, their advantages and disadvantages?

17. Formation of professional abilities and skills (mastering the skills of calculating the material balance, drawing up a technological block diagram for the industrial production of medicinal products:

— task content:

1. Creation of aseptic conditions during the production of ophthalmic dosage forms.
2. Methods of stabilization of low-stable dosage forms.
3. Modern classification of ophthalmic dosage forms.
4. Requirements for ophthalmic dosage forms.
5. General technological scheme of production of eye drops.
6. General characteristics of medicated eye films. Excipients used in LPG production.
7. Types of eye drops packaging, their advantages and disadvantages.
8. General characteristics. Classification. Requirements

Lesson content

The purpose of aseptic processing is to preserve the sterility of a product made from components that have each been previously sterilized by one of the methods described above. This is achieved by using the conditions and equipment above and designed to prevent microbial contamination.

Under aseptic conditions, such stages of the production process as filling of containers and sealing, mixing of ingredients with subsequent aseptic filling and. capping

Before the release of each batch of any medicinal product sterilized by the filtration method or manufactured in aseptic conditions, sterility tests on the appropriate number of samples must be carried out.

In addition to the general requirements for eye, ear and nasal dosage forms, such as: apyrogenicity, sterility, stability, absence of mechanical inclusions, specific requirements are also put forward in them. They should NOT damage tissues and NOT disrupt the functions of vision, ears, and respiratory tract. These drugs should NOT be toxic, and should not cause sensitization of the body upon repeated administration, and should not irritate the vascular wall and NOT cause embolism. their physical and chemical properties must be stable. Many preparations for the eyes, nose and ears must necessarily be isotonic, isoionic, isohydric.

Isotonicity is the ability of the solution to have an osmotic pressure equal to the osmotic pressure of body fluids (blood plasma, tear fluid, lymph, etc.).

Isoionicity is the property of other injection solutions to contain certain ions in the ratio and quantities typical for blood serum. Therefore, the composition of iNPhaUsion solutions includes ions K +, Ca 2+, M g2 +, Na + C 1, SO, rota, etc. Currently, plasma-replacing solutions are being produced that contain up to 40 trace elements that play an important physiological role.

An important requirement for eye, ear and nasal dosage forms is their stability during a certain storage time. The stability of the drug is the ability of the medicinal substance to protect its physicochemical properties and pharmacological activity during the time provided for in the NTD.

Among the diverse range of medicines used by modern scientific medicine, dosage forms for the eyes occupy a special place, and their production is the subject of

a separate section of pharmaceutical technology. This is explained both by the unique features of the human eye organ (unique structure and properties), and by the specific mechanisms of absorption, distribution and interaction of medicinal substances with various tissues and eye fluids.

Vulnerability of eye tissues, a large number of diseases of the organs of human vision (abscesses of the eyelids and eye socket, anioma, blepharitis, glaucoma, trachoma, cataracts and a number of other diseases) necessitated the creation and constant improvement of drugs used in ophthalmological practice.

No less important is the task of creating a simple, convenient, aesthetic, informative and economically profitable packaging of ophthalmic drugs, which will allow for a long time to store them in a sterile and chemically unchanged state, and at the time of use to ensure speed and simplicity of administration.

Ophthalmological drugs are produced in liquid (drops, other injection solutions, lotions), soft (ointments, suspensions, emulsions), solid (inserts, powders, trituration tablets, pencils) and other dosage forms.

These dosage forms are subject to the same requirements as other injection solutions. They should be as free from mechanical and microbial contamination as possible, have the exact concentration of active substances, be isotonic, sterile and stable, and in some cases have a prolonged effect and buffer properties.

Production of eye medicines is carried out in aseptic conditions, this is due to the fact that they are applied to the conjunctiva of the patient's eye. Normally, the tear fluid contains lysozyme, which has the ability to lyse microorganisms that have entered the conjunctiva, but in eye diseases, the content of lysozyme (muromidase) in the tear fluid decreases, and the eye becomes insufficiently protected from the action of microorganisms. With this in mind, the conditions for the technological process of production and all preparatory operations must be the same as during the effectiveness of sterile dosage forms.

Eye drops and ointments have the largest specific gravity among ophthalmic dosage forms.

Eye drops are the simplest form of administration of active substances, prevention and treatment of many eye diseases.

As solvents for eye drops, water is used for other purposes. Injections, sterile fatty oils (peach, almond, etc.).

A necessary condition for the industrial production of eye drops is stability, since serial production requires a rather long sheMF life of eye drops. Preservatives, pH regulators, buffer systems, and antioxidants are used to stabilize eye drops.

Hypertonic and hypotonic aqueous solutions during instillation cause comfort and are poorly tolerated by patients, therefore eye drops require isolation. In addition to isotonicity, the pH value of solutions should have a limit of 3.5-8.5.

The bioavailability of ophthalmological pharmaceuticals is largely determined by the occasional contact of the active substance with tissues in the precorneal spaces of

the eyes. Increasing the duration of action (prolongation) of active substances reduces the dose and frequency of instillations, often avoiding side effects.

Prospective solvents for obtaining eye drops of prolonged action, which increase the bioavailability of drugs, are solutions of methylcellulose, 25% solution of PEG-400, 0.1-0.3% solutions of microbial polysaccharide - aubasidan.

The choice of the method of thermal sterilization of eye drops depends on the degree of stability of the active substances in the solutions during heating. Most often, sterilization is carried out with steam under the benefit of solutions of heat-labile substances - by the method of tyndalization or sterile filtration.

Most often, a dropper tube is used for packing eye drops.

U ski ointments are prescribed for lubricating the skin and the edges of the eyelids or for laying the ointment behind the lower eyelid in the conjunctival eye bag.

The technology of production of eye ointments is carried out according to the stages and operations typical for the production of ordinary ointments. However, there are some peculiarities. Active substances, not soluble in the ointment base, are crushed and sifted through a sieve with a diameter of 0.1 mm. The ointment base should NOT have extraneous inclusions and impurities, be neutral, sterile and should be easily distributed on the mucous membrane of the eye. The pH of the ointment must correspond to the pH of the lacrimal fluid, otherwise lacrimation occurs and the active substance is quickly washed out.

CLASSIFICATION OF OTHLIC MEDICINAL FORMS AND REQUIREMENTS FOR THEM

According to the definition of the State Pharmacopoeia of Ukraine, ophthalmic medicinal products are sterile liquid or solid preparations intended for application to the eyeball and (or) conjunctiva or for introduction into the conjunctival sac. Ophthalmic drugs are classified as follows:

- eye drops;
- eye lotions;
- ocular soft medical media b;
- eye inserts.

In addition, they also include:

- ophthalmic injections:

a) subconjunctivally, which are injected into the conjunctival sac, from where the medicinal substance diffuses through the sclera into the eyes;

b) retrobulbar, which are injected behind the eyeball;

- eye sprays;
- ointments for the eyelids, intended for use on the outer surface of the eyelid;
- liquids for processing contact lenses - sterile, moisturizing and disinfecting aqueous solutions for storing, cleaning and facilitating the application of contact lenses or contact lenses of ophthalmic devices used for eye research.

To date, the requirements for drugs used in ophthalmological practice have increased significantly. Modern pharmaceutical codes, specifications of different countries, the State Pharmacopoeia of Ukraine do NOT make a significant difference between drugs for the treatment of eye diseases and parenteral drugs. Both of them should be freed from mechanical and microbial contamination as much as possible.

Medicinal products for the eyes must be: sterile, stable, isotonic (osmolar or osmolality), contain an exact dosage of the medicinal substance, and not have mechanical impurities visible to the naked eye, some must have a prolonged effect, be convenient to use.

The role of aseptic conditions is especially increasing when shaving ophthalmic drugs that are NOT subject to heat treatment (sterilization), as well as those containing thermolabile medicinal substances (sprays, emulsions, suspensions, etc.). When heated in them, the processes of crystallization, flocculation and coalescence increase sharply. Compliance with the rules of asepsis is the only way to ensure the proper quality of such drugs.

In practice, this is achieved due to the fact that thermolabile substances are dissolved under aseptic conditions in pre-sterilized solvents or in the basis for the preparation of the drug in sterile dishes, adding preservatives and stabilizers as needed. To ensure sterility, some solutions are filtered through filters capable of retaining microorganisms. Filling of the primary container and sealing should also be carried out in aseptic conditions. These manipulations are carried out in special blocks, modules, boxes, where the degree of cleanliness is equal to class A or B.

Ophthalmic drugs containing heat-stable substances are prepared in class C or D production facilities with mandatory sterilization (thermal, gas or radiation).

Prolongation of the action of medicinal substances is important in the therapy of many diseases, as it ensures a stable concentration of active ingredients at a therapeutic level for a long time.

The requirements for long-acting drugs are that the optimal level of the medicinal substance in them should be ensured during the specified time, its concentration should NOT undergo significant fluctuations as it is released from the dosage form, and the techniques used to obtain the effect prolongations should be economical and NOT have a negative effect on the body. Among the methods of prolongation, the following are distinguished: the use of narrow solvents, the addition of biosoluble polymeric substances to the composition in the development of new dosage forms with an adjustable rate of release of active substances.

To increase the duration of action of medicinal substances in eye drops, they tried to replace water with various oils: sterile fish oil, refined sunflower oil, one of these solvents was not widely used for various reasons. Recently, bio-soluble polymer materials of synthetic origin have been proposed to replace water, the use of which for the deposition of medicinal substances removes harmful effects, this is due to the negative effect of polymer products on the body. At the same time, the study of the

biodegradation of these polymers in the body and in simulated environments is a necessary step on the way to improving old and creating new materials that are capable of being destroyed under the influence of environmental factors.

An alternative form of extended-release eye medication is eye inserts.

Ophthalmic pharmaceutical forms (OPF) include liquid (drops, lotions), soft (ointments, suspensions, emulsions), solid (films, powders, trituration tablets, pencils) and other forms. In ophthalmological practice, they are used with various medicinal substances for prophylactic, therapeutic and diagnostic purposes.

Medicinal preparations for the eyes must contain the exact dosage of medicinal substances and be stable, sterile, and not have mechanical contamination visible to the naked eye, and some of them must be isotonic and have a prolonged effect.

The need to make them in aseptic conditions is due to the fact that they are applied to the conjunctiva of the patient's eye. Normally, the tear fluid contains lysozyme, which has the ability to lyse microorganisms that have entered the conjunctiva. However, with eye diseases, the content of lysozyme (miromidase) in the tear fluid decreases and the eyes are insufficiently protected against the action of microorganisms. In this regard, the conditions for the technological process of GMF production and all preparatory operations should be the same as for the production of other sterile dosage forms.

Ophthalmic drugs of factory production are produced in the form of drops, ointments and films according to the nomenclature of frequently encountered extemporaneous prescriptions.

Eye drops (Guttae ophthalmicae) are water and oil solutions or the thinnest suspensions of medicinal substances.

Water for injections, sterile fatty oils (peach, almond, etc.) are used as solvents for eye drops.

A prerequisite for the industrial production of eye drops is stability, so multi-batch production requires that the shelf life of eye drops be quite long.

Preservatives, substances that regulate the pH of the environment, buffer systems, and antioxidants are used to stabilize eye drops.

Some unstable drugs may be available as a dry substance or triturated tablets in vials that are dissolved in water for injection or other sterile solvent before use.

Hypertonic and hypotonic aqueous solutions when instilled into the eyes cause discomfort and are poorly tolerated by patients, so eye drops require isotonization. In addition to isotonicity, the pH of the solutions has a value, which should be within the range of pH equal to 4.5-9.0.

The bioavailability of GMF largely depends on the time of contact of the medicinal substance with tissues in the precorneal region of the eyes. Increasing the duration of action (prolongation) of medicinal substances allows you to reduce the dose and frequency of taking the medicinal product, often avoiding side effects.

Natural oils and synthetic polymers are used in eye drops to prolong the action of medicinal substances. Prospective solvents for obtaining eye drops with prolonged action that increase the bioavailability of drugs are methylcellulose, 25% solution of PEG-400, 0.1-0.3% solutions of microbial polysaccharide - aubasidan.

After dissolution and stabilization of the medicinal substance, the solution is filtered through a sterile filter.

The choice of the method of thermal sterilization of eye drops is determined by the degree of stability of medicinal substances in solutions when heated. Most often, sterilization is carried out with steam under pressure, for solutions of thermolabile substances, the method of tyndalization or sterile filtration is used.

Eye ointments (Unguentae ophthalmica) are prescribed for lubricating the skin and edges of the eyelids or for placing the ointment under the lower eyelid in the conjunctival sac.

The technology of obtaining eye ointments is carried out according to the stages and operations typical for the production of ordinary ointments. However, there are some peculiarities.

Medicinal substances insoluble in the ointment base are crushed and sifted through a sieve with a diameter of 0.1 mm. The ointment base should NOT have extraneous inclusions and impurities, be neutral, sterile and easily distributed on the mucous membrane of the eye. The pH of the ointment should correspond to the pH of the lacrimal fluid, otherwise lacrimation occurs and the medicinal substance is quickly washed out.

Eye films (Membranulae ophthalmicae) are mechanically strong and hard plates of an oval shape with smooth edges and flat surfaces, 6-9 mm long, 3-4.5 mm wide, 0.35 mm thick, with an average weight of 0.015 g, which are prepared with bio-solubility non-toxic polymers with medicinal substances for introduction into the conjunctival cavity of the eye.

In ophthalmology, medicated eye films (SMF) are used to replace frequent instillations of aqueous eye drops and prolong the effect of medicinal substances by extending the contact time.

The solubility of eye films with various medicinal substances is determined by the composition of the base and can be 35-90 minutes. Aqueous solutions of MC, PVA, polyacrylamide derivatives are used as film-forming agents.

During the production of LPG, the following physico-chemical properties are controlled: gloss, integrity, surface roughness, elasticity, strength and adhesion.

LPG is packaged in plastic pencil cases or blisters made of PVC film and aluminum foil. Packages are placed in cardboard boxes of 20-100 pieces and sterilized with gamma rays with an integral radiation dose of 20 kGy or ethylene oxide.

Thus, GLP made it possible to expand the possibility of using anti-glaucomycosis and antiviral agents, to simplify the treatment method, and to increase the therapeutic effectiveness in comparison with drops and ointments.

— recommendations (instructions) for performing tasks (professional algorithms, orientation maps for the formation of practical skills and abilities, etc.):

Orientation map for independent work with literature on the subject of the lesson.

№№p.p.	Main tasks	Instructions	Answers
1	2	3	4
1.	Classification of ophthalmic dosage forms and requirements for them	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. - P. 567-577.
2.	Eye lotions	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. – P. 578.
3.	Eye sprays	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. – P. 578.
4.	Ophthalmic soft drugs	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. - P. 579-581.
5.	Quality control of ophthalmic dosage forms	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. - P. 587-588.

— requirements for the results of the work, including the registration: to state the basic concepts and rules of the pharmaceutical enterprise and safety rules, the concept of proper practice, technological block diagrams, to draw up a material balance.

— control materials for the final stage of the lesson: tasks, tasks, tests, etc. (if necessary):

Task:

1. Into which groups and according to what characteristics are ocular MFs classified?
2. What are the requirements of the SPhU for intramural MFs?
3. For what purpose and by what methods isotonization of ocular MF is performed?
4. What is isohydricity of infusion solutions and what are the most common methods of achieving it?
5. What is the importance of isoionicity and viscosity of infusion solutions?
6. What are the main stages involved in the production process of ophthalmic solutions?
7. Describe concentrates, powders and lyophilized dosage forms for intravenous iNPhaUsions.
8. Into which groups and according to what characteristics are eye medications classified?
9. What are the requirements of the SPhU for ophthalmic drugs?
10. What auxiliary substances are used for their production?
11. What is the peculiarity of the production of eye drops using the "Bottlepack" technology?
12. What parameters are used to control the quality of ophthalmic drugs?

18. List of recommended literature (main, additional, electronic information resources) :

Main:

- A.G. Bashura, O.S. Shpichak, E.E. Bogutska; under the editorship A.I. Tikhonov and S.A. Tikhonova - Kh.: Original, 2016. - 462 p.
- Vishnevska, N.P. Polovka, R.S. Korytniuk et al. - Kh.: National Academy of Sciences: Original, 2016. - 378p.
- Workshop on industrial technology of medicinal products: teaching. manual for students higher education institutions with the specialty "Pharmacy" / O.A. Ruban, D.I. Dmytrievskyi, L.M. Khokhlova [and others]; under the editorship O.A. Ruban. – Kh.: National Institute of Medical Sciences; Original, 2015. – 320 p.
- Industrial technology of medicines : education. manual for students' independent work / O.A. Ruban , V.D. Rybachuk , L.M. X ohlova etc. - KH.: NPHAU, 2015. - 120 p.
- Study guide for preparation for the final modular control and State certification in the Industrial Technology of Medicines for full-time and part-time students of the "Pharmacy" specialty / Ed. O.A. Ruban. - Kh.: National Academy of Sciences, 2016 . - 80 p.

- Study guide for independent preparation of students of the Faculty of Pharmacy for the licensing integrated exam "Step 2. Pharmacy" / O.A. Ruban, V.D. Rybachuk, L.M. Khokhlova, D.S. Pulyaev - KH.: NPHAU, 2016. - 63 p.
- Auxiliary substances in the production of medicines: training. manual for students higher pharmacy education closing / O.A. Ruban , I.M. _ Pertsev, S.A. Kutsenko, Yu.S. Oily; under the editorship I.M. Pepper - Kh.: Golden Pages, 2016. - 720 p.
- Technology of drugs for industrial production: tutorial. for university students education class: in 2 h. / V.I. Chuyeshov, E.V. Gladukh, I.V. Saiko et al. – 2nd ed., revision. and additional - Kh.: NPhaU: Original, 2012. - Part 1. - 694 p.
- Technology of drugs for industrial production: tutorial. for university students education class: in 2 h. / V.I. Chuyeshov, E.V. Gladukh, I.V. Saiko et al. – 2nd ed., revision. and additional - Kh.: NPhaU: Original, 2013. - Part 2. - 638 p.
- Modern pharmaceutical technologies: education. manual to laboratory classes of full-time, evening and part-time master's students of the specialty 8.110201 "Pharmacy" / under the editorship. O.A. Ruban. - Kh.: Publishing House of the National Academy of Sciences, 2016. - 256 p.

Auxiliary :

- Mathematical planning of an experiment when conducting scientific research in pharmacy / T.A. Groshovyi, V.P. Martsenyuk, L.I. Kucherenko and others. – Ternopil: TDMU Ukrmedknyga, 2008. – 367 p.
- Regulatory and technical documentation and production validation. Material balance: Educational method. river for audit. and external audit. student work special "Pharmacy" of full-time and part-time education / D.I. Dmytrievskyi, G.D. Slipchenko, I.M. Hrubnyk, D.V. Rybachuk . - Kh.: Publishing House of the National Academy of Sciences, 2008. - 45 p.
- Technology of medicinal products of industrial production: training. manual/ edited by Prof. D.I. Dmitrievsky. – Vinnytsia: Nova kniga, 2008. – 280 p.
- Drug technology. Educational and methodological guide: Education. manual for students higher education hall. / O.I. Tikhonov, P.A. Logvin, S.O. Tikhonova, O.V. Bazulin, T.G. Yarnykh, O.S. Shpychak, O.M. Kotenko; under the editorship O.I. Tikhonova, Kh.: Original, 2009. - 432 p.
- C pyrotometry. Recovery and rectification of ethanol: Textbook. help / D.I. Dmytryevsky, L.I. Boguslavskaya, L.N. Khokhlova and others; Ed. Prof. D.I. Dmitrievsky - Kh.: Izd-vo NPhaU, 2006. - 100 p.
- Pharmaceutical encyclopedia / Chief editor. council and the author of the foreword V.P. Black people - 3rd ed., revised. and additional - K.: "MORION", 2016. - 1952 p.

- Encyclopedia of Pharmaceutical Technology: 3-d Ed. / ed. by J. Swarbrick. – New York; London: Informa Healthcare, 2007. - 4128 p.
- European Pharmacopoeia 8.0 [8th edition] / European Directorate for the Quality of Medicines & Healthcare. - Strasbourg, 2013. - 3638 p.
- Handbook of Pharmaceutical Excipients, 6th edition / R.C. Rowe, P.J. Sheskey, M.E. Quinn. - Pharmaceutical Press and American Pharmacists Association, 2009. - 521 p.
- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeial Center for the Quality of Medicines", 2015. - Vol. 1. - 1128 p.
- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicines", 2014. - Vol. 2. - 724 p.
- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products", 2015. - Vol. 3. - 732 p.
- Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of non-sterile medicinal products in pharmacies" ST-N of the Ministry of Health of Ukraine 42 – 4.5: 2015 // Edited by Prof. O. I. Tikhonov and Prof. T.G. Jarnih - Kyiv, 2015. - 109 p. (Approved by the order of the Ministry of Health of Ukraine No. 398 of 01.07.2015).
- Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of sterile and aseptic medicinal products in pharmacies" ST-N of the Ministry of Health of Ukraine 42 – 4.6: 2015 // Edited by. Prof. O.I. Tikhonov and Prof. T.G. Jarnih - Kyiv, 2015. - 76 p. (Approved by order of the Ministry of Health of Ukraine No. 398 dated 07/01/2015).
- Production technology of extemporaneous medicinal apipreparations and their use in pharmacy, medicine and cosmetology: methodical recommendations / O.I. Tikhonov, T.G. Yarnykh, S.O. Tikhonova, O.G. Bashura, O.S. Shpychak, L.O. Bondarenko, P.S. Sirota, B.T. Kudryk, R.I. Skrypnyk-Tikhonov, N.S. Bohdan, S.G. Bobro, L.V. Kanoshevich, O.E. Bogutska; under the editorship O.I. Tikhonov. - Kh.: Izd-vo NPhaU, 2016. - 75 p.
- Powder manufacturing technology: teaching. manual / L.L. Davtyan, R.S. Korytniuk, A.O. Drozdova, I.O. Vlasenko, Z.V. Malenka, V.P. Popovych, V.V. Gladyshev, S.M. Musoev, T.F. Olifirova, L.I. Vishnevska, O.M. Hlushchenko,

O.O. Khomich; under the editorship L.L. Davtyan, R.S. Korytnyuk - K.: "Education of Ukraine", 2016. - 141 p.

- Pharmacotherapy of mastopathy. Extemporaneous prescriptions. Phytopreparations and homeopathic medicines: methodical recommendations / L.I. Vishnevska,
- S.S. Zuykin. –Kharkiv.: Publishing House of IFNMU-NPhaU, 2017. – 44 p.
- Zujkina S.S. The pharmacotechnological studies of the phytospecies composition for the complex therapy of mastopathy / S.S. Zujkina, L.I. Vishnevska // Herald of pharmacy. – 2017. – No. 2 (90). - P. 43-47.
- Bogutska O.E. The main directions of solving the problem of pharmaceutical incompatibilities / O.E. Bogutska // Modern achievements of pharmaceutical technology and biotechnology: collection of scientific papers. – issue 2. – Kharkiv.: Publishing House of the National Academy of Sciences, 2017. – pp. 29–31.
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- Prospects for the creation of new original drugs based on substances of plant origin / O.A. Ruban, S.A. Malinovska, Murad Al-Tawaiti, S.I. Mazurets // Phytotherapy. – 2012. – No. 2. - pp. 63–65.
- The current state of creation, production and quality control of capsules / M.B. Chubka, L.V. Vronska, N.O. Zarivna et al. // Pharmaceutical journal. - 2012. - No. 2. - P. 165-168.
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- Patel H. New pharmaceutical excipients in solid dosage forms – A review / H. Patel, V. Shah, U. Upadhyay // Int. J. of Pharm. & Life Sci. - 2011. - Vol. 2. – P. 1006–1019.
- Recent trends of treatment and medication peptic ulcerative disorder / D. Bhowmik, Chiranjib, KK Tripathi [et al.] // International Journal of PharmTech Research. - 2010. - Vol. 2. – P. 970–980.
- The effects of powder compressibility, speed of capsule filling and pre-compression on plug densification / M. Llusa , E. Faulhammer , S. Biserni [et al.] // Int. J. Pharm. – 2014. – Vol. 471. – P. 182–188.

Electronic resources:

- www.moz.gov.ua is the official website of the Ministry of Health of Ukraine
- fp.com.ua - website of the magazine "Pharmacist Praktik"
- www.provisor.com.ua – the official website of the magazine "Provisor"
- Compendium: drugs. - [Electronic resource]. - Access mode: http://compendium.com.ua/ - as of October 10, 2016.
- State Register of Medicinal Products of Ukraine. - [Electronic resource]. - Access mode: http://www.drlz.com.ua/ - as of January 10, 2017.
- Database "Equalizer" LLC "Business Credit" - [Electronic resource]. - Access mode: http://eq.bck.com.ua/ - as of September 20, 2016.

Practical lesson No. 6

Topic: " Production of tinctures." Spiritometry"

Purpose: to get acquainted with the terminology in the production of tinctures, to be able to prepare tinctures by the maceration method and evaluate their quality in accordance with the requirements of regulatory and technical documentation, as well as with the rules of their packaging and labeling

Tinctures (Tincturae) are dyed liquid alcohol or water-alcohol extraction from medicinal plant raw materials, which are obtained without heating and removing the extractant.

Spirometry - is a set of methods used to determine the amount of alcohol (anhydrous alcohol, ethyl alcohol) in various types of alcoholic liquids that have practical or technical significance, for example, in brew, alcohol, vodka, wine, beer, liqueurs, etc. similar liquids , the main components of which are alcohol and water.

Cooking methods

To prepare tinctures, the following methods are used: - maceration and its varieties;

- percolation;

- dissolution of thick and dry extracts.

maceration

Previously, the method of maceration, or infusion, (from the Latin Maceratio - soaking) was widely used to obtain tinctures. Currently, its use is gradually reduced, because during extraction by this method it is difficult to achieve complete extraction of medicinal substances from plant material.

Maceration is carried out as follows. Crushed raw materials with the proposed amount of extractant are loaded into the maceration tank and infused at a temperature of 15-20 °C, stirring periodically. If the terms are not specifically stipulated, then

insistence is carried out within 7 days. After that, the extract is drained, the residue is squeezed, the extracted extract is washed with a small amount of extractant, it is squeezed again, the extracted extract is added to the extracted extract, after which the combined extract is brought to the required volume with the extractant.

This method is ineffective - it flows slowly, raw materials are not completely exhausted. The process of intensification of material extraction from methane is carried out using fractional maceration (remaceration), maceration with forced circulation of the extractant, vortex extraction (turboextraction), ultrasound, etc.

Remaceration, or crushed maceration with the separation of extractant, or raw materials and extractant. The total amount of the extractant is divided into 3-4 parts and the raw materials are successively insisted with the first part of the extractant, then from the second, third and fourth, draining the hood each time. The time of infusion depends on the properties of the plant material. Such a holding of the extraction process allows you to more fully exhaust the raw materials with less time spent, as a high concentration difference in the raw materials and the extractant is constantly maintained.

Vortex extraction, or turboextraction **,** is based on the vortex, very intensive mixing of raw materials and extractant with simultaneous grinding of raw materials. The turbine mixer rotates at a speed of 8,000-13,000 rpm. The extraction time is reduced to 10 minutes, the tinctures are standard.

Ultrasonic extraction. Effective use of ultrasonic vibrations to intensify the maceration process. At the same time, the extraction is accelerated and the complete extraction of the active substances is achieved. The source of ultrasound is placed in the treated environment or attached to the body of the maceration tank in a place filled with extractant and raw materials. The greatest effect of the influence of ultrasound is revealed when the cell of the extracted material is well impregnated with ultrasound-conducting extractants. The emerging ultrasonic waves create sign-changing pressure, cavitation and "sonic wind". As a result, the impregnation of the material and the dissolution of the cell contents are accelerated, the speed of the flow around the raw material particles increases, and turbulent and eddy currents appear in the boundary diffusion layer of the extractant. Molecular diffusion inside the cells of the material and in the diffusion layer changes to convective, which leads to the intensification of mass transfer. The occurrence of cavitation causes the destruction of cells. At the same time, extraction is accelerated due to the washing out of extractive substances from destroyed cells and tissue. When voicing, you can get the hood within a few minutes.

Other types of dynamization of maceration include: grinding of raw materials in an extractant environment, for example in a ball mill; remaceration, accompanied by pressing on hydraulic presses or rollers. In the latter case, the process is repeated until equilibrium concentrations are reached. The method allows to reduce losses of active

substances and extractant, as a small amount of extract remains in the meal. The finished tincture contains a high amount of extractive substances.

Percolation - (from the Latin "Percolation through ..."), i.e. percolation of the extractant through plant material with the aim of extracting substances soluble in the extractants. The process is carried out in percolators and includes three successive stages: soaking of raw materials, infusion, percolation itself. Soaking can be combined with infusion, but if the raw material is capable of swelling strongly, the soaking stage must be carried out in a separate container. The raw material is poured with haMF or an equal amount of the extractant, in relation to the mass of the raw material, and left in a closed container for 4-6 hours to swell. Swollen raw materials are loaded into the percolator on a false bottom with optimal density, covered with filter material on top, pressed with a perforated disc and filled with extractant so as to displace air as much as possible. The extractant layer above the raw material should be about 20-40 mm. The iNPhaUsion lasts 24 hours (rarely 48 hours), after which the actual percolation is carried out. Percolation itseMF is the continuous passage of the extractant through a layer of raw materials and the collection of percolate. At the same time, the draining of the percolate and the simultaneous feeding of the extractant from above is carried out at a rate not exceeding 1/24 or 1/48 (for large productions) of a part of the used volume of the percolator per 1 hour. (see educational task 4). At this speed, the percolate is collected in an amount equal to the required volume of tincture. After that, the extractant is recovered from the spent raw materials, and the percolate is sent to the purification stage. Percolation is considered to have been carried out correctly if, simultaneously with the consumption of the calculated amount of extractant, complete extraction of the active substances is achieved, which is determined by the colorlessness of the resulting percolate or by means of appropriate qualitative reactions. The spent raw material (meal) is recovered, that is, the extractant is extracted with the aim of returning it to production. Extraction cleaning. The obtained extractions are cloudy liquids containing a significant amount of suspended particles.

Equipment: visual material, multimedia projector, presentation.

Plan:

Organizational activities (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).

Control of the reference level of knowledge (written work, written test, frontal survey, etc.) (if necessary):

— requirements for students' theoretical readiness to perform practical classes.

Knowledge requirements.

A student of higher education should know:

- rules of work at a pharmaceutical enterprise and safety rules;
- subject and tasks of drug technology;
- basic concepts of drug technology;
- basic requirements for the drug manufacturing process.

A student of higher education must be able to:

- apply work and safety rules during the manufacture of medicinal products;
- to formulate the basic concepts of drug technology;
- formulate and explain the technological aspects of drug production;
- apply basic calculations during preparatory work for the manufacture of medicinal products.

List of didactic units:

- the text of textbooks;
- a bank of test tasks.
- — questions (test tasks, tasks, clinical situations) to check basic knowledge on the subject of the lesson:

Characteristics and classification of tinctures.

2. Preparation of raw materials and extractant for extraction.
3. Obtaining tinctures by extraction. The essence of the extraction process.
4. Device of maceration tanks and percolators.
5. Methods of intensifying the production of tinctures.
6. Determination of alcohol content in tinctures.
7. Calculation of the amount of raw materials and extractant for obtaining tinctures.
8. Factors affecting the completeness and speed of extraction of active substances.
9. Stages of the method of maceration and remaceration (bismaceration).
10. Sequence of stages during percolation. The equipment used.
11. Methods of purification of tinctures.
12. Standardization. Quality control of tinctures.
13. Storage. Packaging, packaging and labeling of tinctures

Lesson content

Modern extraction preparations from medicinal plant raw materials can be divided into three groups according to the production technology:

v total (galenic) drugs;

v new galenic (maximum purified) preparations;

v preparations of individual substances.

Galenic drugs should be considered as a specific group of drugs, which, together with chemical-pharmaceutical and other drugs, are included in the composition of drugs. They are called Galenians after the name of the famous Roman doctor and

pharmacist Claudius Galen, who lived in 131-201 AD. e. The term "galenic preparations" appeared in the XIII century.

Extracts from raw materials in the production of galenic preparations (tinctures, extracts, etc.) are not chemically individual substances, they are complex complexes that often act differently than a separate chemically pure substance. Therefore, the therapeutic effect of galenic preparations is due to the whole complex of biologically active substances, strengthening, weakening or changing the action of the main substances.

In the 60s of the XIX century, new preparations of the galenic type appeared, called neogalenic. They are extracts from medicinal plants, completely or partially freed from accompanying substances, therefore they are also called maximally purified preparations (MP). These are also total drugs, but with a narrow spectrum of action on the body and with their own characteristics. Thus, deep cleaning increases their stability, eliminates the side effect of a number of accompanying substances (resins, tannins, etc.), allows you to recommend them for parenteral use.

The industrial production of medicinal preparations of individual substances was organized in the former our country in the middle of the 20th century. If relatively recently their production was considered difficult to access, thanks to achievements in the field of chemistry, physics, drug technology and pharmacology, their isolation, comprehensive research and analysis became possible. Preparations of individual alkaloids, cardiac glycosides, etc. have become widespread.

Extraction processes form the basis of the production of extractive preparations. In pharmacy, they are widely used for obtaining preparations from medicinal plant raw materials (tinctures, liquid, thick and dry extracts, extracts-concentrates, maximally purified, i.e. new galenic preparations, extracts from fresh plants, etc.) and from raw materials of animal origin (preparations of hormones, enzymes, drugs of non-specific action — pantocrin, vitohepat, etc.)

Extraction in the solid-liquid system and in the liquid-liquid system, or liquid extraction, are distinguished. The most popular in pharmaceutical production is extraction in the solid-liquid system, where the solid is medicinal plant raw materials or raw materials of animal origin, and the liquid is the extractant. Liquid extraction is used in the cleaning of hoods in the production of maximally purified preparations and preparations of individual substances from medicinal plant raw materials.

In everyday activities, it is important for pharmacists to know how extracts from different manufacturers differ. The effectiveness and safety of the use of such drugs depend on many factors. First, it is the quality of plant raw materials, which in turn depends on:

- parts of the medicinal plant used to make the extract, such as roots, leaves, flowers, fruits, etc.;

- the method of growing a medicinal plant — wild or cultivated;

- growing conditions — climate, soil quality, humidity;

- time of harvesting plant raw materials;

- a method of drying or storing plant raw materials, because active substances are often very sensitive to the influence of sunlight and humidity.

Secondly, the extraction process is crucial in the production of phytopharmaceuticals. The quality of the extract is influenced by the type and concentration of the extractant, the ratio of raw materials and the extractant, the extraction method — soaking, filtering, etc.

To improve the quality of extracts, use:

- selection of source material;

- transition from wild gathering of raw materials to cultivation;

- special methods of standardization of extracts — mixing of extracts of different series and of different origins, as well as those obtained from wild-harvested raw materials and those obtained in the process of cultivation.

Thirdly, different series of extract used for the preparation of the medicinal product can differ significantly in the content of active substances, therefore, the method of mixing different series of extracts is used to standardize the content of active substances in the extract.

Because different manufacturers use different production methods, the extracts obtained from different manufacturers are not the same, that is, one extract differs from another. It is not possible to apply scientific data on a particular extract to extracts from another manufacturer. Therefore, pharmacists and pharmacists need to pay attention to the fact that only those extracts whose quality and effectiveness have been proven by clinical studies can be recommended in everyday work. Extracts from raw materials in the production of galenic preparations (tinctures, extracts, etc.) are not chemically individual substances, they are complex complexes that often act differently than a separate chemically pure substance. Therefore, the therapeutic effect of galenic preparations is due to the whole complex of biologically active substances, strengthening, weakening or changing the action of the main substances.

Tinctures are transparent, colored liquid alcohol extracts from RM, obtained without heating and removing the extractant. Tinctures are widely used in medical practice as independent preparations for internal and external use, and they can also be part of drops, ointments, plasters, etc. When obtaining tinctures, the mass-volume ratio between the raw material and the finished product is adopted. Usually, 5 parts by volume of the finished product are obtained from 1 part by weight of non-potent RM, i.e. in a ratio of 1: 5. From one part of the potent substance, 10 parts by volume of tincture are obtained, i.e. 1:10. Exceptions are bitter tincture, tinctures of calendula, hawthorn, arnica, which are prepared in a ratio of 1:10, mint tinctures - 1:20, sophora tinctures - 1: 2. The process of preparing tinctures consists of successive stages: preparation of RM and extractant, extracting, cleaning, standardization, packing,

packaging and labeling. Preparation of raw materials includes grinding and screening of RM. According to the requirements of NTD, plant raw materials must have a certain particle size before extraction, after which it is sieved. The preparation of the extractant boils down to the calculation of the required amount and the dilution of the rectified alcohol or to the strengthening of the previously obtained recovery according to the "cross" rule or the formulas: X = V or X = V (b + a + c)

Where: V is the volume of ethanol of the required concentration; b - required concentration in percent by volume; a - actual concentration in percent by volume; c - volumetric concentration of weak ethanol used for dilution. Most tinctures are made using 70% ethanol, rarely 40% (tinctures of belladonna, barberry, St. John's wort, foxglove, etc.). Other concentrations are extremely rare: 90% (tinctures of mint, capsicum), 95% (tincture of lemongrass). When calculating the amount of extractant needed to obtain the required volume of tincture, the volume of alcohol absorbed and retained by the medicinal raw material is taken into account. The total amount of extractant of a given concentration to obtain a tincture is calculated by the formula: V = V1 + RK, (4) where V1 is the volume of the tincture (finished product), l or ml; P - amount of plant material, kg or g; K - coefficient of absorption of the extractant by raw materials, which for grass and leaves is 2-3; for bark, roots, rhizomes - 1.3-1.5. Obtaining extracts. Tinctures are obtained by dissolving thick or dry extracts, but more often by the extraction method. Dissolving thick or dry extracts. As a method of obtaining tinctures, they are used in the case of using poisonous raw materials or to speed up production.

The method boils down to simple dissolution in a reactor with a stirrer of the calculated amount of dry or thick extract in alcohol of the required concentration. The obtained solutions are filtered. Breast elixir, etc. are produced in this way. Extracts in the production of tinctures are obtained by the following methods: maceration, maceration using turboextraction and extractant circulation, fine maceration, percolation. Maceration (from the Latin soaking).

In pharmaceutical practice, several methods of maceration are used, which differ in the extraction time, the ratio of the extractant and raw materials, the sequence of the operation, etc. Maceration from the international pharmacopoeia. Crushed raw materials and ¾ part of the extractant are placed in a closed vessel and infused for 5 days. The mixture is periodically stirred. The extract is drained, the meal is squeezed out and washed with clean extractant. To wash the raw materials, take enough extractant to obtain a given amount of tincture. Maceration (classic version). Crushed raw materials with the proposed amount of extractant are loaded into the maceration tank and infused at a temperature of 15-200C, stirring periodically. If the terms are not specifically stipulated, then iNPhaUsion is carried out within 7 days.

After infusion, the extract is drained, the residue is squeezed and washed with a small amount of extractant, squeezed again. The squeezed extract is added to the

merged extract first, after which the combined extract is brought to the required volume with an extractant. The described maceration is now rarely used. New forms of maceration with maximum dynaminization of all types of diffusion are used. One of these forms is maceration using turboextraction or vortex extraction. The method is based on the vortex mixing of raw materials and extractant with simultaneous grinding of raw materials. The turbine mixer rotates at a speed of 8000-13000 rpm. The extraction time is reduced to 10 minutes, and the tincture is standard.

Maceration with the circulation of the extractant can be carried out in any container that has a false bottom and a lower fitting for draining the hood. In the process of infusion, the extract circulates with the help of a pump in the upper part of the container until it is completely saturated with active substances, that is, until equilibrium. At the same time, the infusion time is reduced several times. Another type of dynamic maceration, when the adjustment of hydrodynamic conditions achieves a significant acceleration of free diffusion in the extractant that washes the raw material, is the use of vibration and pulsation of the mixture of crushed raw materials and the extractant, which are achieved with the help of electromagnetic and other vibrators. Intensification of the maceration process with simultaneous grinding of raw materials in the medium of the extractant with the help of high-speed stirrers, in a ball mill, using RPA (rotor-pulsation apparatus) allows to speed up the process, therefore, simultaneously with intensive mixing during grinding of raw materials, a large number of cells are revealed. At the same time, the process of washing extractive substances from destroyed cells is added to the extraction process. Extracts are quickly saturated, but they contain many small particles of plant material, which will make further cleaning much more difficult. Fine maceration or remaceration consists in re-extraction of the original plant material with separate alternating portions of fresh extractant. The process most often occurs in percolators (extractors, diffusers).

The extractor is a vertical cylindrical device with a body and a steam jacket. A perforated disk is placed in the lower part of the housing, that is, a false bottom, on which the filter material is placed. To facilitate the unloading of spent raw materials (meal), the lower cover is equipped with a counterweight. Crushed dry plant material is loaded through the top cover, filter material and a perforated disc are placed on top as cargo. Then the raw materials are poured with the extractant to a "mirror", 30-40 mm thick (10-20 mm in laboratory conditions) and left to infuse for 24 hours. After a day, the hood is drained completely, and the raw materials are poured again with fresh extractant to the "mirror" and after iNPhaUsing for 1.5 hours, a second plum is obtained.

Similarly, the third and fourth plums are received after 1.5 hours each. All plums unite. Their number should be equal to the required volume of tincture. The extractant is recovered from the spent raw materials, and the combined plums are sent for cleaning.

Percolation - (from the Latin "Percolation through ..."), i.e. percolation of the extractant through plant material with the aim of extracting substances soluble in the extractants. The process is carried out in percolators and includes three successive stages: soaking of raw materials, infusion, percolation itself. Soaking can be combined with infusion, but if the raw material is capable of swelling strongly, the soaking stage must be carried out in a separate container. The raw material is poured with half or an equal amount of the extractant, in relation to the mass of the raw material, and left in a closed container for 4-6 hours to swell. Swollen raw materials are loaded into the percolator on a false bottom with optimal density, covered with filter material on top, pressed with a perforated disc and filled with extractant so as to displace air as much as possible. The extractant layer above the raw material should be about 20-40 mm. The infusion lasts 24 hours (rarely 48 hours), after which the actual percolation is carried out. Percolation itself is the continuous passage of the extractant through a layer of raw materials and the collection of percolate. At the same time, the draining of the percolate and the simultaneous feeding of the extractant from above is carried out at a rate not exceeding 1/24 or 1/48 (for large productions) of a part of the used volume of the percolator per 1 hour. (see educational task 4). At this speed, the percolate is collected in an amount equal to the required volume of tincture. After that, the extractant is recovered from the spent raw materials, and the percolate is sent to the purification stage. Percolation is considered to have been carried out correctly if, simultaneously with the consumption of the calculated amount of extractant, complete extraction of the active substances is achieved, which is determined by the colorlessness of the resulting percolate or by means of appropriate qualitative reactions. The spent raw material (meal) is recovered, that is, the extractant is extracted with the aim of returning it to production. Extraction cleaning. The obtained extractions are cloudy liquids containing a significant amount of suspended particles.

Extracts are purified by settling at a temperature not higher than 100C until a clear liquid is obtained. After settling for at least 2 days, filter by decantation. Standardization, packaging, labeling. Tinctures must meet the requirements of NTD. They determine: the content of active or extractive substances (on a dry basis), alcohol content or density, and heavy metals. Ready-made tinctures, if necessary, are adjusted to the norm by adding a pure extractant or tinctures with a different content of active substances, having previously performed calculations according to formulas 2-3. (see back 5 and 7). The finished tincture that meets the requirements of NTD is poured, sealed and labeled on semi-automatic and automatic lines into various glass containers. Store tinctures in a well-closed glass container in a cool (150 °C) place protected from light.

Formation of professional abilities and skills (mastering the skills of calculating the material balance, drawing up a technological block diagram for the industrial

production of medicinal products:

— ***task content:***

Characteristics and classification of tinctures.

2. Preparation of raw materials and extractant for the extraction process.

3. Methods of obtaining tinctures.

4. Obtaining tinctures by extraction. The essence of the extraction process.

5. Calculation of the amount of raw materials and extractant for obtaining tinctures.

6. Sequence of stages during percolation. Used equipment.

7. Preparation of tinctures by dissolving thick and dry extracts.

8. Methods of purification of tinctures.

9. Factors affecting the completeness and speed of BAC extraction.

10. Device of maceration tanks and percolators.

11. Methods of intensification of maceration.

12. Determination of alcohol content in tinctures.

13. Differences in methods for determining the concentration of alcohol in pharmaceutical preparations and intravenous alcohol solutions.

14. Quality control of tinctures.

15. Packaging, packaging and labeling of tinctures.

1. How many raw materials and extractant are needed to obtain 150 ml of valerian tincture? (the absorption coefficient is 1.3).

2. What volume of 95% ethanol is needed to prepare 150 ml of valerian tincture? How to prepare extractant?

3. What amount of raw materials and extractant is needed to prepare 350 ml of belladonna tincture?

4. Calculate the percolation rate in drops per minute, if the diameter of the percolator is 5 cm, the height of the layer of loaded plant material is 11 cm, and 1 ml of percolate contains 40 drops.

recommendations (instructions) for performing tasks (professional algorithms, orientation maps for the formation of practical skills and abilities, etc.):

Orientation map for independent work with literature on the subject of the lesson.

№№p.p.	Main tasks	Instructions	Answers
1	2	3	4
1.	Tinctures	Characteristics of the specified	Ruban O.A., Saiko I.V. Industrial technology of

		concepts	medicines. – Kh.: NPhaU: Original, 2016. – P. 253.
2.	Maceration and remaceration.	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. - P. 227.

— requirements for the results of the work, including the registration: to state the basic concepts and rules of the pharmaceutical enterprise and safety rules, the concept of proper practice, technological block diagrams, to draw up a material balance.

— control materials for the final stage of the lesson: tasks, tasks, tests, etc. (if necessary):

Task:

19. List of recommended literature (main, additional, electronic information resources) :

Main:

- A.G. Bashura, O.S. Shpichak, E.E. Bogutska; under the editorship A.I. Tikhonov and S.A. Tikhonova - Kh.: Original, 2016. - 462 p.
- Vishnevska, N.P. Polovka, R.S. Korytniuk et al. - Kh.: National Academy of Sciences: Original, 2016. - 378p.
- Workshop on industrial technology of medicinal products: teaching. manual for students higher education institutions with the specialty "Pharmacy" / O.A. Ruban, D.I. Dmytrievskyi, L.M. Khokhlova [and others]; under the editorship O.A. Ruban. – Kh.: National Institute of Medical Sciences; Original, 2015. – 320 p.
- Industrial technology of medicines : education. manual for students' independent work / O.A. Ruban , V.D. Rybachuk , L.M. X ohlova etc. - Kh.: NPHAU, 2015. - 120 p.
- Study guide for preparation for the final modular control and State certification in the Industrial Technology of Medicines for full-time and part-time students of the "Pharmacy" specialty / Ed. O.A. Ruban. - Kh.: National Academy of Sciences, 2016 . - 80 p.
- Study guide for independent preparation of students of the Faculty of Pharmacy for the licensing integrated exam "Step 2. Pharmacy" / O.A. Ruban, V.D. Rybachuk, L.M. Khokhlova, D.S. Pulyaev - Kh.: NPHAU, 2016. - 63 p.

- Auxiliary substances in the production of medicines: training. manual for students higher pharmacy education closing / O.A. Ruban , I.M. _ Pertsev, S.A. Kutsenko, Yu.S. Oily; under the editorship I.M. Pepper - Kh.: Golden Pages, 2016. - 720 p.
- Technology of drugs for industrial production: tutorial. for university students education class: in 2 h. / V.I. Chuyeshov, E.V. Gladukh, I.V. Saiko et al. – 2nd ed., revision. and additional - Kh.: NPhaU: Original, 2012. - Part 1. - 694 p.
- Technology of drugs for industrial production: tutorial. for university students education class: in 2 h. / V.I. Chuyeshov, E.V. Gladukh, I.V. Saiko et al. – 2nd ed., revision. and additional - Kh.: NPhaU: Original, 2013. - Part 2. - 638 p.
- Modern pharmaceutical technologies: education. manual to laboratory classes of full-time, evening and part-time master's students of the specialty 8.110201 "Pharmacy" / under the editorship. O.A. Ruban. - Kh.: Publishing House of the National Academy of Sciences, 2016. - 256 p.

Auxiliary :

- Mathematical planning of an experiment when conducting scientific research in pharmacy / T.A. Groshovyi, V.P. Martsenyuk, L.I. Kucherenko and others. – Ternopil: TDMU Ukrmedknyga, 2008. – 367 p.
- Regulatory and technical documentation and production validation. Material balance: Educational method. river for audit. and external audit. student work special "Pharmacy" of full-time and part-time education / D.I. Dmytrievskyi, G.D. Slipchenko, I.M. Hrubnyk, D.V. Rybachuk . - Kh.: Publishing House of the National Academy of Sciences, 2008. - 45 p.
- Technology of medicinal products of industrial production: training. manual/ edited by Prof. D.I. Dmitrievsky. – Vinnytsia: Nova kniga, 2008. – 280 p.
- Drug technology. Educational and methodological guide: Education. manual for students higher education hall. / O.I. Tikhonov, P.A. Logvin, S.O. Tikhonova, O.V. Bazulin, T.G. Yarnykh, O.S. Shpychak, O.M. Kotenko; under the editorship O.I. Tikhonova, Kh.: Original, 2009. - 432 p.
- C pyrotometry. Recovery and rectification of ethanol: Textbook. help / D.I. Dmytryevsky, L.I. Boguslavskaya, L.N. Khokhlova and others; Ed. Prof. D.I. Dmitrievsky - Kh.: Izd-vo NPhaU, 2006. - 100 p.
- Pharmaceutical encyclopedia / Chief editor. council and the author of the foreword V.P. Black people - 3rd ed., revised. and additional - K.: "MORION", 2016. - 1952 p.
- Encyclopedia of Pharmaceutical Technology: 3-d Ed. / ed. by J. Swarbrick. – New York; London: Informa Healthcare, 2007. - 4128 p.
- European Pharmacopoeia 8.0 [8th edition] / European Directorate for the Quality of Medicines & Healthcare. - Strasbourg, 2013. - 3638 p.

- Handbook of Pharmaceutical Excipients, 6th edition / RC Rowe, PJ Sheskey, ME Quinn. - Pharmaceutical Press and American Pharmacists Association, 2009. - 521 p.
- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeial Center for the Quality of Medicines", 2015. - Vol. 1. - 1128 p.
- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicines", 2014. - Vol. 2. - 724 p.
- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products", 2015. - Vol. 3. - 732 p.
- Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of non-sterile medicinal products in pharmacies" ST-N of the Ministry of Health of Ukraine 42 – 4.5: 2015 // Edited by Prof. O. I. Tikhonov and Prof. T.G. Jarnih - Kyiv, 2015. - 109 p. (Approved by the order of the Ministry of Health of Ukraine No. 398 of 01.07.2015).
- Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of sterile and aseptic medicinal products in pharmacies" ST-N of the Ministry of Health of Ukraine 42 – 4.6: 2015 // Edited by. Prof. O.I. Tikhonov and Prof. T.G. Jarnih - Kyiv, 2015. - 76 p. (Approved by order of the Ministry of Health of Ukraine No. 398 dated 07/01/2015).
- Production technology of extemporaneous medicinal apipreparations and their use in pharmacy, medicine and cosmetology: methodical recommendations / O.I. Tikhonov, T.G. Yarnykh, S.O. Tikhonova, O.G. Bashura, O.S. Shpychak, L.O. Bondarenko, P.S. Sirota, B.T. Kudryk, R.I. Skrypnyk-Tikhonov, N.S. Bohdan, S.G. Bobro, L.V. Kanoshevich, O.E. Bogutska; under the editorship O.I. Tikhonov. - Kh.: Izd-vo NPhaU, 2016. - 75 p.
- Powder manufacturing technology: teaching. manual / L.L. Davtyan, R.S. Korytniuk, A.O. Drozdova, I.O. Vlasenko, Z.V. Malenka, V.P. Popovych, V.V. Gladyshev, S.M. Musoev, T.F. Olifirova, L.I. Vishnevska, O.M. Hlushchenko, O.O. Khomich; under the editorship L.L. Davtyan, R.S. Korytnyuk - K.: "Education of Ukraine", 2016. - 141 p.
- Pharmacotherapy of mastopathy. Extemporaneous prescriptions. Phytopreparations and homeopathic medicines: methodical recommendations / L.I. Vishnevska,

- S.S. Zuykin. –Kharkiv.: Publishing House of IFNMU-NPhaU, 2017. – 44 p.
- Zujkina SS The pharmacotechnological studies of the phytospecies composition for the complex therapy of mastopathy / SS Zujkina, LI Vishnevska // Herald of pharmacy. – 2017. – No. 2 (90). - P. 43-47.
- Bogutska O.E. The main directions of solving the problem of pharmaceutical incompatibilities / O.E. Bogutska // Modern achievements of pharmaceutical technology and biotechnology: collection of scientific papers. – issue 2. – Kharkiv.: Publishing House of the National Academy of Sciences, 2017. – pp. 29–31.
- Polovko N.P. Assessment of biopharmaceutical factors in the development and production of new medicines / N.P. Polovko, L.I. Vishnevska, O.S. Shpychak // Modern achievements of pharmaceutical technology and biotechnology: collection of scientific works, issue 2. – X.: NPhaU Publishing House, 2017. – P. 155-160.
- Prospects for the creation of new original drugs based on substances of plant origin / O.A. Ruban, S.A. Malinovska, Murad Al-Tawaiti, S.I. Mazurets // Phytotherapy. – 2012. – No. 2. - pp. 63–65.
- The current state of creation, production and quality control of capsules / M.B. Chubka, L.V. Vronska, N.O. Zarivna et al. // Pharmaceutical journal. - 2012. - No. 2. - P. 165-168.
- Murachanian D. Two-Piece Hard Capsules for Pharmaceutical Formulations / D. Murachanian // Journal of GXP Compliance. - 2010. - Vol. 14. - P. 31-42.
- Patel H. New pharmaceutical excipients in solid dosage forms – A review / H. Patel, V. Shah, U. Upadhyay // Int. J. of Pharm. & Life Sci. - 2011. - Vol. 2. – P. 1006–1019.
- Recent trends of treatment and medication peptic ulcerative disorder / D. Bhowmik, Chiranjib, KK Tripathi [et al.] // International Journal of PharmTech Research. - 2010. - Vol. 2. – P. 970–980.
- The effects of powder compressibility, speed of capsule filling and pre-compression on plug densification / M. Llusa , E. Faulhammer , S. Biserni [et al.] // Int. J. Pharm. – 2014. – Vol. 471. – P. 182–188.

Electronic resources:

- www.moz.gov.ua is the official website of the Ministry of Health of Ukraine
- fp.com.ua - website of the magazine "Pharmacist Praktik"
- www.provisor.com.ua – the official website of the magazine "Provisor"

- Compendium: drugs. - [Electronic resource]. - Access mode: http://compendium.com.ua/ - as of October 10, 2016.
- State Register of Medicinal Products of Ukraine. - [Electronic resource]. - Access mode: http://www.drlz.com.ua/ - as of January 10, 2017.
- Database "Equalizer" LLC "Business Credit" - [Electronic resource]. - Access mode: http://eq.bck.com.ua/ - as of September 20, 2016.

Practical lesson No. 13-17

Topic: Production of thick and dry extracts. Intensification of extraction processes"

Purpose: To study the stages in the production of liquid, thick and dry extracts, as well as the methods of obtaining extracts in the production of liquid extracts. To know the characteristics and classification of extracts and the stages of the technological process of obtaining oil extracts during extraction with oils, volatile solvents, liquefied gases, as well as methods of obtaining extracts in the production of medical oils, which ensure the complete extraction of BAC from RM.

Basic concepts: *Extracts* (from Latin extractum — extract, extract) are concentrated extracts from dried plant or animal raw materials.

Liquid extracts are liquid concentrated water-alcohol extracts from medicinal plant raw materials (PRM), obtained in a ratio of 1:1. At pharmaceutical enterprises, liquid extracts are prepared by weight (from 1 kg of raw materials, 1 kg of liquid extract is obtained).

Dry extracts are concentrated extracts from medicinal raw materials, which are powdery masses with a moisture content of no more than 5%, obtained by removing the applied extractant.

Thick extracts are concentrated extracts from medicinal raw materials, which are viscous masses with a moisture content of no more than 30% (according to European requirements) and 25% (according to the national section of the SPhU).

Equipment: visual material, multimedia projector, presentation.

Plan:

1. Organizational activities (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).
2. Control of the reference level of knowledge (written work, written test, frontal survey, etc.) (if necessary):

— requirements for students' theoretical readiness to perform practical classes.

Knowledge requirements.

A student of higher education should know:

- rules of work at a pharmaceutical enterprise and safety rules;
- subject and tasks of drug technology;
- basic concepts of drug technology;
- basic requirements for the drug manufacturing process.

A student of higher education must be able to:

- apply work and safety rules during the manufacture of medicinal products;
- to formulate the basic concepts of drug technology;
- formulate and explain the technological aspects of drug production;
- apply basic calculations during preparatory work for the manufacture of medicinal products.

List of didactic units:

- the text of textbooks;
- a bank of test tasks.

— questions (test tasks, tasks, clinical situations) to check basic knowledge on the subject of the lesson:

1 1. Characteristics and classification of tinctures.

2. Preparation of raw materials and extractant for extraction.

3. Obtaining tinctures by extraction. The essence of the extraction process.

4. Installation of maceration tanks and percolators.

5. Methods of intensifying the production of tinctures.

6. Determination of alcohol content in tinctures.

7. Calculation of the amount of raw materials and extractant for obtaining tinctures.

8. Factors affecting the completeness and speed of extraction of active substances.

9. Stages of the maceration and remaceration (bismaceration) method.

10. Sequence of stages during percolation. The equipment used.

11. Methods of purification of tinctures.

12. Standardization. Quality control of tinctures.

13. Storage. Packaging, packaging and labeling of tinctures.

14. Methods of obtaining extractions in the production of medical oils, which ensure the completeness of extraction of BAC from RM?

Lesson content

Extracts (from the Latin extractum — extract, extraction) are concentrated extracts from dried plant or animal raw materials.

They can be classified depending on the consistency into liquid extracts (*Extracta fluida*), thick extracts (*Extracta spissa*) and dry extracts (*Extracta sicea*); from the used extract: aqueous (Extracta aquosa), alcoholic (*Extracta spirituosa*), ethereal (*Extracta aetherea*), oily (*Extracta oleosa*) and obtained with the help of liquefied gases. In addition, standardized extracts (*Extracta standartisata*) or extracts-concentrates are distinguished.

Liquid extracts are only alcoholic; others can be alcohol, water, ether, etc.

Liquid extracts

Liquid extracts are liquid concentrated water-alcohol extracts from medicinal plant raw materials (PRM), obtained in a ratio of 1:1. At pharmaceutical enterprises, liquid extracts are prepared by weight (from 1 kg of raw materials, 1 kg of liquid extract is obtained).

Liquid extracts have found wide distribution in the pharmaceutical industry because they have the following advantages: 1) the same ratio between the active substances contained in medicinal raw materials and in the finished drug; 2) convenience in measuring in pharmacies with burettes and pipettes; 3) the possibility of obtaining without the use of evaporation allows obtaining liquid extracts containing volatile substances (essential oils).

The negative characteristics of liquid extracts include: 1) their saturation with accompanying substances extracted from plant raw materials; 2) the appearance of sediments with slight temperature drops or partial loss of alcohol; 3) the need for hermetic closure and storage of the wine at a temperature of 15-20 °C; 4) contain large volumes of extractant, are poorly transportable drugs.

Methods of obtaining

Liquid extracts are obtained by methods of percolation, repercolation (in various variants), fractional maceration of various modifications, dissolution of thick and dry extracts.

Percolation in the production of liquid extracts at the stages of swelling and iNPhaUsion does not differ from percolation in the production of tinctures. At the actual percolation stage, the process is carried out similarly and at the same speed; the difference is only in the collection of ready hoods. For liquid extracts, the hoods are divided into two portions. The first portion in the amount of 85% relative to the mass of raw materials is collected in a separate container. Then percolation is carried out in another container until the raw materials are completely exhausted. At the same time, 5-8 times (according to the mass of raw material loaded into the percolator) more weak extracts, which are called "leaves", are obtained. Releases are evaporated under vacuum at a temperature of 50-60 °C to 15% relative to the mass of raw materials

loaded into the percolator. After cooling, the thickened residue is dissolved in the first portion of the hood. Extracts are obtained in a ratio of 1:1.

Repercolation, i.e. repeated (repeated) percolation, which makes it possible to make maximum use of the solvent capacity of the extractant, to obtain concentrated extracts when the raw materials are completely exhausted. In all cases, the process is carried out in a battery of percolators (from 3 to 10) working in communication. In the battery, the finished product is drained from the percolator, which always has fresh raw materials, and the fresh extractant is fed into the percolator, where the raw materials are the most exhausted. Extractors from the first percolator process raw materials in the next percolator, and so in the entire battery — the next raw material is extracted using extracts obtained from previous percolators. In this way, from the first to the last percolator in the battery, the raw material and extractant move countercurrently. As raw materials are depleted, the position of the "main" and "tail" percolators changes.

There are different repercolation options with the distribution of raw materials into equal and unequal parts, with a finished and unfinished cycle, which allow you to get concentrated extracts without further evaporation.

Repercolation with the distribution of raw materials into equal parts with an unfinished cycle is carried out in a battery of percolators

The first portion of the raw material intended for loading is pre-soaked with an equal or half volume of the extractant relative to the mass of the raw material. After swelling for 4-6 hours, the material is placed in percolator I and infused for 24 hours with double the volume of the extractant relative to the mass of the raw material. After the specified time, percolation is carried out until the raw material is completely exhausted, with the extraction divided into the first portion in the amount of 80% of the mass of the raw material, which is considered a finished product; the second portion (less concentrated extracts) — in an amount equal to the mass of raw materials and intended for soaking raw materials for percolator II; the third portion — release 2 in a double amount in relation to the mass of raw materials and intended for infusion of raw materials in percolator III; the fourth portion — release 3 in an amount that is almost 6 times greater than the mass of raw materials, and intended for extraction (percolation) of raw materials in percolator II. From percolator III, 100% of the finished product is obtained relative to the mass of raw materials in the percolator and releases are collected for working with raw materials in the next percolator. From the last percolator, 100% of the finished product and releases are obtained, which are used to process the next batch of similar raw materials. All portions of the finished product obtained from each percolator are combined.

Extracts - (from Latin Extractum - extract, extract) are concentrated extracts from RM. They can be classified depending on the consistency (liquid, thick and dry) or on the extractant used.

Liquid extracts are liquid concentrated water-alcohol extracts from RM, obtained in a ratio of 1: 1. At pharmaceutical enterprises, liquid extracts are prepared by mass (1 kg of liquid extract is obtained from 1 kg of raw materials). If the extracts contain active substances that are determined quantitatively, then instead of bringing them to a standard volume (or mass), they are brought to the concentration of active substances as in the raw material.

As an extractant in the production of liquid extracts, 50-70% ethanol is usually used, less often other concentrations.

Liquid extracts are applied independently in the form of drops or as part of complex liquid MF.

The process of production of liquid extracts includes the following stages:

• preparation of RM and extractant;

• RM extraction;

• hood cleaning;

• standardization; packaging; packaging and labeling.

Preparation of RM and extractants is carried out in the same way as in the preparation of tinctures. Calculation of the required amount of extractant is carried out according to the formula: $V = P\ n + P\ k$ (6)

where n is the number of volumes of the extractant required for complete exhaustion of the raw material (usually 5 to 10 volumes of the extractant are required and depends on the properties of the raw material) other designations are the same as in formula (4). If the hood for liquid extracts is not evaporated to the required volume, then $n = 1$ is taken.

RM extraction is carried out by the methods of fractional maceration in various modifications, exhaustive percolation, various types of repercolation, and countercurrent extraction.

The fleeting fractional maceration option does not allow extraction to be carried out effectively even at the first infusion, therefore, during a 2-hour extraction of dry raw materials, equilibrium is not reached, and therefore, it is not used, the capacity of the extractant is fully extracted, and the extracts come out insufficiently saturated. In the last, 3rd percolator, spent raw materials (meal) containing quite a lot of BAS are received, so the processing of raw materials is carried out with fairly saturated extracts from the 1st and 2nd percolators. Therefore, this version of fractional maceration is used in laboratory conditions or for small productions, when a small amount of the finished product is obtained.

Percolation in the production of liquid extracts at the stages of soaking and infusing raw materials is no different from percolation in the production of tinctures. At the actual percolation stage, the process is carried out similarly and at the same speed as for tinctures. The difference lies in the collection of ready extracts. For liquid extracts, extraction is divided into two portions. The first portion in the amount of 85%

in relation to the mass of raw materials is collected in a separate container, percolation is carried out in another container until the raw materials are completely exhausted. At the same time, they receive 5-8 times (in relation to the mass of raw materials loaded into the percolator) more weak extracts, which are called "release". This "release" is evaporated under vacuum at a temperature of 50-60 °C to 15% in relation to the mass of raw materials loaded into the percolator. After cooling, this thickened residue is dissolved in the first extraction portion. Extracts are obtained in a ratio of 1:1 in relation to raw materials. After cleaning, in case of poor quality, dilute with ethanol of the appropriate concentration to the standard content of active substances or volume.

Repercolation , i.e. repeated (repeated) percolation, allows you to make maximum use of the dissolving ability of the extractant and obtain concentrated extractions when the raw materials are completely exhausted. The process is carried out in several percolators (from 3 to 10), which work in a relationship, the so-called battery of percolators. The number of percolators in the battery depends on the properties of the raw material: the harder the raw material is extracted, the greater the number of percolators included. Supply of the extractant to the battery of percolators can be carried out according to the principle of direct flow and countercurrent.

There are different options for repercolation with the distribution of raw materials into equal and unequal parts, with a finished and unfinished cycle, for raw materials with large and small bulk mass.

Repercolation with the distribution of raw materials into equal parts with a completed cycle is carried out in a battery of percolators. Raw materials, divided into equal parts, are loaded into percolators. In the first percolator, the raw materials are soaked for swelling, which takes place within 4-6 hours, after which the extractant is fed into the percolator to the "mirror" and infused for 24 hours. Then it is percolated into a separate container, obtaining 80% of the finished product (H.P.1- 80%) in relation to the mass of raw materials in this percolator. Percolation is continued until the raw materials are completely exhausted in another container - they get "release 1". "Batch 1" carries out soaking, infusion and percolation of raw materials in the P-th percolator, from which the finished product (H.P.2-100%) is obtained in an amount equal to 100% of the mass of raw materials in the percolator and "batch 2". Release 2 is carried out soaking, infusion and percolation of raw materials in the 111th percolator from which the finished product 3 is obtained (H.P.3-100%) in an amount equal to 100% of the mass of raw materials in the percolator and "release 3". This is how the process is carried out in each subsequent percolator, if there are more than 3 of them. The discharge of the last percolator is evaporated to 20% of the finished product merged from the 1st percolator. At the same time, for 300 kg of raw materials, a liquid extract is obtained: 80 + 100 + 100 + 20 = 300 l (kg), i.e. the ratio is 1: 1.

Repercolation with the distribution of raw materials into equal parts with an unfinished cycle is carried out as in the previous case. The difference is that the

"releases" from the last percolator are not evaporated, but transferred to a portion of fresh raw materials in the 1st percolator. This option is used when there is a large amount of raw material and it is processed over a long period of time. At the same time, the quality of the finished product is higher, so there is no evaporation, and, therefore, inactivation of biologically active substances.

Repercolation according to Bosina and Chulkov [Textbook, Vol. 2, pp. 96-102].

Repercolation with the distribution of raw materials into unequal parts according to the pharmacopoeia of the USA and Germany. According to the US pharmacopoeia, raw materials are taken as 100% and loaded into percolators in a ratio of 5: 3: 2. Work begins with the largest portion of raw materials and processes it with pure extractant. Percolate is collected in two steps: finished product 1 in the amount of 20% of the total amount of raw materials and release, which is used for swelling, infusion and percolation in the P-th percolator. From the 2nd percolator, the finished product 2 is obtained in the amount of 30% of the total amount of raw materials and release 2, used for the 3rd percolator. From the 3rd percolator, 50% of the finished product is collected in relation to the mass of raw materials. A total of 20 + 30 + 50 = 100% of the finished product is obtained for 100% of the raw material, i.e. 1:1.

According to the German pharmacopoeia, all dry raw materials are loaded into three percolators in the ratio of 5:3.25:1.75 and the process is carried out similarly to the one described above for the US pharmacopoeia. Repercolation with the division of raw materials into unequal parts according to the US and German pharmacopoeias can be used for small productions when a small amount of product is obtained, therefore, in these modifications of repercolation, the raw materials in the 2nd and 3rd percolators are not completely exhausted.

About *cleaning* the extraction. Obtained by any of the methods described above, extracts in the production of liquid extracts stand for at least 2 days at a temperature not higher than 10 ° C until a clear liquid is obtained. The settling is sometimes allowed to be carried out in the presence of adsorbents, which contributes to better cleaning and greater stability during storage and transportation. The settled transparent part of the extract is filtered from accidentally introduced impurities and lastly the rest of the extracts with sediment is filtered. Filtered hoods are thoroughly mixed and standardized.

Standardization , packing, packaging. Determine the content of active substances according to the methods specified in individual articles, alcohol content (GF XI, issue 2, p. 26), or density (GF XI, issue 1, p. 24), dry residue (GF XI, issue 2, p. 161), and heavy metals (GF XI, issue 1, p. 161). According to the requirements of NTD, liquid extracts are poured, sealed and labeled on semi-automatic and automatic lines into glass containers of various capacities.

Store in packaging that ensures stability during the specified sheMF life and, if necessary, in a cool place protected from light. Precipitation may occur during storage.

Oil extracts or medical oils (Oleo medicata) are extracts from RM obtained using vegetable or mineral oils. Medicinal oils were quite widely found in the nomenclature of galenic preparations of past centuries. They were obtained from alkaloid-containing plants (blackberry, belladonna, dope, hemlock), personal etheromas (wormwood, chamomile, burdock, poplar buds) and some of which were taken from other plants (arnica, walnut, St. John's wort) by infusing finely chopped raw materials on olive or sesame oil heated to 60-70 ° C. Extracts obtained in this way are typical extracts with the only difference that vegetable oils are used as an extractant, and therefore the complex of extracted substances will have a lipophilic nature.

Obtaining medical oils is currently carried out according to two main schemes:

1. Vegetable oil is used as an extractant, and then an oil extract is obtained;

2. Volatile solvents are used as an extractant (ethanol 70%, methylene chloride, dichloroethane, chloroform, ether, liquefied gases: carbon dioxide, haldon-12, etc.), and then a concentrate of lipophilic complexes is obtained, which is blended (adjusted to the standard) with oil vegetable (most often sunflower).

Currently, in medical practice, oil extracts are used from the leaves of blekota (bleni oil), dope leaves (dope oil), St. John's wort, eucalyptus leaves (chlorophyllipt), rosehip pulp oil (*Extractum Rosae oleosum*), carotolin (*Carotolinum*), rosehip seed oil (*Oleum Rosae*), sea buckthorn oil (*Oleum Hippophae*). Approved for medical use is a new medicinal-chewing preparation Aromelin, obtained by extraction with liquefied gases (Hladon-12) from pressed chokeberry fruits. Aromelin has an anti-inflammatory, wound-healing, anti-burn effect that is 3-10 times better than that of sea buckthorn oil.

When extracting with oils, the technological process of obtaining medical oils includes:

• preparation of RM and extractant;

• RM extraction;

• extraction cleaning;

• standardization, packaging and labeling of the finished product. Preparation of RM and extractants. RM is crushed to a fine particle size, and oils are heated to 60-75 °C. Extraction of RM is carried out with heated oil at a temperature of 50-65 ° C by the method of maceration or counter-current extraction in batteries of percolators. The obtained extract is sent for cleaning. cleaning from oil extractions is carried out by filtering through print filters. After that, the cleaned extractions enter the standardization stage. Standardization of oil extracts is carried out according to the content of active substances, acid number (content of free acids). The standard finished product is packaged in a dry glass container, packed well. Store in a cool, dark place.

When extracted with volatile solvents, the technological process of the production of medicinal oils includes:

• preparation of RM and extractant;

• RM extraction;

• removal of the extractant - obtaining a concentrate;

• blending and standardization;

• packaging, packaging of the finished product. Preparation of RM is carried out in the same way as with oil extraction. RM extraction is carried out by the method of circulation extraction, countercurrent extraction in batteries of percolators or extraction with liquefied gases.

In circulation extraction, methylene chloride, dichloroethane, chloroform, ether or other volatile solvent with a constant boiling point are used.

In the production of bleached oil using an improved technology, the countercurrent extraction method is used in batteries of percolators with a mixture of 70% ethanol and 10% ammonia solution.

Extraction with liquefied gases is carried out according to the given general scheme: raw materials with a moisture content of no more than 7%, crushed to a particle size of 0.1-0.2 mm are loaded into extractors, which are then hermetically closed. Liquefied gas under pressure (55-65 atm. for carbon dioxide and 4.5-5.5 atm. for hladon-12) from the assembly enters the lower part of the extractors through the lower valves while the upper valves are open, which are closed after over raw material extractant forms a mirror. Supplying the extractant from the bottom allows you to displace air from the raw material and thereby exclude the formation of stagnant zones where extraction is extremely slow.

Depending on the type of raw material, extraction can be carried out in different ways by transferring the extractant from the 1st, 2nd and 3rd extractors, or it can be carried out in parallel. The infusion time also depends on the properties of the raw materials and the extractant. According to the technology of the proposed DNCLZ, when extracting with hladon-12, the insistence lasts for 3:00 at a temperature of 18-25 °C under a pressure of 4.5-5.5 atm and a ratio of raw materials to the solvent of 1:5. Extracts enter the evaporator to remove the extractant. In the evaporator, the pressure is much lower than in the extractors, thanks to which the reagent turns into a gas and enters the condenser, where it cools, condenses and enters the collector in the form of a liquid, which has a level indicator. From the assembly, the extractant is fed again to the raw material. The finished product - lipophilic concentrate is removed from the evaporator through the lower valve.

The advantage of the method is that the solvent is in a closed cycle and is used repeatedly. At the end of the extraction process, the extractant is poured from the extractors into the evaporator, and the pressure in the extractors is reduced and the extractant is removed from the meal. Meal in the dischargers through the discharge bottoms.

At DNSLZ, research was conducted on the use of liquefied chlorofluoroderivative gases (chladons) such as methane, ethane, propane, and butane as extractants from RM. Under normal conditions, these are gases, under excess pressure they are colorless,

easily mobile liquids, the viscosity of which is much lower than that of organic solvents. Refrigerators are chemically indifferent to the extracted BAC and structural materials of the devices. They are non-toxic, do not form explosive mixtures with air, are fire- and explosion-proof.

The analysis of the extraction results showed that the studied haldons extract essential oils, coumarin derivatives, furanochromones, carotenoids, tocopherols, sesquiterpenes, terpenoids, sterols, some iridoids, chlorophylls, alkaloids and a number of other natural compounds. The yield of extracted substances during treatment with different refrigerants of the same type of raw material is not the same. The most selective solvent with respect to essential oils was chladone SZ18 (ts-C_4F_8), which practically does not extract fatty oils. Extracts obtained with the help of hladons of the methane series [khladon-I (SSIzR); hladon-12- (SSURz); chladon-22 ($CHCIF_2$)] contained a mixture of essential and fatty oils, carotenoids, terpenoids and other natural substances. The extracts, semi-active with C318 chladon and chladon-114- ($C_2CN_2P_4$), do not contain chlorophyll, which distinguishes these extractants from chladons of the methane series. It was established that refrigerants have a selective ability relative to natural substances. Therefore, by subjecting RM to sequential treatment with different refrigerants, it is possible to obtain separate groups of BARs. It was also established that chladones do not extract water-soluble substances (polysaccharides, proteins, phenolic compounds, etc.). Therefore, it is advisable to use the meal after treatment with colds to obtain other compounds extracted with polar solvents. Consecutive processing of raw materials with refrigerants, then with more polar solvents (water, water-alcohol mixtures, alcohols, acetone, etc.) will allow comprehensive use of valuable plant raw materials.

Removing the extractant . In circulation, the extractant from the concentrate is distilled off under vacuum, sometimes water is added to remove extractant residues and lower the distillation temperature. When extracting with liquefied gases, the latter are removed from the concentrate, as mentioned above, by reducing the pressure. As a result, a concentrate is obtained in the evaporator, which has undergone blending and standardization.

Blending and standardization of concentrates. The product - a lipophilic complex obtained after extraction with volatile extractants - is mixed with sunflower oil in calculated quantities according to the requirements of NTD. Blending is not carried out during the production of rosehip oil.

Adoniside. Obtaining adoniside in pharmacy. F. D. Zilberg proposed to modify the production of adonylene in order to increase the yield of medicinal substances from the montenegro herb. She called the drug obtained by her method adonizide; it is a transparent, slightly yellowish liquid with a bitter taste. For the production of 1 ton of adonisida, the following are consumed: Hydrate of aluminum oxide 0.625 kg Chopped herbs - 75 LED 383.7 100% ethyl alcohol 270 l Medical chloroform (GOST 5996-51)

171 kg Technological process. The production of adoniside is divided into the following stages. Grinding Dry grass of Montenegrin spring is crushed with the help of an "excelsior". adonizide Preparation of the extractor. Chloroform, 96° alcohol, and distilled water (if any) are poured into the measuring cup-mixer from the measuring cups, not shown in the figure, in such proportions that the mixture contains 95 parts by volume of chloroform and 5 parts by volume of alcohol. The resulting liquid was later called by F.D. Zilberg a universal extractant, because it relatively well extracts all cardiac glucosides from vegetable raw materials. At the same time, ballast substances enter this mixture in negligible quantities. Extraction. Chopped grass of Montenegro is loaded through the upper hatch into the extractor 1. The universal extractor is poured into it - enough to cover all the grass. The mixture is insisted at a temperature of 45-50° C. The extracted extract from the extractor is fed through pipelines 2 or 3 into the evaporator (distillation cube) 4. The evaporator is heated with dead steam (through a steam jacket). Evaporated vapors pass through pipeline 6 into refrigerator 7, and from there into collector 8 and into extractor 1. In addition, evaporated vapors from the boiler via pipelines 5 and 6 can, if desired, be distilled directly into the extractor. Such a method of extraction is usually called circulation. According to this method, extraction proceeds until the plant material is completely exhausted. After this, the extraction of the extractor is stopped. The remaining extract is discharged through pipeline 3 into the evaporator. The attractant, absorbed in the grass, is driven away with sharp or dull steam. After passing through the cooler 7, the extractor vapors are collected in the collector 8. The condensate settles and water is separated from it. After that, they unload the used plant material through the lower hatch, load the extractor with new material, fill it with a universal extractor and insist according to the previous method. Evaporation The rest of the obtained extraction is evaporated in the same evaporator or better — in a separate vacuum apparatus approximately to the weight of the plant material taken for extraction. At the same time, proteins, carbohydrates, tannins and saponins do not pass into the alcohol-chloroform extract from the grass, but cardiac glucosides, chlorophyll, resinous substances, fats, oils and organic acids are extracted. During evaporation, due to the fact that a large amount of chloroform and alcohol remains in the obtained extract, part of the dissolved substances precipitates and some amount remains in the solution. In order to finally isolate water-insoluble substances, an almost equal amount of distilled water is added to the cubic residue. Distillation is continued, preferably under vacuum, until alcohol and chloroform are completely removed. As a result, all water-insoluble substances (resins, fat-like substances, oils, chlorophyll, etc.) fall into the sediment. At the same time, the distillate, consisting of chloroform and other impurities, is collected in a separate receiver - a settling tank with a tight-fitting lid, in order to avoid volatilization of chloroform (a poisonous substance). Settling and filtering. An aqueous solution of glucosides is pumped into a settling tank. After some time, the liquid is drained from the sediment, passed first through calico and paper, and then through a vacuum filter, in which two sheets of filter paper are

placed and a layer of aluminum oxide is poured over them (the latter operation serves to remove ballast from a concentrated aqueous solution of glucosides, and aluminum oxide adsorbs glucosides only in a very small amount). Before filtering, fine-grained aluminum oxide hydrate is slightly calcined. This calcination ends when water vapor stops emitting from the surface of the powder. After cooling, aluminum oxide is immediately used for adsorption of ballast substances or poured into jars with a polished cork.

Packaging, marking. The product, which meets the requirements of the NTD, is packaged in a glass container made of dark glass, tightly closed and labeled. Store in a cool, dark place.

3. Formation of professional abilities and skills (mastering the skills of calculating the material balance, drawing up a technological block diagram for the industrial production of medicinal products:

— task content:

1. Be able to make calculations of raw materials and extractant, draw up a work order.

2. Load the maceration tank and percolator with RM and extractant.

3. Obtain tinctures by various extraction methods.

4. Determine the ethanol content by the boiling point of the tincture and the distillation method.

5. Compile the material balance and technological scheme for the production of the obtained tincture.

— recommendations (instructions) for performing tasks (professional algorithms, orientation maps for the formation of practical skills and abilities, etc.):

Orientation map for independent work with literature on the subject of the lesson.

№№p.p.	Main tasks	Instructions	Answers
1	2	3	4
1.	Theoretical foundations of extraction	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. – P. 216-223.
2.	Extraction methods.	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016.

			- P. 226-250.
3.	Recovery of extractants from spent raw materials	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. - P. 250-256.
4.	Extracts are liquid	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. – P. 256-258.
5.	The extracts are thick and dry	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. – P. 258--270.

— requirements for the results of the work, including the registration: to state the basic concepts and rules of the pharmaceutical enterprise and safety rules, the concept of proper practice, technological block diagrams, to draw up a material balance.

— control materials for the final stage of the lesson: tasks, tasks, tests, etc. (if necessary):

Task:

Task 1. Preparation and research of St. John's wort extract (St. John's wort oil) (*Extractum Hyperici oleosum. Oleum Hyperici*)

Task 2. How many raw materials and extractant should be taken to prepare 425 liters of liquid extract by the method of accelerated fractional maceration using the counterflow type? In what quantities should pure extractant be fed to the 1st percolator at each loading? K = 2.5.

4. List of recommended literature (main, additional, electronic information resources) :

Main:

- A.G. Bashura, O.S. Shpichak, E.E. Bogutska; under the editorship A.I. Tikhonov and S.A. Tikhonova - Kh.: Original, 2016. - 462 p.
- Vishnevska, N.P. Polovka, R.S. Korytniuk et al. - Kh.: National Academy of Sciences: Original, 2016. - 378p.

- Workshop on industrial technology of medicinal products: teaching. manual for students higher education institutions with the specialty "Pharmacy" / O.A. Ruban, D.I. Dmytrievskyi, L.M. Khokhlova [and others]; under the editorship O.A. Ruban. – Kh.: National Institute of Medical Sciences; Original, 2015. – 320 p.
- Industrial technology of medicines : education. manual for students' independent work / O.A. Ruban , V.D. Rybachuk , L.M. X ohlova etc. - KH.: NPHAU, 2015. - 120 p.
- Study guide for preparation for the final modular control and State certification in the Industrial Technology of Medicines for full-time and part-time students of the "Pharmacy" specialty / Ed. O.A. Ruban. - Kh.: National Academy of Sciences, 2016 . - 80 p.
- Study guide for independent preparation of students of the Faculty of Pharmacy for the licensing integrated exam "Step 2. Pharmacy" / O.A. Ruban, V.D. Rybachuk, L.M. Khokhlova, D.S. Pulyaev - KH.: NPHAU, 2016. - 63 p.
- Auxiliary substances in the production of medicines: training. manual for students higher pharmacy education closing / O.A. Ruban , I.M. _ Pertsev, S.A. Kutsenko, Yu.S. Oily; under the editorship I.M. Pepper - Kh.: Golden Pages, 2016. - 720 p.
- Technology of drugs for industrial production: tutorial. for university students education class: in 2 h. / V.I. Chuyeshov, E.V. Gladukh, I.V. Saiko et al. – 2nd ed., revision. and additional - Kh.: NPhaU: Original, 2012. - Part 1. - 694 p.
- Technology of drugs for industrial production: tutorial. for university students education class: in 2 h. / V.I. Chuyeshov, E.V. Gladukh, I.V. Saiko et al. – 2nd ed., revision. and additional - Kh.: NPhaU: Original, 2013. - Part 2. - 638 p.
- Modern pharmaceutical technologies: education. manual to laboratory classes of full-time, evening and part-time master's students of the specialty 8.110201 "Pharmacy" / under the editorship. O.A. Ruban. - Kh.: Publishing House of the National Academy of Sciences, 2016. - 256 p.

Auxiliary :

- Mathematical planning of an experiment when conducting scientific research in pharmacy / T.A. Groshovyi, V.P. Martsenyuk, L.I. Kucherenko and others. – Ternopil: TDMU Ukrmedknyga, 2008. – 367 p.
- Regulatory and technical documentation and production validation. Material balance: Educational method. river for audit. and external audit. student work special "Pharmacy" of full-time and part-time education / D.I. Dmytrievskyi, G.D. Slipchenko, I.M. Hrubnyk, D.V. Rybachuk . - Kh.: Publishing House of the National Academy of Sciences, 2008. - 45 p.

- Technology of medicinal products of industrial production: training. manual/ edited by Prof. D.I. Dmitrievsky. – Vinnytsia: Nova kniga, 2008. – 280 p.
- Drug technology. Educational and methodological guide: Education. manual for students higher education hall. / O.I. Tikhonov, P.A. Logvin, S.O. Tikhonova, O.V. Bazulin, T.G. Yarnykh, O.S. Shpychak, O.M. Kotenko; under the editorship O.I. Tikhonova, Kh.: Original, 2009. - 432 p.
- C pyrotometry. Recovery and rectification of ethanol: Textbook. help / D.I. Dmytryevsky, L.I. Boguslavskaya, L.N. Khokhlova and others; Ed. Prof. D.I. Dmitrievsky - Kh.: Izd-vo NPhaU, 2006. - 100 p.
- Pharmaceutical encyclopedia / Chief editor. council and the author of the foreword V.P. Black people - 3rd ed., revised. and additional - K.: "MORION", 2016. - 1952 p.
- Encyclopedia of Pharmaceutical Technology: 3-d Ed. / ed. by J. Swarbrick. – New York; London: Informa Healthcare, 2007. - 4128 p.
- European Pharmacopoeia 8.0 [8th edition] / European Directorate for the Quality of Medicines & Healthcare. - Strasbourg, 2013. - 3638 p.
- Handbook of Pharmaceutical Excipients, 6th edition / RC Rowe, P.J. Sheskey, M.E. Quinn. - Pharmaceutical Press and American Pharmacists Association, 2009. - 521 p.
- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeial Center for the Quality of Medicines", 2015. - Vol. 1. - 1128 p.
- State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicines", 2014. - Vol. 2. - 724 p.
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Practical lesson No. 18-19

Topic: " Production of drugs under pressure"

Purpose: to study the peculiarities of the technology of industrial production of drugs under pressure, to study the main technological operations and equipment necessary for the production of drugs under pressure.

Basic concepts: *Aerosols* are the smallest liquid droplets or solid particles suspended in a gaseous medium.

Active substances are the main part of the medicinal product, which are under pressure, and all other components are auxiliary and are used for the purpose of issuing active ingredients in the required form.

Solvents are used to dissolve active substances and ensure the distribution of a small amount of LR solution in a large volume of air with the help of a propellant.

Excipients - this group includes emulsifiers, surfactants, solubilizers, preservatives, thickeners and others. They are designed to ensure the proper quality of the aerosol,

create the necessary form of release of the aerosol packaging and more efficient use of the aerosol.

Equipment: visual material, multimedia projector, presentation, packaging container, examples of packaging.

Plan:

Organizational activities (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).

Control of the reference level of knowledge (written work, written test, frontal survey, etc.) (if necessary):

— requirements for students' theoretical readiness to perform practical classes.

Knowledge requirements.

A student of higher education should know:

- rules of work at a pharmaceutical enterprise and safety rules;
- subject and tasks of drug technology;
- basic concepts of drug technology;
- basic requirements for the drug manufacturing process.

A student of higher education must be able to:

- apply work and safety rules during the manufacture of medicinal products;
- to formulate the basic concepts of drug technology;
- formulate and explain the technological aspects of drug production;
- apply basic calculations during preparatory work for the manufacture of medicinal products.

List of didactic units:

- the text of textbooks;
- a bank of test tasks.

— questions (test tasks, tasks, clinical situations) to check basic knowledge on the subject of the lesson:

1. Basic regulatory and technical documents that regulate the activities of the technologist and are used for the preparation of medicinal products under pressure ;
2. Methods of preparation of medicines under pressure ;
3. Stages of the technological process (general and partial); stability of medicinal products under pressure .
4. General characteristics. Classification. Requirements

5. Formation of professional abilities and skills (mastering the skills of calculating the material balance , drawing up a technological block diagram for the industrial production of medicinal products:

— task content:

1. 1. Classification of aerosols, advantages and disadvantages.
2. Excipients used in their production.
3. Technological scheme of production; the equipment used.
4. Quality control of aerosols.
5. The main components of aerosol packages, valve-spray system type, classification of propellants and aerosol concentrates.
6. Production of aerosols, quality control in accordance with the SPHU.

Lesson content

Pressurized pharmaceutical preparations are preparations in which the active and auxiliary substances are under the pressure of a displacer gas (propellant) in an aerosol can, hermetically sealed with a valve. Preparations from aerosol packaging are obtained in the form of liquid and solid particles, particles and films dispersed in a gaseous medium. Bons are intended for inhalation, application to the skin, introduction into the body cavity, etc.

There are several *classifications* of drugs under pressure:

1) Depending on the physical and chemical properties of the composition, they are classified into two- and three-phase systems. In two-phase systems, the liquid phase is usually a solution of active substances in a propellant or a mixture of propellant with a solvent, that is, this system has two phases: gaseous and liquid. In three-phase there are three separate phases: gaseous, solid and liquid

2) Depending on the size of the particles of the dispersed phase, they are divided into spraying (particle diameter up to 50 μm, propellant concentration - up to 80%), shower (particle diameter up to 200 μm, propellant concentration - 30-70%) and foam (particle diameter over 200 μm, propellant concentration - up to 30%).

3) Depending on the application, aerosols are medical and pharmaceutical.

Production of medicinal products under pressure in the form of solutions consists of several stages: preparation of a solution of the active component (concentrate), freeing it from insoluble impurities, packing into containers, sealing, filling with propellant, testing for strength and tightness, standardization, packaging design for further transportation.

An aerosol is a medicine that is under gas pressure in special containers and contains one or more active substances. Propellants provide the pressure necessary for the release of the drug from the container. Medicinal products under pressure are a solution, emulsion or suspension; they are intended for local application to the skin, mucous membranes or for inhalation. In addition to medicinal substances, their composition may also include auxiliaries - emulsifiers, solvents, as well as sliding

substances that protect the valve from clogging. Medicinal aerosols are divided into pharmaceutical and medical.

A pharmaceutical aerosol is a ready-made medicinal form consisting of a cylinder, a valve-spraying system and contents of various consistencies that can be expelled from the cylinder with the help of a propellant. The composition of the aerosol includes medicinal, auxiliary substances and necessarily one or more propellants.

A medical aerosol is an aerosol of one or more medicinal preparations in the form of liquid or solid particles obtained with the help of special stationary devices intended for inhalation administration in the conditions of a medical institution.

According to their purpose, pharmaceutical aerosols are classified into the following groups: inhalation, otolaryngological, dermatological, dental. proctological, gynecological, ophthalmological, special purpose (diagnostic, dressing, hemostatic, etc.). The great popularity of medical aerosols is explained by a number of advantages that favorably distinguish them from other medicinal forms:

- high efficiency of action with relatively small consumption of medicinal substances. Their activity is enhanced by spraying the drug, which increases its free surface many times over;

- during spraying, particles of approximately the same size are formed, which makes it possible to adjust their size; it is especially important for the treatment of bronchial asthma and respiratory diseases;

- special valves can be used to dose different medicinal substances;

- the cylinder is completely sealed, which protects substances from fluctuations in atmospheric conditions, drying, pollution, etc.,

- when the drug is packaged in sterile conditions, sterility is preserved for the entire sheMF life;

- medicinal substances from aerosols are quickly absorbed and can be used to provide first aid;

- the economic advantage is the high efficiency of the action in combination with the reduction of the consumption of active substances;

- the possibility of applying medicinal substances directly to the affected areas;

- obtaining products in the form of small splashes, foams, powders, etc. opens wide opportunities for the use of aerosols in various fields of medicine;

- the aerosol method of application is simple, does not cause painful sensations.

A large number of various chemicals are used to create aerosols. All of them can be divided into five main groups: active agents, solvents, aromas, auxiliary substances and propellants.

Active ingredients are the main part of any aerosol formulation. The rest of all the ingredients are auxiliary and serve to issue them in the required form.

For the preparation of various aerosol preparations, organic solvents and water are widely used, which serve to obtain a solution of the active substance and ensure, with the help of a propellant, the distribution of a small amount of it in a large volume

of air. To provide a pleasant and mask an unpleasant smell, the composition of the aerosol may include odorous substances. The type of fragrance (flavoring agent) should correspond to the nature of the product for which it is intended. Benzaldehyde, various essences, essential oils, etc. can be used as aromas.

The group of auxiliary substances includes surface-active substances (emulsifiers, solubilizers), preservatives, consistency substances and others. They are designed to ensure the proper quality of the aerosol, create the necessary form of packaging discharge and more effective use of the drug. Dispersing or scavenging gases, which create pressure inside the cylinder, are important for the release of an aerosol product. These gases are called propellants.

Propellants are classified by their saturated vapor pressure, state of aggregation under normal conditions, and chemical nature.

Depending on the pressure of saturated steam, they can be divided into main and auxiliary. Individual substances, which at 20 °C can produce an internal excessive pressure in the package of at least 2 atm, are called basic propellants. These include freon-12, -22, -142, as well as propane, isobutane, etc. To reduce the pressure, the main propellants are combined with auxiliary propellants, which have a saturated vapor pressure of about 1 atm. and individually cannot serve as pushing agents. These include freon-11, -114, -21, butane, etc.

According to the aggregate state, all substances used as propellants are divided into three main groups.

1. Liquefied gases:

a) organofluorine compounds (fluorine and chlorofluorocarbons, or otherwise - freons);

b) hydrocarbons of the paraffin series (propane, butane, isobutane);

c) chlorinated hydrocarbons (vinyl chloride, methyl chloride, etc.).

2. Compressed (difficult to liquefy) gases. This includes nitrogen, nitrous oxide, carbon dioxide, etc.

3. Volatile organic solvents (methylene chloride, ethylene chloride, etc.).

Freons are most widely used as propellants in pharmaceutical aerosol preparations.

Aerosol packaging consists of a cylinder, valve and contents. The cylinder containing the solution, suspension or emulsion of the drug and the propellant is hermetically sealed with a valve with a spray head.

A siphon tube is immersed in the contents of the cylinder, designed to supply the drug to the hole in the valve stem. The valve allows you to adjust the dose of the drug. Above the contents of the cylinder is a layer of compressed gaseous propellant, which puts pressure on the contents and the walls of the cylinder and promotes the release of the medicinal product.

With a slight vertical pressure on the valve head or with a slight tilt to the side (depending on the design of the valve), a conical jet or ribbon-like mass is emitted from

the hole in the head. Depending on the contents of the cylinder, the jet may resemble fog (solutions of medicinal substances), smoke or dust (suspensions). The ribbon-like mass can represent abundant foam or a "worm" squeezed out of the pipe (emulsions, ointments, creams).

The valve of the aerosol package must ensure its tightness at a pressure in the cylinder of up to 20 kgf/cm2. It can be spring or springless.

According to the principle of releasing the contents of the cylinder, the valves are divided into dosing valves and multiple continuous valves. According to the purpose - for liquid and viscous systems, for suspensions, foams, etc.

Depending on the material from which the cylinders are made, they are divided into several groups: metal, glass, plastic and combined.

The capacity of packages can be different: from 3 ml to 3 l, except for glass, the capacity of which is limited to 300 ml.

Metal cylinders are most often made of aluminum, their inner surface is covered with protective varnishes. Various polymer materials, anti-corrosion varnishes or copolymers are used for these purposes.

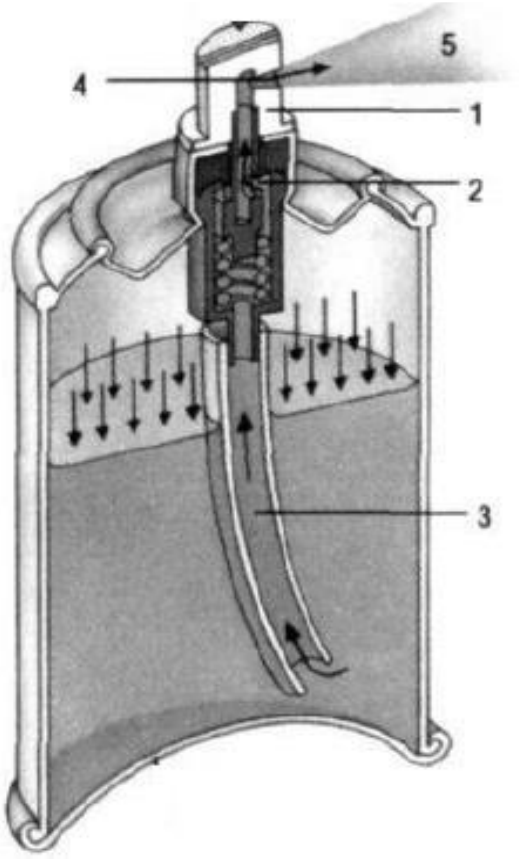

Fig. 8. Device of an aerosol can in:
1 - valve head; 2 - valve; 3 - siphon tube; 4 - nozzle; 5 - atomized substance.

A wide range of plastic cylinders made of polypropylene, nylon, polyethylene, polyformaldehyde, delrin, celcon, etc. are used abroad.

Depending on the degree of displaceability of the components of the main formulation with the propellant, aerosols are divided into solution aerosols, emulsion aerosols, suspension aerosols, and combined systems.

The production of aerosols includes the manufacture of cylinders, valve-spraying systems, preparation of repellents or their mixtures, concentrates, filling of aerosol cylinders and their quality control.

The production of aluminum monoblock cylinders is carried out by forming them from flat blanks on impact presses, and the cylinder neck is formed on special multi-spindle cone-forming machines. At the same time, 12-14 or more operations are performed depending on the diameter of the balloon.

Glass cylinders are made from neutral borosilicate glass HC-1 or HC-2 on automatic high-performance glass forming machines. The process of their production is associated with double annealing in horizontal furnaces with a temperature maximum of 640-650°C, to eliminate or weaken the residual internal stress of the glass.

After forming, the glass cylinders are covered with a polyethylene or polyvinyl chloride protective coating.

Plastic aerosol cans are made by the method of vacuum forming (monoblock) or injection molding on molding or casting machines.

Valve-spraying systems are manufactured at plastic processing plants.

A standard valve-spray system has the following elements:

- *The atomizer (nozzle)* is used to activate the valve and to spray medicine. It can be of different design and configuration, depending on the aggregate state of the medicine and the route of its administration.
- *The stem* serves to open and close the valve. The stem cavity is part of the expansion chamber.
- *The cuff* seals the joint of the stem with the hole in the cup (capsule) of the valve and is sometimes a nipple that closes or opens the hole in the stem.
- *The case* is the place where all the parts are assembled, and its cavity is part of the expansion chamber.
- *The siphon tube* serves to supply the contents from the lower part of the cylinder to the valve.
- *The gasket* seals the attachment points of the valve on the cylinder.
- *The cup (or capsule)* is intended for assembling all the parts of the valve and attaching it to the cylinder.

According to the method of evacuating the drug, valves are divided into valves of continuous and dosing action, which in turn are classified into:

- *standard valves* - used for evacuating products of the perfumery and cosmetic, chemical, pharmaceutical, food industry, leather goods, etc.;
- *universal valves* - spray the contents at any angle and are used to evacuate products of the chemical and perfumery and cosmetic industries;

- *Reversible valves* - spray the contents only in an inverted position and are used mainly for evacuating products of the pharmaceutical industry.

The principle of operation of a standard aerosol valve is as follows: the valve is actuated by pressing the spray head vertically downwards. Together with the head, the rod moves down, compressing the spring. The hole in the stem enters, from under the rubber gasket, into the cavity of the pocket filled with the product. The product goes into this hole and enters the head for spraying through the cavity of the rod. When the head is released, the spring raises the rod up and the valve action stops.

To date, 4 alternative directions for the creation of harmless extruding agents (propellants) have been identified, new spraying methods have been developed, and existing designs of aerosol packages are being improved:

- packaging from raw materials that do not CONTAIN phenol: saturated paraffin hydrocarbons of the methane series (propane, butane, isobutane) and compressed gases (nitrogen, nitrous oxide, carbon dioxide, etc.);
- cylinders in which the propellant is separated from the product and is not released into the environment (Fig. 2);
- packaging with a pump-type mechanical sprayer;
- compressed polymer and other cylinders.

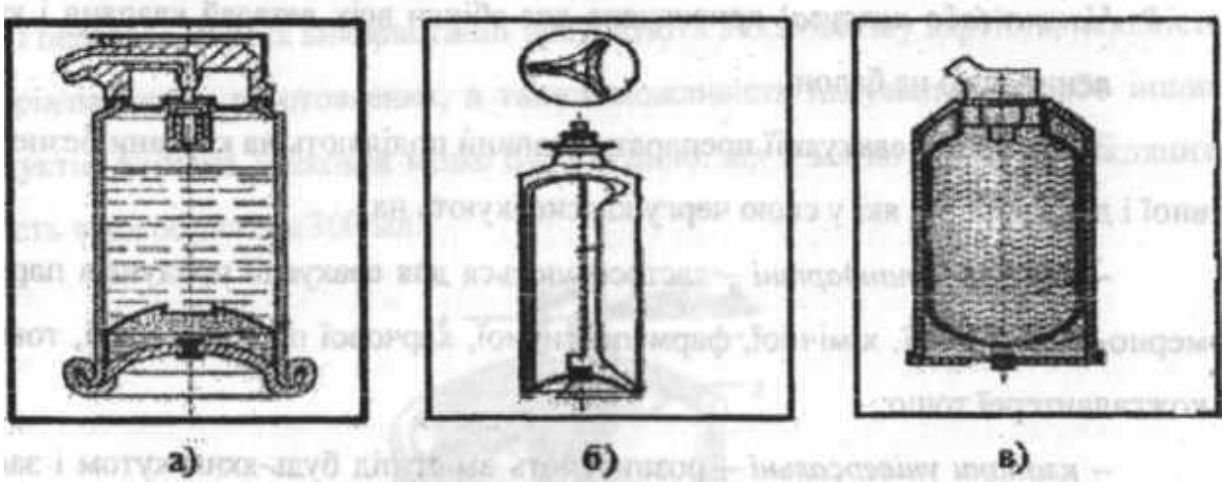

Fig. 2. Two-chamber aerosol packages:
a - aerosol packaging with a piston;
b - aerosol packaging with an insert;
c - aerosol packaging with an inner bag.

Aerosol preparation technology consists of the following stages (see the technological block diagram of aerosol production):

1. production preparation;
2. preparation of raw materials and solvent;
3. preparation of cylinders for filling;
4. preparation and cleaning of aerosol concentrate;
5. packing concentrate into cylinders;

6. clogging of aerosol cans;
7. filling aerosol cans with propellant;
8. checking cylinders for strength and tightness;
9. quality control of drugs under pressure;
10. packaging, labeling is ready: products.

Standardization:

- organoleptic control (appearance, control for the presence mechanical inclusions);
- physical and chemical control (internal pressure of the cylinder, tightness, determination of the percentage yield of the contents of the container, determination of the average weight of the drug in one dose (for dosing valves), determination of the dispersion of aerosol particles, standards for filling the cylinder);
- chemical control (qualitative and quantitative analysis of active substances);
- biological control

Preparation and transportation of propellant mixtures.

The most complex and specific operations for enterprises producing aerosol packaging are the preparation of mixtures of liquefied propellants and their supply to the filling line. In Ukrainian, enterprises of the chemical industry have organized the production of only one mixture, chladons 11 and 12 in a 50:50 ratio. If the recipe requires a different ratio of chladons or other mixtures, they are prepared in different ways at special stations.

Two methods are used to transport (supply) propellants to the filling line:

1) pressurization of the propellant from the capacity in which it is stored with the help of excess pressure created in the capacity either by nitrogen or by heated vapors of the refrigerants themselves;

2) pumping by pumps.

Concentrates-solutions are prepared, like ordinary solutions of medicinal substances, in reactors with a heat exchanger and a stirrer. Solutions are freed from impurities by settling, filtration or centrifugation.

If concentrates-solutions are obtained with the help of viscous solvents (fatty oils), the dissolution is carried out by heating, and the cleaning is carried out under pressure. In the case of using volatile solvents (ethyl alcohol), dissolution of substances is carried out in closed reactors, and filtration - under pressure. Systems may include stabilizers and preservatives. Standardization of concentrate solutions is carried out taking into account the percentage content of active substances or the density of the solution.

A decisive factor in the technology of medicinal products under pressure in the form of solutions is the pressure inside the container, the control of which can serve as a quantitative characteristic of some physicochemical properties: the completeness of

the release of the contents, dispersibility, as well as the solubility of the propellant in the concentrate. The greater the ability of the concentrate to dissolve the propellant, the lower the pressure in the container.

Testing of medicinal products under pressure is carried out at factories by the quality department in accordance with the NTD for this drug. It should be noted that the quality of this group of drugs depends on many factors and requires a special form of control, because it is impossible to make changes to the composition of the drug after the container is closed.

Standardization of medicinal products under pressure includes several types of control: organoleptic, physicochemical, chemical, microbiological and biological control (for the presence of cardiac glycosides, etc.).

The internal pressure in the container must meet the requirements of a separate article. It is determined by a manometer, the accuracy class of which should be 2.5. Filled packages are checked for strength and tightness.

Qualitative and quantitative indicators are controlled by methods of analysis of individual ingredients of the medicinal product.

Containers during their transportation have their own specific features compared to the current rules adopted for other medicinal forms. The storage conditions specified on the packaging and in the technical documentation should be observed (avoid impacts, exposure to direct sunlight and high temperatures).

Medicinal products under pressure are packed in strong wooden boxes, if the drug is flammable, cardboard transport containers are allowed for less dangerous drugs.

— recommendations (instructions) for performing tasks (professional algorithms, orientation maps for the formation of practical skills and abilities, etc.):

Orientation map for independent work with literature on the subject of the lesson.

№№p.p.	Main tasks	Instructions	Answers
1	2	3	4
1.	General characteristics and classification of aerosols.	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. – P. 432 - 434.
2.	Structure of aerosol packaging.	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. - P. 434-439.

3.	Propellants used in aerosol systems	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NPhaU: Original, 2016. - P. 440-442.

— requirements for the results of the work, including the registration: to state the basic concepts and rules of the pharmaceutical enterprise and safety rules, the concept of proper practice, technological block diagrams, to draw up a material balance.

— control materials for the final stage of the lesson: tasks, tasks, tests, etc. (if necessary):

Task:

Task 1. Determine the average mass of one dose, which will be released by aerosol, if the mass of the cylinder with a sprayer is 35.05 g, and after 15 presses - 30.15 g. Explain the reasons that when pressing the stem of the dosing valve may not provide portioned discharge of the contents of the cylinder.

Task 2. Draw up a work order for obtaining 600 packages of the drug "Ingalipt", if Krosh, at the stage of preparation of the aerosol concentrate and its packaging, is 1.025, and at the stage of filling the cylinders with propellant - 1.012.

6. List of recommended literature (main, additional, electronic information resources) :

Main:

- A.G. Bashura, O.S. Shpichak, E.E. Bogutska; under the editorship A.I. Tikhonov and S.A. Tikhonova - Kh.: Original, 2016. - 462 p.
- Vishnevska, N.P. Polovka, R.S. Korytniuk et al. - Kh.: National Academy of Sciences: Original, 2016. - 378p.
- Workshop on industrial technology of medicinal products: teaching. manual for students higher education institutions with the specialty "Pharmacy" / O.A. Ruban, D.I. Dmytrievskyi, L.M. Khokhlova [and others]; under the editorship O.A. Ruban. – Kh.: National Institute of Medical Sciences; Original, 2015. – 320 p.
- Industrial technology of medicines : education. manual for students' independent work / O.A. Ruban , V.D. Rybachuk , L.M. X ohlova etc. - KH.: NPHAU, 2015. - 120 p.
- Study guide for preparation for the final modular control and State certification in the Industrial Technology of Medicines for full-time and part-time students of the "Pharmacy" specialty / Ed. O.A. Ruban. - Kh.: National Academy of Sciences, 2016 . - 80 p.

- Study guide for independent preparation of students of the Faculty of Pharmacy for the licensing integrated exam "Step 2. Pharmacy" / O.A. Ruban, V.D. Rybachuk, L.M. Khokhlova, D.S. Pulyaev - KH.: NPHAU, 2016. - 63 p.
- Auxiliary substances in the production of medicines: training. manual for students higher pharmacy education closing / O.A. Ruban , I.M., Pertsev, S.A. Kutsenko, Yu.S. Oily; under the editorship I.M. Pepper - Kh.: Golden Pages, 2016. - 720 p.
- Technology of drugs for industrial production: tutorial. for university students education class: in 2 h. / V.I. Chuyeshov, E.V. Gladukh, I.V. Saiko et al. – 2nd ed., revision. and additional - Kh.: NPhaU: Original, 2012. - Part 1. - 694 p.
- Technology of drugs for industrial production: tutorial. for university students education class: in 2 h. / V.I. Chuyeshov, E.V. Gladukh, I.V. Saiko et al. – 2nd ed., revision. and additional - Kh.: NPhaU: Original, 2013. - Part 2. - 638 p.
- Modern pharmaceutical technologies: education. manual to laboratory classes of full-time, evening and part-time master's students of the specialty 8.110201 "Pharmacy" / under the editorship. O.A. Ruban. - Kh.: Publishing House of the National Academy of Sciences, 2016. - 256 p.

Auxiliary :

- Mathematical planning of an experiment when conducting scientific research in pharmacy / T.A. Groshovyi, V.P. Martsenyuk, L.I. Kucherenko and others. – Ternopil: TDMU Ukrmedknyga, 2008. – 367 p.
- Regulatory and technical documentation and production validation. Material balance: Educational method. river for audit. and external audit. student work special "Pharmacy" of full-time and part-time education / D.I. Dmytrievskyi, G.D. Slipchenko, I.M. Hrubnyk, D.V. Rybachuk . - Kh.: Publishing House of the National Academy of Sciences, 2008. - 45 p.
- Technology of medicinal products of industrial production: training. manual/ edited by Prof. D.I. Dmitrievsky. – Vinnytsia: Nova kniga, 2008. – 280 p.
- Drug technology. Educational and methodological guide: Education. manual for students higher education hall. / O.I. Tikhonov, P.A. Logvin, S.O. Tikhonova, O.V. Bazulin, T.G. Yarnykh, O.S. Shpychak, O.M. Kotenko; under the editorship O.I. Tikhonova, Kh.: Original, 2009. - 432 p.
- C pyrotometry. Recovery and rectification of ethanol: Textbook. help / D.I. Dmytryevsky, L.I. Boguslavskaya, L.N. Khokhlova and others; Ed. Prof. D.I. Dmitrievsky - Kh.: Izd-vo NPhaU, 2006. - 100 p.
- Pharmaceutical encyclopedia / Chief editor. council and the author of the foreword V.P. Black people - 3rd ed., revised. and additional - K.: "MORION", 2016. - 1952 p.

- Encyclopedia of Pharmaceutical Technology: 3-d Ed. / ed. by J. Swarbrick. – New York; London: Informa Healthcare, 2007. - 4128 p.
- European Pharmacopoeia 8.0 [8th edition] / European Directorate for the Quality of Medicines & Healthcare. - Strasbourg, 2013. - 3638 p.
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Practical lesson No. 20

Topic: " Final control No. 3 "

Purpose: Checking the knowledge of the applicants on previous topics.

1. The pharmaceutical enterprise masters the production of new products. Which section of the industrial technological regulations describes the appearance and physical and chemical properties of the finished product:

A Characteristics of the final product of production

B. Description of the technological process

C. Characteristics of raw materials, materials and semi-finished products

D Characteristics of auxiliary raw materials and materials

E. Information materials

2. Which section of the regulation describes the sanitary preparation of industrial premises:

A. Description of technological process stages and industrial sanitation

B. Safety technology, fire safety and industrial sanitation

C. Safe production operation and environmental protection

D Information materials

E. General characteristics of production

3. Specify the analytical regulatory document that establishes requirements for the composition of the drug and the process of its production:

A. Technological regulation, pharmacopoeial article

B. Technical regulation

C. State standard (GOST)

D Industry Standard (OST)

E. Technical conditions

4. The industrial and technical department is developing technical regulations. Several pieces of equipment were replaced at the factory. Which section of the technical regulations needs to be changed urgently.

A. Hardware diagram

B. Department of labor protection

C. GDC table

D Accident elimination plan

E. List of instructions

5. At the pharmaceutical enterprise, various ready-made medicinal products are manufactured in accordance with technological regulations. During what term is the industrial regulation valid:

A is 5 years old

B. 3 years

C. 8 years old

D. 1 year

E. 6 months

6. A regulatory document that establishes requirements for specific products and services that regulates the relationship between the supplier and the consumer. Which document corresponds to this definition:

A. Technical conditions;

B. Standard;

C. Technical regulations;

D Technological regulation;

E. Methodological guidelines.

7. What are not regulated by the GMR rules:

A. requirements regarding the bioavailability of the drug;

B. pharmaceutical terminology;

C. requirements for buildings and production premises;

D. personnel requirements;

E. the need for validation.

8. The cost factor is:

A. The ratio of the mass of the initial components to the mass of the finished product.

B. The amount of substance used to obtain a given amount of the drug.

C. The ratio of the mass of the finished product to the mass of the raw materials.

D The ratio of the mass of material losses to the mass of raw materials.

E. The sum of the masses of losses and starting material

9. Validation is a concept related to GMR and means:

A. That the system is working as intended.

B. Profitability of the enterprise.

C. Control over the work of the VTK of the enterprise.

D Product sterility.

E. Inspection of the quality of GLZ.

10. GMP rules regulate:

A. All answers are correct.

B. Pharmaceutical technology.

C. Requirements for buildings and premises of farm production.

D Personnel requirements.

E. The need for validation.

11. The need for validation:

A. Conducting preclinical tests of pharmaceutical preparations.

B. Organization of production of GLZ.

C. Conducting clinical trials.

D Retail Rules.

E. Rules of wholesale trade.

12. GMP rules regulate:

A. Conducting clinical trials

B. Organization of production of GLZ.

C. Conducting preclinical research of pharmaceutical preparations.

D Retail Rules.

E. Rules of wholesale trade.

13. The material balance is:

A. The ratio between the amount of raw materials, finished products, production waste and material losses.

B. Amount of material losses.

C. The ratio between the amount of finished product and waste.

D Description of the technological process.

E. The ratio of the amounts of energy introduced into the technological process and released after its completion.

14. Choose a machine for medium grinding of vegetable raw materials:

A. Grass and root cutter

B. Vibrating mill

C. Drum mill
D Rod mill
E. Jet mill

15. Different equipment is used in the production of solutions at pharmaceutical enterprises. What devices are used for mechanical mixing of liquids?
A. Vane, turbine mixers.
B. Liquid whistles.
C. Pulsators.
D Reactors.
E. Barboter.

16. When choosing grinding equipment, the physical and chemical properties of the material are taken into account. Determine the method of grinding for fibrous material with a cellular structure.
A. Cutting, erasing
B. Impact, chipping, abrasion
C. Crushing, impact
D Crushing, abrasion
E. Impact

17. In the case of production of solutions at pharmaceutical enterprises, different equipment is used. What devices are used for mechanical mixing of liquids?
A. Shovel agitators
B. Compressors
C. Pulsators
D Liquid whistles
E. Pumps

18. Different types of dryers are used at the pharmaceutical enterprise. Which dryers belong to the contact type?
A. Valtsevi
B. Tapes
C. Air circulation
D Pneumatic
E. Spraying

19. Different types of dryers are used in the process of manufacturing phyto- and organic preparations. Which dryer is the most appropriate to use for drying heat-labile substances?
A. Lyophilic

B. Valtseva
C. Strychkova
D Drying cabinet
E. Drumbannu

20. A variety of equipment is used to filter solutions. What filters are used for vacuum filtration:
A. Notch filters
B. Print filters
C. Frame filter presses
D Bag filters
E. Centrifuges

21. What should be the correct set of clothing when working in "clean" rooms according to the GMP recommendation?
A. Overalls, helmet, mask, shoe covers, gloves
B. Pants suit, mask, shoe covers
S. Overalls, mask, shoe covers, gloves
D. Trouser suit, headdress, gloves, overshoes
E. Trouser suit, helmet, overshoes

22. For the production of sterile products in GMP factory conditions, the WHO classifies "clean" areas in accordance with the requirements for air characteristics into the following cleanliness classes:
A. A, B, C, D
B. A, B, C, R, D
C. I, II and III
D. I and II
E. A and B

23. According to the GMP requirements of the WHO, clean rooms for the production of sterile products are classified according to the requirements for characteristics into cleanliness classes. What purity class is not available for pharmaceutical companies?
A. E;
B. In;
C. With;
D. D;
E.A.;

24. Which regulatory and technical document establishes requirements for the

quality of medicinal products or medicinal plant raw materials, is approved for a limited period.

A. Provisional pharmacopoeial article (VFS)
B. Pharmacopoeia article (FS)
C. Technological Industrial Regulation (TPR)
D. Industry standard (OSTU)
E. State standard (GOST)

25. A regulatory document that sets requirements for specific products and services and regulates the relationship between the supplier and the consumer. Which document fits this definition?

A. Technical conditions;
B. Methodological guidelines.
C. Technical regulations;
D. Standard;
E. Technological regulations;

1
What brand of glass belongs to the first class?
A. USP-1
B. AB-1 (free glass)
C. NS-2 (neutral glass-2)
D. NS-2 A (neutral glass-2A)
E. MTB (medical container colorless)

2
What brand of glass can be used to make ampoules for tocopherol solution?
A. AB-1
B. NS-3
C. NS-1
D. HT-1
E. SNA-1

3
What brand of glass belongs to the second class?
A. AB-1 (free glass)
B. USP-1
C. NS-1 (neutral glass-1)
D. NS-3 (neutral glass-3)
E. SNS-1 (neutral photosensitive glass)

4
What brand of glass is not used for the manufacture of ampoules:

A. MTB (medical container colorless)
B. AB-1 (free glass)
C. NS-1 (neutral glass-1)
D. NS-3 (neutral glass-3)
E. SNS-1 (neutral photosensitive glass)
5
During the production of ampoules, to change the properties of glass, various components are introduced into its composition. What is the purpose of adding boron oxide to glass?
A. To increase the chemical resistance of glass
B. To reduce the melting temperature of ampoule glass
C. To give the glass the necessary color
D. To increase the mechanical strength of glass
E. To increase the thermal stability of glass
6
When assessing the quality of ampoules, chemical resistance is determined. Specify the methods of determining this indicator:
A. With the help of various acid-base indicators, with the help of a pH meter, weight methods
B. Visual, weight
C. Polarization-optical
D. Method of autoclaving followed by titration with hydrochloric acid solution
E. The method of impacting glass samples with sodium carbonate solution and sodium hydrogen carbonate solution
7
Specify the device for determining the residual voltage in the ampoule glass:
A. Polariscope-polarimeter
B. Densimeter
C. pH meter
D. Photoelectric colorimeter
E. Spectrophotometer
8
To determine the residual voltage in the ampoule glass, the following method is used:
A. Polarization-optical
B. Methylene blue solution
C. Using a pycnometer
D. Using a "drum eraser"
E. Using the Soxhlet apparatus
9

How does the residual stress in the glass affect the quality of ampoules:

A. Mechanical stability decreases

B. Mechanical stability increases

C. Chemical resistance increases

D. The size of the ampoule increases

E. The color of the ampoule changes

10

In the ampoule shop, before using the ampoules, it is necessary to remove the residual voltage. What operation is performed for this:

A. Annealing of ampoules

B. Drying in tunnel ovens

C. Washing with desalted water

D. Capillary cutting

E. Softening of glass with gas burners

11

According to which parameter is the calibration of glass wire at glass factories:

A. By outer diameter

B. By inner diameter

C. By the thickness of the walls

D. By length

E. By mass

12

The technological stage "Preparation of ampoules for filling" includes operations of drying and sterilization of ampoules. Choose the equipment and equipment to perform this operation:

A. Tunnel dryer, drying cabinets, drying cabinets of laminar flow of heated air

B. Drying cabinets of laminar flow of heated air, Krupina chamber, ultrasonic installation

C. AP-7 and AP-18 type steam sterilizers, Rezepina apparatus

D. Ultrasonic installation, tunnel dryer, drying cabinets

E. Krupin's chamber, ultrasonic installation, Rezepin's apparatus, laminar heated air flow drying cabinets

13

In the production of ampoules, glass with the necessary heat resistance is selected. Indicate what this property of ampoule glass provides so that the ampoules meet the requirements of regulatory and technical documentation:

A. Withstand sharp temperature fluctuations

B. Easy cutting of capillaries

C. High-quality sealing of ampoules

D. Load bearing during production and transportation
E. Ability to protect light-sensitive substances
14
What percentage of the ampoules tested for the "heat resistance" indicator should be intact:
A. 98%
B. 75%
C. 30%
D. 50%
E. 95%
15

When testing the thermal stability of 100 ampoules from one batch, 20 ampoules cracked. Whether heat-resistant glass was used in their manufacture:
A. No, there must be 98 integers
B. No, there must be 95 integers
C. No, there must be 90 integers
D. Yes, there should be 80 integers
E. Yes, there should be 75 integers
16
In the production of ampoules, glass with the required low melting point is selected. What provides this property of ampoule glass:
A. High-quality and fast sealing of ampoules
B. Easy cutting of capillaries
C. Load bearing during production and transportation
D. Withstand sharp temperature fluctuations
E. Ability to protect light-sensitive solutions
17
Different brands of glass are used in the production of ampoules for injection solutions. Indicate what brand of glass can be used to make ampoules for solutions that are sensitive to light:
A. SNA-1
B. NS-1
C. NS-3
D. AB-1
E. HT-1
18
What brand of glass should be used in the manufacture of ampoules for 0.01% cyanocobalamin solution?

A. Light protective neutral (SNS-1)
B. Bezborne (AB-1)
C. Neutral (NS-2)
D. Neutral (NS-1)
E. Neutral (NS-2A)

19

The ampoule workshop of the enterprise produces solutions for injections. From the proposed list, select the brands of ampoule glass used in the production of novocaine injection solution:

A. NS-3, NS-1, USP-1
B. NS-1, NS-2, NS-3
C. SNS-1, NS-2A, NS-3
D. OS-1, USP-1, NS-2
E. HT-1, SNS-1, AB-1

20

Which solutions for parenteral administration from the listed substances are subject to special purification in the absence of the "for injection" variety?

A. Magnesium sulfate, calcium chloride, glucose
B. Gelatin, novocaine, sodium sulfite
C. Sodium nitrite, ergot, calcium chloride
D. Hexamethylenetetramine, novocaine
E. Ascorbic acid, analgin

21

At a pharmaceutical enterprise, demineralized water is obtained using membrane separation methods. Choose a method in which the passage of water through a semipermeable membrane is carried out under the influence of external pressure:

A. Reverse osmosis
B. Electrodialysis
C. Evaporation through a membrane
D. Dialysis
E. Sorption

22

Specify the requirements for water for injections that significantly differentiate it from purified water:

A. Absence of pyrogens
B. Absence of heavy metals
C. Absence of sulfates, chlorides
D. Absence of nitrites and nitrates
E. Absence of reducing agents

23

Indicate from which impurities calcium gluconate is purified in the absence of the "for injection" grade.

A. From impurities of calcium oxalate

B. From impurities of iron salts

C. From impurities of manganese and iron salts

D. From impurities of calcium sulfate and iron

E. From dyes and pyrogenic substances

24

For what purpose is activated carbon used in the manufacture of injection solutions:

A. For the purpose of cleaning some injection solutions

B. To create a buffer system

C. As an antioxidant

D. To increase the chemical resistance of ampoule glass

E. To remove residual voltage in ampoules

25

To remove impurities from the glucose injection solution, special cleaning is carried out with the help of the following substances:

A. Adsorption of impurities on activated carbon

B. By adding calcium hydroxide followed by filtration

C. By adding hydrochloric acid followed by adsorption on activated carbon

D. Preliminary treatment with activated carbon followed by stabilization with hydrochloric acid

E. By adding iron oxide followed by adsorption of impurities on activated carbon

26

At a pharmaceutical enterprise, one of the methods of sterilizing heat-labile substances is the tyndalization method. Indicate what the essence of this method is:

A. Three times heating of the solution to 40-60°C with breaks per day for thermostating

B. Autoclaving at a temperature of 119-121°C and a pressure of 1.01.1 atm

C. Sterilization at 100°C with flowing steam

D. Sterilization by dry heat at 180-200°C for a long time

E. High and ultra-high frequency current sterilization

27

The ampoule workshop of the enterprise produces glucose solution. Indicate from which impurities glucose is purified in the absence of the "for injection" variety:

A. From pyrogenic substances and dyes

B. From sulfates and iron

C. From manganese and iron

D. From pyrogenic and protein substances
E. From impurities of protein nature and dyes

28

Specify the methods of control of solutions for parenteral administration on mechanical inclusions:

A. Visual and optical
B. Limulus test
C. Amperometric methods
D. Gravitational methods
E. NMR and UV spectroscopy

29

One of the operations of the technological process of obtaining solutions for injections is filtering solutions. What filters are used for sterile filtration?

A. Candle filters
B. Print filters
C. Filter fungus
D. Nutch filters
E. HNDHFI filter

30

Euphilin solution for injections is manufactured at the pharmaceutical enterprise. Specify the features of preparation of this solution:

A. Cleaning by sterile filtration
B. Cleaning the solution from coloring and pyrogenic substances
C. Dissolution of the medicinal substance during heating
D. Preparation of a solution of higher concentration
E. Adding stabilizer

31

Specify the optimal method of drying sterile powders for injections:

A. In freeze dryers
B. In chamber vacuum-drying devices
C. In spray dryers
D. In fluidized bed dryers
E. In chamber air circulation dryers

32

Name the main operations at the ampoule stage:

A. Filling ampoules with solution, sealing ampoules, quality assessment
B. Washing ampoules, filling ampoules with solution, sealing ampoules
C. Washing ampoules, drying and sterilization, quality assessment
D. Filling, washing, sterilization

E. Sealing, sterilization, packaging.

1

Which solutions for parenteral administration from the listed substances are subject to special purification in the absence of the "for injection" variety?

A. Magnesium sulfate, calcium chloride, glucose
B. Gelatin, novocaine, sodium sulfite
C. Sodium nitrite, ergot, calcium chloride
D. Hexamethylenetetramine, novocaine
E. Ascorbic acid, analgin

2

Which solvent is not used in the production of injection solutions:

A. Mineral oils
B. Mineral oils
C. Water
D. Glycerin
E. Ethyl oleate

3

Which oil is not used to prepare injection solutions:

A. Vaselinova
B. Peach
C. Olive
D. Sonyashnikova
E. Corn

4

The ampoule workshop of the enterprise produces calcium gluconate solution for injections. Indicate from which impurities calcium gluconate is purified in the absence of the "for injection" grade.

A. From impurities of calcium oxalate
B. From impurities of iron salts
C. From impurities of manganese and iron salts
D. From impurities of calcium sulfate and iron
E. From dyes and pyrogenic substances

5

The ampoule workshop produces solutions for injections. Specify the stabilizer for 1% solution of morphine hydrochloride for injection.

A. Hydrochloric acid solution 0.1 N
B. Sodium chloride solution 0.1 N
C. Aminopropylene glycol
D. Rongalite

E. Sodium metabisuMFite

6

To stabilize 5%, 10%, 20% solutions of novocaine, which are manufactured in industrial conditions, use:

A. Hydrochloric acid 0.1 n

B. Antioxidants in combination with hydrochloric acid

C. Meadows

D. Buffer solutions

E. Weibel stabilizer

7

What stabilizer should be taken to stabilize glucose solutions:

A. Weibel stabilizer

B. Kurshman stabilizer

C. Stabilizer 0.1M NaOH

D. Stabilizer 0.1M HCl

E. Carboxymethyl cellulose

8

The ampoule workshop of the enterprise produces solutions for injections. Specify the composition of Weibel's reagent, which is used in the production of glucose injection solutions:

A. Hydrochloric acid, sodium chloride, water

B. Water, hydrochloric acid, sodium hydroxide

C. Hydrochloric acid, sodium bromide, water

D. Hydrochloric acid, sodium nitrite

E. Hydrochloric acid, calcium chloride, water

9

In what quantity is the Weibel stabilizer added to parenteral solutions.

A. 5%

B. 13%

C. 15%

D. 7%

E. 1%

10

Solutions for injections are made in the ampoule workshop. Indicate which group of solutions the ascorbic acid solution for injections belongs to:

A. Solutions that are easily oxidized

B. Solutions of substances that require special cleaning

C. Solutions of substances that are not subject to thermal sterilization

D. Salt solutions formed by weak bases and strong acids

E. Salt solutions formed by strong bases and weak acids

11

The ampoule workshop of the enterprise produces a caffeine-benzoathunatrium solution for injections. What stabilizer is added to stabilize the solution:

A. 0.1 M sodium hydroxide solution

B. Sodium metabisuMFite

C. 0.1 M solution of hydrochloric acid

D. 0.1 M solution of hydrochloric acid and sodium chloride

E. Sodium bicarbonate and sodium suMFite

12

A solution of magnesium sulfate for injections is produced at a pharmaceutical enterprise. Specify the features of preparation of this solution:

A. Preparation of the solution, cleaning from impurities of manganese and iron salts

B. Preparation of solution without thermal sterilization

C. Preparation of a solution of higher concentration and purification from impurities of calcium sulfate and iron

D. Dissolution of the medicinal substance during heating and purification from impurities of calcium oxalate

E. Cleaning the solution from dyes and pyrogenic substances

13

To remove impurities from the glucose injection solution, special cleaning is carried out with the help of the following substances:

A. Adsorption of impurities on activated carbon

B. By adding calcium hydroxide followed by filtration

C. By adding hydrochloric acid followed by adsorption on activated carbon

D. Preliminary treatment with activated carbon followed by stabilization with hydrochloric acid

E. By adding iron oxide followed by adsorption of impurities on activated carbon

14

Solutions for injections of salts of weak acids and strong bases require stabilization. Specify which stabilizers are used for these solutions:

A. 0.1 M sodium hydroxide solution

B. 0.1 M solution of hydrochloric acid

C. Trylon B

D. Ascorbic acid

E. Butyloxytoluene

15

The ampoule workshop of the enterprise produces oil solutions for injections. What solvent is used in the production of a 20% injection solution of camphor in oil:

A. Peach oil
B. Olive oil
C. Polyethylene glycol 400
D. Vaseline oil
E. Benzyl benzoate

16

The ampoule workshop of the enterprise produces an oil solution of camphor for injections. Indicate what volume of oil solution must be prepared to fill 200 ampoules of 1 ml each.

A. 230 ml
B. 220 ml
C. 210 ml
D. 200 ml
E. 240 ml

17

The ampoule workshop of the enterprise produces glucose solution. Indicate from which impurities glucose is purified in the absence of the "for injection" variety:

A. From pyrogenic substances and dyes
B. From suMFates and iron
C. From manganese and iron
D. From pyrogenic and protein substances
E. From impurities of protein nature and dyes

18

Specify the methods of control of solutions for parenteral administration on mechanical inclusions:

A. Visual and optical
B. Limulus test
C. Amperometric methods
D. Gravitational methods
E. NMR and UV spectroscopy

19

Benzyl alcohol is used as part of solutions for parenteral administration as:

A. Antimicrobial preservative
B. Antioxidant
C. Buffer solution
D. pH regulator
E. Isotonicity regulator

20

One of the operations of the technological process of obtaining solutions for injections

is filtering solutions. What filters are used for sterile filtration?

A. Candle filters
B. Print filters
C. Filter fungus
D. Nutch filters
E. HNDHFI filter

21

A solution for injections is prepared in the ampoule shop. Indicate which group of solutions Eufilin for injections belongs to:

A. Solutions that are not subject to thermal sterilization
B. Salt solutions formed by weak bases and strong acids
C. Solutions of substances that require special cleaning
D. Salt solutions formed by strong bases and weak acids
E. Solutions that are easily oxidized

22

Euphilin solution for injections is manufactured at the pharmaceutical enterprise. Specify the features of preparation of this solution:

A. Cleaning by sterile filtration
B. Cleaning the solution from coloring and pyrogenic substances
C. Dissolution of the medicinal substance during heating
D. Preparation of a solution of higher concentration
E. Adding stabilizer

23

When calculating the isotonic concentration of solutions for injections, the value of blood plasma depression is used. Specify its value:

A. 0.52
B. 0.34
C. 0.10
D. 0.45
E. 0.90

24

Specify the optimal method of drying sterile powders for injections:

A. In freeze dryers
B. In chamber vacuum-drying devices
C. In spray dryers
D. In fluidized bed dryers
E. In chamber air circulation dryers

25

Name the main operations at the ampoule stage:

A. Filling ampoules with solution, sealing ampoules, quality assessment
B. Washing ampoules, filling ampoules with solution, sealing ampoules
C. Washing ampoules, drying and sterilization, quality assessment
D. Washing ampoules, drying, filling ampoules with solution, sealing ampoules, quality assessment
E. Filling ampoules with a solution, sterilization, washing, quality assessment

26

In the ampoule workshop, ampoules are filled with a volume that is greater than the nominal one. For what purpose it is carried out:

A. To ensure the correct dose when filling the syringe
B. To be able to take part of the solution for analysis
C. To remove air bubbles from the solution
D. To account for production losses
E. To ensure the stability of the solution

27

Which of the specified methods of filling ampoules allows you to prevent contamination of capillaries with thick and viscous solutions:

A. Syringe
B. Vacuum
C. Turbo vacuum
D. Vapor condensation
E. Filling in an environment of inert gases

28

The pharmaceutical enterprise produces solutions for injections. Which method can be used to fill ampoules with an oil solution:

A. Syringe
B. Vacuum
C. Vapor condensation
D. Turbo vacuum
E. Ultrasonic

29

The ampoule workshop of the enterprise produces a 5% oil solution of tocopherol acetate for injections. Indicate which method of filling ampoules is rational to use when filling ampoules with this solution.

A. Vapor condensation
B. Vacuum
C. Syringe
D. Syringe and vacuum
E. Syringe and steam-condensing

30

For which injection solutions ampoulation is carried out in an environment of inert gases (nitrogen, argon, carbon dioxide)?

A. A substance that is easily oxidized
B. Essential oils
C. powders
D. Hydrolytically unstable substances
E. Photosensitive substances

31

To which group of infusion solutions belong polyvinylpyrrolidone, polyvinyl alcohol, hemodeze, neohemodeze, polydeze:

A. Detoxifying solutions
B. Hemodynamic, anti-shock fluids
C. Regulators of water-salt balance
D. Preparations for parenteral nutrition
E. Solutions with the function of oxygen transfer

32

What is the peculiarity of the calcium gluconate solution technology?

A. Dissolving in hot water
B. Prepared in aseptic conditions without further sterilization
C. Preliminary sterilization of the powder
D. Filling the bottle with a solution for 2/3 of the volume
E. Stabilization with a solution of 0.1 M hydrochloric acid

33

Solutions for injections are made in the ampoule workshop. Indicate which group of solutions the ascorbic acid solution for injections belongs to:

A. Solutions that are easily oxidized
B. Solutions of salts formed by strong bases and weak acids
C. Solutions of substances that are not subject to thermal sterilization
D. Salt solutions formed by weak bases and strong acids
E. Solutions of substances that require special cleaning

34

The pharmacist prepared an injection solution with an easily oxidizing substance that needs stabilization with an antioxidant. Specify this substance:

A. Ascorbic acid
B. Diphenhydramine
C. Sodium chloride
D. Urotropin
E. Calcium gluconate

35

The pharmacist prepared an injection solution of ascorbic acid. Specify the substance needed to stabilize the solution:

A. Sodium sulfite
B. Sodium citrate
C. Sodium acetate
D. Sodium chloride
E. Sodium bromide

36

What is the peculiarity of the calcium gluconate solution technology?

A. Dissolving in hot water
B. Stabilization with a solution of 0.1 M hydrochloric acid
C. Prepared in aseptic conditions without further sterilization
D. Preliminary sterilization of the powder
E. Filling the bottle with a solution for 2/3 of the volume

1

What brand of glass belongs to the first class?

A. USP-1
B. AB-1 (free glass)
C. NS-2 (neutral glass-2)
D. NS-2 A (neutral glass-2A)
E. MTB (medical container colorless)

2

What brand of glass can be used to make ampoules for tocopherol solution?

A. AB-1
B. NS-3
C. NS-1
D. HT-1
E. SNA-1

3

What brand of glass belongs to the second class?

A. AB-1 (free glass)
B. USP-1
C. NS-1 (neutral glass-1)
D. NS-3 (neutral glass-3)
E. SNS-1 (neutral photosensitive glass)

4

What brand of glass is not used for the manufacture of ampoules:

A. MTB (medical container colorless)

B. AB-1 (free glass)
C. NS-1 (neutral glass-1)
D. NS-3 (neutral glass-3)
E. SNS-1 (neutral photosensitive glass)

5

During the production of ampoules, to change the properties of glass, various components are introduced into its composition. What is the purpose of adding boron oxide to glass?

A. To increase the chemical resistance of glass
B. To reduce the melting temperature of ampoule glass
C. To give the glass the necessary color
D. To increase the mechanical strength of glass
E. To increase the thermal stability of glass

6

When assessing the quality of ampoules, chemical resistance is determined. Specify the methods of determining this indicator:

A. With the help of various acid-base indicators, with the help of a pH meter, weight methods
B. Visual, weight
C. Polarization-optical
D. Method of autoclaving followed by titration with hydrochloric acid solution
E. The method of impacting glass samples with sodium carbonate solution and sodium hydrogen carbonate solution

7

Specify the device for determining the residual voltage in the ampoule glass:

A. Polariscope-polarimeter
B. Densimeter
C. pH meter
D. Photoelectric colorimeter
E. Spectrophotometer

8

To determine the residual voltage in the ampoule glass, the following method is used:

A. Polarization-optical
B. Methylene blue solution
C. Using a pycnometer
D. Using a "drum eraser"
E. Using the Soxhlet apparatus

9

How does the residual stress in the glass affect the quality of ampoules:

A. Mechanical stability decreases
B. Mechanical stability increases
C. Chemical resistance increases
D. The size of the ampoule increases
E. The color of the ampoule changes

10

In the ampoule shop, before using the ampoules, it is necessary to remove the residual voltage. What operation is performed for this:

A. Annealing of ampoules
B. Drying in tunnel ovens
C. Washing with desalted water
D. Capillary cutting
E. Softening of glass with gas burners

11

According to which parameter is the calibration of glass wire at glass factories:

A. By outer diameter
B. By inner diameter
C. By the thickness of the walls
D. By length
E. By mass

12

The technological stage "Preparation of ampoules for filling" includes operations of drying and sterilization of ampoules. Choose the equipment and equipment to perform this operation:

A. Tunnel dryer, drying cabinets, drying cabinets of laminar flow of heated air
B. Drying cabinets of laminar flow of heated air, Krupina chamber, ultrasonic installation
C. AP-7 and AP-18 type steam sterilizers, Rezepina apparatus
D. Ultrasonic installation, tunnel dryer, drying cabinets
E. Krupin's chamber, ultrasonic installation, Rezepin's apparatus, laminar heated air flow drying cabinets

13

In the production of ampoules, glass with the necessary heat resistance is selected. Indicate what this property of ampoule glass provides so that the ampoules meet the requirements of regulatory and technical documentation:

A. Withstand sharp temperature fluctuations
B. Easy cutting of capillaries
C. High-quality sealing of ampoules
D. Load bearing during production and transportation

E. Ability to protect light-sensitive substances

14

What percentage of the ampoules tested for the "heat resistance" indicator should be intact:

A. 98%

B. 75%

C. 30%

D. 50%

E. 95%

15

When testing the thermal stability of 100 ampoules from one batch, 20 ampoules cracked. Whether heat-resistant glass was used in their manufacture:

A. No, there must be 98 integers

B. No, there must be 95 integers

C. No, there must be 90 integers

D. Yes, there should be 80 integers

E. Yes, there should be 75 integers

16

In the production of ampoules, glass with the required low melting point is selected. What provides this property of ampoule glass:

A. High-quality and fast sealing of ampoules

B. Easy cutting of capillaries

C. Load bearing during production and transportation

D. Withstand sharp temperature fluctuations

E. Ability to protect light-sensitive solutions

17

Different brands of glass are used in the production of ampoules for injection solutions. Indicate what brand of glass can be used to make ampoules for solutions that are sensitive to light:

A. SNA-1

B. NS-1

C. NS-3

D. AB-1

E. HT-1

18

What brand of glass should be used in the manufacture of ampoules for 0.01% cyanocobalamin solution?

A. Light protective neutral (SNS-1)

B. Bezborne (AB-1)

C. Neutral (NS-2)
D. Neutral (NS-1)
E. Neutral (NS-2A)

19

The ampoule workshop of the enterprise produces solutions for injections. From the proposed list, select the brands of ampoule glass used in the production of novocaine injection solution:

A. NS-3, NS-1, USP-1
B. NS-1, NS-2, NS-3
C. SNS-1, NS-2A, NS-3
D. OS-1, USP-1, NS-2
E. HT-1, SNS-1, AB-1

20

Which solutions for parenteral administration from the listed substances are subject to special purification in the absence of the "for injection" variety?

A. Magnesium sulfate, calcium chloride, glucose
B. Gelatin, novocaine, sodium sulfite
C. Sodium nitrite, ergot, calcium chloride
D. Hexamethylenetetramine, novocaine
E. Ascorbic acid, analgin

21

At a pharmaceutical enterprise, demineralized water is obtained using membrane separation methods. Choose a method in which the passage of water through a semipermeable membrane is carried out under the influence of external pressure:

A. Reverse osmosis
B. Electrodialysis
C. Evaporation through a membrane
D. Dialysis
E. Sorption

22

Specify the requirements for water for injections that significantly differentiate it from purified water:

A. Absence of pyrogens
B. Absence of heavy metals
C. Absence of sulfates, chlorides
D. Absence of nitrites and nitrates
E. Absence of reducing agents

23

Which solvent is not used in the production of injection solutions:

A. Mineral oils
B. Fatty oils
C. Water
D. Glycerin
E. Ethyl oleate

24

Which oil is not used to prepare injection solutions:

A. Vaselinova
B. Peach
C. Olive
D. Sonyashnikova
E. Corn

25

The ampoule workshop of the enterprise produces calcium gluconate solution for injections. Indicate from which impurities calcium gluconate is purified in the absence of the "for injection" grade.

A. From impurities of calcium oxalate
B. From impurities of iron salts
C. From impurities of manganese and iron salts
D. From impurities of calcium sulfate and iron
E. From dyes and pyrogenic substances

26

The ampoule workshop produces solutions for injections. Specify the stabilizer for 1% solution of morphine hydrochloride for injection.

A. Hydrochloric acid solution 0.1 N
B. Sodium chloride solution 0.1 N
C. Aminopropylene glycol
D. Rongalite
E. Sodium metabisuMFite

27

To stabilize 5%, 10%, 20% solutions of novocaine, which are manufactured in industrial conditions, use:

A. Hydrochloric acid 0.1 n
F. B. Antioxidants in combination with hydrochloric acid
G. Meadows
H. Buffer solutions
I. Weibel stabilizer

28

What stabilizer should be taken to stabilize glucose solutions:

A. Weibel stabilizer
B. Kurshman stabilizer
C. Stabilizer 0.1M NaOH
D. Stabilizer 0.1M HCl
E. Carboxymethyl cellulose

29

The ampoule workshop of the enterprise produces solutions for injections. Specify the composition of Weibel's reagent, which is used in the production of glucose injection solutions:

A. Hydrochloric acid, sodium chloride, water
B. Water, hydrochloric acid, sodium hydroxide
C. Hydrochloric acid, sodium bromide, water
D. Hydrochloric acid, sodium nitrite
E. Hydrochloric acid, calcium chloride, water

30

In what quantity is the Weibel stabilizer added to parenteral solutions.

A. 5%
B. 13%
C. 15%
D. 7%
E. 1%

31

Solutions for injections are made in the ampoule workshop. Indicate which group of solutions the ascorbic acid solution for injections belongs to:

A. Solutions that are easily oxidized
B. Solutions of substances that require special cleaning
C. Solutions of substances that are not subject to thermal sterilization
D. Salt solutions formed by weak bases and strong acids
E. Salt solutions formed by strong bases and weak acids

32

For what purpose is activated carbon used in the manufacture of injection solutions:

A. For the purpose of cleaning some injection solutions
B. To create a buffer system
C. As an antioxidant
D. To increase the chemical resistance of ampoule glass
E. To remove residual voltage in ampoules

33

A solution of magnesium sulfate for injections is produced at a pharmaceutical enterprise . Specify the features of preparation of this solution:

A. Preparation of the solution, cleaning from impurities of manganese and iron salts
B. Preparation of solution without thermal sterilization
C. Preparation of a solution of higher concentration and purification from impurities of calcium sulatfe and iron
D. Dissolution of the medicinal substance during heating and purification from impurities of calcium oxalate
E. Cleaning the solution from dyes and pyrogenic substances

34

To remove impurities from the glucose injection solution, special cleaning is carried out with the help of the following substances:
A. Adsorption of impurities on activated carbon
B. By adding calcium hydroxide followed by filtration
C. By adding hydrochloric acid followed by adsorption on activated carbon
D. Preliminary treatment with activated carbon followed by stabilization with hydrochloric acid
E. By adding iron oxide followed by adsorption of impurities on activated carbon

35

At a pharmaceutical enterprise, one of the methods of sterilizing heat-labile substances is the tyndalization method. Indicate what the essence of this method is:
A. Three times heating of the solution to 40-60°C with breaks per day for thermostating
B. Autoclaving at a temperature of 119-121°C and a pressure of 1.01.1 atm
C. Sterilization at 100°C with flowing steam
D. Sterilization by dry heat at 180-200°C for a long time
E. High and ultra-high frequency current sterilization

36

Solutions for injections of salts of weak acids and strong bases require stabilization. Specify which stabilizers are used for these solutions:
A. 0.1 M sodium hydroxide solution
B. 0.1 M solution of hydrochloric acid
C. Trylon B
D. Ascorbic acid
E. Butyloxytoluene

37

The ampoule workshop of the enterprise produces a caffeine-benzoathunatrium solution for injections. What stabilizer is added to stabilize the solution:
A. 0.1 M sodium hydroxide solution
B. Sodium metabisulfite
C. 0.1 M solution of hydrochloric acid

D. 0.1 M solution of hydrochloric acid and sodium chloride
E. Sodium bicarbonate and sodium sulfite

38

The ampoule workshop of the enterprise produces oil solutions for injections. What solvent is used in the production of a 20% injection solution of camphor in oil:

A. Peach oil
B. Olive oil
C. Polyethylene glycol 400
D. Vaseline oil
E. Benzyl benzoate

39

The ampoule workshop of the enterprise produces an oil solution of camphor for injections. Indicate what volume of oil solution must be prepared to fill 200 ampoules of 1 ml each.

A. 230 ml
B. 220 ml
C. 210 ml
D. 200 ml
E. 240 ml

40

The ampoule workshop of the enterprise produces glucose solution. Indicate from which impurities glucose is purified in the absence of the "for injection" variety:

A. From pyrogenic substances and dyes
B. From sulfates and iron
C. From manganese and iron
D. From pyrogenic and protein substances
E. From impurities of protein nature and dyes

41

Specify the methods of control of solutions for parenteral administration on mechanical inclusions:

A. Visual and optical
B. Limulus test
C. Amperometric methods
D. Gravitational methods
E. NMR and UV spectroscopy

42

Benzyl alcohol is used as part of solutions for parenteral administration as:

A. Antimicrobial preservative
B. Antioxidant

C. Buffer solution
D. pH regulator
E. Isotonicity regulator

43

One of the operations of the technological process of obtaining solutions for injections is filtering solutions. What filters are used for sterile filtration?

A. Candle filters
B. Print filters
C. Filter fungus
D. Nutch filters
E. HNDHFI filter

44

A solution for injections is prepared in the ampoule shop. Indicate which group of solutions Eufilin for injections belongs to:

A. Solutions that are not subject to thermal sterilization
B. Salt solutions formed by weak bases and strong acids
C. Solutions of substances that require special cleaning
D. Salt solutions formed by strong bases and weak acids
E. Solutions that are easily oxidized

45

Euphilin solution for injections is manufactured at the pharmaceutical enterprise. Specify the features of preparation of this solution:

A. Cleaning by sterile filtration
B. Cleaning the solution from coloring and pyrogenic substances
C. Dissolution of the medicinal substance during heating
D. Preparation of a solution of higher concentration
E. Adding stabilizer

46

When calculating the isotonic concentration of solutions for injections, the value of blood plasma depression is used. Specify its value:

A. 0.52
B. 0.34
C. 0.10
D. 0.45
E. 0.90

47

Specify the optimal method of drying sterile powders for injections:

A. In freeze dryers
B. In chamber vacuum-drying devices

C. In spray dryers
D. In fluidized bed dryers
E. In chamber air circulation dryers

48

Name the main operations at the ampoule stage:

A. Filling ampoules with solution, sealing ampoules, quality assessment
B. Washing ampoules, filling ampoules with solution, sealing ampoules
C. Washing ampoules, drying and sterilization, quality assessment
D. Washing ampoules, drying, filling ampoules with solution, sealing ampoules, quality assessment
E. Filling ampoules with a solution, sterilization, washing, quality assessment

49

In the ampoule workshop, ampoules are filled with a volume that is greater than the nominal one. For what purpose it is carried out:

A. To ensure the correct dose when filling the syringe
B. To be able to take part of the solution for analysis
C. To remove air bubbles from the solution
D. To account for production losses
E. To ensure the stability of the solution

50

Which of the specified methods of filling ampoules allows you to prevent contamination of capillaries with thick and viscous solutions:

A. Syringe
B. Vacuum
C. Turbo vacuum
D. Vapor condensation
E. Filling in an environment of inert gases

51

The pharmaceutical enterprise produces solutions for injections. Which method can be used to fill ampoules with an oil solution:

A. Syringe
B. Vacuum
C. Vapor condensation
D. Turbo vacuum
E. Ultrasonic

52

The ampoule workshop of the enterprise produces a 5% oil solution of tocopherol acetate for injections. Indicate which method of filling ampoules is rational to use when filling ampoules with this solution.

A. Vapor condensation
B. Vacuum
C. Syringe
D. Syringe and vacuum
E. Syringe and steam-condensing

53

For which injection solutions ampoulation is carried out in an environment of inert gases (nitrogen, argon, carbon dioxide)?

A. A substance that is easily oxidized
B. Essential oils
C. Powders
D. Hydrolytically unstable substances
E. Photosensitive substances

54

What iNPhaUsion solutions are injected into the body when it is necessary to correct the composition of the blood in case of dehydration caused by diarrhea, brain swelling, toxicosis:

A. Regulators of water-salt balance and acid-alkaline balance
B. Hemodynamic antishock drugs
C. Detoxifying solutions
D. Preparations for parenteral nutrition
E. Solutions with the function of oxygen transfer

55

To which group of infusion solutions belong polyvinylpyrrolidone, polyvinyl alcohol, hemodeze, neohemodeze, polydeze:

A. Detoxifying solutions
B. Hemodynamic, anti-shock fluids
C. Regulators of water-salt balance
D. Preparations for parenteral nutrition
E. Solutions with the function of oxygen transfer

56

What is the peculiarity of the calcium gluconate solution technology?

A. Dissolving in hot water
B. Prepared in aseptic conditions without further sterilization
C. Preliminary sterilization of the powder
D. Filling the bottle with a solution for 2/3 of the volume
E. Stabilization with a solution of 0.1 M hydrochloric acid

57

Solutions for injections are made in the ampoule workshop. Indicate which group of

solutions the ascorbic acid solution for injections belongs to:
A. Solutions that are easily oxidized
B. Solutions of salts formed by strong bases and weak acids
C. Solutions of substances that are not subject to thermal sterilization
D. Salt solutions formed by weak bases and strong acids
E. Solutions of substances that require special cleaning
58
The pharmacist prepared an injection solution with an easily oxidizing substance that needs stabilization with an antioxidant. Specify this substance:
A. Ascorbic acid
B. Diphenhydramine
C. Sodium chloride
D. Urotropin
E. Calcium gluconate
59
The pharmacist prepared an injection solution of ascorbic acid. Specify the substance needed to stabilize the solution:
A. Sodium sulfite
B. Sodium citrate
C. Sodium acetate
D. Sodium chloride
E. Sodium bromide
60
What is the peculiarity of the calcium gluconate solution technology?
A. Dissolving in hot water
B. Stabilization with a solution of 0.1 M hydrochloric acid
C. Prepared in aseptic conditions without further sterilization
D. Preliminary sterilization of the powder
E. Filling the bottle with a solution for 2/3 of the volume
1
Which of the ophthalmic medicinal forms of industrial manufacture are called minimsis:
A. Eye lotions
B. Eye dosage forms of prolonged action
C. Solutions for washing eye lenses
D. Gelatin oval discs for single use
E. Ocular dosage forms and single use
2
Depending on the solubility, eye inserts are divided into:
A. emulsions, fat-soluble, combined

B. Biodissolving, lachrymatory, mixed
C. Single-acting, non-soluble, biosolubility
D. Water-soluble, fat-soluble, combined
E. Water-soluble, insoluble, combined
3
At the pharmaceutical enterprise, single-use ophthalmic dosage forms - lamellae - are produced. Which of the listed substances is used for their preparation?
A. agar
B. collagen
C. methylcellulose
D. is elatin
E. chitosan
4
The following film-forming substances are used for the production of eye films as biosoluble polymers:
A. Phenolformaldehyde and perchlorvinyl resins
B. Collagen, acetyl starch, methyl cellulose, derivatives of acrylic acid
C. Oil and epoxy resins, casein
D. Burshtin, rosin, copal and others
E. To arabamido and melaminoformaldehyde resins
5
At the pharmaceutical enterprise, medicated ophthalmic films with a bio-soluble polymer are manufactured. Specify which of the listed substances are used for their preparation:
A. Collagen
B. Methylcellulose, Na-carboxymethylcellulose
C. polyvinylpyrrolidone, polyvinyl alcohol
D. Starch, dextran
E. Gelatin, gelatoses
6
Which of the excipients is NOT used to adjust the viscosity of eye drops?
A. hydroxypropylmethyl cellulose
B. magnesium silicate
C. polyvinyl alcohol
D. polyvinylpyrrolidone
E. methylcellulose
7
A suspension of steroid hormones for ophthalmology is manufactured at a pharmaceutical enterprise. Specify which auxiliary substances are used to stabilize the dispersed phase.
A. Methyl cellulose

B. Twin -80
C. Spen -80
D. proxanol
E. PEG-400 and 0.1% sodium chloride solution
8
At the pharmaceutical enterprise, ophthalmic drugs are manufactured in dropper tubes. Specify the method of their sterilization:
A. radiation
B. dry heat
C. autoclaving
D. nitriding
E. filtration
9
At the pharmaceutical enterprise, single-use ophthalmic dosage forms - lamellae - are produced. Which of the listed substances is used for their preparation?
A. Gelatin
B. Collagen
C. Methylcellulose
D. Agar
E. Chitosan
10
At the pharmaceutical enterprise, ophthalmic drugs are manufactured in dropper tubes. Specify the method of their sterilization:
A. Gas
B. Suhozharovy
C. Autoclaving
D. Radiation
E. Filtering

11
Medicinal substances are introduced into the ointment depending on their properties. How should a pharmacist introduce diphenhydramine into a vaseline-lanolin base:
A. Pre-dissolve in a minimum amount of water
B. Grind with glycerin
C. Grind with part of the molten base
D. Dissolve in molten base
E. Grind with alcohol or ether
12
For the preparation of eye ointments, ointment bases of an alloy of petroleum jelly and lanolin are used. Specify the method of its sterilization
A. Dry heat

B. Ethylene oxide
C. Liquid steam
D. Pasteurization
E. Tyndalization
13
In eye drops, prepared on an oil basis, additionally control:
A. Acid and peroxide numbers
B. Microbiological purity
C. Transparency
D. Identity
E. Sterility
14
The company produces eye drops. For what purpose is sodium chloride added to the composition of eye drops?
A. Creation of an isotonic solution
B. Preventing the growth of microorganisms
C. Removal of pyrogens
D. Prevention of glass leaching
E. Elimination of hydrolysis
15
Solutions of protected colloids are used to prepare drops for the nose. What technological operation should be carried out when making a solution of protargol?
A. Pour a thin layer on a wide surface of water without stirring
B. Dissolve in purified water by shaking
C. Dissolve in purified water when heated
D. Dissolve in a small amount of glycerin
E. Grind with a small volume of purified water
16
The pharmaceutical company manufactures sterile aqueous solutions intended for wetting and washing the eyes, as well as for impregnation of materials that are applied to the eye. Name them:
A. Eye lotions
B. Eye sprays
C. Eye drops
D. Eye ointments
E. Eye inserts.
17
Specify the duration of infusion in the production of tinctures by the maceration method:
A. 7 days
B. 1-2 days

C. 24 hours
D. 3-4 hours
E. 14 days

18

Specify the methods of obtaining tinctures:

A. Maceration, percolation, dissolution of extracts
B. Dissolving extracts
C. Percolation, dissolution of extracts
D. Rectification, maceration
E. Percolation, dissolution of plant material

19

When making liquid dosage forms, the following liquid ingredients are dosed by volume :

A. Valerian tincture.
B. Dimexide
C. Methyl salicylate
D. Polyethylene glycol-400
E. Perhydrol

20

While preparing an infusion of althea root, the pharmacist made a mistake in the temperature of the water for preparing this extract, and the final product turned out to be cloudy. What temperature is needed for water to extract this raw material?

A. room
B. 40
C. 100
D. 60
E. 80

21

Transparent liquid water-alcohol extracts from dried or fresh medicinal plant materials, which are obtained without heating and removing the extractant, are called:

A. Tinctures
B. Liquid extracts
C. Thick extracts
D. Extracts-concentrates
E. Oil extracts

22

Which extraction method is a type of maceration?

F. Bismaceration
G. Percolation
H. Repercolation
I. Dynamization

J. Countercurrent extraction

23

An alcoholic solution of boric acid is produced in a chemical workshop. What filters are used to filter this solution?

A. Print filters
B. Nutch filters
C. Membrane filters
D. Bag filters
E. Paper filters

24

The pharmaceutical company produces camphor oil for external use. Specify which oil is used as a solvent:

A. Sonyashnikova
B. Peach
C. Vaseline
D. Olivkova
E. rain

25

Oil is used in the production of a number of medicinal forms. The method of obtaining this oil is:

A. Pressing
B. Enfleurage
C. Distillation with water
D. Steam distillation
E. Sublimation

26

During the production of decoctions, the volume of which is 1000-3000 ml, the time of infusion in a boiling water bath of the composition:

27

A. 40 minutes
B. 25 minutes
C. 30 minutes
D. 45 minutes
E. 15 minutes

28

A pharmacist prepares an extraction ointment. Specify the component that must be used to make this type of ointment:

A. 64 parts of sugar and 36 parts of water
B. 73 parts of sugar, 22 parts of water, 5 parts of 90% alcohol
C. 50 parts of sugar and 50 parts of water
D. 32 parts of sugar, 33 parts of water, 2 parts of 90% alcohol

E. 45 parts of sugar and 55 parts of water

29

Galenic preparations include:

A. Tinctures
B. Pellets
C. Capsules
D. Aerosols
E. Sponsored

30

Tween-80 is introduced into emulsion systems. State the role of tween-80 in emulsions:

A. Emulsifier
B. Antioxidant
C. Preservative
D. Corrector of taste
E. Solvent

31

The pharmacist prepared a solution of cholargol. Specify the type of dispersed system:

A. Colloidal solution
B. The real solution
C. Suspension
D. Emulsion
E. Aerosol

32

What mainly determines the choice of extractant when obtaining individual substances:

A. Selectivity in relation to active substances
B. The ability to eliminate hydrolysis
C. Heat resistance
D. Pharmacological indifference
E. Cost

33

The phytochemical workshop of the enterprise produces calendula tincture. Specify which raw materials are used for the manufacture of this drug:

A. Flowers
B. Roots, rhizomes and grass
C. Grass
D. Leaves and essential oil
E. Roots

34

The enterprise manufactures galena preparations. Galen preparations include:

A. The amount of biologically active substances
B. Only individual active substance

C. Odor correctors
D. Correctors of taste
E. Preservatives

35

Specify the potent medicinal plant material from which the infusion is prepared in a ratio of 1:400:

A. Foxglove leaves
B. Rhizomes with valerian roots
C. Althea root
D. Sage leaves
E. Stinging nettle herb

36.

The phytochemical workshop produces tinctures. This dosage form is:

A. Alcoholic extracts from medicinal plant raw materials obtained without heating and removing the extractant
B. Aqueous extracts from medicinal plant raw materials
C. Water-ethanol extracts from medicinal plant raw materials containing 25% moisture
D. Oil extracts from medicinal plant raw materials
E. Extracts from medicinal plant raw materials obtained using ether or chloroform

37

Tinctures are made at the pharmaceutical enterprise. For the manufacture of an experimental series of the drug, it is necessary to specify the equipment used for grinding raw materials:

A. Grass cutters
B. Excelsior
C. Vibromlin
D. Dismembrator
E. Rolls

38

Which of the following extractants has a number of advantages, including affordability?

A. Water
B. Ethyl alcohol
C. Methyl alcohol
D. Methylene chloride
E. Ethyl ether

39

Indicate which extractant is used at pharmaceutical enterprises for the production of tinctures:

A. Ethyl alcohol
B. Acetone
C. Chloroform
D. Diethyl ether
E. Peach oil

40

A tincture with an inflated content of active substances was obtained in the phytochemical workshop. To bring the tincture to the standard, it is necessary:

A. Dilute with the extractant to the standard
B. Consider an irreparable defect
C. Deposit excess active substances
D. Leave unchanged
E. Filter through sorbents

41

The phytochemical workshop of the pharmaceutical enterprise produces valerian tincture. Specify the technological features of the production of this drug:

A. It is prepared in 70% ethanol in a ratio of 1:5
B. It is prepared in 70% ethanol in a ratio of 1:10
C. It is prepared in 90% ethanol in a ratio of 1:5
D. It is prepared in 90% ethanol in a ratio of 1:10
E. It is prepared in 95% ethanol in a ratio of 1:10

42

One of the methods of obtaining tinctures in factory conditions is that the total amount of extractant is divided into 3-4 parts and the raw material is successively extracted with the first part of the extractant, then the second, third and fourth, draining the hood each time; the time of infusion depends on the properties of the plant material. What is the name of this method?

A. Remaceration
B. Maceration
C. Percolation
D. Vortex extraction
E. Maceration with forced circulation of the extractant

43

Specify the type of moisture that is tightly bound to the material and that is not completely removed during drying:

A. Crystallization
B. free
C. Hygroscopic
D. Osmotic

44

Extractive substances are released from plant raw materials due to:

A. Molecular and convective diffusion
B. Molecular and cellular diffusion
C. Convective and cellular diffusion
D. Coacervation
E. Adsorption and readsorption of the extractant by plant raw materials

45

In the manufacture of phytochemical preparations, extraction of extractive substances from plant raw materials occurs due to:

A. Molecular and convective diffusion
B. Molecular and cellular diffusion
C. Convective and cellular diffusion
D. Coacervation
E. Absorption and adsorption of the extractant by plant raw materials

46

Specify the methods of obtaining tinctures:

A. Maceration, percolation, dissolution of extracts
B. Dissolving extracts
C. Percolation, dissolution of extracts
D. Rectification, maceration
E. Percolation, dissolution of plant material

47

The phytochemical workshop of the enterprise produces tinctures by the maceration method. Specify the sequence of technological operations when obtaining tinctures by this method:

A. Insisting for 7 days with periodic mixing of the obtained extract, cleaning the extract, standardization, packaging
B. Soaking for swelling, infusing for 24-48 hours, obtaining a hood, cleaning the hood, standardization, packaging
C. Insisting for 24-48 hours, obtaining a hood, cleaning the hood, standardization, packaging
D. Insisting for 7 days, obtaining a hood, cleaning the hood, standardization, packaging
E. Soaking for swelling, infusing for 7 days, obtaining a hood, cleaning the hood, standardization, packaging

48

Which of the methods of obtaining tinctures is ineffective and characterized by incomplete extraction of extractive substances:

A. Maceration
B. Repercolation with evaporation
C. Percolation
D. Repercolation with the distribution of raw materials into unequal parts

E. Extraction using ultrasound

49

Specify the duration of infusion in the production of tinctures by the maceration method:

A. 7 days
B. 1-2 days
C. 24 hours
D. 3-4 hours
E. 14 days

50

The phytochemical workshop of the enterprise is mastering the production of the drug from fresh plant raw materials. What extraction methods are used when obtaining preparations from fresh plant raw materials:

A. Maceration with 90% ethyl alcohol, bismaceration
B. Percolation, maceration with 70% ethyl alcohol
C. Repercolation, countercurrent extraction
D. Extraction in the liquid-liquid system, maceration
E. Vortex extraction, circulation extraction

51

Which extraction method is a type of maceration?

A. Bismaceration
B. Percolation
C. Repercolation
D. Dynamization
E. Countercurrent extraction

52

The phytochemical workshop of the enterprise produces tinctures by the percolation method. At what speed is percolation carried out:

A. 1/24 or 1/48 part of the working volume of the percolator per hour.
B. 1/50th of the working volume of the percolator in 30 minutes.
C. 1/20 part of the working volume of the percolator per hour.
D. 1/40 part of the working volume of the percolator per hour.
E. 1/10th of the working volume of the percolator in 30 minutes

53

The phytochemical workshop of the enterprise produces tinctures by the percolation method. What ratio of raw materials - extractant must be observed when soaking raw materials:

A. 1:1, 1:0.5
B. 0.5:1, 1:5
C. 1:5, 1:10

D. 1:2, 1:1
E. 0.5:2, 1:2

54

The phytochemical workshop of the enterprise produces tinctures by the percolation method. What amount of raw materials and extractant is necessary to obtain 100 liters of nettle tincture, if K = 1.5:

A. 20 kg of raw materials, 130 liters of extractant
B. 10 kg of raw materials, 45 liters of extractant
C. 100 kg of raw materials, 100 liters of extractant
D. 50 kg of raw materials, 175 liters of extractant
E. 20 kg of raw materials, 150 liters of extractant

55

While preparing an iNPhaUsion of althea root, the pharmacist made a mistake in the temperature of the water for preparing this extract, and the final product turned out to be cloudy. What temperature is the water needed to extract this raw material?

A. Room temperature
B. 40 º C
C. 100 º C
D. 60 º C
E. 80 º C

56

What methods of cleaning the hood are used in the production of tinctures:

A. Settling at a temperature of 8-10 °C, filtration
B. Extractive cleaning methods in the liquid-liquid system
C. Denaturation, filtration, sorption
D. Dialysis, advocacy
E. Solvent replacement, settling, filtration

57

One of the methods of purification of tinctures is settling. In the production process, it is necessary to determine at what temperature it is rational to use this method:

A. 10-15°C
B. Not higher than 10°C
C. 20°C
D. 18°C
E. 45°C

58

Different equipment is used to filter solutions. What filters are not used to filter alcohol solutions?

A. Nutch filters
B. Print filters
C. Frame filter presses

D. Bag filters
E. Filter funnels

59

What methods are used to determine the alcohol in the tincture:

A. Distillation, by boiling point
B. Distillation, biological
C. Chemical, biological
D. By boiling point
E. With the help of an alcohol meter and a hydrometer

60

In what ratio are tinctures prepared from potent raw materials:

A. 1:10
B. 1:5
C. 1:25
D. 1:40 a.m
E. 1:100

61

The phytochemical workshop of the enterprise produces belladonna tincture. Indicate in what ratio of raw materials and finished products the extractor is loaded:

A. 1:10
B. 1:1
C. 1:2
D. 1:20
E. 1:5

62

The phytochemical workshop of the pharmaceutical enterprise produces valerian tincture from fresh raw materials. Specify the technological features of the production of this drug:

A. It is prepared in 70% ethanol in a ratio of 1:5
B. It is prepared in 90% ethanol in a ratio of 1:5
C. It is prepared in 90% ethanol in a ratio of 1:10
D. It is prepared in 70% ethanol in a ratio of 1:10
E. It is prepared in 95% ethanol in a ratio of 1:10

63

Which quality indicator **is not investigated** during the analysis of tinctures:

A. Residual content of solvents
B. Density
C. Dry residue
D. Quantitative content of active substances
E. Heavy metals

64

The phytochemical workshop of the enterprise produces calendula tincture. Specify which raw materials are used for the manufacture of this drug:

A. flowers
B. Roots, rhizomes and grass
C. Grass
D. Leaves and essential oil
E. Roots

65

When obtaining ethyl alcohol, a rectification process is used. Specify the principle of the process:

A. This is the separation of a mixture of intermixable liquids with different boiling points into separate fractions
B. This is distillation with inert gases
C. This is the washing of spent raw materials with 3-5 times the amount of ethanol
D. This is a technological technique for obtaining liquid extracts
E. This is deep vacuum distillation

66

Galenic preparations include:

A. Tinctures
B. Granules
C. Capsules
D. Aerosols
E. Spangles

67

Define the term "contact drying":

A. The drying process in phytochemical production when the materials to be dried are heated with a heat carrier through an impermeable wall that conducts heat
B. The process of drying in phytochemical production by direct contact of materials to be dried with a hot gaseous coolant
C. Drying process in phytochemical production by contact heating or infrared heat generation
D. The process of drying in phytochemical production by means of contact introduction or generation of heat by high frequency currents
E. Drying process in phytochemical production by contact feeding or heat generation in a microwave field

1

The driving force of the diffusion process in the extraction of plant raw materials is:

A. The difference in concentrations of the active substance in the raw material and the extractant
B. High temperature of the extractant

C. High polarity of the extractant
D. Brownian motion of particles
E. The presence of a film membrane

2

What phenomena do not take place in the process of extraction of plant raw materials?

A. Adsorption
B. Dialysis of the extractant inside the cell
C. Desorption
D. Dissolution of cell contents
E. Diffusion

3

In the production of maximally purified extraction preparations, specific methods of hood cleaning are used. Specify the method related to salting:

A. Action of saturated solutions of strong electrolytes
B. The process of influencing the heating hood
C. Dialysis
D. Effect of UV radiation
E. Ultrasonic treatment

4

An extract from medicinal plant raw materials is obtained in the phytochemical workshop. Specify the product characterized by the same ratio between the active substances contained in the raw material and the finished product:

A. Liquid extract
B. Tincture
C. Thick extract
D. Dry extract
E. Extract concentrate

5

When making liquid extracts in accordance with the requirements of the pharmacopoeia, the raw materials and the extractant must be taken in the ratio:

A. 1:1
B. 1:3
C. 1:5
D. 1:10
E. 1:4

6

The phytochemical workshop of the enterprise produces liquid extracts. How many parts by volume of liquid extract are obtained from one weight part of medicinal plant raw materials:

A. 1.0
B. 0.5

C. 10.0
D. 5.0
E. 2.0
7
At the pharmaceutical enterprise, liquid extracts are produced by the percolation method. What is the first portion of percolate in relation to the mass of raw materials?
A. 85%
B. 80%
C. 90%
D. 75%
E. 60%
8
In the phytochemical workshop, one percolator is used to obtain the liquid extract. By what method is the process of obtaining the extract carried out:
A. Percolation
B. Repercolation with separation of raw materials into unequal parts according to the US Pharmacopoeia
C. By Bosin's method
D. By repercolation with a completed cycle
E. Chulkov's method
9
Which method of obtaining liquid extracts is accompanied by a further stage of evaporation of the extracts:
A. Repercolation with an unfinished cycle
B. Circulating extraction
C. Repercolation with a completed cycle
D. Repercolation according to Chulkov
E. Repercolation with the distribution of raw materials into unequal parts
10
For the production of the extraction drug, the phytochemical workshop selected: extractant - water; equipment - grinding rolls, a reactor with a steam "shirt", a filter. Specify the production of which extractive preparation is being discussed.
A. Aloe liquid extract
B. Thick licorice extract
C. Lantoside
D. Adoniside
E. Plantaglucid
11
Indicate which extractant is used at pharmaceutical enterprises for the production of liquid extracts:
A. Ethyl alcohol

B. Acetone
C. Chloroform
D. Diethyl ether
E. Peach oil

12

At a pharmaceutical factory, a liquid extract of hawthorn is produced by the percolation method. Specify the amount of the first extract when obtaining 200 liters of extract:

A. 170 liters
B. 50 liters
C. 70 liters
D. 150 liters
E. 200 liters

13

Which of the extraction methods is the most accelerated:

A. Vortex extraction
B. Maceration
C. Percolation
D. Repercolation
E. Circulating extraction

14

A liquid extract of Eleutherococcus is produced at a pharmaceutical factory. What equipment should be used at the hood cleaning stage:

A. Settlers of periodic action, print-filters
B. Filters "Vladipor", "Milipor"
C. Sediminators of continuous action, notch filters
D. Vacuum evaporator, filter "Khnihfi"
E. Centrifuges, notch filters

15

Specify the maximum moisture content in thick extracts according to the requirements of the Federal Ministry of Ukraine.

A. 30%
B. 20%
C. 10%
D. 5%
E. 75%

16

The pharmaceutical enterprise produces thick extracts. Specify the technological stage not provided for in their manufacture:

A. Drying
B. Extraction
C. Extraction cleaning

D. Evaporation
E. Standardization

17

What is the principle of operation of the Soxhlet apparatus when obtaining extracts:

A. Multiple circulation of the extractant through the raw material
B. Molecular diffusion of the extractant under static conditions
C. Use of pseudo rarefaction
D. Action of ultrasonic cavitation
E. Countercurrent extraction

18

The main working parts of the vacuum-evaporative circulation apparatus "Symax" are:

A. Heating flask, "trunk", expansion flask, refrigerator, receiver
B. Spray nozzles, scraper shaft, body with heated walls, splash guard
C. Pump, nozzles, heat exchanger of the evaporation chamber, fan, separator, working capacity
D. Extractor, siphon tube, heating bulb, refrigerator
E. Expansion flask, shaft with scrapers, fan, separator

19

The phytochemical workshop of the enterprise produces extracts by the circulation extraction method. Which extractant is not suitable for this method?

A. Ethyl alcohol
B. Ether
C. Chloroform
D. A mixture of chloroform and ether
E. Methylene chloride

20

What equipment is used for continuous countercurrent extraction with simultaneous movement of raw materials and extractant?

A. Spring-blade extractor
B. Percolator with RPA
C. Soxhlet apparatus
D. Mixer
E. A battery of diffusers

21

In the production of thick extracts, the hood thickening stage is carried out. Specify the equipment for thickening, which consists of a receiving flask, a heater, a refrigerator-condenser, a collecting flask:

A. Circulating vacuum-evaporating apparatus
B. Rotary direct current device
C. Foam evaporator
D. Evaporative cube

E. Reactor with steam heating

22

The phytochemical workshop of the enterprise produces a thick extract of male fern. Select the extractant and method of obtaining for the production of this product:

A. Diethyl ether, circulation method
B. 40% ethyl alcohol, TSANDI method
C. 0.25% ammonia solution, bismaceration
D. Chloroform water, percolation
E. Water, vortex extraction

23

Name the extract for the production of which diethyl ether was used:

A. Thick extract of male fern
B. A thick extract of the trefoil bean plant
C. Thick extract of belladonna leaves
D. Dandelion root extract
E. Adoniside

24

When making which thick extract is a Soxhlet type apparatus used:

A. Buckwheat extract is thick
B. Male fern extract is thick
C. Valerian extract is thick
D. Pepper mustard extract is thick
E. Licorice extract is thick

25

Why is settling at a temperature of 8-10 °C during the purification of the primary extract?

A. At this temperature, ballast substances precipitate
B. To save production
C. For simultaneous cooling of the extract
D. To preserve the active substances
E. All answers are correct

26

Dandelion roots and wormwood are extracted with water containing a preservative. What substance is used as a preservative:

A. 0.5% solution of chloroform in water
B. 0.25% solution of ammonia in water
C. 0.1 M solution of hydrochloric acid
D. 0.1% solution of Nipagin in water
E. 3% acetic acid

27

The phytochemical workshop of the enterprise produces a thick extract of wormwood.

Select the extractant and the method of production for the production of this product:

A. Chloroform water; percolation
B. 0.25 % ammonia solution; bismaceration
C. 70% ethyl alcohol; percolation or repercolation
D. 40% ethyl alcohol; the TSANDI method
E. Water; vortex extraction

28

Indicate the purpose for which boiling water is used in the production of a thick extract of water legume:

A. In order to inactivate enzymes
B. To dissolve glycoside meniactin
C. For fume hood disinfection
D. For degreasing vegetable raw materials
E. For hood lighting

29

The pharmaceutical enterprise produces a dry extract-concentrate of thermopsis, in which the concentration of active substances exceeds the norm. Specify the substance used to dilute the extract:

A. Lactose
B. Ethyl alcohol
C. Pectin
D. The water is purified
E. Sodium chloride

30

The phytochemical workshop of the enterprise produces dry extracts according to two technological schemes. From the equipment listed below, choose the one that is used at the drying stage when obtaining a dry extract, if the thickening stage is not provided:

A. Spray dryer, sublimation dryer
B. Vacuum drying cabinet, belt dryer
C. Roll vacuum dryer, chamber dryer
D. Air fountain dryer, drum dryer
E. Dryer with infrared rays

31

Which vacuum evaporation device provides natural circulation of the evaporating liquid:

A. Vacuum evaporation apparatus with a central circulation pipe
B. "Centriterm"
C. "Volcano"
D. Vacuum evaporator with countercurrent mixing condenser
E. Ball vacuum-evaporating apparatus

32

What is the basis of the operation of spring-blade, screw and disk extractors?

A. The principle of active counterflow of raw materials and extractant
B. The principle of active movement of the extractant
C. Use of carbon dioxide as an extractant
D. Circulation of the extractant
E. Dispersion of raw materials using electric discharges

33

Concentrated extracts are produced at the pharmaceutical enterprise. Indicate the ratio in which dry extracts-concentrates are prepared:

A. 1:1
B. 1:2
C. 1:5
D. 1:10
E. 1:1000

34

To obtain extracts-concentrates, use:

A. Ethanol 20-40%
B. Ethyl alcohol
C. Purified water
D. Ethyl ether
E. Chloroform water

36

During the analysis of the dry extract-concentrate of thermopsis, an excessive content of active substances, moisture content of 5% was established. How to act in this case:

A. Dilute to normal with lactose
B. Dilute with alcohol or water to normal
C. Dry under vacuum
D. Dry to normal, then add the estimated amount of lactose
E. Reject series

37

In the manufacture of phytochemical preparations, extraction of extractive substances from plant raw materials occurs due to:

A. Molecular and convective diffusion
B. Coacervation
C. Absorption and adsorption of the extractant by plant raw materials
D. Molecular and cellular diffusion
E. Convective and cellular diffusion

41

Which of the following indicators characterizes the quality of thick extracts?

A. Moisture content
B. Content of fillers

C. Alcohol content
D. Density
E. Transparency

45

What mainly determines the choice of extractant when obtaining individual substances?

A. Selectivity in relation to active substances
B. Ability to eliminate hydrolysis
C. Heat resistance
D. Pharmacological indifference
E. Cost

48

The pharmaceutical enterprise manufactures galena preparations. Galen preparations include:

A. The amount of biologically active substances
B. Only individual active substance
C. Corrigents of smell
D. Corrigents of taste
E. Preservatives

49

The phytochemical workshop of the enterprise produces the most purified extractive preparations. At the same time, specific methods of cleaning the hood are used. Select the method that applies to dialysis from the following definitions:

A. The property of biopolymer molecules not to pass through semipermeable membranes
B. The process of the effect of heating on the hood
C. The process of extraction from one liquid using another
D. Gas absorption process
E. The process of exposure to electrolyte

50.

Specify the conditions under which the freeze-drying process takes place:

A. The hood is frozen, placed in a sublimation chamber, where a deep vacuum is created, the drying temperature is 20-30 ^{o}C
B. The hood is slightly evaporated at high temperatures, after which sublimation is carried out
C. Sublimation dryers are not used for the production of extraction preparations due to the use of ethyl alcohol as an extractant
D. The thickened extract in the form of a thin layer (0.5-0.8 cm) is placed on the sheets and dried at a temperature of 50-60 ^{o}C
E. The thickened extract in the form of a thin layer (0.5-0.8 cm) is placed on sheets and dried at a temperature of 50-60 ^{o}C and a pressure of 80-87 kPa

51.
In the process of standardizing the production of thick extracts, the mass loss should not exceed:
A. 25-30%
B. 5%
C. 40%
D. 35%
E. 1%
52
Propellants are used in the production of aerosols. Indicate what role propellants play in aerosols:
A. They create pressure in the package
B. Solvents for medicinal substances
S. Stabilizers
D. Emulsifiers
E. Dispersants
53
The aerosol workshop of the enterprise uses propellants of various groups in its work. Choose propellants belonging to the group of compressed gases:
A. Nitrogen, nitrous oxide, carbon dioxide
B. Refrigerants (freons)
B. Propane, butane, isobutane
D. Vinyl and methyl chloride
E. Methylene chloride, ethylene chloride
54
The aerosol workshop of the enterprise uses propellants of various groups in its work. Choose propellants that belong to the group of volatile organic solvents:
A. Methylene chloride, ethylene chloride
B. Refrigerants (freons)
C Propane, butane, isobutane
D. Vinyl and methyl chloride
E. Carbon dioxide
55
Aerosols include active components, solvents, propellants. Which of the substances listed below are used as propellants?
A. Freon 11, carbon monoxide, propane-butane
B. isopropyl myristate, neon, sulfur oxide
C Propylene glycol monostearate, argon, helium
D. Linetol, Myristic acid, benzocaine
E. Hydrogen sulfide, hydrogen, triethanolamine

56
The effectiveness of aerosol therapy is largely determined by the size of the particles of the dispersed phase. What depends on the size of the aerosol particles obtained when spraying the contents of the aerosol:
A. Outlet diameter, saturated fuel vapor pressure
B. Grinding levels, container volumes
C. With the homogeneity of the system, the speed of spraying
D. Calculation of percentage of solid phase content, filling temperature
E. Fractional composition, method of filling the container
57
The workshop of a pharmaceutical enterprise that produces aerosol forms uses liquefied gases as a propellant. Which of the proposed substances belong to the group of liquefied gases?
A. Refrigerants or freons
B. Nitrogen
C Nitrous oxide
D. Methylene chloride
E. Ethylene chloride

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