MINISTRY OF HEALTH OF UKRAINE

ODESSA NATIONAL MEDICAL UNIVERSITY

Department of Pharmaceutical Chemistry and Drug Technology

APPROVE
Vice-Rector for Scientific and Pedagogical Work

_____ Eduard BURYACHKIVSKY

September 01, 2024

METHODOLOGICAL DEVELOPMENT FOR LECTURES FROM THE ACADEMIC DISCIPLINE "DRUG TECHNOLOGY" 8TH SEMESTER

Level of higher education : second (master's **)**

Area of knowledge: 22 "Healthcare"

Specialty: 226 "Pharmacy, industrial pharmacy"

Educational and professional program: Pharmacy, industrial pharmacy

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Approved:

Meeting of the Department of Pharmaceutical Chemistry and Drug Technology
Odessa national medical university

Protocol No. 1 from " 28 " August 2024 river

Manager Department _____ Volodymyr HELMBOLDT

(signature) *(First name, last name)*

Developers:

Assoc. Prof. Zamkovaya A.V., Assoc. Fizor N.S.

Lectures No. 11

Topic: "Tablets, characteristics and classification. Direct compression" - 2 hours.

Relevance of the topic: Drug technology (industrial technology of drugs) means) – is one of the fundamental technological sciences. It consists of several key aspects, which important for modern medicine and patients:Effectiveness and safety - Modern technologies allow the production of medicinal products drugs with high efficacy and safety for patients. Accurate dosage, control qualities and absence impurity do medicine more effective and safe. Innovations in medical in the field of: New technology allow create innovative medicines that can be more targeted and effectivemedical therapy. For example, medicine, designed for accurate influence on specific cells or genes, provide more effective treatment. Minimization side effects effects: Technologies allow elaborate medicinal formulas that minimize side effects and negative effects on the body. This provides more comfortable and safe treatment for patients. Fast production and supply process: The use of modern technologies allows speed up the process of producing medicines, which is especially important in conditions rapidly changing medical environment, such as spread diseases or epidemics. Individual approach to treatment: Technologies allow elaborate medicine, which take into account individual features patient, which leads to a personalized approach to treatment and increases its effectiveness efficiency.Economy and accessibility Improved technology production can reduce production costs, making medicines more available for wide circles patients, providing economic efficiency in field health care.

Thus, the use of modern technologies for the production of medicinal products drugs there are important factor for improvement efficiency treatment, security patients and general state public health.

Goal: to get acquainted with main in stages industrial production medical forms and disciplines "Technology medicines", dates characteristic production tablets method direct pressing and with pre-granulation and describe modern state pharmaceutical industry tabletscovered with a shell and medical capsules.

Basic concept:

Pressing **(** actually tableting) **is** the process of forming tablets fromgranulated or powdered material under by action pressure.

Direct compression **is** the process of compressing non-granulated powders. Direct pressing allows to eliminate 3 - 4 technological operations and, thus, has advantage before tableting with previous granulation of powders.

Dedusting **is** the process of removing dust from the surface of tablets coming out of the press. dust fractions.

Granulation **–** directed amalgamation particles, that is, process transformation powdered material in grains certain magnitudes, What necessary for improvement flowability tableted mixtures and prevention its delamination.

Plan and organizational structure lectures:

No. No. p.p.	**Main stages of the lectureand their content.**	**Goals inlevels abstractions.**	**Type lectures, equipment lectures.**	**Distribution time.**
1	**2**	**3**	**4**	**5**
I	***Preparatory stage***			
1.	Definition educational goals.		Lecture combined	1%
2.	Software positive motivation.			2%
	Basic stage Presentation lecture hall material.			90%

II 3. III4. 5.	Plan: 1. Characteristic tablets as medicine forms. Types and groups tablets. 2. Properties powdery medical substances. 3. Basic groups excipients in production tablets. 4. Objectives and main types granulations at production tablets. 5. Coating tabletsshells. 6. Ways improve tablets as medicalforms. ***Final stage*** Resume lectures, general conclusions. Lecturer's answers to possible question. Tasks for self-training student.	I II III	Slides List literature, question, task.	 2% 3% 2%

Structurally logical scheme content lectures

1. Characteristic tablets as medical forms. Types and groups tablets.

2. Properties powdery medical substances.

3. Basic groups auxiliary substances in production tablets.

4. Goals and main types granulations at production tablets.

5. Coating tablets shells.

6. Ways improve tablets as medical forms.

Content lecture hall material (text lectures)

1. Characteristic tablets as dosage form. Types and groups tablets.

Tablets (*Tablets* , from Latin *table* — board, *table* — tablet, tile)

- dosed medical form, received pressing medical or mixtures medicinal and auxiliary substances, intended for internal, external, sublingual, implantation or parenteral use.

Tablets produced by the chemical and pharmaceutical industry, constitute about 40% production ready-made medical means. Tablet production worldwide is growing by 10-15% annually. According to WHO, such pace will survive until the end XX Art.

Characteristic tablets

Tablets as medical form received wide spread in everything world. IN Currently, tablet preparations account for about 80% of the total volume ready-made medicines means.

Positive qualities tablets provide:

— an appropriate level of mechanization of the main stages and operations of production, whichcontributes high productivity and hygiene;

- precision dosage are introduced in pills medical substances;

- portability of tablets, convenient for dispensing, storage andtransportation;

- continued preservation medical substances in compressed condition;

- for substances not enough stable – possibility causing protectiveshells;

- possibility disguise unpleasant organoleptic

properties (taste, smell, coloring power), which is achieved by causing coatings;

- combination medical properties, incompatible by physicochemical properties in others medical forms;

- localization actions medical substances in certain department gastrointestinal tract – by causing shells, soluble in sour or alkaline environment;

- prolongation actions medical substances (by causing coatings,using special technologies and warehouse core tablets);

- regulation consistent absorption several medical substances with pills in organism in defined gaps time (multilayered tablets);

- warning errors at vacation and reception medicines — causing on surface tablets relevant inscriptions.

However pills have and some disadvantages:

- action medical means in tablets developing relatively slow;
- pills impossible to introduce in organism at vomiting;
- at storage pills can be cemented at this increasestime disintegration;
- to warehouse tablets can enter auxiliary substances, not have therapeutic value, and sometimes cause some side effects (for example, talc annoying mucous membrane shell stomach);
- separate medicinal drugs (for example, sodium or potassium bromide) form in zone dissolution highly concentrated solutions, which can cause strong irritation mucous membranes shells (this drawback eliminated by dissolution tablets in certain quantities water);
- not all sick, especially children can free devour pills.

Classification tablets

1. By in a way receiving distinguish two classes tablets:

Pressed, received by pressing powders on tabletmachines with different manufacturability. This method is main.

Molded, or triturative pills, received formation tabletedmasses. They constitute about 1-2% from total volume production tablets. Triturated tablets contain small doses of medicinal and diluting substances: mass they may be to 0.05 river

Classification tablets on constructive sign:

1. By composition; simple (single-component / and complex (multicomponent).

2. By structure: frame, single-layer and multi-layer (at least 2-x layers), with coating or without him.

Frame, or skeletal pills ,have insoluble frame, voids whose filled medical substance. Tablet represents by yourself as would sponge, soaked medicine. At reception frame its not dissolves, keeping geometric form, and medical substance diffuses in gastrointestinal highway.

Single-layer pills consist of with pressed mixtures medical and auxiliary substances and uniform throughout volume dosage form.

In multilayer tablets, medicinal substances are arranged in layers. Application chemically incompatible substances causes their minimal interaction.

3. Tablet coatings are classified as: coated,film and pressed dry.

Tablet forms, What are produced by the chemical-pharmaceutical The most diverse in industry: cylinders, spheres, cubes, triangles, quadrilaterals, etc. The most common there are flat-cylindrical form with chamfer and biconvex form, convenient for swallowing. In addition, punches and dies for tablet production more simple in manufacturing and not call special difficulties at their installation on tablet machinery.

Size tablets fluctuates from 4 to 25 mm in diameter, most common

— from 4 to 12 mm, pills diameter over 25 mm are called briquettes. Tablets with a diameter of more than 9 mm have one or two risks applied

perpendicularly, allowing the tablet to be divided into two or four parts. and like this in a way vary dosage medical substances.

Mass tablets in basically constitutes 0.05—0.8 m, What is determined dosage medical substances and the number incoming in their composition auxiliary substances.

The tablets should be of regular shape, without jagged edges, smooth and homogeneous surface, have sufficient strength and not crumble. Geometricform and dimensions tablets are determined standard — OSTom 64-072-89

"Medicines. Tablets. Types and sizes". It provides for the release of two types tablets: flat-cylindrical without chamfer and with chamfer, biconvex without coating and with coating: film, pressed and coated. Flat-cylindricalTablets are available in 14 sizes with diameters ranging from 4.0 to 20.0 mm; biconvex tablets without coating - 10 sizes - from 4.0 to 13.0 mm, pills with coating — from 5.0 to 10.0 mm (table. 14.2). Diameter tabletsis determined in dependencies from their masses (table. 14.3).

The height of flat-cylindrical tablets should be within 30-40% of diameter. Some tablets (in the CIS countries these are tablets containing drugs), have on surfaces inscriptions with by name drug in in the form of concave prints, Yes as convex letters on ends tablets much more prone to abrasion and destruction.

IN dependencies from appointment and way application tablets distinguish the following groups:

Oriblettae - tablets that are taken orally. Medicinal substances are absorbed mucous shell stomach or intestines. These pills accept internally, drinking with water. Oral group tablets there are main.

Resoriblettae - pills, which apply sublingually; medicinal substances are absorbed mucous shell cavities mouth.

Implantabulettae - pills, aseptically manufactured, are applied for implantation. Calculated on slow motion absorption medical substances with purpose prolongation medical effect.

Injectables — pills, What are made aseptically, are appliedfor receiving injectable solutions medical substances.

Solublettae - pills, which are used for preparation solutionsvarious pharmaceutical appointment.

Dulciblettae bacilli, pain, urethra, vagitoria — pressed urethral,vaginal and rectal dosage forms.

Scale: mass-diameter "Medicines. Tablets. Types and sizes" (OST64-072-89)

Mass pills, g	**Diameter pills, mm**
From 0.02 to 0.04	4
From 0.04 to 0.08	5
From 0.08 to 0.15	6
From 0.15 to 0.20	7
From 0.20 to 0.30	8
From 0.30 to 0.40	9
From 0.40 to 0.65	10-11
From 0.65 to 0.85	12
From 0.50 to 1.10	13
From 0.65 to 1.35	14
From 0.80 to 1.65	15
From 0.95 to 2.00	16
More 1.8	20

2. Properties powdery medical substances

Properties weekend medical substances many in Why determine rational method of tableting. The starting materials used are loose substances in in the form of powdery (size particles 0.2 mm) or granulated (size particles from 0.2 to 3 mm) forms, What have next properties:

— physical - density, form, size and nature

particle surface, specific surface area of particles, adhesion forces (sticking to surface) and cohesion (sticking together of particles inside the body), surface activity, temperature melting and other;

— chemical — solubility, reactionary ability and other;

— technological — volumetric density, degree consolidation, flowability, humidity, factional composition, dispersion, porosity, pressed and other;

- structural and mechanical - plasticity, strength, elasticity, viscositycrystalline grilles and etc.

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

Physico-chemical properties

Particle shape and size . Powdered drug substances are coarsely dispersed systems and have particles of various shapes and sizes. Majority with them there are crystalline systems; amorphous state meets less often. Many drugs have anisodiametric particles. (asymmetrical, multi-axle). They can be elongated forms, When length much exceeds transverse dimensions (sticks, needles etc), or lamellar, When length and width much more thickness (records, scales, signs, leaves etc). Smaller part powdery substanceshas particles isodiametric (symmetrical, equiaxed) - it spherical education,

blocks, polyhedra etc.

Form and size particles powders depends: in crystalline substances (chemical-pharmaceutical preparations) - from the structure of the crystal lattice and conditions particle growth during the crystallization process, in crushed plant materials - from the anatomical and morphological features of crushed plant organs and the type grind machine.Size particles powders determine on their length and width, measuredby with help microscope, supplied micrometric net, at increase in400 or 600 times.

The shape of the particles is determined by the ratio of the average particle length to average width. At this method particles conditionally divided on three main types: elongated — relation lengths to widths - 3:1; lamellar

- length exceeds width and thickness, but not more than in 3 times; exactly spring — have spherical, multifaceted form, close to isodiametric.

There is 6 crystalline systems: cubic, hexagonal, tetragonal, rhombic, monocligical, triclinic. The largest number of crystalline products are the following substances: monoclinic systems -40, cubic -10, hexagonal -7, tetragonal -5, rhombic -28, triclinic -10%.

It is known that only substances belonging to the cubic system are compressed. in pills directly, that is, direct pressing, without granulations and auxiliary substances (sodium chloride, potassium bromide).

Usually powders, What have form particles in in the form of sticks, are characterized by fine dispersion, good compactability and sufficient porosity (analgin, norsulfazole, akrihin and etc.).

Powders with equiaxed particle shape - coarse, with small degree consolidation, small porosity (lactose, hexamethylenetetramine, salol). The more complex the surface of the powder particles, the greater the adhesion and Less flowability, and vice versa.

Physical properties powders are determined specific and contact surface and true density.

Specific surface — total surface, which one occupies powdery substance, and the contact surface is the surface formed by the collision betweenparticles powder.

For tableting, the chemical properties of the starting materials are important. substances, such as: the presence of water of crystallization, solubility, wettability and hygroscopicity.

Wettability powdery medical substances — their ability interact with different liquids (lyophilicity) and first by all with with water (hydrophilicity). On surfaces solid particles medical substances contained

a certain number of hydrophilic groups (-OH, -SON, -COOH, etc.) or oxygen groups atoms, which there are structural elements their crystalline grilles, ago The wettability of the surface of powders has a different value, depending on the intensity interactions intermolecular forces.

Visually predisposition surfaces powders to wetting with water manifests itself:

and) complete wetting - liquid fully spreads on surfaces powder;

b) partial wetting — water part spreads on surfaces;

in) complete non-wetting — drop water not spreads, keeping form, close to spherical.

Hydrophobic (not wetted by water) substances can be perfectly wetted other liquids, for example, organic solvents.

Lyophilicity tableting powdery substances is determinedthe filality coefficient, which is the ratio of the specific warmth wetting polar liquid. (water) to specific warmth wetting non-polarliquid. It is known that What formation on surfaces solid particles monomolecular layer wetting liquids always accompanied allocation Yes invited warmth wetting.

Practical value wetting and consists of in ago, What in a pill, receivedpressing good wettable with water substances, light penetrates water, What accelerates tablet disintegration.

Hygroscopicity . If elasticity steamed in in the air more, than their elasticityon surfaces solid particles, then powdery mass, prepared to tableting, will begin to absorb vapors from the air and dissolve in the absorbed water. The kinetics of moisture absorption is determined by the gravimetric method (normal ordinary conditions, extreme (desiccators over with water — 100% relativehumidity), or in climate-czech camera.

If substance strongly hygroscopic, it causes application auxiliary substances — moisture stimulators.

Crystallization water . Molecules water crystallization determine mechanical (strength, plasticity) and thermal (attitude to temperatures air environment) properties of the crystal and have a significant impact on behavior of a crystal under pressure. The phenomenon of "cementation" is also closely related to presence water of crystallization in tableted substances.

Electric properties . Phenomenon electrification powdery medical substances

at their processing and pressing gives foundation make conclusion: at under consideration the nature of the bonding of particles in tablets, along with the deformation, must be taken into account dielectric characteristics into account. Under mechanical stress they will be susceptible to to polarization, all asymmetric crystals containing polar groups in their structure or in an adsorbed water film. For nonpolar substances, the formation superficial charges is excluded.

Technological properties

The technological properties of powdered medicinal substances depend on from their physicochemical properties.

Fractional (granulometric) composition, or distribution of powder particles by size, has a certain influence on the degree of flowability, and therefore on the rhythmic work tablet cars, stability masses received tablets, precision dosage medical substances, and also on high-quality characteristics tablets (external appearance, disintegration, strength and others). The fastest and most convenient method for determining dispersion is **sieve analysis.** Machinery its consists of in ago, What 100.0 g researched powder siftthrough a set of sieves (hole diameter 2.0, 1.0, 0.5, 0.25 and OD mm). A portion of the material placed on the largest (top) sieve and the entire set of sieves shaken by hand or on a vibrating machine) for 5 min, and then find the mass of each fraction andits percentage contents.

Research factional warehouse pharmaceutical powders, What subject to tableting, showed that most of them contain in the predominant quantities small faction (Less 0.2 mm) and ago have bad flowability. They badly are dosed by in volume on tablet cars, pills are leaving unequal on mass and strength. Factional composition powders can change by

using directional granulation, which allows you to obtain a certain amount large factions.

Very important there are definition such volumetric indicators powders, as bulk and relative density and porosity.

Bulk (volumetric) density - mass per unit volume of loosely packed of powdered material. Bulk density depends on the shape, size, density particles

powder (granule), their humidity. By meaning bulk densities can be predict the volume of the matrix channel.

Definition of bulk density powder is carried out on the device models 545R-AK-3 Mariupol (formerly Zhdanivska) Technological Plant equipment.

Weighing 5.0 g powder with accuracy to 0.001 g and fall asleep its in measuring cylinder. Install amplitude oscillation (35-40 mm) by with help regulatory screw and after marks by scale fix position lock nut. Frequency oscillation establish by with help transformer within 100-120 rpm on the counter. Then turn on the device toggle switch and are watching by mark equal powder in cylinder. When level powder becomes permanent (usually to 10 min), the device is turned off.

The compressibility of powdered preparations is affected by the shape particles, their ability to move and deform under pressure. Coefficient compaction is an important technological factor; in particular, the greater it is, the more time is spent on pressing. At this is spent more efforts and on pushing out pills with depths matrix channel.

At tableted most important technological properties there are flowability, compression and sliding properties allow the tablet to be easily pushed out of the matrices.

Flowability - the ability of a powder system to flow out of a funnel capacity or "flow" under its own weight and ensure uniform filling the matrix channel. Material that has poor flowability in the funnel, sticks to its walls, What violates rhythm its receipt in matrix. It leads to that, What given mass and density tablets will be fluctuate.

At definition flowability powders with small bulk density it is allowed to use a sample weighing 30.0 g. Using the VP- 12A is determined also angle natural slope — angle between creative cone loose material and horizontal plane. Angle natural slope changes in wide within - from 25 to 30°C for good loose materials and 60-70 °C — for related materials. Flowability powders there are comprehensive characteristic, which is determined dispersion and shape of particles, moisture

content of the masses, granulometric composition. This technological characteristic can be used when choosing a technology tableting. Powdered mixtures, What contain 80-100% small factions (particle size less than 0.2 mm), are poorly dosed, so it is necessary to carry out directed enlargement of particles of such masses, i.e. granulation. If fine fractions contained up to 15%, possible using the method pressing.

Compressibility is the ability of powder particles to coalesce under pressure, i.e. the ability of particles under the influence of forces of electromagnetic nature (molecular, adsorption, electrical) and mechanical couplings to mutual attraction and clutch with formation stable, strong pressing.

Direct methods definition compressibility no.

Compressibility is characterized by the strength of the model tablet after removal pressure. The better the compressibility of the powder, the higher the tablet strength. If The compressibility is low, the tablet is fragile, and sometimes completely collapses. at pushing out with matrices.

The compressibility of a tablet can be assessed by its compressive strength. Strength determined on devices KHNIKHFI or TVT of the company "Erveka" and expressed in kilograms or newtons. The higher the tablet strength, the better the compressibilityand formability tablet masses.

Installed, What for substances with strength tablets:

— above 7 kg/cm2, pure solvents are used for the granulation process;if these are coarsely dispersed powders with good flowability, then they are pressed directly, that is, direct pressing;

- 4-7 kg/cm2 enough application ordinary bind

substances:

- 1-4 kg/cm2 requires the use of highly efficientbinding substances.

By results definition compressibility tablet masses do conclusion about technology tableting.

Powder compressibility is the ability of its particles to cohesion and

adhesion. under pressure, that is, the ability of particles of matter under the influence of forces of various nature and mechanical engagements to mutual attraction and adhesion with the formation of a strong compact pills. Under pressure particles powder as if are soldered, stick together, are linked between yourself, and weak structure dispersed system is transformed in homogeneous solid body.

Suggested three theories pressing (or tableting): mechanical,capillary-colloidal and electrostatic.

Mechanical theory . Pressing there are determining operation at manufacturing tablets. IN modern industrial presses is carried out bilateral compression powder upper and lower punches. At movement punches in matrices there is a gradual change state powder.

All process breaks down on three stages :

1) consolidation (pressing);

2) formation compact bodies;

3) volumetric compression formed compact body.

Capillary-colloid theory. According to theories P. and. Rebinder forces interfacial interactions are largely determined by the nature of the solid and the presence of liquid phases. The strength of structured systems depends on the amount water and its location.

3. Basic groups auxiliary substances in production tablets

Auxiliary substances in tablet production intended give the tablet mass requires technological properties that ensure accuracy dosage, mechanical strength, decay and stability tablets in process storage.

Auxiliary substances, What are used in production tablets, are divided on groups in dependencies from appointment. Basic groups and nomenclature auxiliary substances given in table

Requirements to auxiliary substances:

- they must be chemically indifferent;

— should not have a negative impact on the patient's body, as well as on quality tablets with them cooking, transportation and storage.

Fillers (diluents) are added to obtain a certain mass of tablets. With a small dosage of the medicinal substance (usually 0.01 - 0.001 g) or withtableting potent, poisonous and others substances their can use with purpose regulation individual technological indicators (strength, disintegrability etc). Fillers determine technological properties masses for tableting and physical and mechanical properties ready-made tablets.

Binders substances . Particles majority medical substances have low adhesion strength between them, so their tableting requires high pressure, which often there are reason untimely wear press tool tablet machines and receiving poor quality tablets. For achievement necessary adhesion forces at relatively low pressures to tableted substances add binding substances. Filling between partial space, they increase contact surface particles and cohesive ability. Auxiliary substances, What are applied in production tablets

Group	Substance	Number,%
Fillers (thinners)	Starch, glucose, saccharose, lactose (milk, sugar) magnesium carbonate basic, magnesium oxide, sodium chloride, sodium bicarbonate, white clay (kaolin), gelatin, microcrystalline cellulose (MCC), methylcellulose (MC), sodium salt Carboxyl methyl cellulose (Na CMC), calcium carbonate, calcium phosphate, glycine (aminoacetic acid), dextrin, amylopectin, ultraamyl pectin,	Not normalized

Astringents	Water cleaned, alcohol ethyl, collapsible paste, sugar syrup, solutions: carboxymethylcellulose (CMC), oxyethyl cellulose (OEC), oxypropyl-methylcellulose (OPMC); polyvinyl alcohol (PVA), polyvinylpyrrolidone (PVP), alginate acid,	Not normalized Recommend 1-5%
Leavening agents: swelling gas-producing improve wettability	Starch wheat, potato, corn, rice, pectin, gelatin, MC, NaCMC, amylopectin, ultraamylopectin, agar agar, alginic acid, potassium and sodium alginate, etc. A mixture of sodium bicarbonate with citric or tartaric acidacids etc. Starch wheat, potato, corn,	Not normalized Not normalized Not is normalized. Twin-80 not
Antifrictionno: sliding lubricating	Starch, talc, polyethylene oxide-4000, aerosil and other Stearic acid, calcium and magnesium stearate, etc. Starch, talc, polyethylene oxide-4000, stearic acid acid, calcium and magnesium stearate and etc.	Talc is not more than 3%, aeroforce not more 10%, stearicacids, calcium and
Film-forming Vatel	Acetylphthalyl cellulose (AFC), MC, OPMC, PVP, PVA, ethyl cellulose	Not are being normalized

Corrections: taste smell colors: dyes pigments	Sugar, glucose, fructose, saccharose, xylitol, mannitol, sorbitol, asparkam, glycine, dulcinea and etc. Essential oils, fruit juice concentrates, citral, menthol, vanillin, ethyl vanillin, fruity essences and etc. Indigo carmine, acid red 2C, tropeolin 00, tartrazine, eosin, ruberosum,	Not normalized
PlasticsTories	Glycerin, tween-80, Vaseline butter, acidoleic, polyethylene oxide-400, propylene glycol and etc.	Twin-80 not more 1%
Extenders and substances for creation hydrophobic	Wax white, oil sunflower, butter cotton, monopalmitin, trilaurin, paraffin and other	Not are being normalized
Solvents	Water cleaned, alcohol ethyl, acetone, chloroform, ammonia, acid hydrogen chloride and etc.	Not are being normalized

Special value have binding substances at pressing complex powders. IN process works tablet machinery they can exfoliate, which results in tablets with different contents of the input ingredients. Application kind binding substances, their number depends from physical-chemical properties pressed substances.

Functions binding substances can perform different substances.

Water is used in all cases where simple moistening provides normal granulation powdered masses.

Alcohol ethyl use for granulation powders hygroscopic, most often when the composition of the tableting mass includes dry extracts from plant raw materials - these substances with water and aqueous solutions form a sticky, sloppy, poorly

granulating mass. Concentration applied alcohol usually that above, than more hygroscopic powder.

For powders, What form with with water and alcohol crumble, not granulated masses, apply solutions Navy, mechanism actions whose installed and theoretically solved by E.E. Borzunov. In this case, the ability to connect high molecular weight compounds is determined not only their concentration and viscosity, but and size molecules.

Loose-filling substances. At pressing medical substances sharply decreases porosity and that by ourselves is getting complicated penetration liquids within pills. For improvement disintegrability or dissolution disintegrating agents are used to ensure mechanical destruction tablets in a liquid medium, which is necessary for the rapid release of the active ingredient substances. Disintegrants are also added to the composition of tablets if the drug is not soluble in water or if the tablet is capable of cementing when storage. IN case using in qualities baking powder mixtures sodium bicarbonate with lemon or guilty acids necessary consider their interaction in wet environment, and therefore, right choose order their introduction during wet granulation in tablet mass.

Efficiency actions loosening substances is determined three ways:

- by definition speed absorption and quantities absorbed waterpowdery mass;
- disintegration time of tablets containing different concentrationsloosening substances;
- by definition speed swelling and maximum water containersbaking powder, by high-speed photography under microscope.

In general, all disintegrants ensure the destruction of tablets on small particles when they come into contact with liquid, resulting in a sharp increasing the total surface area of particles, which facilitates release and absorption active ingredients.

Antifriction agents. One of the problems of tablet production is receiving good fluidity granulate in nourishing devices (funnels, bunkers). Received granules or powders have rough surface, What complicates their absorption with boot funnels in matrix nests. In addition, granules can stick to the die walls and punches

due to friction, developing in contact zones particles with press tool tablet machinery. For removal or reduction these unwanted phenomena apply antifriction substances, presented group sliding and lubricants.

Slippery substances, adsorbing on the surface of particles (granules), eliminate or reduce their roughness, raising their fluidity (flowability). The biggest efficiency slip have particles, What have spherical form.

Lecture No. 12

Topic: " Granulation. Types of tablet machines." - 2 hours.

Relevance of the topic: Drug technology (industrial drug technology) is one of the fundamental technological sciences. It consists of several key aspects that are important for modern medicine and patients: Efficacy and safety - Modern technologies allow the production of drugs with high efficiency and safety for patients. Accurate dosing, quality control and the absence of impurities make drugs more effective and safe. Innovations in the medical field: New technologies allow the creation of innovative drugs that can be more targeted and effective drug therapy. For example, drugs designed to precisely affect specific cells or genes provide more effective treatment. Minimization of side effects: Technologies allow the development of drug formulas that minimize side effects and negative effects on the body. This provides more comfortable and safe treatment for patients. Fast production and delivery process: The use of modern technologies allows the production process of drugs to be accelerated, which is especially important in a rapidly changing medical environment, such as the spread of diseases or epidemics. Personalized medicine: Technology enables the development of medicines that take into account the individual characteristics of the patient, which leads to a personalized approach to treatment and increases its effectiveness. Cost-effectiveness and accessibility Improved manufacturing technologies can reduce production costs, making medicines more accessible to a wider range of patients, ensuring cost-effectiveness in the healthcare sector. Thus, the use of modern technologies for the manufacture of medicines is an important factor in improving the effectiveness of

treatment, patient safety and the overall state of public health.

Objective: to get acquainted with the main stages of industrial production of dosage forms and the discipline "Drug Technology", to characterize the production of tablets by direct compression and with preliminary granulation and describe the current state of the pharmaceutical industry for film-coated tablets and medical capsules.

Basic concepts:

Granulation **is** the directed enlargement of particles, i.e. the process of transforming a powdered material into grains of a certain size, which is necessary to improve the flowability of the tableted mixture and prevent its delamination.

Infrared rational dryers **.** As thermal radiation in such dryers are applied special mirrored lamps, nichrome spiralsincandescence.

Sledding machinery. IN given tipi machines bootable crater moving at work on special on skids.

Plan and organizational structure lectures:

No. No. p.p.	**Main stages of the lectureand their content.**	**Goals inlevels abstractions.**	**Type lectures, equipment lectures.**	**Distribution time.**
1	**2**	**3**	**4**	**5**
I	***Preparatory stage*** Definition educational			1%

1.	goals.		Lecture combined	
	Software			2%
2.	positive motivation.			
	Basic stage			
	Presentation lecture hall material.			90%

II 3. III4. 5.	Plan: 1. Characteristic tablets as medicine forms. Types and groups tablets. 2. Properties powdery medical substances. 3. Basic groups excipients in production tablets. 4. Objectives and main types granulations at production tablets. 5. Coating tabletsshells. 6. Ways improve tablets as medicalforms. ***Final stage*** Resume lectures, general conclusions. Lecturer's answers to possible question. Tasks forself-training student.	I II III	Slides List literature, question, task.	2% 3% 2%

Structurally logical scheme content lectures

1. Characteristics of tablets as a dosage form. Types and groups of tablets.
2. Properties of powdered medicinal substances.
3. Main groups of excipients in the production of tablets.
4. Objectives and main types of granulation in tablet production.
5. Coating tablets with shells.
6. Ways to improve tablets as a dosage form.

Content of the lecture material (lecture text)

Goals and main types granulations at production tablets.

Granulation - directed amalgamation particles, that is, process transformation powdered material grains of a certain size.

Granulation is necessary to improve the flowability of the tableted mass, which occurs as a result of a significant reduction in the total surface area of the particles when their clumping into granules and, consequently, a corresponding reduction in the friction that occurs between particles while driving.

Existing in present time ways granulations are divided on main types: 1) dry granulation, or granulation grain; 2) moisture granulation, or granulationpushing; 3) structural granulation.

Method dry granulation. Lies in stirring powders and their moisturizing solutions gluing substances in enameled mixers with by further drying them to a granular mass. Then the mass with the help of rollers or mills "Excelsior" transform on coarse powder. Granulation grinding used in those cases, When dewy material reacts with material at wiping wounds. IN some cases, if medicinal substances decompose in presence water, under time drying enter in chemical reactions interactions or are exposed physical changes (melting, softening, change colors) — they are briquetted.

IN present time, applying method dry granulation, to warehouse tableted masses powders enter dry adhesive (for example, microcrystalline cellulose,

polyethylene oxide), What provide underpressure clutch particles, as hydrophilic, Yes and hydrophobic substances.

Wet granulation method. In production, wet granulation is oftenis carried out in granulators of type 3027 (Mariupol ZTO). Granulation, or rubbing damp masses, is carried out with purpose consolidation powder and receiving uniform grains — granules, What possess good flowability.

Data in a way granulation are exposed powders, What have badflowability and insufficient ability to the clutch between particles.

IN both cases in mass add adhesive solutions, What improve coupling between particles.

Method wet granulation includes next operations:

1) mix powders;

2) moistening the powder with a solution of binding substances andmixing;

3) granulation wet masses;

4) drying wet granules;

5) processing dry granules.

Mixing powders . Carried out to achieve a homogeneous massand uniformity distribution current substances tablets.

For mix and hydration powdery substances are appliedmixers different structures:

1) with rotating blades;

2) screw;

3) mixed drums.

At mixing powders it is necessary:

- to larger quantities add Less;

- poisonous and potent substances, What are applied in

small quantities, previously sifted through sieve, add to masses separate in portions in in the form of triturations, that is, in breeding with filler in

concentrations 1:100;

- colored substances and substances with a high specific by mass to download in mixer in the last one queue;

- light-flying ethereal oils introduce in dry granulated mass before pressing at the powdering stage, to avoid their weathering.

Practice production tablets shows, What time, necessary for mixing simple recipes (two- and three-component) in a dry state, is 5-7 min, for more complicated — 10-12 min.

After mix dry powders in mass separate in portions add moisturizer, What necessary for prevention her lumpiness.

When wet mixing powders, the uniformity of their distribution is significantly measure is improving, not observed separation particles and stratification masses, improving its plasticity. Mixing wet powders is accompanied by some compaction of the mass due to the displacement of air, which allows for denser solid granules. Mixing time of wet masses: for simple mixtures 7-10 min, for complex ones - 15-20 min. Optimal number humidifier is determined experimentally (coming out with physical- chemical properties of powders) and is specified in the regulations. The error may lead to marriage: if you add too little moisturizer - granules after drying will be spill, if many — mass will be viscous, sticky and badly granulated. The mass with optimal humidity is a moist, dense mixture, not sticks to hands, but crumbles at squeezing on separate lumps.

Granulation of wet mass . Wet mass is granulated on special granulator machines, principle works whose consists of in ago, What material wipes with blades, elastic rollers or others devices through perforated cylinder or grid. Granulators there are vertical andhorizontal.

Currently, wet granulation is the main type of granulation in production tablets, however he has number disadvantages:

— prolonged exposure to moisture on medicinal and auxiliarystreet vendors substances;

— deterioration disintegration (solubility) tablets;

- necessity using special equipment;

- duration and the complexity of the process.

Drying wet granules. Use different types dryers:

1) shelf dryers with forced circulation air;

2) dryers with silica gel column.

If necessary, regenerate the liquids contained in the desiccants materials, apply dryers, in whose air is skipped through silica gel. At this valuable couple adsorbed, and warm air again used for drying material.

Infrared rational dryers. As thermal radiation in such dryers are applied special mirrored lamps, nichrome spirals incandescence, placed in focus parabolic reflectors, metal and ceramic panel radiators with electric, steam or gas heating.

Freeze dryers . In recent years, they have been widely used in industry way drying materials in frozen condition in conditions deep vacuum. It was called sublimation drying, or molecular drying. Way allows save main biological qualities dried material, When is happening evaporation solid bodies without melting, passing by liquid phase.

Main advantage dryers - high productivity: time drying material, depending on its physical properties and shape, lasts from 20 to 50 min; they consume little energy and occupy small working area.

Dried granules must have some moisture before pressing, which is called residual. The residual moisture for each tableted drug is individual. and should be optimal, that is, one in which the process proceeds in the best possible way Thus, the quality of the tablets meets the requirements of the GF, and the strength is the highest compared to pills, received with granules this w drug with another degree humidity. Undried granules stick to the punches, fill unevenly matrix and require elevated quantities antifriction substances. Overdried granules hard are pressed, and pills can have broken edge.

Processing of granules . During the drying process, the granules may stick together into separate pieces. lumps. with purpose software uniform factional warehouse dried The granules are passed through granulators with mesh sizes of

1.5 mm, which largely ensures a constant weight of tablets. The granules are then powdered, adding antifriction substances, and transmit on stage tableting.

Structural granulation. Has a characteristic effect on moistened material, which leads to the formation of rounded, and under certain conditions - quite homogeneous by in size granules.B present time exist three ways granulations given type, used in pharmaceutical production: granulation in dragee boilers; granulation spraying drying and structural granulation.

For granulations in dragee boilers loading mixture powders and atrotation boiler from speed 30 rpm produce hydration by serving solutionbinding substances through nozzle. Particles powders stick together between yourself, are drying out warm by air and in result friction acquire about At the end of the process, sliding elements are added to the dried granulate. substances.

Types tablet machines

Pressing on tablet machines is carried out with a press tool that consists of with matrices and two punches.

The main types of tablet machines are eccentric, or impact, and rotary.

Eccentric machinery there are sledge and intermediate .

Sledding cars . IN given tipi machines bootable crater moving at work on special on skids. Material, What arrives with boot funnels, falls in channel matrices, attached to matrix table. After this crater with material is deleted, upper punch goes down, compresses material and rises.

Intermediate machines . Tablet machines of intermediate type in design and The principle of operation is similar to that of sledges, but they differ from them in their immobility.loading hopper and matrices.

Rotary tablet machines. Widely used, have a large number matrices and punches.

Factors affecting the main qualities of tablets - mechanical strength, decomposability and average mass.

Mechanical strength tablets depends from many factors. IN case using the direct compression method, the strength of the tablets will depend on physicochemical properties pressed substances.

The strength of tablets obtained by wet granulation depends on quantity, nature binding (gluing) substances, from quantities pressure pressing and moisture content of the tableted product material.

Number gluing substances and optimal humidity, as rule, are indicated in industrial regulations. Pressure pressing is being selected for of each drug and is controlled by measuring the strength of the tablets and time their disintegrability. Excessive pressure pressing often leads to stratification tablets. Except that, is happening sharp reduction time, What reduces penetration liquids in a pill, increases time its disintegration.

Moisture content above optimum leads to tablet sticking masses to press tool. Insufficient contents moisture, that is, overdrying material, leads to stratification in moment pressing or w to insufficient mechanical strength.

Disintegration and solubility tablets also depends from many factors:

- quantities and nature binding substances;

- quantities and nature loosening substances, which gives opportunity disintegratetablet.

- pressure pressing;

— physicochemical properties substances, What are included to pill —first of all from ability their to lubricity, swelling and solubility.

Medium mass tablets also depends from row components:

- flowability material;

- factional composition;

- forms boot funnels and the angle slope;

- the rotation speed of the matrix table, i.e. from the speedpressing.

Influence auxiliary substances and kind granulations on bioavailability medical substances with tablets

No pharmaceutical factor makes such a significant and complex influence on action drug, auxiliary substances.

IN pre-pharmaceutical period medicines introduction auxiliary substances was considered only as introduction indifferent fillers and form formers, without which

it is impossible to do when obtaining the appropriate dosage forms.

It has been proven that the method of obtaining dosage forms largely determines stability drug, speed its release with medical forms, intensity absorption, and in final summary — therapeutic efficiency. For example, from choice way granulations at receiving tablets The degree of preservation of a number of medicinal substances in finished medicinal products depends forms. Especially undesirable application wet granulations at receiving tablets containing reserpine, antibiotics and other substances, as it is possible decomposition drugs.

1. Granulation conditions have a great influence on the disintegration of tablets. The most commonly used humectants in industry are starch gelatin paste and solutions are not optimal for many drugs, because increase their time disintegrability. Increasing strength tablets with with help high-viscosity granulating liquids at others equal conditions leads to magnification time disintegrability; better disintegrability among highly viscous liquids usually provide solutions polymers: MC, OPMC, PVP, NaKMU. Harmful effects of hydrophobic lubricants (talc, magnesium and calcium) stearate), worsen disintegrability tablets with complicated penetration digestiveliquids in porous structure pills, substantially decreasing or fully

is eliminated, if tableted masses contain strongly swelling substances(CMC, MC).

2. Compression affects the rate of drug release, which, in yours queue, maybe to disturb process its absorption in places absorption.

3.One with methods improvement biopharmaceutical properties tablets is to create them based on inclusion complexes cyclodextrins with medicinal substances. Yes, using complex α-cyclodextrin substantially improves dissolution digoxin, Cavinton; observed magnification speed dissolution of salicylic acid in complex with (3-cyclodextrin.

WITH purpose maintenance concentrations medical substances in organism on at a certain constant level in the manufacture of some tablets are used auxiliary substances, What slow down speed release medical substances. For example, prolonged-release salbutamol tablets have been developed, which contain auxiliary substance — acrylic resin.

Lecture No. 13

Topic: "Coating tablets with shells. Granules. Pellets. Dragees."

– 2 hours.

Relevance of the topic: Drug technology (industrial technology of drugs) means) – is one of the fundamental technological sciences. It consists of several key aspects, which important for modern medicine and patients:Effectiveness and safety - Modern technologies allow the production of medicinal products drugs with high efficacy and safety for patients. Accurate dosage, control qualities and absence impurity do medicine more effective and safe. Innovations in medical in the field of: New technology allow create innovative medicines that can be more targeted and effectivemedical therapy. For example, medicine, designed for accurate influence on specific cells or genes, provide more effective treatment. Minimization side effects effects: Technologies allow elaborate medicinal formulas that minimize side effects and negative effects on the body. This provides more comfortable and safe treatment for patients. Fast production and supply process: The use of modern technologies allows speed up the process of producing medicines, which is especially important in conditions rapidly changing medical environment, such as spread diseases or epidemics. Individual approach to treatment: Technologies allow elaborate medicine, which take into account individual features patient,leading to a personalized approach to treatment and increasing its effectiveness efficiency. Economy and accessibility Improved technology production can reduce production costs, making medicines more available for wide circles patients, providing economic efficiency in field healthcare. Thus, the use of modern technologies for the manufacture of medicinal products drugs there are important factor for improvement efficiency treatment, security patients and general state public health.

Goal: to get acquainted with main in stages industrial production medical forms and disciplines "Technology medicines", dates characteristic production tablets method direct pressing and with previous

granulation and describe modern state pharmaceutical industry tablets covered with a shell and medical capsules.

Basic concept:

Pressing **(** actually tableting) **is** the process of forming tablets fromgranulated or powdered material under by action pressure.

Direct compression **is** the process of compressing non-granulated powders. Direct pressing allows to eliminate 3 - 4 technological operations and, thus, has advantage before tableting with previous granulation of powders.

Dedusting **is** the process of removing dust from the surface of tablets coming out of the press. dust fractions.

Granulation – directed amalgamation particles, that is, process transformation powdered material in grains certain magnitudes, What necessary for improvement flowability tableted mixtures and prevention its delamination.

Plan and organizational structure lectures:

o. No. p.p.	**Main stages of the lectureand their content.**	**Goals inlevels abstractions.**	**Type lectures, equipment lectures.**	**Distribution time.**
1	**2**	**3**	**4**	**5**
I 1. 2.	***Preparatory stage*** Definition educational goals. Software positive motivation. ***Basic stage*** Presentation lecture hall		Lecture combined	1% 2%

	material.			90%

II 3.	Plan: 1. Characteristics tablets as medicine forms. Types and groups tablets. 2.Propertiespowdery medical substances. 3. Basic groups excipients in production tablets. 4. Objectives and main types granulations atproduction tablets. 5.Coating tabletsshells. 6.Paths improve tablets as medical forms. ***Final stage*** Resume lectures, general conclusions. Lecturer's answers to possible question. Tasks forself-training student.	 I II III	Slides List literature, question, task.	 2% 3% 2%

Structurally logical scheme content lectures

1. Characteristic tablets as medical forms. Types and groups tablets.
2. Properties powdery medical substances.
3. Basic groups auxiliary substances in production tablets.
4. Goals and main types granulations at production tablets.

5. Coating tablets shells.

6. Ways improve tablets as medical forms.

Content lecture hall material (text lectures)

Coating tablets shells

Coating tablets shells has multilateral value and next goals:

1) protection of tablets from extreme environmental factors (strokes, abrasion and etc.);

2) protection from influences surrounding environment (light, moisture, oxygen andcarbon dioxide air);

3) disguise unpleasant taste and smell, contained in tablets medical substances;

4) protection from dyeing abilities medical substances, What contained intablets (e.g. tablets activated coal);

5) protection contained in tablets medical substances from sour reactions gastric juice;

6) protection mucous mouth, esophagus and stomach from annoying leg actions medicalsubstances;

7) localization therapeutic actions medical substances in certain department gastrointestinal tract;

8) prevention violations processes digestion in stomach, possible at neutralization gastric juice medicinal substances main character;

9) prologue therapeutic actions medical substances in tablets;

10) overcoming incompatibilities different substances, are located in one tablet,by their introduction to the composition shells and kernels;

11) improving the presentation of tablets and their ease of use. At coating tablets shells apply different auxiliary substances, conditionally What are subdivided on next groups: adhesives, What provide adhesion materials coating to kernels and one to one (sugar syrup, PVP, CMC, MC, AFC, OPMC, EC, PEG, etc.); structural substances that create frames (sugar, magnesium oxide, calcium oxide, talc,

magnesium carbonate basic); plasticizers, which provide coating properties plasticity (vegetable oils, MC, PVP, CMC, tweens and etc.); water repellents, What provide coating properties moisture resistance (aeroforce, shellac, polyacrylic resins, zein); dyes, employeesto improve appearance or to indicate a therapeutic group substances: (tropeoline 00, tartrazine, acid red 2C, indigo carmine, etc.); flavoring agents that give the coating a pleasant taste (sugar, citric acid, cocoa, vanillin, etc.).Applies more 50 names film formers.

Tablets coating in dependencies from their warehouse and way causing share for such groups:

1. Pressed (or dry) coating.
2. Film coating.
3. Dragee coating (causing sugar shells).

Pressed coating

Causing shells pressing ("dry" coating) carry out by using tablet machines of the "Draycott" type from the English company "Zavdat" or domestic RTM-24 D. Machine represents by yourself double aggregate, What consists of with two rotors.

On the first rotor ordinary in a way are pressed pills - kernels biconvex shape, transmitted using a special transporting device on second rotor, where applied coating.

The main advantage of this coating method there are exceptions using in technology solvents. Ago pressed coating rational for tablets hygroscopic and sensitive to influence moisture substances (antibiotics).

WITH purpose extensions effect current substances enter to warehouse as kernels, Yes and coating. The coating disintegrates rapidly in the stomach (initial dose), and the core (a tablet) disintegrates gradually, maintaining a certain constant concentration substances in the body. This method allows to overcome the incompatibility of substances in the one tablet various substances, introducing them into the composition shells and kernels.

Film coating

Film coating is called thin (about 0.05— 0.2 mm) shell, which is formed on pill after drying out inflicted on its surface solution film-forming substances.

They have next advantages:

1. Possibility electoral solubility of tablets in stomach or intestines.
2. Regulation speed adsorption medical substances.
3. Possibility of combination in one dosage formincompatible medications "substances.
4. Preservation physical, chemical and mechanical

properties nuclei tablets at application film coatings.

5. Preservation of original geometric parameters tablets, their forms, marking, branded designations.
6. Reducing the mass of the film coating volume withcomparatively with coated.
7. Possibility of automating the coating process, intensification production and abbreviation production area.

IN dependencies from solubility film coating share on suchgroups:

and) water-soluble;

b) soluble in gastric juice;in) enteric-coated;

d) insoluble.

Water-soluble coating and coating, soluble in stomach. Water-soluble Coatings improve the appearance of tablets, adjust their taste and smell, protect from mechanical damage. Coating, soluble in stomach, protect tablets from exposure to moisture in the air; they break down in the body for 10-30 minutes. To obtain water-soluble coatings, polyethylene oxide and polyvinylpyrrolidone is applied to tablets in the form of 20-30% solutions in 50-90% ethyl or isopropyl alcohols, methylcellulose and sodium salt carboxymethyl cellulose — in in the form of 4-7% aquatic solutions.

Coatings soluble in gastric juice are benzylamino and diethylaminobenzylcellulose, d-aminobenzoate, sucrose, glucose, fructose, mannitol, vinylpyridine, zein and gelatin.

Enteric-coated coating

Enteric-coated coating protect medical substance, What contained intablet, from the action of the acidic reaction of gastric juice, protects the gastric mucosa from annoying actions some medicines, localize medical substance in intestines, prolonging its action to a certain extent. Enteric coatings have also more expressed, than in listed above groups coatings moisture-proof effect.

Process dissolution enteric soluble shells in organism conditioned by the influence on them of a complex of enzymes and various solubilizing substances, which contained in intestinal juice. For receiving enteric-coated coatings in qualities film formers are used high molecular weight connection with properties of polyelectrolytes with a large number of carboxyl groups. They dissociate in neutral or alkaline environment with formation insoluble salts. Natural substances used: shellac, carnauba wax, casein, keratin, paraffin, ceresin, spermaceti, cetyl alcohol, and also synthetic products, stearic acid in combination with fats and bilious acids, butyl stearate, phthalates dextrin, monosuccinates acetyl-, methylphthalylcellulose. Most often, enteric coatings are used to obtain Acetylphthalylcellulose, as a substance, is most resistant to the effects of gastric juice. The listed film-forming agents are applied to tablets in the form of solutions inethyl, isopropyl alcohol, acetone or in mixtures the specified solvents. To obtain colored shells, pigments are added to the solutionsand dyes. Enteric-soluble coating withstand (2-4 hour and more) influence gastric juice, which allows such tablets to pass unchanged through stomach; in intestinal w juice they are falling apart for 1 hour, providing release medical substances in intestines.

Insoluble coating.

Basic appointment coatings given type — protection pills from mechanical damage and from influence atmospheric moisture, elimination unpleasant smell and medicinal taste substances, continuation its actions. To coatings attributed ethylcellulose, monolaurate polyethylene sorbitol, surfactants, etc. Mechanism of

drug release fromtablets with insoluble shells consists of in next. After receiptpills in gastrointestinal highway May juices penetrate in her through micropores shells and call or dissolution content pills, or its swelling. IN the first case dissolved substances diffuse through film in in the opposite direction - towards the gastrointestinal tract under the influence of the difference concentrations, in to the second — is happening gap shells by score magnification volume pills, after what medicinal substance is released ordinary in a way.

Requirements to film-forming substances:

1. Complete harmlessness for organism.
2. Good solubility in widely available organic solventssolvents.
3. Good film-forming properties.
4. Chemical indifference.
5. Stability during long-term storage (preservationstrength, elasticity and solubility).
6. Accessibility.

Methods causing film coatings

There are 3 ways causing film coatings on tablets:

1. Diving in solution film-forming substances.
2. Layering in dragee boilers.
3. Receiving coverage in suspended layer.

The first method is based on immersing the tablets one by one. another side covers solution. This way enough complex and suitable only for causing on pills viscous, but not too sticky solutions. IN present time in communication with not enough high productivity it is applied rarely.

The most widely used method of applying film coatings is This method is inexpensive and suitable for solutions of almost any viscosity, different high productivity. For causing coating biconvex pills placed in dragee boiler, in period workshe rotates at a speed 20-25 rpm

Film coating slightly increases the weight of the tablets. Thanks to the use of volatile organic solvents, excluded continued stage drying shells. Duration process causing film coverage is 2-4 hours.

Film coatings can be applied not only to tablets, but also to granules or on powder particles material.

The main disadvantage causing film coatings in industrial scale there are significant magnification concentrations steamed, often poisonous and flammable organic solvents in workshop premises, which requires taking appropriate fire safety measures, installing a powerful supply and exhaust ventilation and employee safety.

The closed-loop unit UZTS-25 is capable of capturing solvent vapors, regenerate their and again let in production. On this installation produce

pills PASK - Sodium (sodium salt paraaminosalicylic acid acids) with film enteric coating.

Dragee coating

Dragee (from French dragee — causing sugar shells) coating is the oldest type of tablet coating, used since beginning XX Art. **Basic appointment shells** — protection tablets from external influences, disguise unpleasant taste and smell medical substances, improving the appearance of tablets. Sometimes added to the shells substances, that protect pill from the influence gastric juice.

Tablet core should be mechanically strong.

It due to by action on pill at dragee four factors:

- total weight of tablets, which depends on the boiler loading (from increase loading and speed rotation boiler is growing possibilitydestruction of tablets);
- free fall of tablets from the upper point of the rotating boiler to the lower one (this power directly proportional to the weight of the tablets and height, with which they are fall);
- kinetic energy rotating tablets in boilers (tablet not simply arbitrarilyfalls, and is being created rotary moment, power whose depends from masses pills and speed rotation boiler);

- wedge-shaped effect liquids, used at dragee.

Tablets, What are subject to dragee coating, not must have flat form,that to avoid their sticking together.

For teasing are recommended two types tablets:

- from average oval surfaces, depth curvature constitutes close 15% diameter, height by center — 25-30% diameter (p = 0.75 d);
- from standard curvature surfaces (small oval), depth curvature constitutes 10% diameter, height on center - not Less 25% diameter pills (p = l,ld).

Until 1975, domestic chemical and pharmaceutical plants had technology coating tablets method sugar-flour teasing.

Stages technological process teasing tablets:

1. Coating, or primer.

2. Layering, or knurl.

3. Smoothing, or polishing.

4. Glossy.

Wrapping, or primer , consists of in ago, What mobile pills in in a coating boiler moistened with sugar syrup of 64-70% concentration and sprinkled with wheat flour or a mixture of it with magnesium carbonate main. After abscission pills rotating 25-30 min, after what their dried warm air (40-50 °C) for 30-40 minutes. Tablet moistening operations, abscission, free rotation and drying repeat 2-3 times. Stage The coating, if necessary, is used to isolate the tablet core from moisture penetration, especially in first moments of hydration tablets. The coating stage is followed by the layering or knurling stage. In all in the technological cycle of dragee coating is the most important stage, since it is here that is happening, in mainly, education all over shells.On this stages alone factories apply sugar-flour dough for **layering** , others - pills moisturized sugar syrup and showered magnesium carbonate basic or a mixture of it with wheat flour in equal quantities.

After disposable submissions sugar-flour dough The tablets are allowed to rotate freely, stirring them in a cauldron for 30-40 minutes. Then pills dried warm by air 20-30 min. Operations submissions test, free The rotation and drying of the tablets are repeated many times until a certain masses tablets. The layering stage is followed by the smoothing or polishing stage, which carry out by with help sugar syrup with by adding small quantities gelatin (to 1%) and dyes. On this stages is happening removal inequalities, roughness.Lastly stage process teasing there are stage glossing, that is, addition tablets shine, commodity appearance.

Its carry out two ways.

- Applying first way, are preparing glossy mastic.

Glossy eye mastic in quantities 0.05—0.06% with hands apply on rotating warm tablets and allow the tablets to rotate freely for 30-40 minutes. Then tablets are sprinkled with a small amount of talc to speed up the absorption gloss.

Stages suspension method teasing tablets.

1. Causing coating on pills with unpainted suspensions.

2. Coating tablets from colored suspensionor colored syrup.

3. Glossing tablets.

Suspension teasing tablets carry out as on ordinary dragee boilers, Yes and on automatic lines firms "Shtenberg" (Germany) and "Pellegrini" (Italy).

Technological regime teasing consists of in next.

IN coated boiler loading core tablets in quantities 25-30% from volume of the boiler, previously run-in and dust-free. Include the boiler drive and on rotating pills serve 2-2.5% suspensions method irrigation or wsprinkling with with help injectors. Tablets give "to roll out" 4-5 min. The angle of inclination of the boiler to the horizontal is 45°, the rotation speed is 20-25 rpm After What are the tablets for? warm by air 40-45 °C for 3-4 min.

The operations of supplying the suspension, running-in and drying are repeated many times, until obtaining certain masses tablets.

About regime causing painted coating on basis painted suspensions or colored

syrup and glossy tablets it was said above.

Suspension method coating tablets shells allowed automate process, reduce costs, to increase productivity labor in 3-5 times.

New technology has improved the quality of film-coated tablets :

and) decreased their average weight;

b) improve freight appearance;

c) the stability of film-coated tablets has increased —term suitability drugs increased with 1 year to 4 years;

d) the food product - flour, which led tocracking coating.

Triturative pills

Tablets, received formation moistened masses, are called triturated tablets (Tabulettae friabiles). Unlike pressed ones, triturative pills not are exposed actions pressure; clutch particles these tabletsis carried out as a result of autohesion during drying, so the tablets have small strength.

Triturated tablets are made in cases where the use of pressure undesirable for any reason (for example, nitroglycerin tablets, when (using pressure may cause an explosion), or dosing of medicinal substances small, and addition big quantities auxiliary substances inappropriate. To make such pills because of small size (1-4 mm) and masses medical substances (20-40 mg) on serial tablet presses technically difficult, and in majority cases impossible. Triturative pills expedient produce in those cases, When necessary pills quickly and light dissolve in water (tablets for the preparation of eye drops and injection solutions), as they are not needed antifriction substances, What there are, as rule, insoluble in water compounds.

Triturated tablets are obtained from crushed medicinal and auxiliary substances. substances. Lactose, sucrose, glucose, starch and their derivatives are used as mixtures. The powder mixture is most often moistened with ethanol (40-95%), it is taken in a precisely defined amount until it becomes plastic, but not viscous mass. For formation trituration tablets created special enough complex machinery with productivity to 200 thousand tablets in change. Loading crater machines are filled with a mushy mass, which is mixed with the help of a winged

mixer is rubbed into perforated plates - through, cylindrical holes, made of chemically resistant material (plastic, ebonite, stainless steel).Next, the rubbed mass is pushed out of the plates by a system of small punches, and formed pills are drying out directly in matrices, on in the air or are transferred to drying cabinets (temperature drying 30-40 °C).

Triturative pills standardize on content active substances and physical-chemical indicators in accordance to pharmacopoeial articles "Pills".Triturative pills not feel on mechanical strength, and definition disintegration and solubility have some differences.

Packaging, packaging and marking tablets

Tablets are issued in different packaging, calculated for acquisition sick or therapeutic institution. Application optimal packaging — basic way prevention decrease qualities tableted drugs at Therefore, the choice of packaging type and packaging materials is decided in each specific case individually, depending on the physicochemicalproperties include to the composition tablets of substances.

One with the most important requirements, What are presented to packaging materials, there are protection tablets from exposure to light, atmospheric moisture, oxygen air, microbial insemination.

For packaging tablets in present time used such traditional packaging materials such as paper, cardboard, metal, glass (cardboard envelopes, glass test tubes, metal pencil cases, glasses on 50, 100, 200 and 500 tablets, iron bankswith pressed lid on 100-500 tablets).

Near with traditional materials widely are applied film packaging with cellophane, polyethylene, polystyrene, polypropylene, Polyvinyl chloride and different combined films on their basis. Most promising film contour packaging obtained on the basis of combined materials method heat welding: acellular (tape) and cellular (blister).For tape packaging widely are applied in different combinations: laminated cellophane tape, aluminum foil, laminated paper, polymer film, laminated polyester or nylon. Packaging are made, applying heat sealing two combined materials. Packaging carry out on special vending machines (A1-AUZ-T and A1-AU4-T).

Cellular packaging consists of with two main elements: films, with whose thermoforming produces cells, and heat-sealing or self-adhesive films for sealing the cells of packages after filling them with tablets. As thermoforming films most often applies hard (unplasticized) or weakly plasticized polyvinyl chloride (PVC) thickness 0.2—0.35 mm and more. Film PVC good is forming and thermally bonded with different materials (foil, paper, cardboard, covered thermolacquer layer). It most common material, What used for packaging non-hygroscopic tablets.

For hygroscopic medical drugs recommended use polypropylene, but he more difficult is susceptible formation, except that, he more hard, than PVC. Polystyrene also good is forming, but because of high moisture permeability applies rarely. In qualities films, assigned for closing cells, more often aluminum foil is used. It is coated with glue on the inside or heat-sealing film, with external varnish. Aluminum foil impermeable to water vapor and gases, protects drugs well from penetration smells. Packaging, What has in qualities one with layers aluminum foil, different smaller permeability, and consists of quite with aluminum foils — will provide high tightness.

Thermoformed film is continuously wound from a roll and fed to rotating drum formation, where she warming up infrared emitters to plastic state and then with with help vacuum sucks to cells drum, accepting necessary form. Further film arrives on guiding table, where is happening loading cells films tablets. Then film from above covered aluminum foil or paper, wound from a roll and using two thermal glue drums - cold, drive and hot, free rotates, sticks together with by her. Tapewith pills is being cut down on by cutting stamp. Ready packaging on tray are lowered from the machine, and the remaining cut tape is wound into a roll, then is being deleted with machinery.

Productivity machines 3600-9600 packages on hour.

For all types of packaging apply the following data: ministry, factory-manufacturer, name of the tableted drug in Russian and Latin languages, number tablets, composition, number series and price.

The box is sealed with a wrapping paper band. paper or tape. On box stick

label with paper label or writing with designation goods, manufacturing plant, numbers series, quantities packages.

Boxes put in a container or packaged in a plywood box or plank. Bottom and walls box are lining wrapping paper, free spacefill lignin. In the box invest packing letter.

Conditions storage tablets

Storage conditions how they affect the stability of medicinal substances in tablets and on their physicochemical indicators (strength, disintegration). When stored in excessively dry air, the tablets lose moisture, which is one of the main reasons for their cementation and, as a result, almost complete loss abilities disintegrate. At elevated humidity air, usually, decreases tablet strength, disintegration time can both increase and decrease decrease.Negative influence on quality tablets also provide increase air temperature and action direct sunlight.Therefore pills keep at room temperature in dry, protected from the light place. After a year of storage, the disintegration of the tablets is checked in accordance with with requirements GF.

6. Ways improve tablets as medical forms

Development of methods for coating tablets by pressing, and also the use of a number of other technological principles, have significantly expanded problem tableting and opened ways for improve tablets as dosage form and creation new drugs prolonged actions.

Multilayer pills

Multilayer (layered) tablets make it possible to combine medicinal substances, incompatible by physicochemical properties in others medicalforms, prolong action medical substances in certain gaps time and regulate the sequence of their absorption. With the help of multilayer tablets, it is possible to achieve a prolonged effect of the medicinal substance. It is obvious that the dose of the substance will initially have an effect, placed in shell, and then (let's say, through 3 hour) will begin show action dose of the same medicinal substance, which is placed in the middle of the tablet. If in layers pills will be to be different medicinal substances,

then action their will manifest differentiated, successively, in order dissolution layers.

Tablets with insoluble skeleton

Promising also pills with insoluble skeleton. Medical substance with him gradually is released leaching. Such pill compare from sponge, pores whose filled soluble substance (mixture medical substances with soluble filler - - sugar, lactose, polyethylene glycol etc.). The tablets do not disintegrate in the digestive tract and retain their geometric shape. form. Some inorganic materials (barium sulfate, gypsum, di- and trisubstituted calcium phosphate, titanium dioxide) and organic (polyethylene, polyvinyl chloride, refractory waxes, cute aluminum and other) substances. Skeletal pills can be received by simple pressing medical substances, What form skeleton. They can be also multilayer-whey, for example, three-layered, with the medicinal substance being mainly in average layer. Dissolution its begins with lateral surfaces pills, in that while from large surfaces (upper and lower) only diffuse initially auxiliary substances with average layer through capillaries, What formed in external layers.

Tablets with ion exchangers

Continuation actions medical substances perhaps by magnification molecules medical substances deposition its on ion-exchange resin. Substances, related with ion-exchange resin, become insoluble and their release with tablets in digestive tract founded exclusively on exchange ions.

Speed release medical substances changes in dependencies from degree grinding of ion exchange resin (grains with a size of 300-400 microns are most often used), and also from the quantity branched ego chains.

Materials of activation applicants higher education under time carrying outlectures: question, situational tasks etc:

Question:

1. What these are pills as medical form?
2. Specify main groups auxiliary substances, which use inproduction of tablets.

3. In whose cases in production tablets apply thinners?

4. Explain the purpose of binding agents. In which casesapply dry binding substances?

5. What such fluffing substances? On which groups they are divided by mechanism actions?

6. Point examples auxiliary substances, What call destructionpills by score their swelling.

7. Indicate the purpose of sliding substances. What conditional groups do they belong to?share?

8. With which one purpose in tablet production used starches to whose groups auxiliary substances its can to attribute?

9. Wtih which one purpose in tablet used in production sugar?

10. In why essence process granulation and with which one purpose powdery substances before going through a stage granulation?

General material and bulk-methodical software lectures:

- educational rooms – audience departments;
- equipment - computer, tables;
- equipment – multimedia projector;
- illustrative materials – presentation, slides.

Question for self-control:

1. Name it ways granulation, What are applied in tabletproduction and their distinctive features.
2. Explain the principle of wet granulation. What are thein ways it is carried out?
3. What such dry granulation, as it is carried out and in whose casesis it applicable?
4. Which granulation methods are technically more advanced andpromising. What is this? can explain?
5. What such running-in granules and with which one purpose she is being held?
6. Which medicinal substances can tablet without granulation?
7. How can the technological properties of powders be improved?and to carry out direct pressing?

8. Name it main nodes RTM and explain principle its work.
9. What represents by yourself tablet machine double pressing?
10. Explain appointment coatings, What are applied on pills.
11. Specify the coating applied to tablets by the method ofcultivation (trenchment) and recalculate stages this process.
12. What is the essence and advantages of the dragee coating method ?using suspensions?
13. What such film coating? As they are divided in dependencies from solubility?
14. Point examples substances, What form film coating, solublein intestinal juice.
15. What kind in ways apply film coating on pills?
16. What such pressed coating?
17. As receive multilayer pills?
18. What such frame pills and which ones in ways their receive?
19. What are trituration tablets and what stagesconsists of process their receiving?
20. Specify the main indicators that determine qualitytablets.
21. As is determined average mass pills and which deviation from averagemasses are allowed in individual tablets?
22. Specify boundaries permissible deviations in content existing substances in tablets.
23. Which one? should be strength pills? How its to evaluate?
24. How is the disintegration of tablets determined? What are the requirements fordisintegrable presents GF to tablets, uncovered covered with a shell?
25. Which requirements of disintegrable presents GF to tablets with coating,soluble in intestines?
26. Name it factors, What affect on biological accessibility activesubstances in tablets.
27. Specify requirements, What are presented GF, of dissolution activesubstances from tablets. Describe method of determination.

28. What represent by yourself dragee and granules as medicinal forms? Rate theirprospects. Give a definition.
29. WITH what consists of process receiving pills and granules?
30. Which auxiliary substances are applied in production dragee and granules?
31. By which ones indicators controlled quality dragee and granules?
32. Name it drugs, What are issued in in the form of dragee and granules.

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Lectures No. 14

Topic: "Production of medical microcapsules. Microencapsulation methods. - 2 hours.

Relevance of the topic: Drug technology (industrial technology of drugs) means) – is one of the fundamental technological sciences. It consists of several key aspects, which important for modern medicine and patients:Effectiveness and safety - Modern technologies allow the production of medicinal products drugs with high efficacy and safety for patients. Accurate dosage, control qualities and absence impurity do medicine more effective and safe. Innovations in medical in the field of:

New technology allow create innovative medicines that can be more targeted and effectivemedical therapy. For example, medicine, designed for accurate influence on specific cells or genes, provide more effective treatment. Minimization side effects effects: Technologies allow elaborate medicinal formulas that minimize side effects and negative effects on the body. This provides more comfortable and safe treatment for patients. Fast production and supply process: The use of modern technologies allows speed up the process of producing medicines, which is especially important in conditions rapidly changing medical environment, such as spread diseases or epidemics. Individual approach to treatment: Technologies allow elaborate medicine, which take into account individual features patient, which leads to a personalized approach to treatment and increases its effectiveness efficiency. Economy and accessibility Improved technology production can reduce costs on production, What does medicine more accessible for wide circles patients, providing economic efficiency in field health care. Thus in a way, using modern technologies production medical drugs there are important factor for improvement efficiency treatment, security patients and general state public health.

Objective: To become familiar **with** the industrial production of gelatin capsules and microcapsules, with the technologies of their production, to know about quality control, packaging and labeling of the finished product.

Basic concepts:

Hard capsules are designed for dosing loose powdery and granular substances.

Hard capsules are designed for dosing loose powdery and granular substances.

Spansules are hard gelatin capsules for internal use containing a mixture of microcapsules (microdrages) with different dissolution times.

Structurally logical scheme content lectures

1. Technological scheme for the 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. Microcapsule dosage forms

Content lecture hall material (text lectures)

The term "capsules" refers to two types of factory-made products:

1) special tanks made of gelatin mass for placing different doses of medicinal substances in them;

2) ready-to-dose LF gelatin capsules and microcapsules filled with powdered, granular, pasty and liquid medicinal substances.

Hard capsules are designed 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 lid; both parts must fit freely into each other without forming 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 capsules;
- sealing of capsules;
- capsule control;
- drying of capsules;
- grinding of capsules;
- washing capsules;
- regeneration of rejected capsules.

Tubatin is a children's LF, which is a soft gelatin capsule with an "elongated neck" and is intended for young children who do not know how to swallow tablets. 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 (microdrages) with different drug dissolution times, i.e. prolonged

action.

Currently, encapsulation of LF 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 should not have air inclusions, mechanical

contamination, dents and overflows. The permissible deviations of the average mass of each capsule should not exceed ± 10%, unless otherwise indicated.

MICROCAPSULES

Microencapsulation is a technological process of placing microscopic solid, liquid or gaseous substances in a thin shell, which provides their isolation from the external environment. Microcapsules have the form of individual particles or agglomerates ranging in size from 1 to 5000 microns. In medical practice, microcapsules ranging in size from 100 to 500 microns are most often used. The technology of shell formation has recently improved so much that it allows coating particles smaller than 1 micron. Such particles with a shell are called nanocapsules, and the process of their formation is called nanoencapsulation. The shape of microcapsules is determined by the aggregate state of their contents and the method of production: liquid and gaseous substances give microcapsules a spherical shape, solids give them an oval or irregular geometric shape. Microencapsulation has become widely used in the pharmaceutical industry. It is used to stabilize unstable drugs (vitamins, antibiotics, vaccines, serums, enzymes), mask the taste of unpleasant medicinal substances (castor oil, fish oil, aloe extract, caffeine, chloramphenicol, benzedrine), convert liquids into bulk products, regulate the release rate or ensure the release of a biologically active substance in the desired area of the gastrointestinal tract, isolate incompatible substances, improve flowability, and create new types of diagnostic products. Most pharmaceutical drugs are produced in microencapsulated form to increase the duration of therapeutic action when administered orally into the body while simultaneously reducing the maximum level of drug concentration in the body. This method achieves a reduction of at least half the number of drug doses and the elimination of irritating effects on tissues due to the adhesion of tablets to the stomach walls. Gastrolabile drugs are placed in shells that

are stable in acidic environments, which are destroyed in slightly alkaline and neutral environments of the intestine. An important area of application of microencapsulation in pharmacy is the combination in a single dose of medicinal substances that are incompatible when mixed in a free state. Microencapsulated drugs are better stored and more convenient to dose.

STRUCTURE OF MICROCAPSULES

Microcapsules consist of a substance to be encapsulated and a material from which they are made, a shell. The substance to be encapsulated is called the content and forms the core of the microcapsules, and the encapsulating material forms the shell. The content of microcapsules (the internal phase, or core) can be 15-99% of their mass. It can vary depending on the method and conditions of preparation (temperature, degree of dispersion, viscosity of the medium, presence of surfactants), the ratio of the amounts of the shell material and the substance to be encapsulated, etc. The internal phase can be an individual substance, mixtures, dispersions or solutions of substances. The content of microcapsules may 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 core component. The thickness of the shell ranges from 10 to 200 microns and can be single-layer or multilayer, elastic or rigid, with different resistance to water, organic solvents, etc. The thickness of the microcapsule walls 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, a certain permeability, strength and stability during storage. Most substances are inert under normal conditions and are approved for medical use. Typical shell materials are organic polymers: proteins (gelatins, albumin), polysaccharides (dextrans 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., According to solubility, shell materials are divided into water-soluble

(gelatin, gum arabic, polyvinylpyrrolidone, polyacrylic acid, etc.), water-insoluble (silicones, latexes, polypropylene, polyamide, etc.), and 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 selected microencapsulation method. According to the technological principle and depending on the content of plasticizers, there are 2 types of capsules: 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 of 0.1 to 1.5 ml. They encapsulate viscous liquids, oil solutions, pasty drugs that do not interact with the form-forming substance - gelatin. The contents of the capsules can consist of one or more drugs with the possible introduction of various explosives permitted for medical use. Soft capsules are manufactured in factory conditions by two methods: dropwise and pressing. In laboratory conditions, it is allowed to obtain soft capsules by immersion. 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 lid, which must freely fit one into the other without forming gaps. To ensure a "lock", they may have special grooves or protrusions. Depending on the average capacity, they are produced in 8 sizes (GF 11 p. 143). Hard capsules are obtained by immersion.

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

- For hard capsules
- For soft capsules
- Preparation of gelatin mass
- Manufacturing (molding) of capsule shells
- Production of capsule shells, their filling and sealing;
- Drying capsule halves, removing them from the pins
- Washing and drying capsules
- Capsule halves package
- Standardization, packaging and labeling of finished products
- Capsule filling

- Standardization, packaging and labeling of finished products

The 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 ones - after their drying and assembly. In most cases, the filling process of hard capsules can be carried out at other enterprises. To obtain capsules, film-forming high-molecular substances are used that are able to create elastic films and have a certain strength. One of the most common molding materials for the production of capsules is gelatin. To obtain a stable capsule shell, the gelatin base may include various excipients: plasticizers (glycerol, sorbitol, etc.), stabilizers (sodium metabisulfite, sodium benzoate), preservatives (salicylic acid, nipagin), flavorings (ethyl vanillin, fruit essences, essential oils), dyes (tartrazine, indigo, acid red 2C), pigments (titanium dioxide white). The quality assessment of capsules is carried out in accordance with the requirements of the State Federal University of Pharmacy, GF 11 type. or other NTD. Capsules should be produced in tightly closed packaging that protects against moisture. Most often, contour, glass or polymer containers are used. Among other encapsulated MFs, tubatins, rectal capsules and spansules should be distinguished.

Tubatin is a children's MF, which is a soft gelatin capsule with an "elongated neck" and is intended for young children who do not know how to swallow tablets. When biting the neck of the capsule, the child sucks out the contents. One of the varieties of soft capsules is rectal gelatin capsules. Rectal capsules have the shape 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 wetted with water, which facilitates its use. Such capsules, unlike fatty suppositories, are stable at elevated temperatures (45-50 °C), release the drug much faster, and do not irritate 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 this state even weak peristalsis of the rectal walls is sufficient for its rupture at the suture site and the release of the contents.

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

action.

Microcapsules are individual particles of spherical or rounded shape with a diameter of 5 to 5000 microns (more often 100-500 microns), covered with a thin shell of film-forming material of various nature. Particles less than 1 micron are called Nanocapsules. The content of microcapsules (internal phase or core) can reach 15-99% of their mass. This value can vary depending on the method and conditions of production (temperature, degree of dispersion, viscosity of the medium, presence of surfactants), the ratio of the amounts of shell material and encapsulated substance, etc. The internal phase can be an individual substance, mixtures, dispersions or solutions of substances. In the pharmaceutical industry, microencapsulation has found wide application. It is used to stabilize unstable drugs (vitamins, antibiotics, vaccines, serums, enzymes), mask the taste and smell of drugs (castor oil, fish oil, aloe extract, caffeine, chloramphenicol, benzedrine), convert liquids into bulk products, regulate the release rate or ensure the release of BAS in the desired area of the gastrointestinal tract, isolate incompatible substances, improve flowability, and create new types of diagnostic products. The thickness of the shell ranges from 0.1 to 200 microns and can be single-layer or multi-layer, elastic or rigid, with different resistance to water, organic solvents, etc. The choice of shell material depends on the purpose, properties and method of core release, as well as the selected microencapsulation method. These same factors determine the structure of microcapsules. Currently, the following main types of microcapsules are distinguished:

• With one shell; double or multilayer shell. If the shell material for some reason cannot be applied directly to the encapsulated substance, then intermediate microencapsulation of this substance is carried out by a convenient method in another material. The hard 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 manufacture “capsules in a capsule”, when one or more microcapsules of another substance are placed inside the outer shell in the medium of one of the substances.

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

• impermeable to the core and the environment;

• semi-permeable;

• permeable to the nucleus.

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

The essence of physical methods of microencapsulation is the mechanical application of a shell to solid or liquid particles of the MR. Physical methods include methods of spraying in a pseudo-fluidized layer or in vacuum, extrusion, spraying, coating, dispersion, etc. Physico-chemical methods of microencapsulation are based on phase separation and are distinguished by simple equipment, high productivity, and the ability to enclose the medicines in any state of aggregation (solid, liquid, gas) in a shell. They allow obtaining microcapsules of various sizes and with specified properties, as well as using an exceptionally wide range of film-forming agents and obtaining shells with various physico-chemical properties (different thickness, porosity, elasticity, solubility, etc.). When obtaining microcapsules by these methods, the MR is dispersed in a solution or melt of the film- forming substance.

Chemical encapsulation methods 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 rather conditional, since in practice a combination of different methods is often used. The quality of the obtained microcapsules is assessed by the following parameters: Organoleptic indicators, fractional composition, bulk density, flowability, relative density, release rate of contents from microcapsules, qualitative and quantitative content of BAS. Currently, the range of areas of practical use of microencapsulated drugs is very wide - from medicine to space research. In medicine, microcapsules themselves, as MFs, are used

extremely rarely, but they are often included in the composition of other MFs. Microcapsules are used to produce such MFs as emulsions, suspensions, ointments, suppositories, retard capsules, retard tablets, preparations for parenteral administration. Research is ongoing on the use of microcapsules in injection and ophthalmic forms, implantable tablets and in other prolonged-action drug systems.

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Lectures No. 15

Topic: "Soft" medicinal Forms. Characteristics, classification.

Ointment bases. , excipients. - 2 hours.

Relevance of the topic: Drug technology (industrial technology of drugs) means) – is one of the fundamental technological sciences. It consists of several key aspects, which important for modern medicine and patients:Effectiveness and safety - Modern technologies allow the production of medicinal products drugs with high efficacy and safety for patients. Accurate dosage, CONTROL qualities and absence

impurity do medicine more effective and safe. Innovations in medical in the field of: New technology allow create innovative medicines that can be more targeted and effectivemedical therapy. For example, medicine, designed for accurate influence on specific cells or genes, provide more effective treatment. Minimization side effects effects: Technologies allow elaborate medicinal formulas that minimize side effects and negative effects on the body. This provides more comfortable and safe treatment for patients. Fast production and supply process: The use of modern technologies allows speed up the process of producing medicines, which is especially important in conditions rapidly changing medical environment, such as spread diseases or epidemics. Individual approach to treatment: Technologies allow elaborate medicine, which take into account individual features patient, which leads to a personalized approach to treatment and increases its effectiveness efficiency. Economy and accessibility Improved technology production can reduce costs on production, What does medicine more accessible for wide circles patients, providing economic efficiency in field health care. Thus in a way, using modern technologies production medical drugs there are important factor for improvement efficiency treatment, security patients and general state public health.

Objective: to get acquainted with the main stages of industrial manufacturing soft dosage forms and the discipline "Drug Technology", give a characteristic pharmaceutical development of soft dosage forms, and describe the current state pharmaceutical industry.

Basic concept:

Ointment — soft medical form for external application. Ointment consists of a medicinal substance and the so-called medicinal base (vaseline, lanolin, naphthalene etc). IN to yours ointment bases contain fats (pork, beef).

Cream - it emulsion, What contains half water and half oils. Creams alsocontain solid particles medicines, appointed for assimilation skin.

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

Pasta — suspension ointment with quantity powdery substances, according to

recommendations State Federal University, over 20% (earlier 25%).

Liniments — medical form only for external application (more often, by rubbing) represents by yourself liquid ointment or mixture different irritating substances with oils, oils with solutions meadows, soapy water or soap-alcohol solutions.

Homogeneity — one with key properties space in classicalmechanics. It means that the parallel transfer of a closed system in it reference as a whole does not change the mechanical properties of the system, and, in particular, does not affects on result measurements.

Sterility – the absence in the environment, organism, or any material or product viable microorganisms and their dispute.

Homogeneous ointments are systems characterized by the absence of interfacial interface between medicinal substances and basis ointments.

Heterogeneous ointments - it systems, What have divide phases with different border layers. To them belong suspension (or triturative), emulsion and combined ointments.

Plan and organizational structure lectures:

No. No. p.p.	**stages of the lectureand their content.**	**Goals in levels abstractions.**	**Type lectures, uipment lectures.**	**istributiontime.**
1	**2**	**3**	**4**	**5**

I1. 2. II3.	***Preparatory stage*** Definition of traininggoals. Software positive motivation. ***Main stage*** Presentation lecture hall material. Plan: 1. What are soft dosage forms and theirclassification 2. Definition emulsions, suspensions, asLF, region application. 3. 3.Features preparation emulsion and	I II III	Lecture combined Slides	1% 2% 90%

	suspension preparations. 3. Method of obtaining and equipment that used in production of soft dosage forms. 4. By what methods ointments, creams, gels are obtained for pharmaceutical factories? 5. What factors cause stability of suspensions and emulsions? 6. What role do they play? excipients inproduction of suspensionsand emulsions 7. From which stages the process is underwayreceived dispersion drugs? 8. What drugs used for manufacturing suspensions and emulsions? What principle turbine works mixers and RPA? 10.Current statedevelopment pharmaceutical industry. ***Final stage*** Resume lectures, general conclusions. Lecturer's answers topossible question. Tasks forself-training student.		List literature, question, task.	

III	4. 5.	turbine works mixers and RPA? 10.Current statedevelopment pharmaceutical industry. ***Final stage*** Resume lectures, general conclusions. Lecturer's answers topossible question. Tasks forself-training student.		2% 3% 2%

Structurally logical scheme content lectures

1. What such soft medicinal forms and their classification

2. Definition of emulsion, suspension, as LF, scope of application. 3.Features preparation emulsion and suspension drugs.

3. Method receiving and equipment, which used in productionsoft dosage forms.

4. What kind methods receive suspensions and emulsions on pharmaceuticalfactories?

5. Which factors cause stability suspensions and emulsions?

6. Which role are playing auxiliary substances in production suspensions andemulsions

7. WITH whose stages consists of process received dispersion drugs?

8. Which drugs use at manufacturing suspensions and emulsions?

9. Which principle works turbine mixer and RPA? B. Tests for self-control with standard answers. IN. Tasks for self-control with answers.

10.Modern state development pharmaceutical industry.

Content lecture hall material (text lectures)

Ointment - a mild LF intended for application to the skin, wounds or mucous membranes shells. Ointments consist of with foundations and one or several medical substances, evenly in her distributed. To warehouse ointments are included stabilizers,preservatives.

Characteristic and classification. Ointments widely are applied in different areas medicine: at treatment dermatological diseases, in otolaryngology, surgical, proctological, gynecological practice, and also asa means of protecting the skin from adverse external influences (organic substances, acids, alkalis). Recently, ointments have also been used to affect internal organs and all organism with purpose treatment, prevention and diagnosticsdiseases.

Medicinal substances that apply to all are used in the form of ointments. pharmacological groups: antiseptics, anesthetics, hormones, vitamins, antifungal drugs, analgesics, and etc.

Depending on the consistency, there are: ointments, pastes, creams, gels, liniments.Requirements to ointments:

1. Should have a soft consistency for ease of application to the skin and mucous shells and education on surfaces equal continuous film.

2. Medicinal substances in ointments should be as dispersed as possible and distributed throughout the ointment to achieve the necessary therapeutic effect and dosing accuracy medical substances.

3. Or must be stable, not contain mechanical inclusion.

4. Their composition not should change at storage and application.

5. Concentration medical substances and mass ointments should answer written in recipes.

There are sprat classifications: by place application, character actions and type dispersion systems.

By place causing ointments:

- dermatological

- for nose

- dental

- vaginal

- rectal; by with help special syringes

- urethral

- rectal

For example, ointments, What are applied on mucous membrane shell sensitive to microorganisms, ago their are preparing in aseptic conditions. Except that, dispersion eyeointments much higher, than in dermatologist.

By character actions:

1) ointments, have a local effect on the upper layer of the skin or the surface of the mucous membraneshells;

2) ointments of resorptive action (resorption - absorption, absorption), depth penetration into the skin or mucous membrane, reaches the blood. Channels and has an effect on the whole body (ointment "Nitrong" - contains a 2% oil solution of nitroglycerin and is taken for Prof. Angina attacks. The effect occurs after 30 - 40 minutes and stored 3 - 5 hours).

WITH points vision technology more value has classification by type dispersion systems:

- homogeneous ointments;

- heterogeneous ointments.

Homogeneous - in them medicinal substances distributed in basis by type solution, that is, proven to molecular dispersion.

Heterogeneous - characterized by the presence of an interfacial surface betweenmedicinal substances and the basis.

Foundations for ointments.

Foundations provide necessary mass ointments and like this in a wayproper concentration medical substances, soft consistency, are doing

substantive influence on stability ointments. Degree release medical substances with ointments, the speed and completeness of their development largely depend on the nature and properties of the base. For example, 2% boric acid ointment on a

consistent emulsion-based exhibit the same therapeutic activity as the similar ointment 10% concentrations, prepared on Vaseline. What in a way, ointment trace consider as the only one whole, and basis as active part ointments. To basics is being put forward number requirements:

- necessary structural and mechanical properties;
- not to succumb microbial contamination;
- soft consistency
- biological security;
- neutral reaction;
- lightness allocation with places causing;
- pharmacological be indifferent, not should do irritable andsensitizing actions, promote storage initial value pH- skin or mucous shells;
- properties foundations must answer appointment ointments;
- not change under by action factors external environment
- physicochemical stability
- not enter in reaction from introduced to her medicinal substances
- necessary absorption ability

and) soft consistence necessary for amenities causing on skin and mucous shells.

b) The chemical inertness of the bases guarantees the absence of interaction with medicinal products substances, changes under by action external factors (air, light, moisture, temperature) and, therefore, stability is ensured ointments.

c) the absence of allergenic irritants and the sensitizing effect of ointments depends from harmless biological basics.

d) importantly, that foundations not violated physiological functions skin. External layer skin has sour reaction, which hinders reproduction microorganisms. Therefore, maintaining the original pH value of the skin is of great importance value.

e) presence microorganisms maybe be reason repeated infection inflamed skin and mucous membrane, and also decrease activitiesmedical substances.

f) the issue of ease of removing ointment residues from the underwear, skin surface, especially with their fibrous areas.

g) properties foundations must answer goals appointment ointments.

Foundations for superficially active ointments not must promote depth absorption of medicinal substances. Bases for ointments with resorptive action, on the contrary, to ensure the absorption of medicinal substances through the skin layer. Basics protective ointments must quickly dry up and tight adjoin to surfaces skin.There are several classifications of ointment bases: by physical properties, by chemical composition, sources receiving and etc.

Most appropriate there are classification by degree kinship properties of medicinal substances and bases, if possible, dissolution of medicinal substances substances and base. According to this principle, all ointment bases are divided into 3 groups: lipophilic, hydrophilic, lipophilic-hydrophilic bases.

Classification ointment basics.

Most progressive classification ointment basics there are system, which takes into account ability foundations absorb liquid, What agreed with technological principles production ointments.

By this classification ointment foundations share on four groups: hydrophobic, absorption, washable, water-soluble.

Hydrophobic bases include individual substances and their mixtures with bright discovered hydrophobic properties (vaseline, petrolatum, animal fats, vegetable and mineral oils).

To class *absorption* basics belongs to group basics, capable incorporate up to 50% or more of water or aqueous solutions of medicinal substances from formation emulsions type in/m (lanolin, hydroline).

To groups *water-washable* basics belong to emulsion foundations type m/v, made with using surfactants substances (South Africa), highly hydrophilic inorganic (bentonites), organic (water-soluble esters cellulose) substances and their mixtures.

Water-soluble ointment bases combine a large group of hydrophilic bases, formed by water-soluble high-molecular compounds of synthetic or of natural origin. They also include numerous hydrophilic-colloidal foundations — starchy, alginate, pectin hydrogels.

Foundations for ointments		
Lipophilic: 1. Fats and their derivatives (pork fat , oils vegetable, fats hydrogenated) 2. Waxes (wax bee, spermaceti, lanolin) 3.Hydrocarbons foundations (Vaseline, petroleum jelly, paraffin, oil Vaseline, ceresin) 4. Silicone Bases (esirol– aeropower and etc.)	Hydrophilic: 1. Gels high molecular weight Carbohydrates and proteins (starch, esters, cellulose, gelatin, collagen) 2. Synthetic gels Navy (PEO-400,PEO-1500, PEO-4000, PVP etc. 3. Inorganic gels Clay compounds Minerals (bentonite foundations)	Lipophilic-hydrophilic: 1.Adsorption (lipophilic base + emulsifiers PAH) 2. Emulsion (lipophilic base+ emulsifiers PAV+ water)

Lipophilic bases are chemically heterogeneous substances that have pronounced hydrophobicity.

This includes fats and their derivatives, waxes, hydrocarbons and silicone bases. (Fats hydrogenated - products, received at catalytic hydrogenation oils

vegetable. At this unsaturated glycerides become extreme, and liquid oils change their consistency to soft and hard depending on degree hydrogenation. Hydrogenated fats are more stable at storage).

Hydrophilic bases - a characteristic feature is the ability to dissolve in water. Hydrophilic foundations not leave fatty traces, better washed away with skin and linen.

Disadvantage their there are small stability to microbial contamination. Here are included gels VM carbohydrates and proteins, synthetic IUDs, inorganic substances.

Lipophilic-hydrophilic bases - they can easily be introduced as water, as well as fat-soluble substances, aqueous solutions of medicinal substances. As mandatory components included here surfactant emulsifier.

Technology ointments.

The main task of technology in the manufacture of ointments is to medicinal substances were maximally dispersed and evenly distributed throughout throughout mass foundations; consistence ointments provided b lightness causing and even distribution on skin or mucous shells; stability ointments guaranteed b its immutability warehouse at application and storage.

Technology ointments consists of with the following stages:

1. preparation foundations for ointments and medical substances;

2. introduction medical substances in basis;

3. homogenization ointments;

4. standardization;

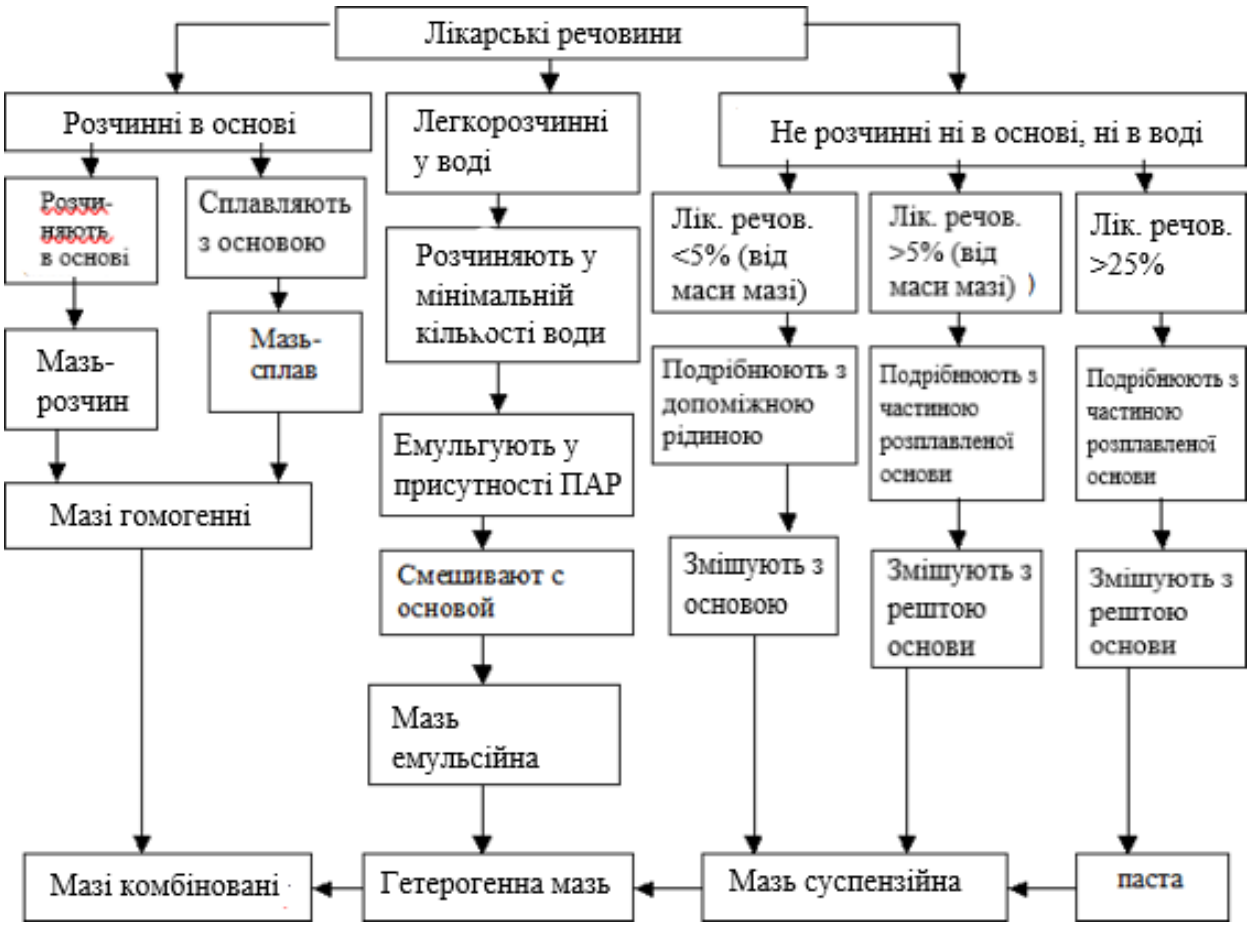
5. packaging and storage.

1. Preparation of the base for ointments. The base is melted in a barrel or tank (in balls) and transfer to the cooking pot. If several components are melted start with refractory substances. If necessary, filter the base through canvas or gauze. Medical substance grind sieving through sieve.

2. Introduction of medicinal substances into the base. Adding medicinal

substances to the base is carried out in 2 roller mixers or in reactors with steam shirt or electric heating, well-off 3rd powerful mixers: anchor, scapular, turbine, What provide good mixing and grinding components of the ointment.

Introduction medical substances to ointments .



· Depending from way introduction medical substances and character distribution their in basics ointments are classified: homogeneous, suspension, emulsion and combined.

Alloy ointments (combination of 2 or more soluble components)homogeneous

Ointments-solutions (contain medicine). Substances, dissolved in basis.

Preparation ointments begin with melting foundations, after what in received molten dissolve medicinal substances).

Suspension - ointments containing medicinal substances that are not soluble in water and basis, What are distributed in her by type suspensions.

Emulsion - characterized by the presence of a liquid dispersion phase, which does not dissolve in the base and is distributed in it by the type of emulsion (dispersion phase - H_2O_2, linetol, glycerin, tar, liquid Burova, and also solutions medical substances).

Combined - the most complex multi-component systems contain liquid and solid ingredient, one of which dissolves in water, another in the base, the third does not there, not there.

3. homogenization of ointments - if mixing fails to obtain the required degree of dispersion of medicinal substances. It is carried out in millstones mills or roller mills, and also apparatus RPA.

4. Standardization - the ointment is standardized according to the content of medicinal substances, meaning pH and degree of dispersion firm. parts in suspension ointment.

5. Packaging and storage - in glass banks, n / there are and aluminum tubas. Packaging in tubas - by with help turbocharged vending machines. They keep ointments in cool, protected from light place. Ointment, prepared pharmacies, keep 10 day

Basic areas for improvement qualities and technology ointments.

1) expansion assortment ointment basics and their choice depending from application ointments and from age sick.

2) Increased physical stability of suspension and emulsion ointments can be achieved by adding thickeners, emulsifiers and etc. Auxiliary substances.

3) Chemical stability - use of antioxidants (butyloxyanisole, α- tocopherol etc.)

4) Microbiological stability - by with help preservatives (acid sorbic 0.2%, mixture 1:3 nipagin and nipazole, alcohol benzyl 0.9%).

5) The packaging problem is due to modern requirements for the level of microbial contamination in non-sterile medicinal means. Are being created combined (laminated) materials, combining the best properties of aluminum foil, polymers, paper. Are being created disposable packaging use.

Materials of activation applicants higher education under time carrying

outlectures: question, situational tasks etc:

Question:

1. What such soft medicinal forms and their classification

2. Definition of emulsion, suspension, as LF, scope of application. 3.Features preparation emulsion and suspension drugs.

3. Method receiving and equipment, which used in productionsoft dosage forms.

4. What kind methods receive suspensions and emulsions on pharmaceuticalfactories?

5. Which factors cause stability suspensions and emulsions?

General material and bulk-methodical software lectures:

- educational rooms – audience departments;
- equipment - computer, tables;
- equipment – multimedia projector;
- illustrative materials – presentation, slides.

Question for self-control:

2. Name it drugs, What are issued in in the form of MLF.

3. Which role are playing auxiliary substances in production suspensions and emulsions?

4. WITH whose stages consists of process received dispersion drugs?

5. Which drugs use at manufacturing suspensions and emulsions?

6. What is the working principle of turbine mixers and RPA?

B. Tests forself-control with standards answers.

IN. Tasks for self-control with answers.

7. IN Why features modern state pharmaceutical industry?

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- **Lecture No. 16**

Topic: "Technology of homogeneous and heterogeneous ointments. Standardization, filling, packaging. - 2 hours."

Purpose: Liniments are among the ancient medicinal forms that find wide use in everyday life, on different productions, in cosmetics and medicine withto protect the skin of the hands and exposed parts of the body (face, neck) from the effects of organic solvents, acid solutions, alkalis and other chemical irritants and allergens; for softening the skin, nourishing it with vitamins, fats, to remove pigment spots spots, treatment and removal of warts, freckles and other cosmetic imperfections skin. A special place liniments are used, widely used in various fields medicine: dermatology, gynecology, proctology, laryngology, etc. Sometimes liniments appoint as medicine general actions with purpose resorption, that is, absorption, What contained in them medical substances in thicker skin, subcutaneous fiber oreven into the bloodstream. They are applied to the skin, wounds, mucous membranes by smearing, rubbing or by with help bandage.

Basic concept:

Plan:

Liniments (or liquid ointments) - medical form for external application, What represents by yourself thick liquids or gelatinous masses, What are melting at body temperature.

Liniments occupy as would intermediate position between liquid and soft medicinal forms: they very close to others groups ointments by substances used, method of application, at the same time technological manufacturing methods, liquid consistency combine them with liquid medicinal forms.

The name liniment comes from the Latin word *linire (to rub)* and indicates way application given medical forms - by rubbing in skin. This a characteristic feature distinguishes liniments from other groups of ointments and liquid medicines forms for external application (drops, washings, lotions).

Liniments are an ancient medicinal form that has not lost its importance in the present. time. In DF XI, liniments are included in the general article "Ointments". In DF X, they highlighted separately article No. 376 "Liniments".

Modern extemporaneous recipe liniments diverse and maybe be enough complicated. Significant number liniments is released industry. It liniments-solutions: capsin, capsitrin, pepper-camphor, pepper-ammonia, chloroform complex, methyl salicylate complex, turpentine complex, sanitas; Liniment emulsions: ammoniac, naphthalene; liniment suspensions: balsamic on Vishnevsky; combined liniments: chloramphenicol, streptocide.

Wide application liniments in medical practice stipulated their

advantages:

- medicinal substances with liniments light are absorbed skin, that is, havehigh biological accessibility;
- in comparable with ointments liniments easier are applied on skin;
- Less leave traces on skin and clothes sick.
- *Disadvantages given medical forms:*
- low stability row prescriptions;
- inconvenience transportation.

Classification liniments. There is medical and physicochemical classification. By

The therapeutic effect of liniments is *analgesic, irritating (distracting), anti-inflammatory, viscous, drying, insecticidal, fungicidal.* Most often meet analgesics and irritating liniments.

By their physicochemical nature, liniments are dispersed systems with liquid dispersion environment. By character dispersion environment liniments divide on *fatty, alcohol, soap-alcohol, vasoconstrictors.*

Fatty liniments (Linimenta pinquia sen Olimenta) as a dispersion medium contain fatty oils or fat-like substances (lanolin). Most often sunflower, linseed, and castor oils are used. Fatty liniments include may be included as liquid medicinal substances (chloroform, turpentine, ether, tar), Yes and powdered (camphor, menthol, novocaine, dermatol and etc.).

Alcoholic liniments (Linimenta spirit) contain alcohol or tinctures (most often tincture pepper legume), and also different medicinal substances.

Soap-alcohol liniments (Saponimenta) as dispersion environment contain alcohol solutions of soap. They can be liquid (if they contain potassium soap) or dense, jelly-like (if they contain sodium soap). When rubbed in the skin, they cause emulsification of sebum, so they quickly penetrate it, taking medicine substances.

Vasolimenta are characterized by the presence of vaseline oil. In communication with chemical inertness Vaseline oils they enough stable at storage. Inpresent time soap and alcohol liniments and vasoconstrictors are applied rarely.

By the type of dispersed systems, liniments are divided into homo- and heterogeneous. To *homogeneous* include *liniment solutions* and *extraction,* to *heterogeneous - liniment suspensions, emulsions* and *combined.*

OWN TECHNOLOGY LINIMENTS

Liniment solutions - *it transparent mixtures (true or colloidal solutions) fatty oils with ethereal oils, chloroform, methyl salicylate, ether, turpentine.* They may include various solid substances soluble in registered liquids: camphor, menthol, anestezin and etc.

Liniment solution, which includes a potent, light-sensitive substance - chloroform, odorous - turpentine and photosensitive - sunflower oil. Allthree liquid

components mutually soluble one in one.

In accordance to *physicochemical classifications* ointments divide by consistency, type dispersed systems and ointment bases. Depending on the consistency, there are: *liquid* ointments (or liniments), *creams, gels, actually ointments,* dense ointments - *to eat, dry* semi-finished ointments, intended for dilution water or fats.

By type dispersed systems (in dependencies from degree dispersion medicinal substance and character its distribution in basis) distinguish *homogeneous* and *heterogeneous* ointments.

Homogeneous ointments are *systems characterized by the absence of interfacialinterface between medicinal substances and ointment base.*

In this case, the medicinal substance is distributed in the base by solution type, that is, proven to molecular or micellar degree dispersion. To homogeneous include: *ointment solutions, ointment alloys* and *extraction ointments.*

Heterogeneous ointments - it systems, What have divide phases with different border layers. To them belong *suspension* (or triturative), *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 whichis formed and appropriate type ointments.

By type (character) ointment basics distinguish ointments, prepared on: *hydrophobic (lipophilic), hydrophilic* and *diphilic (hydrophilic-lipophilic)* basics.

Such in a way, medical classification gives general idea about ointments (purpose, application, etc.), and the physico-chemical one reflects the technology of ointments and criteria their quality.

Quality control of liniments is carried out by deviation in mass, as well as by organoleptic indicators: uniformity, absence of foreign inclusions, color, smell. Liniments are usually packaged in glass bottles with screw caps. According to the instructions of the pharmacopoeia, liniments, like all ointments, are stored in a cool, dark place, unless otherwise indicated in their own articles. Heterogeneous liniments

are additionally labeled with the words "Shake before use". Liniments of a thick consistency are released in wide-mouthed bottles.

Increasing the stability of a number of liniment formulations can be achieved by the correct selection and use of new emulsifiers, thickeners, etc. To increase chemical stability and slow down the decomposition of lipophilic bases, the promising use of antioxidants (α-tocopherols, butyloxyanisole, etc.)

The reduction of microbial action is facilitated by the introduction of preservatives into the composition of liniments (benzyl alcohol, nipagin, nipazole, sorbic acid) and the development of new types of packaging.

Lecture No. 17

Topic: "Industrial production suppositories" - 2 hours

Relevance of the topic: Drug technology (industrial technology of drugs) means) – is one of the fundamental technological sciences. It consists of several key aspects, which important for modern medicine and patients: Effectiveness and safety - Modern technologies allow the production of medicinal products drugs with high efficacy and safety for patients. Accurate dosage, CONTROL qualities and absence impurity do medicine more effective and safe. Innovations in medical in the field of: New technology allow create innovative medicines that can be more targeted and effective medical therapy. For example, medicine, designed for accurate influence on specific cells or genes, provide more effective treatment. Minimization side effects effects: Technologies allow elaborate medicinal formulas that minimize side effects and negative effects on the body. This provides more comfortable and safe treatment for patients. Fast production and supply process: The use of modern technologies allows speed up the process of producing medicines, which is especially important in conditions rapidly changing medical environment, such as spread diseases or epidemics. Individual approach to treatment: Technologies allow elaborate medicine, which take into account individual features patient,which leads to a personalized approach to treatment and increases its effectiveness efficiency. Economy and accessibility Improved technology production can reduce production costs, making medicines more available for wide circles patients, providing economic efficiency in field health care.

Thus, the use of modern technologies for the production of medicinal products drugs there are important factor for improvement efficiency treatment, security patients and general state public health.

Objective: To study the general technological scheme of suppositories, to get acquainted with proper by the rules production. Learn industrial methods production suppositories with various medicinal and auxiliary substances, to carry out continuous control and be able to standardize the finished product in accordance with requirements of regulatory and technical documentation, be able to draw up

technological schemes production.

Basic concept:

Suppositories (from Latin *Suppositories* - substitute, to put) - medical form famous to humanity not one millennium. Solid single-dose medications means

Rectal suppositories (*Suppositories rectalia*) intended for introduction in straight line intestine.

Vaginal suppositories (*Suppositoria vaginalia*) are used for introduction in vagina.

The sticks (*Bacilli*) are intended for insertion into the urethra, canal necks uterus, fistulous and wound walks, auditory hole.

Plan and organizational structure lectures:

No. No. p.p.	**Main stages of the lectureand their content.**	**Goals in levels abstractions.**	**Lecture type, equipment lectures.**	**Distributiontime.**
1	**2**	**3**	**4**	**5**
I1. 2. II 3.	***Preparatory stage*** Definition of training goals. Software positive motivation. ***Main stage*** Presentation lecture hallmaterial. Plan: 1. The concept of suppositories . **2.** Manufacturing methods suppositories on	II	Lecture combined Slides	1% 2% 90%

	production. Storage suppositories **drugs .** ***Final stage*** Resume lectures, general conclusions.	III		2%
III4.	Lecturer's answers to possible question.			3%
5.	Tasks forself-training student.		List literature, question, task.	2%

Structurally logical scheme content lectures

1. Concept about suppositories .
2. Methods production suppositories on production. .
3. Storage suppositories drugs .

Content lecture hall material (text lectures)

Suppositories (from Latin *Suppositoria* - to substitute, to place) - medicinal The form has been known to mankind for more than one millennium. For the first time about rectal suppositories mentioned in the oldest papyri dating back to 2600 BC. e. 3 written attractions known, What in gray hair antiquity residents Mesopotamia and Egypt used suppositories for treatment, which included herbal and animal fats, honey, frankincense, juices plants, resins and etc. These substances were used as foundations about to XVIII century, then to end second decades XX century as suppository basis was used onlycocoa butter. Nowadays, a large number of suppository bases have been introduced for whose characteristic undeniable advantages before oil cocoa.

General properties

Suppositories - solid single-dose medicinal means. Form, volume and The consistency of the suppositories should be suitable for rectal use. They contain one or more active substances, dispersed or dissolved in downtime or difficult basis, which maybe to dissolve or disperse in water orfuse at temperature body.
Distinguish between rectal suppositories (candles), vaginal and sticks.

Medical means for rectal application can be classified as:

- rectal suppositories;
- rectal capsules;
- rectal solutions and suspensions;

- powders and pills for preparation rectal solutions or suspensions;
- soft medicines for rectal use;
- rectal foam;
- rectal tampons.

Rectal suppositories (*Suppositoria rectalia*) are intended for insertion into the straight line intestine.

Vaginal suppositories (*Suppositories vaginalis*) use for introduction in vagina.

Sticks (*Bacilli*) intended for introduction in urinary channel, channel necks uterus, fistulous and wound walks, auditory hole.

General property suppositories - their ability at room temperature to be in condition solid bodies, and at temperature bodies become in liquid. This property has important value at medical application such medical forms. Hardness suppositories gives possibility overcome the reflex resistance of muscles and tissues, and the liquid consistency in the body cavities - evenly distribute medicinal substances across the mucous membrane, which can keep on organism as local (local), Yes and resorptive (system) action.

In recent years, the industrial production of such dosage forms has increased, conditioned significant their advantages before others forms. Suppositories canapply under time ambulance urgent assistance, ago What their pharmacological effect turns out much earlier, than in oral dosage forms. This is due to the rapid absorption of drugs in the large intestine. intestines and their penetration into the blood, bypassing the liver through the middle and lower hemorrhoidal veins. In terms of duration of action, suppositories are close to injectables. drugs, but their administration does not violate the integrity of the skin. In addition, Rectal administration of medication very often makes it possible to reduce the single dose dose due to their prolonged release from suppositories. Many drugs in oral administration are inactivated by enzymes of digestive juices, exhibit unfavorable influence on gastrointestinal highway and liver - these defect deprived rectal medicinal forms.

The rate of absorption of drugs from suppositories is affected by such physiological factors, as state direct intestines, blood circulation surfaces absorption, muscular tone and layer mucus on wall surfaces rectum.

Most influential factor on absorption active substances from suppositories is the nature of the base, which accounts for up to 90% of the mass of the suppositories. Auxiliary substances closely are in contact and with different by force interact with This determines the degree of their release from the rectal form and affects on completeness and speed absorption.

Rectal suppositories can have form cone, cylinder from pointed at the end or another form; maximum diameter is usually not exceeds 1.5cm.

Mass one suppository should be in within from 1to 4g, length

- 2.5-4cm with a width at the base of no more than 1.5cm. The weight of a suppository for children is be from 0.5 up to 1.5 g.

Vaginal suppositories can be spherical (balls - *globules*), egg-shaped (ovals - *ovula*) or have form tongue - flat body from

rounded at the end (pessaries - pessary). Mass these medical forms fluctuates inwithin from 1.5 to b d.

Sticks have form cylinders from pointed at the end thickness 2-5 mm and length up to 10cm.

CHARACTERISTIC BASICS I AUXILIARY SUBSTANCE

3 views of physical and chemical science consider suppositories as dispersed systems, What consist of with dispersion environment, presented.by the basis, and dispersed phases, role whose perform medicinal substances. Depending from properties medical substances suppositories can create different dispersedsystems.

Homogeneous systems are formed in cases where the drug substancedissolves in basis, and *heterogeneous systems - I am* what? medicinal substances are introduced in basis by type emulsions or suspensions.

IN structure suppositories distinguish main (medical substances) and auxiliary (carriers) or basis) components.

To suppository basics is being put forward series requirements:

- They must retain sufficient hardness at room temperature.temperature;
- temperature melting or dissolution has be close to human body temperature bodies;
- not lifelong irritate the mucous membrane shell direct intestines and cause others unwanted actions, that is, must be physiologically indifferent;
- not must prevent release and therapeutic actions medicalsubstances;
- not must interact with medicinal substances, which enter in suppository mass.

From specified general requirements closely related and technological requirementsto basics. To them include:

- chemical and physical stability foundations in process production and storage suppositories;

- ability light form and save necessary hardness atintroduction;
- ability emulsify necessary number solutions;
- have certain plasticity, viscosity, time full deformations, that is,certain structural and mechanical properties.

Hereby requirements satisfy lipophilic and hydrophilic foundations, which are applied in pharmaceutical industry different countries.

Lipophilic foundations. As suppositories foundations State Federal University offers use butter cocoa, its alloys with paraffin and hydrogenated fats, vegetable and animal hydrogenated fats, solid fat, lanolin, alloys hydrogenated fats with wax, hard paraffin and other bases permitted to medical application.

Lyophilized foundations have answer like this requirements:

- quickly fuse in rectum;
- temperature melting not should exceed 37 °C;
- have sufficient hardness and little interval between temperature melting and freezing;
- have sufficient viscosity;

- good absorb liquids;
- be stable at storage.

Butter cocoa in our time in pharmacopoeias row countries remains official basis. It consists of from mixtures triglycerides: tristearin, tripalmetin, triolein, trilaurin, triarachin. The composition of cocoa butter explains polymorphic modifications of this basics of different physical properties.

When melting this base at a temperature above 36 °C and further cooling in different conditions, and also at storage at temperature above 10
°C butter cocoa passes in modification with low point melting (23-24

°C) and a low pour point (17-18 °C), which causes difficulties in in the formulation of suppositories. Cocoa butter also does not emulsify aqueous solutions well, capable of rancidity due to the high content of oleic acid (about 30%). In addition that, it may contain viable pathogens microorganisms.

To improve structural and mechanical properties and the ability to release medical substances to this one foundations add different auxiliary substances: lecithin, white wax, starch, microcrystalline cellulose, aerosil, palm tree oil.

About such w properties, as and butter cocoa, have oil lavra petiolate and oil coriander.

Hydrogenated fats allow create suppositories foundations, devoid of the defects of cocoa butter. Back in 1934, A. G. Bosin developed a suppository basis butyrol — alloy hydrogenated fats from paraffin. As substitute oilscocoa now widely are used alloys hydrogenated fats from fat-like substances, emulsifiers or hydrocarbons products.

IN industrial production suppositories used basis Nizhny Novgorod Chemical and Pharmaceutical Plant, which includes30% cocoa butter, 49-60% hydrogenated sunflower oil and 10-21% paraffin; lanole base, What consists of with 60-80 % lanolin (mixture esters acids phthalic and high molecular weight alcohols), 10-20% cooking fat and 10-20% paraffin.

Of particular interest for the industrial production of suppositories is firm confectionery fat on palm kernel basis and on basis plasticized salomasa. These fats

have fine-grained crystalline structure that melts in a narrow temperature range without noticeable phase transformations, which favorably distinguishes them from cocoa butter and a number of other suppository bases.

Wax is used to increase the melting point of alloys, paraffin, ozokerite and spermaceti. Lanolin, lecithin, cholesterol enter for better emulsification liquids.

Fatty and fat-like bases, depending on their composition, have different viscosities and plasticity, and the choice of the method of manufacturing suppositories depends on this form.3 of known foreign lipophilic bases, especially interesting are the bases Vitepsol,estarinum, lazupol.

Vitepsol, or Imhausen (Germany) is a mixture of virgin lauric triglycerides and stearic acids, What contains additives emulsifier monoglycerin lauric acid ester. Melting point 33.5-35.5 °C. Full time deformation of foundations in within 15 minutes.

Vitepsol is produced in different groups H, V, S, E, which differ in the interval physicochemical properties.

Estarinum is released in in the form of several modifications, What differ physicochemical characteristics. IN chemical regarding basis represents by yourself mixtures of mono-, di- and triglycerides saturated fatty acids.

Lazupol consists of with esters acids phthalic with higher alcohols (e.g. cetyl and (or) stearyl).

Released sprat modifications Lazupol, What differ melting points (34-37 °C), solidification and emulsification ability aquatic solutions.

All described foreign lipophilic bases emulsify aqueous solutions well. medical substances, quickly freeze, have temperature melting, close to body temperature.

Hydrophilic foundations. Hydrophilic foundations must answer requirements:

- quickly and completely dissolve in mucous secretionsshells;
- not irritate mucous shells;
- mix with hydrophobic medicinal substances orabsorb their;

- be chemically and pharmacologically indifferent.

Modern hydrophilic foundations presented main in a way *with ethylene glycols* condensed polymers ethylene oxide and water. Domestic industry are issued polyethylene glycols, What differ molecular by mass - PEG-400, -1500, -2000, -4000, -6000.

Abroad, polyethylene glycol bases are known under the name "karbovax" (CTTTA), "skurol" (France), "moaned", "suppofarm" (Germany). This group basics capable to dissolve in secrets mucous membranes shells, fully to release medicinal substances, not irritating mucous membrane shell, has long shelf life, high physiological indifference, relatively available by cost.

Gelatin-glycerin and *soap-glycerin foundations* much less often used in the production of suppositories, although included in pharmacopoeias row countries.

Trace to note, What polyethylene oxide foundations incompatible with salts silver, mercury, bromides, iodides, salicylates, phenol, tannin, some sulfonamides. Except that, this basis slow and not fully dissolves in rectum, dehydrates and irritates mucous membrane shell.

Gelatin - glycerin base is incompatible with acids, alkalis and astringents means. When stored quickly dries up and moldy.

These foundations have disadvantages: low structural and mechanical properties, insufficient stability, low resorption ability.

To eliminate these defects and ensure optimal structural and mechanical characteristics of suppository bases are enhanced by adding aluminum and magnesium stearates and other salts of fatty acids, as well as tween, emulsifiers T-2, No. 1, bentonite, glucose, starch, aerosil.

For prevention instability basics to them add antioxidants, preservatives, stabilizers.

METHODS OBTAINING SUPPOSITORIES IN INDUSTRIAL CONDITIONS.

TECHNOLOGICAL EQUIPMENT PRODUCTION

Suppositories in industrial production are made two methods

— *pouring* molten masses in forms and *pressing* on special equipment.

Pouring method . Industrial production of suppositories by this method is being held most often by technological scheme, which consists of with such stages:

1. preparation foundations;
2. preparation medical substances and obtaining concentrate;
3. introduction medical substances in basis;
4. formation (and packaging) suppositories;
5. packaging suppositories.

First they prepare reactors, various containers, collections, pumps and other equipment by thorough treatment with hot steam, water from detergents, rinsing and drying. Sanitizing is carried out premises and preparation working staff.

Preparation of the base. First, the base components are weighed. In the reactorstainless steel with steam jacket and stirrer melts the components base at a temperature of 60-70 °C and stirring for 40 minutes. Base filtered through a filter press using brass mesh or belting, and analyzed by melting point, solidification point and time of complete deformation and transmit in hardware department.Then basis by with help compressed air serve in reactor, in to whom is preparing suppository mass. After this in mass enter medicinal substances.

Introduction medical substances in basis. Medical substances enter in basisin in the form of aquatic solutions (water-soluble), fatty solutions (fat-soluble) or suspensions of ground powders in bases (insoluble in water and fats). The obtained solutions or suspensions are called *concentrates.*

Water-soluble components dissolve in water, heated to 45 °C, fat-soluble - in the melted fat base. The resulting concentrates filter through calico, and then mix from remainder bases. Substances, insoluble in water and basis, enter in in the form of suspensions. Pre-ground medicinal substances are mixed in a reactor with equal or one and a half times the amount of base heated to a temperature of 40-50 °C. The resulting concentrate cool and grind on colloidal mills or for thermolabile substances — by with help three-roller a maser. Except that, for To obtain high-quality

suspensions, rotary-pulsation systems can be used. devices, rotary-toothed pumps and other equipment. Time grinding concentrate continues from 2to 4 hours for obtaining necessary degree dispersion of medicinal substances, which enter in basis by type suspensions.

Finished concentrate using a pump (through a hose with a nylon sieve) merges in reactor (from turbine or anchor mixer) for mix from remainder foundations. Operation preparation suppository masses is being held at permanent stirring and temperature 45-50 °C. After positive analysis (homogeneity mix components, temperature freezing and melting, time full deformation) mass is served on stage outpouring suppositories.

Then suppositories form and packaged.

For *outpouring suppositories* are used *automatic lines type*

«Sarong 200 S» from direct dosage masses in formed cells with polyvinyl chloride film with further styling products in packs.

3 two rolls (position *1)* are fed one at a time, vertically placed ribbon aluminum foil or polyvinyl chloride films. Both ribbons first pass separately and in the cutting block (position *2)* are cut into vertical direction, that perform impeccable formation. Except that, The incisions facilitate subsequent separation of the packaged suppositories from the stripes. IN positions *3* both ribbons are forming (coined) in cup-shaped halves, which in the future (position *4)* are connected in complete form and in positions 5heat-sealed. At this from above each forms remains open the filling hole through which the filling needle (items *6, 7)* injects molten suppository mass. Thus, the foil-formed packaging simultaneously serves foundry form. Filling double-walled capacity 7 holds almost 30 liters of mass. The required mass temperature is constantly maintained using water heating with a continuously operating mixer. Dosage is carried out using a pump. In the next position *8*, the package is hermetically sealed closed and fitted (position *9)* between separately welded suppositories additional transverse ribs stiffness (cold embossing). Further (items *10* and *11)* strips are cut from the tape for a certain number of suppositories (5, *6, 10).* Cut off strip arrives on cooling plot (position *12),* after passage whose is formed

ready packaging. External surface foil (thickness 40 microns) covered stretched polypropylene film (12.5 microns), and the inner one is polished for welding when heated or layered polyethylene high pressure by mass 20 g/m ^{2}.

Productivity lines 16 000—20 000 pieces by hour.

For outpouring suppositories used also *automatic line*

"Farmo Dui FD 22/U" (Italy), which has approximately the same scheme. Productivity22000-25000 pieces per hour.

Sometimes outpouring suppositories are made on machines with separate operations casting and packaging. IN such cases are used *semi-automatic devices "Franco-Crespi"*. Outpouring rectal and vaginal candles here is happening without operations packaging. Device equipped with:

- two nutritious bunkers from steam heating and bladedmixers (70-600 rpm), in which is given by suppository mass;
- receivers-dispensers;
- dosing pumps;
- three synchronously rotating disks;
- nests of metal molds (36 molds each)are located on the two extremes rotating disks);
- refrigeration installation;
- with a knife, which heated, for removal excess masses;
- device for pushing out suppositories in reception rooms collections and trays.

After forming, the suppositories are rejected based on appearance, is being held their analysis. Dry suppositories at temperature 10-15 °C for 2-3 hours from additional blowing by air for removal cooling and lubricating components.Ready suppositories are coming on *packaging* and *packaging* by with help semi-automatics.

Semi-automatic for packaging suppositories valid by such scheme. Suppositories manually are invested in cells rotating disk, from whose horizontal

they are pushed out through the inlet formed by the cellophane by a pusher ribbons. Candles are accepted holder, pressing stamps cover and are packing candles in cellophane. By with help cut-off device, is happening their distribution by 5 pieces and cut.

The packaged candles are fed into machines, where they are placed 10 pieces in a cardboard boxes, where the leaflet is placed, are labeled series number and the term suitability.

Store the finished product in a dry place, protected from light, at temperature not above 20 °C,y tight closed containers. On label additionally indicate: the name of the active substance and its content in a dosage unit medical means; way application; conditions storage; term suitability.

When preparing suppositories by pouring, their mass depends on size of the nest shape (volume), specific gravity of the medicinal substances used and foundations.

Firstly, When medicinal substances are included to warehouse suppositories in an amount of up to 5%, or well soluble in the base, this can be ignored minor volume, What they will take in forms.

Second, When substances are included in suppositories foundations in big quantities, not can neglect that volume foundations, which will be displaced at pouring in forms. IN these cases necessary find accurate correlation between the volume occupied by the medicinal substances and the volume of the base, otherwise the accuracy dosage will be broken. It correlation is expressed "coefficient" replacement" and "inverse coefficient" replacement".

The substitution coefficient E_{is} The amount of medicinal substance that is replaces one mass part of the fat base with a specific gravity of 0.95, i.e. this the amount of medicinal substance occupies the same volume as one mass part fatty foundations.

Inverted coefficient replacement $1/E_w$ are called number fatty base that replaces one mass part of the medicinal substance. That is, the amount fatty basis is equivalent by volume 1.0g of medicinal substances.In tables given value *E* and *1/E F* for medical substances, What most often used in suppository medical forms.

The disadvantage of the pouring method is that the mass may separate under time dosage and freezing especially in those cases, When to warehouse suppository masses included insoluble ingredients with big density or liquids, which badly are mixed with with water. That prevent this, necessary increase viscosity foundations, avoid high temperatures at pouring masses and conduct mixing the mass before pouring in forms.

Important value in improvement technology production suppositories has a method of *non-thermal preparation by pressing the compositions* chilled and crushed basics from medicinal substances.

The substitution coefficient of fatty and gelatin-glycerol bases for some medical substances

Medicinal substance	$E_{ж}$	V-E»	£ж-г	!/£;ж.г
Ampiox	1,14	0,88	0,94	1,06
Ampicillin	1,0	1,0	0,826	1,21
Analgin	1,27	0,79	1,05	0,95
Anesthesin	1,33	0,75	1,1	0,91
Antipyrine	1,25	0,80	1,03	0,97
Apilak	1,48	0,68	1,22	0,82
Barbamil	1,81	0,55	1,55	0,67
Barbital	1,06	0,94	0,875	1,14
Sodium barbital	1,81	0,55	1,50	0,67
Benzylpenicillin sodium salt	1,2	0,83	0,99	1,01

Bismuth nitrate basic	4.8	0.21	3.96	0.25
Glucose	1.23	0.81	1.02	0.98
Braiding aluminum-potassium	1.8	0.56	0.49	0.67
Dermatol	2.6	0.38	2.15	0.465
Dicloxacycline	1.1	0.91	0.91	ID
Ethacridine lactate	1.50	0.63	1.31	0.76
Euphyllin	1.25	0.80	1.03	0.87
Ichthyol	1.1	0.91	0.91	1.1
Calcium gluconate	2.01	0.50	1.66	0.60
Calcium lactate	1.53	0.65	1.26	0.70
Camphor	0.98	1.02	0.81	1.23
Acid ascorbic	1.73	0.58	1.43	0.70
Acid boron	1.60	0.625	1.32	0.76
Acid tartaric	1.03	0.97	0.85	1.17
Acid lemon	1.27	0.79	1.05	0.95
Cocaine hydrochloride	1.18	0.85	0.975	1,025
Xeroform	4.8	0.21	3.96	0.25
Levomycetin	1.59	0.63	1.31	0.76
Letter foxgloves (powder)	1.81	0.55	1.50	0.67
Lincomycin	1.20	0.83	0.99	1.01
Menthol	1.09	0.92	0.90	1.11
Metacycline	1.14	0.88	0.94	1.06
Methacillin	1.08	0.93	0.89	1.12
Morphine hydrochloride	1.18	0.85	0.97	1.03
Sodium bromide	2.22	0.45	1.83	0.546

Sodium bicarbonate	2.12	0.47	1.73	0.57
Sodium salicylate	2.50	0.40	2.06	0.48
Novobiocin sodium	1.20	0.83	0.99	1.01
Novocaine	1.40	0.71	1,156	0.865
Oxacillin	1.04	0.96	0.86	1.16
Oil castor oil	1.0	1.0	0.826	1.21
Osarsol	1.45	0.69	1.20	0.83
Papaverine hydrochloride	1.59	0.63	1.31	0.76
Paraffin	1.0	1.0	0.826	1.21
Protargol	1.40	0.71	1,156	0.865
Resorcinol	1.41	0.71	1,165	0.858
Sulfur precipitated	1,141	0.71	1,165	0.858
Streptocide	1.61	0.62	1.33	0.75
Tannin	0.90	1.10	0.74	1.35
Theophylline	1.23	0.81	1.02	0.98
Phenylsalicylate	1.40	0.72	1.16	0.86
Phenobarbital	1.40	0.72	1.16	0.86
Phenol	1.10	0.91	0.91	1.10
Ferumu lactate	1.59	0.63	1.31	0.76
Furazolidone	1.81	0.55	1.50	0.67
Quinine hydrochloride	1.20	0.83	0.99	1.01
Quinozol	1.36	0.74	1.12	0.89
Chloral hydrate	1.20	0.83	0.99	1.01
Zinc oxide	4.00	0.25	3.30	0.30
Zinc sulfate	2.0	0.50	1.65	0.61

By method pressing on eccentric tablet machines at cooling punch, matrices and casing can receive from 40to 100 thousand. suppositories by hour. Suppository mass usually cooled in refrigeration camera to 3-5 °C, grind and sifting. To warehouse granulate enter lactose, sucrose, aeroforce, starch for adjustment technological properties.

Advantage this method consists of in opportunities prevent destruction thermolabile medicinal substances, absence of sedimentation of the active substance andto avoid its possible incompatibility with molten suppository basis.

This method maybe to apply at use plastic basics. Because mass dosed by volume, need use coefficient replacement medical substances.

In the process of manufacturing pressed suppositories, it is not necessary to apply significant effort for pushing out, ago What particles fatty foundations play back role effective lubricants in wall-mounted layers because of their intensive plastic leakage.

The compression method is particularly suitable for the production of suppositories with cordial glycosides, some thermolabile hormonal drugs, biogenic stimulants, because during the cooking process is provided high precision dosage, thermal stability medical substances.

STANDARDIZATION SUPPOSITORIES. NOMENCLATURE

In accordance to State pharmacopoeia Ukraine suppositories control by such indicators: description, identification active substances and antimicrobial preservatives, average mass and homogeneity masses, decay, homogeneity content, temperature melting or time full deformations, dissolution, accompanying impurities, microbiological purity, quantitative definition active substances and antimicrobial preservatives. At necessity additionally control acidic and peroxide numbers, and also size particles.

Suppositories have be homogeneous. Homogeneity determine visually, on longitudinal slices have be missing interspersed.

Homogeneity masses or average mass determine weighing 20 suppositories with accuracy to 0.01g. Deviation in mass not must exceed

±5 %.If no others indications, suppositories with content current substances Less2mg or less than 2% of the total mass shall pass the test for homogeneity content current substances in units dosed medical means.

For suppositories, manufactured on lipophilic basics determine temperature melting, which not should exceed 37 °C. Temperature melting measure open capillary method (SFU, Mr. 2.2.15).

If it is difficult to determine the melting point, the time of complete melting is determined. deformations, which has be not more 15 minutes.

Definition time full deformations spend according to with methodology application1to article "Medical means for rectal application" (SFU).

For suppositories, which made on hydrophilic basics, determine time dissolution by methodology "Dissolution" test for solid dosed forms (SFU, Mr. 2.9.3).Time dissolution has be not more 60min.

The disintegration test for suppositories is carried out according to the “Disintegration suppositories and pessaries" (SFU, Mr. 2.9.2). Suppositories on fatty basics mustto fall apart for 30 minutes, and on hydrophilic - through 60min.

Nomenclature suppositories. IN nomenclature suppositories and vaginal balls industrial production included such name (examples (of prescriptions):

Cefecon (Suppositoria «Cefeconum»). Composition: salicylamide 0.6g, amidopyrine0.2g, phenacytine 0.2g, caffeine (or caffeine benzoate sodium) 0.05 g.

Betiol (Suppositories "Bethiolum"). Composition: extract belladonna 0.15 g, ichthyol 0.2 g.

Anuzol (Suppositoria «Anusolum»). Composition: extract belladonna 0.02g (or 0.015g), xeroform 0.1g, zinc sulfate 0.05g, glycerin 0.12g.

Anestezol (Suppositoria «Anaesthesolum»). Composition: anesthesine 0.1g, dermatol 0.04g, menthol 0.004g, zinc oxide 0.02g.

Suppositories with glycerin (SuppositoriacumGlycerino). Composition: glycerin 1.44g (or 2.46g), stearic acid 0.12g (or 0.25g), sodium carbonate crystalline 0.06g (or 0.13g) .

Suppositories with digitoxin (Suppositories with Digitoxin) contain digitoxin 0.00015g.

Biological antiseptic suppositories (Suppositoria antiseptica biologica). Composition: dry mixtures bovine plasma and thromboplastin 0.9g, chloramphenicol 0.02g, novocaine 0.12g, extract belladonna 0.015 g.

Candles apilaku (Suppositoria "Apilacum") contains apilaku lyophilized 0.005g (or 0.01g).

Neo-Anuzol (Suppositories "Neo-Anusolum"). Composition: zinc oxide 0.2g, bismuth nitrate basic 0.075g, tannin 0.05g, iodine 0.005g, resorcinol 0.005g, methylene blue 0.003g.

Candles with ichthyol (SuppositoriacumIchthyolo)contain ichthyol 0.2 g.

Osarbon (Giobuli «Osarbonum»). Composition: osarsolu 0.35g, acids boron 0.3g,glucose 0.3g.

Osarcid (globuli "Osarcidum"). Composition: osarsol 0.3g, glucose 0.2g, acidboric acid 0.3g, streptocide 0.3 g.

Prospects development rectal medical forms

Rectal suppositories —promising medical form, What developing by several directions.

Lyophilized suppositories. Thanks to porous structure and big internal surfaces such suppositories quickly are falling apart in insignificant quantities secretions of the rectal mucosa and release medicinal substances that contained in them. Produced their from aquatic suspensions or emulsions auxiliary andmedicinal substances; after pouring into molds, they are subjected to deep freezing chewing (lyophilization).

Porous suppositories. For magnification surfaces contact mucous rectal lining with inserted suppositories and accelerated release medical components proposed porous suppositories, which are made

pouring molten masses in forms with further vacuuming at vacuum depth 80 kPa **(600** mm mercury (Art.).

Hollow suppositories are filling emulsions, suspensions or solutions of medicinal substances, also contribute to a faster release medical substances.

Multilayer suppositories. IN in a row countries patented two-i multilayer

suppositories. Shell such suppositories are made with foundations with less high melting point. It contains medicinal substances with local action(anesthesin, extract belladonna). IN rod enter substances, which do resorptive action on organism. For rod use basis, What has morehigh temperature melting.

Suppositories with film coatings. Controlled delivery medical substances at rectal introduction maybe to be carried out using suppositories from film coatings, which slow down diffusion active component, or laying suppositories in capsules.

Colored suppositories. The color of suppositories is of great importance, intended not so much for visual identification different pharmacological groups substances, how many to protect suppositories from the effects of a certain spectrum of rays,What call oxidation, destruction input components.

Production rectal ointments, capsules, aerosols, tampons

Soft medicinal means for rectal application last sometimes have become widespread in medical practice. They are represented by creams, gels, ointments and are single-dose medicines in containers equipped withappropriate applicators.

A significant, up to 50 g, single administration of a mild drug allows increase number applied medical substances. Except that, big number foundations in these medical forms allows appoint medicinal substances, which at others ways introduction can cause irritation.

Rectal capsules are one of the promising dosage forms. This is a solid single-dose medical form, in basically similar to soft capsules. They represent by yourself containers with gelatinous films by form suppository, filled

a single dose of a medicinal substance in the form of a liniment, ointment, emulsion or solution. Shell capsules is preparing with higher varieties gelatin with additive 30-36

% glycerin, which provides elasticity and relative strength of the capsules, as well as relatively fast their dissolution in straight line intestine. To advantages this one rectal formsapplies possibility choice available basics, more wide interval storage and use temperatures compared to suppositories, full mechan- nization and process automation encapsulation.

Rectal solutions and suspensions (enemas) - liquid medicinal means,

intended for introduction in straight line intestine with purpose obtaining general or local actions. They can be used from diagnostic goal. It is known that What from aqueous solutions introduced into the rectum in the form of an enema, medicinal substances are absorbed very well quickly. However, some of the solution spills out outside. In In such cases, it is more convenient to administer medicinal solutions using rectal pipettes-rectiols, consisting of an elastic can with a tip. Spray can executed in in the form of corrugated container capacity 2.5-5ml. Tip harshly attached to him and made with polyethylene. The use of oleogels, liniments, and ointments to fill rectoceles opens wide opportunities for expanding the range of proctological dosage forms. Rectal solutions and suspensions are produced in containers with a capacity of 2.5 ml to 2000ml.

Rectal tampons are a solid single-dose dosage form intended for for introduction in lower part direct intestines on certain time. They represent by yourself a plastic rod wrapped in cotton wool with medicinal substances adsorbed on it substances. Cotton swab covered thin layer alginate. Before application swab on some time immerse in water, as a result what shellfrom alginate swells and does not interfere with the diffusion process medical substances. Swab enter in straight line intestine on 2 hours. Apply, as rule, for treatmenthemorrhoids.

Rectal foams have undergone intensive development in our time. Foams are profitable differ from others medical forms, which are applied in proctology. Ointments and creams not penetrate in folds mucous membranes shells and in more deep zones

intestines. Suppositories not provide treatment all plots anal channel; they are characterized by a shorter-term therapeutic effect on leveled with foams.

Foams are formed when leaving the aerosol packaging if the composition concentrate are included foaming agent (its role perform South Africa) and emulsified or dissolved propellant (usually liquefied under pressure gas). After dispensing through the valve-spray system of the aerosol can the propellant evaporates and gas bubbles, increasing in volume, form foam — rough dispersion steamed propellant in emulsion or another type system.

Foams occupy great volume at low specific mass. It allows small quantities

emulsions, translated **in** foam, process significant surfaces or fill large volumes. The foam is applied locally and painlessly to the affected surface, providing heat and gas exchange and creating a barrier for infection wounds from the outside.

The presence of surfactants gives it excellent adhesion and the ability to clean the affected area. surface from necrotic tissues; expanding, the foam penetrates the wound pockets and cavities. At correct choice auxiliary substances foam remain stable for a long time, ensuring the prolongation of the effect of drugs preparations. A small amount of the preparation when converted into foam takes up a large volume, however concentration medical substances in intermembrane-cilia liquid remains at the same time high.

In foam can transfer different dispersed systems: solutions, emulsions, suspensions, What opens big opportunities for creation combined drugs.

Foam preparations in aerosol packaging, which are used in proctology, contain in to his/her warehouse antiseptics, anesthetics, corticosteroids, anti-inflammatory substances nonsteroidal structures. More in detail about foamy drugs in aerosol packaging stated in head "Medical means, What are located under pressure.

Materials of activation applicants higher education under time carrying out

lectures: question, situational tasks etc:

Question:

1. What such suppositories?

2. Basic groups suppositories.

3. Specify foundations for production suppositories MLF.

4. Explain appointment auxiliary substances. IN whose cases their used?

5. Point examples auxiliary substances.

6. Specify which value pH have suppositories?

7. How can the technological properties of suppositories be improved?

Generalmaterial and educational and methodological software lectures:

- educational rooms – audience departments;
- equipment - computer, tables;
- equipment – multimedia projector;
- illustrative materials – presentation, slides.

Question for self-control:

1. Which requirements qualities of suppositories presents State Federal University?
2. Rate prospects industrial production suppositories.
3. WITH what consists of process receiving different suppositories?
4. Name it drugs, What are issued in in the form of suppositories.

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Regime access to texts lecturesfor students pharmaceutical faculty: https://info.odmu.edu.ua/chair/drugs/files/390/ua

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- Scientific library NUPh: Regime access :http://dspace.ukrfa.kharkov.ua; http://lib.nuph.edu.ua
- www.moz.gov.ua – official website Ministries security health Ukraine
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Lecture No. 18

Topic: "Production of medical plasters, characteristics, classification, industrial production. Mustard plasters. - 2 hours.

Relevance of the topic: Drug technology (industrial technology of drugs) means) – is one of the fundamental technological sciences. It consists of several key aspects, which important for modern medicine and patients: Effectiveness and safety - Modern technologies allow the production of medicinal products drugs with high efficacy and safety for patients. Accurate dosage, CONTROL qualities and absence impurity do medicine more effective and safe. Innovations in medical in the field of: New technology allow create innovative medicines that can be more targeted and effective medical therapy. For example, medicine, designed for accurate influence on specific cells or genes, provide more effective treatment. Minimization side effects effects: Technologies allow elaborate medicinal formulas that minimize side effects and negative effects on the body. This provides more comfortable and safe treatment for patients. Fast production and supply process: The use of modern technologies allows speed up the process of producing medicines, which is especially important in conditions rapidly changing medical environment, such as spread diseases or epidemics. Individual approach to treatment: Technologies allow elaborate medicine, which take into account individual features patient,which leads to a personalized approach to treatment and increases its effectiveness efficiency. Economy and accessibility Improved technology production can reduce production costs, making medicines more available for wide circles patients, providing economic efficiency in field health care.

Thus, the use of modern technologies for the production of medicinal products drugs there are important factor for improvement efficiency treatment, security patients and general state public health.

Objective: to get acquainted with the main stages of industrial manufacturing medical forms and disciplines "Technology medicines", dates characteristic production plasters TTS and describe modern state pharmaceutical

industry.

Basic concept:

Patches (Emplastra) - a dosage form for external use, which sticks to skin, affects on skin, subcutaneous fabrics and in some cases does general action on organism. It one with the oldest medical forms.

Calloused plaster (Emplastrum ad nails) — has in to his/her *in stock:* acids salicylic 20.0 parts; rosin 27.0 parts; paraffin 26.0 parts;
petrolatum 27.0 parts.

Plasters leaden — contain in to his/her warehouse leaden soap. Lead cutefuse with resins, waxes, medicinal substances, do not pollute clothing, stable during storage.

Adhesive plaster (*Leucoplastrum*). Sticky plaster elastic anointed (Emplastrumadhaesikkoekasticumextensum). Plaster has such *composition:* rubber natural 25.7 parts; rosin 20.35 parts; zinc oxide 32 parts; anhydrous lanolin 9.9 parts; liquid paraffin 11.3 parts; neozone D 0.75parts.

Cerigel (Cerigelum) contains: polyvinyl butyral 4.0 parts; cetylpyridinium chloride 0.2 parts; ethyl alcohol 96% 100.0 parts. Glue — colorless opalescent, something knitting liquid from smell alcohol.

Basic concept:

Plan and organizational structure lectures:

No. No. p.p.	**Basic stages lectures and their content.**	**Goals in levels**	**Type lectures, equipment**	**Distribution time.**

		abstractions.	**lectures.**	
1	**2**	**3**	**4**	**5**
I 1. 2. II 3. III	***Preparatory stage*** Definition of training goals. Software positive motivation. ***Main stage*** Presentation lecture material.Plan: 1. Plasters 2. Plasters leaden 3. Rubber plasters 4. Plasters liquid, or leather adhesives ***Final stage*** Resume lectures, general conclusions. Lecturer's answers to possible question. Tasks for self-training student.	I II III	Lecture combined Slides List literature, question, task.	1% 2% 90% 2% 3% 2%

Structurally logical scheme content lectures

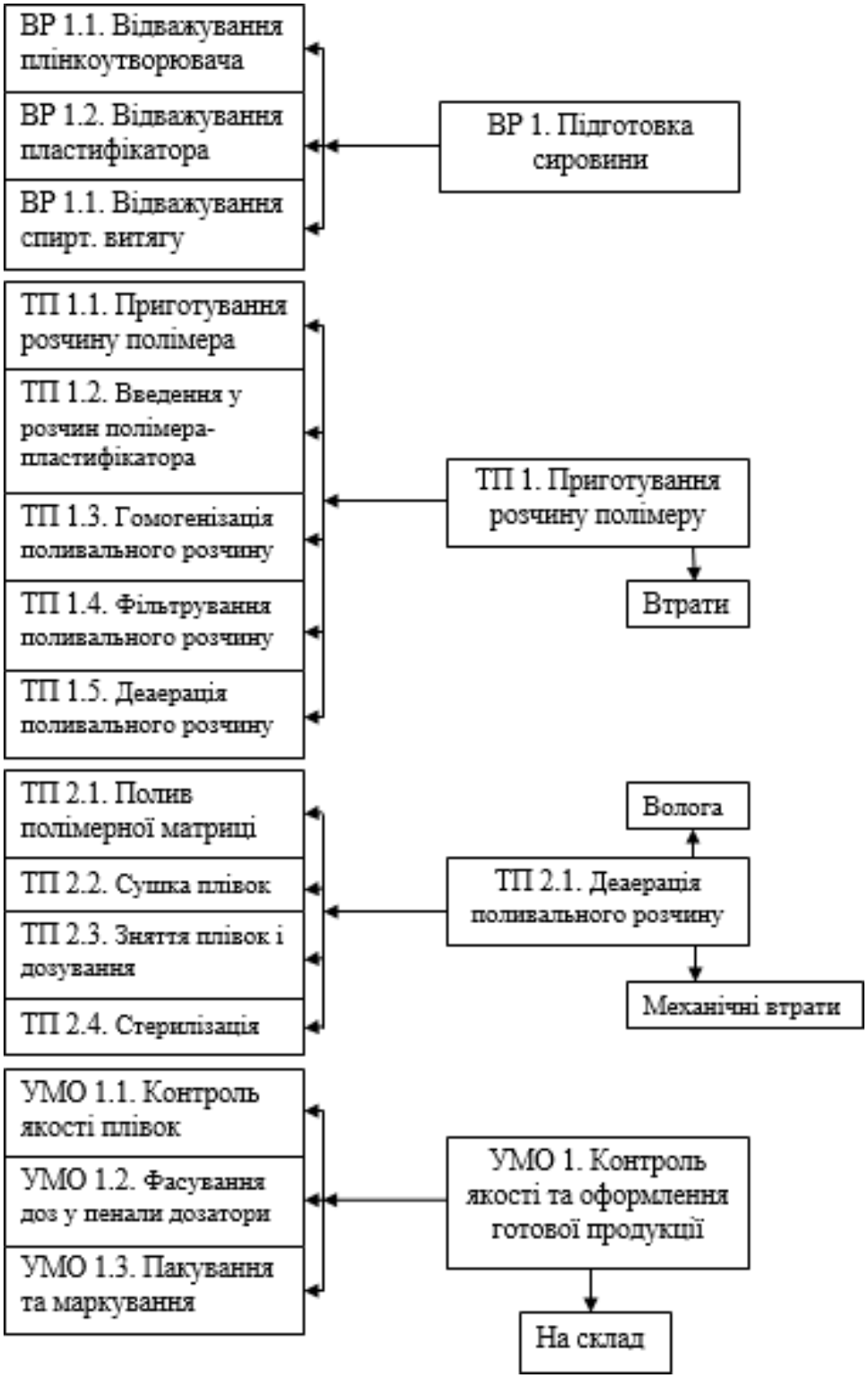
1. Plasters
2. Plasters leaden

3. Rubber plasters

4.Plasters liquid, or leather glues

Content lecture hall material (text lectures)

STRUCTURAL AND LOGICAL DIAGRAM OF PHYTOFILM TECHNOLOGYFOR TREATMENT THERMAL BURNS



1. Plasters

Modern pharmaceutical technology considers as one of its basic tasks creation of new dosage forms with high therapeutic activity, which provide controlled release medical means and their specific delivery to the site of the pathological process. This is extremely important because; There are groups of serious chronic diseases that require treatment take into account not only the effect of the drug itself, but also the method of its deliveryin organism. So heavy disease, characteristic of our time, there are atherosclerosis, the social significance of which, unfortunately, is great. One of the causes of its dominant roles in row modern pathologies there are not enough effective pharmacotherapy. Medical drugs for treatment and prevention atherosclerosis is not so much, and the range of dosage forms is limited pills or injectable solutions. WITH medical means hypolipidemic actions in present time most common statins and fibrates, but known and such domestic medicinal drugs as diisopropylammonium dichloroacetate (DIPROMISSARY), which is low-toxic, and the synthesis is inexpensive and simple. However, when it is Oral administration may cause side effects in the gastrointestinal tract, so it is not very widely used in the form of traditional dosage forms - tablets. Therefore, the improvement of this drug through the development of original and effective medical forms is relevant and possible.

Among the various drug delivery systems, the most widespread is expressed scientific and industrial potential, and also commercial success received trans der formal therapeutic systems (TTS), representing by yourself alternative forms oral and parenteral traditional dosage forms that are capable of continuously delivering a drug into the body withat a rate that creates a constant level of drug concentration in the bloodstream drug, close to the minimum therapeutic level. TTS have many indisputable advantages and obvious advantages before others medicinal forms and ago can be used for medical means, oral way introduction few effective, and injectable there are not enough gentle.

By with his/her structure and design transdermal therapeutic systemrepresents by yourself plaster. Ago enough often in literature can to meet the "crossover" of the concepts of TTS and the transdermal patch, which is reallymain model modern TTS.

Despite on all advantages transdermal plasters, What provide necessary effect by penetration current substances through unharmed skin, in basically, their manufacturers there are companies France, Germany, Japan, Sweden.

Therefore, research into the possibility of using a transdermal patch as a dosage form for hypolipidemic drugs, in particular for dipromonia, - question current and significant with scientific and practical positions.

Plasters (*Emplastra*) - a dosage form for external use, which sticks to skin, affects on skin, subcutaneous fabrics and in some cases does general action on organism. This one with the oldest medicinal forms.

Plasters at room temperature have appearance solid masses. At temperature bodies they soften, and at temperature 65-100 °C - melt. By these conditions their can float with different medicinal and auxiliary substances and mixed with powdered materials. In addition, plasters can be produced in liquid form, in glass bottles, aluminum tubes, aerosol cans.

Depending from medical purpose plasters share on epidermal, endermatic and diadermic.

Epidermal patches are used to protect the skin from harmful effects, for closing skin defects, bringing wound edges closer together and fixing bandages on skin surface.

Endermatic plasters contain medicinal substances, What affect onsick skin.

Diadermic plasters contain medicinal substances, What penetrate throughskin and affect deep-seated tissues, or have a general effect on organism.

Epidermal patches should have good stickiness and adhere tightly. to skin and not irritate its. They can not contain medical substances, speaking as bandage material. As a result "greenhouse" effectepidermal patches help soften the skin, enhance the processes circulation and resorption. Endermatic and diadermatic patches are more soft by consistency, ago What have to provide maximum release medicinal substances and their penetration into different depths of tissue or providing resorptive actions.

Plasters are produced in the form of a plastic mass on a substrate (canvas, chiffon, calico, paper, etc.); solid plaster masses (cylinders, bars, tiles, sticks);

liquid solutions (leather adhesives).

To warehouse plaster masses are included medicinal substances and basis. As medicinal substances used are antibiotics, sulfur, salicylic acid, extracts, tinctures etc.

Plaster basis maybe contain natural (rosin) and synthetic resins,wax, paraffin, ceresin, petrolatum, 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). To its warehouse are included plasticizers (linetol, vegetable oils, dibutyl phthalate, alcohol cetyl and others), antioxidants, fillers, etc.

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

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

2. Plasters leaden

Lead plasters contain lead soap. Lead soaps fuse with resins, waxes, medicinal substances, do not pollute clothing, stable during storage.

Simple leaden plaster (*Emplastrum Plumbisimplex*). Homogeneous solid The mass is grayish or yellowish in color, and becomes viscous and sticky when heated. Preparation not should be fatty to the touch and to have a bitter taste scent.

Apply as basis for preparation others plasters and externally at purulent-inflammatory skin diseases, boils, carbuncles and etc.

Composition: plumb bob oxide (lead (sigh) — 10.0 g; oils sunflower — 10.0 g; pork fat purified — 10.0 g; water purified sufficient number. IN chemical regarding plaster represents by yourself mixture lead salts. In basis industrial way production plaster lies reaction saponification fats plumb bob oxide in presence water at temperature boiling masses. The main equipment is enameled or stainless steel reactors. (excluded using copper and copper-tinned boilers), which have steam shell and mixer.

Preparation simple lead plaster. IN reactor placed calculated number pork fat and oils sunflower melt, regulating temperature by serving deaf couples. Volume reactor should exceed number reactionary masses not Less than in 4-5 times, ago

What mass under time cooking strongly foams. Leaden glet rub in small powder, sift through silk sieve and mix from two in parts freshly digested water purified. I molten, but not overheated mixture fats add suspension lead oxide in water in portions without residue with constant stirring and heating. At this is happening reaction saponification, in result whose is formed fatty salt lead (lead soap). IN chemical regarding leaden plaster represents by yourself mixture lead salts oleic, palmitic and stearic acids from significant advantage the last ones.

Process cooking is necessary conduct at at a temperature of 100 — 110 °C for 2-3 hours. During the cooking process, add to the reaction mass every 5 minutes hot water in small portions, making sure that it does not boil completely boiled away, as evidenced by the presence of fine-bubble foam. The mass is constantly mix, ago What reaction is happening on boundaries fat — plumb bob oxide, What have different densities and tend to separate. Adding large amounts water slows down process, What contributes stratification systems.

Absence foam at long heating masses indicates on that, What water boiled away, and the temperature of the mixture may exceed 110°C. Adding the next portions water leads to sprinkling masses, ago necessary be careful.In process cooking initial reddish color mixtures gradually passes in whitish-gray, and under end cooking — in whitish.

The cooking of the patch is considered complete if a small sample, poured into cold water, is a plastic mass that does not smear or stick when kneaded sticks to fingers.

The finished patch is freed from glycerin by repeated stirring. masses in warm water by with help dough mixers, What heated. Laundered like this in a way plaster again translate in reactor and heated to 105-110 °C to complete removal of water. A sample of dried lead plaster, taken with a spatula, should be pulled out into a thin transparent thread. Poorly dried and insufficiently The patch, freed from glycerin, becomes hard and brittle during storage, becomes bitter and moldy. The quality of the plaster is affected by the quality of the original fats, lead oxide is not should contain impurity lead (Pb_30_4), What almost not soaps up fats.The water used must not contain carbonates, sulfates and carbon dioxide, which transform plumb

bob oxide in plumb bob sulfates and carbonates, which not oxidize fats.

Standardization ready drug is being held by reactions truthfulness and quantitative content of lead oxide. The preparation should not contain peroxide, lead carbonate and lead oxide. Loss on drying is not should exceed 3%.

A simple lead patch can be applied on its own, as well as to be part of others plasters and lead ointment (diachyl).

Plasters on basis simple lead plaster accepted divide on *lead-resin* and *lead-wax.*

Lead composite plaster (*Emplastrum Plumbicompositum*) — lead- resin plaster of the following *composition:* 85.0 parts of simple lead plaster; rosin 10.0 parts; oils turpentine 5.0 parts.

Leaden plaster and rosin are melting in reactor with steam heating. To semi-chilled masses at continuous stirring add turpentine. 3obtained mass squeeze out or are pumping out sticks.

Used as a mild irritant. Epilin patch 4% -(*Emplastrum Epilini*) belongs to lead-wax plasters and has the following *composition:* epilin citrate 4.0 parts; lead simple plaster 51.0 parts; lanolin anhydrous 20.0 parts; wax 5.0 parts; water purified 20.0 parts.

Homogeneous sticky mass light yellow or brownish-yellow colors soft consistency. Plaster shouldn't have rancid smell.

Applicable as depilatory means at fungal diseases skin. *Preparation epiline plaster.* IN reactor from steam shell and mixer placed previously brave simple leaden plaster, wax and anhydrous lanolin. The mixture is melted with constant stirring,Filter hot through a sieve. Epilin citrate dissolve in measured quantities water, enter in fusion and emulsify at stirring to formation homogeneous masses and complete its cooling. Finished
plaster are packed in banks with dark glass.

Standardization ready product spend by reactions truthfulness andquantitative content epiline citrate (3.8 - 4.2 %), organoleptic indicators. The patch "Ureaplast" (*Emplastrum "Ureaplastum"*) contains urea 20.0 parts; water 10.0 parts; bee wax 5.0 parts; lanolin 20.0 parts;

lead plaster 25.0 parts.

It is used as a keratolytic agent in the treatment of onychomycosis. PLASTERS RESIN-WAX

The basics resin-wax plasters there are alloys resin and wax. To their warehousecan enter also fats and carbohydrates. Most widely appliescallous plaster.

Callus plaster (*Emplastrum ad clavos*) contains *:* acids salicylic 20.0 parts; rosin 27.0 parts; paraffin 26.0 parts;
petrolatum 27.0 parts.

Homogeneous soft, sticky, but not viscous mass of yellow or dark yellow color. The melting point is not above 60 °C. Molten plaster has characteristic scent rosin.

Applicable as means for removal callus (keratolytic means).

Preparation of a corn plaster. In a reactor with a steam jacket and a weighed amount of rosin, paraffin and petrolatum is placed in a stirrer and are melting. Alloy filter in warm in the form of through kapron grid. INfiltrate dissolve at stirring acid salicylic. Received The homogeneous mass is poured into 3.0g molds and cooled. Each piece plaster wrap in paraffined paper and are packing in cardboard pencil cases.

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

3. Rubber plasters

Rubber plasters were first proposed in 1888 and represent by yourself mixture rubber from resins, medicinal and auxiliarysubstances. They acquired wide dissemination thanks to to many advantages compared to other plasters. Rubber plasters last a long time retain their stickiness; significant amounts of medicinal substances can be added to them substances without changing their consistency; they are harmless to human organism; not enter in interaction with medicinal substances and convenient in application.

To rubber plasters belong adhesive plaster, adhesive plaster bactericidal,

callous "Salipod", pepper, mustard seeds.

Adhesive plaster (*Leucoplastrum*). Sticky plaster elastic anointed (*Emplastrum adhaesivum elasticum extensum*). The patch has the following *composition:* rubber natural 25.7 parts; rosin 20.35 parts; zinc oxide 32 parts; anhydrous lanolin 9.9 parts; liquid paraffin 11.3 parts; neozone D 0.75 parts.

All starting materials must be free of water. Residual moisture in materials should not exceed 0.5%, because the patch will initially sticky and wet, and then it will fall off the fabric and crumble. Rosin provides plaster mass bigger adhesiveness and contains resinous acids, which manifest irritating effect on the skin. To neutralize these acids, zinc oxide, in result what are formed to resynthesize. Zinc oxide does

drying effect, thereby preventing excessive smearing of the patch. Lanolin and Vaseline butter perform role plasticizers. For elimination process

"aging" in mass enter anti-aging — substances, What slow down oxidation rubber. It neozone D (phenyl-P-naphthylamine), paraoxydephenylamine, edgeright (aldolanaphthylamine). As a solvent apply gasoline.

Technology preparation. Adhesive plasters receive on basis rubbersimple long-term mixing (for 6 hours) separately prepared:

- rubber glue (solution in gasoline rosin and rubber);
- pastes (homogenized mixture of lanolin withanti-aging);
- zinc foundations (homogenized mixture lanolin, wax and zincoxide).

The prepared plaster mass is applied to a moving chiffon ribbon using with help adhesive coating (spreading).

On stuffed ribbon are omitted than 5, establishing clearance 0.35 - 0.40mm. The adhesive mass from the hopper is applied to the fabric in front of the knife. As the tape moves The knife evenly distributes the leukocyte mass across the entire width of the tissue. Speed of movement ribbons 7.5—8.5 m/min.

At passing ribbons over heated stove (temperature 100 – 105 °C) gasoline evaporates from the applied layer of leucomas, its vapors are sucked off through pipe *6.* For more complete evaporation gasoline towards movement ribbons heated air is supplied under pressure. The tape then passes through the drive shaft *4*over by

stream cold air (4-16) °C), which is served through hole *8* fan 7, after which it is wound onto the take-up roller. Upon completion receiving the tape onto roller *2,* the machine is turned off and the rollers are swapped, repeating the process of applying the leukomass to the tissue again. The required layer plaster masses achieved in result 5—6 smears. Layer plaster massesshould be of such thickness that a piece of chiffon with the spread mass measuring 5x5cm had mass 0.64—0.65 g for chiffon article 85.

The tapes are rewound from the roll using unwinding machines on cardboard spools in rolls length 1 and 5.2m. Further rolls cut on coilsof different sizes.

Sucked off couples gasoline are passing through adsorber, where they are absorbed and then desorbed. The regenerated gasoline is reintroduced into production.

Adhesive plaster maybe to graduate in small packaging in in the form of stripes 4x10 cm and 6x10 cm in size on stapled canvas, covered with a protective layercellophane, on 10 pieces in package.

In the finished plaster, the following are determined: the uniformity of the applied layer (per 1m ^{2} the patch must contain at least 120 g of leukomas); peel-off adhesiveness - at least 10 kPa; acid number 32-37;number zinc oxide 29-34 %.

An adhesive plaster can serve as a base for applying medicinal substances. Such, in particular, there are **adhesive plaster bactericidal** (Emplastrum adhesive bactericidal), What consists of with gauze gaskets, soaked solution antisepsis *composition:* furatsilin 0.02%; synthomycin 0.08 %; brilliant green 0.01% in 40% ethyl alcohol), and has a fixing adhesive tape tape. The patch is covered with a protective layer of starched gauze and cellophane. Plaster produced in various sizes.

Pepper plaster (EmplastrumCapsici). It is a homogeneous adhesive a yellow-brown mass with a peculiar odor, applied to paper or cloth, sizes 12x18, 10x18, 8x18cm, and two pairs of plasters are placed in a package, covered with a protective layer of cellophane.

It is used as a painkiller for gout, arthritis, sciatica, lumbago and distracting remedy for colds diseases.

Technology production pepper plaster consists of with processes preparation

rubber glue, paste pepper and flour base.

Rubber glue is prepared in a reactor with a steam jacket and a stirrer, which receive dissolving in gasoline rubber, rosin and antioxidant. Separatelyare preparing pasta pepper. For this mix thick extract legume pepper11 %-value from part molten and chilled to temperatures 40—50°Lanolin, add belladonna extract thick 0.3% and 0.3% tincture arnica. Pasta pepper enter in rubber glue and mix 30 min. IN reactor with pepper paste and rubber glue add a solution of rosin in gasoline and mix 60 min.

For preparation flour foundations take wheat flour, mix from heated lanolin, vaseline oil and a solution of rosin in gasoline. This basis ground fabric ribbon with madapolam, to the point or chintz, and then apply pepper leukomas on installation USPL-1. On this equipment a one-time application of the plaster mass and its drying are provided. The basis movement ribbons in drying camera laid down spiral-shaped trajectory. Dryer compact, small sizes and in technological cycle has three zones. IN the first Two zones use heated air (35-40 °C and 65-75 °C, respectively, The speed of the web is 0.8-1 m/s. In the third zone, the patch cools. Length ribbons is 250—300 m. General duration dryingplaster masses 50min. Yet more promising chamber-loop drying installation that allows the use of any backing materials (paper, non-woven materials). The tape with the adhesive mass *3* moves, using supporting rollers *4* passes drying rooms blocks *1* and heated heated by air through gas distribution cassettes *2*. The steam-air mixture enters the adsorber for gasoline regeneration.

Calloused adhesive plaster "Salipod" (Emplastrum adhesive ad nails "Sali-podum"). To warehouse adhesive plaster preschool installations fishing and sulfur.

Released in in the form of rectangular stripes fabrics in size 6x10i 2x10cm, from above protected cellophane.

Plaster styptic "Feracryl" (Emplastrum haemostaticum "Feracrylum") represents by yourself ribbon adhesive plaster with gasket, What consists of from layers gauze, soaked solution feracryl. Feracryl — it incomplete

ferric salt of polyacrylic acid, which has the ability to form clots from proteins blood.

Mustard seeds

Mustard plasters (*Sinapismata*) are a variety of rubber plasters that are issued in in the form of rectangular stripes paper in size 8x12.5 cm, coveredpowder skimmed seed mustard thick 0.3—0.55mm.

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

Applicable as antiphlogistic counterattraction.

The raw material for mustard powder is mustard seeds. (*Seminar Sinapisjunceae (Sinapisjunceae*) and black (*Seminar Sinapis nigrae*) mustard, What contains glycoside sinigrin, which splits under by action enzyme myrosin on glucose, potassium hydrosulfate and essential mustard oil (allyl isothiocyanate). Essential oil causes severe irritation and hyperemia of the skin. Seeds after falling (removal) of the shell is subjected to grinding to medium fineness and from them A hydraulic press is used to extract the fatty oil. The remains of the fatty oil from the cake extract in devices type Soxhlet. Presence fatty oils negatively affects the quality of mustard plasters - the therapeutic effect slows down and their shelf life decreases (mustard powder becomes bitter and flakes off)from paper).

Preparation of mustard greens. The technological process consists of five stages:

1. preparation rubber glue;
2. preparation mustard masses;
3. smearing masses on paper, drying, cutting roll andinvestment mustard plants in feet;
4. packaging;
5. recuperation gasoline.

Preparation rubber glue. For this in glue mixer placed steamed for 24—36

hours and cut on pieces rubber, addgasoline and turn on the paddle mixer for 30-40 minutes. Then the mass is filtered. Received glue (1.35— 2 %-th solution rubber in gasoline) represents by yourself thick sedentary mass, What light is transformed in jelly-like mass in measure weathering gasoline.

Preparation of mustard paste. Mustard paste is a mixture of rubber glue and mustard powder in a ratio of 1:1—1.1:1. The content of essential oil in mealshould be at least 1.11%. The rubber glue is placed in a mixer, added sifted from big particles and outsiders impurity mustard powder and Mix until a homogeneous mass is obtained. The finished mustard mass is pumped serve on the table with a bathroom for smearing.

Production mustard plants. Process smearing, drying and slitting is performed on a continuous machine. Paper rolled into roll, passes through clearance between stove table and a bathroom. Passing by under a bathroom, The paper is covered on top with a layer of mustard paste 0.3-0.5 mm thick, then enters the drying chamber (drying time 45 minutes, air temperature 80 °C). Steam-air mixture, What is formed in camera, from gasoline gradually sucked and is served to the stage recovery gasoline.

Dried ribbon cut on leaf cutter car on letters in size75(76)x90 cm, which are cooled for 24 hours, then the sheets are cut into individual mustard plants and rejected.

Packaging. Mustard seeds are packed in packages on 10 pieces. Every tenth sinapism has on one side inscription about way application. Packages are packed in packs of 600 pieces and stored in a dry place. Shelf life8 months. In the presence of moisture, sinigrin hydrolysis occurs, and mustards lose activity.

Standardization ready products is being held by quantitative content allyl isothiocyanate, which must contain at least 0.0119 g in mustard plasters (100 cm ^{2}).
Mustard powder, immersed in water for 5-10 s at a temperature of 37 °C and applied tight to skin hands, should cause strong irritation, burning and redness skin no later than through 5 minutes.

Now are releasing also "Mustard package", What represents by yourselfheat-sealed bag made of porous paper that does not get wet, on both sides or on one side

and paper with polymeric coating with the second. Package full mustard mixture. Mustard-pack is released in size 11x10 cm and divided on four identical bags. Every bag evenly full mustard mixture.

4. Plasters liquid, or leather adhesives

Liquid plasters, or leather adhesives (Emplastra liquida) are viscous liquids that leaves an elastic sticky residue on the skin after the volatile solvent has evaporated strong film. They are used as epidermal and endermatic plasters. The adhesive film in them is formed due to film formation during drying. solutions rosin, nitrocellulose (in form collodion), perorvinyl and formaldehyde resins in organic solvents (ether, ethanol, acetone, less often chloroform, dimethylformamide). For granting films larger elasticity toThe composition of the adhesives includes vegetable oils, linethol, dibutyl phthalate, triacetin, alcohol cetyl Liquid plasters are released in bottles and in aerosol packaging. The latter are widely used as sterile dressing material. in inpatient and outpatient treatment in gynecology, dermatology and surgery.

Adhesives are conventionally divided into *collodion adhesives,* which include collodion, collodion elastic, callous liquid, liquid Novikova, colaplast and microplastic and*resinous* — cleol, furaplast, glue BF-6, cerigel.

Collodium (*Collodium*). *Composition* of the preparation: colloxylin 4.0 parts; alcohol ethyl 96% 20.0 parts; ether medical 76.0 parts. It shows by yourself colorless or yellowish, transparent or slightly opalescent syrupy liquid from the smell of ether. Contains 4% colloxylin.

Preparation of collodion. The required amount of alcohol is weighed into the reactor. Colloxylin is crushed carefully because it is an explosive substance. (mixture mono- and dinitrocellulose cellulose), dare and placed in reactor,Wetting it with alcohol, add the rest of the alcohol and a measured amount of ether. They leave in good closed reactor to complete dissolution colloxylin.

Because colloxylin — explosive substance, ago its often are transporting in the form of safe water jelly beans At cooking water patch with jelly displace ethanol, and formed at this alcohol gel colloxylin dissolve in on air. Collodion is released in bottles of 5 and 15 ml.

Used to secure surgical dressings and coverings to the skin small wounds.

CONTROL qualities ready products spend on cleanliness. For this to 5mldrug add 20ml water, shake and filtered out from sediment, What formed. Filtrate should have neutral reaction. Sukhoi remainder mustbe from 3.8to 4.2%.

Collodion elastic (*Collodium elasticum*) -collodion, to whose added 3 %oil castor oil as plasticizer.

Corneal liquid (*Liquor adclavos (adclavos*) contains in to his/her *in stock:* acids salicylic 1 part; ethanol 96% 1 part; collodion 8 parts; diamond green 0.01 parts.

Liquid Novikova (*Liquor Novicovi*) has *composition:* tannin 2 parts; brilliant green 0.2 parts; ethanol 96 %-value 0.2 parts, oils castor oil 0.5 parts and collodion 20 parts.

Applicable for processing small wounds skin and cracks.

Colaplast (*Collaplastum*) — it 5 %-th solution oils castor oil in collodion.

Microplastum is a 1% solution of *levofloxacin* in colaplasty.

Resin glue presented cleol, furaplast, glue BF-6, cerigslem.

Cleol (*Cleolum*) consists of: with rosin 45.0 parts; alcohol ethyl 95%-of 37 parts; ether medical 17.0 parts; oils sunflower 1.0 part.

Glue represents by yourself transparent glue thick liquid yellowish- or reddish-brown colors from the smell of ether, weakly acidic reaction.

Applicable for fixation surgical bandage on surfaces skin.

Preparation *of cleol.* The required amount of alcohol is weighed into the reactor. Rosin grind, dare and are packing in gauze bag, which hang in reactor from alcohol for dissolution rosin (gravitational way).To received solution add measured number sunflower oils and ether,

dissolve at stirring. Solution defend for days and filtered.Pouring in vials on 50.0ml.

Standardization drug spend by acidic by number (60—93) and dry remainder (45-54) %).

Furaplast (from **perchlorovinyl)** (*Furaplastumcum Perchlorvinyl*). Its

composition: furatsilina 0.25 parts; resins perchlorovinyl (film former) 100.0 parts; dimethyl phthalate (softener) 25.0 parts; acetone 400.0 parts; chloroform 475.0 parts. It is a light yellow liquid syrupy consistency with the smell of chloroform. Available in glasses orange glass on 50 ml.

Applicable for processing small injuries skin with formation elastic films, stable to influence water.

BF-6 glue is a 20% ethanol solution of synthetic formaldehyde resins from the resole group. Contains polyvinyl butyral (butvar) as a plasticizer. Released in vials on 10th 20ml.

Applicable for processing sad and cracks.

Cerigel (*Cerigelum*) contains: polyvinyl butyral 4.0 parts; cetylpyridinium chloride 0.2 parts; ethyl alcohol 96% 100.0 parts. Glue — colorless opalescent, somewhat viscous liquid from smell alcohol.

Released in glass vials on 400ml. They keep liquid adhesives in tightin sealed bottles in a cool, dark place, away from fire.

Applicable for formation films on hands surgeon and medical staff before operations and medical manipulations-

we at blanks blood, production bacterial drugs and blood substitutes. Plaster has significant antibacterial activity.

Films and sponges made from animal tissues. In modern medicine a group of drugs is used that can be conditionally classified as patches — These are hemostatic and wound-healing preparations from animal tissues in the form of films and sponges.

Film fibrinous isogenic (*Membranula fibrin isogene*) represents by yourself fibrin derived from human plasma fibrinogen and impregnated with a solution glycerin.

Has a hemostatic effect, promotes tissue regeneration and wound healing. Film, abandoned in organism, dissolves.

Released in in the form of films **in** sterile glass test tubes.

Isogenic fibrin sponge (*Spongia fibrinosa isogena*) - porous fibrin, obtained from human blood plasma. In appearance it is a dry porous mass white or

cream-colored, in size 2x2x1or 6x2x1cm.

Applicable locally for hemostasis at injuries and operating bleeding. Dissolves in wounds.

Released in sterile glasses.

Sponge **hemostatic** collagen (*Spongia haemostatic collagenica*) made from a 2% collagen solution with the addition of furacilin and acidboron.

Dry, porous mass of yellow color in the form of plates, soft, elastic consistency, What absorbs well liquid.

Detects hemostatic and antiseptic action, stimulates regeneration fabrics.

Available in the form of plates measuring 5x5 or 10x10 cm, packaged in packages with polyethylene.

Film "Clothes" (Membrane "Oblecolum") -it plates with collagenwith by adding 1:100 oil sea buckthorn.

Apply externally for treatment wounds.

They release plates in size 5x5 or 10x10cm in polyethylene packages.

Sponge gelatinous (*Spongia gelatinosa*) is formed from specially processed gelatin food. Dry porous mass white color.

It has a hemostatic effect. Released in packaging on 0.6 g.

Sponge antiseptic with kanamycin (*Spongia antiseptic Kanamycin* ()

— dry porous mass yellowish color. Contains gelatin from by adding kanamycin sulfate, furatsilin, calcium chloride.

Has hemostatic and antimicrobial action.

Released in in the form of pieces by mass 0.5 — 0.7 g in transparent paper andpolyvinyl chloride packages; 10 each sponges in the package.

· **Materials of activation applicants higher education under time carrying outlectures: question, situational tasks etc:**

Question:

1. What such TTS?

2. As classify TTS.

3. Specify foundations for TTS.

4. Explain appointment auxiliary substances. IN whose cases theirused?

5. Point examples auxiliary substances.

6. Specify which value pH have for TTS?

7. Or use alcohols in production TTS?

8. As can improve technological TTS?

9. Which requirements qualities of TTS presents State Federal University?

10. Rate prospects industrial production TTS.

General material and bulk-methodical software lectures:

- educational rooms – audience departments;
- equipment - computer, tables;
- equipment – multimedia projector;
- illustrative materials – presentation, slides.

Question for self-control:

1. What such Band-aids?

2. As classify plasters.

3. Specify foundations for plaster.

4. Explain appointment auxiliary substances. IN whose cases theirused?

5. Point examples auxiliary substances.

6. Specify which value pH have for Band-aids?

7. Or use alcohols in production Band-aids?

8. As can improve technological Band-aids?

9. Which requirements qualities of plasters presents State Federal University?

10. Rate prospects industrial production plasters.

11. WITH what consists of process receiving different Band-aids?

12. Name it drugs, What are issued in in the form of plasters.

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- Lecture materials, methodological developments for seminar classes and

independent works on department social pharmacies: Regime access : http://socpharm.nuph.edu.ua.

- Scientific library NUPh: Regime access :http://dspace.ukrfa.kharkov.ua; http://lib.nuph.edu.ua
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Lecture No. 19

Topic **: "Transdermal therapeutic systems. General characteristics, classification, controlled release system"** - 2 hours

Topicality topics: Technology medicines (industrial technology medicalmeans) – there are one with fundamental technological Sciences. She consists of several key aspects that important for modern medicine and patients: Effectiveness and safety - Modern technologies allow the production of medicinal products drugs with high efficacy and safety for patients. Accurate dosage, CONTROL qualities

and absence impurity do medicine more effective and safe. Innovations in medical in the field of: New technology allow create innovative medicines that can be more targeted and effective medical therapy. For example, medicine, designed for accurate influence on specific cells or genes, provide more effective treatment. Minimization side effects effects: Technologies allow elaborate medicinal formulas that minimize side effects and negative effects on the body. This provides more comfortable and safe treatment for patients. Fast production and supply process: The use of modern technologies allows speed up the process of producing medicines, which is especially important in conditions rapidly changing medical environment, such as spread diseases or epidemics. Individual approach to treatment: Technologies allow elaborate medicine, which take into account individual features patient,which leads to a personalized approach to treatment and increases its effectiveness efficiency. Economy and accessibility Improved technology production can reduce production costs, making medicines more available for wide circles patients, providing economic efficiency in field health care.

Thus, the use of modern technologies for the production of medicinal products drugs there are important factor for improvement efficiency treatment, security patients and general state public health.

Goal: Learn general technological scheme production nano- and radiopharmaceuticals drugs, to get acquainted with proper by the rules production. Learn methods stabilization nano- and radiopharmaceuticals drugs, be able get nano- and radiopharmaceuticals drugs with different medicinal and auxiliary substances, carry out gradual CONTROL and be able standardize finished product in accordance to regulatory and technical requirements documentation, be able draw up technological schemes production.

Basic concept:

- *transdermal therapeutic systems* (TTC) - dosage forms for dosed, continuous administration of medicines into the bloodstream through the skin, bypassing the gastrointestinal tract and avoiding the disadvantages of injection

administration.

- *hydration of the surface epithelium* — the higher the hydration, the higher the permeability;
- *pH value* — according to the pH distribution theory, only non-ionized forms of medicines can overcome the barrier of lipid membranes in significant quantities.
- *presence of penetrants* — medicines transport through the skin can be more intense when using special substances.

Plan and organizational structure lectures:

No. No. p.p.	**Main stages of the lectureand their content.**	**Whole levels abstractions.**	**Lecture type,lecture equipment.**	**Distribution time.**
1	**2**	**3**	**4**	**5**
I	***Preparatory stage*** Definition of traininggoals. Software positive motivation.		Lecture combined	1%
P 1. 2. 3.	***Main stage*** Presentation lecture hall material. Plan: The concept of*transdermal therapeutic systems* (TTC). Description of transport of LR. TTC classification according to the technological principle	I	Slides	1% 2% 90%

III4. 5. 6.	***Final stage*** Resume lectures, general conclusions. Lecturer's answers topossible question. Tasks forself-training student.	II III	List literature, question, task.	2% 3% 2%

Structurally logical scheme content lectures

1. Concept about TTS.
2. Advantages of TTS.
3. Membrane transdermal systems .
4. Structure of transdermal therapeutic systems

Content lecture hall material (text lectures)

TRANSDERMAL THERAPEUTIC SYSTEMS

It is known that some medicinal substances (acetylsalicylic acid, indomethacin, scopolamine, nitroglycerin, etc.), which are administered orally, significantly affect the gastrointestinal tract and often cause its diseases. Although the introduction into the blood by injection prevents their harmful effects on the gastrointestinal tract, it cannot ensure uniform, dosed and long-term administration of drugs. Therefore, in many countries of the world, dosage forms for dosed, continuous administration of medicines into the bloodstream through the skin have been developed, bypassing the gastrointestinal tract and avoiding the disadvantages of injection administration. These are *transdermal therapeutic systems* (TTC). Transdermal drug delivery has a number of advantages:

+ the ability to avoid problems associated with oral administration: inactivation or reduction in drug activity as a result of metabolism in the gastrointestinal tract and liver, as well as associated adverse reactions;

+ ensuring a constant concentration of the drug in the blood without concentration fluctuations and associated adverse reactions;

+ possibility of immediate discontinuation of treatment in case of adverse reactions;

+ reducing the frequency of administration by delivering the required dose of the drug over a longer period of time;

+ convenience of using the drug by patients;

+ reduction of the required dose of the drug, as drug losses associated with metabolism are reduced.

At the same time, there are some limitations to transdermal delivery of medicines:

+ possible skin irritation or contact sensitization, caused by adverse interaction of active or inactive components of the system with the skin;

+ transdermal drug delivery system can only be used for substances that have certain physicochemical properties and the ability to penetrate the skin in a therapeutically effective amount.

When using TTC It is necessary to take into account not only the physicochemical properties of the medicines, but also the physiological state of the skin surface (inflammation, degree of damage to the stratum corneum, permeability, age and ethnic differences, etc.).

The process of dermal absorption of LR depends on the intensity of blood supply and the chemical composition of the skin surface. The blood supply to the skin comes from the deep part of the dermis. In the skin, 60 *% of the blood* is venous. Healthy skin is a good barrier to various environmental factors. Keratin, which is formed in the cells of the epidermis, gives it resistance to various mechanical, physical and chemical effects. Lipids, which are expelled by the sebaceous glands, mixing with the lipids of keratinocytes, form a fatty lubricant on the surface of the skin, which ensures its permeability and bactericidal properties. From the point of view of the physicochemical laws of diffusion, the skin is considered as a simple membrane.

A randomized model has been proposed to describe the transport of medicines

across the surface epithelium. According to this model, medicines transport can occur along three parallel routes:

1) through cellular and intercellular space;

2) through the intracellular space;

3) through lipid layers placed between protein-rich cells and the surface epithelium.

The rate of release of medicines depends on the surface area of the skin area on which the medicines is located, as well as on the composition of the TTC and the method of application.

Among the factors that affect skin permeability are:

- *hydration of the surface epithelium* — the higher the hydration, the higher the permeability;
- *solubility of medicines in the surface epithelium* ;
- *the presence of excipients* - solvents and surfactants can enhance the permeability of LR through the skin;
- *pH value* — according to the pH-distribution theory, only non-ionized forms of LR can overcome the lipid membrane barrier in significant quantities. Diffusion of ionized drugs through the skin will be insignificant, especially at pH values that favor ionization of molecules;
- *binding of medicines to the skin* - the skin acts as a reservoir for some medicines molecules. In this case, the bound fraction of LR is unable to diffuse into deeper layers, which reduces the degree of permeability and increases the absorption time;
- *metabolism of medicines in the skin* — metabolism of medicines during transport through the skin affects bioavailability and is the reason for significant differences between the results of *in vivo studies* and *in vitro.* Oxidation, reduction, and hydrolysis are kinetic processes that affect the transport of medicines through the skin;
- *presence of penetrants* — transport of LR through the skin can be more intense when using special substances that enhance skin permeability, penetrants. Ionogenic surfactants provide transdermal passage by destroying the lipid layers

of the surface epithelium and by denaturing keratin.

Based on existing TTC classifications Technological and pharmacokinetic principles are laid down.

TTC classification According to the technological principle, there are four types:

1) *systems based on semipermeable membranes* (transderm-skop — with scopolamine; transderm-nitro — with nitroglycerin; catapres TTC — with clonidine; estraderm — with estradiol);

2) *polydisperse systems based on adhesives saturated with medicinal substances* (systems with nitroglycerin - Nitrodur II , Deponit, Minitran; system with isosorbide dinitrate - Frandol);

3) *dispersed systems based on polymeric non-cohesive matrices* that provide a given diffusion rate (systems with nitroglycerin - nitrodur, NTS);

4) *polydisperse microreservoir-type systems* (with nitroglycerin - nitrodisk; contraceptive system with progestin and estrogen).

Membrane transdermal systems are a complex structure consisting of four layers:

a) impermeable upper membrane;

b) a permeable layer containing the medicinal substance;

c) a microporous membrane filled with a non-polar material (e.g., paraffin);

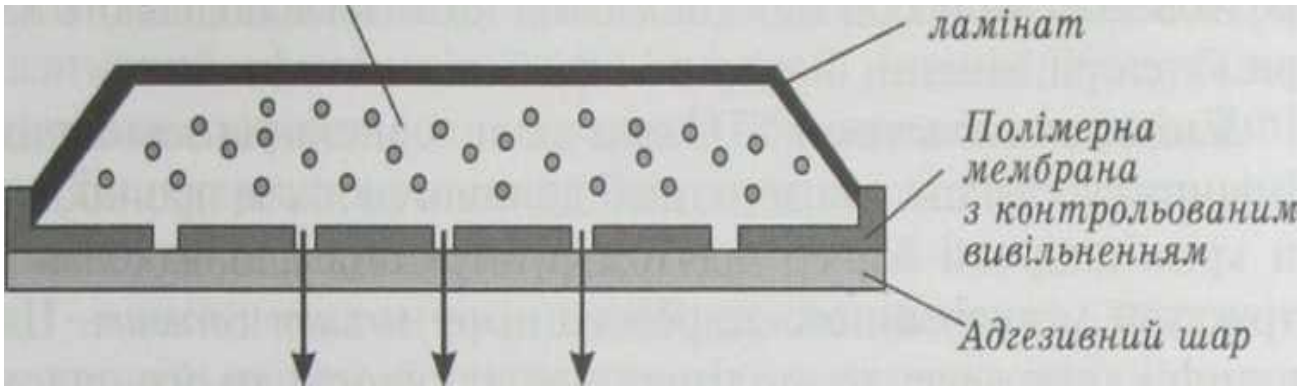
d) an adhesive layer that ensures contact of the system with the skin. In early TTC models each function was provided separately by one of components (Fig. 16.2). These systems, known as "raviolli" (raviolli systems), are made by introducing a solution or gel with medication into the space between the main membrane and the reservoir with medication, then they are thermally welded with a membrane that controls the level of drug release, covered around the perimeter with glue that sticks together when pressed, and a protective film. The manufacturing process is inconvenient, and the patch itself is quite bulky

Achievements and prospects for the development of pharmaceutical technologies.

Structure of transdermal therapeutic systems

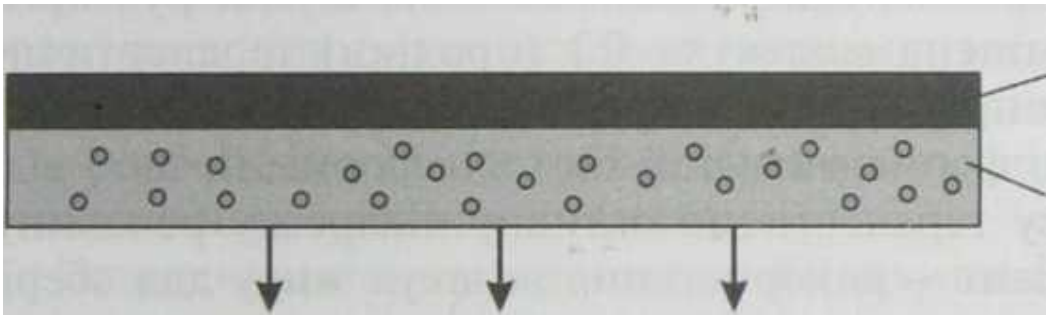
Ravioli - mun

Hermetic metal-plastic



Matrix type

Sealed lining



Adhesive matrix reservoir with drug

In the new TTCs , so-called matrix systems (matrix systems), the adhesive that sticks together when pressed, performs various functions: adhesion, storage, drug release, and control of the drug release rate (Fig. 16.2). The process of manufacturing a matrix system is relatively simple, and the patch is very thin. However, it is sometimes difficult to find an adhesive that will last for the duration of its action. TTC can dissolve drugs and release them without crystallization or phase separation. Moreover, the dissolution and release of the drug can reduce the adhesive force and adhesion to the skin.

Technologies for improving TTC . Today, many approaches are being investigated to overcome the barrier properties of the skin and improve the possibilities of using TTC . To achieve new developments, it is necessary to develop technologies by which drug permeability could become reversible, predictable and controlled. Methods for improving technologies are divided into three categories: chemical, biochemical and physical.

Chemical improvement TTC leads to the use of external chemical substances to

help drugs penetrate the skin barrier by disrupting the ordered structure of the intercellular fat layer *stratum* This modification leads to improved fluidity of this layer and solubility of drugs in the stratum corneum .

In *biochemical modification,* the drug molecule undergoes a short-term physicochemical change that facilitates its movement through the stratum corneum. The modified drug molecule (prodrug) is therapeutically inactive. After penetration into the stratum corneum, it undergoes hydrolytic or enzymatic biotransformation to restore the original therapeutically active drug substance.

Another option is to use lipid vesicles to store drugs (similar to liposomes), which can penetrate the skin and self-deposit in the stratum corneum, where they can act as controlled-release systems.

Physical enhancement of transdermal drug delivery systems uses external stimuli to drive the drug across the skin. External forces induce reversible physical changes within the stratum corneum. Three approaches are used: *iontophoresis, phonophoresis,* and *electrophoresis.* These approaches help deliver large ionic molecules of peptides or proteins that cannot be delivered by passive diffusion across the skin. In addition, the level of delivery is well controlled by the magnitude and duration of the external stimuli.

Currently, research on the development of TTC are carried out in the following areas: search for new polymer materials; expansion of the range of solvents; expansion of the range of medicines that can be used in TTC .

Materials of activation applicants higher education under time carrying out lectures: question, situational tasks etc:

Question:

1. Describe the role of TTS and their placein medicine and pharmacy?
2. Using TTS in production medical drugs.
3. Give definition concept
4. What are *the systems based on semipermeable membranes* ?

General material and bulk-methodical software lectures:

- educational rooms – audience departments;
- equipment - computer, tables;

- equipment – multimedia projector;
- illustrative materials – presentation, slides.

Question for self-control:

1.C what consists of process receiving different TTS?

2.Name it drugs, issued in in the form of TTS.

3. Basic principles and directions of TTS development.

4. Describe TTC improvement technologies .

List used sources:

1. Educational manual for independent works students Faculty of Pharmacy for the licensing exam "Step 2. Pharmacy" / V.Yu. Anisimov, O.I. Belyaeva, G.G. Vidavskaya, V.O. Helmboldt, A.V. Zamkova, I.V. Lytvynchuk, A.V. Nikitin, B.V. Prystupa, I.B. Petkova, Ya.V. Rozhkovsky, S.B. Meeting, L.M. Unguryan, N.C. Physiotherapist Odesa: Odessa National Medical University. university 2020. - 240 with.

Regime access to texts lecturesfor students pharmaceutical faculty: https://info.odmu.edu.ua/chair/drugs/files/390/ua

Literature, which used lecturer for preparation lectures.

Main:

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"Ukrainian Scientific Pharmacopoeial Center for the Quality of Medicines" - 2nd ed. – Kharkiv: State Enterprise “Ukrainian Scientific Pharmacopoeia” quality center medical means", 2014. – T. 2. – 724 p.

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Electronic informational resource

- Lecture materials, methodological developments for seminar classes and independent works on department social pharmacies: Regime access : http://socpharm.nuph.edu.ua.
- Scientific library NUPh: Regime access :http://dspace.ukrfa.kharkov.ua; http://lib.nuph.edu.ua
- www.moz.gov.ua – official website Ministries security health Ukraine
- nuph.edu.ua – official website National pharmaceutical university
- library@nuph.edu.ua – website libraries NUPhU
- Website departments ZTL National University of Physics and Technology. – Regime access: ztl.nuph.edu.ua.
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Lecture No. 20

Topic: "Production nano- and radiopharmaceuticals drugs" - 2 hours

Topicality topics: Technology medicines (industrial technology medicalmeans) – there are one with fundamental technological Sciences. She consists of several key aspects that important for modern medicine and patients: Effectiveness and safety - Modern technologies allow the production of medicinal products drugs with high efficacy and safety for patients. Accurate dosage, CONTROL qualities and absence impurity do medicine more effective and safe. Innovations in medical in the field of: New technology allow create innovative medicines that can be more targeted and effective medical therapy. For example, medicine, designed for accurate influence on specific cells or genes, provide more effective treatment. Minimization side effects effects: Technologies allow elaborate medicinal formulas that minimize side effects and negative effects on the body. This provides more comfortable and safe treatment for patients. Fast production and supply process: The use of modern technologies allows speed up the process of producing medicines , which is especially important in conditions rapidly changing medical environment, such as spread diseases or epidemics. Individual approach to treatment: Technologies allow elaborate medicine, which take into account individual features patient,which leads to a personalized approach to treatment and increases its effectiveness efficiency. Economy and accessibility Improved technology production can reduce production costs, making medicines more available for wide circles patients, providing economic efficiency in field health care.

Thus, the use of modern technologies for the production of medicinal products drugs there are important factor for improvement efficiency treatment, security patients and general state public health.

Goal: Learn general technological scheme production nano- and radiopharmaceuticals drugs, to get acquainted with proper by the rules production. Learn methods stabilization nano- and radiopharmaceuticals drugs, be able get nano- and radiopharmaceuticals drugs with different medicinal and auxiliary substances, carry out gradual CONTROL and be able standardize finished product in accordance to requirements

regulatory and technical documentation, be able draw up technological schemes production

Basic concept:

Radiopharmaceutical drug (English: *radioparmaceutica drug*) — any which pharmaceutical product, which contains one or more radionuclides (radioactive isotopes) incorporated into a composition with diagnostic or therapeutic purpose. Requirements, regarding storage radiopharmaceuticals drugs.

Radiopharmaceutical preparation has have passport, What contains such information: activity drug number drug in milliliters or milligrams; specific; concentration solution; time measurement; precision measurements taken.

Plan and organizational structure lectures:

No. No. p.p.	**Main stages of the lectureand their content.**	**Goals inlevels abstractions.**	**Lecture type, equipment lectures.**	**Distribution time.**
1	**2**	**3**	**4**	**5**
I	***Preparatory stage*** Definition of training goals. Software positive motivation			
1. 2.	***Main stage*** Presentation lecture hallmaterial. Plan: The concept of radiopharmaceutical drug . Diagnostic method by with help radiopharmaceuticalof		Lecture combined	1% 2%

II 3. III 4. 5. 6	the drug . Measurement radioactivity andspecific activities radiopharmaceuticaldrug Storage radiopharmaceuticals drugs ***Final stage*** Resume lectures, general conclusions. Lecturer's answers to possible question. Tasks forself-training student.	 I II III	 Slides List literature, question, task.	 90% 2% 3% 2%

Structurally logical scheme content lectures

5. Concept about radiopharmaceutical drug .

6. Method diagnostics by with help radiopharmaceutical preparation .

7. Measurement of radioactivity and specific activityradiopharmaceutical preparation .

8. Storage radiopharmaceuticals drugs

Content lecture hall material (text lectures)

RADIOPHARMACEUTICAL PREPARATION (English) *radiopharmaceuticals* drug)

— any pharmaceutical product that contains one or more radionuclides (radioactive isotopes) introduced into the composition with diagnostic or For diagnostic purposes, short-lived R.p. are used, the action of which is whose register in organism by with help special devices (scintillators, single-photon emission tomographs and positronic (two-photon) emission tomographs), which catch γ-radiation tagged radionuclide. As tagged radionuclide most often use technetium-99. It short-lived nuclide with a half-life of about 6 hours. Used for diagnostics practically all organs. R.p., tagged technetium, constitute over 80% nomenclature R.p. For the purpose of diagnosis and treatment, they are also used radioactive isotopes Thallium-201 and -199, iodine-123 and -131, fluorine and etc.

The diagnostic method using R.p. is called scintigraphy, its uniqueness consists of in accuracy, reliability, opportunities reusable application, and the main thing — abilities diagnose disease on early stage. To R.p. put forward such requirements: good to be absorbed with blood certain organ, to retain radionuclide not associated with the drug (no more than 5% radiochemical impurities), to succumb biological decay and withdrawal with organism for certain time, provide creation minimal radiation loads on organism patient, to be characterized harmlessness, sterility and apyrogenic, be inexpensive and available.

The technology of R.p. consists of several stages: obtaining the necessary radioisotope; production of carrier reagent isotope; production tropical to organ drug, control quality.Measurement radioactivity and specific activities R.p. spend on animals; purity is determined by partition paper chromatography methods (or electrophoresis) and radiometric analysis. Radionuclide purity drug represents by yourself relation activities main radionuclide to general activity of the drug, expressed as a percentage, and is not a constant characteristic, and changes with by the way time. Radionuclide impurities — it impurities others radioactive nuclides (in percentage) to activities main nuclide on certain time (date); determination of radionuclide purity of R.p. is carried out by nuclear spectroscopy and radiometry; radiochemical purity, investigated chromatography methods and electrophoresis, corresponds in relation to activities radionuclide in the main chemical substance included in the drug, to the total activity R.p., expressed as a percentage. Radiochemical impurities are impurities of chemical compounds, different from the main substance that makes up the drug, but contain the sameradionuclide. The level of radiochemical impurities is expressed as a percentage of the total activity of the radionuclide in the preparation. Quantitative analysis is carried out by determining radionuclide activity in R.p. by β-, γ- and X-ray radiation regarding the standard sample by comparison. The R.p. must have a passport containing the following information: drug activity in millicuries (or becquerels); amount of drug in milliliters or milligrams; specific activity in millicuries (or becquerels) per 1 ml; total content of the substance in milligrams on 1 ml; concentration solution in milligrams on 1 ml; time measurement; accuracy measurements taken. R.p. are stored in accordance with the current Basic Sanitary Rules of Workwith radioactive substances and sources ionizing radiation, approved by the Ministry of Health of Ukraine, as well as special requirements. Expiration date R.p. is determined chemical stability and radiochemical composition of the drug, degree decrease activities drug with by the way time (by by law radioactive decay), increase relative content long-lived radionuclide impurities that have half-lives longer than the main one radionuclide. Recently, for the diagnosis and treatment of malignant neoplasms use radioactive drugs. Except that , radio pharmaceutical drugs allow diagnose

disease heartily - vascular systems ,kidneys , biliary ways , thyroid glands, etc.

Advantage using this one groups drugs consists of in simplicity application and relative harmlessness.

Feature assessments qualities radioactive drugs there are using near with chemical and physicist - chemical radiometric methods analysis .

Authenticity radionuclide in drug consider confirmed, if hardware spectrum ionizing radiation , removed with source ,

identical spectrum , semi-soluble from exemplary solution with that the same radionuclide and removed in those under the same conditions. absence exemplary sources and solutions with necessary radionuclide for installation authenticity radionuclide trace determine specific value energies individual lines spectrum ionizing radiation and their intensity . Measurement activities radionuclides are carried out by betta - or gamma- radiation, and also X-ray radiation in dependencies from type of radiation, What is released data nuclide .

Definition radionuclide cleaning is carried out method nuclear spectroscopy and radiometry, using various methods if necessary quantitative chemical separation of impurities.

Chemical separation of impurities significantly increases the efficiency of analysis.Radionuclide analysis includes three main stages:

1) detection of radionuclide impurities;2) identification impurities;

3) definition activities .

Radionuclide purity , as rule , should be not lower 99.5 %.

Radiochemical purity is most often investigated by methods chromatography and electrophoresis

Term suitability is determined next factors:

- Stability chemical and radiochemical warehouse drug ;

- Decrease in drug activity over time by lawradioactive decay ;

- Growth relative content long tenacious radionuclide impurity ,have periods half-life more , than basic radionuclide .

Representatives this one groups drugs:

Solution sodium phosphate , tagged phosphorus -32 , for injections (SolutionSodium phosphatidylcholine phosphorous -32 note for injectionibus) ***Na 3 P ^{32} O 4***

Properties . Colorless transparent liquid . Specific activity 2-10 μm/ ml. Relative activity R ^{32} in in the form of orthophosphate not Less 98 %.

Identification.

1. WITH nitrate zirconium in concentrated nitrogenous acid is formed white friable precipitate.
2. The absorption curve (beta radiation) of the drug should beidentical curve absorption betta - radiation exemplary solution R ^{32} .
3. Activity drug decreases with period half-life 14.2day. Radiochemical composition determine chromatographically (on paper) .

Specific activity measure on counting installation with detector betta - radiation by comparing the count rates from the tested solution and exemplary solution R ^{32} .

Quantitative definition phosphorus. Spectrophotometrically (on reactions with vanadate and ammonium molybdate). The optical density of the colored solution measure at 410 nm.

Storage. IN special cabinets for radioactive substances. Term suitability not more than 2 months.

Therapeutic use for polycythemia, myeloma, chronic leukemia ; for diagnosis of malignant neoplasms.

Solution sodium - iodohippurate, tagged iodine -131, for injections

Properties: Clear, colorless or slightly yellowish liquid. Specific activity not less than 0.1 mcurie / ml. relative activity of iodohippurate sodium at least 98 %.

Identification. Determined spectrophotometrically and by gamma-ray spectrum. radiation.

The activity of the drug decreases with a half-life of 8 days.Radiochemical composition determine chromatographically (on paper) .

Specific activity measurements are carried out using γ- or γ-radiation.

Quantitative definition about – iodohippurate sodium. Spectrophotometry (in UV- region) .

Storage. In special cabinets for radioactive substances whentemperature from +4 up to +10 ° WITH. Term suitability not more 20 days.

Application. For research functional activities kidneys.

Decontamination of work areas and equipment In all areas where are being carried out works with open radioactive sources, daily wet cleaning is carried out at least once a month. –Working equipment fastens by premises for works each class and stored in specially designated places. Radioactive contamination of external surfaces equipment, equipment, tool, laboratory dishes, surfaces working spaces should not exceed permissible levels of total pollution, What installed NRBU-97. IN all premises with permanent stay staff, appointed for works from sources radiation in open, daily wet cleaning should be carried out. Periodically, but not less often one once on month, is being done general cleaning with deactivation walls, floors, doors and external surfaces equipment. Cleaning is being organized with maximum application means mechanization. Dry cleaning production premises, by except vacuum, is prohibited. In premises permanent stay staff, where are working with sources in open in form, has be provided constant stock deactivating means and detergents solutions, What are getting there with taking into account properties radionuclides and their compounds, with which ones is going work, and also the nature of the surfaces to be decontaminated. After completion of the work, each employee has to remove own working place and at need decontaminate equipment, tools, work utensils that were used in the process of working with open sources. IN case pollution radioactive substances premises or their individual sections shall immediately begin decontamination. If pollution happened powder dry substance, then its collect slightly damp a rag, previously turning off ventilation. Big number spilled radioactive liquids are covered with shavings. After the main part of them number will be deleted, remains pollution are destroying processing special washing means. Deactivation contaminated surfaces carried out using soft brushes, swabs moistened with detergents, or in a way

flushing. After deactivation special washing by means surface abundantly washed with water and wipe dry clean with a rag.

Then spend control purity surfaces appropriate radiometric device. Radioactive pollution external surfaces equipment, instruments, laboratory glassware, surfaces of work spaces and departments for storing workwear should not exceed permissible levels. Used brushes, tampons collect in plastic bags or in others containers and delete asradioactive waste. As detergents means can to be used such solutions:

1) washing powder - 10 ml, lye - 10 ml, water - up to 1 l. 2) oxalic acid - 5 g, table salt - 50 g, detergent DS-RAS - 10 ml, water - up to 1 l. If not succeeded effectively to spend deactivation specified means, then for For additional surface treatment, a solution of potassium permanganate -40 g is used, sulfuric acid (specific gravity - 1.84) - 5 ml, water - up to 1 liter. Potassium permanganate dissolved in 1 liter of water heated to 600C, then cooled to room temperature temperature. In solution are pouring sulfuric acid acid and mix. If arable material unstable to solutions, What contain acids, for deactivation use alkaline solution caustic soda ash -10 g, trilon B - 10 g, water - up to 1 liter. Dissolve caustic soda in water, add Trilon B, mix until complete dissolution. For decontamination of valuable equipment and devices, prepare next solutions: - lemon acid - 10 g, water - to 1 l; - sorrel acid - 20g, water - up to 1 l; - sodium hexametaphosphate - 10-20 g, water - up to 1 l; - detergentOP-7 - 4 g, hydrochloric acid - 20 ml, sodium hexametaphosphate - 4 g, water - up to 1 liter. Acid or sodium hexametaphosphate is dissolved, stirring, in 1 liter of water at room temperature. At necessity deactivation surfaces with varnish- colored coating upper layer are being removed mechanical (combing) or chemical (using special solvents) methods. Clothing (aprons, sleeves, etc.) made of polyvinyl chloride and polyethylene can be deactivated in sodium hexametaphosphate solution - 10-20 g, water - up to 1 l. After decontamination floor and equipment carefully washed with water and wipe dry 84 Such premises have special requirements for ventilation, carry out constant dosimetric control by level radiation Air pollution. 3.5. Personal protection and hygiene measures at work with radioactive substances All personnel, which works or visits places works with open sources radiation, should be provided

personal protective equipment depending on the type and class of work. Since working with radioactive substances, sources of ionizing radiation and stay there, where with by them are working there are potentially dangerous. According to NRB stands out three classes works – AND , II and III. At works I-th class and individual species works II. class personnel provided overalls, hats, special underwear, stockings, easy shoes (rubber boots or shoe covers), gloves, paper towels and disposable handkerchiefs, and also with respiratory protection equipment (respirators, gas masks). When working In class II and certain types of work of class III, personnel are provided with gowns, hats, gloves, light shoes, and if necessary, protective equipment organs breath. InN premises for works with open radioactive sources prohibit: employees from being without the necessary means personal protection; storage of food products, tobacco products, cosmetics; working with a pipette without a bulb. Manipulations with a pipette are carried out with help rubber pears or use automatic dispensers from variables tips. All works with radioactive substances perform in cuvettes, covered layer filtering paper, which after works make up in plastic bags for collecting radioactive waste. After work is finished Each employee is required to clean their workplace, decontaminate dishes, tools and other equipment to extremely permissible levels, controlling their cleanliness radiometric devices. At exit from The premises where work with radioactive substances is carried out must be withdraw overall, mittens and others means individual protection, carefully to wash hands and verify their cleanliness on radiometric device. At immediateprocessing of leather, regardless of the degree of its contamination and the deactivating agent,up to 90-98% of unfixed radionuclides present on it are removed. Whenminor pollution (exceeding permissible levels by no more than 2.5 times) radioactive substances good are deleted under 85 time washing warm flowing with water with 72 %-m economic soap by with help hairy brushes. With a brush use without pressure, that not cause damage skin and penetration radioactive substances within organism. Water has be flowing with a temperature not higher than 35 $^{\circ}$C, since the use of hot water worsens the cleaning results. In the case when radioactive fixation has occurred substances in result their reactions with proteins skin, ordinary processing by with help water and cute not

effective. For removal final activities use detergents means depending from chemical properties radioactive substances: adsorbents (kaolin paste, "Novost" powder, etc.), complexing agents (Trilon B, trisodium salt, citric acid, unithiol, oxathiol, soda solution and etc.), weak solutions of acids (most often hydrochloric and citric). These agents destroy connections isotope with proteins skin, sorb radioactive substances and light washed away from skin. For deactivation leather covers can use the drug "Protection" and detergents solutions

Recipes detergents means, What are used for deactivation skin

No. solution	Composition	Mass, g	No. solution	Composition	Mass, g
1	Kaolin paste:kaolin (powder)soapy shavingssoda Water hot	64 15 3 18	5	Potassium permanganateWater	40 1000
2	Detergent OP10 (OP-7) Polycomplexon Water	50 10 950	6	Lemonacid Water	3 1000
3	Detergent OP10(OP-7) Trisodium salt Antibacterial preparation	4 30 1	7	Sodium bicarbonate Water	20 1000

	Water	1000			
4	Trilon B Sodium bisulfate Starch Sodium carbonate Water	5 5 5 35 1000	8	Salty acidWater	20 1000

At deactivation necessary consider chemical patterns, for example, pollution radioactive phosphorus unnecessary wash soap, because at this are formed insoluble phosphates. IN this case betteruse synthetic detergents, such as OP-10 or 2%-m solution soda.

Radioactive iodine light is being deleted at processing with water with soap and next using oxidizers (permanganate potassium) and processing sulfite solution. Using soap and water is effective for contamination of 42K and 24Na. IN others cases better to use complex forming means: Trilon B (for contamination with 90Sr and 59Fe); unithiol and oxathiol (for polluted 198Au and 203Hg); kaolin soap (at polluted 226Ra). At small pollution leather covers torso necessary carefully wash under the shower with 72% household soap or OP10. When necessity more thorough deactivation for 2 minutes spend processingsolution 3 (table 3.5). Heavily contaminated skin areas are first treated with a strong solution of potassium permanganate and a 5% solution of sodium sulfate. Then carefully are washing under shower. For rub-down processed surfaces skineasy use disposable napkins or cotton-gauze tampons, which then delete as solid radioactive waste.

If radioactive pollution accompanied small damage skin, then a.m. necessary few times to rinse warm with running water, and then artificially induce bleeding under a stream of water. Facial skin is disinfected with soap and water, hair with shampoo and water, until whose add 3% solution lemon acids. Eyes washed under with a stream of warm water with widely revealed eyelids. For prevention pollution tearful channels jet water send from internal corner eyes to external. IN case hit

radioactive substances to mouth necessary few times rinse its warm with water, and teeth and gums clean dentalwith a brush and paste, then rinse with a 3% citric acid solution. If a single treatment of body parts did not provide the necessary cleanliness, decontamination repeat. Ineffective repeated processing indicate on fixation isotope skin. This is signal for taking such persons under medical supervision. Radiation control is carried out by employees who have undergone special training. preparation, or representatives services radiation security.Individual CONTROL by doses irradiation staff spendone time on month; CONTROL by level pollution workers surfaces, equipment, workwear working and their leather cover - every time afterworks with radioactive substances; level pollution adjacent premises controlled once a quarter, control of the content of radioactive substancesin in the air workers premises - not less often two times per month, and in sewage waters -1 time on quarter. Data all species radiation control are registering in magazine.Staff who clean the premises and work with radioactive solutions and powders should be provided (except marked) plastic aprons and armbands or plastic half-robed, rubber shoes. At transition with premises for works more high class to premises more low class necessary control levels radioactive pollution means individual protection, especially safety shoes and hands. Protection from radiation irradiation includes:

1. Sealing sources radiation radiation;

2. Such a planning of the placement of working places to reduce any possibility radiation irradiation personnel;

3. Rational application sanitary and technical devices, equipment, means and events;

4. Using special protective materials; 5. Usingmeans individual protection;

5. Compliance rules personal hygiene.

Individual protection from radiation irradiation provides the following:

- Abbreviation duration working time in conditions irradiation;
- Magnification distances from sources radiation;
- Software employees special bathrobes, hats, gloves (to protect hands),

arm warmers, glasses (to protect the cornea)eyes) etc.

- Software employee rubber shoes, shoe covers, aprons with leaded rubber.
- When working with radioactive aerosols and dust, workers must to provide respirators, gas masks.
- After completing the work, you must take a shower using soap. economic, special shampoos.
- Accept food and smoke in places irradiation prohibited;
- All workers, under working conditions from a radiation source radiation, must be provided with complete good nutrition. In premises for carrying out class I work there must be sanitary permit to rooms II. class. In premises, where are being held works II. class should be equipped sanitary inspector to rooms IIIrd class or a shower room with separate lockers for each employee.For works IIIrd class is expected shower ordinary type.

Materials of activation applicants higher education under time carrying outlectures: question, situational tasks etc:

Question:

5. Describe the concept of "nanotechnology". What is the role and place of nanodrugs in medicine and pharmacy?

6. Using nanotechnology in production medical drugs.

7. Give definition concept "address" delivery medicines. Name it requirements, whichare presented address systems delivery medicines.

General material and bulk-methodical software lectures:

- educational rooms – audience departments;
- equipment - computer, tables;
- equipment – multimedia projector;
- illustrative materials – presentation, slides.

Question for self-control:

2. Describe nanomaterials, name their types and classification. nanomaterials.

3. Basic principles and directions nanotechnology. Nanodrugs. Features their production. Nanosystems, ways receiving nanosystems.

4. Describe concept "radiopharmaceutical" preparation". Describe production, application and main diagnostic propertiesradiopharmaceuticals drugs.

5. Assortment and composition radiopharmaceuticals drugs on pharmaceutical market Ukraine.

6. Features their technology and control quality.

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