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
" __ " _____2025

METHODOLOGICAL DEVELOPMENT TO PRACTICAL CLASSES FROM THE ACADEMIC DISCIPLINE (8th SEMESTER)

Faculty, course Pharmaceutical, course 4

Academic discipline Drugs technology
(name of academic discipline)

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

Protocol No. _dated _____ ___, 2025.

Head of the department _____ Volodymyr HELMBOLDT
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Developers:
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Practical lesson No. 21-22

Topic " Physico-chemical and technological properties of powders and granules "

Purpose: To study the material balance at the stages of the technological process and the technological properties of powdered and granular medicinal substances for the optimal tableting process and the selection of auxiliary substances.

Basic concepts: *Powders* (lat. pulveres — powders) are solid medicinal preparations for internal or external use, which consist of one or more medicinal substances and have free-flowing properties. Powders can be mechanical mixtures of crushed free-flowing medicinal substances (organic and inorganic nature) with thick substances and liquids in small quantities that do not affect their flowability.

Requirements: high degree of dispersion, flowability, uniformity of distribution of substances throughout the mass of the powder (homogeneity of mixing), dosing accuracy, stability; for some - sterility and uniformity of distribution of active substances in the mass.

Grinding is the process of reducing the size of particles of solid pharmaceuticals with the help of various devices.

The degree of grinding is the ratio of the average initial size of a piece of material to its average cross-sectional size after grinding.

Mixing is a process that achieves homogeneity, that is, the same ratio of constituent particles in any part of the resulting mixture.

Sieving is a process whose goal is to obtain a product with the same particle size as determined by sieve analysis.

Material balance is the ratio between the amount of raw materials, materials, semi-finished products and intermediate products used in production, and the amount of finished products, by-products, waste and losses actually obtained, i.e. the ratio of theoretically possible and practically obtained output of finished products.

This relationship is illustrated by the material balance equation, which has the form:

C1 = (C2 + C3 + C4) + C5,

where C1 is the amount of raw materials; C2 — quantity of finished products; C3 — number of by-products; C4 — amount of waste; C5 is the number of losses.

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:

Tests from the base of KROK-2

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. Crystal forms of medicinal substances.
2. The purpose and method of determining the fractional composition of powder and granules.
3. Influence of the size of powder particles and granules on the tableting process.
4. Determination of bulk, true and relative density of powders.
5. Influence of physical and chemical properties on bulk density.
6. Determination of flowability.
7. Influence of flowability on the tableting process.
8. Pressed powdered materials.
9. Value of extrusion pressure during the production of tablets.

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.	Physico-chemical properties of powdered medicinal substances	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. - Kh.: National University of Applied Sciences: Original, 2016. - P. 65-68.
2.	Technological properties of powdered medicinal substances	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. - Kh.: National University of Applied Sciences: Original, 2016. - P. 68-78.

— 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:

Tests from base of KROK-2.

Lesson content.

PROPERTIES OF POWDER-LIKE MEDICINAL SUBSTANCES

The properties of the original medicinal substances largely determine the rational method of tableting. As raw materials, loose substances in the form of powder (particle size 0.2 mm) or granular (particle size from 0.2 to 3 mm) forms are used, which have the following properties:

— physical — density, shape, size and character of the surface of particles, specific surface of particles, forces of adhesion (sticking on the surface) and cohesion (sticking of particles inside the body), surface activity, melting point, etc.;

— chemical — solubility, reactivity, etc.;

•— technological — bulk density, degree of compaction, flowability, moisture, fractional composition, dispersity, porosity, compressibility, etc.;

— structural and mechanical — plasticity, strength, elasticity, viscosity of crystal lattices, etc.

These properties are often divided into two large groups: physical and chemical and technological.

PHYSICAL AND CHEMICAL PROPERTIES

Shape and size of particles. Powdered medicinal substances are roughly dispersed systems and consist of particles of various shapes and sizes. Most of them are crystalline systems; the amorphous state is less common.

There are 6 crystal systems: cubic, hexagonal, tetragonal, rhombic, monoclinic, triclinic. It is known that only substances belonging to the cubic system are pressed into tablets without granulation and auxiliary substances (sodium chloride, potassium bromide).

The shape of the particles is determined by the ratio of the average length of the particles to the average width. At the same time, the particles are conditionally divided into three main types: elongated - the ratio of length to width is more than 3: 1; lamellar - the length exceeds the width and thickness, but not more than 3 times; equiaxed - have a spherical, polyhedral shape, close to isodiametric.

Usually, powders that have the form of particles in the form of sticks are characterized by fine dispersion, good compaction and sufficient porosity (analgin, norsulfasol, acrichin, etc.). Powder with equiaxed particles - coarsely dispersed, with a low degree of compaction, low porosity (lactose, hexamethylenetetramine, salol). The more complex the surface of the powder particles, the greater the adhesion and less flowability, and vice versa.

For tableting, such properties of substances as: presence of water of crystallization, wettability and hygroscopicity are important.

In many drugs, the particles are anisodiametric (asymmetric, multiaxial). They can be elongated, in which the length significantly exceeds the transverse dimensions (sticks, needles, etc.), or lamellar, when the length and width are significantly greater than the thickness (plates, scales, tablets, leaves, etc.). A smaller part of powdery substances has isodiametric (symmetrical, equiaxed) particles — these are spherical formations, blocks, polyhedra, etc.

The shape and size of powder particles depend: in the case of crystalline substances (chemical-pharmaceutical preparations) — on the structure of the crystal lattice and the conditions of particle growth during the crystallization process, in crushed plant materials — on the anatomical and morphological features of crushed plant organs and the type of crushing machine.

The size of powder particles is determined by their length and width, which are measured using a microscope equipped with a micrometer grid, at a magnification of 400 or 600 times.

The shape of the particles is determined by the ratio of the average length of the particles to the average width. With this method, particles are conditionally divided into three main types: elongated - the ratio of length to width is more than 3:1; lamellar - the length exceeds the width and thickness, but not more than 3 times; equibasic — have a spherical, polyhedral shape close to isodiametric.

There are six crystal systems: cubic, hexagonal, tetragonal, rhombic, monoclinic, triclinic.

Among the crystalline products, the largest amount is made up of substances: about 40% of the monoclinic system, 10% of the cubic system, 7% of the hexagonal system, 5% of the tetragonal system, 28% of the rhombic system, and 10% of the triclinic system.

It is known that only substances belonging to the cubic system are pressed directly into tablets, that is, by direct pressing, without granulation and auxiliary substances (sodium chloride, potassium bromide).

Usually, powders that have the form of particles in the form of sticks" are characterized by fine dispersion, good compaction and sufficient porosity (analgin, norsulfazole acrichin, etc.).

Equiaxial powders; in the shape of the particles, they are coarsely dispersed, with a low degree of compaction, and slight porosity (lactose, hexamethylenetetramine). The more complex the surface of the powder particles, the greater the adhesion and the lower the flowability, and vice versa.

The physical properties of powders are determined by the specific and contact surface and actual density.

The specific surface is the total surface occupied by a powdery substance, and the contact surface is the surface formed when powder particles collide with each other.

The actual density of the powder is determined by the ratio of the mass of the drug to its volume at zero porosity of the powder. Any liquid that wets but does not dissolve the powder is used as a comparison. The determination is carried out using a volume meter (a pycnometer for powdered solids).

Wettability The wettability of powdered medicinal substances refers to their ability to interact with different liquids (lyophilicity) and primarily with water (hydrophilicity). On the surface of the solid particles of medicinal substances there is one or another amount of hydrophilic groups (—OH, —COOH, etc.) or oxygen atoms, which are structural elements of their crystal lattices, so the wettability of the surface of the powders has a different value depending on the intensity of the interaction of intermolecular forces . Visually, the propensity of the surface of the powders to be wetted by water is revealed: a) complete wetting — the liquid spreads over the surface of the powder; b) partial wetting — water partially spreads over the surface; c) complete; non-wetting - the drop of water does not spread, maintaining a shape close to spherical. Hydrophobic (not wetted by water) substances can be well wetted by other liquids — for example, organic solvents.

The practical value of wetting is that water easily penetrates into a tablet obtained by pressing well-wetted substances, and this accelerates the disintegration of the tablet.

Hygroscopicity. If the elasticity of vapors in the air is greater than their elasticity on the surface of solid particles, then the powdery mass prepared for tableting will begin to absorb steam from the air and dissolve in the absorbed water. The kinetics of moisture absorption is determined by the mass method in ordinary (normal)

conditions, in extreme conditions (desiccator over water — 100% relative humidity) or in a climatic chamber.

If the substance is very hygroscopic, then this requires the use of auxiliary substances - moisture stimulators.

Crystallization water. Crystallization water molecules determine the mechanical (strength, plasticity) and thermal (dependence on the air temperature) properties of the crystal, significantly influence the behavior of the crystal under pressure. The phenomenon of "cementation" is also closely related to the presence of water of crystallization in tableted substances.

Electrical properties. The phenomenon of electrification of powdered medicinal substances during their processing and pressing gives a reason to conclude that, considering the nature of the connection of particles in tablets, in addition to deformation ones, it is necessary to take into account also dielectric characteristics. When subjected to mechanical action, all asymmetric crystals that contain polar groups in their structure or in the adsorption water film will be subject to polarization. Formation of surface charges is impossible for non-polar substances.

The technological properties of powdered medicinal substances depend on their physical and chemical properties.

Fractional (granulometric) composition, or the distribution of powder particles by size, affects the degree of its flowability, and therefore, the rhythmic operation of tablet machines, the stability of the weight of the received tablets, the accuracy of the dosage of the medicinal substance, as well as the quality characteristics of the tablets (appearance, disintegration, strength, etc.).

The fastest and most convenient method of determining dispersion is sieve analysis. The technique of this analysis consists in the fact that 100.0 g of the studied powder is sifted through a set of sieves (hole diameter 2.0; 1.0; 0.5; 0.25 and 0.1 mm). The weight of the material is placed on the largest (upper) sieve and the entire set of sieves is shaken (by hand or on a vibrating device) for 5 minutes, and then the mass of each fraction and its percentage content are found.

Studies of the fractional composition of pharmaceutical powders subject to tableting have shown that most of them mainly contain a fine fraction (less than 0.2 mm) and therefore have poor flowability. They are poorly dosed by volume on tablet machines, tablets are formed of unequal weight and strength. The fractional composition of powders can be changed with the help of directional granulation, which makes it possible to obtain a certain number of large fractions.

It is important to determine such volumetric indicators of powders as bulk density, bulk volume.

These indicators are determined according to the methods of the SFU (clause 2.9.15).

The milling process is widely used in pharmaceutical practice for various purposes. Grinding can be an auxiliary process to ensure further dissolution, extraction,

drying, etc., which proceed faster and more completely, the more surface involved solids. In this case, the crushed material plays the role of a semi-finished product, as it is used by the enterprise to obtain solutions, tinctures, extracts, etc.

Grinding can be the main process for obtaining a commercial product (powders and medicinal preparations) with a certain particle size, in this case, the technological scheme for obtaining a crushed product consists of several consecutive technological operations: grinding of material; screening; mixing (when obtaining complex powders and collections).

Shredded is the process of reducing the size of particles, which allows to significantly increase the speed of chemical and diffusion processes, the accuracy of dosage of drugs, and in some cases to increase the pharmacological activity of drugs.

In technological practice, grinding is characterized by the degree of grinding of the substance. The degree of grinding is the ratio of the diameter of the pieces of material before grinding D to the diameter of the particles of the crushed material d.

Depending on the size of the initial material and the size of the crushed material, the following types of grinding are conditionally distinguished:

	i	D, mm	dk
Coarse (shredding)	2-6	1000-200	250-40
Medium (shredding)	6-10	250-50	40-10
Fine (shredding)	10-50	50-25	10-1
fine (shredding)	50-100	25-3	1-0.4
Colloidal (ground)	100-10000	0.2-0.1	Up to 0.001

In pharmaceutical practice, large, small, smallest and smallest grinding is widely used. Solid substances of mineral and organic origin can be crushed. Depending on the structure, all solids are divided into two groups: amorphous and crystalline. From a technological point of view, a third should be added to these two categories - materials with a cellular structure (plant and animal raw materials).

When carrying out the grinding process, the NTD requirements for the size of the particles of the crushed material are guided, and the choice of machines is determined by the specified degree of grinding and the properties of the crushed material.

Shredding machines can be classified according to different features:

- by purpose: preliminary and final grinding;

- according to the method of grinding the material: cutting tools (grass cutters, root cutters); crushing and abrasive (rollers, runners, millstones); impact-centrifugal mills (hammer mills, cross mills, disintegrators, dismembrators); shock-abrasive (ball and rod mills); ultrafine grinding machines (vibrating mills, colloid and jet mills);

- according to the degree of crushing of the material (crushers for coarse, medium and fine crushing, fine mills and colloid and jet machines),

- according to the nature of the working tool (disc, ball, knife, rotary, etc.)

Due to the fact that grinding is associated with the consumption of a significant amount of energy, the question of the economy of this process is important. Determination of energy consumption is one of the main problems of the theoretical foundations of grinding. Rittinger hypothesized that the work expended in grinding is proportional to the newly exposed surface in the ground material. Later, Kick proposed a "volumetric" theory of crushing, according to which the energy consumption for crushing a given material is directly proportional to its volume. V.N. Kirpichev proposed an equation for calculating the energy for grinding:

$$A = (\sigma 2 \cdot V) / (2E),$$

where A is the grinding work,

σ - value of destructive stresses,

V - volume of crushed material,

E is the modulus of elasticity of the crushed material.

According to the observations of P.A. Rebinder, the energy spent on grinding the material is the sum of the work that goes into the deformation of the grinding body and the formation of new surfaces:

$$A = (\sigma 2 \cdot V) / (2E) + K \cdot F,$$

where K-proportionality coefficient,

F - newly formed surface during the destruction of the body.

Screening. Crushed materials are always heterogeneous in particle size. For this reason, it is necessary to separate larger or smaller particles from the main mass. This process is called sieving, screening or sieve classification and is carried out using sieves. As a result of sieving, the raw material is divided into 2 fractions: sifted (material that passed through the mesh) and screened (retained on the sieve).

The main part of sieving machines are sieve cloths, which are divided into: woven, stamped, grating. The shape of the holes of the nets can be square, round, rectangular, depending on the method of obtaining the nets and the material from which they are made.

Woven sieves are obtained by interweaving thin threads or wires. They use natural silk, synthetic materials (kapron, mylar), special grades of stainless steel, brass (copper and zinc alloy), phosphor bronze. Fabrics of woven sieves are produced in compliance with a certain ratio between the width of the holes and the thickness of the threads in accordance with the so-called "sieve formula": the width of the mesh holes is 6 / ή; thread thickness - 4 / ή, where ή is the number of threads per 1 cm of screen cloth.

Attributing the constant numbers 6 and 4 to the number of threads makes it possible to determine the width of the holes and the thickness of the threads. According to this formula, the width of the mesh holes should be 1.5 times the thickness of the thread (6:4). Wicker sieves are relatively cheap, but not very strong. Their nets are easily pulled out, the threads shift, the size of the holes changes. To increase strength,

silk woven sieves are in some cases reinforced with a metal support. Metal wire nets are pressed in places where the threads cross or they are made from shaped bent wires.

Stamped, perforated grids are metal plates with frequent round, oval or square holes. Stamped nets are very strong. Such sieves are widely used in industry, but they have rather large openings - at least 0.3 mm.

Trolley sieves are a combination of metal (cast iron, steel) shaped plates. Despite the extreme strength, sieves are used extremely rarely, because they differ in low productivity.

In industrial conditions, mechanical designs of sieves are used: rotating, swinging, vibrating.

Rotating sieves are a drum of cylindrical, conical or polygonal shape (burat), the walls of which are made of mesh or perforated metal sheets. The cylindrical drum sieve rotates on the shaft and is installed slightly inclined to the horizontal (at an angle of 4-70). To eliminate material scattering, the drum is placed in a casing. The sieve surface of the drum consists of sections. Each section is a flat removable sieve with holes that increase in size as the material progresses. The advantage of rotating sieves is the possibility of differentiating the material into several fractions with different particle sizes. Despite the simplicity of construction and maintenance, rotating sieves are used relatively rarely due to the small productivity per unit surface of the sieve, and the mesh holes are easily clogged, since the material is not shaken.

Shaking sieves are used for sifting plant material. They are a flat oscillating box on spring supports, installed obliquely at an angle of 7-140 to the horizontal, with a number of oscillations of 60-400 rpm and an amplitude of 5-225 mm. The rocking motion is created by a crankshaft, connecting rod or eccentric mechanisms. Productivity is low, and the mesh hole is easily clogged, since the movement of the material is smooth in the horizontal plane.

Vibrating sieves are similar to rocking sieves, but have a higher frequency of oscillations (1800 cycles/min and higher) and small amplitudes (0.3-5 mm). These sieves are widely used in the pharmaceutical industry. Their high productivity is explained by the fact that at a high frequency of vibration of the sieve, its holes are not clogged with material, due to continuous tossing on the grid.

According to the design, three types of vibrating screens are distinguished depending on the vibrating device: electromagnetic, gyrational, inertial.

The electromagnetic sieve is especially effective for sieving fine powders, as the vibrating movements prevent clogging of the holes of the sieve fabric. Progressive reverse movement is carried out due to periodic magnetization and demagnetization of the armature attached to the sieve. When the current passes, the electromagnet attracts the armature, and with it the sieve, but this movement to the right entails the opening of the contacts. The return movement (to the left) of the sieve is carried out by means of springs.

The gyratory screen is a box mounted on elastic supports. The principle of circular vibration is used in gyratory sieves: an eccentric shaft directs an oscillating motion in a circle to the box with an amplitude of oscillation equal to the eccentricity of the shaft. It works from fast-moving eccentrics, which are rigidly connected to the surface or mounted in the walls of the box.

Inertial sieve. The circular movements are created by an unbalanced shaft passed through the sieve body. Since an unbalanced shaft creates inertial vibrations of the shaft, such sieves are called inertial. The sieve box is mounted on springs. A shaft with two pulleys carrying unbalanced loads (Unbalances) rotates on racks and bearings. When the pulleys rotate, centrifugal forces of inertia arise, which cause vibration of the shaft and, accordingly, the screen.

When sieving, it is necessary to create safety equipment in connection with the toxicity of dust or some medicinal substances. For this purpose, the sieves are placed in a hermetic case or placed in isolated cabins connected to the draft. For individual additional protection of the eyes and respiratory tract, respirators and goggles are used.

The productivity of the sieves and the quality of material screening depend on several factors: the shape and size of the mesh openings, the thickness of the material layer on the sieve, the moisture content of the material, the speed of movement of the material on the sieve, the nature of the movement and the length of the material path. In addition, the method of feeding the material, the frequency of sieving, etc., is important. Quantitative accounting of all factors is time-consuming, so productivity is determined empirically, but accounting for all factors is necessary for the rational operation of the sieve.

A thick layer of material on the sieve impairs performance, as it complicates the contact of the material with the mesh, increases the sliding of small particles on the surface of the material, as a result of which sieving does not take place completely. Installing the sieve at an angle to the horizontal helps to spread the material in a thin layer and create better conditions for sieving.

The moisture content of the material is of great importance for the performance of the sieve. Raw material sticks together and clogs the holes of the mesh, dry material is sifted better, but sieving is complicated by phenomena arising as a result of friction of the material against the mesh. In this case, when the particle sifts through the material and the mesh is charged with different charges, the material clogs the mesh openings. With the charge of the same name, the material tends to scatter in all directions. To combat the phenomena, metal sieves are grounded. Removing the charge from silk sieves is difficult. In production, brushes are used to wipe the material when clogging the nets.

The speed of movement on the screen surface has a significant impact on the performance of the screen. However, at very high speeds, the contact of small particles with the sieve becomes difficult, and they can fall into the sieve. Low speeds slow down the sifting process.

The longer the material path, the more efficient the screening. A longer path allows sieving at a low speed, with a small thickness of the material. If the movement path of the material on the sieve is small, intensive movement of the material (shaking) is advisable. With a calm free sliding of the matyukal on the surface of the mesh, small particles can remain in the upper layers, without coming into contact with the holes of the sieve, and go to the sieve. It is more profitable to shake the material on a sieve, which is taken into account in some sieve designs.

Technological properties

These include:

Fractional (granulometric) composition - the distribution of powder particles by size, has a certain influence on the degree of flowability, and, therefore, on the rhythmic operation of tablet machines, the stability of the mass of the received tablets, the accuracy of the dosage of the medicinal substance, as well as on the quality characteristics of the tablets (appearance, disintegration , strength).

Studies of the fractional composition of pharmaceutical powders that are subject to tableting have shown that most of them contain a large amount of fine fraction (less than 0.2 mm) and therefore have poor flowability. They are poorly dosed by volume on tablet machines. The fractional composition of powders can be changed using directional granulation, which allows obtaining larger fractions.

Bulk (bulk) *density* is the mass of a unit volume of loosely packed powdery material. Bulk density depends on the shape, size, density of powder particles (granules), and their moisture content. The volume of the matrix nest can be predicted by the value of the bulk density.

But the most important technological properties are flowability, compressibility and sliding.

Flowability - the ability of the powdery mass to pour out of the loading funnel under the force of its own weight and ensure uniform filling of the matrix nest. The material, which has poor flowability in the funnel, sticks to its walls, which disrupts the rhythm of its entry into the matrix. This leads to the fact that the given mass and density of tablets will fluctuate.

Flowability is calculated according to the formula:

$$V_c = \frac{m}{t \pm 20}$$

where: V_c - s and mass , kg/ s

m - weight of the weight, kg

t is the total time of the test , p

20 - time of shaking, p

The flowability of powders can be used when choosing a tableting technology. Powdery mixtures containing 80-100% of fine fraction (particle size less

than 0.2 mm) are poorly dosed, so it is necessary to carry out directed particle agglomeration of such masses, i.e. granulation. If the fine fraction contains up to 15%, it is possible to use the direct pressing method.

The compressibility of the powder is the ability of its particles to bond and adhere under pressure. At the same time, the powder particles coalesce, stick together, and stick together to form a homogeneous solid body. Compressibility can be estimated by the tablet's compressive strength. The higher the strength of the tablet, the better the compressibility of the tablet mass.

It is established that for substances with the strength of tablets:

- above 7 kg / cm, pure solvents are used for the granulation process; if these are coarse powders with good flowability, they are pressed directly, that is, by direct pressing;
- 4 - 7 kg / cm is enough to use ordinary binders;
- 1 - 4 kg / cm requires the use of highly effective binders.

The force of pushing tablets out of the matrix . To push the pressed tablet out of the matrix, you need to use force to overcome the friction and adhesion between the side surface of the tablet and the wall of the matrix. Additives of lubricants are predicted taking into account the force of ejection. The pressed tablet is pushed out by the lower punch. At the same time, the pressing force of the tablet is recorded on the manometer of the tablet press. The calculation of pushing forces is made according to the formula:

$$P_{вытал} = \frac{P_{ман} \cdot S_{пл}}{S_{бок}}$$

where: $P_{вишт}$ - ejection pressure , MPa;

$P_{ман}$ - pressure gauge reading, MPa;

$S_{пл}$ - plunger area, m;

$S_{бок}$ - the area of the side surfaces and the tablet, m;

The area of the side surface of the tablet is calculated according to the formula:

$$S_{бок} = 2 \cdot \pi \cdot r \cdot h$$

where: *r* is the radius of the pill, m;

h – in the hundredth tablet, m.

Mixing of powdered products, as well as mixing of paste-like materials is used in the technology of obtaining most LF and is carried out in special mixers. Mixers are classified: by the nature of the mixing process (convective or diffuse), a design feature (drum mixers with a rotating body and rotating blades), the method of impact on the mixture (gravitational, centrifugal), the nature of the mixing process occurring in them (periodic or continuous), and others signs

Mixers with a rotating body. One of the simplest mixers of this type are ball mills, which work at a low number of revolutions. The speed of rotation of the ball mill is regulated in such a way that the balls do not fall, but roll. If the mill rotates long enough, they give good mixing. The disadvantage is that the material is subjected to additional grinding, which is not always desirable. Drum mixers do not have this drawback.

Drum mixers are cylindrical, prismatic or star-shaped (cross-shaped) chambers that rotate around a horizontal axis driven by an electric motor. The inner surface of the drum is polished or lined with a smooth plate to prevent powder sticking. To improve the mixing effect, so-called baffles are arranged on the walls - vertical, spiral or rectangular blades located at an angle to the direction of rotation. The drums rotate at a speed of 6-8 rpm and are designed for mixing only loose materials.

Mixers with rotating blades. This type of mixers includes trough-type paddle mixers, the so-called "universal" mixers, suitable for mixing loose and plastic masses.

Inside the trough with a rounded bottom rotates a shaft carrying a sigmoidally curved blade that rotates at a low speed (up to 50 rpm). Mixers with two blades rotating at different speeds in opposite directions (17-24 rpm and 3-10 rpm) are often used. Due to the low speed of rotation of the blades, mixers of this type are not very productive, mixing in them takes quite a long time. Single-shaft and double-shaft screw mixers are used for continuous mixing of loose, plastic and other materials. Two-shaft screw mixers are horizontal troughs, inside which two parallel shafts with blades rotate at different speeds, one of them mixes the material, the other transports it. The material enters through the hopper and moves, mixing along one shaft, then is transferred by a paddle wheel to another shaft and moves along it in the opposite direction. The finished mixture is discharged from the mixer. Disadvantages of mixers of this type are the unwanted additional grinding of crystalline substances and the formation of wall "dead zones" where quality mixing of the material does not occur.

The centrifugal mixer consists of a body inside which an open hollow cone rotates on a vertical axis, with the larger base facing up. The mixing material is mixed in the inner surface of the cone from the bottom up under the action of centrifugal forces of inertia, is ejected from the body and an outer layer is formed, inside which intense mixing takes place. When mixing inside the cone, the material encounters on its way knives mounted on a freely rotating frame with blades that rotate at a lower speed and contribute to additional mixing.

Mixing of components in a pseudo fluidized layer occurs under the influence of air with a certain speed and pressure. When the gas pressure exceeds the resistance of the material, the layer of solid particles becomes fluid. The solid particles move intensively in the gas flow, and the entire layer resembles a boiling liquid - a pseudo-liquefied state.

A quantitative characteristic of the mixing process is the homogeneity of the composition of any of the samples taken from different zones of the mixer. The

following factors influence the mixing process: surface forces (electrostatic, molecular, Van der Waals), shape and size of particles, and their density. The time of mixing simple and complex prescriptions in the dry state is from 3 to 12 minutes, and in the moistened state from 5 to 20 minutes. When mixing, it is also necessary to take into account the nature of the powdered material (poisonousness, toxicity, coloring, volatility, etc.). The basic principle of mixing: a smaller quantity is added to a larger quantity to avoid the loss of small substances.

Grinding, sieving and mixing processes are the main operations in the production of powders and medicinal preparations.

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. Khohlova etc. - Kh.: NFaU, 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 "KROK 2. Pharmacy" / O.A. Ruban, V.D. Rybachuk, L.M. Khokhlova, D.S. Pulyaev - Kh.: NFaU, 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.: NFaU: 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.: NFaU: 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 NFaU, 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 NFaU, 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-NFaU, 2017. – 44 p.
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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.
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- 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, K.K. 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. 23-25

Topic: " Production of tablets by the method of direct pressing and with preliminary granulation "

*Goal***:** To study technological schemes for the production of tablets by direct pressing and using preliminary granulation. Be able to rationally select auxiliary materials and equipment, carry out quality control, packaging and labeling of the finished product

*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: Pressing – (actual tableting). This is the process of forming tablets from granular or powdery material under pressure. In modern pharmaceutical production, tableting is carried out on special presses - rotary tablet machines (RTM). Pressing on tablet machines is carried out by a press - a tool consisting of a matrix and two punches.

The technological cycle of tableting on RTM consists of a series of consecutive operations: dosing of material, pressing (tablet formation), its ejection and reset. All the listed operations are carried out automatically one by one with the help of the corresponding executive mechanisms.

Direct pressing **.** This is a pressing process of NOT granulated powders. Direct pressing allows you to eliminate 3-4 technological operations and thus has an advantage over tableting with preliminary granulation of powders. However, despite the apparent advantages, direct pressing is slowly being introduced into production. This is explained by the fact that for the productive operation of tablet machines, the pressed material must have optimal technological characteristics (flowability, compressibility, moisture, etc.). Such characteristics are possessed only by a small number of non-granular powders - sodium chloride, potassium iodide, sodium and ammonium bromide, hexomethylenetetramine, bromocamphor, etc. substances having an isometric shape of particles of approximately the same granulometric composition, which do not contain a large number of small fractions. They press well.

One of the methods of preparation of medicinal substances for direct pressing is directed crystallization - obtaining a tabletable substance in crystals of a given flowability, compressibility and humidity is achieved through special crystallization conditions. Acetylsalicylic acid and ascorbic acid are obtained by this method.

The wide use of direct pressing can be ensured by increasing the flowability of non-granulated powders, high-quality mixing of dry medicinal and auxiliary substances, and reducing the tendency of substances to delaminate.

Dedusting . Dust removers are used to remove dust fractions from the surface of tablets coming out of the press. Tablets pass through a rotating perforated drum and are cleaned of dust, which is sucked by a vacuum cleaner.

Granulation is a directed agglomeration of particles, that is, the process of transforming a powdery material into grains of a certain size, which is necessary to improve the flowability of the tablet mixture and prevent its delamination. The improvement in flowability occurs as a result of a significant decrease in the total surface area of the particles during their gluing into granules and, therefore, a

corresponding decrease in the friction that occurs between the particles during movement. Stratification of the powdery mixture usually occurs due to the difference in the particle sizes and specific density values of the medicinal and auxiliary components included in its composition. Stratification of the tablet mass is a dangerous and unacceptable process that causes a violation of the dosage of components.

*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;
- characteristics of tablets as a dosage form. Types and groups of tablets ;
- positive and negative aspects of direct pressing ;
- The main directions of production of tablets by direct pressing .
- Stages of the technological process of obtaining tablets by direct pressing
- Stages and equipment of production of tablets with preliminary granulation

A student of higher education must be able to:

- - to give distinction in the ology of granulation . Positive and negative aspects of this process.
- to know with means of structural granulation.
- know when to use dry granulation (granulation by grinding).
- to know the characteristics and groups of auxiliary substances in the production of tablets.

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. Calculate the working prescription for the production of 100 kg of acetylsalicylic acid tablets of 0.5. The average weight of tablets is 0.55. Crash = 1.05.

2. Determine the amount of starch for the production of 2 kg of ascorbic acid tablets of 0.05, average weight 0.2. Sahara 0.11 m Krash = 1.09.

3. Determine the amount of starch for the production of 200,000 phenobarbital tablets of 0.1 g. The average weight is 0.2 g (sugar 0.08, talc 0.0036). Crash = 1.15.

Lesson content

Definition of tablets as a dosage form

Tablets (Tabulate, from Latin tabula — board, tabulate — board, tile) — a solid medicinal form containing one dose of one or more active substances, obtained by pressing a certain volume of particles. Tablets are intended for oral administration. Some tablets are swallowed whole, some are pre-chewed, others are dissolved or dispersed in water before use or left in the mouth, where the active substance is released.

Even in the "Canon of Medical Science" by Abu Ali Ibn Sina, such medicinal forms as cakes are mentioned (they are a prototype of modern tablets). Tablets, depending on the purpose and dosage, are divided into dosed forms for direct use and non-dosed, for storage and subsequent use.

The first information about pills appeared in the middle of the 19th century. In 1844, in England, Brokedon received a patent for the preparation of potassium bicarbonate tablets by pressing. In 1846-1897, the production of tablets was established in SILA, France, and Switzerland. In 1872, tablets were first offered in Germany by Rosenthal,

In our country, the first large tablet workshop was opened in 1895 at the factory of military and medical supplies.

In 1900, Professor L. F. Ilyin, a member of the commission "On Pressing Medicines from the Stock of the Field Pharmacy at the Pharmacy Department of the Factory of Military Medical Supplies", wrote the first dissertation "On Pressed Medicines, or Tablets". In 1901, for the first time, tablets as a dosage form were included in the Swedish Pharmacopoeia.

Tablets produced by the chemical and pharmaceutical industry make up approximately 40% of the production of finished medicines. The production of tablets worldwide is growing annually by 10-15%. According to WHO, such rates will remain until the end of the first decade of the 21st century.

Characteristics of tablets

Tablets as a medicinal form have become widespread throughout the world. Today, tablet preparations make up more than three quarters of the total volume of finished medicines. The positive qualities of the tablets provide:

'— the proper level of mechanization at the main stages and operations, which ensures high productivity, cleanliness and hygiene of the production of these medicinal forms;

— accuracy of dosage of medicinal substances included in the tablet;

— the portability of tablets, which ensures the convenience of dispensing, storing and transporting them;

— long-term integrity of medicinal substances in a compressed state;

— for substances that are not stable enough — the possibility of applying protective coatings;

— the possibility of masking unpleasant organoleptic properties (taste, smell, color), which is achieved by applying coatings;

— a combination of medicinal properties incompatible in terms of physico-chemical properties in other medicinal forms;

— localization of the action of the medicinal substance in a certain part of the gastrointestinal tract by applying membranes soluble in an acidic or alkaline medium;

— prolonging the effect of medicinal substances (by applying certain coatings, using special technology and composition of core tablets);

— regulation of sequential absorption of several medicinal substances from a tablet at specified time intervals (multilayer tablets);

-- prevention of errors when dispensing and taking medicines due to the application of appropriate inscriptions on the surface of the tablets.

However, tablets have some disadvantages:

— the effect of medicines in tablets develops relatively slowly;

— the tablet cannot be administered during vomiting and unconsciousness;

— during storage, tablets may become cemented, while the decomposition time increases;

— the composition of tablets may include excipients that have no therapeutic value, and sometimes cause some side effects (for example, talc irritates the mucous membrane of the stomach);

— certain drugs (for example, sodium or potassium bromide) form highly concentrated solutions in the dissolution zone, which can cause severe irritation of the mucous membranes (this defect is eliminated by dissolving the tablets in the appropriate amount of water);

— not all patients, especially children, can easily swallow pills.

Classification of tablets

According to the method of production in industrial conditions, two classes of tablets are distinguished:

1. Pressed, which are obtained by pressing medicinal powders on tablet machines with different productivity. This method is the main one.

2. Formed or triturated tablets, which are obtained by forming a tablet mass. Trituration tablets contain small doses of medicinal substances and fillers: their weight can be up to 0.05 g.

Tablets are also classified according to the structural feature:

1. By composition: simple (one-component) and complex (multi-component).

2. According to the structure of the building: frame, single-layer and multi-layer (at least two layers), with or without coating.

Frame (or skeleton) tablets have an insoluble frame, the cavities of which are filled with a medicinal substance. A separate tablet is like a sponge impregnated with medicine. When taken, its frame does not dissolve, keeping its geometric shape, and the medicinal substance diffuses into the gastrointestinal tract.

Single-layer tablets consist of a pressed mixture of drugs and auxiliary substances and are uniform throughout the entire volume of the dosage form.

Medicinal substances are arranged in layers in multilayer tablets. The use of chemically incompatible substances causes their minimal interaction.

3. Tablet coating is classified into: coated, film and pressed.

The forms of tablets produced by the chemical and pharmaceutical industry are very diverse: cylinders, spheres, cubes, triangles, quadrilaterals, etc. The most common is a flat-cylindrical shape with a chamfer and a biconvex shape that is convenient for swallowing. In addition, punches and dies for the production of tablets are simpler and very easy to install on tablet machines.

Most of the existing filling and packaging machines are also adapted to work with flat-cylindrical and biconvex tablets.

The flat-cylindrical form of tablets without a chamfer is not recommended for production, because during packaging and transportation, the sharp edges of the tablets are destroyed, as a result of which the marketable appearance is lost.

The size of the tablets varies from 3 to 25 mm in diameter. Tablets with a diameter of more than 25 mm are called briquettes. The most common are tablets with a diameter of 4 to 12 mm. Tablets with a diameter of more than 9 mm have one or two lines drawn perpendicularly and allow dividing the tablet into two or four parts and thus varying the dosage of the medicinal substance.

The weight of the tablets is mainly 0.05-0.8 g and is determined by the dosage of the medicinal substance and the amount of auxiliary substances in their composition.

Tablets should have the correct shape, be whole, without jagged edges, their surface should be smooth and uniform. Tablets should be strong enough and not crumble. The geometric shape and dimensions of tablets are determined by the standard - GOST 64-072-89 "Medicinal agents. Tablets. Types and sizes". It mainly involves the production of two types of tablets: flat-cylindrical without a chamfer and with a chamfer, biconvex without a coating and with coatings: film, pressed and coated. Abroad, the choice of tablet forms is much larger. Flat-cylindrical tablets are produced in 14 standard sizes with a diameter ranging from 4.0 to 20.0 mm; uncoated biconvex tablets are produced in 10 standard sizes — from 4.0 to 13.0 mm, coated tablets — from 5.0 to 10.0 mm (Table 14.2). The diameter of the tablets is determined by their mass (Table 14.3).

The height of flat-cylindrical tablets should be within 30-40% of the diameter. Some tablets (in the CIS countries - these are tablets containing drugs) have an

inscription with the name of the drug on the surface, they are made in the form of concave impressions, since the convex letters on the end of the tablets are much more likely to be erased and destroyed.

Depending on the purpose and method of use, tablets are divided into the following groups:

Oriblettae - tablets, used orally. Medicinal substances are absorbed through the mucous membrane of the stomach or intestines. These tablets are taken internally with water. The oral group of tablets is the main one.

Resoriblettae — tablets, used sublingually; Medicinal substances are absorbed through the mucous membrane of the oral cavity.

Implantabulettae — tablets produced aseptically, are used for implantation. Designed for slow absorption of medicinal substances in order to prolong the therapeutic effect.

Injectabulettae — tablets made aseptically, are used to obtain injection solutions of medicinal substances.

Solublettae are tablets used to prepare solutions for various pharmaceutical purposes.

Dulciblettae bacilli , boli , urethratoria , vagitoria — pressed urethral, vaginal and rectal dosage forms.

Oral tablets can be classified as:

— on tablets without a shell;

— coated tablets;

— "effervescent" tablets;

— soluble tablets

— tablets are dispersed

— enteric-dissolving tablets;

— tablets with modified release;

— tablets for use in the oral cavity.

Technological process of manufacturing tablets

Direct pressing

The direct pressing method has some advantages. It allows you to achieve high labor productivity, significantly reduce the time of the technological cycle due to the elimination of some operations and stages, exclude the use of several items of equipment, reduce production areas, and reduce energy and labor costs. |Direct pressing makes it possible to obtain tablets from wet, thermolabile and incompatible substances. Currently, less than 20 names of tablets are obtained by this method. This is explained by the fact that most medicinal substances do not have properties that ensure their direct pressing. These properties include: isodiametric shape of crystals, good flowability (fluidity) and stretchability, low adhesiveness to the press instrument of the tablet machine

Direct pressing is a set of various technological measures that allow to improve the main technological properties of the tableted material: flowability and crossability, and to obtain tablets, bypassing the granulation stage.

Today, tableting without granulation is carried out:

1) with the addition of auxiliary substances that polish the technological properties of the material;

2) forced feeding of tablet material from the loading hopper of the tablet machine into the matrix; ,

3) with preliminary directed crystallization of pressed substances

The size, strength of particles, compressibility, fluidity, moisture content and other properties of substances are of great importance for direct pressing. Coarse-dispersed powders with equiaxed particle shape and low porosity are characterized by the highest fluidity, such as lactose, phenylsalicylate, hexamethylenetetramine and other similar preparations included in this group. Therefore, such preparations can be compressed without prior granulation. Medicinal powders with a particle size of 0.5-1.0 mm, a natural slope angle of less than 42°, a bulk mass of more than 330 kg/m3, and a porosity of less than 37% have proven themselves to be the best.

They consist of a sufficient number of isodiametric particles with approximately the same fractional composition and, as a rule, do not contain a large number of small fractions, they are united by the ability to pour out evenly from the funnel under the influence of their own weight, that is, the ability of arbitrary volumetric dosing, and also quite good compressibility

However, the vast majority of medicinal substances are not capable of arbitrary dosing due to the significant (more than 70%) content of small fractions and the unevenness of the particle surface, which causes strong interparticle friction. In these cases, auxiliaries are added that improve fluidity properties and belong to the class of sliding auxiliaries.

Tablets of vitamins, alkaloids, glucosides, acetylsalicylic acid, bromocamphor, phenolphthalein, sulfadimesine, phenobarbital, ephedrine hydrochloride, ascorbic acid, sodium bicarbonate, calcium lactate, streptocid, phenacetin and others are obtained by this method.

Preliminary directional crystallization is one of the most complex methods of obtaining medicinal substances suitable for direct pressing. This method is carried out by two methods:

1) recrystallization of the finished product in the required mode;

2) by selecting certain conditions for crystallization of the synthesized product.

Applying these methods, a crystalline medicinal substance with crystals of a fairly isodiametric (equiaxial) structure is obtained, which freely pours out of the funnel and, as a result, is easily amenable to arbitrary volumetric dosing, and this is an indispensable condition for direct pressing. This method is used to obtain tablets of acetylsalicylic and ascorbic acids.

To increase the compressibility of medicinal substances during direct pressing, dry adhesive substances are introduced into the composition of the powder mixture - most often microcrystalline cellulose (MCC) or polyethylene oxide (PEO). Due to its ability to absorb water and hydrate individual layers of tablets, MCC has a beneficial effect on the process of releasing medicinal substances. It is possible to make strong tablets from MCC, which, however, do not always disintegrate well.

To improve the disintegration of MCC tablets, it is recommended to add ultraamylopectin.

For direct pressing, the use of modified starches is indicated. The latter enter into a chemical interaction with medicinal substances, significantly affecting their release and biological activity.

Milk sugar is often used as a means of improving the flowability of powders, as well as granulated calcium sulfate, which has good fluidity and ensures the production of tablets with sufficient mechanical strength. Cyclodextrin is also used, which helps increase the mechanical strength of tablets and their disintegration.

In direct tableting, maltose is recommended as a substance that ensures a uniform rate of falling asleep and has a slight hygroscopicity. The lactose mixture is also used

The technology of making tablets consists in the fact that medicinal products are carefully mixed with the necessary amount of excipients and pressed on tablet machines. Disadvantages of this method are the possibility of delamination of the tablet mass, dosage changes during pressing with a small amount of active substances, and the use of high pressure. Some of these defects are reduced to a minimum during tableting by forced feeding of pressed substances into the matrix. Some constructive replacements of machine parts are carried out, i.e. vibration of the shoe, rotation of the matrix to a certain angle during the pressing process, installation of star-shaped mixers of various designs in the loading hopper, suction of material into the matrix hole using a vacuum that is created by itself, or a special combination with a vacuum line

But, despite the successes achieved in the field of direct pressing, in the production of tablets, this method is used for a limited number of medicinal substances.

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.	Technological process of manufacturing tablets	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. - P. 86-92.

2.	Technological process of making tablets by direct pressing and granulation method	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. - P. 92-106.
3.	Types of tablet machines	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. - P. 106-108.
4.	Factors affecting the quality indicators of tablets	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. - P. 108-110.

— 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:

Testes from the base of KROK-2

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

Main 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. Khohlova etc. - Kh.: NFaU, 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 "KROK 2. Pharmacy" / O.A. Ruban, V.D. Rybachuk, L.M. Khokhlova, D.S. Pulyaev - Kh.: NFaU, 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.
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Practical lesson No. 26-28

Topic: " Industrial production of coated tablets. Quality control "

Purpose: To study technological schemes for the production of coated tablets, granules, dragees. Be able to rationally select a coating method, auxiliary substances and equipment, carry out quality control, packaging and labeling of the finished product

Basic concepts: ***Film coatings*** are created on tablets by applying a solution of a film-forming substance followed by removal of the solvent. At the same time, a thin (0.05 - 0.2 mm) shell is formed on the surface of the tablets. Depending on the solubility, film coatings are divided into the following groups: water-soluble, soluble in gastric juice, soluble in the intestines, and insoluble coatings.

Water-soluble coatings protect against mechanical damage, but do not protect against the influence of air moisture. Water-soluble shells form PVP, MC, oxypropylene methyl cellulose, Na KMC, etc. They are applied in the form of water-ethanol or water solutions.

Coating, soluble in gastric juice. These are films that protect tablets from moisture, but do not prevent their rapid destruction in the stomach (within 10-30 minutes). These include polymers that have basic substituents in the molecule, mainly amino groups, such as diethylaminomethylcellulose, benzylaminocellulose, paraaminobenzoates of sugars and acetylcellulose, etc. Solutions of these substances in organic solvents are used for coating: ethanol, isopropanol, acetone.

Insoluble coatings are films with a microporous structure. They are solutions of ethyl and acetyl in ethanol, isopropanol, acetone, toluene, chloroform, ethyl acetate, etc. With the addition of plasticizers. The mechanism of release of the medicinal substance: digestive juices quickly penetrate through the pores of the insoluble membrane and dissolve the medicinal substance or cause its swelling. In the first case, the medicinal substance diffuses through the film in the reverse direction, in the second case, the membrane ruptures, after which the medicinal substance is released in the usual way.

Dragee **-** solid dosed MF for internal use, which is obtained by multiple layering (dragging) of medicinal and auxiliary substances on sugar granules (grit). Dragees have

a spherical shape, weight 0.1 - 0.5 g. In the form of dragees, medicinal substances that are difficult to tablet are released. Dragee allows you to hide the unpleasant taste of medicinal substances, reduce their irritating effect, and protect against the influence of external factors. However, in this MF it is difficult to ensure dosage accuracy, disintegration in the required terms, and quick release of medicinal substances. Dragee is not recommended for children. In view of the above, this MF is not promising.

Pellets **-** this is MF in the form of round or cylindrical granules containing a mixture of medicinal and auxiliary substances (sugar, lactose, starch, glucose, talc, etc.). They are easy to swallow, which makes it possible to use them in pediatric practice.

Equipment: visual material, multimedia projector, presentation, sieve, grinding machine, mixer, dispenser (for example, auger), packaging container, examples of packaging .

Plan:

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

9. 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:

- purpose of tablet coating.
- types of coatings and their application technology.
- excipients used in the coating of tablets with shells.
- suspension method of teasing. Its advantages.
- requirements for the geometric shape of tablets-cores during Dragging.
- parameters affecting the process of covering tablets with shells during Dragging.

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. Film coatings. Types and properties. Application methods.
2. Pressed coatings. Stages of the technological process and equipment.
3. Definition of granules and dragees as dosage forms.
4. Excipients used in the production of granules and dragees.
5. Granule and dragee production technology.
6 . Quality control of granules and dragees

Lesson content

In case of unsatisfactory technological properties of powdered masses, namely, poor compressibility and flowability, granulation must be carried out in advance to ensure the required quality of the tablets.

Granulation is a directed agglomeration of particles, that is, it is a process of transformation of a powdery material into grains of a certain size, which is necessary for: 1) improving the flowability of the tablet mixture, 2) improving compressibility, 3) preventing delamination, 4) ensuring dosing accuracy, 5) reducing dustiness of workers premises

The following granulation methods are used in the chemical and pharmaceutical industry:

- Granulation by pressing, or wet granulation.
- Dry granulation or briquetting.
- Granulation is structural.
- Granulation is mixed.

Pressing granulation, or wet granulation, includes the following stages:

1) mixing medicinal powders with auxiliary substances;

2) moistening the mixture of powders with solutions of adhesives and binders to obtain a mass that forms a lump, but does not stick to the fingers;

3) obtaining wet granules, i.e. wiping the wet mass through perforated plates; drying of wet granules;

4) obtaining dry granules, for which the dry mass is rubbed through perforated plates to break up lumps and obtain homogeneous granules;

5) powdering of dry granules.

Wet granulation is currently the main type of granulation in the production of tablets, but it has a number of disadvantages:

- long-term effect of moisture on medicinal and auxiliary substances; deterioration of the ability to disintegrate (dissolution rate) of tablets;
- duration and complexity of the process;
- the need to use special equipment;
- energy intensity of the process.

Dry granulation, or briquetting, is used in those cases when medicinal substances in the presence of water or in the process of drying at an elevated temperature change their physical and chemical properties, decompose or lose their pharmacological activity.

So. briquetting is used for:

- hygroscopic materials that enter into a chemical reaction when moistened and undergo physical changes: hardening, softening, color change;

- thermolabile materials that, under the action of heating during drying, enter into chemical reactions of interaction or undergo physical changes: melting, softening, color change;

– substances with good compressibility, which do not require additional binding of particles with adhesives.

Briquetting is carried out as follows:

1. The medicinal substance is mixed with excipients.

2. From a mixture of powders, briquettes are pressed on tablet machines (briquetting machines) arbitrarily, that is, without observing a certain mass of tablets.

3. The resulting briquettes are crushed on ribbed rollers or mills.

4. The obtained powder is sifted on sieves with a hole size of 1-2 mm.

5. The resulting granulate is pulverized in mixers, after which tablets are pressed.

Structural granulation can be carried out in three ways:

- In the teasing cauldron.

- Spraying.

– In a fluid "boiling" layer.

The granulate in the brewing boiler is obtained as follows: medicinal and auxiliary substances are loaded into the brewing boiler and mixed at a speed of rotation of the boiler 30 rpm. Then, with the help of a nozzle, a solution of a binding substance is applied. Upon contact with the solution, small granules are formed. Then the boiler rotation speed is reduced to 3-5 rpm, and a stream of warm air is supplied to dry the granules. At the end of the process, slippery substances are added to the dried granulate. Granulation by spraying is carried out as follows: a suspension of auxiliary substances and a moisturizer (without medicinal substances) is prepared in advance and fed into the spray dryer using nozzles in the form of small drops. Drying is carried out with air at a temperature of about 150 °C. At the same time, granules with a size of 10-70 μm are obtained, which are then mixed with medicinal substances. Granules have good flowability and compressibility, so tablets obtained from such granulate have high strength and are pressed at low pressure. If there is a significant difference in the specific gravities of the granulate and the medicinal substance, delamination of the tablet mass is possible. As a result of excessive drying of the suspension, peeling of the upper part of the tablet ("capping") during pressing is also possible. When processing powdered drugs, the particle size of which is close to 100 nm, their ability to agglomerate under the action of special adhesion forces is used. The granulation plant is presented in fig. 5.6, works by the method of pseudo-liquefaction. It is a vertical cylindroconical apparatus made of stainless steel, in the lower part of which there is a bottom 13 made of stainless wire mesh. The diameter of the mesh holes is designed for the finest grinding of the drug. In the middle part of the apparatus, the walls of which

are polished to a mirror surface, there is a nozzle that moves in a vertical plane, 11. Depending on the properties of the granulating liquid, the type of nozzle and the type of pump are selected experimentally. The liquid intended for irrigation and granulation is supplied to the nozzle by a high-pressure pump. In the cylindrical part of the device there are bag filters 10 made of nylon, attached to the body of the device.

During granulation, air enters the filter sleeves and leaves in a purified form through valve 4 of the first segment to the outside. The settled dust is discharged into the chamber 8; cleaning is in progress.

According to the method of production, two types of tablets are distinguished - pressed and molded or triturated.

Tablets are also classified according to the structural feature:

1. By composition: simple (one-component) and complex (multi-component).

2. According to the structure of the building: frame, single-layer and multi-layer (at least 2 layers), with or without coating.

3. According to the nature of the coating: coated, film and pressed dry coating.

Tablets obtained by pressing have different shapes, weights and sizes. Round tablets with a flat or biconvex surface are most often produced. Pharmaceutical tablets have diameters ranging from 4 to 25 mm. Tablets with a diameter of more than 25 mm are called briquettes.

Tablets should have the correct shape, be whole, without jagged edges, their surface should be smooth and uniform. Tablets should have sufficient strength and should not crumble.

Direct pressing is a set of various technological techniques related to solving problems aimed at increasing the pressing of powders and achieving homogeneity of multicomponent mixtures.

At present, three methods of direct tableting are known: with the addition of appropriate excipients that improve the fluidity properties of the drugs, forced feeding of pressed substances into the matrix and pre-directed crystallization of the drugs.

The size, strength of the particles, pressing, fluidity, humidity and other properties of substances are of great importance for direct pressing. Thus, for obtaining sodium chloride tablets, the oblong shape of the particles is acceptable, and the round shape of this substance is almost impossible to press. The best fluidity is observed in coarse-dispersed powders with equiaxed particle shape and low porosity - such as lactose, phenyl salicylate, hexamethylenetetramine and other similar preparations included in this group. Because such drugs can be compressed without prior granulation.

The most common method of direct pressing is the addition of auxiliary substances to the pressed preparations, which improve the fluidity properties. As such, they use microcrystalline cellulose and its sodium salt, 30% whey, Sorbitan, a mixture

of anhydrous glucose, starch and calcium stearate, xylitol mixed with sugar, a mixture of mannitol with glucose and starch, Aerosil, a mixture of magnesium stearate and talc, and others.

The technology of preparing tablets consists in the fact that medicinal products are thoroughly mixed with the necessary amount of excipients and pressed on tablet machines. Pressing on tablet machines is carried out by a press tool consisting of a matrix and two punches. The disadvantage of this method is the possibility of delamination of the tablet mass, dosage changes when pressing a mixture with a small amount of active substances, and high pressure is used. Some of these disadvantages are minimized during tableting by forced feeding of pressed substances into the matrix. The implementation of this method by producing! by some structural changes of machine parts, i.e. vibration of the shoe, rotation of the matrix to a certain angle during the pressing process, installation of star-shaped mixers of various designs in the loading funnel, suction of material into the matrix hole using a self-forming vacuum or a special connection with a vacuum line.

Perhaps, the most promising will be the forced supply of pressing substances based on the vibration of loading funnels in combination with an acceptable design of the gel stirrer.

The issue of direct pressing would be solved more simply if the pressed preparations had a certain shape of particles, which ensures good fluidity and sufficient pressing. For this, directional crystallization is used in the synthesis process. This method is used to obtain acetylsalicylic and ascorbic acids.

But, despite the successes achieved in the field of direct pressing in the production of tablets, this method is used for a limited range of medicinal substances.

In the case of unsatisfactory technological properties of powder-forming masses, namely poor compressibility and flowability, granulation must be carried out beforehand to ensure the required quality of the tablets.

Granulation this is a directed consolidation of particles, i.e. E. This is the process of transforming a powdery material into grains of a certain size, which is necessary for: 1) improving the flowability of the mixture for tablets; 2) improvement of pressing; 3) prevention of delamination; 4) ensuring dosage accuracy; 5) reduction of dustiness of work premises.

The following granulation methods are used in the chemical and pharmaceutical industry:

1. Pressing granulation or wet granulation.
2. Dry granulation or briquetting.
3. Granulation is structural.
4. Granulation is mixed.

Wet granulation is currently the main type of granulation in the production of tablets, however, it has a number of disadvantages:

- Long-term exposure to moisture on medicinal and auxiliary substances;

deterioration of the disintegration (dissolution rate) of tablets; duration and complexity of the process;

- The need to use special equipment;

- Energy intensity of the process.

Dry granulation or briquetting is used in cases where medicinal substances in the presence of water or during drying at elevated temperature change their physical and chemical properties, decompose or lose pharmacological activity.

Yes, briquetting is used for:

1) hygroscopic materials that enter into a chemical reaction when moistened and undergo physical changes: hardening, softening, color changes;

2) heat-labile materials that, under the action of heating during drying, enter into chemical reactions of interaction or undergo physical changes: melting, softening, color change;

3) substances with good pressed properties, which do not require additional binding of particles with adhesives.

Structural granulation can be carried out in three ways:

1. In the teasing cauldron.

2. Spraying.

3. In a fluidized bed.

When tableting drugs, mixed granulation is often used, which is a modified method of wet granulation, where there is no operation of wiping the wet mass.

Auxiliary substances in the production of tablets give the mass the necessary technological properties, good dosing and pressing and ensure the production of tablets of the required quality. The range and basic norms of auxiliary substances are defined in GF 11 edition. (general article "Tablets") and private articles.

Auxiliary substances are divided into groups depending on the indication: fillers (thinners), binders, looseners, antifreeze substances, film formers, corrigents, plasticizers, extenders and solvents.

The following requirements apply to excipients:

they must be chemically indifferent;

should not have a negative impact on the patient's body and on the quality of tablets during their preparation, transportation and storage.

10. 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 tablets of hexamethylenetetramine 0.3 g by direct pressing

Composition per tablet:

Hexamethylenetetramine - 0.30 g
Potato starch -0.03 g
Tablet weight: 0.33 g

Task No. 2 . Preparation of 0.5 g analgin tablets by pressing with prior granulation
Composition per tablet:
Analgin - 0.500 g
Ground medical talc - 0.013 g
Calcium stearate - 0.005 g
Potato or corn starch - 0.002 g
The weight of the tablet is 0.520 g

— 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.	Covering tablets with shells	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. – P. 110 – 113.
2.	Rolled, film, pressed coverings.	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. – P. 113 – 124.
3.	Quality control of tablets	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. – P. 124 – 125.
4.	Packing, packaging and storage conditions of tablets	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. – P. 125 – 126.

— 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 No. 1 . Preparation of mukaltin tablets 0.05 g by pressing with preliminary granulation

Composition per tablet:

Mukaltin - - 0.050 g

Sodium bicarbonate - 0.087 g

Food citric acid - 0.020 g

Calcium stearate - 0.003 g

Sugar -0.140 g

The weight of the tablet is 0.300 g

Task No. 2 . Preparation of tablets of streptocide 0.3 g by pressing with preliminary granulation

Composition per tablet:

Streptocide - 0.30000 g

Potato starch - 0.02446 g

Calcium stearate or stearic acid - 0.00224 g

Sugar - 0.00330 g

The weight of the tablet is 0.33,000 g

11. 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. Khohlova etc. - Kh.: NFaU, 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 "KROK 2. Pharmacy" / O.A. Ruban, V.D. Rybachuk, L.M. Khokhlova, D.S. Pulyaev - Kh.: NFaU, 2016. - 63 p.
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- 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.
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- Encyclopedia of Pharmaceutical Technology: 3-d Ed. / ed. by J. Swarbrick. – New York; London: Informa Healthcare, 2007. - 4128 p.
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Practical lesson No. 29-31

Topic: "Production of medical capsules"

Goal: Study the industrial production of gelatin capsules and microcapsules, master their production technologies, conduct quality control, packaging and labeling of the finished product

Basic concepts: *The term "capsules" refers to two types of factory-produced products:*
1) special tanks made of gelatin mass for placing different doses of medicinal substances in them;
2) ready dosed MF - gelatin capsules and microcapsules filled with powdered, granular, pasty and liquid medicinal substances.

Hard capsules are intended for dosing loose powdery and granular substances. They have the shape of a cylinder with hemispherical ends and consist of two parts: a body and a cover; both parts freely fit into each other without creating gaps.

Soft capsules - for liquid and pasty medicinal substances. They have a spherical, ovoid, oblong or cylindrical shape with hemispherical ends.

Obtaining soft gelatin capsules. It consists of the following operations:

- preparation of gelatin solution;
- production of capsule shells;
- filling of capsules;
- sealing of capsules;
- capsule control;
- drying capsules;
- capsule grinding;
- washing capsules;
- regeneration of rejected capsules.

Tubatins are children's LF, which are soft gelatin capsules with an "extended neck" and are intended for small children who cannot swallow pills. When biting the neck of the capsule, the child sucks out the contents.

Spansules are hard gelatin capsules for internal use, containing a mixture of microcapsules (microdrags) with different drug dissolution times, i.e. prolonged action.

Equipment: visual material, multimedia projector, presentation, methodological developments, laboratory utensils, electronic dispenser, electric soldering iron, pipette, drying cabinet .

Plan:

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

13. 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:

1. Definition of capsules as a dosage form.
2. Types of capsules, their purpose.
3. Methods of making capsules. The equipment used.
4. Characteristics of soft gelatin capsules. Tubatins.

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 . Technological scheme of production of soft gelatin capsules.
2 . Characteristics of hard gelatin capsules.
3 . Packaging and storage of capsules.
4. Characteristics of the microcapsule shell, its varieties.
5. Physical methods of microencapsulation.
6 . Characteristics of chemical methods for obtaining microcapsules.
7 . Standardization of microcapsules.
8. Medicinal forms from microcapsules

Lesson content.

Currently, LF encapsulation is becoming widespread. Capsules are a dosed LF consisting of medicinal raw materials enclosed in a shell. They are intended for oral, less often rectal and vaginal use. Capsules can be transparent or opaque, colored or uncolored, but they must not have air inclusions, mechanical contamination, dents and overflows. Permissible deviations of the average weight of each capsule should not exceed ± 10%, unless otherwise specified.

MICROCAPSULES

Microencapsulation is a technological process of placing microscopic solid, liquid or gaseous substances in a thin shell, which ensures their isolation from the external environment.

Microcapsules have the form of individual particles or agglomerates with a size of 1 to 5000 μm. In medical practice, microcapsules with a size of 100 to 500 μm are most often used.

The technology of shell formation has recently improved so much that it allows coating on particles smaller than 1 micron. Such particles with a shell are called nano-capsules, and the process of their formation is called nanoencapsulation.

The shape of microcapsules is determined by the state of aggregation of their contents and the method of production: liquid and gaseous substances give microcapsules a spherical shape, solid ones - an oval or irregular geometric shape.

In the pharmaceutical industry, microencapsulation has become widely used. With its help, they stabilize unstable drugs (vitamins, antibiotics, vaccines, serums, enzymes), mask the taste of unpleasant medicinal substances (castor oil, fish oil, aloe extract, caffeine, chloramphenicol, benzedrine), turn liquids into liquid products, regulate the speed release or ensure the release of a biologically active substance in the required area of the gastrointestinal tract, isolate incompatible substances, improve flowability, create new types of products for diagnostic purposes.

Most pharmaceuticals are produced in microencapsulated form to increase the duration of the therapeutic effect when administered orally into the body with a simultaneous decrease in the maximum level of concentration of the drug in the body. In this way, it is possible to reduce, at least by half, the number of doses of the drug and eliminate the irritating effect on tissues due to the adhesion of tablets to the walls of the stomach. Gastrolabile drugs are placed in shells, stable in acidic environments, which are destroyed in slightly alkaline and neutral environments of the intestines.

An important area of application of microencapsulation in pharmacy is the combination in one dose of medicinal substances that are incompatible when mixed in the free state. Microencapsulated drugs are better stored and more convenient to dose.

STRUCTURE OF MICROCAPSULES

Microcapsules consist of the substance to be encapsulated and the material from which they are made, the shell. The substance that is encapsulated is called the content and forms the core of the microcapsule, while the encapsulating material forms the shell.

The content of microcapsules (internal phase, or core) can be 15-99% of their mass. It can vary depending on the method and conditions of production (temperature, degree of dispersion, viscosity of the medium, presence of surface-active substances), the ratio of the quantities of the shell material and the encapsulated substance, etc. The internal phase can be an individual substance, mixtures, dispersions or solutions of substances. The composition of the contents of microcapsules can include an inert filler as a medium in which the active substance was dispersed, or it is necessary for the further functioning of the main component of the core.

The thickness of the shell varies from 10 to 200 μm and can be single-layer or multi-layer, elastic or rigid, with different resistance to the action of water, organic solvents, etc. The thickness of the walls of the microcapsules decreases with an increase in the amount of encapsulated substance or a decrease in the size of the microcapsules themselves.

A large number of natural and synthetic compounds that form a film are used for microcapsule shells. These shells adhere well to the encapsulated substance, providing tightness, elasticity, some permeability, strength and stability during storage. Most substances are inert under normal conditions and approved for medical use. Typical shell materials are organic polymers: proteins (gelatins, albumin), polysaccharides (dextran and gums), waxes, paraffin, cellulose derivatives (methyl-, ethyl-, acetyl-, acetylphthalyl-, nitro-.carboxyethyl substituted), polyvinyl alcohol, polyvinyl acetate , polyvinyl chloride, polyethylene and others, polyacrylamide, , polysulfides, polycarbonates, polyesters, polyamides, various copolymers, as well as inorganic materials — metals, carbon, silicates, etc.,

By solubility, shell materials are divided into water-soluble (gelatin, gum arabic, polyvinylpyrrolidone, polyacrylic acid, etc.), water-insoluble (silicones, latexes, polypropylene, polyamide, etc.), water-soluble (zein, shellac, spermaceti, acetylphthalyl cellulose, etc.) .

The choice of shell material depends on the purpose, properties and method of core release, as well as on the chosen microencapsulation method.

According to the technological principle and depending on the content of plasticizers, 2 types of capsules are distinguished: hard and soft.

Soft capsules can have a spherical, ovoid, oblong or cylindrical shape with hemispherical ends, with or without a seam. Capsules can be of different sizes, with a capacity from 0.1 to 1.5 ml. They encapsulate viscous liquids, oil solutions, and paste-like liquids that do not interact with the mold-forming substance - gelatin. The contents of the capsules can consist of one or more drugs with the possible introduction of various BBs approved for medical use. Production of soft capsules in factory conditions is carried out by two methods: drip and pressing. In laboratory conditions, it is allowed to obtain soft capsules by the immersion method.

Hard capsules are intended for dosing loose powdery, granular and microencapsulated substances. They have a cylindrical shape with hemispherical ends and consist of two parts - a body and a cover, which should fit freely into each other without creating gaps. They can have special grooves or protrusions to provide a "lock". Depending on the average capacity, they are produced in 8 sizes (GF 11 p. 143). Hard capsules are obtained by the dipping method.

The production of capsules is a complex technological process and consists of the following main stages:

For hard capsules For soft capsules Preparation of gelatin mass

- Manufacturing (forming) of capsule shells Manufacturing of capsule shells, their filling and sealing;

Drying capsule halves, removing from pins Washing and drying capsules

- Assembly of capsule halves Standardization, packaging and labeling of finished products

Filling capsules

- Standardization, packaging and labeling of finished products

Technological schemes for obtaining drugs in soft and hard capsules differ, therefore, the filling of soft capsule shells is carried out immediately after their manufacture, and hard capsules - after their drying and packaging. In most cases, the process of filling hard capsules can be carried out at other enterprises.

Film-forming high-molecular substances capable of creating elastic films and having a certain strength are used to obtain capsules. Gelatin is one of the most common molding materials for the production of capsules. To obtain a stable capsule shell, the composition of the gelatin base may include various substances: plasticizers (glycerin, sorbitol, etc.), stabilizers (sodium metabisulfite, sodium benzoate), preservatives (salicylic acid, nipagin), flavoring substances (ethyl vanillin, fruit essences, ether oils), dyes (tartrazine, indigo, acid red 2C), pigments (white titanium dioxide).

Evaluation of the quality of capsules is carried out in accordance with the requirements of the State Federal Office of Ukraine, SPh 11 edition. or other NTD. Capsules must be issued from a tightly closed package that protects against the influence of moisture. Contour, glass or polymer containers are most often used.

Among other encapsulated LF, it is necessary to single out tubatins, rectal capsules and spansules.

Tubatins are children's MF, which are soft gelatin capsules with an "extended neck" and are intended for small children who cannot swallow pills. When biting the neck of the capsule, the child sucks out the contents.

Rectal gelatin capsules are one of the types of soft capsules. Rectal capsules have the form of an "elongated" drop with a volume of 0.6 ml to 1.8 ml and consist of a thin layer of gelatin, the surface of which becomes slimy when moistened with water, which facilitates its use. Unlike fat suppositories, such capsules are resistant to elevated temperatures (45-50 ° C), release LV much faster, and do not have an irritating effect on the intestinal mucosa. The gelatinous membrane swells under the influence of the weakly basic secretion of the rectum (pH 7.3 - 7.6), and in such a state, even weak peristalsis of the walls of the rectum is sufficient for its rupture at the place of the suture and the release of the contents.

Spansules are hard gelatin capsules for internal use, containing a mixture of microcapsules (microdrags) with different drug dissolution times, i.e. prolonged action.

Microcapsules are individual spherical or rounded particles with a diameter of 5 to 5000 μm (more often 100-500 μm), covered with a thin shell of film-forming

material of various nature. Particles smaller than 1 μm are called Nanocapsules. The content of microcapsules (internal phase or core) can reach 15-99% of their mass. This value may vary depending on the method and conditions of production (temperature, degree of dispersion, viscosity of the medium, presence of surfactant), the ratio of the quantities of the shell material and the encapsulated substance, etc. The internal phase may be an individual substance, mixtures, dispersions or solutions of substances.

Microencapsulation is widely used in the pharmaceutical industry. With its help, they stabilize unstable drugs (vitamins, antibiotics, vaccines, serums, enzymes), mask the taste and smell of drugs (castor oil, fish oil, aloe extract, caffeine, chloramphenicol, benzedrine), turn liquids into loose products, regulate the speed release or ensure the release of BAS in the required area of the gastrointestinal tract, isolate incompatible substances, improve flowability, create new types of products for diagnostic purposes.

The thickness of the shell varies from 0.1 to 200 μm and can be single-layer or multi-layer, elastic or rigid, with different resistance to the influence of water, organic solvents, etc. The choice of shell material depends on the purpose, properties and method of core release, as well as on the chosen microencapsulation method.

The same factors determine the structure of microcapsules. Currently, the following main types of microcapsules are distinguished:

• With one shell; double or multi-layer shell. If, for some reason, the shell material cannot be applied directly to the encapsulated substance, then intermediate microencapsulation of this substance in another material is produced by a convenient method. The creative shell has a two-layer structure.

• "Capsule-in-capsule" and emulsion in microcapsules or microcapsules in a liquid medium in a common shell. If it is necessary to enclose substances in a common shell, it is possible to make "capsules in a capsule", when one or more microcapsules of another substance are placed inside the outer shell in the environment of one of the substances.

Depending on the purpose and properties of microencapsulating substances, there are 3 types of permeability of microcapsule shells:

• impermeable to the core and environment;

• semi-permeable;

• permeable to the nucleus.

The release of LV from microcapsules is largely determined not only by the chosen material and the permeability of the shell, but also by the method of microencapsulation, which can be divided into three main groups: physical, physicochemical, and chemical.

The essence of physical methods of microencapsulation consists in the mechanical application of a shell on solid or liquid particles of LR. Physical methods include sputtering in a pseudo-fluidized layer or in a vacuum, extrusion, spraying, coating, dispersing, etc.

Physico-chemical methods of microencapsulation are based on the single phase relationship and are characterized by simple equipment, high productivity, and the ability to encapsulate LR in any aggregate state (solid, liquid, gas). They make it possible to obtain microcapsules of various sizes and with specified properties, as well as to use an exceptionally wide range of film-formers and to obtain shells with different physical and chemical properties (of different thickness, porosity, elasticity, solubility, etc.). When obtaining microcapsules by these methods, LR is dispersed in a solution or melt of a film-forming substance.

Chemical methods of encapsulation are based on the formation of protective coatings around the cores of the microencapsulated substance as a result of polymerization or polycondensation of film-forming components.

It should be emphasized that such a classification, which is based on the nature of the processes occurring during microencapsulation, is quite conditional, since a combination of different methods is often used in practice.

The quality of the obtained microcapsules is evaluated according to the following parameters: organoleptic indicators, fractional composition, bulk mass, flowability, relative density, rate of release of contents from microcapsules, qualitative and quantitative BAC content.

Currently, the range of areas of practical use of microencapsulated drugs is very large - from medicine to space research. In medicine, microcapsules themselves, as MF, are used extremely rarely, but they are often included in the composition of other MF. On the basis of microcapsules, such MF as emulsions, suspensions, ointments, suppositories, retard capsules, retard tablets, preparations for paraetheral use are made. Research is ongoing on the use of microcapsules in injectable and ophthalmic forms, implantable tablets and other long-acting medicinal systems.

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 VMS 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.

14. 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 1. Preparation of gelatin mass to obtain soft capsules (without gelatin swelling process)

Storage:

Gelatin 26%

Glycerin 8%

Sorbitol 5%

Nipagin 0.2%

Purified water 60.8%

Preparation.

Task 2. Obtaining shells and research of soft gelatin capsules

Preparation.

Task 3 **.** Obtaining shells and studying hard gelatin capsules

Preparation.

Task No. 4. Preparation of chloramphenicol microcapsules by simple coacervation method

Description.

Preparation.

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— 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.	Modern classification and general characteristics of the dosage form - gelatin capsules	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. – P. 158 – 170.
2.	Production of soft gelatin capsules	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. – P. 164 – 166.
3.	Production of hard gelatin capsules	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. – P. 164 – 166, 170 - 172.
4.	Machines for filling capsules	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. – P. 172 – 177.
5.	Quality control and packaging of capsules	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. – P. 177 – 178.

— 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):

15. 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. Khohlova etc. - Kh.: NFaU, 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 "KROK 2. Pharmacy" / O.A. Ruban, V.D. Rybachuk, L.M. Khokhlova, D.S. Pulyaev - Kh.: NFaU, 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.: NFaU: 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.: NFaU: 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 NFaU, 2006. - 100 p.
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- Encyclopedia of Pharmaceutical Technology: 3-d Ed. / ed. by J. Swarbrick. – New York; London: Informa Healthcare, 2007. - 4128 p.
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Practical lesson No. 32-34

Topic: " Industrial production of soft drugs "

Goal: To study the definition of emulsion, suspension as a dosage form, scope of application. Features of preparation of emulsion and suspension preparations. Production methods and equipment used in the production of suspensions and emulsions

Basic concepts: *Ointment* — a soft medicinal form for external use. The ointment consists of a medicinal substance and the so-called medicinal base (vaseline, lanolin, naphthalene, etc.). In their basis, ointments contain fats (pork, beef).

Cream is an emulsion containing half water and half oil. Creams also contain solid particles of drugs intended for absorption by the skin.

Gel is a structured system consisting of high-molecular and low-molecular substances.

The paste is a suspension ointment with the amount of powdery substances, in accordance with the recommendations of the Federal State Administration of Ukraine, more than 20% (previously 25%).

Liniments - medicinal form for external use only (more often, by rubbing) is a liquid ointment or a mixture of various irritating substances with oils, oils with alkali solutions, soap-water or soap-alcohol solutions.

Homogeneity is one of the key properties of space in classical mechanics. It means that the parallel transfer of the closed frame of reference in it as a whole does not change the mechanical properties of the system, and, in particular, does not affect the result of measurements.

Sterility is the absence of viable microorganisms and their spores in the environment, organism, any material or product.

Homogeneous ointments are systems characterized by the absence of an interphase interface between medicinal substances and the base of the ointment.

Heterogeneous ointments are systems that have a phase separation with different boundary layers. These include suspension (or trituration), emulsion and combined ointments .

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

Plan:

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

17. 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;
- the subject and tasks of the technology of production of soft dosage forms;
- basic concepts of the technology of industrial production of soft dosage forms;
- basic requirements for the process of industrial production of soft 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. What are soft dosage forms and their classification
2. Definition of emulsion, suspension, as MF, scope of application.
3. Features of preparation of emulsion and suspension preparations.
3. Method of obtaining and equipment used in the production of soft dosage forms .
4. By what methods are suspensions and emulsions obtained at pharmaceutical factories?
5. What factors determine the stability of suspensions and emulsions?
6. What role do auxiliary substances play in the production of suspensions and emulsions
7. What stages does the process of obtaining dispersion preparations consist of?
8. What preparations are used in the production of suspensions and emulsions?
9. What is the principle of operation of turbine mixers and RPA? B. Tests for self-control with standard answers. B. Tasks for self-control with answers.

Lesson content

Soft drugs for external use are intended for local action or transdermal delivery of active substances, or for emollient or protective action. They should be uniform in appearance. Soft medicinal products for external use consist of a simple or complex base, in which one or more active substances are usually dissolved or dispersed. Depending on the composition, the base can affect the activity of the medicinal product. The base can consist of natural or synthetic substances and can be single-phase or multi-phase. According to the nature of the base, the drug can exhibit hydrophilic or hydrophobic properties; it may contain suitable excipients such as antimicrobial preservatives, antioxidants, stabilizers, emulsifiers, thickeners and penetrants.

Soft medicinal products intended for use on skin with severe damage must be sterile.

Containers for soft drugs for external use must meet the requirements of the articles "Materials used for the manufacture of containers" (3.1 and subsections) and "Containers" (1.2 and subsections), unless otherwise specified in a separate article.

In accordance with the requirements of the Federal Drug Administration, soft medicinal products for external use can be classified into:

· ointments,
· creams,
· gels,
paste,
poultices,
· medical plasters,

· skin patches.

Depending on their structure, ointments, creams and gels usually exhibit viscoelastic properties, and at high shear rates have a non-Newtonian type of flow, for example, plastic or pseudoplastic, and exhibit thixotropic properties. Pastes often show dilatancy.

When developing soft medicinal products for external use, which include antimicrobial preservatives, the authorized body must be provided with data confirming the need for use and the effectiveness of the selected preservatives. The method of determination and criteria for evaluating the effectiveness of preservatives must meet the requirements of the article "Effectiveness of Antimicrobial Preservatives".

During the production, packaging, storage and sale of soft medicinal products for external use, appropriate measures must be taken to ensure the necessary microbiological purity in accordance with the requirements of the article "Microbiological purity of medicinal products" (5.1.4). Sterile soft medicinal products for external use are manufactured using materials and methods that ensure sterility, prevent contamination of medicinal products and the growth of microorganisms in accordance with the requirements of the article "Methods of preparation of sterile products" (5.1.1).

When developing soft medicinal products for external use in single-dose containers, it should be confirmed that the nominal content can be withdrawn from the container. In the production of soft medicinal products for external use, measures must be taken to ensure compliance with the established rheological properties. If necessary, the following optional tests can be used: consistency measurement by penetrometry, viscosity determination (relative viscosity) and a suitable test that confirms the appropriate release of the active substance/substances.

In the production of soft drugs for external use, which contain one or more active substances that are not soluble in the base (for example, emulsions or suspensions), it is necessary to take measures to ensure the uniformity of the obtained drug. In the production of soft medicinal products for external use, which contain dispersed particles, measures should be taken to ensure the required particle size depending on the intended use and its control.

TRIAL

Homogeneity of dosage units. Soft medicinal products for external use, produced in single-dose containers containing 1 dose of the drug, or in containers with a dosing device, and intended for transdermal delivery of the active substance or substances must pass tests for the uniformity of the dosage units. Soft medicinal products, in which the active substance or substances are dissolved, must pass the test by the calculation-weighing method, and soft medicinal products, in which the active substance or substances are in the form of suspensions, by the method of direct determination of the

homogeneity of the content. Tests are carried out as indicated for liquid dosage forms. This test does not apply to medicinal products containing herbal medicinal products and raw materials.

For soft medicinal products produced in containers with a dosing device, which contain the active substance/substances, in the form of a solution, must withstand such a test. The dose is released and discarded. After at least 5 seconds, the container is shaken for 5 seconds, the dose is released and discarded. The specified operation is repeated three more times. After that, the container is weighed, the dose is released and the container is weighed again. The mass of an individual dose is calculated as the difference of two masses. The above procedure is repeated for nine more containers. The homogeneity of the content of the active substance is determined by the calculation-weight method.

Soft medicinal products released in containers with a dosing device, which are suspensions, must withstand such a test. They use a device that allows you to quantitatively hold the dose after pressing the valve of the spraying device.

Shake the container for 5 seconds, release the dose and throw it away. After at least 5 seconds, shake the container again for 5 seconds, release the dose and discard it. The specified operation is repeated three more times. After 2 s, press on the valve, directing the dose of the drug into the sample collection. The contents of the collection are combined by successive washings and the content of the active substance in the combined solution is determined. The above procedure is repeated for nine more containers. The homogeneity of the content is determined by the method of direct determination.

STERILITY .

If the label states that the drug is sterile, it must pass the sterility test.

Storage

If the medicine contains water or other volatile components, store in airtight containers. Sterile medicinal products - in sterile, airtight containers with control of the first opening.

Marking

The label states:

- name of all excipients;
- sterile, if necessary.

Ointments belong to the number of ancient medicinal forms that are widely used in everyday life, in various industries, in cosmetics and medicine in order to protect the skin of the hands and exposed parts of the body (face, neck) from the effects of organic solvents, solutions of acids, alkalis and other chemical irritants and allergens; for softening the skin, nourishing it with vitamins, fats, for removing pigment spots, treating and removing hair, warts, moles and other cosmetic defects.

A special place is occupied by ointments widely used in various fields of medicine: dermatology, gynecology, proctology, laryngology, etc. Sometimes ointments are prescribed as drugs of general action for the purpose of resorption, that is, the absorption of medicinal substances contained in them into the thickness of the skin, subcutaneous tissue or even into the bloodstream.

In modern pharmacies, ointments make up an average of 10-15%. they are applied to the skin, wounds, mucous membranes by smearing, rubbing or using bandages; sometimes tampons soaked in ointment are inserted into body cavities, or special syringes are used.

Ointment is a soft medicinal form intended for application to the skin, wounds or mucous membranes.

Ointments consist of a base and medicinal substances evenly distributed in it. Preservatives, surfactants and other auxiliary substances approved for medical use may be added to the ointment.

According to the physico-chemical classification: ointments are free comprehensively dispersed formless (structureless) or structured systems with a plastic-elastic-viscous dispersion medium. At room temperature, due to high viscosity, ointments keep their shape and lose it when the temperature rises, turning into thick liquids. They differ from typical liquids in the absence of noticeable fluidity.

Ointments as a medicinal form have their positive and negative qualities. Positive qualities: the possibility of introducing various medicinal substances (liquid, soft, solid) into the composition of ointments; the possibility of prescribing ointments with the purpose of local or resorptive action; achieving a high concentration of medicinal substances in the skin, tissues, biological fluids of the body: relative simplicity and safety of using ointments in comparison with other medicinal forms (injectable, oral, etc.); economy and manufacturability of ointments.

Negative qualities: some ointments have a limited spectrum of pharmacological activity (one-way therapeutic effect, for example, only anti-inflammatory); certain compounds of ointments on hydrophobic bases cause a pronounced "greenhouse" effect, which limits their use in medical practice; some ointments irritate the skin.

Requirements for ointments. Ointments must have certain consistent properties characterized by rheological parameters: plasticity, viscosity, relaxation period, which largely depends on the degree of pharmacodynamics of ointments.

The soft consistency of ointments ensures the convenience of their application when smeared on the skin, mucous membranes, as well as the release of medicinal substances from them. Rheological parameters serve as a criterion for evaluating the quality of ointments both during production and during their storage.

Ointments should have optimal dispersion of medicinal substances and their uniform distribution, which guarantees the maximum therapeutic effect and the stability of the compound during storage. At the same time, they must be stable, without extraneous impurities and with the exact concentration of medicinal substances.

CLASSIFICATION OF OINTMENTS

There is a medical and physico-chemical classification of ointments. According to the medical classification, ointments are divided by action and place of application. Depending on the action, ointments of superficial and deep action are distinguished.

Ointments of surface action are ointments that are not absorbed by the skin, the effect of which is limited mainly to the epidermal layer or the surface of the mucous membrane. These include covering, protective and cosmetic ointments.

Coverings soften dry epidermis, prevent its drying and contamination, protect damaged skin from microbial infection.

Protective ones are similar in purpose to covering ones. They are used for preventive purposes in various industries. They must protect the skin from exposure to poisonous substances, solutions of acids and alkalis, solvents and other aggressive liquids.

Cosmetic ointments and creams are intended for the treatment or elimination of cosmetic skin defects.

Deep-acting ointments are absorbed by the skin and are divided into penetrating and resorptive.

Ointments that penetrate to more or less deep layers of the skin are classified as penetrating. The degree and depth of their penetration into the skin depend on the type of ointment base, properties of medicinal substances included in their composition, methods of application and other conditions.

Of the ointment bases, only lipid-soluble ones penetrate the skin, and vegetable and animal fats, close in composition to human skin fat, penetrate better than others. Vaseline and other hydrocarbons do not penetrate the skin by themselves. The main barrier for absorption is the epidermis layer. The dermis, rich in lymphatic and blood vessels, does not prevent absorption.

The penetration of ointment bases and medicinal substances into the deep layers of the dermis occurs, presumably, mainly through the ducts of the sebaceous glands. Ointment bases penetrate much worse into healthy skin with an intact epidermis than into skin deprived of the epidermis as a result of an injury, a painful process, etc.

Medicinal substances contained in the ointment penetrate healthy skin to varying degrees. Volatile (iodine, mercury, essential oils), soluble in lipids (bases of alkaloids and some other substances) usually penetrate deeply. On the contrary, medicinal substances that are not soluble in lipids penetrate the skin much worse. Medicinal substances contained in the ointment in a dissolved form act more intensively than those contained in the form of a suspension. Penetration of medicinal substances from ointments applied to damaged skin with the epidermis removed is approximately the same as from ointments applied to the mucous membrane. Penetrating ointments are, for example, ointments with antibiotics.

Ointments with resorptive effect differ in that the medicinal substances contained in them penetrate from the place of application of the ointment into the bloodstream. They are used mainly in those cases when it is necessary to strengthen or supplement the effect of the drug taken orally, or when another method of administration is inconvenient or impossible.

Resorption of medicinal substances differs from their penetrating action. It depends mainly on the chemical structure of medicinal substances and to a lesser extent on the type of ointment base. Deeper resorption, as well as penetration, is observed for substances soluble in lipoids. Ointments with a resorptive effect include, for example, "Nitrong" ointment (contains a 2% oil solution of nitroglycerin and is used to prevent angina attacks), as well as ointments containing some hormones, vitamins, alkaloids, etc.

According to the place of application, ointments are distinguished: dermatological (ointments actually), applied to the skin; ophthalmic, applied to the conjunctiva of the eye; for the nose, applied to the mucous membrane of the lower concha; vaginal, urethral and rectal. The last three types of ointments are administered using special syringes.

According to the physicochemical classification, ointments are divided by consistency, type of dispersion systems and ointment bases.

Depending on the consistency, the following are distinguished: liquid ointments (or liniments), creams, gels, actual ointments, thick ointments - pastes, dry semi-finished ointments intended for dilution with water or fats.

Homogeneous and heterogeneous ointments are distinguished by the type of dispersion systems (depending on the degree of dispersion of the medicinal substance and the nature of its distribution in the base).

Homogeneous ointments are systems characterized by the absence of an interphase interface between medicinal substances and the base of the ointment.

In this case, the medicinal substance is distributed in the base according to the type of solution, that is, brought to the molecular or micellar level of dispersion. Homogeneous include: ointments-solutions, ointments-alloys and extraction ointments.

Heterogeneous ointments are systems that have a phase separation with different boundary layers. These include suspension (or trituration), emulsion and combined ointments.

The different physical state of medicinal substances in ointments is mainly explained by their properties (solubility or insolubility in water and oil, etc.), depending on which the corresponding type of ointment is formed.

According to the type (character) of ointment bases, ointments prepared on: hydrophobic (lipophilic), hydrophilic and diphilic (hydrophilic-lipophilic) bases are distinguished.

Thus, the medical classification gives a general idea of ointments (purpose, application, etc.), and the physicochemical classification reflects the technology of ointments and their quality criteria.

BASES FOR OINTMENTS, REQUIREMENTS FOR THEM AND THEIR CLASSIFICATION

Ointment bases can be in the form of individual or a sum of various substances that determine the required volume, appropriate consistency and some specific features of the ointment. Due to its consistency, the base is an excellent lubricant for the skin, which makes it soft, smooth, elastic and protects it from drying out. Under the action of the base, the natural fatty protection of the skin is strengthened, cracks and sores heal faster, water evaporation decreases, due to which the stratum corneum swells and natural heat is retained, which achieves significant protection against humidity and cold. The last circumstance is of significant importance for swimmers who are in the water during the competition. In addition, the foundations absorb external contamination of the skin well and facilitate its removal.

Pork fat is easily mixed and fused with other fats, waxes, hydrocarbons, resins and fatty acids, does not lose an ointment-like consistency when absorbing up to 20% of water (due to the presence of a small amount of cholesterol). Under the influence of external factors (heat, light, air oxygen, etc.), pork fat easily turns bitter, acquiring an unpleasant smell, an acidic reaction and an irritating effect.

Although lard is one of the best bases for ointments, its use is very limited because it is a food product.

SPh of Ukraine IX recommends the use of fat in the preparation of sulfuric acid ointment, potassium iodide ointment, and mercury gray ointment. The latter is prepared with the addition of beef fat.

Beef fat (*Sebum bovinum*) belongs to the group of solid fats, as it contains up to 58% triglycerides of solid saturated fatty acids palmitic and stearic and relatively little triglycerides of unsaturated linoleic acids. It has a yellowish color and a weak smell, its melting point is 42-52 °C. At room temperature, it is hard and brittle, which is why it is unsuitable as an ointment base in its pure form. Sometimes it is used to thicken fat-based ointments.

Lamb fat has similar properties and uses.

Goose fat (*Adeps anserinum*) - a soft mass of yellowish-cream color with a melting point of 26-34 °C; belongs to the number of difficult-to-congeal fats, is used in the composition of ointments for frostbite.

Vegetable fats (oils). Most of the vegetable fats belong to the number of liquids, so they are not used in their pure form as bases. They are widely used as additives to solid bases (fats, waxes, hydrocarbons), forming alloys of a soft consistency. In the technology of ointments, oils are used: almond, apricot, peach, sunflower, plum, cotton, olive, etc.

However, technical, low-refined hydrocarbons should be used carefully to avoid negative effects on the skin or mucous membranes.

Silicone bases. The works of M. T. Alyushin marked the beginning of the use of silicone fluids as a base for ointments. Currently, our industry produces polydimethyl, polydiethyl and polymethylphenyl silicone fluids.

Of the listed silicone fluids, polydiethyl siloxanes have the best compatibility with medicinal substances and other base components. They are mixed with petroleum jelly or vegetable oils (except castor oil), fused with petroleum jelly, paraffin, ceresin, fats, spermaceta, wax, etc.

Menthol, camphor, phenyl salicylate, tar, phenol and other medicinal substances dissolve well in polydiethylsiloxane liquids.

Unlike fatty oils, silicone fluids do not become bitter during storage. They are also used for the production of protective ointments and creams, because they do not get wet with water and do not decompose under the influence of mineral acids.

The introduction of MCs in fat-based ointments gives them hydrophilicity and a faster release of medicinal substances, improving the contact of medicinal substances with the affected areas of the skin. Possessing adsorption properties, MC absorbs various types of secretions from damaged skin and creates a protective film on the surface of the skin. MC is compatible with many medicines.

Sodium carboxymethyl cellulose (Sodium-KMC). Solutions of sodium-CMC as a basis for ointments are used in a limited way, although they have prospects.

Bases based on MC and sodium-CMC are usually obtained by mixing them with glycerin according to the following instructions:

1) methylcellulose 6.0 g, glycerin 20.0 g, water 74 ml;

2) sodium-CMC 6.0 g, glycerin 10.0 g, water 84 ml. Preservatives are added to the bases. Other cellulose derivatives produced in the production plant deserve attention

scale

Bases from clay minerals. The composition of clays and argillaceous rocks includes the most characteristic and specific minerals for them: kaolinite - the main mineral of medical white clay, montmorillonite-bentonite clays, etc. They consist of 90% of oxides of silicon, aluminum, iron, magnesium and water. Calcium, sodium, potassium, and titanium oxides are also included in minerals in small quantities. Some of these oxides are absent in some minerals.

For pharmaceutical purposes, bentonite and other clay minerals should be used completely free of coarse impurities and sand. This is achieved by desilting followed by drying (and simultaneous sterilization) of the mineral powder.

According to their condition, clay minerals are highly dispersed systems. They are characterized by an active physical and chemical interaction with water (they swell and hold it firmly). So, for example, sodium forms of bentonite swell when wet with water,

increasing in volume by 15-18 times. The formed soft gels are well distributed on the skin and accept many medicinal substances, because they have chemical indifference.

The ability of bentonite to turn into a gel upon adding water makes it possible to use it for the production of dry concentrates in the form of powders or tablets.

According to the simplest prescriptions, the bentonite base consists of 13-20% of the sodium form of the mineral, 10% of glycerin and 70-77% of water.

Phytosterol bases. Phytosterol is a white or slightly yellowish powder, oily to the touch, obtained during the hydrolysis of pine wood.

When shaken with hot water, it swells and absorbs up to 120% of water, forming ointment-like products of various densities, has the ability to stabilize emulsion systems.

For the production of ointments, a base consisting of phytosterol (12-15%) and water (85-88%) is proposed. Phytosterol is mixed with cold water and the mixture is heated to 50-60 °C for 4-6 hours with constant stirring. A white or slightly yellowish mass is formed, which is easily and evenly spread on the skin. It easily mixes with medicinal substances and does not mix with vaseline, fats and oils.

With long-term storage, the phytosterol base dries out. However, upon subsequent mixing of the remaining phytosterol with warm water (50-60 °C), a mass with the original properties is formed again. This property of phytosterol makes it possible to obtain dry concentrates of ointments. Phytosterol base by itself dries inflamed skin.

Characteristics of lipophilic-hydrophilic (diphilic) bases. These are compositions of different composition, which have both lipophilic and hydrophilic properties. They are characterized by the ability to mix with both fat-soluble substances and aqueous solutions of medicinal substances.

An emulsion base is recommended, which includes sodium lauryl sulfate - 2 parts, white wax - 1 part, propylene glycol - 10 parts, cetyl alcohol - 15 parts, purified water - 72 parts. Wax, propylene glycol and cetyl alcohol are melted in a water bath. The resulting alloy is vigorously mixed with a warm (60 °C) aqueous solution of sodium lauryl sulfate until a homogeneous mass is obtained. it can be used to make ointments with sulfonamides, precipitated sulfur, salicylic and benzoic acids, mercury preparations, etc.

Emulsion bases of the following compounds are proposed:

Triethanolamine 2.0

Stearic acid 15.0

Lanolin b/v2.0

Vaseline oils 25.0

Glycerin 5.0

Purified water up to 100.0

A heated solution of triethanolamine and glycerin in water is added to the alloy of stearic acid, lanolin and petroleum jelly and mixed well until cooling.

Hydrogenated sulfofat 8.0

Sodium alginate 2.0

Paraffin 30.0

White wax 2.0

Purified water up to 100.0

First, an aqueous solution of sodium alginate is prepared, which, swelling, forms a gel, other components are fused and mixed with the gel.

Emulsion waxes7.0

Vaseline oils7.5

Glycerin 12.5

Esilon-510.0

Sodium benzoate 0.2

Purified water 62.8

It is made by mixing in a mortar an alloy of emulsion waxes, esilon-5, petroleum jelly and glycerin with a heated solution of sodium benzoate in water. This base is used to make ointments with anesthetics (anesthesin, novocaine, trimecaine, dicaine).

For the production of eye ointments with pilocarpine hydrochloride, a base consisting of emulsifier 3 and - 15 parts, cinnamon alcohol - 0.15 parts and purified water - 77.85 parts is used.

Emulsion bases of the W/O type, when left on the skin for a long time, can cause its maceration, which further promotes the resorption of the drug. They are characterized by small values of plastic viscosity and yield point, so they are easily applied to the skin. Being emulsions of the second kind, they are less able to change their consistency during storage.

According to their properties, fatty sugars are surfactants and, therefore, can be emulsifiers. F. A. Zhoglo synthesized and studied a number of sucrose mono- and diesters. He established that diesters of palmitic and stearic acids in the amount of 2% are able to combine with petroleum jelly (47%). water (45%), methylcellulose (1%) and ceresin (5%) to form a stable, consistent emulsion of the W/O type. Methylcellulose and ceresin in it play the role of a thickener.

In their pure form, fatty sugars are colorless crystalline substances without taste or smell. In the body, they break down into fatty acids, glucose and fructose. They do not have an allergic effect on the skin, maintain constant pH values of the skin and a normal water balance.

On the basis of the T-2 emulsifier, E. N. Kutumova proposed an ointment base, which, according to FS 42-124-72, is called "water-vaseline consistent emulsion" and has the following composition:

Vaseline 60.0

Emulsifier T-2 10.0

Purified water 30.0

Vaseline and emulsifier are fused while stirring in a water bath, hot water (90-95%) is gradually added, stirred again until the temperature drops to 30 °C, and left in a cool place until the next day.

The mass of an ointment-like consistency is white with a yellowish tint. It is included in SPh of Ukraine IX as a basis for the manufacture of simple sulfur, turpentine and potassium iodide ointments.

Two emulsion bases are recommended for pharmacy production of ointments. The composition of the first includes anhydrous lanolin - 168 parts, petroleum jelly - 240 parts, purified water - 72 parts.

The second emulsion base consists of anhydrous lanolin, sunflower oil and purified water, taken in equal quantities. First, lipophilic components are fused, then hot water is added while stirring, emulsification is continued until the base is completely cooled.

The shelf life of these foundations is limited at a temperature not higher than 25 °C for the first foundation - 15 days, for the second - 5 days.

Absorption bases. Along with emulsion bases, anhydrous alloys of surfactants with components having hydrophilic and hydrophobic properties have found wide application.

A number of researchers attribute these peculiar consistent semi-finished products to a special class of ointment bases, calling them absorbent. Due to the presence of surfactants, these bases are able to mix with water, aqueous solutions of medicinal substances, forming emulsions of the W/O or M/W type. In this regard, the term "absorbent" refers only to the property of the base to incorporate water.

An absorption base of the following composition is proposed:

Alcohols of wool wax 6.0

Vaseline 10.0

Ceresin 24.0

Vaseline oils 60.0

These ingredients are fused in a water bath at 70-80 oC. and the mixture is stirred until cooling. It is allowed to change the concentration of ceresin and petroleum jelly in order to obtain the basis of any desired consistency. To obtain an emulsion base based on wool wax alcohols, 50% of water heated to 70-80 °C should be added to the melted ingredients of the absorption base while mixing. Various medicinal substances can be added to this base: sulfur, zinc oxide, boric and salicylic acids, hydrocortisone, chloramphenicol, potassium iodide, streptocid, etc. The stability of the ointment is maintained for more than 2 years.

Along with surfactants, oils, and waxes, many absorbent bases include hydrocarbons. This is due to the desire to reduce the adverse effect of hydrocarbons on the skin, mucous membrane, and wound surfaces.

For the production of ointments, alloys of petroleum jelly with anhydrous lanolin are also used in different ratios: 9:1, 8:2. 6:4.

Numerous studies show that the bases for ointments according to their ability to ensure the most intensive release and resorption of drugs can be placed in the following series: hydrophilic, emulsion type O/W. W/O emulsion type, absorbent and hydrophobic. But it is impossible to observe the above-mentioned dependence of the activity of the ointment on the nature of the base when obtaining ointments with new medicinal preparations. There is a lot of data that shows that in each specific case, first of all, it is necessary to take into account the direction of action of the drug, its properties, the nature of the interaction with the components of the base and other factors.

MAZEY'S OWN TECHNOLOGY

Production of homogeneous ointments. Ointment-alloys are a combination of several melting, mutually soluble components. The composition of such ointments can include fats, waxes, hydrocarbons, resins, plasters, oils and other substances. The ingredients can be both solid and soft or liquid.

The components are melted in a water bath in a porcelain or enamel cup. The general technology of ointments-alloys is as follows: first of all, the most refractory substances are melted and other ingredients are added to the obtained melt in order of decreasing melting temperature; liquid components are added last; if necessary, the obtained liquid melt is filtered through cheesecloth into a heated mortar (50-55 °C) and stirred until cooling. At the same time, the ointment becomes loose, soft, easily smears due to the fact that mixing prevents the formation of microcrystalline frameworks, as well as the crystallization of some solid ingredients that give the ointment a coarse-grained structure.

Mixing is especially appropriate if the ointment contains paraffin, otherwise it may separate in the form of large crystals. In addition, when mixing the ointment, a loose porous structure is obtained due to the incorporation of air.

The relative melting point of the substances that make up the ointments-alloys is given below in the following order:

Filtration of small amounts of ointment (10.0-20.0 g) in the process of their manufacture according to prescriptions leads to large losses, therefore pharmacies use pre-filtered bases.

Examples of alloy ointments: spermaceti ointment (*Unguentum Cetacei*) - an alloy of 1 part of wax with 2 parts of spermaceti and 7 parts of peach oil; diachylon ointment (*Unguentum Diachylon*) - an alloy of equal parts of a simple lead patch and vaseline: official naftalan ointment (SPh of Ukraine IX Art. 728) and others.

Rp.: Naphthalani liquidi raffinati 70.0
Paraffini 18.0
Petrolati 12.0
Misce, fiat unguentum
Yes. Signa. For bandages.

Melt petrolatum (melting point - 60-62 °C), paraffin (melting point - 50-54 °C) is added to the obtained melt while stirring, and finally - naphthalene oil. The alloy is stirred in a warm mortar until it cools completely.

Solution ointments are ointments containing medicinal substances that are soluble in an ointment base (regardless of their nature).

Medicinal substances are dissolved in a molten base in a porcelain (porcelain) cup with careful heating in a water bath.

If the composition of the ointment contains a liquid in which a soluble substance is prescribed, then it is dissolved in this liquid, and then mixed with other components.

If medicinal substances are easily dissolved in the ointment base and are prescribed in small quantities (up to 5%), then they are first rubbed with an equal amount of fatty or petroleum jelly until completely dissolved, then the base is added in parts, thoroughly mixed until homogenous.

When making ointments-solutions, the following must be taken into account:

- if the medicinal substance has volatile properties (camphor, menthol, etc.), it is dissolved in a semi-cooled melt (45-50 °C);

- do not prepare supersaturated solutions, because dissolved substances may crystallize upon cooling;

- many drugs soluble in hydrophobic bases lower the melting point of the latter due to the formation of eutectics, therefore, in order to obtain sufficiently dense ointment-solutions, sealing components (10% wax or paraffin) are introduced into the composition of the ointment bases.

Rp.: Menthol 0.1

Vaseline 10.0

Misce, fiat unguentum

Yes. Signa. Ointment for the nose.

In a mortar, 0.1 g of menthol is ground with a few drops (0.1 g) of petroleum jelly until completely dissolved and thoroughly mixed with petroleum jelly.

The official prescription of camphor ointment (SPh of Ukraine IX Art. 721) has been slightly changed: according to FS 42-751-73, paraffin is included in its composition.

Rp.: Camphorae10.0 seu10.0

Vaseline60,054,0

Paraffmi-8.0

Lanolin anhydrici30.0 28.0

Misce, fiat unguentum

Yes. Signa. For shoulder rubs.

Anhydrous lanolin and petroleum jelly are melted (according to the fusion rule) in a water bath, and in the obtained melt, cooled to 45-50 °C, camphor (a volatile substance) is dissolved and stirred until it cools. The technology of this ointment with

paraffin is similar. Ointment is a combined system: ointment-alloy and ointment-solution.

QUALITY ASSESSMENT OF OINTMENTS

The quality of prepared ointments is evaluated in the same way as other medicinal forms, that is, documentation (recipe, passport), packaging, design, absence of delamination and mechanical inclusions, deviations in mass are checked. Authenticity is determined visually by appearance and organoleptic signs (smell, color, etc.), which depend on the properties of the constituent medicinal substances and the used ointment bases.

The homogeneity of ointments is determined by the size of the particles of the solid phase (SPh of Ukraine XI). For this, a biological microscope is used, equipped with a MOB-1 eyepiece micrometer with an eyepiece magnification of 15x and an objective lens of 8x. The price of the division of the eyepiece micrometer is calibrated by the object-micrometer for penetrating light (OPM). A sample of the ointment is selected as specified in the article "Selection of samples of medicinal products", and it should be at least 5.0 g. If the concentration of medicinal substances in ointments exceeds 10%, then they are diluted with a suitable base to a content of about 10% and mixed. When selecting, you should avoid crushing the particles.

Determination method. A 0.05 g sample is taken from the average ointment sample and placed on the untreated side of the glass slide. The other side of the specimen glass is processed in the following way: a square with a side of about 15 mm and diagonals is applied to the middle of it with a diamond or some other abrasive material. Lines are painted with a pencil on the glass. The glass slide is placed in a water bath until the base melts, a drop of 0.1% sudan III solution for fat, hydrocarbon and emulsion bases of the B/O type or 0.15% methylene blue solution for hydrophilic and emulsion bases of the O/B type is added and mixed. The sample is covered with a cover glass (24x24 mm). Fix it by pressing lightly and view the segments formed by the diagonals of the square in the four fields of view. For the analysis of one drug, five determinations of the average sample are carried out. In the field of view of the microscope, there should be no particles, the size of which exceeds the norms specified in their own articles.

Determination of the pH of ointments is necessary to control the stability of medicinal substances and the base during storage. Violation of pH indicates a change in their physical and chemical properties.

An important criterion for the quality of ointments is the indicators of their structural and mechanical (rheological) properties. The consistency of ointments affects the processes of their manufacture and packaging, spreadability of ointments and the release of medicinal substances from them.

One of the important factors on which the consistency depends is the ultimate shear stress, which characterizes the ability of the ointment to offer some resistance during spreading and extrusion (the ability to squeeze out of tubes, dispensers, etc.).

Important rheological characteristics of ointments are plastic viscosity, which can be determined on a rotary viscometer, as well as plastic strength, which is determined on a conical plastometer.

IMPROVEMENT OF OINTMENT TECHNOLOGY

The direction of improvement includes the expansion of the range of bases for ointments and their purposeful selection depending on the purpose of the ointment. As an example, we can cite Nitrong ointment, in which the base (paraffin, ethanol, oxypropyl cellulose, petroleum jelly) promotes uniform absorption of nitroglycerin by the skin. The ointment has a prolonged effect and is prescribed as an additional means in combination with orally administered drugs for the prevention of angina attacks.

For the effect of drugs on local processes in the rectum or on the body as a whole, the use of rectal ointments is promising, because the medicinal substances are easily and quickly absorbed.

The given examples do not limit the further improvement of ointments. Ointments fixed on paper, prepared in the manner of mustard seeds, may also be promising.

Improvements in the technology of ointments and their quality are carried out in the following areas:

-increasing the chemical, physical, and microbiological stability of bases and ointments;

- development of accessible and objective methods for evaluating the quality of ointments;

- improvement of packaging;

- development and introduction of elements of small mechanization in the production of ointments in pharmacies;

- expansion of the assortment and unification of the formulation of ointments and pastes. The main directions of development of ointments can be divided into the following stages:

1. The study of biological processes that occur during the effect of the medicinal product on damaged and intact skin.

2. Creation of soft medicinal forms with a controlled effect and release of drugs that provide the expected therapeutic effect in the specified place and at the expected time.

3. Search for carriers that ensure the delivery of medicines to the site of the disease.

There is a medical and physico-chemical classification of ointments. According to the medical classification, ointments are divided by action and place of application.

Depending on the action, ointments of superficial and deep action are distinguished. According to the place of application, ointments are distinguished:

Dermatological (actually ointments) that are applied to the skin;

Ophthalmics, which are applied to the conjunctiva of the eye;

For the nose, applied to the mucous membrane of the lower concha;

Vaginal

Urethral

Rectal

The last three types of ointments are administered using special syringes.

According to the physico-chemical classification, ointments are divided by consistency. Type of dispersion systems and ointment bases. Depending on the consistency, they distinguish:

liquid ointments (liniments)

creams

gels

Ointment itself

· thick ointments - pastes

semi-finished dry ointments intended for dilution with water or fats.

According to the type of dispersion systems (depending on the degree of dispersibility of the medicinal substance and the nature of its distribution in the base), the following are distinguished: · Homogeneous · Heterogeneous ointments. Homogeneous ointments are systems characterized by the absence of an interphase interface between medicinal substances and the base of the ointment. In this case, the medicinal substance is distributed in the base according to the type of solution, that is, brought to the molecular or micellar degree of dispersion. Homogeneous include: ointments-solutions, ointments-alloys and extraction ointments. Heterogeneous ointments are systems that have a phase separation with different boundary layers. These include suspension (trituration), emulsion and combined ointments. The different physical state of the medicinal substances in the ointment is explained mainly by their properties (solubility or insoluble in water and oil, etc.), depending on which the corresponding type of ointment is formed. According to the type (character) of ointment bases, ointments prepared on: Hydrophobic (lipophilic), hydrophilic Diphilic (hydrophilic-lipophilic) bases are distinguished. Thus, the medical classification gives a general idea of ointments (purpose, application, etc.), and the physicochemical classification reflects the technology of ointments and their quality criteria. Different ointment bases Ointment bases can be in the form of individual or a sum of different substances that determine the required volume, appropriate consistency and some specific features of the ointment. Due to its consistency, the base is an excellent lubricant for the skin, which makes it soft, smooth, elastic and protects it from drying out. Under the influence of the base, the natural fatty protection of the skin is strengthened, cracks and sores heal faster, water evaporation decreases, due to which

the stratum corneum swells and natural heat is retained, which achieves significant protection against humidity and cold. The last circumstance of the mass is essential for swimmers who are in the water during the competition. In addition, the foundations absorb external contamination of the skin well and facilitate its removal. These and other studies show that ointment bases are not just an indifferent carrier, but an active component of ointment pharmacodynamics. The choice of the ointment base depends on the physicochemical properties of the prescribed drugs and the nature of the ointment's action. The base, which would provide the maximum therapeutic effect of the ointment, must meet the following requirements:

Have good spreadability, i.e. necessary structural mechanical (consistent) properties: viscosity, plasticity, fluidity, thixotropy, etc.;

· Accept medicinal substances well, i.e. have an absorbent capacity;

· Do not change under the influence of air, light, temperature fluctuations and do not react with medicinal substances that are introduced into it, that is, have chemical resistance;

· To be pharmacologically indifferent, not to have an irritating and sensitizing effect, to help maintain the original pH value of the skin or mucous membrane;

· Do not undergo insemination by microorganisms;

It should not stain clothes, not be too sticky, wash off easily with or without soap.

The properties of the base should correspond to the purpose of the ointment: the bases of protective ointments used for preventive purposes should dry quickly and adhere tightly to the surface of the skin; bases for surface-acting ointments should not be absorbed; bases for resorptive ointments should, on the contrary, penetrate deeply into the skin, reach the blood vessels and promote the absorption of medicinal substances. However, there are no ointment bases that fully meet these requirements. Therefore, in order to obtain the required quality of the base, mixtures of different substances (complex ointment bases) are often used.

CLASSIFICATION OF FUNDAMENTALS.

Substances used as bases for ointments differ in their sources, chemical composition, and physical and chemical properties. This is reflected in the classification of the basics given in various training manuals, textbooks, reviews and articles. A significant drawback of many proposed classifications is that they mix bases for ointments with their individual components.

Depending on the sources of production, ointment bases and their components are divided into natural and artificial. The last group includes bases, which are various synthetic or semi-synthetic substances or their mixtures, both with each other and with natural substances.

Based on their chemical composition, bases are divided into glycerol esters and beggar fatty acids, complex esters of these acids with high-molecular monoatomic

alcohols, high-molecular hydrocarbons and their amines, inorganic compounds, polysaccharides, etc.

The basis of the classification should be the most characteristic feature that allows combining substances into a single, organically connected group. Such a characteristic feature of all substances or compositions of bases is their ability to interact with water.

According to the intensity of interaction with water, all bases are divided into three groups:

· hydrophobic

· hydrophilic· diphilic

This group includes:

fatty

· hydrocarbons

· Silicone bases.

Fat bases. Among fatty bases, the most widely used are fats of animal and vegetable origin, as well as products of their industrial processing. They are triglycerides of higher fatty acids and are similar in composition to the sebaceous secretions of the skin. Fats are indifferent, well absorbed, mix with many medicinal substances and release them well, relatively easily washed off with warm soapy water.

But at the same time, they are not stable enough and decompose (bitter) with the formation of free fatty acids, aldehydes and other compounds that can enter into chemical reactions with medicinal substances present in the composition of ointments and have an irritating effect on the skin.

Pig fat (*Adeps suillus depuratus*. *Axungia porcina depurata*) is obtained by melting the fat that covers the internal organs of the pig. It is a mixture of triglycerides of oleic acid and tripalmitin and tristearin. The product is white in color, has a soft, delicate consistency, has a very weak smell, melts at a temperature of 34-35 °C, does not irritate the skin and does not interfere with skin breathing when fresh, penetrates the epidermis quite easily and gives medicinal substances well to the skin.

Beef fat (*Sebum bovinum*) belongs to the group of solid fats, as it contains triglycerides of solid saturated fatty acids of palmitic and stearic acids and relatively few triglycerides of unsaturated linoleic acids. It has a yellowish color and a weak smell, its melting point is 42-52 °C. At room temperature, it is hard and brittle, therefore, in its pure form, it is unsuitable as an ointment base. Sometimes it is used to thicken fat-based ointments.

Lamb fat has similar properties and uses.

Goose fat (*Adeps anscrinum*) - a soft mass of yellowish cream color with a melting point of 26-34 °C; belongs to the group of hard-solidifying fats, used in ointments for frostbite.

Vegetable fats (oils). Most of the vegetable fats belong to the number of liquids, so they are not used in their pure form as bases. They are widely used as additives to solid bases (fats, waxes, hydrocarbons), forming alloys of a soft consistency. In the

technology of ointments, oils are used: almond, apricot, peach, sunflower, plum, cotton, olive, etc.

Hydrogenated fats are products of industrial processing of fats and vegetable oils.

The process of hydrogenation of natural fats is carried out in reactors at elevated temperature (180-240 °C) and pressure, in the presence of catalysts (usually copper-nickel) and with a constant supply of hydrogen.

As a result of hydrogen saturation of glycerides of unsaturated fatty acids, the latter are transformed into saturated ones, forming products of any consistency with different melting temperatures, up to solid products that have greater stability of physicochemical parameters.

Hydrogenated fats can be used:

a) independently as bases for ointments, if they are viscoplastic;

b) as components of bases for ointments, if they are solid or semi-liquid.

SPh of Ukraine XI recommends using the following ointment-like products as ointment bases:

Salomas, hydrofat or (*Adeps hydrohcnisatus*), which is obtained from refined oil; similar to pork fat, but more dense. Vegetable lard (*Axungia vegetabilis*) is an alloy consisting of 88-90% hydrofats and 10-12% vegetable oil. Hydrocarbon bases. In 1876, petroleum jelly was introduced into pharmaceutical practice as a base for ointments. At this time, liquid and solid paraffins were also used as components of the bases for ointments. Combinations of liquid and solid hydrocarbons made it possible to create ointment bases of the required consistency, which would not be bitter, were neutral and compatible with a large number of medicines.

Vaseline (*Vaselinum*) is a purified mixture of solid, soft and liquid hydrocarbons. obtained from oil.

A homogeneous ointment-like mass without odor, white or yellowish in color. When smeared on a glass plate, it gives an even, non-slip film. Mixes with fatty oils and fats in all ratios. When melted, it gives a clear liquid with a weak smell of paraffin or oil. The melting point is 37-50 °C. It is not saponified by alkali solutions, does not oxidize, does not become bitter in air and does not change under the action of concentrated acids.

Vaseline is widely used as an independent ointment base for surface-acting dermatological ointments. For use on mucous membranes and increasing the resorptive capacity of petroleum jelly, it is combined with lanolin.

For eye practice, vaseline of the "eye ointment" variety is used, cleaned of renewing impurities and subjected to hot filtering and sterilization.

Along with the pharmacopoeia, medical vaseline is also used, which is obtained by fusing ceresin, paraffin, purified petrolatum or their admixtures with purified petroleum oil.

Petrolatum is not a mixture of solid paraffin with mineral oil, a light brown mass with a melting point above 60 °C. It is obtained during the deparaffinization of

petroleum aviation oils. For medical purposes, it is additionally purified and used in complex bases for ointments as a filler.

Paraffin (*Paraffinum solidum*) is a white crystalline mass, greasy to the touch. It consists of high-molecular hydrocarbons, has a melting point of 50-57 °C, is used as an additive to bases in order to thicken their consistency. In hot climates, SPh of Ukraine X recommends adding 10% paraffin or wax to the usual base.

Vaseline oil, or liquid paraffin (*Oleum Vaselini*, *Paraffinum liquidum*) is a fraction of oil obtained after distillation of kerosene. Colorless oily liquid without smell and taste, insoluble in water and easily mixed in all respects with vegetable oils (except castor oil). It is used with the aim of obtaining a base of a softer consistency.

Ozokerite (*Osokeritum*) is a waxy natural mineral, or mountain wax, a mixture of high molecular weight hydrocarbons. It is used in complex bases in the form of tar-free ozokerite - a light yellow mass that melts at a temperature above 60 °C.

Wax (*Ceresinum*) is refined ozokerite, which is an amorphous colorless brittle mass that melts at 68-72 ° C. It is chemically indifferent. It fuses well with fats and hydrocarbons, forming alloys that do not crystallize. It is used to obtain complex ointment bases (artificial vaseline). Artificial vaseline (*Vaselinum artificiale*) is a complex alloy made from liquid and solid paraffins, de-tarred ozokerite or ceresin, sometimes with the addition of petrolatum. In the simplest case, it is an alloy of 1 part of paraffin and 4 parts of petroleum jelly (*Unguentum Paraffini*). The alloy is prone to syneresis and becomes grainy during storage. The quality of these alloys is usually the better, the more complex the combination of components. Naphthalan oil (*Naphthalanum liquidum*, *Naphtha Naphthalani*) is a thick grayish black liquid with a greenish fluorescence and a peculiar smell. Mixes in all proportions with glycerin, oils and fats. It has a disinfecting and pain-relieving effect. An effective treatment for first and second degree burns. There are a number of prescriptions with naphthalene oil for the treatment of scabies, itching, eczema, erysipelas, arthritis, sciatica and other diseases.

CHARACTERISTICS OF HYDROPHILIC BASES.

Hydrophilic ointment bases contain substances of different chemical nature, combined by the common property of dissolving or swelling in water. They are gels of high molecular weight compounds (natural or synthetic) or highly dispersed hydrophilic clays.

Some of these bases are well absorbed through the skin, others form more or less elastic protective films on the skin, that is, they lose water due to evaporation. Since the evaporation of water is associated with the absorption of heat, hydrophilic bases have a cooling effect that resembles the effect of a wet bandage. Hydrophilic bases are compatible with many medicinal compounds and are easily released from the external aqueous phase into body tissues.

Starch-glycerin base, or glycerin ointment (*Unguentum Glycerini*) is a whitish translucent mass of gelatinous consistency, easily soluble in water and mucous membrane secretions. This last circumstance contributed to its long-term application as a basis for the manufacture of ointments that are applied to mucous membranes. According to DF IX, starch-glycerin ointment is prepared by mixing 7 parts of wheat starch with an equal amount of purified water, followed by the addition of 93 parts of glycerin while gently heating in a water bath until 100 parts of a homogeneous mass are obtained. The base is resistant to microflora, but unstable in the physico-chemical relation, because it undergoes syneresis during storage.

Collagen bases.

Collagen is a natural biopolymer, which is a fibrillar protein of connective tissue of animals. It is obtained from certain areas of the skin in the form of a paste-like mass or solution. Collagen was previously used for the manufacture of a number of medical products (suture material, vascular prostheses, etc.). Then they began to make films from it, which contain medicinal substances for various purposes. Collagen is very promising for ointments, because it provides a pronounced therapeutic effect and a prolonged effect.

Tragacanth-glycerin dragees, which contain 3% tragacanth and up to 40% glycerin, were proposed as hydrophilic bases.

In foreign practice, pectin, algin, mucin, and other bases from plant-based IUDs have been used.

In our country, the possibilities of using solutions of polysaccharides of microbial origin as a basis for ointments were investigated.

Methylcellulose (MC) is a simple ether obtained by the interaction of alkaline cellulose and methyl chloride. The introduction of MCs in fat-based ointments gives them hydrophilicity and a faster release of medicinal substances, improving the contact of medicinal substances with the affected areas of the skin. Possessing adsorption properties, MC absorbs various types of secretions from damaged skin and creates a protective film on the surface of the skin. MC is compatible with many medicines.

Sodium carboxymethyl cellulose (Sodium-KMC). Solutions of sodium-CMC as a basis for ointments are used in a limited way, although they have prospects.

Bases based on MC and sodium-CMC are usually obtained by mixing them with glycerin according to the following instructions:

1) methylcellulose 6.0 g, glycerin 20.0 g, water 74 ml;

2) sodium-CMC 6.0 g, glycerin 10.0 g, water 84 ml.

Preservatives are added to the bases.

Other cellulose derivatives that are produced on a production scale deserve attention.

Oxypropylmethylcellulose (OPMC) and acetophthalylcellulose (APC) are known as bases for ointments.

Polyethylene oxide (polyethylene glycol) (PEO) bases are obtained by fusing solid and liquid polyethylene oxide.

PEO - the base consists of 60.0 g of PEO-400 and 40.0 g of PEO-4000 or 70.0 g of PEO-400 and 30.0 g of PEO-1500. PEO-4000 (PEO-1500) is melted in a water bath at 70 ° C, PEO-400 is added and mixed with a mechanical stirrer for 30 minutes until a homogeneous soft cream-like mass is obtained.

Polyethylene glycol base is neutral, non-toxic, does not macerate the skin with long-term use, easily releases medicinal substances, is not an environment for the development of microorganisms.

In addition, PEO bases have the ability to dissolve hydrophilic and hydrophobic medicinal substances; weak bactericidal effect due to the presence of primary hydroxyl groups in the molecule; osmotic activity, which contributes to the treatment of contaminated wounds. In such cases, PEO ointments act as washing and cleaning agents.

Polyethylene gels (for example, Aerosil 4 parts, Vaseline oil 84 parts, Paraffin 6 parts, High-pressure polyethylene 15 parts) are part of protective ointments (to protect the skin from the effects of alkalis, acids), cooling emulsion creams, etc. they are indifferent, poorly washed off the surface of the skin, incompatible with water and aqueous solutions of medicinal substances, alcohol, birch tar, ichthyol.

Bases from clay minerals. The composition of clays and argillaceous rocks includes the most characteristic and specific minerals for them: kaolinite - the main mineral of medical white clay, montmorillonite-bentonite clays, etc. They consist of 90% of oxides of silicon, aluminum, ferrum, magnesium and water. Calcium, sodium, potassium, and titanium oxides are also included in minerals in small quantities. Some of these oxides are absent in some minerals.

Characteristics of lipophilicity-hydrophilic (diphilic) bases.

These are different compositions that have both lipophilic and hydrophilic properties. They are characterized by the ability to mix with both fat-soluble substances and aqueous solutions of medicinal substances.

This group of bases includes both anhydrous alloys of lipophilic bases with emulsifiers capable of absorbing a significant amount of water (absorption bases) and water-containing emulsion bases.

Lipophilicity-hydrophilic bases, unlike hydrocarbons, ensure significant resorption of medicinal substances from ointments, do not interfere with gas and heat exchange of the skin, and have good consistent properties. Thus, it is one of the most common and promising bases.

The most common representative of this group is lanolin (*Lanolinum*). which is obtained from washing waters of sheep's wool.

Therefore, this substance is often called wool wax (*Adeps lanae*). A natural mixture of esters of high molecular weight cyclic alcohols, fatty acids and free high molecular weight alcohols. Purified lanolin is a white-yellow mass, thick, knitting,

ointment-like consistency, with a peculiar weak smell; melting point 36-42 0 C. Lanolin is insoluble in water, but mixes with it, absorbing (emulsifying) more than 150% of it, without losing its ointment-like consistency. The use of anhydrous lanolin (*Lanolinum anhydricum*) is based on this important and valuable property, because with its help, a large amount of aqueous liquids can be introduced into the ointment. Anhydrous lanolin has a fairly high stability and chemical indifference. It is able to be absorbed by the skin and mucous membranes, does not irritate them, easily fuses with fats, hydrocarbons and wax. The disadvantage of anhydrous lanolin as a base - high viscosity, stickiness and difficulty of spreading - does not allow using it in its pure form. For this reason, it is almost always used in a mixture with other bases and most often with petroleum jelly.

SPh of Ukraine X recommends using water lanolin (*Lanolinum hydricum*), if the type of lanolin is not specified in the recipe. Aqueous lanolin is a thick yellowish-white viscous mass, which consists of 70 parts of anhydrous lanolin and 30 parts of water. When heated, like any emulsion system, it delaminates.

Spermacet (*Cetaceum*) is a solid waxy product obtained from sperm whale fat. It is a complex ether of ethyl alcohol and palmitic acid, melting point 45-54 °C, stable during storage. Easily fuses with fats, wax, petroleum jelly. These alloys have a certain density, a kind of slipperiness and the ability to absorb liquids, forming rough emulsions, they are often used in cosmetics to make creams.

Wax (*Sega*). Beeswax is a hard, granular, brittle mass from yellow to brown in color with a faint smell of honey. It melts at a temperature of 63 65 °C.

Beeswax fuses well with fats, hydrocarbons and other waxes. Due to the presence of 11 higher alcohols, the wax is able to emulsify certain amounts of water. It adds plasticity to bases and ointments and increases their density.

The introduction of medicinal substances into the ointment is carried out taking into account their physical and chemical properties and prescribed quantities.

Medicinal substances that are insoluble neither in water nor in the base (zinc oxide, basic bismuth nitrate, white clay, dermatol, norsulfazole, sulfur, streptocide, talc, etc.), as a rule, are introduced into suspension ointments in the form of powders, ground to the maximum degree of dispersion according to Deryagin's rule by type of suspension.

Water-soluble substances that require a significant amount of water to dissolve (sodium tetraborate, boric acid, sulfonamide preparations, etc.) are also introduced into suspension ointments.

By type of suspension, zinc sulfate and resorcinol are introduced into dermatological ointments.

If the total amount of these substances is up to 5%, they are rubbed with a liquid that is similar in properties to the base: hydrophilic base - purified water, vaseline - vaseline oil, fatty base - kernel oil. Are liquids taken according to Deryagin's rule? from the mass of dry matter.

If the total amount of these substances is more than 5%, they are ground according to Deryagin's rule from the mass of the dry substance of the fusible base.

Medicinal substances soluble in water (salts of alkaloids, potassium iodide, novocaine, silver nitrate, etc.) are introduced mainly into the composition of emulsion ointments, dissolving them in a minimum amount of water or in the base, if the base is hydrophilic.

If the base is hydrophobic and the total amount of these substances is up to 5%, they are dissolved in water, aqueous solutions, liquid extracts, if they are prescribed in the recipe and emulsified with lanolin. If the hydrophilic liquid is not prescribed in the recipe, it is calculated from aqueous lanolin (30%) and emulsified with aqueous lanolin (70%). Medicinal substances soluble in fats (camphor, menthol, thymol, chloral hydrate, crystalline phenol, anesthesin up to 2%, phenylsalicylate, etc.) They are introduced into single-phase solution ointments, dissolving them in a fatty base or its constituent part.

If the total amount of these substances is up to 5%, they are rubbed with a liquid that is similar in properties to the base: vaseline - vaseline oil, fatty base - kernel oil. Liquids take as much as substances.

If the total amount of these substances is more than 5%, they are ground with an equal amount to the mass of dry substances of the fusible base.

These substances are introduced into hydrophilic bases in the form of a suspension.

Production of combined ointments.

These ointments can be considered as mixed type ointments, which consist of separate types of ointments. Combined ointments are complex multicomponent ointments that contain several medicinal substances with different physicochemical properties, which require the production of various types of ointments: suspensions, emulsions, solutions, alloys.

The production of combined ointments is regulated by the same rules that are provided for in the technology of individual types of ointments. At the same time, taking into account the presence of combinations (for example, ointment-suspension and solution or ointment-emulsion and ointment-solution, etc.), a different sequence of technological stages is possible, which must be rational.

In pharmacy conditions, the production of combined ointments is carried out in the same mortar, if necessary, moving the previously obtained part of the ointment to the spout or to the wall of the mortar. Therefore, if the composition of the combined ointment includes medicinal substances that form a suspension type of ointment, it is more appropriate to prepare the suspension ointment first in the mortar.

Combined ointments are made in the following sequence:

Ointment-suspension

· Ointment-solution· Ointment emulsion.· * Ointments-alloys can be prepared as needed

Technological stages of preparation of suspension ointments

1. Compliance with the sanitary regime and preparation of the workplace
2. Distillation of medicinal substances
3. Mixing according to the rules for preparing complex powders.
4. Plumbing of the base
5. Dispersion with an auxiliary liquid or submerged base
6. Mixing

Technological stages of preparation of ointments-solutions

1. Compliance with the sanitary regime and preparation of the workplace
2. Distillation of medicinal substances
3. Mixing according to the rules for preparing complex powders.
4. Plumbing of the base
5. Dispersion with an auxiliary liquid or submerged base
6. Mixing

Technological stages of preparation of ointments-emulsions

1. Compliance with the sanitary regime and preparation of the workplace
2. Distillation of medicinal substances
3. Mixing according to the rules for preparing complex powders.
4. Emulsifier cuttings
5. Dissolving in purified water
6. Emulsification

The production of combined ointments is carried out in the same mortar, if necessary, moving the previously obtained part of the ointment to the spout or to the wall of the mortar.

QUALITY ASSESSMENT OF OINTMENTS

The quality of prepared ointments is evaluated in the same way as other medicinal forms, that is, documentation (recipe, passport), packaging, design, absence of delamination and mechanical inclusions, deviations in mass are checked. Authenticity is determined visually by appearance and organoleptic signs (smell, color, etc.), which depend on the properties of the constituent medicinal substances and the used ointment bases.

The homogeneity of ointments is determined by the size of the parts of the solid phase. A biological microscope is used for this. A sample of the ointment is selected as noted in the article "Sampling of medicinal products", and it should be at least 5.0 m. If the concentration of medicinal substances in the ointment exceeds 10%, then they are diluted with the appropriate base to a content of about 10% and mixed. When selecting, you should avoid crushing the parts.

Determination method. A 0.05 g sample is taken from the average ointment sample and placed on the untreated side of the glass slide. The other side of the specimen glass is processed in the following way: a square with a side of about 15 mm

and diagonals is applied to the middle of it with a diamond or some other abrasive material. Lines are painted with a pencil on the glass. The glass slide is placed in a water bath until the base melts, a drop of 0.1% solution of Sudan III is added (for fatty, hydrocarbon and emulsion bases of type B / O) or 0.15% solution of methylene blue (for hydrophilic and emulsifiable bases of type Pro / B) and mix. The sample is covered with a cover glass (24x24 mm). Fix it by pressing lightly and view the segments formed by the diagonals of the square in the four fields of view. For the analysis of one drug, five determinations of the average sample are carried out. In the field of view of the microscope, there should be no particles, the size of which exceeds the norms specified in the articles.

Determination of the pH of ointments is necessary to control the stability of medicinal substances and the base during storage. Violation of pH indicates a change in their physical and chemical properties.

An important criterion for the quality of ointments is the indicators of their structural, mechanical (rheological) properties. The consistency of ointments affects the processes of their manufacture and packaging, the spreadability of ointments and the release of medicinal substances from them.

One of the important factors on which consistency depends. - this is the maximum shear stress, which characterizes the ability of the ointment to offer some resistance during spreading and extrusion (the ability to squeeze out of tubes, dispensers, etc.)

Important rheological characteristics of ointments are plastic viscosity, which can be determined on a rotary viscometer, as well as plastic strength, which is determined on a conical Plastometer.

PACKAGING AND STORAGE OF OINTMENTS

In pharmacies, ointments are packed in glass, porcelain or plastic jars with a capacity of 10.0 to 100.0 g with plastic lids that are screwed on or tightened. In all cases, parchment or waxed paper or cardboard pads with a double-sided polyethylene coating are placed under the lid, and the ointment is prepared accordingly before leaving. Ointments and pastes, which contain substances that change under the influence of light, are released in light-proof jars.

Ready ointments and pastes are transferred from the mortar to the jars with the help of a spatula and a celluloid plate, which collects the ointment first from the core, and then from the walls of the mortar. Banks should be selected according to the volume of ointment. When filling the jar with ointment, there should be no free spaces (voids), for which it is necessary to apply the ointment in separate portions and seal it by tapping the bottom of the jar against the palm of your hand.

It should be noted that along with indisputable advantages (chemical inertness, impermeability of medicinal substances, water vapor, gases, the possibility of sealing, availability), glass jars also have disadvantages: low mechanical strength, inconvenience of transportation, labor-intensive washing. Plastic cans made of

polystyrene with lids are also used, but they are unsuitable for storing ointments that contain tar, methyl salicylate, turpentine, camphor, phenol, essential oils.

As you know, the medical and perfume industries widely use tubes for dispensing ointment-like products. Despite the fact that tubes are more rational and hygienic, pharmacies rarely use them for dispensing extemporaneous ointments. The advantage of leaving ointments in tubes is that the ointments are protected from the effects of the external environment and do not pollute when used; tubes are light, portable.

There are metal (tin, aluminum) and plastic tubes. They have a cylindrical body for filling the ointment, made of stainless steel or a hard polymer material, inside which slides a piston with a rod that pushes the ointment into the tube through a mouthpiece that is attached to the lid of the housing or molded with the lid. After filling, the tubes are subjected to rolling and branding also with the help of small-sized devices. Strictly speaking, almost the entire process of making ointments in pharmacies can be mechanized.

In some cases, with minor resorptive ointments that contain poisonous substances, there is a need for accurate dosage of the drug. For this, ointments are released in graduated cartridges, closed on one side by a movable piston. By moving the piston, ointments are divided into the required doses. In factory production, it is possible to pack individual doses of ointment into shells made of cocoa butter, formed in the form of individual balls.

The stability of various ointments depends on many conditions: the physicochemical properties of the medicinal substances and the base, the purity of the components of the ointment, storage conditions (temperature, light, humidity, etc.), the type of container and packaging. Usually less stable are ointments prepared on emulsion bases, hydrophilic gels.

According to the instructions of the SPh of Ukraine, all ointments should be stored in a cool place protected from light in tightly closed jars.

IMPROVEMENT OF OINTMENT TECHNOLOGY

The direction of improvement includes the expansion of the range of bases for ointments and their purposeful selection depending on the purpose of the ointment. As an example, we can cite Nitrong ointment, in which the base (paraffin, cytanol, oxypropyl cellulose, petroleum jelly) promotes uniform absorption of nitroglycerin by the skin. The ointment has a prolonged effect and is prescribed as an additional means in combination with orally administered drugs for the prevention of angina attacks.

For the effect of drugs on local processes in the rectum or on the body as a whole, the use of rectal ointments is promising, because in this case medicinal substances are easily and quickly absorbed.

The given examples do not limit the further improvement of ointments. Ointments fixed on paper, prepared according to the type of mustard seeds, can also be promising.

Improvements in the technology of ointments and their quality are carried out in the following areas:

· Increasing the chemical, physical, microbiological stability of bases and ointments;

· Development of accessible and objective methods for evaluating the quality of ointments;

· Improvement of packaging;

· Development and implementation of elements of small mechanization in the production of ointments in pharmacies;

· Expansion of the assortment and unification of the formulation of ointments and pastes.

The main directions of the development of ointments can be divided into the following stages:

1. Study of biological processes that occur during the effect of the medicinal product on damaged and intact skin.

2. Creation of soft dosage forms with controlled exposure and release of drugs that provide the expected therapeutic effect in a certain place and at the expected time.

3. Search for carriers that ensure the delivery of medicines to the site of the disease.

18. 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:

— 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 soft drugs. Excipients for soft medicines.	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. - Kh.: National University of Applied Sciences: Original, 2016. - P. 370-373.
2.	Ointment bases are hydrophobic,	Characteristics of the specified	Ruban O.A., Saiko I.V. Industrial technology of

	hydrophilic, diphilic.	concepts	medicines. – Kh.: National University of Applied Sciences: Original, 2016. – P. 375 - 390.
3.	Technology of industrial production of homogeneous and heterogeneous ointments.	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: National University of Applied Sciences: Original, 2016. – P. 390 - 391.
4.	Standardization, packing and packaging of MLF	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. - Kh.: National University of Applied Sciences: Original, 2016. - P. 396-399.

— 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):

Tests of the base KROK-2

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. Khohlova etc. - Kh.: NFaU, 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 "KROK 2. Pharmacy" / O.A. Ruban, V.D. Rybachuk, L.M. Khokhlova, D.S. Pulyaev - Kh.: NFaU, 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.: NFaU: 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.: NFaU: 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 NFaU, 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 NFaU, 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-NFaU, 2017. – 44 p.
- Zujkina SS 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. – Kh.: NFaU 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, K.K. 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. 35-36

Topic: " Industrial production of suppositories"

Goal: Study technological schemes of suppository production. Be able to rationally select auxiliary materials and equipment, carry out quality control, packaging and labeling of the finished product

Basic concepts:

Pouring method - pouring the molten mass into molds and pressing it on special equipment. Industrial production of suppositories in this way is most often carried out according to a technological scheme, which consists of the following stages:

1) preparation of the base;
2) preparation of medicinal substances and preparation of concentrate;
3) introduction of medicinal substances into the base;
4) formation (and packaging) of suppositories;
5) packaging of suppositories.

Pressing method - on eccentric tablet machines, during cooling of the punch, matrix and casing, it is possible to obtain from 40 to 100 thousand suppositories per hour. The suppository mass is usually cooled in a refrigerator to 3-5 °C, crushed and sieved. Lactose, sucrose, aerosol, starch are added to the granulate to adjust the technological properties

Bases - from the point of view of physical and chemical science, suppositories are considered as dispersed systems consisting of a dispersion medium represented by the base and a dispersed phase, the role of which is performed by medicinal substances. Depending on the properties of medicinal substances, suppositories can create different dispersion systems.

Equipment: visual material, multimedia projector, presentation, sieve, grinding machine, mixer, 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;
- subject and tasks of drug technology;
- basic concepts of drug technology;
- basic requirements for the process of manufacturing suspensions.

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. Characteristics of the suppository as a dosage form. Let them go .
2. Positive and negative aspects of using suppositories .
3. Methods of production of suppositories in industry .
4. Stages of the technological process of obtaining suppositories .
5. Pouring method in the production of suppositories .
6. Method of pressing in the production of suppositories .
7. Basics that will be used for the manufacture of suppositories .
8. Groups of auxiliary substances in the production of suppositories .
10. Paratour equipment for the production of suppositories .

Lesson content

Suppository drugs are becoming more and more common in the medical practice of all countries. This is explained by their positive properties and the absence of negative effects characteristic of oral and injectable drugs.

Suppository drugs can have both general and local effects on the body. Suppositories are dosage forms that are solid at room temperature and melted or dissolved at body temperature. There are rectal suppositories (candles), vaginal and urethral suppositories (sticks).

Rectal suppositories can have the shape of a cone, a cylinder with a pointed end or another shape with a maximum diameter of 1.5 cm. The weight of one suppository should be between 1 and 4 g. The weight of a suppository for children should be between 0.5 and 1.5 g. ML C is classified according to the SPh of Ukraine according to the following characteristics:

- according to water affinity: hydrophilic and hydrophobic (lipophilic);
- by the ability to adsorb water and the absorption mechanism;
- by type of dispersion systems: single-phase (solutions, alloys), two-phase (oil/water emulsions (w/w), suspensions, colloidal dispersions of higher fatty alcohols or acids (stabilized by hydrophilic surfactants) and multi-phase systems (multiple w/w emulsions / m and in / m / in, as well as combined systems);
- by rheological properties at the set storage temperature and application conditions;
- concentration and dispersion of auxiliaries and/or drugs.

According to the set of features, ointment-like drugs for local use (Unguenta) can be classified as:

ointments (Ointments);
creams (Creams);
gels (Gels);
pastes (Pastes);
liniments (Liniments).

Bases - carriers for MLF are divided by degree kinship components foundations to water on such groups : hydrophobic , absorbent , water-repelling and water soluble Such classification takes into account ability foundations to absorption liquid secretions skin and tissues , and agrees with technological principles preparation ointment.

The class of hydrophobic bases includes individual substances or their mixtures with pronounced hydrophobic properties, which are practically immiscible with polar liquids or aqueous solutions of solvents. This is primarily a large group of hydrocarbons (yellow and white vaseline, artificial vaseline, solid and liquid paraffin, petrolatum, naphthalene oil, ozokerite, ceresin), polyethylene gels (alloys of polyethylene in vaseline oil) and silicone bases. This also includes natural, vegetable fats and wax. Ointments based on these bases do not have high therapeutic activity and are used as emollients and covering agents. They have a prolonged effect, as they slowly release LV.

The absorbent class includes a group of bases capable of incorporating up to 50% or more of water or aqueous solutions of LV with the formation of emulsions of the w/m type (lanolin, hydrolines). Absorption bases absorb wound exudate well, provide good contact between LR and the absorption surface.

The group of detergents includes emulsion bases of the m/w type, prepared using surfactants, stabilized with hydrophilic inorganic (bentonites), organic (water-soluble cellulose ethers) substances and their mixtures, etc. They release LV well, mix easily with aqueous solutions, have a cooling effect.

Water-soluble ointment bases unite a large group of hydrophilic bases formed by water-soluble UMS of a synthetic or natural nature (polyethylene glycols, cellulose ethers, soluble lanolin).

This also includes numerous hydrophilic-colloid bases (starch, algin, pectin hydrogels), which by their nature represent colloidal systems of the type of elastic jellies obtained by the interaction of macromolecules of organic polymers with water. Ointments on these bases easily release LR, have good contact with the skin and tissues, absorb purulent secretions, are easily removed from the surface, are indifferent, do not stain linen.

The technological process of production of ointments, gels, pastes and liniments at chemical and pharmaceutical enterprises consists of the following stages of production: production preparation, preparation of medicinal and auxiliary substances, preparation of the base; introduction of liquid into the base, homogenization, packaging, packaging and labeling of finished products

CHARACTERISTICS OF BASES AND AUXILIARY MATERIALS

From the point of view of physical and chemical science, suppositories are considered as dispersed systems consisting of a dispersed medium represented by the base and a dispersed phase, the role of which is performed by medicinal substances. Depending on the properties of medicinal substances, suppositories can create different dispersion systems. ,

Homogeneous systems are formed in those cases when the medicinal substance is dissolved in the base, and heterogeneous systems — if the medicinal substances are introduced into the base by the type of emulsion or suspension,

In the structure of suppositories, main (medicinal substances) and auxiliary (carriers or base) components are distinguished. A number of requirements are put forward to suppository bases:

— they must retain sufficient hardness at room temperature

— the melting or dissolving temperature should be close to the temperature of the human body;

— should not irritate the mucous membrane of the rectum and cause other undesirable effects, i.e. should be physiologically indifferent;

— should not interfere with the release and therapeutic effect of the medicinal substance;

— should not interact with medicinal substances that are injected into the suppository mass.

The technological requirements for the foundations are closely related to the specified general requirements. These include:

— chemical and physical stability of the base during the manufacturing and storage of suppositories;

— the ability to be easily formed and maintain the necessary hardness during injection;

— the ability to emulsify the required amount of solutions;

— have a certain plasticity, viscosity, time of full deformation, i.e. certain structural and mechanical properties.

These requirements are met by lipophilic and hydrophilic bases used in the pharmaceutical industry of various countries.

Lipophilic bases. As suppository bases, SPh of Ukraine suggests using cocoa butter, its alloys with paraffin and hydrogenated fats, vegetable and animal hydrogenated fats, solid fat, lanol, alloys of hydrogenated fats with wax, solid paraffin, and other bases approved for medical use.

Lyophilic bases must meet the following requirements:

- melt quickly in the rectum;

— the melting temperature should not exceed 37 °C;

— have sufficient hardness and a small interval between the melting and solidification temperatures;

— have sufficient viscosity;

— absorb liquids well;

— be stable during storage.

Of the known foreign lipophilic bases, Vitepsol, Estarinum, and Lazupol bases are particularly interesting.

Hydrophilic bases. Hydrophilic bases must meet the requirements

— to dissolve quickly and completely in secretions of mucous membranes;

- do not irritate mucous membranes;

— mix with hydrophobic medicinal substances or absorb them;

— to be chemically and pharmacologically indifferent.

Modern hydrophilic bases are represented mainly by polyethylene glycols — condensed polymers of ethylene oxide and water. The domestic industry produces polyethylene glycols that differ in molecular weight — PEG-400, -1500, 42000, -4000, -6000.

METHODS OF OBTAINING SUPPOSITORS IN INDUSTRIAL CONDITIONS. PRODUCTION TECHNOLOGICAL EQUIPMENT

Suppositories in industrial production are made by two methods — pouring the molten mass into molds and pressing on special equipment.

Pouring method. Industrial production of suppositories in this way is most often carried out according to a technological scheme, which consists of the following stages:

1) preparation of the base;

2) preparation of medicinal substances and preparation of concentrate;

3) introduction of medicinal substances into the base;

4) formation (and packaging) of suppositories;

5) packaging of suppositories.

First, reactors, various containers, manifolds, pumps and other equipment are prepared for operation by thorough treatment with hot steam, water with detergents, rinsing and drying. Sanitary treatment of premises and training of working personnel are carried out.

Preparation of the base. First, the base components are weighed. In a stainless steel reactor with a steam jacket and a stirrer, the components of the base are fused at a temperature of -60-70 °C and stirred for 40 minutes. The base is filtered through a filter press, using a brass mesh or belting, and analyzed for melting point, solidification and time of complete deformation and transferred to the hardware department,

Then, with the help of compressed air, the base is fed into the reactor, in which the suppository mass is prepared. After that, medicinal substances are injected into the mass.

Introduction of medicinal substances into the base. Medicinal substances are introduced into the base in the form of aqueous solutions (water-soluble), fat solutions (fat-soluble) or suspensions of ground powders in bases (insoluble in water and fats). The resulting solutions or suspensions are called concentrates.

Water-soluble components are dissolved in water heated to 45 °C, fat-soluble components are dissolved in part of the melted fat base. The resulting concentrates are filtered through calico, and then mixed with the rest of the base.

Substances insoluble in water and base are introduced in the form of a suspension. Pre-ground medicinal substances are mixed in a reactor with an equal or one-and-a-half amount of base heated to a temperature of 40-50 °C. The resulting concentrate is cooled and ground on colloidal mills or, for heat-labile substances, with the help of three-roll maseters. In addition, rotary pulsation devices, rotary gear pumps and other equipment can be used to obtain high-quality suspensions. The grinding time of the concentrate lasts from 2 to 4 hours to obtain the necessary degree of dispersion of the medicinal substance, which is introduced into the base according to the type of suspension.

The finished concentrate is pumped (through a hose with a kapron screen) into a reactor (with a turbine or anchor stirrer) for mixing with the rest of the base. The

operation of preparing the suppository mass is carried out with constant stirring and a temperature of 45-50 °C. After a positive analysis (homogeneity of the mixing of components, temperature of solidification and melting, time of complete deformation), the mass is submitted to the stage of pouring suppositories.

Suppositories are then formed and packaged.

For pouring suppositories, lines of the "Sarong 200 S" type are used (with direct dosing of the mass into the formed cells made of polyvinyl chloride film with subsequent packing of the products into bundles.

One vertically placed strip of aluminum foil or polyvinyl chloride film is supplied from two rolls. The two strips first pass separately and are cut in a vertical direction in the cutting unit to achieve a flawless formation. Both strips are formed (forged) into cup-shaped halves, which are then joined into a complete form and heat-welded. At the same time, a filling hole remains open on top of each form, through which the filling needle pours the molten suppository mass. Thus, the packaging formed from foil simultaneously serves as a casting mold. The filling double-walled container contains almost 30 liters of mass. The necessary temperature of the mass is constantly maintained with the help of water heating with a continuously operating stirrer. Dosing is carried out using a pump. At the next position, the package is hermetically sealed and equipped with additional transverse stiffening ribs (cold compression) between separately welded suppositories. Next, strips are cut from the tape for a certain number of suppositories. The cut strip enters the cooling section, after passing through which a ready-made package is formed. The outer surface of the foil (thickness 40 μm) is covered with a stretched polypropylene film (12.5 μm), and the inner one is polished for welding when heated or layered with high-pressure polyethylene weighing 20 g/m^2.

The productivity of the line is 16,000—20,000 pieces per hour.

By the method of pressing on eccentric tablet machines with cooling of the punch, matrix and casing, it is possible to obtain from 40 to 100 thousand suppositories per hour. The suppository mass is usually cooled in a refrigerator to 3-5 °C, crushed and sieved. Lactose, sucrose, aerosol, starch are added to the granulate to adjust the technological properties

The advantage of this method is the ability to prevent the destruction of heat-labile medicinal substances, the absence of sedimentation of the active substance and to avoid its possible incompatibility with the molten suppository base.

This method can be used when using plastic bases. Since the mass is dosed by volume, it is necessary to use the coefficient of substitution of medicinal substances.

In the process of manufacturing pressed suppositories, it is not necessary to apply significant forces for pushing out, because the particles of the fat base play the role of an effective lubricant in the wall layer due to their intensive plastic flow. The pressing method is particularly suitable for the production of suppositories with cardiac glycosides, some thermolabile hormonal drugs, and biogenic stimulants, because the preparation process ensures high dosage accuracy and thermal stability of medicinal

substances. PREPARATION OF MEDICINES AND EXPOSURES, as a rule, is reduced to grinding, sieving, weighing and (or) dissolution of the drug.

PREPARATION OF THE BASE. The components of the ointment base are subjected to melting, mixing or emulsification followed by filtration from mechanical impurities. Melting bases and their components (vaseline, lanolin, wax, emulsifier No. 1, emulsion waxes, polyethylene oxide-1500, etc.) are melted in EK-40, EK-60, EK-125, EK-250 electric boilers or boilers with PK-125, GR-250 steam shirts.

ADMINISTRATION OF DRUGS INTO THE BASE is carried out depending on their physical and chemical properties. Crushed solids or their aqueous solutions are added to the base with constant stirring, for which mixers of various designs with anchor, blade and turbine stirrers are used.

Suppositories in industrial conditions are manufactured in the following ways:

pouring the molten mass into molds;

pressing on special equipment.

The most commonly used method is pouring the molten mass into molds.

After the stage of homogenization of the suppository mass, the mixture is poured. The most widely used for pouring suppositories is the automatic line "Sarong 200S" with direct dosing of mass into molded cells made of polyvinyl chloride film with subsequent stacking of products in bundles. Productivity of the line is 16,000 - 20,000 pcs. in an hour After the suppositories are formed, they are rejected based on their appearance, and their analysis is carried out. Dry suppositories at a temperature of 10-15 °C for 2-3 hours with additional air blowing to remove cooling and lubricating components. Ready suppositories come in a package.

The method of non-thermal preparation of this dosage form by pressing compositions of cooled and crushed bases with liquid has an important importance in improving the technology of suppositories.

By the method of pressing on eccentric pressing machines with punch cooling, matrices can be obtained from 40 to 100 thousand suppositories per hour. The advantage of this method is the possibility of preventing the destruction of thermolabile drugs, the absence of sedimentation of the active substance, and the prevention of its possible incompatibility with the molten suppository base.

The final stage of any technological process is product quality control. Suppositories are controlled according to the following indicators: shape, uniformity, average weight of suppositories and deviations from it. For suppositories prepared on lipophilic bases, the melting temperature is determined, which should not exceed 37 ° C. If the definition of the melting temperature is difficult, the time of complete deformation is determined, which should be no more than 15 minutes. For suppositories made on hydrophilic bases, the dissolution time is determined, the

suppository must dissolve within 1 hour. Suppositories also determine the quantitative content and uniformity of dosage of active substances.

PACKAGING AND PACKAGING SMF. SMF packaging is produced in a container made of various materials that do not allow adsorption, diffusion of the content, its contamination, which ensure ease of use and the possibility of labeling.

SMF is stored in a cool place protected from light.

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 medicinal products:

— task content:

Task 1. Preparation of the thesis emulsion

Description.

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.	Suspensions - give definitions	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. – P. 253.
2.	Classification of suspensions	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: 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):

Tests from the base of KROK-2

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. Khohlova etc. - Kh.: NFaU, 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 "KROK 2. Pharmacy" / O.A. Ruban, V.D. Rybachuk, L.M. Khokhlova, D.S. Pulyaev - Kh.: NFaU, 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.: NFaU: 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.: NFaU: 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 NFaU, 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 NFaU, 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-NFaU, 2017. – 44 p.
- Zujkina SS 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. – Kh.: NFaU 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.

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- 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, K.K. 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. 37-38

Topic: " Production of plasters and TTS"

Goal: To study the production technology of plasters and TTS. Be able to rationally select auxiliary materials and equipment, carry out quality control, packaging and labeling of the finished product

Basic concepts: *Mustard sticks* are sheets of paper coated on one side with a thin layer of defatted dry powder obtained from black mustard seeds. In medical practice, it is this powder that acts on the skin for the purpose of irritation and distraction.

Plaster - (from buckwheat. Emplastron - ointment), dosage form for external use - a plastic mass that softens at body temperature and sticks to the skin. It consists of salts of fatty acids mixed with wax, rosin, medicinal and other aromatic and medicinal substances. A sticky plaster (glucose plaster) is used to fix non-bandaged bandages

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. Characteristics and classification of plasters.
2. Industrial production of plasters.
3. Industrial production of mustard seeds
4. Liquid plasters.

Lesson content

Mustards, their pharmacological features

Different pharmacological substances that excite receptors can have different degrees of selectivity of use.

Things that have a universal stimulating effect on different types of receptors are labeled as irritants. Such drugs of factory production include mustard seeds.

Mustard sticks are sheets of paper coated on one side with a thin layer of defatted dry powder obtained from black mustard seeds. In medical practice, it is this powder that acts on the skin for the purpose of irritation and distraction. First of all, mustard

seeds cause reddening of the skin, expansion of the vascular network and a rush of blood to the place of their application. At the same time, the excitability of the autonomic nervous system - sympathetic and parasympathetic - increases. As a result of the reflex increase in the tone of the sympathetic nervous system and the accumulation in the blood of the products of nervous excitement (adrenaline, norepinephrine), the protective function of the child's body increases. It is on this principle that the use of mustard dressings as stimulators of a child's immunity during a cold is based.

The distracting effect is the creation of an additional focus of nervous irritation with the help of mustard. It is needed, for example, if the child has stenosing laryngotracheitis, which is accompanied by difficulty breathing, a deep cough, hoarseness of voice. For a distracting effect, mustard seeds are placed on the calves of the legs.

The active substance of mustard is essential mustard oil and volatile phytoncides, which are released under the influence of water and an enzyme present in the mustard itself.

Stimulating agents, stimulating receptor formations, are able to cause various reflex reactions. When acting on skin receptors, irritating substances have a beneficial effect on internal organs, muscles, joints that are related to a certain area of the skin. The "distracting" effect is manifested in the fact that with inflammatory diseases of internal organs, muscles, nerves, joints, irritating substances, affecting skin receptors, 1) reduce pain sensations and 2) improve the functional state of the affected organ.

A vivid example of a distracting effect can be the use of mustard seeds for inflammatory lung diseases, myositis, neuralgia, etc. At the same time, applying mustard seeds to the appropriate areas of the skin reduces pain and promotes faster recovery. The irritant in this case is mustard essential oil, which is released when using mustard seeds.

Before use, mustard seeds are placed for a short time in warm water (approximately 38 °C). If you place mustard seeds in very hot or, on the contrary, cold water, its effect may not be manifested. This is due to the fact that the active principle of mustard seed powder, which is covered with mustard seeds - mustard oil - is formed as a result of an enzymatic reaction that occurs only when mustard seeds are placed in warm water. At a low temperature, this reaction does not occur, and at a high temperature, the enzyme necessary for its treatment is destroyed.

2. Plasters, their types, properties

Plaster - (from buckwheat. Emplastron - ointment), dosage form for external use - a plastic mass that softens at body temperature and sticks to the skin. It consists of salts of fatty acids mixed with wax, rosin, medicinal and other aromatic and medicinal substances. A sticky plaster (glucose plaster) is used to fix non-bandaged bandages.

Depending on the medical purpose, patches are distinguished:

* Epidermal. They have the necessary stickiness and may not contain medicinal substances, they are used as a dressing material, bringing the edges together earlier, hiding skin defects, protecting it from traumatizing factors of the external environment, in the treatment of some skin diseases;

* Endermatic. They contain medicinal substances (keratolytic, depilatory, etc.), applied in case of skin diseases;

* Diadermal. They contain medicinal substances that penetrate through the skin and have an effect on deep-lying tissues or a general (resorptive) effect. A variety of diadermal patches are transdermal therapeutic systems (TTS).

According to the aggregate state, plasters can be solid or liquid.

Patients with hypersensitive skin can use a patch made of soft, breathable non-woven material with an applied layer of polyacrylate glue, which is gentle on the skin. It has a reliable gluing ability, while it is removed painlessly and without residues.

For the production of modern adhesive plasters, the latest world achievements are used: the latest materials, technologies, equipment, etc. The production technology involves the use of non-drying glue that does not retain gasoline. It forms a film that retains stickiness for a long time. Even with a small pressure at room temperature, it immediately ensures the adhesion of the patch to the skin.

The use of plasters in everyday medical practice, the maximum convenience of their use makes them indispensable for certain medical purposes.

Any nurse in the procedure or intensive care unit is well acquainted with the problem of reliable and at the same time aseptic fixation of the needle in the vein, as well as with the system for intravenous infusion, intravenous catheters of various types, including "butterfly needles". Special plasters make it possible to relieve the nurse, who is always burdened with various problems, from additional difficulties associated with fixation on the patient's skin. The shepherds presented below are epidermal in their variety.

First of all, it is a 3-strip fixing patch for needles and tubes of systems for infusion of solutions, blood transfusions, devices for infusion into small veins (butterfly needles) made of both transparent film and non-woven material (Fig. 1).

There are also special patches for fixing intravenous catheters, which have a U-shaped cutout for the catheter port (Fig. 2).

All types of patches have a non-sticky, absorbent "pad" to cover the puncture site. A distinctive feature of these plasters is that, providing a reliable fixation, they can be easily torn off by hand in the longitudinal and transverse directions without leaving traces on the skin after use and almost without tearing off even a hair. Patches have a special hypoallergenic sticky layer, which is important for patients prone to allergic reactions.

Plasters have:

* bactericidal, antiseptic and anti-inflammatory properties; * increase the body's ability to resist adverse environmental conditions; * affect the mental and emotional

state of a person; * have pronounced dermatological and cosmetic properties, actively restore and preserve the health of the skin, * renew the mechanisms of self-regulation of our body* have bioenergetic value.

Patches are a medicinal form for external use that sticks to the skin, affects the skin, subcutaneous tissues and in some cases has a general effect on the body. This is one of the oldest medicinal forms.

Plasters at room temperature have the appearance of a solid mass. They soften at body temperature, and melt at 66-100 °C. Under these conditions, they can be fused with various medicinal and auxiliary substances and mixed with powdered materials. In addition, plasters can be produced in the form of liquids, in glass bottles, aluminum tubes, aerosol cans.

Depending on the medical purpose, plasters are divided into epidermal, endermatic and diadermal.

Epidermal plasters are used to protect the skin from harmful effects, to close skin defects, to close the edges of wounds and to fix bandages on the surface of the skin.

Endermal patches contain medicinal substances that affect the diseased skin.

Diadermic plasters contain medicinal substances that penetrate through the skin and affect deep-seated tissues, or have a general effect on the body.

Epidermal patches should have good stickiness, adhere tightly to the skin and not irritate it. They may not contain medicinal substances, acting as a dressing material. As a result of the "greenhouse" effect, epidermal patches contribute to the softening of the skin, strengthen the processes of blood circulation and absorption. Endermic and diadermic plasters are softer in consistency, because they should ensure the maximum release of medicinal substances and their penetration to different depths of the tissue or provide a resorptive effect.

Plasters are produced in the form of a plastic mass on a substrate (canvas, chiffon, colencor, paper and others); solid plaster masses (cylinders, bars, tiles, sticks); liquid solutions (leather glues).

The plaster mass includes medicinal substances and a base. Antibiotics, sulfur, salicylic acid, extracts, tinctures, etc. are used as medicinal substances.

The plaster base may contain natural (rosin) and synthetic resins, wax, paraffin, ceresin, petroleum jelly, lanolin, lead salts of higher fatty acids (lead soap), fats, rubber, nitrocellulose, copolymers of vinylpyrrolidone with vinyl acetate, polymethacrylates and acrylates, volatile solvents (ether, gasoline, ethanol).

Its composition includes plasticizers (linetol, vegetable oils, dibutyl phthalate, cetyl alcohol, and others), antioxidants, fillers, etc.

Depending on the composition, plasters are classified as lead (lead-resin and lead-wax); resin-waxy; rubber; liquid (leather glues).

The technology of making plasters depends on which group they belong to.

Lead plasters contain lead soap. Lead soaps fuse with resins, socks, medicinal substances, do not contaminate clothes, are stable during storage.

Simple lead plaster (*Emplastrum Plumbi simplex*). A homogeneous solid mass of grayish or yellowish color, becomes viscous and sticky when heated. The drug should not be greasy to the touch and have a bitter smell.

It is used as a basis for preparing other plasters and externally for purulent-inflammatory skin diseases, boils, carbuncles, etc.

Composition: lead oxide (lead lead) — 10.0 g; sunflower oil - 10.0 g; purified pork fat - 10.0 g; a sufficient amount of purified water.

Chemically, the patch is a mixture of lead salts. The basis of the industrial method of plaster production is the saponification reaction of lead fats with oxide in the presence of water at the boiling temperature of the mass. The main equipment is enameled or stainless steel reactors (the use of copper and tinned copper boilers is excluded), which have a steam jacket and a stirrer.

Preparation of a simple lead patch. The calculated amount of pork fat and sunflower oil is placed in the reactor and fused, adjusting the temperature by supplying blind steam. The volume of the reactor should exceed the amount of the reaction mass by at least 4-5 times, because the mass foams strongly during cooking. Lead slag is ground into a fine powder, sifted through a silk sieve and mixed with two parts of freshly boiled purified water. A suspension of lead oxide in water is added to the melted, but not overheated mixture of fats in portions without residue with constant stirring and heating. At the same time, a saponification reaction takes place, as a result of which a fatty lead salt (lead soap) is formed. Chemically, lead plaster is a mixture of lead salts of oleic, palmitic and stearic acids with a significant preference for the latter.

The cooking process must be carried out at a temperature of 100 - 110 °C for 2-3 hours. During the cooking process, hot water is added in small portions to the reaction mass every 5 minutes, making sure that it does not boil completely, as evidenced by the presence of small bubbles. The mass is constantly stirred, because the reaction occurs at the boundary between fat and lead oxide, which have different densities and tend to separate. Adding large amounts of water slows down the process, which contributes to stratification of the system.

The absence of foam when the mass is heated for a long time indicates that the water has boiled off, and the temperature of the mixture may exceed 110 °C. Adding successive portions of water leads to spattering of the mass, so you need to be careful.

In the process of cooking, the initial reddish color of the mixture gradually turns into whitish-gray, and towards the end of cooking - into whitish.

Cooking the patch is considered finished if a small sample, poured into cold water, is a plastic mass that does not smear and does not stick to the fingers when kneaded.

The finished patch is freed from glycerin by repeatedly mixing the mass in warm water with the help of a heated dough mixer. The patch washed in this way is again transferred to the reactor and heated to 105-110 °C until the water is completely removed. A sample of dried lead plaster, taken with a spatula, should be drawn into a

thin transparent thread. Poorly dried and insufficiently freed from glycerin plaster becomes hard and brittle during storage, becomes bitter and moldy.

The quality of the patch is affected by the quality of the original fats, lead oxide should not contain suric impurities (Pb304), which almost does not saponify fats. The water used should not contain carbonates, sulfates and carbon dioxide, which turn lead oxide into lead sulfates and carbonates, which do not oxidize fats.

Standardization of the finished preparation is carried out according to the reactions of truth and quantitative content of lead oxide. The preparation should not contain peroxide, lead carbonate and lead oxide. Weight loss during drying should not exceed 3%.

A simple lead plaster can be used independently, as well as be part of other plasters and lead (diachial) ointment.

Plasters based on a simple lead plaster are usually divided into lead-resin and lead-wax plasters.

Composite lead plaster (*Emplastrum Plumbi compositum*) — lead-resin plaster of the following composition: simple lead plaster 85.0 parts; rosin 10.0 parts; oil of turpentine 5.0 parts.

Lead plaster and rosin are fused in a steam-heated reactor. Turpentine is added to the semi-cooled mass with continuous stirring. Sticks are squeezed or pumped out of the obtained mass.

It is used as a mild irritant.

Plaster spiliny 4% (Emplastrum Epilini) belongs to lead-wax plasters and has the following composition: epilin citrate 4.0 parts; simple lead patch 51.0 parts; anhydrous lanolin 20.0 parts; wax 5.0 parts; purified water 20.0 parts.

A homogeneous sticky mass of light yellow or brownish yellow color with a soft consistency. The plaster should not have a bitter smell.

It is used as a depilatory agent for fungal skin diseases.

The bases of resin-wax plasters are alloys of resins and wax. They can also include fats and carbohydrates. The most widely used callus patch.

Corn patch (Emplastrum ad clavos) contains: salicylic acid 20.0 parts; rosin 27.0 parts; paraffin 26.0 parts; petrolatum 27.0 parts.

A homogeneous soft, sticky, but not viscous mass of yellow or dark yellow color. The melting point is not higher than 60 °C. The melted plaster has a characteristic smell of rosin.

It is used as a means to remove calluses (keratolytic agent).

Preparation of a corn patch. A weighed amount of rosin, paraffin and petrolatum is placed in a reactor with a steam jacket and a stirrer and fused. The alloy is filtered while warm through a kapron mesh. Dissolve in the filtrate at mixing salicylic acid. The resulting homogeneous mass is poured into 3.0 g molds and cooled. Each patch is wrapped in waxed paper and packed in cardboard pencil cases.

Standardization of finished products is carried out according to qualitative and quantitative reactions to salicylic acid (19-21%), organoleptic indicators, melting point.

Liquid plasters, or skin glues (Emplastra liquida) are viscous liquids that leave an elastic sticky strong film on the skin after application of a volatile solvent. They are used as epidermal and endermatic plasters. The plaster film in them is formed due to film formation during drying of solutions of rosin, nitrocellulose (in the form of collodion), perchlorvinyl and formaldehyde resins in organic solvents (ether, ethanol, acetone, less often chloroform, dimethylformamide). To give the film greater elasticity, vegetable oils, linetol, dibutyl phthalate, triacetin, and cetyl alcohol are added to the composition of the adhesives. Liquid plasters are produced in bottles and aerosol packaging.

The latter are widely used as a sterile dressing material for inpatient and outpatient treatment in gynecology, dermatology and surgery.

Glues are conventionally divided into collodion glues, which include collodion, elastic collodion, callous liquid, Novikov's liquid, colaplast and microplasg, and resin glues - klsol, furaplast, BF-6 glue, cerigel.

Collodium (*Collodium*). The composition of the drug: Koloxylin 4.0 parts; 20.0 parts of 96% ethyl alcohol; ether medical 76.0 parts. It is a colorless or yellowish, transparent or slightly opalescent syrupy liquid with an ether smell. Contains 4% koloxylin.

Preparation of collodion. The required amount of alcohol is weighed into the reactor. Coloxylin is carefully crushed, because it is an explosive substance (a mixture of mono- and dinitrocellulose cellulose), weighed and placed in a reactor, wetting it with alcohol, the rest of the alcohol and a measured amount of ether are added. Leave in a well-closed reactor until the koloxylin is completely dissolved.

Because coloxylin is an explosive substance, it is often transported in the form of safe water slurry. When preparing the plaster, the water is displaced from the jelly with ethanol, and the koloxylin alcogel formed at the same time is dissolved in ether. Collodion is available in bottles of 5 and 15 ml.

It is used for fixing surgical bandages on the skin and covering small wounds.

Quality control of finished products is carried out for cleanliness. For 20 ml of water is added to 5 ml of this preparation, shaken and filtered from the formed precipitate. The filtrate should have a neutral reaction. The dry residue should be from 3.8 to 4.2%.

Elastic collodion (*Collodium elasticum*) is collodion to which 3% of castor oil is added as a plasticizer.

Corn liquid (*Liquor ad clavos*) contains: salicylic acid 1 part; 1 part of 96% ethanol; collodion 8 parts; diamond green 0.01 part.

Novikov's liquid (*Liquor Novicovi*) has the composition: tannin 2 parts; diamond green 0.2 parts; 0.2 parts of 96% ethanol, 0.5 parts of castor oil and 20 parts of collodion.

It is used to treat small skin wounds and cracks.

Mustard sticks are a variety of rubber plasters, which are produced in the form of rectangular strips of paper measuring 8x12.5 cm, covered with a powder of defatted mustard seeds 0.3-0.55 mm thick.

The composition of mustards includes mustard powder 98.0 parts; natural rubber to obtain a mass of 100.0 parts; B-70 aviation gasoline 100.0 parts; paper.

It is used as an anti-inflammatory distraction.

The raw material for obtaining mustard powder is the seed of Sarepta (Semina Sinapis junceae) and black (Semina Sinapis nigrae) mustard, which contains the glycoside sinigrin, which is split under the action of the myrosin enzyme into glucose, potassium hydrosulfate

1 essential mustard oil (allyl isothiocyanate). Essential oil causes severe irritation and hyperemia of the skin. After collapsing (removing) the shell, the seeds are ground to medium fineness and fatty oil is squeezed out of them with a hydraulic press. The remains of fatty oil from the cake are extracted in Soxhlet-type apparatus. The presence of fatty oil negatively affects the quality of mustard seeds - the therapeutic effect is slowed down and their stability during storage is reduced (mustard powder becomes bitter and peels off from the paper).

Preparation of mustards. The technological process consists of five stages:

1) preparation of rubber glue;

2) preparation of mustard mass;

3) spreading the mass on paper, drying, cutting the roll and placing mustard seeds in the feet;

4) packaging;

5) gasoline recovery.

Preparation of rubber glue. To do this, rubber steamed for 24-36 hours and cut into pieces is placed in the glue mixer, gasoline is added and the paddle mixer is turned on for 30-40 minutes. Then the mass is filtered. The resulting glue (a 1.35-2% solution of rubber in gasoline) is a thick, slow-moving mass that easily turns into a jelly-like mass as the gasoline evaporates.

Preparation of mustard mass. Mustard mass is a mixture of rubber glue and mustard powder in a ratio of 1:1—1.1:1. The content of essential oil in macus should be at least 1.11%. Rubber glue is placed in a mixer, mustard powder sifted from large particles and extraneous impurities is added and mixed until a homogeneous mass is obtained. The finished mustard mass is served with a pump on a table with a tub for spreading.

Production of mustard seeds. The process of spreading, drying and cutting is carried out on a continuous operation unit. Rolled paper passes through the gap

between the table top and the tub. Passing under the bath, the paper is covered with a layer of mustard mass 0.3-0.5 mm thick, then enters the drying chamber (drying time 45 min, air temperature 80 °C). The vapor-air mixture formed in the chamber with gasoline is gradually sucked off and fed to the gasoline recovery stage.

The dried tape is cut on a sheet-cutting machine into sheets of 75(76) x 90 cm size, which are cooled for 24 hours, then the sheets are cut into separate mustard seeds and discarded.

Packaging. Mustard seeds are packaged in bags of 10 pieces. Every tenth mustard has an inscription on one side about the method of application. Packages are placed in bundles of 600 pieces and stored in a dry place. The storage period is 8 months. In the presence of moisture, hydrolysis of sinigrin occurs, and mustards lose their activity.

Standardization of finished products is carried out according to the quantitative content of allyl isothiocyanate, which must be at least 0.0119 g in mustard seeds (100 cm2). severe irritation, burning and redness skin no later than after 5 minutes.

Nowadays, they also produce "Mustard bag", which is a heat-sealed bag made of porous paper that does not get wet, on both sides or on one side and paper with a polymer coating on the other. The package is filled with mustard mixture. The mustard bag is produced in the size of 11x10 cm and is divided into four identical bags. Each bag is evenly filled with mustard mixture.

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:

— **Manufacturing formulation of Emplastrum Plumbi simplex (FS 42-1732-81)**

Specification for raw materials

No. z/p	Starting substances and materials	ND	Content, %	components, g Quantity
1.				
2.				
3.				
4.				

Description .

Storage .

Expiration date –.

Application:

A brief description of the technology for obtaining a simple lead plaster

Composition:

Preparation. .
Trial.

— 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.	Characteristics and classification of plasters	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. – P. 399-402.
2.	Industrial production of plasters	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. - P. 402-407.
3.	Industrial production of mustard seeds	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. - P. 407-410.
4.	Liquid plasters	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. - P. 410 - 411.
5.	Characteristics and classification of therapeutic systems	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. – P. 589 - 591.
6.	Therapeutic systems with controlled release	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. – P. 591 - 596.
7.	Oral therapeutic systems	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. – P. 596 -

			600.
8.	Transdermal therapeutic systems	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. – P. 600 - 604.

— 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:

Tests of the base KROK-2

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. Khohlova etc. - Kh.: NFaU, 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 "KROK 2. Pharmacy" / O.A. Ruban, V.D. Rybachuk, L.M. Khokhlova, D.S. Pulyaev - Kh.: NFaU, 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.: NFaU: 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.: NFaU: 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 NFaU, 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 NFaU, 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-NFaU, 2017. – 44 p.

- Zujkina SS 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. – Kh.: NFaU 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, K.K. 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. 39

Topic: " Production of nano- and radiopharmaceuticals"

Goal: To study technological schemes for the production of radio- and nanopharmaceuticals . Be able to rationally select auxiliary materials and equipment, carry out quality control, packaging and labeling of the finished product .

Basic concepts: *Radiopharmaceutical drug (eng. radioparmaceutica drag) — any pharmaceutical product* that contains one or more radionuclides (radioactive isotopes) included in the formulation for diagnostic or therapeutic purposes.

Radionuclide impurities are impurities of other radioactive nuclides (in percentage) to the activity of the main nuclide for a certain time (date);

Radiochemical impurities are admixtures of chemical compounds different from the main substance that makes up the drug, but contain the same radionuclide .

Equipment: visual material, multimedia projector, presentation, 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;
- 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 role and place of nanopreparations in modern medicine.
2. History of creation of nanopreparations.
3. Materials used in the production of nanopreparations.
4. Advantages and disadvantages.
5. Technology of obtaining nanopreparations.
6. Equipment used in the production of nanopreparations. Quality control.

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 medicinal products:

— task content:

1. Production and use of radiopharmaceuticals.
2. Assortment and composition of radiopharmaceuticals on the pharmaceutical market of Ukraine.
3. Features of technology and quality control of radiopharmaceuticals.
4. Use of nanotechnology in the production of medicinal products.
5 . Special conditions necessary for the manufacture of radiopharmaceuticals
6. Groups of auxiliary substances in the production of nano- and radiopharmaceuticals .
7. Equipment for the production of nano- and radiopharmaceuticals .

Lesson content

Today, scientific research in the field of nanotechnology is recognized as a priority all over the world, and progress related to the development of nanomaterials for the electronic, automotive, aerospace industry, and especially medicine, is gaining more and more scope. The latest achievements in nano- and bio-nanotechnology affected many areas of health care: such concepts as nanomedicine appeared, as well as nanopharmacology, which deals with the development of a new generation of medicinal preparations - the so-called nanomedicines. The use of specific radioindicators, called radiopharmaceuticals, to visualize the function of organs and pathological conditions is a unique feature of nuclear medicine. Unlike other imaging techniques, such as computed tomography, magnetic resonance imaging, and ultrasound, nuclear medicine studies are able to map physiological function and metabolic activity, thereby providing more specific information about organ function or dysfunction.

GENERAL CHARACTERISTICS. CLASSIFICATION. REQUIREMENTS

For the first time, the term "nanotechnology" was used by Norio Taniguchi, an engineer from the University of Tokyo, in 1974. Today, nanotechnology is used in various fields, including medicine and pharmacy, which are developing the most intensively.

Nanotechnology is an interdisciplinary field of fundamental and applied science and technology, dealing with a set of theoretical foundations, practical methods of research, analysis and synthesis, as well as methods of production and application of products with a given atomic structure through the controlled manipulation of individual atoms and molecules, which are aimed at creating and practical use of nanoobjects and nanosystems with specified properties and characteristics.

In medicine and pharmacy, nanosystems are used for the delivery of medicinal substances, diagnostics and the creation of implants. One of the priority areas of nanotechnology development in pharmacy is the targeted delivery of drugs. The importance of which is evidenced by the progressive growth of publications on this topic in international scientific journals.

More than 50% of pharmaceutical manufacturing companies actively working in this field use nanotechnology to develop systems for the delivery of active pharmaceutical ingredients (APIs) to organs and tissues - targets. There are already two blockbusters among nanopreparations that, despite other successful drugs, together have a turnover of 5 billion dollars. Over the past 20 years, nanotechnologies have made significant progress in the development of drug delivery systems that have solved the solubility and bioavailability issues of APIs and helped reduce side effects. The specific forms and small sizes of drugs made it possible to deliver various therapeutic agents to hard-to-reach targets, for example, to overcome the blood-brain barrier or to deliver active substances inside the cell nucleus.

Targeted drug delivery is a system of nanoobjects, the activity of which and the method of delivery to the target tissue (organ) are determined by the properties of this object.

The address delivery system has the following requirements :

- the ability to circulate in the blood for a long time;
- accumulate in the lesion;
- effectively transfer molecules of active substances into cells and their organelles;
- be compatible with peptides, nucleic acids and maintain physical stability in whole blood;
- allow changing the drug release profile;
- have the ability to carry a marker, with the help of which it is possible to track the accumulation of API in the lesion in real time, while its size can vary in the range of 10 - 300 nm.

The use of delivery systems is aimed at reducing the adverse side effects of medicines. To date, there are 5 main areas of application of nanotechnology in

medicine and pharmacy: API, new methods of treatment at the nanometer level, in vivo and in vitro diagnostics, medical implants.

Nanodelivery systems are classified depending on the nature of the carrier: organic and inorganic; depending on the aggregate state and morphological features (liposomes, micelles, fullerenes, dendrimers, clusters, nanospheres, nanocrystals). A nanocarrier, as a rule, consists of a molecule from which a particle is created; API, a surface modifier that provides targeted delivery.

Nanoparticles, which will be used as medicinal products and their carriers, will play an important role due to their unique chemical, biological, pharmaceutical and physical properties due to their dimensions (polymeric, inorganic nanoparticles, liposomes, etc.). Medicines can be encapsulated in nanoparticles or manufactured as nanoparticles. Their surface can be modified with coatings, layers or connections to ensure improvement of their characteristics (biocompatibility, directionality, shape recognition ability and participation in biological communication).

Being in the state of nanoparticles, medicinal products have a number of advantages: they are protected from destruction during transport to the destination, nanoparticles actively or passively accumulate in the target organ and release the required dose of the drug at the required time, it is possible to use nanoparticles as contrast agents of diagnostic systems and many another An increase in the ratio of the surface area of the drugs to the volume while reducing the size will cause an increase in their therapeutic activity, which will open a wider range of therapeutic methods and reduce its toxic effect on the human body.

Thus, nanoparticles or nanotechnologies make it possible to change the properties of the original drugs in a positive way:

- delivery and direction of medicines;
- increasing the therapeutic effect and duration of the drug due to controlled mechanisms of absorption and/or binding to nanoparticles;
- stability of the drug;
- manipulation and influence on body tissues;
- longer bioavailability;
- influence on the pharmacokinetics of drugs by changing the size of the constituent nanoparticles of the drug;
- visualization of processes using the unique physical and chemical properties of nanoparticles;
- the potential effect of the drug.

In order to apply nanotechnology in drug delivery, it is necessary to use at least some of the unique defined physicochemical properties of nanoparticles. Thus, increasing the solubility of the drug with the help of nanoparticles consists in the use of small sizes of these particles, which have a much larger surface area and at the same time are purposefully absorbed by specific tissues.

The following types of nanomaterials are distinguished as nanomaterials:

1. nanoporous structures;
2. nanoparticles, nanotubes and nanofibers;
3. nanodispersions (colloids);
4. nanostructured surfaces and films;
5. nanocrystals;
6. nanoclusters.

The classification of nanomaterials depends on:

- **purpose** (functional, compositional, structural);
- **the number of measurements** (three-dimensional particles obtained by explosion of conductors, plasma synthesis, restoration of thin films, etc.; two-dimensional objects - films obtained by methods of molecular layering, ion layering, etc.; one-dimensional objects - whiskers , these objects are obtained by the method of molecular layering, by introducing substances into cylindrical micropores, etc.; nanocomposites are materials obtained by introducing nanoparticles into any matrix);
- **aggregate state and morphological features** (nanosuspensions, liposomes, mixed micelles, crystalline structures (lyotropes), microemulsions, nanoemulsions, nanocapsules, surfactants, polymer nanoparticles, solid lipid nanoparticles;
- **the nature of the carrier** (polymeric nanoparticles, lipid nanoparticles, viral nanoparticles, organometallic nanoparticles).

The main concepts in the creation of nanomedicines are molecular objects - the drug and the target. ***A target*** is a macromolecular biological structure that is probably related to a certain function, the violation of which leads to a disease and on which a certain action must be taken. The most common targets are receptors and enzymes. ***API*** is a chemical compound (usually low molecular weight) that specifically interacts with the target and in one way or another modifies the response of the cell, which is created by the target. If the target is a receptor, then the drug will most likely be its ligand, that is, a compound that interacts in a specific way with the active site of the receptor.

There are two methods of obtaining nanosystems, they are shown in Fig. 1.

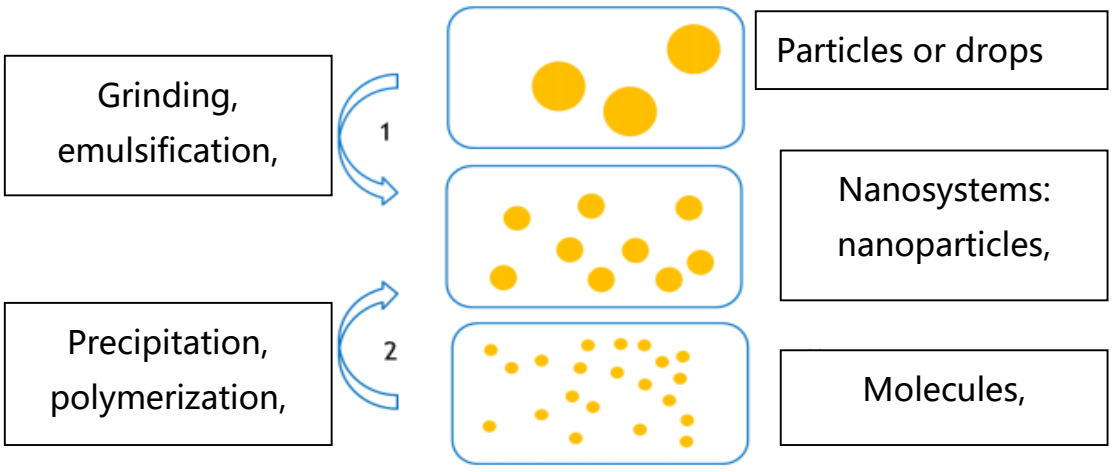

Figure 1. Methods of obtaining nanosystems

The first method includes grinding in a liquid medium of medicinal substances that are poorly soluble in water using an air jet, direct homogenization and, with microprecipitation in the presence of surface active modifiers, ultrasonic crystallization, liquid supercritical technology, cryo-grinding, spray drying.

The first "top-down" method is by reducing the size of the particles of the solid or liquid phase.

The second - "from the bottom to the top", by precipitation. The second way is to obtain nanocapsules (liposomes, niosomes, dendrimers, micelles). The scheme for obtaining micelles is shown in Fig. 2.

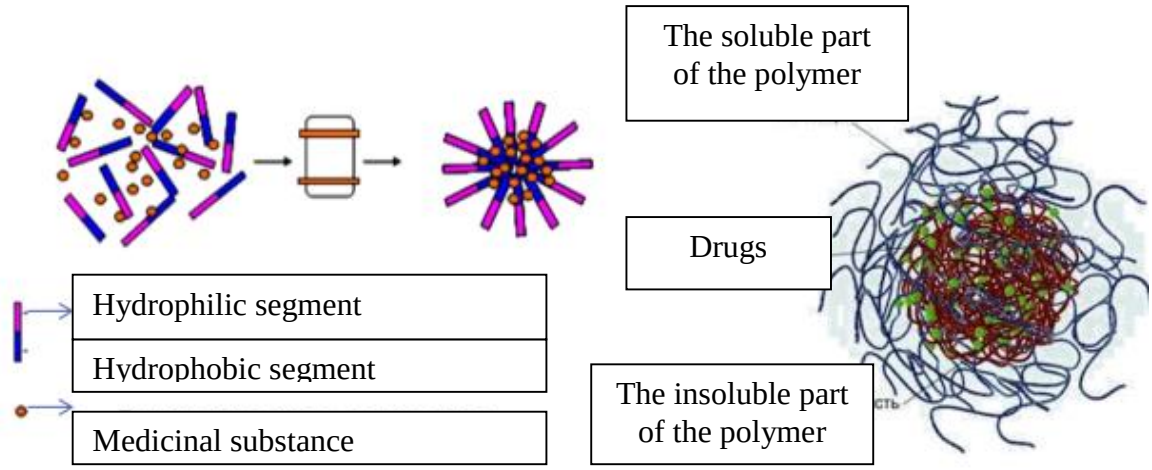

Figure 2. Scheme of obtaining a polymer micelle

Despite the successes in the development of this field, issues related to the long-term safety and toxicity of medicinal nanoforms, as well as their biocompatibility and decomposition, remain unresolved.

Radiopharmaceutical preparation (RPP) is a medicinal preparation approved for administration to a person for diagnostic or therapeutic purposes, which contains a certain radioactive nuclide in its molecule.

Currently, there are more than 100 radiopharmaceuticals developed using a reactor or cyclotron, which are used to diagnose a number of common diseases and to treat some diseases, including cancer. Although radiopharmaceuticals were considered as a treatment immediately after the discovery of radioactivity, the first significant use came much later, with the advent of cyclotrons to accelerate particles to produce isotopes. Subsequently, nuclear reactors made it possible to prepare a larger number of radioisotopes. For example, radioactive iodine (iodine-131), first introduced in 1946 for the treatment of thyroid cancer, remains the most effective method for the treatment of thyrotoxicosis and thyroid malignancy.

Some terms and definitions of RFP

Activity of radioactive material (Activity of radioactive material) - the number

of nuclear transformations (N) occurring in a given amount of material in a short period of time (t). This is often called absolute activity.

Isotopes **are** nuclides with the same serial number but different atomic mass.

Half-life (radionuclide) - for a single radioactive decay process: the time during which the initial number of radionuclide nuclei is halved. Denoted: $T_{1/2.}$

Radioactivity (Radioactivity) is the property of some nuclides to undergo radioactive decay.

Radioisotopes (Radioisotope) - a radioactive isotope of a certain element.

Radionuclide (Radionuclide) is a nuclide that is radioactive.

Radionuclide purity of the drug - the ratio of the activity of the main radionuclide to the total activity of the drug, expressed as a percentage, is not a constant characteristic of this drug, but changes over time.

Radiochemical purity (Radiochemical purity) - the ratio of the activity of a radionuclide, which is present in the drug in the declared chemical form of the main substance, to the total activity of the radionuclide in this drug, expressed as a percentage. Over time, the radiochemical purity decreases.

Chemical impurities (Chemical impurities) - impurities of extraneous chemical compounds and elements, the sources of which are starting substances and reagents, as well as by-products of incomplete or parallel reactions.

Nuclear isomers are nuclides that have the same mass number and atomic number, but differ in the energy state of their nuclei.

Radiopharmaceuticals (RFPs) differ from traditional medicines by the absence of any pharmacodynamic effect on the human body, which is due to the introduction of small amounts of a labeled chemical compound. The effect of therapeutic RFP is not due to the effect of a chemical compound, but to the radiation included in its radionuclide structure. The diagnostic use of RFP is based on the peculiarities of their pharmacokinetics, which allows obtaining an image of an organ and determining its anatomical and topographical characteristics or assessing the functional state of an organ or system without disturbing the physical conditions of its operation. The volume of RFLP production is extremely small compared to other medicinal products. Quite often, the number of packages in a series is 3-5 units. The shelf life of the drugs, depending on the half-life of the corresponding radionuclides, ranges from several minutes to several days.

The production of RFPs, unlike conventional pharmaceuticals, is still on a small scale, and the implementation of GMP guidelines that can be applied to the pharmaceutical industry is difficult and expensive. Ensuring GMP compliance is a challenge for a small-scale manufacturer. All technological operations must be performed in special premises and on special equipment designed for the production / manufacture of radiopharmaceuticals. The simultaneous production and / or manufacture of different RFP in the same working area (hot chamber, laminar zone or cabinet) is not allowed, which is caused by the need to reduce to a minimum the risk

of cross-contamination with radioactive substances or mixing of starting materials.

The preparation of the dosage form of the final RFP in practical nuclear medicine usually includes a specific (limited) activity on the date (and, if necessary, the hour) agreed with the consumer for the delivery of ready-to-use RFP, generators, kits and radiopharmaceutical precursors. All conditions that may affect the quality of the product (for example, radiochemical purity and sterility) must be clearly defined and must include permissible values for protection against radioactivity.

Because of their short half-life, some radiopharmaceuticals allow release for sale until quality control testing is completed. Specifications and quality control procedures for the most common radiopharmaceuticals are given in the State Pharmacopoeia of Ukraine or in the registration dossier.

List of quality indicators to which radiopharmaceutical medicinal products of industrial production and / or manufactured in medical institutions must comply

1. Preparations of industrial production: composition; description; authenticity; pH; volumetric activity; radionuclide impurities; radiochemical purity (radiochemical impurities); chemical impurities; quantitative definition; physiological distribution in body tissues (if necessary); quality indicators characterizing monoclonal antibodies, if they are available; bacterial endotoxins or pyrogenicity; sterility; packaging; labeling; transportation; storage; expiration date.
2. Preparations manufactured in medical institutions: composition; description; solubility; authenticity; transparency; chroma; pH; quality indicators characterizing monoclonal antibodies, if they are available; loss in mass during drying; mechanical inclusions (visible, invisible); quantitative definition; bacterial endotoxins or pyrogenicity; sterility; packaging; labeling; transportation; storage; expiration date.

The main diagnostic properties of RFP are determined, on the one hand, by the radionuclide, and on the other hand by the chemical compound and its behavior in the human body. When choosing a radionuclide, factors such as emitted radiation, energy and output of quanta, half-life, as well as possibilities and conditions of its production are taken into account.

Each radionuclide and nuclear isomer is characterized by a half-life and specific spectra (energies) of ionizing radiation unique to it. These include the spectra of alpha, beta, gamma radiation, conversion and Auger electrons, bremsstrahlung radiation, and characteristic X-ray radiation.

Radionuclides are identified by:

- by spectrum (gamma, beta and X-ray radiation);
- along the half-attenuation layer (beta radiation);
- by half-life (any radiation).

To determine the half-life, measure the amount of activity (or any amount proportional to it, for example, the counting rate, the area of the spectrum section, etc.) depending on time. The detector is chosen depending on the type of radiation emitted

by the analyzed nuclide.

The activity of the radionuclide in the preparation (as well as the specific, molar and volumetric activity) is indicated for a certain date, and for preparations containing a radionuclide with a half-life of less than 10 days, also for a certain time. For preparations containing a radionuclide with a half-life of less than 1 day, the activity is indicated in minutes.

In most cases, to determine the radionuclide purity and/or radionuclide impurities of RFP, the authenticity of each present radionuclide is pre-established and their activity is measured. Gamma spectrometry is often used to determine radionuclide purity. However, this is not a completely reliable method. Control of the drug for the content of radionuclide impurities is not carried out if: the content of radionuclide impurities is indicated in the document on the radioactive raw material used to obtain the drug; radionuclide is ultra-short-lived or short-lived, then the determination of its radionuclide purity is difficult, and its testing is carried out at the production stage.

Determination of radiochemical purity requires the separation of various chemical compounds containing the radionuclide and the calculation of the percentage of activity associated with the main chemical form. Radiochemical impurities can be formed as a result of: radionuclide production; further chemical operations; incomplete drug separation; chemical changes as a result of storage. Thin-layer and paper chromatography are most often used.

For diagnostics, short-lived radiopharmaceuticals are used, the effect of which is recorded in the body with the help of special devices (scintillators, one-photon emission tomographs and positron (two-photon) emission tomographs), which capture the γ-radiation of a labeled radionuclide. Technetium-99 is most often used as a labeled radionuclide. It is a short-lived nuclide with a half-life of about 6 hours. Used for diagnosis of almost all organs. Technetium-labeled radiopharmaceuticals make up more than 80% of the RFP nomenclature. Radioactive isotopes of thallium-201 and -199, iodine-123 and -131, fluorine, etc. are also used for the purpose of diagnosis and treatment. The method of diagnosis using radiopharmaceuticals is called scintigraphy, its uniqueness lies in accuracy, reliability, the possibility of repeated use, and most importantly, the ability to diagnose diseases at an early stage. A radiopharmaceutical product must have a passport containing the following information: activity of the drug in millicuries (or becquerels); the amount of the drug in milliliters or milligrams; specific activity in millicuries (or becquerels) per 1 ml; total substance content in milligrams per 1 ml; concentration of the solution in milligrams per 1 ml; measurement time; the accuracy of the measurements.

Storage and transportation

Storage conditions should ensure reduction of the radiation dose to an acceptable level. In the pharmacopoeial article or NTD, the specific storage conditions of the drug are specified, which are determined by its specific properties and ensure the preservation of its quality (temperature regime, etc.). Radiopharmaceutical medicinal

products must be carefully closed and stored in an area designated for these purposes. During storage, the material of the primary packaging may change color as a result of irradiation. A change in color does not mean a deterioration in the quality of the drug. The transportation of RFP is carried out in accordance with the current safety rules for the transportation of radioactive substances.

Packaging and labeling

Packaging and labeling of RFP should be carried out in accordance with the current legislation of the country in this area regarding radioactive drugs for medical purposes. At the same time, it is necessary to take into account that comprehensive information about the drug should be contained in the passport and instructions for the medical use of RFP. The labeling of the primary packaging of the RFP (usually a bottle for medicines) should contain a minimum of information in order to ensure the minimum radiation load on the eyes of medical personnel. The label of the primary packaging (vials) with the sign of radiation danger indicates: the name of the drug, dosage form, activity (for capsules or dragee activity of each unit) on the set date (and time), batch number, expiration date. The label of the secondary packaging (packaging transport set) with the sign of radiation danger indicates: the name of the manufacturer; its trademark (if available); name of the drug; INN in the state language; dosage form, composition; "Sterile" (only for injectable dosage forms); information that the drug is intended for diagnosis or for therapeutic use; way of introduction; total radioactivity on the specified date and, if necessary, time; for solutions, data on radioactivity are provided in the appropriate amount (for example, in MBq per ml of solution); for solutions, the total volume is indicated; any special storage requirements regarding temperature and lighting; if necessary, the name and concentration of antimicrobial preservatives are indicated; for capsules (drags) additionally indicate the activity of each unit and the number of capsules (drags) in the package.

Precautions

All RFP procedures are carried out in accordance with current regulatory documents that regulate the rules for working with radioactive substances, including their storage and transportation.

— 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 of	Characteristics of the specified	Ruban O.A., Saiko I.V. Industrial technology of

	nanopreparations.	concepts	medicines. – Kh.: NFaU: Original, 2016. – P. 432 - 434.
2.	General characteristics of radiopharmaceuticals.	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: Original, 2016. - P. 434-439.
3.	Production technology of nano- and radiopharmaceuticals	Characteristics of the specified concepts	Ruban O.A., Saiko I.V. Industrial technology of medicines. – Kh.: NFaU: 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.

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. Khohlova etc. - Kh.: NFaU, 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 "KROK 2. Pharmacy" / O.A. Ruban, V.D. Rybachuk, L.M. Khokhlova, D.S. Pulyaev - Kh.: NFaU, 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.: NFaU: 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.: NFaU: 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 NFaU, 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 NFaU, 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-NFaU, 2017. – 44 p.
- Zujkina SS 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. – Kh.: NFaU 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, K.K. 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. 40

Topic: "Under bag control No. 4 "

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

1. Grinding equipment is classified by the grinding method. What machines does a roller crusher belong to?

A) They are crushed

B) Abrasive

C) Impact-centrifugal

D) Percussion

D) Cutting

2. Specify which devices are used for packaging ointments in industrial conditions:

A. Screw machines

B. Disc dispensers

C. Vacuum dispensers

D. percolator

E. Mazeterki

3. To which group of auxiliary substances does calcium stearate belong?

A) Anti-friction

B) Plasticizers

C) Dyes

D) Fillers

D) Loosening agents

4. Specify the auxiliary substance that is added to the mass for tableting in an amount of more than 1% in accordance with the SPh of Ukraine:

A) Aerosil

B) Twin-80

C) Stearic acid

D) Calcium stearate

D) Magnesium stearate

5. Tablets are produced in the tablet workshop. Tell the disintegration time of soluble tablets according to the requirements of the Federal Ministry of Ukraine:

A. 15 min

B. 5 min

C. 3 min

D. 60 min

6. Physical incompatibility was detected. Specify the combination of medicinal substances that, when mixed, form a eutectic:

A. Camphor and menthol.

B. Glucose and phenylsalicylate.

B. Streptocide and Antipyrine.

G. Ascorbic acid and glucose.

D. Basic bismuth nitrate and magnesium oxide

7. The ability of the powdered mass to pour out of the container of the watering can or "flow" under the force of its own weight and ensure uniform filling of the matrix channel is called:

A. Turnover

B. Compressedness

C. Granulation

D. Teasing

E. Spraying

8. Choose the maximum permissible concentration of calcium stearate in tablets according to SPh of Ukraine:

A. 1%

B. 13%

C. 5%

D. 7%

E. 10%

9. During packaging and transportation, raw materials are partially crushed and ground. Too much grinding spoils the appearance and reduces the quality of raw materials. Specify what is used to separate the crushed particles:

A. Sieve

B. Mortars

C. Tweezers

D. Scalpel

E. Filters

10. The pharmaceutical company plans to produce potassium bromide tablets. Which method of obtaining is optimal?

A. Direct pressing

B. Formation

C. Pressing with preliminary wet granulation

D. Pressing with preliminary dry granulation

E. Direct pressing with auxiliary substances

11. Powders are a solid dosage form for internal or external use. There is a missing stage in the production of powders:

A. Granulation

B. Sifting

C. Grinding

D. Packaging

E. Mixing

12. Various medicines are manufactured at the pharmaceutical enterprise. Specify the name of the dosage form consisting of solid individual dry particles of varying degrees of pulverization:

A. Powders

B. Emulsions

C. Suspensions

D. Dry extract

E. Tablets

13. To which group of excipients does calcium stearate belong?

A) Anti-friction

B) Plasticizers

C) Dyes

D) Fillers

D) Loosening agents

14. Which group of excipients improves wetting and water permeability of the tablet:

A. Baking powders

B. Fillers

C. Binders

D. Anti-friction

E. Corrections

15. Different groups of excipients are used in the production of tablets. Which of the listed groups of substances ensure the strength of tablets:

A. They bind

B. Loosening agents

C. Sliding
D. Corrections
E. Lubricants

1

Specify the auxiliary substance added to the mass for tableting in an amount of more than 1% according to the SPhU:

A. Aerosil
B. Twin-80
C. Stearic acid
D. Calcium stearate
E. Magnesium stearate

2

Tablets are manufactured at a pharmaceutical company. The following are used as lubricants in the production of tablets:

A. Calcium stearate
B. Starch paste
C. water
D. Solutions of the Navy
E. Tartrazine

3

In the process of producing tablets at an industrial enterprise, substances are used that improve their ejection from the matrix. What substance is used for this purpose?

A. Stearic acid
B. Monopalmitin
C. Indigo carmine
D. Alginic acid
E. Ultramylopectin

4

Which group of auxiliary substances in the production of tablets improves wetting and water permeability of tablets:

A. Baking powders
B. Fillers
C. Binders
D. Anti-friction
E. Corrigents

5

Various groups of excipients are used in the production of tablets. Which of the listed groups of substances ensure the strength of tablets:

A. Binders
B. Loosening
C. sliding

D. Corrigents
E. Lubricating

6

What binder is used for wet granulation :

A. Starch paste
B. Pectin
C. Gum
D. Mucus
E. Aerosil

7

Tablets are manufactured at a pharmaceutical company. Specify the methods of preparation of tablets according to the SPh of Ukraine.

A. Pressing, forming, teasing
B. Pressing, extrusion, forming, freeze drying
C. Formation, teasing
D. Pressing, teasing, extrusion
E. Pressing, granulation, freeze drying

8

Sodium chloride tablets are manufactured at a pharmaceutical enterprise . Specify the method by which they are prepared.

A. Direct pressing, without auxiliary substances
B. Formation
C. Direct pressing with the addition of auxiliary substances
D. Pressing with preliminary wet granulation
E. Pressing with previous dry granulation

9

What technology should a technologist offer for the industrial production of sodium chloride tablets:

A. Direct pressing
B. Wet granulation
C. Granulation with spray drying
D. Teasing
E. Dry granulation

10

The pharmaceutical company plans to produce potassium bromide tablets. Which method of obtaining is optimal?

A. Direct pressing
B. Formation
C. Direct pressing with auxiliary substances
D. Pressing with preliminary wet granulation
E. Pressing with previous dry granulation

11

In the tablet shop, tablets are produced by various methods. From which medicinal substances are tablets obtained by the method of direct pressing without auxiliary substances:

A. Sodium chloride, potassium bromide, ammonium bromide
B. Hexamethylenetetramine, sulfadimezin, streptocid
C. Sodium chloride, bromocamphor, streptocid
D. Potassium iodide, sulfadimesin, PASK-sodium
E. Phenyl salicylate, lactose, hexamethylenetetramine

12

The pharmaceutical company plans to produce phenobarbital, ephedrine hydrochloride, and sodium bicarbonate tablets. Which method of obtaining is optimal?

A. Direct pressing with the addition of auxiliary substances
B. Formation
C. Direct pressing without additives
D. Pressing with preliminary wet granulation
E. Pressing with previous dry granulation

13

The pharmaceutical company plans to release riboflavin tablets with ascorbic acid. Specify a rational method of preparation of these tablets.

A. Formation
B. Pressing with previous dry granulation
C. Direct pressing without additives
D. Pressing with preliminary wet granulation
E. Direct pressing with the addition of auxiliary substances

14

Granulation in tablet production is:

A. Directional agglomeration of powder particles for subsequent tableting
B. Fine grinding of the powder mass
C. Compression of the powder in the matrix
D. Pouring powder from the container of the watering can
E. Distribution of powder by size

1 5

Powders that have:

A. Poor fluidity
B. Good compression capacity
C. Good flowability
D. Bulk density
E. Porosity

1 6

For the granulation of tablet mixtures, an apparatus is used, in which the components

are mixed, the mixture is moistened, granulated, the granulate is dried, and the powder is powdered. Specify this device:

A. Apparatus with a fluidized bed for granulation of SG-30 mixtures
B. Dragging boiler
C. Spray dryer
D. Press granulator
E. The granulator is vertical

1 7

Mixers are used to mix moistened powdery materials:

A. With rotating blades
B. With a rotating body
C. Pneumatic
D. With fluidization
E. Centrifugal action

1 8

Which dryers apply in those cases when _ in material are contained valuable liquids [alcohol , ether , chloroform and other] or he is thermolabile ?

A. Sorptive
B. Radiation
C. Pneumatic dryers
D. Pseudo-liquefaction
E. Sublimation

1 9

What is the main advantage of dielectric drying?

A. Uniform heating of the material over the entire thickness
B. Preservation of native properties of the material being dried
C. Possibility of drying liquid and pasty materials
D. The compactness of the equipment
E. Relatively low drying temperature

2 0

Convective drying is carried out:

A. By direct contact of wet materials with a hot gas coolant
B. By heating wet materials with a coolant through an impermeable wall that conducts heat
C. By supplying heat with high-frequency currents
D. Ultrasonic radiation
E. sublimation of ice under deep vacuum

2 1

Designs of dryers are very diverse, but they all have several elements common to all dryers. Choose a structural element common to all convective type dryers:

A. Radiator for heating

B. Several rectangular chambers with shelves where the material dries in a stationary state
C. Shiber (damper), with the help of which part of the warm exhaust air is mixed with fresh air
D. Horizontal belt conveyor
E. Gas distribution chamber with a fan

2 2

In the drying chamber, 1 or 2 empty metal drums, which are heated from the inside by steam, rotate slowly. The surface of the drum is moistened with a thin layer and dries after an incomplete rotation of the drum. For which dryer is this description typical:

A. Roller vacuum dryer
B. Strichkova
C. Spraying
D. Dryer with dielectric heating
E. Sublimation dryer

2 3

Choose the equipment for granulation that should be used in the production of tablets that contain heat-labile substances:

A. Spray dryer
B. Rotary tablet machine
C. Teasing cauldron
D. Installation of a fluidized bed
E. "Draykota" type machine

24

Tablets are manufactured in aseptic conditions at the enterprises. A feature of the technology of which tablets is sterilization by dry heat:

A. Implantation
B. Prolonged
C. Framework
D. Trituration
E. Sublingual

25

Quality control of tablets at pharmaceutical enterprises involves determination of abrasion resistance. Indicate how many tablets are taken for the test, if the weight of the tablet is less than 0.65 g:

A. 20
B. 5
C. 50
D. 100
E. 2

26

The solubility test is used for quality control:

A. Tablets
B. Aerosols
C. Ointment
D. Liniments
E. Tincture

27

At the pharmaceutical enterprise, tests are conducted to determine the dissolution and disintegration of tablets. At what temperature are the tests conducted:

A. 37 °C
B. 20 °C
C. 50 °C
D. 18 °C
E. 30 °C

28

The quality of tablets is evaluated according to various indicators. Specify the devices that are used to determine the dissolution of tablets (according to SPhU).

A. A device with a rotating basket, a device with a shovel, a flow device
B. A device with a basket, a flow device
C. A device with a shovel; swinging basket
D. Flow device
E. Rotating basket

29

Indicate how the tablet dissolution test is regulated according to the SPhU:

A. The amount dissolved in 45 min. the substance must be at least 75% in water
B. The amount dissolved in 30 min. the medicinal substance must be at least 97% in water
C. The amount dissolved in 15 min. the medicinal substance must be at least 75% in water
D. The amount dissolved in 15 min. the pepsin solution of the medicinal substance must be at least 75%
E. The amount dissolved in 20 min. in a 0.9% solution of sodium chloride, the substance must be at least 75%

30

The main indicators of the quality of tablets according to the requirements of the SFU are divided into organoleptic, physical, chemical and biological. Define chemical indicators.

A. Disintegration
B. Average tablet weight
C. Appearance
D. Content of microorganisms

E. Strength indicators

31

The quality of tablets is evaluated according to various indicators. Specify the device that is used to determine the disintegration of tablets.

A. A swinging basket
B. Flow device
C. The KhNDHFI device
D. A device with a shovel
E. Friabilator

32

The pharmaceutical enterprise produces Aspirincardio tablets, during quality control the disintegration of the tablets was determined. Specify the device with which, according to the State Federal Office of Internal Affairs, this control can be carried out:

A. A device of the type "swinging basket"
B. A device of the type "rotating basket"
C. Densimeter
D. X-ray machine
E. Gas-liquid chromatograph

33

Tablets are manufactured at a pharmaceutical company. The disintegration time of tablets not covered with a shell is no more than:

A. 15 minutes
B. 20 minutes
C. 30 minutes
D. 5 minutes
E. 10 minutes

34

Tablets are produced in the tablet workshop. Tell the disintegration time of soluble tablets according to the requirements of the Federal Ministry of Ukraine:

A. 15 minutes
B. 5 minutes
C. 25 minutes
D. 60 minutes
E. 40 minutes

35

During the production of tablets, continuous quality control of the finished product is carried out according to various indicators. Select the correct mode for the "disintegration" test if the tablets are coated with a water-soluble coating:

A. No more than 30 minutes
B. At least 1 hour
C. At least 30 minutes

D. No more than 45 minutes
E. No more than 15 minutes
36
Tablets covered with enteric coatings are manufactured at pharmaceutical enterprises. Indicate how long they should not disintegrate in an acidic environment according to the requirements of the Federal Drug Administration:
A. 1:00
B. 2 hours
C. 4 hours
D. 3 hours
E. 5 hours
37
In the tablet shop, tablets are made, covered with a shell that dissolves in the intestine. Specify the disintegration time of the tablets:
A. Should not disintegrate within 1 hour in a 0.1 M hydrochloric acid solution, and after washing with water should disintegrate within 1 hour in a 0.1 M sodium bicarbonate solution
B. Should not disintegrate within 30 minutes in a 0.1 M hydrochloric acid solution, and after washing with water should disintegrate within 30 minutes in a 0.1 M sodium bicarbonate solution
C. No more than 15 minutes
D. No more than 30 minutes
E. No more than 45 minutes
38
Granules are produced at the pharmaceutical enterprise. Specify the disintegration time of effervescent granules:
A. No more than 5 minutes
B. 15 minutes
C. 20 minutes
D. 45 minutes
E. 60 minutes
39
During the evaluation of the appearance of the tablets, the marbling of the surface was found, which is:
A. Uneven color, local, local discoloration
B. Violation of the roundness of the form
C. Holes, chips, parts of tablets
D. Exfoliation, since the tablets
E. Uneven coating surface
40
When conducting quality control of tablets at pharmaceutical enterprises, a test is

carried out to determine the abrasion resistance of tablets. Specify which device is used to perform this test:

A. Drum wiper (friabilator)
B. Goniometer
C. Spring dynamometer
D. Laboratory indicator of the decay process
E. Laboratory indicator of the dissolution process

41

The pharmaceutical company manufactures Septefril tablets. Specify the device for determining the wearability of tablets according to the SPhU:

A. Friabilator
B. Areometer
C. Device with a "swaying basket"
D. Polarimeter
E. Densimeter

42

A pharmaceutical company produces tablets. What device is used to determine their splitting strength:

A. The KhNDHFI device
B. Adj. VP-12A
C. Friabilator
D. Device "swinging basket"
E. Device model 545R-AK-3

43

Tablets are manufactured at a pharmaceutical company. Indicate for which tablets the mechanical strength is not determined:

A. Nitroglycerin tablets
B. Tablets of sodium chloride
C. Streptocide tablets
D. Acetylsalicylic acid tablets
E. Potassium bromide tablets

44

Triturating tablets are made in the tablet shop. What quality indicators are not determined for these tablets?

A. Abrasion, resistance to crushing
B. Homogeneity of content
C. Microbiological purity
D. Disintegration and dissolution
E. Uniformity of dosage

45

Controlling the number of tablets at pharmaceutical enterprises involves determining

the average weight. Specify how many tablets with a mass of 0.5 g for the test:
A. 20
B. 5
C. 50
D. 100
E. 10
46
Quality control of the manufactured tablets includes determination of the content of auxiliary substances talc and aerosol. Indicate by what method the determination is made:
A. Gravimetric
B. Titrimetric
C. Photocolorimetric method
D. Spectrophotometric
E. Chromatographic
47
Indicate for what purpose binders are used in the production of tablets:
A. * To achieve the required particle adhesion force
B. To improve the taste
C. To increase flowability
D. To obtain the required mass
E. To improve tablet disintegration
48
Indicate for what purpose fillers are used in the manufacture of tablets:
A. To obtain a certain mass of tablets
B. To improve taste
C. To improve the fluidity of the granulate
D. To improve the adhesion of particles to each other
E. To improve tablet disintegration
49
When pressed, the tablets stick to the press tool. Choose the reason for sticking from the following:
A. Excess moisture of the tablet mass and pressure
B. Heterogeneity of granulate
C. Unsatisfactory fluidity of the tablet mass
D. High specific density of powders
E. Tableted powder has plate-shaped crystals
50
Tablets without a shell, the main mass of which consists of acids and carbonates, have the name:
A. Effervescent

B. Pressed
C. Acidic
D. Soluble
E. Caplets
51
According to the SFU, different types of tablets for oral administration are classified. What type of pulsatile-release tablets are APIs?
A. Modified-release tablets
B. Effervescent tablets
C. Chewable tablets
D. Soluble tablets
E. Dispersible tablets
1
Tablets obtained by the formation of moistened masses are called:
A. Coated tablets
B. Effervescent tablets
C. Trituration tablets
D. Film-coated tablets
E. Tablets with modified release
2
In the tablet shop, tablets are made by the molding method. Indicate in which cases tablets are prepared by this method:
A. If the use of pressure is undesirable; when the dose of the medicinal substance is insufficient, and the addition of auxiliary substances is undesirable
B. If the medicinal substance interacts with water
C. If the medicinal substance is explosive
D. If the medicinal substance changes its properties under pressure
E. If a very large dose of the medicinal substance
3
Nitroglycerin tablets are manufactured at a pharmaceutical enterprise. Specify the method by which they are prepared:
A. Formation
B. Direct pressing without additives
C. Direct pressing with the addition of auxiliary substances
D. Pressing with preliminary wet granulation
E. Pressing with previous dry granulation
4
Tablets are manufactured at a pharmaceutical company. Specify the correct sequence of technological stages in the production of tablets by the molding method:
A. Auxiliary work, mixing dry powders, obtaining a wet mass, forming tablets, drying, quality control, packing, packaging

B. Auxiliary work, mixing dry powders, forming tablets, drying, quality control, filling, packing
C. Auxiliary work, obtaining a wet mass, forming tablets, drying, quality control, packing, packaging
D. Auxiliary work, mixing of dry powders, forming tablets, quality control, packing, packaging
E. Auxiliary works, forming tablets, drying, quality control, filling, packaging
5
Nitroglycerin tablets are manufactured at a pharmaceutical enterprise. Specify the correct sequence of technological stages and operations in the production of these tablets:
A. Auxiliary work, mixing dry powders, moistening the mixture with binding liquids, rubbing the wet mass into perforated plates, pushing out the rubbed mass with punches, drying tablets, standardization, packing, packaging
B. Mixing dry powders, moistening the mixture with binding liquids, forming tablets, standardization, packaging
C. Auxiliary work, mixing dry powders, wiping wet mass through a granulator, tableting, standardization, packing, packaging
D. Wetting the mixture with binding liquids, rubbing the wet mass into perforated plates, tableting, standardization, packaging
E. Auxiliary works, granulation, tableting, standardization, packing, packaging
6
Nitroglycerin tablets are made in the tablet shop. Specify the equipment used in the manufacture of these tablets:
A. Special tablet machines for forming tablets
B. Tablet machine "Draykota"
C. RTM-24 rotary tablet machine
D. Teasing cauldron
E. Eccentric "shoe" machine
7
In the tablet shop, tablets are made by the molding method. Indicate which quality indicator is not determined for these tablets:
A. Mechanical strength
B. Disintegration
C. Solubility
D. Quantitative content of active substances
E. Uniformity of dosage
8
The medicinal form for internal use in the form of round or irregularly shaped grains, containing a mixture of medicinal and auxiliary substances, which is not covered with a shell, is called:

A. Pellets
B. Dragee
C. Powder
D. Tablets
E. Sponsored

11

According to the SFU, granules can be classified as:

A. "Effervescent"; covered with a shell; with modified release; enteric soluble
B. Covered with a shell; with modified release
C. Enteric soluble, gastric soluble
D. "Effervescent"; solid
E. With a modified release; covered with a shell

12

Different types of tablets are manufactured at the pharmaceutical company. Specify the structure of the framework tablets.

A. Mesh matrix in which the medicinal substance is included
B. Film-coated tablets
C. Tablets covered with a fat-soluble coating
D. Coated tablets
E. Dispersions of medicinal substances in polyethylene

13

What is the name of tablets that have a large weight and the length of which exceeds the width and height?

A. Briquettes
B. Effervescent
C. Caplets
D. Vaginal
E. Pressed

14

The plant produces tablets with a pressed coating. Specify the equipment used for this:

A. Double pressing tablet machine
B. Dragging boiler
C. S. Marmeriser
D. Eccentric tablet machine
E. Trituration machine

15

When coating tablets with shells, various auxiliary substances are used. Which of the following substances belong to the adhesives that ensure the adhesion of the core coating materials:

A. Sugar syrup, PVP, KMC, MC, AFC, OPMC
B. Magnesium oxide, calcium oxide, talc, magnesium carbonate

C. Aerosil, shellac, polyacrylic resins, zein
D. Tropeolin 00, tartrazine, acid red 2C, indigo carmine
E. Sugar, citric acid, cocoa, vanillin

16

Tablets are covered with a shell in order to protect them from the effects of moisture, light, mechanical damage, masking unpleasant taste and smell. Specify substances that ensure moisture resistance of the coating.

A. Zein
B. PEG
C. Tartrazine
D. tweens
E. Calcium oxide

17

Film-coated tablets are manufactured at a pharmaceutical enterprise. Which of the proposed substances is used to obtain a water-soluble film coating?

A. Hydroxypropylene-methylcellulose
B. Talc
C. Camphor
D. Zinc oxide
E. Starch

18

What film coatings do not exist:

A. Fat soluble
B. Water soluble
C. Soluble in gastric juice
D. Enteric soluble
E. Insoluble

19

Which of the coatings allows you to protect the stomach from the negative effects of the active components of the tablets?

A. Enteric soluble
B. Water soluble
C. Gastrically soluble
D. Fat soluble
E. Any

20

Enteric coatings are one of the types of tablet coatings. Specify the place of their dissolution:

A. In the intestines
B. In the stomach
C. In the oral cavity

D. In the rectum
E. In the vagina
21
Preparation of drugged coatings on tablets is carried out in the following devices:
A. Obductors
B. Double pressing machines
C. Machines with a suspended layer
D. Apparatus of centrifugal action
E. Spray dryers
22
Specify the correct technological scheme for applying a dry pressed coating to tablets:
A. Feeding granulate to the matrix for coating, feeding the core tablet, feeding granulate from above, pressing
B. Feeding the granulate for the lower part of the coating into the matrix, the subsequent filling of the granulate for the upper part of the coating, pressing
C. Feeding the tablet core into the matrix, filling the granulate, pressing
D. Feeding the granulate for the lower part of the coating into the matrix, feeding the core tablet, pressing
E. Feeding granulate coating into the matrix, feeding core tablets, pressing
23
Tablets covered with a shell are manufactured at a pharmaceutical enterprise. Specify the required speed of rotation of the cauldron for coating the tablets with powdered sugar suspension:
A. 18-20
B. 30
C. 40
D. 15-20
E. At least 45
24
The tablet workshop of the enterprise produces tablets covered with a suspension coating. Suggest the composition of the suspension for the technological operation of coating the core tablets:
A. Granulated sugar, water, polyvinylpyrrolidone, aerosol, basic magnesium carbonate, titanium dioxide, dye
B. Granulated sugar, methylcellulose solution, titanium dioxide, polyvinylpyrrolidone
C. Granulated sugar, dye, magnesium carbonate, magnesium oxide, sodium carboxymethyl cellulose
D. Sugar-sand, alcohol-water mixture, sodium carboxymethylcellulose, magnesium oxide, aerosol, dye

E. Sodium carboxymethylcellulose, granulated sugar, water, glycerin, magnesium oxide, Aerosil, titanium dioxide

25

The tablet workshop of the enterprise produces tablets covered with a suspension coating. From the listed ingredients, choose substances that act as a suspension carrier when applying a suspension coating:

A. 70% sugar syrup
B. Aerosil
C. Polyvinylpyrrolidone
D. Basic magnesium carbonate
E. Titanium dioxide

26

What quality parameter is not determined for tablets covered with a shell:

A. Abrasion resistance
B. Solubility
C. Ability to disintegrate
D. Average mass and deviation from it
E. Uniformity of dosage

27

At the pharmaceutical enterprise, multiple layering of medicinal and auxiliary substances on sugar granules is carried out in a cauldron. What is the finished medicinal form called?

A. Dragee
B. Granules
C. Tablets
D. Medulla
E. Microcapsules

28

A pharmaceutical enterprise produces dragees. Specify the equipment necessary for the industrial production of the dosage form:

A. Dragging boiler
B. Vertical granulator
C. Friabilator
D. Tablet machine "Draykota"
E. RTM-12

1

The production of gelatin capsules is based on various principles. What are the features of the technological process of the production of capsules by the dipping method:

A. Capsules are formed using pins
B. Forming capsules using two concentric toothed rolls

C. The formation of a spherical drop with the simultaneous inclusion of a liquid medicinal substance
D. Formation of tape from gelatin mass, formation of capsule halves with simultaneous filling and sealing
E. Production of capsules by coacervation method
2
The production of gelatin capsules is based on different principles. What is the peculiarity of obtaining capsules by pressing:
A. Forming capsules using concentric nozzles
B. Forming capsules by dipping pins
C. The formation of a spherical drop with the simultaneous inclusion of an active substance in it
D. Forming capsules from gelatin ribbons by stamping
E. Formation of capsules during evaporation of a volatile solvent
3
The pharmaceutical company manufactures hard gelatin capsules. What method is used to obtain hard capsule shells?
A. Diving
B. Casting
C. Pressing
D. Rotational matrix
E. Formation
4
The production of gelatin capsules is based on various principles. What are the features of the technological process of the production of capsules by the dipping method:
A. Capsules are formed using pins
B. Forming capsules using two concentric toothed rolls
C. The formation of a spherical drop with the simultaneous inclusion of a liquid medicinal substance in it
D. Formation of a ribbon from gelatin mass, formation of capsule halves with simultaneous filling and sealing
E. Production of capsules by coacervation method
5
The immersion method is used to obtain hard gelatin capsules. Specify the equipment used for this production:
A. "Bathroom", frames with pins
B. Capsule pressing machine, drying unit
C. "Draykota" type machine, ball mill
D. Fluidized bed device
E. RPA, piston for indentation
6

In the production of hard gelatin capsules, I use the immersion method. Name the technological equipment used for this method of obtaining capsules:

A. "Dipping bath", frames with pins, drying unit, automatic unit for trimming
B. Disks, piston for compression, metered hopper
C. Grids, drying unit, cutting unit
D. Chassis frames, drying unit, rotors with scrapers
E. Matrix table, hopper for filling, receiver

7

A change in which conditions can lead to the process of coacervation:

A. All answers are correct
B. Change in electrolyte concentration
C. A change in the concentration of IMS
D. Changing the pH of the environment
E. Temperature change

8

Physico-chemical methods of obtaining microcapsules include:

A. Coacervation method
B. Teasing method
C. Spray method
D. Spraying in a fluidized bed
E. Liquid dispersion method

9

Modern methods of microencapsulation are divided into three main groups: physical, chemical and physico-chemical. Specify the method that refers to physical:

A. Extrusion
B. Coacervation
C. Polymerization
D. Polycondensation
E. Spray drying

10

The physical methods of microencapsulation include:

A. Spraying in a fluidized bed
B. Physical adsorption
C. Coacervation
D. Polymerization
E. Extractive substitution

11

According to the SPhU, the content of solid medicinal products - capsules can be:

A. Solid, liquid or pasty
B. We claim
C. Soft

D. Gaseous
E. Hard, soft

12

Medicines in the form of capsules, the shell of which is formed from rice flour, have the name:

A. Wafers
B. Medulla
C. Sponsored
D. Tubatyn
E. Caplets

13

During the production of capsules, excipients of various groups are added to the gelatin base. Specify the group of excipients used to increase the strength and reduce the fragility of capsules:

A. Plasticizers
B. Hydrophobizers
C. Dyes
D. Preservatives
E. Adhesives

14

During the production of capsules, excipients of various groups are added to the gelatin base. Specify the substance belonging to the group of plasticizers:

A. Polypropylene
B. Potassium metabisulfate
C. Eosin
D. The essence is aromatic
E. Mint oil

15

Gelatin capsules are manufactured at a pharmaceutical enterprise. What is the purpose of glycerin in gelatin mass?

A. Gives elasticity to the shell
B. Increases the porosity of the shells
C. Increases resistance to the effects of gastric juice
D. It has antimicrobial properties
E. Accelerates the disintegration of shells

16

The workshop of the enterprise produces soft gelatin seamless capsules. Specify the method of receipt:

A. Drip
B. Dip
C. Stamping

D. Outpouring
E. Dissolution

17

The pharmaceutical enterprise organizes the release of an oily solution of retinol acetate in the form of capsules. Specify the method that should be chosen for the production of this drug:

A. Drip method
B. Pressing method
C. The rolling method
D. Casting method
E. Layering method

18

According to the technology of the drop method of making capsules, and encapsulation are subject to:

A. Light-flowing liquid non-aqueous medicinal substances
B. Pea-like substances
C. Granulated medicinal substances
D. Microgranulated substances
E. Pastes and liquids with high viscosity

19

To improve which properties of the filler, when filling hard gelatin capsules, slippery auxiliary substances -0.1% - 0.3% aerosols or magnesium stearate together with 0.5% - 1% talc are added?

A. Flowability
B. Ability to contact formation
C. Regulation of moisture content
D. Homogeneity
E. Homogeneity of mixing

20

Define the medicinal form of tubatin:

A. Soft capsules with an elongated neck
B. Soft rectal capsules in the form of an elongated drop
C. Spherical capsules obtained by the immersion method
D. Egg-shaped capsules obtained by pressing
E. Hard capsules with a cap filled with microcapsules

21

Artificially obtained, hermetic spherical particles formed by bimolecular lipid layers, more often phospholipids, in the cavities between which there is a forming sphere. They are called:

A. Liposomes
B. Pellets

C. Capsules
D. Sponsored
E. Tubatyn

22

What technological method ensures the delivery of the drug to the cell?

A. Liposomization
B. Granulation
C. Application of the shell
D. Solubilization
E. Microencapsulation

23

The pharmaceutical enterprise produces gelatin capsules. To ensure the antimicrobial resistance of the shells, the following are introduced into the gelatin mass:

A. Preservatives
B. Plasticizers
C. Film formers
D. Dyes
E. Stabilizers

24

During the organoleptic evaluation, the shells of hard gelatin capsules contained air. What technological error was made in the process of manufacturing gelatin mass?

A. Vacuum is not connected
B. Agitation speed exceeded
C. Increased temperature
D. Long mixing time
E. Insufficient number of stabilizers

25

Modern methods of microencapsulation are divided into three main groups: physical, chemical and physico-chemical. Specify the method of preparation for microcapsules that contain thermolabile substances:

A. Vacuum deposition
B. Teasing
C. Suspension
D. Extrusion
E. Dispersion

26

To prevent the possible leakage of volatile fillers, the capsules are subjected to additional sealing. Specify the sealing methods that are used for this:

A. Thermomechanical welding
B. Separate filling
C. Drying

D. Solvent removal
E. Coating of capsules with metals

27

Various methods are used in the production of microcapsules. What methods belong to chemical:

A. Polymerization, polycondensation
B. Dispersion
C. Simple coacervation
D. Dissolution
E. Teasing

28

At the pharmaceutical enterprise, microcapsules are produced by the teasing method. Specify the equipment used in the production of microcapsules by this method:

A. Teasing cauldron
B. Dismembrator
C. With mixer - granulator
D. Friabilator
E. Disintegrator

29

Enter the name of the finished dosage form, which is gelatin capsules filled with microcapsules:

A. Sponsored
B. Tubatyn
C. Pearls
D. OROS type tablets
E. Microcapsules

30

When evaluating the quality of gelatin capsules, solubility is determined. Indicate in which case the series is considered standard when determining this indicator:

A. If at least 75% of the active substance has dissolved in water in 45 minutes
B. If 75% of the active substance dissolves in water in 60 minutes
C. If at least 55% of the active substance has dissolved in water in 30 minutes
D. If at least 85% of the active substance has dissolved in water in 90 minutes

31

During quality control of capsules, the average weight is determined. Specify the number of capsules that must be taken to determine this indicator according to the SPhU:

A. 20
B. 15
C. 10
D. 5

E. 3

32

Name the method of obtaining microcapsules, the essence of which is to apply a shell made of metallic silver, zinc, etc., to the solid particles of the encapsulated substance:

A. Galvanization

B. Polymerization

C. Suspension of nuclei

D. Teasing

E. Coacervation

33

Microcapsules have the form of individual particles or agglomerates. Specify their size:

A. From 1 to 5000 microns

B. From 100 μm

C. From 500 μm

D. From 3000 to 8000 microns

E. Up to 100 μm

34.

Specify what the semipermeable shell of microcapsules is:

A. It is impermeable to the nucleus, but permeable to low molecular weight substances

B. It is impermeable to low molecular weight substances, but permeable to the nucleus

C. It is a membrane through which only water and gastric juice can penetrate

D. It is a membrane through which only water and gastric juice can penetrate under the influence of heat, pressure, and ultrasound

E. The core is released as a result of the mechanical destruction of the shell

1

The pharmaceutical company manufactures soft drugs. Specify the name of a soft medicine that melts at body temperature:

A. Liniment

B. Ointment

C. Gel

D. Cream

E. Paste

2

The ointment workshop of the enterprise is mastering the production of a new ointment. Specify the technological operation that ensures the uniformity of the distribution of the medicinal substance in the base:

A. Homogenization

B. Preparation of the base

C. Standardization
D. Packaging
E. Packaging

3

At pharmaceutical enterprises, a technological stage - homogenization - is carried out during the production of zinc ointment. What equipment is used to carry out this stage:

A. Two- and three-roll maseters, RPA
B. Mixers with anchor stirrers
C. Electric boilers of various brands
D. Boilers with steam heaters
E. Drum mills

4

The pharmaceutical enterprise plans to produce heterogeneous ointments. Specify the equipment needed for homogenization of ointments:

A. Three-roll maseter, rotary-pulsation device (RPA.)
B. Electric panel for melting bases
C. Reactor-mixer
D. Mixer with paddle stirrers
E. Disintegrator

5

Ointments are subject to homogeneity requirements. Which equipment can be used to achieve a high degree of homogenization in the production of ointments:

A. RPA
B. Propeller stirrer
C. Autolyzer
D. bubbler
E. Anchor stirrer

6

The ointment workshop of the enterprise produces soft medicinal forms. A rotary-pulsation apparatus is used for homogenization of ointments. The use of a rotary-pulsation device allows you to combine:

A. Preliminary grinding of powdered components, homogenization of the ointment
B. Standardization of the dosage form, melting of the base
C. Melting of the base, preliminary grinding of powdery components
D. Homogenization of ointment, filling and packaging of ointment
E. Packing and packaging of the ointment, melting the base

7

When preparing ointments containing amorphous substances (sulfur, zinc oxide, starch), using a rotary-pulsation apparatus (RPA), it is possible to exclude the following stage:

A. Stages of preliminary grinding of medicinal substances

B. Mix
C. Homogenization
D. Standardization
E. Introduction of medicinal substance into the base

8

The ointment workshop of the enterprise produces ointments (gels) on water-soluble bases. Specify the component to get them:

A. Methyl cellulose
B. Hydrogenated fats
C. Silicones
D. Vaseline
E. Wax

9

Sterile liniments are manufactured at a pharmaceutical enterprise. Specify the equipment that allows you to receive a sterile liniment:

A. Magnetostrictive emitters
B. Rotary-pulsation device
C. Propeller mixers
D. Turbine mixers
E. Colloid mills

10

The pharmaceutical company manufactures soft drugs. Specify which quality indicator is determined only for heterogeneous soft medicinal products:

A. Particle size
B. pH
C. Identification
D. Microbiological purity
E. Quantitative definition

11

The ointment workshop of the enterprise may use the following equipment during the production of ointment at the packaging stage:

A. Screw and piston dosing machines
B. Rezepin's machine gun
C. Rotary machines
D. Eccentric machines
E. Disc machines

12

Specify which devices are used for packaging ointments in industrial conditions:

A. Screw machines
B. Disc dispensers
C. Vacuum dispensers

D. Percolators
E. Mazeterka
13
Choose the dosage form when using the active substance that does not undergo primary metabolism in the liver:
A. Suppositories
B. Capsules
C. Syrups
D. Oral suspensions
E. Tablets
14
The workshop for the production of soft dosage forms produces suppositories of various shapes. Define pessaries:
A. Vaginal suppositories with a rounded end
B. Rectal cone-shaped suppositories
C. Torpedo-shaped rectal suppositories
D. Egg-shaped vaginal suppositories
E. Spherical vaginal suppositories
15
The pharmaceutical company manufactures suppositories. Indicate which method is the most optimal to use for the manufacture of suppositories with thermolabile substances.
A. Pressing
B. Pouring into forms
C. S. Pumping
D. Teasing
E. Lyophilization
16
The workshop for the production of soft dosage forms produces suppositories on various bases. Choose suppository bases that have lipophilic properties:
A. Cocoa butter, alloys of cocoa butter with hydrogenated fats, vegetable and animal hydrogenated fats, solid fat, lanol, wax, paraffin
B. Alloys of cocoa butter with hydrogenated fats, alloys of polyethylene glycols with different molecular weights, gelatin-glycerol gels, vegetable and animal hydrogenated fats
C. Gelatin-glycerin gels, vegetable and hydrogenated fats, solid fat, lanol, wax, paraffin, alloys of polyethylene glycols with different molecular weights
D. Vegetable and animal hydrogenated fats, solid fat, lanol, wax, paraffin, gelatin-glycerin gels
E. Alloys of polyethylene glycols with different molecular weights, gelatin-glycerol gels, vegetable and animal hydrogenated fats

17
Lipophilic suppository bases include:
A. *Alloys of hydrogenated fats
B. Polyethylene oxide base
C. Gelatin-glycerin base
D. Collagen base
E. Soap-glycerin base
18
The workshop for the production of soft dosage forms produces suppositories on various bases. What bases are lipophilic:
A. Cocoa butter, vitebsol, hydrogenated fats
B. Gelatin-glycerin base, soap-glycerin base, polyethylene glycol
C. Cocoa butter, polyethylene glycol
D. Polyethylene glycols, hydrogenated fats
E. Lanol, vitebsol, soap-glycerin base
19
In the manufacture of rectal suppositories, the following auxiliary substances are added to ensure the hardening process:
A. Cocoa butter
B. Glycerin
C. Paraffin
D. Vaseline
E. Dry powders
20
In the production of suppositories in industrial conditions, one of the stages of the technological process is the production of concentrates. What in this case are concentrates:
A. Obtained solutions or suspensions of medicinal substances of low concentration
B. Concentrated solutions of medicinal substances prescribed in small quantities
C. Internal pharmacy preparation of medicinal substances
D. Medicinal substances soluble in the base
E. Medicinal substances soluble in water
21
Suppositories on hydrophilic bases are manufactured at the pharmaceutical enterprise. Specify which parameter is determined during the standardization of these suppositories:
A. Dissolution time
B. Dry residue
C. Boiling temperature
D. Resuspension
E. Mechanical strength

22

The pharmaceutical company manufactures various medicinal products. For which dosage form does the State Pharmacopoeia of Ukraine regulate the "time of complete deformation":

A. Suppositories
B. Tablets
C. Dragee
D. Pellets
E. Capsules

23

Specify which devices are used for packaging ointments in industrial conditions:

A. * Screw machines
B. Vacuum dispensers
C. Maseterki
D. Percolators
E. Disc dispensers

24

Specify the optimal method of manufacturing suppositories in industrial conditions:

A. * Pouring into molds
B. Pressing
C. Pumping
D. Lyophilization
E. Stamping

25

To prepare the ointment, the pharmacist additionally used paraffin. Indicate what role paraffin plays in technology:

A. Sealant
B. Foundation
C. For dispersing powders
D. Preservative
E. Emulsifier

26

The pharmaceutical company produces ointments. Specify the name of the stage that allows you to obtain a homogeneous ointment:

A. Homogenization
B. Obtaining the base
C. Dispersion
D. Production of ointment concentrate
E. Mixing components with the base

27

Water lanolin consists of:

A. * 70 parts of anhydrous lanolin and 30 parts of water
B. 80 parts anhydrous lanolin and 20 parts water
C. 5 parts anhydrous lanolin and 95 parts water
D. 90 parts lanolin anhydrous and 10 parts water
E. 50 parts of anhydrous lanolin and 50 parts of water

28.

When preparing the ointment base, the components are loaded:

A. In strict order of decreasing melting point
B. In strict order of decreasing adsorption properties
C. In random order
D. In order of increasing mass of components
E. All answers are correct

29.

To pump the molten ointment base from the boiler to the reactor, it is most appropriate to use gear pumps. Specify the reason:

A. Because they work well in viscous environments
B. Because only they can be heated
C. Therefore, the diameter of the pump corresponds to the reactor pipeline
D. The most economical type of pumps
E. All answers are correct

30

Define the term "inverse substitution coefficient"

A. The amount of fatty base that replaces one mass part of LR
B. The amount of LR that replaces one mass part of a fatty base with a specific mass of 0.95
C. The amount of LR that occupies the same volume as one mass part of the fat base
D. The number of hydrophilic compounds that replace water molecules in the base
E. The number of hydrogenated fats that bind to the base

31.

State the advantages of the disk method of dosing capsules:

A. The method allows you to adjust the dosage; the mass of the filler can be adjusted by changing the pressure and increasing or decreasing the level of the filler
B. The method allows partial filling of capsules
C. The method is intended for dosing two fillers into one capsule
D. The method is intended for the use of fillers of clearly defined sizes (tablets, cores, dragees, capsules, etc.)
E. All answers are correct

32.

State the advantages of the double slide method when dosing capsules:

A. The method allows partial filling of capsules

B. The method allows you to adjust the dosage; the mass of the filler can be adjusted by changing the pressure and increasing or decreasing the level of the filler
C. The method is intended for dosing two fillers into one capsule
D. The method is intended for the use of fillers of clearly defined sizes (tablets, cores, dragees, capsules, etc.)
E. All answers
33.
Specify the advantages of the method of forming rolls when dosing capsules:
A. The method is intended for the use of fillers of clearly defined sizes (tablets, cores, dragees, capsules, etc.)
B. The method allows you to adjust the dosage; the mass of the filler can be adjusted by changing the pressure and increasing or decreasing the level of the filler
C. The method is designed for dosing two fillers into one capsule
D. The method allows partial filling of capsules
E. All answers are correct
34.
Specify the features of rectal capsules:
A. They consist of a thin layer of gelatin, the surface of which becomes slimy when moistened with water
B. Such capsules are not stable at elevated temperatures, which facilitates the release of LR
C. The release of LR is slow compared to suppositories, so their use is not widespread
D. Due to the poor permeability through the gelatin shell, in order to achieve a therapeutic effect, the amount of LR in the rectal capsule should be a dose one and a half times greater than the dose in the suppository
E. All answers are correct
35.
When determining the uniformity of the mass of a unit of a dosed medicinal product with an average weight of a capsule of less than 300 mg per SPhU, the permissible deviation should:
A. Do not exceed 10%
B. Not to exceed 5%
C. Not to exceed 7.5%
D. Not to exceed 20%
E. Do not exceed 15%

1. Suppositories are manufactured at a pharmaceutical enterprise. Indicate which method is the most optimal to use for the production of suppositories in industrial conditions:
A Molding
B Rolling

D Stamping
E Lyophilization

2. Lipophilic suppository bases include:
A Hydrogenated fat alloys
B Polyethylene oxide base
C Gelatin-glycerol base
D Collagen base E Soap-glycerin base

3. Suppositories are manufactured at a pharmaceutical enterprise. Indicate which method is the most optimal to use for manufacturing suppositories in industrial conditions:
A. Molding
B. Rolling out
C. Pressing
D. Stamping
E. Lyophilization

4. Lipophilic suppository bases include :
A. Alloys of hydrogenated fats
B. Polyethylene oxide base
C. Gelatin-glycerin base
D. Collagen base
E. Soap-glycerin base

1 . The effective half-life never exceeds the time:
A. Biological half-life.
B. Can exceed both physical and biological .
C. Physical half-life .
D. Physical half-life .
E. Neither physical nor biological.
2 . Radiochemical pollution can become:
A. The reason for the change in the biological behavior of RFP.
B. The reason for the change in the overall activity of the drug .
C. The reason for the lack of biological effect of RFP.
D. All of the above.
E. Cause of radiation damage .
3. Radiochemical purity can be established by the following methods:
A. Chromatographic .
B. Definition of general activity .

C. Electrophoretic .
D. Biological effect of RFP .
E. To all of the above .
4. Radiochemical purity is:
A. The presence of unlabeled chemicals in the RFP.
B. The fate of the radionuclide in the RFP in the required chemical form.
C. The share of the total activity of the drug due to the radionuclide .
D. Change in the biological behavior of RFP.
E. Absence of biological effect of RFP.
5. Over time, radiochemical purity ...:
A. Increases over time.
B. Increases .
C. Does not change .
D. C decreases with time.
E. Decreases .
6. Depending on the purpose, nanomaterials are classified into:
A. Nanosuspensions, polymers, nanoparticles.
B. Functional, compositional, structural.
C. Organometallic, mixed, microemulsions.
D. Single-layer liposomes, mycelium, nanocapsules.
E. Multilayered liposomes, lipoproteins, monolithic nanoparticles.
7. Nanoobjects are ..
A. Structural elements whose linear size in at least one dimension is 10 - 100 nm;
B. Structural elements of microcapsules;
C. Small spherical particles obtained by combining powders of active substances and fillers;
D. Structural elements of the drug provide connection with peptides;
E. Substances that provide solidification of reactive oligomers.
8 . Types of nanomaterials have the following classification:
A. Nanoparticles, nanotubes, nanofibers.
B. Liposomes, dendrimers, micelles.
C. H anoporous structures, nanoparticles, nanodisperse, nanostructured surfaces, nanoclusters.
D. Nanosystems, nanoobjects.
E. Nanobiotechnological, nanomedical, nanoorganic.
9. Fullerenes are:
A. Graphene grids rolled into tubes with a distance between the walls of 0.35 nm.
B. Molecular compounds that have the form of convex closed polyhedra, consisting of even, formed only by an even number of carbon atoms in sp^2-hybridization.
C. Lipid nanoparticles.
D. Nanoparticles in aggregate state.

E. Ferromagnetic particles.
10. Nanoparticles are obtained by:
A. Using a dismembrator.
B. Grinding, homogenization.
C. Ultrasonic crystallization, coacervation.
D. Mechanical activation, homogenization with microprecipitation.
E. Sublimation drying.

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