ODESSA NATIONAL MEDICAL UNIVERSITY
PHARMACEUTICAL FACULTY
DEPARTMENT OF TECHNOLOGY OF MEDICINAL PRODUCTS

DIARY

EDUCATIONAL PRACTICE
FROM INDUSTRIAL DRUGS TECHNOLOGY

Student _____
(Full Name)

Pharmacrutical Faculty

Course _____ group _____

Specialty pharmacy

20 _____ / 20_____ academic year

The practice in industrial technology of medicines is one of the types of practical training of students, during which the formation of initial professional skills is carried out.

Training Practice on Industrial Technology of Medicines:

a) is based on students' study of such disciplines as propaedeutic practice, pharmacy technology of medicines, industrial technology of medicines, pharmacognosy, pharmacology, pharmaceutical chemistry and integrates with these disciplines;

b) is aimed at consolidating the practical skills and theoretical knowledge on industrial technology of medicines obtained during studying at a higher educational institution and adapting them to the real conditions of modern pharmaceutical enterprises;

c) lay the foundations for professional practical skills in the processes of grinding, dissolving, evaporating, drying, extraction, etc., the ability to read and compile technological schemes of production, to make a material balance of the production stage;

d) provides the basis for students' study of theoretical and practical issues of the manufacture of drugs in industrial conditions, equipment and apparatus used in pharmaceutical industries, the determination of the optimal type of packaging, the study of the prospects for the development of finished pharmaceutical products.

In accordance with the curriculum, the training practice in the technology of finished medicines for students of the pharmaceutical faculty is held in the 9th semester.

The organizational and methodological management of practice is carried out by the Department of Technology of Medicine together with the Department of Practice of the University.

The head of the practice is obliged to supervise the course of practice, write a diary, organize a practice placement.

Aim: to consolidate, expand and deepen the theoretical knowledge of medicine technology and practical skills acquired during training, with the aim of acquiring practical skills in the manufacture of medicines necessary for solving specific problems in the future practice of pharmacist-technologist.

Objective: assimilation of provisions of normative documents regulating the conditions and rules for the preparation and storage of medicinal products at work; study of modern problems and methods of obtaining finished pharmaceuticals, technological equipment of pharmaceutical enterprises, scientific organization of labor, prospects of development of industrial production of medicinal products; perfect mastery of all technological operations in the preparation of various dosage forms, their packaging, putting into leave, quality control.

As a result of passing the practice student must **know:**

- Basic provisions of safety and pharmaceutical procedures at work;
- the content of the group articles of the State Pharmacopoeia of Ukraine (DFU);

• the main provisions of the existing orders and other regulatory documents of the Ministry of Health of Ukraine regarding the prescription, manufacture, quality control and delivery of medicinal products;

• the timing of the plant's pharmaceutical technology;

• Classification of medicinal products and medical forms;

• the nomenclature and types of industrial medicines;

• physical and chemical properties of medicinal products;

• modern assortment of medical and auxiliary substances, general characteristics and the field of application of auxiliary substances;

• methods of dosing and devices used for dosing medicines of different aggregates;

• Requirements relating to purified water, water for injections, storage order and expiration date;

• physical and chemical properties of solvents (water, ethyl alcohol, mineral and grease oils, glycerol, etc.);

• Theoretical basis of technology of various medical forms;

• basic rules for the introduction of medicinal products into pharmaceutical forms;

• principles of using technological equipment of pharmaceutical companies;

• the appointment of packaging and packaging material and the rules of its choice for the packaging of cooked medicines;

• main criteria for evaluation and quality control of semi-finished products and finished products in industrial production of medicines.

- be able to:

• adhere to the rules of occupational safety and safety;

• use normative, reference and scientific literature for solving professional problems;

• prepare solid, liquid, soft dosage forms (tablets, solutions, suspensions, emulsions, injectable solutions, eye drops, liniments, ointments, suppositories) in conditions of industrial production taking into account the theoretical bases and requirements of regulatory documents;

• calculate the amount of the components of the prescription, the total volume or weight of the medicinal product;

• to choose the optimal version of the technology and to prepare a medicine according to it with a progressive assessment of quality;

• to conduct production of technological schemes;

• to acquire skills to improve the technological process, to be able to estimate the losses and output of the finished product, to make a material balance and a block diagram of production;

• to consolidate practical skills when using technological equipment of pharmaceutical companies;

• assess the quality of the prepared preparation in accordance with the analytical and regulatory documentation (IDA);

• to observe the storage conditions and the type of packaging in order to ensure the stability of the dosage forms;

• To carry out a complex of measures ensuring compliance with the sanitary regime at enterprises, and to control the aseptic preparation of medical forms;

• Objectively use the advanced foreign experience of pharmaceutical manufacturers.

INSTRUCTIONS FOR SAFETY:

1. Students should familiarize themselves with the instruction on sanitary conditions at the enterprise and strictly observe it during the training practice.

2. Before starting a business practice, students should familiarize themselves with the safety and fire safety rules developed and approved by the safety engineer.

3. Only the items necessary for the work should be present at the workplace. Textbooks, tutorials, briefcases should be located in specially designated places.

4. It is not allowed to taste and use for the self-treatment of medicinal substances from the working rod, as well as take them from the laboratory. During operation, it is prohibited to accumulate a number of padlocks in your workplace.

5. When working with poisonous and potent substances it is necessary to strictly observe safety.

6. After the work is completed and the finished product delivered to the students, it is necessary to bring the work place to the order.

Student's signature _____

PROGRAM AND CONTENT OF PRACTICE

№	Name of the class and its contents	Number of hours
1.	General introduction to the pharmaceutical company; rules of the internal order. Guidance on safety and health regulations	4
2.	Production of solid dosage forms according to GMP requirements (tablets, granules, dragees)	2
3.	Production of solid dosage forms according to GMP requirements (capsules in gelatin capsule)	2
4.	Production of sterile medicines according to GMP requirements (pharmaceutical forms for injection in ampoules, vials, infusion solutions in containers, etc.)	4
5.	Production of soft dosage forms according to GMP requirements (ointments, gels, suspensions, emulsions, suppositories, patches, etc.).	4
6.	Production of phytochemicals according to GMP requirements	4
7.	Filling and packaging of finished products	4
8.	Familiarity with the work of the Department of Quality Control of Drugs and the Central Laboratory of Laboratory	4
	Dif test	2
	Hours in general	**60**

Practical lesson № 1 _____ date

Topic: GENERAL KNOWLEDGE OF PHARMACEUTICAL ENTERPRISE; RULES OF INTERNAL RETAIL. INSTRUCTIONS FOR THE SAFETY AND LABOR PROTECTION TECHNIQUES.

Aim: to study the organizational structure of the pharmaceutical enterprise, the characteristics of its workshops and departments, the relationship with the auxiliary workshops (divisions) of the enterprise, the description of workplaces (service areas), general requirements for premises and personnel, rules of safety and sanitary conditions at the enterprise;

familiarization with the instruction on the rules of safety and occupational safety;

assimilation of the basic terms used in the industrial production of medicinal preparations, familiarization with normative-methodical documentation, drafting of regulations.

Control questions:

1. Main activity of the Ministry of Health of Ukraine and the State Pharmacological Center.
2. Normative documents in Ukraine.
3. Basic principles of the registration system.
4. The essence and significance of the material balance.
5. Registration dossier.
6. Protocols of production, validation forms and cards.
7. Pharmaceutical development.
8. Basic terms and definitions.

INFORMATION MATERIAL

1. The main terms of the industrial drug technology

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2. Organizational structure of the pharmaceutical enterprise, characteristics of its shops and departments

3. GMP requirements for the organization of production and quality control of drugs

4. Normative documentation in the production of ready-made medicines

Industrial production of drugs is regulated by the relevant normative and technical documentation (NTD), approved in accordance with the established procedure.

Regulatory technical documentation (NTD) should ensure the improvement of the quality and efficacy of medicinal products, to continuously improve on the basis of scientific and technological achievements and to be timely reviewed in order to replace the outdated indicators in accordance with the needs of public health, protection of the country and exports.

5. Basic provisions of the technological regulation for the production of drugs

Trainig tasks for practical work:

Task № 1

Define NTD category:

A) technological document of the current serial production of commodity products.

B) technological document that concludes scientific research in laboratory conditions when developing a production technology for a new type of product or a new technological method of production for a serially manufactured product.

Task № 2

Determine the NTD approved for a limited period that sets the quality requirements for a medicinal product or medicinal plant material.

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Task № 3

Determine the functions of the technological control department at the pharmaceutical enterprises.

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Task № 4

Determine the NTD, approved for a limited period, which sets the quality requirements for a medicinal product or medicinal plant material.

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Task № 5

To establish the organizational structure of normative documentation at the pharmaceutical company.

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Theoretical question of self-control

1. Organizational structure of the enterprise and the scheme of connections of its divisions.
2. Structure of normative and technical documentation at pharmaceutical enterprises.
3. Basic principles of the registration system of medicinal products.
4. The main parts of the registration dossier.
5. Specifications for raw materials, intermediate products, finished products.

6. Quality control of pharmaceuticals at a pharmaceutical company.

7. The essence of the material balance.

8. What is the difference between the material balance of the series from the material balance of the stage?

9. What documents reflect the contents of the technological regulations?

10. What are the main raw material indicators reflecting the certificate?

Tasks for self-control

To draw up the scheme of the basic principles of the registration system of medicinal products.

Situational tasks.

1. The term of registration of the medicinal product has expired. Is it possible to implement it further? If so, then under what conditions? The answer is to justify.

2. Technological industrial and temporary regulations for the medicinal product were approved in 2010. Have they lost their strength? The answer is to justify.

3. Pharmaceutical enterprise produces production of new products. Technologist - the operator for each production series was the protocol production series. Evaluate the actions of the operator-technologist. The answer is to justify.

Direct Manager _____

(signature)

Practical lesson № 2 _____ date

Topic: MANUFACTURE OF SOLID DRUG FORMS UNDER GMP REQUIREMENTS (TABLETS, GRANULES, MADE)

Aim: learn to use SPhU, NTD and reference literature to find the necessary information for the preparation of tablets, granules, pills; to know the classification and characterization of auxiliary substances used for the manufacture of solid dosage forms; to count the amount of medicinal and auxiliary substances for tablet preparation taking into account the expenditure factor;

learn how to chop and sift solid medicinal and vegetable raw materials; be able to choose the best tableting technology; be able to analyze and receive tablets by direct pressing and pressing with pre-granulation; to be able to classify and offer the application of film, draffed and pressed coats; to analyze the quality of the coated tablets;

to carry out basic technological operations at reception of tablets, granules, dragees.

Control questions:

1. Shredding at pharmaceutical plants. What is the choice of machines for shredding?
2. Explain the principle of mechanical separation of the material and specify the type of sieve used in the pharmaceutical industry.
3. To name the types of mixers for powdered materials, to specify the principles of work.
4. Major groups of excipients used in tablet production.
5. Stages of the technological process of obtaining tablets.
6. The main types of granulation.
7. Auxiliary substances and basic technological operations in obtaining a mass for covering tablets with shells

INFORMATION MATERIAL

Grinding - the process of reducing the size of particles of solid materials, using mechanical effects. It can be a major process and auxiliary.

In technological practice, grinding is characterized by a conditional index - the degree of grinding of matter.

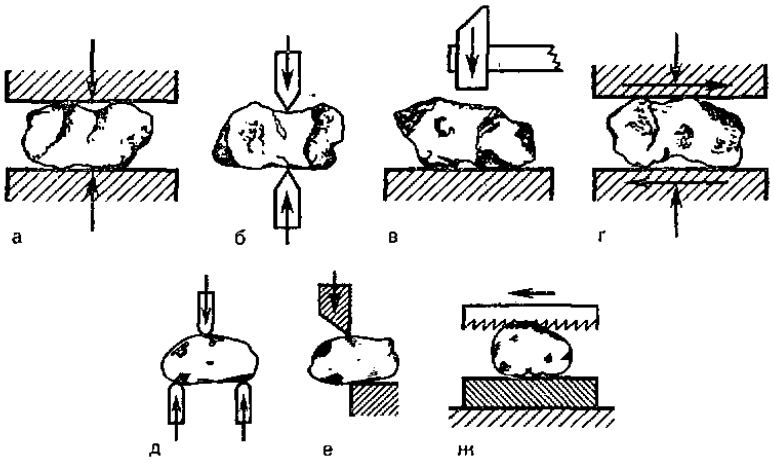
The degree of shredding (i) is the ratio of the diameter of the pieces of material to the milling (D) to the diameter of the particles obtained after grinding (d)

When conducting the grinding process, the requirements of the State Pharmacopoeia or DSTU shall be guided by the size of the particles of the crushed material. Grinders are selected depending on the properties of the substance and the degree of its crushing and are classified as follows:

- By the way of grinding (cutting machines, washing machines, crushing machines, shock machines, shock-centrifugal machines and others).

- By degree of crushing (crusher of large, medium and fine crushing, mill thin and colloidal crushing)

- By the nature of the working tool (machines disk, ball, rotary, etc.).



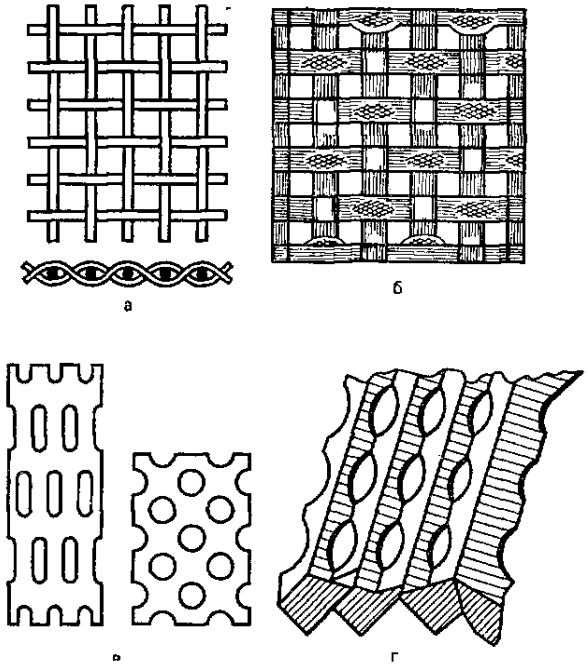
Methods of grinding.
a - crushing;
b - split; c - a punch;
d - abrasion; e - breakdown; f - irisation;
g -the same - sawing.

1. The structure and the principle of the operation of milling machines

The *separation* of the crushed material into fractions (classes) is carried out according to the size of the particles. The following methods of separation are

known: mechanical - on sieves; hydraulic - depending on the rate of precipitation of particles in water; air (separation) - by the velocity of their precipitation in the air.

In the pharmaceutical industry, the classification of the crushed material is carried out using various sieves. In such cases, mechanized sieves are used. The work of sieves is estimated by two indicators: the efficiency of sifting or the coefficient of effectiveness. Efficiency of sieve and efficiency of sifting are influenced by factors: the shape and size of the holes of the grid, the thickness of the material layer on the screen, its moisture, speed, the nature of the material movement, the length of its path.



Types of mesh sieve.
a, b - braided,
c - in - stamped;
d - Grain

2. Devices for the classification of crushed material

Mixing - a process in which several powder-like components, which are separated, after a thorough mixing and even distribution of each of them to mix the volume of the material, form a homogeneous mixture. The degree and speed of mixing depend on a large number of variables: the physical and chemical properties of individual components (particle size distribution, particle shape, surface characteristics, bulk density, moisture content, fluidity, particle friction coefficient, etc.); the characteristics of the mixing devices (dimensions and geometry of the mixer, the size of the agent, the type and location of the loading and unloading devices, structural materials and the degree of their purity) and the conditions of the mixing operation (the mass of each component added, the ratio of volumes of the mixture and mixer, method, sequence, location and speed of adding components, mixing speed). Mixers are classified: by the nature of the mixing process (convective or diffusion), the constructive feature (drum mixers with a rotating body and worm-lobed), the way of influencing the mixture (gravity, centrifugal), the nature of the process of mixing in them proceeds (periodic or continuous).

3. Devices for mixing solid materials

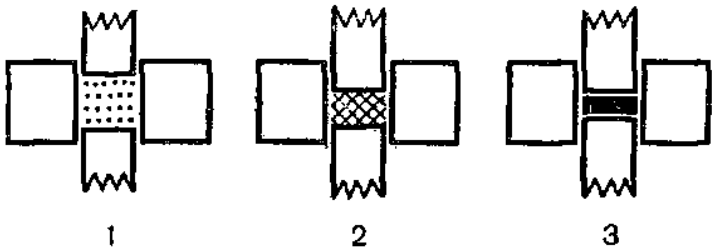
Granulation is the process of transforming powdered material into particles (grains) of a certain size. It allows to prevent bundle of multicomponent pelletized masses, to improve the flowingness (fluidity) of powders and their mixtures, to ensure uniform velocity of their entry into the matrix of the tablet machine and the high accuracy of the dosage and the uniform distribution of the active component, and therefore, a greater guarantee of the therapeutic properties of each tablet. The task of granulation is to ensure the close convergence of particles of powdered material and the formation of homogeneous and solid granules of a certain size from them.

The granulation is carried out in the following ways: wet (pressing of moist masses), in a weighed layer followed by spray drying; dry compaction, etc.

4. Principle of work of devices for granulation

The *pressing* (the actual tabletting) can be defined as the process of forming pellets of granular or powder-like material under pressure.

In modern pharmaceutical production, tabletting is carried out on special presses - rotary tablet machines (RTM). In the world of practice, high-performance tablet presses, equipped with devices for automatic control of the weight of tablets, pressure compression are created.



Stages of pressing bulk materials.

The entire compression process can be schematically divided into three stages of pressing: sealing (sub-compression), forming a compact body, volume compression of a compact body.

5. Device and principle of tablet machines

The *application of the shells* has the following objectives: to give the tablets a good appearance to increase their mechanical strength, to hide the unpleasant taste, the smell, to protect from the influence of the environment (light, moisture, air oxygen), localize or prolong the action of the medicinal substance contained in the tablet, protect the mucous the esophagus and stomach shell from the destructive action of the drug substance.

Coatings applied to tablets, depending on their composition and method of application can be divided into three groups: drapeed, film and pressed.

5. Equipment for coating tablets on tablets

Teaching tasks for practical work:

Task № 1

Grind 250 g of sugar on a ball mill and make a material balance for this stage, determine the percentage of yield, the percentage of technological costs and the expense ratio.

Perform a sieve analysis of crushed sugar and set the fractional composition (2, 1, 0.5, 0.25 mm) in grams and percent.

Number of crushed material, g	**Particle size, %**				
	+2мм	-2мм +1мм	-1мм +0,5мм	-0,5мм +0,25мм	-0,25мм

Sift crushed sugar. To make a material balance taking into account the waste at this stage. Calculate the percentage of output, cost and expense ratio.

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Task № 2

Determine the performance of a ball mill, grinding 15 kg of raw material in 20 minutes.

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Task № 3

Prepare sodium chloride tablets for 0,9 20 pcs. List the indicators that evaluate the quality of the finished product. Make a material balance on finished products in the form of equations and tables, calculate output, loss, expense ratio.

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The substance is consumed	Quantity, g.	End product received.	Quantity, g
sodium chloride		Tablets sodium chloride 0,9	
		Costs	
total		total	

Task № 4

Identify the possible causes of the following types of tablet deviation:

Deflection	Cause
From time to time	
Sticking up	
Marble	
Poor tablet strength	

Task № 5

Find the purpose of each of the components of the suspension used for the suspension method of teasing.

Suspension component	Assignment
A. Sugar syrup	1. Filler
B. Polyvinylpyrrolidone	2. Stabilizer
C. Aerosil	3. The carrier of the suspension
B. Magnesium carbonate is basic	4. Dye
G. Titanium dioxide	5. Form a spatial grid

Theoretical issues for self-control

1. Why is it necessary to shred the plant material without a residue?
2. On what factors depends on the performance of screens?
3. What are the pills as a dosage form?
4. How can the technological properties of powders be improved and direct compression?
5. What groups of auxiliary substances are involved in the production of tablets?
6. Explain the purpose of the binders. In which cases are dry binders used?
7. Give examples of excipients that cause the destruction of the tablet due to their swelling.
8. How is wet granulation performed? Disadvantages of this method.
9. Methods of structural granulation. In what cases is structural granulation performed?

Tasks for self-control

1. Classify shredders used in the industrial production of medicines. Fill in the "Method of Grinding" column in the table.

Method of grinding	Machine type	Examples of processed products
	Shchekova crusher	Root root, soap root, birch mushroom (chaga)
	Hammer crusher, dismemberer, disintegrator	Root eleutherococcus, mushroom chaga, bark of grass, rhizosphere of zamanichi, rhizome of male fern, anestezin, syntomycin, furatsilin, gall, root of stomach
	Ball mills	Stearic acid with starch, xerox, sugar, streptocide with fish oil, syntomycin with castor oil, glucose
	Colloidal mills	Crystalline and chemical substances
	Tapeworms, cornices	Green leafy plantain, grass green plantain, root with valerian rhizomes

2. Make a material balance at the stages of crushing and sifting 50kg boric acid with a ball mill. At the milling stage, 2 kg of losses were obtained, and when sifting, 44 kg of pure fraction, 2 kg of waste and 1 kg of by-products were obtained. Find out, technological losses, cost standards at each stage and general.

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3. Why is the degree of shredding, if D = 10mm, d = 0,12mm?

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4. Calculate the amount of starch to produce 1000 tablets of 0.5 g of nonsulfazole with an average weight of 0.575 if the amount of talc in the finished tablets should be no more than 2%.

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5. Calculate the amount of liter of alcohol 96% to be taken to moisturize 7.5 kg of a mixture of riboflavin with ascorbic acid if the amount of moisturizer should be 40% of the weight of the drug.

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Situational tasks.

1. In which number of turns of a drum with a diameter of 0,49 m will mixing powders in a ball mill?
2. What kind of tablet quality affects the uniformity of the pressed mass and how is it provided? The answer is to justify.
3. Tablet shop of the enterprise produces tablets covered with a shell that dissolves in the intestine. The operator-operator as auxiliary substances uses for such coverage of ethylcellulose and acetyl-phthalic cellulose. Evaluate the actions of the operator-technologist. The answer is to justify.

Direct Manager _____
(signature)

Practical lesson № 3 _____ date

Topic: MANUFACTURE OF SOLID DRUG FORMS UNDER THE GMP REQUIREMENTS (CAPSULES IN THE GELATIN WALLPAPER).

Aim: of the lesson: to learn to use SFU, NTD and reference literature to find the necessary information for the preparation of capsules in the gelatine shell; to study assortment and properties of auxiliary substances for the production of capsules in a gelatine shell;

study methods of producing capsules; be able to choose the optimal technology of their production; know how to obtain solid and soft gelatin capsules, types of machines, their structure and working principles;

to draw up block diagrams for production of capsules, basic technological operations upon their receipt, equipment selection at each stage and definition of quality indices.

Control questions:

1. Methods of obtaining and properties of gelatin as a form-forming substance.
2. What types of medical capsules are used in medical practice?
3. What is the difference between the production of hard and soft gelatin capsules?
4. What preservatives are most often included in the gelatin mass for the production of capsules?
5. The essence of obtaining capsules by the method of pressing, the droplet method, the principles of their implementation?
6. General characteristics of microcapsules, the main objective of the process of microcapsulation, the main methods for obtaining microcapsules.
7. Groups of excipients when receiving microcapsules.

INFORMATION MATERIAL

Capsules (from the Latin *Capsula* - case, shell, box) - a dosage form, consisting of a medicinal product, enclosed in a shell. Medical capsules are solid drugs with peculiar membranes (solid or soft of different shapes and capacities) to fill them with dry, dense or liquid medicines. Capsules may contain one or more active substances.

In medical capsules, drugs that have an unpleasant smell and taste (in order to mask these properties), have irritating effects on the mucous membrane or substances that destroy the tooth enamel, dyes, as well as, if necessary, the prolongation or localization of the action of drugs in the intestine.

The gelatin mass for the preparation of capsules includes gelatin, glycerol and other plasticizers, preservatives, water, as well as colorants.

Distinguish:

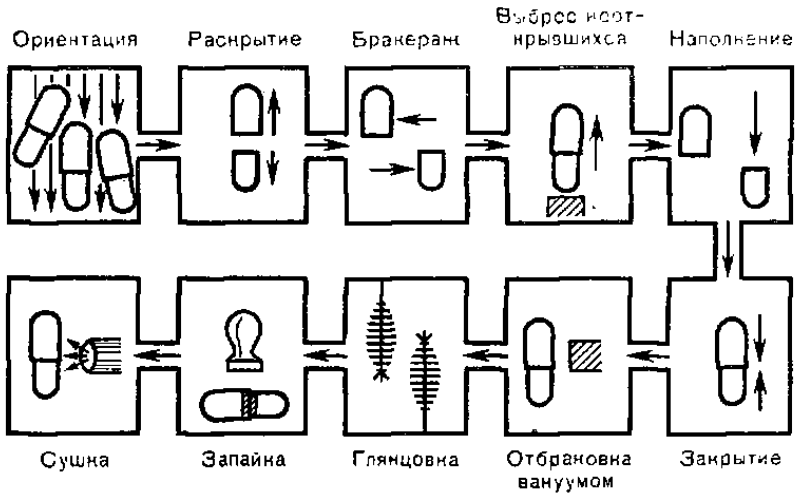
a) gelatin capsules, soft or elastic (*capsulae gelatinosae elasticae seu molles*), having the appearance of spherical or oval vessels;

b) gelatine capsules solid (*capsulae gelatinosae durae*) of the same shape and size as soft gelatin capsules;

c) gelatine capsules with caps (*capsulae gelatinosae operculatae*), consisting of two closed hemispherical surfaces on one side and thin hollow cylinders that are tightly inserted into each other.

Types of gelatin capsules

Depending on the type of capsule, the composition of the mass changes: in solid capsules glycerin may be absent or placed in small amounts (up to 0.3%), for soft capsules the amount of glycerin is increased to 20-25%.



The process of filling capsules with a medicinal substance.

Capsules are mainly for oral use, less for rectal, vaginal and other methods of administration.

1. Equipment for gelatinous membranes - forming capsules

Microcapsules are small particles of solid, liquid or gaseous material, coated with a thin film of film-forming material of different nature. They represent separate particles of a spherical or round shape in the diameter from 0.5 microns to 6500 microns, with a shell thickness of 0.1 to 200-400 microns, a shell weight of 1-70 percent. The most widely used in medical practice are microcapsules of 100-500 μm in size. Particles less than 1 μm are called nanocapsules and are intended for parenteral administration.

The shape of the microcapsule is determined by the aggregation state of the contents and by the method of obtaining the microcapsules.

As materials for shells of microcapsules use natural and synthetic polymers. They are represented by water soluble compounds (gelatin, gum arabic, PVP), water-insoluble compounds (silicones, lakteksy, polypropylene, polyamide), enteric compounds (zein, shellac, spermaceti, АФЦ). Use waxes and lipids (paraffin, spermaceti, beeswax, stearic acid).

The main types of microcapsules:

1. With one shell
2. With a double or multilayer sheath
3. "Capsule in capsule";
4. Emulsion in microcapsules or microcapsules in a liquid medium in a general envelope.

Methods for obtaining microcapsules are divided into 3 groups:

- Physical;
- Physico-chemical;
- Chemical.

2. Devices for microcapsulation

Teaching tasks for practical work:

Task № 1

Prepare gelatin mass for soft capsules (without the process of swelling gelatin).

Prepare technology. In the closed capacity of a laboratory installation equipped with a water shirt, an automatic temperature controller and a shovel stirrer, enter the calculated amount of purified water and heat up to 70-75 °C, in conservative water dissolve preservatives, plasticizers, and then load gelatin with the stirred plug. Mix until completely dissolved for 20-30 minutes. After disconnecting the mixer and heating, the gelatin mass is left in the reactor for 1 hour with a vacuum connection to remove the bubbles from the mass of air. The prepared mass is transferred to stabilize the thermostat with a controlled temperature and maintained at 45-50 °C for 1.5-2 hours. Before starting the capsule, control the viscosity value, which should be within (650-700) 103 Pa.

Task № 2

Form soft gelatin capsules by immersion method (in laboratory conditions).

Formation of capsules. Metal forms are washed with gauze swab moistened with peach oil and cooled at 3-5 ° C for 30 minutes. The cooled forms are slowly immersed in the gelatin mass for 1-2 sec.

For a uniform distribution of masses of forms slowly raise, simultaneously turning them in a horizontal position around its axis. When the film is thickened, the form is placed in the refrigerator for gelatinization at a temperature of 5 ºC for 6-7 minutes.

The cooled frame is taken out of the refrigerator, removed from the gelatin shells and placed on a plastic plate with nests. Properly prepared capsules should be transparent and free of air bubbles and mechanical impurities.

Task № 3

Fill soft gelatin capsules with castor oil and suck.

Filling capsules. Conduct filling with castor oil using a syringe, which is injected into the opening of the capsule, without wetting the edge of the oil.

Waxing capsules. Sealing of capsules is achieved by sealing with an electric soldering iron, heated to a temperature of 55-56 °C. The molten mass hermetically closes the neck of the capsule. The vaporization can be carried out with a drop of melted gelatin mass, which is applied to the neck of the capsule using a metal loop.

The capsules are dried at a temperature of 23-26 °C. and washed with isopropyl alcohol, then dried again..

Task № 4

Conduct quality control of capsules according to the following indicators: description (appearance), homogeneity of mass; homogeneity of the contents of capsules, definition of decay.

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Theoretical issues of self-control

1. What are the ways in which capsules are produced and can all of them be used to produce soft gelatin capsules, hard capsules with caps?
2. What properties of the capsules affects the violation of the temperature regime of mass dissolution?
3. What is the scheme of obtaining capsules by immersion method and for what purpose gelatin mass for a long time stands?
4. For what purpose and what excipients are used in obtaining capsule-soluble?
5. Is it possible to release poisonous and potent substances in capsules?
6. How is the thickness of the shells of hard and soft gelatinous capsules checked and the precision of dosage of the drug?
7. Physical methods of microcapsulation.
8. Physico-chemical methods of microcapsulation.
9. Receipt of microcapsules by chemical methods.
10. Characteristics of shells of microcapsules and its varieties.
11. Form, size and structure of microcapsules.

Tasks for self-control

1. Using literature sources, fill in a table of two columns, one of which is to indicate a group of methods for obtaining microcapsules, in another one - the methods related to this group.

Group of methods for obtaining microcapsules	**Methods related to this group**
Physical	
Physico-chemical	
Chemical	

2. To make a working copy of the production of 14000 pieces of hard gelatin capsules of acetylsalicylic acid of 0,1 g, taking into account the expense coefficients at each stage, if at the stage of production of gelatin mass the expense ratio is equal to 1, 040, at the stage of preparation of the contents of the capsule, the expense ratio is equal to 1,009, per the stages of formation of capsules - 1,030, at the stage of filling capsules - 1,010. To make the equation of the material balance. Determine output and loss percentages for a given production.

Stage Process		**Capsule Structure**			
Medicinal substance	**Quantity**	**1**	**2**	**3**	**4**
Acetylsalicylic acid			Kp		Kp
Potato starch			Kp		Kp
Talc			Kp		Kp
Metabisulfite sodium		Kp		Kp	Kp
Polypropylene		Kp		Kp	Kp
Gelatin		Kp		Kp	Kp
Water is purified		Kp		Kp	Kp

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Situational tasks.

1. In case of casual control in the production of soft gelatin capsules, unevenness of thickness was detected. What is the reason? The answer is to justify.

2. In the walls of soft gelatin capsules air bubbles formed. What is the reason? The answer is to justify.

3. With the progressive control of microcapsules, their deformation is observed. What is the reason? The answer is to justify.

Direct Manager _____

(signature)

Practical lesson № 4 _____ date

Topic: MANUFACTURE OF STERILIAN MEDICINAL PRODUCTS UNDER THE GMP REQUIREMENTS (MEDICAL FORMS FOR INJECTION IN AMBULAS, FLAKONS, INFUSION SOLUTIONS IN CONTAINERS AND al.)

Aim: to learn to use SFU, NTD and reference literature to find the necessary information for the preparation of sterile drugs; to study assortment and properties of auxiliary substances for the production of injections, infusions or implants in the human body, as well as eye medical forms;

to study methods for the production of primary packaging for sterile products; to master the methods of obtaining water for injections in industrial conditions; be able to choose the optimal technology of manufacturing parenteral solutions; know ways to get eye medicine forms; types of cars, their structure and working principle;

to make a block diagram of the production of sterile drugs, the main technological operations upon their receipt, the selection of equipment at each stage and the definition of quality indicators.

Control questions:

1. What are the conditions for the production of sterile dosage forms? List the classes of cleanliness of production facilities.
2. What are the requirements for injecting drug precursors?
3. List the requirements for water for injection. List how to get it. What are the ways to improve its quality?
4. List the requirements for ampoule glass. Name its composition and properties.
5. The concept of osmolality and osmolarity.
6. Characteristics of injectable solutions, their use.
7. Modern classification and requirements for infusion solutions.
8. Features of the factory production of eye medical forms.

INFORMATION MATERIAL

All sterile and aseptically manufactured pharmaceutical forms can be classified as follows: medicines for parenteral use for administration by injection, infusion or implantation into the human body (solutions, emulsions, suspensions, powders, pills for solutions and implants, freeze-dried solutions), eye medical forms (eye drops, ointments, films, etc.), sterile lotions.

To ensure all the indicators of quality of the finished product, special conditions are created for the stages and operations of the technological process, special requirements for the purity of industrial premises, the work of the technological equipment, ventilation, the system of preparation of the main and auxiliary materials, as well as certain requirements to the personnel are presented.

At different stages of technology, the probability of contamination and contamination is different. Usual urban air contains from 100 000 to 1 000 000 particles in the size of 0.5 microns or more in 1 liter.

Classification of clean zones by the maximum allowable number of particles in the air, pcs / m3

Classes of purity	Equipped with state		Functioning state	
	0,5 mkm	5mkm	0,5 mkm	5 mkm
A	3500	0	3500	0
B	3500	0	3500	2000
C	350 000	2000	3 500 000	20 000
D	3 500 000	20 000	Not specified	

Stamps and ampoule glass

Stamps of glass	The composition of the glass. % of weight								
	SiO_2 ±0,50	Al_2O_3 ±0,20	B_2O_3 ±0,25	CaO± +MgO ±0,30	Na_2O ±0,25	K_2O ±0,20	Fe_2O_3 ±0,30	MnO_2, ±0,50	BaO ±0,20
НС-3	72,80	4,50	6,00	6,90	8,10	1,70	-	-	-
НС-1	73,00	4,50	4,00	8,00	8,50	2,00	-	-	-
СНС-1	67,00	4,10	5,20	6,30	7,50	2,00	2,90	5,0	-
НС-2,НС-2А	73,00	3,5	2,50	8,00	11,00	2,00	-	-	-
	73,00	3,0	-	9,50	13,50	1.00	-	-	-
АБ-1	74,00	5,0	8,00	1,20	5,00	2,80	-	-	4,00
ХТ	72,00	6,0	10,50	0,80	6,70	1,80	-	-	2,20
ХТ-1									

The production of ampoules is made of glass tubes (medical wires) and includes the following main stages: glass-wire manufacturing, washing and drying of wire, manufacturing ampoules.

1. Equipment for manufacturing, calibrating, washing and drying of glass

Ampoules are glass containers of different capacities (1; 2; 3; 5; 10; 20 and 50 ml); and a mold consisting of an expanded part - a body (pulki), which contains medicinal substances (in solution or in another state) and 1-2 capillaries ("stems"), which serve to fill and empzle ampoules. Capillaries can be even or interleaved.

2. Equipment for manufacturing ampoules and preparing them for filling

The purified water PhA 42-2619-89 (Aqua purificata), which is used in the manufacture of injectable dosage forms, should be maximally chemically treated and comply with the requirements of the NTD. In each series of water obtained, it is necessary to check the pH (5,0-6,8), the presence of reducing agents, acetic anhydride, nitrates, nitrites, chlorides, sulphates, calcium and heavy metals. The presence of ammonia - no more than 0.00002%, dry residue - is not more than 0.001%.

3. Equipment for water treatment

4. Equipment for filtration of injectable solutions, filling of ampoules, sealing and sterilization

Traning tasks for practical work:

Task № 1

Prepare a 10% solution of glucose with the appropriate composition:

Glucose anhydrous 100.0 g

solution of hydrochloric acid 0.1 M to pH 3.0-4.0

Sodium chloride 0,26 g

Water for injections up to 1 liter

The technological process begins with the washing and drying of neutral glass bottles. Internal washing is carried out with the help of laboratory installations of vacuum or syringe sink. The drying and sterilization of the vials are carried out in a drying oven at a temperature of 180-200 ° C.

According to the prescription, weigh the required amount of glucose (with its moisture content) for the "injection" grade and dissolve in a sterile measuring flask of 50 ml in half the amount of water for injection. The calculated amount of sterile solution of the stabilizer Weibel is added to the solution. After dissolving glucose, the solution is diluted with water for injection into the label and mixed. The resulting solution is adjusted by the content of glucose and pH, filtered using a sterile glass filter with a maximum pore size of 0.3 microns and filled bottles with a syringe method, taking into account the filling standards.

The vials are sealed with rubber stoppers and circled with aluminum caps, after which they are subjected to Sterilization with a fluid vapor at a temperature of 100 °C. for 30 minutes or a vapor under pressure at 120 °C. for 8 minutes.

The quality control of the solution in vials is carried out according to the following technological parameters: determination of tightness, volume, control for the presence of mechanical inclusions, determination of pH and transparency of the solution.

Task № 2

Specify the composition of the Weibull reagent.

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Task № 3

To characterize ways of detecting pyrogenic substances and methods of liberating solutions from them.

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Theoretical tasks for self-control

1. What chemical transformations occur on the surface of ampoule glass during prolonged contact with solutions of neutral, alkaline and cystic reactions of the medium?
2. What are the indicators for assessing the quality of ampoule glass?
3. How is pyrogenic water and injection solutions tested?
4. Pyrogenic substances. Properties and ways to detect them.
5. Methods of liberating solutions from pyrogenic substances.
6. What measures are used to stabilize solutions of easily hydrolyzing medicinal substances?
7. What are the features of filtration of injectable solutions? List the requirements for filtering materials.
8. What methods of sterilization are used in the technology of injection solutions?
9. What is the essence of the preparation of bottles and closures for filling?
10. What packaging is used for eye medical forms? Advantages and disadvantages.
11. Assortment of domestic and foreign infusion drugs.
12. Freeze-dried dosage forms.

Tasks for self-control

1. Using the literature sources to fill in the table: to indicate the groups of infusion solutions depending on the functions performed when administered to the body, the purpose and examples of medicinal substances.

Group of Infusion Solutions	**Purpose**	**Examples of Medicinal Substances**

2. To create a working record for the preparation of 120 vials of 200 ml of solution for infusion "Reopoliglyukin" with the appropriate composition: dextrin 10 g / l, sodium chloride 9 g / l; water for injections up to 1000 ml if the expense ratio is 1,046.

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3. 38 liters of 18% solution of magnesium sulphate are prepared. How much should I add magnesium sulfate to get 20% solution?

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4. Cooked 150 ml of caffeine solution of sodium benzoate. The analysis showed that the solution contains 15% of the drug. How much water should I add to get 10% solution?

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Situational tasks.

1. Control for mechanical inclusions is carried out by inspecting the vials in black and white against 60 watts. For a more objective assessment of the quality of the solution with this parameter, the technologist used other methods. Evaluate his actions.

Direct Manager _____
(signature)

Practical lesson № 5 _____ date

Topic: MANUFACTURE OF MILK MEDICAL FORMS UNDER GMP REQUIREMENTS (MAZI, GELI, SUSPENSION, EMULSION, SUPPORTS, PLASTICS AND ETC.)

Aim: learn how to use SPhU, NTD and reference literature to find the necessary information for the preparation of soft dosage forms; to study assortment and properties of auxiliary substances for the production of ointments, gels, suspensions, emulsions, liniments, and also medicinal forms for rectal and vaginal use;

to study methods of production of soft medical forms in industrial conditions; be able to calculate the amount of medicinal substances that are included in the composition, to select the bases for the preparation of SMF, to choose the optimal technology for their manufacture; to rationally choose equipment, to know the types of machines, their structure and working principle;

to make a block diagram of production of soft dosage forms, basic technological operations upon their receipt, equipment selection at each stage and determination of quality indices.

Control questions:

1. Requirements for ointments and ointment bases.
2. Ointment bases. Classification. Characteristic.
3. Assortment of auxiliary substances in the manufacture of soft drugs
4. Introduction of medicinal substances to ointment bases.
5. General characteristics of suppositories.
6. Classification of suppository foundations.
7. Features of the introduction of active substances in the suppository basis, depending on the physical and chemical properties.
8. Prospects for development of rectal and vaginal dosage forms.

INFORMATION MATERIAL

Production of suspensions and emulsions. Emulsion - a uniform appearance, a dosage form consisting of mutually insoluble fine dispersed liquids and intended for internal, external or parenteral use. Emulsions belong to microheterogenic systems, which consist of disperse phase and dispersion medium. There are two main types of emulsions - dispersion of oil in water (m/v) and water in oil (w/m). For their preparation, as an oil phase, peach, olive, sunflower, castor oil, vaseline and essential oils, as well as fish oil, balsams and other non-water-miscible liquids are used. In addition, e and "multiple" emulsions, in which in a dispersed phase drops, the dispersed liquid is a dispersion medium. In developing the composition and technology of emulsions production, it is necessary to take into account the general properties of the inputs, the method of obtaining, the rheological, electrical and dielectric properties, as well as the stability during storage.

Suspension is a liquid dosage form comprising, as a dispersed phase, one or more crushed powdered substances dispersed in a liquid dispersion medium. The size of the disperse phase particles in the suspensions can range from 0.1 to 1 μm (in thin suspensions) or more than 1 μm (in coarse dispersion suspensions).

Manufacturing of suspensions and emulsions at pharmaceutical enterprises is carried out in various ways: intensive mechanical mixing with the help of high-speed mixers and rotary-pulsating apparatuses, solid milling in a liquid medium on colloid mills of various constructions, ultrasonic dispersion using magnetostrictive and electrosurgical emitters, condensation method.

When obtaining suspensions by the dispersion method, the greatest attention is paid to the grinding of the medicinal substance, because it is this factor that most influences the stability of the resulting suspensions.

1. Equipment for mechanical dispersion

Under the action of ultrasonic waves, a cavitation phenomenon occurs on the liquid, that is, ultrasonic waves have their own pressure on the liquid, which is

imposed on constant hydrostatic pressure. If a sound wave propagating in a liquid at 101.3 kPa (1 atm) spreads in the liquid, then at the time of compression, the total pressure in the liquid will equal 202.6 kPa (2 atm). The liquids are compressive-resistant and very sensitive to stretching, so at the time of their rarefaction there is a large number of gaps in areas where their strength is weakened, for example, in the presence of foreign solid particles. These cavities, called cavitation bubbles, are stored for some time, after which they "lock up". At the same time, local pressure develops, which reaches hundreds of atmospheres and leads to the destruction of solids located near the bubble.

Ultrasonic cavitation is achieved with the help of mechanical, electromechanical and magnetostrictive radiators.

2. Equipment for ultrasonic dispersion

The State Pharmacopoeia of Ukraine defines ointments as soft medicines for local use, intended for local therapeutic or protective action, or for penetration of medicinal substances through the skin.

Ointments consist of bases and medicinal substances, evenly distributed in it. Ointments must have certain structural and mechanical (rheological) characteristics: elasticity, ductility, viscosity, relaxation periods. The nature and strength of the ointment significantly affects the type of disperse system. Ointment solutions and emulsions can detect both local and resorptive effects, while suspension-based ointments are primarily local.

The technology of ointments consists of the following basic stages: the preparation of the basis for ointments and medicinal substances, the introduction of medicinal substances into the basis, homogenization of ointments, standardization, packing and storage of ointments.

3. Equipment for the production of ointments

Suppositories are solid, single dose medicines. They contain one or more active substances, dispersed or dissolved in a simple or complex base, which may dissolve or disperse in water or melt at body temperature. Rectal suppositories may have the shape of a cone, an acute cylinder or other shape; the maximum diameter is usually not more than 1.5 cm. Suppositories in industrial production are made by two methods - pouring the molten mass into molds and pressing on special equipment.

4. Equipment for the production of suppositories

Traning tasks for practical work:

Task № 1

Make a calculationfor the compilation of the working recipe and material balance in the form of an equation and table for the preparation of 150 kg of calendula ointment on a consistent basis. At the same time, take into account that the cost coefficient at the stage of cooking of the basis is equal to 1,005; Cost factor at the stage of introduction of the medicinal substance into the basis of 1,003; at the stage of homogenization - 1,007.

Composition: tincture of calendula 10 parts.
the basis of 90 parts

Basis composition: Vaseline 60 parts
water purified 30 parts
emulsifier T-2 10 parts

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Composition of the		Process Stage		
Medicinal substance	**Quantity**	**1**	**2**	**3**

Task 2

Make a technological scheme of production of ointment of calendula on a consistent basis in stages with indication of the equipment used at each stage

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Task № 3

Prepare 150 g of sulfuric ointment ointment on an emulsion basis.
Sulfur Ointment is simple / Unguentum sulfuratum simples
Storage:
Purified powder cells 50 g
consistency emulsion
Water / Vaseline 100 g
Composition of water / liquid petroleum emulsion
Vaseline 60 g
Emulsifier T-2 10 g
Water 30 g

Making technique: In a porcelain glass, a T-2 emulsifier, a petroleum jelly, and a flask at 85 ° C in a water bath are placed on 0,5 liters. Distilled water is added, heated to 90 ° C., and emulsified with a propeller mixer for 15 minutes prior to cooling. In the mortar, the sulfur is mixed with the emulsion and homogenized. Packed in glass jars of 25, 30, 50 m.

Theoretical issues of self-control

1. Parameters characterizing the structural and mechanical properties of soft drugs.
2. What factors determine the stability of suspensions and emulsions?
3. What role do auxiliary substances play in the production of suspensions and emulsions?
4. From what stages is the process of obtaining dispersive drugs?
5. Factors that affect the stability of ointments.
6. What is the homogenization of ointments and in which cases is it obligatory?
7. What are the advantages of РПА against other machines in the production of suspension ointments?
8. Give examples of industrial ointments. What are the features of their technology?
9. What are the basic rules for the introduction of medicinal substances into the suppository basis?
10. How is the process of forming suppositories carried out? Which automata are used for this purpose? What is the principle of their work?
11. Standardization of soft dosage forms.
12. Determination of homogeneity of suspension ointments for SPhU.

Tasks for self-control

1. Using literary sources, pick up the matching: name - definition.

Name of the medical form Determination of the SPhU	**Name of the medical form Determination of the SPhU**
Ointment	multiphase drugs containing lipophilic and aqueous phases
Creams	are composed of liquids in which gelation has been achieved using suitable gel formers
Liniments	consist of a single-phase basis in which solid or liquid substances can be dispersed
Paste	soft medicines for external use that melt at body temperature
Gels	soft medicines for external use containing a significant amount of solids uniformly distributed in the base

2. Using literary sources, give a description of the basics for suppositories.

HYDROPHOBIC	**HYDROFILIC**

Natural Fats	Hydrogenated fats and their alloys	Alloys of products of esterification of macromolecular alcohols with fatty acids and other acids	

3. Using literary sources, pick up the matching pairs: deviation of the quality index from the norm - control parameters that have been violated - equipment on which the parameter is controlled.

Deflection of the Quality Score from the norm.	**Control parameters that have been violated.**	**Equipment in which the parameter is controlled**
A. Container leaks	1. The volume of the dispenser	a. Melting boiler
B. Excessive deviations from the quantitative content of active substances	2. The distance between the joining tools	b. Rotary - pulsating apparatus (RPA)
C. Insufficient content of containers	3. Time of homogenization	c. Enclosure device
D. Insufficient degree of grinding of solid particles	4. Temperature	d Tube filling machine
E. Excessive acid and peroxide numbers	5. The speed of the planetary mixer	e. Reactor

4. Using literary sources, indicate what indicators (basic and auxiliary) control the quality of soft drugs according to the requirements of the State Pharmacopoeia of Ukraine.

Basic	**Additional**
1.	1.
2.	2.
3.	3.
4.	4.
5.	5.
6.	6.

Situational tasks.

1. At the pharmaceutical enterprise, when receiving an ointment with a high degree of viscosity for homogenization, the worker used a portable propeller stirrer. Will he achieve sufficient homogenization? Why?

2.On the pharmaceutical company introduced a new drug - suppositories, which include biogenic stimulants, which at high temperature collapse. The suppositories were prepared by pouring, the drying was carried out at a temperature of 15 °C. for 2 hours. Evaluate the activities of the technologist.

3. The pharmaceutical company manufactured suppositories with digitoxin at 0.00015 g. Before the technologist - the operator became the question of what method to produce them. Evaluate his actions.

Direct Manager _____

(signature)

Practical lesson № 6 _____ date

Topic: PRODUCTION OF PHYTOXIMIC PREPARATIONS UNDER GMP REQUIREMENTS

Aim: to learn to use SFU, NTD and reference literature to find the necessary information for the preparation of phytochemicals; to study the modern range of extras and requirements to them; factors influencing the extraction process;

to study methods of obtaining extractives; stages of the technological process of preparation of total drugs, Novogalenov, preparations of individual substances; choose the optimal technology for their production; to rationally choose equipment, to know the types of machines, their structure and working principle;

to draw up a block diagram of the production of extractive preparations from plant and animal raw materials, the main technological operations upon their receipt, the selection of equipment at each stage and the definition of quality indicators.

Control questions:

1. Factors influencing the completeness and speed of extracting of active substances.
2. The essence of the seizure process.
3. The modern range of extragrants and the requirements offered to them.
4. Ways to intensify the production of tinctures.
5. Essence of methods for obtaining liquid extracts.
6. Determination of completeness of exhaustion of raw materials.
7. Extractants used in the production of dense and dry extracts. 8. Methods of cleaning the lifts in the production of dense and dry extracts

INFORMATION MATERIAL

The main purpose of the production of phytopreparations is the isolation of medicinal substances from the total mass of ballast, which is achieved, mainly through the extraction (extraction), which represents a very complex process. It consists of several separate independent processes, are closely interwoven with each other: diffusion, osmosis, dialysis, dissolution and desorption of substances contained in plants.

The following factors influence the extraction process:

- Molecular weight of the recovered substance;
- Charge of colloidal particles;
- Living protoplasm;
- Anatomical structure of plant material;
- The degree of grinding of plant material;
- Extractant type;
- Temperature of the extraction process;
- Viscosity of extractant;

- The difference in concentrations within the plant material and in the surrounding liquids;
- Duration of extraction;
- Pressure;
- Mixing and other.

Thus, the completeness and speed of extraction depend on many factors, the influence of which must be skillfully regulated.

Knowledge of theoretical bases of extraction makes it possible to correctly conduct this production process and thus provide the most complete and in the shortest possible time extract of active substances.

The method of countercurrent extraction consists in the multistage promotion of the extractant from the more depleted to less depleted raw material to saturation with extractive substances. In the industry, countercurrent extraction is carried out in different ways: in the battery of extractors, when the raw material is in a stationary state, and only the extractor moves; in extractors of continuous action, diffusers, where the raw material and the extractor move towards each other.

1. Device of extractors of different design.

The essence of the circulatory extraction method is the multiple extraction of the plant material of the same portion of the flying extractant (ether, chloroform, methylene chloride, etc.).

2. Equipment for circulating extraction

In order to increase the efficiency of extracting active substances from the raw material, extraction is carried out in a turbulent flow of the extractant, with vibration, fluid ripple through the layer of raw materials, using ultrasound, electric material processing, etc.

3. Equipment for intensifying the extraction process

Recuperation (from Lat. Recuperatio - return, reception again) - technological reception, carried out in order to return to production part of valuable solvents from waste raw materials, condensates, etc.

Rectification (from the Latin Rectificatio - correction, purification) consists in the separation of mixtures of intermixing liquids with different boiling temperatures on individual components, in systems containing azeatropics - on azeatrope mixture and one of the components.

5. Rectification installations

Traning tasks for practical work:

Task № 1

Preparation and study of tinctures of St. John's wort

Storage:

Herbs St. John's wort of large-scale 20 g

alcohol 40% to get 100 ml

Application: with functional disorders of cardiac activity, with angina pectoris, with flashing arrhythmia and paroxysmal tachycardia.

Description: Transparent liquid of dark brown color.

Preparation is carried out by percolation method and vortex extraction method with full theoretical and practical substantiation in comparison with the percolation method, taking into account the yield of extractive and active substances, the consumption of raw materials and extractants, the extraction time and the norm cost for the performance of these works.

The grinding is obtained in the device "Microizommelchite cloth RT-2" (speed of the mixer 3000-5000 rpm).

To obtain 100 ml of the finished product, 20 g of the large-flowered grass of the St. John's wort (1-8 mm) are placed in a glass of the apparatus and poured 140 ml of 40% alcohol (taking into account the absorption coefficient, including the

apparatus at a speed of 5,000 rpm and extracted for 5 minutes, then turned off for 10 minutes, after which the extraction is repeated 2 times.Therefore, the extraction (without taking into account breaks) takes 15 minutes.Extraction is poured into the cylinder through a funnel with cotton wool, pressed with a two-layer gauze wipes, and the pressed liquid is added to the extract. and getting tincture less than 100 ml of raw material is washed with 40% alcohol, pressed and added to tincture.

The extract is poured into a glass with a corked stopper and left to clean from ballast substances for 3-4 days in a cool place (8-10 °C).

Conduct research: establish authenticity, purity, determine the dry residue, the content of alcohol, active substances.

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Task № 2

Make appropriate calculations for the preparation of extractant to obtain 100 kg of liquid nettle extract

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Task № 3

Make a technological scheme for obtaining a dry extract of the leaves of the steppe in stages, indicating the equipment used at each stage

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Theoretical questions of self-control

1. What is the place and role of mass transfer processes in pharmaceutical technology?
2. Bring the classification and characteristics of the extraction drugs.
3. Features of extraction of fresh and dehydrated raw materials.
4. Preparation of the raw material for extraction, the value of the size of the particles and the nature of the crushing.
5. The effect of extractive ability, selectivity, desorption, polarity, viscosity, surface tension, and environmental reaction of the extractant to increase the speed and completeness of extraction.
6. The main technological factors affecting the completeness and speed of extraction.
7. Ways to intensify mass transfer.
8. Physical basis of rectification processes.

Tasks for self-control

1. Using the literature sources, fill out the table:

Extractors and main methods of extraction

Method of extraction	**Extractor type**	**Device and operating principle**	**Scope and extractor**
one time			
repeated with cross-current of solvent			
multiple protivotochnaja			
circulating			

2. Using literary sources, fill out the table:

The main methods of extraction division

Extraction Method	**Features**	**Type Extractor**	**Application**
one time			
repeated with cross-current of solvent			
multiple with anti-motion of solvent			
continuous protivochnaya			

protivotohnaya with reflux			
extraction with two solvents			

3. Calculate the percolation rate if the height of the raw material and the mirror in the percolator is 16 cm, the diameter is 2 cm.

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4. Determine the content of ethanol in the tincture of the vistrynik, if the boiling point of the tin is 81.10, the atmospheric pressure is 750 mm.Hg.

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Situational tasks.

1. Explain the essence of evaporation under vacuum and indicate the effect of temperature on the quality of extraction drugs

2. What types of drying plants can be used rationally when receiving phytopreparations?

Direct Manager _____
(signature)

Practical lesson № 7 _____ date

Topic: FACILITATION AND PACKING OF READY PRODUCTS

Aim: to study the State standards for packaging and packaging materials; learn how to use SPhU, NTD and reference literature to find the necessary information for packaging finished dosage forms;

to study the modern assortment of packaging and packing material in the pharmaceutical industry; packing in the conditions of large enterprises;

to study the influence of the sorption of components of drugs on the packaging of finished medicines on their preservation;

to study methods of production of polymeric containers, medical glass, cardboard-paper, metal, rubber and composite packaging;

to pick up equipment, to know the types of machines, their structure and the principle of working for the packaging of solid, soft, liquid medicinal products.

Control questions:

1. Basic terms and definitions concerning the packaging of medicinal products.
2 GMP Requirements for the Packaging of Medicinal Products.
3. Requirements for materials of primary packaging.
4. Impact of packaging on the stability of finished products.
5. Corking means. Classification, assortment.
6. Containers for medicinal products. Assortment.
7. Requirements for materials for the production of consumer packaging and sealing products.

INFORMATION MATERIAL

Packaging and packing of products are the final operations in the manufacture of finished dosage forms. The nature of these operations and the conditions for their implementation vary depending on the type of products (tablets, powders, ampoules, liquid medicines, ointments) and how to work with them (manual operations, mechanization, flow lines).

Packaging - all operations, including packaging and labeling, which must be passed through unpackaged products, to become finished products (Manual 42-01-2001).

Primary (internal) packaging - capacity or other form of packaging that is directly in contact with the medicinal product (Requirements for information on the use of the medicinal product / Order of the Ministry of Health of Ukraine No. 163 dated May 3, 2001).

One of the most important requirements for packaging is the protection of drugs against the effects of light, atmospheric moisture, air oxygen, microbial insemination. The use of optimal packaging is the main way of preventing the quality of medicinal products from being reduced during storage.

At present, the following types of packaging of tablet formulations are used: contour packaging (cellular and non-cellular); glass jars and bottles; tubes and metal pencils; cardboard pancakes.

Contour-shaped packaging consists of two main elements: the film from which thermoforming cells are obtained, and the thermosetting film or the self-adhesive film, which glued the cell after filling them with tablets. As a thermoformed film, the most commonly used rigid, unplasticized or weakly plastifitsirovanny polyvinyl chloride (PVC). Coating of PVC film with polyvinylidene chloride or halogenated ethylene reduces gas and vapor permeability; PVC laminating with polyester or nylon is used to obtain a cellular package that is safe for children. For hygroscopic drugs it is recommended to use polypropylene. Aluminum foil is more often used as a film for closing cells. On the inside, it is covered with glue or thermosetting film, and from the outside - varnish. Aluminum foil is impermeable to vapors of water and gases, well protects preparations from penetration of odors.

1. Machines for the packaging of tablets in a polymer film and foil.

Direct Manager _____

(signature)

LIST OF CONTROLLED QUESTIONS FOR PREPARATION TO THE LITERARY:

1. Mixing. Mixing of powdered materials. Classification of mixers.
2. Powders. Classification. Powder technology. Automatic powder dispensers.
3. Methods for cleaning solutions. Centrifugal drainage and filtration. Super-centrifuge. Filters: press and print, filter press.
4. Syrups. Characteristic. Classification. Production of syrups.
5. Fragrant waters. Fragrant waters. Equipment for receiving distilled aromatic waters.
6. Alcoholmetry. Concentration of alcohol, methods and devices for its determination.
7. Determination of the content of anhydrous alcohol in water-alcohol solutions. Accounting for alcohol.
8. Extraction drugs. Theoretical foundations of extraction.
9. Factors that affect the extraction process. Viscosity. Surface-active substances. Hydrodynamics of a layer of vegetable raw material.
10. Equipment for extraction: maceration tanks, communicated and non-communicated batteries of extractors. Continuous Extractors.
11. Recuperation and rectification of alcohol. Recovery of alcohol from spent raw material by displacement of water and distillation with water. Equipment.
12. Maceration, possibilities of its intensification. Percolation
13. Extracts. Classification by consistency and extractive agent used. Liquid extracts - methods of obtaining.
14. Nomenclature of liquid extracts. Dense and dry extracts - methods of obtaining.
15. Preparations of animal raw materials. Features of animal raw materials.
16. Technology of preparation of drugs for internal use and parenteral administration. Standardization.
17. Enzyme preparations. Characteristic. Classification. Enzymes of higher plants.
18. Enzymes of microbiological synthesis. Strains of microbiological synthesis and requirements put forward to them.
19. Preparation and disinfection of nutrient media, purification and sterilization of air.
20. Microbiological control of production stages. Conducting fermentation processes. Fermenters
21Cultivation and reproduction of sowing material. Preparation of sowing material in the shop of pure culture.
22. Basic fermentation. Isolation of fermentation products. Aparature for the processing of fermentation products.
23. The meaning of granulation. Granulation is dry, moist, powdered granulate.
24. The effect of the form of granulation on the biological availability of drugs. Analysis of granulate.
25. Pressing. Tablet presses: shock and rotary.

26. Comparative characteristics of tablet presses and the principle of their work. The Effect of Pressure Pressure on the Therapeutic Effectiveness of Pills. Direct pressing
27. Methods of application of shells. Purpose of drawing.
28. Teaching technology: rooting, grinding, gloss, polishing. Blowers Film coatings.
29. Types and properties of film coatings. Apparatus.
30. Pressed coatings. Film coating technology. Apparatus.
31. Surface coating technology. Machines of double and triple pressing.
32. Substances in the manufacture of gelatin capsules. Ways of receiving.
33. Automated lines, presses. Filled capsules with medicinal substances.
34. Machines screw, rotary, piston. Assortment of medicinal products in gelatin capsules of factory production, precision of dosing.
35. Microcapsulation of medical prescriptions. Ways to get microcapsules.
36. Plasters. Mustard Receiving technology. Equipment.
37. Rectal dosage forms. Characteristics of suppositories. Equipment for the production and packaging of suppositories.
38. Aerosols. Characteristic. Aerosol inhalation. Composition and principle of the aerosol can.
39. Methods of filling aerosol. Quality assessment. Precision of content dosing. Qualitative and quantitative composition.
40. Medicines of factory production, which are prepared in conditions of asepsis.
41. Medicinal forms for injection: solutions in ampoules, suspensions, emulsions, powders, pills.
42. Requirements for injectable forms. Sources of contamination of injectable solutions.
43. Classes of cleanliness of premises. Requirements for personnel, overalls, equipment.
44. Receiving water for injections in the factory. Distillation devices.
45. Glass. Obtaining, technical requirements for it. Classes of glass Investigation of chemical and thermal stability of ampoules.
46. Preparation of a snowstorm: calibration, washing methods. Production of ampoules on semi-automatic machines.
47. Preparation of ampoules for filling. Apparatus for the discovery of capillaries. Anomalies of ampoules.
48. Vacuum, syringe and steam condensation washing ampoules. Use of ultrasound for washing ampoules. Drying and sterilization.
49. Production of injectable solutions in factory conditions. Dehydration. Additional cleaning in the process of obtaining solutions. Filter materials. Filtering devices. Metal, ceramic, glass, fluoroplastic membrane filters. Sterilization by filtration.
50. Filling ampoules. Apparatus for filling. Vomiting of ampoules. Warming in a stream of inert gases. Shelf quality control.

51. Methods of sterilization of solutions in ampoules. Control of sterilization mode. Check tightness.
52. Evaluation of the quality of finished products. The notion of a sterile series
53. Eye medicine forms. Features of the technology of eye medical forms of factory production.
54. Biotechnology in the manufacture of medicines. Scientific and technical preconditions for the formation of biotechnology.
55. Fundamentals of biotechnological production. Manufacturing of drugs on the basis of microbiological synthesis.
56. Isolation of biosynthesis products. Purification of biosynthesis products.
57. Genetic engineering. Methods of obtaining drugs based on genetic engineering.
58. Packaging of finished dosage forms. Packing materials. Container. Packing of medical forms.
59. The modern range of packaging and packaging materials used in the pharmaceutical industry.
60. Apparatus for washing containers. Packing in conditions of increase of enterprises.
61. Dosing devices for powders, liquids, ointments, tablet packs, dragees, capsules and others. Prospects for packaging EMF.
62. Solid disperse systems. Media carriers of the first generation. Microcapsules. Microspheres.
63. Methods of industrial production of suspensions, emulsions, ointments. Phase mixing.
64. Grinding in a liquid environment. Shredding using ultrasound. Equipment.
65. Design features and operating principle of the mixer reactor, mill mill, three-roller mazekerka.
66. Tubing filling machines. The main factors influencing the rheological properties of ointments.

LIST OF MANDATORY PRACTICAL SKILLS WHO STUDENT MUST LEAVE IN THE STUDY OF THE INDUSTRIAL TECHNOLOGY OF MEDICINAL PRODUCTS.

1. Determine the average mass and deviation from it (according to SPh XI) for tablets that are not coated and coated.
2. Determine the bulk mass of bulk materials (powders, granulates, microcapsules).
3. Prepare tritium pills and evaluate their quality.
4. Determine the flowingness and angle of natural deviation of bulk materials.
5. Determine decomposition, solubility (by SPh XI) for non-coated tablets, coated, gastro-dissolute and intestinal soluble membranes.
6. Investigate the quality of the SPh XI tablets.
7. Determine the strength of the SPh XI tablets.
8. Conduct direct compression.
9. Obtain granules by wet granulation.
10. Check the thermal stability of the ampoules.
11. Make a work record for glucose solution in ampoules.
12. Open the ampoules and conduct their washing with syringe and vacuum methods.
13. Determine chemical resistance of ampoule glass by means of indicator methods (using a universal indicator, phenolphthalein, methyl red), potentiometric method.
14. Make a working record for obtaining a given number of ampoules of a certain capacity of the camphor solution in the oil.
15. Determine the dilution, in which ampules of this volume should be filled.
16. To control the injection solution in ampoules for the absence of mechanical inclusions.
17. Determine the amount of water to be added to the solution at a higher concentration to obtain the required concentration.
18. Make a working record for obtaining a given amount and a given concentration of a solution of caffeine-benzoate sodium.
19. Determine the amount of novocaine needed to produce a given number of ampoules of the indicated capacity.
20. Determine chemical stability of ampoule glass by potentiometric method.
21. Check the ampoules with aqueous solution for sealing the seal.
22. Check the ampoules with an oily solution for sealing the seal.
23. To conduct an additional cleaning of the glucose solution (sodium chloride, magnesium sulfate, calcium chloride).
24. Determine the presence of residual stress in amputee glass and propose measures to eliminate it.
25. To investigate the quality of the injection solution in ampoules for SPh XI.
26. To prepare ampoules with isotonic solution of sodium chloride.
27. Controlling the injection solution in ampoules to match the filling.

28. Prepare a given amount of alcohol-water mixture of the official concentration of strong alcohol and alcohol-water mixture of weak concentration (given in volumetric percentages).

29. Determine the concentration of ethanol using a metal alcohol tester.

30. Determine the content of ethanol in mass percentage, if the specified content of it in the mixture in volumetric percentages. Use interpolation in two variants.

31. Determine the volume of anhydrous ethanol under normal conditions if its mass and concentration are known at a temperature below 20 °C.

32. Recalculate 96% and 95% ethanol, if the amount of ethanol obtained is other concentrations. Use the breeding formulas and tables VI of the Standards Committee.

33. Determine the volume of anhydrous ethanol, if known volume of ethanol of the given concentration.

34. Determine the concentration of ethanol in the recuperator, if its density is known at a temperature below normal (20 °C).

35. Transfer volumetric percentages by mass using interpolation.

36. List the methods for determining the concentration of alcohol in the alcohol-water mixture.

37. Prepare a given volume of ethyl alcohol of the official concentration of strong alcohol and water. Check the solution obtained.

38. Determine the content of ethyl alcohol in a spirit-water mixture using a glass spiritometer.

39. Carry out cleaning, determine its completeness for the alcohol-alcohol extract from walnuts.

40. Make a working copy for a dense extract.

41. To assemble the Soxhlet apparatus, load it with raw material and extractant for adoniside.

42. Determine the rate of percolation in drops per minute, if the diameter of the percolator is known, the height of the layer of the loaded raw material and the number of drops in 1 ml percolate.

43. Determine the amount of moisture to be evaporated from a known amount of gaseous extract, the moisture content of which is higher than standard.

44. Determine the amount of solvent required to convert the standard content of alkocolides if the known volume of tinctures and alkaloid content is higher than standard.

45. Calculate the amount of raw material with known biological activity, necessary for the production of a given amount of lantzide, adonizide.

46. Determine the amount of liquid to be added to the specified amount of dense extract, the moisture content of which is lower than the standard one.

47. To recover the ethanol from the hardener by the method of displacement with water.

48. Make a rectification facility and recover the water-alcohol mixture.

49. To recover the alcohol by distillation from washing waters.

50. To make the installation and to perform the recovery of ethyl alcohol from scrap by the method of distillation with water vapor.

51. Prepare a simple sugar syrup.

52. To make packing and labeling of the finished product.

53. Determine the amount of water that needs to be added to the given mass of a simple sugar syrup which has a density above the standard for the production of standard density dough.

54. Determine the number of solutions of basic aluminum acetate with a density higher and lower than standard, which must be taken for mixing to obtain the prescribed mass of a solution of standard density.

55. Determine the amount of lead acetate solution with a density higher than standard to obtain a given mass of solution with a standard density.

56. Prepare Althea or Sweet Syrup.

57. To select the optimal package for liquid extracts, tablets, injection solutions in ampoules, capsules, eye drops, ointments, powders.

58. Prepare soft and hard gelatin capsules by immersion method.

59. Determine the average mass and deviation from her soft and hard capsules.

60. To determine the decay of soft and hard gelatin capsules.

61. To study the quality of hard and soft gelatin capsules for DF XI.

62. Dry the medicinal raw material on the zebra shaker and determine the fractional composition of the resulting powder.

63. Prepare a complex powder using a ball mill as a mixer.

64. Grind the powder with a ball mill. Determine the fractional composition and compile the material balance.

65. Determine the number of wicker and stamped sieve.

66. To prepare an ointment using a three-rope Mazeeter. Determine pH and homogeneity. To make packing and labeling of finished products.

67. Determine whether the benign lineint of streptocide, if it is stratified after 6 hours in a thermostat at 45 °C.

68. What conclusions about the method of preparation of liniments can be made, if two liniments of the same composition, obtained in different ways, one sterile, and the other - no.

69. Specify the size of the emulsion drops for parenteral nutrition. Answer substantiate.

70. Give an estimation to the actions of the technologist, if he made the filtration stage when manufacturing 10% of the sunflower oil emulsion.

71. Give an assessment of the actions of the apparatus, if at the time of the manufacture of the ointment, he introduced the essential oil in the last resort at a temperature of 44 °C.

72 Indicate any possible changes in the prescription if streptocide linimentation includes streptocide, fish oil, emulsifier No. 1, and water.

73. To determine the material losses, the regulated cost factor and to make a material balance for the receipt of ointment.

74. Determine the size of particles in suspension ointments.

75. Determine the melting point and the time of complete deformation of suppositories made on a lipophilic basis.

76. Determine the time of dissolution of suppositories made on hydrophilic bases.

77. Determine the time of sedimentation stability of the suspension.

78. Prepare an emulsion using a turbine mixer.

79. Determine the type of emulsion.

80. Determine the bias voltage of the ointment using the Geppler resonance gauge and calculate the dynamic viscosity.

81. Determine the time of the emulsion bundle.

82. Determine the thermal stability of the emulsion.

83. Make a technological scheme for obtaining solutions for injections in ampoules prepared from preparations requiring sterilization.

84. Check the aerosol packaging for hermetic proreties.

85. Investigate the quality of injectable solutions for transparency.

RECOMMENDED EDUCATIONAL AND METHODOLOGICAL ANALYTICS

a) legal acts:

1. State Pharmacopoeia of Ukraine / State-owned enterprise "Scientific Expert Pharmacopoeia Center". - 1st kind.-Kharkov: RIREG, - 2001.-556s.

2. State Pharmacopoeia of Ukraine / State Enterprise "Scientific-Expert Pharmacopoeia Center". - 1st kind. - Kharkiv: RIREG, 2001. - Supplement 1. - 2004 - 520 p.

3. Law of Ukraine dated 04.04.96 No. 123/96-VR "On Medicines" with Appendices and Changes from 1997 to 2013.

b) *basic literature:*

1. Technology of medicines for industrial production: a textbook for the studio. higher tutor zakl .: in 2 ch. / VI Chuyshev, E.V. Gladukh, I.V.Saiko and others. - 2nd species., Processing. and add - X .: NFaU: Original, 2012. - 694 p. : il

2. Technology of medicines for industrial production: a textbook for studio. higher tutor zakl .: in 2 ch. / VI Chuyshev, E.V. Gladukh, I.V.Saiko and others. - 2nd species., Processing. and add - X .: NFaU: Original, 2013. - Ch. 2. - 638 p. : il

3. Equipment of technological processes of pharmaceutical and biotechnological productions: teaching. tutorial for studio higher tutor institution. / M.V.Stasevich, A.O.Milyanich, I.O.Huseva [and others.]: Ed. VP Novikova - Vinnitsa: A New Book, 2012.-408 pp .: Il.

c) additional literature:

1. Pharmaceutical and medico-biological aspects of medicine: teaching. sits for students, masters, asp., ed., sciences. co-worker and specialists in pharmacy / I. M. Pritsev, O. Kh. Piminov, M. M. Slobodyanyuk [and others]; for ed. I.M.Pertseva; National pharmacy un - 2nd form, processing. and add - Vinnitsa: N. Kn., 2007. - 725 p. : il., tabl.

2. Theoretical fundamentals of pharmaceutical technology: A manual for students. / V. I. Chueshov, I. V. Saiko, E. V. Gladuk and others .// - 2 ed. - X: Publishing house NFUU, 2003. - 210s.