MINISTRY OF HEALTH PROTECTION OF UKRAINE
ODESSA NATIONAL MEDICAL UNIVERSITY

Faculty Pharmaceutical .
(faculty name)

Department Pharmaceutical chemistry and drug technology
(name of department)

I APPROVE
Vice-rector for scientific and pedagogical work
_____ Eduard BURYACHKIVSKY
" 01 " September 20 23 _

METHODOLOGICAL DEVELOPMENT TO THE LECTURE AND FROM THE ACADEMIC DISCIPLINE

Faculty, course Pharmaceutical, course III

Academic discipline Drugs technology
(name of academic discipline)

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

Protocol No. 1 dated August 28 , 2023 .

Head of Department _____ Volodymyr HELMBOLDT
(signature) (First name, last name)

Developers:
Ph.D., Assoc. Tsisak A.O.

Lecture 1: "State regulation of the manufacture of medicines in pharmacies. General issues of drug technology" - 2 hours.

1.Actuality of theme.

The rationale behind the topic. In their daily practice, pharmacists need to work with recipes, normative-technical documentation and reference books. The pharmacist is responsible for leave from pharmacies only properly prepared medical forms, and for this it needs to control the correct prescription and obtaining a prescription. To cope with their responsibilities, the pharmacist will be to represent the structure of the recipe to be able to use DF, other normative-technical documentation. This explains the theoretical and practical need for studying of this subject.

2. The objectives of the lecture:

- **training:** training to formulate the basic concepts and terminology of technology of medicinal forms;
- **educative:** Professional development focused on significant individual substructures; training students in modern professional thinking; providing mastering leading domestic value of clinical, scientific and educational development problems in schools lectures; mastering skills ethics and medical ethics.

3. Plan and organizational structure of the lecture.

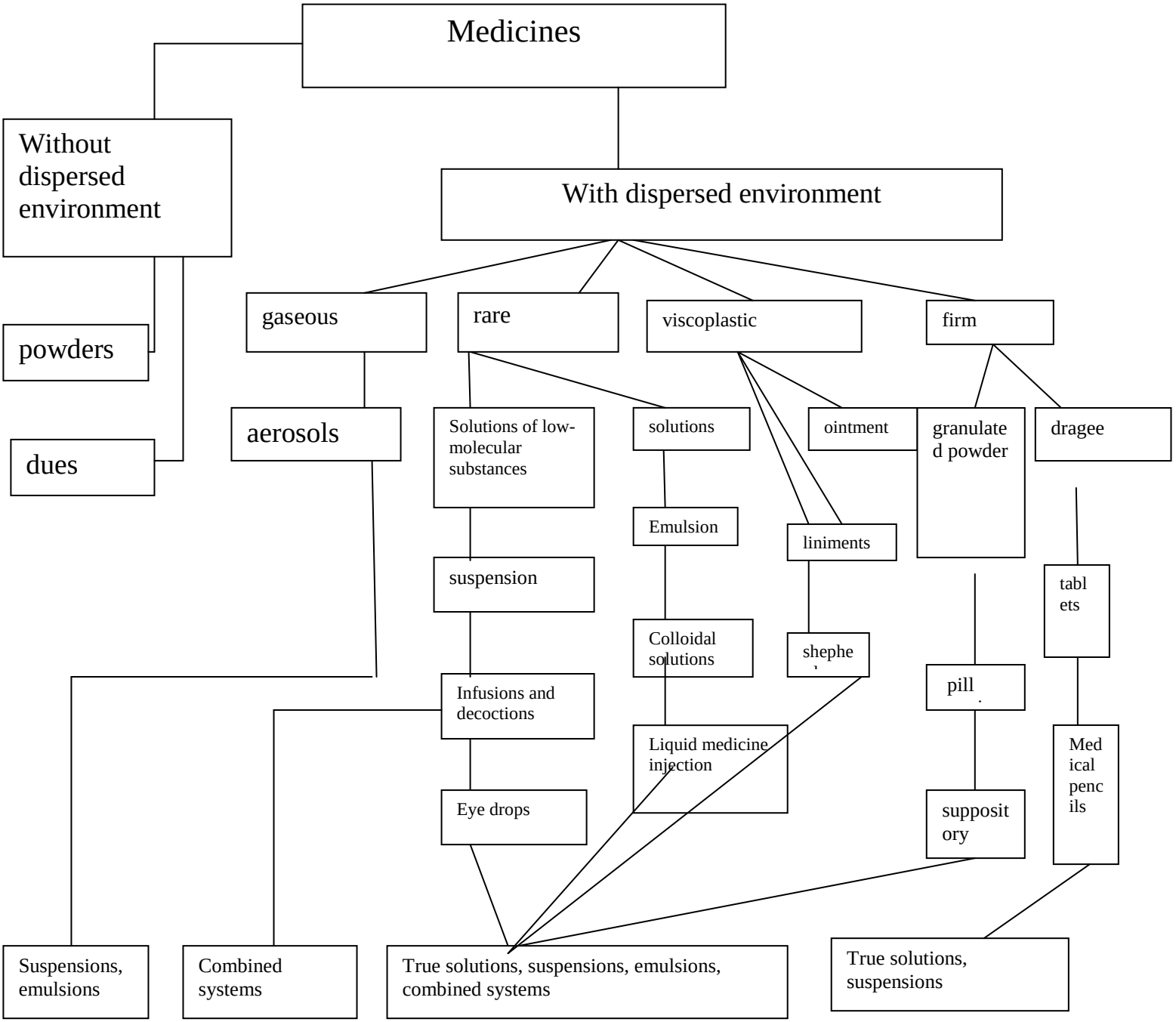
№№ pp	The main stages of lectures and their contents.	The objectives in the levels of abstraction.	Type of the lecture, lecture equipment.	Distribution of time.
1	2	3	4	5
	Preparatory stage			
1.	Learning objectives.			
2.	Provide positive reinforcement.			
	The main stage			
3.	Presentation of lecture material. Plan: 1. Technology of medicines as a science. The purpose and objectives of the TLZ. 2. Basic terms and concepts technology medical products. 3. Characteristics and classification of drug excipients. 4. State regulation of drug	I II III II I	References, visual material. State Pharmacopoeia, the main regulatory and technical documentation	85% - 90%
4.				

6. 7.	manufacturing. 5. The main regulatory and technical documentation. 6. Quality control in pharmacies. ***The final stage*** Summary of lectures, general conclusions. Lecturer answers to possible questions. Tasks for self student.		References, issues, tasks.	

4. Content of lectures:

1. Technology of medicines as a science. The purpose and objectives of the TLZ.
2. Basic terms and concepts technology medical products.
3. Characteristics and classification of drug excipients.
4. State regulation of drug manufacturing.
5. The main regulatory and technical documentation.
6. Quality control in pharmacies.

The content of the lecture material:



TECHNOLOGY OF MEDICINE AS A SCIENTIFIC DISCIPLINE

Public health is engaged in a comprehensive review of medicines called drugscience, that is, the science of medicines. It covers a range of scientific sectors and disciplines.

Modern pharmacology at the same time, is divided into two separate sections: pharmacology that studies the action of drugs on the body, and pharmacy.

Word "pharmacy" comes from the ancient Egyptian word "farmaki", which means "the one that gives recovery and security," or from the Greek word "Pharmacon" - drug.

Pharmacy is a complex of Sciences (technology of medicines, pharmaceutical chemistry, pharmacognosy, organization and Economics of pharmacy, management and marketing) that explore issues relating to drugscience, namely:

1. Synthesis and analysis of drugs.

2. The development of new theories and methods of manufacture of dosage forms.

3. The study of natural resources of plant, animal, mineral origin and refining them into drugs.

4. Development of new machines and devices, means of mechanization and modernization of existing industrial and pharmaceutical production.

5. Quality control, storage and dispensing of medicines.

6. A study of the planning, organization and management of pharmaceutical business, management, marketing.

7. Improvement of educational-methodical work of pharmaceutical educational institutions and training of highly qualified personnel.

Modern pharmaceutical science must get ahead of practice, opening up new ways of improving drug provision of population of Ukraine.

The value of pharmacy to protect the health of the population determined by the role drugs played in the modern system of treatment and preventive measures.

IP Pavlov in 1895, noted that the drug is "a universal weapon of the doctor", and attached great importance to their study.

It becomes apparent that the broad use of therapeutic measures (physiotherapy, radiotherapy, hydrotherapy, etc.) in no way reduces the importance of medications, so prevention of many diseases and cure them without the use of drugs is impossible. Indeed, it is difficult to imagine modern surgery without the use of anesthesia,

painkillers or disinfectant drugs. Unthinkable, and a serious struggle with infections without the use of sulfonamides, antibiotics and disinfectants.

However, with the advent of new and effective drugs has increased the need for modern scientific substantiation of methods of production and improvement of

technology of medicinal forms with the aim of obtaining stable drugs with optimal therapeutic effect.

Technology of medicine - the science of the theoretical foundations and production processes of processing of drugs in pharmaceutical products (drugs) by giving them a specific medicinal forms on the basis of established physical, chemical, mechanical and other laws.

The word "technology" comes from the Greek techne, the skill, ability and logos-science, study. The literal translation of "technology of drugs" means "the study of the ability to prepare medicines."

By definition encyclopedic dictionary (1982), technology is the totality of methods of processing, manufacture, change of status, properties, form of raw materials or material carried in the process of production. The task of technology as the science - identification of physical, chemical, mechanical and other laws to determine and use in practice the most efficient and economic production processes. The main goal of drug technology as a scientific discipline - to explore scientifically-based, technically advanced methods of conversion of drugs in dosage forms and preparations.

Technology of drugs relies heavily on data General subjects (chemistry, physics, mathematics), life Sciences (physiology, pharmacology, Microbiology and pharmaceutical subjects (pharmacognosy, pharmaceutical chemistry, organization and economy of pharmacy, management and marketing**.**

Most closely the technology of medicines associated with pharmaceutical disciplines. By definition of Professor AA Ovsky, it is the top pharmacy. Technology of medicine as a separate scientific discipline of pharmaceutical in the course of its development has experienced several different stages. At the initial stage of development, it takes more matters of technology, production of dosage forms and was called "the course of practical work," "practice prescription", "pharmacy practice", "pharmaceutical formulation", "pharmaceutical propedeutics". Outdated meaningless title "pharmaceutical propedeutics" in 1920 it was proposed to replace the accurate term "technology of medicinal forms", and in 1924 the decision of the First Congress on pharmaceutical education this title was finally secured. Since 1955 it has been called a "technology of drugs". During this period it grew into an independent leading pharmaceutical discipline, which defines the content of the practical activity of a pharmacist.

Established by the time of conditions a fundamentally new system of pharmaceutical education, the significant achievements of pharmaceutical science (developed new ways of producing drugs, new dosage forms), the development of industrial pharmacy has accelerated the process of differentiation technology medicine technology medicine pharmacy and factory production (see chart 1).

Factory (industrial) production is large-scale and is mechanized pharmaceutical companies (plants, factories).

Pharmaceutical manufacturing is engaged in the manufacture of drugs in individual formulations, manufacturing unotron blanks, filling, and is carried out in pharmacies. It features a large assortment of small-batch products. In terms of the pharmacies preparing drugs that are unstable during storage and a complex, with individual dosage.

Pharmacy and factory production are complementary, developed and improved-analyysi in parallel.

Now our discipline is called "chemist's technology of drugs" that most accurately reflects not only the essence of this science, but its complete independence. Sequential study of the course of technology of medicines, pharmacy first, and then a factory shows their close relationship, sequence, and defines the tasks of industrial pharmacy.

In the US, our science is called "theoretical and practical pharmacy" in the England, France, Holland - "herbal pharmacy" and "prescription art".

One of the first textbooks on technology of medicinal forms was the textbooks of AI Eberhard (1929) and SG Kovalev (1930, 1934), PP. F. Shubin (1942, 1948), IA Murav'eva (1961), JK Sander (1967).

A number of textbooks were written in national languages: Azerbaijani - PK Aliyev (1951), Estonian - N. Ya Veiderpass (1964).

In 1962 was published textbook GP Pivnenko "pharmaceutical technology of drugs" (in Ukrainian), which best reflects the course of pharmaceutical technology of drugs based on the achievements of domestic and foreign science.

New technological methods of manufacture of dosage forms in pharmacies was presented at the "Workshop on pharmaceutical technology of drugs" GP Pivnenko (1964, 1972) (in Ukrainian), and then in the "Manual for practical training in chemist's technology of drugs", edited by YA Blagovidova and VM Ivanova (1968), was reprinted several times.

Modern science put before technology of medical forms a row quite new investigational and practical tasks, the decision of that will allow qualitatively to change going both near the questions of creation of medical forms and to medicinal preparation.Basic from them: it is realization of fundamental complex researches in area of technology, biopharmacy and pharmakokinetics of medicinal facilities; it is development of new types of medical forms and improvement of existing; - creation of the prolonged medicinal preparations, and also medical forms, using in pediatric and geriatrics practice; it is a search of new auxiliary substances, expansion of assortment of preservatives and stabilizators for injection medical forms; it is the use

of modern packing material;it is expansion of researches on questions mechanization and automation of technological processes productions in pharmacies.By a task to technology of medical forms as educational discipline is: - are studies of students of activity of pharmacist-technologist; - study of theoretical foundations, acquisition of professional skills and skills in the manufacture of pharmaceutical forms, as well as determining the effects of storage conditions and the type of packaging on the stability of medicinal products.The tasks set before the technology of medicinal forms as a branch of pharmacy, can be solved only at the level of scientific research, high qualification of personnel and the integration of science with production.

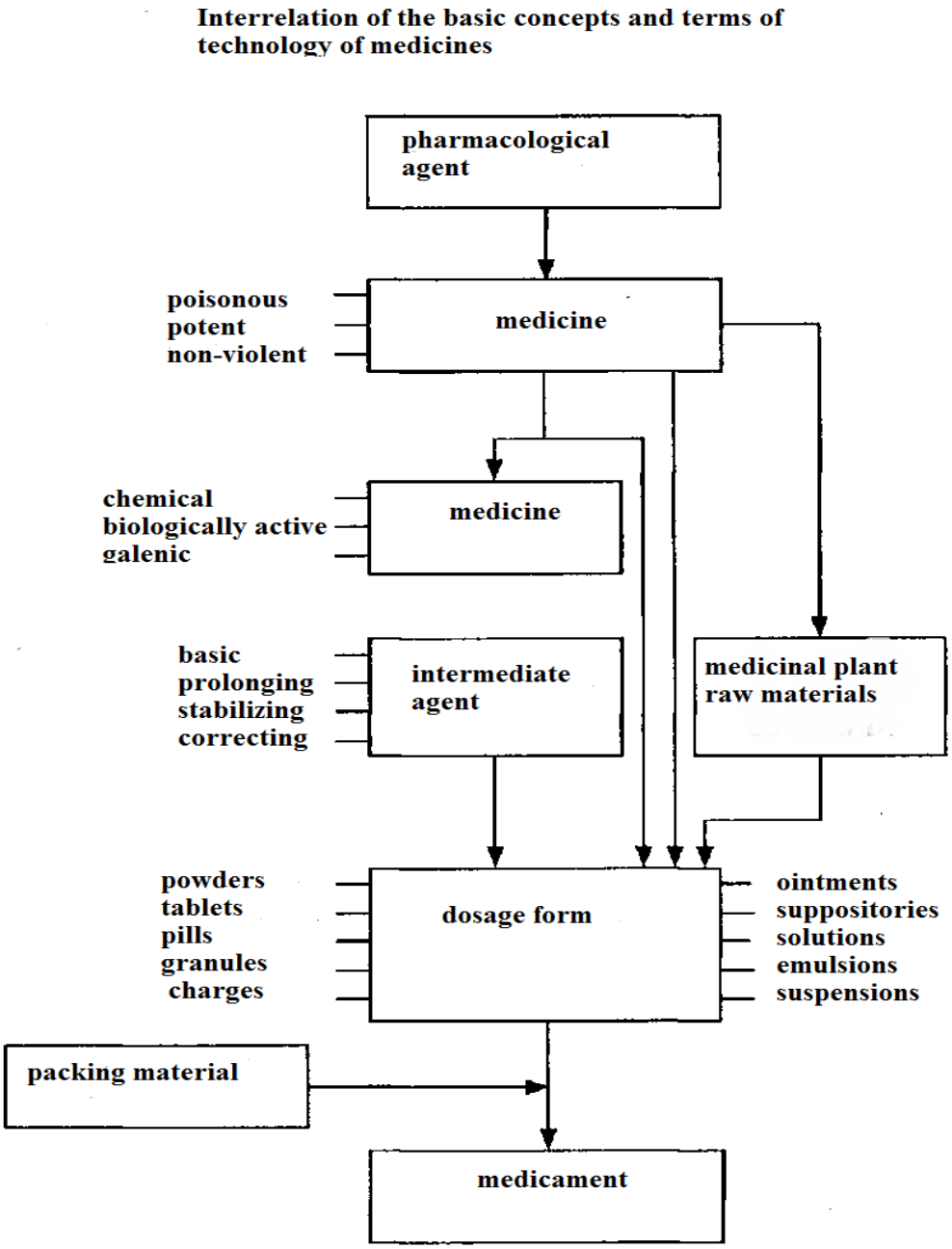
MAIN TERMS AND CONCEPT OF TECHNOLOGY OF MEDICINES

The term (terminus - lat border, border) is a word or phrase, which is an exact, unambiguous name of a certain notion of a special field of science, technology, etc. Terminology has a direct relation to the essence of this science, the development of which produces a review, streamlining of terms, as well as restriction or complete elimination of synonyms. There are new terms for new concepts, in the old terms a new meaning is added, that is, terminology is subjected to conscious intervention, regulation, ordering, unification and standardization. An arbitrary interpretation of scientific terms is inadmissible. The only "Terminological Dictionary" was put into effect in 1980 and in 1982. It contained the definition of basic concepts in the field of medicinal products and clinical pharmacology. More modern terminology, including the basic terms of the technology of medicinal forms, is given in the Law of Ukraine "On Medicinal Products" (1996) .Terms and their concepts have not only information and legal, but also methodological significance, since a clear definition allows you to properly plan and conduct scientific research .Terminology of medicine technology consists of names of medical forms (tablets, powders, extracts, etc.), designation of technological processes and operations, machines and apparatus. In technological terminology, pharmacological, pharmaco-pharmacological and pharmaco-chemical terms are common in comparison with other pharmaceutical sciences.

A pharmacological agent is a substance or a mixture of substances with established pharmacological activity. After obtaining positive results of clinical examinations and authorization of the authorized person for medical use, it receives the name of the medicinal product. Medicinal product - a pharmacological agent authorized by the authority of that body of the country for use in order to treat, prevent and diagnose a human or animal disease.Medicines represent a significant group of a variety of substances, differing in appearance, origin and composition. They can be plant and animal origin, organic and inorganic nature, substances individual and complex, have different aggregate state, etc. In order to systematize

medicinal products, based on their composition, can be divided into two groups: 1. Medicinal substances.2. Medicinal herbal and animal raw materials (and microbial agents). Medicinal substance is a medicinal product that is an individual chemical compound or biological substance. It can be used for the preparation of dosage forms without pre-treatment. Depending on the specificity of the preparation and the purification method in the production conditions, the medicinal substances are divided into several groups.

Scheme



Chemicals - are individual chemical compounds, of synthesis or purified natural substances origin, they produce chemical industry. In their bulk, they are designed to meet the needs of different sectors of the economy, but many of them are both widely

used drugs, for example, sodium chloride, sodium sulfate, silver nitrate, hydrochloric acid, sodium bicarbonate, potassium permanganate, etc.

Chemico-pharmaceutical substances - by their very nature, are also individual chemical products. They are manufactured by the enterprises of the chemical and pharmaceutical industry and are one of the main and important groups of medicinal products, which are dominated by organic synthesis products, for example, sulfanilamide preparations (streptocide, nursulfazol, phthyvazide, etc.). Chemico-pharmaceutical substances - biologically active substances, isolated in their pure form from raw materials of plant and animal origin (for example, alkaloids, glycosides, etc.).

Vitamins - can exist in the form of individual chemical compounds (ascorbic acid - vitamin C, nicotinic acid - vitamin PP, riboflavin - vitamin B2), as well as in the form of extracts and concentrates. Produced mainly by enterprises of specialized industry.

Antibiotics - are products of the life of different microorganisms. They are extracted by biologic synthesis when growing microbes in different environments. Widespread antibiotics are penicillin, biomycin, streptomycin, gramicidin, and others. In most cases, they are individual chemical compounds. Some of them receive synthetic (levomitsetin) or semi-synthetic (methicillin, oxacillin, etc.) methods.

Organotherapeutic substances - are complex complexes of biologically active hormone substances (adrenaline). Obtained from organs and tissues of animal organisms. A number of hormones are synthesized (sex hormones). This group includes enzymes (pepsin, etc.). Produced by enterprises of the meat and dairy industry.

Substances from plant and animal raw materials. This group includes essential and fatty oils, fats derived from parts of plants and animals. It also includes numerous products, which are shredded parts of plants and animals (for example, powder of salve tubers, softwood leaves, altea root, etc.), as well as powders of gums, resins and others.

Galen drugs - named after the ancient Roman scholar Claudius Galen. Characterized by chemical complexity. In them along with the active substances contained and related. Prepare them most often from medicinal plant raw materials (tinctures, extracts, oils, syrups, fragrant waters, etc.). A special subgroup of galenic preparations is made up of so-called Novogalenic drugs, which are also extracts (like extracts and tinctures), but are more liberated from ballast substances. There are other varieties of galenic preparations (extracts from fresh plants, canned juices, condensed, and others).

Immunological substances are vaccines and serums or inanimate microorganisms, various antigens and antibodies. Produced by institutes of vaccines

and serums, institutes of epidemiology, microbiology and hygiene, as well as a number of regional sanitary and epidemiological stations. This is a specific group of drugs, for which the role of a pharmacy worker is reduced only to proper storage and timely release.

Substances of radioactive isotopes - represent a very active group of chemical and pharmaceutical substances included in the medical catalog. Due to isotopes of radioactive elements, it is possible to use intra-nuclear energy in the form of radiation energy for external and intracavitary irradiation. Radioactive substances in the minimum doses are used for rectal and parenteral administration. With the help of nuclear reactors, preparations of radioactive sodium, silver, iodine, cobalt and other elements that are released in the form of various compounds are obtained, for example, silver nitrate with radioactive silver, etc.

Medicinal substances by physical properties are divided into solid, liquid, soft and gaseous. The range of medicinal substances is constantly changing. Less effective are replaced by means more valuable in therapeutic or prophylactic terms. Medicinal raw materials are natural substances in raw form or are subjected to a simple, initial processing, which require the application of one or another processing or purification. Medicinal plant raw material is a plant material authorized by an authorized body in the prescribed manner for medical use. This group includes dried herbs, leaves, flowers, roots, bark and other organs of medicinal plants. Medicinal herbal raw materials are used as such in drugstores (for the preparation of dues, infusions and decoctions), as well as for the preparation of galena and novoagalene preparations in the conditions of serial production. Medicinal raw materials of natural origin are products of bee products: propolis, pollen, bee poison, honey. They are used for the receipt of medicinal products in the conditions of both pharmacies and chemical and pharmaceutical enterprises.

Propolis (Propolis - bee glue, lacquer, bee balm, "foundation", bee or wax resin) - dark gray with a greenish tint of mass, heterogeneous in a fracture, with a specific odor. Almost insoluble in water, ether, chloroform, acetone. Propolis contains at least 25% of the total amount of phenolic compounds (flavonoids, flavonols, oxyric acids, coumarins, etc.), not more than 20% wax and not more than 15% of mechanical impurities (FS 42U-18-95) .

Flower Pollen (Flower Pollen) is male reproductive cells of flowering plants, which are formed on the basis of an enlarged part of stamens (in almonds), collected by bees and formed in the baskets by a third pair of legs. In appearance - the lumps of irregular shape weighing from 5 to 20 mg, from light yellow to dark brown color, with a specific pleasant characteristic of the bees overnight smell. According to botanical origin, it is subdivided into homogeneous (monoflore), obtained from one species of plants, and inhomogeneous (polyphonic) - from several species of plants.

As part of the pollen, about 250 different types of compounds and substances (proteins, water, amino acids, minerals, vitamins, etc.) were detected (DSTU 3127-95).

Bee poison (Venerium Apisum - a secret made in the poisonous glands of honey bees) - gray with yellowish or boring shade of powder, practically insoluble in water. The activity of phospholipase A enzymes is not less than 100 ME (international units), hyaluronidase is not less than 70 ME.

Honey (Mel - Succulent Separation, deposited in Apis Mellifica Bees) is a thick syrup-like, almost transparent liquid that subsequently turns into a grainy, opaque mass of yellowish-white, yellow or light brown, sweet flavor, a pleasant honey odor. The main component of honey is carbohydrates (95%), proteins, amino acids, minerals, vitamins, and others. (GOST 19792-87). It should be borne in mind that the drugs themselves are not given to patients, they are only the starting material for the manufacture of medicinal products by providing them with the appropriate dosage form. Characteristics of the medicinal product and classification are given in Scheme 3. Auxiliary substances are additional substances necessary for the preparation of a medicinal product. In the technology of medicine it is allowed to use only auxiliary substances that are dosed for medical use by the relevant normative documentation: State pharmacopoeia, pharmacopoeial articles (FS), temporary pharmacopoeial articles (TFS) or special DST. The state register contains the section "Substances". Until recently (prebiopharmaceutical period of linguistics), auxiliary substances were considered only as indifferent fillers, form-makers, and the choice of auxiliary substances was dictated purely by technological, and often simply economic considerations. For their application it was only necessary to prove that they are pharmacologically indifferent, provide the pharmaceutical form with appropriate technological properties and are economically affordable.

For example, the search for a "universal basis for ointments or suppositories", "universal solvent for injections", "universal extractant" for extractors from plant and animal raw materials, "universal diluent" for the manufacture of tri-turations, tablets, etc. began. Modern pharmacy has abandoned the former understanding of auxiliary substances as indifferent form-makers. Substances have certain physical and chemical properties. Depending on the nature of the medicinal substance, the conditions of production and storage of the medicinal form, they are able to enter into more or less complex interactions with both medicinal substances and environmental factors (eg, inter-tissue fluid, contents of the gastrointestinal tract, etc.). It has been proved that auxiliary substances can greatly influence the pharmacological activity of medicinal substances: to amplify or reduce it, or to change the nature of therapeutic action altogether. In some dosage forms (eg, ointments, suppositories, aerosols, etc.),

substandard substances make up more than 90% of volume and regulate all the basic properties, including the completeness and rate of absorption of active substances. Therefore, the study of the pharmacological action of any medicinal substance does not make sense if it is not conducted in the presence of those excipients, which in the future will compose the composition of a particular dosage form of the drug. Each case of the use of auxiliary substances requires a special study, the purpose of which is the choice of auxiliary substances that provide sufficient stability of the drug, maximum bioavailability and its specific pharmacological action. Using various auxiliary substances, it is possible to create dosage forms with improved taste and given properties, for example, providing localization and duration of action, the determined rate of absorption of medicinal substances. Thus, the search, study and application of new auxiliary substances is a rather complicated and very topical problem of modern pharmaceutical technology.

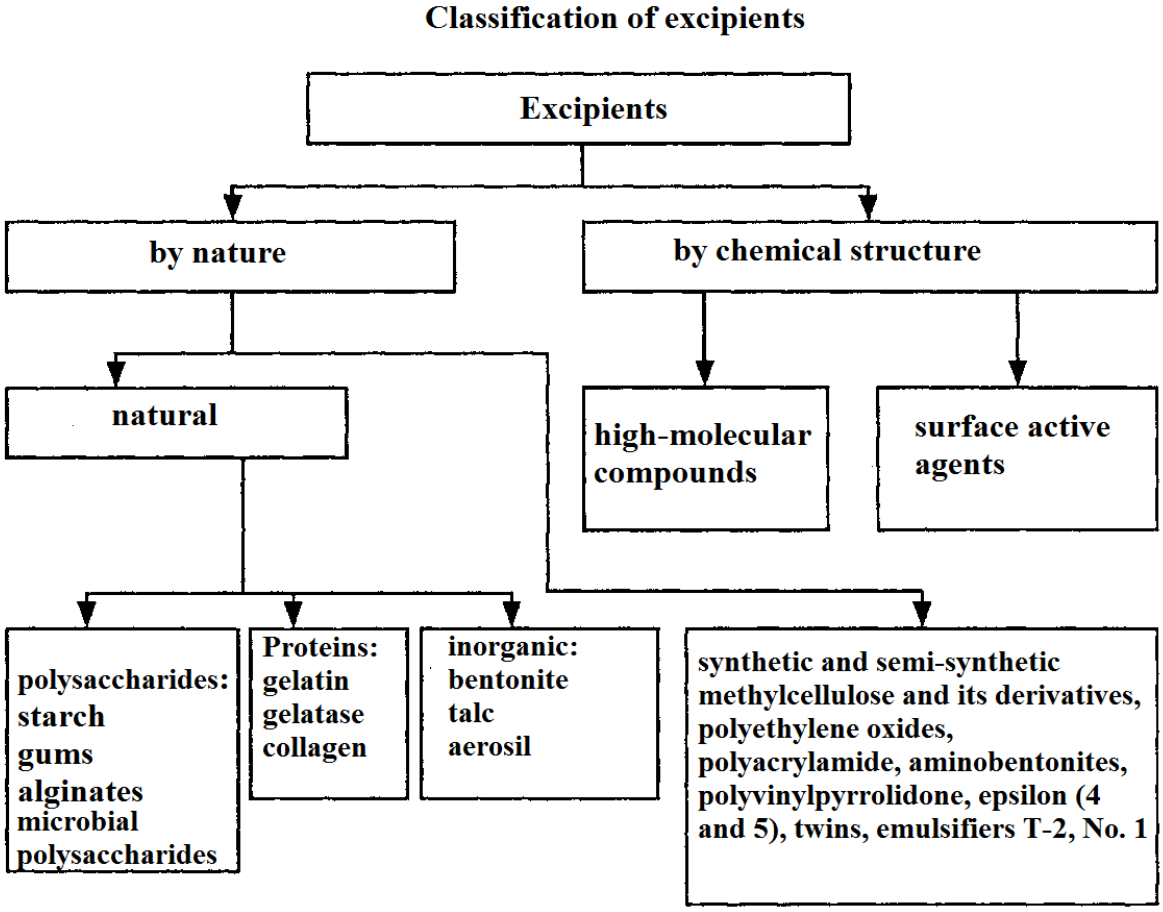
- should not carry out allergic and other toxic effects;

- must comply with the requirements of the maximum permissible microbial contamination (ob-seeding), if possible, be subjected to sterilization;

- should be economically affordable.

In order to systematize, facilitate the further study and proper selection of auxiliary substances, they are classified according to the influence of technological characteristics of dosage forms (as form-forming substances), as well as the nature and chemical structure of compounds.Based on the functions of auxiliary substances as form -makers and taking into account the effect on the pharmacokinetics of drugs, they are divided into the following groups: solvents; bases for ointments; substances to cover; substances that increase the viscosity; stabilizers; preservatives; cohorts prolongers; solubilizers; dyesClassification of auxiliary substances by nature and chemical structure (see Scheme 4), proposed by the Department of Technology of Medicines 1 st IMI. Sechenov (TS Kondratyev, LO Ivanov, etc.), according to which they are divided into natural, synthetic and semisynthetic. This classification is suitable for knowledge of the physical, physicochemical and physicomechanical properties of auxiliary substances, which is necessary for the use of these compounds in the techno logical process for the purpose of proper choice depending on the specificity of the dosage forms.

Figure 4



Natural auxiliaries have a big advantage over synthetic ones due to high biological harmlessness. Approximately 1/3 of the auxiliary substances used are natural and their search continues. Plant biopolymers are used as emulsifiers, stabilizers, propellants. The disadvantage of inorganic auxiliary substances (especially polysaccharides and proteins) is the instability of microorganisms. As part of the microflora of inorganic compounds, not only conditionally pathogenic, but also pathogenic microorganisms can appear. Because of this, auxiliary substances may be the main source of microbial contamination of medicinal products. To reduce microbial contamination to the maximum permissible values, they are usually sterilized or added to antimicrobial substances (preservatives). Synthetic and semi-synthetic auxiliaries are also widely used in the technology of pharmaceutical forms. This is facilitated by their availability, the ability to synthesize substances with given properties. It should also be taken into account that synthetic and semi-synthetic auxiliaries can replace a number of food products. Characteristics of natural, synthetic and semi-synthetic auxiliaries are elucidated in detail in the technology of each dosage form.organism, etc. But at the same time, the medical forms are

presented with certain general requirements: - they should provide the maximum therapeutic effect and have a minimal side effect (negative); - must provide a given duration of action; - should be comfortable in use; - must be stable when stored and transported. Biofarmation is the theoretical basis of drug technology.

Biopharmaceuticals - a science that studies the dependence of therapeutic effects of drugs on the body from various factors (pharmaceutical, biological, etc.). Biofarmation is a scientific discipline of pharmacy dealing with the influence of the physical and physicochemical properties of a medicinal substance and a medicinal product on the quantitative characterization of the therapeutic effect in a human or animal organism after the administration of a medicinal substance in various dosage forms.It appeared after the establishment of evidence of therapeutic inequivalence of drugs, that is, drugs of one composition, but manufactured by different pharmaceutical companies, had different therapeutic efficacy. This was due to a number of reasons: the shattering of medicinal substances, the selection of auxiliary substances and the difference in technological processes, the so-called pharmaceutical factors. In the literature, the term "pharmaceutical factors" has spread primarily due to the clinical confirmation of experimental data on the existence of a relationship between the effectiveness of drugs and the methods of their obtaining.Since the therapeutic effectiveness of drugs is determined by the processes of their absorption (absorption), distribution and elimination (withdrawal) from the macroorganism, biopharmacy pays special attention to the study of these processes, as well as the influence on them of the physicochemical properties of medicinal substances. Therefore, all investigated dosage forms are now considered in biopharmaceutical aspects. The main task of biopharmacy in modern medicine technology is to maximize the therapeutic efficacy of drugs and minimize their possible side effects on the body. Studies on the evaluation of the bioavailability of drugs helps to solve this fact. This means that in the pharmaceutical complex of knowledge, where previously their only physical and chemical constants served the only criteria, new provisions are introduced that have purely biological, medical justification.

PHARMACEUTICAL FACTORS AND THEIR CONTENTS

All pharmaceutical factors that can influence the biological effects of medicinal products can be divided into 5 groups:

1. Physical state of the medicinal substance (particle size, crystal shape, presence or absence of charge on the surface of particles, etc.). Polymorphism.

2. The chemical nature of the medicinal substance (salts, acids, bases, esters, complex compounds, etc.)

3. Substances (their nature, physical condition and quantity).

4. Kind of dosage form and ways of its introduction into the body.

5. Technological operations taking place at the receipt of a medicinal product. Pharmaceutical factors play an important role in the development of the composition and technology new medicines and improving already existing ones. In the practical work of the pharmacist-technologist, the most important factors are: the physical state of the drug substance, the presence of auxiliary substances and their nature. Proceeding from these factors, the right choice of technology of medicinal products, mechanization of stages of the technological process is necessary. The pharmacist-technologist does not choose, Medicinal substances as well as the pharmaceutical form, in the pharmacy because there is a certain prescription recipe, where the doctor indicates which medicinal substance should be used and what dosage form to prepare. The study of pharmaceutical factors will help the pharmacist-technologist to choose the optimal technology of manufacturing drugs, which would ensure the maximum release of the drug substance from the dosage form with the required method of administration. Physical state of the drug substance. The size of the particles depends to a great extent on the speed and completeness of the absorption of the drug in any method of administration, except intravascular, as well as its concentration in biological fluids, mainly in the blood. Thus, it turns out that such an ordinary technological operation, like grinding, has a direct bearing on the therapeutic effect of medicinal products. It was first proved for sulfanilamide substances, then steroids, derivatives of salicylic acid, antibiotics, painkillers, diuretics, anti-diabetic, cardiological and other drugs. For example, in the case of the identical doses of sulfadimezine micronized and obtained in the factory production without further grinding, it was determined that in blood plasma of humans, when applied micronized sulfadimezin, its content is 40% higher, the maximum concentration is reached 2 hours earlier, and the total the amount of substance that is absorbed is 20% higher. With a decrease in the size of the particles of grizeofulvin from 10 to 2.6 microns, its absorption in the gastrointestinal tract increases dramatically, which reduces the usual therapeutic dose by 2 times. Similar results were obtained with the use of micronized acetylsalicylic acid - anti-inflammatory action was increased approximately 2-fold. However, the choice of the size of the particles of the drug in each particular case must be scientifically substantiated. One can not consider the correct desire to obtain a micronized powder in each case, because often a sharp decrease in the size of the particles of the drug causes either the rapid inactivation of the drug, or the rapid removal of the substance from the body, or increases its undesirable effect on the body.In pharmacy practice, the required particle size is achieved with the adherence to the present conditions of grinding: the choice of mortar, the time of shredding, the order of shredding and mixing of medicinal substances. All these rules are set out in the chapter "Powders". Polymorphism (from Greek rolie - many, morphe - form) - the ability of the same substance to form

different crystals in shape. Polymorphic modifications form many chemical substances, including medicinal substances. At the same time, the same chemical substance has different physical properties. This applies primarily to organo-substances that can exist in two or more crystalline modifications. Formation of various polymorphous modifications of medicinal substances is possible at their receiving (allocation), purification and drying, as well as in the manufacture and storage of medicinal forms.Polymorphic transformations are especially common among salicylates, barbiturates, sulfanilamides, hormonal preparations. For example, acetylsalicylic acid is found in six crystalline forms, cortisone acetate - in heel. The consideration and rational use of the phenomena of polymorphism of medicinal substances are essential for pharmaceutical and medical practice. The fact that polymorphic modifications of the same drug substance have different solubility, melting point, oxidation resistance, and therefore, different surface properties, which depend on the rate of absorption of medicinal substances and their stability in medicinal forms. Thus, acetylsalicylic acid (polymorphic modification II) has a 50% better solubility compared to Form I and 1. 5 times more activity and biological availability. The rate of dissolution of anhydrous caffeine and theophylline exceeds the rate of dissolution of their solvated forms. A vivid example of the therapeutic significance of the fact of polymorphism may be insulin. Precipitated insulin is, after a reaction with zinc chloride, an irreducible complex, which, depending on the pH, may be amorphous or crystalline. When an urgent short-term action is not feasible, use an easily absorbed amorphous zinc insulin. Crystal zinc-insulin is absorbed slowly and provides a prolonged action of the hormone. The chemical nature of the medicinal substance. One and the same medicinal substance can be used as a medicinal product in various chemical states (salt, acid, base, complex compound, etc.). In the simplest cases, this may relate to the formation of one or another active substance. For example, when replacing the hydrogen ion in ascorbic acid with sodium ion, while preserving the basic function of vitamin C, the drug acquires new properties that are not characteristic of ascorbic acid - the ability to change the electrolyte balance of the organism to a greater extent than ascorbic acid, to suppress the function of the insulatory apparatus in the cause For diabetes mellitus. Or another example: alkaline quinine from the base can be converted into various salts: sulfate, chloride, bromide. When preserving the pharmacological action of quinine, its salts, having different solubility, will have different absorption kinetics. The concentration of hydrogen ions affects solubility, the distribution factor of drugs, as well as the membrane potential and surface activity. So, when passing through the lipid barrier (the wall of the stomach, intestine), the role of ionization plays an important role. Medicinal substances can be in an ionized or nonionized form, which affects their therapeutic action.

Excipients. Creating a dosage form in almost all cases requires the use of one or another auxiliary substance. The success of organic chemistry and leeches led to the creation of hormonal or similar type of action drugs. Routine doses of such drugs are milligrams or even a fraction of milligrams, which leads to the mandatory use of "auxiliary substances" in the pharmaceutical form and enhance their role in the pharmacokinetics of the drug. Substances are not indifferent and in all cases they have somehow or other effect on the release of the drug. Often milk sugar is used for these purposes. However, in his presence, for example, increases in the absorption of testa-tosterone, decreases the activity of isoniazid. Aminocapronic acid, in combination with double sugar, has the same activity as pure aminocapron, but a 3-5-fold amount of sugar significantly reduces its activity. Therefore, in each individual case, the choice of the excipient should be individual in relation to the particular medicinal substance. Among the works devoted to the study of the influence of auxiliary substances on the activity of medicinal preparations, particular attention is paid to the ointment and suppository bases, their type (hydrophilic, hydrophobic, emulsion), viscosity, physical and chemical properties, concentrations of emulsifiers used, surfactants and others. Suction activators. For example, ointments with antibiotics (in particular, with penicillin), cooked on petroleum jelly, due to poor resorption, are ineffective. In this case, a basis is needed which includes 6 hours of vaseline and 4 parts of lanolin, which is now used for the manufacture of many antibiotic ointments. It is established, for example, that acid boron does not produce bacteriostatic action when using fatty bases, but is effective when using ointments on hydrophilic bases, which contain a large amount of water. Obviously, the therapeutic effect detects the resulting solution of boric acid. On the other hand, iodine is low active in bases containing a large amount of water. When studying the diffusion of novocaine from ointments, it has been found that it is higher than the emulsion bases of type M / V than from the emulsion bases of type B / M. Thus, the introduction of substances into different types of emulsion bases makes it possible to obtain ointments possessing a different degree of absorption. The rate of diffusion of medicinal substances from ointment bases also affects the structural and mechanical properties of the bases. Thus, for example, the introduction of aerosil in the amount of 5-8% in hydrocarbon bases leads to an increase in the viscosity of ointment bases, resulting in the release of salicylic acid decreases. There is a large number of works that show the ability of dimethyl sulfoxide (DMSO) to easily penetrate the intact skin, transport, deposit and prolong the receipt of medicinal substances in the body. Thus, the addition of DMSO in eye drops accelerates the penetration of antibiotics into the eye tissue, the use of the same methyl cellulose allows to keep the medicinal substances in the tissues for a long time, thus prolonging the action, which is very important in the treatment of many chronic diseases of the organs of vision. The

influence of surfactant on the kinetics of streptomycin sulfate introduced in suppositories has also been studied. Streptomycin sulfate has been shown to be absorbed in the rectal administration of suppositories based on cocoa butter. The addition of surfactant (the best effect is provided by tween-80) allows you to create therapeutic concentrations of antibiotics in the blood for four hours and provides its anti-tuberculosis action. It must be taken into account that auxiliary and medicinal substances can interact with each other. It is now assumed that regardless of the nature of the connection in the vast majority of cases, the end result in the system of the drug substance - the adjuvant substance is the reaction of complex formation and adsorption. A large number of drugs with complex molecules easily enter complexation reactions. The formed complexes can be very strong and weaken the basic pharmacological properties of the drug substance. The intensity of the technological processes taking place in the manufacture of medicinal products can significantly affect the reaction of complex formation, accelerating or controlling it in the corresponding direction. Particularly responsible in this respect are the stages of dissolution, filtration, recrystallization, melting, mixing, etc., which undergoes a change in the aggregate state of medicinal and auxiliary substances, the intensity and growth of the number of contacts between them. To auxiliary substances that can form complexes with medicinal substances include: nonionic surfactants, starch, polyethylene oxides, gelatin, etc. Formations of compounds characterized by other than the starting materials, properties-they may have poor solubility, high stability and low adsorption capacity. For example, when using in the dosage forms PEO-4000, PVP as a thickener, the complex formed with phenobarbital has a very weak ability to dissolve and absorb. In pharmacies, the choice of auxiliary substances should be given special attention in such medicinal forms as ointments, suppositories, pills. For example, according to DF IX, potassium ointment with iodide, mercuric gray, sulfuric acid should be readily prepared on fat or on a pumice or emulsion basis with an emulator T-2. The use of vaseline in this case does not achieve the desired therapeutic effect. Tablets with alkaloids should be prepared using as a filler of starch-sugar mixture, because when applying plant powders and extracts there is adsorption of alkaloids on them and incomplete release in the gastrointestinal tract. This confirms the need for an individual approach in the selection of auxiliary substances. Kind of medical form and ways of its introduction into an organism. The medical form, representing the material form of manifestation of the dialectical unity of active and auxiliary substances and corresponding technological operations, affects the processes of absorption of medicinal substances present in it and manifestation of their unwanted side effects. Biopharmacy attaches serious attention to the theoretical substantiation of the dosage form, clarification of its role and place in pharmacotherapy. Biopharmacy has enriched the existing understanding of the

medical form associated with the convenience of prescribing, transporting and storing medical preservatives. Currently, there is no doubt that the optimal activity of a medicinal substance is achieved by its appointment in a rational medical form. For example, more liberal than suppositories, the absorption of izadrina hydrochloride is observed in the appointment of it in the form of sublingual tablets. The choice of the dosage form simultaneously determines the method (route) of the introduction of the drug into the body. It is clear that the rate of action of a drug depends on which route for its application is chosen. For example, in the rectal process, the drug can be absorbed in about 7 minutes, and in the oral form only after a few minutes (on average). When a rectal method of administration, some of the medicinal substances penetrate the bloodstream by passing the liver and not subject to the chemical influence of its enzymes, as well as gastric juice, bile and juice of the pancreas. Consequently, the effect of the drug in this case is greater than in the case of oral use. When choosing a dosage form it is important to know the purpose of the use of the medicinal substance and the drug. For example, in ophthalmology, in the case when short-term action of a medicinal substance is required - enlargement of the pupil to look at the vessels of the fundus, more rationally use atropine sulfate in eye drops. On the contrary, the use of pylocarpine hydrochloride used for the treatment of glaucoma (increased intraocular pressure) is appropriate in ophthalmic drug films, because it allows for preparate 1-2 times a day, as opposed to eye drops, which instillation is carried out through each 2-3 hoursFocusing on the role of the pharmaceutical form in pharmacotherapy, biopharmacy simultaneously opens the beneficial opportunities for continuous improvement of the methods of obtaining and studying the dosage forms themselves.Technological factors. Biopharmaceutical research has allowed to give a scientific explanation of the role of technological processes and methods of obtaining drugs in the development of pharmacotherapeutic effect. It has now been proved that the method of obtaining dosage forms largely determines the stability of the drug, the rate of release from the dosage form, the intensity of its absorption, and, ultimately, its therapeutic efficacy. Thus, for example, the degree of conservation of reserpine in the final dosage form depends on the choice of the granulation method in obtaining the tablets. In this respect, the so-called wet granulation (granulation of corrosion) is especially undesirable, which leads to a loss of 14% of the drug. This same method of granulation causes a significant reduction in the therapeutic effectiveness of antibiotics erythromycin and neomycin and contributes to the decomposition of acetylsalicylic acid, dichloramine, penicillin and other medicinal substances. One can also cite this example. The chosen method of emulsifying castor oil depends on the degree of its dispersion, and hence the rate of saponification of the oil in the alkaline medium of the intestine and the subsequent laxative effect.Thus, when developing the composition and technology of any drug, particular attention should be paid to the

release of the active substance, which depends to a large extent on the pharmaceutical factors - in pharmacy practice, primarily on the particle size, the correct choice of auxiliary substances, and pharmaceutical technology. Therefore, modern pharmacy pays great attention to the development of rational, scientifically sound methods of obtaining medicines, taking into account the provisions of biopharmaceuticals on the possibility of influencing technological processes on the activity of drugs.

STATE REGULATION OF PRODUCTION OF DRUGS

State regulation of the production of medicinal products is a set of requirements, legalized by the relevant documents, to the quality of medicinal products, auxiliary substances and materials, the technological process and medicinal preparations as a finished product. Improper storage of the medicinal product, incorrect preparation or dosage can lead to a reduction or loss of the therapeutic effect, or even before the toxic effect of the medicinal product. However, in contrast to other subjects of consumption, the quality of medicinal products can not be determined by the patient. This especially emphasizes the importance of state regulation of production and quality of medicinal products. The establishment of rules for conducting individual operations, norms of quality and costs of raw materials, requirements for the finished product not only promotes the receipt of high-quality products, but also reduces material losses, which increase especially in violation of the technological regime.The standardization of the production of medicinal products is carried out mainly in four directions: 1. Restrictions on the range of persons authorized to prepare medicines (the right to pharmaceutical work) .2. Rationing of prescriptions of medicinal products.3. Ration of the quality of drugs and adjuvants used for the manufacture of medicinal products.4. Rationing of the conditions and technological process of making medicines.

THE RIGHT TO MANUFACTURING DRUGS (ON PHARMACEUTICAL WORK) which increase especially in violation of the technological regime. The standardization of the production of medicinal products is carried out mainly in four directions: 1. Restrictions on the range of persons authorized to prepare medicines (the right to pharmaceutical work) .2. Rationing of prescriptions of medicinal products.3. Ration of the quality of drugs and adjuvants used for the manufacture of medicinal products.4. Rationing of the conditions and technological process of making medicines.

THE RIGHT TO MANUFACTURING DRUGS (ON PHARMACEUTICAL WORK) which increase especially in violation of the technological regime. The standardization of the production of medicinal products is carried out mainly in four directions: 1. Restrictions on the range of persons

authorized to prepare medicines (the right to pharmaceutical work) .2. Rationing of prescriptions of medicinal products.3. Ration of the quality of drugs and adjuvants used for the manufacture of medicinal products.4. Rationing of the conditions and technological process of making medicines.

THE RIGHT TO MANUFACTURING DRUGS (ON PHARMACEUTICAL WORK) Ration of the quality of drugs and adjuvants used for the manufacture of medicinal products.4. Rationing of the conditions and technological process of making medicines.

THE RIGHT TO MANUFACTURING DRUGS (ON PHARMACEUTICAL WORK) Ration of the quality of drugs and adjuvants used for the manufacture of medicinal products.4. Rationing of the conditions and technological process of making medicines.

THE RIGHT TO MANUFACTURING DRUGS (ON PHARMACEUTICAL WORK)

In the "Fundamentals of the legislation of Ukraine on health care" it is stated that medical and pharmaceutical activities can be carried out only by persons who have received the corresponding professional education and meet the same qualification requirements. The only qualification requirements for persons engaged in certain types of medical and pharmaceutical activity, including in the field of folk and non-traditional medicine, are established by the Ministry of Health of Ukraine.Proceeding from this legislation, the controller-technologist is responsible for checking recipes for the correctness of their prescribing and registration, compatibility and ingredients, single and daily doses of poisonous and potent drugs. The Professor-Technologist manages the work of pharmacists in the manufacture of medicinal products, intra-ocular preparations, controls the implementation of all technological requirements during their preparation. He controls the compliance with the sanitary regime in the production premises and controls the serviceability and accuracy of all weighing instruments in accordance with the requirements of the State Committee of Standards.

RECORDING OF MEDICINAL DRUGS

Medicines prepared according to standard prescriptions by the pharmaceutical industry in large numbers are called officinal - medicamenta officinalia (from the Latin officina - workshop, pharmacy) .Medicines intended for individual use and prepared in a pharmacy by prescription of a doctor, are called trunk - medicamenta magistralia (from the Latin magister - teacher, the head, in this case - the doctor who made the prescription) or extemporal (from the Latin ex tempore - immediately cooked) Accordingly, all prescriptions for medicinal products are divided into officinal, manual and main (extemporal) .Official formulations (Formulae officinales) are approved by the state legislature - the Pharmacopoeia Committee of the Ministry

of Health of Ukraine. These prescriptions can be included in the State Pharmacopoeia - in pharmacopoeia articles (FS) or in temporary pharmacopoeial articles (TFS).

Manuals (Formulae manuales, lat. Manus - hand)- standard propolis, repeatedly tested by practical medicine. They can be included in special collections, manuals or recipes. Masterpieces (Formulae magistrates) - prescriptions prescribed by a physician to a sick person. Thus, the composition of medicinal products is determined by appropriate prescriptions. This division into groups is arbitrary, because individual extemporal drugs, if widely used, can be prepared on a large scale and become ophthalmic. In the pharmaceutical industry, the composition of the prescriptions of medicinal products is regulated by a recipe. The word "recipe" comes from lat. recipere - brothersThe recipe is called a written application (instruct) of the doctor to a pharmacist (in the pharmacy) on the manufacture of the medicinal product and release to his patient with an indication of the method of administration. The recipe has an important medical significance. It is a document that serves as the sole basis for the release from the pharmacies of most drugs and the use of their patients, based on the instructions of the doctor about the dose and the order of admission, taking into account the individual approach to the patient.The preparation of each recipe requires a serious and thoughtful consideration from the doctor, because the careless or improperly prescribed recipe can cause difficulty and delay in the manufacture and release of the drug, and in case of gross mistakes it can become the cause of an accident. In addition to the basic medical value, the recipe also has legal, technological and economic significance. The legal significance of the recipe is that it gives the right to purchase medicines and is determined by the rational use of the prescribed prescription for the patient, the date of prescription prescription, the presence of PI IB. and age of the patient, name the doctor, using the appropriate prescription forms taking into account the pharmacological action of medicinal products. In special cases, it can be a real proof, because persons who prescribe recipes and prepare medicines for them are legally responsible. The technological (technical) value of the recipe is that it serves as the basis and guidance of a pharmacist in the manufacture of a medicinal product (it indicates which medicines should be taken and in what dosage form they should be converted). The economic (financial-economic) value is that the recipe is a document on the expenditure of drugs and auxiliary materials; serves as the basis for calculations between the treatment and prophylactic institution and the pharmacy in cases of free-of-charge or preferential dispensing of drugs to ambulatory patients. The prescription determines the cost of the drug. In self-supporting pharmacies, along with the valuables in monetary terms, for medicinal substances in list A and ethyl alcohol, they account for the cost of their quantities in the formulation. The recipe serves as the basis for forecasting the financial activity of a pharmacy institution, as well as the

determination of the need for medicines. The rules for prescribing recipes are established by the order of the Ministry of Health of Ukraine No. 117 of 30.06.94. The right to prescribe recipes is provided only to persons with higher medical education-doctors. Doctors of medical and prophylactic institutions, including clinics of research institutes, medical educational institutions, legal and physical persons engaged in medical practice on a business basis, other doctors or authorized medical workers in the manner prescribed by these Rules, with In the presence of appropriate indications it is necessary to issue sick recipes, certified by their signature and personal stamp.Recipes should be dispensed with, taking into account the age of the patient, the order of payment for medicines and the nature of the action of medicinal products on forms printed in a typographic way on the established forms.Recipes are written in Latin, which has become international in this area. In some countries recipes are issued in the national, English, French or Spanish languages. At the same time, the structure of the recipe does not differ from that adopted in Ukraine, although it has some simplifications. For example, the prescription of a prescription ointment in Latin:

1RP:

Unguenti Ichthyoli 50.0

D.S. Apply to the affected area of skin 2 times a day.

In English:

1. Rp.: Ointment of Ichthammol 50.0

Apply twice daily to affected scin.

In french:

2. Rp.: Pommade d'ichthyolammonium 50 g

Appliquer sur la region affecte 2 fois on jour.

In spanish:

3. Rp.: Pomada de ictamol 50 g

Aplicates a part of afectadas 2 veces diaridis. Ingredients of the recipe.

The recipe must be written out in ink or a ball pen, clearly in the sequence below with the mandatory filling of all the graphs provided in the form (Fig. 4). It should be remembered that corrections in the recipe are not allowed: if the mistakes are made, the recipe must be rewritten.1. Inscriptio - inscription (from Latin inscribere - insert). The inscription indicates the first name, address and phone number of the institution where the recipe was issued. The code of the health care institution is printed entirely or the stamp is put. At the reception of the private practitioner, the surname, home address and telephone number (if any) must be indicated.

Datum is the date of issue of the recipe (the whole number, month, year is indicated) .1. Nomen aegroti - the surname, the initials of the patient. The recipe indicates the surname and initials of the patient, his age. Information about the age of the patient is necessary in connection with the fact that the pharmacist has the responsibility to control the correct appointment of a physician of poisonous and potent medicinal substances. If the patient is the doctor who prescribes the recipe, then "rgo te" (for me) is written.3. Nomen medici - the surname and initials of the doctor (legibly) .4. Invocatio - appeal (from lat. Invocare - to call, to beg). In the recipe, this part is presented in one word Recipe - take (which is usually written in abbreviated form: Rp.: Or R.:) And legally characterizes the order of the doctor of the pharmacist. It shows that this document is a recipe and is subject to all the rules of the recipe.5. Designatio materiarum or Orginatio - transfer of medicinal substances from which the medicinal product is prepared. This is the most important part of the recipe. Medicinal substances are prescribed in Latin in the generic term by chemical names (according to the nomenclature of the State Pharmacopoeia). When listing ingredients, each substance is written on a separate line with capital letters. The names of potent and potent drugs should always be written altogether. It is forbidden to reduce the names of the ingredients close to those that do not allow to establish which medicinal product is prescribed. For example:

1. **Stamp of medical-prophylactic establishment**	Polyclinic № 20 Darwin St.	Inscriptio	
2. **Date (legal and special values)**	t. 43-19-36	Datum	
3. **Full name of the patient, age**	10/08/1999 Ivanov NV 10 years of age	Nomen aegroti	
4. **Name of doctor**		Nomen medici	
5. **Recipe (doctor's referral to a pharmacist)**	Rp.: (Recipe)	Invocatio	**Designatio materiarum**
6. **Basic substances** **Promoting substances** **Corrective** **Consistency**	Codeini phosphatis 0,06 Natrii benzoatis 1,0 Sirupi simplicis 10 ml Aquae purificatae 200 ml	Basis Adjuvans Corrigens Constituens (Menstruum)	
7. **Ordinance**	Misce. Da.	Subscriptio	
8. **Notation** **Mode of application**	Signa. По 1 чайній ложці 3 рази в день	Signatura	
9. **Signature of doctor**	Doctor	Subscriptio medici	
10. **Personal physician seal** **Other seals**			

Fig. 1. Recipe and its components

In this case, we can mean: sodium sulfate (Na2SO4), sodium sulfide (Na2S), sodium sulfite (Na2SO3). All these substances have a completely different application. The use of the most important prescription abbreviations is allowed only in accordance with the accepted medical and pharmaceutical practice (see appendix 1). After the name of the medicinal product on the right side, its quantity is indicated. When prescribing medicinal substances, dosed in biological units of action (antibiotics, some other substances), in the recipe indicate the number of units of action (OD). In those cases, when medicines are dispensed in identical quantities, after the name of the last of them, before the designation of the number, write "apa" - on an equal footing. Liquid medicines are prescribed in milliliters and drops, all the rest - in grams. If the amount of liquid is less than one milliliter, then it is usually prescribed in drops, indicating their number in Roman numerals. For example, gtt IV (gtt - guttas - drop). What is the amount of auxiliary substances, the doctor may not specify the amount of them, and prescribe "qs" (quantum satis - as needed). Of course, drugs are prescribed in order of their decreasing importance. First, the basic drug is written, then prescribing the substances that take the basic

drug (adjuvans - the literal translation - the one that helps, contributes). Further, a substance that corrects the taste or smell of a medicinal preparation (corrigens), then - form-forming, or consistency substances, giving the form of drugs (constituens - filler) can be prescribed. Sometimes the doctor does not prescribe auxiliary substances in the recipe, but they are meant as completely defined on the basis of the rules established by the pharmacopoeia. For example, water is purified - for medicines, vaseline - for ointments, sugar in powders, solid fat bases in suppositories, and so on.7. Praescriptio or subscriptio - order, signature. After the transfer of medicinal substances it is indicated which dosage form should be prepared and the basic technological operations to be performed (mixing, entertaining, etc.) in which the medicinal product should be dispensed (in capsules, ampoules, in dishes dark glass, etc.) When prescribing dosage medications indicate the number of doses. Accepted abbreviations are widely used to denote the dosage form, for example: Mfung. (Misce fiat ungventum) - mix to ointment; Mf.pulv DD No. 6 (Mistake fiat pulvis. Da tales doses No. 6) - mix to get powder.

Signatura - signature, designation. Begins with the words Signa, or Signatur (the tag, let it be marked), is often written abbreviated - S. Signature content is intended for the patient, it indicates how to use the drug. Therefore, the signature is written in Russian or in national languages. Such general instructions as "External", "Internal", "Known," "To use as it is written", etc., are unacceptable, and so forth, as this deprives the pharmacist of checking the doping of poisonous, narcotic or potent medicinal products and can lead to incorrect administration of the drug to the patient. The method of treatment should be detailed, indicating the dose, frequency, and, if necessary, the time of admission, that is, before or after food, onset, and so on.9. Subscriptio medici - personal signature of the doctor and his personal seal. Signature While prescribing a prescription, the doctor accepts responsibility for the correctrum of this drug. This last part of the recipe is legally valid. In addition to the above, special assessments of doctors can be found in the recipes. For example, in the case of emergency need for the patient to leave a medicinal product the doctor writes in the upper right corner of the recipe the following inscriptions: Cito! (Quickly); Let's go! (As soon as possible); Static! (Immediately); Periculm in mora! (Procrastination is dangerous); Antidotum (protiotrute). If necessary, repeat the patient's prescribed medicine, the doctor makes the repetatur on the recipe, or vice versa, if repeat it is undesirable - pop repetatur, and affix the signature. When the physician knowingly knows that the prescribed medicinal product will have to be re-received by the patient, then he should write "Repetatur bis, ter" (and so on) in the prominent place of the primary recipe, which means (repeat twice , thrice, etc..) in cases provided for in Sections 20-24 of the Rules, the doctor makes the following in the recipe: "Chronic Patient",

"for special Purpose" .Recipes for medicines written on special forms of f- 3, valid for 5 days, are listed in paragraph 15 of the Rules - 10 days, and others - within two months from the day of the prescription.A recipe that does not comply with at least one of the requirements of the said Regulation or containing incompatible medicinal substances shall be considered invalid and no medication is allowed on it. The recipe is repaid by stamp " In drugstores of medical and prophylactic establishments, medicinal preparations are prepared on the basis of requirements issued in the form approved by the order of the Ministry of Health of Ukraine, in the presence of a stamp, seal and signature of the head of the institution or his deputy from the medical unit. The requirements must include the name of the department (room), the dosage and purpose of the medicinal product. In drugstores of medical and prophylactic establishments, medicinal preparations are prepared on the basis of requirements issued in the form approved by the order of the Ministry of Health of Ukraine, in the presence of a stamp, seal and signature of the head of the institution or his deputy from the medical unit. The requirements must include the name of the department (room), the dosage and purpose of the medicinal product.

NORMAL QUALITY OF MEDICINAL PRODUCTS

The quality of drugs is directly dependent on the quality of raw materials, the method and the conditions for their manufacture. Therefore, while exercising control over their production, the state establishes the same requirements and special quality standards for medicines, auxiliary substances and materials. Thus, the standardization of the quality of medicinal products is the process of establishing and applying standards. The standard is a normative document developed and approved by a recognized body, in which rules, requirements, general characteristics related to different types of activities or their results are established for achieving ordering in a defined area. Standards are based on the generalized achievements of science , technology, practical experience and aimed at achieving optimal benefits for society. Depending on which standardization organization (international, regional or national) adopts standards, they are respectively divided into international, regional and national. By scope, standards are divided into state (DST), sectoral (OST), republican (PCT) and enterprise standards (STP). For example, the standards that apply to medicinal products are industry standard technical documentation (NTD) and are approved by the Ministry of Health. The order of their development is regulated by OST 42U-1 -92 "Procedure for the development, approval of normative and technical documentation for medicinal products and medicinal raw materials". Standards should periodically be reviewed in the light of modern advances in science and

technology. NTD defining the requirements for the quality of medicinal products are subdivided into the following categories: State Pharmacopoeia (DF), Pharmacopoeial Article (FS), Temporary Pharmacopoeia Article (VFS). Pharmacopoeia article (FS) is a normative and technical document that establishes requirements for a medicinal product, its packaging, conditions and termin storage and methods of quality control of medicinal product. First, for each new medicinal product, a temporary pharmacopoeial article (VFS) is approved for a certain period (most often for 3 years). If, after this time, a medicinal product, normalized by this WFS, has justified itself in medical practice and its production becomes stable, then a permanent FS is being developed for it. When preparing it, the WFS makes the necessary clarifications, corrections and additions. If necessary, the WFS may continue. Current FSs are periodically reviewed. WFS and FS of all categories after their approval are registered with the assignment of the mark consisting of the 42U- index, the registration number and the year of approval or revision of the article (the last two digits) .Example: Guttae ophtalmicae «Propomics »FS 42U-34 / 42-113-96 Eye drops« Propomix »instead of VFS 42-2023-90FS and WFS have the following structure: warehouse; description; solubility; authenticity; transparency and colorfastness; the limit of acidity or alkalinity, pH; dry residue; alcohol content, etc.Separate sections can be combined or lowered, and if necessary, other specifics for the given object can be entered. The sections on packaging, marking, transportation and storage periods are mandatory, indicating the relevant DSTs, which regulate packaging materials, sealing agents, marking symbols. In addition, the course of the presentation indicates the NTD, requirements of which must meet the individual components of dosage forms and all the methods used for analysis. At the end of the articles, information is provided on the main pharmacological action of the medicinal product. FS for medicinal products of the highest therapeutic value and widely included in medical practice, as well as high qualitative indicators, are included in the State Pharmacopoeia.The creation of new drugs and the development of NTD, which normalizes their quality, is the only inseparable process that is carried out in a definite sequence. The procedure for the establishment and introduction of medicinal products is established by the order No. 87 of September 4, 1996 (State Committee of Commerce and Industry of Ukraine, since 2000 - the State Department of quality control, safety and production of medicines and medical products). New medicinal substances and medicines created from them are developed in scientific research institutes, laboratories and departments of pharmaceutical universities. Upon completion of the pilot studies to be carried out at the modern scientific level, the NTD and samples of the finished product (together with the manufacturer) are sent to the Pharmacological Committee of the Ministry of Health of Ukraine (since

2000 - the State Pharmacological Center of Medicinal Products). The Committee issues permission for a clinical trial of new drugs presented, which is usually carried out at once in several medical institutions in the country. When obtaining positive results of clinical examinations, the Pharmacological Committee recommends that the use of the medicinal product and its pharmaceutical form in medical practice be permitted. After admittance to the medical application, registration and approval of the NTD for medicinal products, raw materials, prescriptions for medicinal forms are carried out by the Pharmacopoeia Committee of the Ministry of Health of Ukraine. The work of both committees on admission and rationing of new medicines is completed by the order of the Ministry of Health of Ukraine on the permission for medical use and industrial production, as well as their inclusion in the State Register of Medicinal Products.Pharmacopoeia. Pharmacopeia is of great importance in pharmaceutical practice. Pharmacopoea comes from two Greek words: pharmacon - medicines and rovei - I do, prepare, that is literally it can be translated as a "guide to the preparation of drugs". Initially, pharmacopoeias were really collections of drugs with a description of how they were cooking. Modern pharmacopoeia is a collection of standards for medicinal products and provides only the basic principles of manufacturing medical forms. State Pharmacopoeia is a collection of compulsory medical-pharmacies-national standards and regulations that regulate qualitymedicines. Pharmacopoeia has a legislative character, obligatory for all medical, including veterinary establishments and enterprises of the country, which manufacture, store, control and use medicinal products.The first Russian Pharmacopoeia was published in 1866, the second edition - in 1871, Ill - in 1880, IV in 1891, V in 1902, and VI in 1910.In pharmacies of these years, due to the rapid growth of the chemical industry, chemical drugs are largely reflected, which has even led to the underestimation and oblivion of a number of herbal medicinal products. They reflect successes in the field of analytical chemistry, which allowed the transition from organoleptic tests to more advanced methods of analysis. In 1925 the State Pharmacopoeia, the seventh edition was issued. Then there were additional copies of this edition, issued in 1929, 1934 and 1942.In 1946, the VIII edition of the State Pharmacopoeia was issued, and in 1952 it was an additional edition of this edition, which made a number of corrections and additions. In the same year, the first supplement to the State Pharmacopoeia VIII was issued. In 1961 the State Pharmacopoeia IX edition (DF IX) containing 781 drugs was issued. This pharmacopoeia included new, effective medicines made from domestic raw materials and excluded outdated. In 1968 the X edition of the State Pharmacopoeia (DF X) came out. The progress of domestic science allowed to expand and improve pharmacopoeia with normative documents a little. The latest advances in

physics, chemistry, and biology have allowed us to develop a number of more advanced methods of treating contraceptives. There was a large number of new antibiotics, synthetic and highly effective herbal medicines. More advanced methods of producing dosage forms in pharmacy and in factory conditions are developed. All this was reflected in DF X. All of these pharmacopoeias were issued in one volume, which included private and general pharmacopoeial articles for medicinal substances and medicinal forms, as well as medicinal plant raw materials, and general articles describing the physical, physico-chemical and biological methods of drug analysis. Includes information about reagents and indicators. The annexes provided a number of help tables. After the release of DF X, the system for the development and approval of pharmacopoeial articles for medicinal products was changed. In connection with this, there was a need to issue the State Pharmacopoeia XI Edition (DF XI) on a new basis. Unlike previous editions, the DF XI was supposed to be issued in several parts, consisting of separate volumes, having a serial number number. However, in the current historical conditions (the collapse of the USSR), only two volumes were published. In the first volume of the DF XI "General Methods of Analysis" (published in 1987), 9 articles were first introduced on contemporary methods of analysis, such as: "Gas chromatography", "Methods of phase solubility", "Electrophoresis", "Fluorescent chromatography" and othersOf the presented physico-chemical methods of analysis for technology, the most important is the article "solubility", which is slightly different from the typical DF X: the soluble substances are defined as moderately soluble, refined solubility technique. In the section "Methods of analysis of medicinal plant material" included 7 general articles, which determine the main diagnostic features for the morphological groups of raw materials. The section "Sampling of packaged products" is included for the first time. Issue 2 DF XI (issued in 1989) includes "General methods of analysis, biological control methods", "Methods of quality control of medical immunobiological drugs" and "Medicinal herbal raw materials" .The first section includes mainly general articles on dosage forms, of which the first presented: "Suspensions", "Aerosols", "Studies on microbiological number." Other articles are supplemented and redone in the light of modern achievements. For example, in the article "Sterilization", for the first time introduced methods for sterilization by filtration of the diaphragm and deep filters, as well as radiation; the article "Injection" introduces the definition of infusion, toxicity and pyrogenicity tests; In the article "Mash" a microscopic method for determining the solid phase dispersion in suspension media was introduced; In the article "Suppositories" an index of "dissolution" was introduced for suppositories prepared on the hydrophilic bases.Of particular interest and importance for technology are general articles on

dosage forms, methods of their manufacture, requirements for them and indicators of quality assessment. They also contain excipients that the pharmacist can use if they are not indicated in the recipe (solvents, bases for ointments and suppositories, etc., stabilizers for injectable solutions, emulsifiers for emulsions, etc..), Often with an indication of their number. The recommendations for the introduction of medicinal substances into the pharmaceutical form, the degree of dispersion, the sequence of technological operations, etc., are given. Special attention is directed to the requirements proposed for the medicinal form: precision of dosing, permissible deviations in mass or volume, transparency for solutions, sterility for injectable solutions and TP, which is very important for the technological process and the assessment of the quality of the dosage forms. In some cases, when the quality of the dosage form can not be standardized, the process of its manufacture is standardized in the pharmacopoeia. For example, in the article "Infusions and decoctions", the quality of which is difficult to assess in pharmacy conditions, specific instructions are given on their technology: the conditions for the extraction of medicinal raw materials, the standardity of raw materials and their dispersion, etc., are established.In the section " The project of the first part of the State Pharmacological Center (prepared for the V National Congress of Pharmacists of Ukraine, 1999) is written in Ukrainian and Russian. General and private articles of the PFU project consist of two parts: the European (which is the literal translation of the relevant article of the European Pharmacopoeia) and the national one, which does not contradict the European and complement its national peculiarities. The draft of the first part of the SPF includes 30 general articles: 7 articles on dosage forms, 9 - on pharmacoecological tests and 14 - on methods of analysis. The article "Residual amounts of organic solvents" has been in force in Ukraine since February 1, 1998. Specialists from all the well-known pharmaceutical centers of Ukraine (Pharmacopoeia Committee, NCTSC, NFAU, etc.) Participated in the preparation of the State Pharmacopoeia project. DFU is the first pharmacopoeia of Ukraine. At present, almost all countries of the world have state pharmacopoeias. They are issued by governmental bodies and reflect the achievements of the pharmaceutical science of this country. So, published Pharmacopoeia of Germany. Czechoslovakia, Scandinavian countries, etc. The leading pharmacies are Great Britain (1980), USA (1985), Japan (1982). In 1951, p. The World Health Organization (WHO) of the United Nations issued the first volume of the International Pharmacopoeia (English), then went Volume II and supplemented it in 1959. They were published in English, French and Spanish. In 1967, the second edition of the International Pharmacopoeia, a collection of non-legislative specifications, came into being. They are offered as reference material so that national specifications can be developed on the same basis in any

country. The articles of the 2nd edition of the supplement were prepared through cooperation with the members of the WHO Expert Advisory Council on International Pharmacopoeia, as well as with a large number of specialists from different countries. In 1969, the second edition of the International Pharmacopoeia was first published in Russian. In 1979 the I volume of the International Pharmacopoeia III was published (MF III), and in 1981, p. - II volume, which in 1983 was released in Russian. The main objective of the MF is to ensure that pharmacopoeial medicines and pharmaceutical forms made from them are of equal quality in all countries that have accepted the International Pharmacopoeia for guidance. Manuals (from the Latin manualis - manual, that is, the manual) are collections of prescriptions of medical forms not included in the acting pharmacopoeia. Quite often in mana-lakh is given the short technology of the described medicinal preparations. Manuals have the character of official, semi-official and unofficial publications, since they can be issued by both public (professional) organizations and individual scholars. The first Soviet "Pharmaceutical Manual" was published in 1949. It contains the most commonly used complex drugs information under certain conditional names, often associated with the names of doctors who first proposed these prescriptions. These include, for example, prescriptions for Bekhterev's medicine, Zelenin's drops, and many others. A total of 405 prescriptions, expressed in rational dosage forms and in their composition, contain available ingredients, mainly of domestic origin. The second part of the manual is a list of 70 prescriptions, the components of which were physically or chemically incompatible with each other, as well as prescriptions, in the manufacture of which there were some features ("complicated" recipes) .Similar manuals are issued in other countries, including "Pharmaceutical Formulas", issued in 1944 in England; in its one volume more than 10,000 records. Among the contemporary unofficial publications is published in 1999 under the editorship of the Academy. OI Tikhonova "Handbook of Extemporal Recipe. Alopathy and homeopathy." In it for the first time more than 2,000 registers of extemporal formulation of medicinal products according to diseases are generalized and systematized. The manual also includes the labeling of homeopathic remedies. In 2000, the second edition of this book "Extemporal Recipe (Technology, Application)" came out. Issue 1 "Liquid dosage forms" includes 123 prescriptions describing their technology. The prescriptions are systematized on medicinal forms and dispersion classification. Among foreign publications, the Formulaire de Magistrale du Syndicat (FMS, 1992) is a compilation of prescription drugs, compiled by the commission of French pharmacists, which ensures its publication and distribution. Interesting structure of this compilation: the prescriptions of medicines are classified into sections by

dosage forms, and in each section of the prescription drug forms are classified as diseases. The collection includes a memorial to doctors on the rules for prescribing prescriptions with the obligatory indication of the title of the collection. Formules Magistrales (ARIS, 1994 p.) - issued by the association of independent pharmacists from Charleroi-Ville. The collection contains prescriptions of the most commonly prescribed prescription drugs, with their cost. The authors draw the attention of doctors prescribing drugs to doses that can be changed in each particular case. The guide includes information about new drug release rules.The publication of official and unofficial collections of main (extemporal) prescriptions gives a lot to both the pharmacist and doctors. In such sources, you can find a lot of successful combinations of drugs.

Good pharmacy practice is a guarantor of the quality of medical supplies. One of the constituent elements of NAP is compliance with the conditions and technological process of the production of extemporal drugs. Production and quality control of medicines are interdependent. Therefore, the relevant requirements for them are dealt with in one section.Rationing conditions for the manufacture of medicinal products includes:

> observance of the complex of sanitary-hygienic measures (microclimate, illumination, air pollution, equipment, etc.), which is thoroughly studied in the course of hygiene;

> compliance with the sanitary regime, and in the manufacture of a number of medical forms - the conditions of asepsis;

> observance of the rules of work with poisonous, narcotic and substances equated with them;

> safety precautions. The rules that regulate the conditions for the manufacture of medicinal products in pharmacies are established by the relevant state authorities (orders of the Ministry of Health of Ukraine No. 139 dated 14.06.93 p., No. 44 of March 16, 1993 p.) .In the process of production, sources of pollution of medicinal products may be impurities that come from the apparatus during synthesis, due to imperfect methods of purification (impurities of heavy metals, lead and, which is very dangerous, arsenic). In the initial vegetative raw materials, there are also impurities of mineral and organic origin, which in one degree or another are reflected in the purity of the extract. Relevant impurities in quantities above the permissible standards can cause toxic effects on the human body or affect the stability of medicinal products. Sources of microbial contamination (microbiological contamination) of non-sterile medicinal products can be: medicinal and auxiliary substances, packing and poaching materials, and also the possibility of infection of medicinal preparations in the process of manufacturing from working personnel, equipment, etc. is not excluded.

Medicines are most often contaminated by saprophytes, widely distributed in the environment: soil, water, air, on plants, etc. Unlike pathogenic microorganisms, many saprophytes have a large set of enzymes and can disperse a variety of substances. In particular, yeast and filamentous fungi are capable of destroying glycosides and alkaloids, ascorbic acid, glucose, vitamins, and others. Many microorganisms inactivate antibiotics, break down proteins, lipids, cause the decomposition of galenic preparations. Microbial lesions are the basis for ointments, their components and ready-made ointments. Thus penicillins, actinomycetes easily break down paraffin, mineral oils, vaseline, beeswax and others. In all cases, factors such as the concentration of medicinal substances, humidity, ambient temperature, as well as the nature and degree of primary colonization, etc., influence the intensity of the destruction of medicinal products. The products of destruction of medicinal substances can also serve as a nutrient medium for microorganisms.Currently, in many countries, including ours, due to the danger of microbial contamination, temporary maximum permissible norms of non-pathogenic microorganisms in non-sterile medicinal products included in DF XI have been developed.Pharmacy workers should observe the requirements of the sanitary-anti-epidemic regime of pharmacy and personal hygiene of pharmacists (Order of the Ministry of Health of Ukraine No. 139 dated June 14, 1993) for the preservation of high quality medicinal products, their physical and chemical stability and apirogenicity.

Instructions include:

- requirements for premises and equipment of pharmacies;
- sanitary requirements for cleaning of premises, maintenance of equipment of pharmacies;
- requirements for personal hygiene of pharmacies;
- sanitary requirements for receiving, transporting and storing water purified and water for injections;
- sanitary requirements for the manufacture of medicines in aseptic conditions;
- sanitary requirements in the manufacture of non-sterile dosage forms;
- the procedure for handling rubber stoppers and cleaning the pharmacy dishes.

It is equally important to normalize the conditions of production by properly preserving medicines and auxiliary materials. In the instructions on the organization of storage in pharmacies of different groups of medicines and medical products (see Annex 2) provided:

- maintenance of equipment of pharmacies;
- requirements for personal hygiene of pharmacies;

- sanitary requirements for receiving, transporting and storing water purified and water for injections;

- sanitary requirements for the manufacture of medicines in aseptic conditions;

- sanitary requirements in the manufacture of non -sterile dosage forms;

- the procedure for handling rubber stoppers and cleaning the pharmacy dishes.

It is equally important to normalize the conditions of production by properly preserving medicines and auxiliary materials. In the instructions on the organization of storage in pharmacies of different groups of medicines and medical products (see Annex 2) provided:

- transporting and storing water purified and water for injections;

- sanitary requirements for the manufacture of medicines in aseptic conditions;

- sanitary requirements in the manufacture of non-sterile dosage forms;

- the procedure for handling rubber stoppers and cleaning the pharmacy dishes.

It is equally important to normalize the conditions of production by properly preserving medicines and auxiliary materials. In the instructions on the organization of storage in pharmacies of different groups of medicines and medical products (see Annex 2) provided:

- requirements for the device and operation of storage facilities;

- general requirements for the organization of storage of medicinal products;

- requirements for the storage of medicinal products, depending on their physical, physical and chemical properties and the influence on them of factors of the environment.

Details of this information will be considered in the relevant sections of the textbook. The standardization of the technological process is one of the factors ensuring the high quality of the manufactured drugs. Violation of technology may be due to poor quality medicines. For example, in the manufacture of infusion of grass with a normal biological activity in violation of the temperature regime, a drug with reduced or lost biological activity can be obtained. Therefore, it is necessary to control all stages of production from the initial to the final moment of each technological operation, the sequence of transition and the connection between them. In this case, determine the basic parameters (speed of heating or cooling, mixing time, pH value of the medium, etc.). The completion of the technological operation must be determined by the established basic technological indicator. For example, a defined temperature, pH, dispersion of the suspension, etc. In industrial conditions, the stages of the technological process of production

are regulated by regla-tion. The technological regulation is a normative document in which technological methods, technical means, norms and norms of production of a medicinal product are defined (structure, rules and procedure of development and approval of regulations are stipulated by MLA 09-001-98 "Regulations on the production of medicinal products") Pharmacological conditions of the technological process stage are regulated by DF, technological instructions, information sheets that comply with the orders of the Ministry of Health of Ukraine (Order No. 197 dated September 7, 1993, etc.). the first general stage of manufacturing for all dosage forms is preparatory work. This is the preparation of premises, auxiliary facilities, equipment, packaging materials, medical and auxiliary substances. After the preparatory work, the stages of the technological process are sequenced in accordance with the specificity of the dosage form. For example, in the manufacture of liquid dosage forms, it is necessary to observe the prescribed order of dissolution and mixing of medicines taking into account their physical and chemical properties; when making powders it is necessary to observe the rules of mixing, grinding, the introduction of coloring agents, etc. (This information will be indicated in the relevant sections of this textbook).

Normalized and common for all medical forms are the final stages of the technological process: packaging and registration for release. All medicines are packaged depending on their aggregate state and intended for packing material, which is allowed for medical purposes. There are common rules for the registration of drugs that are being prepared in pharmacies. All medical preparations make labels of a certain size and specimen. Depending on the method of administration, the labels are divided into internal, external, for injections, for ophthalmic dosage forms. Labels have different signal colors: green - for medicines prescribed inside; orange - for exterior use; pink - for eye medical forms; blue - for injection. All labels must have the following designations: the emblem of medicine, the pharmacy number, the prescription number, the surname and initials of the patient; the method of application, the date of manufacture of the medicinal product, the signature of the person who prepared the medicinal product, and the cost, as well as the posting statement "Keep away from children". On the labels of medicinal preparations intended for injections, their composition is indicated. For a special attention to the appointment of a medicinal product, the warning signs are used: "Children", "Heart". For medicinal preparations that are prepared individually and depending on the dosage form and purpose, use the labels "Powders", " Mixture "," Drops "," ointment "," Eye drops "," Eye ointment ". Great emotional impact on the patient has the appearance of packaging, its perfection, purity, tightness. It has been established that a slowly decorated and released drug, poorly sealed, leaking and contaminating the container from the outside, may not require the necessary

therapeutic action, despite the fact that it contains all the necessary medicinal substances. The packaging should be the bearer of scientific, advertising and aesthetic information, should fit into the technological scheme as one of the elements of the process, intensifying or, at least, not reducing productivity. Quality control of medicines in pharmacies. In the state valuation of the production of medicinal products, much attention is paid to quality control of the finished product.

State control over the quality of medicinal products is carried out by the state constituents through official NTDs (DFs, acting orders, instructions, etc.). The quality control of medicines in pharmacies involves a range of measures that ensure the manufacture of medicinal products of the proper quality. These include:

> compliance with sanitary norms and rules, sanitary and hygiene and anti-epidemic regimes, rules of aseptic manufacturing of medicines, pharmaceutical order in accordance with existing normative-methodical documents and orders;

> provision of terms and conditions of storage in the pharmacy of medicinal products in accordance with the physical and chemical properties and requirements of the State Pharmacopoeia, acting orders and instructions;

> careful review of the recipes coming to the pharmacy, and the requirements of treatment and prevention institutions in order to verify the correctness of their prescription, compatibility of drugs included in the composition of medicines; the compliance of prescribed doses of the patient's age;

> observance of the technology of manufacture of medicinal products in accordance with the requirements of the State Pharmacopoeia, acting orders and instructions.

The quality and effectiveness of the sanitary-anti-epidemic regime in pharmacies is determined by the results of bacteriological control. The objects of bacteriological control in pharmacies are: water purified and water for injection, medicines, pharmacy dishes, plugs and other auxiliary materials, inventory, equipment; hands and clothes for the staff; air environment.

1. Written control: carried out by a pharmacist and pharmacist-technologist in the manufacture of medicinal products according to individual prescriptions and requirements of treatment and prevention institutions by filling in the written control passport (PCT). The passport is filled in immediately after the manufacture of the medicinal product in accordance with the technology. The passport indicates: the date, the number of the recipe (requirements), the medicines taken (in Latin) and their number, the number of doses, the subscriptions of those who prepared, packaged and checked the drug. In the case of preparation of a medicinal product, the practitioner shall include the signatures of a trainee and a person responsible for industrial practice. For medicinal preparations containing poisonous drugs, the

letter "A" is placed on the top of the passport, and the letter "D" is given on the medical forms for children. All calculations are made for the preparation of the drug and recorded on the back of the passport. When using semi-finished products and concentrates, their concentration and quantities are indicated. When making powders, suppositories and pills, the weight of individual doses and their number is indicated. The size of the pill or suppository mass, the amount of isotonic and stabilizing substances added to eye drops and injection solutions are indicated both in the passports and on the reverse side of the recipes. The passport shall indicate the coefficients used for calculating the water absorption for medicinal plant material, the coefficients of increasing the volume of water solutions at the dissolution of medicinal substances, calculation formulas used in calculations. Prepared medicines, recipes and filled PPK are passed to the chemist for a technologist or person performing his functions. The control means to check the adequacy of records in the control panel of the prescription and to make the correctness of the calculations. If the medicinal product is checked by a pharmacist-analyst with complete chemical control, the passport contains the analysis number and signature of the pharmacist-analyst. When a medicinal product is manufactured and discharged by the same person, the control of the control panel is also required. In the manufacture of injectable solutions, all records are stored in a special journal. The control panel is kept in the pharmacy for one month.

2. Questioning control: carried out by the technologist and applied selectively. After manufacturing a pharmacist no more than 5 drugs, pro-vizor-technologist calls the first ingredient included in the drug, and in the complex medicines indicates its amount, after which the pharmacist must name all the ingredients taken and their number.

3. **Organoleptic control:** carried out by an analyst or pharmacist-technologist and consists in checking the appearance of the dosage form, its color, taste, smell, homogeneity of mixing, the absence of mechanical inclusions in liquid dosage forms. Homogeneity of the mixing of powders, ointments, pills, suppositories is checked up to the mass separation by dose. The check is carried out selectively by each pharmacist during the working day (but not less than three dosage forms per day). On the taste, dosage forms for internal use are checked selectively and in cases of doubt as prepared dosage forms. Particular attention is paid to medicines for children. The results of organoleptic control of the dosage forms are recorded in the journal.

4. Physical control is carried out by the analyst or pharmacist-technologist and it is necessary to check the total mass or volume of the dosage form, the number and weight of the individual doses included in this dosage form (but not

less than 3 doses) are also controlledquality of clogging. Physical control is subject to: - each series of packing and intrapackage preparation (from 3 to 5 units of samples from each series or preparation; - selectively dosage forms prepared on individual recipes per day (but not less than 3% of the total amount); - dosage forms requiring sterilization, after packaging before sterilization.

5. Chemical control is carried out by a pharmacist-analyst (qualitative and quantitative) andthe pharmacist-technologist (selectively - qualitative) and is to determine the correspondence andthe quantitative content of medicinal substances included in the dosage form. Water purified, water for injection, all drugs coming from the warehouse, solutions-concentrates, semi-finished products, packing are subject for qualitative analysis; selectively -all types of dosage forms prepared according to recipes (requirements). All solutions for injection before and after sterilization; eye drops and ointments containing narcotic and poisonous substances; all dosage forms for newborns, solutions of hydrochloric acid (for internal use), atropine sulfate, mercuric dichloride and silver nitrate; all concentrates, half-dresses and intrapulmonary procreation; stabilizers used in the manufacture of injections and eye drops; concentration of ethyl alcohol are subject to the complete chemical analysis; selectively - all types of medical forms (but not less than eight, prepared for change) .Particular attention is paid to the control of children's medical forms, eye and those containing narcotic and poisonous substances.

6**. Control at departure** is carried out by a technologist-supervisor. All medicines prepared at the pharmacy are subject to control. Checked: Packing (must correspond to the weight (volume) and type of dosage form, as well as the properties of the inbound ingredients), registration (must comply with the requirements of the current regulations); the compliance of the doses of medicinal products listed in the prescription with the list A and B of the patient;

5. Materaly enhance students during the presentation of lectures

1. Identify the components of the recipe according to the algorithm of its structure.
2. To indicate the peculiarities of registration of recipes containing poisonous, narcotic, psychotropic substances, as well as hypnotics, antipsychotics and tranquilizers in the clause No. 16 of the Order of the Ministry of Health of Ukraine No. 117 dated June 30, 1994.
3. Specify the terms of the recipes if the list includes substances in the general list.
4. Determine for the table doses higher single and daily doses of atropine sulfate and papaverine hydrochloride for adults.
5. What should a pharmacist do in the event of an incorrectly prescribed prescription in the pharmacy?

6. Technology of medical forms as a science, its tasks and directions of development.
7. Basic terms and concepts in the technology of drugs: medicines, active substances (substances), excipients, finished medicinal products, pharmaceutical form, State Pharmacopoeia (DF), pharmacopoeial article (FS), temporary pharmacopeial article (TPS), technical conditions (TU), state standards (DSTU), International Pharmacopoeia, State Register of Medicinal Products of Ukraine, quality of medicinal product, expiry date of medicinal products.
8. What orders regulate the conditions of preparation, storage and release of drugs from pharmacies?
9. What are the main directions of state regulation of the production of medicines in Ukraine?
10. What documents regulate the quality of medicines?

Tests

1.The pharmaceutical enterprise is developing new products. In which section of the technological regulations describes the appearance and physico-chemical properties of the finished product:

A. * Characteristics of the final product of production
B. Information materials
C. Characteristics of raw materials, materials and intermediates
D. Statement of the technological process
E. Characteristics of auxiliary raw materials and materials

2. Which normative and technical document sets out the requirements for the quality of medicinal means or medicinal plant raw materials, approved for a limited period.

A * Temporary Pharmacopeial Article (TFS)
B Technological industrial regulation (TPR)
C Pharmacopeia article (FS)
D State Standard (GOST)
E Industry standard (GSTU)

3. The normative document, which establishes the requirements for specific products and services, and regulating the relationship between the supplier and the consumer. How long does it take?

A * Specifications;

B Standard;
C Technical regulations;
D Technological regulations;
E Methodological guidelines

3. Point, which issiues pharmacy doesn`t explore.

A. Consumer demand

B. Synthesis and analysis of drugs.
C. The development of new theories and methods of manufacture of dosage forms.
D. The study of natural resources of plant, animal, mineral origin and refining them into drugs.
E. Quality control, storage and dispensing of medicines.

4. What is a pharmacological agent?

A. is a substance or a mixture of substances with established pharmacological activity.
B. adjuvant
C. surface shell
D. a drug substance that promotes the cleavage in the body

5. Choose the solid dosage form.

A. Pills
B. Ointment
C. Potion
D. Aerosol
E. Patch

6. Choose the liquid dosage form.

A. solution
B. ointment
C. potion
D. aerosol
E. patch

7. What factor does not affect the quality of the finished product?

A. Location of the enterprise
B. raw materials
C. production technology
D. production equipment

8. What scientific discipline is closely connect with medicine technology?

A. *Pharmacology
B. organization and economy of pharmacy
C. pharmacognosises
D. management and marketing

9. What factor can not be attributed to the functions of auxiliary substances?

A. Strengthening the action of active substances
B. Masking of taste and smell
C. Filling the dosage form to the desired weight
D. Disintegration in a specific part of the gastrointestinal tract
E. Giving the attractive appearance

6.General material and guidance of the lecture:

- educational premises: - small lecture pharmaceutical audience at the department of pharmacy;
- Illustrative materials: - National Pharmacopoeia and normative and technical documentation.

7. Materials for self-training of students:

1. To familiarize with the basic normative documents regulating manufacture of medicines:
- Law of Ukraine "On Medicines";
- By orders of the Ministry of Health of Ukraine;
- National Pharmacopoeia.

8. Literature lecturer who used to prepare the lecture.

1. Technology drugs. Textbook: Textbook for Universities / AI Tikhonov, PA Logvyn, S. Tikhonov, A. Mazulin, TG Yarnyh, OS spiers, O. Mikhail Kotenko; Edited by AI Tikhonov - Kharkov: Pharmacy; Original, 2009. - 432 p.
2. Technology Medicine: Textbook / A. Marchuk, NB Androshchuk - Kyiv: Health, 2008. - 488 p.

More:
1. Soft medicinal forms: extemporaneous compounding: Guidelines / AI Tikhonov, T. Yarnyh, AV Lukienko etc .; Ed. OI Tikhonov. - H .: Izd pharmacy; Golden Pages, 2003.-128 with.
2. Aseptic drug forms, extemporaneous compounding: Guidelines / AI Tikhonov LV Bondarev, TG Yarnyh NF Orlovetska etc .; Ed. AI Tikhonov and T. Yarnyh. - H .: Izd pharmacy; Original, 2005. - 184 p.
3. Solid dosage forms: extemporaneous compounding: Guidelines / AI Tikhonov, T. Yarnyh, S. Gritsenko, etc.; Ed. AI Tikhonov - H .: Izd pharmacy; Golden Pages, 2003. - 176 p.

4. Liquid formulations: extemporaneous compounding: Guidelines / AI Tikhonov, T. Yarnyh NF Orlovetska etc .; Ed. AI Tikhonov and T. Yarnyh. - H.: Izd pharmacy; Original, 2005. - 160 p.

Lecture 2: "Solid dosage forms. Technology of powders with medicinal substances, differing in prescribed amount, bulk density and structure of particles. Technology of powders with poisonous and potent substances. Powder technology with colorful, fragrant, hard-to-grind substances and extracts" - 2 hours.

1. **Actuality of theme.**

Powders have been used since ancient times and are among the first drugs that began to provide a certain form. Despite the expiry date of application, powders have not lost their significance and now, because medicines used in the form of powders have certain positive properties. Powders are fairly common drugs, and in the general formulation of pharmacies they occupy about 30% in relation to other drugs. Powders - one of the oldest dosage forms, which until now is widely used in medical practice. The therapeutic effect of this dosage form largely depends on the choice of optimal technology based on the physico-chemical properties of the drugs and their amounts. Therefore, the study of classification, the basic and specific rules of manufacturing is of great importance for the assimilation of the theoretical foundations of the technology of powders of any composition.

2. The objectives of the lecture:

-training:

• Learn to prepare simple and complex powders with medicinal substances that differ in physical and chemical properties and quantity, evaluate their quality in release.

• Learn how to prepare complex powders with poisonous and potent substances, evaluate their quality and quality in release.

• Learn to prepare complex powders with colored (dyestuff), fragrant and severely degradable drugs, evaluate their quality and make them ready for release

• Learn how to prepare complex powders with extracts (dry, thick, solutions of dense extracts), and also use semi-finished powders.

- educative: The upbringing of students from the notion that a medicinal product should be considered as an object used for the preparation of various medicinal products, and drugs, in turn, as a form of application of medicinal products, that is, drugs in this case are already subject to patients.

3. Plan and organizational structure of the lecture.

№№ pp	The main stages of lectures and their contents.	The objectives in the levels of abstraction.	Type lecture, lecture equipment.	Distribution of time.
1	2	3	4	5
	Preparatory stage			

1. 2.	Learning objectives. Provide positive reinforcement. ***The main stage*** Presentation of lecture material. Plan: 1. Determination of powders as dosage forms. Biopharmaceutical evaluation. 2. Requirements of DFU and DF XI to powders. 3. Classification of powders. 4. Stages of the technological process. 5. General rules for the preparation of powders. 6. Assessment of the quality of powders ***The final stage*** Summary of lectures, general conclusions. Lecturer answers to possible questions. Tasks for self student.	I II III II I	According to the publication, "Methodological recommendations for planning, preparation and analysis of lectures. " (Ed. 2001). References, issues, tasks.	85% - 90%
3. 4. 6. 7.				

4. Content of lectures:

1. Determination of powders as dosage forms. Biopharmaceutical evaluation.
2. Requirements of DFU and DF XI to powders.
3. Classification of powders.
4. Stages of the technological process.
5. General rules for the preparation of powders.
6. Assessment of the quality of powders

Powders - one of the most ancient medical forms used in medical practice in 2500-3000 years BC and has not lost its value until now. An analysis of the extemporal formulation has shown that in the form of powders various drugs of organic and inorganic nature, dense substances and liquids in quantities that do not affect their viability are prescribed.

The technology of powders is quite simple to execute. However, the knowledge gained under the basic rules of preparing powders, serve as a basis for

studying more complex dosage forms: suspensions, ointments, suppositories, pills for both pharmacy and factory production.

Powders - a solid dosage form for internal and external application, consisting of one or several chopped powders and has the property of flowing.

The advantages of powders as a pharmaceutical form can be attributed:

- ease of preparation, accuracy of dosing;
- versatility of the composition (in the form of powders it is possible to combine different composition and properties of medicinal substances);
- convenient storage and transportation.

Disadvantages of powders:

- slower therapeutic action compared with liquid dosage forms;
- poor storage capacity due to a large specific surface (easily lose or absorb water, oxidize, etc.);
- an inconvenience of taking odorous, colorful and substances having an unpleasant taste;
- subacute effect on the mucous membrane of the gastrointestinal tract.

During the internal use, the powders have a constant contact with the mucous membranes, starting with the oral cavity and esophagus, which causes the manifestation of allergic reactions and irritating effect.

Some disadvantages of powders can be eliminated, which is done in practice. For example, volatile and coloring substances are released in capsules. For medicinal substances that cause irritation of the mucous membrane (eufilin, acetylsalicylic acid, sodium bromide, etc.), as well as for substances that undergo metabolic transformation in the stomach to form inactive or undesirable products, enteric soluble colonies (in the form of tablets or capsules). Thus, the coating of sulfadimezin and sulfapiridazine with acetylphthalylcellulose (AFC) can reduce the process of their acetylation in the stomach and increase the content of the active form of dasgs in the blood by 15-20%.

Unfortunately, the industry produces a limited number of pills with intestinal coating (lyophil, solizim, bonaphtoone, naphthamon, and furadonin), and in one dosage. Distribution of them at the dose is inadmissible because of violation of the intestinal coating. Therefore, in the conditions of pharmacies there is a need for obtaining intestinal soluble forms. For this, powders are placed in the capsule (see the description of the medical capsules on page 177).

CLASSIFICATION AND METHODS FOR POWDERING

Classification of powders.

Depending on the composition, the powders are divided into simple (Pulveres simplices), consisting of one ingredient, and complex (Pulveres compositi), consisting of several ingredients (sometimes up to 10).

Depending on the nature of the dosage, the powders are classified into dosed (that is, divided into separate doses - Pulveres divisi) and undoped (ie, unbranched - Pulveres indivisi).

Depending on the method of application, there are powders for the internal (Pulveres ad usum internum), or oral (Pulveres peroralia), and external (Pulveres ad usum externum) applications.

Powders for internal (oral) application are a pharmaceutical form consisting of solid free dry particles of different degree of crushing. Powders for internal use include most extemporal powders in a dosage range of 0.1 to 1.0 g per serving. They should have a relatively high degree of dispersion, which provides rapid dissolution of the substance in juices of the gastrointestinal tract, and high adsorption capacity.

Powders for external use include: powders used to treat wounds and various lesions of the skin or mucous membranes; powders for injections, used for infusion into the body cavity (nose, ear, nasopharynx, etc.); toothpicks; nail powders; powders for prepareing solutions for rinses, napkins, washings, etc .; powders to fight insects - duets.

The main requirements for powders: fluffiness; uniform distribution of substances in the total mass of the complex powder; homogeneity of mixing; precision of dosing; stability.

Depending on the medical purpose and the method of application, the powders must have a certain particle size. If there are no guidelines in separate articles, the powders for internal use should be shredded to 0.16 mm (DF XI).

Powders intended for use as suction and inhalation, as well as duets, should be chopped to particles of 0.1 mm in order to achieve a maximum increase in the total surface of these powders.

Dental powders also require fine grinding, because the content of large solid particles in them can damage the enamel of the teeth.

Inhaled powders, on the contrary, in order to avoid getting into the larynx and bronchi, can be shredded to an average particle size of 0.2 mm. When inhaled, such a powder should only enter the upper respiratory tract, but not in bronchi and alveoli.

Powders for the preparation of various solutions at home, as a rule, are released from pharmacies without further grinding (potassium permanganate, boric acid, sodium bicarbonate).

Powder - fine powder, intended for application on the skin with therapeutic or prophylactic purpose. Powders used for wounding, damaged skin or mucous membranes, as well as powders for infants should be prepared in aseptic conditions, and if they can withstand the effects of high temperatures - be sterilized. This is due to the fact that many of the ingredients that are part of the powder (for example, white clay, talc, etc.) may contain pathogenic microorganisms.

TECHNOLOGICAL STAGES OF PREPARATION OF POWDERS

For greater consistency and convenience, consideration of the technological stages, the preparation of powders, can be divided into two stages:

- Transformation of crude substances into the powdered state and obtaining a homogeneous mixture consisting of particles of more or less the same size. To do this, use the following technological steps: grinding, sifting (in the conditions of the pharmacy are used rarely) and mixing.
- Receiving from a powder mixture of separate corresponding doses. Stages: pre-packing, packing and design.

The necessity of performing certain technological steps in the preparation of powders depends on the composition of the prescription, their medical purpose and the physical and chemical properties of the drugs (aggregate state, density, color, odor, etc.).

Pulveratio is important for powders. As a rule, fine-grained substances have a greater therapeutic effect. The finer the drug, the faster and more fully it can be absorbed, and insoluble substances are better adsorbed by the mucous membranes and provide a better therapeutic effect. Grinding is also important for optimal mixing and precise dosage. When crushed, the size of the particles of drug substances is leveled, after which they are easy and well mixed and do not straighten out when dosed.

Shredding is a process of reducing the size of solids particles using different gadgets.

The choice of the method of grinding depends on the nature of the material to be crushed, and on the required fineness of the resulting powder. The grinding is achieved by means of various mechanical efforts:

a - crushing; b - split; in - strike; g-abrasion; D - cutting (Figure 89).

In the used grinding techniques, these efforts are usually combined. Thus, for example, grinding in a mortar is characterized by a combination of abrasion with crushing ducts, and grinding in a disk mill "excelsior" is associated with breaking and sti-tion, etc. For grinding solids it is better to combine a blow from the crush-

(crystalline salts); for viscous materials - rubbing with breaking; for brittle materials - splitting and rubbing.

The shredding processes are associated with significant energy consumption for the formation of new overheads, overcoming the forces of grip between particles (overcoming the internal friction during the course of their deformation during the destruction), overcoming external friction between the materials to be crushed and the working parts of the equipment.

The theory of crushing was first proposed by Rittinger. It is based on the hypothesis that the grinding operation is directly proportional to the distribution surface, or otherwise, is inversely proportional to squares of linear dimensions (this is the so-called superficial theory of grinding). Later, Kick's theory belongs to the fact that the work spent in chopping is directly proportional to the volume or mass of the body (volume theory of grinding). Both of these theories complement each other and can be applied: Rittinger's theory - for fine grinding, mainly rubbing; Kick's theory - for rough crushing, mainly crushing and impacting. However, both theories do not fully reflect all the phenomena that occur during fragmentation.

The founder of physicochemical mechanics, Academician PA Rebinder, was united by the unified theory of grinding. According to observations by P. A. Rebinder, the energy expended on the grinding of the material represents the sum of the work going on the deformation of the shredded body and the formation of new surfaces. With an increase in the number of teaspoons, their specific surface area increases (the ratio of the total surface of the particles to their volume), and thus free surface energy increases. This dependence can be expressed by the following equation:

$$\Delta F = \Delta S \times \sigma,$$

ΔF – increase in size of free surface power of particles ;

ΔS – increase in size of free surface of particles

σ – surface tension of compound

$\Delta F \rightarrow \min$

At mechanical grinding simultaneously there are two processes: the separation of particles under the action of applied force and the aggregation of small particles under the action of forces of mutual attraction.

When the processes of separation and aggregation of particles acquire the same speed, that is, they are in equilibrium, further grinding of substances does not make sense, therefore, the optimal time of grinding is established. It is not the same for different substances and when crushed in a mortar is about 2-3 minutes. With further crushing, the powder becomes loose, sometimes it is moisturized by absorption from the air of moisture, gases, particles can be bonded to larger

aggregates or adsorption (adherence) of the powder to the walls of the mortar, that is, there is a decrease in the free energy surface.

Thus, as a result of grinding, powders are formed, which consist of particles of defined sizes, differing in degree of shredding.

The degree of grinding - this is the ratio of the average initial size of a piece of material to its average size in the width after shredding.

If a larger degree of shredding is required than achieved at the time of stabilization, it is necessary to saturate the free surface energy of small particles, which involves the use of special techniques:

- crushing of powders in the presence of excipients (eg, milk sugar);
- grinding with the addition of volatile liquids (95% ethanol, ether).

When grinding in a mortar several ingredients at once, they are ground separately from each other, so it is more rational to grind the mixture of substances than each of them separately, except for heavy-duty medicinal substances, where it is necessary to add auxiliary liquids (Table 8).

Smooth solvents are also used when rubbing especially poisonous dasgs (for example, mercuric dichloride, arsenic anhydride) to reduce dust formation. It should be borne in mind that mercury oxycinnate explodes in the event of a strong rupture, so rub it carefully.

Grinding of viscous substances is performed in the presence of milk sugar, which is carried in a ratio of 1: 1 to the taken basic substance.

Medicinal substances such as phyton, zinc oxide, magnesium oxide, mercuric amidocloride, quinine salt, acetylsalicylic acid, magnesium carbonate and others, when triturated, are densely adhered to the walls of the mortar and are compressed, so they are recommended to rub carefully, without much effort. If necessary, sugar before grinding can be dried at a temperature of 40-60 ° C and rubbed in a heated mat, because even with insignificant humidity sugar breaks and adheres to the walls of the mortar.

Insoluble in water: sulfur, butadiene, terpinhydrate - very electrified when rubbed, causing spraying, especially when trying to collect them with a celluloid plate. Therefore, these substances, to avoid losses, should be rubbed simultaneously with the prescribed water-soluble substances or fluids.

In pharmacy conditions, mortars or different apparatuses are used for grinding solids (often in combination with mixing): runners, disintegrators, shotguns, hammers, drum mills, etc., allowing to mechanize the process of making powders.

Stumps (Mortaria) are manufactured in various shapes and sizes (Figures 90, 91, 92). They are made of different materials: porcelain, glass, steel, copper, brass, agate.

Porcelain refers to soft materials of high hardness, resistant to moderate loads to abrasion, so it is most suitable for the manufacture of pharmaceutical stupas. Industry manufactures mortars of various sizes. Depending on the volume of work, there are seven room numbers (Table 9).

The powder (pistilla), by which the crushed medicinal substances that are found in the mortar, must correspond to the size of the mortar. The inside surface of the mortar and the head of the blender must not be glazed, as the blender will slip. The surface of the head of the shredder should have as much contact with the surface of the mortar as possible, otherwise the shredded particles will be delayed in the bends not accessible to the shredder. As the roughness of the mortar surfaces of the piece is smoothed, the size of the pop decreases, resulting in deterioration of the mortar's properties as a grinding apparatus. When crushing poisonous substances and those that irritate the mucous membranes, it is necessary to use special mortar with lids (covers) or cover the mortar with paper, cover the face with a gauze mask with a cotton layer and wear protective glasses.

When grinding, it is necessary to take into account the maximum loading of the mortar, which, according to V. D. Kozmin, should not exceed 1/20 volume, in order to ensure optimal grinding of medicinal substances. When crushing the substances in the mortar, the crusher is rotated with a hand brush without the involvement of the shoulder and elbow joints. The stove is held in the left hand, tightly pressed to the table.

When crushing a small amount of medicinal substances is lost in the pores of the mortar. Fill the pores of the mortar with the rubbing substance first. The number of losses is determined by the structure of the substance, and in order to establish the sequence of their addition, it is necessary to know the amount of losses of medicinal substances in the mortar (determined experimentally, see Table 10).

For other sizes, the value of the loss calculated for the mortar number 1 is multiplied by the coefficient of the working surface, which shows how many times the loss of substance increases with the size of the mortar compared with losses when using mortar number 1.

Depending on the characteristics of solids, their losses due to "rubbing" can fluctuate within a fairly wide range. For example, in mortar number 1 glucose losses do not exceed 7 mg, while for bismuth of nitrate basic they make up 42 mg. Using the table of losses, it is easy to decide on which ingredient it is necessary to start prepareing the complex powder.

If there is no auxiliary substance (sugar) in the formulation, the grinding should begin with the substance that is discharged in greater quantities and the least amount is lost in the pores of the mortar.

Sowing (*curbatio*). The crushed medicinal products must be sieved through the sieve.

The purpose of this operation is to obtain a product with the same size of casting that solves the sieve analysis.

Sowing is regulated by a special article DF XI "Determination of Powder and Sieve Shredding".

Sieves are metal, made by stamping a metal sheet, and fabrics made of silk (StSt 4403-77), kapron (CSt 17-46-82) and metal (StSt 214-83) threads. Distinguish open screens, representing empty cylinders, made of metal or wood, the bottom of which is stretched by a suitable fabric with a certain size of the holes, and closed, consisting of the actual screen, the receiver, in which the sifted material arrives, and the covers protecting it is from cutting (Figure 93.94).

When carelessly used in silk-made screens, the location of the yarns may be changed, resulting in a powder of different particle sizes.

The silk screen number indicates the number of openings per inch.

The number of the metal wire mesh corresponds to the size of the holes in the mill in millimeters.

The number of breakdown sieves with round holes corresponds to the diameter of the hole in millimeters, multiplied by ten.

The sieve number with the longitudinal holes corresponds to the width of the hole in millimeters, multiplied by ten. It must be assumed that the shredded material does not interact with the material of the screen and does not change its composition.

The sifting result directly depends on the pressure under which the powder passes, on the size of the sieve openings, as well as on the duration and force with which the sifting is carried out. Therefore, when sifting it is necessary to take into account the influence of these factors and to carry out this process not very quickly, thoroughly mixing the powder.

In order to obtain powders free of smaller particles, they resort to the method of "double sifting", which consists in the fact that the smaller powder is released by sifting through the next thicker sieve.

When sifting, it is convenient to use a vibration sieve (Figure 95).

In the conditions of the pharmacy during the preparation of powders, the drugs directly in the mortar bring to the desired size of the particles, which is determined visually, without the help of sieves.

Mixtio is a process in which homogeneity is achieved, that is, the same ratio of component particles in any part of the resulting mixture.

The displacement process is the main operation in the preparation of complex powders. With insufficiently thorough mixing of the ingredients, the individual doses of the powder, obtained with its subsequent dosage, may contain different amounts of medicinal substances. It can adversely affect the medical effect of the drug, and when using potent and toxic substances even - to lead to poisoning.

The method and procedure for mixing the powders depends on the weight ratio of the registered ingredients and their physical and chemical properties (aggregate state, wet wiping, etc.). Depending on the above factors, very important practical provisions have been developed which should be observed when mixing the powders. The main ones are:

Medicinal substances of complex powder are discharged in equal or approximately equal quantities (the ratio in mass does not exceed 1: 5).

In this case, there are two possible mixing options.

1. If the physicochemical properties of medicinal substances are approximately the same, then they are mixed, taking into account the amount of losses when crushed in a mortar.

2. If the physicochemical properties of the medicinal substances are different, then the mixing and grinding begin with a coarse-grained substance, and then it is added to the fine-crystalline substance.

Amorphous substances (talc, magnesium oxide, starch, etc.) are mixed with the powder mass without further grinding.

Lightly dispersible substances are added in the last place and mixed carefully.

Rp .: Analgini
Butadioni aa 0,15
Misce fiat pulvis
Da tales doses No. 6
Signa 1 powder 2 times a day.

In this case, when mixing medicinal substances it is necessary to take into account that butadion is highly electrified and sprayed, and also has a larger amount of losses in the case of rubbing, so it is rationally placed first in a mortar analgin. In a mortar, rub 0.9 g of analgin first, and then add 0.9 g of butadiene and mix. Weigh out 0.30 g in wax capsules.

About the dispersal of medicinal substances are judged not by the size of their density, but by their volumetric mass.

Volume mass - is the mass (weight) of 1 cubic centimeter of matter in air-dry powdered state in conditions of free filling in any capacity.

Volumetric mass characterizes the degree of dispersibility of medicinal substances. The smaller the bulk mass of the substance, the more the substance is prone to spraying. In tabl. 11 shows the densities and volumetric masses of some

medicinal substances. Dispersibility of substances is also due to the size of the forces of adhesion between the particles and to a large extent depends on the moisture content of powder ingredients.

Rp .: Magnesia oxydi
Bismuthi subnitta "aa 0,25
Misce fiat pulvis
Da tales doses No. 12
Signa 1 powder 2 times a day.

In this case, the bulk mass of magnesium oxide is equal to 0,387 (the substance is easily sparged), and the bismuth of the main nitrate - 1,735. Losses when rubbed in a mortar for basic nitrate bismuth - 42 mg, and for magnesium oxide - 16 mg. Therefore, part of the magnesium oxide is rubbed pores of the mortar, then the basic nitrate is added to the bismuth, and then the magnesium oxide is added to the parts and mixed.

Pharmaceutical substances of complex powder are discharged in different quantities (ratio in weight more than 1: 5). In this case, the order of prepareing powder is available: the first crushed medicinal product, which is included in a larger number and has less losses in the pores of the mortar. Then, the crushed powder is poured into the capsule, filling in a mortar a small amount (approximately as much as the next ingredient). Mixing begins with the ingredient prescribed in the smallest amount, gradually adding other substances in the order of growth of the prescribed quantities, given the crystalline structure and the scattering of medicinal substances.

Pharmaceuticals of complex powder (in multicomponent prescriptions) can be dispensed both at the same time and in equal amounts, and in different quantities. In this case, it is necessary to follow all the above-mentioned provisions, without violating the main right-hand mixing: from smaller to larger.

Rp.: Phenobarbitali 0,3
Dibazoli 0,1
Papaverini hydrochloridi 0,2
Sacchari 2,0
Misce, fiat pulvis
Divide in partes aequales № 10
Signa. 1 powder 2 times a day.

Into the mortar, place 2,0 g sugar, grind, pour some of it into a capsule, fill in the mortar with an amount equal to the mass of dibasol (0,1 g), add dibasole, mix with sugar, rubbing the mixture, then add 0, 2 grams of papaverine hydrochloride

and mix at rupture. In the end, add phenobarbital (0.3 g), parts of sugar from capsules and mix to homogeneity.

In this case, it is important not to mix the powder mixture, but to prolong the shredding and mixing of the first portions of the weight of the substances.

The process of mixing in the preparation of complex powders is much easier and faster than powdering.

The quality of the mixing of medicinal products is judged by the degree of their dispersion and homogeneity of the resulting mixture, which is determined by pressing the filler on the prepared powder mass. When looking at the mass of the prepareed powder, the individual particles of the ingredients should not be detected by the naked eye. A mixture containing colored medicinal products should not have colored particles.

Stones with the prepared mass to the sensation so that it does not get dust, is recommended to cover with a plate of plastic or other material.

Dosage (Divisio) is a division of powder mass into separate dose levels.

The accuracy of the dosage depends on the correctness and sensitivity of the weights, the correct weighing, the homogeneity of the powder mixture.

In pharmacy practice, the dosage of powders is usually done using hand-held pharmacy scales (see Chapter 9), which is a labor-intensive process and requires certain skills. In order to accelerate this operation, other devices described in Section 10, whose construction principle is based on the dosage of powders, both in volume and mass, are currently proposed. Dosage by weight is more accurate than dosage by volume. Therefore, poisonous and potent medicinal substances should not be dosed in volume.

In accordance with the requirements of DF XI deviation in the mass of powders should not exceed the following values:

Weight of powder, g	Permissible deviations,%
to 0.1	± 15
0.11-0.30	+10
0.31-1.00	± 5
more than 1,0	± 3

Packaging of powders and medical capsules. For packaging of powders, depending on their physical and chemical properties, various packaging materials are used: writing, paraffin and waxed paper, parchment and subheading, cellophane, polyethylene film, cardboard, etc.

Each individual dose of powder is poured into pre-laid rows of paper capsules, which are taken from the number of registered powders, and then

wrapped. Filled capsules make up three (five) for convenience of account and put in a paper package or box.

Capsules of glued paper (simple capsules) are used for packaging nonhygroscopic and non-volatile substances; from waxed and paraffined paper - for the packaging of hygroscopic substances, as well as substances that change under the influence of oxygen, carbon dioxide, which easily weathered. Waxes and paraffin capsules are not suitable for the packaging of powders soluble in wax or paraffin (essential oils, camphor, menthol, phenylsalicylate, etc.). Camphor and menthol form an eutectic alloy with wax.

Parchment capsules are used to pack volatile and soluble waxes and paraffin substances (menthol, thymol, camphor, etc.). Cellophane capsules are used in the same cases as parchment. Parchment and cellophane slightly pass the vapor and gases, at the same time they are greaseproof.

In recent years, it has been practicable to release powders in special packages of polyethylene film. However, not all substances can be released in this package because of its gas permeability (eg iodine, camphor).

Undiluted powders are released in paper bags, cardboard and plastic boxes. Powders containing a significant amount of crystallization water that are easily weathered, such as sodium tetraborate, sodium sulfate, magnesium sulfate, etc., are placed in parchment paper or parchment paper before placing them in a package or carton. Powders containing easily decomposed substances (potassium permanganate, etc.) are released in glass jars (or tubes) enclosed with a plug.

It is desirable to dispose of the powder in a special package with an additional inner lid, which has small spray holes.

According to the doctor's instructions, powders can be released in special medical capsules.

Medical capsules (Capsulae) - a dosage form, consisting of a medicinal product, enclosed in a shell. Gelatin capsules were first proposed in France in the XIX century. Nowadays they are very widely used in Western Europe, America, where they are filled with medicines. They are intended for the protection of drugs from the influence of the environment, masking unpleasant taste and smell, to prevent the action of drugs on the teeth, the mucous membrane of the mouth or stomach. Capsules are usually prescribed for ingestion. However, there are capsules for subcutaneous administration, for administration to the rectum.

The capsule shell is made of gelatin or other substances, the plasticity of which is ensured by the addition of such substances as glycerol and sorbitol. The shell may include adjuvants such as surfactants, non-transparent fillers, preservatives, sweeteners, dyes authorized for medical purposes, and flavors. The surface of the capsules may be marked.

Solid, liquid or viscous medicinal substances may be released in capsules. In pharmacy practice, the most commonly used capsules are prescribed medicines such as ethacrytidine lactate, resorcinol and others. The contents of the capsules may consist of one or more active substances and such excipients as solvents, diluents, humectants and diluents, or without the excipients. The contents of the capsule should not destroy the shell.

However, the shell under the influence of digestive juices should collapse and release the contents of the capsule.

There are four types of capsules: Capsulae durae operculatae, Capsulae molles, Capsulae enterosolubiles, and capsules with modified release (Capsulae retard seu Capsulae cum liberatione modificata).

For release of powdered substances, only solid gelatin capsules are used, which are empty cylinders with rounded bottoms, which enter tightly into one.

The capsule is manufactured by the factory method, eight rooms - from 000 (the largest size) to five (the smallest size). They contain 0.1 to 1.5 g of powdered substances, respectively. The most commonly used capsules number 2-5, because capsules of larger sizes are difficult to swallow.

The capacity of gelatin capsules, given in Table 12, depends on the degree of compression of the powder, the bulk density, and so on.

Filling the capsules with powders: first, weighed doses are laid out on open paper capsules, then each dose by means of frequent pressing on a powder smaller in diameter by a cylinder (bottom) is filled until the whole amount of powder enters.

For poorly stuffed medicinal substances, a small amount of alcohol is allowed to pre-moisten. In the extreme case, the powder gently poured into the bottom of the capsule.

After that, close it with another cylinder (lid). If the lid jumps, then with the help of a fleece the edges of the edges slightly moisten with water. Now use special devices to fill gelatin capsules.

In accordance with the requirements of DF XI, gelatine capsules should be transparent and with stirring for 10 minutes with 20 times the amount of water heated to 35-40 ° C, should give a transparent liquid, which has no foreign smell and taste.

Soft capsules in the form of spherical, oval or oblong receptacles are intended primarily for the release of liquid drugs (eg, castor oil oil). The soft capsule shell may be firm or elastic depending on the content of the plasticizers.

Intestinal capsules are capsules with variable release, ie, their purpose is to resist gastric juice and release active substance or substances in intestinal juice. They can be made by applying, on hard or soft capsules, acid-resistant coatings.

Voids (intestine soluble capsules) or by filling capsules with granules or particles coated with an acid-resistant coating.

Appearance of powders. Powders, prepared in pharmacies, make up the main label "Powders". If necessary, stick a warning label: "Store in a dry, cool place protected from light".

Powders containing medicinal substances in list A must be prepared in accordance with the special rules established by the Ministry of Health of Ukraine.

ASSESSMENT OF QUALITY AND IMPROVEMENT OF POWDER TECHNOLOGIES

The assessment of the quality of the powders includes questioning, physical, organoleptic, chemical (selective) control and control during the release.

In assessing the quality of powders, first of all, the analysis of documentation (recipe, control panel), testing of compatibility of drugs, checking of doses of medicinal substances of lists A and B and norms for the release of narcotic drugs is carried out. Check the color, taste, and smell of the properties of the input medicinal substances. Determine the variation in the mass of individual doses to allowable standards that meet the requirement of the general article DF XI. Homogeneity is checked after pressing the head of the blender to the mass of the powder (at a distance of 25 cm from the eye there should be no visible individual particles, sequins). Sourdough is checked by pouring powder from one capsule to another, while there should be no laceration. Check the design of powders - the conformity of lable, packaging.

In order to increase labor productivity, ensure the high quality of medicinal products and provide rapid medical care, it is necessary to improve all technological stages of powders:

- development and introduction of available means of small mechanization in the stages of shredding, mixing and dosing of powders;
- use of semi-finished products for increasing labor productivity;
- introduction of auxiliary powders to overcome the incompatibility of drugs;
- improvement of packaging to increase the shelf life of medicines and provide local action of drugs (polyethylene films, capsules);
- implementation of theoretically grounded approach to the choice of technology (adherence to the rules of mixing powders, etc.).

5. Materaly enhance students during the presentation of lectures

Control questions:

1. Determination of powders as dosage forms, their classification and requirements

to them.
2. Ways of prescribing powders in recipes.
3. Degree of shredding of medicinal substances in powders, depending on medical application.
4. Technological stages of preparation of simple and complex powders.
5. Factors influencing the order of the mixing of medicinal substances in the powder.
6. Preparation of complex powders, which include medicines of differing density, bulk density, structure of particles.
7. Preparation of powders with medicinal substances, registered in equal and different quantities.
8. Basic equipment used for grinding, mixing and dosing of powders.
9. Rules for selecting the packaging material in accordance with the physical and chemical properties of the inbound ingredients and their dosage.
10. Evaluation of the quality of powders in accordance with the requirements of the normative and technical documentation (buoyancy, homogeneity of mixing, degree of dispersion, accuracy of dosage, packing, registration for release, storage).

Test tasks:

1**. The pharmacist has prepared powders, which include camphor. What capsules he needs for packing them?**

* Parchment
Paper
Volcanic
Paraffin
Zelofan

2**. The analyzer-technologist prepared 10,0 triturations of ethylmorphine hydrochloride (1: 100). What amount of poisonous substance and filler did he has taken?**

* 0.1 g ethylmorphine g / x and 9.90 g sugar
0.01 g ethylmorphine g / x and 9.99 g sugar
0.1 g ethylmorphine g / h and 10.0 g sugar
0.05 g of ethylmorphine g / x and 9.95 g of sugar
1.0 g ethylmorphine g / x and 9.0 g sugar

3**. Pharmacist should be weighed down the medicinal substance of the general list - glucose. What minimum amount of glucose can be weighed on manual single-grams?**

* 0.02
0.01
0.03
0.04
0.05

4. **The recipe contains 0,0001 atropine sulfate. Specify the amount of**

trituration of atropine sulfate (1: 100) required for the preparation of 10 powders:

* 0.10
0.20
0,50
0.01
0.02

5. **To test the trituratization of platyphilin hydrotartrate (1:10). Specify the optimum filler for the preparation of trituration:**

* Milk sugar
Sugar - refined
Starch of corn
Starch of rice
Mannit

6. **A pharmacist has prepared a prescription drug.**

Rp .: Magnesia oxydi
Sodium hydrocarbonatis ana 0,2
M. f. powder
D.T. d No. 12
S. One powder 3 times a day.

Specify the best technology option:

* Crumbed with sodium bicarbonate, added magnesium oxide, mixed.
Submerged magnesium oxide, added sodium bicarbonate, mixed.
Chopped sodium bicarbonate with alcohol, added magnesium oxide, mixed.
Grind a portion of magnesium oxide, add sodium bicarbonate, then the residue of magnesium oxide, mixed.
Chopped magnesium oxide with alcohol, added sodium bicarbonate, mixed.

7. **A pharmacist prepares pills of platyphylline hydrotartrate. Specify the minimum weight of the poisonous substance that it can weigh on handy single-gram scales:**

* 0.05
0.02
0.03
0.1
0.15

8. The proprior prepared 20.0 triturations of atropine sulfate (1: 100). Specify the amount of poisonous substance and filler:

* 0.20 and 19.8
0.02 and 19.98
0.1 and 19.0
2.0 and 18.0
0.20 and 20.0

9. The pharmacist has prepared the drug according to the name .:

Rp .: Papaverini hydrochloride 0.01
Sachar 0.25

M.f. powder
D.D. No. 10
S. One powder 3 times a day
Calculate the mass of one powder
* 0.26
0.23
0.22
0.28
0.25

10. In the pharmacy, you need to prepare powders containing 0,02 g of the extract of belladonna. How much of a dry extract (1: 2) was picked up by a pharmacist for the preparation of 10 powders?

* 0.4 g
0.6 g
0,5 g
0.8 g
0,2 g

6. General material and guidance of the lecture:

- training rooms;
- equipment;
- illustrative materials.

.

7. Materials for self-training for students:

1. To familiarize with the basic normative documents regulating manufacture of powders:

- Law of Ukraine "On Medicines";
- By orders of the Ministry of Health of Ukraine;
- National Pharmacopoeia

8. Literature lecturer who used to prepare the lecture.

Basic literature:

1. Technology drugs. Textbook: Textbook for Universities / AI Tikhonov, PA Logvyn, S. Tikhonov, A. Mazulin, TG Yarnyh, OS spiers, O. Mikhail Kotenko; Edited by AI Tikhonov - Kharkov: Pharmacy; Original, 2009. - 432 p.

2. Technology Medicine: Textbook / A. Marchuk, NB Androshchuk - Kyiv: Health, 2008. - 488 p.

More:

1. Soft medicinal forms: extemporaneous compounding: Guidelines / AI Tikhonov, T. Yarnyh, AV Lukienko etc .; Ed. OI Tikhonov. - H .: Izd pharmacy; Golden Pages, 2003.-128 with.

2. Aseptic drug forms, extemporaneous compounding: Guidelines / AI Tikhonov LV Bondarev, TG Yarnyh NF Orlovetska etc .; Ed. AI Tikhonov and T. Yarnyh. - H .: Izd pharmacy; Original, 2005. - 184 p.
3. Solid dosage forms: extemporaneous compounding: Guidelines / AI Tikhonov, T. Yarnyh, S. Gritsenko, etc.; Ed. AI Tikhonov - H .: Izd pharmacy; Golden Pages, 2003. - 176 p.
4. Liquid formulations: extemporaneous compounding: Guidelines / AI Tikhonov, T. Yarnyh NF Orlovetska etc .; Ed. AI Tikhonov and T. Yarnyh. - H.: Izd pharmacy; Original, 2005. - 160 p.

Lecture 3: «Liquid dosage forms. Technology of concentrated solutions and mixtures. Technology solutions of SPL, non-aqueous solutions. Special cases of manufacturing aqueous solutions. Droplets technology» - 2 hours.

1. Relevance of the topic.

The preparation of liquid dosage forms is not possible without the use of a solvent which is a suitable dispersion medium. One of these solvents is purified water. Pharmacological indifference, availability, easy obtaining, the ability to dissolve many medicinal substances - these properties of purified water make it the most commonly used solvent in medical practice. The purpose of this lecture is to consider the advantages and disadvantages of purified water as a solvent, to compare and analyze the methods of its obtaining, to highlight promising means and methods of obtaining water for injections, to consider the most important issues of obtaining, using, transporting and storing water. Pharmacists should have questions about the technology of manufacturing liquid dosage forms and be prepared for the realization of their knowledge. A rational ratio of active substances, methods of their administration and preparation allows the creation of highly effective medicines.

2. The objectives of the lecture:

- training

- to formulate in students the basic concepts of technology of liquid dosage forms;

- to determine the requirements for the liquid dosage forms, to teach how to classify the RLF

- to explain the types of solvents; equipment and methods of obtaining solvents;

- to teach how to orientat in the main directions of state regulation of the production of liquid dosage forms;

- to learn how to read recipes in Latin, to analyze their constituent parts and to assess the correctness of the writing;

-educative

To develop the skills of using the DF and the International Pharmacopoeia, other normative and technical documents, as well as reference literature to find information on the composition, preparation, storage and release of drugs.

This lecture is aimed at developing a professional meaningful personality structure; education for students of modern professional thinking.

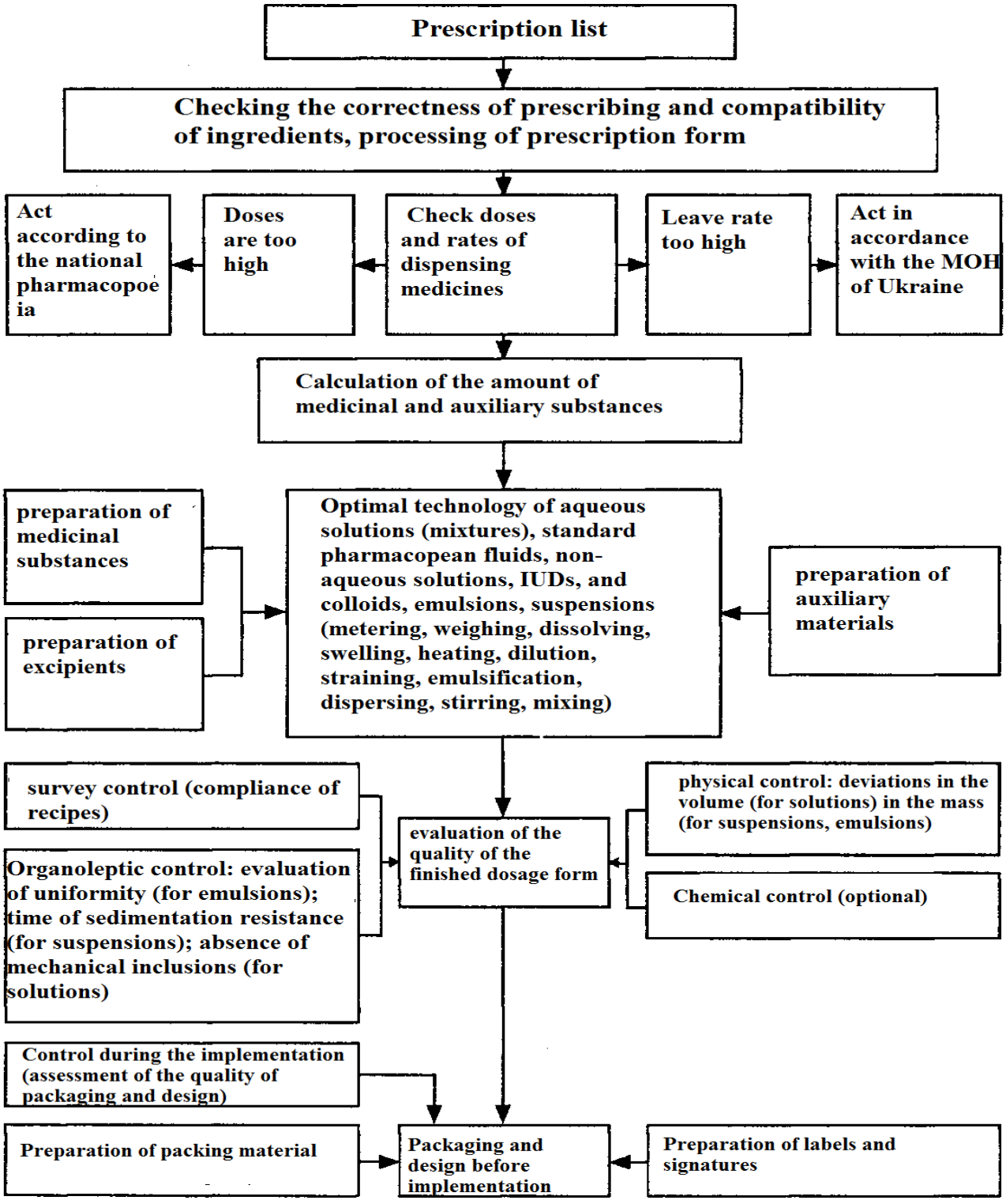
3. Plan and organizational structure of the lecture.

№№ pp	The main stages of lectures and their contents.	The objectives in the levels of abstraction.	Type lecture, lecture equipment.	Distribution of time.
1	2	3	4	5
	Preparatory stage			
1.	Learning objectives.			
2.	Provide positive reinforcement.			
	The main stage			
3.	Presentation of lecture material. Plan: 1. Classification of liquid dosage forms. 2. Basic terms and concepts of liquid dosage forms. 3. Characteristics of solvents for RLF. 4. Purified water, equipment for its receipt.	I II III II I	According to the publication, "Methodological recommendations for planning, preparation and analysis of lectures. " (Ed. 2001).	85% - 90%
4.	5. State regulation of the production of liquid dosage forms.			
6.				
7.	6. Basic normative and technical documentation. 7. Quality control of RLF in pharmacy conditions.		References, issues, tasks.	
	The final stage			
	Summary of lectures, general conclusions. Lecturer answers to possible questions. Tasks for self student.			

4. Content of lectures:

1. Classification of liquid dosage forms.
2. Basic terms and concepts of liquid dosage forms.
3. Characteristics of solvents for RLF.
4. Purified water, equipment for its receipt.

5. State regulation of the production of liquid dosage forms.
6. Basic normative and technical documentation.
7. Quality control of RLF in pharmacy conditions.
8. Discharge of standard pharmacopoeial liquids. Features of preparing of some aqueous solutions.
9. Non-aqueous solutions. Prospects for improving the quality and technology of dosage forms.



Liquid dosage form is a form of delivery of drugs obtained by mixing or dissolving active substances in water, alcohol, oils and other solvents, as well as by extracting active substances from plant material.

All liquid dosage forms by its physical and chemical nature can be free all-in one dispersed systems in which the drugs (i.e. dispersed phase) are uniformly distributed in a liquid dispersion medium.

Depending on the degree of shredding of the dispersed phase and the nature of its connection with the dispersion medium (solvent), the following physical and chemical systems are distinguished: real solutions of low- and high-molecular compounds, colloidal solutions (ash), suspensions and emulsions. Individual dosage forms can be combined disperse systems - a combination of the main types of disperse systems (infusions and decoctions, extracts, etc.).

Applying the appropriate technological techniques (dissolution, peptization, suspension or emulsification), the drug substance (solid, liquid, gaseous) can be reduced to a greater or lesser degree of dispersion, from ions and molecules to coarse particles, visible under a microscope or naked eye. This is very important for the therapeutic effect of the drug substance on the body, which has been repeatedly confirmed by biopharmaceutical research.

CLASSIFICATION OF LIQUID MEDICINAL FORMS

For medical purposes, liquid dosage forms are distinguished for internal use (ad usum internum), for external use (ad usum externum) and for injectable administration (pro injectionibus).

Liquid medicines for internal use are usually called mixurs (from the Latin word mixturae - mix).

Liquid medicines for external use are divided into rinses, washings, lotions, dipping, enema etc.

By combination, liquid drugs are divided into simple and complex. Simple - these are solutions containing only one dissolved ingredient, complex - containing two or more.

Depending on the nature of the solvent, the solutions are divided into water and non-aqueous (alcohol, glycerol, oil).

Wide use of liquid dosage forms is due to the fact that they have a number of advantages over other forms of medicine:

- a variety of ways of appointment;
- reduction of irritating properties of certain medicinal substances (bromides, iodides);
- Simplicity and ease of use, especially in pediatrics and geriatric practice;
- the possibility of masking unpleasant taste;- during internal administration they are

absorbed and act faster than solid dosage forms (powders, pills, etc.), whose effect is detected after dissolving them in the body;

- the softening and enveloping effect of a number of medicinal substances is most complete when it is used in the form of liquid drugs;- some medicinal substances: m

agnesium oxide, chalk, coal, white clay, bismuth nitrate basic show the best adsorption effect in the form of thin slurries.

However, the liquid dosage forms also have some disadvantages:

- the solutions are poorly stored, since the substances in the dissolved form are more easily subjected to hydrolysis and oxidation processes than in dry;

- solutions are a favorable environment for the development of microorganisms, hence the small storage period of liquid dosage forms - no more than 3 days;

- less convenient for transportation, require more time for preparing and special packaging;

- For the precision of the dosage, liquid drugs are inferior to solid dosage forms. For example, powders are dosed in a pharmacy, and mixtures - rather conventional dosage measures: table spoons, drops.

To eliminate these disadvantages, some dosage forms used in liquid form are prepared at the factories in the form of dosage forms (tablets, dry mixes, powders) that should be dissolve in water by the patients themselves before use.

SOLUTIONS FOR THE PREPARATION OF LIQUID MEDICINAL FORMS

In the process of preparing liquid dosage forms, a solvent is always used, which is a suitable dispersion medium. Solvents include chemical compounds or mixtures capable of dissolving various substances, that is to form monolayer systems with them - solutions consisting of two or more components.Purified water, ethyl alcohol, glycerin, fatty and mineral oils, less often - ether, chloroform are used as solvents in medicinal practice. At present, it is possible to expand the range of solvents a little at the expense of organosilicon compounds, ethylene and propylene glycols, dimethyl sulfoxide (DMSO) and other synthetic substances.

The solvent requirements for the preparation of liquid drugs are following:

- solvents must be stable when stored, chemically and pharmacologically indie-fertile;

- should have high dissolving power;

- should not have unpleasant taste and smell;

- should be cheap, accessible to the public and have an easy way of obtaining;

- should not be flammable;

- should not serve as an environment for the development of microorganisms. According to the chemical classification solvents are divided into inorganic and organic compounds.

Water purified (Aqua purificata). Among the norganic compounds, the most commonly used solvent in medical practice is water purified (by DF X - distilled water).

Water is pharmacologically indifferent, available and dissolves a lot of medicinal substances, but at the same time it quickly hydrolyzes some medicinal substances and breeds microorganisms.

Purified water can be obtained by distillation, ion exchange, electrolysis, reverse osmosis. The quality of cleaned water is regulated by FS 42-2619-89: it must be colorless, transparent, odorless and not flavored; pH may vary within the range of 5.0-7.0; should not contain reducing agents, nitrates, nitrites, chlorides, sulfates, ammonia traces and other impurities.

The methods of obtaining purified water are the most common method of distillation (distillation).

Distillation of water should be carried out in accordance with the order of the Ministry of Health of Ukraine No. 139 dated June 14, 1993 in a specially equipped for this premises (distillation). Walls should be painted with an oil paint or laid out with a facing tile and kept in absolute cleanliness. In these premises it is prohibited to do other work like to wash dirty dishes, to wash clothes, to store foreign objects. As a matter of fact, only sterilization of solutions of medicinal substances can be allowed.

The quality of cleaned water is influenced by the initial composition of drinking water, the structural features of aquatic distillers, as well as the conditions for collecting and storing water. In order to receive water purified in cities, usually tap water is used that meets the sanitary requirements set for drinking water. Regarding the water used by rural pharmacies (caves, rivers, etc.), it requires preliminary water preparation, since it usually contains both dissolved and mechanical, and colloidal-suspended impurities: organic matter, ammonia, water hardness salts and other substances. Methods of cleaning depend on the nature of impurities contained in water.

Mechanical impurities are usually separated by settling, followed by drainage of water by decantation or by filtration. For this purpose, filters made in the form of capacities of cylindrical shape, filled with anthracite or quartz sand are used. The receptacles have a lid and bottom, equipped with a device for input, output and distribution of water inside the filter. Filters can be single-layered (for example, only an anthracite layer) or double-layered (anthracite and quartz sand). Loading

height varies depending on the amount of suspended particles and the desired flushing effect.

Destruction of organic impurities. Before distilling up to 100 liters of water containing organic impurities, add 2.5 g of potassium permanganate (or 1% solution of potassium permanganate 25 ml per 10 l of water) in the form of a solution of 2.5 g, mix and leave to stand for 6-8 hours. The active oxygen released, oxidizes organic matter:

$$2KMO_4 + H_2O = 2KOH + 2MO_2 + 3O$$

Then water is drained and filtered.

Binding of ammonia. On 10 liters of water add 5,0 g of aluminum sulfate or alumina calcium in dissolved form:

$$\mathbf{2KAl(SO_4)_2 + 2NaCl = K_2SO_4 + 3Na_2SO_4 + 2AlCl_3}$$

At the same time there is an adverse reaction: the excess of alum is reacted with chlorides, often present in water, with the release of gaseous hydrogen chloride, which easily passes into distillates:

$$\mathbf{A1Cl_3 + 3H_2O \rightarrow Al(OH)_3 + 3HCl}$$

If, after using the peanuts, purified water gives a reaction with silver nitrate, it is necessary to add another two-substituted sodium phosphate before distillation.

To bind hydrogen chloride to 10 liters of water, add 3.5 grams of sodium phosphate of two-substituted (at the rate of 2/3 of the number of alum):

$$\mathbf{Na_2HP0_4 + HC1 = NaCl + Na_2P0_4}$$

In the presence of carbon dioxide and other volatile impurities, add lime water. After passing 20-30 minutes, water is decanted, filtered and then distilled.

Softening of water. The unwanted presence of calcium and magnesium salts in water, which give it temporary and constant hardness, resulting in the distillation of water on the walls of the evaporator scum. In addition, during distillation of solid water, the heating elements of the distiller quickly fail. Temporary hardness causes the presence of calcium and magnesium bicarbonates. They can be freed by boiling water. In this case, the hydrocarbonates are converted into carbonates and fall in a precipitate which is filtered out:

$$Ca\,(HCO_3)_2 \rightarrow CaCO_3 \downarrow + H_2O + CO_2$$

But in this case, the water is saturated with carbon oxide, which is slowly removed during boiling, thereby reducing the pH of the purified water. Therefore, in order to eliminate temporary hardness, it is advisable to use calcium hydroxide:

$$Ca\,(HCO_3)_2 + Ca\,(OH)_2 \rightarrow 2CaCO_3 + 2H_2O$$

The constant hardness of water is due to the presence of calcium and magnesium chlorides, sulfates and other salts. It is eliminated by treating water with sodium carbonate:

$$CaCl_2 + Na_2CO_3 \rightarrow CaCO_3 + 2\ NaCl$$

$$MgSO_4 + Na_2CO_3 \rightarrow MgCO_3 \downarrow + Na_2CO_3$$

Available for each pharmacy is a lime-soda softening water. Its essence is added in water simultaneously to a solution of calcium hydroxide and a solution of sodium carbonate. Under the action of calcium hydroxide eliminates the temporary (carbonate) hardness, since calcium and magnesium bicarbonates pass into carbonates and fall in the precipitate.

$$Mg\ (HCO_3)_2 + Ca\ (OH)_2 \rightarrow CaCO_3 \downarrow + MgCO_3 \downarrow + 2H_2O$$

Under the influence of sodium carbonate salts of a constant (non-carbonate) hardness fall: sulfates, chlorides and other salts of calcium and magnesium. Calcium hydroxide also binds carbon dioxide in water:

$$\mathbf{CO_2 + Ca(OH)_2 \rightarrow CaCO_3\downarrow + H_2O}$$

Coagulation of colloidal impurities. Colloidal moths can only be removed after preliminary consolidation of suspended particles. To destroy the colloidal system, it is necessary to neutralize the electric charge of particles. Deprived charge particles under the influence of forces of mutual attraction are connected-coagulate. The aggregated particles have a mass in which they lose their kinetic stability and fall into the precipitate. Neutralization of the charge of colloidal particles is achieved by addition to the water of another resin as well as colloidal nature, but the particles of which carry the opposite charge.

The compounds of silicic acid in water, in the colloid-dispersed state, carry negative charges, therefore, only substances which are charged in water are suitable for their coagulation. As such a substance is most commonly used in aluminum sulphate or alumina calcium alum. The treatment of water before distillation should be done in separate containers to avoid contamination of aquatic distillers.

The water supply, prepared in this way, nevertheless contains a sufficient amount of salts, which during distillation settle on the walls of the evaporator and the electrically heated elements, which significantly reduces the efficiency of the distiller and often disables the electric heaters. Therefore, the most promising creation of aparatov in combination with water-conditioning. Electromagnetic water treatment is now proposed.

The method of magnetic water treatment consists in passing it through the gaps formed in the case of a special device between moving and stationary magnets. As a result of the influence of the magnetic field on the water, the conditions of crystallization of salts during distillation change. Instead of a dense on the walls of the distillers formed loose slimes, and in the water column - suspended. When using the device, a daily water drain from the slime machine is required. An electrochemical dialysis apparatus with the use of semipermeable membranes is proposed, as well as an ion exchange plant for the production of desalinated water using granulated ion exchangers and ion-exchange cellulose fiber.

Distillation of water. The general principle of obtaining distilled water is that the drinking water that has undergone a water treatment is placed in an aquadistable, consisting of the following main parts: evaporator, passive section (helmet and connecting tubes), condenser (refrigerator) and collector. To control the water level in the evaporation chamber there is a water-proof glass. Evaporator with water is heated to boil. Water vapor enters the condenser, where they are splashed and in the form of a distillate enter the collection. All non-volatile impurities present in the source water remain in the aquatic distillery.

Depending on the heating source, aquatic distillers are divided into apparatuses with fire, electric and steam heating. Under the modern nomenclature, aquatic distillers are classified in the following: DV - fire hydrodynamic, DEV - aquadistable electric with water, DEVZ - aquadistable electric with water preparation and collection and others. By design, the devices are periodic and circulating (continuous action). In aquatic distillers of periodic action, purified water is obtained in separate portions. To fill the evaporator with the source water, the distillation process is interrupted.

Circulating aquatic distillers are automatically filled up when distilled with hot water from the condenser and distilled water can go out continuously. In pharmacies, mainly use aquadistiles of continuous action: DE-1, DE-25, DE-4 with the use of electric heating (figures denote the productivity of the devices in liters per hour), and aquadistiles fire Dv-10, DV-4, a source of heating in which there is a standard gas cooker. They can be used instead of electric in pharmacies with centralized gas supply in the presence of liner gas pipeline in the distillation.

The main parts of the DE-25 apparatus (fig. 99) are evaporation chamber with reflecting screens for steam separation, condenser, electric heater, level sensor, valve, demountable crane, power cable with wire, base, hatch cover, nipple for draining water. The steam separator is of great importance for obtaining the high quality of purified water, because as a result of the splash, the substances contained in the source water enter the distillate.

In the evaporator, electric heaters are installed. At the beginning of the work, tap water, which continuously flows through the valve, fill the evaporator to the set level. In the future, as boiling water will enter the evaporative chamber only partially, the main part will merge through the tube into the equalizer, and further through the seam in the sewer or can be used for economic needs. The equalizer is combined with the evaporation chamber and serves for constant maintenance in it of the necessary level of water. The device is equipped with an automatic device-a level sensor that protects electric heaters from distillation in the event of a decrease in water level below the permissible level. In case of stopping water supply or at low pressure, electric heaters are automatically switched off. The work of the device is controlled by signal lamps located at power shield.

For reception use distilled water and other aquatic distillers.

When using any aquadistilator, the following conditions must be observed.

All parts of the water vapor or steam vaporizer must be made of materials (glass, stainless steel, etc.) that do not give water components or are removed with pure tin and should be kept in absolute cleanliness and serviceability. Every day before distillation it is necessary to pass a pair for 10-15 minutes, not including a refrigerator. The first portions of purified water, obtained within 15-20 minutes, are drained and only then start collecting water.

It is necessary to ensure that the evaporation chamber (cube) is filled with water to 2/3 of the volume, and maintain the water level during distillation not less than 1/5 of the volume, otherwise the burning of impurities remaining at the bottom of the cube may occur and getting into the receiver of volatile products formed at the same time. Do not allow strong boiling water in the cube to reduce the number of droplets formed.

Place the condenser (refrigerator) as far right as possible from the boiler of the pouring cube, so that the steam could pass a longer path, during which small droplets of water admired by steam, could settle on the walls of the steam line, not reaching the refrigerator.

It is important to wipe the inner surface with cotton wool, soaked with a mixture of alcohol with ether, and then with a solution of hydrogen peroxide, if the structure of the device allows it to do this during the use of a new device. After this, it is necessary to pass through it a pair without cooling for 10-30 minutes and overtake not less than 40-60 liters of water.

After the installation of aquadistiles, it is important to know that the use of purified water for the intended purpose is only allowed after 48 hours of operation of the apparatus and checking the quality of water in accordance with the requirements of DF XI and FS 42-2619-89.

Cleaned water should be collected in clean sterilized or steam-coated collections. Purified Type 3 collectors (Figure 104) are made of stainless steel, having a cylindrical shape.

Capacity of collections 6, 16, 40, 100 and 250 l. They are equipped with a water tube and drain cock. The upper part of the case has a hatch for cleaning and sanitary treatment of the inner surface. The hatch is covered with a lid, equipped with an air filter. Collections are joined to the aqueduct with the help of a fitting. They are usually installed on brackets or on a stand, so that the water can be fed to workplaces by gravity. Before use, the internal surface of the collection should be thoroughly cleaned and rinsed with a soda solution or mustard suspension (1:20), and then rinsed several times with tap water and freshly cleaned water. In the course of operation, the collection is not necessary periodically (1 -2 times a month) washed with the use of detergents.

Small amounts of water (as an exception) are assembled into glass cylinders of chemically resistant glass, otherwise the pH may change, which adversely affects medications that decompose in alkaline media.

Cleaned cylinders should be thoroughly closed with two holes: one for the tube in which the water comes, the second for a glass tube with sterile cotton, which is filtered by the air entering the vessel. Cotton need to be changed periodically (at least once a day). The collection should be connected to the aquadistilator with the aid of glass tubes, which must be in close contact with the condenser tube. Rubber tubes are used only for the connection of glass tubes. Collections are installed on pallets or on a cylindrical disperser.

Control of the quality of cleaned water. Purified water should be subjected to chemical and bacteriological control. An analysis on the absence of chlorides, sulfates, calcium salts, etc (from each cylinder, and at water supply through the pipeline - at each workplace) should be perfomed every day. Quarterly a complete chemical analysis is done; two times a quarter it is sent to a local sanitary-bacteriological laboratory for bacteriological research.

The purified water is stored in aseptic conditions for no more than 3 days in closed containers made of materials that do not change the properties of water and protect it from mechanical inclusions and microbiological contaminants.

Water demineralized (Aqua demineralisata) (or desalinated) in quality corresponds to purified water and has recently been increasingly used instead of it. The high content of salts in the source water worsens the conditions of distillation, as well as the quality of purified water. Therefore, it is very important to desalinate solid natural water before distillation.

Different plants are used for desalting (demineralization) of water. The principle of their action is based on the fact that water is free from salts by passing

it through ion exchange columns (Figure 105). The bulk of such plants - columns filled with cationic and anion resins. The activity of cationit is determined by the presence of a carboxylic or sulfone group, which has the ability to exchange hydrogen ions on alkali and alkaline earth metal ions

$$R(SO_3H)_2 + Ca(HCO_3)_2 = R(SO_3)Ca + 2\ H_2O + CO_2$$

$$RNH_3OH + NaCl = RNH_3Cl + NaOH$$

Anionites - most often products of polymerisation of amines with formaldehyde, which exchange their hydroxyl groups on anions.

In practice, for example, cationite KU-1, sulfugyl SK-1 and anion exchange ED-10P are used. These same adsorbents can also be used to obtain softened water in order to eliminate the scale in the overflow cubes. And the kg of the above cation exchangers can bind cations contained in 70-80 liters of water or other potable water. When loading in a column of 30 kg of cation exchanger (KU-1, KU-2 or sulfovglyl SK-1) it can be used within 10-15 days and receive 100-150 liters of high-quality desensitized water every day.

When loading 15 kg of anion exchanger EDE-10P and AB-17 it is possible to continuously process water for 20-25 days, after which to regenerate. Plants have capacities for solutions of acids, alkali and purified water, which are necessary for the regeneration of resins. Regeneration of cation exchangers is carried out by acid (3-5% hydrochloric or sulfuric acid): Regenerated cation exchanger is washed with purified (desalinated) water until there is no acid reaction. Anionites are recovered with alkaline solution (2-5%).

Regenerated anion exchanger is washed with unsalted water until there is no alkalic reaction in the filtrate on litmus.

Water is first passed through a cation exchanger, and then with an anion or in reverse order (convection system), or water is passed through one column containing both cation exchanger and anion exchanger (mixed column).

In a pharmacy practice, a demineralizer containing cation exchanger and anion exchanger, a gauge for monitoring the electrical resistance of desalinated water and a system for shutting down the supply of tap water can be used when reducing the electrical resistance of dissoled water below the permissible level. The kit also includes a regenerator designed to restore ion exchange capacity of resins.

Demineralizator is expedient to use in inter-hospital, large hospitals and other pharmacies for delivery of desalinated water in a washing room and in an aqueduct. Demineralizator productivity of 200 l / h with the capacity of interregeneration period 400 l.

Ethanol, ethyl alcohol (Spiritus aethylicus, spiritus vini). Ethyl alcohol (C2H5OH) is a cooled clear, colorless moving fluid with a characteristic smell and burning taste, boiling at 78 ° C.

For pharmaceutical purposes, ethanol, obtained by digestion of raw materials containing polysaccharides, mainly potatoes and grains is used. The preparation of medicinal forms is not used for ethanol of other origin because of the presence of inadmissible admixtures (alcohol of methyl and other compounds).

Ethyl alcohol can be attributed to non-aqueous solvents with a certain proportion of conventionality, since non-absolute ethanol is used, and water-alcohol solutions of varying strength. The concentration of the aqueous alcohol solution is expressed in volumetric percentages, indicating the number of milliliters of absolute ethanol in 100 ml of solution at 20 ° C.

In some cases, ethanol is used as a good solvent for many organic and inorganic compounds (organic acids, essential oils and fatty oils, camphor, menthol, iodine, tannin, levomitsetin, alkaloids, etc.) and in others as a medicinal product in the form of solutions containing alcohol. The dissolving ability of ethanol depends on its concentration. For example, castor oil is readily soluble in anhydrous (absolute) alcohol, 85% ethanol dissolves about 10% of castor oil, 70% - only 1%, and 40% - practically does not dissolve it.

Alcohol is mixed in all proportions with water, glycerol, ether, chloroform. It is neutral, does not oxidize with oxygen, has bacteriostatic and bactericidal effects depending on the concentration of the solution. The greatest antiseptic properties have alcohol of 70%, because it easily penetrates inside the cell through the shell of microorganisms and kills the protoplasm. In concentrations above 70%, alcohol causes denaturation of the protein shell, which prevents its penetration into the cell into the protoplasm, and therefore the bactericidal property of the alcohols of higher concentrations does not manifest.

To the negative properties of alcohol should be attributed to its non-indifference, the inhaling effect. A fatal dose of 96% ethyl alcohol is about 210-300 ml. It promotes the removal of proteins, enzymes, is readily engaged, has a high hygroscopicity, is incompatible with oxidizing agents (the presence of a hydroxyl group in the molecule): potassium permanganate, bromine, strong nitric acid, etc. Futility and volatility depend on its durability. With some salts (calcium chloride, magnesium nitrate), ethyl alcohol gives crystalline compounds.

The quality of ethanol is regulated by DF X (*Spiritus aethylicus* 95%).

When mixing ethyl alcohol and water there is a contraction (compression), which is accompanied by heat release and volume change, and the volume of the mixture is always less than the sum of both volumes. For example, when mixing 500 ml of ethyl alcohol and 500 ml of water, the volume of the resulting mixture

will be not 1000 but 940 ml. This phenomenon is associated with the formation of alcohol hydrates of various composition with the mutual separation of molecules of alcohol and water when they are located in space. The maximum compression is observed in a water-alcohol mixture having a strength of 54-56%. At an alcohol concentration of 35% and below, the phenomenon of contraction during the dilution of alcohol is no longer observed. Alcohol strength below 40% has, like water, hydrolytic properties and in concentration above 40% of this ability does not have.

Strength of alcohol is determined by alcoholometers, refractometric method or by the density of alcohol solution.

Breeding alcohol with water or mixing alcohol and water solutions of different concentrations is just daily operations in the pharmacy. However, given the specifics of ethyl alcohol, when mixed with water, it is necessary to calculate the required amount of alcohol and water each time. In order to facilitate these calculations and to prevent possible errors in the annexes to the DF XI, reference tables are provided, which pharmacist-technologist should learn to use with brewing alcohol. Keep alcohol in well-sealed bottles of dark glass in a cool place, away from the fire.

Chloroform (*Chloroformium*). It is a colorless, transparent, mobile volatile liquid with a characteristic smell and sweet taste. Mix in all proportions with alcohol, ethyl, ether. In chloroform highly soluble drugs, insoluble in water: boric acid, butadiene, camphor, levomycetin, chlorobutanol hydrate, menthol and others. It has, like all the halogen-derivative, narcotic and disinfectant effect, it refers to the potent substances (List B), therefore its use is limited.

It is used mainly in medicinal forms for external use. In non-aqueous solutions, chloroform is usually prescribed in combination with any basic solvent: alcohol with ethyl, oils and others. Widely used chloroform in the technology of liniments. Unlike alcohol, ethyl chloroform is dosed by mass. Couples not flaming, but harmful to health. Store in well-sealed containers in a cool, light-protected place.

Ether Medical (*Aether medicinales*). It is a colorless, transparent flammable liquid, a peculiar smell, pungent taste. Medical ether is often referred to simply ether. It dissolves many medicinal substances; dissolves in 12 parts of water, mixed in all ratios with alcohol, ethyl, chloroform, petroleum ether, fatty and essential oils. On dissolving ability it is analogous to chloroform: it dissolves the same medicinal substances and approximately at the same concentration as in chloroform.

Ether pair is poisonous. It has a tendency to fall on the floor, very mobile and can accumulate at a distance from the source of evaporation of the ether. The ether

is at a temperature of 40 ° C. The ether, just like chloroform, has a narcotic effect, belongs to the list B, in non-aqueous solutions is used rarely and only in combination with other solvents, it is dosed by weight.

In the technology of finished medicines the ether is used in the manufacture of some tinctures and extracts, as well as in the production of a pile.

Given the slight flammability of the ether, the explosion of its steam with air, when working with it, safety must be strictly observed. Keep the ester in a well-sealed container in a cool, dark place away from the fire.

Glycerinum (Glycerinum) is a colorless, syrupy transparent hygroscopic liquid of sweet taste, neutral reaction, dissolved in water, alcohol and in a mixture of ether with alcohol, but is not soluble in ether, chloroform and fatty oils. In glycerol readily dissolves: boric acid, sodium tetraborate, chloral hydrate, sodium bicarbonate, tannin, protargol, and others. Glycerin solutions are easily washed off with water and have less adsorption of dissolved substances than are different from grease oils.

In the pharmaceutical practice, not an absolute glycerin (as well as ethanol) is used, but diluted with water with a content of glycerol 86-90% and a density of 1,225-1,235, that is, with a water content of 12-15%.

This is due to the fact that anhydrous glycerin is very hygroscopic and has irritating properties. It is applied mainly in medicinal forms for external use.

Solutions of glycerin in concentrations of 25% and above exhibit an antiseptic effect, more diluted -green nutrient medium for microorganisms. Due to the high viscosity of dissolution in it of medicinal substances at room temperature is slow, so it should be made when heated in a water bath to a temperature of 40-60 ° C. Glycerin is stored in well-sealed containers because of high hygroscopicity.

Fats and oils (Olea pinguia) are blends of esters of glycerol and higher fatty acids. In appearance, it is transparent or slightly colored oily liquid without odor or with a weak characteristic odor. In medical practice, only cold-pressed oils are used.

Fats and oils are used in the technology of ear and nose drops, ointments, liniments, injectable solutions and as a solvent for nonpolar and malopolar drugs: camphor, menthol, phenyl salicylate, benzoic acid, crystalline phenol, thymol, alkaloids, some vitamins, etc. Like all fats, vegetable oils do not mix with water, slightly soluble in ethyl alcohol but easily soluble in ether and chloroform.

For the manufacture of medicinal forms most often use almond (Oleum Amygdalarum), peach (Oleum Persicorum), olives (Oleum Olivarum), sunflower (Oleum Helianthi) and other oils. The quality of each of them is regulated by the DF by the determined indicators: density, acid, iodine, peroxide number, number of saponification, etc.

Dissolution of medicinal substances in them, as well as in glycerol, should be done when heated in a water bath.

Being biologically harmless, pharmacologically indifferent, vegetable oils, unfortunately, have low chemical stability. The presence of unsaturated fatty acids in their composition is the reason for the peeling of vegetable oils. In this case, as a result of oxidation and hydrolysis of fats, peroxide compounds, aldehydes and other products are formed. The oils get unpleasant taste and smell.

Light, air oxygen, as well as moisture, various microorganisms amplify these processes. Preserve fatty oils in well-sealed and filled top containers in a cool, dark place.

Vaseline oil (Oleum vaselini, paraffinum liquidum) - a liquid paraffin, is an oil fraction obtained after kerosene burning. It is a colorless, clear, oily liquid without flavor and odor, representing a mixture of boundary hydrocarbons (C10H12-C15H32). Mix in all ratios with ether, chloroform, gasoline, oils, except castor, is not soluble in water and alcohol. Vaseline oil is a free solvent for iodine, camphor, menthol, thymol, iodoform, benzoic acid and other medicinal products. By its dissolving ability it can be compared with vegetable oils.

However, it should be noted that compounds containing hydroxyl and carbonyl groups in vaseline oils dissolve much worse than in greasy oils. For example, resorcinol is soluble in greasy oils, and in vaseline is practically insoluble.

Vaseline oil is not absorbed through the skin and mucous membranes and slows the resorption of medicinal substances. Its significant disadvantage is that, when applied to the skin, it greatly impedes its gas and heat exchange, which, of course, is unwanted in inflammatory processes.

For this reason, and also because of its limited dissolving power, vaseline oil in non-aqueous solution technology is used less often than vegetable oils and mainly in rubbish and drops for the nose. More widely it is used in the manufacture of ointments.

Keep the petroleum jelly tray in sealed containers in a place protected from light.

Dimethoxide (Dimexidum) is a dimethyl sulfoxide. This is a sulfur-organic compound, a derivative of sulfur dioxide, in which one oxygen atom is replaced by two methyl groups in the molecule. The pharmaceutical practice came in relatively recently, in our country synthesized in 1966. It is a colorless, transparent liquid or colorless crystals with a specific odor, very hygroscopic. Dimethoxide is well mixed with alcohol, ethyl acetate, acetone, glycerol, chloroform, ether and castor oil. It is mixed with water in all proportions, in the ratio 2: 1 forms hydrate with water, which is accompanied by a significant release of heat.

Dimexid readily dissolves medicinal substances of different chemical nature. Apparently, this is due to the high polarity of dimethoxide (dielectric permittivity 49.0 at 25 ° C), as well as the ability to form associatives, compounds of compounds (adducts) and other properties.

Interest in this solvent is due not only to its high dissolving ability but also the property to quickly penetrate through damaged tissue, carrying with it medicinal substances. In addition, dimethoxide has analgesic, anti-inflammatory and antipyretic effects, as well as antimicrobial activity. These properties of dimethoxide, along with its biological harmlessness, allow us to predict its wider use in the technology of various medical forms (emulsions, liniments, ointments), as well as to speak about the possibility of reducing the doses of medicinal substances in solutions prepared on the dimethoxide.

Store dimexid in tightly closed cans in a place protected from light. In the manufacture of liquid drugs, solvents are also used as PEO-400, Esilon-4, Ysi-lon-5, the characteristics of which are given in the section "Solutions of the GMC".

TECHNOLOGICAL STAGES OF MANUFACTURE OF LIQUID MEDICINAL FORMS

All liquid dosage forms are made by mass-volume method (Order of the Ministry of Health of Ukraine № 197 dated 07.09.93), which provides the required mass of medicinal substance in the prescribed volume of solution. By mass, usually prepare solutions, where as a solvent used liquids of high density, viscous, volatile, as well as emulsions and some medicinal forms by author's proprietary. By volume, prepare solutions of ethyl alcohol of different strengths, solutions of standard pharmacopoeial liquids. In the mass-bulk method, the soluble material is taken by weight, and the solvent is added to obtain the required volume of solution.

If the solvent in the recipe is not specified, then make aqueous solutions. Under the word "water", if there are no special instructions, refer to purified water.

The process of manufacturing liquid dosage forms consists of the following stages: preparatory work (selection of appropriate dishes and plugs to it); weighing and measuring medicines and solvents; mixing or dissolving, extracting, dispersing or emulsifying the constituents of the drug; strain or filter; assessment of the quality and design of the medicinal product before departure.

Depending on the dosage form, the solubility of the medicinal substances and the type of solvent, certain technological steps are used.

Selection of dishes (bottles) and stoppers. The vial and cork are picked up in advance, taking into account the volume of liquid dosage forms manufactured and the properties of their components.

The bottle should be clean and dried. The lid should be screwed up to the humps free of stops and should not rotate. If the liquid medicinal products contain photosensitive substances, they are placed in a vial of orange glass.

Weighing and measuring. When weighing and measuring medicinal products, the basic rules laid down in section 9 are followed.

Mixing, dissolving, extracting, dispersing, emulsifying. All these technological processes for liquid dosage forms serve as the basis for the formation of a disperse system. The presence or absence of a dispersed phase in these processes depends on the solubility of drugs in water or other solvents.

When manufacturing liquid dosage forms by dissolving dry medical substances, the following rules should be followed:

> The first is always measured in the stand (a pot with a wide throat) calculated amount of purified water, which dissolves dry medicinal substances: first, the list A or B, then the general list, taking into account their solubility and other physical and chemical properties. Such a sequence of solutions is necessary to prevent or eliminate the processes of drug interactions, which most likely occurs in solutions with high concentration;

> large-crystalline medicinal substances (copper sulfate, gallium, potassium permanganate, etc.) to accelerate the dissolution process, first, in a mortar with a small amount of solvent;

> heat-resistant substances that slowly dissolve (sodium tetraborate, boric acid, mercuric dichloride, riboflavin, etacridine lactate, etc.), dissolve in a hot solvent or when heated;

> to accelerate the dissolution process, shake or stir the solution with a glass rod

When manufacturing liquid dosage forms by mixing or adding liquid components, the following rules should be followed:

> mixing of liquids is carried out in order to increase of their quantity;

> fragrant waters, tinctures, liquid extracts, alcohol solutions, flavor and sugar syrups, and other liquids are added to the aqueous solution in the last place in the bottle for delivery in the following order: water non-fat and non-liquid liquids; alcohol solutions in the order of increasing the concentration of alcohol; odorous and volatile liquids;

> liquid medicinal products containing essential oils (ammonia-anise drops, thoracic elixir, citral solution, etc.) are added to the mixture by mixing with sugar syrup (if it is present in the prescription) or with an equal amount of the mixture;

> tinctures, emulsion-aniseed drops and other volatile liquids should not be added to warm solutions;

> medicinal products with high viscosity (ihtiol, dense extracts, etc.) are pre-mixed in a mortar with a part of the solvent and after the addition of the remaining pores are transferred to the vial for delivery.

Cooling (colatio) and filtration (filtratio). These processes are used in pharmacy practice to separate the liquid phase from all suspended particles (mechanical impurities) that enter the liquid dosage forms when contaminating solvents and soluble substances from devices and dishes in the form of fibers, dust, etc. Filtration is carried out with the help of funnels made of different materials, of different capacities and types.

Glass funnels (Figure 106) come in different shapes: at an angle of 45 °is very convenient for separating the liquid part of the drug from small solids using a folded filter; with spherical thickening at the transition to a narrow part where a cotton swab is placed, suitable for filtration, and also for filtering with strain. The rate of stratification depends on the density of the wool in the spherical part of the funnel; at an angle of 60 ° - chemical, convenient for use in the use of smooth filters for collecting sediment, as well as in the manufacture of injectable solutions.

The draft is selected in such a way that it contains 25-30% of the liquid for filtration or filtration.

The choice of the method of cleaning the solution depends on its purpose. Solutions for internal and external application are filtered, eye drops, concentrated and injectable solutions are filtered.

This process is used to separate large particles, for which the liquid is pro-let through a lump of cotton wool or several layers of gauze, less often cloth, silk, capron and other fabrics.

Hygroscopic cotton wool should be long-fiber and clean enough to contain acid, alkaline and reducing substances; chlorides, sulfates, calcium salts are allowed only in minimal quantities. The most suitable for strain medical cotton wool of the grade "eye" (not lower than the grade I, DST 5556-75). Cottage chewing gauze (DST 11109-74) can be used only low fat, without impurities of starch and other substances. Gauze filters have high throughput and almost no mechanical contamination.

The process is run through a cotton swab, pre-rinsed with purified to remove small fibers. The purity of the drug in this case will depend on the density of the lumbar sac, enclosed in the mouth of the funnel. Excess hardness of a cotton swab is not desirable, because it slows down the rate of stratification.

Mucus, emulsions, infusions and broths are filtered through a double layer of gauze or cloth.

The filtration is used to separate all suspended particles (including small ones) by means of a filtering material having pores or capillary moves. The word "filter" comes from the Latin filtrů - felt.

Depending on the mechanism of the delay of the particles distinguish filters deep (flattened) and membrane (screen). In the in-depth filter, the particles are usually delayed at the intersection of the filter fibers, ie mechanically or as a result of adsorption on the filter material. As deep filters use cotton-fiber materials (cotton wool, gauze), glass in the form of sintered powder or fibers, pulp-asbestos filters, materials from polymeric fibers.

Membrane filters are screens of average sizes of nop in the narrow range (see section 25). Such filters quickly get littered, therefore, for filtering solutions using combined filters using medical cotton wool, filter paper and household cotton gauze.

All filtering materials in quality should fully meet the requirements of the relevant normative and technical documentation. they must have a certain strength, have a structure that provides effective delay of particles at high permeability, does not allocate fiber or particles to solution, do not interact with drugs, withstand thermal sterilization, pressure or dilution during the filtration.

In pharmacy practice, filtering paper can be used to filter solutions. This is glued paper made of cotton fiber. There are the following types of filter paper for standard datas: filtering (grade B), medium filter (brand C) and slow-filtration (brand M). The ratio of the filtration rate between these filter papers is as follows: B: C: M = 4: 2: 1. Ash content should not exceed 0.8%.

For certain types of work, the filter paper is sealed by treating with hydrochloric or hydrofluoric acid. In accordance with the requirements of DF XI, the filter paper should consist of pure fiber without dark places and impurities of wood, chlorides, iron salts (DST 120-26-76). If the filter paper contains at least insignificant traces of iron salts, then filtration of the solution of sodium salicylate or other salicylic preparation becomes purple or pink in color. The development of adrenaline hydrochloride loses its physiological effect.

Flexible and smooth filters are used to filter liquid dosage forms (gravity flow).

The folding filter has a large filtering surface and thanks to a large amount of folds it does not stick to the walls of the funnel, so the filtering is fast.

Make a folded filter made of a square piece of filter paper, which is folded in half, and then several times diagonally. When folding the filter, it is not necessary to fold s to the top so that the narrow end of it turns out sharp, otherwise the filter tip is softened and when filtering the paper in this place can break. The height of the filter should be lower than the upper edge of the funnel by 0.5-1 cm in order to

prevent the filtering fluid from transfusion through the edge of the funnel. The end of the filter must enter the narrow part of the funnel, not to "hang" and not stick to its walls, and the folds of the filter should touch their catching parts to the funnel.

A smooth filter is made of a square piece of filter paper, folded and lean over a diagonal, the outer end of which is cut in a circle. By expanding one layer, a cone is obtained.

For filtering with smooth filters, use a glass funnel with a 60 ° angle.

To delay fibers that are separated from the outer surface of the filter, and to protect it from possible rupture, a lump of cotton wool is put in a funnel. When filtering, the liquid is poured into the filter walls sideways, and the funnel is placed so that its end is slightly below the neck of the vial.

Filter and strain can be done using a metal or wooden base.

In order not to contaminate the finished medicinal product with fibers of cotton or paper, sticking to the walls of the bottle and very difficult to wash, filter and filter the part of the drug first, collect the filtrate in a separate dish and then pour it again into the filter, and then filter into the vial for delivery. It is also necessary to take into account the adsorption capacity of paper and cotton wool, which is associated with some loss of liquid medicinal preparations, and this loss depends on the size of the filter and the number of wool taken. Hence, the size of the filter and the amount of cotton should be minimal. If liquid drugs are manufactured in quantities of 100 ml or more, then such a minor loss is not significant, since it is invested in the established norm.

In cases where small amounts of solutions are filtered (10-30 ml), a significant loss of solution occurs and the concentration of the diluted medicinal product decreases.

To avoid this, use special technological techniques, which will be said when making drops (see section 15).

When filtering aqueous solutions, it is important to know that paper is electrified negatively as a result of the dissociation of cellulose molecules and therefore, adsorption phenomena occur in the filtration (less in the filtration), leading to a slight decrease in the concentration of active substances. Cations of alkaline and alkaline-earth metals are adsorbed little, cations of heavy metals - more. According to their adsorption capacity, they can be arranged in a definite order (a series of Kolgotovs):

$$Pb^{2+} > Hg^{2+} > Ca^{2+} > Ag^{+} > Zn^{2+}$$

Significant adsorption occurs in the filtration of solutions of alkaloids, colorants (methylene blue, ethacridine lactate), enzymes (pepsin). Solutions containing oxidants (potassium permanganate, silver nitrate) are recovered by

fiber. The influence of filter paper and cotton wool on oxidation solutions depends on a number of factors: the quality of the filter paper, the time of contact of these solutions with the paper and cotton wool, the concentration of the filtered solutions.

The method of filtering through a paper (free flow) is poorly productive and labor-intensive due to insufficient filtration rate (2-3 l / h) and frequent flaking of the fibers from the filter material. To improve the process of filtering liquid dosage forms in pharmacies, it is suggested to use glass filters. These are porous glass plates obtained by fusing glass powder, inserted into a funnel of conical or cylindrical shape. They are used in cases where either the filtration solution decomposes in contact with the paper, or the paper adsorbs the dissolved medications. When applied, the adsorption of the released substances is significantly reduced. Glass filters are suitable for filtering solutions of alkaloids, colorants, enzymes, oxidizing agents, protected colloids and some others. These filters are manufactured with a different diameter pop (Table 14). No. 1 - 90-150 microns (size of pp corresponds to a cotton swab), № 2 - 40-90 microns (size of pc corresponds to a dense filter paper), No. 3 - 20-40 microns and No. 4 - 10-20 microns (pop size corresponds to a very dense filter paper). The most large filters of the number 1 and number 2, through which the fluid passes arbitrarily without vacuum, is usually used for straining solutions for internal and external application. Filters # 3 and # 4 require the creation of a vacuum. They are used to filter eye drops and injectable solutions.

Before filtration, non-used glass filters were washed with warm (50-60 ° C) purified water. When the content in the washing waters of a large amount of glass dust filters are treated with concentrated sulfuric acid for 15-20 hours, after which repeatedly washed with warm water purified to a negative reaction to sulfate ions in washing waters. After use, the filters are thoroughly washed with warm water (from the tubular branch of the funnel), strongly contaminated, treated with acid sulfuric acid, concentrated with the addition of 1% solution of sodium nitrate or perchlorate with safety precautions. An important advantage of glass filters is the possibility of their sterilization. Lack of glass filters is their fragility. They are inconvenient when filtering concentrated solutions: the pores of filters quickly clog up.

ASSESSMENT OF QUALITY AND FORMATION OF LIQUID DRUGS BEFORE DISCOUNT

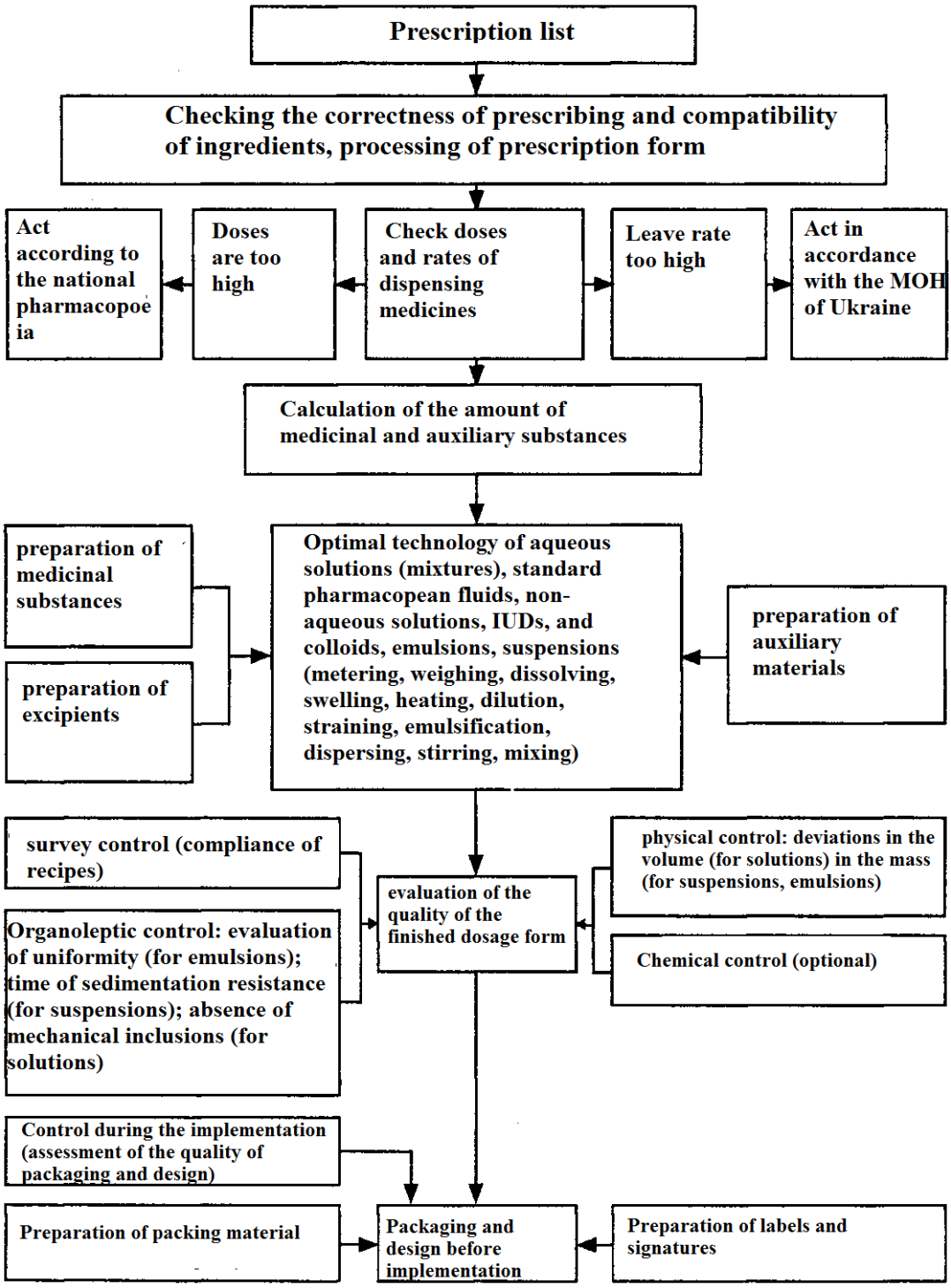
Finished medicines are checked for purity and the dishes they contain are leakproof. If the vial with the finished product turns over with a stopper then with a slight tap on the palm of the hand, the liquid should not be leaked through the plug. Clogged bottle with liquid drug (solution) is slightly shaken, flipped over and

viewed in direct and reflected light. No foreign particles should be visible in the liquid.

The vial is stamped with a "Internal" or "External" label, which has been issued accordingly. Solutions containing poisonous substances, seal, make a sign and an additional label "Be careful". If the medical prescription requires special storage conditions, additional labels are labeled, for example, "Keep in a cool place", "Shake up before use", etc.

The assessment of the quality of liquid dosage forms is carried out in accordance with the requirements of the normative and technical documentation. The structural and logical scheme of technology and quality control of liquid dosage forms is presented in Scheme 6.

Scheme 6. STRUCTURAL-LOGICAL SCHEME OF TECHNOLOGY AND CONTROL OF QUALITY OF LIQUID MEDICINAL FORMS



CONCENTRATED SOLUTIONS FOR FLEXIBLE INSTALLATIONS

The preparation of concentrated solutions is regulated by the instructions of the DF XI and "Instruction on the manufacture of pharmaceutical forms with liquid dispersion medium in pharmacies" approved by the order of the Ministry of Health of Ukraine No. 197 dated September 7, 1993.

Concentrated solutions are an undoped form of pharmacy preform, used to make dosage forms with a liquid dispersion medium, by dilution or in combination with other medicinal substances.

Concentrated solutions are working solutions of medicinal substances at a clearly greater concentration than these substances are prescribed in recipes, calculated on the corresponding water dilution to the concentration indicated in the recipe. they are usually called "concentrates". The use of concentrated solutions has a number of advantages over the preparation of mixtures of dry substances: the work of the pharmacist is facilitated, the quality improves and the release of drugs to patients is accelerated.

The nomenclature of concentrated solutions is determined by the requests of the extemporal formulation entering the pharmacy and depending on the need, the list of concentrated solutions may vary. In the instructions for the manufacture of pharmaceutical formulations with liquid dispersion medium in pharmacies in Appendix 1 (see appendix 3 of the textbook), an exemplary list of concentrated solutions, often used in the manufacture of liquid medicinal products, is given.

In the manufacture of concentrated solutions, concentrations close to saturated should be avoided, as decreasing the temperature of the solution may lead to the decomposition of the decomposed substance.

Due to the fact that concentrated solutions can become an environment for the development of microorganisms, they should be prepared in aseptic conditions on freshly distilled purified water. All used auxiliary materials, as well as dishes for their manufacture and storage, should be pre-sterilized and the resulting solutions are necessarily filtered (not strained).

Concentrated solutions after manufacture are subjected to complete chemical control (truth, quantitative content of active substances). All prepared concentrated solutions are recorded in a laboratory journal and on the label of the receptacle in which they are stored, the name and concentration of the solution, the number of the series and analysis, the date of manufacture is indicated.

Stocks of concentrated solutions are stored in tightly sealed bottles in a cool and light-protected place at a temperature of 20-22 ° C or in a refrigerator (3-5 ° C).

In pharmacies, concentrated solutions are made in such quantities, which can be used during the prescribed shelf life. Limit storage times for individual solutions are set depending on their stability from 2 to 10 days.

If the solution is an environment for the reproduction of microorganisms, then its shelf-life is small, for example: 5 and 20% glucose solution is stored for two days. With an increase in the concentration of glucose solution to 40 and 50%, its shelf life is increased to 15 days. The latter is due to the rising osmotic pressure of the solution, which reduces the survival conditions of microorganisms.

Changes in color, clouding of solutions, the appearance of flakes, raids is a sign of their uselessness, even if the shelf life has not expired.

Preparation of concentrated solutions. Concentrated solutions are made by mass-volume method using dimensioned dishes. You can also calculate the amount of water you need by using the volume increase factors or the density value of the solution (see tutorial appendix 3).

For example, you need to prepare 1 liter of 20% (1: 5) potassium bromide solution.

1. Preparing the solution in a measuring dish.

In a sterile 1 liter volumetric flask, 200.0 g of potassium bromide are weighed down through a funnel and dissolved in a small amount of freshly prepared (cooled) purified water. Then water is added to the label. The solution is filtered into a matte-glass or dark glass with a corked stopper, checked for numerical and quantitative composition, labeled with a designation of the name and concentration of the solution, the date of its manufacture, the serial number and the analysis number.

2. Preparation of the solution using CCD.

If we take into account the increase in volume equal to 0,27 ml / m for potassium bromide, then the volume, which takes 200,0 g of potassium bromide, is 54 ml (200,0 x 0,27), then the water for making the solution is 946 ml (1000 ml - 54 ml). In this case, the use of measuring cookware is not required.

946 ml of freshly brewed (chilled) purified water are measured in the stand and dissolved in 200,0 g of potassium bromide. Then do as above.

3. Preparation of the solution, taking into account its density.

The density of 20% potassium bromide solution is 1,144, that is, 1 liter of this solution should have a mass of 1144.0 g (according to the formula P = V x d, where P is the mass of the solution, V is the volume and d density). Since in this solution of potassium bromide is taken by weight, the water should be 1144.0 - 200.0 = 944.0 g. The volume of the solution at that will be 1 liter, and its mass - 1144.0 g.

944 ml of freshly brewed purified water are measured in the stand and dissolved in 200,0 g of potassium bromide in it. If it is impossible to measure the required quantity of water, it is weighed into a pre-made old stand. After dissolution, filter as above.

In determining the amount of solvent needed to make 20% potassium bromide solution in different ways (based on the density of the solution and using the volume increase factor), we obtain data that differ in 2 ml (946 and 944 ml respectively), which can be explained the experiment's mistake.

Medicinal substances (crystalline hydrates) are weighed against the actual moisture content.

For example, it is necessary to prepare 1 liter of 50% solution of glucose (humidity where a is the amount of anhydrous glucose indicated in the prescription; b - moisture content in glucose,%.

$$x = \frac{a \times 100}{100 - b},$$

$$x = \frac{500 \times 100}{100 - 10} = 555{,}5 \text{ г.}$$

The glucose is weighed on the basis of the actual moisture content in it, the quantity of which is determined by the formula:

In a measuring flask, pour a small amount of hot water, dissolve 555.5 g of a sample. After complete dissolution of the substance and the cooling solution, bring the solution to 1 liter with water and filter. Conduct a complete chemical analysis (truth, purity, quantitative composition). Depending on the result of the quantitative analysis, the concentrated solutions are rotated with water or strengthened by the addition of the dry drug to the required concentration

1. If the solution is stronger than necessary, it is diluted to the desired concentration of water, the quantity of which is calculated by the formula:

$$X = \frac{A\,(C - B)}{B},$$

where X - amount of water needed to brew the prepared solution, ml;
A - the volume of the prepared solution, ml;
B - necessary concentration of solution, %;
C is the actual concentration of the solution,%.

$$X = \frac{3000\,(23 - 20)}{20} = \frac{9000}{20} = 450 \text{ мл (води).}$$

20,0 г – 100 мл

690,0 г – x

$$x = \frac{100 \times 690{,}0}{20{,}0} = 3450 \text{ мл.}$$

For example, it was necessary to prepare 3 l of 20% (1: 5) of potassium bromide solution. The analysis showed that the solution contains 23% of the drug. Using the formula above, find the amount of water needed to dilute the solution:

Of this amount (690.0 g) you can prepare 3450 ml of 20% potassium bromide solution:

23,0 – 100 мл

x – 3000 мл

$$x = \frac{23{,}0 \times 3000}{100} = 690{,}0 \text{ г.}$$

Consequently, in order to obtain a solution of the required concentration, it is necessary to add 450 ml of freshly-sweetened and chilled water of purified and to check the concentration again.

2. If the solution is weaker than necessary, it must be strengthened by the addition of a medicinal substance, the amount of which is calculated by the formula:

$$X = \frac{A\,(C - B)}{100 \times d - B},$$

where X is the amount of dry matter to be added to strengthen the solution, g; A - the volume of the prepared solution, ml; B - required concentration of solution,%; C - actual concentration of solution,%; d is the density of the solution of the required concentration.

For example, it was necessary to prepare 1 liter of 20% solution of potassium bromide. The analysis showed that the solution contains 18% of the medicinal substance (which, like in the first case, does not correspond to acceptable deviations).

Using the formula above, find:

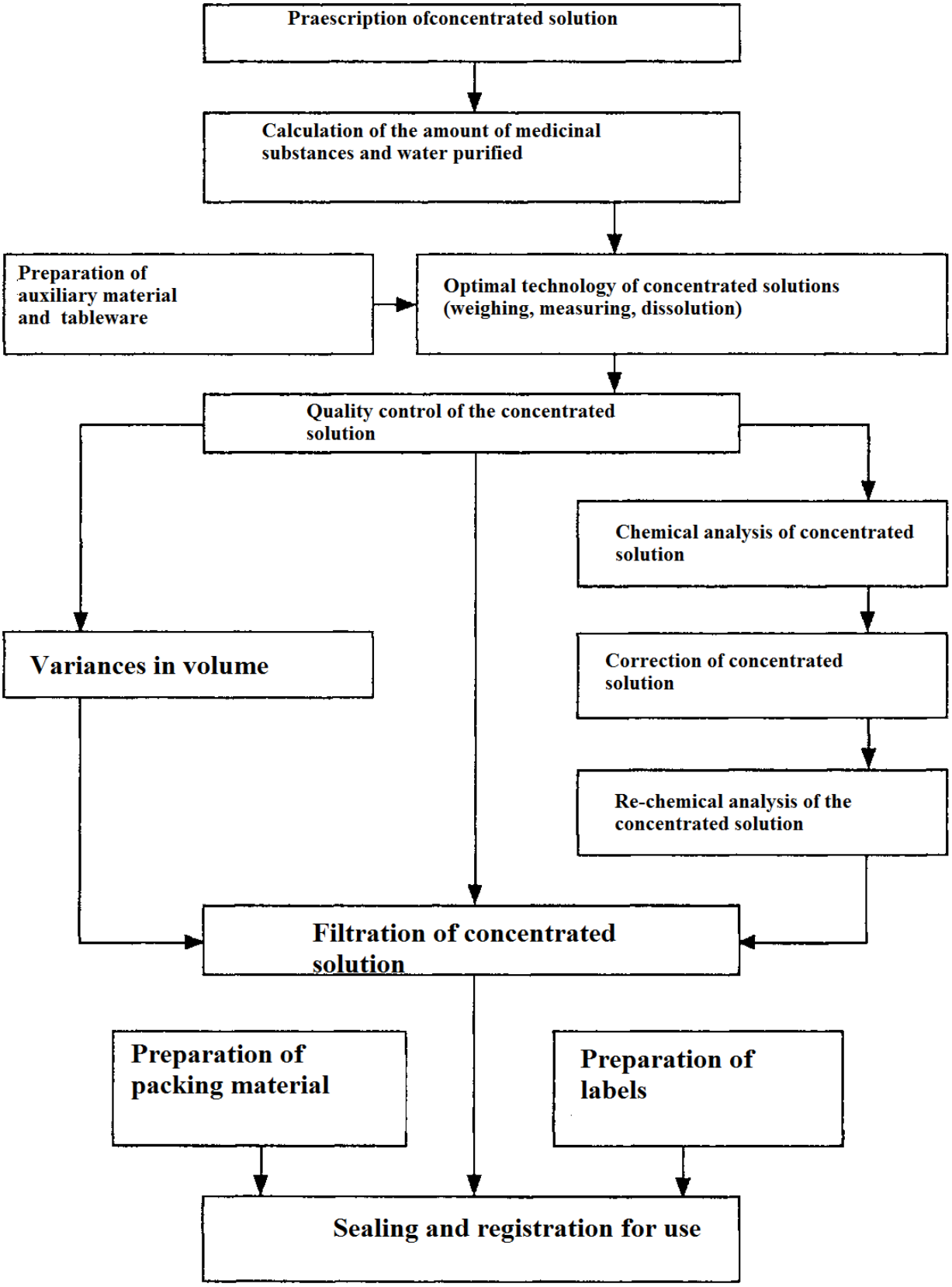
$$X = \frac{1000\,(20 - 18)}{(100 \times 1{,}144) - 20} = \frac{2000}{94{,}4} = 21{,}18 \text{ г,}$$

Thus, to strengthen the solution, it is necessary to add 21,18 g of potassium bromide. After strengthening the solution, it is again filtered and analyzed. Acceptable deviation of concentration in solutions containing substances up to 20% inclusive is ± 2% of the indicated; in solutions with a concentration of 21% and above - ± 1%.

The structural and logical scheme of the technology of concentrated solutions is given in scheme 7.

Scheme 7.

STRUCTURAL AND LOGICAL SCHEME OF TECHNOLOGIES OF CONCENTRATED SOLUTIONS


Praescription ofconcentrated solution
Calculation of the amount of medicinal substances and water purified
Preparation of auxiliary material and tableware
Optimal technology of concentrated solutions (weighing, measuring, dissolution)
Quality control of the concentrated solution
Chemical analysis of concentrated solution
Variances in volume
Correction of concentrated solution
Re-chemical analysis of the concentrated solution
Filtration of concentrated solution
Preparation of packing material
Preparation of labels
Sealing and registration for use

For example, it was necessary to prepare 1 liter of 20% solution of potassium bromide. The analysis showed that the solution contains 18% of the medicinal substance (which, like in the first case, does not correspond to acceptable

$$X = \frac{1000\,(20 - 18)}{(100 \times 1{,}144) - 20} = \frac{2000}{94{,}4} = 21{,}18 \text{ г.}$$

deviations).

To strengthen the solution it is necessary to add 21,18 g of potassium bromide. After strengthening the solution, it must be filtered and analyzed again. Acceptable deviation of concentration in solutions containing substances up to 20% inclusive is ± 2% of the indicated; in solutions with a concentration of 21% and above - ± 1%.

The structural and logical scheme of the technology of concentrated solutions is given in scheme 7.

PREPARATION OF LIQUID MEDICINAL FORMS USING CONCENTRATED SOLUTIONS AND DRY MEDICINAL PRODUCTS

A very important issue in the manufacture of liquid dosage forms by mass-volume method is to determine the total volume, which is calculated by summing all volumes of liquid ingredients (in accordance with the Order of the Ministry of Health of Ukraine No. 197 of 09.07.93 p.). The total volume includes: solvent, aqueous and alcohol solutions of medicinal substances, tinctures, liquid extracts and all other prescribed liquids, prescribed in recipes in milliliters.

If it is necessary to establish the volume of liquid dosage forms, which include viscous, volatile and also liquids with a higher density, take into account their density. The number of dry substances in the determination of the total volume is not taken into account. When determining the fill volume, it is necessary to consider the method of prescribing the solvent. Example:

Rp .: Sodium hydrocarbonatis 2.0
Tincturae Valerianae 6 ml
Sirupi simplicis 10 ml
Aquae purificatae 200 ml
Misce Da Signa 1 tablespoon 3 times a day.

In the above list the amount of solvent is specified. In this case, the calculation of the total volume of the mixture is carried out by summation of volumes of liquid ingredients: 200 ml of purified water + 6 ml of tincture of valerianum + 10 ml of syrup of sugar, which will make 216 ml. The mixture can be prepared using a concentrated sodium hydrogen carbonate solution of 5% (1:20).

Calculation: Sodium hydrocarbonate solution 5% (1:20) 20 x 2.0 = 40 ml Water purified 200 - 40 = 160 ml

Control panel

Date Recipient No
Aquae purificatae 160 ml
In a solution of sodium hydrocarbonetis 5% (1:20) 40 ml
Sirupi simplicis 10 ml (or 13.0)
Tincturae Valerianae 6 ml
Vwhole = 216 ml
Prepared by: (signature)
Checked out: (signature)

If the amount of the solvent is indicated "to a certain volume", then the liquid ingredients are included in the volume of the aqueous solution.

Example:

Rp .: Nartii hydrocarbonatis 2,0
Tincturae Valerianae 6 ml
Sirupi simplicis 10 ml
Aquae purificatae 200 ml
M. D. Signa. 1 tablespoon 3 times a day.

The total volume of the mixture in this case is 200 ml. Number of treated water: 200 - (40 + 6 + 10) = 144 ml. PC

Date № of recipe

Aquae purificatae 144 ml

Solutionis Natrii hydrocarbonatis 5 % (1:20) 40 ml

Sirupi simplicis 10 ml (чи 13.0)

Tincturae Valerianae 6 ml

$V_{whole.}$ = 200 ml

Prepared by: (signature)

Checked out: (signature)

It should be noted that in the medicine prescribed syrup sugar in volume but because as it is a viscous liquid, it can be dosed and takien into account by weight with a density of 1,3 g / ml (ie, weigh 1 instead of 10 ml of syrup , 3 x 10 = 13.0 g).

As for the tincture of valerian, then it is measured with a pipette or measuring cylinder and added in the final turn to the finished potion. This is due to the fact that the addition of alcoholic solutions to water is the allocation of substances insoluble in water.

If extraction drugs are added in the last turn, then the replacement of the solvent in a large volume of solution will occur with a sharp change in the concentration of ethyl alcohol, resulting in the formation of many centers of crystallization, the suspension is fine, for a long time is suspended, is easily dispensed. If extraction preparations are measured first and added to them an aqueous solution - the solvent replacement will occur slowly, resulting in less than the centers of crystallization, the precipitate turns coarse-grained (fluctuating).

When adding tinctures to concentrated salt solutions there is a phenomenon of vialization of extractive substances from tinctures in the form of large particles.

When making mixtures of concentrated solutions, the following rules are followed:

- First of all, in a bottle, water purified, then concentrated solutions of poisonous and potent substances is measured and then concentrated solutions of medicinal substances of the general list in the order of their prescription;

- the medicines are not filtered and made immediately in the bottle.

Taking into account all these requirements for the given prescription, the medicine is made as follows: 160 ml of purified water is measured in a leave-up bottle, then 40 ml of 5% solution of sodium bicarbonate, 10 ml of sugar syrup and lastly 6 ml of tincture of valerianum are measured here. The bottle is sealed and sealed to leave.

In the absence of concentrated solutions, the mixture is prepared taking into account the percentage of dry medicinal substances in the total volume of solution (see pages 234-235).

1. If the liquid dosage form consists of dry medicinal substances in a total amount of up to 3% and the concentrated solutions are absent, then they are dissolved in the measured quantity of prescribed water or other liquid without taking into account the CCD.

Example:

Rp.: Analgini	3,0
Kalii bromidi	4,0
Tincturae Belladonnae	8 ml
Tincturae Valerianae	10 ml
Aquae purificatae	200 ml
Misce. Da.	
Signa. 1 tablespoon 3 times a day.	

Opalassiyuschey a potion, which consists of highly active substances (analgin and tincture of belladonna, prepared on 40% alcohol), a photosensitive substance potassium bromide and tincture valerian, prepared on 70% alcohol.

Testing of single and daily doses of analgin and tinctures of belladonna is carried out by comparing them with higher single and daily doses for reception in the following sequence, as indicated on page 234

Total volume of the drug: 200 ml + 10 ml + 8 ml = 218 ml.

3.0 g of analgin (a concentrate which is absent) in a volume of 218 ml will consist of:

218 мл – 3,0 г

100 мл – x

$$x = \frac{3{,}0 \times 100}{218} = 1{,}7, \text{ тобто менше 3 \%}$$

When dissolved in 3.0 g of analgin (KOO = 0.68 ml / r), the volume will increase by 2.04 ml (0.68x3.0 = 2.04).

For a volume of more than 200 ml allowed deviation is ± 1%. For a volume of 218 ml this deviation will be 2.18 ml. Apparently, the variation in the volume taking 3.0 g of analgin does not exceed the permissible norm, because 2.18 ml is more than 2.04 ml. In such cases, the CCD is not take into account.

Calculation: Potassium bromide solution 20% (1: 5) 5 x 4 = 20 ml

Water purified 200 - 20 = 180 ml

In the stand, measure 180 ml of purified water, which dissolves 3,0 g analgin. The solution is filtered into a leave-up bottle and first add 20 ml of a 20% solution of potassium bromide, then 8 ml of tincture of belladonna is added and 10 ml of tincture of valerian. Clog up and draw up to leave.

2. Liquid dosage forms containing dry matter in the total amount of 3% are made using concentrated solutions or in a measure the dishes or volume of water needed to dissolve dry substances are determined by calculation, taking into account the CRO.

Rp: Solution Calcium chloride 5% in 200 ml
Glucose 60.0
Sodium Bromide 3.0
Misce Da Signa 1 tablespoon 3 times a day.

Mixture is a solution, which includes a photosensitive substance - sodium bromide, strongly hygroscopic substance - calcium chloride and glucose, registered in a concentration of more than 3%. The mixture is made using concentrated solutions.

Calcium chloride is a very hygroscopic substance that dissolves in air to the consistency of syrup solution. It is not easy to use crystalline calcium with chloride (wet crystals and dirty weights, when weighing, there is no certainty in the exact dosage, because the unknown content in this salt of hygroscopic water). To avoid damage to the drug and inaccurate dosing of calcium chloride, a concentrated solution of 50% or 20% is made from it and it is used for the manufacture of liquid medicinal products. The solution is stable and well preserved for a long time.

Calculation: Calcium chloride solution 50% (1: 2) 10,0x2 = 20 ml

Glucose solution 50% (1: 2) 60.0 x 2 = 120 ml

A solution of sodium bromide 20% (1: 5) 3.0 x 5 = 15 ml

Water purified 200- (20 + 120 + 15) = 45ml

45 ml of purified water, 20 ml of 50% concentrated calcium chloride solution, 120 ml of 50% concentrated glucose solution, 15 ml of 20% concentrated solution of sodium bromide are measured in n a bottle

In the absence of a concentrated glucose solution, the amount of solvent is calculated using an increase in volume for glucose. When 60.0 g of glucose is dissolved , the volume of the solution will increase by 41.4 ml (0.69 x 60 = 41.4). Therefore, the amount of purified water to obtain 200 ml of solution will be 123.6 ml (200 - 20 - 15 - 41.4 = 123.6).

In 123.6 ml of heated water, dissolve 60.0 g of glucose, cool the solution, simulate the bottle for delivery and add the calculated amount of concentrated calcium chloride and sodium bromide.

3. If the medicinal product is given in a dry form in a quantity less than C% and in the amount in excess of 3%, then in calculating the water it is necessary to take into account the volume that each of the medicinal substances will take.

4. Liquid dosage forms in which purified water, and fragrant waters or other liquids (pertussin, water extracts from plant raw materials, polyethylene oxide-400, ethyl alcohol, etc.) are not used as a solvent ,all are made without the use of concentrated solutions of medicinal substances and recording of CCD when dissolving substances.

Rp .: Sodium hydrocarbonate 2.0
Sodium benzoate 1.5
Anchovy anionic liquor 4 ml
Syrupi sacchari 10 ml
Aquae Menthae 100 ml
Misce Da Signa 1 tablespoon 3 times a day.

Opalescents with amniotic-anisive drops, which are added to aqueous solutions by a special method.

In the stand, measure 100 ml of mint water, which dissolves 2,0 g of sodium hydrocarbonate and 1,5 g of sodium benzoate. The solution is filtered into the vial for delivery. In vitreous jar add 4 ml of amniotic-drops, mix and transfer to a vial for delivery.

If sugar syrup is not indicated in the formulation, the ammonia-aniseed drops are pre-mixed with approximately equal amount of aqueous solution. With the direct addition of ammonia drops to aqueous electrolyte solutions, the anetol contained in the vanilla oil is deposited, which is deposited with flakes on the walls of the bottle.

DISCHARGE OF STANDARD PHARMACOPOEIAL LIQUIDS. FEATURES OF PREPARING OF SOME AQUEOUS SOLUTIONS.

Standard pharmacopoeial solutions (liquids) are aqueous solutions (factory-made) of certain medicinal substances in a strictly defined concentration, as established in the relevant articles of the DF.

These include solutions of solid, liquid or gaseous substances (a solution of potassium acetate, a drill fluid, a hydrochloric acid, an ammonia solution, hydrogen peroxide, formalin, etc.). In the manufacture of liquid dosage forms from the listed standard solutions are guided by the relevant instructions DF as well as the provisions of "Instructions for the manufacture of pharmaceutical forms with liquid dispersion medium in pharmacies" (Order of the Ministry of Health of Ukraine No. 197 dated 07.09.93 p.). These liquids are readily mixed with water and their solutions are made directly in the bottle for delivery, which initially measures the water and then the calculated amount of liquid. If necessary the solution is filtered.

Standard pharmacopoeial solutions can be prescribed under two names: conditional and chemical, which depends on the calculation of their number.

If in the formulation the liquid is registered under the conventional name, then at the dilution, the concentration of the standard solution is taken as unit (100%).

If the chemical name is given, then the calculations shall be based on the actual content of the substances in standard solutions using the following formula:

$$X = V \times \frac{B}{A},$$

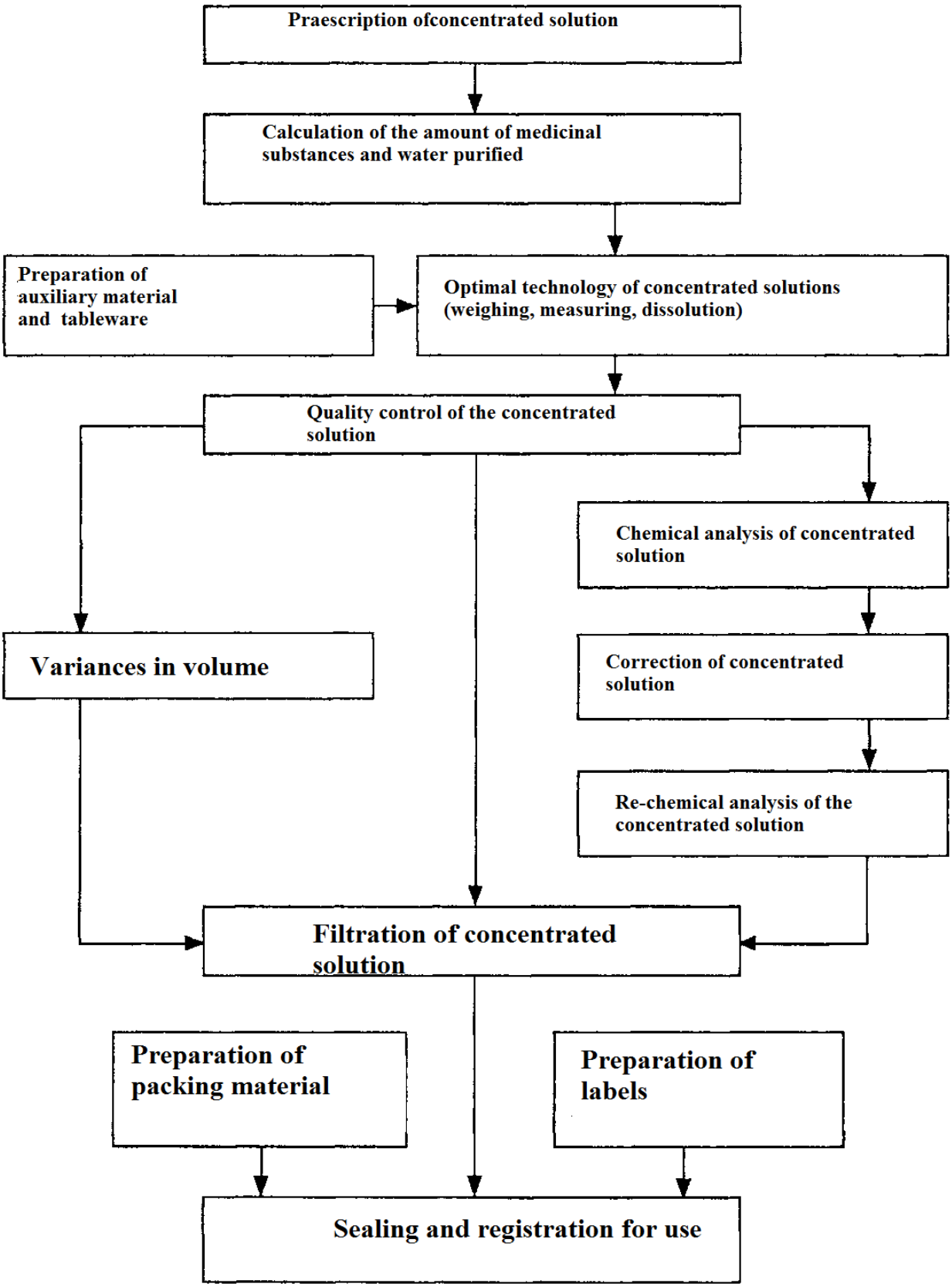
where X is the volume of standard liquid, ml;

V is volume of solution to be prepared, ml;

B is prescribed concentration of solution,%;

A is the actual concentration of the standard liquid to be diluted,%.

The amount of water in both cases is calculated by the difference between the total volume of the prepared solution and the calculated amount of standard liquid.



WATER SOLUTIONS

In the manufacture of aqueous solutions and other liquid dosage forms, you must strictly observe the rules given above.

For the manufacture of liquid dosage forms the medicinal products of pharmaceutical quality are used. If the drug substance in the DF is indicated in crystalline and anhydrous form, then the substance is used in a crystalline form. Depending on the properties of medicinal substances, their solubility, stability and the purpose of solutions of roses, several methods of their manufacture can differ.

Solutions with readily soluble drugs. The dissolution of the majority of solids is arbitrary, especially in those cases where the concentration of medicinal substances in the prescribed solutions is far from the limit of solubility.

When calculating the amount of purified water, take into account the percentage of the medicinal substance (or the sum of substances). If solutions are made up to a concentration of C%, then the water is taken up by volume as long as the solution is prescribed in the recipe, because a small amount of the drug does not substantially change the volume of the cleanser when it is dissolved.

Example:

Rp .: Solutionis Analgini 2% 150 ml

Da Signa 1 tablespoon 3 times a day.

Mixture is a solution with a well soluble drug substance in list B, written down to 3%.

If solutions for internal use prescribe toxic and potent substances, then first of all pay attention to the correctness of their dosage.

Calculation: Analgin 3.0 g

$$x = \frac{2 \times 150}{100} = 3{,}0 \text{ г.}$$

2,0 - 100 ml

x - 150 ml

Water purified 200 ml

Dosage Check: The volume of the solution is 150 ml

number of receptions - 150: 15 = 10

t.s.d. 3,0:10 = 0,3 g h.s.d. = 1,0 g

t.s.d. 0,3 x 3 = 0,9 g h.d.d. = 3,0 g

Doses are not inflated

In the stand, 150 ml of purified water is measured. Weigh 3.0 g of analgin, pour out into the stand and dissolve. Stir in the vial for delivery. Clogged and decorated.

Solutions in concentrations higher than 3% are made in measuring dishes or counting the amount of water using the coefficients of increasing volume (see Annex 2 to the Order of the Ministry of Health of Ukraine No. 197 dated 07.09.93 p.).

> The volume increase factor (ml / g) indicates an increase in the volume of solution in ml at the dissolution of 1.0 g of substance at 20 ° C.

Rp .: Solution Magnesium sulfate 20% 150 ml
Da Signa 1 tablespoon 3 times a day.

Mixture is a solution with a well soluble drug magnesium sulfate (crystalline hydrate), discharged in an amount of more than 3%. It is not necessary to grind magnesium sulfate in front because it is readily soluble in water.

The technology of the solution using the measuring dishes. In the measuring cylinder place about 80 ml of purified water. On BW-100 weigh 30,0 g of magnesium sulfate, pour into a cylinder and stir until it is completely dissolved using a glass paste. Then bring the solution to a volume of 150 ml. Processed in a pre-selected vial and accordingly issued for release.

Control panel
Date Recipient No
Magnesium sulfate 30.0
Aquae purificatae ad 150 ml
V total = 150 ml
Prepared by: (signature)
Checked out: (signature)

The technology of the solution using the volume increase factor (KIV). For magnesium sulfate, the CCD is 0.50.

Calculation: Magnesium sulfate 30.0 g

Water purified 150 ml - (30,0 x 0,50) = 135 ml

In the stand, 135 ml of purified water is measured, in which 30,0 g of magnesium sulfate is dissolved, filtered in a vial for release and decorated.

Control panel
Date Recipient No
Aquae purificatae 135 ml
Magnesium sulfate 30.0
Vtotal = 150 ml
Prepared by: (signature)
Checked out: (signature)

An exception to this rule is a solution of sodium thiosulfate 60% used to treat scabies.

Rp.: Solution in sodium thiosulphate 60% in 100 ml

D.S. External (solution number 1)

The prescription of this solution is author's, so it is made by weight (60.0 g + 40.0 g) = 100.0 g. If it is necessary to prepare 100 ml of solution in mass-volume concentrating, it is necessary to make certain calculations. 100.0 g 60% solution of sodium thiosulfate has a volume of 73.5 ml, so for the manufacture of 100 ml of solution should be taken sodium thiosulfate 81.63 g:

$$x = \frac{60,0 \times 100}{73,5} = 81,63\ \%.$$

60.0 - 73.5 ml

x - 100 мл

In a measuring bowl, 81.63 grams of sodium thiosulfate are dissolved in a portion of the water, and the volume of the solution is adjusted to 100 ml with water (or a TSO sulfate is taken into account, depending on the KOO: 100 - (81.63 x 0.51) = 58 ml).

It is prohibited to prepare a solution by dissolving 60,0 g of sodium thiosulfate and giving the solution obtained to a volume of 100 ml, as the mass-volume concentration of the medicinal substance in the solution will be only 46,37%.

Special cases of making solutions. This group of solutions is quite large. Preparing each of them has its own peculiarities.

Solutions with slowly soluble drugs. The slow solubility of medicinal substances in water can be due to various factors: the strength of the crystal lattice, the low diffusion rate of heavy ions or the relatively poor wettability of the drug substance with a solvent. To accelerate the dissolution, additional technological techniques are used: dissolving in a hot solvent or grinding in a mortar.

To slowly soluble in cold water are heat-resistant medicinal substances: boric acid, sodium tetraborate, alumina alumina, caffeine, calcium gluconate, copper sulfate, ethacridine lactate, furatsilin and others.

Rp .: Solution Acid boric 2% 200 ml

Da Signa For rinsing the oral cavity.

1.0 g of boron acid dissolves in 25 ml of cold water and 4 ml of boiling water, so it is dissolved in hot water when shaking. Measuring cylinder measure 200 ml of hot water, pour into the stand and dissolve with stirring 4,0 g of boric acid. After cooling, the solution is filtered to the vial for delivery.

Rp .: Solution Cupri sulfate 3% 200ml

Da Signa For swaddling.

A solution for external use with a slowly soluble co-crystalline drug. The solubility of copper sulphate in water is good 1: 3. However, due to poor water wettability of crystals (a substance of a coarse-grained crystal), the dissolution is suppressed by grinding in a mortar with water.

In the stand, measure 200 ml of water. In a mortar, 6,0 g of copper sulphate are placed and dissolved when rubbed with a portion of water, then the remaining water is added. The solution is for dipping, so it is filtered into a vial for delivery. The vial is sealed and drawn up for leave.

Rp .: Solutionis Furacilini (1: 5000) 250ml
Da Signa To rinse.

Solution for external use with low solubility in water (1: 4200) substance. Furacillin solutions are made on an isotonic sodium chloride solution (0.9%), which enhances the pharmacological action of furatsillin.

In a flask of heat-resistant glass, measure 250 ml of purified water, add 2.25 g of sodium chloride and 0.05 g of furatsillin (weighed according to the rules for coloring matters). The contents are heated in a flask until the furatsilin is completely dissolved and filtered to the vial. Make up for leave.

Codeine solutions. Codeine is slowly and slightly soluble in cold purified water (1: 150), soluble in hot (1:17), easily soluble in 90% alcohol (1: 2,5), in dilute acids and therefore the production of its solutions has its own features. For example, to make 100 ml of 1% solution of codeine, 1.0 g of matter is dissolved in 3 ml of 95% ethyl alcohol (in a measuring cylinder or flask) by light shaking. The alcoholic solution is diluted with purified water to obtain a volume of 100 ml. If necessary, it can be thinned. The resulting solution can be stored for 10 days.

Solutions of calcium gluconate. Calcium gluconate is difficult and slowly dissolved in cold water (1:50), easily - in boiling (1: 5), practically insoluble in ethanol. Solutions make 5-10% concentration, using special technological applications, because when heated it can form persistent supersaturated solutions. For purification of solutions of calcium gluconate add activated charcoal in the amount of 3-5% of the mass of the substance.

Rp .: Solutionis Calcii gluconatis 5% 100ml
Da Signa For 1 teaspoonful 2-3 times a day before meals.

5.0 grams of calcium gluconate is added to the flask of heat-resistant glass, added 97.5 ml of purified water and heated to full dissolution of the substance. To the solution add 0,25 g of crushed activated charcoal (1 tablet of carboline) and boil on low heat for 10 minutes, shaking the contents of the bulb several times.

The solution is filtered hot through a paper filter. After cooling (20 ° C), the solution is adjusted to a volume of 100 ml, checked for transparency (the solution should be colorless) and poured into a vial that is plugged in and drawn up for release.

Mortar solutions of dichloride. It is used as a strong antiseptic in the form of 0.1% solution on the skin and 0.1-0.2% solution on the mucous membranes. Sulma slowly breaks in cold water (1: 18,5), when heated, its solubility rises (1: 3).

RP: Solution: Hydrargyri dichloride (1: 1000) in 200 ml
Da Signa To disinfect the skin.

The solution for external use with a particularly poisonous (list A) is a slowly soluble in water substance. Pay attention to the design of the prescription and the drug.

In the stand, measure 200 ml of warm purified water, dissolve 0,2 g mercury of dichloride (sulam), weighed on special hand weights for substances of List A according to the rules of weighing of poisonous medicinal substances, tint with a solution of eosin (1%) and filter through cotton wool in the bottle for leave. Clogging, mark with a seal, sticking labels: "Poison" (with the image of a skull with crossed bones), "Be careful", "0,1% solution of mercury dichloride". At the signature, make an estimate that the solution is painted with eosin.

In the manufacture of solutions of very low concentration of mercury, dichloride is better dissolved initially in a test tube in a small amount of water (when heated) and in the manufacture of more concentrated solutions intended for disinfection, it is recommended to add an equal amount of sodium chloride. Addition of sodium chloride slightly reduces the disinfectant properties of the solution but thus disappears acidic reaction of the solution and prevents the release of basic salts, which can be formed as a result of hydrolysis of mercury dichloride.

In drugstores to accelerate the work often use a concentrated solution of mercuric dichloride (1:10) containing the same amount of substance, sodium chloride and eosin. The solution may also be prepared by dissolving tablets of 0.5 and 1.0 g mass containing a mixture of equal amounts of dichloride mercuric chloride and sodium chloride epoxy-poured. In DF X there is a prescription of tablets for the production of solutions of sulam for the external use of the following composition:

Mercury dichloride 0.5 or 1.0 g, Sodium chloride 0.5 or 1.0 g. Eosin - a sufficient amount.

Concentrated solution and mercuric dichloride tablets should also be stored in the cabinet for substances in list A.

Phenol solutions.

Rp .: Solution Phenol purée 2% 100 ml
Da Signa To rinse.

Solution for external use with fragrant medicinal substance. Phenol crystalline (carbolic acid) is very slowly dissolved in water. For convenience, its aqueous solutions are obtained from liquid phenol (Phenolum purum liquefactum), which is made by adding to the 100.0 g phenol molten in a water bath, 10 ml of water. On this basis, the liquid phenol is taken up 10% more than crystalline. According to the recipe for preparation of the solution, 97.8 ml of water are measured and 2.2 ml of liquid phenol are added.

Phenol in pure form or in solutions with a concentration above 5% is released with the labels "Be careful", "Carbolic acid".

Solutions with drugs are strong oxidants. Silver nitrate and potassium permanganate are strong oxidizing agents. They are easily destroyed in the presence of organic matter, in particular, in the filtration of solutions. In addition, the filter paper adsorbs silver ions (up to 3 mg per 1.0 g of paper). Therefore, oxidants are better dissolved in pre-filtered or filtered water, and if necessary, filtered through a glass filter number 1 or number 2. It is established that the destruction of oxidants is reduced with a decrease in the concentration of solutions (up to 5%), and especially if the filter and cotton wool is pre-rinsed with hot water, then the concentration does not change significantly.

Rp .: Solution Kalii permanganate 0.1% 300ml
Da Signa For wounds.

In a pre-prepared vial of orange-colored glass for dispensing, weigh 300 ml of freshly distilled filtered purified water and dissolve 0,3 g of potassium permanganate in it, carefully weighed on BP-1 on a circle of parchment paper (barium substance; potassium dust of permanganate irritates the nasopharynx). After complete dissolution of the substance, the solution is prepared for release in a dark vial (to avoid activating the recovery process).

An important condition for obtaining stable solutions is the use of benign, purified water that does not contain organic matter. It is necessary to use only fresh-distilled water. Water stored for more than a day is often found to be contaminated with microorganisms and their livelihoods which have a restorative ability.

If potassium permanganate is prescribed in the form of concentrated solution (3.4, 5%), then to accelerate the dissolution, carefully rub it in a mortar with a portion of warm, filtered purified water, and then add the rest of the solvent.

Rp .: Argenti nitratis 0.12

Aquae purificatae 200 ml
Da in vitro nigro
Signa 1 tablespoon 3 times a day before meals.

Mixture is a solution that easily disintegrates with a list A drug substance. It is not necessary to check the single and daily dose.

In a bottle for dropping dark glass, measure 200 ml of filtered purified water and dissolve 0.12 g silver nitrate in it. In the case of contamination, the solution is pro-filtered through a glass filter No. 1. In the absence of a glass filter, a solution can be made through a cotton swab carefully washed with hot water. Solutions of silver nitrate are released in sealed form with the label "Be careful".

Release of solutions with a concentration above 2% is allowed only in the hands of the doctor or on his behalf. In manufacturing, follow all the rules of work with poisonous gin wines. Make a signature (with the inscription "For internal use").

Solutions with medicinal substances that form soluble salts of iodine solutions. Crystalline iodine soluble in water 1: 5000. For medical purposes, solutions of iodine with a concentration of at least 1% are used. To obtain more concentrated solutions use the ability of iodine to form readily soluble complex compounds of potassium or sodium iodides (perioidids are formed). The most commonly used in the practice of Lugol solution: 5% - for internal and 1% - for external use.

If no potassium iodide is indicated in the recipe, it is added in duplicate in relation to the weight of the prescribed iodine.

In pharmacies most often make aqueous and glycerol solutions Lugol. Aqueous solutions are used internally for 5-10 drops in milk for the treatment and prevention of endemic goiter and other diseases, as well as externally for lubricating the mucous membrane of the pharynx, larynx; Glycerol solutions of iodine are used only externally.

Rp .: Solution Lugoli 20 ml
Da Signa At 7 drops 3 times a day after eating milk.

Iodine is a potent substance. In DF X, higher single and daily doses for 5% iodine alcohol in drops are given. In the drops table, only 5% alcohol solution of iodine is given (1 g - 49 drops, 1 ml - 48 drops). Since the aqueous solution of iodine is prescribed in the recipe, it is necessary to find the ratio between the number of drops in the aqueous and alcohol solutions of iodine.

1 g of 5% alcohol solution of iodine - 49 drops.

1 g of 5% aqueous solution of iodine - 20 drops.

20 drops 5% of aqueous iodine is 49 drops. 5% alcohol. p-iodine

1 drop 5% aqueous solution of iodine - starch. 5% alcohol solution of iodine

1 drop 5% aqueous solution of iodine - 2,45 drops. 5% alcohol solution of iodine

$$x = \frac{49}{20} = 2{,}45 \text{ крап.}$$

Based on this relationship, check the doses:

t.s.d. (according to the recipe 7 x 2,45 = 17,5 drops 5% alcohol solution of iodine

t.d.d. 17.5 x 3 = 51.45 dots. 5% alcohol solution of iodine h.s.d. 20 drops; h.d.d.- 60 drops

Doses are not inflated.

Calculation:

Iodine 1.0

Potassium iodide 2.0

Water purified with consideration CIV of iodine in potassium iodide solution = 0.23; CIV of calium iodide = 0.25

20 - (0.23 + 0.25 x 2) = 19.3 ml.

In this case, the increase in volume can not be taken into account, because the volume of 20 ml permissible deviation is ± 4%.

Weigh 2.0 g of potassium iodide, place it in a vial and let it dissolve in approximately 2 ml of purified water (solubility 1: 0.75), pre-measured in a vial (20 ml). On a circle of parchment paper weigh 1.0 g of iodine and pour into a stand. Due to the volatility of iodine and the ability of its vapor to act on metal (prisms and rocker weights), weighing should be carried out as quickly as possible. Wash cups after weighing iodine with wool soaked with strong alcohol (to remove iodine residues, a pair of poisonous ones). After complete dissolution of crystalline iodine in a concentrated solution of potassium iodide, add the entire solvent and, if necessary, filter the solution through a small cotton swab in a bottle for the release of opaque glass. The bottle is sealed with rubber or polyethylene stoppers. Solution osarsoula. Ossarol is a preparation of arsenic (list A). Very little soluble in water, it's easy - in a solution of sodium bicarbonate. In this case, as a result of the neutralization reaction, the water-soluble salt of osarsol is formed. If sodium bicarbonate is not indicated in the recipe, then it is added at a rate of 0.61 g per 1.0 g of osarsoul.

Rp .: Osarsoli 1,5
Iodi 0.06
Kalii iodidi 0.3

Sodium hydrocarbonatis 4.0
Glycerini 15.0
Aquae purificatae 15 ml
Misce Da Signa For vaginal tampons.

Sodium bicarbonate is dissolved in water and add osarsool to the solution with constant shaking (observing the rules of work with poisonous substances). Potassium iodide dissolves in several drops of water, based on its solubility (1: 0.75). In a concentrated solution of potassium iodide, iodine is dissolved, glycerol is added, and then the solution is stirred. Prepared for release according to the rules.

Solutions with drugs that mutually worsen solubility. We note that the dissolution of solids may be accompanied by a chemical change with the formation of new substances.

Rp .: Sodium benzoate 4.0
Solution Calcium chloride 5% 150 ml
Misce Da Signa 1 tablespoon 3 times a day.

In the process of manufacturing the mixture according to general rules a precipitate of badly soluble in water of calcium benzoate is formed. Therefore, this medicinal product is prepared separately in two supports, mixing the calculated amounts of water and concentrated solutions, after which both solutions are poured into the vial for delivery - a clear solution is obtained.

NON-AQUEOUS SOLUTIONS

In medical practice, solutions are widely used for non-aqueous solution-nicks (non-aqueous solutions) as lotions, rinses, lubricants, washing, intranasal drops, inhalations.

Depending on the properties of the solvent distinguish non-aqueous solutions on volatile, non-volatile and combined solvents.

Volatile liquids are used as solvents include ethyl alcohol, chloroform, ether. Unleavened are glycerin, fatty oils (peach, almonds, sunflower seeds), vaseline oil, dimethoxide, PEO-400 and others, the characteristics of which are presented in the section "Solvents". Naturally, the more solvents are used, the more is diverse the recipe of this group of solutions.

Preparing solutions on volatile solvents. In this case, it is necessary to envision the possibility of significant losses of the solvent and the corresponding increase in the concentration of the solution due to evaporation during the manufacturing process. To avoid these losses, it is not desirable to carry out such

operations as heating, filtering or straining. In addition, ethyl alcohol, ether, with the exception of chloroform is flammable so the dissolution in this case should be carried out in compliance with safety (away from the fire).

Alcohol, ether and chloroform solutions are made directly in release bottles. Vials should be clean and dry, because the water is poorly mixed with organic solvents (except for alcohol) and changes their dissolving power.

In the manufacture of alcoholic solutions, unlike aqueous, in a dry bottle for release put a medicinal substance that dissolves first (if it is volume and loose, then use a dry funnel), and then the solvent, because the powder is poured , the alcohol-soaked bottle neck is hard.

The process of these solutions is made, if necessary, through a small lump of dry wool using a funnel, covered with a glass. To process essential fluids is especially not desirable. The precipitated ether solution and the solvent lost should be weighed by adding ether. Ethyl alcohol most often is used as a volatile solvent in pharmacy.

Alcoholic solutions. Ethyl alcohol and its aqueous solutions are used to dissolve different medicinal substances (organic acids, bases, alkaloids, essential oils, iodine, camphor, resorcinol, menthol, hydrogen peroxide, formalin and other substances). Spirtetiloid can also be used as a medicinal product that has a disinfectant, refreshing and irritating properties, for compresses etc.

The preparation of alcoholic solutions of medicinal substances is regulated by the DF and the "Instruction on the manufacture of pharmaceutical forms with liquid dispersion medium in pharmacies" (Order of the Ministry of Health of Ukraine No. 197 of 07.09.93 p.).

If the recipe does not indicate the concentration of ethyl alcohol, then use 90%. An exception is a 10% solution of iodine, which is made using 95% alcohol by the word SF X article. 356, as well as some solutions, in accordance with the approved normative and technical documentation (see appendix 3 of the textbook). If the strength of ethyl alcohol is indicated as a percentage, the volume percentages should be understood.

Rp .: Acidi salicylici 0.3
Spirits aethylici 30 ml
Misce Da Signa Wipe off your feet.

The recipe must be decorated with a stamp of a medical institution, a personal pechet and a doctor's signature, a seal of the medical institution "For recipes".

To make 1% salicylic acid solution use 70% alcohol.

In a clean, dry bottle, with well-chosen cork, place 0,3 g of salicylic acid, measure the measuring cylinder with 30 ml of 70% ethyl alcohol and quickly close

the stopper to prevent the weathering of the alcohol. Medicinal products are signed up.

If the pharmacy has finished 70% alcohol, it is made of alcohol available concentration.

Breeding alcohol with ethyl water to the desired concentration requires the proper calculations. For this purpose, the alcoholometric tables DF XI are used: № 3 - a table for obtaining alcohol of different strength at 20°C, № 4 - a table showing the amount (in ml at 20°C) of water and alcohol of varying strength, which must be mixed to obtain 1 liter of alcohol strength of 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90%.

In a pharmacy, as a rule, comes an alcohol containing it anhydrous alcohol in excess of 96% (96.1-96.7). Therefore, for the manufacture of standard water-alcohol solutions, the available strong alcohol is drawn using the table number 5 (DF XI), which specifies (in ml at 20 ° C) the amount of water and alcohol of different strength (95.1-96.5) , which must be mixed to obtain 1 liter (at 20 ° C) strength strength 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95%.

In the order of the Ministry of Health of Ukraine No. 197 dated September 7, 1993, tables are given showing compliance of volumes (ml) of ethanol of different concentration of weight (g) of alcohol (at a temperature of 20 ° C).

Concentration of the starting alcohol is given in volumetric percentages for 95%; 96%; 96.1%; 96.2%; 96.3%; 96.4%; 96.5%; 96.6%; 96.7%.

$$X = \frac{V \times Б}{A},$$

where X is the amount of strong alcohol, ml;

V - amount of ethyl alcohol required concentration, ml;

A - concentration of strong alcohol, ml;

B - required concentration,%.

For the manufacture of 70% alcohol in the above recipe, the amount of 90% alcohol is 23.3 ml:

$$x = \frac{30 \times 70}{90} = 23{,}3 \text{ мл}$$

The amount of water needed to make 70% alcohol can not be calculated by deducting 90% of the volume of alcohol from the total volume of the solution, because it is necessary to take into account the contraction - the decrease in volume. The detected amount of 90% alcohol (23.3 ml) is measured by measuring cylinder at 20 ° C., add about 7 ml of water, the solution is stirred and cooled to 20 ° C., and then brought to the required volume of water to 30 ml. In the absence of

the necessary measuring dishes, the amount of water for brewing the ethyl alcohol is calculated on the table number 3.

per 1000 ml of 90% alcohol - 310 ml of water

23.3 ml of 90% alcohol - x ml of water

$$x = \frac{23,3 \times 310}{1000} = 7,22 \text{ мл}$$

Table number 4 (SF XI) can calculate the amount of both components: alcohol 90% - 23.34 ml water - 7.2 ml

Since the substantive and quantitative accounting in pharmacies leads by weight, simultaneously do the recalculation of volumetric units in weight.

The volume increase factor when dissolving powders registered in quantities of more than 3% in alcohol solutions is not taken into account (CVI for alcoholic solutions and suspensions are used only when analyzing the dosage form).

Rp .: Acidi salicylici 1,5
Laevomycetin 3.0
Camphorae 1.0
Sp. aethylic in 50 ml
Tincturae Calendulae 10 ml
Misce Da Signa Wipe face skin.

In the realize bottle put 3.0 g of levomycetin, 1.5 g of salicylic acid, 1.0 g of camphor, add 50 ml of 90% ethyl alcohol and shake. After dissolving recoïvin add 10 ml of tincture of calendula.

Preparing solutions of non-volatile solvents. Solutions of medicinal substances of non-volatile solvents are made by weight because the significant viscosity of solvents leads to large losses in measuring. The mass of such solutions consists of the sum of the quantities of medicinal substances and solvent. Considering that the dissolution in viscous solvents proceeds slowly it is expedient to carry it out with heating taking into account the properties of medicinal substances. However, in this case, the preparation of saturated solutions should be avoided because when the solution is cooled, the soluble substance may precipitate. Solutions on viscous solvents are made directly in the vial for dispensing and filtered only in extreme cases and only through the gauze.

Glycerin solutions are widely used as various lubrication. In the form of glycerin-new solutions, prescribe boric acid, sodium tetraborate, iodine, tannin, ichthyol and other substances. Glycerin has a significant viscosity so the manufacture of glycerol solutions can occur with heating and without heating which completely depends on the thermal stability of the input medicinal

substances. When heated to 40-50^{o} C, the viscosity of glycerin decreases and the dissolution process is accelerated. Sodium tetraborate and boron acid can be dissolved in warmed glycerol, when dissolved, they form a glycosyberic acid, which adds acidic solutions to the solutions. To neutralize glycosyric acid, sodium bicarbonate is often prescribed along with boric acid. It should be added in two small portions because the neutralization reaction proceeds violently and spray solution can occur.

Rp .: Acid boric acid 1.0
Glycerin 90.0
Misce Da Signa To wet the tampons.

In a dry vial, a boron acid is placed in a dry vial, packed on technical scales and weighed 90,0 g of glycerin, heated in a water bath at a temperature of 50-60 ° C. until complete dissolution of boric acid. Make up for leave.

Rp .: Sodium tetraborate 1.0
Aquae purificatae
Glycerin aa 5.0
Misce Da Signa Lubrication

The solubility of sodium tetraborate in water is 1:25, in glycerol 1: 2,5. Consequently, 1.0 g of sodium tetraborate (through a dry funnel) is placed in a vial for dispensing, weighed it (without a funnel) and weighed glycerine, closed with a stopper and warmed up in a water bath by immersing the vial in warm water until the total dissolution of sodium tetraborate is dissolved. Then add 5 ml of purified water.

In the manufacture of glycerol iodine solutions, heating is undesirable.

Rp .: Iodi 1.0
Calcium iodide 2.0
Aquae purificatae 3 ml
Glycerin 94.0
Misce Da Signa For tampons with vulvovaginitis.

First make a concentrated solution of potassium iodide. In a holiday vial of orange glass, measure the water purified and dissolve potassium iodide in it, then iodine, the vial is packed on technical pharmacological scales, weigh glycerol, shake to obtain a solution and make up for leave. If no water is prescribed in the recipe, it should be taken in a minimum amount (equal to the amount of potassium iodide).

Oily solutions. Fatty oils as well as vaseline oil are good solvents for many medicines that are widely used in the form of ear and intranasal drops.

In order to accelerate the dissolution apply light heating. If an oil substance, for example, menthol, camphor is prescribed in an oil solution, then to dissolve

dissolution losses, preheated oil is carried out at a temperature not higher than 40°C.

Rp .: Mentholi 0.1
Ole Ole Vaseline 10,0
Misce Da Signa Drops in the nose.

In a dry vial, weigh out 10,0 g of vaseline oil, warm in a water bath not above 40-50 ° C, and then dissolve 0,1 g of menthol (a fragrant wine of recipe). Processed as needed.

When making oil solutions it is necessary to pay attention to the manufacture of ears-drops with carbolic acid.

In SF X there are two preparations of phenol: crystalline and liquid. If the recipe does not indicate which one should apply, then use a crystalline form. Liquid phenol is used for the manufacture of only aqueous solutions.

Rp .: Acid carbolici 0.4
Ole Helianthi 20.0
Misce Da Signa Ear drops.

In a dry vial, put 0.4 g of crystalline phenol, weighed on hand-made scales on a parchment paper mug (trying not to touch hands to avoid burns). The vial is packed on technical pharmacy scales, where 20,0 g of sunflower oil are weighed, closed by a previously picked up gasket and shaken until full dissolution of phenol.

Non-aqueous solvents also include eutectic alloys obtained as a result of the mutual dissolution of two solids having high cryoscopic concentrations or low melting temperatures, or both.

Eutectic alloys are prepared by placing the prescribed medicinal substances in the bottle for release, which is well sealed with a stopper and placed in warm water (40°C) until they are completely melted. When making significant quantities of liquid eutectic alloys, sometimes rubbing and mixing in a mortar are used.

Rp .: Camphorae
Chloral hydrate aa 1.5
Misce Da Signa Tooth drops.

In a dry vial for release put camphor and chloral hydrate, tightly close the stopper, place in warm water (40°C) and withstand until full melt-formed liquid.

Rp .: Iodi 10.0
Dimexid ad 100.0
Misce Da Signa Lubricate the nails, feet.

10 g of iodine are placed in a dry vial, loaded with a vial and weighed 90,0 g of dimethoxide and shaken to dissolve (1: 1 solubility of iodine in dimethoxide).

Preparing solutions on combined solvents. If combined formulations are prescribed in recipes (for example, water is purified, ethyl alcohol, glycerol, etc.), then, first of all, they are guided by the solubility of the medicinal substances and

also take into account the properties of the individual solvents - the volatility and viscosity - and accordingly choose the most appropriate technological techniques and their consistency. In calculations, different methods of dosing of ethyl alcohol, ether, glycerin, dimethoxide and others are taken into account. In addition, the volume displaced by drugs is, if necessary, deducted from the volume of the solvent that has the most dissolving power in relation to the drug substance.

Rp .: Acidi Salicylici 1.0
Resorcin 2.0
Acid boric 1,5
Aetheris medicinalis 30.0
Spiritu aethylici 70%
Aquae purificatae aa 50 ml
Misce Da Signa Wipe face's skin in the morning and evening.

From the prescribed medicinal substances, boron acid is readily soluble in hot water (1: 3), salicylic acid is slightly soluble in water (1: 500), but readily - in 70% ethyl alcohol (1: 5.5) and ether (1: 2), resorcinol is very readily soluble in water. The solvent is the most volatile air. It is dosed by weight, purified water and ethyl alcohol - by volume.

The volume of the drug based on the density of the ether (0.7160 g / cm3) is: 50 + 50 + 30.0: 0.7160 = 141.8 ml.

In a dry vial put acid salicylic acid and dissolve in 50 ml of 70% ethyl alcohol. Add prepared in the stand solution of boric acid and resorcinol in 50 ml of purified water. In the last turn add 30.0 g of ether. Draw up a signature before the release.

Rp .: Analgini 2.0
Butadioni 0.5
Furacilini 0,3
Dimexidi 30,0
Spiritus aethylici 50 ml
Misce. Da. Signa. Lubricate the affected areas of the skin.

The solubility of analgin and furatsilina in dimethoxide is much higher than in ethyl alcohol. Butadion by contrast easily dissolves in ethyl alcohol and is worse soluble in dimethoxide.

In a bottle for release, weigh 30,0 g of dimethoxide and dissolve analgin and furatsilin in it. In a stand in 50 ml of 90% ethyl alcohol dissolve butadiene. Both solutions are drained together and shaken. If necessaryshpuld be filtered.

IMPROVING QUALITY AND TECHNOLOGY OF SOLUTIONS

The improvement of the quality of solutions is primarily due to the expansion of the range of solvents that are highly soluble in relation to most medicinal

substances chemically and pharmacologically indifferent which provide the necessary biodoscope and high stability and consequently increase the shelf life.

In addition, the general tendency to reduce the use of narcotic drugs in the technology of drug forms of ethyl alcohol, limiting the use of vegetable oils that are easy to peel and are food, raises the question of their replacement by other solvents. In this regard, the introduction of polyethylene oxide-400 pharmacy, dimethoxide and silicone fluids into practice, and also promotes new, promising solvents, is of great interest.

5. Materiels of activating students during the presentation of a lecture / problem, problem situations, etc.

Control questions:

1. Characteristics of solutions as disperse systems, their classification.
2. Ways of obtaining purified water; the equipment used for this purpose, the principle of its work.
3. Requirements for the quality of purified water in accordance with the State Food Inspectorate and the order of the Ministry of Health of Ukraine No. 626 dated December 15
4. Concentrated solutions, their purpose, conditions of preparation in pharmacies in accordance with the instruction to the order of the Ministry of Health of Ukraine No. 197 dated September 7, 1993
5. Calculations of the amount of medicinal substances and water for the preparation of concentrated solutions in various ways:
- using the measuring dishes;
- using the ratio of increase in volume;
- taking into account the density of the solution.
6. Control of the quality of concentrated solutions, correction of their concentration, storage conditions. Accounting for prepared concentrated solutions.
7. The device of the burette installation, rules of care and use of it.
8. Characteristics of liquid dosage forms as disperse systems, requirements for them, their classification.
9. Methods of prescription and designation of concentration of solutions, testing of doses of poisonous, narcotic and potent medicinal substances in mixtures.
10. Factors influencing the accuracy of dosage by volume.
11. Nomenclature of standard pharmacopoeial liquids, their concentration and prescribing methods.
12. Rules for calculating the quantities of purified water and standard pharmacopoeial liquids depending on the method of their prescription according to the order of the Ministry of Health of Ukraine No. 197 dated 09.09.93.

13. Features of preparation and storage of solutions of standard pharmacopoeial liquids.
14. Evaluation of the quality of solutions of standard pharmacopoeial liquids in accordance with the requirements of the normative and technical documentation, packaging, registration for release, rules of storage.
15. Which standard fluids have two names: conditional and chemical?
16. Characteristics of non-aqueous solvents used in pharmacy practice.
17. Features of technology solutions for volatile and non-volatile solvents.
18.What concentration should I release the hydrochloric acid, if in the recipe there is no designation?
19. What is the principle of diluting hydrochloric acid?
20. Packing, registration for the release and storage of solutions of pharmacopeia liquids and non-aqueous solutions.

Test tasks:

1. **The pharmacist prepared 150 ml of 10% glucose solution. Specify which amount of Liquid Weybel he added to stabilize the solution?**

* 7.5ml
5 ml
10 ml
15 ml
3 ml

2. The pharmacist prepared an injectable solution of sodium bicarbonate. Specify the maximum volume of the vial.

* 80%
100 %
50 %
40 %
60 %

3. A pharmacist prepared a 1% aqueous iodine solution. Specify the features of the solution preparation.

* dissolution in a solution of potassium iodide
dissolving in hot water
dissolution in freshly distilled water
rubbing in a mortar with water
dissolve in cold water

4. How long does a pharmacist need to sterilize 250 ml of 5% glucose with a vapor under pressure at a temperature of 120 ° C?

* 12 min.
8 min
30 min
15 min.

1 year

5. The pharmacist has prepared a solution for injection, which contains a salt formed by a strong base and a weak acid. Specify the required stabilizer.

* sodium hydroxide
sodium sulfate
hydrochloric acid
ascorbic acid
cysteine

6. In the prescription, a solution of formalin 5% - 100 ml is prescribed. What amount of 37% formaldehyde should be taken by a pharmacist to prepare a solution.

* 5 ml
12.5 ml
4.5 ml
10 ml
15 ml

7. A pharmacist prepares a solution for injection with a substance that needs to be stabilized with a 0.1 M solution of chloride acid. Specify this substance:

* Novocaine
Calcium chloride
Potassium chloride
Hexamethylenetetramine
Sodium benzoate

8**. The pharmacist has prepared an injectable solution, with the addition of a stabilizer - sodium bicarbonate. Specify the substance that needs the use of this stabilizer:**

* Sodium Thiosulfate
Novokain
Ephedrine hydrochloride
Sodium chloride
Glucose

9**. The pharmacist prepared an injectable solution, using a stabilizer - 0.1 M sodium hydroxide solution. Specify the substance that needs the use of this stabilizer:**

* Caffeine sodium benzoate
Diazole
Sodium hydrocarbonate
Sodium chloride
Glucose

10. The pharmacist has prepared an injectable solution with an easily oxidizing substance that needs to be stabilized with antioxidant. Specify this substance:

* Acid ascorbic acid
Diededrol
Sodium chloride

Urotropin
Calcium gluconate

11**. A formalin solution of 5% to 100 ml is prescribed. What amount of 37% formaldehyde should be taken by a pharmacist to prepare this solution.**

* 5 ml
12.5 ml
4.5 ml
10 ml
15 ml

12. The pharmacist prepared the dosage form with the following words: Rp: Sol. Acid Acid 3 \ - 100ml D.S. To rub off. Specify the quantity of standard pharmacopoeial fluid and water:

* 10ml 90ml
3 ml and 100 ml
3 ml and 97 ml
15 ml and 85 ml
10 ml and 100 ml

13. For the manufacture of eye drops, use a solution-concentrate of riboflavin (1: 5000). Indicate the amount of solution to be measured if the prescription contains 0,001 riboflavin:

* 5ml
2ml
3 ml
4ml
1 ml

14. For the patient it is necessary to prepare a solution of potassium permanganate. What solvent is used in this case to ensure the stability of the active ingredient?

* Purified freshly prepared water.
Water purified.
Ethyl alcohol.
Demineralized water.
Glycerin.

15. The product contains 3.0 sodium benzoate. What volume of 10% concentrated solution should be used?

* 30 ml.
2 ml
8 ml
10 ml
20 ml

16. To accelerate the preparation of mixtures, use a 5% (1:20) concentrated solution of sodium bicarbonate. What volume of this solution is necessary for the preparation of a mixture containing 2.0 sodium bicarbonate?

* 40 ml.
30ml

20 ml
10 ml
2, 5 ml.

17. A solution of hydrogen peroxide is released from pharmacies at various concentrations. What concentration should be released to the patient if the concentration does not appear in the recipe?

* 3%.
30%.
20%.
10%.
2%.

18. For the patient the prescribed lotion:
Rp .: Sol. Liquoris Burovi 10 \ - 100 ml
Da.Signa. Lotion.
What volume of Burof liquids should be measured for the preparation of this medicinal product?

* 10 ml.
90 ml
20 ml
80 ml
50 ml

19. Patient prescribed medicine:
Rp .: Sol. Asci hydrochloric acid 2% - 100 ml
Da.Signa. 1 item l 3 pounds a day before meals.
What amount of chloride dilute solution (1:10) should be measured for its preparation?

* 20 ml.
25 ml
15 ml
10 ml
5 ml

20. The patient is prescribed 3% alcoholic solution of borate acid. What concentration of ethyl alcohol is used to prepare this solution according to the requirements of normative documents?

* 70%.
95 %.
90 %.
60 %.
40 %.

6.General materials and guidance of the lecture:

- training rooms;
- equipment;

- codoscope; Slides;
- illustrative materials.

7. Materials for self-training of students:
a). on the topic of the lecture / literature, questions, tasks, test tasks /;
b). on the topic of the next lecture / literature, list of basic questions, test tasks /.

8. Literature used by the lecturer to prepare the lecture.
Basic literature:
1. Technology drugs. Textbook: Textbook for Universities / AI Tikhonov, PA Logvyn, S. Tikhonov, A. Mazulin, TG Yarnyh, OS spiers, O. Mikhail Kotenko; Edited by AI Tikhonov - Kharkov: Pharmacy; Original, 2009. - 432 p.
2. Technology Medicine: Textbook / A. Marchuk, NB Androshchuk - Kyiv: Health, 2008. - 488 p.
Additional:
1. Soft dosage forms: Extemporal formulation: Methodical recommendations / O. I. Tikhonov, T. G. Yarnykh, O. V. Lukienko and others; Ed. OI Tikhonov - X .: View of NFaU; Golden Pages, 2003.-128 p.
2. Aseptic dosage forms: Extemporal formulation: Methodical recommendations / O. I. Tikhonov, L. V. Bondareva, T. G. Yarnykh, N. F. Orlovetsky and others; Ed. OI Tikhonova and TG Yarnyh. - X .: View of NFaU; Original, 2005. - 184 p.
3. Solid dosage forms: Extemporal formulation: Methodical recommendations / O. I. Tikhonov, T. G. Yarnykh, S. V. Gritsenko and others; Ed. OI Tikhonova - Kh.: View of NFaU; Golden Pages, 2003. - 176 pp.
4. Liquid dosage forms: Extemporal formulation: Methodical recommendations / O. I. Tikhonov, T. G. Yarnykh, N. F. Orlovetsky, and others; Ed. OI Tikhonova and TG Yarnyh. - X .: View of NFaU; Original, 2005. - 160 s ..

Lecture 4. «The technology of Naval Solutions. The technology of colloidal solutions» - 2 hours.

1. Relevance of the topic.

Justification topic. Pharmacists should have questions about the technology of manufacturing liquid dosage forms and must be prepared for the realization of their knowledge. Colloidal solutions have high bioavailability, they are non-toxic which allows them to be used in gynecology, otolaryngology, ophthalmology, pediatric and geriatric practice. A rational ratio of active substances, methods of their introduction and preparation allows to create highly effective medicines.

2. Objectives of the lecture:

- training

- basic concepts and terms of technology of medical forms;

- to master the preparation of some aqueous solutions, HMC solutions, colloidal solutions;

- to orient in the main directions of state regulation of the production of medicinal products of this section;

- read recipes in Latin, analyze their constituent parts and assess the correctness of the prescription;

- use the DF and the International Pharmacopoeia, other normative and technical documents, as well as the reference literature for the search for information on the composition, preparation, storage and release of medicinal products.

- educative

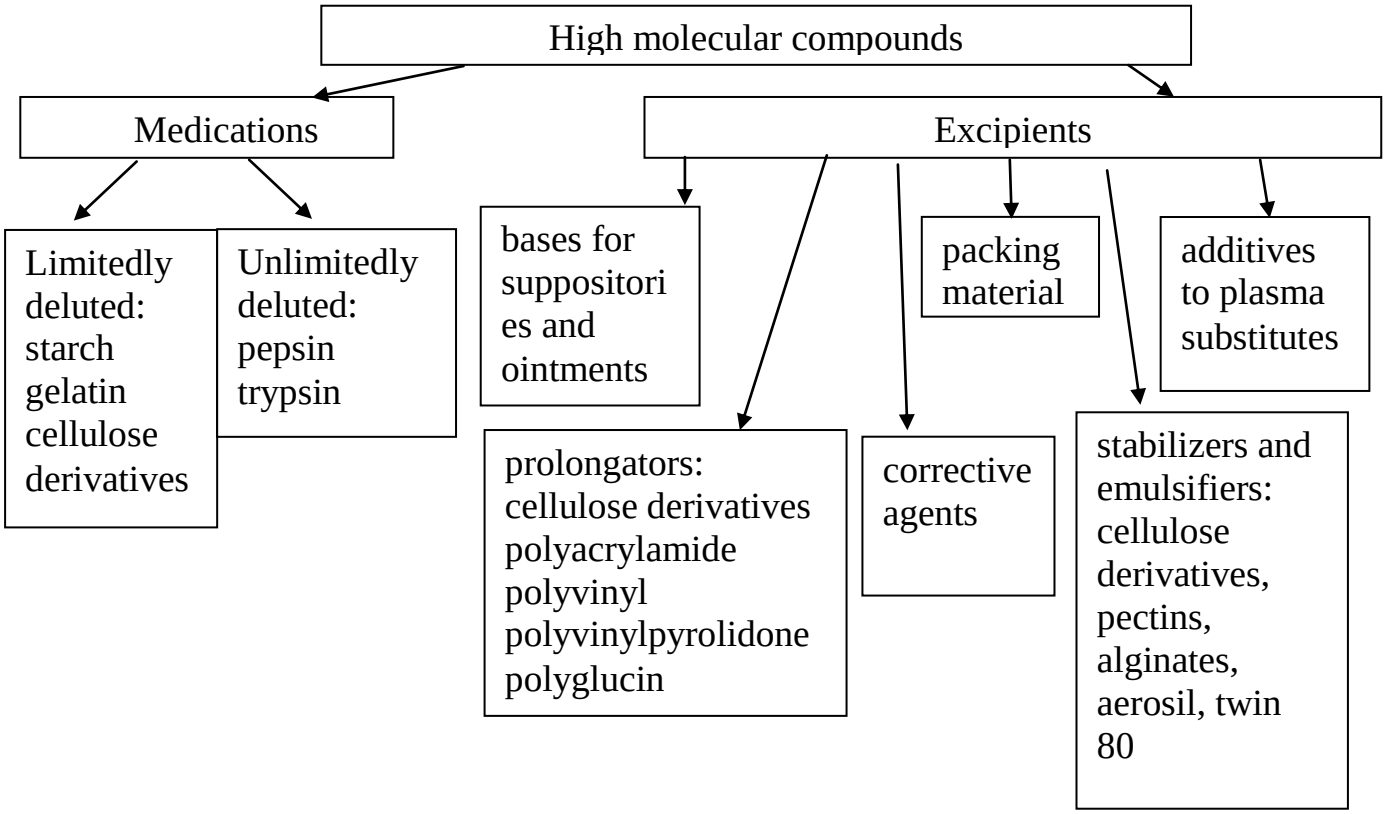
This lecture is aimed to develop a professional meaningful personality structure; to teach modern professional thinking.

3. Plan and organizational structure of the lecture.

№	The main stages of the lecture and their contents.	Goals at levels of abstraction.	Type of lecture, equipping lecture.	Distribution of time.
1	2	3	4	5
	Preparatory stage			
2.	Definition of educational goals. Ensuring positive motivation.	I		2% 2%
3.	**The main stage**			
	Presentation of the lecture material. **Plan:** 1. HMC solutions. Influence of structure of HMC on their solubility. Preparation of solutions of pepsin, gelatin, starch, methylcellulose and other semi-synthetic and synthetic HMC.	II III	References, visual material. State Pharmacopoeia, basic normative and technical documentation.	85% - 90%
	2. Rules of work with high-molecular compounds and protected colloids;	II		
	3. Characteristics and properties of colloidal solutions;			
	4. Influence of the structure of the HMC on the dissolution process is limited and infinitely diluted substances;			2%
	5. Position of solutions of pepsin, gelatin, starch, methylcellulose; protargol, collargol and ichthyol;		List of literature, questions, tasks.	2% 2%
	The final stage Summary of lectures, general conclusions. Answers of the lecturer on possible questions. The task for self-education of a student.	I		

4. Contents of the lecture material:

High molecular compounds in pharmacy



High molecular compounds are called natural or synthetic substances with a molecular weight of several thousand (not less than 10-15 thousand) to a million or more.

The molecules of these compounds are giant bodies, consisting of hundreds and even thousands of individual atoms, connected with each other by the forces of the main valences and therefore these molecules are called macromolecules.

Molecules of high molecular weight compounds (HMWC) are often long threads that are interwoven with each other or rolled into tufts and their length is considerably larger in diameter. Thus, the length of the cellulose molecule is 400-500 nm and the propeller is 0.3-0.5 nm. Consequently, these molecules are sharply anisodiametric and when collided with the corresponding solvent they form the real (molecular) solutions.

A characteristic feature of most of the HMC is the presence in their molecules of repeatedly repeated links. This repetition depends on the degree of polymerization. From here, these substances have a second name “polymers”

Studies of recent decades have proved that HMWC solutions can not be attributed to typical colloidal systems, although they have the properties characteristic of colloidal solutions: the originality of the particles of the dissolved substance; motion similar to Brownian; small diffusion velocities in their solutions

due to the large size of the molecules of the HMWC as a result of which they are not able to penetrate through the semipermeable membranes; small values of osmotic pressure; slower flow in solutions of a number of processes (including chemical, increased propensity to form various chemical complexes, etc.). All this indicates that the solutions of the HMWC combine the properties of both true and colloidal solutions. This is explained by the fact that in solutions of the HMC, the dissolved substance is fragmented into a molecule, and, consequently, these solutions are homogeneous and single-phase systems. When dissolving the HMWC, solutions are formed unilaterally so they do not require special additives for their formation. Solutions of the HMWC are thermodynamically equilibrium systems that are stable for a long time, if there is no influence of external factors (for example, solutions of electroliters). Solutions of the HMWC for molecular-kinetic properties are no different from solutions of low molecular compounds. In spite of the fact that macromolecules are not detected in an ultramicroscope, they have the ability to light dispersion, which leads to opalescence or some turbidity of the solution.

The properties of the HMWC and their solutions are detailed in the course of organic, physical and colloidal chemistry.

All HMWC, due to their large molecular mass are not volatile and can not overdo it. For the same reason, the HMWC is very sensitive to the impact of various external factors. Macromolecules easily decay under the influence of even small amounts of oxygen and other destructive agents. Most of the HMWC with increasing temperature soften gradually and do not have a definite melting point. In these substances, the decomposition temperature is lower than the boiling point and therefore they can only be in a condensed state.

Giant chain-like molecules of the HMWC are heterogeneous on separate links and have a different character. Separate links consist of atomic groups with a polar nature. Among the polar atomic groups are -COOH, -NH_2, -OH and others. These radicals interact well with polar liquids (water, alcohol, etc.) - hydrate, in other words, they are hydrophilic. Along with the polar macromolecule, they contain nonpolar, hydrophobic radicals -CH_3, -CH_2 -C_6H_5 etc. that can be solvated with nonpolar liquids (benzene, petroleum ether, etc.) but can not be hydrated. In natural HMWC polar groups are almost always dominated so when they enter the water they behave like hydrophilic substances. The more polar regions in the molecule of the HMWC, the better it is soluble in water.

Properties of the HMWC depend on the size and shape of their molecules. Thus, HMWC having spherical molecules (hemoglobin, glycogen, pepsin, trypsin, pancreatin, etc.) are usually powder-like substances and when dissolved almost do

not swell. Solutions of these substances have a low viscosity even at comparatively large concentrations and obey the laws of diffusion and osmotic pressure.

Derivatives with very asymmetric linear (branched) elongated molecules (gelatin, cellulose and its derivatives) dissolve slowly and form highly viscous solutions that do not obey the laws inherent in solutions of low molecular weight substances. The dissolution of the HMWC with linear molecules is accompanied by swelling which is the first stage of their dissolution. The reason for swelling is when it is dissolved there is not only diffusion of dissolved soluble molecules into the solvent as it happens when dissolving the low molecular weight substance (LMWS) but also the diffusion of solvent in the HMWC. The swelling is as follows: the molecules of a low molecular weight solvent fluid the mobility of which is many times greater than the mobility of macromolecules penetrate into the immersed in it HMC, filling the free spaces between macromolecules. Next, the solvent starts to flow inside the swelling substance in an increasing amount.

Once the bonds between the macromolecules are destroyed, that is, when the threads are sufficiently pushed apart, the macromolecules, having acquired the ability to heat motion, begin to slowly diffuse into the phase of the solvent. Swelling transitions into dissolution, forming a homogeneous true (molecular) solution. Thus, the dissolution of the HMWS with linear macromolecules proceeds in two stages: the first (solvatation-hydration) is accompanied by the release of heat that is the decrease of free energy and volume compression. The main purpose of this stage when dissolved is reduced to the destruction of bonds between individual macromolecules. In the second stage of swelling, the liquid is absorbed without heat release. The solvent is simply diffusely absorbed into the mesh loop, formed by macromolecules submerged. At this stage, absorption of a large amount of solvent and an increase in the volume of swollen HMWC is 10-15 times, as well as the mixing of macromolecules with small solvent molecules which can be considered as a purely osmotic process.

It should be borne in mind that the swelling of such a compound does not always end with its dissolution. Very often, after the known degree of swelling, the process is stopped. Swelling can be unlimited and limited.

Unlimited swelling ends with dissolution. The compound initially absorbs the solvent and then at the same temperature it passes into the solution. With limited swelling the macromolecular compound absorbs the solvent but it does not dissolve in it no matter how much time it is in contact.

The limited swelling of such a compound always ends with the formation of an elastic gel (chilly). However, limited swelling due to limited dissolution, often changing conditions unfettered. So gelatin and agar-agar which swell limited in

cold water, swel in unheard-of-water in warm water which is used when dissolving these substances.

HMWC swelling is selective. They swell only in liquids that are close to them in a chemical structure. So compounds having polar groups swell in polar solvents and hydrocarbons only in nonpolar liquids.

Solutions of the HMWC if they are in the thermodynamic equilibrium are aggregatelike the real solutions. However, with the introduction of large amounts of electrolytes, the isolation of the HMWC from the solution is observed. Therefore, this phenomenon is not identical coagulation of types of colloidal systems, which occurs when the introduction of small amounts of electrolyte and is an irreversible process.

Isolation from the solution of the HMWC occurs when the addition of large amounts of electrolyte and is a reversible process - after removing from the siege of the electrolyte or washed by dialysis, the HMWC is again able to dissolve. Different are mechanisms of both phenomena.

Coagulation occurs as a result of the compression of the double electric layer and the reduction or complete disappearance of the electric charge, which is the main factor of stability. Isolation from a solution of a polymer with the addition of a large amount of electrolyte due to a simple decrease in the solubility of the HMWC in a concentrated solution of electrolitol and is called vulgating. The soluble action of various sediments is a consequence of their own solvation, at which the cost of the solvent occurs that leads to lower solubility of the HMWC. When adding neutral salts their ions hydrated, subtract water from the molecules of the HMWC. When hanging, the main role is played by the valence of the ions and their ability to hydrate. The soluble role of the electrolytes mainly depends on the anions and the anion can be arranged in the following order for sulfate-ion, citrate-ion, acetate-ion, chloride-ion, rhodanide ion.

Not only anions but also cation such as lithium, sodium, potassium, rubidium, cesium, have a cure. Of these compounds, compounds containing sodium and potassium cations are most commonly used. They take the second place after anions for a refreshing action. When the electrolyte is added, the solubility of the HMWC decreases and it falls into the precipitate.

The higher the ability to hydrate ions, the stronger their stinging effect. Therefore, when preparing solutions of the HMWC for prescriptions, which include sediments, it is expedient to add the latter to the solution of the HMWC in dissolved form. The HMWC must necessarily dissolve in a pure solvent because in the solution of salts of dissolution of these substances it is difficult. Dehydration, dissolved compound and hence its vulgarisation can be caused by nonionized substances, for example, by alcohol. Also concentrated solutions of sugar (syrups)

are also active. These substances are hydrated by macromolecules. The solvent spent on their hydration already loses the ability to participate in the dissolution of the initially dissolved HMWC. Sugar and alcohol have a strong dehydrating effect when introduced in significant amounts, so they need to be added to the solution of the HMWC by shaving parts.

Under the influence of these factors, there is also a coacervation phenomenon - dividing systems into two layers. The coacervation is different from the salting because the substance (disperse phase) is not separated from the solvent in the form of a solid, plasticized sediment but first it is collected in the invisible eye of the invisible fat droplets which gradually merge into a drop of large size and then there is stratification on 2 layers: first - a concentrated layer of polymer and solvent; the second - diluted solutions of the same polymer. Under the influence of low temperatures, such phenomena as gelatinization or scrubbing and syneresis are possible.

From the scrubbing the gelling differs in that there is no division of the system with the formation of a precipitate and the whole system as a whole passes into a special intermediate form of its existence - chalice or gel and this condition is characterized by complete loss of fluidity. For example, a solution of gelatine shines with a decrease in temperature; when the temperature rises it regains its fluidity and can be applied. The process of scrubbing can occur in the gel itself which can lead to a division of the system into 2 phases: a concentrated gel and a solvent containing the molecules of the HMWC. This apparent shading, occurring in the gel, is called syneresis and is typical for solutions of starch.

HMWC and their solutions are very important in all sorts of industries, agriculture of medicine and pharmacy. In medicine, they are used as drugs (enzymes, polysaccharides, mucus, extracts, etc.) and as adjuvants in the preparation of various dosage forms (suppository and ointment bases, emulsifiers, stabilizers, prolongers, solubilizers, corrigents, as additives in the manufacture of blood substitutes) as well as packaging material when dispensing drugs for the manufacture of bottles, films, stoppers, cans and other packaging products.

MANUFACTURE OF NON-EXHAUSTED SOLIDS

To infinitely swollen HMWC most commonly used in pharmaceutical practice, include pepsin, licorice extracts, belladonna and others. The preparing solutions of infinitely swollen substances is guided by the general rules for the manufacture of solutions of low molecular weight substances, taking into account the properties of medicinal substances and solvents.

Rp .: Pepsin 2.0
Acid hydrochloric 5 ml

Aquae purificatae 200 ml
Misce Da Signa For 1-2 tablespoons 2-3 times a day during meals.

Mixture-solution, which includes an infinitely swollen HMWC (enzyme) - pepsin, well soluble in water, and a potent substance - an acid hydrochloric acid.

The peculiarity of the technology of pepsin mixes is to adhere to the mixing sequence of the components. Since pepsin is inactivated in strong acids, the mixing of propylated components is carried out in the following sequence: first, an acid solution is prepared and pepsin is dissolved therein.

Calculation:
Pepsin 2.0 g
Acid solution
hydrochloric acid (1:10) 50 ml
Water purified 205 - 50 = 155 ml

In the stand, 155 ml of purified water are measured, 50 ml of hydrochloric acid solution is added in dilution 1:10, and 2.0 g of pepsin is dissolved in the resulting solution, stirring until it is completely dissolved. The solution is optionally filtered through a glass of several layers of gauze (preferably through a glass filter No. 1 or No. 2) into the bottle for delivery. The solution should be transparent. Turbidity of the solution indicates an impurity in pepsin of soluble foreign proteins. If there is a precipitate it must be removed by injection. Filtration of pepsin solutions through paper filters is not recommended because pepsin is easily adsorbed by a paper filter since in the acidic medium the protein as an amphoteric compound produces a positive charge so the paper when hydrolysed is charged negatively. Release pepsin solutions in vials of orange glass with the additional label "Keep in a cool, dark place".

Mixture with dry and dense extracts. The technology of dry extracting mixtures does not differ from the technology of powdered medicine formulations. When preparing mixtures from dense extracts they are added to the liquids in two ways depending on the amount of the prescribed extract.

Rp .: Sodium benzoate
Sodium hydrocarbonatis aa 2.0
Extracti Glycyrrhizae 4.0
Aquae purificatae 200 ml
Misce Da Signa 1 tablespoon 3 times a day.

Mixture with the HMWC is a thick extract of licorice recorded in large quantities. Due to the fact that the industry produces two extracts of licorice - thick and dry in the absence of an exact indication in the recipe, refer to a dense extract.

In the stand, measure 140 ml of purified water. A thick extract of licorice is weighed on a small circle of filter paper and glued it to the rounded part of the filler (head) with paper upward, the filter paper is wetted with water or 70% ethyl alcohol, separated from the extract. The remaining extract on the crusher's head is rubbed in a mortar with a small amount of water first then gradually adding new portions of water until the extract is completely dissolved. Stir from the mortar into a vial for delivery where 20 ml of a 10% solution of sodium benzoate and 40 ml of a 5% solution of sodium bicarbonate are added.

Rp .: Analgini 2.0
Solution Calcium chloride 10% in 200 ml
Extracti Belladonnae 0.15
Misce Da Signa 1 tablespoon 3 times a day.

Mixture with the HMWC is a thick extract of belladonnathat is registered in large numbers. In this case, it is convenient to use a solution of a dense extract of belladonna 1: 2 (Extractum Belladonnae solutum), which is added in drops to a solution of salts in a double amount relative to the initial thick extract.

Calculation:
Analgin 2,0 m
20% solution of calcium chloride (1: 5) 20.0 x 5 = 100 ml
The solution of the extract of belladonna is a thick (1: 2) drops of 18 (0.1 g thick extract = 6 drops).
Water purified 200 - 100 = 100 ml

In a bottle for release, measure 100 ml of purified water then 100 ml of 20% solution of calcium chloride and, in the end, calibrated pipettes - 18 drops of a solution of a thick extract of belladonna.

MANUFACTURE OF SOLUTIONS LIMITED TO INCREASING IRS

An example of limited swelling substances in cold water and infinitely swell when heated are gelatin and starch.

RP .: Solution Gelatine 5% 50.0
Da Signa 1 tablespoon in 2 hours.

Weigh 2.5 g of dry gelatin and place in a porcelain cup, pour 10 times the amount of cold water and leave to swell for 30-40 minutes. Then add the rest of the water, the mixture is placed in a water bath (temperature 60-70 ° C) and when stirred, complete dissolution of gelatin and obtain a clear solution. Provide water to the required mass. If necessary, the resulting solution is filtered into the vial and released with the label "Keep in a cool place", as under the influence of microorganisms there can be a deterioration of the solution. The patient needs to be

clarified that before using the dosage form, it should be warmed up because the solution may be thickened.

For internal use and enemas prepare a 2% starch solution, according to the GF of the form VIII. Solutions of such concentration are prepared in those cases where their concentration is not indicated in the recipe. Example:

Rp .: Solution Amyli 2% 100.0

Da Signa Ha 2 enemas.

Can just be written out

Rp .: Mucilagin Amyli 100.0

Da Signa Ha 2 enemas.

The solution is prepared by weight as follows: 2 parts of starch are mixed with 8 parts of cold water and when stirred add up to 90 parts of boiling water. Mix it and heat to boil. If necessary, you can strain through the gauze. Solutions are unstable, microbial spoilage, so they are prepared exteMpore.

The starch solution is used as an enveloping agent to protect the sensitive endings of the mucous membrane from the effects of irritants.

Methylcellulose (MC) refers to the limited swelling substances in hot water and infinitely swell in cold. When heated above 50 ° C in aqueous solutions, coagulation of MC is possible but when cooling there are reciprocal processes and MC is completely transformed into a solution. However, prolonged heating of solutions leads to a decrease in viscosity. For the manufacture of aqueous solutions MC fill with water heated to 80-90 ° C (for a more complete and rapid dissolution) in the amount of 1/2 of the required volume of the resulting solution. After cooling to room temperature add the remaining cold water, stir and leave in the refrigerator for 10-13 hours until complete dissolution of methyl cellulose. The resulting clear solution of methylcellulose is passed through a glass filter No. 2. The cooled solutions are transparent.

It should be borne in mind that IUDs are prescribed more often in combination with various drugs that can react with them, because each time it is necessary to consider their interoperability.

CHARACTERISTICS OF COLLOID SOLUTIONS

Colloidal solutions are an ultramicroheterogenic system in which the structural unit is a complex of molecules, atoms and ions called micelles.

The size of the particles of the dispersed phase of colloidal solutions (from the Greek kolla - glue and eidos -vid) is in the range from 1 to 100 nm (0.1 microns). The nucleus of a micelle is formed in the cause of the accumulation of individual molecules of hydrophobic matter. The double layer of ions surrounding the nucleus

(adsorption and diffusion) arises either as a result of adsorption of ions or as a result of the dissociation of superficially located core molecules under the influence of the external environment. The compounds from which double-layer ions are called ionogen-like groups.

According to the Fayans rule, the ions that have common chemical elements with the nucleus are adsorbed on the surface of the nucleophilic micelle core. All these ions are called potentiometric ions. Electrically charged particles limited by adsorption layer are called granules. Ions that neutralize the granule form a ion atmosphere around the nucleus, distributed between the adsorption and diffusion layers. These ions are called counterion. Typically, in the adsorption layer of the micelle, potentials-determining ions are located and in the diffusion it is counterion. Thus, the micelle can be regarded as a complex of granules and anti-ions. The detailed micelle building is considered in the course of physicoloid chemistry.

In pharmaceutical practice, mainly hydrosols that is disperse systems where the dispersion medium is water.

Due to the large particle size, colloidal solutions have characteristic properties: low diffusion ability, low osmotic pressure, low dialysis ability, ability to dissipate light in all directions when considering solutions in reflected light (typical Tin-dale cone is formed). The micelles in the colloidal solution are in a chaotic motion. They are characterized by Brownian motion.

Colloidal solutions are sedimentally stable systems.

Sedimentation is a process of staining particles under the influence of force of weight. The precipitation of particles in colloidal solutions is a detrimental to the Brownian motion, which distributes particles along the entire volume.

Colloidal solutions are aggregation and thermodynamically unstable systems, since particles have excessive surface energy. As a result of reduction of surface energy, coagulation of colloidal solutions may occur.

Coagulation is the process of combining particles in disperse systems with the formation of larger complexes.

The consolidation of particles in colloidal solutions arises under the influence of molecular forces of adhesion and surface tension of a liquid. The forces of intermolecular attraction contribute to the adhesion of particles when they collide and the forces of surface tension of the liquid - to reduce the surface of the collision of the liquid with particles. However, typical colloidal solutions remain stable over certain terms which can be explained by the presence of factors that interfere with the combination of colloidal particles. One of such factors is the presence of colloidal particles of electrical charge of the same name, which makes them repel and consequently do not connect to large aggregates. Colloidal

solutions can be stable only in the presence of a third component - a stabilizer, which adsorbs on the surface of the distribution of particles - the medium, prevents coagulation. The stability of colloidal systems is also improved by the appearance of solvate layers from solvent molecules.
Colloidal solutions are non-equilibrium systems: they do not have the properties of reversibility (if the colloidal solution is evaporated or precipitated with an electrolyte, and then again add water, then the colloidal solution will not work). It should also be borne in mind that during prolonged storage can occur so-called "aging", which is manifested in the adhesion of particles, which leads to their coagulation. This phenomenon also distinguishes colloidal solutions from the true ones.

The stability of colloidal solutions is disturbed due to the unwanted adhesion of particles, with the addition of electrolytes (which, by hydrating, subtract water from the micelle of the colloidal solution, that is, the water shell around the colloidal particles is broken, in the result of which the particles are enlarged and their deposition occurs), with change temperature, pH of the medium under the influence of light.

The stability of the system is ensured by the presence of charge on the surface of the particle (dissociation of matter, adsorption of the same names of ions), solvate layer, shell of the HMC, surfactant around particles of the dispersed phase which prevents their adhesion.

The mechanism of the stabilizing action of the HMC and the surfactant is that they are adsorbed on the surface of the particles and are oriented at the boundary of the phase distribution in such a way that the polar part is directed to the polar fluid, and the nonpolar one to the nonpolar particles, forming a monomolecular adsorption layer on the surface of the phase. Ions of surfactant, adsorbed on the surface of the distribution, have superficial activity, thus increasing the repulsive forces between the particles and decreasing their surface tension, which contributes to aggregate stability. In addition, around the film surfactant, surrounding the lobe, the molecules of the solvate layer (in the water - hydrated shell) are oriented. Such colloids are called "protected".

Since the size of the proteins protected colloids is such that they do not pass through the physiological membranes, they are deprived of the ability to absorb, and their preparations, therefore, are only local.

MANUFACTURE OF SOLUTIONS OF PROTECTED COLLOIDS

In pharmaceutical practice, mainly used three protected colloidal drugs. This is a collargol, protargol and ichthyol.

Collargol and protargol are used as astringent, antiseptic, anti-inflammatory agents. Their solutions are used to lubricate the mucous membranes of the upper respiratory tract, in the ophthalmic practice, for washing the bladder, purulent wounds, etc.

Argentum proteinicum is an amorphous powder of brown-yellow color, odorless, slightly bitter and slightly viscous, is easily soluble in water, is protected by colloidal silver, containing 7,3- 8.3% (on average 8%) of silver oxide. The role of the protective colloid is carried out by products of hydrolysis of the protein (albuminates). The drug is described in GF IX, Art. 398

RP .: Solution Protargoli 2% 100 ml

Da Signa To wash the nasal cavity.

When preparing protargol solutions, its ability to swell due to the contents of a large amount (about 90%) of protein is used. After swelling, the protargol passes into the solution itself.

Cover 2,0 g of protargola with a thin layer on a surface of 100 ml of water and leave at rest. The drug swells, and the particles of the protargola, gradually dissolving, fall to the bottom of the stand, giving access to subsequent portions of water to the drug. It is not recommended to mix the protargol solution, since when shaking the powder, it fills in the chest, foam is formed, which envelops the particles of the protargolum and slows down its peptization.

The resulting solution if necessary is filtered into a vial for letting through a fluff lint of cotton wool, washed with hot water. The protargol solutions can be filtered through the impenetrable filter paper or the glass filters No. 1 and No. 2. The ash filter paper contains iron, calcium and magnesium ions that cause the coagulation of the protargola and eventually the loss of the drug on the filter.

If in the solutio (except for water) prescribed glycerin then the protargol is initially rinsed in a mortar with glycerol and after its swelling gradually add water. In addition, it should be borne in mind that the solutions of protargola should be released in glasses of dark glass because light is a factor that affects the coagulation of colloidal drugs. Under the influence of light the oxide contained in the protargol silver disintegrates by oxidizing the products of the hydrolysis of the protein resulting in the transformation of protargol into metallic silver. The protargol solution should not be prepared for storage.

Argentag colloidale solutions are greenish-black or bluish-black plates with metallic luster, soluble in water, containing 70% silver oxide and 30% protein hydrolysis products (sodium salts of lysalbin or tribal-new acids) that act as a protective colloid. The B. Kolargol list is also described in GF IX. Due to the small amount of protein (about 30%) there is a slow dissolution of the drug in water.

Therefore, two methods of manufacturing depending on the concentration of the prescribed solution can be used to accelerate the dissolution.

1. In a glass bottle for release, filtered (can be strained), purified water, pour collargolum and the contents of the glass should be shaken until the collagen is fully transferred into the solution. This method is convenient at small concentrations of collargol (up to 1%).

Rp .: Solutionis Collargoli 2% 200 ml

Da Signa For swaddling.

2. If you have to prepare solutions of greater concentration, then do as follows: the collar is placed in a mortar, in this case 4,0 g, add a small amount of water purified, leave the mixture for 2-3 minutes to swell, rub, and then gradually when stirring add the rest of the water.

The collargol is swollen for a relatively long time, so it is more rational to use the second method. If necessary, the solution of collargol is filtered through a glass filter No. 1 or No. 2 or filtered through a loose cloth of cotton wool, washed with hot water. The solution is photosensitive, so it is released in a vial of orange glass.

Solutions of ichthyol (ammonium salt of sulphonic acids of shale oil) – Ichtyolum is almost black or brown syrup liquid of a peculiar sharp smell and taste. Soluble in water, glycerol, alcohol-ether mixture. Aqueous solutions during shaking are very foaming. Description of the preparation is given in GF IX. It is a natural protected colloid.

Rp .: Solution Ichtyoli 1% 200 ml

Da Signa For lotions.

Weigh 2.0 g of ihthiol into an old porcelain cup (or a container of parchment paper), gradually add 200 ml of water with continuous stirring with a glass rod, then, if necessary, filter into the bottle for delivery.

Rp .: Solution Ichtyoli 2% 100ml
Glycerin 10.0
Misce Da Signa For tampons.

In a tare stand, weigh out 10.0 g of glycerol (viscous liquid) and then weigh 100 ml of purified water, shake to homogeneity. Ichthyol weigh in a porcelain porcelain cup, then add a solution of glycerin in water and grind until completely dissolved, leaving part of the water-glycerine solution in the support. The resulting solution of ihthyol, if necessary is filtered through a loose lint of cotton wool into a bottle of 150 ml. Porcelain (porcelain) cup is rinsed with the remainder of the water-glycerol solution and the same is washed cotton swab. The vial is sealed and drawn up for leave.

For the manufacture of glycerine solutions of ihthyol, the vial is placed in hot water to facilitate the dissolution of ihthiol.

Rp .: Solution Ichtyoli 10% 100 ml
Calcium iodide 2.0
Misce Da Signa For 2 tablespoons microclysters.

In this case, it is necessary to choose the optimal version of the technology to avoid the effect of the coagulating electrolyte - potassium iodide. To this end it is advisable to add it to ihtiol in the form of aqueous solution. Weigh 10,0 g of ihtiolum into a tare cup and add 80 ml of water while stirring. The solution is filtered into a vial, for which 10 ml of 20% potassium iodide solution are measured and shaken to homogeneity.

SULFURS OF NAPOLICOIDS

Solutions of semi-colloids are systems that under certain conditions are true solutions and when the concentration of the dispersed phase changes they become solos in the colloid state. In this case, the substance (dispersed phase) simultaneously consists of molecules, ions and various aggregates in the form of a micelle of varying dispersion. The micelles are formed as a result of the association of dissolved molecules. At the same time, the concentration of the solute increases which contributes to the increase of the colloidal fraction. On the contrary as the temperature rises the micelle formation becomes more complex, since the intermolecular bonds are weakened and the molecular-kinetic movement is amplified. Such solutions used in medical practice include solutions of tannins, cats, some organic bases (ethcardine lactate).

Due to the sharply expressed surface activity, the half-colloids are easily adsorbed on non-polar surfaces and hydrolyze them. The ability to associate molecules in solutions of tannins and other tannins, which increases with increasing concentrations is especially apparent. Production of solutions of semicolonials is carried out in pharmacies under the rules of manufacturing of solutions.

Aqueous solutions of tannid. In aqueous solutions of tannins, which are derivatives of phenol, micelles are formed not only due to adhesion of molecules in hydrophobic areas, but also due to the formation of hydrogen bonds.

Rp .: Tannini 3.0
Aquae purificatae 100 ml
Misce Da Signa For wetting the skin with burns.

The solution for external use, which includes tannin, which is related to semi-colloids (concentration of 3%).

In the stand, measure 98.2 ml of warm purified water and dissolve 3.0 g of tannin (KOO = 0.61). The solution is filtered through a cotton swab into a vial and made up for leave.

Aqueous solutions are soap. Milas, which are fatty acid salts, can exist in aqueous solutions in the form of nonionized molecules, ions, soap hydrolysis products, aggregates (micelles) and fatty acid molecules. In rather concentrated solutions, micelles are spherical. They consist of molecules that are connected by their hydrocarbon groups and facing out (in water) ionogenous, strongly polar groups. At higher concentrations of soap in solutions, micelles of another composition (lamellar micelles) are formed in solutions.

In alcohol, soap forms molecular solutions, because alcohol is a solvent for both the polar and nonpolar soap molecules.

In the recipe of pharmacies there may be liquid dosage forms that represent the combination of solutions of the HMC, colloidal and semi-colloidal solutions.

5. Materials of activating students during the presentation of a lecture / problem, problem situations, etc.

Control questions:

1. Give the definition of "high-molecular compounds".
2. Characterization and classification of macromolecular compounds (IMS), their classification.
3. Use of the HMC in pharmacy.
4. Dependence of dissolution of the HMC on the structure of their molecules.
5. List unlimited swelling macromolecular compounds.
6. Features of the technology of solutions of pepsin, gelatin, starch and methylcellulose.
7. Characteristics and properties of colloidal solutions.
8. Technology of solutions of protected colloids: collargol, protargol, ihtiol.
9. Rules for the addition of medicinal substances to solutions of the HMC and protected colloids.
10. Assessment of the quality and storage of solutions of naval vessels and colloids in accordance with the requirements of the normative and technical documentation.

Test tasks:

1. A pharmacy received a recipe for an ointment with a colic. What auxiliary substance was used by an assistant to dissolve collargol?

* water
glycerin

Vaseline oil
ethyl alcohol
Sunflower oil

2. A pharmacist has prepared a prescription drug.:

Rp .: Sol. Protargoli 0,3% - 10 ml
Glycerin 1.0
D.S. For washing
Specify the best technology option:

* Protargol rub in a mortar with glycerol and add water.
Glycerin is dissolved in water and added to protargolum.
Dissolve the protargol in the support and add glycerol.
Into the vial weigh the protargolum, dissolve in water, add glycerol.
In a vial we glycerin, water, protargol are sequentially weighed.

3. The patient is prescribed a solution according to the following words:
Rp .: Acid hydrochloric acid 2% - 100 ml
Pepsin 2.0
Da.Signa. By Art. l 3 pounds a day before meals.
How to dissolve pepsin to provide therapeutic activity of the drug?

* In a pre-cooked solution of acid chloride.
In 20 ml of acid chloride solution.
In 98 ml of purified water.
Rub off 10 ml of purified water.
Dissolve in water purified by stirring.

4**. For the preparation of drugs, solutions of high molecular weight compounds are used. What process should be preconditioned for the preparation of solutions of finely swollen substances?**

* Pour the optimum amount of water purified to swell.
Dissolve in a small volume of acid chloride.
Dissolve in purified filtered water.
Rub with a small amount of cleaned water.
Dissolve in water purified when heated.

5. To prepare nosal drops, use solutions of protected colloids. What process should be performed during the preparation of the protargol solution?

* Pour over a wide surface of water with a thin layer without mixing.
Dissolve a small amount of glycerin.
Dissolve in water purified by shaking.
Rub with a small amount of cleaned water.
Dissolve in water purified when heated.

6. The ointment for the nose containing protargol is prepared for the patient. How should a pharmacist enter protargol in the ointment base?

* First, rub with glycerin, and then with water.
Grind with water or alcohol.
Grind with alcohol or ether.
First, rub with the base, and then with glycerin

Pour a thin layer on the surface of the water.

7. A pharmacist has prepared an ozarsol solution. Specify the features of this solution.

* dissolved in a solution of sodium bicarbonate
dissolved in freshly distilled water
dissolve in hot water

8. The difference between the oligomer of polymer is:

*The degree of polymerization
The nature of monomer
The long macromolecular chain
There is no correct answer

9. A repeating group of atoms bound together in a polymer molecule is called:

*The degree of polymerization
The polymer
The element link
The monomer

10. Which polymers are not softened by heating:

*Thermoplastic
Thermosetting
Thermoplastic and thermoreactive
It is impossible to correspond unambiguously

6. General material and methodological support of the lecture:

- training rooms;
- Codoscope; Slides;
- illustrative materials.

7. Materials for self-training of students:

a). on the topic of the lecture / literature, questions, tasks, test tasks;
b). on the topic of the next lecture / literature, list of basic questions, test tasks.

8. Literature used by the lecturer to prepare the lecture.

Basic literature:

1. Technology of medicines. Educational and methodical manual: A manual for higher education institutions / O. I. Tikhonov, P. A. Logvin, S. O. Tikhonova, A. V. Mazulin, T. G. Yarnykh, O. S. Shpichak, O. M. Kotenko; Edited by O. I.

Tikhonov - Kharkiv: NFaU; Original, 2009. - 432 pp.
2. Technology of medicines: Textbook / O. S. Marchuk, N. B. Androschuk - Kyiv: Medicine, 2008. - 488 p.

Additional:

1. Soft dosage forms: Extemporal formulation: Methodical recommendations / O. I. Tikhonov, T. G. Yarnykh, O. V. Lukienko and others; Ed. OI Tikhonov - X .: View of NFaU; Golden Pages, 2003.-128 p.
2. Aseptic dosage forms: Extemporal formulation: Methodical recommendations / O. I. Tikhonov, L. V. Bondareva, T. G. Yarnykh, N. F. Orlovetsky and others; Ed. OI Tikhonova and TG Yarnyh. - X .: View of NFaU; Original, 2005. - 184 p.
3. Solid dosage forms: Extemporal formulation: Methodical recommendations / O. I. Tikhonov, T. G. Yarnykh, S. V. Gritsenko and others; Ed. OI Tikhonova - Kh.: View of NFaU; Golden Pages, 2003. - 176 pp.
4. Liquid dosage forms: Extemporal formulation: Methodical recommendations / O. I. Tikhonov, T. G. Yarnykh, N. F. Orlovetsky, and others; Ed. OI Tikhonova and TG Yarnyh. - X .: View of NFaU; Original, 2005. - 160 s ..

Lecture 5: « Suspension technology. Emulsion technology»-2h

1.Relevance of the topic. Justification topics. Pharmacists should ladet issues of technology for manufacturing suspension first and be ready to implement the AI of their knowledge. Suspensionshave high bioavailability, they are non-toxic, which allows their use in gynecology, otolaryngology, ophthalmology, in pediatric and geriatric practices. The rational ratio of active substances, methods of their introduction and preparation allows you to create highly effective drugs.

2. Objectives of the lecture:

-training:

- basic concepts and terms of the technology of dosage forms;
- master the preparation of suspensions;
- navigate in the main directions of state regulation of the production of drugs in this section;
- read recipes in Latin, analyze their components and evaluate the correctness of discharge;
- use DF and International GF, other regulatory and technical documents, as well as reference books to search for information on the composition, preparation, storage and dispensing of drugs.
- formed in abstraction degrees of lecture material presentation /;

- educational:

- This lecture is aimed at the development of a professional significant personality structure;
- education of students of modern professional thinking.
- bringing up students of the concept that a drug should be considered as a subject that is used to prepare various drugs, and drugs, in turn, as a form of use of drugs, that is, drugs in this case are already subject to treatment by patients.

3. Plan and organizational structure of the lecture.

№	The main stages of the lecture and their content.	Goals in levels of abstraction.	Type of lecture, lecture equipment.	Timedistribution
1	**2**	**3**	**4**	**5**
1.	***P preparatory stage*** Definition of learning objectives. Providing positive motivation.	I		5%
2.	***The primary stage*** Statements of the lecture material. Plan: 1. Definition of suspension.Features of some suspensions. 2. Rules for working with suspensions. 3.Characteristics and properties of suspensions. 4.Characteristics of emulsions as a dosage form and dispersion system; 5. Requirements for emulsion wells. eight. Types of oil emulsions and methods for their determination; 6.Characteristics as emulsifiers, their mechanism of action and classification; 7.General rules and methods for the preparation of oil emulsions.Calculate the amount of emulsifier, water and oil; eleven. Stages of the technological process of preparation of emulsions. 8. The introduction of drugs with different physico-chemical properties in the composition of oil emulsions. Features of the introduction phenylsalicylateand sulfonamides. 9.Evaluation of the quality of emulsions, the rules for blocking, processing and storage according to the requirements of regulatory documents.	II III II	References, visual material. State Pharmacopoeia, main regulatory documentation	85% - 90%
3.	***The final stage*** Summary of lectures, general conclusions. The lecturer's answers to possible questions.	I	References, questions, tasks.	10-15%

	Tasks for student self-training.			

4. The content of the lecture material:

Suspensions are a liquid dosage form containing, as a dispersed phase, one or more powdered powdered medicinal substances distributed in a liquid dispersion medium.

Suspensions (suspensions) are microheterogeneous disperse systems consistingfrom a solid dispersed phase and a liquid dispersion medium.Depending on the particle size of the suspension, there are:

- *rough*, which are called scrambled mixtures (Mixturaeagitandae), have a particle size of the dispersed phase (i.e. medicinal substance) more than 1 micron, quickly settle on standing, so they are filtered (if necessary, only the solvent is filtered)
- *thin*, which are called cloudy or opalescent mixtures (Mixturaeturbidae),particle size from 0.1 to 1 μm, differ from coarse suspensions in that the precipitate forms more slowly in them.

Depending on the method of application, suspensions are distinguished for internal, external and parenteral use. If medicinal substances for internal use are prescribed in the form of suspensions, they are called suspension mixtures. As external means, suspensions are prescribed for lubrication, douching, etc. Less often suspensions are used for injections, mainly intramuscular (they are not used for internal administration).

In the pharmacy practice, most often used suspensions in which the dispersion medium is water, aqueous extracts from medicinal plant materials, glycerin, fatty oils, etc.

Suspensions can be ready for use, and also in the form of powders or granules for suspensions, to which water or another suitable liquid is added before use in the amount indicated in its own articles.

Suspensions are formed in the following cases:

-with assignment composed of liquid medicines solid ingredients which are insoluble in the prescribed solvent (e.g., if the water solvent is registered, and as a medicinal substance - zinc oxide, camphor, phenyl salicylate, and other substances)

- when assigning solid soluble substances in amounts exceeding their solubility limit (for example, boric acid has a solubility in cold water of 1:25, and written out - 1:30, therefore, its undissolved particles will be in the form of a precipitate;
- when new medicinal drugs are formed as a result of chemical reactions substances insoluble in a prescribed solvent (for example, if you mix solutions of calcium chloride and sodium bicarbonate, a precipitate of calcium carbonate is formed)

-when mixing two solvents worsens the solubility conditions of medicinal substances (for example, anethole is released when ammonium-anisic drops are added to aqueous solutions of salts.)

In medical practice, suspensions have a certain value:

-Provide the ability to introduce solid insoluble substances in the liquid, they have a high degree of dispersion, which is why they show their therapeutic effect faster and more fully, which has been proven in numerous biopharmaceutical studies;

- allow to ensure prolonged action and regulate its duration by changing the size of the particles of the medicinal substance.For example, a suspension of amorphous zinc insulin with particles of about 2 microns causes a short-term decrease in blood sugar.The suspension of the crystalline drug with particles of 10-40 microns has a long-term therapy to tiche th action. A mixture of amorphous and crystalline drug provides an early onset of therapeutic effect and its duration.

It should be noted that the suspensions are difficult to dose. Poisonous and potent substances due to the difficulties of dosing them in suspensions, as a rule, are not released. An exception is the case when the amount of a substance in List B, written out in a prescription, does not exceed the highest single dose in the whole volume of the medicinal form. The issue of the release of potent substances in suspensions is solved individually in the individual case.Suspensions are also not available in cases where toxic precipitations are formed as a result of chemical interaction between medicinal substances.

FACTOR, INFLUENCING THE STABILITY OF HETEROGENEOUS SYSTEMS. LAW STOKS

Suspensions do not have the ability to diffuse, osmotic pressure, they do not observe spontaneous chaotic movement of particles.A characteristic feature of suspensions is their ability tosettle.Therefore, one of the important requirements for suspensions is their stability.

Sustainability Suspensions depends primarily on the properties of medicinal substances, contained in them, namely: these substances are surface hydrophilic or hydrophobic.Suspensions of hydrophilic substances are stable, because hydrophilic particles are moistened with a dispersion medium and a water (hydrate) shell is formed around each of them, preventing the aggregation of small particles into larger ones.

Hydrophobic particles are not protected by such a shell, since they cannot form a stabilizing water shell when in contact with water, and therefore easily and spontaneously (under the action of molecular forces) stick together, forming aggregates-flakes (coagulation) quickly precipitate.If during coagulation of suspensions flakes are formed , poorly moistened with water, they float on the surface.The ascent of large layered aggregates of a hydrophobic substance onto the surface of water is called *flocculation (from the Latin wordflocculi-flakes).*Flocculation increases with shaking, because the surface of the hydrophobic substance is poorly wetted and this contributes to the fixation of air bubbles at the solid phase.

The stability of suspensions depends on the degree of dispersion (grinding) of dispersed phase particles and their electric charge, which exists a prepyats coagulation and coarsening of particles ation.The grindingmaterial, the stability of the suspension, the more accurate its dosage, effective action.

Stability depends on the ratio of the densities of dispersed particles of the dispersed phase and the dispersion medium. If the density of the dispersed phase is greater than the density of the dispersion medium, then the fractions quickly settle.If the density of the dispersed phase is less than the density of the dispersion medium, then the proportions float. If the density of the dispersed phase is approximately equal to the density of the dispersion medium, then the suspension is most stable.

Cutting sedimentation and aggregate stability of suspensions.

Aggregate stability is resistance against the adhesion of particles. During the sedimentation of suspensions, two different cases can be observed: in one case, the particles are deposited separately, not connecting with each other. Draft occurs more freely. Such a dispersed system is called aggregate stable.

However, it is also possible that the suspension solid particles coagulate under the action of molecular attractive forces and settle in the form of whole flakes.So and the systems are called unitbut unstable.

Sedimentation stability is stability against sedimentation of particles, associated only with their size.

In any suspension, the solids will sedimentate (settle) at a rate depending on the degree of dispersion of the solid particles and some other factors.

Stokes law. In general, the deposition speed is displayed in the odds mu le Stokes. When the particle radius of the dispersed phase is less than 0.5 μm, the Stokes formula does not applicable because the Brownian movement prevents their sedimentation . For spherical particles with a diameter of 0.5 to 100 μm, the sedimentation rate of particles of the dispersed phase obeys the Stokes formula.

The sedimentation rate is directly proportional to the radius of the fractions of the dispersed phase, the differences in the densities of the dispersed phase and the dispersion medium and is inversely proportional to the viscosity of the dispersion medium.

$$V = \frac{2 r^2 \times (d_1 - d_2) \times g}{9 \times \eta},$$

where V is the speed of movement (precipitation), cm / s;

r - the radius of the dispersed phase particles;

d_{one} - density of particles of the dispersed phase, g / cm $^{3;}$

d_2 - density of the dispersion medium, g / cm $^{3;}$

η - absolute viscosity of the dispersion medium, g / cm x s;

g - acceleration of gravity, cm / s ^{2}

When applying the Stokes formula, it should be borne in mind that the particles of the dispersed phase must be strictly spherical in shape, absolutely hard and smooth;In addition, the Stokes formula does not reflect the phenomena occurring at the interface and depend on whether the substances are hydrophobic or hydrophilic.

Since stability is a quantity in its inverse speed sedimentation, the Stokes formula can be slightly transformed and obtained:

$$U = \frac{1}{V} = \frac{9 \times \eta}{2 r^2 \times (d_1 - d_2) \times g},$$

Where U - stability of the suspension.

Sustainability Suspension the larger the radius of the particles of the dispersed phase, the closer the density of the phase and the medium, the larger the viscosity of the dispersion medium. And therefore, to improve the stability of suspensions, use the following techniques:

- increase the viscosity of the dispersion medium. This is achieved by the introduction of surfactants , viscous liquids (glycerin, syrups), hydrophilic colloids, starch, and others;

- try to disperse the solid particles of the dispersed phase as thin as possible. This is achieved by careful grinding in a mortar substance initially in dry form, and then in the presence of a small amount of liquid.

When grinding substances in a dry form, the degree of dispersion is in the aisles of up to 50 microns, and if they are further crushed in the presence of water, the particle size is in the range of 0.1-5 microns.

The need to add fluids is explained by the fact (as follows from Fig. 113) that the hardness of the substance being crushed decreases and, in addition, wetting fluids penetrate into small cracks of solid particles formed during grinding of the substance and create a wedging pressure (P), the opposite effect of the concave meniscus, the so-called Laplace pressure (P). Microcracks widen, and further grinding of the substance occurs. This phenomenon is known as the Rebinder Effect. The higher the wetting energy, the more pronounced the wedging effect and better splitting of the substance will occur.

B.V. Deryagin established that *The maximum effect of dispersion in a liquid medium is observed when adding 0.4-0.6 ml of liquid per 1.0 g solids* (40-60%). In accordance with this, in the technology of drugs there is *Deryagin's rule: for fine grinding of a solid powdered substance, liquid is taken in half the amount of its mass.*

Hydrophilic substances are more easily destroyed in the presence of water than in the presence of non-polar liquids. To facilitate the dispersion of hydrophobic substances, it is more advantageous to use alcohol or ether.

Stabilization of suspensions. Aggregate stability of the suspension is obtained when their fractions are coated with solvation shells consisting of molecules of the dispersion medium. T Which inhibit coarsening shell particles, being for minutes and diluted suspension stabilizing factor.

Stabilization of suspensions. Aggregate stability of the suspension is obtained when their fractions are coated with solvation shells consisting of molecules of the dispersion medium. Such shells prevent the coarsening of particles, being a stabilization factor for diluted suspensions.

To increase the stability of suspensions of hydrophobic substances that do not form protective hydration layers on their surface, they should be lyophilized, that is, they should add a hydrophilic colloid (stabilizer), thereby giving them a property of wettability. Natural or synthetic high-molecular substances are used as

stabilizers: gum, proteins, gelatin, vegetable mucus, natural polysaccharide complexes, methylcellulose, sodium carboxymethylcellulose, polyvinylpyrrolidone, polyglucin, tweens, spines, bentonites. All of these surfactants reduce the supply of surface energy in the system. The protective effect is most pronounced in IUD suspensions. Solutions of these substances not only have greater stability, but also transfer this property of hydrophobic particles. The stabilizing effect of these substances lies in the formation of hydrated layers on the surface of the suspension particles, as well as in the coverage of these particles with long chain-like macromolecules.

The ratio between the solid phase of the suspension and the protective IUD depends on the degree of hydrophobicity of the drug and the hydrophilic properties of the protective substance and is established experimentally.

To determine the surfactant concentration required for wetting hydrophobic substances, the drug powder is crushed to 40 μm, dried to constant weight and placed in a desiccator over dried calcium chloride. Then, 0.02 g of this substance is applied to 1 cm 2 of the surface of a solution containing surfactants of various concentrations in a glass with a capacity of 30 ml and diameter 45 μm.

The time of immersion of the powder in the surfactant solution is fixed with a stopwatch.Based onthedataobtained, a graph is plottedagainst thetime of immersion of thepowder on the concentration of surfactant.From the point of intersection of the tangents near the inflection point, they are set perpendicular to the abscissa axis. The point of intersection of the perpendicular with the abscissa axis indicates the surfactant concentration necessary for wetting pharmaceutical powders.

According to the results of the experiments, it is concluded that the concentration of surfactants is reasonable, and hydrophilization of the drug is provided.This amount should be optimal.If the limit is exceeded, a process occurgelling.With an insufficient number of IUDs, the opposite phenomenon can occur – asstabilization, because the share of the IUD isnot enough to cover and protect the entire surface of suspended particles.

The particles of suspensions can be stabilized and by adding electrolytes, they form a zeta-potential of a certain sign and size in the boundary layer. The appearance of zeta potential in suspensions is explained in the same way as charging the micelle core in hydrophobic sol: adsorption of ions from solution and dissociation or hydrolysis of the surface layer of the solid phase.

It should be borne in mind that electrolytes stabilize suspensions only in certain concentrations. If the electrolyte concentration is exceeded, then the stabilizing effect of the electrolyte becomes coagulating.

Suspension manufacturing methods

Suspensions of medicinal substances are prepared by two methods: *dispersive* and *satsionnym capacitor*.

The basis of the dispersion method is the principle of obtaining a certain degree of dispersion by grinding powdered drug substance.

The basis of the condensation method is a combination of molecules into larger particles — aggregates characteristic of suspensions.

In the manufacture of suspensions by the dispersion method , large particles (coarse suspensions) are released, and in the manufacture of suspensions by the condensation method, fine particles (thin suspensions).

The technology of suspensions should include such technological methods that would ensure the formation of suspensions with finely dispersed particles. Suspensions with a drug concentration of 3% or more are prepared by weight.

Suspension preparation by the dispersion method. Depending on which substances are included in the suspension (hydrophilic or hydrophobic), the method of dispersion will be different.

Hydrophilic substances include magnesium oxide, zinc oxide, starch, white clay, bismuth basic nitrate and d . To hydrophobic - camphor, menthol, thymol, sulfur, phenyl salicylate and other similar substances.

Preparation of suspensions with hydrophilic substances. In the manufacture of suspensions with hydrophilic substances, the solid medicinal substance is first triturated in a mortar in a dry form, and then (according to the Deryagin rule) with half the amount of liquid (by weight of dry matter). The resulting mixture in the form of a slurry (pulp) is diluted with water and poured into a vial for tempering.

Rp.: Zincioxydi 10.0
Aquaepurificatae 100 ml
Misce . Da . Signa . For lotions.

Suspension for external use, the composition of the cat is a hydrophilic substance - zinc oxide. 10.0 g of zinc oxide was triturated in a mortar initially in dry form , and then added 6.4 ml of water and thoroughly ra washed to ensure maxi mal dispersion. Then the rest of the water is added in parts and transferred to the vial for tempering, trying to wash out the dispersions of zinc oxide by washing off the stucco walls .

Labeled "Exterior" and "Shake before use."
PPK
date No recipe
Zinci oxydi 10.0
Aquae purificatae 100 ml

m_{total} = 110 ml
Prepared: (signature)
Checked: (signed)

Reception shaking. For more fine and stable suspensions EC owl reception agitation (which is a kind of dispersion method). It is used for the manufacture of suspensions with hydrophilic substances that are highly dense.

Rp.: Bismuthisubnitratis 2.0
AquaeMenthae 200 ml
Misce . Da . Signa . 1 tablespoon 3 times a day.

In this case, 2.0 g of bismuth nitrate is thoroughly triturated in a mortar, then 1 ml of mint water is added (according to Deryagin's rule), triturated, 5 or 10-fold amount of mint water (about 10 ml) is added, mixed and left for 2 -3 minutes to large particles settled, and the thin mixture is poured into a vial for dispensing. The residue is again triturated, add 5-10-fold amount of water, stirred, allowed to stand, and then poured into a vial for tempering. This operation is repeated until the whole substance is transferred to the fine-dispersed state. After screwing up with water noticeable sedimentation occurs within 2-3 hours. Initial dispersionmixture is easily restored by shaking before use.

In this mixture one of the stabilizing factors - the surface potential - arises as a result of the electrolytic dissociation of the surface layer of suspended particles of bismuth nitrate of the main nitrate.

The stability of mixture suspensions with hydrophilic substances is significantly increased if substances that increase the viscosity of the dispersion medium are introduced into the recipe without being a surfactant.

As viscous liquids, it is advisable to introduce into the mixtures sweeteners and other syrups (if they are not prescribed in the prescription, we can advise your doctor). Then the solid is thoroughly ground in a dry form, then with a small amount of syrup (half the amount relative to the substance), then the rest of the syrup is added and diluted with water. Syrups increase the viscosity of the mixture, as a result of which the sedimentation rate of suspended particles of the drug substance decreases, and it is precisely dosed.

When making suspensions with swelling hydrophilic substances, they are first triturated in a dry form (if other powders are prescribed in the recipe, they are mixed with these substances), and then mixed with water, not rubbed with half the amount of water.

Production of suspensions with hydrophobic substances. It is not possible to obtain a stable suspension of hydrophobic substances by simple rubbing with a liquid. In such cases, the hydrophobic compound is mixed with a hydrophilic colloid to form on the surface of solids particulate adsorptive membranes, providing the required stability of the suspension.

For substances with *mild pronounced hydrophobic properties* (terpin hydrate, phenyl salicylate, sulfa drugs, etc.).Apricot gum, gelatin, 5% methylcellulose or tween-80 are used as stabilizers.

For substances with *pronounced hydrophobic properties* (menttol, camphor , etc.). The number of stabilizers is increased by 2 t i m e s . Hydrophilisate properties of these protective substances are manifested in the presence of water. For the formation of primary pulp the right amount of water, equal to half the amount of the drug and a protective substance.

Rp.: Therpinihydrati 2.0
Natriihydrocarbonatis 2.0
Aquaepurificatae 100 ml

Misce. Da. Signa. 1 tablespoon 3 times a day.

Mixtura suspension with Terpingidrat - a substance with unsharply pronounced hydrophobic properties. Therefore, suspensions with terpingidrata are marked by a tendency to flocculation. This leads to rapid precipitation.

In a stand measure 80 ml of distilled water and 20 ml of 5% sodium bicarbonate solution with a burette. In a mortar, rub down 2.0 g of terpinghydrate with 10 drops of alcohol (the substance is highly powdered), then add 1.0 g of gelatose and 1.5 ml of sodium bicarbonate solution. All carefully ground to obtain a pulp (homogeneous mixture). Then add (in small portions) a solution of sodium bicarbonate, pouring the resulting suspension into a vial for tempering

PWC

DateNo recipe

Aquae purificatae80 ml

SolutionisNatriihydrocarbonatis 5%-20 ml

Therpinihydrati 2.0

Gelatosae 1.

V_{total} = 100 ml

Prepared:(signature)

Checked: (signed)

Rp .: Mentholi 0.5

Natrii hydrocarbonatis

Natriitetraboratis 1,5

Aquaepurificatae 100

Misce. Da. Signa. Rinse.

Suspension for external application with a hydrophobic aromatic and volatile vesch hydrochloric menthol, with pronounced hydrophobic properties.

In a stand measure 100 ml of water and dissolve sodium bicarbonate and sodium tetraborate (take sodium bicarbonate in the form of a 5% solution - 3o ml). Put 0.5 g of menthol in a mortar , triturate with 5 drops of alcohol (as a hardly powdered substance), add 1.0 g of a 5% solution of methylcellulose and triturate until a homogeneous slurry is obtained. Then add about 15 drops of an aqueous solution of salts (according to Deryagin's rule), triturate and add a solution of salts in small portions. After mixing, wash off the contents of the mortar into the vial for tempering.

In the manufacture of suspensions with a hydrophobic substances different approach requiring a preparation of suspensions of sulfur, because it relates to the number of specific substances with pronounced hydrophobic properties. Sulfur is adsorbed on the surface of air bubbles and its fractions float to the surface in the form of a foam layer. It is not always advisable to use conventional substances to stabilize sulfur suspensions, since they reduce its pharmacological activity. As a stabilizer for sulfur suspensions for external use, potash or green soap is used based on 1.0 g of sulfur 0.1 0.2 g of soap. Soap is not used if the suspension includes salts of heavy or alkaline-earth metals, since this forms insoluble precipitates. It should also be borne in mind that medical soap is incompatible with acids.

Rp .: Sulfuris praecipitati2.0
Glycerini 5.0
Aquaepurificatae 100 ml
Misce. Da. Signa. Rub into the scalp.

Sulfur is ground with part of glycerin 0,8- 1.2 g . Glycerin has high hydrophilic properties, wets the surface of sulfur particles and promotes their grinding. To the resulting pulp add the remaining glycerol and purified water, washing the mixture into a vial for tempering. At the end, 0.2 g of potash soap is added and the vial is thoroughly shaken.

Rp.: Sulfurispraecipitati2.0
Streptocidi 3.0
Camphorae 3.5
Acidisalicylici 2,
Glycerini 3.0
Sp. aethylici 50 ml
Sol. acidiborici 3% 50 ml
Misce. Da. Signa. To wipe the skin.

2.0 g of salicylic acid, 1.5 g of boric acid, 3.5 g of camphor are weighed into the vial for tempering, 50 ml of ethyl alcohol 90% are added. The bottle is sealed and shaken to dissolve the powders. In the stand measure 50 ml of purified water. In a mortar, grind 3.0 g of streptocide with 15 drops of 95% alcohol (a heavy powder), add 2.0 g of sulfur, 3.0 g of glycerin, and triturate to a uniform slurry. Add 50 ml (parts) of purified water, washing the suspension into a vial for tempering.

In the manufacture of suspensions in a volume of 1–3 l, it is possible to use means of mechanization — the SES-1 mixer.

Suspension preparation by condensation method. In pharmaceutical practice, the condensation method finds wide application in the manufacture of suspensions. The following cases of the formation of suspensions are distinguished:

- due to chemical interaction;
- due to the replacement of the solvent.

The condensation method for obtaining suspensions is based on the preparation of highly dispersed particles of disperse phase substances in the molecular or ionic state. The process of formation of these compounds depends on a number of conditions: on temperature; on solute concentration; from mix order.

In pharmaceutical conditions, such mixture-suspensions are most often released as a result of the reaction of exchange decomposition, more rarely due to the reaction of hydrolysis, redox and other reactions.

For fine dispersions requires that the starting materials were able to again rank or colloidal dispersion systems.

Rp.: Calciichlondi10.0
Natriihydrocarbonat 4.0 Aquaepurificatae 200 ml
Misce. Da. Signa. 1 tablespoon 3 times a day.

An insoluble substance is formed by mixing solutions of calcium chloride and sodium bicarbonate. As a result of the exchange decomposition, fresh calcium carbonate is formed:

$$Cacl_2 + 2NaHCO_3 \rightarrow CaCO_3 \downarrow + H_2O + 2NaCl$$

In order to obtain calcium carbonate in a finely dispersed state, it is necessary to prepare first two solutions: a solution of calcium chloride and a solution of sodium bicarbonate, and then these solutions are drained. The result is a thin precipitate of calcium carbonate. It is better to use concentrated solutions: 50% calcium chloride solution and 5% sodium bicarbonate solution. Then 100 ml of purified water is measured in a bottle for dispensing, 20 ml of a 50% solution of calcium chloride and 80 ml of a 5% solution in sodium bicarbonate are added.

Rp.: Plumbi acetates
Zincisulfatisana 1.5
Aquaepurificatae 100 ml
Misce. Da. Signa. For urethral injection.

$$Pb(CH_3COO)_2 + ZnSO_4 \rightarrow PbSO_4 \downarrow + Zn(CH_3COO)_2$$

In this case, a precipitate of lead sulfate is formed as a result of the exchange decomposition reaction .

In this example, separate dissolution of substances cannot be used, as in the previous one, so crystals of lead sulfate with sharp edges will fall out. When douching, such crystals can injure mucous membranes and cause an acute inflammatory process. Therefore, the slurry is prepared as follows: In a mortar solid triturated Ingram gradients of first in the dry state, and then water was added to half amount by weight of solids to obtain a pulp, is added and the remaining water was emptied into a vial to break away.

According to the solvent replacement method, thin suspensions are released than with mechanical dispersion. Most often, opalescent and turbid mixtures are formed by adding liquid extracts, ammonia-anisic drops to aqueous solutions of tinctures (see “ Cooking liquid dosage forms using concentrated solutions and dry drugs”, p. 245). In turbid mixtures, sediments, as a rule, are formed rather thin and dissolve well in a liquid medium upon agitation.

QUALITY ASSESSMENT, STORAGE AND IMPROVEMENT OF SUSPENSIONS

Assessment of the quality of suspensions is carried out in accordance with the Global Fund XI. Check the homogeneity of the particles of the dispersed phase, the time of sedimentation, resuspendable, dry residue.

The homogeneity of the dispersed phase particles. Determined by microscopy. There should not be heterogeneous large particles. Particle size should be as specified in private articles.

Time settling. The size of the supernatant during storage is judged on the stability of the suspensions. The smaller the height of the settled layer, the greater the stability.

Resuspended . If the stability of the suspension is disturbed, they should restore a uniform distribution of particles throughout the volume after 24 hours of storage during balancing for 15–20 seconds, after 3 days of storage for 40–60 seconds.

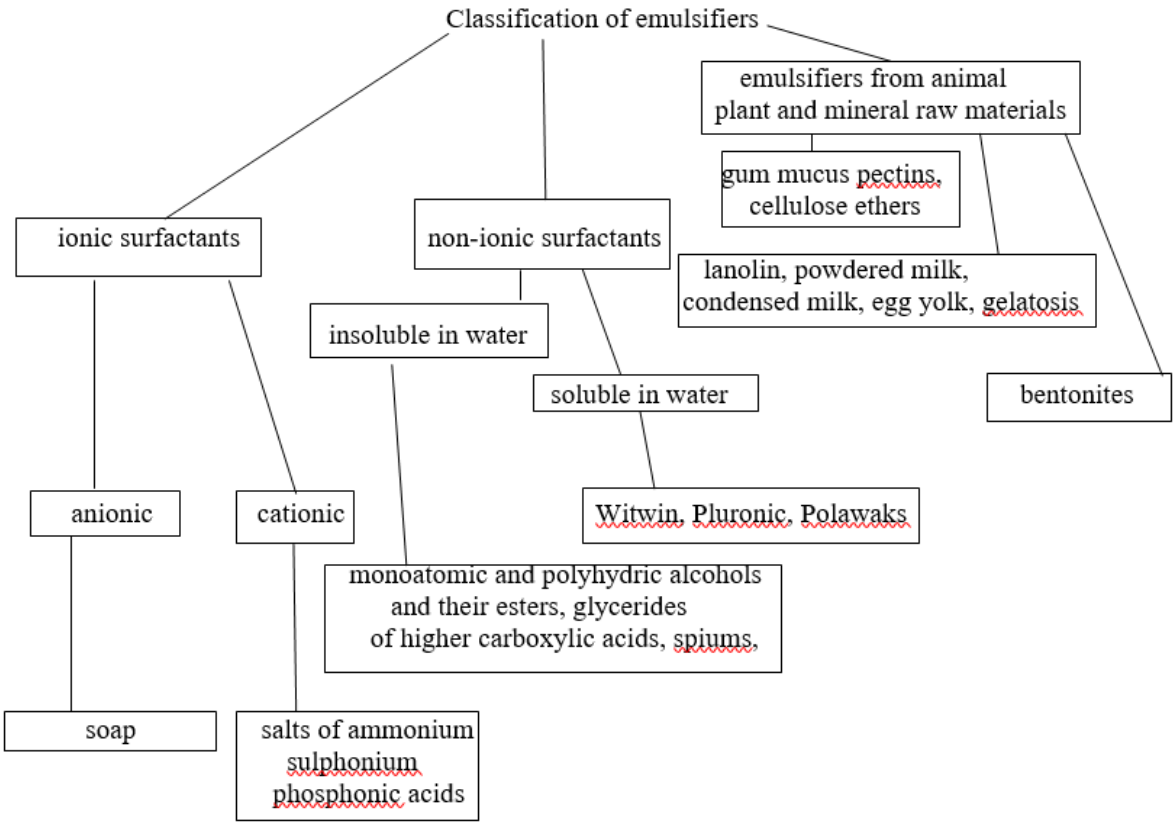
Dry residue. Determined to verify the accuracy of dosing suspensions. To do this, measure the required amount of the suspension is dried and set the mass of the dry residue.

The deviation in the content of active substances in 1 g (ml) of the suspension should not exceed ± 10%.

All suspensions are dispensed in colorless glass vials so that you can see the results of agitation, with the additional label “Shake Before Use”. Keep the suspension mixture in a cool place.

Currently, a promising manufacture of "dry suspensions" (in the form of powders or granules), representing a mixture of medicinal substances with a stabilizer, sometimes with the addition of a preservative. Prepare them in the factory. Dry suspensions are convenient for transportation, can be stored for a long time.

The main directions of improvement of suspensions include: the search for new stabilizers , preservatives; introduction of instrumental methods of quality assessment; development of means of small mechanization.



Emulsions - uniform in appearance dosage form, which consists of mutually insoluble finely dispersed liquids, intended for internal, external or parenteral use.

For the manufacture of emulsions, peach , olive, sunflower, castor essential oils, liquid paraffin, as well as fish oil, balms and other water-immiscible liquids are used. Emulsions must be stabilized with emulsifiers.

The size of particles (droplets) of the dispersed phase in emulsions varies from 1 to 50 microns. But more highly dispersed systems can be prepared.

Emulsions as a dosage form have their positive and negative qualities.

The positive qualities of emulsions include:

- it is possible to prescribe immiscible liquids in some medicines, which is very important for the accuracy of their dosing;

-with grinding oil increases its free surface; this promotes the rapid action of drug substances soluble in it, and also accelerates the process of hydrolysis of fats by the enzymes of the gastrointestinal tract, gives a quick therapeutic effect;

- in emulsions there is an opportunity to mitigate the irritating effect of certain medicinal substances on the gastric mucosa;

- it is possible to mask unpleasant tastes and smells of fatty and essential oils, resins, balms and some medicines, the reception of viscous oils is facilitated , they are poorly dosed;

-emulsions are valuable drugs in pediatric pharmacotherapy.

The negative qualities of emulsions include:

- low resistance, because they quickly collapse under the influence of various factors;

-emulsions are a favorable environment for the development of microorganisms;

- the relative duration of production (this requires appropriate technological methods, practical experience)

-the need to use emulsifiers to keep the phase in a dispersed state. Due to the fact that emulsions are an unstable and heterogeneous dispersed system, which is easily destroyed by various factors, they are prepared only for a short time.

Types of emulsions. Two immiscible liquids can form two types of emulsions, depending on which of the liquids will be transformed into the dispersion phase and the dispersion medium above. There are emulsions of the type oil-water (B / B) and water-oil (B / O).

In the B / B emulsions, the dispersion medium is water, and the dispersed phase is fatty or essential oils, balsams and other hydrophobic liquids. In B / O emulsions, oil is the dispersion medium, and water is the dispersed phase.

B / V type emulsions are used for internal or parenteral use. For external use, the emulsions used are B / V and B / O.

Emulsions B / B is also known as direct or first order and emulsion B / O - reverse, or other first kind (indelible water). These two types of emulsions differ significantly in their properties and formation conditions. In addition, they also distinguish multiple emulsions, in which a dispersed liquid in a drop of the dispersed phase is a dispersion medium. They may be B / M / B or B / B / O. There are several ***ways to determine the type of emulsions.***

The dilution method is based on the fact that emulsions of type B / B retain their stability when diluted with water and lose stability when diluted with oil. Reverse B / O type emulsions retain their stability when adding oil and become inhomogeneous when water is added.

A drop of the test emulsion is placed on a glass slide and a drop of water is placed next to it - the drops will merge if the B / C emulsion is applied. In another experiment, a drop of oil is applied next to the drop of emulsion. The drops will coalesce if the tested emulsion is of the B / O type. This experience can be done in test tubes.

The method of dyeing is based on dyeing the dispersion medium soluble in a dye, selectively soluble in either water or oil.

A drop of water-soluble paint (for example, methylene blue) is applied to a drop of the test emulsion and observed under a microscope. If the emulsion is of type M / B, then the dispersion medium will turn blue and you will see unpainted oil droplets - “eyes”. And if the emulsion is B / O, then the grains of methylene blue will remain lying on the surface of the drop, because the paint cannot penetrate into water droplets, because it is insoluble in oil. If the paint is soluble in oil (for example , Sudan III), then the oil phase will be colored and the water droplets will be unpainted.

The conductometric method is based on the fact that an emulsion of the type M / V has a high electrical conductivity, while an emulsion of the type B / O is insignificant.

The method of a waxed plate is that when you put a drop of a proven emulsion on a glass plate covered with a layer of paraffin, the drop will grow if the dispersion medium is oil (B / O type emulsion) and does not spread if it has water (M / V type emulsion) .

THEORETICAL BASES OF EMULSION FORMATION

Emulsions are thermodynamically unstable systems. The task of manufacturing aggregatively resistant emulsions is reduced mainly to the search for the most effective emulgator for a given message component.

Emulsifiers are diphilic surfactants and are oriented to be distributed at the interface between two liquids. And I conditionally classify them according to the structure and properties of molecules , the mechanism of action, and medical purpose. .

Emulsifiers should always be sufficiently high representatives of homologous rows and have both hydrophilic and hydrophobic particles in the composition of molecules, varying in volume (area) of the occupied surface and balanced so that the polar part should have a strong affinity for water in order to stipulate sufficient solubility of the substance and strong hydration, and the hydrocarbon part must be sufficiently developed, for example , the hydrocarbon chain must be of sufficient length to provide education micelles by adhesion of hydrocarbon groups, and when they were concentrated in solution and in the adsorption layer, they lead to the development of gel-like structures. These requirements are satisfied by fatty soaps, as well as, to varying degrees, other sweet emulsifiers, alkaline salts of the corresponding organic acids: naphthenic soaps, resin (rosin) soaps, and alkyl and

alyl sulfates and the corresponding sulfonic acids, both in acid form and in the form of alkali salts. In addition such surfactants count loidnyh electrolytes is a nionaktivnye well known e and cationic soaps, typified by inorganic salts nical, e.g., hydrochloric , salts of the corresponding nitrogen-containing organic bases of both fat and aromatic series. All such sweet substances are usually effective wetting agents, blowing agents, emulsifiers and peptizing agents and are of great importance in pharmacy for drug technology (see p. 274 “Classification of the IUD”). When choosing emulsifiers to stabilize emulsions, it is necessary to consider the mechanism of their stabilization, toxicity, pH value, chemical compatibility with medicinal substances amy . The emulsifier is added in an amount of from 0.1 to 25%.

The surface-active properties of emulsifiers can be judged by the magnitude of the *hydrophilic-lipophilic balance (HLB).* HLB is *the ratio of hydrophilic and hydro- PHOBN groups in a molecule, the value of which is expressed by a certain number*. Yes. South Africa with HLB 1,5-3 - defoamers. 3-6 - emulsifiers of type B / O. 7-9 wetting agents, 8-18 of emulsifiers of type B / B, 13-15 - foaming agents, 15-18 - solubilizers. According to the HLB value of emulsifiers, it is possible to characterize the type of emulsion being created. According to the theory of the formation of emulsions and the mechanism of the stabilizing action of emulsifiers, there were several scientific ideas. For example, the theory of phase volume (W. Ostwald), the theory of viscosity (N. N. Holmes, WD Child), hydration theory (R. Fischer), the theory of interfacial surface tension reduction (1 Langmuir, WD Harkins, etc.).

The logical continuation of the latter theory is the theory of the formation of the absorption shell on the surface of the dispersed phase (G. Clowes. W. Bancroft and in). Modern provisions of this theory were subsequently developed by domestic scientists (P. A. Rebinder and others), According to which the mechanism of the stabilizing action of emulsifiers lies in the fact that they, adsorbed on the phase boundary, reduce surface tension and accumulate at the interface, and most importantly - enveloping droplets of the dispersed substance, form an adsorption film. The film, sho formed, has mechanical strength, prevents the formation of large particles, the merging of droplets in a continuous layer (coalescence) and provides emulsion resistance (it “binds” the dispersed phase drops). School of Academician Rebinder experimentally proved that the film, which was formed - the main factor in the stabilization of emulsions. Protective films may consist of one or several molecular layers of an emulsifier (mono- or multi-molecular film).

In the manufacture of an emulsion in the process of mixing the components of the emulsifier is concentrated on the interface of two immiscible liquids. During the further manufacturing process the formation of the corresponding type emulsion depends upon the type of emulsifier, which determines the values of the surface tension on both hundred Rhone formed shell produced corresponding areas hydrophilic and hydrophobic parts of the surfactant.

So, for example, soaps with monovalent cations are colloidly soluble in water, but not in oil, which makes it possible to form a shell that is wetted with water

rather than oil, therefore the surface tension on the water side is lower than on the oil side. Since the inner surface of the shell surrounding the ball is smaller than the outer one, the shell tends to bend so as to envelop a drop of oil in the water. As a result, a surface with a higher surface tension is reduced to a minimum compared with a surface having a lower surface tension. On the other hand soap shell with di- and trivalent cations (such soaps colloidally soluble in oil but not in water) is better wetted with oil than with water. In this case, the surface tension on the oil side is lower than that on the water side, and the shell tends to bend so as to envelop the water droplets that are in the bulk of the oil phase. These representations are schematically depicted by J. Clos and A. I. Tikhonov (Fig. 116.3).

The interfacial layer consists of one row of molecules, with its polar part towards water, and the non-polar one towards oil. The polar groups and hydrocarbon radicals are simultaneously solvated by the water and oil phases, and this adsorption-solvation layer has a certain mechanical strength.

The type of emulsion created depends on the solubility of the emulsifier in one phase or another. The dispersion medium becomes the phase in which the emulsifier preferentially dissolves . It follows that to obtain stable emulsions of the M / V type, it is necessary to use hydrophilic emulsifiers (with HLB 8-18) - gums, proteins, alkaline soaps, mucus, pectins, saponins, some plant extracts, polyoxyethylene glycol ethers in higher fatty alcohols, acids, with foams (twin-80, preparation OS-20), etc.

To obtain stable emulsions of type I / O need to apply oleophilic emulsifiers (HLB from 3-6) -lanolin derivatives, cholesterol, phytosterol, natural salts, cetyl alcohol and myricyl, magnesium and aluminum soaps, oxidized races vegetable oils, Pentol, emulgatorT 2, distilled monoglycerides (MHD), many synthetic substances. These emulgatorsare used in pharmacy practice only in the production of medicines for external use.

It is proved that the most stable emulsions are formed by emulsifiers, which have the ability to form gelatinous or viscous films.

Synergism and antagonism of emulsifiers. Phase reversal. In the preparation of emulsions, combined emulsifiers are sometimes used. For example, a mixture of gum arabic and tragacanth. In this case, it is possible to achieve an increase in the degree of dispersion and stability of emulsions, that is, synergism of emulsifiers is observed (one substance enhances the action of the other). Note, however, that s The dependence of the properties emulgator emulsion may deteriorate, whereas emulsifiers act as antagonists.

If an emulsifier of the opposite type is added to an O / B type emulsion, one type of emulsion can transfer to another, that is, an M / B type emulsion can turn into a B / O type emulsion. The same can happen with a significant excess of the emulsified phase. This phenomenon is called reversing the phases of the emulsions. Etc. and this is first formed, both types of emulsions, but then remains or one resistant system prevails. To increase the stability (stability) of emulsions, sometimes emulsifiers of the opposite type are combined. For example, in an emulsion of the type M / B, stabilized by sodium oleate, up to 1% of calcium or

aluminum chloride is added. In this case, as a result of the exchange reaction, a part of sodium ions in sodium oleate is replaced by calcium ions orluminescent to form an emulsifier of the opposite type and therefore along with the emulsion of the direct type M / B an emulsion of the opposite type B / O is formed, that is, in the B / H emulsion of the oil, the particles will not be pure oil, but the B / O type, uniformly distributed in the aqueous phase. Due to the small amount of emulsifier of the opposite type of phase reversal, there is observed here , however, the stability of such emulsions and their resistance to desiccation significantly increases . A classic example of the stability of emulsions due to the presence of emulsifier direct and reverse types are milk and butter.

As a rule, colloid emulsifiers used for the manufacture of pharmaceutical emulsions give strong films of gel-like structure, the mechanical properties of which can be used to prevent its breakthrough , which is necessary for coalescence.

Factors affecting the stability of emulsions. Emulsions must have physical , chemical and microbiological stability.

For the *physical stability of the* emulsion, the residual amount of emulgator is very important . It must be borne in mind that a certain amount of emulsifier can saturate only a certain surface. This means that with an insufficient amount of emulsifier, the degree of dispersion will be small . Oil balls in this case are so large, that the film can not withstand the weight of the balls and breaks. Therefore, it is necessary for each emulsifier and oil to know the optimal ratios that would provide the necessary degree of dispersion and stability of the emulsion The stability of the emulsion depends not only on the properties of the used emulsifier, but also on the degree of dispersion of the phase. The closer the density of the dispersed phase to the density of the dispersion medium, the lower the interfacial surface tension, the higher the viscosity of the dispersion medium, the more stable the emulsion.

The size of the droplets of the dispersed phase depends on the magnitude of the decrease in the surface tension at the interface and the id of the energy spent on the grinding of the particles of the dispersed phase. Especially greater stability of the emulsion is obtained as a result of homogenization , that is, with an additional vigorous mechanical action on the finished emulsion. When homogenizing, not only increases the dispersion of the emulsion, but it becomes monodisperse, which significantly increases its stability.

The emulsion is homogenized with the help of a special device, a homogenizer. For this, a coarse emulsion is passed under high pressure through the narrow channels present in the homogenizer . The e if dispersion of large droplets meat phase and destroyed obtained fine emulsion. In this case, the diameter of the drops may decrease by a factor of ten compared with the original.

The chemical stability of emulsions is determined by the stability of medicinal substances, the lack of chemical reactions between the ingredients of the emulsions.

Chemical instability can affect the physical stability of emulsions (destruction as a result of saponification, oxidation, hydrolysis, components, their interaction with each other and the packaging material).

For the purpose of chemical stabilization of emulsions, they are kept in a package of inert materials in a cool place protected from exposure to light and air, and antioxidants (butyloxytoluene, butyloxyanzole, propyl gallate, etc.) are introduced.

The microbiological stability of emulsions is an important requirement that determines their quality. In the manufacture of emulsions (as well as other dosage forms) it is necessary to observe all measures to ensure the microbial purity of medicinal and auxiliary substances.

EMULSION TECHNOLOGY

The preparation of oil emulsions is regulated by the State Fund XI (p. 161). Oil emulsions are prepared by grinding an emulsifier with emulsified liquid and water in a mortar. When e is to 10.0 g of oil taking 5.0 g w elatozy and 7.5 g of water. If the emulsifier in the recipe is not specified, then pharmacists at their discretion, given the purpose of the emulsion, the physico-chemical properties of the incoming ingredients, select the appropriate emulsifier. It should be borne in mind that the emulsifier will render proper emulsifying action only when the emulsifier , water and oil are taken in certain quantities.

In the absence of indication of the oil in the emulsion using peach, olive or sunflower. In the absence of instructions on the concentration for the manufacture of 100.0 g of the emulsion take 10.0 g of oil.

If necessary, preservatives (nipagin, nipazol, sorbic acid, etc.) are introduced into the emulsion composition and are approved for medical use. Preparation of oil emulsions consists of two stages:

- obtained primary emulsion (hull)
- dilution of the primary emulsion with the required amount of water.

Getting the primary emulsion - the most crucial moment of manufacture of the emulsion. If the emulsion does not come out and after adding water you can see large drops of oil, then you should not correct this emulsion. It must be re-cooked.

In the manufacture of the primary emulsion it is necessary to adhere to certain technological methods.

1. An emulsifier is first added to the mortar, which is thoroughly ground, and then oil and water are added.

2.The pestle must be rotated in a spiral with vigorous mass rubbing all the time in one direction. When moving the pestle in a viscous medium in one direction, the oil particles are drawn into the threads, which, when torn, give a drop of coated emulsifier.

If the pestle is moved in different directions, the oil pulling in the thread decreases, and the balls formed in this process collide and coalesce, the process of dispersing is impeded. The pestle must be kept so that it maximizes with

the walls of the mortar. He must not only rub the emulsified mixture, but also kill air into it.

3. In the manufacture of primary emulsions, it should also be borne in mind that very cold oils (at temperatures below 15 ° C) can hardly be emulsified. In this case, solid triglycerides precipitate and do not succumb to the transformation into a fine dispersion . In such cases, the oil is slightly heated.

4. For a better mixing of the ingredients that make up the primary emulsion, it is recommended to several times collect a celluloid plate a thick mass from the walls of the mortar and pestle into the center of the mortar. Then gradually add the rest of the water while stirring.

Three methods can be used to obtain the primary emulsion.

Continental (Bodrimont method). A dry mortar was placed optimal amount of emulsifier and carefully triturated it, then oil was added and uniform py hamster pestle oil is mixed with an emulsifier to obtain a homogeneous mass, thereby forming oleozol. To this mixture was added dropwise water in an amount equal to half the sum of the mass of oil and emulsifier (if taken gelatose or acacia) and continuing outrub to characteristic crackle. In this case, the mixture takes the form of a creamy mass, and when applying a drop of water, which is lowered along the wall of the mortar, it leaves a white mark; this indicates that the primary emulsion is ready and there is no free oil surface. If the primary emulsion is not ready, then a drop of water deposited on its surface does not spread.

At the end of emulsification, it is advisable to leave the obtained primary emulsion for 5-10 minutes to destroy the reverse type emulsion, always form, and then mix again. In this method, the swarm leaves the emulsion only if the mortar and emulsifier are dry. If the emulsifier is NOT dry, the oil will not be able to wet the wet emulsifier.

English way. An optimal amount of emulsifier is placed in the mortar, which is triturated, and then mixed with water until a homogeneous mass is obtained, and a hydrosol is formed . With this thorough mixing, drops are added to the mixture. When all the oil has been applied, the rest of the water is added to the primary emulsion.

This method is laborious, but practice has shown that it gives good results. In this case, emulsions are of good quality, even if the mortar and emulsifier are not sufficiently dry, which is very important, and especially if you have to work with an emulsifier such as gelatose, which is very hygroscopic and always contains moisture.

Russian way. The optimal amount of emulsifier is placed in the mortar. The porcelain (porcelain) cup of water is weighed and the water surface oil is weighed, the mixture was poured into a mortar and triturated to obtain a primary emulsion. This method is quite simple and convenient when the emulsion does not include substances soluble in oil.

As you can see, the methods of obtaining the primary emulsion are marked by the sequence of mixing the components and some technological methods.

Dilution of the primary emulsion. The finished primary emulsion is diluted with the necessary amount of water to a given mass. When this water is added in

several stages with stirring . If water is diluted too quickly, the phases of the emulsion may be destroyed or reversed. Therefore, dilutions of the primary emulsion are made gradually with stirring. The finished emulsion is filtered, if necessary, through two layers of gauze into a calibrated vial for tempering and adjusted to the desired mass with water. Properly prepared emulsion is a homogeneous liquid, resembling milk with a characteristic smell and taste, depending on the taken oil.

Calculate the number of components. When determining the mass of oil, water and emulsifier, the main points are:

-The amount of oil is determined in words in the recipe;

- the amount of emulsifier - its emulsifying ability;

- the amount of water for the formation of the primary emulsion - the solubility of the emulsifier in water.

Therefore, the recipe for obtaining the primary emulsion is different depending on the used emulsifier. For example, if gelatose is used as an emulsifier for the manufacture of 100.0 g of emulsion, then 5.0 g of gelatose and water are half the amount of oil and emulsifier (10 + 5) per 10.0 g of oil: 2 = 7.5 ml . Water for dilution of the primary emulsion 100 - (10 + 5 + 7.5) = 77.5 ml.When using other emulsifiers for 10.0 g of oil is taken:

-2.0 g Tween 80 (in 2-3 ml of water);

-2.0 g of potash or soda soap (or a mixture of 1.0 g of potash in combination with 1.0 g of emulsifier T-2 in the form of a gel for benzyl benzoate emulsion)

-10.0 g of dry milk (in solution with 10 ml of water);

- 1.0 g methylcellulose (in the form of a 5% solution - 20 ml)

- 0.5 g of sodium carboxymethylcellulose (in the form of a 5% solution - 10 ml, in combination with 0.5 g of methylcellulose in a 5% solution - 10 ml)

- 2.0 g polyoxyl 40-stearate (melted and mixed with 10.0 g oil in a warm mortar , add 2-3 ml of water, emulsify and dilute with water to 100.0 g)

- polyoxyl 40-stearate with tween-80 (1.0 g of tween-80 in a warm mortar is mixed with 1.0 g of polyoxyl 40-stearate, 10.0 g of oil is added, triturated, 2-3 ml of water are added, emulsion is pressed and diluted with water to 100.0 g)

-5.0 g of starch (in the form of 10% paste - 50 ml)

-lecytin (1.2% by weight of the emulsion)

-T-2 (15% by weight of oil)

phosphatides (1-1.5% by weight of the emulsion).

The solubility of tweens depends on the length of the polyethylene oxide chains. For example, in the manufacture of an oil emulsion with tween-20 per 10.0 g of oil, emulsifier 5.0 m is taken , water is 7.5 ml (half the amount of oil and emulsifier). In this case, the emulsifier is layered on the oil, and then water is added and ground. Obtained primary emulsion , which was diluted to 100.0 g. Similarly prepare emulsions with tween-40 and tween-60.

Nowadays, in pharmaceutical practice, tweens are widely used (as solubilizers) to obtain clear solutions of oils. Using tween-20, an aqueous solution

of mint oil was obtained . Twin-60 dissolves pink and mint oils, twin-80 - pink and lavender.

Addition of medicinal substances in the emulsion. The composition of oil emulsions often includes various medicinal substances, the method of administration of which may affect the therapeutic effect of drugs. Therefore, it is necessary to take into account the properties of these substances, their concentration and quantity.

1. *If medicinal substances are soluble in water,* they are dissolved in a portion of the water intended for dilution of the primary emulsion. The solution of these substances is added to the finished emulsion last. It is impossible to add such substances directly to the primary emulsion, and even more so to introduce them into the primary emulsion, because the destruction of the emulsion can occur due to the viscosity of the electrolyte or a large concentration of the substance. The use of concentrated solutions is permitted if their volume is 1 / 2-1 / 3 less than the volume of water intended for dilution of the primary emulsion.

Rp.: EmulsioleiPersicorum 100.0

Coffeini-natriibenzoatis 0,5

Misce. Da. Signa. 1 tablespoon 3 times a day.

Oil emulsion type B / B with a water-soluble substance - caffeine-sodium benzoate (list B).

5.0 g of gelatose is placed into a porcelain (porphoric) mortar and carefully rubbed , then 7.5 ml of water is added, mixed, hydrosols are obtained, and then 10.0 g of peach oil are added gradually (preferably dropwise) with careful grinding and emulsification . Mass several times from the walls of the mortar and pestle collected celluloid plate. Check the readiness of the primary emulsion, and then water is gradually added to it, which is calculated:

100 - (7.5 - 5.0 + 10.0) = 77.5 ml.

Since caffeine-benzoate sodium is included in the emulsion, about 20-25 ml of water is left to dissolve it (or use a 10% concentrated solution of 5 ml), and the rest of the water is diluted with a primary emulsion. After that, add a solution of caffeine sodium benzoate.

CWP

date No recipe

Gelatosae 5.0
Aquaepurificatae 85 ml
Oleipersicorum 10.0
Coffeini-natriibenzoatis 0,5

m_{total} = 100.5 "
Prepared: (signature)
Checked: (signed)

Chloral hydrate, sodium bromide, alcohol solutions, syrups, extracts are added in the same way.

2. *If medicinal substances soluble in oils* (camphor, menthol, thymol, as well as fat-soluble vitamins, hormonal and other drugs), then they are dissolved in oil before its introduction into the primary emulsion. The amount of emulsifier is calculated taking into account the mass of the oil solution.

An exception to this rule is the intestinal antiseptic phenyl salicylate. It is not recommended to dissolve it in oil, as it is poorly hydrolyzed in the intestine, as a result of which the solution does not have an antiseptic effect.

3 *If medicinal substances are not soluble in water and oils*, then they are added in the form of fine powders by thorough grinding with a prepared emulsion, and if necessary, an emulsifier is added in the required amount.

Rp.: EmulsioleiRicini 200.0

Camphorae 1.0

Misce. Da. Signa. 1 tablespoon 3 times a day.

Oil emulsion type M / B with aromatic, volatile substance - camphor - soluble in oil. 20.0 g of castor oil is weighed into a porcelain cup and 1.0 g of camphor is dissolved in it , by heating (up to 40 ° C) in a water bath. In a mortar placed 4.2 g of tween-80, add an oil solution of camphor, mixed. Drops add 5 ml of water and emulsify to obtain the primary emulsion. The finished primary emulsion was diluted with water (201.0 - (21.0 + 4.2 -and- 5.0) = 170.8 ml) which was added in several portions.

Rp.: Emulsioleosi 100.0

Phenylii salicylates

Bismuthisubnitratisana 2.0

Misce. Da. Signa. 1 tablespoon 3 times a day.

Emulsion type M / B, which consists of phenyl salicylate, which is unsharply expressed hydrophobic properties, and bismuth nitrate main - a hydrophilic substance with high density.

20.0 g of 5% methyl cellulose solution is weighed into a small porcelain (porcelain) cup , transferred to a mortar, 10.0 g of almond or peach oil are added in small portions , mixed thoroughly until the primary emulsion is ready , and then 70 ml of purified water is added in portions .

2.0 g of phenylsalicylate is ground in a mortar as an importantly powdered substance with 20 chambers of ethyl alcohol. After weathering, the alcohol is mixed with 2.0 g of a 5% solution of methylcellulose, then 2.0 g of bismuth basic nitrate is added, and about 4.0 g of the emulsion is added to the mixture while rubbing. The resulting mass is diluted with an emulsion and transferred to a beaker for tempering.

Rp.: Benzyliibenzoatis 20.0

Saponisviridis 2.0

Aquaepurificatae 78 ml

Misce. Da. Signa. Lubricate the skin of the hands.

20.0 g of 5% methyl cellulose solution is weighed into a small porcelain (porcelain) cup, transferred to a mortar, 10.0 g of almond or peach oil are added in

small portions, mixed thoroughly until the primary emulsion is ready, and then 70 ml of purified water is added in portions

In the pharmaceutical practice of other countries, for example, Bulgaria, the emulsion with benzyl benzoate is prepared according to the recipe: benzyl benzoate 100.0 g, triethanolamine 2.0 g, oleic acid 8.0 g, purified water to 300.0 g.

In addition to the manufacture of emulsions in mortars, other methods are now offered:

-shaking in special installations;

-mixing with agitators or turbines;

-crushing using ultrasound or high frequency currents.

QUALITY ASSESSMENT, STORAGE AND IMPROVEMENT OF EMULSIONS

Evaluation of the quality of emulsions is carried out in accordance with the GF XI and its own pharmacopoeial articles on the following indicators: the homogeneity of the particles of the dispersed phase, the time of separation, heat resistance, viscosity.

The homogeneity of the dispersed phase particles. The particle size specified under microscopeation , should not exceed the parameters set forth in own entries.

Peeling time. Delamination of emulsions is determined using a centrifuge. The emulsion is considered stable, if not observed delamination of the system in a centrifuge with a speed of 1.5 thousand / Min.

Heat resistance of emulsions. An emulsion is considered stable if it withstands a heating temperature of 50 ° C without delamination.

Viscosity in emulsions is determined by pharmacopoeial techniques with the help of special devices - viscometers, etc.

When storing emulsions, their uniformity may be disturbed as a result of settling . When settling, the particles of the dispersed phase do not merge, but gather in the upper layers, so the dispersed oil particles, although covered with the adsorption membrane of the simulator , but due to the fact that they are lighter than water, float to the surface. Such an emulsion is easily recovered by vigorous shaking. Therefore, the emulsion is settled, leave is subject, since *settling* is a reversible process.

You must be able to distinguish the process of settling the emulsion from the irreversible process of separation, which consists in slowly and gradually reducing the degree of dispersion of the oil phase, if it is an M / V type emulsion, and of the aqueous phase, if it is an E / O type emulsion , then they begin to stick together (coalescence) into a solid mass, the liquids are stratified, and such an emulsion cannot be recovered. Delamination occurs the faster, the weaker the surface protective shell of the globules (fractions) of the oil.

According to these major trends in the improvement of pharmaceutical emulsions, this is an increase in physical stability and prolongation of the action of medicinal substances in their composition.

The most promising ways of prolonging the action of medicinal substances included in the emulsion composition is the development of medicinal preparations based on multiple emulsions, as well as the modification of the physicochemical properties of the dispersion medium through the introduction of hydrophilic solvents, solubilizers, etc.

To improve the stability of emulsions, it is advisable to use a complex of synthetic non-ionic surfactants (emulsifiers B / B and B / O), have a pronounced stabilizing effect.

No less important role in the stabilization of emulsions belongs to the rational technology, which includes not only certain temperature regimes and the order of mixing components, but also the use of modern equipment.

Therefore, a promising direction for the development of emulsions is the introduction of small-scale mechanization (dispersants, homogenizers, etc.) to expand the range of stabilization of tori; introduction of instrumental quality assessment methods.

5. Materials activating students during the presentation of the lecture / task question, problem situations, etc.

Control questions:

1. Characterization of suspensions as a dosage form and dispersion system.
2. Requirements for suspensions.
3. Cases of the formation of suspensions.
4. Classification of suspensions depending on the composition and method of preparation.
5. Factors affecting the stability of heterogeneous systems.
6. Dispersion method of preparation of suspensions with hydrophilic and hydrophobic medicinal substances. Reception shaking.
7. The value of the Rebinder effect and the rules of Deryagin in the preparation of suspensions.
8. Condensation method for producing suspensions (chemical dispersion, solvent change).
9. Evaluation of the quality of suspensions, the rules of packaging, processing and storage in accordance with the requirements of regulatory and technical documentation.

Test items:

1.The pharmacist has prepared a suspension, which includes 2 g of streptocide. Is an amount of 5% methylcellulose solution necessary to stabilize the suspension?

* 2.0
0.5
1.0
5.0
0.2

2.The patient must prepare a suspension, which includes 2 g of menthol. Specify the amount of 5% methylcellulose solution to add to stabilize the suspension?

* 4.0
0.5
1.0
0.4
2.0

3.A pharmacist prepares a suspension containing 2.0 phenylsalicylate. Specify the optimal amount of 5% methylcellulose solution needed to stabilize the suspension.

* 2.0
1.0
3.0
4.0
5.0

4.In the preparation of suspensions, the medicinal substance is triturated with a small amount of liquid. Specify the optimal amount of it according to the Deryagin rule, necessary for grinding 20 g of zinc oxide

* 10 ml.
5 ml.
2 ml.
1 ml.
0.5 ml.

5.Sustainability of the suspension increases with the introduction into their composition of substances that increase the viscosity of the dispersion medium. Specify the substances that provide these properties.

* Glycerol.
Purified water.
Ethanol.
dimexide
Ether ..

6.The method of preparation of suspensions depends on the properties of the substance, which are included in their composition. Specify substances with hydrophobic properties:

* Camphor, menthol.
Sodium bicarbonate, sodium sulfate.
Borate acid, calcium carbonate.
Zinc oxide, talc.
White clay, bentonite.

7. A pharmacist prepared a suspension with a hydrophobic substance. Specify the disperse system stabilizer

* TV and n-80
Sodium chloride
Hydrochloric acid solution

A solution of sodium hydroxide and
E silon

Test questions:

1.Characteristics of emulsions as a dosage form and dispersion system, their use.

2. DF requirements in emulsions.

3.Types of oil emulsions and methods for their determination.

4.Characteristics of emulsifiers used in the preparation of emulsions, their classification and mechanism of action.

5.General rules and methods for preparing oil emulsions. Calculations of the amount of emulsifier, water and oil.

6.The introduction of medicinal substances with different physicochemical properties of amy in the composition of oil emulsions. Features of the introduction of phenyl salicylate and sulfonamides.

7.Evaluation of the quality of emulsions, the rules of packaging, processing and storage in accordance with the requirements of regulatory and technical documentation.

Test items:

1. A pharmacist prepared 150.0 emulsions. Specify the amount of oil he took, if the doctor did not indicate in the prescription.

* 15.0
10.0
30.0
5.0
20.0

2. The recipe is written 100.0 oil emulsion. Specify the amount of oil, gelatin and purified water, which are necessary for the manufacture of the primary emulsion by continental method:

* 10.0; 5.0; 7.5 ml
20.0; 10.0; 30 ml
5.0; 10.0; 7.5 ml.
10.0; 5.0; 1.5 ml
5.0; 5.0; 5 ml.

3. The doctor prescribed 100 g of fish oil emulsion. The amount of fish oil need to weigh the pharmacist for its preparation?

* 10.0 g .
20.0 g .
15.0 g .
3.0 g .
1.0 g .

4. The doctor prescribed an emulsion of olive oil, which includes anesthesin. Specify the feature of anesthesin administration:

* Dilute the anesthesin in the oil before preparing the emulsion.
Dissolve the anesthesin in the finished emulsion.

Dissolve the anesthesin in purified water.
Dissolve anesthesin in the primary emulsion.
Dissolve in alcohol and add to the primary emulsion

6. General material and methodological support of the lecture:
- *educational premises;*
- *equipment;*
- *equipment;*
- *illustrative materials.*

7. Materials for self-preparation of students:
a) on the topic of the lecture presented / literature, questions, tasks, test tasks
b) on the topic of the next lecture / literature, a list of key questions, test items

8. The literature used by the lecturer to prepare the lecture.
Basic literature:

1. Technology drugs. Textbook: Textbook for Universities / AI Tikhonov, PA Logvyn, S. Tikhonov, A. Mazulin, TG Yarnyh, OS spiers, O. Mikhail Kotenko; Edited by AI Tikhonov - Kharkov: Pharmacy; Original, 2009. - 432 p.
2. Technology Medicine: Textbook / A. Marchuk, NB Androshchuk - Kyiv: Health, 2008. - 488 p.

Additional:

1. Soft dosage forms: thermal preparation: Methodical recommendations / A. I. Tikhonov, T. G. Yarnikh, A. V. Lukienko and others; Ed. A.I. Tikhonov. - M.: Publishing house NUPh; Golden Pages, 2003.-128 p.
2. Aseptic dosage forms: thermal recipe: Methodical recommendations / A. I. Tikhonov, L. V. Bondareva, T. G. Yarnikh, N. F. Orlovskaya and others; Ed. A.I. Tikhonov and T. G. Yarnikh. - M.: Publishing house NUPh; Original, 2005. - 184 p.
3. Solid dosage forms: thermal recipe: Guidelines / A. I. Tikhonov, T. G. Yarnikh, S. V. Gritsenko and others; Ed. A.I. Tikhonov - M.: Publishing House of the NUPh; Golden Pages, 2003. - 176 p.
4. Liquid dosage forms: thermally assisted ATGM: Methodical recommendations / A. I. Tikhonov, T. G. Yarnikh, N. F. Orlovskaya and others; Ed. A.I. Tikhonov and T. G. Yarnikh. - M.: Publishing house NUPh; Original, 2005. - 160 p.

Lecture 6: «Technology infusions, decoctions of the PRM. Liquid drugs using extracts, concentrates. Mucus.»- 2 h.

1. Relevance of the topic. Substantiation of the topic. In recent years, there has been increased attention to herbal medicine. Water extracts from medicinal plant materials (MPM) have a high bioavailability, as compared with individual medicinal substances have a milder effect on the body, with virtually no side effects.

At present, there can be no universal technology of water extraction from plant raw materials containing various groups of active substances. For each raw material there should be an individual rational technology, with the help of which the maximum of active substances is obtained.

2. Objectives of the lecture:

- training:

- to formulate the basic concepts and terms of the technology of infusions and decoctions;
- focus in the main directions of state regulation of production of infusions and decoctions;
- read recipes in Latin, analyze their components and evaluate the correctness of discharge;
- use DF and the International Pharmacopoeia, other regulatory and technical documents, as well as reference books to search for information on the composition, preparation, storage and dispensing of drugs.

- educational:

-This lecture is aimed at the development of a significant professional personality structure; nurturing students of modern professional thinking.

3. Plan and organizational structure of the lecture.

№№ Pp	The main stages of the lecture and their content.	Objectives at the levels of abstraction.	Type of lecture push lecture	Time distribution
1	2	3	4	5
1.	***Preparatory stage***			
	Definition of learning objectives.			2%
	Providing positive motivation	I		2%
2.	***Main stage***			
	Statements of the lecture material. Plan: 1. Methods of prescribing infusions and decoctions.			
	2. Rules of preparation of infusions and decoctions of vegetable raw materials and the addition of medicinal substances to them according to the requirements of the State Pharmacopoeia.	II III	References, visual material. The State Pharmacopoeia, the main regulatory and technical documentation.	85% - 90%
	3. Features of the preparation of aqueous extracts from herbal raw materials containing alkaloids, cardioglycosides, essential oils, tannins, anthracene derivatives, saponins and the like.	II		
	Special cases of preparation of infusions and decoctions (“double” infusions, decoctions of senna leaves, etc.). Author's recipe of water extracts (Dryagin's mixture, Quater, Ravkina, etc.).			
	Quality assessment, storage of water extracts, blockage and clearance for release.			
3.	***The final stage***			
	Summary of lectures, general conclusions.	I		
	Lecturer's answers to possible questions.		References, questions, tasks.	2%
	Tasks for student self-training..			2%
				2%

4. The content of the lecture material:

By their physico-chemical nature, aqueous extracts are combined dispersed systems: a combination of true solutions or solutions of high molecular compounds with colloidal solutions. Sometimes emulsified or suspended components are transferred to the hoods.

Water extracts are widely used in medical practice by themselves, as well as as components of medicines in the form of mixtures, rinses, lotions, washes, baths, inhalations.

The positive qualities of this dosage form include:

- the maximum therapeutic effect of the action of the complex of biologically active and su-track substances contained in plant raw materials;
- prolonged action;
- no side effect common to many chemicals;
- for some of the active substances contained in the plant material, methods for isolating them in their pure form or chemical structure have not been developed, and therefore they cannot be synthesized or obtained in any other way;
- ease of manufacture.

The negative qualities of water extraction include:

- instability during storage (microbial, chemical, thermodynamic), which limits the shelf life;
- non-standard extraction through numerous factors affecting their quality in the manufacture;
- cooking duration.

THEORETICAL BASIS OF THE PROCESS OF EXTRACTION OF MEDICAL PLANT RAW MATERIALS

The process of extracting active ingredients from raw materials is very complex and consists of the stages of *swelling,* the *formation of primary juice inside the cells and mass transfer* .

The process of extracting plant material is not a simple dissolution of the plant constituents. It should be considered as a series of physicochemical processes taking place both inside the cell and on its surface. Along with the processes of dissolution occur the phenomena of diffusion, osmosis, adsorption, etc. For extraction, dried material is most often used, in which as a result of moisture loss the volume of protoplasm decreases, and the voids in the cell membrane are filled with air.

Stage swelling. In the first moments of contact with the extractant, the cells of the dry plant material swell. The duration of this process depends mainly on the histological structure of the plant material, on the degree of its grinding, and on the nature of the extractant. In the course of cell swelling, the air is displaced from them by the extractant, first pulling out both soluble and insoluble substances from external, mainly destroyed cells.

The stage of formation of the primary juice inside the cells. Then the extractant penetrates the insoluble membranes into the deeper cells and dissolves the substances contained in them, forming a concentrated solution with a high osmotic pressure - “primary juice”.

Stage of mass transfer . As a result of the high concentration of "primary juice inside the cells, a significant osmotic pressure is created, causing a diffusion exchange between the contents of the cells and the surrounding fluid with a lower osmotic pressure. This is the basis of the extraction process, which leads to the dilution of the resulting concentrated solution with an extractant that is outside the cells. This process of diffusion and osmosis occurs until equilibrium is reached, that is, the concentration of substances that pass through the cell wall, in the cells and outside will be the same.

When this happens molecular and convective diffusion.

Molecular diffusion is the transfer of matter through the chaotic motion of molecules, which depends on the kinetic energy of the particles (molecules). The speed of molecular diffusion depends on the temperature of extrusion (as it increases, the speed of movement of molecules increases), the size of the surface separating the substance, the thickness of the layer through which diffusion passes. Finally, the movement of a substance requires a certain time (the longer the diffusion lasts, the greater the amount of substance passes from one medium to another).

The formula is given for diffusion flowing in one direction. In 1905, A. Einstein derived the time dependence of the diffusion coefficient.

Convective diffusion is the transfer of a substance as a result of the reasons causing the movement of a liquid: shock, temperature change, mixing. This type of diffusion is much faster and occurs due to convection, that is, transfer of mass from one place of the moving medium to another.

Ehis process can be expressed by the equation Fika Shchukarev

$$\frac{DS}{d\tau} = - DF \frac{dc}{dx}$$

$\frac{DS}{d\tau}$ - diffusion rate

D- molecular diffusion coefficient

F- area of diffusion exchange (total area of grinding plant material)

$\frac{dc}{dx}$ - concentration gradient (change in the concentration of a substance at a distance dx) - the diffusion process is directed towards a decrease in concentration

Due to the fact that the extraction process under the conditions of the pharmacy is carried out with the same amount of extractant, the active substances

are never completely extracted from the plant material, which is one of the drawbacks of the existing methods.

To increase the efficiency of the extraction process, it is necessary to maintain the maximum possible concentration of substances inside and outside the plant material by feeding "fresh" portions of the extractant until the equilibrium state occurs. This is achieved by mixing. On this basis, DF XI prescribes that upon receipt of infusions and decoctions of the infusion of raw materials with frequent mixing.

Thus, stretching consists of the following main processes: diffusion, desorption, dissolution, dialysis and leaching, which occur spontaneously and simultaneously.

Factors that affect the completeness and speed of extraction of active substances. The dynamics of the extraction process, and consequently, the quality of the infusions and decoctions are influenced by the following factors *: the ratio between the amount of raw material and extractant; standard of raw materials; histological structure of raw materials; the degree of grinding of raw materials: the material used equipment; temperature and time of infusion; influence of enzymes and microflora: chemical composition of active substances; pH of the medium.*

The ratio of raw materials and extractant. Infusions and decoctions in recipes can be prescribed in various ways:

1. Indicate the amount of the original plant materials and the volume of water extraction. For example:

Rp . Infusi herbae Hyperici ex 10.0-200 ml
Da. Signa. For rinsing the mouth .

According to the words, it is necessary to prepare 200 parts by volume of infusion from 10 parts by weight of the herb of Hypericum.

2. Only the exhaust volume is indicated. In this case, the doctor gives the pharmacist the right to decide on the amount of plant raw materials in accordance with the instructions of DF XI.

If the amount of medicinal plant materials in the general list is not specified in the recipe, infusions and decoctions are prepared in the ratio (1:10). For example:

Rp .: Infusi herbae Leonuri 200 ml
Da . Signa . 1 tablespoon 3 times a day.

In this case, it is necessary to prepare 200 volume parts of the infusion from 20 weight parts of the grass of motherwort.

Infusion of adonis herb, rhizomes with valerian roots is prepared at the rate of 1:30 (according to DF X, water extracts from a knotweed, lily of the valley grass, centaury root, sena, cyanosis, dog soap, tubers of sea onions are prepared in the same ratio).

Extractions from medicinal plant materials containing potent substances (thermopsis herbs, leaves of digitalis, etc.) are prepared according to a doctor's

prescription, and in the absence of indications about the amount of raw materials - in a ratio of 1: 400 and mainly from extracts-concentrates.

To get full-fledged extracts, you need to use the maximum possible amount of water under the given conditions, because the doctor in the prescription indicates the amount (volume) of the finished extraction, and not the water necessary to obtain it. It should be borne in mind that some of the liquid after extraction is always retained (absorbed) by the plant material, therefore the prepared extract is less than what was taken of water. To obtain the required amount of extract, you have to add water, which leads to a partial dilution of infusion or decoction. This is undesirable, because the loss of active substances is proportional to the amount of liquid that remains in the raw material. By squeezing the raw materials, these losses can be somewhat reduced, but it is impossible to completely get rid of them, because under the influence of capillary forces, part of the extraction will always remain irreversibly in the plant material. In addition, water loss occurs due to evaporation and wetting of the walls of the hospital. In this regard, for the manufacture of water extracts, it is advisable to take water a little more than necessary by the recipe of the finished extract.

The amount of water absorbed depends on the histological structure and the degree of grinding of raw materials. Therefore, it is necessary to use individual coefficients of water absorption by raw materials.

The coefficient of water absorption (K) shows the amount of fluid retained by 1.0 g of vegetable raw materials of the standard degree of grinding after it is squeezed in a perforated glass.

For the most commonly used types of raw materials Kv are given in DF XI, as well as in the order of the Ministry of Health of Ukraine No. 197 dated 09/07/93 (see Appendix 3). If Ki is not specified, then it is recommended to use generally accepted coefficients: for roots - 1.5; bark, flowers and herbs - 2.0; seeds - 3.0.

Thus, the amount of water needed to make an infusion or decoction is determined by summing the extraction volume indicated in the recipe and the additional amount of water, which is calculated by multiplying the mass of raw material by the water absorption coefficient.

For example, to obtain 200 ml of infusion from the grass of the motherwort water should be taken: 200 + (20.0 x 2) = 240 ml.

This additional amount of water significantly improves the process of extracting the active substances and increases their content in the prepared infusions and decoctions, and the more difficult the active substances dissolve in water, the better is the addition of water.

However, in the manufacture of hoods, taking into account the coefficient of water absorption, their volume still turns out to be slightly less, therefore, according to DF XI, water is added to the filtered extract after pressing the raw material through the same raw material to the volume prescribed in the recipe.

The amount of water required to obtain the hood, can not be reduced, because it will reduce the extraction of active substances from raw materials. Therefore, in multicomponent prescriptions for liquid dosage forms containing aqueous extracts

and powdered substances, in the case of preparing infusions and decoctions of vegetable raw materials, it is impossible to use concentrated salt solutions.

Standard raw materials. The composition and concentration of aqueous extracts, the strength and nature of their action on the body depend on the feedstock and, in particular, on the content of active substances in it. The amount of the latter in the plant material varies depending on the conditions and zoning of plants, the time of collection, the mode of drying and other factors. *Standard is called raw materials, which meets the requirements of NTD* . Medicinal raw materials must be supplied to pharmacies with an indication of the percentage of active substances or biological activity in units of action (ED) on the label of the package

According to DF XI, only standard can be used to obtain aqueous extracts, or raw materials with a high content of active substances and increased biological activity.

In this case, it is necessary to recalculate non-standard raw materials according to the formula: $X = \frac{A \times B}{Б}$,

de X - the amount of raw materials with a high content of active substances ;

A - the amount of raw material prescribed in the recipe, g;

B - the actual amount of active ingredients in raw materials, expressed as a percentage or

the amount of IU in 1.0 g of raw materials ;

B - the standard content of active substances in the same units.

For example, a thermopsis herb with a content of 2.5% alkaloids entered the pharmacy (standard of raw materials according to DF is 1.5%), then according to the presented recipe:

Rp .: Infusi herbae Thermopsidis ex 0.5 - 200 ml

Da . Signa . On 1 tables about th bed ke 3 times a day.

It is necessary to take instead of 0.5 g of thermopsis grass - 0.3 g.

$$X = \frac{A \times B}{Б} = \frac{0{,}5 \times 1{,}5\%}{2{,}5\%} = 0{,}3 \text{ г}$$

It is unacceptable to use raw materials containing less active substances than that provided by DF XI, because this results in water extracts with a high content of associated substances that are cloudy and less persistent during storage.

Histological structure of raw materials. The speed of extraction depends on the structure of the cell membranes, which is a significant obstacle to the passage of the extractant, and to a greater extent than they are thicker and denser. If the cell membrane is very dense, the cellular tissue is not sufficiently loose, and there are few intercellular passages and channels, then extraction proceeds more slowly. Of great importance is the composition of the cell membrane. The skeleton of the cellular tissue consists of cellulose. Cell tissue of many plants is impregnated with cutin, cerin and lignin, which impede the wetting of cellulose. Pectins, which are impregnated cell walls, swell under the action of cold water, and form boiling hydrosol in boiling water. The presence of other hydrophobic and hydrophilic substances in plant material also delays stretching.

In the manufacture of aqueous extracts, the choice of the method of extraction of plant material, as a rule, is determined by its histological structure. From loose raw materials (flowers, leaves, herbs), usually infusions are prepared, from dense (bark, roots, rhizomes) -steals. Exceptions: roots with rhizome of valerian (prepare infusion), bearberry leaves, senna, cowberry (decoctions).

The degree of grinding of plant material. To obtain water extracts, plant materials are used in dried, crushed and sifted form. Grinding of plant materials is caused by the need to facilitate the penetration of the solvent into the thickness of the material, which has a cellular structure of different anatomical structure and contains an unequal amount of hydrophilic substances that improve the wettability of raw materials.

With an increase in the degree of grinding of plant materials, the surface of its contact with the extractant increases, which facilitates its penetration into the cells, and, consequently, the process of extraction is accelerated.

However, very fine grinding in practice turns out to be irrational. Fine powder is easier to caking, and with a significant content of pectin in it, mucus and starch, the dissolution and swelling of these substances is facilitated and lumps are formed (due to the gluing of the lysing cells), which settle to the bottom of the vessel. All this greatly slows down the process of extraction. In addition, with the increase in destroyed cells, the leaching process is enhanced, which results in a turbid extract, which is likely to deteriorate.

According to DF X, leaves, flowers and herbs were chopped up to 5 mm, bearberry leaves, eucalyptus, cowberry and other leathery leaves - up to 1 mm; stems, bark and roots - up to 3 mm; fruits and seeds - up to 0.5 mm. The particle size of the corn stigmas should be no more than 10 mm.

However, for each type of plant raw materials, an optimal degree of grinding should be established, which ensures the completeness and speed of extraction of the active substances.

Therefore, DF XI indicates that vegetable raw materials should be shredded in accordance with the requirements of NTD (that is, the degree of grinding of certain types of raw materials should be specified in their own articles). The optimal particle size of the raw materials should not exceed 7 mm. For example, the grass of St. John's wort is 7 mm, the leaves of the sena are 7 mm, the bark of viburnum is 7 mm, the leaves of lingonberry, bearberry, wild rosemary sprouts 3 mm,

eucalyptus leaves 5 mm, alder seedlings 10 mm. Of all the known principles of crushing plant materials (crushing, cutting, grinding, splitting, abrasion, etc.) most often used in the pharmacy: cutting (for herbs, leaves, roots) with the help of herbs or koreneriz, crushing and abrasion in a mortar (for seeds and fruits). As a rule, the raw materials in pharmacies come already crushed, or cut-pressed or bricketed, which is the most optimal,because the pieces crushed by the rolls of raw materials do not contain air inside, which contributes to the rapid penetration of the solvent into the cells and more complete use of raw materials.

The temperature and duration of the extraction process (extraction kinetics). The mode of extraction, that is, the temperature conditions of extraction and the duration of the contact of the plant material with the extractant, affecting the qualitative and quantitative composition of the extract.

Increasing the temperature increases the rate of diffusion exchange and therefore speeds up the extraction. At the same time, hot water separates pieces of raw materials, separates plant tissues, facilitating the penetration of water into the deeper layers of pieces of raw materials. In most substances, extractable, with increasing temperature increases solubility and diffusion. It is important that the temperature rises gradually, and therefore, pectins, proteins, gums have time to dissolve and prodifunduvi before you curl or swell. In addition, the effect of temperature leads to the death of microorganisms, which is very important to preserve the quality of aqueous extracts.

On the other hand, prolonged exposure to high temperature leads to the destruction heat-labile substances, for example, cardiac glycosides group of essential oils. Heating is also undesirable given the significant increase in the output of related substances and the loss of volatile components.

In the pharmacy practice for the preparation of aqueous extracts use the methods of hot extraction - Infusa calide parata (infusions, decoctions, mucus) and cold extraction - Infusa frigide parata (only for infusion of Althea root).

According to the requirements of DF X and XI, infusions are heated in a boiling water bath for 15 minutes, decoctions - for 30 minutes. After the termination of the indicated periods of extraction, it is cooled at room temperature: infusions - within 45 minutes, decoctions - 10 minutes.

In the manufacture of water extracts from medicinal plant materials with a volume of 1000–3000 ml, the heating time in a water bath for infusions is increased to 25 minutes, for decoctions - 40 minutes; cooling time remains the same (45 and 10 minutes, respectively).

In the case of instructions in the recipe "Seiu" (if necessary, to quickly prepare the aqueous extract), the infusion is carried out for 25 minutes, followed by artificial cooling.

Thus, the process of infusions and decoctions differs only in the duration of thermal exposure. The question of the duration of the temperature regime of infusion for infusions and decoctions has not yet been developed sufficiently, despite the fact that it is these factors that are most likely to influence the kinetics of the extraction process. In the pharmacopoeias of different countries are different modes of insistence.

The duration of the cooling and the temperature of the stretching process greatly influence the quality of the preparation. To the question of the value of the duration of cooling infusions and decoctions must be approached differentially depending on the chemical composition of the medicinal raw materials.

According to DF XI, infusions are filtered only after complete cooling, no earlier than 45 minutes. This is due to the fact that a 15-minute infusion in a water bath is usually not enough to completely extract the active substances from vegetable raw materials and an additional extraction process takes place during cooling.

For some cooling infusions, it is also important because their active ingredients are more soluble in cold than in hot water. For example, the digitalis glycosides (in particular, digitoxin) or adonis (adon o Vernozide) coagulate when heated in an infusion on a boiling water bath and go back into solution only during the cooling of the infusion.

In other cases, in the process of cooling the hood, it self-purifies from some accompanying (ballast) substances, which are not soluble in cold water and precipitate (resin, etc.).

The cooling stage for decoctions is shorter than for infusions, which is due to the long duration of their infusion in a water bath and the content of a significant amount of IUDs, the solutions of which, after cooling, thicken and poorly percolate.

Enzymes and microflora. As you know, medicinal plants contain numerous enzymes that are substances of protein nature. Under the influence of enzymes in a living plant, very complex processes of formation and decomposition of various substances occur.

Most of the enzymes, while in a living plant, determine the vital processes in it. Moreover, during the life of the plant, the actions of the enzymes are directed and regulated by the plant. When the plant dies off, a deep decomposition of substances (including active ones) begins as a result of the chaotic action of enzymes - this process is called autolysis: complete self-dissolution (destruction) of substances entering the cell.

The activity of enzymes takes place mainly in a humid and weakly acidic environment. Short-term exposure to temperatures above 60-70 ° C usually leads to denaturation and inactivation of enzymes.

In this regard, a number of researchers propose to fill in plant material with hot water. However, as shown by studies of other scientists, the action of enzymes is not instantaneous. Therefore, if you pour the plant material with cold water and put it to heat, then in 5-10 minutes, until the water temperature reaches 60-70 ° C (enzyme inactivation temperature), a noticeable decomposition of the active substances will not occur.

At the same time, the use of cold water creates the best conditions for the extraction of active substances from plant material, containing a significant amount of protein substances. During the drying of plant materials, a protein film is formed at the cell walls. Protein under the action of cold, with gradual heating, water swells and dissolves. Until the moment when water is heated to the temperature of

protein coagulation, it is distributed throughout the cell cavity and drops out in the form of small flakes, which do not interfere with the extraction process.

The destructive activity of enzymes stops when the plants are dried. Therefore, its drying is of great practical importance for the stabilization of plant materials. All types of fresh plants should be dried as soon as possible after they are harvested. In pharmacies, water extracts are prepared only from dried plant materials, which are stored in a dry and ventilated room (the methods and conditions of drying can be different, described in detail in manuals on pharmacognosy).

In the manufacture of aqueous extracts, it must be borne in mind that plant raw materials are not free from microorganisms. Even in well-preserved raw materials, various soil microorganisms are usually found. Microflora can get into the hood and from the air during manufacture and, causing various fermentation processes (lactic acid, acetic acid, alcoholic fermentation), lead to damage. The temperature of a boiling water bath leads to the death of microorganisms. If necessary, various preservatives approved for medical use are added to water lifts in the manufacturing process.

5. Material activating of students during the presentation of the lecture / problem questions, problem situations, etc. /.

Control questions:

1. Characteristics of infusions and decoctions as dosage forms and disperse systems. Ways of prescribing infusions and decoctions.
2. The theoretical basis of the extraction process from plant materials.
3. Factors affecting the extraction process.
4. Rules for the preparation of infusions and decoctions of medicinal plant materials and the addition of various medicinal substances to them in accordance with the requirements of regulatory and technical documentation.
5. Apparatus used for making infusions and decoctions.
6. Features of the technology of infusions and decoctions of raw materials containing alkaloids, cardiac glycosides, essential oils, tannins, saponins.
7. Special cases of cooking infusions and decoctions ("double" infusions, decoctions of the leaves of the seine, etc.).
8. Author's recipe of water extracts.
9. Features of the preparation of aqueous extracts from raw materials containing mucus (althea root, flax seeds, etc).
10. Quality assessment, packaging rules, design and storage of infusions and decoctions in accordance with the requirements of regulatory and technical documentation.

Test items:

1. A pharmacist prepared an infusion of Althea roots. In what proportion did he take the amount of medicinal plant materials and extractant?

* 1: 20
1:10
Half past one
1: 100
1: 400

2. The pharmacy is preparing water extracts from LSR. Specify the group of BAR extraction of which is carried out in a tightly closed information and filtering after complete cooling?

* essential oils
alkaloids
cardiac glycosides
tannins
saponins

3. A pharmacist prepared an infusion of rhizome with valerian roots. What is the ratio of raw materials and extractant for the preparation of exhaust?

* 1:30
1: 400
1:10
1:20
1:40

4. A pharmacist prepared 100 ml of chamomile infusion. Specify the amount of raw materials and extractant he used to prepare the hood (Kvodopogl. = 3,4)

* 10 g of chamomile flowers, 134 ml of water
20 g of chamomile flowers, 234 ml of water
10 g of chamomile flowers, 200 ml of water
20 g chamomile flowers, 200 ml of water
5 g of chamomile flowers, 234 ml of water

5. A pharmacist prepared 200 ml of oak bark decoction. Specify how to filter this hood:

* immediately
in 10 minutes
after complete cooling
in 3-4 hours
after 45 minutes

6. Shelf life of infusions, decoctions, mucus she made in the pharmacy is:

* Two days
One year
Ten days
Three days
Five days

7. The doctor prescribed 100 ml of infusion of 0.25 g of thermopsis herb. Specify the amount of dry extracts of thermopsis herb concentrate that the pharmacist should weigh:

* 0.25 g .

0.5 g .
0.3 g .
0.2 g .
0.1 g

8. Patient ntu released from the pharmacy mint leaves . What recommendations regarding the preparation of an infusion should pharmacist give when dispensing medicinal plant materials?

* Prepare the infusion in a tightly closed container.
Cook infusion on an open fire.
Prepare the infusion at room temperature.
After insisting extract the strainer immediately.
After 15 min Infusion hood cooled artificially.

9. For the patient prepare the tincture of the roots of Althea. Should the pharmacist apply the infusion to prepare this medicine?

* 30 min. at room temperature.
60 min at room temperature.
15 minutes. infusion in a water bath and 45 min. cooling at room temperature.
30 min. insist on a water bath and 10 min. cooling at room temperature.
30 min. insisting on a water bath and filtering immediately without cooling.

10. The patient was released from the pharmacy sage leaves. What recommendations regarding the preparation of an infusion should pharmacist give when dispensing medicinal plant materials?

* Prepare the infusion in a tightly closed container.
Cook infusion on an open fire.
Cook only a decoction.
After insisting extract the strainer immediately.
After 15 min Infusion hood cooled artificially.

6. General material and methodological support of the lecture:

- *educational premises;*
- *equipment;*
- *equipment;*
- *illustrative materials* .

7. Materials for self-preparation of students:

a) on the topic of the lecture presented / literature, questions, tasks, test tasks /;

b) on the topic of the next lecture / literature, a list of key questions, test items /.

8. The literature used by the lecturer to prepare the lecture.

Basis literature:

1. Drug technology. Teaching aid: Textbook for higher educational institutions / VI Tikhonov PA Logwin, SA Tikhonov AV Mazulya and n, TG

Yarnih, A. Špičák, A M. Kotenko; Edited by A.I. Tikhonov - Kharkiv: NUPh; Original, 2009. - 432 p.

2. Medicine technology: study guide / O.S. Marchuk, N. Would. Androschuk - Kiev: Medicine, 2008. - 488 p.

3. Production of medicines. Quality control and regulation: prak.ruk. / ed. Sh.K. Gad; per. from English V.V. Coastal. - SPb .: Profession, 2013. - 960 pp.

Additional:

1. Soft dosage forms: Exttemporal formulation: Methodical recommendations / A. I. Tikhonov, T. G. Yarnikh, A. V. Lukienko, etc .; Ed. A.I. Tikhonov. - X .: Type of NUPh; Golden Pages, 2003.-128 p.

2. Aseptic dosage forms: Ecological temporal formulation: Methodical recommendations / A. I. Tikhonov, L. V. Bondareva, T. G. Yarnikh, N. F. Orlovetska, etc .; Ed. A.I. Tikhonov and T. G. Yarnikh. - X .: Type of NUPh; Original, 2005. - 184 p.

3. Solid dosage forms: Ecsttemporal formulation: Methodical recommendations / A.I. Tikhonov, T.G. Yarnikh, S.V. Gritsenko and others; Ed. A.I. Tikhonov - Kh .: Type of NUPh; Golden Pages, 2003. - 176 p.

4. Liquid dosage forms: Ecstemporal formulation: Methodical recommendations / A.I. Tikhonov, T.G. Yarnikh, N.F. Orlovetska and others; Ed. A.I. Tikhonov and T. G. Yarnikh. - X .: Type of NUPh; Original, 2005. - 160 p.

Lecture 7: «Soft dosage forms. Linimenta. Ointments are homogeneous. Ointments heterogeneous, combined»- 2 h.

1. Relevance of the topic. Substantiation of the topic. Liniment are among the ancient dosage forms that are widely used in everyday life, in various industries, in cosmetics and medicine in order to protect the skin of hands and exposed parts of the body (face, neck) from the effects of organic solvents, solutions of acids, alkalis and other chemical irritants and allergens; to soften skin, nourish it with vitamins, fats, remove pigment spots, treat and remove warts, freckles and other cosmetic skin imperfections.

A special place is occupied by liniments, which are widely used in various fields of medicine: dermatology, gynecology, proctology, laryngology, etc. even into the bloodstream. They are applied to the skin, wounds, mucous membranes by smearing, rubbing or using dressings.

2. Objectives of the lecture:

- training:

- to formulate in students the basic concepts of technology of liniments;

-define requirements for liniments;

- teach to navigate in the main directions of state regulation of the production of liniments

- teach to read recipes in Latin, analyze their components and evaluate the correctness of discharge;

educational:

-To develop skills to use SPh and the International Pharmacopoeia, other regulatory and technical documents, as well as reference books to search for information on the composition, preparation, storage and dispensing of drugs.

3. Plan and organizational structure of the lecture.

№№ pp	The main stages of the lecture and their content.	Objectives at the levels of abstraction.	Type of lecture, lecture equipment	Time distribution
1	2	3	4	5
1.	***Preparatory stage***			
	Definition of learning objectives.			2%
	Providing positive motivation	I		2%
2.	***Main stage***			
	Statements of the lecture material.			
	Plan:			
	1. Classification of liniments.		References,	5%
	2. Basic terms and concepts of liniments.		visual material.	5%
			State	10%
			Pharmacopoeia,	20%
	3. State regulation of the production of liniment.	II	basic regulatory	20% -30%
			and technical	10%
	4. Basic regulatory and technical documentation.		documentation	10%
		III		5-10%
	5. Quality control of liniments in a pharmacy.			2%
				2%
		II		
3.	**The final stage**			
	Summary of lectures, general conclusions.		References,	
	Lecturer's answers to possible questions.	I	questions,	10-20%
	Tasks for self- study student.		tasks..	

4. The content of the lecture material:

Liniment (or liquid ointment) - dosage form for external use, which is a thick liquid or gelatinous mass, melting at body temperature.

Liniment takes an intermediate position between liquid and soft dosage forms: they are very close to other groups of ointments for the substances used, method of application, at the same time, manufacturing techniques, liquid consistency combine them with liquid dosage forms.

The name of the liniment comes from the Latin word *linire (rub)* and indicates the method of using this dosage form - by rubbing it into the skin. This characteristic feature distinguishes liniments from other groups of ointments and liquid dosage forms for external use (drops, washes, lotions).

Liniment - an ancient dosage form , which has not lost its value in the present. In DF XI, liniments are included in the general article “Ointment”. In DF X, they are highlighted in a separate article No. 376 "Liniment".

In the directory of MD Mashkovsky "Drugs" are about 20 formulations of liniments. Pharmacopoeial prescription of liniments are presented in table. 22

The modern ex temporal recipe of liniment is diverse and can be quite complex. A significant amount of liniments produced by the industry. *These are liniments-solutions: capsin, capsitrin, pepper-camphor, pepper-ammoniac, complex chloroform, methyl salicylate complex, complex turpentine, sanitas; liniments-emulsions: ammonia, naphthalgin; liniments-suspensions: balsamic according to Vishnevsky; combined liniments: chloramphenicol, streptotsida.*

The widespread use of liniments in medical practice is due to their advantages:

- medicinal substances from liniment are easily absorbed by the skin, that is, they have a high biological availability;

- in comparison with ointments, liniments are easier applied to the skin;

- fewer marks are left on the skin and clothes of the patient.

- The disadvantages of this dosage form:

- low stability of a number of formulations;

- inconvenience of transportation.

Classification of liniments. There is a medical and physico-chemical classification. For the therapeutic effect of liniments are *analgesic, irritating (distracting), anti-inflammatory, astringent, desiccant, insecticidal, fungicidal* . The most common analgesic and irritating liniment.

Physico-chemical nature of the liniments are dispersed systems with a liquid dispersion medium. By the nature of the dispersion medium, the liniments are divided into *fatty, alcoholic, soap-alcoholic, vazolimeti* .

Fatty liniments (Linimenta pinquia sen Olimenta) as a dispersion medium contain fatty oils or fat-like substances (lanolin). The most commonly used sunflower, flaxseed, castor oil. The composition of fatty liniments can include both liquid medicinal substances (chloroform, turpentine, ether, tar), and powdered (camphor , menthol, novocaine, dermatol, etc.).

Alcohol liniments (Linimenta spirituosa) contain alcohol or tinctures (most often pepper tincture), as well as various medicinal substances.

Soap-alcohol liniments (Saponimenta) as a dispersion medium contain alcohol solutions of soap. They can be liquid (if they contain potassium soap) or dense, gel-like (if they contain sodium soap). When rubbed into the skin cause emulsification of sebum, so quickly penetrate into it, seizing medicinal substances.Vasoliatings (Vasolimenta) are characterized by the presence of

vaseline oil. Due to the chemical inertness of vaseline oil, they are quite stable during storage. Nowadays, soap-alcohol liniments and vazimentimentov are rarely used.

According to the type of dispersed systems, the liniments are divided into homo - and heterogeneous. Treat homogeneous: liniments-solutions and extraction, to heterogeneous - liniments-suspensions, emulsions and combined.

OWN LINES TECHNOLOGY

Liniments-solutions - *a transparent mixture (true or colloidal solutions) fatty oils, essential oils, chloroform, methyl salicylate, ether, turpentine.* Their composition may include a variety of solids that are soluble in prescribed liquids: camphor, menthol, anestezin, etc. A typical example of liniment-solution is complex rubbing with turpentine :

Rp .: Chloroformii 10.0
Olei helianthi
Olei Therebinthinae aa 20.0
Misce. Da. Signa. Vtirat s in the affected joint.

Liniment-solution, which includes a potent, photosensitive substance - chloroform, odorous - turpentine and photosensitive - sunflower oil. All three liquid components are interdependent in one.

In the dry oh A tared glass for orange glass leave is weighed out 20.0 g of sunflower oil, then (without removing from the balance) 10.0 g of chloroform and last of all - 20.0 g of turpentine. Shut up, shake up to uniformity and make out for holiday.

WPC

Date No recipe

Olei helianthi 20.0
Chloroformii 10.0
Olei therebinthinae 20.0

$M_{total.}$ = 50 ml

Prepared: (signature)
Checked: (signature)

Rp .: Mentholi 2.0
Camphorae 3.0
Olei Helianthi 80.0
Methylii salicylatis 5.0
Misce . Da. Signa. Rub into the sore joint

Liniment-solution, which consists of volatile, odorous substances - menthol and camphor, forming a eutectoid mixture, odorous, volatile, light- sensitive substance - methyl salicylate, light-sensitive - sunflower oil.

Dry substances are prescribed (menthol, camphor) well soluble in sunflower oil, however, due to the formation of a eutectic mixture, they should be dissolved in turn or in separate portions of solvent.

To a dry flask to leave a dark glass placed 2.0 g menthol, tar ir comfort and weighed 80.0 g of sunflower oil, dissolved (by heating on a warm water bath). After the menthol is completely dissolved, 3.0 g camphor is added and dissolved. At last, add 5.0 g of methyl salicylate. Shut up, shake and make out to leave.

To jinyment-solutions are also gel-like mass, melting at body temperature. For example, iodine-chloroform-paraffin liniment - Rosenthal paste .

Rp .: Iodi 0.3
Paraffini 15.0
Spiritus aethylici 95% 10 ml
Chloroformii 80.0
Misce. Da. Signa. For warm dressings.

Liniment-solution at the time of manufacture and use, which consists of two potent photosensitive substances - iodine and chloroform. Iodine is slowly soluble in alcohol, well - in chloroform, therefore, it is better to dissolve it in chloroform. Paraffin is soluble in chloroform when heated. Chloroform mixes well with alcohol.

0.3 g of iodine, weighed on parchment paper, are placed in a dry flask for dispensing, 15.0 g of paraffin grated on a grater are added, tared and 80.0 g of chloroform are weighed out. Then tightly closed with a stopper and heated in a warm water bath (temperature 40-50 ° C) to dissolve. After cooling, add 10 ml of 95% alcohol.

Shut up, shake up to uniformity. They are issued for leave with a signature with additional labels: “Warm up in warm water before use”, “Store in a cold dark place”, “Apply with a net or dots”.

Heated chloroform when dissolving paraffin must be very carefully, not tightly covering the glass so that the vial does not break. The patient should be warned that before applying the liniment should be heated in warm water, opening the lid, until the paraffin is completely dissolved. Apply this drug to the skin in the form of a mesh or dots, and not over the entire surface, because Rosenthal paste is an irritant liniment, and if it is rubbed into the skin, it causes severe burns.

In the manufacture of this drug, you can use ready-made 10% solution of iodine in 95% ethyl alcohol (if available at the pharmacy). In this case, paraffin is dissolved in chloroform in a glass for tempering (when heated), and then, after cooling, 7 ml of 95% ethyl alcohol and 3 ml of 10% iodine solution are added.

The composition of the paste of Rosenthal may include various medicinal substances, for example :

Rp .: Iodi 1.0
Kalii iodidi 2.0
Paraphinii 20.0
Spiritus aethylici 70% 20 ml
Chloroformii 130.0

Misce. Da. Signa. For warm dressings.

As is known from previous material, iodine is readily soluble in aqueous solutions of potassium iodide to form a complex compound, is readily soluble in alcohol th. Therefore, the technology of liniment according to this recipe will be as follows .

In a dry flask for tempering from dark glass, paraffin is dissolved in chloroform by heating. Potassium iodide is dissolved in a stand of 5.8 ml of purified water, iodine is dissolved in the obtained saturated solution of potassium iodide. 14.6 ml of 95% alcohol are added, transferred to a beaker for tempering with a chloroform paraffin solution, sealed, shaken and arranged for tempering.

If other medicinal substances, for example, novocaine, menthol, atropine sulfate, are additionally included in the paste of Rosenthal, they are administered according to the general rules: dissolved in the solvent in which they are better soluble: novocaine, atropine sulfate - in water; menthol - in alcohol, and then mixed with other components.

Liniment-suspensions are two-phase systems, which are thin suspensions of powdered medicinal substances that are not soluble in prescribed liquids.

Most often they include the following substances: zinc oxide, talc, xeroform, calcium carbonate, starch, sulfa drugs. Glycerin, fatty oils, alcohol, water, etc. are used as a dispersion medium. They are prepared according to the general rules for the manufacture of suspensions .

Rp .: Xeroformii
Picis liquidae Betulae aa 3.0
Olei Ricini 100.0
Misce. Da. Signa. For application to wounds .

Liniment-suspension which includes fragrant substance - insoluble tar and a first base, odorous, photosensitive - xeroform (Wisniewski liniment). For grinding xeroform as a suitable liquid, it is advisable to use tar (a less viscous substance than castor oil).

In a mortar is placed 3.0 g of xeroform weighed on a hand-held balance, ground in a dry form. Then add half the amount of tar - 1.5 g (measure drops) and crush xeroform according to the rule of Deryagin. While stirring, add 1.5 g of tar that remained, and parts of 100.0 g of castor oil (previously weighed in a glass for vacation). Transferred to the flask for the holiday, sealed and make out.

Balsamic liniment according to Vishnevsky is sometimes called Vishnevsky's ointment, which is connected with the method of using this drug - it is not rubbed into the skin, like most liniments, but smeared or applied to wounds using a sterile dressing.

In the Vishnevsky liniment recipe, the following substitutions are possible: xeroform - on dermato- l, tar - on Balsam Shostakovsky (vinylinum), and castor oil - on fish oil. For example :

Rp .: Xeroforrnii 3.0
Vinilini (Balsami Schostakovsky) 6.0
Olei ricini 100.0
Misce. Da. Signa.For application to wounds.

Vinylinum (polivinilbutil ester) - is a thick viscous liquid of characteristic odor, practically insoluble in water, it mixes well with oils. The manufacture of the drug in this recipe is similar to the previous recipe.

Currently, the Vishnevsky liniment is produced mainly in the factory. To increase stability during storage (prevention of xeroform sedimentation), 5% of aerosil is introduced into its composition (suggested by N. T. Alyushinim).

Rp .: Iodoromiii 10.0
Glycerini 45.0
Spiritus aethylici 95% 45 ml
Misce, fiat linimentum Da.Signa. For rubbing .

Liniment-suspension with insoluble in alcohol and glycerol odorous substance - iodoform. Iodoform is ground in a mortar in a dry form, and then about 4.0-6.0 g of glycerin, previously weighed into a vial (45.0 g), is added, carefully triturated, and the rest of the glycerin is added. Transferred from the mortar to the vial for tempering. The rest of the suspension is rinsed with 45 ml of alcohol in a bottle and arranged for dispensing .

Rp .: Zinci oxydi
Talciaa 5.0
Amyli
Olei Riciniaa 10.0
Olei Helianthi 70.0
Misce. fiat linimentum
Da. Signa. To put on the leg.

Liniment suspension containing medicinal substances not soluble in fatty oils. Powdered substances are placed in the mortar in the order of prescription, ground, about 10.0 g of sunflower oil (from a holiday wide-mouth bottle in which 70.0 g of sunflower oil are weighed in advance) is added and carefully ground to obtain a thin pulp. Then, in 2-3 doses remaining oil is added and stirred from time to time removing the mass from walls of the mortar and pestle tselluloi th bottom plate. 10.0 g of castor oil is weighed into the dispensing bottle, weighed, add it to the mortar and mix until a homogeneous mass is obtained. The finished liniment is transferred to the tempering bottle and drawn up for the release.

Liniments emulsion - *a two-phase system, which can be an emulsion of the M / B or B / A.* They consist of a mixture of fatty oils with alkalis or contain solutions of soap. Emulsifier or specified in prescription, or formed as a result of the interaction of components that make up the liniments. A typical example of what constitutes a B / B emulsion is ammonium liniment, or volatile .

Rp .: Olei Helianthi 74.0
Liquoris Ammonii caustici 25 ml
Acidi oleinici 1.0
Misce. Da. Signa. For rubbing

Emulsion liniment type M / B which contains an odorous liquid - ammonia solution. The emulsifier is ammonium oleate, which is formed as a result of the

neutralization reaction. The emulsion is formed easily, by shaking up two liquids with an emulsifier, so there is no need to prepare in a mortar.

74.0 g of sunflower oil are weighed into the flask, 1.0 g of oleic acid (drops) are added and stirred. Then add 25 ml of ammonia solution, seal and shake. Make out to leave.

Liniment is unstable and is preparing for a short time. During storage, ammonium oleate is converted to oleic acid amide (type II emulsion), the phases of the emulsion are converted and thicker. Such liniment before the holiday is not suitable. M. T. Aleshin proposed replacing sunflower oil in ammonia liniment with a polydiethylsiloxane liquid - esilon-4. Ammonium liniment prepared on the epsilon-4, stable throughout the year.

In emulsion liniments, limelining (DF VIII), which was previously widely used for burns, also applies. It consists of equal parts of flaxseed oil and lime water. The emulsifier is calcium oleate, which is formed by neutralizing the free fatty acids of linseed oil with lime water. Since this is an emulsifier of the second kind, an emulsion of type B / O is formed. In the manufacture shake in a glass for the sale of equal parts of lime water and linseed oil. Currently, limestone liniment is practically not used.

The combined liniments are a combination of various disperse systems: emulsions, suspensions, solutions. Prepare them according to the general rules for the manufacture of individual dispersed systems. Powdered medicinal substances are introduced into the composition of combined liniments, depending on their physicochemical properties: soluble in oil - introduced into the oil phase; soluble in water - in the aqueous phase to obtain an emulsion; insoluble, neither in water nor in oil, are injected as a suspension into the finished emulsion. For example :

Rp .: Linimenti ammoniati 50.0
Mentholi 0.5
Misce. Da. Signa. Rub the lower back .

Combined liniment emulsion-solution, which consists of fragrant, volatile substances, - ammonia solution and menthol; two viscous liquids - sunflower oil and oleic acid. Menthol is well soluble in oil, therefore, it must be introduced into the oil phase to obtain an emulsion.

0.5 g of menthol is placed in a glass for dispensing dark glass, the container and 37.0 g of sunflower oil are weighed out and dissolved. Add 0.5 g of oleic acid, dissolve, add 12.5 ml of ammonia solution, seal and shake vigorously.

Examples of combined liniments are syntomycin (1%, 5% and 10%), streptocide (5%) and levomycetin (1%).

Rp .: Laevomycetini 1.0
Olei ricini 20.0
Emulgentis 9.0
Thymoli 0.15
seu acid salicylici 0.125
Aquae purificatae ad 100.0

Misce. Da. Signa. For bandages .

Combined liniment: emulsion-suspension-solution. Castor oil with water and an emulsifier (emulsifier No. 1 of Ugryumov is used) forms an emulsion. Levomycetin - not soluble in water or oil, forms a suspension. Thymol (or salicylic acid) is introduced as a preservative. Since protection against microbial contaminated with N spine needs and to the aqueous phase, a preservative rational dissolve in water.

To prepare the oil, castor oil is fused with emulsifier No. 1, then with vigorous stirring a solution of preservative in warm water is added and emulsified. Levomycetin is crushed according to the Deryagin rule and injected into the finished emulsion. As part of the recipe includes an antibiotic (chloramphenicol), prepared under aseptic conditions. Tween-80 or T-2 emulsifier can also be used as an emulsifier.

In difficult cases of manufacturing of a liniment, the following is written

Rp .: Novocaini 0.5
Chloroformii 10.0
Mentholi 0.3
Olei Helianthi 30.0
Sol. Ammonii caustici 10 ml
Misce. Da. Signa. For rubbing .

Combined liniment: emulsion-solution, which includes two potent photosensitive substances - novocaine and chloroform; odorous volatile - menthol and ammonia solution. Sunflower oil with ammonia forms an emulsion. The emulsifier is the ammonium salts of free fatty acids of sunflower oil. Since there are few free fatty acids in the oils, the emulsion is coarse.

The difficulty is the introduction of novocaine. It is not soluble in oils, soluble in water. However, in an aqueous solution of ammonia with the hydrochloride salt of novocaine, a quaternary ammonium base of novocaine is released, insoluble in water, but well soluble in chloroform.

In a glass for tempering from dark glass, menthol is dissolved in sunflower oil. Novocain is dissolved in a stand in a solution of ammonia. The base of novocaine that has fallen is dissolved in chloroform and added to the flask for tempering, sealed, shaken vigorously and arranged for tempering .

QUALITY CONTROL, STORAGE AND IMPROVEMENT OF THE TECHNOLOGY OF LININGS

The quality control of liniments is carried out according to the deviation in mass, as well as by organoleptic indicators: uniformity, absence of impurities, color, smell.

Pack usually liniments in glass bottles with screw caps. In accordance with the instructions of the pharmacopoeia, liniments, as well as all ointments, are stored in a cool, dark place, unless otherwise indicated in personal articles. Heterogeneous liniments are decorated with an additional label “Shake before use”. Liniment thick consistency is released in wide mouth bottles.

The structural-logical scheme of technology and quality control of liniments is shown in scheme 11.

Improvement technology linimentov held in several directions.

The use of small-scale mechanization (installation for the preparation of ointments - UPM-2; mixers for emulsions and suspensions - WEH; tissue shredding - PT-2; dosing devices) allows not only to speed up and facilitate the manufacture of liniment, but in some cases in the manufacture of emulsion liniment to increase their quality.

Improving the stability of a series of liniment preforms can be achieved by correctly selecting and using new emulsifiers, thickeners, etc. To improve chemical stability, slow down the decomposition of lipophilic bases, the use of antioxidants (a-tocopherols, butyloxyanisole, etc.) is promising.

Reducing microbial action promotes the introduction of the cons liniments ervantov (benzyl alcohol, nipagin , n and pazol and , sorbic acid), and the development of new types of packaging.

Ointments are among the ancient dosage forms, are widely used in everyday life, in various industries, in cosmetics and medicine in order to protect the skin of hands and exposed parts of the body (face, neck) from exposure to organic solvents, solutions of acids, alkalis and other chemical irritants and allergens . To soften the skin, nourish it with vitamins, fats, remove pigment spots, treat and remove hair, warts, freckles and other cosmetic defects.

It occupies a special place ointment, widely used in various fields of medicine: dermatology, gynecology, proctology, general relativity . Laryngology, etc. Sometimes ointments prescribed as a general action of drugs for the purpose of bone resorption, ie the absorption they contain medicinal substances in the skin, subcutaneous tissues, and even into the bloodstream.

In the modern formulation of pharmacies ointments average 10-15%. they are applied to the skin, wounds, mucous membranes by smearing, rubbing or using dressings; sometimes tampons soaked in ointment are injected into the body cavity , or special syringes are used.

Ointments - soft dosage form intended for application to the skin, wounds or mucous membranes .

Ointments consist of base and medicinal substances, evenly distributed in it. In the ointment can be entered preservatives, surface-active and other excipients permitted for use.

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

Ointments as a dosage form have their positive and negative qualities. *Advantages* : the possibility of introducing into the composition of ointments of various medicinal substances (liquid, soft, solid) ; the possibility of prescribing ointments for the purpose of local or resorptive action; to achieve e the

high concentration of drug in the skin, tissues, biological fluids ; relative simplicity and safety of ointments compared with other dosage forms (injection, oral, etc.); profitability and manufacturability of ointments.

Negative qualities : some ointments have a limited range of pharmacological activity (unidirectional therapeutic effect, for example, only anti-inflammatory), separate ointment compounds on hydrophobic bases cause a pronounced "greenhouse" effect, which limits their use in medical practice . H ome ointment to the skin irritating.

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

The soft texture of ointments provides ease of application when smearing on the skin, mucous membranes, as well as the release of these drugs. Rheological parameters serve as a criterion for assessing the quality of ointments both during production and during their storage.

Ointments should have an optimal dispersion of medicinal substances and their uniform distribution, guarantees the maximum therapeutic effect and the invariance of the compound during storage. At the same time, they must be stable, free of impurities and with an exact concentration of medicinal substances.

CLASSIFICATION OF OILS

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

Ointments *surface action* - it ointments, skin not absorbed, the action of which is limited mainly layer of the epidermis or mucous surface. These include coatings, protective and cosmetic ointments.

The integuments soften the dry epidermis, prevent its drying and pollution, and protect damaged skin from microbial infections.

Protective in their intended use are close to the coverslip. Apply them for prophylactic purposes in various industries. They must protect the skin from the effects of toxic substances, solutions of acids and alkalis, solvents and other corrosive liquids.

Cosmetic ointments and creams are designed to treat or eliminate cosmetic skin imperfections.

Ointments *the deep*- soaked skin, and are divided into penetrating and resorptive.

To penetrate include ointments, penetrating into more or less deep e layers of the skin. The degree and depth of their penetration into the skin depends on the type of ointment base, the properties of medicinal substances in their composition, methods of application and other conditions.

From ointment bases, only soluble in lipids penetrate the skin, and among them vegetable and animal fats, similar in composition to human skin fat, penetrate better than others. Vaseline and other hydrocarbons themselves do not penetrate

the skin. The main barrier to absorption is the epidermis layer. Dermis, rich in lymphatic and blood vessels, does not interfere with absorption.

The penetration of ointment bases and medicinal substances into deep layers of the dermis probably occurs mainly along the ducts of the sebaceous glands. Ointment bases penetrate into healthy skin with intact epidermis much worse than skin without epidermis due to injury, disease process, etc.

Medicinal substances contained in the ointment penetrate healthy skin to varying degrees. Volatile (*iodine, mercury, essential oils*), lipid-soluble (alkaloid bases and some other substances) usually penetrate deeply. On the contrary, medicinal substances insoluble in lipids penetrate the skin much worse. Medicinal substances contained in the ointment in a dissolved form act more intensively than those contained in the form of a suspension. The penetration of medicinal substances from ointments applied to the damaged skin with the epidermis removed is approximately the same as that from the ointment applied to the mucous membrane. Penetrating ointments are, for example, antibiotic ointments.

Ointments of resorptive action are distinguished by the fact that the medicinal substances contained in them penetrate from the site of application of the ointment into the bloodstream. They are used mainly in cases where it is necessary to strengthen or supplement the effect of the drug, taken orally, or when another route of administration is inconvenient or impossible.

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

At the place of application, there are ointments: *dermatological* (actually ointments) applied to the skin; *ophthalmic* , applied to the conjunctiva of the eye; for the *nose* , which are applied to the mucous membrane of the inferior turbinate, *vaginal, urethral and rectal.* The last three types of ointments are introduced using special syringes.

According to the *physico-chemical classification of* ointments are divided by consistency, type of dispersed systems and ointment bases.

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

According to the type of dispersed systems (depending on the degree of dispersion of the drug substance and the nature of its distribution at the base), *homogeneous* and *heterogeneous* ointments are distinguished .

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

In this case, the drug is distributed in the solution based on the type that is brought to molecular or micellar minutes fineness. By Homogenous ennym include *ointments, solutions, ointments alloys and extraction ointment*.

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

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

By type (nature) of ointment bases, ointments prepared on: hydrophobic (lipophilic), hydrophilic and diphilic (hydrophilic-lipophilic) bases are distinguished.

Thus, the medical classification gives a general idea of the ointment (purpose, application, etc.), And the physico-chemical - reflects the technology of ointments and criteria for their quality.

BASES FOR OILS, REQUIREMENTS FOR THEM AND THEIR CLASSIFICATION

Ointment bases can be in the form of individual or the sum of various substances that determine the required volume, the appropriate consistency and some specific features of the ointment. Due to its consistency, the base is an excellent lubricant for the skin, making it soft, smooth, supple and prevents from drying out. Under the action of the base, the natural fat protection of the skin is enhanced, cracks and abrasions heal faster, water evaporation is reduced, due to which the horny layer swells and the natural heat is retained, thus achieving significant protection against moisture and cold. The latter circumstance is essential for swimmers who are in the water during the competition. In addition, the basics well absorb external contamination of the skin and facilitate its removal.

There is a complex relationship between the medicinal substance and the base, do not allow to consider it as an inert carrier that does not participate in the action of the ointment. Ointments must be considered as a unity of form and content. The form must be active in relation to the manifestation and disclosure of its content.

It has been proven that the medicinal substance itself, used as an ointment, can act quite differently depending not only on how it is introduced into the ointment, but also on what ointment base it is combined with. For example, the ointments of many antibiotics on petrolatum are inactive, but the same ointments prepared on hydrophilized petrolatum-lanolin base have a pronounced antibiotic effect.

Salicylic acid in the form of a 5% ointment on petrolatum has a predominantly surface effect. The same ointment, prepared on an emulsion basis, has a pronounced keratolytic effect.

Replacing the petrolatum-lanolin base with a water-soluble polyethylene oxide increases the activity of chloramphenicol by 30 times.

These and other studies show that the ointment base is not just an indifferent carrier, but an active component of the pharmacodynamics of the ointment.

The choice of the ointment base depends on the physicochemical properties of the prescribed drugs and the nature of the action of the ointment. The basis, which

would provide the maximum therapeutic effect of the ointment, must meet the *following requirements* :

- To have smearing ability, that is, the necessary structural and mechanical (consistent) properties: viscosity, plasticity, fluidity, thixotropy , etc.;

- Good to take medicinal substances, that is, to have an absorbent capacity;

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

- To be pharmacologically indifferent, not to have an irritating and sensitizing effect, to help preserve the original pH of the skin (3-4 units) or the mucous membrane;

- Do not succumb to contamination by microorganisms;

- It should not be dirty clothes, not be too sticky, it is easy to wash off with soap and without it;

- The properties of the base should be consistent with the purpose of the ointment: the basis of protective ointments, used for prophylactic purposes, should dry quickly and fit snugly to the skin surface; Bases for superficially operating ointments should not be soaked up; Basics for resorptive ointments should, on the contrary, penetrate deeply into the skin, reach the bloodstream and facilitate the absorption of medicinal substances.

However, ointment bases that would fully meet these requirements, no. Therefore, to obtain the necessary quality of the base often used mixtures of various substances (complex ointment bases).

The classification of grounds . Substances used as a basis for ointments differ in their sources, chemical composition, physicochemical properties, etc. This is reflected in the classification of the grounds given in various textbooks, textbooks, reviews and articles. A significant disadvantage of many proposed classifications is that they mix the bases for ointments with their individual components.

Depending on the sources of obtaining ointment bases and their components are divided into *natural* and *artificial*. The last group includes the basics, a variety of synthetic or semi-synthetic substances or their mixtures with each other, as well as with natural substances.

According to the chemical composition, the bases are divided into *glycerol esters with higher fatty acids, herd esters of these acids with high molecular weight monohydric alcohols, high molecular weight hydrocarbons and their amines, inorganic compounds, polysaccharides* , etc.

The classification should be based on the most characteristic feature that allows you to combine substances into a single, organically related group. Such a characteristic feature for all substances or basic compositions is their ability to interact with water. In terms of intensity and interaction with water, all bases are divided into three groups: *hydrophobic, hydrophilic, and diphilic*. This classification is considered the most rational. She adopted GF XI.

Hydrophobic bases have a pronounced lipophilicity, that is, the ability, as a rule, to mix completely with fats, fat-like substances or to dissolve in them. Exceptions to this rule are rare and belong to the category of

incompatibility. For example, castor oil is poorly mixed with hydrocarbons. The characteristic feature of this group of bases is that they do not mix with water and do not emulsify it, except for those small amounts of water or aqueous solutions that they can hold due to their viscosity.

Hydrophilic bases: gels of high molecular weight carbohydrates and proteins (cellulose ethers, starch, gelatin, agar), gels of inorganic substances (bentonites), gels of synthetic high-molecular compounds (polyethylene oxide, polyvinylpyrrolidone, polyacrylamide), etc.

A characteristic property for this group of fundamentals is active interaction with water: they either mix with it indefinitely, or are wetted or swell in it.

Diphilic (lipophilic-hydrophilic) bases - anhydrous alloys of lipophilic bases with emulsifiers (an alloy of petroleum jelly with lanolin or with other emulsifiers). B/O type emulsion bases (a mixture of vaseline with water lanolin , consistent emulsion water / vaseline, etc.) and O/B use sodium, potassium, triethanolamine salts of fatty acids, tween-80, etc. as emulsifiers .

The proposed classification makes it possible to more clearly characterize the properties of the ointment bases, which are technologically important, helps to make a more correct choice of the basis depending on the physicochemical properties of the medicinal substance, to determine the method of its introduction. In addition, the separation of the ointment bases on these groups makes it possible to a certain extent to judge the rate at which the medicinal substance is received from the ointment in the tissue and body fluids.

Characteristics of lipophilic bases. This group includes: fat, hydrocarbon and silicone bases.

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

But at the same time, they are not sufficiently stable and decompose (go rancid) with the formation of free fatty acids, aldehydes and other compounds that can enter into chemical reactions with medicinal substances in the composition of ointments and act irritatingly on the skin.

Pork fat (Adeps suillus depuratus. Axungia porcina depurata) is produced by melting fat that covers the internal organs of the pig. It is a mixture of 62-68% triglycerides of oleic acid and up to 35% tripalmitin and tristearin a . The product is white in color, soft and delicate, has a very faint odor, melts at 34-35 ° C, does not irritate the skin fresh and does not interfere with skin breathing, penetrates the epidermis quite easily and transfers the medicinal substances mixed with it to the skin.

Pig fat is easily mixed and fused with other fats, waxes, hydrocarbons, resins and fatty acids, does not lose its oily consistency when it absorbs up to 20% of water (due to the presence of a small amount of cholesterol). Under the influence

of external factors (heat, light, air oxygen, etc.) Pig fat easily burns , acquiring an unpleasant odor, acid reaction and irritating effect .

Although lard is among the best bases for ointments, its use is very limited, as it is a food product.

DF IX recommends the use of fat in the manufacture of simple sulfuric ointment, potassium iodide ointment and mercury sulfur ointment. The latter is prepared with the addition of beef tallow.

Beef tallow (Sebum bovinum) is a solid fat , since it contains up to 58% of the three glycerides of the solid saturated palmitic and stearic fatty acids and relatively few triglycerides of unsaturated acids like linoleic acid. It has a yellowish color and a faint odor, its melting point is 42-52 ° C. It is hard and brittle at room temperature, therefore it is unsuitable as an ointment base in its pure form. Sometimes it is used to seal ointments on fatty bases.

Lamb fat has similar properties and uses.

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

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

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

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

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

Hydrogenated fats can be used:

a) independently as a basis for ointments, if they are viscous-plastic;

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

DF XI as an ointment base recommends the use of such ointment-like products: Salomas, or hydro-grease (Adeps hydrohenisatus), obtained from refined vegetable oils, with like with pork fat, but more dense.

Vegetable fat (Axungia vegetabilis) - alloy consisting of 88-90% hydrofat and and 10-12% vegetable oil.

Kombizhir (Adeps compositus) - an alloy consisting of 55% salomas, 30% vegetable oil and 15% beef, pork or hydrogenated whale fat.

Hydrocarbon bases . In 1876, in pharmaceutical practice was called U p en petrolatum as a base for ointments. At that time, liquid and solid paraffins also began to be used as components of the bases for ointments. The combination of liquid and solid hydrocarbons made it possible to create ointment bases of the

required consistency, which did not burn out , were neutral and compatible with a large number of drugs.

Vaseline (Vaselinum) (DF IX century. 746) is a purified mixture of solid, soft and liquid hydrocarbons derived from petroleum.

Uniform, stretching filaments , odorless, greasy mass, white or yellowish. When smearing on a glass plate gives a smooth non-slip film. With fatty oils and fats mixed in all ratios. When melting gives a clear liquid with a faint smell of paraffin or oil. Melting point is 37-50 ° C. It is not saponified with alkali solutions, does not oxidize, but does not taste bitter in air and does not change under the action of concentrated acids.

Vaseline is widely used as an independent ointment base for surface dermatological ointments. For use on the mucous membranes and an increase in the resorptive capacity of vaseline, it is combined with lanolin.

For ophthalmic practice, Vaseline grade “for eye ointments”, purified from reducing impurities and subjected to hot filtration and sterilization, is used.

Along with the pharmacopoeial, petrolatum according to GOST 3682-52, obtained by fusing ceresin, paraffin, purified petrolatum or their impurities with purified petroleum oil, is also used.

Petrolatum (Petrolatum) is a mixture of solid paraffin with mineral oil, a light brown mass with a melting point above 60 ° C. It is obtained by dewaxing petroleum aviation oils. For medical purposes, it is additionally cleaned and used in complex bases for ointments as a filler.

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

Vaseline oil or liquid paraffin (Oleum Vaselini, Paraffinum liquidum) is a fraction of the oil obtained after the distillation of kerosene. Colorless, oily, odorless and tasteless oily liquid, insoluble in water and easily mixed in all respects with vegetable oils (except castor oil). It is used to obtain the basis of a soft consistency.

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

Ceresin (Ceresinu m) - refined ozokerite, which is an amorphous colorless breaking mass melts at 68-72 ° C. Chemically indifferent. It is well fused with fats and hydrocarbons, forming alloys, does not crystallize. It is used to obtain heavy ointment bases (artificial petrolatum).

*Vaseline artificial (*Vaselinum artificiale) - CA complex alloys prepared from liquid and solid paraffins, deresinated ozokerite or ceresin, sometimes with the addition of petrolatum. In the simplest case, it is an alloy of and parts of paraffin and 4 parts of vaseline oil (Unguentum Paraffini). The alloy is prone to syneresis and becomes granular during storage. The quality of these alloys is usually the better, the more complex their combination.

Naphthalan *oil* (Naphthalanum liquidum, Naphtha Naphthalan i) is a thick, curd black substance with greenish fluorescence and a peculiar odor. Mixed in all proportions with glycerin, oils and fats. There is a disinfectant and painkiller. Effective remedy for burns I and II. There are a number of formulations with Naftalan oil for the treatment of scabies, itching, eczema, erysipelas of the skin, arthritis, radiculitis and other diseases.

Included in the naphthalan ointment (Unguentum Naphthalani), which is a mixture of 70 parts of naphthalan refined oil, 18 parts of paraffin and 12 parts of petrolatum (Listing IX).

In the domestic literature there is information about the use of technical hydrocarbons in the composition of the main ointments. So, for the treatment of scaly lichen, eczema, neurodermatitis, ointments containing amide chloride mercury, xeroform, bismuth basic nitrate, prepared on artificial Vaseline Bohl (solid paraffin - 1 part, autol or turbine oil - 2 parts) are recommended. For the treatment of eczema, psoriasis, dermatosis, an ointment based on it is recommended; it consists of technical autol No. 17 - 60%, paraffin wax - 30% (the composition of the ointment includes dermatol and bismuth nitrate of the main 5% each).

However, the use of technical, little purified hydrocarbons should be carefully to avoid negative effects on the skin or mucous membranes.

Silicone bases. The works of M. T. Alyushin laid the foundation for the use of silicone fluids in the composition of essential ointments. At present, our industry produces *polydimethyl, polydiethyl, and polymethylphenyl silicone fluids.*

Of these silicone fluids, polydiecylsiloxanes have better compatibility with medicinal substances and other base components . They are mixed with vaseline th or vegetable oils (except castor) fused with vaseline, paraffin, ceresin, fats, spermaceti wax, etc.

Menthol, camphor, phenylsecyllate, tar, phenol and other medicinal substances are well dissolved in polydiecylsiloxane liquids .

Unlike fatty oils, silicone liquids do not burn when stored. They are also used for the manufacture of protective ointments, creams, as they are not wetted by water and do not decompose from exposure to mineral acids.

Along with esilon-4 and esilon-5 , silicon dioxide $Si0_2$, commonly known as oxyl or aerosil, is widely used in pharmaceutical practice. It is a white amorphous powder, non-porous, highly dispersed, and has a high adsorption capacity. Aerosil can contain, without loss of flowability, 15-60% of various liquids, does not swell in water, but binds it, forming a suspension, which can then be turned into a homogeneous ointment base.

In the manufacture of soft dosage forms, it is advisable to use Aerosil with a high specific surface, i.e. Aerosil A-380 (the industry produces A-175, A-300, A-380, differing in the degree of dispersion). As an auxiliary th Aerosil substance used as a thickener and stabilizer of ointment bases in a concentration to 5%.

The known esilon-aerosil base is 84% esilone-5, thickened with 16% aerosil. It is a colorless, highly viscous transparent gel, neutral or weakly acidic with a peculiar smell.

The esilon-aerosil base has a high chemical stability, does not stratify and does not taste bitter during long-term storage, provides local surface action and stability of medicinal substances. It can also be used as a protective ointment to protect the skin from pressure sores, in the treatment of intestinal fistulas, etc.

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

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

Soap bases are obtained by dissolving soap when heated in water or as a result of the interaction of glycerin and stearic acid with solutions of sodium or potassium carbonates. The concentration of soap ranges from 5 to 10%. They are easily absorbed into the skin, mix well with fatty bases, forming emulsion systems.

Basics on the basis of my l have an alkaline reaction and therefore can not be considered indifferent.

Potassium (green) optionally soap has walk ointment greases properties E , and is often used in the composition against ochesotochnyh ointments.

Gelatin-glycerin bases are made with different contents of gelatin, glycerin and water.

Gelatin gels in a concentration of up to 3% - gentle fusible jelly that dilutes when rubbed into the skin, slowly absorbed, are widely used in the manufacture of various creams.

Gels containing more than 5% gelatin, thick, elastic, non-melting at body temperature, difficult to liquefy, applied to the skin in the molten state with a brush.

Gelatinous bases are easily affected by microorganisms and require preservation, they are dried during storage.

Starch-glycerin base, or glycerin ointment (Unguentum Glycerini) is a whitish translucent jelly consistency mass, easily soluble in water and secretions of the mucous membranes. This latter circumstance contributed to its long-term use as a basis for the manufacture of ointments applied to mucous membranes. According to DF IX, starch glycerin ointment is prepared by mixing 7 parts of wheat starch with an equal amount of purified water and then adding 93 parts of glycerin with gentle heating in a water bath until 100 parts of a homogeneous mass are obtained. The basis is resistant to microflora, but physically and chemically unstable, as it undergoes syneresis during storage.

Collagen bases. Collagen (VFS 42-726-78) is a natural biopolymer that is a fibrillar protein of the connective tissue of animals. Get it from certain areas of the skin in the form of a pasty mass or solution. Collagen was previously used for the manufacture of a number of medical devices (suture material, vascular prostheses,

etc.). Then from it began to receive films containing medicinal substances for various purposes. Collagen is very promising for ointments, as it provides a pronounced therapeutic effect and prolonged action.

Tragacanth-glycerin jelly containing C% tragacanth and up to 40% glycerol were proposed as hydrophilic bases.

In foreign practice have found application: pectin, algin, mucin and other bases from the plant Navy.

In our country, we investigated the possibility of using solutions of polysaccharides of microbial origin as the basis for ointments.

Methylcellulose (MC) is a simple ether obtained by the interaction of alkali cellulose and methyl chloride. Preparation of aqueous solutions of the MC, see on page 286.

The introduction of the MC in the ointment on the basis of fat provides them with hydrophilicity and faster release of drugs, improves the contact of drugs with the affected skin. Possessing adsorption properties, MC absorbs various kinds of secretions of damaged skin and creates a protective film on the skin surface. MC is compatible with many drugs.

Sodium carboxymethylcellulose (sodium-CMC). Solutions of sodium-CMC as a basis for ointments are used with limited, although they have prospects.

The bases on the basis of MC and sodium-CMC are usually obtained by mixing them with glycerin according to the prescriptions:

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

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

Preservatives are added to the base. Other cellulose derivatives produced in manufacturing scale.

The use of hydroxypropylmethylcellulose (OPMC) and acetophthalylcellulose (APC) is known as a base for ointments.

Polyethylene oxide (polyethylene glycol) (PEO) bases receive fusion of solid and liquid polyethylene oxide.

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

Polyethylene glycol base is neutral, non-toxic, with prolonged use it does not macerate the skin, it easily releases medicinal substances, it is not a medium for the development of microorganisms.

Besides. PEO bases have the ability to dissolve hydrophilic and hydrophobic medicinal substances; have a weak bactericidal effect due to the presence of primary hydroxyl groups in the molecule; osmotic activity favorably affects the treatment of contaminated wounds. In such cases, ointments on PEO act as flushing and cleansing agents.

Polyethylene gels (for example, aerosil 4 hours, vaseline oil 84 hours, paraffin 6 hours, high-pressure polyethylene 15 meters). Part of protective ointments (to protect the skin from the effects of alkalis, acids), soft emulsion creams, etc. They

are indifferent, poorly washed off the skin surface, incompatible with water and aqueous solutions of drugs, alcohol, birch tar, ichthyol.

Basics of clay minerals. Clays and clay rocks contain the most characteristic and specific minerals for them: kaolinite — the main mineral of medicinal white clay, montmorillonite-bentonite clays, etc. They are 90% composed of oxides of silicon, aluminum, iron, magnesium and water. In insignificant quantities oxides of calcium, sodium, potassium, titanium are also included in the composition of minerals . Some of these oxides are missing in individual minerals.

For pharmaceutical purposes, bentonite and other clay minerals should be used completely purified from coarse impurities and sand. This is achieved elevation yv aniem followed by drying (and simultaneous sterilization) mineral powder.

According to their state, clay minerals are highly dispersed systems. They are characterized by an active physicochemical interaction with water (swell and firmly hold). For example, sodium forms of bentonites, when wetted with water, swell, increasing in volume by 15-18 times. Formed soft jelly is well distributed on the skin and perceive many medicinal substances, as they have chemical indifference.

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

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

Phytosterol basis. Phytosterol is a white or slightly yellowish powder, fat to the touch, obtained by hydrolysis of pine wood.

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

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

For long term storage of phytosterols th base dries. However, upon subsequent mixing of the phytosterol s with warm water (50-60 ° C) is again formed mass having initial properties. This property of phytosterol ov makes it possible to obtain dry ointment concentrates. Phytosterol oh base itself dries the inflamed skin.

Characteristics of lipophilic-hydrophilic (diphilic) bases. These are compositions differing in composition, having both lipophilic and hydrophilic properties. They are characterized by their ability to mix with both fat-soluble substances and aqueous solutions of medicinal substances.

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

Lipophilic-hydrophilic bases, in contrast to hydrocarbons, provide significant resorption of medicinal substances from ointments, do not interfere with gas and heat exchange of the skin, have good consistent properties. Thus, it is one of the most common and promising foundations.

The most common representative of this group is lanolin (Lanolinum), which is obtained from the wash water of sheep wool. Therefore, this substance is often called wool wax (Adeps lanae). A natural mixture of esters of high molecular weight cyclic alcohols, fatty acids and free high molecular weight alcohols (cholesterol and isocholesterol). Purified lanolin is a mass of white-yellow color, thick, viscous, ointment-like consistency, with a peculiar faint odor, melting point is 36-42 ° C. In water, lanolin is insoluble, but it mixes with it, absorbing (emulsifying) it by 150%, without losing at this ointment consistency. The use of anhydrous lanolin (Lanolinum anhydricum) is based on this important and valuable property, because with it you can inject a large amount of aqueous liquids into the ointment. Anhydrous lanolin has a rather high stability and chemical indifference. It is able to be absorbed by the skin and mucous membranes, without irritating them, it is easily fused with fats, hydrocarbons and wax. The lack of anhydrous lanolin as a basis - high viscosity, stickiness and difficulty of smearing - does not allow its use in pure form. For this reason, it is almost always used in a mixture with other basics and most often with petroleum jelly.

DF X recommends using water lanolin (Lanolinum hydricum, if the type of lanolin is not indicated in the recipe. Water lanolin is a thick yellowish-white viscous mass consisting of 70 parts of anhydrous lanolin and 3 parts of water. When heated, like any emulsion system, it stratified.

Lanolin deficiency - an adverse effect on the skin, which manifests itself in the form of allergic reactions, especially in dermatological patients. To improve the properties of lanolin, they began to subject it to various treatments. As a result, the resulting acetylated lanolin derivative. And cethylated lanolin has less stickiness, ability to mix with mineral stones, better plasticization properties, and is devoid of allergic properties. Used as a softening additive in ointments.

Methods have been developed for the preparation of hydroxyethylated lanolin derivatives, which are called water-soluble *lanolins* (" *vodlans* "). Emulsifying properties of their low, but they are good stabilizers and plasticizers, etc. idayut emulsions best-of s appearance and durability s in storage.

From lanolin by hydrolysis get higher fatty alcohols. Unseparated mixture of alcohols is produced in the form of small pieces, which are melted at a temperature of about 60 ° C and is called wool wool alcohols, which are used as emulsifiers in the manufacture of B / O type emulsions.

In order to improve the properties of wool wax alcohols (increase resistance to acids and alkalis, obtain products of stable composition, reduce oxidative damage, etc.) and x is subjected to oxyethylation. Ethoxylated alcohol derivatives of s stabilize emulsion type B / B, and may be solubilizers .

To increase the yield of alcohols, lanolin is subjected to hydrogenation. Hydrogenation of lanolin is carried out by methods used in the hydrogenation of fats. Hydroline was obtained, which can be used as an emulsifier for the preparation of emulsion bases for ointments. Hydroline , in comparison with lanolin , has low values of acid and ether numbers. It is light yellow in color, almost odorless, has less stickiness and a higher emulsifying ability.

Spermaceti (Cetaceum) is a solid waxy product derived from sperm whale oil. It is an ester of ethyl alcohol and palmitic acid , melting point 45-54 ° C, stable during storage. It is easily fused with fats, waxes, vaseline. These alloys have a certain density, a peculiar slipperiness and ability to absorb aqueous liquids, forming coarse emulsions, therefore they are often used in cosmetics for making creams.

Wax (Cera). Beeswax is a hard, grainy, breaking mass from yellow to brown with a faint smell of honey. Melts at a temperature of 63-65 ° C.

From yellow wax (Cera flava) under the influence of sunlight in the air or by chemical treatment get white wax (Cera alba). For the manufacture of ointments is better to use wax yellow.

Beeswax alloyed well with fats, hydrocarbons and other waxes. Due to the presence of higher alcohols, wax can emulsify certain amounts of water. It adds the basics and ointments plasticity and increases their density.

Often, a mixture consisting of yellow wax (10 parts), almond oil (35 parts), purified water (25-30 parts) is used as a base. Sometimes, to soften the skin as an ointment, a composition consisting of yellow wax (7 parts), spermaceti (8 parts), almond oil (60 parts), purified water (25 parts) is used.

Emulsion bases for ointments, like all emulsions, are microheterogeneous disperse systems. They consist, as a rule, of a liquid, insoluble or slightly soluble in another liquid or highly viscous substance. In most cases, for the manufacture of emulsion ointment bases used liquid pronounced polarity (water, aqueous solutions of glycerol, carbohydrates, ethylene glycol and the like. P.) and nonpolar or low-polarity e substances (fats, hydrocarbons, silicone fluids, etc.). Emulsion bases for ointments are concentrated emulsions of both the first and second kind, in which the content of the dispersed phase reaches 50-70% or more. Due to the excess of free surface energy at the interfacial surface, the emulsion bases are unstable, therefore, to obtain stable compositions, surfactants, so-called emulsifiers are introduced into their composition.

Ointments on emulsion bases are characterized by low viscosity values, reduce skin dryness, increase its softness and elasticity, maintain normal water balance of the skin, reduce inflammation, have a good presentation.

Emulsion bases of type O / B have a good consistency, an excellent aesthetic look, they do not leave a greasy mark on the skin, they are easily washed off. The dispersion medium of these bases is water, therefore, as a result of its evaporation, ointments are prepared with their help, characterized by a cooling effect on the skin and mucous membranes.

To stabilize the bases, both ionic (cationic and anionic) and nonionic surfactants are used as emulsifiers . Cationic PA In are cetylpyridinium chloride - a

white powder, soapy to the touch, soluble in water and alcohol, easily soluble in ether. When shaking aqueous solutions, a rich foam is formed. As an emulsifier, O / B is used in a concentration of 0.1-0.5%. Cationic PA in use is limited because of their high toxicity. Anion-active PA In are applied much more widely. Anionic emulsifiers are soaps and alkyl sulfates.

Emulsifiers - milled alkali metals. Sodium, potassium and ammonium salts of fatty acids emulsify well vegetable and hydrogenated fats. They are more suitable for the manufacture of liquid ointments (linimentov).

Emulsifiers are polyvalent soaps. Multivalent metallic soaps (zinc, calcium) can form B / O type highly dispersed emulsions with a high water content (up to 70%) as a dispersed phase.

Triethanolamine soap emulsifiers are also capable of stabilizing bases with their anions, forming surface adsorption layers in the oil phase.

Emulsifiers-alkyl sulfates are sulfate esters of higher alcohols. The most widely used sodium salts of alkyl sulfates today are sodium lauryl sulfate, sodium cetyl sulfate, sodium steryl sulfate.

Along with alkyl sulfates, some alkyl sulfonates, for example, sodium cetyl sulfonate, are also used.

Significantly more non-ionic emulsifiers are used in pharmaceutical practice, the hydrophilic properties of which are sharply enhanced by oxygen.

Emulsifiers -tvin prepared by treatment with foams(Spans) ethylene oxide in the presence of a catalyst - sodium hydroxide.

Depending on which of the Spencer s reacts esterification and what degree of polymerization of ethylene oxide, are following Tweens having the tradename Tween-20, Tween-40, Tween-60, Tween-80, and others. All of them have a liquid consistency , well dissolved in water and organic solvents.

Emulsifier № 1 (Ugryumova PS) (PS 42-285-72 : a mixture of sodium x sulfuric ester salts SEASON -molecular alcohols Single shallot ovogo fat with a melting temperature of 49 ± 2 ° C and free Vysokomolek middle molecular weight fatty alcohols (cetyl, O Ktadetsilovogo etc.). This is a solid mass of brownish color, oily to the touch, with the smell of sperm whale fat. 1 part of the emulsifier is capable of emulsifying 9 parts of water.

Recommended emulsion base, which consists of sodium lauryl sulfate - 2 parts, white wax - 1 part, propylene glycol - 10 parts, cetyl alcohol - 15 parts, purified water - 72 parts. The water bath fused wax, propylene glycol and cetyl alcohol. The resulting alloy is vigorously mixed with warm (60 ° C) aqueous sodium lauryl sulfate solution until a homogeneous mass is obtained. E e may be used for the manufacture of ointments with sulfonamides, precipitated sulfur, salicylic and benzoic minutes acids, mercury and other drugs.

Proposed emulsion bases of the following compounds:

Triethanolamine	2.0
Stearic acid	15.0
Second-hand lanolin	2.0
Vaseline oil	25.0
glycerin	5.0

Purified water to 100.0

To the alloy of stearic acid, lanolin and vaseline oil, add a heated solution of trietanolamine and glycerin in water and mix well until cooling.

Hydrogenated sulfozhir and 8.0
Sodium Alginate 2.0
paraffin wax 30.0
White wax 2.0
Purified water to 100.0

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

Emulsion waxes 7.0
Vaseline oil 7.5
Glycerol 12.5
Evilonu- 5 10.0
Sodium benzoate 0,2
Purified water 62.8

Make a mixture of emulsion waxes, esilone- 5, vaseline oil and glycerin oil with a heated solution of sodium benzoate in water in a mortar. This base is used for the manufacture of ointments with anesthetics (anestezin, Novocain, Trimecain, Dikain).

For the manufacture of eye ointments with pilocarpine hydrochloride, a base is used, consisting of emulsifier No. 1 - 15 parts, cinnamon alcohol - 0.15 parts and purified water - 77.85 parts.

Emulsion bases such as B / O with a long stay on the skin can cause its maceration, which further contributes to the resorption of the drug. They are characterized by small values of plastic viscosity, yield strength, and therefore are easily applied to the skin. Being a different kind of emulsions, they are less able to change their consistency during storage.

Emulsifiers - higher fatty alcohols and their derivatives. Valuable components of the ointment bases are the saponet saponification products: cetyl and stearic alcohols, having a melting point of 50 and 59 ° C, respectively. Both are good emulsifiers. Ointment bases containing 5–10% of them are capable of incorporating up to 50% aqueous solutions, forming B / O type emulsions.

Derivatives of higher fatty alcohols include emulsifier K, used in the manufacture of cosmetic ointments. It is a potassium salt of high molecular weight alcohol (fraction enriched in ethyl alcohol) and phosphoric acid.

The alloy consisting of 30% emulsifier K and 70% of high molecular weight alcohols of sperm whale fat is called emulsion wax. It is a solid homogeneous mass of light cream color, well fused with fats, oils, hydrocarbons.

Emulsifiers - derivatives of polymeric glycerin. This group includes ointment bases prepared with solid emulsifiers T-1 and T-2. T-1 is a mixture of incomplete mono- and di-esters of diglycerin and with stearic acid. T-2 is a mixture of incomplete di -esters of triglycerols and stearic acid.

Emulsifiers - Span (Span) This name has incomplete esters of sorbitan and higher fatty acids. Depending on which acid reacts with sorbitan , Spene formed

has different properties and differ in numerical terms : Span-20, Span-40, C pa n-60, Span-80 (respectively, esters of sorbitan and lauric , palmitic, stearic, oleic acids).

Despite the fact that almost all Spenes stabilize B / O type emulsions , Spen-80 is a B / C emulsifier .

Commercially, sorbitol oleate is produced, which is a mixture of sorbitan mono- and diesters and oleic acid. In appearance, it is a highly viscous, stretching filament, a mass of light brown color. Recommended for the manufacture of emulsion bases for ointments.

Emulsifier-Pentol - PA B, which is a mixture of mono-, di- and tetra esters chetyrohatomny x alcohol s foams taeritrita and oleic acid. Vaseline alloys with 5% pentol form stable, highly dispersed B / O type emulsion systems with 50-60% water. The basis is steady at storage, freezing and heating.

Emulsifiers - fat sugar . Giro sugars are incomplete sucrose esters with higher acids (“sugar soaps”).

The starting materials for the production of fat sugars are sucrose and individual fatty acids (stearic, palmitic, lauric, etc.) or a mixture of coconut, palm and other vegetable oils.

According to the properties of fat sugar is PAIR and, therefore, can be emulsifiers. F. Zhoglo synthesized and studied a number of sucrose mono- and diesters. He found that palmitic and stearic acid diesters in the amount of 2% are capable of using liquid paraffin (47%). water (45%), methylcellulose (1%) and ceresin (5%) to form a stable grease emulsion of the type B / O. Methylcellulose and ceresin in it act as a thickener.

In its pure form, fat sugars are colorless, odorless and tasteless crystalline substances. In the body break down into fatty acids, glucose and fructose. Do not allergic to the skin, maintain constant skin pH values and normal water balance.

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

Vaseline	60.0
Emulsifier T-2	10.0
Purified water	30.0

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

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

For the pharmaceutical manufacturing of ointments, two emulsion bases are recommended. The composition of the first is anhydrous lanolin - 168 parts, vaseline -240 parts, purified water - 72 parts.

The second emulsion base consists of anhydrous lanolin, sunflower oil and purified water, taken in equal amounts. First, lipophilic components are fused, then

hot water is added with stirring, emulsification is continued until the base is completely cooled.

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

Absorption bases. Along with emulsion bases, anhydrous alloys of VAPOR with components have been widely used, have hydrophilic and hydrophobic properties.

These peculiar consistent semi-finished products are a number of researchers refer to a special class of ointment bases, calling them absorption. Due to the presence of PAR, these bases can be mixed with water, aqueous solutions of medicinal substances, forming emulsions of the type B / O or M / V. In this connection, the term “absorption” means only the property of the base to incorporate water.

The proposed absorption basis of such a composition:

Woolen Wax Alcohols	6.0
Vaseline	10.0
Ceresina	24.0
Vaseline oil	60.0

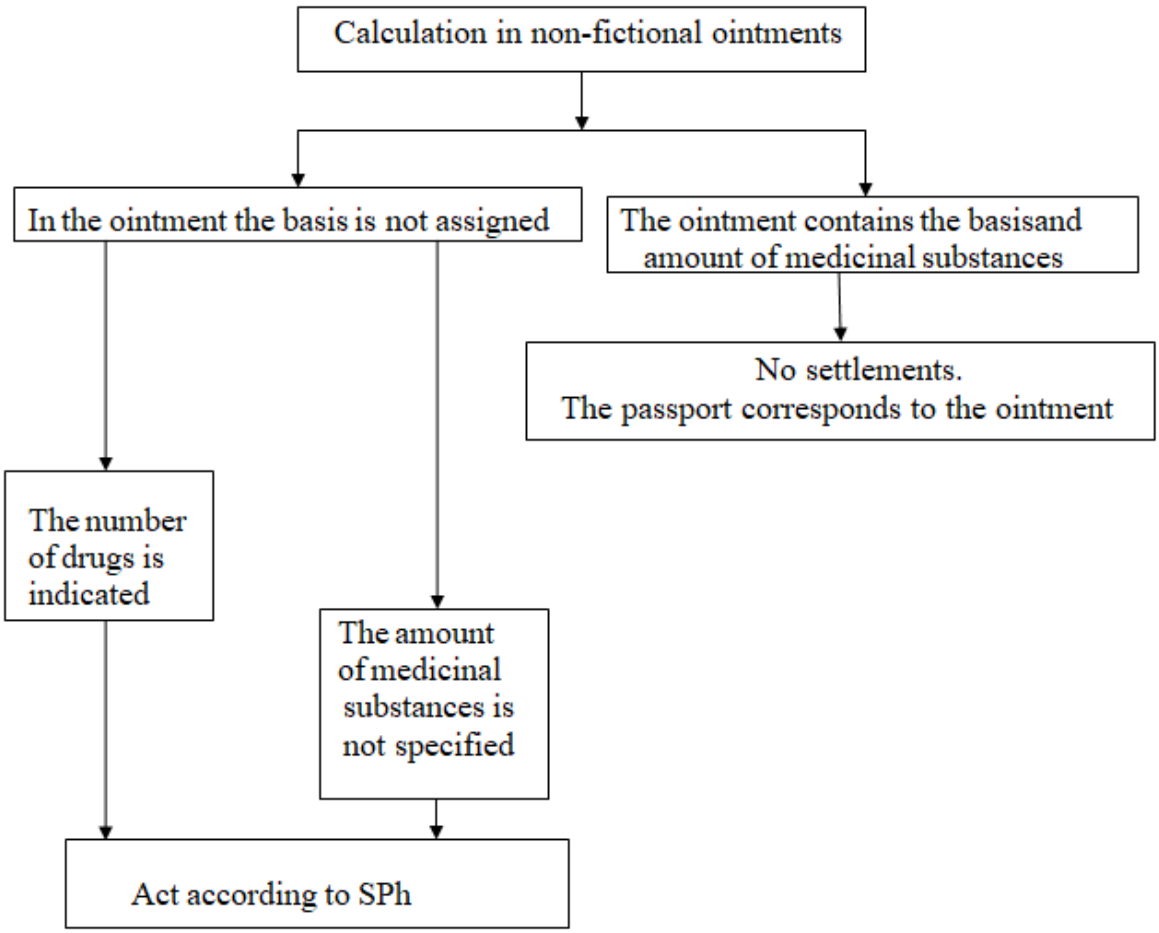
These ingredients are melted in a water bath at 70-80 ° C. and the mixture is stirred until cooling. It is allowed to change the concentration of ceresin and vaseline oil in order to obtain the basis of any desired consistency. For emulsion base on wool wax alcohols , should , to p ac melted ingredients absorption bases add with stirring 50% water, heated to 70-80 ° C. In this framework can be introduced various medicinal substances: sulfur, zinc oxide, boric and salicylic acids, hydrocortisone, chloramphenicol, potassium iodide, streptocide, etc. The stability of the ointment is more than 2 years.

The composition of many absorption bases next to PAR, oils, waxes include hydrocarbons. This is due to the desire to reduce the adverse effects of hydrocarbons on the skin, mucous membranes, wound surfaces.

For the manufacture of ointments are also used alloys of vaseline with anhydrous lanolin in various ratios: 9: 1, 8: 2. 6: 4.

Numerous studies show that the basics for ointments by their ability to provide the most intensive release and resorption of drugs can be arranged in the following row: hydrophilic, emulsion type B / B, emulsion type B / O, absorption and hydrophobic. But to observe the above-mentioned dependence of the activity of the ointment on the nature of the base when receiving ointments with new drugs is impossible. There are many data that show that in each case, first of all, it is necessary to take into account the direction of action of the drug, its properties, the nature of interaction with the components of the base and other factors.

Calculation of drugs and fundamentals



$m_{ointment}=m_{ointment}=\sum$ all the ingredients

$m_{alkalis}=m_{ointment}-\sum$ medical substances

$m_{ointment}= S_{all\ the\ ingredients}$

$m= 10\%$ from $m_{ointment}$

$m_{alkalis}=m_{ointment}-S_{medical}$ substances

Next, carry out calculations of drugs and bases, as shown below. In the absence of an indication of the concentration of the medicinal substance in the recipe, 10% ointment should be prepared. Ointments, the prescriptions of which are standardized (that is, officinal), are prepared in accordance with the composition and concentration of the medicinal substances indicated in the reference document.

The manufacture of ointments consists of several successive technological stages: melting, dissolving, dispersing, emulsifying, mixing, packaging, and dispensing. In the process of technology, stepwise control is carried out (completeness of dissolution, homogeneity of mixing, etc.), as well as evaluation of the finished ointment according to technological indicators of quality.

Because ointments like physicochemical dispersions may be homogeneous and heterogeneous E , their technology could include all of the major steps or some of them (melting and mixing, melting, dissolution, mixing etc. AP.).

The introduction of medicinal substances in the ointment is carried out taking into account their physico-chemical properties and the prescribed amounts (see. "Own technology of ointments").

Medicinal substances that are not soluble in water or in the database (zinc oxide, bismuth nitrate basic, white clay, dermatol, norsulfazol, sulfur, streptotsid, talc, etc.), As a rule, are introduced into the composition of suspension ointments in the form of powders, ground to the maximum degree of dispersion. Water-soluble substances that require a significant amount of water (sodium tetraborate, boric acid, sulfa drugs, etc.) are also added to suspension ointments. This also applies to substances that are soluble in fats.

Medicinal substances soluble in water (salts of alkaloids, potassium iodide, novocaine, silver nitrate, etc.) Introduce mainly into the composition of emulsion ointments, dissolving them in a minimum number of drivers.

Medicinal substances soluble in fats (camphor, menthol, thymol, chloral hydrate, crystalline phenol, anesthesin up to 2%, phenyl salicylate, etc.) are introduced into single-phase ointment solutions, dissolving them in a fatty basis.

Thus, the method of manufacturing the ointment is chosen taking into account the physicochemical properties of the prescribed substances and the dispersed system is formed. To mix the ingredients of the ointment, use mortars of the appropriate size or mechanization for the manufacture of ointments.

OWN OIL TECHNOLOGY

Making homogeneous ointments. Ointment alloys - a combination of several fusible inter-soluble components. The composition of such ointments may include fats, waxes, hydrocarbons, resins, patches, oils and other substances. Ingredients can be both hard and soft or liquid.

The fusion of the components is carried out in a water bath in a porcelain or enamelled cup. The general technology of ointment-alloys is as follows: first of all, the most refractory substances are melted and other ingredients are added to the resulting melt in decreasing order of the melting temperature; liquid components are added last; If necessary, the obtained liquid melt is filtered through gauze into a pre-heated mortar (50-55 ° C) and stirred until cooling. At the same time, the ointment becomes friable, soft, easily smeared due to the fact that the mixing prevents the formation of microcrystalline frameworks, as well as cr istalization of some solid ingredients that render the ointment a coarse-grained structure.

Stirring is especially advisable if paraffin enters into the ointment, otherwise it can stand out in the form of large crystals. In addition, with stirring ointments get loose porous structure as a result of incorporation of air.

The comparative smoothness of the substances that make up the ointment alloys is given below in this order:

1. Ceresin
2. Ozokerite
3. Wax yellow — Used as components in the ointment bases as sealants
4. Wax white
5. Netrolatum
6. Prafin solid
7. Spermacet
8. Beef tallow
9. Anhydrous lanolin
10. Vaseline — Used independently or as part of the ointment bases
11. Hydrogenated fat
12. Naftalan
13. Liquid oils

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

Examples of ointment alloys: spermaceti ointment (Unguentum Cetacei) - an alloy of 1 part of wax with 2 parts of spermaceti and 7 parts of peach oil; Ointment diahilna I (Unguentum Diachylon) - Alloy equal parts patch lead to claim growth and petrolatum: officinal ointment NAFTALAN (IX DF 728 in.) and others.

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

Melt petrolatum (t melting - 60-62 ° C), adding paraffin (t melting - 50-54 ° C) and, last but not least, naphthalene oil to the resulting melt while stirring. The alloy is stirred in a warm mortar until it is completely cooled down.

PWC

date No recipe
Petrolati 12.0
Paraffini 18.0
Naphthalani liquidi raffinati 70.0

$m_{zag.}$ = 100 ml Preparation method: (signatures)

Checked: (signatures)

Ointment solutions are ointments containing medicinal substances that are soluble in the ointment base (regardless of their nature).

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

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

If medicinal substances dissolve easily in an ointment base and are prescribed in small amounts (up to 5%), they are first triturated with an equal amount of fatty or petroleum jelly until complete dissolution, then the base is added in parts, thoroughly mixed until homogeneous.

In the manufacture of ointment solutions, the following should be considered:

> If the medicinal substance has volatile properties (camphor, menthol, etc.), T o it is dissolved in a semi-frozen melt (45-50 ° C);

> Do not prepare saturated solutions, as solute may crystallize upon cooling ;

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

Rp .: Mentholi 0.1
Vaselini 10.0
Misce, fiat unguentum
Da. Signa. Ointment for the nose.

In a mortar, 0.1 g of menthol is triturated with a few drops (0.1 g) of petroleum jelly until complete dissolution and thoroughly mixed with petroleum jelly.

The original recipe of camphor ointment (SPh of the IX century. 721) is not changed a : according to FS 42-751 -73, paraffin was introduced into its composition.

Rp .: Camphorae	10.0 seu	10.0
Vaselini	60.0	54.0
Paraffmi	-	8.0
Lanolini anhydrici	30.0	28.0

Misce, fiat unguentum
Da. Signa. For rubbing .

Anhydrous lanolin and Vaseline is melted (according to the rule of fusion) in a water bath and in the resulting melt cooled to 45-50 ° C, dissolve camphor (volatile substance) and stir until cooled. The technology of this ointment with paraffin is similar. Ointment is a combined system: ointment, alloy and ointment solution.

Rp .: Anasthesini 0.25
Mentholi 0.1
Vaselini 20.0
Misce, fiat unguentum
Da. Signa. For rubbing in.

Ointment solution , which consists of medicinal substances, soluble in petrolatum, but such, which, when mixed, form a eutectic alloy, insoluble in petroleum jelly. Therefore, in this case, you need a consistent dissolution of the substances in the base. In melted petroleum jelly, first anesthesin is dissolved, and then menthol, and then stirred until the ointment is completely cooled.

In the manufacture of ointments, solutions according to recipes, to avoid wasting time on fusing bases and dissolving medicinal substances, it is advisable to use pre-prepared semi-finished products - ointment concentrates, diluted with the base according to the requirements of the recipe.

Extraction ointments are obtained by extracting the molten base of active ingredients from plant or animal materials.

Representatives of this group of ointments are: ointment from Spaniard flies, ointment of swamp larva, ointment from walnut leaves, etc. These ointments are prepared in the factory, therefore their technology is covered in the course of the plant medicine technology.

The manufacture of heterogeneous ointments and pastes.

Ointment suspensions are ointments containing solid powdered, crushed to the smallest size of medicinal substances, insoluble in the base and in water and distributed in it according to the type of suspension.

Ointment suspensions may contain one or several medicinal substances, and each of them has its own interface. On this basis, ointment suspensions are divided into two-, three- and multiphase systems.

Suspension ointments are prepared by thorough grinding of solid powdered substances with ointment and ointment . The peculiarity of the ointment-shaped suspensions is a high degree of viscosity of the dispersion medium, eliminates sedimentation of the suspension phase or its flocculation. Unlike aqueous suspensions, in the manufacture of and tritational ointments, the inclusion of even hydrophobic (with respect to the base) solid components into ointment bases usually does not meet any difficulties and does not require the use of protective substances.

The therapeutic activity of suspension ointments, as well as liquid suspensions, also depends on the degree of dispersion of the insoluble drug substance. So, the most important technological moment - as thin as possible grinding the solid phase.

The process of dispersion of solid particles in the presence of liquids from a physico-chemical point of view is due to the following factors: the mechanical action promotes a uniform distribution of particles by mass; small particles formed as a result of dispersion are isolated from each other by a liquid that prevents their coarsening; solvation of the powder is particularly helpful in dispersing.

In the manufacture of ointments, the grinding of a solid phase should be carried out in the presence of liquids, reduce the hardness of the particles and enhance the effect of others due to the wedging effect . However, viscous liquids, which are ointment bases, are not suitable for this purpose, since they very slow down the movement of particles and require great effort during grinding.

The dispersion of the solid phase is carried out using a small amount of vegetable or mineral oil, is added specifically in this case, or by using part of the molten base.

Since the amount of solid phase in suspension ointments in practice can vary widely from fractions of a percent to 50% or more, it has become necessary to use various technological methods.

If insoluble drugs are part of the ointment in an amount up to 5% of the total mass of the ointment, then they are thoroughly ground in a mortar, first in a dry form, and then in the presence of a liquid suitable for the base. Depending on the nature of the base, petroleum jelly (with hydrocarbon bases), peach or almond (with fat bases) and water or glycerin (with hydrophilic bases) are used as an auxiliary liquid. These liquids are taken in half the amount by weight of medicinal substances (Deryagin rule).

If the amount of insoluble substances in the ointment is from 5 to 25%, then they are triturated in a mortar, first in a dry form, and then with a half amount by weight of dry substances of the molten base. The use of auxiliary liquids in this case is impractical, as it will lead to the dilution of the ointment and a decrease in the concentration of medicinal substances.

Typical present firs suspension ointments are camping officinal and ointment mercury white kseroformna I , zinc and others. The main formulations of trituration ointments have an exceptional variety.

Rp .: Unguenti Streptocidi 3% 10.0
Da. Signa. Zmazuvati wounds.

This is a suspension ointment with a solids content of less than 5% (3%). Streptocide (0.3 g) as a complex substance to be ground is crushed in the presence of a few drops of alcohol or ether, and then triturated with a few drops (0.15 g) of vaseline oil and vaseline mass is added in 2-3 doses with petroleum jelly under constant stirring. obtain a homogeneous mass.

PWC
date No recipe
Streptocidi 0.3
Olei Vaselini gtts IX
Vaselini 9.7

$m_{zag.}$ = 10,0 ml
Prepared: (signature)
Checked : (signature)
Rp .: Furacilini 0.2
Vaselini 100.0
Misce, fiat unguentum
Da. Signa. Apply to the affected skin.

Furacilin I (FS 42-94-72) antiseptic ointment, which accelerates the processes of granulation and wound healing. This is a suspension-type ointment with a solids content of less than 5%.

0.2 g of furatsilina placed in a mortar and carefully triturated with a few drops (0.1 g) of vaseline oil. To the resulting mass is gradually added with stirring 99.7 g of petroleum jelly.

It is proposed to rub furatsilin with 6 ml of boiling water (from water lanolin - 30%) in the out-temporal formulation of an ointment containing aqueous lanolin to ensure high dispersion of furacilin (less than 50 microns), mix it with anhydrous lanolin and petroleum jelly, mix until uniform .

Rp .: Resorcini 0.4
Vaselini ad 10.0
Misce, fiat unguentum
Da. Signa. Apply to the affected skin.

Rp .: Unguenti Xeroformii 100.0
Da. Signa. Ointment for dressings.

Suspension ointment with the drug substance, soluble in water, is introduced by the type of suspension.

First, resorcinol is triturated with a few drops (0.2 g) of vaseline oil, then petrolatum is added to the total mass of the ointment (10.0 g) and triturated to homogeneity.

Rp .: Zinci oxydi 10.0
Vaselini 90.0
Misce, fiat unguentum
Da. Signa. Apply to the affected skin.

Zinc ointment (DF X, Art. 737). In a mortar, 10.0 g of zinc oxide is ground (not pressing the pestle too much), then half of the amount (5.0 g) of melted vaseline is added, and then the rest of vaseline is added in several stages during grinding.

Rp .: Streptocidi 1.0
Acidi salicylici 0,3
Vaselini 20.0
Misce, fiat unguentum Da. Signa. Hand ointment.

Ointment suspension with the content of insoluble substances more than 5%. Streptocide is placed in a mortar, preheated, crushed with 5 drops of alcohol 95%, salicylic acid is added, and triturated in the presence of 0.6-0.7 g of melted vaseline. Then in 2-3 steps add the rest of vaseline and mix until a homogeneous mass. Ready ointment light yellow, homogeneous in appearance ..

Rp .: Hydrargyri amidochloridi 0,5
Bismuthi subnitratis
Xeroformii aa 1,0
Lanolini
Vaselini aa 10.0

Misce, fiat unguentum

Da. Signa. When weeping eczema.

Multiphase suspension ointment, which consists of three solids, insoluble in water or in the base.

The total content of medicinal substances is 2.5 g, that is, about 11% of the total mass of the ointment. When used for grinding powders of vaseline oil, the latter would need 1.25 g (half the amount by weight of the powders), which is more than 7% by weight of the ointment. This amount is too large and contributes to the excessive dilution of the ointment. The correct method would be grinding powders in a heated mortar with a portion of the molten base.

When rubbing several powders, one should start with the most coarse drug. Such a case is mercuric amidochloride. It is placed in a mortar and thoroughly ground. Then add bismuth nitrate basic and continue grinding. Lastly, xeroforms are added to the mortar, mixed, and a portion (1.3 g) of molten vaseline is added and ground. The residue of vaseline and water lanolin is mixed into the obtained uniform pulp and the ointment is mixed until a homogeneous mass, occasionally removing it from the walls of the mortar and pestle with a celluloid plate. The finished ointment is transferred to a selling jar and made to leave.

Pastes are ointments containing more than 25% of the solid phase. They are characterized by a dense consistency. When the temperature of the human body paste only softens, rather than melting, and therefore may linger for a longer time on the skin. Depending on the destination paste are divided into dermatological, dental and dental. Among the dermatological pastes, in turn, distinguish between therapeutic and protective.

Dermatological pastes are prepared by mixing powdered drugs with a molten base. The addition of liquids , for grinding solids , should be avoided, since this leads to a softening of the pasta. The insoluble medicinal substances entering the paste are ground to a fine powder, mixed in a heated mortar and gradually, with thorough stirring, the whole melted base is added to them.

If the amount of powders included in the paste is very large (more than 75%), then phase reversal may occur. The mixture begins to crumble due to the fact that the base ceases to be a continuous phase and turns into small particles that adhere to the powder particles, turns from a dispersed phase into a dispersion medium.

Rp .: Acidi salicylici 0.4

Zinci oxydi

Amyli aa 5.0

Vaselini 10.0

Misce, fiat pasta

Da. Signa. Pasta lassara.

Zinc oxide, salicylic acid and starch do not dissolve in water and petrolatum. Salicylic acid when rubbed produces dust that irritates the mucous membranes.

In a evaporated porcelain (porcelain) cup, vaseline is melted in a water bath. Zinc oxide is crushed in a heated mortar (up to 50 ° C), mixed with salicylic acid and part of molten vaseline (5.0 g). Starch is added in portions to the semi -

cooled mass (starch can form starch paste when mixed with hot petroleum jelly), the remaining molten petroleum jelly is added and mixed until a homogeneous mass is formed.

Dental pastes.This group of drugs include various pasty mixtures of drugs, most often with oily liquids, should have a thick consistency.

From the point of view of medical application, dental pastes cannot be attributed to the type of ointment, since they are not used for applying to the skin or mucous membranes, but are inserted into the canals of the tooth to kill the nerve, anesthetize, and disinfect the tooth cavity. However, based on the physicochemical characteristics of toothpastes, their consistency, internal structure and technology, they fully correspond to dermatological pastes in this regard, therefore they are studied in this section.

For the manufacture of dental pastes, various powdered substances are used, glued into a pasty mass with the help of various liquids (glycerin, clove oil, creosote, less often others).

The main conditions for obtaining dental pastes are the finest grinding of powdered components and careful dispensing of liquids. It should be borne in mind that even a slight excess of liquid results in soft and branded products. To avoid this, it is advisable to give powdered ingredients in 2 parts and with an excess of liquid condense the mass of powders. Dental pastes are prepared in small glass mortars or on thick glass plates with a narrow flat spatula or scalpel.

An example of dental pastes are: arsenic, yodoformnaya, trikrezolova I , and others.

Rp .: Tricresoli 24.0
Formalini 6 ml
Boli albae 48.0
Glycerini ad 100.0
Misce, fiat pasta
Da. Signa. Toothpaste tricresol - formalin.

The white clay are ground and mixed with m rikrezol ohms and formalin, and then added in 2-3 doses glycerol (22.0 g) with stirring until a homogeneous doughy mass.

Toothpastes are designed to move the teeth and mouth. And they are made in perfumery factories.

Ointment-emulsions are heterogeneous systems consisting of two phases and have an interface between the phase and medium .

They contain aqueous solutions or water-soluble medicinal substances that form emulsion with ointment base , mainly type B / O. In contrast to tritational, ointment emulsions penetrate the skin more quickly, and medicinal substances, while in the aqueous phase, also act faster.

In the manufacture of emulsion ointments out of the amount of liquid that can be absorbed by the base.

> Medicinal substances, easily soluble in water and discharged in small quantities (up to 5%), dissolved in a minimum amount of water. If they are discharged in large quantities, they are dissolved in water (with the exception of collargol, protargol, tannin), and injected into the ointment by type of suspension.

> Dry and thick extracts are introduced into the composition of ointments after their previous grinding with an alcohol-water-glycerin (1: 6: 3) mixture. When mixing the aqueous solutions of medicinal vesch ETS emulsion is formed with the base on the I system, which obeys the general laws that govern the behavior of emulsions. For the formation of a stable emulsion system, it is necessary to use an emulsifier, for which lanolin is most often used. Spermaceti and wax are used much less frequently, as they have weak emulsifying properties. The technique of making emulsion ointments is reduced to thorough mixing in a mortar of lanolin or another emulsion with an aqueous solution of medicinal substances until it is completely absorbed, after which the base is mixed.

Ointment emulsion type B / O.

Rp .: Kalii iodidi 5.0
Natrii thiosulfatis 0.1
Aquae purificatae 4,4 ml
Lanolini anhydrici 13.5
Basis emulsionis 27.0
Misce, fiat unguentum
Da. Signa. For rubbing.

Potassium iodide and sodium thiosulfate are dissolved in water and the resulting solution is emulsified with anhydrous lanolin. While stirring, to the resulting emulsion is added a water / vaseline consistent emulsion base. The ointment should have a yellowish color. The addition of sodium thiosulfate is designed to bind free iodine, which can be released even after short storage. The presence of a brown color ointment indicates the release of free iodine, in which case the ointment is not suitable for use. If iodine is prescribed as part of this ointment, then it is prepared without the addition of sodium thiosulfate.

Rp .: Novocaini 1.0
Kalii iodidi 0.5
Lanolini
Vaselini aa 5,0
Misce, fiat unguentum
Da. Signa. Lubricate the affected skin

Emulsion ointment type B / O with soluble substances. As part of the ointment ingredients are easily soluble in water.

Calculation: Wet purified (from water lanolin):

100% - 5.0

30% - x x = 1.5 ml (30 drops)

Lanol and anhydrous 5.0 - 1.5 = 3.5 g

Novocaine and potassium iodide are placed in a mortar and dissolved in 1.5 ml of water, which is part of aqueous lanolin (3o%), replacing it with anhydrous lanolin after appropriate calculations. Then was added 3.5 g anhydrous lanolin and

emus lgiruyut aqueous solution ohm drugs. Vaseline is added to the resulting emulsion and mixed until a homogeneous mass is formed.

PWC

Date No recipe
Novocaini 1.0
Kalii iodidi 0.5
Aquae purificatae 1,5 ml (gtts XXX)
Lanolini anhydric 3.5
Vaselini 5.0

m $_{zag.}$ = 11.5 ml Preparing : (signature)
Perevir: (signature)

Rp .: Protargoli 1.0
Lanolini 3.0
Vaselini 12.0
Misce, fiat unguentum
Da. Signa. Apply to the nasal mucosa .

Emulsion ointment type B / O with protargol that forms a colloidal solution. Protargol is introduced into the ointment necessarily in the form of a sol, for which it is first triturated in a mortar with a small amount of glycerin (per 1.0 g of protargol - 6-8 drops of glycerin), and then with water. If the water in the recipe is not spelled out, then water is used to dissolve protargol, which is part of water lanolin.

In this case, in a mortar, rub protargol with 6-8 drops of glycerin, after which it is dissolved in water (0.9 ml). The resulting solution of protargol is emulsified with 2.1 g of anhydrous lanolin, petrolatum is added and mixed until homogeneous.

Rp .: Collargoli 3.0
Aquae purificatae 1 ml
Lanolini 2.0
Vaselini 15.0
Misce, fiat unguentum
Da. Signa. Ointment for the nose.

Collargol (3.0 g) is triturated in a mortar with water (20 drops) and left for a few minutes, then aqueous lanolin (2.0 g) is added and mixed until the solution is absorbed, then petroleum jelly is added and mixed until uniform.

It is often nasal ointment, incl . and water borne e , administered in pure petrolatum. Since these ointments are poorly distributed on the moist mucous membrane, it is necessary to recommend the introduction of 5-10% lanolin to the doctor. If necessary, the introduction of vaseline ointment significant quantities of aqueous solution, lanolin additive can be carried out without notifying the

physician with a binding score of the recipe. The amount of vaseline must be reduced accordingly.

B / B type ointment *emulsions* are predominantly cooling ointments. They are characterized by a high content of water or aqueous solutions, which give these ointments softness, friability. Being applied to the skin, they have a calming effect, cooling, depending on the evaporation of water. Cooling ointments are indicated for inflammatory processes, acute and subacute forms of eczema, dermatitis. Action emulsion type ointments In / In is compared with the effect of wet dressings.

Emulsion of type B / B gives ointment, it is easily washed off from the skin with water, leaving no greasy spots. In addition, a significant amount of water-soluble drugs, such as ichthyol, as well as oily liquids, such as tar, etc. can be easily added to this ointment . Such drugs in amounts up to 10% can be mixed with the finished base, and in large quantities emulsify. These ointments have a specific feature: when applied to the skin in a relatively short period of time (5-15 minutes), they form a dense, soft layer to which the linen does not stick or become soiled. This layer keeps on the skin for a long time.

Among ointments, emulsions of the O / B type are protective ointments. Emulsifier, they usually act soaps formed during the manufacture of an ointment.

Rp .: Kalii carbonatis 1.0
Natrii tetraboratis 0,5
Olei vaselini 15.0
Stearini 10.0
Aquae purificatae 70 ml
Misce, fiat unguentum
Da. Signa. Protective ointment.

In a warm aqueous solution of potassium carbonate and sodium tetraborate, a thin stream of oil with stearin is added with constant stirring. In this case, potassium stearate is formed, and at the same time , mass thickens . After homogenization , a soft ointment with an alkaline reaction comes out from the blunt , which, when rubbed into the skin, is well and easily absorbed into the stratum corneum of the epidermis. After evaporation of the aqueous phase, a thin film (soap-oil) remains on the skin, impermeable to organic solvents, resins, varnishes, which makes it possible to use it as a protective one.

It is even better as an emulsifier to use triethanolamine - a syrupy pale yellow liquid that is miscible with water, alcohol, glycerin and most organic solvents. With fatty acids, triethanolamine easily gives soaps, which are part of dermatological ointments, increase the penetrating ability of medicinal substances. Triethanolamine emulsions do not irritate the skin. Widely used in the cosmetic industry (see 33).

Bentonite clays also have emulsifying properties.

Rp .: Picis liquidae 3.0
Bentoniti 2.0
Aquae purificatae ad 30.0

Misce, fiat unguentum

Da. Signa. Apply to damaged skin.

The tar is thoroughly mixed with bentonite. When dispersing tar in oligol bentonite, adhere to drops of tar with their lipophilic sites, while hydrophilic sites remain free. With the subsequent addition of water (in parts, with continuous rubbing), the hydrophilic parts of bentonite adsorb well, and the mass swells , taking on a soft, oily consistency.

The manufacture of combined ointments. These ointments can be considered as mixed-type ointments, consisting of individual types of ointments.

Combined ointments are complex multicomponent ointments containing several medicinal substances with different physicochemical properties that require the manufacture of various types of ointments: suspensions, emulsions, solutions, alloys.

The manufacture of combined ointments is governed by the same rules provided for in the technology of certain types of ointments. At the same time, taking into account the presence of the resulting combinations (for example, ointment-suspension and solution, or ointment-emulsion and ointment-solution, etc.). A different sequence of technological stages is possible, it must be rational.

In the pharmaceutical conditions for the manufacture of combined ointments carried out in the same mortar, if necessary, displacing the previously received part of the ointment to the nose or on the wall of the mortar. Therefore, if the combination ointment contains medicinal substances that form a suspension type of ointment, it is better to prepare an ointment suspension first in a mortar.

There are two methods for the manufacture of suspension- emulsion ointments: first prepare a suspension ointment, then an emulsion or vice versa (ointment-emulsion, then ointment-suspension) and get a combined dispersion system.

When the solid phase is added to the finished emulsion ointment or when it is initially mixed with a fat-like ointment base, the solid matter fractions are located in the ointment base next to the droplets of the emulsified phase.

Another technological option is possible in which the solid phase having hydrophilicity is moistened first with water or with an aqueous solution. If on the next mixing the resulting aqueous suspension is obtained with an ointment base combined system - the emulsion is an aqueous suspension in the fat minutes environment. The proportions of the solid phase in these cases are included inside the emulsified droplets of the aqueous phase, which in turn are distributed in the fatty base. In the latter case often are ointments , more active e therapeutically than in the first case. Thus, the technology affects the therapeutic efficacy of the ointment.

Rp .: Ephedrini hydrochloridi	1.0
Mentholi	0.15
Protargoli	1.0
Lanolini	2.0
Vaselini	8.0

Misce, fiat unguentum

Da. Signa. Ointment for the nose.

The ointment consists of ephedrine hydrochloride and Protargolum, soluble in water, forming conductive ointment-emulsion, and menthol -soluble base, defining ointment-solution (in an amount up to 5%).

First, it is advisable to prepare an ointment solution, and then an ointment emulsion. Considering the fact that dissolving protargol and ephedrine hydrochloride together is undesirable (the effect of the electrolyte on a colloidal solution), an ointment is prepared as follows. In a mortar, rub the 0.15 menthol with a few drops of vaseline oil (0.15 g) and mix with a portion of the petroleum jelly. The resulting mixture is pushed to the spout of the mortar. Ephedrine hydrochloride is added to the mortar and dissolved in 1/2 part of water (6 drops), which is part of aqueous lanolin (30%). The resulting solution is emulsified with a part of anhydrous lanolin, mixed with menthol solution in petroleum jelly and pushed to the spout of the mortar. Then the rotargol is ground with 6 drops of glycerin, dissolved in the remaining water (6 drops), this is mixed with the rest lanolin, mixed with the content of the mortar and the rest of vaseline to obtain a homogeneous mass.

Rp .: Ephedrini hydrochloridi 0.1
Dimedroli 0.2
Mentholi 0.3
Zinci oxydi 2.0
Lanolini 8.0
Vaselini 20.0
Misce, fiat unguentum
Da. Signa. Ointment for the nose.

Combined ointment: menthol - ointment solution, ephedrine hydrochloride and dimedrol (readily soluble in water) - ointment-emulsion, zinc oxide (not soluble in water or in base) - ointment suspension with a solids content of more than 5%.

In a porcelain (porcelain) evaporating dish on a water bath, about 1 / 3-1 / 4 parts of petroleum jelly are melted at a temperature not higher than 50 ° C and 0.3 g of menthol is dissolved in it. Put 2.0 g of zinc oxide into a warm dry mortar and carefully triturate with a small amount (= 1.0 g) of menthol solution in petrolatum, then add the remaining menthol solution in petroleum jelly and mix to the absence of individual visible zinc oxide particles. The resulting mass is removed celluloid plate from the walls of the mortar and placed on the edge of the mortar (or shifted to the spout). 0.1 g of ephedrine hydrochloride and 0.2 g of dimedrol are placed in the freed mortar and dissolved in 2.4 ml of water (30% aqueous lanolin). 5.6 g of anhydrous lanolin is added to the solution and mixed until complete absorption of the liquid phase. The resulting emulsion is thoroughly mixed with previously prepared ointment. suspension and remains Xia Vaseline until homogeneous light yellow color with a characteristic smell of menthol.

Rp .: Streptocidi 0.5
Bismuthi subnitratis 1.0
Basis polyaethylenoxydi 10.0

Misce, fiat unguentum

Da. Signa. Maz s dermatology .

Combined ointment: ointment-solution (by streptotsida) and ointment-suspension (by bismuth of the main nitrate). Streptocide dissolved in claim olietilenoksidn th basis is an alloy-PEO 1500 and PEO-400 in the ratio (3: 7).

The base is fused in a porcelain (porcelain) cup in a water bath, streptocide is dissolved in the alloy. In a pre-heated mortar, bismuth nitrate of the basic is first ground in a dry state, and then a part of the streptocide solution in the molten base. Gradually add the rest of the solution in parts and mix until cooling. Combined (suspension and partially emulsion) can be considered an ointment of the following composition :

Rp .: Kalii iodidi

Lanolini 10.0

Misce, fiat unguentum

Da. Signa. Apply to the nail plate.

This ointment is used to treat nail fungus (onychomycosis) and is designed for the ability of potassium iodide to loosen the nail plate. Technology ointment is as follows: potassium iodide is thoroughly ground in a mortar with 3 ml of purified water (30% from aqueous lanolin). Then, to the suspension of potassium iodide and partially its solution in water, 7.0 g of anhydrous lanolin are mixed while rubbing.

Typical combined ointments are also ointments that are prepared on emulsion bases. They, as a rule, are made in the conditions of the integrated production. However, with ready-made bases or available emulsifiers, they can also be prepared in pharmacy conditions. For example, in the presence of T-2 emulsifier, it is possible to prepare a consistent emulsion, and on its basis ointments with various disperse systems.

Rp .: Sulfuris praecipitati 100.0

Basis emulsionis 200.0

Misce, fiat unguentum

Da. Signa. Rub into the skin.

Sulfuric ointment simple (FS 42-1380-80). The combined ointment on an emulsion consistent basis water / vaseline.

Sulfur is gently but carefully ground in a pre-heated mortar, a portion (50.0-60.0 g) of the base is added and dispersed. Then add the base, remained, and mix thoroughly until a homogeneous mass.

QUALITY ASSESSMENT OF OILS

The quality of the prepared ointments is evaluated in the same way as other dosage forms, that is, they check the documentation (recipe, passport), packaging, design , absence of stratification and mechanical inclusions, deviations in weight. The identification is carried out visually in appearance and organoleptic characteristics (smell, color, etc.), which depend on the properties of the components of medicinal substances and used ointment bases.

The uniformity of ointments is determined by the size of the particles of the solid phase (GF XI). To do this, use a biological microscope equipped with an eyepiece micrometer MOB-1 with an increase in the eyepiece 15x and lens 8x. The dividing price of an ocular micrometer is calibrated against an object-micrometer for penetrating light (RPS). A sample of the ointment is taken, as indicated in the article "Sampling of drugs", and it must be at least 5.0 g. If the concentration of medicinal substances in ointments exceeds 10%, they are diluted with an appropriate basis for a content of about 10% and mixed. At selection it is necessary to avoid crushing of particles.

Method of determination. From the average sample ointment take a portion of 0.0 5 g and placed on the untreated side of the glass slide. The other side of the glass slide is processed in the following way: in the middle with its diamond or some other abrasive material a square with a side of about 15 mm and diagonals is applied. Lines paint with a pencil on the glass. A glass slide is placed in a water bath until the base is completely melted, a drop of 0.1% Sudan III solution is added for fatty, hydrocarbon and emulsion bases of B / O type or 0.15% solution of methylene blue for hydrophilic and emulsion bases of O / B type and mixed . The sample is covered with a cover glass (24x24 mm). They fix it by weak pressing and look through the four fields of view of the segments formed by the diagonals of the square. For the analysis of one drug, five determinations of the average sample are carried out. In the field of view of the microscope should be no particles whose size exceeds the norm,specified in their own articles.

Determining the pH of ointments necessary to control the stability of medicinal substances and bases during storage. Violation of the pH indicates a change in their physico-chemical properties.

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

One of the important factors on which the consistency depends is the ultimate shear stress, which characterizes the ability of the ointment to exert some resistance in smearing and elasting (the ability to be squeezed out of tubes, dispensers, etc.).

Important rheological characteristics ointment is plastic viscosity, which may be determined in a rotary viscometer, and the plastic strength, determined on a conical plastometer e .

IMPROVING THE TECHNOLOGY OF OILS

The direction of improvement is the expansion of the range of bases for ointments and their targeted choice depending on the purpose of the ointment. An example is the Nitrong ointment, in which the base (paraffin, cetanol, hydroxypropyl cellulose, petrolatum) promotes the uniform absorption of nitroglycerin by the skin. The ointment acts by prolonging and is prescribed as an additional agent in combination with orally used drugs for the prevention of strokes.

For the effects of drugs on local processes in the rectum or on the body as a whole, promising use of rectal ointments, as this drug is easily and quickly absorbed.

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

Improving the technology of ointments and their quality is carried out in the following areas:

- Improving the chemical, physical, microbiological stability of bases and ointments;
- Development of affordable and objective methods for assessing the quality of ointments;
- Improved packaging;
- Development and implementation of elements of small-scale mechanization in the manufacture of ointments in pharmacies;
- Expansion of the range and standardization of the formulation of ointments and pastes. The main directions of development of ointments can be divided into the following stages:

1. The study of biological processes occurring during exposure of the drug to damaged and intact skin.
2. The creation of soft dosage forms with controlled influence and release of drugs that provide the expected therapeutic effect in a certain place and in the expected time.
3. Search for carriers that provide delivery of medicines to the site of the disease.

5. Material of activation of students during the presentation of a lecture / problem questions, problem situations, etc. /.

Control questions:

1. Characteristics of ointments as a dosage form, and a disperse system, their classification (for medical purposes, place of application, consistency and physical and chemical properties of the inbound ingredients). Requirements for ointments.
2. Classification bases for ointments and requirements for them. Principles of selection of the bases.
3. Characteristics of hydrophobic and hydrophilic bases.
4. The main technological stages and rules for the preparation of homogeneous ointments: solutions, alloys.
5. Pharmacopoeial prescription of ointment solutions.
6. Evaluation of quality, storage of homogeneous ointments in accordance with the requirements of normative-technical documentation, packaging and processing for the release.
7. Characteristics of the diphilic bases for ointments and emulsifiers, which are used for their preparation.

8. Characteristics of suspension (triturative) ointments and methods of their preparation, depending on the percentage of medicinal substances. Prophylactic impressions of suspension ointments.

9. introduction to dermatological ointments of some medicinal substances (resorcin, zinc sulfate).

10. Pastes their classification. Features of the preparation of dermatological pastes.

11. Characteristics of liniments as a dosage form and dispersion system, their classification.

12. Rules for the preparation of liniments of various disperse systems: solutions, suspensions, emulsions, combined.

13. Pharmacopoeial and difficult to register linimentov.

14. Quality assessment, storage of liniments in accordance with the requirements of regulatory and technical documentation, packaging and clearance for tempering.

Test items:

1.The doctor prescribed sulfuric ointment for scabies. Specify the basics that should be used for its preparations in a pharmacy:

* Pork fat or emulsion base
wax or petrolatum
cocoa butter or butyrol
soap-glycerin or starch-glycerin
lanolin or paraffin

2. A pharmacist prepares the ointment according to the prescription:

Rp.: Streptocidi 1.0
Vaselini 9.0 m. f. unq.
DS For the treatment of burns.

Specify a rational way of introducing the substance into the base:

* Streptocide is dispersed with 0.5 melted vaseline
streptocid dispersed with 4.5 melted vaseline
streptocid is dispersed with 0.5 unmelted vaseline
streptocid is dispersed with 4.5 not melted vaseline
streptocid dispersed with 9.0 melted vaseline3.

3. The pharmacist must prepare an ointment, which consists of substances that are not soluble either in base or in water in an amount of more than 5%. How to enter them to the base?

* Grind with a portion of the molten base
grind with all non-melted foundation
grind with a piece of non-melted base
grind with a base fluid
grind with alcohol-water-glycerin mixture

4. Pharmacy received recipe for production streptocid hydrochloric ointment without concentration. What concentration will the pharmacist prepare the ointment for?

*10%
5%
1%
20%
2%

5. The pharmacy received a prescription for ointment with a collar. As the excipient used for the dissolution assistant Collargol?

* water
glycerol
vaseline oil
ethanol
sunflower oil

6. The patient needs to prepare 50.0 xero formic ointment. What is the amount of xeroform used by the pharmacist?

* 5.0
10.0
3.0
2.5
0.5

7. To prepare the ointment, the pharmacist additionally used paraffin. What role does paraffin have in technology?

* seal
the foundation
preservative
for dispersing powders
emulsifier

8. The pharmacist must prepare a yellow mercury ointment. Specify the optimal technology (in aseptic conditions):

* The substance is ground with vaseline oil, sterile vaseline and lanolin are added.

The substance is dissolved in water, sterile petroleum jelly and lanolin are added.

The substance is ground with a melted sterile base.

The substance is ground with glycerin, add the base

The substance is ground with alcohol, sterile vaseline and lanolin are added.

9. A patient has come to the pharmacy, a cat orom needs to prepare camphor ointment. What concentration of ointment should be prepared by a pharmacist, guided by the requirements of regulatory documents?

* 10%.
20%.
15%.
5%.
1%.

10. The patient is prepared 50 g of zinc ointment. Should the pharmacist weigh out the amount of zinc and vaseline?

* 5.0 g and 45.0 g
10.0 g and 40.0 g
2.5 g and 47.5 g
1.0 g and 49.0 g
0.5 g and 49.5 g

11. A pharmacist prepared liniment-solution. Choose dishes for cooking:

* Bottle for holiday
Cylinder
Stand
Mortar
Volumetric flask

12. A pharmacist prepared Vishnevsky suspension liniment. Specify the mode of administration of xeroform:

* Grind dry, mixed with half the amount of tar.
Crushed with alcohol.
Grind dry, mixed with the entire amount of tar.
Dissolved in the entire amount of oil.
Crushed, mixed with butter.

13. The patient needs to prepare Vishnevsky's liniment. What substances can be used as a basis for liniment, guided by the requirements of regulatory documents?

* Castor oil or fish oil.
Sunflower or cottonseed oil.
Oil camphor or henbane.
Vaseline oil or petroleum jelly.
Vaseline or lanolin water.

14. Rosenthal liniment is prescribed to the patient. What components are included in its composition?

* Paraffin, alcohol, chloroform, iodine.
Castor oil, calcium chloride, alcohol.
Chloroform, methyl salicylate, turpentine.
Iodine, potassium iodide, glycerin.
Sunflower oil, ammonia solution, oleic acid

15. The patient needs to prepare a protective cream. What substance most protects the skin from the action of harmful environmental factors ?

* Zinc oxide.
Oil cotton .
Almond oil.
Calcium chloride.
Sodium chloride.

16. The pharmacy received a prescription:

Rp: Xeroformii
Picis Liquidae Betulae ana 3.0
Olei Ricini 100.0

MDS For lubrication of wounds. Specify the type of dosage form:

* liniment
ointment emulsion
paste
combination ointment
ointment solution

6. General material and methodological support of the lecture:

- educational premises;
- overhead; slides;
- illustrative materials.

7. Materials for self-preparation of students:

a) on the topic of the lecture presented / literature, questions, tasks, test tasks /;
b) topics of the next lecture / literature, list of main questions, test items /.

8. The literature used by the lecturer to prepare the lecture.

Basis literature:

1. Drug technology. Teaching aid: Teaching aid for higher educational institutions / V.I. Tikhonov P.A. Logvin, S.A.Tikhonova, A.V. Mazulin, T.G. Yarnikh, A.S. Shpichak, A.M. Kotenko; Edited by A.I. Tikhonov - Kharkiv: NUPh; Original, 2009. - 432 p.

2. Medicine technology: study guide / O.S. Marchuk, N. Would. Androschuk - Kiev: Medicine, 2008. - 488 p.

3. Production of medicines. Quality control and regulation: prak.ruk. / ed. Sh.K. Gad; per. from English V.V. Coastal. - SPb .: Profession, 2013. - 960 pp., Ill.

Additional:

1. Soft dosage forms: Exttemporal formulation: Methodical recommendations / A. I. Tikhonov, T. G. Yarnikh, A. V. Lukienko, etc .; Ed. A.I. Tikhonov. - X .: Type of NUPh; Golden Pages, 2003.-128 p.

2. Aseptic dosage forms: Ecological temporal formulation: Methodical recommendations / A. I. Tikhonov, L. V. Bondareva, T. G. Yarnikh, N. F. Orlovetska, etc .; Ed. A.I. Tikhonov and T. G. Yarnikh. - X .: Type of NUPh; Original, 2005. - 184 p.

3. Solid dosage forms: Ecsttemporal formulation: Methodical recommendations / A.I. Tikhonov, T.G. Yarnikh, S.V. Gritsenko and others; Ed. A.I. Tikhonov - Kh .: Type of NUPh; Golden Pages, 2003. - 176 p.

4. Liquid dosage forms: Ecstemporal formulation: Methodical recommendations / A.I. Tikhonov, T.G. Yarnikh, N.F. Orlovetska and others; Ed. A.I. Tikhonov and T. G. Yarnikh. - X .: Type of NUPh; Original, 2005. - 160 p.

Lecture №8: **«Preparation of suppositories by rolling out and pouring out»** - 2h.

1. Relevance of the topic. Substantiation of the topic. Suppository dosage forms have been known since antiquity. From a technological point of view, in the history of suppositories there are distinguished: the first period is the time before the introduction of cocoa butter, as suppository bases (approximately to the XVIII century), the second is the time of its indivisible predominance as the basis.

(Approximately until the end of the second decades of the 20th century). And the third is the time for extensive searches for cocoa butter substitutes (present). Such a periodization in the history of the suppository is quite natural and necessary, since, on the one hand, the properties, the introduction of the suppository are mainly determined by the foundation, and on the other, the nature of the applied foundation as a whole is due to the development of pharmacy and medicine, progress in the development of medicines and their introduction into practice.

In recent years, industrial output and the nomenclature of suppositories have increased in our country. Suppositories with ichthyol, belladonna extract, nystatin, methyluracil, piroxicam, diphenhydramine are produced. The suppositories prescribe steroid hormones, thyroid hormones, various vitamins, antibiotics, alkaloids, phenothiazine derivatives, pyrozolone, etc.

The importance of rectal suppositories as a means of rapid delivery of drugs in life-threatening cases has increased. Suppositories are available for the relief of hypertensive crises, spasm of blood vessels and bronchi, rapid recovery of heart rhythm and respiratory distress. In some cases, medicinal substances, administered as suppositories, enter the bloodstream faster than with subcutaneous administration, and have a therapeutic effect in smaller doses (estrogenic hormones). The promise of this dosage form becomes apparent when you consider that some medicinal substances taken orally are inactivated by the digestive juices and injure the gastrointestinal tract.

2. Objectives of the lecture:

- training:

- to study the methods of suppository preparation: manual shaping, pouring;
- To teach students to carry out calculations related to the preparation of suppositories;
-define requirements for suppositories, teach classify suppositories,
- Teach to navigate in the main directions of state regulation of the production of suppositories;
- To teach reading recipes in Latin, to analyze their components and to evaluate the correctness of the statement;

- educational:

-Upbringings skills to use the SPh and SPh International, other regulatory and technical documents as well as reference books to find information on the composition, preparation, storage and dispensing of medicines.

3. Plan and organizational structure of the lecture.

№№ pp	The main stages of the lecture and their content.	Goals in levels of abstraction	Type of lecture, lecture equipment.	Time distribution
1	2	3	4	5
1.	***Preparatory stage***			
	Definition of learning objectives.			2%
	Providing positive motivation.	I		2 %
2.	***The primary stage***			
	Statements of the lecture material.plan:		References, visual	
	1 Suppository preparation methods		material.	10-20%
	2. Calculations associated with the preparation of suppositories;		State Pharmacopoeia	20 -30%
	3. Methods of preparation of suppositories;	II	main regulatory technical	30 -40%
	4 ..Suppository quality control in pharmacy conditions.	III	documentation.	
	5. Methods of improvement			
		II		
3.	***The final stage***			
	Summary of lectures, general conclusions.		References, questions, tasks	20% 10 -20%
	Lecturer's answers to possiblequestions.	I		
	Task for student self-training .			

4. The content of the lecture material:

Suppositories are dosage forms that are solid at room temperature that melt or dissolve at body temperature.

The name “suppositories” is a collective term assigned to a group of dosage forms intended for introduction into easily accessible body cavities, natural channels and pathological holes. The Latin word suppositorius means fake, comes from supponere - enclose.

Suppository dosage forms have been known since antiquity. From a technological point of view, in the history of suppositories, there is a distinction: the first period is the time before the introduction of cocoa butter as a suppository base (approximately until the 18th century), the second is the time of its undivided

advantage as the basis (approximately by the end of the second decade of the 20th century) and the third is time search for cocoa butter substitutes (our days). Such a periodization in the history of suppositories is quite natural and necessary, since, on the one hand, the introduction properties of suppositories are mainly determined by the foundation, and on the other, the nature of the applied foundation is generally determined by the development of pharmacy and medicine, advances in drug development and their introduction into practice.

In recent years, our country has increased industrial output and the nomenclature of Supozitoriv. Suppositories with ichthyol, belladonna extract, nystatin, methyluracil, piroxicam, diphenhydramine are produced. In suppositories, steroid hormones, thyroid hormones, various vitamins, antibiotics, alkaloids, phenothiazine derivatives, pyrazolone, etc. are prescribed.

The value of rectal suppositories as a means of rapid delivery of drugs in life-threatening cases has increased. Suppositories are available for stopping hypertensive crises, spasm of blood vessels and bronchi, quick recovery of heart rhythm and respiratory disorders. In some cases, medicinal substances, administered as suppositories, enter the bloodstream faster than with subcutaneous administration, and give a therapeutic effect in smaller doses (estrogenic hormones). The promise of this form is even more evident when one considers that certain medicinal substances are ingested, are activated by digestive juices, injuring the gastrointestinal tract.

Depending on the site of administration, suppositories are distinguished:

- Rectal (suppositoria rectalia suppositories), intended for insertion into the rectum;
- Vaginal (balls - suppositoria vaginalia), designed to enter into the vagina;
- Bacilli (bacilli) for insertion into the fistular passages, ureter, cervical canal, auditory canal, etc.

Rectal suppositories may have the shape of a cone, a cylinder with a pointed end (or cigars), torpedoes, that is, bodies with a pointed end and a thickening in the middle. Their length should be from 2.5 to 4 cm, and the maximum diameter of 1.5 cm, the mass should be allowed in the range from 1.0 to 4.0 g.

Vaginal suppositories can be sferichny (balls) - globuli, ovoid (ovules) - ovula or in the form of a flat body with a rounded end (pessaries) - pessaria, which is derived from the Latin word pes-sarium, which means a ring that serves to contain displaced uterus. Their mass of guilt is in the range from 1.5 to 6.0 g.

The rods have the shape of a cylinder with a tailing end and a diameter of not more than 1 cm. The length of the rods usually does not exceed 10 cm, and the mass should be from 0.5 to 1.0 g.

The geometric shape of the candle is important, since the speed of its introduction depends on the shape. With the introduction of a candle in the rectum, the and must overcome the reflex resistance of the sphincter, which closes the anal opening. If the candle is of a conical shape, then as it is introduced, the resistance of the sphincter increases and this increasing resistance acts on the candle at thetime of its full immersion. On a candle of a cylindrical shape, the muscles only oppose when entering the sharpened part of it, since after that its diameter is the

same to the very end. With the introduction of a cigar-like candle, resistance is felt until the introduction of the wide part, after which, thanks to reflex compression and inertial force, the candle quickly enters the rectum. Rational rectal shape - a form of torpedoes (cigars).

Of all the above vaginal forms, pessaries are the most rational, since with the same mass they have a relatively larger surface than ovules, and especially balls, and pass from solid to liquid much faster.

Despite the fact that the suppository dosage forms have a different purpose and place of entry, they all have a common characteristic: at room temperature, they are solid bodies, and at the place of use they turn into liquid. Their suppositories are based on this medical purpose, because their hardness makes it possible to overcome the reflex resistance of the muscles and tissues of natural and pathological channels, and the fluid formed provides a uniform distribution throughout the mucous not only of the base, but also of the drugs included in it both locally and receptively.

Vaginal suppositories are prescribed mainly for the purpose of local exposure: disinfectant, astringent, cauterizing, anesthetic, against puzzling. Rectal suppositories are considered as a medicinal form not only for local, but also for resorptive action in violation of cardiovascular activity, neuropsychiatric disorders, and so on. The zastosuvannya in the latter cases is explained by the rate of exposure to drugs, recognized as suppositories. Drugs are absorbed in the lower part of the rectum through the lymphatic and venous systems of the pelvis, and they enter the bloodstream without passing through the middle and lower hemorrhoidal veins. It is believed that according to the speed of action of medicinal substances suppositories can compete with dosage forms for intramuscular injections. Therefore, in the manufacture of a suppository, it is necessary to check the doses of toxic and potent substances, just as in dosage forms for internal or injectable use.

From the physico-chemical point of view, suppositories should be considered as dispersed systems consisting of a dispersion medium (base) and a dispersed phase (various drugs in solid and liquid state). Depending on the properties of medicinal products, supporters can form various dispersed systems. Heterogeneous systems are established in cases when the medicinal substance is distributed in the base by the type of suspension or emulsion, homogeneous - when the medicinal substance is dissolved in the base.

Requirements for suppositories. In addition to this form, and mass, deviations in the mass of suppor tory should not exceed ± 5%. Medicinal substances contained in them must be accurately metered. The mass of the base for suppositories indicated in the recipe should not decrease without agreement with the doctor, as this leads to an increase in the concentration of the active substances in the suppositories. Suppositories should have the correct and, accordingly, the same shape, homogeneous mass, sufficient hardness (mechanical strength) and melt at body temperature. The suppository mass should be homogeneous, without inclusions, marrow and spangles.

Suppository basics

For the manufacture of suppository dosage forms should be used fundamentals, with specific features. To suppository bases are imposed on the requirements:

- Sufficient hardness at room temperature and the ability to melt at a temperature not higher than 37 ° C, that is, the ability to drastically change from the solid state in the liquid, bypassing the softening stage — the oil-like stage; sufficient viscosity, lack of odor, ensuring maximum contact between the medicinal substances and the mucous membrane
- Chemical and pharmacological indifference, no irritant. resistance to external factors (light, heat, moisture, oxygen, microorganisms)
- The ability to easily take the appropriate form, mix with as much as possible of medicinal substances, not to interact with them and to be stable during storage;
- The ability to easily release medicinal substances, contribute to the manifestation of their pharmacological action, depends on the properties of the basics, and the method of introduction of medicinal substances into the base;
- The presence of appropriate rheological parameters and optical structural and mechanical properties.

The quality of the foundations is determined by the SPh XI or by the NTD. When checking the quality of fatty bases, it is necessary to determine the melting temperature, acid and iodine numbers (they should not exceed the values established for these bases), tests for the absence of impurities. Very important for the quality of the basics are their hardness and plasticity, on which the convenience of entering suppositories prepared on these bases depends. To determine the fatty bases, the Osminin instrument is used, which shows the load value in g / cm needed for a standard size bar of oil to be cut with a wire of 0.25 cm in diameter for 1 minute. For this purpose, a “penetrometer” device can be used, the application of which measures the depth of immersion in oil of a standard cone of a certain weight within a specified time, as well as a “hardness meter” and some other devices.

Currently, for the manufacture of suppositories used a wide range of bases that differ in physico-chemical properties. They can be divided into two groups: hydrophobic and hydrophilic.

Hydrophobic bases. SPh XI recommends using cocoa butter, alloys of cocoa butter with paraffin and hydrogenated fats, vegetable and animal hydrogenated fats, solid fats A and B, lanol, alloys of hydrogenated fats with wax, hard paraffin and other bases permitted for medical use as hydrophobic bases.

Cocoa butter (Oleum Cacao seu Butyrum Cacao) is produced by hot pressing from the purified seeds of a chocolate tree, filtered and poured into molds. After cooling, it is a dense homogeneous mass of light yellow color with a faint aromatic smell and a pleasant taste.

For the first time cocoa butter was applied in 1766 by the French pharmacist Antoine Bom. At room temperature, it is a solid product, chemically characterized by the content of mixed triglycerides: tristearin, tripalmitin, triolein. trilaurine, triarahina. It has a pronounced melting point (30-34 ° C), mixed

with various medicinal substances. Adding a small amount of anhydrous lanolin turns into a plastic mass. It is characterized by polymorphism and the variability of the melting point associated with it. When storing cocoa butter at a temperature above 10 ° C, it undergoes a phase transformation, which leads to the formation of a vitreous modification that melts at a temperature of 24-26 ° C (suppositories will be deformed in the patient's hands). The most stable (of the existing a b1 and b forms) is the b modification of cocoa butter.

In addition, it should be noted that when heated above the melting point (35 ° C), it is difficult to solidify. Therefore, it is used mainly only for the method of manual downloading and pressing of suppositories.

Cocoa butter contains up to 30% oleic acid, which causes it to burn (it turns white and gradually loses its fragrance). It is difficult to use in the hot season: it is poorly emulsifying water and aqueous solutions (only 4-5%). Cocoa butter contains viable microorganisms, so candles that contain solutions of medicines, mold, and medicines decompose.

English laurel oil (Oleum Cinnamomi pedunculali) is obtained from the nuclei of laurel fruits. This is a mass of yellowish solid consistency, pleasant aromatic taste, melts in the mouth, occupies an intermediate place in quality between coconut oil and cocoa butter. Melting point 34-35 ° C. It is very important that at this temperature the oil, bypassing the ointment-like consistency, immediately goes into a liquid state. Sweet laurel oil in the form of suppositories has the same properties as cocoa butter.

Coriander oil (Oleum Coriandri) is obtained as a by-product from seed residues after the distillation of the essential oil. Fat coriander oil contains about 50% of the dense part, consists of petroselinic acid triglycerides, having a melting point of 30-3 1 ° C. The oil can be used as a candle base as a substitute for cocoa butter. From the plants of the umbrella family, except coriander oil, fatty oils of cumin and anise were isolated and studied. Their solid part consists mainly of triglycerides of petroselinic acid, which contain about 20%, their melting temperature is 29-31.5 ° C. For their physico-chemical and other properties, the listed oils approach coriander, therefore they can be used as suppository bases.

Hydrogenated fats. As cocoa butter substitutes, alloys of hydrogenated fats with fat-like substances, emulsifiers or hydrocarbon products are widely used.

Substances such as wax, paraffin and spermaceti are used to increase the melting point of alloys, and lanolin, lecithin, cholesterol and others - to improve the sensibility of the alloys with water.

It was established experimentally that the addition of 8% hydrogenated fat (melting temperature 46 ° C) and 4% paraffin (melting point 56 °C) increase the smoothness of the mass by 2-3 °C, and its hardness increases by 2-3 times. Replacing wax with wax does not give the desired result due to the peculiar viscosity of the wax.

For the first time, an alloy of hydrogenated fats with 4% paraffin called butyrol was proposed in 1934. A. G. Bosini. Currently, the butyrol base consists of 50% hydrogenated fats, 20% paraffin, 30% cocoa butter (HFC 42-836-73), has a melting point of 37 ° C and a cocoa butter hardness of 66.5%.

With hydrogenated fats, most commonly used fat is fat having a melting point of 32-34 ° C, obtained by hydrogenating cotton or sunflower oil and subsequent purification. According to the SPh XI, hydrogenated fats are accepted as the suppository bases of many pharmacopoeias of the world. For example, the Swiss SPh has taken hydrogenated peanut butter, the British have sunflower oil, etc.

Hydrogenated fats with surfactants additives. This group of suppository bases is currently gaining the most popularity. For example, Yu. A. Blagovidova, I. S. Azhgikhina found that the alloy of hydrogenated cotton oils with 4-5% T-2 emulsifier (GHM-5T) is not inferior in its properties to cocoa butter and has some advantages due to the content of emulsifier T 2, which contributes to the absorption of aqueous solutions and enhances the absorption of medicinal substances. The basis is recommended for the manufacture of suppositories by pouring with various substances: norsulfazole, sulfadimezin, sodium sulfapiridazine, nobiotsin sodium salt, etc. - 2 or with 3% emulsifier propylene glycol monostearate.

Products of thermal fractionation of fats and hydrogenates. At the basis of the production of these products, there is a release from natural or hydrogenated fats with chemical or temperature indications of narrow fractions of glycerides that are similar in properties to cocoa butter. The first basis of this type - sebuvinolum (Sebuvinolum) is a fraction of beef tallow; it has a hardness of what is oil and melting temperature of 36-37 ° C. This base is used for the manufacture of suppository dosage forms by the method of lithiation. I. S. Azhgikhina proposed acetonoroscin fraction of hydrogenation of beef tallow and palmweed grease oil. After removal of acetone, solid products are obtained, to which one of the emulsifiers is added to obtain the base: T-2 in an amount of 3%, propylene glycol monostearate (PGMS) - 5 or 10%, sugar glycerides (SG) - 0.5%, sucrose distearate (DSS) - 0.5%.

Fatty and fat-like bases, depending on their composition, have different viscosity and plasticity, on which the use of one or another method of making suppository dosage forms depends. Bases containing fats may zgirkats. Many drugs are worse adsorbed from fatty and fatty bases, have the least activity and are partially removed from the channels along with the base.

By hydrophobic bases am include esterification products aimed high molecular alcohols with fatty acids derived semisynthetically. From glycerol esters, the most interesting are glycerol and lauronic acid esters, phthalic acid ester and high alcohols, etc.

Imhausen H (Imhausen H), or Witepsol H (Witepsol H) is an imported patented base (Germany), consisting of lauric and stearic acid triglycerides. The emulsifier is monoglycerol ester of lauric acid. Melting point 33.5-35.5 ° C. Time of complete deformation of suppositories within 15 minutes.

Lazupol (Lasupolum G) is included, as a basis, in the pharmacopoeias of a number of foreign countries. It is a mixture of phthalic acid esters with higher alcohols, for example, cetyl and free alcohols. Melting point 34-37 ° C. Full deformation time within 15 minutes.

Lanolev basis has the following composition:

lanolin 60.0 (80.0)
confectionery fat 20.0 (10.0)
paraffin 20.0 (10.0)
Obtained by fusing ingredients.

Lanol is a mixture of phthalic acid esters with high molecular weight sperm alcohols. It is a hard waxy mass of yellow-brown color, peculiar smell. Melting point is 35.5-37.5 ° C. Lanol is used for the manufacture of suppositories by the pouring method.

Solid fat In the pharmacy practice use solid fat type A and B. Solid fat type A contains 100% solid confectionery fat. It is recommended when using the casting method, for suppositories, which include lipophilic (vegetable oils, oil solutions) and powdered substances in an amount up to 15%. Type B solid fat contains 95-99% solid confectionary fat and 1-1.5% stearic acid monoglyceride (T-1 emulsifier or No. 1 emulsifier). It is recommended for the manufacture of suppositories with Vodozhiron insoluble powders and liquid extracts.

Hydrophilic bases. SPh XI hydrophilic bases s recommended: gelatin in - glitseri new and soap-glycerol gels, alloys of different molecular weight polyethylene oxide and other permitted for use.

The process of absorption of drugs from these bases occurs regardless of their melting point, since the absorption is due only to the rate of diffusion of drugs from the base and the rate of dissolution of the bases themselves. These bases can be used for the manufacture of candles, balls and sticks by casting only.

Gelatin-glycerol basis (Massa gelatinosa) consists of gelatin, glycerol and water and, in various pharmacopoeias found in various ratios. The content of gelatin in the base can vary from 10% (France) to 20% (Hungary). Density Gelatin s of glycerine bases depends on the amount of gelatin: it is less than, the base is softer and melts more quickly. The degree of drying of the base depends on the amount of glycerol, especially during long-term storage: the more glycerol, the slower its drying. Therefore, depending on the requirements for the base, change the number of its constituent parts. It absorbs substances soluble in water and glycerin. The Official Recipe of Gelatin in - glycerin basis: gelatin - 1, water - 2, glycerin - 5 parts.

Making the base: chopped gelatin is poured with purified water at room temperature and allowed to swell for 30-40 minutes, after which glycerol is added and heated until a transparent homogeneous mass is formed. Finished base should be 8.0 g.

Gelatin in -glitserinovaya base has a number of drawbacks. Due to its low mechanical strength, it is most often used for the manufacture of vaginal suppositories. If the administration and a significant amount of elec trol of in observed phenomenon Sinersis. Gelatin is also incompatible with acids, alkalis and viscous agents. Gelatin with heavy metal salts forms insoluble products. When storing gelatin in a glycerol base, it dries quickly and molds, because it is a good medium for the development of microorganisms.

Soap-glycerin base (Massa sapo-glycerinata) is a solution of soap in glycerin. Prepare this basis by various methods depending on the initial components and

their quantity. Austrian and Polish Pharmacopoeias recommend preparing soap with stearic acid and sodium carbonate. According to the pharmacopoeias of other countries (USA, Hungary, Holland), the bases are obtained by fusing the finished medical soap with glycerin. The following copybook is given in the Hungarian Pharmacopoeia: medical soap - 10 parts, glycerin-90 parts, water - 10 parts.

The official formula of the soap-glycerin base on DF X for 20 suppositories has the following composition: glycerol 60.0 g, sodium carbonate (crystalline) 2.6 g, stearic acid 5.0 g.

Preparation of the base: in 60.0 g of glycerin, 2.6 g of sodium carbonate are dissolved by heating in a water bath, then 5.0 g of stearic acid is added in small portions. The mixture is evaporated to 66.0 g, the soda soap is formed - $C_{17}H_{35}COONa$:

As follows from the above equation, to neutralize 5.0 g of stearic acid you need

$$\frac{286,16 \times 5}{568,6} =$$

2.51 g of crystalline sodium carbonate.

Mix to remove carbon dioxide and the disappearance of the foam, then the mass is poured into molds so that each candle contains 3.0 g of glycerin.

It is also possible to use as a base for suppositories 8-10% diluent of soap in glycerin, which is more rational and easier to manufacture. Prepare fused Niemi medical soap, consisting, mainly, of sodium palmitate, stearate and glycerine. This produces a dense enough the jelly.

Candles, obtained on the soap-glycerin-based (mylets), have significant hygroscopicity and, as a rule, are used without the addition of other drugs. They act as a weakening, it is associated with a local irritant effect, and causes a reflex motility of the intestine. When you release the candles should be wrapped in foil.

Synthetic foundations. From water-soluble synthetic bases in domestic practice as well as abroad, use products of varying degrees of polymerization of ethylene oxide, which have complete physiological indifference. It is known that solid polymers of ethylene oxide are used in Germany under the name “Postonal”, and with a soft consistency - “Postonal B”, in France they are called “Scurol”, the United States produces “Carbowax”, approaching the melting temperature to post-melt human body temperature.

Polyethylene oxide bases. The receipt of polyethylene oxide, their properties and use as a basis for ointments is mentioned above (see Crop. 281). By combining polyethylene oxides of different consistency, it is possible to obtain bases with the desired structural and mechanical properties. For pendently from the melting point, degree of polymerization, molecular weight, hardness and other vlas tivostey PEO can be used not only as an ointment bases, but also as a base for suppositories.

Polyethylene oxide bases have a number of positive properties:

- They are able to dissolve in the secrets of the mucous membranes, which eliminates the need for selection of substances with exactly the desired melting point;
- The drugs included in them completely give up and do not irritate the mucous membranes:
- Long term is preserved, does not change and does not create an environment for the development of microorganisms;
- When making supozitornih dosage forms can be used molding methods and pouring;
- Can be used in subtropical areas, as well as they tolerate temperature fluctuations;
- Suppositories with polyethylene oxide have a good presentation, relatively cheap;
- The manufacturing process is easily automated.

Disadvantages of polyethylene oxide bases:

- Incompatibility with a large number of medicinal substances - (phenol, resorcin, tannin, salicylates, iodides, bromides, salts of mercury, bismuth, silver, etc.);
- Slow and incomplete solubility in the rectum, therefore, slow and inconstant absorption rate of medicinal substances:
- Polyethylene oxides attract moisture from the surrounding tissues and dissolve in it, causing antiphysiological ecsoosmosis (dehydration of mucous membranes), discomfort in the rectum;
- Solutions of PEO have low viscosity and are able to follow from the cavity.

Due to these disadvantages, the use of polyethylene oxide as a basis for rectal suppositories has decreased. However, they are used for vaginal forms. In the literature for the manufacture of suppository bases can be found various combinations of PEO. The most optimal composition is considered PEO-400 60%, PEO-4000 20%. PEO-1500 20%. Apply and other relationships. Bases are produced by fusing ingredients in a water bath.

In the manufacture of suppositories as preservatives, emulsifiers, thickenings, etc. can be fixed with butyloxytoluene, butyloxyanisole. citric acid, emulsifier No. 1. emulsifier T-1, emulsifier T-2, tween-80. wool wax alcohols, aerosil and other excipients permitted for medical use.

Prescribing Suppositories

Suppositories are prescribed in recipes in two ways: distributive and separate. Separate prescription is rarely used.

1. Distribution method - the number of medicines prescribed per candle or ball and an indication of how much they need to be prepared is given.

The number of basics indicate (qs) or indicate its number.

Rp .: Tannini 0,2	Rp .: Anesthesini 0.05
Amyli 0.3	Xeroformii 0.1
Olei Cacao 2.0	Olei Cacao qs,
Misce, fiat suppositorium	ut fiat globulus vaginalis
Da tales doses No. 10 Signa.	Da tales doses № 6
Signa.1 candle 2 times a day	Signa. 1 ball 2 times a day

Rp .: Tannini 2.0
Amyli 3.0
Olei Cacao 20.0
Misce, fiant suppositoria No. 10
Signa. 1 candle 2 times a day.

The number of drugs in the chopsticks is prescribed similarly to candles and balls, but the number of the base is not indicated, but the dimensions (length and diameter) of the sticks and their number indicate.

Rp .: Iodoformii 0.1
Olei Cacao qs,
ut fiat bacillus longitudine 5 sm et diametro 5 mm
Da tales doses № 6
Signa. Enter into the urethra on 1 stick 2 times a day.

Suppository technology

Suppositories are both homogeneous and heterogeneous dispersed systems, so the main technological task is to evenly distribute the most dispersed drugs not only in the suppository mass, but in each candle, ball or stick, giving them the necessary geometric shape.

If the weight of the candle in the recipe is not specified, then in accordance with the instructions of GF XI they are prepared weighing 3.0 g. In children's practice, the weight of the candle must be indicated in the recipe, it should be from 0.5 to 1.5 g.

If the mass of vaginal suppositories is not specified, they are prepared with a weight of at least 4.0 g. The size of the sticks should be indicated in the recipe.

Methods for the manufacture of suppositories. Suppositories can be made by three methods: by rolling (by hand molding), by pouring into molds and by pressing.

The use of a particular method depends on the properties of the base, its method NOSTA give plastics, solidification rate after melting, fluidity under pressure. To obtain suppositories using the pumping method, only cocoa butter or its substitutes are used; by pressing - cocoa butter, butyrol, PEO (with the press van and many of them soften); by pouring out, water-soluble and all fatty bases (except cocoa butter, which, when heated, turns into a low - melting modification).

In the process of technology, suppositories can easily be contaminated with microorganisms, therefore, when making them, it is necessary to pay special attention to strict compliance with sanitary rules (clean hands and devices, protect the suppository mass from microorganisms, dust, etc.). It is not recommended to touch the mass directly with your hands; if necessary, it is taken using a piece of cellophane or waxed paper.

The introduction of medicinal substances into a suppository depends on the nature of the base, the amount and physicochemical properties of the medicinal substances administered, and, above all, on their solubility in the base.

Introduction of medicinal substances in hydrophobic bases:

1. Medicinal substances soluble in the base (camphor, chloral hydrate, phenol, phenyl salicylate, thymol, anesthesin, etc.), Depending on their amount, dissolve in part or in the whole amount of the molten base. If these substances are introduced in large quantities, then eutectic alloys with a lower melting point are formed. More reduce its chloral hydrate, camphor and phenol. In these cases, it is necessary to add substances, in the amount of 4-5% by weight of the fatty base, which increases the melting point of the mass to 36-3° C. Paraffin, wax, spermacet, etc. are such seals. If the suppositories contain phenol, then taken in crystalline form and dissolved in part of the molten fatty base (in order to avoid cauterizing action).

It should be noted that the method of dissolving medicinal substances in the molten base is more suitable for casting the molten mass into molds. In the manufacture of suppositories by manual molding (download), it is inconvenient.

2. Medicinal substances soluble in water (salts of alkaloids, resorcin, quinosol, novocaine, ethacridine lactate, protargol, collargol, tannin, etc.) are prescribed in an amount up to 5%, first dissolved in a few drops of water or glycerin, or in extreme cases, alcohol is triturated with these liquids, and then emulsified and mixed with the base. Dissolution facilitates the even distribution of small doses of drugs in the base, improves the conditions of absorption and provides rapid local action.

As an emulsifier, water- free lanolin (B / O type emulsion) is used, it is added in minimal amounts to eliminate the formation of a mass of greasy consistency. If the above-mentioned medicinal substances are mixed in undissolved form directly with the fatty base (which is, in principle, possible due to its high viscosity), then their smallest particles are covered with a fatty shell, and the absorption process is very slow. With the introduction of medicinal substances into the fatty base in the form of an aqueous solution without an emulsifier, a mass is formed which is difficult to form and easily disintegrates during operation.

If soluble substance lot (5%) and it requires znach itelnogo amount of solvent, then it was triturated in a mortar, first dry then with a small amount of water (i.e., injected without dissolution of the substance), and then added by portions wells basis. Collargol, protargol and tannin are always administered only in the form of aqueous or water-glycerin solutions, regardless of their number.

3. Medicinal substances that are not soluble either in base or in water (xeroform, dermatol, streptocid, bismuth basic nitrate, theophylline, zinc oxide, osarsol, etc.) are incorporated into the composition in the form of a fine powder. In the manufacture of suppositories by the method of pouring the substance, first crushed to the maximum degree of dispersion (the accuracy of their dosing in suppositories and therapeutic activity significantly depends on this), then a part of the melted base is crushed (according to Deryagin's rule) and the mixture is added to the melted, semi-dried basis. Then the mass is poured into the appropriate form. Thermolabile substances should be added to the base of the base before pouring it into the mold. In the manufacture of suppositories by pumping method, depending on the amount, these medicinal substances are administered in two

ways. If they are prescribed in small quantities, that is, up to 0.1 g per candle, they are first triturated with a few drops of fatty oil (peach, almond, or others), and then mixed with ground base. If these medicinal substances are prescribed in large quantities, that is, more than 0.1 g per candle, then they are thoroughly crushed and mixed with a portion of the molten or finely grated base, and then the rest are added. The direct mixing is, crushed medicinal substances with the entire base does not ensure uniform distribution of bulk substances in a thick base.

4. Medicinal substances in the form of liquids (Ichthyol, salves, oil Naphthalan) having adhesive properties, is introduced direct but blending the milled giro in minutes basis, without adding plasticizer. Liquid ingredients that do not contain volatile substances can be condensed by evaporation at the lowest possible temperature.

5. Thick extracts (for example, belladonna extract, etc.) Injected into the suppository mass after pre-mixing with an equal amount of alcohol-water-glycerin mixture (1: 6: 3) or as a prepared solution (1: 2).

The introduction of drugs in hydrophilic bases.

1. Medicinal substances soluble in water or glycerine are not first dissolved in a portion of the water or glycerin used to make the base, and then added to the molten base ready for pouring into the mold.
2. Medicinal substances that are not soluble in water or in glycerol, first triturated with a portion of the glycerin in a thin suspension, and then added to the finished, molten base before pouring into the form.
3. Medicinal substances, soluble in polyethylene oxide base or collagen gel, are injected directly into the molten part or the entire base (gel), followed by stirring and pouring the finished homogeneous mass into the forms. Insoluble substances are first triturated with the liquid part of the base, and then they are mixed to the whole mass and poured into molds.

Manufacture of suppositories by the method of rolling. The manual rollout method on the positive side is characterized by the fact that it does not require special equipment. This method achieves a uniform distribution in the suppository mass of all ingredients. On the other hand, it is economically inefficient, since in the absence of mechanization a lot of labor is expended, and the resulting products have a worse appearance than in the manufacture of suppositories using the means of mechanization.

The manufacture of uppositories by the method of rolling out involves several stages: preparing the base, injecting medicinal substances and obtaining a suppository mass, dosing, forming suppositories, packaging and design.

Using the method of rolling out, suppositories can be prepared only from plastic bases, which are preliminarily crushed using special tools. The ground base is much easier to dose, more convenient to use for the manufacture of suppositories.

In accordance with the rules outlined, prescribed medicinal substances are introduced into the crushed base, mixing them in a porcelain mortar. The resulting mixture is pressed with a pestle, gradually increasing the pressure on the pestle until a plastic mass is formed that lags behind the walls of the mortar. If the

composition of the suppository mass includes many powdered substances, the mass is difficult to form and crumble. In this case, in order to impart plasticity, it is necessary to add a small amount of anhydrous lanolin (on average at the rate of 1-1.5 g of lanolin per 30.0 g of mass). The amount of the latter depends on the properties of the bulk solids and the temperature in the room (in the summer, less is added in winter). If suppository Torno second mass comprises binders, dense extracts, etc., then adding the lanolin necessity disappears. If an excess amount of lanolin is taken, the mass becomes soft, sticky and cannot be formed.

The resulting mass is chosen from the mortar using waxed paper, compressed into a ball and weighed, the result is indicated on the recipe or signature and in the CPD. After that, the mass is transferred onto a plastic plate or pill-type glass covered with white paper, and using a plate also covered with a smooth white sheet of paper, an equal tetrahedral bar (or cylindrical rod) of equal thickness is extruded. The length of the rod should be equal to the number of divisions of the cutter of the pill typewriter (or twice the number of divisions) corresponding to the prescribed or multiple number of candles or balls. The bar is placed on the lower back of the sawing machine and, pressing it down with the upper cutter, they apply divisions (rice 126), using which with a thin knife the rod is cut into the prescribed number of candles or balls and the accuracy of mass dosing is checked by weighing. Then a plate is added to each individual portion of the mass to form a ball, from which candles of a conical or other shape are extruded by a plate that is inclined at an angle of 30 °.

Ready-made candles, each separately, are wrapped in cellophane, aluminum foil or thin waxed paper, having the shape of a triangle (kerchief) measuring 7.5-12 cm. Rolled candles are placed in cardboard or plastic boxes.

Rp .: Dimedroli
Papaverini hydrochloridi "aa 0.05
Novocaini 0.15
Olei cacao qs
Misce, fiat suppositorium
Da tales doses No. 10
Signa. On 1 candle for the night.

Rectal suppositories of the type B/O emulsion, which include potent medicinal substances, well soluble in water.

Rectal suppositories of the type of emulsion B/O, which contain potent medicinal substances, are well soluble in water.

Checking single and daily doses of potent substances (dimedrol, papaverine hydrochloride, novocain) is carried out by comparing them with the highest single and daily doses for oral administration (the section "Powders").

For preparing suppositories number 10 should weigh: 0.5 g diphenhydramine, Dimedrol 0.5 g, papaverine hydrochloride 0.5 g, Novocain 1.5 g. Since the amount of the base is not indicated in the recipe, it is calculated based on the fact that the

weight of one candle must be 3, 0 g. Therefore, cocoa butter should be taken: 30.0 - (0.5 + 0.5 + 1.5) = 27.5 g.

Medicinal substances are placed in the mortar (according to the rule of making powders), first they are dried first, and then about 1 ml (20 drops) of distilled water is added (based on the solubility of the medicinal substances) and triturated to dissolve. The resulting solution is mixed with a portion of the crushed cocoa butter o, gradually adding the rest. If necessary, add anhydrous lanolin (about 0.5 g). Mix to obtain a homogeneous mass, behind the walls of the mortar, which is weighed. The mass is marked on the back of the recipe and in the passport of the written control. A rod is formed from the mass, divided into 10 portions, and a candle is pumped out from each portion. To control multiple doses weighed mass deviations should not exceed ± 5%. Suppositories should be the same shape, length and thickness.

PWC

Date Recipe No.

Dimedroli	0,5
Papaverini hydrochloridi	0.5
Novocaini	1.5
Aquae purificatae gtts XX	(1 ml = 20 drops)
Olei Cacao	27.5
Lanolini anhydrici	0,5
Massae suppositoriorum	31.5
‘	3.1 № 10

Prepared: (signature)
Checked: (signature)

Rp.: Theophyllini 0,2
Olei Cacao 1.5
Misce, fiat suppositorium
Da tales doses No. 10
Signa.1 candle 2 times a day.

Suppositories of the type of suspension, which include a medicinal substance, practically insoluble in water and base.
First, theophylline (2.0 g) is crushed in a mortar, mixed with a portion of the crushed or melted base (1.0 g), the rest of the cocoa butter is gradually added and crushed to obtain a homogeneous suppository mass. Anhydrous lanolin is added to make plasticity. The resulting suppository mass is metered, form candles, pack and make out to leave.

Rp .: Extract!Belladonna 0.01
Ichthyoli 0.2
Olei cacao qs
Misce, fiat suppositorium

Da tales doses №20

Signa. On 1 candle for the night.

Rectal candles, which include viscous liquids. Weigh out 55.8 g of ground cocoa butter, on the surface of which a small hole is made and 4.0 g of ichthyol are weighed into it. In a mortar, grind 0.2 g of the thick extract of the belladonna with an equal amount of alcohol-water-glycerol mixture, take 0.4 g of the solution of the thick extract of the belladonna (1: 2) and add cocoa butter so that ichthyol, which promotes the gluing of the suppository mass, is added got into the mortar last. From the prepared mass, suppositories are prepared as described. The mass is prepared without adding a plasticizer.

Rp .: Chloral and hydrati 0.5
Cerae flavae 0.25
Olei Cacao 2.0
Misce, fiat supposeitorium
Da tales doses № 6
Signa. On 1 candle for the night.

Suppositories of the type of solution, which include a potent drug substance, soluble in the base and forming a eutectic mixture with it.

Pre-check a single dose of a potent substance. In an evaporation cup, 1.5 g of wax is fused with 1.5 g of cocoa butter (without overheating!). In a mortar, triturate with 3.0 g of chloral hydrate and dissolve in the alloy. Add cocoa butter and knead. The mass is transferred to waxed paper, turned into a dense ball, weighed. From the resulting mass of candles prepared by the method described and make out to leave. Making suppositories by pouring. The casting method, being universal, allows you to prepare suppositories of the same shape using different bases, which is impossible with other methods. The process of making I proho dit significantly faster hygienic and appearance suppositories, pellets and sticks better compared to the downloading method.

As a disadvantage of this method, it is necessary to note a violation of the homogeneity of the mixture during cooling, especially at the expense of liquids, do not mix with the bases and the solid phase.

The casting method consists of the following stages: manufacturing and melting corresponds to a prominent base; mixing prescribed medicinal substances with a molten base; the preparation of molds and the casting of prepared brews in a mass into molds; cooling; packaging; clearance.

If a single substance is prescribed as a basis, for example, butyrol, etc., then it is melted into a dipper or a porcelain dish in a water bath for mixing with medicinal substances. If the base consists of several substances, then the alloy is apparently prepared, and then medicinal substances are added in the form of a solution or the finest powder. The mass should be heated carefully, not allowing the temperature to rise above 38-40 °C. When overheated, the time required for further solidification increases, the quality of the suppositories produced

deteriorates. If it is necessary to heat the base to a higher temperature, it is advisable to heat not the entire amount of the base, but only a part (70-80%), and add the rest in solid form in the melting mass after its temperature drops to 37-38°C.

The prepared suppository mass is quickly poured from the porcelain rye cups into the prepared forms. For pouring out Vikoristovuyu special metal or plastic masks with the number of sockets AOR, 50, 200 or more, with a capacity of 1; 1.5; 2; 3, 4 cm3 (fig. 127, 128).

Before assembling, the cells of the form are wiped with a gauze pad moistened with sterilized vaseline oil, if the suppositories are prepared on water-soluble bases, if the fat bases are soap alcohol.

The filling of the form with the mass should be gradual, otherwise the suppositories are non-uniform and fragile. The filled form is slightly shaken to remove air bubbles from it and placed in the freezer compartment of the refrigerator for 10-15 minutes, after which the frozen mass protruding from the form cells is scraped off with a knife. Frozen suppositories free (after the connector elements of the form) by pressing on their base towards the top.

In the manufacture of suppositories by the method of pouring out, their mass depends on the size of the nest of the form (volume), the density of the medicinal substances used and the base.

In cases where medicinal substances are discharged in an amount of up to 5%, it is possible to disregard the insignificant amount they occupy in the forms. If medicinal substances are included in suppositories in quantities of more than 5% (in this case, the volume occupied by them displaces a significant amount of base), then it is necessary to find the exact ratio between the volume occupied by the prescribed drug substance and the base. Otherwise, dosing accuracy is impaired. This ratio is expressed by a “replacement rate” or “inverse replacement rate”.

The replacement ratio (Hedgehog) is the amount of drug substance that replaces one weight part of the fatty base with a density of 0.95. That is, a given amount of drug substance occupies the same volume as one weight part of the fat base.

For example, the replacement ratio of bismuth nitrate basic, on a fatty basis is equal to 4.8. This means that 4.8 g of bismuth basic nitrate occupy the same volume as 1.0 g of the fat base.

The inverse replacement rate (1 / Hedgehog) refers to the amount of fatty basis, replacing one weight part of the drug substance. That is, the amount of fatty basis is equivalent in volume to 1.0 g of the drug substance.

For example, the inverse replacement rate of bismuth nitrate of the main fatty basis is 0.21. This means that 0.21 g of the fat base occupies a volume equal to the volume of 1.0 g of bismuth basic nitrate. When calculating the amount of basis, it is more convenient to use the inverse replacement rate.

In the table. 26 shows the values of the Hedgehog and 1 / Hedgehog for medicinal substances, which are most often written in suppository dosage forms.

Production of suppositories in hydrophobic bases.

Rp .: Osarsoli 0.2
Acidi borici 0.1
Glucosi 0.3
Butyroli qs
Misce, fiat suppositorium
Da tales doses № 12
Signa. On 1 candle for the night.

Rectal suppositories, which include the list A drug, osarsol, as well as other substances that are not soluble in the base - boric acid and glucose, prescribed in more than 5%. Checking single and daily doses of Osarsol is carried out by comparing them with the highest and single and daily doses for oral administration according to the table DF.
Calculation: Osarsol 0.2 x 12 = 2.4 g
Boric acid 0.1 x 12 = 1.2 g glucose 0.3 x 12 = 3.6 g The amount of suppository base is calculated based on the fact that the form for Wilvan ¬ allows to get suppositories on a fatty basis weighing 2.0 g. Using the replacement rate, make the calculation of the basics:

By coefficient substitution (K_i) Substitution (I / K_g) Osarsol 2.4: 1.45 = 1.66 2.4 x 0.69 = 1.66
boric acid 1.2: 1.6 = 0.75 1.2 • 0.625 = 0.75
glucose 3,6: 1,23 = 2,92 3,6-0,81 = 2,92
Thus, butyrol and must be taken: 2.0 x 12 - (1.66+ 0.75 + 2.92) = 18.67 g .

Osarsol is obtained on demand by a pharmacist. Substances carefully ground in a dry form in accordance with the rules for the manufacture of complex powders. Then, the grinding is continued by parts of the melted base (approximately 4.0 g according to the Deryagin rule). The resulting mixture is transferred from the mortar to the remaining porcelain base in a porcelain dish and mixed thoroughly to evenly distribute the crushed substances.

The mass is quickly poured into pre-lubricated with soap alcohol and cooled forms, placed in a refrigerator for 15-20 minutes. After cooling, scrape the frozen mass protruding from the cells of the form with a knife, unscrew it, remove the suppositories, wrap it, and arrange it for leave.

Production of suppositories in hydrophilic bases. Candles, as a rule, are made on a soap-glycerin basis, and gelatin-glycerin base is used more often for the manufacture of vaginal suppositories. Prepare them only by casting.

Soap-glycerin suppositories are used as a laxative, therefore no other medicinal substances are introduced into the composition of these candles. Record these candles written in SPh IX.

Rp Acidi stearinici 5,0
Natrii carbonatis 2,0
Glycerini 60,0

ut fiant suppositoria № 20
Signa. On 1 candle for the night

In addition, these candles can be written in this way: Rp .: Suppositoria Glycerini 3.0
Da tales doses №20
Signa. On 1 candle for the night.
Their technology is described above (see “Suppository bases”).
Gelatin-glycerin base, compared with fat, has a higher density (1.15), therefore, with the same mass takes less volume. In this regard, in the manufacture of suppositories in gelatin-glycerin-based, it should be taken more than fat, given that its density is higher than fat by 1.21 times (1.15 / 0.95).

Rp .:Protargoli 0.1
Massae gelatinosae qs
Misce fiat globulus vaginalis
Da tales doses No. 10
Signa. 1 bullet 3 times a day.

Vaginal suppositories on gelatin s on-glycerin basis protected colloid. If the nest of the form holds 4.0 g of the fat base, then to obtain 10 balls it would be necessary to 40.0 g (4.0 x 10), and gelatin in α - glycerol base: 40.0 x 1.21 = 48 4 g . In this case, the replacement rate is not taken into account, since the protargol is prescribed less than 5%.
Calculation of gelatin - 1.0 g - 8.0 g base
x = 6.05 g
x g - 48.4 g base
Purified water 6.05 x 2 = 12.1 ml
Glycerol 48.4 - (6.05 + 12.1) = 30.25 g

A gelatin is placed in a weighted porcelain dish, filled with water and allowed to swell for 30-40 minutes. Then, glycerin is weighed into a cup with swollen gelatin and heated in a water bath until gelatin is completely dissolved. Add water to the required mass.

1,0 g of protargol is placed in a porcelain dish, ground with 6-8 drops of glycerin and dissolved in 4-6 drops of water. The amount of water and glycerin taken into account in the manufacture of gelatinous mass. The protargol solution is added, stirring, into a warm gelatin-glycerin mass and the resulting homogeneous mixture, devoid of air bubbles, is poured into pre-prepared forms, smeared with vaseline oil. Place in the freezer of the refrigerator for 10-15 minutes. The frozen balls are released by the connectors of the form elements.

PWC

Date Recipe No.
Gelatinae 6.05

Aquae purificatae 12,1 ml
Glycerini 30.25

Massae gelatinosae ad 48.4
Protargoli 1.0

Massae suppositoriorum 49,4
4.94 № 10
Prepared: (signature)
Checked: (signature)

Rp .: Zinci oxydi 0.25
Acidi borici 0.1
Massae gelatinosae qs
Misce, fiat pessarium
Da tales doses No. 10
Signa. 1 pence per night.

Suspension vaginal suppositories for gelatino in - glycere based on insoluble substances with a content of more than 5%. The volume of the nests of the form provides the output of pessaries on the basis of fat weighing 4.0 g.

Since the substitution coefficients for the drug substances are calculated for the fatty basis, it is advisable to calculate the latter, and then to list the gelatin-glycerol base.

For the manufacture of 10 pessaries only from the fatty base (without medicinal substances), it was necessary to take 40.0 g. Given the volume that 2.5 g of zinc oxide will occupy, the mass of the fatty base must be reduced, using the corresponding replacement drug coefficients.

Using the reverse replacement ratio (1 / Egg) for zinc oxide, equal to 0.25, find the required amount of the base:
40.0 - (0.25 x 10 **)** x 0.25 = 39.375 = 39.4 g .

To switch from fat to gelatin-glycerin base, the mass of fat base must be multiplied by a conversion factor of 1.21: 39, 5 x 1.21 = 47.674 "47.7 g (gelatin 5.96; water 11.92 ml; glycerin 29.8).

The introduction of boric acid into the composition of gelatin in the α-glycerin base has practically no effect on volume, since it is prescribed in an amount of up to 5%.

Crushed gelatin is placed in a pre-stained cup, poured with water and allowed to swell for 30-40 minutes. Glycerin is then added (leaving a portion to dissolve the boric acid and grinding the zinc oxide), the mixture is heated in a water bath, stirring until a homogeneous mass is formed.

In a jar with a slight heat dissolve the boric acid in glycerin. In a mortar, zinc oxide is ground in a dry form, then the resulting mixture is added to the prepared base with a solution of boric acid in glycerol and mixed. The finished suppository mass weighed (add water) and poured into a mold, smeared with a thin layer of

vaseline oil. Cooked pessaries are placed in cardboard boxes and arranged for release.

In calculating the quantity of gelatin in the so-called transition module can be used -glitserinovoy framework, which is the ratio fat base density to the density gelatin-glycerin basis: 0.95: 1.15 = 0.826.

For gelatin and glycerin base, the replacement factor is used, derived by multiplying the replacement rate of the fat base by the transition module.

Thus, the replacement ratio of gelatin to β-glycerol bases

Hedgehog / m = hedgehog x 0,826.

So, for example, if the hedgehog for their thiol is 1.1,

then the hedgehog / m is 1.1 x 0.826 = 0.908-0.91.

Rp .: Ichthyoli 0.25
Massae gelatinosae qs
Misce fiat pessarium
Da tales doses No. 10
Signa. 1 pesar 2 times a day.

Pessaries to gelatin-glycerin basis.

In this case, the mass of pessaries is not specified, therefore, they are prepared with a mass of 4.0 g. Accordingly, the replacement rate for ichthyol on a gelatin-glycerol basis is determined 1.1 x 0.826 = 0.91. This means that 2.5 g of ichthyol replace 2.5: 0.91 = 2.7 g of gelatin-glycerin base. When pouring it into 4-gram forms, it is necessary to take 40.0 - 2.7 = 37.3 g of base. Thus, for such an amount of base, gelatin is taken 4.7 g, water - 9.4 ml, glycerol - 23.3 g and prepared according to the indicated method. Ichthammol added directly in a cup of warm gelatin-glycerin mass stirred until homogeneous and immediately spill out in a greased vaseline oil form. After cooling, the pessaries are taken out, they are taken back and made to leave.

Polyethylene oxide base used for the manufacture of candles and balls as a method of casting and pressing.

Rp .: Sulfadimethoxini 0,2
Basis polyaethylenoxydi qs
Misce, ut fiat suppositorium
Da tales doses №20
Signa. On 1 candle in the morning and in the evening.

Rectal suppositories on a hydrophilic basis, which include a potent substance, soluble in the base - sulfadimethoxin.

Check single and daily doses of sulfadimethoxine. The volume of the nest form gives candles on a fat basis of 2.0 g. The content of the medicinal substance is 10%.

The calculation of the amount of polyethylene oxide bases is carried out taking into account the replacement rate. The density of the polyethylene oxide

bases higher fatty hence suppositories by pouring it should take longer (similar to gelatin-glycerin base).

To manufacture 20 candles from a pure fatty base, it is necessary to take 2.0 x 20 = 40.0 g. Given the inverse replacement rate (1 / Egg) for sulfadimethoxine, the required amount of fatty base is calculated, and then recalculated on a polyethylene oxide base using the conversion factor (1.21):

[40.0 - (0.2 x 20 x 0.74)] x 1.21 = 44.82 - 44.8 m

In a porcelain dish melted 44.8 g of base and dissolved therein 4.0 g sulfadime toxin and with stirring. Next, almost cooled mass is poured into cooled forms, pre-lubricated with vaseline oil. The mold is placed for 10–15 minutes in a refrigerator, after which the ready candles are removed, wrapped and decorated for release.

Determination of the replacement rate and the amount of base experimentally If for the medicinal substance the substitution coefficient is not listed in the table, then it can be determined experimentally on the basis available.

Below is the calculation of the replacement factor for the base containing confectionary fat for chocolate products and food concentrates with a melting point not higher than 36.5 ° C and a hardness lower than 550 g / cm (95%), as well as a solid emulsifier T-2 (VFS 42 - 173-7 2). The components of the base are mixed; when melted in a water bath at a temperature not higher than 55 ° C. A mass of light yellow color with a slight specific smell is obtained, solid at room temperature, melts at a temperature of 36.4-36.9 C. The molten mass should be transparent and free from mechanical impurities. The base is stored in closed glass or porcelain jars in a cool, dark place. Shelf life - 1 year.

With the molten base without the addition of medicinal substances by the method of casting get 30 suppository in (nest capacity 2 cm3) and weighed on a technical scale (2nd class). Then make 30 candles with medicinal substances. To do this, thoroughly grind the quantity of medicinal substances necessary according to the words in the mortar and mix it with about 80% of the calculated molten base and evenly pour it into the same form. After this, the nests of the form are filled with a molten base, filled with (20%), the excess of which is carefully removed with a spatula and the form with suppositories is placed in the freezer compartment of the refrigerator for 10-15 minutes. Frozen suppositories in the amount of 30 pieces are weighed on the same scales.

The substitution factor is calculated using the following formula:

$$F = \frac{P - Q}{A} + 1,$$

where P is the mass of 30 suppositories without medicinal substances, g Q is the mass of 30 suppositories with medicinal substances, g., A is the total mass of medicinal substances contained in 30 suppositories, g.

The calculation of the number of bases required for the manufacture of suppositories, taking into account the substitution factor, is made according to the following formula:

X = P - FA,

where X is the amount of the base, the city required for the manufacture of suppositories, taking into account the substance substitution factor in 30 suppositories, g F is the substitution factor.

For example, for the manufacture of ZO suppositories according to the recipe: streptotsida 0.05 g, novocaine 0.1 g, anestezina 0.15 g, belladonna extract 0.015 g, adrenaline hydrochloride solution (1: 1000) 4 drops, bases for suppositories up to 2.0 g

$$\Phi = \frac{P - Q}{A} + 1 = \frac{59,7 - 61,2}{9,75} + 1 = 0,85,$$

where P is the mass of ZO suppositories without medicinal substances 59.7 g Q - the mass of ZO suppositories with medicinal substances 61.2 g

And - the mass of medicinal substances specified in the recipe, calculated on the ZO suppositories, 9.75 g

Calculation of the amount of the base required for the manufacture of suppositories as indicated in words, taking into account the substitution factor:

X = R-FA = 59.7-0.85.9.75 = 51.41 g.

Table 27 shows the number of medicinal substances and the base required for the manufacture of 30 suppositories by the method of pouring into forms with a capacity of 2 cm 3.

Manufacture of suppositories by pressing. The pressing method is used only for suppository masses having the necessary ductility. Basics in the form of glycerogel, with significant elasticity, can not be compressed. Presses used for the manufacture of candles, can be unattended and with mechanical or automatic dispensing.

In terms of pharmaceutical suppositories prepared using a specially manufactured soup claim ozitornogo press, or may be used refitted tablet machine whose matrix detachable and has the form candles.

The containers in this press, as in the casting molds, have a certain volume. The candles prepared by this press, regardless of their composition, have a constant volume, but their mass depends on the density of the incoming lyricants. Therefore, just as with pouring, it is necessary to use the replacement coefficient to calculate the suppository mass. When preparing the mass for pressing, it should be crushed and, if necessary, dried to give flowability.

The method of pressing with automatic dosage is used in pharmaceutical factories, where mass production of candles is carried out.

In pharmacy conditions, manual non-dosing presses can be used. The prepared suppository mass is first divided into the prescribed number of doses, each individual portion is placed in the nest of the press and pressed with a piston. Candles come out with a smooth surface and the same shape. The homogeneity of the mass at the time of pressing is not violated. This method is distinguished by dosing accuracy and hygiene. However, when working with non-dosing presses a lot of time is spent on the distribution of doses.

Sticks - Bacilli (Bougé - Cereol). The word "bougie" comes from the French bougie - probe. Prepare them to plastically fat-based method of popping out of Bani or pressing on gelatin-glycerin basis - casting.

When prescribing sticks, the length and diameter of the sticks are indicated, without specifying the mass of the base, or the mass of the base and one of the mentioned parameters are indicated. In cases where the number of bases in the recipe is not specified, it is determined by the formulas:

a) for the fatty basis: x = 3.14 (d / 2): x 0.95 x 1 x n:

b) for gelatin-glycerin basis: x = 3.14 (d / 2) 2 x 1.15 x 1 x n;

where x is the number of bases, g

d - diameter of rods, cm; 1 - the length of the sticks, cm; N is the number of sticks.

Rp .: Streptocidi 0.1
Olei cacao qs
ut fiat bacillus longitudine 4 sm
et diametro (crassitudine) 4 mm
Da tales doses №10
Signa. At 1 stick 2 times a day at the fistula course.

Suppositories (sticks) with a potent drug substance, insoluble in water and cocoa butter, is administered in a slurry type.

Substituting the numerical values in the formula, find the values of x:

x = 3.14 x (0.4 / 2) - x 0.95 x 4 x 10 = 4.77 = 4.8 g cocoa butter

Streptocide (1.0 g) is triturated in a mortar into a schonaydribnishi powder and gradually mixed with the calculated amount (4.8 g) of crushed cocoa butter.

For plasticity, add a small amount of anhydrous lanolin and knead, until a homogeneous mass is formed, lags behind the walls of the mortar. The resulting mass is rolled out in the form of a rod and divided into equal parts using a cutter of a pill machine. Each individual batch of mass is pumped out until a flat cylindrical stick of the specified length is formed with one pointed end. The length of the stick is measured with a ruler, and its diameter is determined by itself if the amount of the base was taken correctly.

In the presence of a special press consisting of a cylinder, a piston and a set of dies having openings of different diameters, it is possible to prepare sticks by pressing the resulting mass, pressing the mass through a 4 mm diameter piston. The resulting long rod is cut into 10 equal parts and make one end pointed. You can cook sticks from this mass by pouring it into special shapes that have channels of a certain length and diameter. Before pouring the molten mass, the molds are heated to 50 ° C, otherwise the mass may solidify in the upper part of the channel. Finished sticks released in cardboard boxes with cells of corrugated paper.

Empty suppositories - rectal capsules. By this name is meant solid hollow fatty or on another capsule basis, which are containers of predetermined size, filled with medicinal substances in the form of powder, solution, emulsion, ointment, etc. P. As a rule, such capsules are prepared in pharmaceutical plants by pressing or pouring.

As a base for rectal capsules used cocoa butter and other fatty bases, gelatin-glycerin mixture (64-70% gelatin and 30-35% glycerol), and so on. P. Currently, the most widely used gelatin rectal capsules. An appropriate medicinal substance is placed inside the finished capsule and the hole is carefully poured with the same mass from which the candle was made. After cork is set, the candles are ready for use.

QUALITY ASSESSMENT AND STORAGE

The quality of the prepared suppositories is evaluated in the same way as other dosage forms, that is, they check the documentation (recipe, passport, packaging, design, color, smell, absence of mechanical inclusions).

Specific to the quality of suppositories are: size, shape, which should not correspond to the recipe recipe.

Uniformity of mixing - on the slice of the suppository mass should be homogeneous, without inclusions, the presence of an air core or a funnel-shaped recess is allowed.

The weight of the candles should be in the interval indicated by the State Fund XI. The deviation in the mass of individual candles should not exceed ± 5%.

Ready su n pozitornih dosage form should have s certain rigidity to ensure their use, otherwise they will become useless because they can be deformed in the patient's hands before they are used.

For suppositories prepared on hydrophobic bases, the melting point is determined by method 2a (SPh XI, vol. I, p. 18), which should not exceed 34 ° C, unless otherwise indicated in its own articles. If it is difficult to determine the melting point, then the time of complete deformation is determined using a special device.

Water is supplied to the cabinet with a constant temperature (37 ° C). Into the tube, pour 15 ml of water so that part of it, below the restriction, is filled and held up by a device to equalize the temperature of all its parts for 5 minutes. Then the suppository is lowered into the tube with a pointed tip down, a rod is placed on top of it and a stopwatch is inserted. Mark the time during which the rod will immerse itself to the mark (zero division). This time is taken during the deposition of suppositories, should be within 3-15 minutes. The rod should be lowered only under the influence of its weight.

For suppositories prepared on hydrophilic bases, determine the time of dissolution. To do this, one suppository is placed on the bottom of a vessel with a capacity of 100 ml containing 50 ml of water with a temperature of 37 ± 1 ° C. The vessel is shaken every 5 minutes so that the liquid and the sample gain a rotational movement.

The suppository should dissolve within 1:00, unless otherwise indicated in its own articles.

Determination of the quantitative content and uniformity of dosing of active substances should be specified in their own articles.

Suppositories stored in a cool dry place, unless otherwise indicated in their own articles.

After the manufacture of fat candles and balls, they are wrapped in waxed paper, cellophane or foil, and a gel-like candle is wrapped in waxed or waxed paper. Balls, pessaries are placed in cardboard boxes in corrugated caps, and packs in the folds of paper. Decorated labels "External", "Store in a cool dry place."

On packets of suppositories made on a polyethylene oxide basis, there should be an indication of the need to moisten suppositories before entering the body cavity.

The structural and logical scheme of technology and quality control of suppositories is presented in Scheme 15.

TECHNOLOGY IMPROVEMENT

Improvement of suppository technology is carried out both in the direction of expanding the assortment of suppository bases, improving their quality, and creating new dosage forms, for example:

- Empty suppositories that have a cavity inside to fill it in the pharmacy with medicinal substances. The lack of previous suppositories - when the base is melted on the mucous membrane, highly concentrated solutions of medicinal recichovine can get into, which leads to its irritation;
- Two-layer and multi-layer suppositories consisting of a shell and a rod. The latter can be prepared from low-melting fats with dispersed substances, the shell - from alloys of hydrogenated fats with surfactants. Bilayer suppositories make it possible to combine medicinal substances of different properties;
- Rectal capsules - containers filled with medicinal substances. Rectal capsules are recommended to be cooked with gelatinous mass containing sugar, salicylic acid, sodium metabisulphite and other substances;
- Pressed suppositories are prepared on solid bases by the method of pressing by analogy with tablets. In our country for this purpose and use granular powdergramm to and - magnesium carbonate, magnesium stearate, starch, iron lactate, sodium bicarbonate in a mixture with hydrogenated fats. Perspective rectal enemas, ointments, infusions;
- Lyophilized suppositories are obtained from aqueous suspensions or emulsions, the bulk of which is the active substance, and the amount of auxiliary substances is limited to a minimum. The principle of manufacturing is to deep freeze the emulsion or a homogeneous suspension (lyophilization). The suppositories thus obtained have a porous structure and a large internal surface; the insignificant amount of the secretion of the rectal mucus easily dissolves without causing irritation of the mucous membranes.
- Porous suppositories are prepared by pouring the molten mass into molds, followed by evacuation at a vacuum depth of 600 mm Hg. Such suppositories increase the surface of contact with the mucous membrane of the rectum and facilitate the release of drug components;
- Film coated suppositories control the delivery of drugs, slow down the diffusion of the active ingredient. As a film coating, hydrophilic polymers (cellulose ethers, alginates, gelatin, etc.) are most often used;

- Effervescent suppositories are prepared from a solid high-polymer of water-soluble second substance, the foaming agent forms a foam when dissolved enii suppository in an aqueous medium with gas evolution and foam stabilizer (RSA) capable of reducing the surface tension of water.

Thus, based on the analysis of current trends, it is possible to predict promising directions for the development of suppository dosage forms:

1. Identification of biochemical processes occurring during the action of the drug.
2. Creation of dosage forms with controlled release of ingredients that give the expected therapeutic effect in the right place and at a certain time, as well as with targeted delivery of the medicinal substance to the diseased organ, which makes it possible to achieve a given therapeutic effect with a smaller amount of drugs.

5. Material of activation of students during the presentation of the lecture / problem questions, tasks and problem situations, etc.

Control questions:

1. Characterization of suppositories as a dosage form and dispersion system. Requirements for suppository pits.
2. Classification of suppositories.
3. Methods for prescribing suppositories; checking doses of poisonous, narcotic and potent drugs in them.
4. Classification and characterization of suppository bases; requirements for them. Warehouses of suppository bases.
5. Prescribing sticks and calculating the basis for them, technology.
6. Technological stages of preparation of suppositories by pumping method.
7. Basics for suppositories that are used in the casting method, their classification and requirements for them.
8. Effect of base on the bioavailability of medicinal substances.
9. Calculations of the number of bases for suppositories (hydrophobic and hydrophilic) for the preparation of candles, balls and sticks by casting.
10. Rules for the introduction of medicinal substances with different physicochemical properties into the base when using the casting method.

Test items:

1. In the prescription, the doctor prescribed suppositories in cocoa butter, but it is not in the pharmacy. Specify the basis for replacing it:

* Laurel oil pedunculate
Butyrol
Gelatin-glycerin
Vitepsol
Soap-glycerin

2. The recipe contains suppositories for hemorrhoids on butyrol. Specify the components of this suppository base:

* Cocoa butter, paraffin, hydrogenated fats
Cocoa butter, ozocerite, hydrogenated fats

Cocoa butter, ceresin, hydrogenated fats
Cocoa Butter, Wax, Hydrogenated Fats
Cocoa butter, petrolatum, hydrogenated fats

3. For the preparation of suppositories using various methods: download, casting, pressing. Specify the basis for the preparation of suppositories by pouring:

* Butyrol
paraffin
cacao butter
petroleum jelly
coriander oil

4. A pharmacist prepared a suppository mass with novocaine and cocoa butter, but it turned out to be fragile. Specify the substance that must be added to form a plastic mass:

* Anhydrous lanolin
water lanolin
paraffin
petroleum jelly
wax

5. At the pharmacy, a pharmacist prepares rectal suppositories. Specify the permissible limits for the average weight of these suppositories:

* 1.0-4.0
2.0-5.0
3.0-6.0
4.0-7.0
5.0-8.0

6. In a pharmacy, a pharmacist prepares vaginal suppositories. Specify the permissible limits for the average weight of these suppositories:

* 1.5-6.0
1.0-4.0
2.0-6.5
3.0-7.0
4.0-7.5

7. The pharmacy prepares suppositories using various methods. Specify the method by which you can make rectal suppositories in cocoa butter:

* Download
tabletting
granulation
pouring out
extraction

8. A pharmacist prepares rectal suppositories on Witepsol. Specify the fluid that needs to be lubricated suppository form:

* Soap alcohol
Vaseline oil
ethanol
purified water

Peach oil

9. In the prescription, the doctor prescribed suppositories for a laxative effect on a soap-glycerin basis. Specify from these components it consists of:

* Glycerin, sodium carbonate, stearic acid
Soap, water, glycerin
Sodium carbonate, water, stearic acid
Stearic acid, glycerin, water
Water, sodium carbonate, glycerin

10. A pharmacist prepares rectal suppositories on a polyethylene oxide basis. Specify the liquid that needs to wipe the suppository form:

* Vaseline oil
ethanol
soap alcohol
purified water
Peach oil

6. General material and methodological support of the lecture:

- Training rooms;
- Overhead; slides;
- Illustrative materials.

7. Materials for self-preparation of students:

a) on the topic of the lecture presented / literature, questions, tasks, test tasks /;
b) on the topic of the next lecture / literature, a list of key questions, test items /.

8. The literature used by the lecturer to prepare the lecture.

Basis literature:

1. Drug technology. Study guide: Study guide for higher education institutions / A.I. Tikhonov, P.A. Logvin, S.A.Tikhonova, A.V. Mazulin, T.G. Yarnikh, A.S. Shpichak, A. M. Kotenko; Edited by A.I. Tikhonov - Kharkiv: NUPh; Original, 2009. - 432 p.
2. Medicine technology: study guide / A.S. Marchuk, N. B. Androshchuk - Kiev: Medicine, 2008. - 488 p.
3. Production of medicines. Quality control and regulation: prak.ruk. / Ed. Sh.K. Ged; per. from English V.V. Coastal. - SPb.: Profession, 2013. - 960 p.

Additional:

1. Soft dosage forms: thermal recipe: Methodical recommendations / A. I. Tikhonov, T. G. Yarnikh, A. V. Lukienko and others; Ed. A.I. Tikhonov. - M.: Publishing house NUPh; Golden Pages, 2003.-128 p.
2. Aseptic dosage forms: an extremporal formulation: Methodical recommendations / A. I. Tikhonov, L. V. Bondareva, T. G. Yarnikh, N. F. Orlovskaya and others; Ed. A.I. Tikhonov and T. G. Yarnikh. - M.: Publishing house NUPh; Original, 2005. - 184 p.

3. Solid dosage forms: extremporal formulation: Methodical recommendations / A. I. Tikhonov, T. G. Yarnikh, S. V. Gritsenko and others; Ed. A.I. Tikhonov - M.: Publishing House of the NUPh; Golden Pages, 2003. - 176 p.
4. Liquid dosage forms: an extremporal formulation: Methodical recommendations / A. I. Tikhonov, T. G. Yarnikh, N. F. Orlovskaya and others; Ed. A.I. Tikhonov and T. G. Yarnikh. - M.: Publishing house NUPh; Original, 2005. - 160 p.

Lecture № 9: «Requirements for the manufacture of sterile and aseptic medicines in pharmacies. Solutions for injection. Isotonic, physiological solutions. Suspensions for injection» - 2h.

1. Relevance of the topic. Substantiation of the topic. Dosage forms that should be prepared under aseptic conditions include: dosage forms for injections, dosage forms for treating eyes, dosage forms with antibiotics, dosage forms for children.

All these dosage forms are characterized by the fact that they should not contain microorganisms and their dispute.

The need for sterile and aseptically prepared dosage forms is caused by a special way of using them, for example, injections are introduced into the body through a cannula

with violation of the integrity of the skin and mucous membranes. Availability

in them, microorganisms can lead to infection of the body, and, consequently, to serious consequences.

Dosage forms with antibiotics require aseptic conditions of preparation, since in the presence of microorganisms, antibiotics lose their activity.

The listed dosage forms, regardless of whether they are subject to further sterilization or not, must be prepared under aseptic conditions. Sanitary requirements for the preparation of drugs under aseptic conditions are governed by the order

Ministry of Health of Ukraine No. 139 of 06/14/93. "On approval of instructions) of the sanitary regime of pharmacies.

2. Objectives of the lecture:

- training:

- to study the nomenclature of sterile and aseptic dosage forms,
- Conditions for the preparation of aseptic forms;
- Teach to navigate in the main directions of state regulation of the production of aseptic forms;
- To teach reading recipes in Latin, to analyze their components and to evaluate the correctness of the statement;

-educational:

-To develop skills to use DF and International SPh, other regulatory and technical documents, as well as reference books to search for information on the composition, preparation, storage and dispensing of drugs.

3. Plan and organizational structure of the lecture.

№№ pp	The main stages of the lecture and their content.	Goals in levels of abstraction.	Type of lecture, lecture equipment.	Time distribution.
1	**2**	**3**	**4**	**5**
1.	***Preparatory stage***			
	Definition of learning objectives.	I		2%
	Providing positive motivation.			2%
2.	***The primary stage***			
	Presentation of the lecture material. Plan:			
	1. Nomenclature of sterile and aseptic dosage forms,	II	References, visual material. State	10-20%
	2. Conditions for the preparation of aseptic forms	III	Pharmacopoeia, the main regulatory and	20 -30%
	3. Regulatory documentation.	II	technical documentation.	30 -40%
	4. Filtration of injection solutions.			
	5. Pyrogenic substances and conditions for ensuring apyrogenicity of drugs.			
3.	***The final stage***			
	Summary of lectures, general conclusions.	I	List of literature , questions,	20%
	Lecturer's answers to possible questions.		problems.	10 -20%
	Task for student self-training .			

4. The content of the lecture material:

Dosage forms that should be manufactured under aseptic conditions include: dosage forms for injections, dosage forms for treating eyes, dosage forms with antibiotics, dosage forms for children. All these dosage forms are characterized by the fact that they should not contain microorganisms and their dispute.

The need to obtain sterile and aseptically manufactured dosage forms is regulated by a special method of their use, for example, injections are introduced into the body through a cannula with a violation of the integrity of the skin and mucous membranes. The presence of microorganisms in them can lead to infection of the body, and, consequently, to serious consequences.

Dosage forms with antibiotics require aseptic manufacturing conditions, since in the presence of microorganisms, antibiotics lose their activity.

The listed dosage forms, regardless of whether they are sterilized or not, must be manufactured under aseptic conditions. Sanitary requirements for the manufacture of drugs in aseptic conditions are governed by the Order of the Ministry of Health of Ukraine No. 139 of 06/14/93. "On approval of instructions for the sanitary and anti-epidemic regime of pharmacies."

Characteristics of dosage forms for injection

Injectable dosage forms include sterile aqueous and non-aqueous solutions, suspensions, emulsions and dry solids (powders, porous masses, tablets), which are dissolved in a sterile solvent immediately before administration.

Medicines for injection began to be applied in medical practice somewhat later than other dosage forms. For the first time, the Russian doctor Lazarev performed the subcutaneous injection of drugs in 1851. His device consisted of a barometric tube with a piston, at the free end of which a silver tip was extruded into a needle. A modern syringe was offered in 1852 by Pravc.

The injection method of administration of drugs has positives and disadvantages. The advantages include the following:

- The completeness of absorption and the rate of action of the injected drugs, sometimes after a few seconds
- Drugs are introduced, bypassing such protective barriers of the body as the gastrointestinal tract and liver, where under the influence of enzymes can change, and sometimes disintegrated medicinal substances;
- With this method of administration, the inconveniences associated with the unpleasant smell and taste of drugs are completely excluded;
- The ability to accurately dose the medication;
- Ability to localize the action of medicinal substances;
- The possibility of administering a drug to a patient who is unconscious;
- Ability to replenish the required volume of fluid after significant blood loss
- Ability to procure sterile drugs for future use.

At the same time, the injection route of administration has disadvantages:

- There is a serious danger of introducing infection into the body;

- With the introduction of solutions into the blood there is a danger of embolism due to solid particles or air bubbles with a diameter greater than the diameter of small vessels (with embolism of vessels feeding the brain, death is possible)
- The injury is inflicted on the patient both physically and mentally;
- The use of the input method is associated with the need to attract medical personnel;
- The introduction of drugs can cause a violation of pressure, pH, etc., especially with the introduction of large quantities of the solution intravenously or intraarterially. These physiological disorders are painfully perceived by the body over time (sharp pain, burning, sometimes fever).

Types of injections. Depending on the injection site, the injections are divided into: intracutaneous, subcutaneous, intramuscular, intravenous, intraarterial, cerebrospinal, intracranial, intraperitoneal, intrapleural, intraarticular, etc.

Intradermal injections - injections intracutaneae. With this method of insertion, the needle pierces only the epidermis of the skin and fluid in a very small amount is injected into the space between the epidermis and the dermis. Intradermal injections are used to diagnose infectious diseases (Pirke's reaction), less often with a therapeutic purpose.

Subcutaneous injections - injectiones subcutaneae. Solutions are injected into the subcutaneous tissue. For subcutaneous injections, water and oil solutions, as well as suspensions and emulsions can be used. The rate of absorption depends on the nature of the solvent. Aqueous solutions are absorbed quickly, oil solutions, suspensions and emulsions - slowly.

Intramuscular injection - injectiones intramusculares. The liquid is introduced into the interior of the big muscles first. Intramuscularly, you can enter water and oil solutions, thin suspensions and emulsions. Compared with the subcutaneous tissue, muscles have a greater number of blood vessels, rather than the absorption of drugs. In addition, intramuscular injections are less painful, since muscle tissue contains less sensitive nerve endings than subcutaneous tissue.

Intravenous injections - injectiones intravenosae. The solution is injected into the vein slowly and carefully. The effect of drugs in this case occurs in 1-2 seconds. The intravenous method allows you to enter into the body large quantities of fluid: from 1 to 500 ml, and in some cases more. Often these solutions are administered by the drip method (in this case, the solution is injected into the vein not from a needle, but through a cannula, at a speed of 40-60 drops per minute).

The presence in the blood of the buffer system, regulates the pH value, allows you to enter into the blood solutions sharply acidic or alkaline reactions. With slow administration, even solutions with a pH of 3-10 in small volumes (15-20 ml) do not cause noticeable complications.

Only aqueous solutions can be administered inside the vessels, they mix well with blood (physiological, blood substitutes, glucose solutions, etc.). You can not enter into the blood suspension, emulsion with a particle diameter exceeding the diameter of red blood cells. When administered intravenously, the dose of the drug substance is taken 3 or 4 times less than when taken orally.

Intra-arterial injections - injectiones intraarteriales. The solution is injected into the artery, slowly, carefully, the effect of drugs occurs already in the process of entering. With intravascular injection, the risk of embolism and infection of the body increases dramatically.

Spinal Injection - injectiones cerebrospinales. Liquid is introduced into the epidural or subarachnoid space of the spinal canal. For spinal injections, only true aqueous solutions with a pH of less than 5 and no more than 8 are used. Usually, this method is used to administer anesthetics and antibiotics.

The conditions of distribution and resorption of medicinal substances in the subarachnoid and epidural space are different. So, with the introduction of an anesthetic solution into the subarachnoid space, after 5-7 minutes, the so-called spinal anesthesia occurs, and when injected into the epidural space, only after 20-30 minutes.

The absorption of drugs into the blood with this method of administration is very slow. Spinal injections should be performed by an experienced surgeon, because injuring the tip of a spinal cord with a needle can lead to paralysis of the lower limbs.

Intracranial injection- injectiones subarachnoidales. The solution is injected into the dilated part of the subarachnoid space, and the drugs act instantly. Introduced only true neutral solutions of water. The method is often used to inject penicillin and streptomycin for meningitis.

Intraosseous, intraarticular, intrapleural and other injections are less commonly prescribed.

Currently, a needleless injection method is used. Using a special injector, the solution is injected under pressure into the subcutaneous tissue without compromising the integrity of the skin.

The method of jet injection of medicinal substances in comparison with conventional injections with a needle has the advantages: painlessness of injections, rapid onset of effect, reduction of the required dose, impossibility of transferring "syringe infections", liquid sterilization of the injector, increasing the number of injections per unit time (up to 1000 per hour).

Needleless injectors differ in the following main features: according to the depth of administration of the drug - for intracutaneous, subcutaneous, intramuscular injections and universal; by the number of doses administered - multi-and single-dose, by design - with elastic hydraulic, electromechanical, electromagnetic and pneumatic actuators.

Non-needle injectors BI-1 (“Bee”), BI- 2, BI-3, BI-5 are now being produced. The use of needleless injector contributes to the emergence of an independent highly effective method of parenteral administration.

REQUIREMENTS FOR INJECTABLE DOSAGE FORMS.

SPh XI puts forward the following requirements for injection forms: absence of mechanical impurities, sterility, stability, apyrogenicity, in some solutions is isotonicity, which is indicated in the relevant regulatory documents or recipes.

Injection solutions can be isohydric and iso-ionic according to the requirements of their own articles.

For the implementation of these requirements, you must comply with the special conditions for the manufacture of injection dosage forms. They include: requirements for premises, production equipment, personnel, medicinal and auxiliary substances, solvents, sealing materials, organization and conduct of technological processes (dissolution, stabilization, filtration, sterilization, packaging, labeling).

The most important component of the technological process of all injection dosage forms is the organization of work under aseptic conditions and sterilization.

SOLVENTS

In the manufacture of injection dosage forms as solvents used water for injection, fatty oils, ethyl oleate, as well as complex solvents.

Water for injection (Aqua pro injectionibus). Sanitary requirements for receiving, transporting and storing water for injection are given in the order of the Ministry of Health of Ukraine No. 139 dated 06/14/93. "On approval of the instruction on the sanitary and anti-epidemic regime of pharmacies." It should meet all the requirements of FS 42-2620-89 to purified water and not contain pyrogenic substances.

Organization of work in aseptic conditions

Sources of contamination of sterile solutions can be raw materials, environment, equipment, containers, closures, working personnel.

Aseptics are certain working conditions, a complex of organizational measures that allow to protect the drugs from microorganisms in them to the maximum degree. Asepsis includes a series of consecutive events that complement each other, and the mistake made in one link of this series negates all the work done.

Aseptic conditions provide for the availability of a special room in the pharmacy for the manufacture of sterile and aseptic medicines - an aseptic unit, which must have at least three rooms:

1. The press service (gateway) is intended for personnel training to work.
2. Aseptic is intended for the manufacture of dosage forms.
3. Hardware - it is installed autoclaves, sterilizers, devices, allowing to obtain water for injection.

Requirements for the room. The production of drugs under aseptic conditions is carried out in "clean" rooms, where the cleanliness of the air is normalized according to the content of microbial and mechanical particles.

The aseptic unit is usually located far from the sources of contamination with micro- organisms (a room for patient care, washing, packing, sanitary facilities).

In the premises for the manufacture of drugs in aseptic conditions, the walls should be painted with oil paint or lined with bright tiles, while there should be no projections, eaves, cracks on them. Ceilings are painted with glue or water

emulsion paint. The floor is covered with linoleum with the obligatory welding of joints. Doors and windows must be fitted tightly and have no gaps.

Aseptic unit is equipped with exhaust ventilation with a predominance of air flow over the hood. To reduce the microbial contamination of plant air purifiers recommended that provide effect- cleaning air filter que minutes through filters of ultrafine fibers and ultraviolet irradiation.

For air disinfection in an aseptic unit, unshielded germicidal irradiators are installed: wall (OBN-150), ceiling (OBP-300), mobile type (OBPe-450), bactericidal lamps BUV-25 BUU-30, BUU-60 from the calculation of power - 2 - 2.5 W per 1 m3 of room volume, including for 1-2 hours before the start of work in the absence of people. The switch for these irradiators must be in front of the entrance to the room, and is equipped with a light panel: “Do not enter, the bactericidal irradiator is on”. Entry into the room where the unshielded germicidal lamp is turned on is allowed only after it is turned off, and it is only 15 minutes after the unshielded germicidal lamp is switched off for a long time in the specified room.

In the presence of personnel, screened bactericidal emitters can be used, installed at a height of 1.8-2 m, at the rate of 1 W per 1 m3 of room in the absence of directional radiation on those in the room.

Since ultraviolet irradiators form toxic products in the air (ozone and nitrogen oxides), ventilation must be enabled during their operation.

All equipment and furniture brought into the aseptic unit are pretreated with wipes moistened with a disinfecting solution (solution of chloramine B 1%, solution of chloramine B 0.75% with 0.5% detergent, hydrogen peroxide solution 3% with 0.5% washing facilities). Storage in aseptic unit unused equipment is strictly prohibited. Cleaning aseptic unit is carried out at least 1 time per shift with the use of disinfectants.

Once a week there is a general cleaning of the aseptic unit. At the same time, rooms are freed from equipment as far as possible, and walls and doors and floors are cleaned and disinfected. After disinfection, irradiated with ultraviolet light.

Before entering the premises of the aseptic unit there must be rubber mats that are moistened with a disinfectant solution once a shift. The aseptic unit is separated from other premises of the pharmacy by air gateways.

Requirements for staff. Persons involved in the manufacture of drugs in aseptic conditions must strictly follow the rules of personal hygiene. Upon entering the gateway, they must wear special shoes, wash their hands with soap and a brush, wear a sterile gown, a 4-ball gauze bandage, a cap (with hair carefully taken), shoe covers. The best is to use a helmet and overalls. Gauze bandage should be changed every 4:00. After putting on sterile technological clothing, staff should rinse their hands with water for injection and treat them with 80% ethyl alcohol disinfectant solution, with chlorhexidi solution at a digluconate in 70% alcohol or 0.5% chloramine B solution (in the absence of other substances). Entry from the airlock into the room for the manufacture and packaging of drugs in aseptic conditions in non-sterile sanitary clothing is prohibited. It is also forbidden to go beyond the aseptic unit in sterile sanitary clothing.

Sanitary clothes, bathrobes, gauze, textiles, cotton wool are sterilized in biks in steam sterilizers at a temperature of 132 ° C for 20 minutes or at 120 ° C for 45 minutes and stored in closed biks for no more than 3 days. Before and after work, shoes are disinfected outside and stored in locks. Persons with infectious diseases, open wounds on the skin, carriers of pathogenic microflora until their complete recovery should not be allowed to work.

REQUIREMENTS FOR PRECURSORS AND MATERIALS.

Medicinal substances necessary for the manufacture of drugs in aseptic conditions, are stored in cabinets in tightly closed shtanglas under conditions that exclude their contamination. The shtanglas are washed and sterilized before each filling.

For the manufacture of injectable dosage forms, medicinal substances of the qualification “chemically pure”, “pure for analysis” or “suitable for injections” are used, which meets the requirements of regulatory and technical documentation (TFS, FS, GOST).

However, in some preparations of the “fit for injection” variety there are additional quality requirements (Table 29).

Auxiliary substances (stabilizers, solubilizers, preservatives) must also comply with the requirements of regulatory and technical documentation.

As stabilizers of injection dosage forms, the following substances are used:

Glycerin, the highest grade, GOST 6824-76.

Trilon B h.d.a., GOST 10652-75.

Potassium metabisulfite ch.d.a., GOST 5713-75.

Hydrochloric acid, chemically pure, analytical grade, GOST 3118-77, DF X, Art. 17. Citric acid, chemically pure, analytical grade, GOST 3652-69. Sodium acetate, chemically pure, analytical grade, GOST 199-78. Sodium hydroxide, chemically pure, analytical grade, GOST 4328-77.

Sodium iodide two-water x.h., ch.d.a., GOST 8422-76, DF X, st. 133. Sodium chloride, chemically pure, GOST 4233-77, DF X, Art. 426. Sodium metabisulfite, analytical grade, GOST 10575-76. Sodium sulfite anhydrous ch.d.a., GOST 195-66.

Ethyl alcohol of the highest quality, GOST 5962-67, first grade, DF X, Art. 631.

Sodium bicarbonate, chemically pure, analytical grade, GOST 4201-79, DF X, Art. 430.

Auxiliary material (wadding, gauze, parchment paper, filters, etc.) is sterilized in doubles or ground-in jars at 132 ° C for 20 minutes or at 120 ° C for 45 minutes and remains closed. no more than three days. Disclosed materials must be used within 24 hours. After each sampling material box tightly closed. The fence is made with sterile forceps. In this case, it should be borne in mind that the auxiliary material must be stacked for sterilization in beeks in the form ready for use.

Packaging. Contamination of solutions with mechanical particles and microorganisms can be reduced by means of quality preparation of containers and

closures, as well as by observing the conditions of their storage and transportation directly to the place of spill of the solution. The first-aid kit is cleaned (used, previously disinfected, then cleaned) and sterilized, sealed, and stored in tightly closed cabinets painted from the inside with light oil paint or plastic-coated.

When washing dishes, in addition to removing mechanical impurities, it is necessary to remove as much as possible soluble alkaline compounds, of which there are especially many in an alkaline environment. Washing dishes with the use of soap is of little use, as this may form insoluble calcium soap that pollutes the glass. Detergents and disinfectants are presented in section 8. Dishes are washed by hand using brushes or washing machines.

The cleanliness of the washed dishes and the full rinsing of detergent should be monitored.

Injection solutions made in pharmacies should be dispensed in bottles with neutral glass NS-1 (for medical products, antibiotics) and NS-2 (blood vessels). As an exception, after liberation from alkalinity, AV-1 and MTO glass bottles are used, taking into account that the shelf life of solutions in them should not exceed 24 hours, otherwise glass leaching is possible.

For sealing bottles with injection solutions, use stoppers of rubber grades (pp. 98-99): IR-21 (silicone), 25P (natural rubber), 52-369, 52-369 / 1, 52-369 / I (butyl rubber) , IR-119, IR-119A (butyl rubber). In the foreign literature there are reports of the closure of injection solutions made from polyvinyl chloride.

Requirements for production equipment. The use of small-scale mechanization in the manufacture of injection solutions is allowed provided they can be sterilized. Equipment must be designed and placed in such a way as to ensure its proper preparation for operation, operation and maintenance. The material from which the equipment is made should not react with the components of drugs, and the design of the equipment should exclude the possibility of substances entering the drugs used for its operation (lubricants, coolants, etc.).

Equipment and tools must be regularly subjected to routine inspections, washed, disinfected or sterilized. The equipment should be operated in such a way as to minimize the possibility of contamination by the microorganisms of the finished drugs. Sterilizers should be equipped with devices that automatically record the time and temperature of sterilization.

Filtration for injection. One of the requirements for injection dosage forms is the absence of mechanical inclusions. Injection solutions should not contain particles visible to the naked eye, that is, particles with a size of 10 microns or more. However, it seems advisable to bring the filters up to 5 microns, that is, injection solutions should not contain particles larger than the diameter of the blood cells (5-9 microns). The presence of suspended particles is unacceptable, since embolism is possible with intravascular injection.

The release of injection solutions from mechanical impurities is carried out by filtration. The degree of purification of dispersed systems, along with other factors, is determined by the ability of suspended particles to “stick” to the filter layer. In this case, the fractions are delayed if the forces of their adhesion to the

filter material are greater than the separation forces arising from the hydrodynamic effect of the flow.

In pharmacy practice, the two most common methods of filtration are: gravity flow (see “Liquid dosage forms”, pp. 223-228) and with the help of a vacuum.

The main method of filtering solutions for injection in large-scale production in pharmacies is vacuum. It lies in the fact that a vacuum is created in the receiving tank. Under the influence of the pressure difference, the fluid, passing through the filters, fills the receiving tank. Vacuum pumps of various types, for example, suction surgical or compressor-vacuum apparatus, are used to create a vacuum.

The purity of the solutions depends largely on the choice of filter. Therefore, the choice of the optimal filter is the crucial moment in the technology of injection solutions.

To filter injection solutions, ash-free filters made of filter paper of the type FO (type M - slow-filtering) are used, which detains fine precipitates. Other brands of ashless filters are unsuitable for filtering injection solutions. An unbleached filter paper contains calcium, iron, magnesium salts, and when filtered through such paper, the properties of some solutions change. Glass filters No. 3 and No. 4 are widely used.

The modern method of cleaning injection solutions is membrane microfiltration, a process of membrane separation of microsuspensions under pressure, which allows one to obtain solutions free of mechanical particles (0.02 μm in size) visible and invisible under visual control, including microorganisms.

Thus, polypropylene was proposed for filtering injection solutions under vacuum or pressure. It is used in the form of plates in various filters of a disk design, various press filters in a Millipore type filter holder.

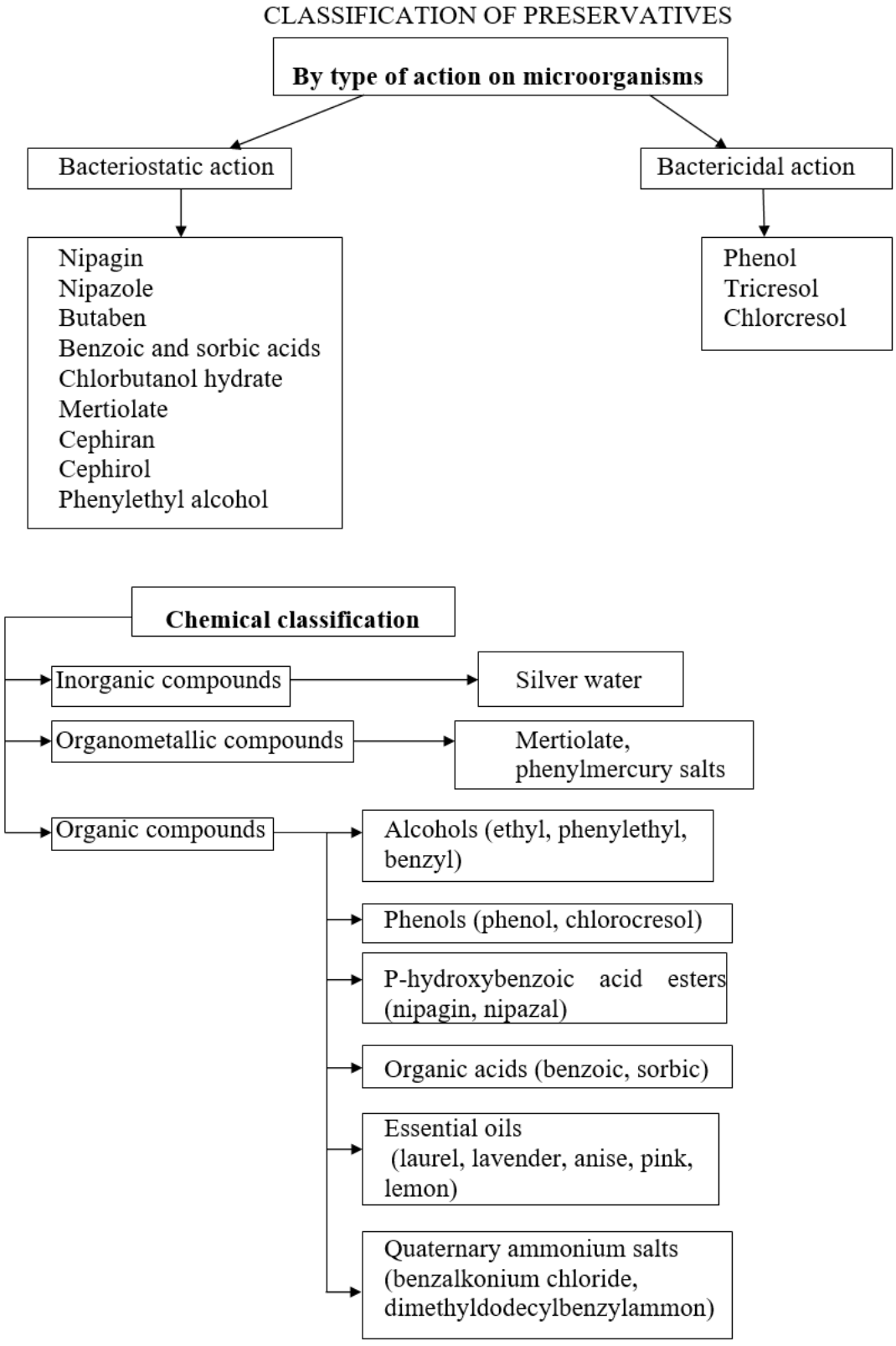
Injection solutions are filtered through 5-7 layers of sterilized polypropylene, all others are filtered through a three-layer filter. Polypropylene plates can be ¬ leather used as a prefilter for membrane filtration. Polypropylene filters can be reused.

Polypropylene filters allow to obtain pure solutions with a high efficiency of the filtration process (for a five-layer filter) on average 2-5 l / h per 1 cm; filtering surface. Also promising is the use of porous filter elements made of pressed titanium powders for fine cleaning of injection solutions.

In combination with filter elements, filter holders should be made of metal or plastic materials permitted for use in contact with liquid forms. Filter holder can be immersed or continuous type. They can be used to filter liquid dosage forms under compressed air pressure or under vacuum. For filtration of liquid dosage forms under vacuum, serial production mechanization tools should be additionally used, and pharmacies are widely used.

Filtering the solutions is combined with their simultaneous bottling in prepared sterile vials. Deviation from the volume indicated on the label (nominal) admits repents within ± 10% for vials with up to 50 ml, ± 5% - dish with 50 ml.

Structural and logical scheme of the content of the topic:



Lecture text

Water for injection (Aqua pro injectionibus). Sanitary requirements for receiving, transporting and storing water for injection are given in the order of the Ministry of Health of Ukraine No. 139 of June 14, 1993 “On approval of the

instruction on the sanitary and anti-epidemic regime of pharmacies". It should meet all the requirements of FS 42-2620-89 to purified water and not contain pyrogenic substances.

Pyrogenic substances (from the Greek word rug - fire, the Latin generatio - birth) call the waste products of microorganisms, toxins, dead microbial cells.

To determine pyrogenicity in Ukraine adopted the method described in the GF XI ("Testing pyrogenicity"). Modern world pharmacopoeias, such as the British 1998, European 1997, United States 1995, Czech 1997 along with the test for bacterial endotoxins also contain the "Test for pyrogens". In addition to the official biological test method for pyrogenicity, a limulus test (lim test) is widely used abroad, based on the formation of a gel in the interaction of bacterial pyrogens with amoebocyte lysate. A similarly sensitive, but simpler method based on the ability of gram-negative microorganisms (the main producers of pyrogenic substances) to form a gel in a 3% potassium hydroxide solution has been developed at NIIF Russia.

The chemical composition of pyrogenic substances is very complex - this is a high molecular weight, they have a liposaccharide or lipopeptide nature. Once in the body, they cause allergic reactions, fever, chills, cyanosis, asphyxiation, even anaphylactic shock. With a high content of pyrogenic substances in solutions for injection can even be fatal. The toxicity of pyrogenic substances is explained by the presence of phosphate groups in them. It is almost impossible to get rid of pyrogenic substances in water and injection solutions of thermal sterilization, because they are thermostable substances. Pyrogenic substances also pass through porcelain bacterial filters. Injection solutions are freed from pyrogenic substances using sorbents (activated carbon, cellulose, etc.).

Water for injection can be obtained by distillation of drinking water under aseptic conditions in apparatus, the design of which allows the release of water vapor from small droplets of un-distilled water.

It is known that pyrogenic substances are not volatile and are not distilled by water vapor. Distillate contamination by pyrogenic substances occurs by the assignment of small water droplets of steam to the refrigerator.

Thus, the main task in obtaining water for injection is the separation of water droplets from the vapor phase. To do this, distillers are now offered, in which, unlike conventional, water vapor passes through special separators. By design, they are centrifugal, film, bulk, volume, combined. In centrifugal separators, the rotational motion of the separated vapor is created and, under the action of acceleration, water particles are intensively released from the steam flow. Film separators consist of a set of plates, through the gaps of which the steam passes, is separated. In volume separators, water droplets fall out of the steam flow under the action of gravity, in combined separators, a combination of two or more types of separation is used. In some devices, the steam goes a long, winding path, and on this path to the condenser gradually loses the droplet-liquid phase. The steam thus purified after condensation gives pyrogen-free water. Currently available are AA-1 devices (Fig. 132), A-10, A-25, Vaponix distiller (USA), which

includes a combination of methods: a sharp change in the steam flow rate, filtering it through a special filter with a hole diameter of 40 microns and droplet separation in a centrifugal field and others.

Device AA-1 produced by the St. Petersburg plant of electromedical equipment "ZMO". It has a nominal capacity of IL / hour. The main parts are the evaporation chamber (10) with traps (8), the condenser (1), the equalizer collector 25 and the electrical panel. The evaporation chamber is externally protected by a steel casing (9), designed to reduce heat losses and prevent maintenance personnel from burns. Four electric heaters (11) with a capacity of 2 kW each are mounted in the bottom (12) of the evaporation chamber. In the evaporation chamber, water (with the addition of chemical reagents) heated by electric heaters (11) turns into steam, which through traps (8) and the steam tube (7) enters the condensation chamber (3), cooled outside with cold water, and condensing, turns into pyrogen-free water, which flows through the nipple (5). To prevent pressure increase in the chambers (3) and (10), a safety slot (6) is equipped, through which excess steam can escape. On one of the legs of the device there is a special bolt (14) with nuts and washers for connecting the ground wire.

The cooling water, continuously flowing through the valve (4) into the water chamber (2) of the condenser (1), is drained through the drain pipe (15) into a collection rectifier (25). Collection rectifier (25), which is connected to the evaporation chamber (10), is designed to constantly maintain the water level.

At the beginning of the operation, the water fills the evaporation chamber to the set level. In the future, as boiling, water will flow into the evaporation chamber partially, the main part through the nozzle (26) will be discharged into the sewer. For visual observation of the water level in the evaporation chamber (10), a water -indicating glass (27) is equipped at the fitting of the equalizer collector (25).

The equalizer collector (25) is also intended for mixing water with chemical reagents that are added to the evaporation chamber to obtain high-quality pyrogen-free water that meets the requirements of the Pharmacopoeia.

For this purpose, there is a special tube in the equalizer collector through which chemical reagents enter the evaporation chamber (10) along with water. Strict dosing of chemical reagents is provided by a special dosing device consisting of two glass vessels (22) with droppers (24), two filters (21) and two dispensers (18) connected by rubber tubes. The dosing device is connected about with a collector-leveler (25) through droppers (24). The dosing device fastenings are carried out on a bracket (19), in which special openings for glass vessels (22) are arranged, which are fixed with rubber rings (20) into special grooves into which dispensers (18) are freely inserted, which are mounted on the bracket (19).) lock nuts (17).

Fig. 1. Apparatus for producing pyrogen-free water AA-1

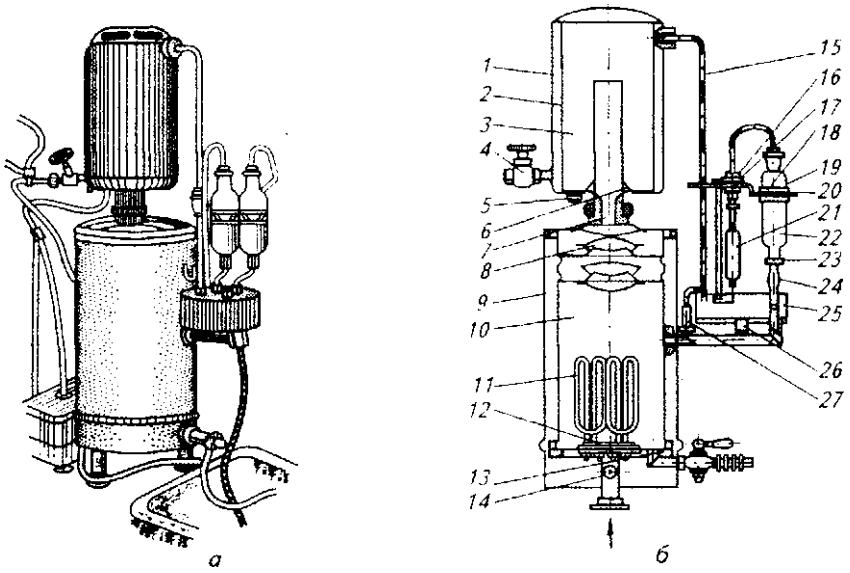


Fig. 1. Apparatus for pyrogen-free

Apparatus A-10 differs from apparatus AA-1 by the presence of semi-automatic control; it turns off electrical heating elements in the event of a water supply cut-off.

The device D-25 differs from other distillers in compactness and profitability. Mage capacity 25 l / h. In the case of cessation of water supply or at low pressure, the device automatically turns off. The operation of the apparatus is controlled by signal lamps. When receiving water for injections, double distillation apparatus is also used. Convenient to use and quite productive (5-6 l / h) Bidistillator BD-1. It consists of a distillation chamber where a primary steam is formed, a double-distillation chamber for the formation of secondary steam, a condenser and a collector. Before entering the double-distillation chamber, the distillate is mixed with chemical reagents, which served by a special device, which consists of two glass vessels with droppers, filters and dispensers. In one vessel filled with a solution of disodium phosphate and potash alum, in one second - a solution of potassium permanganate. The process of obtaining double-distilled water in this apparatus is as follows: tap water enters the condenser, then through an equalizer into the evaporation chamber, where it heats, turns into steam and goes to the condenser. The water from the condenser flows into the collection and, after mixing with chemical substances, enters the double distillation the chamber where it is heated, the other turns into steam, which enters the condenser and after condensation flows into the receiver twice. The distilled water. The most widely used in the conditions of pharmacies found the device, serially produced by domestic industry, brand AEVS-60 (apyrogenic electric avadistillator with a water-drier and collection container). The nominal capacity of the water distiller is 60 l / h. Estimated consumption of consumed tap water 900 l / h.

The device AEVS-4A is an electric water distiller with water treatment for producing pyrogen-free water (Fig. 133).

It consists of an evaporator, a collection of water for injections, an electrical cabinet, an anti-scale magnetic device (PMS), a piping system. This is a stationary installation, working according to the following scheme: the steam generated in the evaporator passes through the separator, the steam line and enters first into the condensation chamber of the collector, and then into its internal cavity, where the distillate is finally cooled to the required temperature. On the tap water line there is a permanent residence for the release of the initial (tap) water from salts and various impurities, then the water enters the cooled jacket of the collector and the evaporator. Upon reaching the water in the evaporation chamber to a predetermined level, the excess of it is discharged into the sewer system. After filling the collection with water, the electric heater in the evaporation chamber is turned off. Productivity of the device is 4 l / h.

AEVS-25 - electric water distiller with water treatment for pyrogen-free water (Fig. 134).

It is a stationary installation and consists of: evaporators of I and II degrees, a collection of water for injection, pipelines and electrical cabinet. On the water line in the evaporators built in

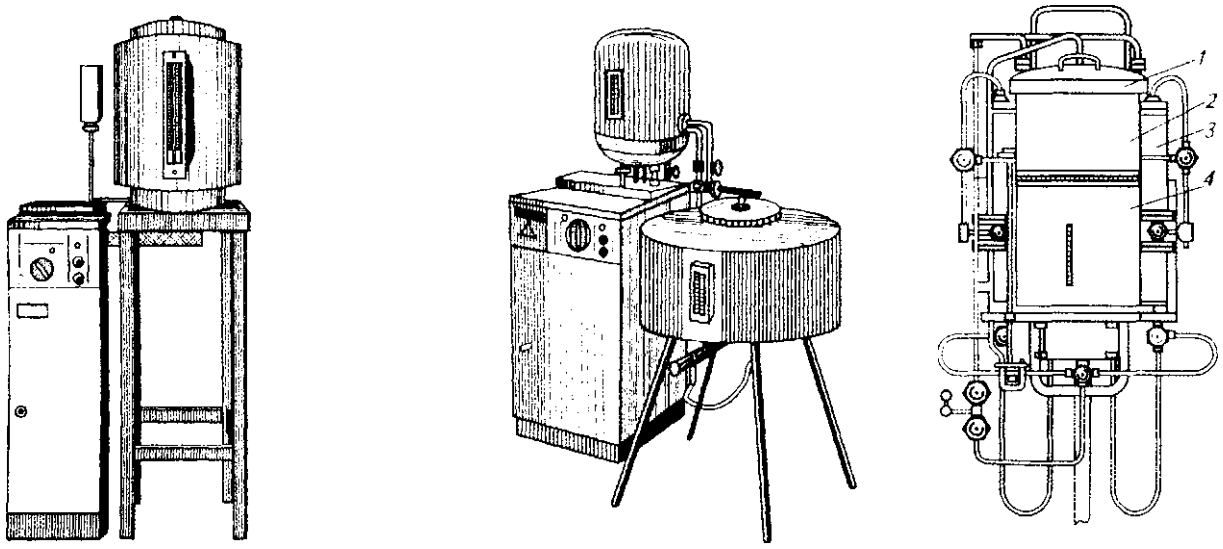


Fig. 2. Aquadistillator AEVS-4A

Figure. 3. Aquadistillator AEVS-25

Figure. 3 Diagram of the apparatus for producing pyrogen-free water design GANDI

Anti-scale magnetic device designed for pre-treatment of source water. At first, water enters the evaporator of the second degree until a smooth device closes the water supply, after which the first stage of the evaporator begins to fill with water. Simultaneously with the water supply to the evaporators, the tap water is fed through a special pipeline into the chilled jacket of the collector. The vapor, which was formed in the evaporator of the first degree, passes through the separator and then enters the heating chamber of the second degree through the steam- wire. In

the heating chamber, the steam loses some of its heat to heat the water and the formation of steam in the evaporator of degree II and partially condenses.

Conductivity of steam mixture from the heating chamber and steam Kotor first the last e l through II degree evaporator separator, fed via conduits in the collection. In the collection, thanks to its water cooling jacket, the final condensation of the steam-water mixture takes place and water is collected for injection. After the reservoir is filled with water to the set upper level, the float is lowered and the limit switch is in the initial position.

The device design TSANII (Fig. 4).

It is a combined installation of ion exchange columns and distillation apparatus, in which tap water is subjected to desalting, and then distillation and sterilization.

The device for the production of pyrogen-free water is portable, since it is made in the form of a vertically located cylinder. Components of the apparatus: evaporator, condenser (2), pyrogen-free water collection (3), demineralization column (4). A device for the regeneration of columns and electric heaters are located in the evaporation chamber. Two demineralization columns, mounted behind the apparatus, made of organic glass and filled with ion exchange resins. One column is involved in the work, and the second (after regeneration) - backup. Each column in the upper part is filled with cation exchanger, and in the lower part with an anion exchanger, both parts are interconnected by a crane. Productivity of the device is 12 liters of pyrogen-free water per hour.

In the distillation apparatus manufactured by Hirano, the steam during the distillation is freed from water droplets using a reflux condenser (nozzle with transverse partitions that do not reach the end). In another apparatus of the same company, the steam from the steam generator is sent to the condenser through a chamber filled with pieces of glass tubes, where it loses the droplet-liquid phase.

Recently, interest in the development of non - distillation methods for obtaining extremely pure water has increased. This is due to advances in technology and technology, requires the use of water of this degree of purification.

Technological schemes of non - distillation preparation of high - purity water include various combinations of activated carbon sorption, ion exchange, membrane technology, ultrafiltration, reverse osmosis and ozonation.

So, at the enterprises of the firms “Christ AG” and “Hoffman La-Roche” (Switzerland) the technological scheme of obtaining extremely pure water for the pharmaceutical industry was developed and put into production (Reider V.P., Bruch M.). As the source, used city tap water without prior treatment. After deionization, water is supplied to the reverse osmosis unit using filtering elements made of porous fibers or spiral elements. The resulting concentrate with 90% elimination of solutes is subjected to UV irradiation, microbial disinfection in a mixed-type ion exchanger (developed by Krist AG) until the water complies with the standard. Next, the water is filtered through sterilizing filters with a pore diameter 0.22 microns. Achieving optimal operating conditions for individual components of the plant and increasing the service life of sterilizing filters made it possible to reduce the cost of water produced by 20%.

Ganzi GC . Parise PL. suggested a combined installation, that the reverse osmosis module and the installation of continuous deionization of water. As the results of research have shown, with such a combination, especially pure water is obtained without the use of chemical regeneration and ion-exchange treatment. Recent developments in continuous deionization technology allow the removal of dissolved carbon dioxide without first determining the acid-base value. The existing complex system makes it possible to obtain water with a low content of microorganisms and pyrogen.

In the preparation of highly pure water, Nebel S. showed the need to use ozone to disinfect the deionizing layer and the deionized water itself. Granular activated carbon and a deionizing layer in some cases contribute to the growth of microorganisms and one UV irradiation cannot ensure complete sterilization of the treated water. It was found that the treatment of water samples with ozone in a concentration of 2.5 mg O3 / l gives a zero indicator of the presence of microorganisms in the resulting water. Further, the water made is deozonurized by UV irradiation.

Margardt K. was shown that when developing components of plants for the production of ultrapure water for the pharmaceutical industry, including ion-exchange processing devices and reverse osmosis plants, it is necessary to include the technological stages of disinfection of reverse osmosis systems, followed by the removal of ozone and carbon dioxide from water.

Hayashi Akio (Japan) showed the possibility of obtaining extremely pure water that meets the requirements of the British Pharmacopoeia. The treated water (volume 35 l), after passing through the deionizer, entered the quartz feed and was treated with UV light with simultaneous transmission of an ozone stream for 20 minutes. Tests have shown the compliance of water with existing standards, the ability to remove from it when using this method, microorganisms, pyrogens and chemical impurities.

So, non-distillation methods make it possible to obtain highly pure water for pharmaceutical production. However, not so simple. In the West, only the XXI US Pharmacopoeia allows to obtain water for injection using reverse osmosis using special equipment. Demineralizer "ELGAMAT DUO Rapids" (England), which desalinates water by ion exchange, etc., Provides a three-stage installation "Osmocarb" (England). Ultraviolet modules are produced by foreign companies such as Asahi Chemical (Japan), Hoffmann La-Roche (Switzerland), Elga (Great Britain), etc.

Of great importance for the quality of water are the way it is collected and stored. The resulting water for injection is collected in clean, sterilized or steamed industrial production collections. The necessary sanitary and hygienic conditions for the storage of water for injection are provided by domestic collections of type SI with a capacity of 40 and 100 liters.

The choice of a collection of SI type for pharmacies depends on the amount of work and the cost of purified water. Collections must have a clear inscription: "Water for injection." If several collections are used simultaneously, they are numbered.

As an exception, water for injection can be stored in sterile glass collections (bottles), which are tightly closed with two openings (caps): one for the tube through which water flows, the second for the glass tube into which a tampon of sterile cotton wool is inserted air filtration (changes every day). In order to protect against dust, the receiver must be closed in a sealed glass box. It is necessary to carefully monitor the cleanliness of the cylinders and connecting tubes through which water enters the collection.

Conventional glass bottles with cortical or ground stoppers are unsuitable for storing water for injection.

Water for injection is used freshly prepared or stored at a temperature of 5. ° C to 10 ° C. When preparing a stock of water for injection, it must be sterilized immediately after distillation in tightly closed vessels at 120 ° C for 20 minutes or at 100 ° C within 30 minutes, or heated in a collection to a temperature of 80-95 ° C in the process of distillation, collection and then stored under aseptic conditions for no more than 24 hours.

TECHNOLOGY SOLUTIONS FOR INJECTION AND QUALITY CONTROL

Solutions for injections are prepared in accordance with the requirements of the Global Fund XI, orders of the Ministry of Health and instructions. The technological process of manufacturing solutions for injection consists of the following stages:

1. Preparatory work.
2. Preparation of the solution (stabilization, isotoning, if necessary).
3. Filtration and packaging.
4. Sterilization of the solution.
5. Control of finished products.
6. Registration.

Preparatory work (personnel training, aseptic block preparation, organization of work under aseptic conditions, preparation of dishes and auxiliary materials, preparation of solvents and preparations) are provided on pages 450-455.

Consider the stage of direct manufacture of solutions for injection.

Preparation of the solution. Production of solutions for injection can be carried out only in pharmacies that have permission to do so, issued by an authorized body.

It is prohibited to prepare solutions for injections in the absence of methods for their complete chemical analysis, sterilization regime, data on the chemical compatibility of the incoming ingredients and technology.

Personal responsibility for the organization of the work of aseptic blocks and the preparation of solutions for injection rests with the heads of pharmacies. They are required to conduct an annual briefing and examination of employees of aseptic units on the rules for preparing solutions for injections, as well as when they are accepted or transferred to work in an aseptic unit. Persons

who do not possess the technology of injection solutions are not allowed to work in the aseptic unit.

Due to the very responsible method of application and the high risk of errors that can be made during operation, the manufacture of injection solutions requires strict regulation and strict adherence to technology.

The simultaneous manufacture of several injection solutions is not allowed, they include various ingredients, or the same, but in different concentrations. At the workplace in the manufacture of injection solutions should not be shtanglas with medicinal substances that are not related to these solutions.

Preparation of injection solutions is carried out by mass-mass method, in which the medicinal substance is taken by weight, and the solvent - to obtain a certain volume of solution. The need to manufacture solutions in bulk concentration is due to the fact that when injected with a syringe, the drug is dosed by volume.

Technological stage “Preparation of a solution” includes three technological operations: preparation of raw materials (calculations, weighing substances and measuring the solvent), direct production of a solution (dissolving substances, if you need to add a stabilizer, obtain the required volume) and primary analysis.

The medicinal substance taken by weight is placed in a sterile volumetric flask, dissolved in a small amount of solvent, and then brought to a certain volume. In the absence of measuring dishes, the amount of solvent needed to prepare a solution is determined by a calculation method using the density of the solution of a given concentration or volume increase factor.

The volume occupied by stabilizers is included in the total volume of the solution, so they are added simultaneously with medicinal substances.

When enlarged manufacturing solutions for injection required capacity of 10 liters or more. In large inter-hospital and hospital self-supporting pharmacies, the dissolution of drugs is carried out in glass 20-liter reactors equipped with electric heating and an electric mixer. In medium-capacity production of interhospital pharmacies, the process of mixing the fluid is mechanized using various type of agitators.

Immediately after preparation of the solution, conduct a survey control. Next, the prepared solution for injection is subjected to complete primary chemical control, is to determine the authenticity (qualitative analysis) and the quantitative content of active substances and stabilizer (quantitative analysis).

The results of the complete chemical control of injection solutions are recorded in a journal in the prescribed form.

In the case of a satisfactory result, proceed to filtration and packaging.

Filtration and packaging solutions for injection. One of the requirements for injection dosage forms is the absence of mechanical inclusions. Injection solutions should not contain particles visible to the naked eye, that is, particles with a size of 10 microns or more. However, it seems advisable to bring the filters up to 5 microns, that is, injection solutions should not contain particles larger than the

diameter of the blood cells (5-9 microns). The presence of suspended particles is unacceptable, since embolism is possible with intravascular injection.

The release of injection solutions from mechanical impurities is carried out by filtration. The degree of purification of dispersed systems, along with other factors, is due to the ability of suspended particles to “stick” to the filter layer. In this case, the fractions are delayed if the forces of their adhesion to the filter material are greater than the separation forces arising from the hydrodynamic effect of the flow.

In pharmaceutical practice, the most common two methods of filtration: by gravity and using a vacuum.

The main method of filtering solutions for injection in large-scale production in pharmacies is vacuum. It lies in the fact that a vacuum is created in the receiving tank. Under the influence of the pressure difference, the fluid, passing through the filters, fills the receiving tank. Vacuum pumps of various types are used to create a vacuum, for example, a suction surgical or compressor-vacuum apparatus.

The purity of the solutions depends largely on the choice of filter. Therefore, the choice of the optimal filter - crucial moment in the technology of injection solutions.

To filter injection solutions, ash-free filters are used from an oval paper filter of the type FO (type M - slow- filtering), which detains fine precipitates. Other brands of ashless filters are unsuitable for filtering injection solutions. Non-bleached filter paper contains calcium, iron, magnesium salts, and when filtered through such paper, the properties of some solutions change. Glass filters No. 3 and No. 4 are widely used.

Characteristics of filter materials and glass filters are presented in detail in the section “Liquid dosage forms”.

The modern method of cleaning injection solutions is membrane microfiltration - a process of membrane separation of microsuspensions under pressure, which allows to obtain solutions free from mechanical particles (0.02 μm in size) visible and invisible under visual control, including microorganisms.

So, for filtering injection solutions under vacuum or pressure, the proposed polypropylene. It is used in the form of plates in various filters of a disk design, various press filters in a filter holder of the “Millipore” type.

Injection solutions are filtered through 5-7 layers of sterilized polypropylene, all others are filtered through a three-layer filter. Polypropylene plates can also be used as a prefilter for membrane filtration. Polypropylene filters can be reused.

Polypropylene filters allow to obtain pure solutions with high filtration process performance (for a five-layer filter) on average 2-5 l / h per 1 cm2 of filtering surface. Also promising is the use of porous filter elements made of pressed titanium powders for fine cleaning of injection solutions.

In combination with filter elements, filter holders should be made of metal or plastic materials permitted for use in contact with liquid dosage forms. Filter holder can be submersible or through type. They can be used to filter liquid dosage

forms under compressed air pressure or under vacuum. For filtration of liquid dosage forms under vacuum, serial production mechanization tools, widely used in pharmacies, should be additionally used.

Filtering the solutions is combined with their simultaneous bottling in prepared sterile vials. The deviation from the volume indicated on the label (nominal) is allowed within ± 10% for bottles with a capacity up to 50 ml, ± 5% - for dishes with a capacity of 50 ml.

For packaging injection dosage forms, two types of packaging are used: ampoules and vials of glass, polyethylene or other material, do not change the properties of medicinal substances (see 8, p. 94).

Ampoules are an improved form of packaging, because they allow you to maintain the sterility of medicines until the moment of their use. This is the factory form of packaging, so their production is considered in the course of technology of factory-made drugs.

From pharmacies of medical institutions, it is customary to release sterile solutions in wide- mouth standard (can be graduated) bottles of various capacities with a standard rubber stopper attached to the hospital department, pressed with an aluminum cap (like antibiotic bottles).

Filtered solutions for injection after bottling are inspected visually for the absence of mechanical impurities.

UK-2 device is used for visual control of cleanliness. Solutions are viewed with the naked eye. The distance of the eye of the controller should be within 25 cm from the vial. The controller must have visual acuity 1 (compensated by glasses). Visible mechanical impurities should appear in sterile injectable solutions.

When mechanical inclusions are detected, the solutions are re-filtered, re-examined, clogged (leak test), labeled and sterilized.

Vials with solutions for injection are labeled by inscription or stamping on the lid, the use of metal tokens or other methods.

Sterilization of solutions for injection should be carried out no later than three hours from the beginning of production under the control of a specially selected specialist.

Control of finished products. After sterilization, secondary control is carried out for the absence of mechanical impurities, qualitative and quantitative analysis. For analysis, one vial of solution is taken from each batch (for one batch of solution, the products obtained in one container from one batch of medicinal substance are counted).

At the same time, the sealing of the vials is checked (the aluminum cap should not be rotated when turning manually) and the volume of the vials filled (± 5%). Control of injection solutions for sterility and pyrogenic substances is carried out in accordance with the requirements of the current instructions.

Thus, the quality control of injection solutions should cover all stages of their manufacture. The results of the stepwise control of the production of solutions for injection are recorded in a special journal in the prescribed form.

Register

registration of individual stages of the manufacture of injection solutions 1

Дата	№ п/п, він же № серії чи № рецепта	Вихідні лікарські засоби		Готовий продукт		Підпис того, хто приготував	Фасування		Підпис того, хто розфасував	Умови стерилізації		Термостат	Підписи		№№ аналізів до і після стерилізації[2]	Кількість флаконів готової продукції, що надійшла для відпуску	Підпис того, хто допустив лікарську форму до відпуску[3]
		назва	кількість	назва	кількість		об'єм	кількість пляшок (фл.)		температура	час		хто провів стерилізацію	хто провірив на відсутність механічних включень			
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18

1. Registration during the day is allowed on a separate sheet of this form, followed by stitching.
2. The number of the analysis before and after sterilization is indicated by a fraction.
3. For this, the responsible person is allocated (head of department, deputy head of department, analyst or pharmacist).

Registration of the manufacture of injection solutions is carried out as they are made.

Solutions for injections are considered to be unsatisfactorily manufactured with non-compliance with their physico-chemical parameters, with the content of visible mechanical impurities, non-sterility and pyrogenicity, violation of the closure fixation, insufficient filling of the volume of the bottles.

Solutions that meet all the requirements, suitable and subject to registration for vacation.

Design solutions for injection. Solutions for injections for outpatients are issued with a basic blue label “For Injections” (it should contain the pharmacy number, composition, method of use, date of manufacture, prescription number), additional label “Sterile” and, if necessary, warning labels about the conditions storage (“Keep in a cool and dark place,” “Keep out of the reach of children”, etc.). On the bottle with the solutions prepared under aseptic conditions without sterilization, an additional label “Prepared Aseptically” is pasted.

Dosage forms for treatment-and-prophylactic institutions are issued with a label, which should contain the following designations: pharmacy number and hospital number, department, date of manufacture, shelf life, prepared, checked, released. No. of analysis, method of use, the composition of the dosage form (indicated in Latin).

STERILIZATION

Sterilization is the process of complete destruction of microorganisms and their spores in medicinal substances, dosage forms, dishes, auxiliary materials, tools and apparatus.

The term "sterilization" is derived from the Latin sterilis, which means sterile. Sterility is achieved by observing asepsis and applying sterilization methods in accordance with the requirements of the Global Fund XI - the article “Sterilization”.

When choosing a method and duration of sterilization, it is necessary to consider the properties, volume or mass of materials to be sterilized.

Sterilization methods can be divided into: physical, mechanical, chemical.

Sterilization methods. These include: thermal or thermal sterilization, sterilization by ultraviolet rays, radiation sterilization, sterilization by high-frequency currents.

Of these methods in the conditions of pharmacies applied thermal sterilization, as well as sterilization by ultraviolet rays. Other methods of sterilization in pharmacies have not yet been applied.

Thermal sterilization. With this method of sterilization, the death of microorganisms occurs under the influence of high temperature due to the coagulation of proteins and the destruction of the enzymes of microorganisms. The most widely used in the pharmacy practice is sterilization with dry heat and steam.

Dry heat sterilization is carried out with dry hot air in air sterilizers at a temperature of 180-200 °C. The effectiveness of sterilization depends on temperature and time. The uniformity of heating objects is determined by the degree of their thermal conductivity and the correct location inside the sterilization chamber to ensure free circulation of hot air. Objects that are sterilized must be packaged in an appropriate container, tightly sealed and freely placed in drying cabinets to ensure quick and uniform penetration of hot air into them. Loading should be carried out in unheated drying cabinets or when the temperature inside the cabinet does not exceed 60 C. Since the hot air has a low thermal conductivity, the heating of the loaded objects is quite slow. The time recommended for sterilization should be counted from the moment of heating the air in the drying cabinet to a temperature of 180-200 ° C.

The air method is used to sterilize heat-resistant powdered drugs (sodium chloride, zinc oxide, talc, white clay, etc.). Powders weighing more than 200 g are sterilized at 180 ° C for 60 minutes or at 200 ° C - 30 minutes. The thickness of the powder layer should be no more than 6-7 cm. The time of sterilization exposure of powders weighing less than 200 g, respectively, is reduced to 30-40 minutes at 180 ° C and to 10-20 minutes - at 200 ° C.

Mineral and vegetable oils, fats, anhydrous lanolin, petroleum jelly, wax are sterilized with hot air at 180 ° C for 30-40 minutes or at 200 ° C - 15-20 minutes taking into account the amount of substance.

Products made of glass, metal, silicone rubber, porcelain, installations for sterilizing filtration with filters and receivers of the filtrate are sterilized at 180 ° C for 60 minutes.

Small glass and metal objects (funnels, pipettes, etc.) are placed in drying cabinets in special bix.

To preserve the sterility of the dishes, if it is not used immediately after sterilization, it should be tightly closed with glass or cotton plugs wrapped in

gauze before sterilization. As an exception, sterilized dishes can be closed with stoppers under aseptic conditions immediately after sterilization, while the bottles and flasks are hot.

Solutions of medicinal substances cannot be sterilized in drying cabinets, as due to the poor thermal conductivity of air, having a temperature of 100-120 ° C, it does not provide rapid heating of solutions to the sterilization temperature. For example, a sodium chloride solution (volume 200 ml) placed in an oven with a temperature of 120 ° C warms up to 60 ° C in an hour. Hot air at a higher temperature can cause decomposition of medicinal substances and glasses rupture due to the pressure difference inside and outside the vials.

For sterilization with dry hot air in pharmacies, it is advisable to use the ShSS-250P drying and sterilization cabinets, the dry heat sterilizer SS-200 and air sterilizers with a small volume of the OP-10, GP-20 and GP-40 sterilization chambers. In large hospital pharmacies there are drying and sterilizing cabinets ShSS-500P and ShSS-1000P.

Steam sterilization is based on a combination of high temperature and moisture. Coagulation of protein substances in these conditions begins at a temperature of 56 ° C. In pharmaceutical practice, several methods of steam sterilization are used, of which the most reliable, fast and economical - sterilization with saturated steam under a pressure of 0.11 MPa (1.1 kgf / cm2) and temperature 120 ° C; 0.20 MPa (2 kgf / cm2) and a temperature of 132 ° C. Under these conditions, not only vegetative, but also spore forms of microorganisms are killed.

Steam sterilization method at 120 ° C is recommended for water and aqueous solutions of medicinal substances. Sterilization exposure time is not more than 30 minutes, depending on the physicochemical properties of the preparation and the volume of the solution. Solutions with a volume of up to 100 ml are sterilized for 8 minutes, a volume of 101-500 ml - 8-12 minutes and a volume from 501 to 1000 ml - 12-15 minutes.

Sterilization of water and aqueous solutions is carried out in hermetically sealed and pre-sterilized vials or ampoules. Fats and oils in hermetically sealed vessels are sterilized at 120 ° C for 2:00. This method is sterilized also products made of glass, porcelain (porcelain), metal, rubber, dressing and auxiliary materials (cotton wool, gauze, bandages, bathrobes, filter paper, rubber stoppers, parchment, etc.). Sterilization time 45 minutes.

Sterilizing filtration units with filters are sterilized for 15 minutes (for filters with a diameter of 13 and 25 mm), 30 minutes (for filters with a diameter of 47, 50, 90 and 142 mm) and 45 minutes (for filters with a diameter of 293 mm).

A method of steam sterilization at 132 ° C for 20 minutes can also be recommended for sterilizing surgical instruments, dressings, underwear, and work clothes. Sterilization of these objects should be carried out in sterilization boxes or two-layer soft pack of coarse calico or parchment paper.

Sterilization with steam under pressure is carried out in steam sterilizers (autoclaves) of various designs. Convenient such steam sterilizers, in which the specified pressure and temperature are automatically maintained, and it is also

possible to dry the auxiliary material (cotton, filter paper, gauze, etc.) after sterilization.

Now sterilizers of type VK-15, VK-30 (fig. 137), GP-280 and others have become common. In the practice of hospital pharmacies, also sterilizers of type GP-400, GPD-280 and GPS-500 can be used, by structure and principle actions are similar to the sterilizer GP-280.

VK-30 and VK-75 vertical steam sterilizers are distinguished by the capacity of the sterilization chamber. They consist of a housing with a sterilization and water steam chambers, a lid, a casing, electric heating elements, an electrical panel, an electrical contact meter , an vacuum tube, an eke torus, safety valve, water-indicating column and pipeline with valves. Sterilization and water steam chambers are combined into a single welded structure, but functionally separated, so that you can block the flow of steam into the sterilization chamber during loading, ejection and unloading of the autoclave, as well as automatically maintain the working pressure in the water vapor chamber for subsequent sterilization. Both cameras are made of stainless steel. The maximum vapor pressure in the sterilization chamber is 0.25 MPa. Both sterilizers operate on a 220/380 V three-phase AC network. Steam sterilizers VKO-50 and RKO-75 differ in the size of the sterilization chamber, the working pressure of which should not exceed 0.2 MPa. Sterilization can be carried out both under pressure and flowing steam.Steam sterilizer VKO-16 of portable type is intended for sterilization by fluid steam. The GK-100 horizontal steam sterilizer is designed to operate at a maximum vapor pressure of 0.2 MPa. The main parts of it are the sterilization and water vapor chambers, a steam generator with electric heating elements, a cover, a casing and an electrical panel. Inside the water vapor chamber is sterilization. Steam from steam generator enters the steam chamber, and then into the sterilization chamber. The condensate formed in the process of operation flows into the steam generator, it is equipped with a safety valve, a pressure gauge and a water indicating column with a funnel for pouring water. Filling the steam generator with water can be carried out either manually through a funnel, or from a water mains through a special pipe, equipped with a valve. The sterilizer operates on a three-phase AC network with a voltage of 220/380 V (fig. 138).

The steam sterilizer GP-280 operates in an automatic cycle and has four sterilization modes that differ in different lengths (from 20 to 30 minutes) and vapor pressure in the sterilization chamber (from 0.1 to 0.2 MPa). The sterilizer consists of a sterilization chamber with a door, a steam generator, an electric pump and a switchboard. The door of the chamber is equipped with a central shutter and has a membrane-type lock, prevents its opening when the steam pressure is excessive inside the chamber. On the control panel of the sterilizer is a pressure gauge, vacuum gauge, gauge glass and control buttons. The steam generator is made in the form of a boiler with a heat insulating jacket, equipped with a safety valve, thermistor, pressure gauge, level sensor and water-indicating column.

The steam sterilizer GPD-280, in contrast to the sterilizer GP-280, is equipped with two doors with centralized valves and a lock. It is built into the wall

opening that separates the aseptic unit and the sterilization room. The steam sterilizer GPS-500 is powered by a centralized source of steam (boilers).

Preparation of devices for sterilization should begin with water filling the water vapor chamber through the funnel of the water indicating column to the upper mark. At the same time, the tap, valve and cover of the sterilizer must be open. After loading the sterilization chamber the lid of the sterilizer is closed, tightly drew it with bolts. Valve and valve must be closed. Then in the manometer set the limits of automatic pressure maintenance and include the device in the network.

Before sterilization begins, air must be completely removed from the sterilizer. To do this, the sterilizer is first heated with an open tap. After 10-15 minutes after the steam goes strong jet, the valve is closed. To check for the absence of air in the sterilizer, one should place the tube from the outlet valve into a test tube with water, turned upside down in a vessel filled with water. At an exit from a sterilizer of steam without air impurity water from a test tube will not be displaced. Removal of air from the sterilizer is extremely necessary, since the air left in it sharply reduces the heat transfer coefficient of the pair (thermal conductivity of steam containing 5% air decreases by 50%), as a result it is impossible to ensure uniform heating of materials, sterilized, and sterilization reliability. Found that anthrax spores during sterilization die at different times, depending on the amount of air in the vapor. If the vapor contains 8% air, at a pressure of 0.1 MPa, the spores die within 3 minutes, if there is 20% - within 10 minutes, and with a content of 37% air, the spores die after 30 minutes.

When the sterilizer is heated in parallel with the pressure increase, the temperature in the sterilization chamber rises. The relationship between temperature and air pressure is expressed as follows: 0.05 MPa - 110.0 ° C, 0.1 MPa - 119.6 ° C, 0.15 MPa - 126.8 ° C, 0.2 MPa - 132 9 WITH.

Sterilization time should be counted from the moment of establishment of the set pressure, it is maintained during sterilization automatically. After the sterilization time has elapsed, the valve connecting the sterilization chamber with the atmosphere is opened, steam and condensate are discharged through it, and after the arrow turns to “0”, the lid is opened and the sterilization chamber is unloaded.

In recent years, new steam sterilizers have been created specifically for solutions with forced cooling of objects; they are sterilized: ГП-400 and others.

The sterilization chamber of the GP-400 sterilizer has a steam jacket and is equipped with a sliding type door, and the loading and unloading device is made in the form of a trolley with a movably placed carriage on which cartridges with hermetically sealed blood vessels are installed. After the vials are loaded, the doors of the sterilization chamber are hermetically closed and by pressing the “network” and “start” buttons the autonomous steam supply system and the air preparation system are sequentially activated and the sterilization process is carried out.

New sterilizers, designed specifically for sterilizing solutions in hermetically sealed containers, can dramatically reduce the time required for this due to forced cooling.

The second important advantage of the sterilizers again is the TC, that at the end of the sterilization process the temperature of the liquid in the vials does not exceed 60-70 ° C. This eliminates the battle of the vials at the stage of unloading the sterilizer and guarantees safety for the staff. In addition, forced cooling shortens the time of exposure to elevated temperature on the drug substance, as a result of which the chemical stability of drugs in solutions increases. Since sterilizers are pressure machines, they are serviceability is monitored by the boiler inspection. Persons working with the sterilizer should be well aware of its structure and strictly follow the safety regulations. Maintenance of sterilizers is permitted only to persons who have reached the age of 18, who have completed autoclave maintenance courses, who have passed a preliminary medical examination and instruction on safe maintenance of sterilizers.

Steam Sterilization It is carried out with saturated water vapor at a temperature of 100 ° C. Flowing steam is used in cases where only vegetative forms of microorganisms need to be killed. If there are spore forms in the object, this method is ineffective. Steam sterilization is carried out in sterilizers, which are cylindrical metal vessels that are closed with a lid with two openings - for a thermometer and steam outlet. At the bottom of the vessel is poured water, over which is a metal stand with holes. Sometimes the apparatus is equipped with double walls, and the steam, proceeding from the steam chamber, is directed into the gap between them. This design ensures the maintenance of a constant temperature during sterilization. In the pharmacy practice sterilizers C-60 (Fig. 139), VKO-16, VK-75 are used.

Heating fluid steam (for DF X) do for 30-60 minutes. The duration of sterilization depends on the physicochemical properties of the medicinal substances and the volume of the solution. It is established that when the sterilizer is heated, the temperature of the solution in the vials lags behind the temperature of the steam chamber. For small volumes, the lag is small (2-3 minutes), and for volumes over 500 ml, it is significant. Therefore, when sterilizing solutions more than 100 ml, the duration of sterilization increases:

up to 100 ml - 30 minutes from 101 to 500 ml - 45 minutes; from 501 to 1000 ml - 60 minutes. Sterilization of solutions with a volume of more than 1 l is prohibited.

Tyndallization - fractional sterilization, consists in heating at a temperature of 60-65 ° C at 1:00 for 5 days or at a temperature of 70-80 ° C for 3 days. The liquid is sterilized , contained in the intervals between heating at a temperature of 25-37 ° C. This method of sterilization is used for medicinal substances and their solutions, they do not withstand heating at 100 ° C. At the same time, not only microorganisms, but also their spores germinating in the intervals between heating. The method of tyndallization in pharmaceutical practice is rarely used. In most cases it is used industrially in the manufacture of ampoules ir IAOD us x solutions. Tindalization is as effective as autoclaving , but lasts longer.

Pasteurization - a single heating of the solution at a temperature of 80 ° C for 30 minutes. It makes it possible to destroy the vegetative forms of microorganisms, but not disputes. The method is not reliable enough. DF X allows you to use this method in the manufacture of solutions of thermolabile substances with the addition of antiseptics (0.5% or 0.3% phenol tricresol). In the presence of an antiseptic, the virulence and viability of microbes is reduced, the growth and reproduction of microbial cells stops. Bacteria spores are not destroyed, but they do not germinate in the presence of antiseptics. The effect of antiseptics increases significantly with increasing temperature of the solution.

Pasteurization and tindalization are allowed only in exceptional cases in accordance with the instructions of their own pharmacopoeial articles.

Monitoring the effectiveness of thermal sterilization methods is carried out using instrumentation, chemical and biological tests.

Bacteriological methods are the most accurate and are carried out using a biotest sterilization. Biotest sterilization of an object from an established material, littered with test micro-organisms, designed to monitor the effectiveness of sterilization / Test microorganisms can be used as a biotest: pure cultures of spore-forming microorganisms of the type B. subtilis, B. stearothermophylus, etc., applied to the material that sterilized.

The chemical sterilization test is based on the property of a number of substances to change their physical state or color under the influence of a certain temperature.

The following substances are commonly used: sulfur (melting point 111-120 ° C), antipyrine (110 ° C), antifibrin (115 ° C), resorcinol (110 ° C), benzoic acid (121-122 ° C), B-naphthol (120-122 ° C), urea (132 ° C), phenacetin (134-135 ° C). To control dry heat sterilization, thiourea (180 ° C), succinic acid (180-184 ° C), barbital (190-191 ° C) and some other substances are used. In recent years, they began to use color temperature indicators (Table 32), which with great accuracy indicate the temperature level (fluctuations of 1-2 ° C).

Sterilization by ultraviolet rays. UV radiation is a powerful sterilizing factor that can kill vegetative and spore forms of microorganisms. UV rays are widely used in various sectors of the national economy for the disinfection of indoor air, water, etc. Their use in pharmacies is of great practical importance and significant advantages compared with the use of disinfectants, since they can be adsorbed by medicines, which because of this foreign odors.

Ultraviolet radiation is an invisible shortwave part of the sun's rays with a wavelength of less than 300 nm. It is believed that UV radiation causes a photochemical disturbance of the enzyme systems of the microbial cell, acts on the cell's protoplasm with the formation of toxic organic peroxides and leads to the photodimerization of thiamine. The effectiveness of the bactericidal action of UV radiation depends on a number of factors: the wavelength of the radiator, the dose and time of exposure, the type of inactivated microorganisms, dust and humidity of the environment. The highest sterilizing ability of the rays have a wavelength of 254-257 nm. Depending on the time of exposure, stages of stimulation, inhibition and death of microbial cells are distinguished. Vegetative cells are more sensitive

to UV radiation than spores. To destroy a spore, a dose is needed on average 10 times higher than to destroy vegetative cells. Dust and humidity of the environment significantly reduce the effectiveness of sterilization by UV rays.

As a source of UV radiation in the practice of pharmacies, special lamps were used (bactericidal UVV). The lamp is produced in the form of a straight tube made of special UV-glass, with electrodes from a double tungsten helix covered with carbonate salts of barium and strontium. The tube contains a small amount of mercury and inert argon gas under a pressure of several millimeters of mercury. The source of UV radiation is a discharge in mercury vapor, occurs between the electrodes when voltage is applied to them. The composition of uviol glass includes up to 72% of oxides of silicon, aluminum, barium. Compared with ordinary glass, it contains a small amount of sodium oxide. UV transmittance for UV glass 75%. These lamps have a strong bactericidal effect. because the radiation maximum is close to the maximum bactericidal action (254 nm). At the same time, the formation of ozone and nitrogen oxides is insignificant, since the share of the waves forming these products is 0.5%. The industry produced lamps BUV-15 was-30, was-60, etc. (Table. 33).

Currently, UV lamps are widely used in pharmacies to sterilize air, purified water when it is supplied through a pipeline, auxiliary materials, etc. For air sterilization, it is advisable to use wall and ceiling germicidal irradiators, hanging them at a height of 1.8-2 m from the floor and placing along the convection air flow evenly throughout the room. In the absence of people, sterilization can be carried out with unshielded lamps at the rate of 3 W per 1 m3 of space. Sterilization time 1-1 / 2:00. It is convenient to use shielded lamps, the light of which is directed upwards; thus, UV rays do not affect the eyes and skin. The presence of shielded lamps allows to disinfect the air in the presence of workers. In this case, the number lamps is determined on the basis of the power of 1 W per 1 m3 of room.

For air sterilization in pharmacies, high-capacity mobile bactericidal irradiators are proposed, consisting of 6 BUV-30 lamps and provide a high sterilization rate. Using this device in a room up to 100 m3 allows for 15 minutes to reduce the contamination of air by 90-96%. The second type of bactericidal irradiation is equipped with a lamp BUU-30P and an appropriate reflector that allows you to direct the rays. It is designed to sterilize rooms up to 20 m3.

When sterilizing air with UV radiation, it is necessary to follow certain rules in order to avoid undesirable exposure of UV rays to the human body. In case of inept use, a burn of the conjunctiva of the eyes and skin may occur, therefore it is strictly forbidden to look at the switched on lamp. In the manufacture of drugs in the field of UV radiation it is necessary to protect the hands of a 2% solution or 2% ointment novocaine or PABK. It is also necessary to systematically ventilate the room to remove the resulting oxides of nitrogen and ozone.

Air exposure time of the lamp can be significantly reduced on if readjustment to add air spray trietilenglikolya or other similar substances.

When sterilizing air with UV rays, it is necessary to take into account the possibility of numerous photochemical reactions of medicinal substances during

radiation absorption. Therefore, all medicines that are in the room for the manufacture of medicines that require asepsis, it is advisable to store in containers that are impermeable to UV rays (glass, polystyrene, colored polyethylene, etc.).

Ultraviolet radiation is used to sterilize purified water. For this purpose, devices with immersion and non-immersed sources of UV radiation are used. In the apparatus of the first type, a bactericidal lamp, covered with a quartz glass casing, is located inside the aqueduct and is washed by water. In vehicles with immersed lamps, they are located above the surface of the irradiated water. Since ordinary glass is practically impervious to UV rays, the water supply at the sites of irradiation is made of quartz glass.

UV lamps can be used to decontaminate prescriptions delivered to the pharmacy, which are one of the main sources of microbial contamination of the air and the hands of the assistant. Of interest is the apparatus for disinfecting prescriptions, which is based on the principle of irradiating them with six bactericidal lamps BUV-30 on both sides. Capacity up to 180 recipes per hour.

Ultraviolet radiation can be used to sterilize auxiliary materials and pharmacy equipment.

Radiation sterilization is a highly efficient and promising method of sterilization, which in recent years has become increasingly common for sterilization of medical products. The possibility of radiation sterilization of drugs is being studied (saline infusion solutions, therapeutic eye films, etc.). The bactericidal effect of ionizing radiation is the result of the impact on metabolic processes in the cell. The sensitivity of microorganisms to ionizing radiation depends on many factors: the presence of moisture, oxygen, pH, temperature, etc.

For radiation sterilization, gamma radiation from the isotopes "° C and 137c, as well as fast electrons from linear accelerators, the antimicrobial action of which is the same, is used. The sterilization dose is 2.5 mrad, but other doses are possible depending on the specific production conditions.

The main advantages of the method: a high degree of inactivation of microorganisms, efficiency at low temperature, the ability to automate the process, sterilization of products in the package.

There is a wide range of medical products that can be sterilized by this method: absorbent cotton, dressings, plastic products, parts for various devices and instruments, biological and bacterial preparations, and antibiotics.

Sterilization with high frequency currents. High-frequency currents are called currents that form an electromagnetic field that changes with a high frequency, causes a change in the orientation of the molecules and the absorption of part of the field energy by the substance. As a result, the substance is rapidly heated and sterilized.

Mechanical sterilization methods. For solutions of medicinal substances that are sensitive to thermal and radiation effects, can be used the method of sterilization by filtration through small-pore filters. Unlike other sterilization methods, in which microorganisms only lose their viability, with sterilizing filtration, they are completely removed from the solution, thereby ensuring its sterility and apyrogenicity. Filtration sterilization method is a kind of solution

filtration (microfiltration). With sterilizing filtration, finer purification is achieved using appropriate filter media in the form of depth and membrane filters.

Depth filters are characterized by sorption and inertial particle containment mechanisms. The large thickness of these filters leads to the fact that they contain particles smaller than the size of the pop filter. So, filters with a maximum diameter of 1.6 microns under certain conditions is sterilizing. Therefore, in depth filters of size nop, they usually take the value of the smallest particles held by this filter in the amount of 100%. However, having a high ability to trap contaminants from solutions, depth filters have several disadvantages. The size of the pores of these filters is much larger than the particle size, they are captured, therefore, in the filtering process, all the necessary conditions must be strictly observed (pH, pressure, temperature, etc.). With prolonged filtering, germination of microorganisms, retained by the matrix, and their ingress into the filtrate is possible. Besides,Most of the depth filters consist of fibrous materials, and therefore there is a threat of detachment of loose fibers and contamination of the filtrate. Once in the body, these fibers can cause various pathological reactions.

In recent years, microporous membrane filters have been widely used for sterilizing filtration and are free from these disadvantages. Membrane filters are thin (100-150 microns) plates of polymeric material, characterized by a sieve delay mechanism and a constant spot size. It is considered that the average size of the filter pop, guarantees obtaining a sterile filtrate, is 0.3 microns. To avoid rapid clogging of the membrane is used in combination with prefilters that have large pores. When sterilizing large volumes of solutions rational use of filters of both types.

About ten types of membrane filters are produced abroad for pharmaceutical purposes (Millipore, Sartorius, Sinpore, Duraport, etc.). In Kazan, membrane filters “Vladipor” are produced from cellulose acetate of the type MFA, from regenerated cellulose of the type MFC, which can be used for cleaning from mechanical impurities and microorganisms solutions of medicinal substances that have a pH in the range of 1.0-10.0. Vladipor filters are available in 10 rooms in the range of nop sizes from 0.05 to 0.95 microns and more.

Filters MFA-3 and MFA-4 with an average size nop of 0.25-0.35 and 0.35-0.45 microns are used to sterilize solutions of medicinal substances. They are produced in the form of plates and disks of different diameters. Filters such as MFA can be sterilized with saturated steam under pressure at 120 ° C, dry hot air at 180 ° C, treated with formaldehyde, ethyl alcohol, hydrogen peroxide, ethylene oxide, UV or gamma rays.

Polymer films with cylindrical pores are also promising - the so-called nuclear filters; The Mifil filters from PA-6 polyamide caprone with a diameter of 0.2 microns nop.

Sterilizing filtration is performed in installations, the main parts of which are the filter holder and the filtering medium. Two types of holders are used - plate in which the filter has the shape of a round or rectangular plate, and cartridges containing one or more tubular filters. Before filtering, sterilization of

the filter is carried out in a holder and a reservoir for collecting the filtrate with saturated water vapor at 120 ° C or hot air at 180 ° C.

The method of membrane filtration (or sterile filtration) is advisable to use for solutions of thermolabile substances, for example, Propomix eye drops (produced by Apitek MP). For this purpose, a filtration unit (UV) product is successfully used in the town of Kirishi. UV productivity at a working pressure of 0.3 MPa (C kgf / cm2) on the Vladipor membrane MFA-A No. 2 with a filter holder FD-142 - 0.08 m3 / h (80 l / h) and FD-293 - 0, 2 m3 / h (200 l / h). Before starting and at the end of the solution filtration, the installation is tested for tightness and integrity of the membrane filter.

The use of filter sterilization makes sense only if the solution itself is poured into the vials under strictly aseptic conditions using equipment with a laminar air flow.

Control of sterilization by this method is carried out by direct seeding of the filtrate samples on nutrient media.

Chemical sterilization methods. For products from rubber, polymeric materials, glass, and corrosion-resistant metals, chemical methods of sterilization with gases and solutions are now used. For gas sterilization use pure ethylene oxide or ethylene oxide with various phlegmatizers (methyl bromide, carbon dioxide, freons, etc.). Sterilization is carried out in gas sterilizers. The sterilization efficiency of this method depends on the sterilizing agent, temperature, and relative humidity of the air.

Objects sterilization pre-packaged in plastic bags or parchment paper. Products, sterilized by the gas method, kept in a ventilated room for one or several days, depending on the type of product and their purpose.

Sterilization with gases can also be used to sterilize air in boxes, auxiliary materials (especially heat-sensitive), dishes, stoppers; dressing materials, patient care products, etc. Gases easily penetrate through packaging materials (paper, cellophane, polyethylene), and after sterilization they easily evaporate. It is necessary to remember about their toxicity, irritant action and when working with them to observe protective measures (special clothes, masks, etc.).

In foreign countries, aerosol preparations, which are liquid physicochemical systems prepared on liquefied gases (fluorotrichloromethane, trifluorotrichloroethane, carbon dioxide, etc.), are widely used for air sterilization. Aerosols can be in the air for a long time, disinfecting it. For air sterilization use ethylene glycol and polyethylene glycol aerosols. Tetylene glycol aerosol is considered the most effective, when spraying it, complete sterility of the air in the room is achieved in a few minutes.

The use of gas sterilization for medicinal substances and solutions (atropine sulfate, promedol, cordiamine, caffeine-sodium benzoate, etc.) is also being studied. In this case, it is necessary, first of all, to find out the possibility of the interaction of gases with medicinal substances. In the foreign literature there are reports of possible sterilization ha Zami antibiotics, pancreatin and other substances.

For sterilization of solutions, it is possible to apply (3-propylolactone, a liquid boiling at 153 ° C. Dissolving in water, it hydrolyzes to (3-hydroxypropionic acid. (3-propylolactone is used at a concentration of 0.2% by volume and incubated at 37 ° C for 2 seconds.

For chemical sterilization with solutions, a 6% solution of hydrogen peroxide and peracid (deoxon-1) is used. Sterilization is done in closed containers of glass, plastic or enamelled. The sterilization efficiency of this method depends on the concentration of the sterilizing agent, the time of sterilization and the temperature of the solution, it is sterilized. During chemical sterilization, the product is completely immersed in the solution, kept there for a certain time, and then washed with sterile water under aseptic conditions.

One of the varieties of chemical sterilization is the preservation of dosage forms, that is, protection from microbial spoilage of drugs in the process of their use by adding to them various chemicals.

By preservatives advances a number of requirements: pharmacological indifference at the concentration used (absence of general toxicity and local irritating action e); wide antimicrobial spectrum; lack of chemical interaction with medicinal substances and other components of drugs; no effect on the organoleptic properties of drugs; storage stability; support of sterility of dosage forms during the whole time of their use, that is, reliable antimicrobial activity.

Preservatives are used only in urgently needed cases when sterilization or other methods cannot be used to store sterility through the complex physico-chemical structure of drugs or because it is impossible to release single-dose packages. Preservatives are also used to preserve sterility with repeated use. The problem of preserving drugs is especially important for sterile and aseptically made dosage forms. Therefore, the characteristics of preservatives are presented in this section (these substances can also be used in the technology of aqueous extracts, emulsions, ointments, prepared on hydrophilic and emulsion bases, etc.). Preservatives are added to injection solutions that contain substances that decompose when heated. Preservatives must be listed in the recipe or in their own articles. Their name and number is written in the PPK.

Medicines for intracavitary, intracardiac, intraocular, and injections that have access to the cerebrospinal fluid, as well as with a single dose exceeding 15 ml, should not contain preservatives.

The need for preservation of dosage forms is now growing even more due to the expansion of the range of finished dosage forms that require long-term storage.

Yu. I. Zelikson suggested that the most frequently used preservatives be classified as follows:

- Inorganic compounds.
- Organometallic compounds.
- Organic compounds: alcohols, acids, esters, salts of quaternary ammonium compounds. Inorganic compounds (preparations of silver, silver water, etc.) - These are mainly salts of heavy metals, provide oligodynamic action, that is, they cause the death of microorganisms at very large dilutions (1-10 μg / l). Apply

mainly to canning eye drops. Silver water is used to disinfect drinking water on ships and in other special conditions in the USA, France, Great Britain and other countries.

Organometallic compounds are organic mercury compounds, have a great antimicrobial activity and are non-toxic to humans in small doses. Such substances include: merthiolate (at a concentration of 0.001-0.02%), metafen (1: 2500), phenylmercuric salts (0.001-0.002%),.

Merthiolate (Merthiolatum, Thoomersal) is the sodium salt of ethyl salicylate. Powder of cream color, it is steady on air, well soluble in water, alcohol. Merthiolate is used for preserving injection solutions (0.001%), eye drops (0.005%), ointments (0.02-0.1%) and emulsions.

Metaphene (Metaphenum, Monosept) - yellow powder without taste and smell, insoluble in water, soluble in meadows. It is used for canning eye drops at a concentration of 1: 2500. The use of metafen and merthiolate in eye drops limits the fact that they are stable only in an alkaline medium, while most of the alkaloids used in ophthalmology are most stable at low pH values.

Phenylmercuric salt. Phenyl t uchi acetate is a white crystalline powder, soluble in water and alcohol. Other phenylmercuric salts of Borat, benzoate, chloride, gluconate and salicylate are suitable for preserving dosage forms.

Of the phenylmercury salts, phenylmercury nitrate is the most widely used for preserving injection solutions in a concentration of 0.001-0.002%, for eye drops -0.004%, emulsion ointments (0.007-0.01%).

This group of compounds - reliable preservatives. Their effect on microorganisms is based on blocking the sulfhydryl groups of enzymes. Organic mercury compounds are effective against pathogens, commonly found in eye solutions. Some authors consider undesirable use of these substances in ophthalmology, since, in their opinion, they cause allergic reactions with prolonged use.

Organic compounds. Ethyl alcohol is used for preserving novogalenovyh drugs in a concentration of up to 20%, as well as in the amount of 10-12% of the aqueous phase for preserving emulsions.

However, the most antiseptic properties of the masses of 70% ethyl alcohol, therefore, being present in galenical preparations up to 20%, it gives a weak preservative effect.

Phenylethyl alcohol is a rose-scented liquid. It is dissolved in water with shaking up to 2%, forming a clear solution in 50% alcohol (1: 1). It is recommended mainly for canning eye drops at a concentration of 0.3%. As a preservative of eye drops, it is accepted by a number of countries (England, USA, etc.). But it has the disadvantage that it is ineffective against many gram-positive microorganisms.

Benzyl alcohol is a liquid with a pleasant aromatic smell and burning taste. It is dissolved in water (1:25), in 50% alcohol (1: 1). Mixed with chloroform. At a concentration of 0.5%, it is used for preserving 15% nebutal injection solution and preparations of radioactive isotopes: at a concentration of 0.9%, for eye drops with non-steroid preparations.

Chlorobutanol hydrate - colorless crystals with a camphor odor, slightly soluble in water (1: 250), easily soluble in 90% alcohol, chloroform, fatty oils and paraffin oil, glycerin. It is widely used in various countries, including ours, for preserving injection solutions, eye drops (0.5%), etc., Since it has a rather wide spectrum of antimicrobial action and little sensitizing ability. Chlorbutanol hydrate is connective with many medicinal substances, effective in solutions with an acidic pH value. However, the preservative is completely inactivated in neutral and alkaline media, incompatible with silver nitrate, sodium sulfathiazole and certain other substances.

Phenols. Phenol solution (0.25; 0.3; 0.5%) is very effective for preserving parenteral solutions (insulin preparations, vaccines and serums). As a preservative of pharmaceuticals, phenol is almost never used. Its disadvantage is that it is highly toxic and sometimes causes pain and burning during injection, as well as allergic conditions. Poor solubility in water does not allow it to be used for preserving aqueous solutions.

Chlorocresol is a colorless crystals with a characteristic odor. Soluble in 250 g of water (preferably hot), ethanol, oils. Chlorocresol is 10–13 times more active than phenol with respect to bacteria and fungi, while less toxic.

It is used for canning eye drops at a concentration of 0.05%, injection solutions-0.1%, ointments - 0.1-0.2%.

Benzoic acid is a white crystalline substance with a faint characteristic odor. 1 g of acid is soluble in 350 ml of water, 3 ml of alcohol, 8 ml of chloroform. Benzoic acid is a well-known preservative. Most often it is used in the form of sodium salt, soluble in water (1 g in 1 ml of water).

Benzoic acid and its salts are used as food preservatives in an amount of 0.1-0.2% in most countries of the world. They strongly affect the yeast, especially in an acidic environment. Benzoic acid and its sodium salt are used as preservatives for sugar and medicinal syrups, emulsions of fish oil and liquid paraffin, suspensions with antibiotics, etc. These preservatives are added to the mass for gelatin capsules. They are mainly used in the manufacture of dosage forms for internal use.

Sorbic acid is a white crystalline powder with a weak irritating odor and Sorbic acid is a white crystalline powder with a weak irritating odor and slightly acid taste, it is poorly soluble in water (0.15%), well soluble in oils (0.6-1%) and alcohol.

For the first time sorbic acid was obtained in 1859. As a result of alkaline hydrolysis of polysaccharides isolated from the fruits of mountain ash - Sorbus aucuparia L - hence its name. In the fruits of mountain ash, the acid is in the form of b-lactone, called parasorbic acid, which content is about 1%.

Now it is synthesized most often by the interaction of crotonaldehyde with malonic acid in the presence of tuhidina.

Sorbic acid is permitted in a number of countries for food preservation. It is less toxic than commonly used acid preservatives and is not harmful to humans, even in large quantities. It helps to increase the immunobiological activity of the body, has a strong fungicidal activity. Used for preserving solutions (0.1%), sugar

and other syrups (0.7%), sometimes in combination with sodium benzoate. Approved for use for preserving hydrophilic and emulsion bases (0.2%). Currently, in addition to sorbic acid, the industry produces its potassium and calcium salts. Calcium salt (unlike potassium) is poorly soluble in water.

Esters of p-hydroxybenzoic acid (parabens). In medical practice, methyl (nipagin) and propyl (nipazol) esters, accepted as preservatives by many foreign pharmacopoeias (USA, Sweden, Great Britain, Germany, etc.), have received the greatest application. They have significantly less toxicity than many other preservatives. These are white crystalline substances, odorless and tasteless. Parabens are poorly soluble in water, soluble in oils and very good in organic solvents. Through better solubility, methyl ether (nipagin) is more often used in aqueous solutions, and butyl (butabo) is more commonly used in oil solutions.

Propyl ether (nipazol) is very valuable because it is equally soluble in water and oils and has greater activity with less toxicity than other esters.

Nipagin is used for preserving injection solutions, sugar syrup (0.01%). The most commonly used combination is nipagin-nipazol (1: 3) for preserving eye drops, ointments, emulsions, etc.

However, parabens have significant drawbacks: low solubility in water, inactivation with a large number of substances (for example, non-ionic surfactants), weak sporicidal effect. Parabens are often irritating and allergic to the skin (especially in people who respond to para - aromatic compounds).

However, parabens, due to a variety of positive properties, are widely used in the cosmetic, food and pharmaceutical industry in our country and abroad.

Quaternary ammonium salts (QAC) - CA synthetic substances with high surface activity and bactericidal action. Of this group of substances, benzalkonium chloride, a mixture of alkyl dimethyl benzyl ammonium chlorides, is most widely used abroad . Benzalkonium and I chloride - crystallization cal substance of white color, is very soluble in water its aqueous solutions are colorless, resistant to changes in temperature, pH of the medium.

At a concentration of 1: 10,000, it is used in almost all foreign countries mainly for preserving eye drops, nose drops, where the absence of irritant action and a quick bactericidal effect are required. This preservative compound with many medicinal substances, with the exception of silver nitrate, sodium sulfathiazole, boric acid. It has a significant bacteriostatic and fungistatic effect. Of the other derivatives of quaternary ammonium compounds, benz alkonium chloride is used at a concentration of 1: 4000 for canning eye drops and at a concentration of 1: 10,000 - 1: 20000 for injection solutions, as well as cetylpyridinium chloride for canning eye drops (1: 5000).

The compound of this group is of considerable interest, the domestic drug is dodecyl dimethyl benzyl ammonium chloride (DMDBAH), which, unlike foreign, is an individual substance with a dodecyl radical (C H, 5). In terms of safety, antimicrobial activity and stability, DMDBAH significantly exceeds benzalkonium chloride. It is a yellowish-white powder with an aromatic odor, very soluble in water, alcohol, acetone; in a concentration of 0.01% allowed for the

preservation of ointment bases. When canning eye drops, DMDBAC maintains sterilization (100 and 120 ° C) and remains active for more than one and a half years.

Thus, as chemical preservatives for dosage forms, various substances can be used. However, there is no universal preservative that could be used for any pharmaceutical products. When deciding what preservative is suitable for this drug, consider its compatibility with other components, check its activity in this particular drug, and also take into account all other requirements for substances subject to preservation.

It should be noted that solutions of medicinal substances that have a strong bactericidal effect do not need sterilization. Such substances include: hexamethylenetetramine, aminazine, diprazin, collargol, protargol, imizin, mercury dichloride, potassium permanganate (0.1% or more), etc.

Stability of drugs means their ability to preserve the physicochemical properties and pharmacological activity stipulated by the requirements of the Pharmacopoeia or NTD for a certain period of storage.

The study of stabilization of injection solutions is an important technological task, since about 90% of medicinal substances require the use of stabilizers or special preparation conditions. This is explained by the fact that the solutions of medicinal substances during thermal sterilization withstand various changes. They can be caused by hydrolysis, oxidation-reduction, decarboxylation, polymerization, photochemical degradation, etc.

Oxidation of substances. Medicinal substances of various chemical structures are subjected to oxidation: derivatives of aromatic amines, phenothiazine, many salts of alkaloids, salts of nitrogenous bases, vitamins and other substances.

In the oxidation process, inactive or toxic substances are formed. The rate of oxidation processes depends on many factors: oxygen concentration, temperature, pH of the medium, the presence of catalysts, the state of aggregation.

The oxidation process can often cause a change in the color of the solutions. For example, phenothiazine derivatives (aminazine, diprazine, etc.) In solutions, they are easily oxidized by atmospheric oxygen to form oxidation products of a dark red color. When sterilization in an alkaline glass dish, glucose solutions are oxidized, caramelized and become yellow and sometimes brown in color. During manufacture and storage of preparations of opium alkaloids (morphine, apomorphine, omnopon et al.), On sobenno in alkaline medium, are oxidized to inactive or toxic substances Accompanying them by a change in color of solution. Morphine, being oxidized, passes into poisonous oxide-morphine, apomorphine is oxidized with the formation of poisonous products of green color.

Among the substances that are oxidized, vitamins occupy a significant place: ascorbic acid and its sodium salt are easily oxidized to form inactive 2,3-diketogulonic acid. This process is significantly accelerated in an alkaline medium, especially in the presence of catalysts - traces of metal ions, while the solutions become yellow. Vitamin B_1 under the influence of oxygen, elevated temperature, sunlight, catalysts is easily oxidized and becomes yellow.

Hydrolysis. Many medicinal substances undergo hydrolytic decomposition into less active, inactive, or poisonous components.

Alkaloids, glycosides, vitamins and other compounds undergo hydrolysis. The rate of hydrolysis depends on the temperature, the presence of catalysts, the nature of the solvent. An important factor in the hydrolytic decomposition of substances is the pH of the medium. It is known that hydrolysis easily gives in to salts of weak bases and strong acids, as well as salts of weak acids and strong bases. Inactive and even toxic products are formed in the process of hydrolysis of dicain, novocainamide, novocaine, atropine sulfate, scopolamine hydrobromide and other substances.

Isomerization. Among medicinal substances there are many optically active compounds (atropine, adrenaline, ergot alkaloids, etc.). Medicinal value are certain isomers, for example, ergotamine. It exists in two isomeric forms, while the levogyrate form is a physiologically active compound and the dextrorotatory form is a low-active substance.

Isomerization depends on the chemical nature of the compound, on the functional group aimed at the asymmetric carbon atom, on the optical activity of the substance, temperature, light, metal ions, pH of the medium and other factors.

The influence of microflora. In the process of manufacturing drugs, various microorganisms capable of excreting waste products (toxins, enzymes) can get into solutions, cause changes in drugs of an oxidative, hydrolytic and other nature, as well as affect the body.

To increase the sustainability of dosage forms for injection, stabilization using physical, chemical and complex methods is used.

Stabilization by physical methods:

- *Boiling water*, followed by its quick cooling;
- *Saturation of water for* carbon *injections* with dioxide or inert gases;
- *Recrystallization of the* starting materials;
- *Treatment of solutions with* adsorbents.

In terms of pharmacies, the most common method of boiling water, followed by its rapid cooling. At the same time, the content of free oxygen in water decreases from 9 to 1.4 mg in 1 liter, which significantly reduces the intensity of redox processes in solutions, ensuring their stability.

By boiling water followed by rapid cooling, a reduction in its carbon dioxide content is also achieved. This is very important for solutions of drugs that decompose in the presence of carbon dioxide, often with the formation of a precipitate. For this reason, solutions of euphyllin 12%, hexenal, etc. are prepared on boiled water for injection.

Method saturation water for injection of carbon dioxide or inert gases more efficiently than boiling, so that water saturated with these gases contains less oxygen compared with boiled (0.18 mg in 1 l). However, it is technically more complicated and requires special equipment. J. Lifshits, A. N. Kotenko proposed an installation for carbon dioxide water saturation under pharmacy conditions.

Carbon dioxide is released by the interaction of hydrochloric acid 25% with sodium bicarbonate. To saturate 1 l of water you need 55 ml of acid and 33.4 g of sodium bicarbonate.

Sodium bicarbonate is placed in a glass so that its volume is not more than half full. A hydrochloric acid is introduced with drops from another glass (the Kipp apparatus can be used). The reaction is very fast, so a clamp is installed to control the flow of acid. Formed carbon dioxide passes through a wash bottle and enters the water. Gas is supplied until a water sample is taken (10 ml) will not give a gray or purple color according to a mixed indicator (methyl orange - indigo). Next, overlap the valve or clamp connecting the glass with sodium bicarbonate and hydrochloric acid. Water saturated with carbon dioxide by this method has a pH of 4.0.

The method of recrystallization of the original substances is used to remove impurities from them. It is advisable to use it for the purification of hexamethylenetetramine, if the drug does not meet the requirement of "suitable for injection," that is, contains impurities of amines, ammonium salts, etc.

The recrystallization of hexamethylenetetramine is carried out as follows: first, the drug is dissolved in hot ethyl alcohol to obtain a saturated solution and cooled after filtration. This forms a crystalline precipitate, which is separated through a filter, dried, and after analysis by pharmacopoeial article e , in case of compliance with its requirements, is used to make solutions for injection. In a pharmacy, this operation is difficult to carry out.

Impurities contained in medicinal preparations can also be removed by adsorbing them from solutions of medicinal substances. The adsorbent is activated carbon of grade A. It acts as an adsorbent not only for low molecular weight chemical impurities (calcium oxalate, for example, in calcium lactate), but also for high molecular weight compounds, in particular for pyrogenic substances, which are mixtures of polypiprotein b and lipopolysaccharides.

For depyrogenation of glucose solutions, as well as the purification of other solutions, carbolen cannot be used, the tablets of which are obtained by wet granulation using starch paste. Chemical stabilization is carried out by adding chemicals (stabilizers or antioxidants) to the solutions by selecting appropriate solvent systems; the introduction of substances that provide the pH value of the environment at which the drug is most stable; transferring the insoluble active substance to soluble salts or complex compounds, etc.

Stabilizers - substances that increase the chemical resistance of medicinal substances in solutions for injection.

Substances used as stabilizers must meet the following requirements: to be safe for the patient, both in pure form and in combination with the components of the drug, are permitted by the pharmacological committee for use in medical practice to perform the functional purpose - to ensure the sustainability of the drug.

The choice of stabilizer depends on the nature of the substance and the nature of the chemical process occurring in the solution.

The stabilizers used can be divided into two groups:

- Substances that prevent the hydrolysis of salts and saponification of esters.
- Antioxidants (antioxidants) - substances that prevent oxidation.

In each case, the addition of stabilizers is determined by the results of studies of the chemical kinetics of decomposition of drugs and biological tests for the harmlessness of the solution. The amount of stabilizer attached is indicated in the GF, as well as existing orders of the Ministry of Health and instructions.

The mechanism of action of stabilizers is reduced to improving the solubility of medicinal substances (solubilization), the creation of a certain pH value of the medium, the prevention of redox processes.

The solubility of medicinal substances is improved by adding hydrotropic cosolvents to the solution, complexing agents (citrates, etc.), or the solubilizer itself (mannitol, sorbitol, carboxylic acids, etc.). For example, a solution of oxyprogesterone capronate 12.5% in oil is made by adding to the peach oil 30% (volume) benzyl benzoate; 2.5% progesterone solution in oil - by adding 20% (by volume) benzyl benzoate. A solution of chloramphenicol 2% receive, using as a solvent solution of hexamethylenetetramine 40% (the solution is prepared aseptically after prior sterilization of chloramphenicol).

Infusion solutions of ciprofloxacin (Woweg) and Alexan infusions concentrate (Heinrich Mack) are prepared using lactic acid as a solubilizer.

A certain pH value of the medium is created by buffer solutions, acids and alkalis.

When considering the issues of stabilization of solutions for injections, medicinal substances can be roughly divided into 3 groups (according to the classification proposed by A. S. Prozorovsky and N. A. Kudakov):

1. Solutions of salts formed by weak bases and strong acids.
2. Solutions of salts formed by strong bases and weak acids.
3. Solutions of easily oxidized substances (stabilized by antioxidants).

Stabilization of salt solutions formed by weak bases and strong acids. This group includes salts of alkaloids and synthetic nitrogenous bases (atropine sulfate, scopolamine hydrobromide, gomatropine hydrobromide, cocaine hydrochloride, pilocarpine hydrochloride, physostigmine salicylate, novocaine, strychnine nitrate, dibazole, etc.). Aqueous solutions of such salts, as a rule, can have a neutral or weakly acid reaction due to hydrolysis, which occurs almost completely.

Salt BA completely decomposes into dissociating acids and weak dissociating acids. Hydroxyl ions, which are formed during the dissociation of water, are associated with the low dissocial base of VON. This leads to a decrease in pH.

$BA + HON = BOH + H^{+} + A^{-}$

In addition to these solutions of free acid, that is, an excess of hydrogen ions, inhibits hydrolysis, causing an equilibrium shift to the left. The decrease in the concentration of hydrogen ions in the solution, for example, as a result of exposure to alkali, separated by glass, shifts the equilibrium to the right, that is, it enhances the hydrolysis.

Heating solutions increases the intensity of salt hydrolysis and increases the degree of dissociation, leading to an equilibrium shift to the right. Therefore, with

the next sterilization and maintaining the pH of the injection solution rises. For the stability of salts of alkaloids and other specified substances, the solutions must have a certain pH.

If the salt is formed by a weak base and a strong acid, then as a stabilizer, inhibits the process of salt hydrolysis and saponification of esters, it is recommended to add hydrochloric acid.

The amount of hydrochloric acid required to stabilize the solution depends on the properties of the drug. The most common rate of stabilizer consumption is 10 ml of 0.1 M hydrochloric acid solution per liter. In the manufacture of small amounts of solutions to ensure accurate dosing, it is advisable to prepare a 0.01 M stabilizer solution: 0.42 ml of diluted (8.3%) hydrochloric acid per 100 ml of solution. The solution is poured into small bottles of 10 ml from neutral glass, sterilized. Compared with a 0.1 M solution of hydrochloric acid, this stabilizer (0.01 m) is added 10 times more. The shelf life of it for 5 days.

To stabilize the solutions of novocaine, it is necessary to add hydrochloric acid to pH 3.8-4.5. With an increase in its concentration, the amount of stabilizer increases (solutions of 0.25, 0.5, 1.2% require 3, 4, 9, 12 ml of 0.1 M , hydrochloric acid solutions per 1 liter of solution, respectively) .

Novocain is a hydrochloride of 3-diethylaminoethyl para-aminobenzoic acid. After sterilization of novocaine solutions, free PABA appears, due to which the pH of the solution shifts to the acid side. The amount of novocaine decomposed in a solution with a neutral or slightly alkaline medium reaches 2.28%, and at pH 8.0 it increases to 11%.

In the foreign literature there are reports of the presence of aniline in solutions of novocaine after sterilization, which is explained by the decarboxylation of para-aminobenzoic acid. The use of solutions of novocaine mixed with aniline is accompanied by side effects (edema, pain). To stabilize 2.5 and 10% solutions of novocaine, add hydrochloric acid 0.1 M 4, 6 and 8 ml, respectively, and 0.5 g of sodium thiosulfate per 1 l of solution.

Solutions of novocaine 5% for spinal anesthesia are prepared aseptically without heat sterilization using sterile auxiliary materials, dishes and sterile substances. Novocain powder is pre-sterilized in glass or porcelain containers with a layer height of not more than 0.5-1 cm with hot air in air sterilizers at 120 ° C for 2:00, the pH of this solution is 5.0-5.3.

The proposed technology of this solution on citrate buffer solvent with the addition of 1.5% polyvinyl as a stabilizer. A solution of novocaine of this composition can withstand heat sterilization and is stable for 30 days. 5 and 10% novocaine solutions used in otolaryngological practice are stabilized by adding 0.3% sodium metabisulfite and 0.02% citric acid or 10 ml of a 0.1 M solution of hydrochloric acid per 1 liter of solution.

To produce a stable solution of novocaine (1-2%) in an isotonic solution of sodium chloride, add 5 ml of a 0.1 M solution of hydrochloric acid per liter.

Novocain is sometimes prescribed in a prescription with adrenaline hydrochloride solution (1: 1000). In these cases, a stabilizer consisting of 0.05 g of

salicylic acid, 0.4 g of sodium sulfite and 0.2 g of sodium metabisulfite is added. The solution is sterilized at 100 ° C for 15 minutes.

Stabilization of salt solutions formed by strong bases and weak acids. This group includes: sodium nitrite, sodium caffeine-benzoate, sodium thiosulfate, aminophylline, etc. In aqueous solutions, these substances readily hydrolyze, dissociate into ions, and the solution becomes alkaline. Dissociate into ions and water molecules. As a result of the interaction of salt ions and water, a weakly dissociating acid HA is formed. This leads to a decrease in the solution of free hydrogen ions and the accumulation of an excess of OH ions, as a result of which the pH of the solution increases.

VA + NON = B^+ + HE^- + ON.

This leads to the formation of difficult-to- dissolve compounds, which produce turbidity or precipitate in solutions, which is unacceptable for injection solutions.

To stabilize solutions of salts of strong bases and weak acids, it is recommended to add stabilizers of the main nature — 0.1 M solution of sodium hydroxide or sodium bicarbonate.

To ensure favorable conditions for the stabilization of drugs, they undergo hydrolysis, the pH of the solution is adjusted to the criterion, corresponds to the minimum decomposition of substances, the addition of various substances or buffer systems. The optimum pH value is specified in the documentation or is established empirically.

So, to stabilize 1 liter of 10 and 20% solution of caffeine sodium benzoate, it is recommended to add 4 ml of 0.1 M solution of sodium hydroxide, and up to 30% solution of sodium thiosulfate sodium bicarbonate in an amount of 20 g per 1 liter.

The sodium thiosulfate solution, having a medium close to neutral , with a slight decrease in pH, decomposes, releasing sulfur and sulfur dioxide.

Euphyllinum is a complex salt of a weak acid (theophylline) and a weak base (ethylenediamine). It easily decomposes in an acidic environment. Adding sodium hydroxide to the solution also leads to decomposition of aminophylline. Therefore, to obtain stable solutions of aminophylline, it is necessary to use a drug with an ethylenediamine content of 18-22% instead of 14-18% theophylline 75-82%, which withstands additional testing (GF X p. 276). Water for injection should be freed from carbon dioxide by boiling or saturating with nitrogen.

Abroad, stable theophylline solutions are obtained by adding aminopropylene glycol or diethylaminopropylene glycol (0.75-1.5 stabilizers are taken per 1.0 g of theophylline). High polymers are also used to stabilize sodium salts — derivatives of barbituric acid, which, being salts of a strong base and a weak acid, are easily hydrolyzed in aqueous solution with increasing pH.

Thus, a change in the pH of the medium is not the only means of protecting medicinal substances from hydrolysis.

In the last decade, there have been many studies on the effect of surfactants on the kinetics of chemical reactions. It has been proven that non-ionic and anion-active surfactants inhibit, and cation-active surfactants accelerate the process of

hydrolysis of a number of drugs. It has been established that in the presence of surfactants, an increase or decrease in reaction rates is due to the formation of micelle associates of surfactant molecules. The surfactant micelles have large colloidal sizes and large volumetric capacity, that is, they have voids into which relatively small molecules of the drug substance can penetrate under the influence of intermolecular attraction forces. Molecules with hydrophobic properties penetrate into the micelle. For example, the inhibitory effect of 0.5% tween-80 is associated with the introduction of dicain molecules into micelles of surfactants. In this case, the anesthetic activity of dikain corresponds to the initial substance. The hydrophilic molecule of a substance occupies a position between the individual molecules of the micelle and joins the outer, most hydrophilic part of the micelle. The complex compounds formed are more resistant than medicinal substances.

In this regard, surfactants are used to suppress the hydrolysis of a number of medicinal substances, for example, anesthetics, antibiotics and others. At the same time, it is necessary to take into account possible changes in the therapeutic action of complex compounds. In each case, the use of stabilizers in their introduction into the composition of the drug requires careful study.

Stabilization of solutions of easily oxidized substances. This group includes: ascorbic acid, vikasol, sodium salicylate, salyuzid, soluble streptocide, sulfacyl sodium, thiamine chloride, ethyl morphine hydrochloride, epinephrine hydrotartrate, phenothiazine derivatives, procainamide, and some other medicinal substances. In the manufacture of solutions, and especially during sterilization, in the presence of oxygen contained in water and in the air space of the vial (above the solution), these substances are easily oxidized to form physiologically inactive compounds. The oxidation process is greatly enhanced under the influence of the so-called sensitizing factors (from the Latin. Sensibilis -chuliness), such as light, heat, pH, etc.

The mechanism of oxidation of easily oxidized substances is based on the Bach-Engler peroxide theory and the theory of branched chain reactions of Semenov. In pharmaceutical practice, there are various methods to slow down the oxidation process. For example, the addition of antioxidants. Antioxidants are auxiliary substances that prevent oxidation. they can be divided into direct and indirect.

Direct antioxidants include strong reducing agents that have a higher ability to oxidize than medicinal substances stabilized by them: rongalite, sodium sulfite, sodium metabisulfite, ascorbic acid, thiourea, cysteine, methionine, etc.

Sodium sulfite stabilizes solutions of streptocide soluble 5 and 10% (2.0 g per 1 liter of solution).

Sodium metabisulfite is added to a solution of sodium salicylate 10% (1.0 g per 1 l of solution), ascorbic acid solution 5% (2.0 g per 1 l of solution). Ascorbic acid itself can be used as an antioxidant for substances with a lower ability to oxidize.

The stabilization mechanism consists in the fact that antioxidants oxidize more easily than the active substances, and oxygen dissolved in the injection

solution is used to oxidize the stabilizer, thereby protecting the preparation from oxidation.

Indirect antioxidants include substances that bind cations of metals (Cu2 +, Fe3 +, Mn2 +, etc.) into practically undissociated compounds, which enter solutions of medicinal substances as impurities from drugs and are catalysts for oxidative processes.

It has been established that the color change of salicylate solutions is due to the oxidation of phenolic hydroxyl in the presence of traces of manganese ions. Ions of heavy metals, participating in an oxidation-reduction chain reaction, are able to detach electrons from various ions present with them in solutions, translating the latter into radicals:

$$Cu^{2+} + RCOO^{-} \rightarrow Cu^{+} + RCOO^{\cdot}$$

$$Cu^{2+} + POOH \rightarrow P^{\cdot}$$

The resulting radical can react with oxygen to form a peroxide radical, which will continue to be involved in the chain reaction. Partly restored while the heavy metal ion can easily be oxidized by oxygen to its original form, after which the process repeats.

$$Cu^{+} \xrightarrow{O_2} Cu^{2+}$$

It is the chain character that explains the catalytic effect of heavy metal ions when they are present in solutions in insignificant amounts. For example, the catalytic effect of copper ions is in fractions of a microgram.

Heavy metal ions often pass into solutions from glass or instrumentation, or may be present in the drug substance as a manufacturing impurity. To obtain stable solutions of easily oxidized substances, it is necessary to get rid of traces of heavy metal ions. Methods for cleaning water from heavy metals and solutions of medicinal substances by filtration through a layer of activated carbon and the sodium form of oxidized cellulose are now proposed.

Indirect antioxidants are complexing agents. These include: many basic carboxylic acids, hydroxy acids (citric acid, salicylic acid, tartaric acid, etc.), ethylene diamine tetraacetic acid disodium salt (Trilon B), and Trilon B calcium salt (thetacin), unithiol, as well as amino acids, thiourea, etc.

Examples of stabilization with unithiol are solutions of thiamine bromide 3 and 6% and thiamine chloride 2.5 and 5%, to increase the stability of which uniothiol 0.2% is used. Trilon B stabilizes solutions of saluzid soluble 5% and lipoic acid 0.5% (at a concentration of 0.01%), solutions of cyclobutonium 0.7% (at a concentration of 0.05%).

To stabilize easily oxidized substances, it was proposed to use high molecular substances (polyglucin, polyethylene glycol, propylene glycol, etc.), among which oxidation and other reactions are slowed down. This is probably explained by the penetration of low-molecular substances into the interior of the high-polymer molecules, which leads to a decrease in their reactivity.

The oxidation of drugs can also be reduced by eliminating the sensitizing effect of light, temperature. Sometimes solutions of certain drugs (for example,

phenothiazine) are prepared under red light. Some solutions are stored in a package with light-protective glass.

Stabilization of solutions for injection is sometimes achieved by the introduction of several stabilizers (stabilization by the complex method). Such a complex can be represented by a combination of different types of stabilizers: several direct antioxidants; direct and indirect antioxidants; antioxidant and pH agent; antioxidant and preservative (antimicrobial stabilization). For example, a solution of diprazine 2 and 2.5% is stabilized with several antioxidants, for injections (ascorbic acid — 0.2%, anhydrous sodium sulfite — 0.1%, sodium metabisulfite — 0.1%).

Antioxidant and pH regulator stabilizes a solution of indigo carmine 0.4%. As a stabilizer, it contains rongalite - 0.05% and sodium - 0.1%.

A solution of apomorphine 1% is made on a solvent containing analgin 0.5 g, cysteine - 0.2 g, 0.1 M hydrochloric acid - 40 ml per 1 l of solution.

Thus, to stabilize the compounds are oxidized, it is necessary to exclude the effect of oxygen on medicinal substances, to create optimal pH values of solutions, to exclude the effect of catalysts in the process of manufacture, sterilization and storage of the drug.

PROPERTY TECHNOLOGY OF INJECTION SOLUTIONS

Glucose solutions. The industry produces glucose solutions for injection at a concentration of 5, 10.25 and 40%. However, injectable glucose solutions in large quantities are prepared in pharmacies. Glucose solutions are unstable compared to long-term storage. The main factor determining the stability of glucose in solution is the pH of the medium. In an alkaline environment, it is oxidized, caramelized and polymerized. At the same time there is yellowing and sometimes browning solution. In this case, under the influence of oxygen, hydroxy acids are formed: glycolic, acetic, formic and others, as well as acetaldehyde and hydroxymethylfurfural (destruction of the bond between carbon atoms). To prevent this process, glucose solutions are stabilized with a 0.1 M solution of hydrochloric acid to a pH of 3.0-4.0, because in this medium there is a minimum formation of 5-hydroxymethylfurfural, what nephroheptotoxic effect.

In a strongly acidic medium (at a pH of 1.0-3.0), D-gluconic (sugar) acid is formed in glucose solutions. With its further oxidation, especially in the sterilization process, it turns into 5-hydroxymethylfurfural, which causes the solution to turn yellow, which is associated with subsequent polymerization. At pH 4.0-5.0, the decomposition reaction slows down, and at pH above 5.0, the decomposition into hydroxymethylfurfural increases again. An increase in pH causes decomposition with a break in the glucose chain.

GF X prescribes stabilizing glucose solutions with a mixture of sodium chloride 0.26 g per 1 liter of solution and 0.1 M hydrochloric acid solution to pH 3.0-4.0.

Under pharmacy conditions, for convenience, this solution (known as Weibel's stabilizer) is prepared in advance according to the following recipe: sodium chloride — 5.2 g of dilute hydrochloric acid (8.3%) —4.4 ml of water for

injection is up to 1 l. In the manufacture of glucose solutions (regardless of its concentration), Weibel's stabilizer is added 5% of the volume of the solution.

The mechanism of the stabilizing action of sodium chloride is not well understood. Some authors have suggested that when sodium chloride is added, a complex compound is formed at the site of the aldehyde glucose group. This complex is very fragile, sodium chloride is mixed from one molecule of glucose to another, replacing aldehyde groups, and thereby inhibits the course of the redox reaction.

However, at the modern level of studies on the structure of sugars, this theory does not reflect the entire complexity of the processes taking place. Another theory explains these processes as follows. As you know, in the solid state, glucose is in cyclic form. Partial ring opening occurs in the solution to form aldehyde groups, with moving equilibrium being established between the acyclic and cyclic forms. Acyclic (aldehyde) forms of glucose are most reactive to oxidation. Cyclic forms of glucose with oxygen bridges between the first and fifth carbon atoms are characterized by high stability. The addition of a stabilizer creates conditions in the solution that promote an equilibrium shift towards a cyclic form that is more resistant to oxidation. It is now believed that sodium chloride does not contribute to the cyclization of glucose, and in combination with hydrochloric acid creates a buffer system for glucose.

During thermal sterilization of glucose solutions without a stabilizer, dienes, carboxylic acids, polymers, and phenolic products are formed. Replacing thermal sterilization by sterilizing filtration, you can prepare a 5% glucose solution with a shelf life of 3 years without a stabilizer.

The quality of glucose itself, which may contain water of crystallization, is of great importance for the stability of the solutions produced. According to FS 42-2419-86, anhydrous glucose is produced, containing 0.5% of water (instead of 10%). It is distinguished by solubility, transparency and color of the solution. Its shelf life is 5 years. When using water glucose it takes more than indicated in the recipe. The calculation is made according to the formula:

$$x = \frac{a \times 100}{100 - б},$$

where x - required amount of glucose

a - the amount of anhydrous glucose specified in the recipe;

b - the percentage of water in glucose according to the analysis.

Rp .: Solutionis Glucosi 40% 100 ml Sterilisa!

Da. Signa. 10 ml intravenously.

For example, glucose contains 9.8% water. Then water glucose should be taken 44.3 g (instead of 40.0 g anhydrous).

$$x = \frac{40 \times 100}{100 - 9{,}8} = 44{,}3 \text{ г}$$

Under aseptic conditions, in a volumetric flask with a capacity of 100 ml, water for injection dissolves glucose (44.3 g) “suitable for injection”, add Weibel stabilizer (5 ml) and bring the solution to 100 ml. Conduct primary chemical analysis, filtered, sealed with a rubber stopper, check for the absence of mechanical

impurities. In the case of positive control, the vials, sealed with stoppers, are rolled around with aluminum caps and labeled, and the tightness of the closure is checked.

Since glucose is a good medium for the development of microorganisms, the resulting solution is sterilized immediately after production at 100 ° C for 1:00 or at 120 ° C for 8 minutes. After sterilization, secondary control of the quality of the solution is carried out and arranged for release. The shelf life of the solution is 30 days. PPK

Date Recipe No.
Glucosi 44.3 (Ow. 9.8%)
Liguoris Wejbeli 5 ml
Aquae pro injectionibus ad 100 ml
Sterilis $V_{zag.}$ = 100 ml

Prepared: (signature)
Checked: (signed)

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

The name isotonic comes from the Greek words isos - smooth, tonus - pressure.

The osmotic pressure of blood plasma and tears in the body is normal at 7.4 atmospheres (72.82 x 104 Pa). With the introduction of any solution of an indifferent substance into the body, it deviates from the natural osmotic pressure of the serum, causes a pronounced feeling of pain, which will be the stronger, the more the osmotic pressure of the solution, introduced, and the body fluid differs.

Plasma, lymph, lacrimal and cerebrospinal fluids have a constant osmotic pressure, but with the injection of the injection solution into the body, the osmotic pressure of the fluids changes. The concentration and osmotic pressure of various fluids in the body is maintained at a constant level by the action of the so-called osmoregulator.

With the introduction of a solution with a high osmotic pressure (hypertonic solution) as a result of the difference in osmotic pressures inside the cell or erythrocytes and the surrounding plasma, water moves from the erythrocyte to the osmotic pressure equalization. Erythrocytes at the same time, getting rid of the water, lose their shape (shrink) plasmolysis occurs.

Hypertonic solutions in medical practice are used to relieve edema. Hypertonic solutions of sodium chloride in concentrations of 3.5, 10% are used externally for the outflow of pus in the treatment of purulent wounds. Hypertonic solutions also have an antimicrobial effect.

If a solution with a low osmotic pressure (a hypotonic solution) is injected into the body, the fluid will penetrate inside the cell or red blood cell. The erythrocytes begin to swell, and with a large difference in osmotic pressures inside and outside the cell, the membrane does not withstand the pressure and breaks - hemolysis occurs.

The cell or erythrocyte in this case die and turn into a foreign body, which can cause blockage of vital capillaries or vessels, resulting in paralysis of individual organs or death. Therefore, such solutions are introduced in small quantities. It is advisable instead of hypotonic solutions to prescribe isotonic.

The isotonic concentration of the prescribed drug is not always indicated in the recipe. For example, a doctor may write a prescription as follows:
Rp.: Solutionis Glucosi isotonicae 200 ml
Sterilisa!
Da. Signa. For intravenous fluids.
In this case, the pharmacist must calculate the isotonic concentration.

Methods for calculating isotonic concentrations. There are several ways to calculate isotonic concentrations: the method based on the Vant-Hoff law or the Mendeleev-Clapeyron equation; method based on the law of Raul (cryoscopic constants) method using isotonic equivalents of sodium chloride.

The calculation of isotonic concentrations according to the law of Vant Hoff. According to Avogadro and Gerard's law, a 1-gram molecule of gaseous substance at 0 ° C and a pressure of 760 mm Hg. occupies a volume of 22.4 liters. This law can be attributed to solutions with a low concentration of substances.

To obtain an osmotic pressure equal to the osmotic pressure of the serum of 7.4 atm., 1 gram molecule of the substance should be dissolved in less water: 22.4: 7.4 = 3.03 l.

But due to the fact that the pressure increases in proportion to the absolute temperature (273 ° K), it is necessary to correct for the temperature of the human body (37 ° C) (273 ° + 37 ° = 310 °). So, for storage in solution of osmotic pressure of 7.4 atm. 1 gram moles of a substance should not be dissolved in 3.03 liters of solvent, but in a slightly larger amount of water.
From 1 gram-mole of non- dissociating substance, a solution must be prepared:

3.03 L - 273
x l-310

$$x = \frac{3{,}03\ л \times 310°}{273°} = 3{,}44\ л.$$

However, in pharmacy conditions, it is advisable to conduct calculations for the manufacture of 1 l of solution:

$$x = \frac{1{,}0}{3{,}44} = 0{,}29\ г/моля.$$

1 g / mol - 3.44 l
x g / mol_v - 1 l

So, for the manufacture of 1 liter of isotonic solution of any medicinal substance (non-electrolyte), it is necessary to take 0.29 g / mol of this substance, dissolve in water and bring the solution to 1 liter:

$$m = 0{,}29\ M \text{ чи } 0{,}29 = \frac{m}{M},$$

m - the amount of substance required for the manufacture of 1 liter of isotonic solution, g;
0,29 - isotony factor of a non-electrolyte substance;
M is the molecular weight of the drug.
the amount of substance required for the manufacture of 1 liter of isotonic solution, g
0,29 - isotony factor of a non-electrolyte substance;
M is the molecular weight of the drug.

For example, it is necessary to calculate the isotonic concentration of the glucose solution. Molecular glucose mass is 180.18. For 1 liter of isotonic solution you need glucose:

$$m = 0.29 \text{ x } M; \; m = 0.29 \text{ x } 180.18 = 52.22 \text{ g / l.}$$

So, isotonic glucose concentration is 5.22%. Then, according to the recipe, for the manufacture of 200 ml of isotonic glucose solution, it is necessary to take it 10.4 g.

5.2 g - 100 ml

x g - 200 ml

The relationship between osmotic pressure, temperature, volume and concentration in a diluted solution of a non-electrolyte can be expressed by the Mendeleev – Klapeyron equation:

$$p\,V = nRT\,,$$

where P is the osmotic pressure of blood plasma (7.4 atm.)
V is the volume of solution, l
R is the gas constant expressed for this case in atmospheric liters (0.082)
T is the absolute body temperature (310 °);
n is the number of gram molecules of the solute.

$$\text{Звідси } n = \frac{P \times V}{R \times T};\; n = \frac{m}{M},\; \text{тоді } \frac{m}{M} = \frac{P \times V}{R \times T},\; \text{чи } m = \frac{M \times P \times V}{R \times T} = \frac{M \times 7{,}4}{0{,}082 \times 310}$$

$$\text{чи } m = 0{,}29 \times M$$

When calculating the isotonic concentration of electrolytes as according to the law of van't Hoff. as in the Mendeleev – Clapeyron equation, it is worth making corrections, that is, the value (0.29 hm) must be divided by the isotonic coefficient “i”, which shows how many times the number of particles increases during dissociation (compared to a non-dissociating substance), and is numerically equal to:

$$i = 1 + a\,(n - 1),$$

where i is the isotonic coefficient;
a is the degree of electrolytic dissociation;
n is the number of particles formed from one molecule of a substance during dissociation.

For example, in the dissociation of sodium chloride, two parts are formed (Na + ion and Cl-ion). then, substituting in the formula the value a = 0.86 (taken from the tables) and c = 2, receive:

$$i = 1 + 0.86\,(2 - 1) = 1.86.$$

So, for NaCl and similar binary electrolytes with singly charged ions and = 1.86. Example for CaCl: n = 3, a = 0.75,

i = 1 + 0.75 (3 - 1) = 2.5.

So, for CaCl2 and similar electrolytes

i = 2.5 ($CaCl_2$, Na_2S0_4, $MgCl_2$, Na_2HP0_3 and in.).

For binary electrolytes with doubly charged ions $CuSo_4$, $MgS\ 0_4$, $ZnS\ 0_4$ and ін. (a = 0.5; n = 2).

i = 1 + 0.5 (2-1) = 1.5.

For weak electrolytes (boric, citric acid, etc.) (a = 0.1; n = 2).

i = one +0.1 (2-1) = 1.1.

$PV = i \cdot \frac{m}{M} \cdot RT$, тоді, вирішуючи рівняння у відношенні m, знаходять:

$$m = \frac{PVM}{iRT} = = \frac{7{,}4 \cdot 1 \cdot M}{i \cdot 0{,}082 \cdot 810} = \frac{0{,}29 \cdot M}{i}.$$

Для натрію хлориду, наприклад, $m = \frac{0{,}29 \cdot 58{,}45}{1{,}86} = 9{,}06$ г/л.

The Mendeleev – Clapeyron equation with an isotonic coefficient is:

So, for the manufacture of 1 liter of isotonic sodium chloride solution, you must take 9.06 g, or the physiological solution will be sodium chloride at a concentration of 0.9%.

To determine isotonic concentrations in the manufacture of solutions, which include several substances, it is necessary to conduct additional calculations. According to Dalton's law, the osmotic pressure of the mixture is equal to the sum of the partial pressures of its components:

$$P = P_1 + P_2 + P_3 + \ldots \text{, etc.}$$

This position can also be transferred to the diluted solutions, in which you must first calculate how much isotonic solution comes out of the substance or substances indicated in the recipe. Then set by the difference, the amount of isotonic solution should give the substance with which the solution is isotonets, after which find the amount of this substance.

Sodium chloride is used to isotonize solutions. If substances not compatible with it are prescribed, sodium sulfate, sodium nitrate or glucose can be used.

Rp .: Hexamethylentetramini 2.0
Natrii chloride qs
Aquae pro injectionibus ad 200 ml
ut fiat solutio isotonica
Sterilisa!
Da. Signa. For injections.

Calculate the amount of isotonic solution obtained by 2.0 g of urotropin (Mm = 140). The isotonic concentration of urotropin will be 0.29 x 140 = 40.6 g or 4.06%.

4.06 - 100 ml

x = 50 ml
2.0 x
Determine the amount of isotonic solution, which must be obtained by adding sodium chloride:

200 ml - 50 ml = 150 ml.

$$x = \frac{0,9 \times 150}{100} = 1,35 \text{ г}$$

Calculate the amount of sodium chloride needed to obtain 150 ml of isotonic solution:

0.9 g - 100 ml
x g - 150 ml

Thus, to obtain 200 ml of isotonic solution containing 2.0 g of hexamethylenetetramine , it is necessary to add 1.35 g of sodium chloride.

Calculation of isotonic concentrations according to the law of Raul, or a cryoscopic method. According to Raul's law, the vapor pressure above the solution is proportional to the molar fraction of the solute.

The conclusion from this law establishes the relationship between a decrease in vapor pressure, the concentration of a substance in a solution and its freezing point, namely: a decrease in freezing temperature (depression) is proportional to the decrease in vapor pressure and, therefore, proportional to the concentration of the solute in the solution. Isotonic solutions of various substances are frozen at the same temperature, that is, they have the same temperature depression of 0.52 ° C.

Depression of the blood serum (At) is 0.52 ° C. So, if the prepared solution of a substance has a depression equal to 0.52 ° C, then it will be isotonic to the blood serum.

Depression (lowering) of the freezing point of a 1% solution of a drug substance (At) shows how many degrees the freezing point of a 1% solution of a drug substance is reduced compared to the freezing point of a pure solvent.

Knowing the depression of a 1% solution of any substance, it is possible to determine its isotonic concentration.

Depression of 1% solutions are given in Appendix 4 of the textbook. Denoting the depression of a 1% solution of a substance At, determine the concentration of the solution, which is a depression equal to 0.52 ° C, according to the following formula:

1% - Δt °
x = 0,52 ° C

1 % – Δt°
x – 0,52 °C

$$x = \frac{0,52}{\Delta t} \%$$

1% glucose solution = 0.1 ° C:

So, the isotonic concentration of glucose solution will be 5.2%. When calculating the amount of substance required to obtain an isotonic solution, use the formula:

$$m_1 = \frac{0,52 \times V}{Dt \times 100},$$

where m1 is the amount of substance required for isotoning, g

V - volume of roses for recipes in the recipe, ml.

$$m_1 = \frac{0,52 \times 200}{0,1 \times 100} = 10,4 \text{ г глюкози необхідно на 200 мл ізотонічного розчину.}$$

When two components in the recipe for the calculation of isotonic concentrations using the formula:

$$m_2 = \frac{(0,52 - \Delta t_2 \times C_2) \times V}{\Delta t_1 \times 100},$$

де m_2 – кількість речовини, необхідна для ізотонування розчину, г;
0,52 °С – депресія температури замерзання сироватки крові;
Δt_2 – депресія температури замерзання 1 % розчину прописаної речовини;
C_2 – концентрація прописаної речовини, %;
Δt_1 – депресія температури замерзання 1 % розчину речовини, узятого дл тонування розчину, прописаного в рецепті;
V – об'єм прописаного в рецепті розчину, мл.

For example:

Rp .: Sol . Novocaini 2% 100 ml
Natrii sulfatis q.s.,
ut fiat sol. isotonica Sterilisa!
Da. Signa. For injections.

Δt_1 – депресія температури замерзання 1 % розчину натрію сульфату (0,15 °С);
Δt_2 – депресія температури замерзання 1 % розчину новокаїну (0,122 °С);
ΔC_2 – концентрація розчину новокаїну (2 %).

$$m_1 = \frac{(0,52 - 0,122 \times 2) \times 100}{0,15 \times 100} = 1,84 \text{ г натрію сульфату.}$$

So, for the manufacture of isotonic solution of novocaine according to the above recipe, you must take 2.0 g of novocaine and 1.84 g of sodium sulfate.

With three or more components in the recipe for the calculation of isotonic concentrations use the formula:

$$m_3 = \frac{0,52 - (Dt_2 \times C_2 + Dt_3 \times C_3) \times V}{\Delta t_1 \times 100},$$

де m_3 – кількість речовини, необхідна для ізотонування розчину, г;
0,52 °С – депресія температури замерзання сироватки крові;
Δt_1 – депресія температури замерзання 1 % розчину речовини, узятого для ізотонування розчину, прописаного в рецепті;
Δt_2 – депресія температури замерзання 1 % розчину другого компонента в рецепті;
C_2 – концентрація другого компонента в рецепті, %;
Δt_3 – депресія температури замерзання розчину третього компонента в рецепті;
C_3 – концентрація третього компонента в рецепті;
V – об'єм розчину, прописаного в рецепті.

For example:

Rp .: Atropini sulfatis 0.2

Morphini hydrochloride 0.4
Natrii chloridis
Aquae pro injectionibus ad 20 ml ut fiat solutio isotonica Sterilisa!

Da . Signa . For injections.
Δt1 - depression of the freezing temperature of a 1% solution of sodium chloride (0.576 ° C);
Δt2 - depression of the freezing temperature of a 1% solution of atropine sulfate (0.073 ° C);
C2 is the concentration of atropine sulfate (1%);
Δt3 - depression of the freezing temperature of a 1% solution of morphine hydrochloride (0.086 ° C);
C3 - the concentration of morphine hydrochloride (2%);
V is the volume of the solution prescribed in the recipe.

$$m_3 = \frac{0{,}52 - (0{,}073 \times 1 + 0{,}086 \times 2) \times 20}{\Delta t_1 \times 100} = 0{,}0955 \approx 0{,}1 \text{ г натрію хлориду.}$$

When calculating the isotonic concentration by the cryoscopic method, the main source of errors is the absence of a strict proportional relationship between concentration and depression. It is important to note that deviations from proportional dependence are individual for each medicinal substance.

So, for a solution of potassium iodide, there is an almost linear (proportional) relationship between concentration and depression. Therefore, the isotonic concentration of some medicinal substances, determined by an experimental method, is close to the calculated one, for others there is a significant difference.

The second source of errors is the error of experience in the practical determination of depression in 1% solutions, as evidenced by the different values of depressions (Δt), published in some sources.

Calculate isotonic concentrations using sodium chloride equivalents. A more versatile and accurate method for calculating isotonic concentrations of pharmacopoeial solutions (adopted by SPh XI), based on the use of isotonic equivalents of medicinal substances for sodium chloride. In pharmacy practice, it is used most often.

The isotonic equivalent (E) of sodium chloride indicates the amount of sodium chloride that creates an osmotic pressure under the same conditions, equal to an osmotic pressure of 1.0 g of the drug substance.

For example, 1.0 g of novocaine is equivalent in its osmotic effect to 0.18 g of sodium chloride (see Appendix 4 of the textbook). This means that 0.18 g of sodium chloride and 1.0 g of novocaine create the same osmotic pressure and the same volumes of water are isotonic under equal conditions.

Knowing the sodium chloride equivalents, any solutions can be isotonuvaty, as well as determine the isotonic concentration. For example:

1.0 g of novocaine equivalent - 0.18 g of sodium chloride, and 0.9 g of sodium chloride - x g of novocaine;

$$x = \frac{0,9 \times 1}{0,18} = 5,0 \text{ г}$$

So, the isotonic concentration of Novocain is 5%.

Rp .: Dimedroli 1.0
Natrii chloridi qs
Aquae pro injectionibus ad 100 ml ut fiat solutio isotonica
Sterilisa !
Da . Signa . Intramuscularly no 2 ml 2 times a day.

For the manufacture of 100 ml of isotonic solution of sodium chloride, it would be necessary to 0.9 g (isotonic concentration - 0.9%). However, part of the solution is isotonated with the drug substance (dimedrol).

Therefore, first take into account how much of the prescribed volume is 1.0 g of Dimedrol. When calculating proceed from the definition of an isotonic equivalent for sodium chloride. According to the table (Appendix 4), it is found that E of dimedrol in sodium chloride is equal to 0.2 g, that is, 1.0 g of dimedrol and 0.2 g of sodium chloride isotonic with identical volumes of aqueous solutions.

Next, determine what amount of sodium chloride must be added to isotoning: 0.9-0.2 = 0.7 g.

Rp .: Solutionis Novocaini 2% 200 ml
Natrii chloridi qs,
ut fiat solutio isotonica Sterilisa!
Da . Signa . For intramuscular administration.

In this case, for the manufacture of 200 ml of isotonic sodium chloride solution, it was necessary to use 1.8 g:

0,9 – 100

x – 200

$$x = \frac{200 \times 0,9}{100} = 1,8 \text{ г.}$$

Прописані 4,0 г новокаїну еквівалентні 0,72 г натрію хлориду:

$1,0_{\text{ новокаїну}} - 0,18_{\text{ натрію хлориду}}$

$4,0_{\text{ новокаїну}} - x_{\text{ натрію хлориду}}$

$$x = \frac{4,0 \times 0.18}{1} = 0,72 \text{ г.}$$

So, sodium chloride is necessary to take 1.8 - 0.72 = 1.08 g .

Rp .: Strichnini nitratis 0.1% 50 ml
Natrii nitratis qs,
ut fiat solutio isotonica Sterilisa!
Da . Signa . On 1 ml 2 times a day under. skin

First, determine the amount of sodium chloride required for the manufacture of 50 ml of isotonic solution:

0,9 – 100

x – 50

$$x = \frac{50 \times 0,9}{100} = 0,45 \text{ г.}$$

Next set, the amount of sodium chloride corresponds to 0.05 g (prescribed) strychnine nitrate:

$1{,}0\ г_{\text{стрихніну нітрату}} - 0{,}12\ г_{NaCl}$

$0{,}05\ г_{\text{стрихніну нітрату}} - x\ г_{NaCl}$

$$x = \frac{0{,}12 \times 0{,}05}{1} = 0{,}006 \approx 0{,}01\ г.$$

So, sodium chloride need 0.45 - 0.01 = 0.44 g.

But in the recipe it is indicated that the solution needs sodium isotonuvata nitrate. Therefore, they recount this substance (equivalent of sodium nitrate in sodium chloride is 0.66):

$0{,}66\ г_{NaCl} - 1{,}0\ г_{\text{натрію нітрату}}$

$0{,}44\ г_{NaCl} - x\ г_{\text{натрію нітрату}}$

$$x = \frac{0{,}44 \times 1}{0{,}66} \approx 0{,}67\ г.$$

Thus, according to the above recipe, 0.67 g of sodium nitrate is necessary for isotoning. Based on known equivalents of sodium chloride, were calculated isotonic equivalents of glucose, sodium nitrate, sodium sulfate and boric acid, are given in Appendix 4 of the textbook. With their use, the calculations are simplified. For example:

Rp .: Solutionis Ephedrini hydrochloridi 2% 100 ml
Glucosi q . s .,
ut fiat solutio isotonica
Da . Signa . For injections

The isotonic equivalent of ephedrine hydrochloride in glucose is 1.556. Prescribed in the recipe 2.0 g ephedrine hydrochloride will create the same osmotic pressure as 3.11 g glucose (2.0 x 1.556). Since the isotonic glucose concentration is 5.22%, it should be taken 5.22 - 3.11 = 2.11 to isotonize the solution of ephedrine hydrochloride.

Calculation of isotonic concentrations by the formulas. Osmotic pressure in aqueous solutions of one or several substances (equal to osmotic pressure of 0.9% sodium chloride solution) can be expressed by the following equation:

$$m_1 \times E_1 + m_2 \times E_2 + \ldots + m_n \times En = m_x \times E_x = 0{,}009 \times V, \text{ звідки}$$

$$m_x = \frac{1}{E_x} 0{,}009 \times \frac{V^n - (m_1 \times E_1 + m_2 \times E_2 + \ldots m_n \times En)}{E_x}; (1)$$

m_x - маса шуканої речовини, г;
E_x – ізотонічний еквівалент по натрію хлориду шуканої речовини;
$m_1, m_2 \ldots$ – маси прописаних у рецепті речовин;
$E_1, E_2 \ldots$ – ізотонічні еквіваленти речовин по натрію хлориду;
V - об'єм розчину.

According to the formula (1) you can determine the number of different medicinal or auxiliary substances, which must be added to the solution to isotony for water injections, eye drops, lotions, rinses. For example:

Rp .: Solutionis Morphini hydrochloridi 1% 100 ml Glucosi qs,
ut fiat solutio isotonica
Sterilisa!

Misce. Da. Signa. On 1 ml under the skin.

$$m_{глюк.} = \frac{1}{E_{глюк.}}(0{,}009 \times V - m_1 \times E_1) = \frac{1}{0{,}18} \times (0{,}009 \times 100 - 1 \times 0{,}15) = 4{,}17 \text{ г.}$$

To isotoning the injectable solution, you need to add 4.17 g of anhydrous glucose grade “for injection”.

Rp .: Solutionis Argenti nitratis 0,5% 10 ml
Natrii nitratis qs,
ut fiat solutio isotonica
Misce. Da . Signa . 2 drops 1 time per day.

$$m_{натр.\ нитрат} = \frac{1}{0{,}66} \times (0{,}009 \times 10 - 0{,}05 \times 0{,}33) = 0{,}11 \text{ г.}$$

Rp .: Solutionis Magnesii sulfatis isotonica 100 ml
Sterilisa !

Da . Signa . 10 ml intravenously **1** time per day,

m **x** E = 0.009 **x** V

$$m_{магн.\ сульфат} = \frac{0{,}009 \times 100}{0{,}14} = 6{,}43 \text{ г.}$$

For the manufacture of an isotonic solution, it is necessary to take 6.43 g of magnesium sulfate grade "for injection".

An isotonic solution of sodium chloride (0.9%) creates an osmotic pressure of 7.4 atm. The same osmotic pressure has blood plasma. Determine the osmotic pressure in the injection solution can be by the formula:

$$P = \frac{(m_1 \times E_1 + m_2 \times E_2 + \ldots + m_n \times En) \times 7{,}4 \times 100}{0{,}9 \times V}, (2)$$

de P-osmotic pressure, atm.

For example:

Rp .: Natrii chloride 5.0
Kalii chloride 1.0
Natrii acetatis 2.0
Aquae pro injectionibus ad 1000 ml Sterilisa!

$$P = \frac{(5 \times 1 + 1 \times 0{,}76 + 2 \times 0{,}46) \times 7{,}4 \times 100}{0{,}9 \times 1000} = 5{,}49 \text{ атм.}$$

Misce . Da . Signa . For intravenous administration ("Acesol"),

Solution "Acesol" hypotonic. It is necessary to prepare a solution so that it is isotonic, keeping the ratio of salts - sodium chloride: potassium chloride: sodium acetate -5: 1: 2 (or the same 1: 0.2: 0.4).

The number of substances that should be in solution (keeping their ratio and at the same time the solution should be isotonic) can be calculated by the formula:

$$мі_{(1,2,3)} = \frac{0{,}009 \times V \times m_{(1,2,3)}}{m_1 \times E_1 + m_2 \times E_2 + m_3 \times E_3}, (3)$$

m_3 – маса натрію ацетату в розчині «Ацесоль», г;
E_1, E_2, E_3 – відповідні ізотонічні еквіваленти по натрію хлориду;
V – об'єм розчину.

$$m''_{натрію\ хлорид} = \frac{0{,}009 \times 1000 \times 5}{5 \times 1 + 0{,}76 + 2 \times 0{,}46} = 6{,}736 \text{ г}$$

$$m''_{калію\ хлорид} = \frac{0{,}009 \times 1000 \times 1}{6{,}68} = 1{,}347 \text{ г}$$

$$m''_{натрію\ ацетат} = \frac{0{,}009 \times 1000 \times 2}{6{,}68} = 2{,}694 \text{ г}$$

(Sum 5 x 1 +1 x 0.76 + 2 x 0.46 road 6.68).

So that the solution was isotonic and at the same time the ratio of salts was maintained as 1: 0.2: 0.4. To it must be attached: sodium chloride 6.736-5 = 1.74 g, potassium chloride 1.347-1 = 0.35 g, sodium acetate 2.694-2 = 0.69 g.

The calculation by the formula (3) can be carried out for hypertonic solutions in order to reduce the amount of substances and bring the solutions to normal (isotony).

Formulas (1), (2) and (3) were first proposed for use in pharmacy practice by an assistant at the Department of Drug Technology at Zaporizhia Medical Institute, Ph.D. in Pharmaceutical Sciences P. A. Logvin.

Along with isotonicity, an important characteristic of the osmotic pressure of the solutions is osmolarity, **Osmolarity (osmolarity)** is the *value of the estimate of the total contribution of various solutes to the osmotic pressure of the solution.*

The unit of osmolarity is pitch per kilogram (pitch / kg), in practice the unit is usually used milliosmol per kilogram (mosmol / kg). The difference between osmolarity and osmolality is that they use various expressions for the concentration of solutions: molar and molar.

Osmolarity - the amount of resin per 1 liter of solution. Osmolality - the amount of resin per 1 kg of solvent. Unless otherwise indicated, osmolality (osmolarity) is determined using an osmometer instrument.

The determination of the osmolarity of the solutions is important when using parenteral nutrition of the body. The limiting factor for parenteral nutrition is the amount of fluid injected, which affects the circulatory system and water-electrolyte balance. Given certain limits of "endurance" of veins, it is impossible to use solutions of arbitrary concentration. Osmolarity of about 1100 moz-mol / l (20% sugar solution) in an adult is the upper limit for administration through the peripheral vein.

The plasma osmolarity is about 300 mosmol / l, which corresponds to a pressure of about 780 kPa at 38 ° C. This is the starting point for the stability of the infusion solutions. The osmolarity value can vary from 200 to 700 mosmol / l.

TECHNOLOGY ISOTONIC SOLUTIONS. Isotonic solutions are prepared according to all the rules for preparing solutions for injections. The most widely used isotonic solution of sodium chloride.

Rp .: Solutionis Natrii chloridi 0.9% 100 ml Sterilisa !

Da . Signa . For intravenous administration.

To prepare the sodium chloride solution, it is preheated in the Dry-Air Sterilizer at 180 ° C for 2:00 in order to destroy possible pyrogenic substances. Under aseptic conditions, sterile sodium chloride is weighed out on sterile teresics, placed in a 100 ml sterile volumetric flask and dissolved in a portion of water for injection, after dissolving it is brought up to 100 ml with water for injection. The solution is filtered into a sterile vial, quality controlled, hermetically sealed with a sterile

rubber stopper under running-in with a metal cap. Sterilized in an autoclave at 120 ° C for 8 minutes. After sterilization, secondary control of the quality of the solution is carried out and arranged for release. The shelf life of the solution prepared in pharmacies is 1 month.

PWC

Date Recipe No.

Natrii chloride 0.9

Aquae pro injectionibus ad 100 ml

Sterilis $V_{zag.}$ = 100 ml

Prepared: (signature)

Checked: (signed)

PLASMA SUBSTITUTING (PHYSIOLOGICAL) SOLUTIONS

Characterization and classification of plasma-substituting solutions. With blood loss, impaired water-electrolyte balance and the acid-base state of the body, there is a need to introduce into the bloodstream significant amounts of blood-substituting liquids. The simplest of them is an isotonic solution of sodium chloride, the introduction of which has a favorable hemodynamic effect. However, this solution cannot maintain a constant ionic composition of the plasma, and in some cases it is necessary to introduce more complex solutions, which include a number of salts present in the blood plasma.

Plasma-substituting solutions (formerly called physiological, or blood-borne liquids) are solutions, the composition of dissolved substances can support the vital activity of cells and organs and do not cause significant changes in physiological balance in the body.

On this basis, it is wrong to call the “physiological” isotonic sodium chloride solution, the introduction of large doses of which leads to a change in the ratio between the mineral salts of the plasma, causes a painful condition in the form of “salt fever”, and sometimes “salt glycosuria”.

At present, the classification has been adopted; it divides plasma-substituting solutions into the following groups:

1. Regulators of water-salt and acid-base equilibrium (Ringer, Ringer-Locke solutions, lactasol, acesol, disol, trisol, chlosol, quartosol, etc.); salt solutions, osmodiuretikov. Carry out the correction of the blood during dehydration.

2. Hemodynamic (protivoshokovye) blood substitutes (polyglukin, reopolyglukine, gelatinol, dextran). Designed for the treatment of shock of various origins and the restoration of hemodynamic disorders, including microcirculation, using heart-lung machines for dilution of blood during operations, etc.

3. Detoxification blood substitutes (hemodez, polydez). Contribute to the removal of toxins during intoxication of various etiologies.

4. Preparations for parenteral nutrition (hydrolysin, amino peptide, polyamine). They serve to ensure the energy resources of the body, the delivery of nutrients to organs and tissues.

5. Blood substitutes with oxygen transfer function. Designed to restore the respiratory function of the blood.

6. Blood substitutes of complex action. Have a wide range of action may include several groups of plasma-substituting solutions.

Requirements for plasma-substituting solutions. Depending on the purpose, there are also requirements for individual groups of infusion solutions, but it's common for them that they must be completely eliminated from the body without disrupting the functions of organs, have constant physical and chemical properties, be non-toxic, pyrogen-free, sterile, stable during long-term storage. .

One of the main requirements for infusion solutions, administered in significant quantities during blood loss, is the observance of the physiological correspondence between the composition of the body fluid and the injection fluid.

Such a match is achieved, provided that the fluid is introduced into the body, will have:

- Compliance with the osmotic pressure of the solution introduced to the osmotic pressure of body fluids (isotonia)
- A certain concentration, composition and ratio of ions (isoionium)
- Determined the pH of the solution (isohydria)
- A certain viscosity.

Thus, plasma solutions, such solutions are called, by their osmotic pressure, ionic composition and pH value are close to blood plasma plasma, they are sometimes called balanced or stabilized solutions, and also under the name of the institution or the name of the author who proposed the solution.

Isotonia (see pp. 488-499).

Isoionium. Plasma substituting solutions should contain ions of vital substances in the ratio in which they are in the blood plasma (Na^{+}, K^{+}, Ca^{2+}, Mg^{2+}, $P04^{3-}$, etc.).

Calcium ions provide a general stimulating effect, potassium ions stimulate the vagus nerve and thus the heart muscle, suppressing the work of the heart. Magnesium ions cause intestinal peristalsis, which is especially important during abdominal operations. Plasma-substituting solutions should contain a foreign-external complex of ions of sodium, potassium, calcium, magnesium, and in the same proportions in which they are located in the blood plasma. Currently, methods have been developed for the manufacture of plasma-substituting solutions enriched with microelements, since the blood contains more than 40 elements that perform an important physiological role.

Scientific studies have shown that, in order to ensure a more or less long-term vital activity of cells, readily assimilable nutrients should be added to the liquid, which are necessary for replenishing the energy expenditure of organs. In order to provide nutrition to the cells and create the necessary redox potential, glucose is injected into physiological solutions. Blood contains glucose in the amount of 5-6 mol. With its help in the liver, heart muscle and other organs is carried out the oxidation of various harmful metabolic products and turning them into harmless to the body products. Therefore, glucose is necessary for equalization of the reduction potential in a physiological solution.

Isohydria. Isohydric called those solutions in which the pH corresponds to the pH of blood plasma or other body fluids into which this solution is administered.

The concentration of hydrogen ions in different body fluids is different, for example, blood serum has a slightly alkaline reaction, the pH ranges from 7.34 to 7.36, and cerebral spinal fluid varies from 7.71 to 7.85. With intense muscular work, the pH in the tissue fluid decreases to 6.6. As mentioned above, for the stability of isotonic solutions, the concentration of hydrogen ions plays an important role as a preservative and stabilizer of solutions. SPh XI recommends that for the manufacture of sterile solutions, especially in factory production, various stabilizers should be added.

In cases where the saline solution is used in large quantities, it becomes necessary to prepare them isohydric, otherwise the concentration of hydrogen ions of the blood will be disturbed. As you know, in the process of vital activity of cells and organs, acidic products of metabolism are formed, neutralized by buffer systems of the blood, such as carbonate, phosphate, and others. That is why similar pH regulators were introduced into infusion solutions. As a result, the solutions become balanced (ekvilibrovanimy).

To maintain a certain pH (equal to the pH value of blood plasma) is used:

1. carbonate system (NaHCO, + C02).

2. phosphate system (Na2HP03 + Na2P04).

3. Protein systems are ampholyte (ampholytes are substances that simultaneously possess the properties of acids and bases in an aqueous solution).

To maintain neutrality, add one and disubstituted phosphates, for acidic - a mixture of weak acid with its salt, for example, acetic acid and sodium acetate. Phosphates and bicarbonates are most commonly added, which regulate the pH in the body, for example, if an acid enters the body, it reacts with sodium bicarbonate (buffer): HCl + NaHCO, = NaCl + H20 + CO2. The acidic environment disappears as a result of the formation of salt, which is an integral part of blood serum, and CO2 is easily excreted from the body.

If a small amount of acid is formed in the blood, the pH value almost does not change with the introduction of solutions, due to the reaction:

NaHCO3 + HCl = NaCl + CO2 + H20 or

Na2HPO4 + HCl = NaCl + Na2PO4

In addition, carbon dioxide makes it possible, when injected into the bloodstream, to cause impairment of the respiratory vasomotor centers and thereby improve breathing and blood circulation.

Viscosity. Conventional plasma solutions have a significant drawback: their effect is short-term and after about 2:00 this solution is removed from the vessels. As a result, the amount of fluid in the bloodstream decreases sharply and blood pressure drops.

The problem of creating plasma-substituting solutions with a viscosity close to that of blood (1.5-1.6 centipoise) is very complex. Based on experimental studies, it became apparent that to ensure the viscosity of infusion solutions, the addition of special substances is necessary. Such substances are high-molecular compounds. They very little change the value of osmotic pressure (large molecular weight) and,

due to the fact that they do not pass into urine, they delay the release of water and the dissolution of salt in it. Searches for substances that could provide liquids with the necessary viscosity continued for a long time. It was proposed to use for this purpose solutions of gum arabic, apricot gum. However, these substances are not absorbed by the body and, remaining in the bloodstream, glue the red blood cells. Solutions of casein, gelatin, gelatin and some proteins,isolated (without special treatment) from the blood of animals, also could not be used for these purposes, since many of them are foreign proteins and cause anaphylaxis and other complications.

Currently, plasma-substituting (infusion) solutions with a viscosity close to that of blood are made with the addition of such components: human blood, heterogeneous protein, high-molecular compounds of plant origin, and synthetic high-density polymers. New and real possibilities of solving the problems of ensuring the viscosity of infusion solutions appeared with the discovery of dextran and the synthesis of polyvinylpyrrolidone.

Dextran (proposed by COLIPP) is a water-soluble high-polymer glucose, which is obtained from beet sugar by enzymatic hydrolysis, that is, by the influence of micro-organisms (Leuconoston mesenteroydes), converting sucrose into a high-molecular compound "dextran", with a molecular weight of 50000 ± 10000, with appropriate conditions make polyglyukin, reopoliglyukin, rondex, reoglyuman.

Plasma substituting solutions containing substances that increase the viscosity, are used as antishock and detoxification.

Solutions-regulators of water-salt and acid-base balance. Under the conditions of pharmacies, plasma-substituting solutions belonging to the first group are prepared mainly. These are Ringer's solutions, Ringer-Locke's solutions, acesol, disol, trisol, quartosol, chlo-salt, etc.

Ringer's solution - Locke.

Rp .: Natrii chloride 1.8
Kalii chloride 0.04
Calcii chloride 0.04
Natrii hydrocarbonis 0.04
Glucosi 0.2
Aquae pro injectionibus ad 200 ml
Sterilisa !
Da . Signa . For intravenous administration.

Saline saline solution for intravenous administration. With the joint presence of sodium bicarbonate and calcium chloride, the formation of calcium carbonate precipitate is possible. Therefore, prepare two solutions. In the manufacture using a sterile 20% solution of calcium chloride.

In a sterile volumetric flask of 100 ml in a part of water for injection dissolve 1.8 sodium chloride, 0.22 glucose with a moisture content of 9%, 0.04 g of potassium chloride, add 4 drops (0.2 ml) of a 20% solution of calcium chloride and water for injection volume is adjusted to 100 ml. The solution is analyzed, filtered into a vial, sealed with a sterile rubber stopper, the control is carried out on mechanical impurities, rolled around with a metal cap, the sealing is checked and sterilized at

120 ° C for 8 minutes, the secondary control is carried out and arranged for tempering.

In another 100 ml volumetric flask, a solution of sodium bicarbonate is prepared (for technology, see Page 488). Sterilization conditions are similar to saline with glucose. Before use, the solutions are drained under aseptic conditions.

These solutions are used in the treatment of patients with acute gastrointestinal infections, accompanied by dehydration, intoxication, acidosis, and lack of blood electrolytes. In tab. 34 shows the composition of the most frequently used plasma-substituting liquids.

Solution "Quartasol". Colorless liquid with a pH of 8.1-8.9. The solution is prepared according to the general rules. When working with sodium acetate, you should use a respirator, rubber gloves, goggles. To avoid the loss of carbon dioxide, which is formed during the hydrolysis of sodium bicarbonate, the dissolution is carried out at a temperature not higher than 20 ° C in a closed vessel, avoiding shaking. The solution is sterilized at 120 ° C.

Petrov's liquid. To obtain a solution capable of lingering in the body for a long time, Professor Petrov proposed a copy of a hypertonic solution containing sodium, potassium, calcium chloride, water for injection and 10% of preserved human blood. The blood in the saline solution is added under aseptic conditions before being administered to the patient, heating the solution to 38 ° C. The solution, due to hypertonic concentration, is slowly excreted by the kidneys and longer than isotonic solutions, retained in the bloodstream.

Polyglucin - 6% depolymerized dextran solution in isotonic sodium chloride solution. The drug quickly increases blood pressure in acute blood loss and keeps it at a high level for a long time. It is used both in pure form and in mixture with salt solutions. Available in hermetically sealed vials of 400 ml. Store at temperatures from +10 to + 20 ° C. Polyglucin freezing is not a contraindication to use.

Reopoliglyukin - 10% solution of partially hydrolyzed dextran in an isotonic solution of sodium chloride. The drug reduces the aggregation of blood cells. You have a detoxifying action. Available in bottles of 400 ml. Store in a dry place at temperatures from +10 to + 20 ° C.

Many diseases and pathological conditions are accompanied by intoxication of the body (poisoning with various poisons, infectious diseases, burns, acute hepatic and renal failure, etc.). For their treatment, targeted detoxification solutions are necessary, the components of which must bind to toxins and quickly remove them from the body. Such compounds include polyvinylpyrrolidone (PVP) and polyvinyl alcohol.

PVP solutions with a molecular weight of from 20 to 40,000 are used as plasma substitutes as a component that provides the viscosity of infusion solutions. Drugs with a molecular weight above 40,000 for administration in the blood are not used, since they linger for a long time in the body and can accumulate in the spleen and liver.

PVP preparations with a molecular weight below 20,000 are rapidly excreted from the body and are used as a detoxifying agent. With the drugs used for this purpose, it is possible to mention gemodez, a water-salt solution containing 6% of

low-molecular-weight PVP and Na +, K *, Ca ++, Mg ++ chlorides. It is a clear, slightly yellowish liquid. It is used for detoxification of the body in toxic forms of gastrointestinal diseases, especially in children (dysentery, dyspepsia), burn disease, scarlet fever, diphtheria and other infectious diseases. The drug binds toxins and quickly removes them through the kidneys.

Close to the mechanism of action for hemodez polidez - C% solution of low molecular weight polyvinyl alcohol in isotonic sodium chloride solution. Introduced intravenously. Being an energy agent, it can be administered with glucose solutions, protein hydrolysates and other therapeutic solutions.

Plasma-substituting solutions containing proteins are used as agents for parenteral nutrition: Hydrolysin solution, casein hydrolyzate, aminopeptide, aminocrovins, fibrinosol, etc.

Plasma substitutes of protein origin include gelatinol - an 8% solution of partially split edible gelatin in an isotonic solution of sodium chloride. Contains a number of amino acids (except tryptophan). It is a clear amber liquid. Used as a plasma-substituting agent for operations, traumatic shock, when preparing for an operation and for detoxifying the body. Available in bottles of various capacities. Store at a temperature of 4-6 ° C. In the case of precipitation the drug can not be used.

Antishock solutions . The introduction of plasma-substituting solutions, whose action is aimed at normalizing blood circulation, was not effective enough in combating shock. To obtain antishock solutions in plasma-substituting liquids, medicinal substances are added to increase blood pressure, normalize the functions of the central and autonomic nervous system, and restore the chemism of the blood and tissues. The antishock fluids include glucose- alcohol solutions, so-called stimulants, and solutions with hypnotics and narcotic substances.

Anti-shock fluids can be divided into three groups:

- Simple antishock solutions containing salts, glucose and ethyl alcohol;
- Complex antishock solutions containing glucose, ethyl alcohol, bromides and drugs;
- Complex antishock solutions containing glucose, ethyl alcohol, bromides, drugs, blood plasma.

Alcohol has an anesthetic, hypnotic effect, and also increases redox processes. The therapeutic effect of glucose-alcohol solutions is enhanced by the addition of sodium bromide, morphine hydrochloride, barbital, urethane, and other sleeping pills and narcotic substances. The mechanism of action of anti-shock fluids is reduced to the normalization of the processes of excitation and inhibition in the central nervous system, the elimination of the flow of neuro-pain sensations, is achieved by the introduction of bromides and drugs. Sleeping pills and narcotic substances, causing sleep, guard the cells from exhaustion. Antishock solutions with an isotonic concentration, as a rule, are rapidly removed from the bloodstream, raise blood pressure and increase the mass of circulating blood for a very short period. In this respect, antishock solutions with hypertonic concentration are effective.

According to the previously given classification, the anti-shock liquid COL1PK can be assigned to the first group according to the prescription of P. A. Seltsovsky, which contains sodium chloride - 7.0 g, potassium chloride - 0.2 g, magnesium sulfate - 0.04 g, glucose - 54 2 g 96% alcohol - 80 ml, Weibel liquids - 3.3 ml, water - up to 1000 ml.

In the antishock fluids of the second group, the therapeutic efficacy of the glucose-alcohol composition is enhanced by bromide and drugs. As an example, Asratyan's antishock fluid can be given, dispensed in the form of two solutions. Solution A contains sodium chloride — 8.0 g, sodium bromide — 0.75 g, sodium bicarbonate — 0.6 g, and water for injections — up to 500 ml. Solution B contains urethane - 1.2 g, barbital - 0.15 g, calcium chloride - 1.5 g, glucose - 17.0 g, alcohol 96% - 15 ml, water up to 50 ml. Before use, both solutions are heated to 20-25 ° C (not more) and mixed immediately before administration.

The antishock solution of A.N. Filatov, similarly to Asratyan's solution, contains calcium chloride, glucose, alcohol and barbital, transfers sterilization and is stored in ampoules for a long time.

Antishock solutions of the third group are complicated by the addition of binders. For example, the anti-shock solution of Belyakov and Petrov includes: sodium bromide 1.0 g, caffeine - 0.2 g, morphine - 0.01 g, plasma - 40 ml, syncol - 400.0 g. Another solution of this group is the latex solution COLIPP contains alcohol 96% - 50 ml, glucose - 50.0 g, Tecodine - 0.04 g, defibrinated plasma - 200 ml and water - up to 500 ml. Due to the content of syncol (6% solution of hydrolyzed dextran in an isotonic solution of sodium chloride) or plasma, which are contained in the vascular bed for a long time, the mass of circulating blood increases in these solutions. The weak side of this group of solutions is the absence of substances in them, normalize the disturbed volume.

Prepare anti-shock solutions in the same way as isotonic and plasma-substituting solutions.

Adding alcohol to injection solutions can be done in two ways:

1. The required amount of alcohol (under aseptic conditions) is added to the ready-made simple solution.

2. In the case of the manufacture of solutions in ampoules (or vials, hermetically sealed,) alcohol is introduced into the solution before sterilization.

In the manufacture of alcohol solutions, the bottles are filled to 3/4 volume, the contents of the bottle should not interfere with the stopper during sterilization. Traffic jams should not have punctures. Bottles corked under running-in with metal caps must be checked for tightness.

Alcohol solutions should be sealed with plugs of the brand IR-21 (beige), IR-119 (gray). When capping with 25P (red) brand stoppers, it is necessary to enclose specially treated parchment paper or non-lacquered cellophane under them.

Banaitis liquid.

Rp .: Solutionis Glucosi 25% 6 5 ml
Natrii chloride 0.5
Calcii chloride 0.12
Spiritus aethylici 60% 12 ml

Sterilisa!

Da . Signa . For intravenous administration.

Banaitis fluid is a plasma plasma-substituting agent used in mild cases of shock and in moderate blood loss.

Weigh 16.25 g of anhydrous glucose, 0.5 g of sodium chloride and 0.12 g of calcium chloride. It is brought to 65 ml with water for injection, filtered, 12 ml of 60% alcohol are added and the bottle is sealed. Sterilized with steam under pressure at 120 ° C for 8 minutes.

The use of plasma-substituting solutions is of great importance for medical practice, since their use reduces the amount of donated blood.

IMPROVEMENT OF INJECTION MEDICAL FORMS TECHNOLOGY

Conducted research in the field of improving the technology of injection dosage forms aimed at improving efficiency and quality requires solving the main problems - it is stabilization, ensuring the absence of mechanical impurities in the preparations, optimization of the production process and its instrumentation.

At present, the chemical stabilization method has become common, which involves the addition of various excipients-stabilizers to drugs, which is not the optimal way to obtain stable drugs from a biological point of view. A physical, or rather technological, method of stabilization, which allows one to obtain stable preparations without the addition of any auxiliary stabilizers, deserves attention.

From a biological point of view, the physical method of stabilization is the most rational and requires a significant expansion of research in this direction.

Thus, the production of frozen infusion solutions (cephalosporin antibiotics and antibiotics of other groups) is widely developed in the United States. These solutions are prepared in a 0.9% solution of sodium chloride or 5% glucose solution and produced in special polymer containers with a capacity of 50 or 100 ml. The shelf life of such solutions -6 months. subject to storage at a temperature not higher than minus 20 ° C.

One of the ways to improve the technology of infusion preparations in terms of ensuring stability is the development of methods for creating aqueous solutions of rare-earth substances. Special attention is attracted to combined, infusion and polyionic drugs that require the study of compatibility and stability. The production of concentrated solutions (concentrates), powders and lyophilized dosage forms for injection is promising.

Concentrates for intravenous injection are sterile solutions intended for use after dilution in the specified volume with an appropriate liquid. Powders and lyophilized dosage forms with shaking with the specified volume of the corresponding sterile liquid form a clear, free from mechanical particles solution. These dosage forms must comply with all requirements for injectables.

The direction of application of amino acid infusion solutions in combination with glucose solutions, fat emulsions is developing.

An important problem is the optimization of the technological process of obtaining injection dosage forms and the improvement of equipment. The process of receiving, filtering, bottling, capping injection drugs should be carried out in a

"clean room". The problem of ensuring the absence of mechanical impurities in injection preparations is solved by creating effective filters, as well as by improving the methods of quality control of the filtrate. The control of the filtrate and solution in the bottles is mainly carried out visually. The systems of automatic control of the purity of solutions (Japan) are used abroad. In our country, an installation has been developed to control the purity of the filtrate behind slices of 2-5 microns or more.

A comprehensive solution to the main problems, taking into account other factors affecting the stability of the drugs, will provide a stable injection of high quality dosage forms.

5. Materials activating students during the presentation of the lecture / problem question, problem situations, etc. /.

Control questions:

1. Characteristics of dosage forms for injection and the requirements for them. Positive and negative sides of dosage forms for injection.
2. Aseptic conditions for the preparation of drugs.
3. Characteristics of solvents used for the preparation of injection solutions.
4. Receipt, storage and quality control of water for injection in accordance with the requirements of NTD (GFC, order of the Ministry of Health of Ukraine No. 626 dated December 15, 2004).
5. Requirements for medicinal and auxiliary substances, TRACKING materials used for the preparation of injectable drugs.
6. Processing dishes, stoppers, caps; auxiliary materials used in the preparation of solutions for injection.
7. Filtration of injection solutions, the apparatus used for this.
8. Technological stages of preparation of solutions for injections.
9. Sterilization methods and apparatus used.
10. Quality assessment, packaging, clearance for tempering and storage of injection solutions in accordance with the requirements of regulatory and technical documentation.
11. Determination of hypo-, hyper- and isotonic solutions. The value of isotoning solutions for injections.
12. Methods for calculating isotonic concentrations (using equivalents, the laws of Raul, Vant-Hoff and the Mendeleev-Clapeyron equation).
13. Principles of selection of isotoning substances.
14. Infusion (physiological) solutions, the requirements for them.
15. Classification of physiological solutions for their medical purpose and composition. The nomenclature of infusion solutions, which are most often used in the form of finished drugs and their requirements.
16. Cases of the use of infusion solutions in medical practice.
17. Features of the technology of infusion solutions.
18. Rules for the preparation of solutions for injection with thermolabile substances and suspensions for injection.

19. Assessment of quality, registration for tempering and storage of drugs in accordance with the requirements of regulatory and technical documentation.

Test items:

1. A pharmacist prepares an injection solution with a substance that requires stabilization with a 0.1 M hydrochloric acid solution. Specify this substance:
   * Novocain
   calcium chloride
   potassium chloride
   hexamethylenetetramine
   sodium benzoate
2. A pharmacist prepared an injection solution with the addition of a stabilizer — sodium bicarbonate. Specify the substance that requires the use of this stabilizer:
   * Sodium thiosulfate
   novocaine
   ephedrine hydrochloride
   sodium chloride
   glucose
3. A pharmacist prepared an injection solution using a stabilizer — 0.1 M sodium hydroxide solution. Specify the substance that requires the use of this stabilizer:
   * Caffeine sodium benzoate
   Dibazol
   sodium bicarbonate
   sodium chloride
   glucose
4. A pharmacist prepared an injection solution with an easily oxidizing substance, which requires stabilization with an antioxidant. Specify the substance:
   * Vitamin C
   Dimedrol
   sodium chloride
   urotropin
   calcium gluconate
5. A pharmacist prepared 100 ml of a 0.5% solution of novocaine for injections. Specify the amount of 0.1 M hydrochloric acid solution necessary for stabilization:
   * 0.4 ml (8krapel)
   0.5 ml (10krapel)
   0.7 ml (14krapel)
   0.9 ml (18krapel)
   1.0 ml (20 drops)
6. A pharmacist prepared 100 ml of 10% glucose solution for injections. Specify the amount of Weibel stabilizer required for cooking:
   * 5 ml
   10 ml
   15 ml

20 ml
25 ml

7. A pharmacist prepares the solution for injection at a temperature of 20 EC, agitates it, fills thick-walled vials at 80% of the volume and sterilizes it in a horizontal position and. Specify the substance for which the technology is characteristic:

* Sodium bicarbonate
aminocaproic acid
glucose
apomorphine hydrochloride
calcium gluconate

8. A pharmacist must sterilize 400 ml of calcium gluconate injection. Specify the time of sterilization of the solution in an autoclave at a temperature of 120 ° C:

* 12 min
10 min
15 minutes.
12 min
8 min

9. A pharmacist must prepare 100 ml of a mixture that contains glucose for a child of 8 months. Indicate by which technological stage, the preparation of children's medicine, will differ from its preparation for adults:

* Sterilization stage
filtering stage
design stage
filtration stage
capping stage

10. A pharmacist prepared eye drops containing silver nitrate. Does he need to take the substance to ensure isotonicity?

* Sodium nitrate
sodium chloride
borate acid
glucose
sodium sulfate

11. A pharmacist prepared 100 ml of isotonic sodium chloride solution. Specify the method of sterilization of the final product:

* steam
air
gas
mechanical
radiation

12. A pharmacy received a prescription for preparing eye drops containing protargol. Specify the substance chosen by the pharmacist for the addition of eye drops.

Do not izotonuyut
sodium chloride

sodium nitrate
sodium sulfate
boric acid

13. A pharmacist prepared eye drops containing silver nitrate. Does he need to take the substance to ensure isotonicity?

* Sodium nitrate
sodium chloride
borate acid
glucose
sodium sulfate

14. The pharmacist must prepare eye drops with pilocarpine hydrochloride. Specify optimal isotonizing agent:

* Sodium chloride
sodium sulfate
glucose
boric acid
sodium nitrite

15. Pharmacies prepare infusion solutions that must meet the requirements of HFCs. Specify additional requirements for such solutions:

* Isotonicity, isovykist, isohydric, isoionic.
Isotonicity, isovykist, isohydricity.
Isotonicity, isoionichnist.
Isoosmoticity, isohydricity.
Isotonicity, isohydric.

16. To achieve isotonicity of solutions, several methods of calculating isotonic concentrations are used. Specify the method of calculation that is most often adopted in pharmacy practice.

* Using equivalents for sodium chloride.
According to the law of van't goff.
Graphic method.
According to the law of Raul.
According to the equation of Mendeleev-Clapeyron.

17. The patient needs to prepare eye drops with riboflavin. Does the substance need to be incorporated into the solution to ensure its isotonicity in the absence of instructions in the recipe?

* Sodium chloride.
Sodium sulfate.
Borate acid.
Glucose.
Sodium nitrate.

18. The pharmacy prepares an infusion 2% glucose solution. Specify the substance that is used to ensure that this solution is isotonic.

* Sodium chloride.
Sodium nitrate.
Sodium sulfate.

Sodium sulfite.
Borate acid.

19. Infusion solutions should be isohydric. Specify the optimum pH value that is acceptable for infusion solutions intended for intravenous administration.
* 7.35-7.45.
7.0-7.2.
7.2-7.4.
7.25-7.45.
7.35-7, 55.

20. Sodium chloride solutions for injections or infusions are prepared in pharmacies. Specify additional requirements for the quality of sodium chloride, intended for the preparation of infusion solutions.
* H.ch., depyrogenation.
Ch.d.a.
Variety "for others" injection "
There are no impurities of manganese salts.
Anhydrous, ch.d.a.

6. General material and methodological support of the lecture:
- Training rooms;
- Equipment;
- Equipment;
- Illustrative materials.

7. Materials for self-preparation of students:
a) on the topic of the lecture presented / literature, questions, tasks, test tasks /;
b) on the topic of the next lecture / literature, a list of key questions, test items /.

8. The literature used by the lecturer to prepare the lecture.
Basis literature:
1. Drug technology. Study guide: Study guide for higher education institutions / A.I. Tikhonov, P.A. Logvin, S.A.Tikhonova, A.V. Mazulin, T.G. Yarnikh, A.S. Shpichak, A. M. Kotenko; Edited by A.I. Tikhonov - Kharkiv: NUPh; Original, 2009. - 432 p.
2. Medicine technology: study guide / A.S. Marchuk, N. B. Androshchuk - Kiev: Medicine, 2008. - 488 p.
3. Production of medicines. Quality control and regulation: prak.ruk. / Ed. Sh.K. Ged; per. from English V.V. Coastal. - SPb.: Profession, 2013. - 960 p.
Additional:
1. Soft dosage forms: thermal recipe: Methodical recommendations / A. I. Tikhonov, T. G. Yarnikh, A. V. Lukienko and others; Ed. A.I. Tikhonov. - M.: Publishing house NUPh; Golden Pages, 2003.-128 p.
2. Aseptic dosage forms: an extremporal formulation: Methodical recommendations / A. I. Tikhonov, L. V. Bondareva, T. G. Yarnikh, N. F.

Orlovskaya and others; Ed. A.I. Tikhonov and T. G. Yarnikh. - M.: Publishing house NUPh; Original, 2005. - 184 p.
3. Solid dosage forms: extremporal formulation: Methodical recommendations / A. I. Tikhonov, T. G. Yarnikh, S. V. Gritsenko and others; Ed. A.I. Tikhonov - M.: Publishing House of the NUPh; Golden Pages, 2003. - 176 p.
4. Liquid dosage forms: an extremporal formulation: Methodical recommendations / A. I. Tikhonov, T. G. Yarnikh, N. F. Orlovskaya and others; Ed. A.I. Tikhonov and T. G. Yarnikh. - M.: Publishing house NUPh; Original, 2005. - 160 p.

Lecture №10: «Ophthalmic dosage forms. Medicinal forms with antibiotics. Children's and geriatric dosage forms» - 2 h

1. Relevance of the topic. Substantiation of the topic. Ophthalmic dosage forms are allocated in a special group in connection with the method of their use. The famous Soviet ophthalmologist, academician V.P. Filatov wrote: "It can be said without exaggeration that the organ of sight is the most precious among the human sense organs."

Currently, in the treatment and prevention of eye diseases, solutions for instillation, ointment, eye films, tablets, lamellae, Injection medication, as well as using contact lenses and electrophoresis are used for local application.

2. Objectives of the lecture:

- training:

- to study the nomenclature of dosage forms for eyes,
- Conditions of preparation of dosage forms for eyes
- Teach to navigate in the main directions of state regulation of the production of eye dosage forms
- To teach reading recipes in Latin, to analyze their components and to evaluate the correctness of the statement;

-educational:

-To develop skills to use DF and International GF, other regulatory and technical documents, as well as reference books to search for information on the composition, preparation, storage and dispensing of drugs.

3. Plan and organizational structure of the lecture.

№№ Pp	The main stages of the lecture and their content.	Goals in levels of abstraction.	Type of lecture, lecture equipment.	Time distribution
1	**2**	**3**	**4**	**5**
1.	***Preparatory stage*** Definition of learning objectives. Providing positive motivation.	I		2% 2%
2.	***The primary stage*** Statements of the lecture material.plan: 1. Nomenclature of eye dosage forms 2. Conditions of preparation of dosage forms for the eyes in a	II	References, visual material. State Pharmacopoeia is the main regulatorytechnical documentation.	10-20%

3.	pharmacy 3. Quality assessment. 4. Eye ointment. Basics for eye ointments. 5. Classification of dosage forms with antibiotics 6. Basic terms and concepts of antibiotic dosage forms 7. Characteristics of dosage forms with antibiotics. 8. State regulation of the production of dosage forms with antibiotics 10. Basic regulatory and technical documentation. 11. Quality control of dosage forms with antibiotics in terms of the pharmacy. ***The final stage*** Summary of lectures, general conclusions. Lecturer's answers to questions. The task for the student самo self-training.	III II I	References, questions, tasks.	20 -30% 30 -40% 20% 10 -20%

4. The content of the lecture material:

In practical ophthalmology, instillation of solutions, bookmarks in the conjunctival sac of ointments, eye films, tablets, lamellae, injection injection of medicinal substances, as well as using contact lenses and electrophoresis are used to treat eye diseases. A variety of dosage forms also corresponds to the listed routes of administration of ophthalmic drugs: solid, liquid, soft and gaseous.

For solid eye dosage forms include: tablets, lamellae, pencils, powders, eye medicinal films; in gaseous - aerosols (eye sprays) to soft - ointments are homogeneous and heterogeneous; to liquid - true water and oil solutions, solutions of high molecular compounds, colloidal solutions, emulsions and suspensions. They are used in the form of eye drops, lotions, washes, solutions for injection and electrophoresis.

The type of dosage form in ophthalmic pharmacotherapy is determined by a number of interrelated factors: the state of the pathological process, general indicators of the patient's state of the patient, the presence of corresponding traumatic injuries of the organ of vision, the degree of permeability of the hemato-ophthalmological barrier, the physicochemical properties of medicinal substances, the features of the pharmacological action of medicinal and auxiliary substances,

etc. Significant role in the processes of activation or inhibition of action I and such factors include drug substances such as pH value, the osmotic pressure of the solution, molecular weight carrier substances etc. For the manufacture of high quality ophthalmic dosage forms, these factors must be considered.

Eye-drops, lotions and ointments are most often manufactured in the eccentric formulation of pharmacies.

Eye drops (GUTTAE OPHTALMICAE)

Eye drops are liquid dosage forms, which are aqueous or oil solutions, as well as thin suspensions of medicinal substances intended for administration to the eye.

Apply them to the mucous membrane of the eye with a sterile eye pipette. Eye drops are prescribed in small quantities (5-10 ml) with the expectation of their use in a short time.

In the form of eye drops, solutions of various medicinal substances are used. Many of them are unstable and change or collapse under the influence of high temperature, sunlight, microflora and other factors.

Especially often prescribed eye drops with vitamins (ascorbic acid, thiamine bromide, riboflavin), salts of alkaloids (atropine sulfate, pilocarpine hydrochloride, etc.), antibiotics (benzylpenicillin, levomycetin, neomycin, etc.). There are about 80 medicinal substances used in ophthalmic practice, and a significant number of various combinations of them.

Requirements for eye drops. Poor quality eye drops and, above all, their contamination with microorganisms can cause serious consequences, including loss of vision. In this regard, the requirements for eye drops should be similar to those provided for injection solutions: sterility, absence of mechanical impurities, stability, comfort, (isotonicity, optimal pH value), prolonged action.

Sterility. Eye drops, as well as concentrated solutions used for their preparation, should be made under aseptic conditions, followed by sterilization.

The method of sterilization of eye drops depends on the resistance of drugs in solutions to temperature effects. On this basis, medicinal substances can be divided into three groups:

1. Medicinal substances whose solutions can be subjected to heat sterilization without the addition of stabilizers (boric acid, nicotinic acid, sodium chloride, furatsilin, etc.)

2. Medicinal substances, the solutions of which can be subjected to heat sterilization after the addition of stabilizers (sulfacyl-sodium, etilmorphine hydrochloride, physostigmine salicylate, Pass-sodium, soluble salyuzid, etc.).

3. Medicinal substances whose solutions do not withstand heat sterilization (protargol, collargol, lidaza, himopsina, trypsin, penicillin, etc.) and are made aseptically without further sterilization.

Under aseptic conditions also prepared solutions of medicinal substances, sterilization regimes which have not been developed.

Eye drops may contain preservatives, buffers, prolongators. Preservation of eye drops provides for the prevention of the development of microorganisms in the dosage form during storage and use.

The mechanism of action of preservatives is reduced to disruption of the cell membrane, protein coagulation, blocking of free sulfhydryl groups, chemical antagonism. Characteristics of the preservatives and the requirements that are put forward to them are given on pp. 468-472.

In ophthalmic dosage forms used their limited range. Thus, from inorganic preservatives, boric acid is more often used in a concentration of 1.9–2% with a pH of about 5.0 (the optimum pH of ophthalmic solutions is 4.5–9.0). In addition, boric acid has buffer properties, prevents changes in the pH of the solution when adding a drug substance, especially from the group of alkaloids, give an acidic solution in solutions (pH below 4.0).

Of organic preservatives, b-phenylethyl alcohol - 0.3-0.5%, benzyl alcohol - 0.9%, esters of p-hydroxybenzoic acid: nipagin-0.05-0.23%, nipazol - 0, 03-0.08% or their mixture (nipagin - 0.18%, nipazol - 0.02%), levomycetin 0.15%, salts of quaternary ammonium bases (benzalkonium chloride, cetylpyridium chloride, dodecyl dimethylbenzylammonium chloride) at a concentration of 1 10000 .

Sorbic acid has found application with acids; it has no irritating and allergic effect on the skin and mucous membranes. Most effective at pH 3.0-4.0; has very strong fungicidal properties, is used in a concentration of 0.05-0.2%.

With organometallic preservatives, ethanolmercurium chloride 0.01% and merthiolate 0.005% are of interest.

Preservatives are added to the dosage form before sterilizing the solution. Due to the low solubility, nipagin and nipazol are dissolved in hot water at a temperature of 30-90 ° C and agitated vigorously .

Cetylpyridinium chloride when agitated in water gives abundant foam, therefore it is necessary to dissolve it in part of the water and carefully (preferably at a water temperature of about 50 ° C).

Stability. In the eye drops must be ensured the stability of medicinal substances. Heat sterilization and long-term storage of eye solutions in glass containers lead to the destruction of many medicinal substances (alkaloids, anesthetics, etc.). As a result of hydrolysis, oxidation, etc. Therefore, when making eye drops, and especially when they are sterilized, much attention should be paid to chemical glass stability, since alkaline glass (the presence of sodium silicate) gives an alkaline reaction to water, during sterilization, the pH can reach 10.0. The rate of destruction of drugs depends not only on the sterilization temperature, but also largely on the pH of the medium.

To store stability, most solutions require a low pH (around 5.0). On this basis, there is a need to manufacture eye drops on buffer solvents. When using buffer solutions, an increase in chemical stability, therapeutic activity, as well as a reduction in the irritant effect of ophthalmic solutions is achieved. SPh XI recommends using sterile isotonic solutions with preservative and buffering properties as solvents in the manufacture of eye drops. But these solutions can be used only as directed by a physician.

The choice of buffer solvent depends on the physicochemical properties of the drug substance. On this basis, they can be divided into two groups. The first group includes drugs, in solutions of which a pH of about 5.0 should be maintained. In this case, it is recommended to use an isotonic solution of boric acid (concentration of 1.9%), whose pH is below 5.0. The solution at the same time has low acidity, well neutralizes alkali, extracted from glass. At the same time, boric acid is neutralized and therefore does not cause a feeling of pain. Such a buffer solvent is recommended in the manufacture of solutions: pilocarpine hydrochloride, dikain, sovkain, mesatone and zinc salts. Eye drops, prepared on a 1.9% solution of boric acid, can be autoclaved at 100 ° C for 15 minutes.

The second group includes medicinal substances, in solutions of which a pH of about 6.8 should be maintained. In this case, phosphate buffer with a pH of 6.8 is recommended. isotonation with sodium chloride. Buffer composition:

A solution of monosodium phosphate 0.8% - 30 ml

A solution of disubstituted sodium phosphate 0.94% - 70 ml

Sodium chloride - 0.43 g

With this phosphate buffer, it is possible to prepare solutions of atropine salts, pilocarpine) and scopolamine. For these same drugs, borate buffer of the following composition is used:

Boric acid - 1.84 g

Sodium tetraborate - 0.14 g

Purified water (pH = 6.8) - 100 ml

However, it can only be used in the manufacture of ex tempore eye drops, because the stability of the drugs in it is maintained for 5-10 days.

There are also borate-acetate (1.9% solution of boric acid and 1.5% solution of sodium acetate) and borate-propionate (1.9% solution of boric acid and 2% solution of sodium propionate) buffer solutions. The preparation of eye drops using buffer solvents is carried out by selecting such a buffer solution, the composition and pH of which would ensure the stability of the drug.

The stabilization of the easily oxidizable salts of physostigmine salicylate and epinephrine hydrochloride in eye drops is accomplished by adding antioxidants (sodium sulfite, sodium metabisulfite, etc.). To increase the stability of 10, 20, and 30% sodium sulfacyl solutions, it is recommended to add respectively 1.0, 3.0, 5.0 g of sodium metabisulfite and 5, 17, and 18 ml of 0.1 M sodium hydroxide solution per 1 liter of solution, respectively.

The solution is sterilized at 100 ° C for 30 minutes. Packed in bottles for running. In a sealed package, the solution is stable for 18 months.

Solutions of sodium sulfacyl 10, 20 and 30%, intended for instillation in adults, as well as newborns for the prevention of gonorrhea, can be prepared as follows:

Sulfacyl sodium - 100.0 g, 200.0 g, 300.0 g

Sodium thiosulfate - 1.5 g

A solution of hydrochloric acid 1 M - 3.5 ml

Water purified to -1l

The vials are sealed under running-in, sterilized at 120 ° C for 8 minutes. The pH value of the solution is 7.5-8.5. The drug is stable for 1 month.

In the manufacture of eye drops in a sterile polymer packaging (tubes-kra-nets), 0.15 g of sodium thiosulfate and 3.5 ml of 1 M hydrochloric acid solution per 1 liter of solution are added as a stabilizer. A solution of ascorbic acid 2% is stabilized by adding sodium metabisulfite (0.1%) or sodium sulfite anhydrous (0.2%). In the case of the manufacture of intra-pharmaceutical preparations, water is saturated with carbon dioxide. Very often, the pH of ascorbic acid solutions has a low pH value (2.9-3.2), which causes discomfort in the patient. To eliminate them, excess acidity is neutralized by adding sodium bicarbonate to a pH of 6.6-7.1.

Eye drops - 0.02% riboflavin solution in combination with 2% potassium iodide and 2% glucose is stabilized with Trilon B in a concentration of 0.03%. The shelf life of these drops is 3 years.

Adding a complex stabilizer — a mixture of 0.1% sodium metabisulfite and 0.03% Trilon B — the shelf life of eye drops containing 0.02% riboflavin, 0.2% ascorbic acid, and 2% glucose, increases to 3 months while maintaining conditions of room temperature and up to 6 months at 4 ° C.

Other methods can be used to stabilize eye drops, namely: adding high polymers, complexones, making solutions in an atmosphere of inert gases, etc. P. These methods can be considered as the potential for a significant increase in the shelf life of the eye drops. Unstable eye drops are produced in the form of hanging dry (lyophilized) substances in vials and dissolved in a sterile solvent immediately before use. This applies to intermedin, acetylcholine and other drugs.

Prolongation of the therapeutic action of eye drops. The disadvantage of many drugs used in the form of aqueous solutions is a short period of their therapeutic action.

For example, the hypotensive effect of an aqueous solution of pilocarpine hydrochloride in a patient with glaucoma persists only for 2:00, which leads to 6-fold instillation of eye drops per day.

In this case, there are fluctuations in intraocular pressure. Frequent instillations of an aqueous solution wash away the tear fluid containing lysozyme, and thereby create the conditions for the occurrence of an infectious process.

This necessitated a search for substances that promote the prolongation (lengthening) of the therapeutic action of eye drops. The recommended viscosity of eye drops is 15-30 centipoise at a temperature corresponding to body temperature.

In order to prolong the action of eye drops, attempts were made to replace water with other solvents with viscosity, which slows down the rapid leaching of medicinal substances from the conjunctival sac. As such components previously used oils (refined sunflower, peach or apricot), tragakant and other substances. But for various reasons they did not receive distribution. High refractive index, chemical instability limited their application.

More effective prolongators for eye drops - synthetic hydrophilic high-medical compounds. SPh XI indicates that for the prolongation of the action of medicinal substances used in eye drops, cellulose derivatives may be included in the solvent.

Which like : methylcellulose (0.5-2%), sodium carboxymethylcellulose (0.5-2%), polivinol (1.5%), microbial polysaccharide aubazidan (0.1-0.3%), and polyglukin others. These substances do not irritate the eyes, in some cases, accelerate epithelization e roses th e hydrochloric cornea, as well as compatible with many drug substances and preservatives.

Despite the fact that the said prolongation guides the components included in the GF XI, they can be added dropwise to the eye only as directed by physician.

The prolongation of the effect of eye drops when using IUD is explained by an increase in the viscosity of the solution and its contact with the mucous membrane of the eye. Thus, methylcellulose in a concentration (0.2–2%) has a high viscosity and a refractive index equal to 1.336 (water refractive index = 1.333), which ensures normal vision. It is used to make eye drops with pilocarpine hydrochloride, homatropine hydrobromide, etylmorphine hydrochloride, zinc sulfate, etc.

Recently, however, there has been a tendency to reduce the production of methylcellulose-based eye drops. This is due to the fact that it inhibits the regeneration of the corneal epithelium, and with subconjunctival administration leads to the growth of tissue. Because as a prolongator in eye drops, sodium carboxymethylcellulose is highly soluble in water and is easily mixed with tear fluid. For example, the number of installations of a 2% solution of pilocarpine hydrochloride prepared from 2 and -sodium carboxymethylcellulose, in a number of patients with glaucoma, was reduced to three times per day instead of six instillations of an aqueous solution.

Significant advantages compared with derivatives of methylcellulose has polyvinyl alcohol (PVA). It does not irritate the mucous membrane of the eye, does not violate the integrity of the corneal epithelium, and, unlike methylcellulose solution, accelerates epithelialization of the eroded cornea.

PVA solutions are compatible with a large number of medicinal substances used in ophthalmology (antibiotics, sulfonamides, salts of alkaloids, zinc sulfate, etc.). At the same time, some substances (resorcinol, boric acid, sodium tetraborate) can cause healthy PVA and make it impossible to use it.

Polyacrylamide was also proposed as a prolongator, the pH of which 1% of the solution is 5.0-7.0. Solutions withstand sterilization, compatible with many medicinal substances, have no irritating properties. 1% solution of polyacrylamide can be used as a solvent for eye drops pilocarpine hydrochloride, atropine sulfate, dikaina, sulfapiridazin sodium, scopolamine hydrobromide. Polyacrylamide has an interferogenic activity, that is, it promotes the production of interferon (an effective means of antiviral therapy) in the absence of a toxic effect on the macroorganism .

A good solvent for obtaining eye drops with prolonged action is a 25% solution of polyethylene oxide-400. It not only prolongs the period of therapeutic effect, but also increases the bioavailability of medicinal substances (dikaina, novocaine, etc.).

Fundamentally new opportunities for the use of medicinal substances gave the use in pharmacy of new polymeric materials, including biosoluble.

Thus, the staff of the Moscow NDI eye diseases. Ophthalmic polymeric films prepared from a 10% solution of polyvinyl alcohol (PVA) and impregnated with

antibiotics, pilocarpine and corticosteroids have been proposed to Helmholtz. However, these films, although they continued the effect of medicinal substances and kept storage for 2 months, had a significant drawback - they did not dissolve in the conjunctive cavity, but only swell, increasing in size. To eliminate this drawback, the proposed films with a biosoluble polymer, for example, eye films with a phenolic hydrophilic propolis preparation (developed by Acad. A. I. Tikhonov).

Due to the prolonged action to obtain a therapeutic effect, the ocular drug films can be applied once a day.

The advantages of eye films are high drug stability, ease of use, hygiene, portability and effectiveness of drugs.

In some countries, in the manufacture of ophthalmic drugs, various polymeric solutions are used that prolong the therapeutic action of medicinal substances. For example, in Germany they use Rosannosy "Izanto", liquid base "Liquidfilm", capable of covering the surface of the eye with an invisible thin film, more than three times extending the therapeutic effect of dissolved medicinal substances.

Isotonicity Many eye drops cause discomfort during instillation (burning or pain). In most cases, the discomfort is due to the disparity between the osmotic pressure and the pH value of the eye drops with the osmotic pressure and the pH value of the tear fluid. Eye drops should be isotonic us lacrimal fluid man and respond to the osmotic pressure of sodium chloride solutions at concentrations of 0.9 (0.2% (0.7-1.1%) that is approximately 286 mOsm / kg. In some cases, permitted the use of hypertonic or hypotonic solutions, which should be indicated in their own articles.

Depending on the magnitude of the osmotic pressure, eye drops can be divided into 3 groups:

1. Eye drops, the osmotic pressure of which is lower than 0.7% of the equivalent concentration of sodium chloride - hypotonic solutions, must be compounded by the calculated amount of sodium chloride. It is especially important that the washings for the eyes be isotonic.

2. Eye drops, the osmotic pressure of which is higher than 1.1% of the equivalent concentration of sodium chloride, and not isotonized, because they are hypertonic.

3. Eye drops, the osmotic pressure of which is in the range of 0.7-1.1% of the equivalent concentration of sodium chloride, and not isotonic because there is isotonic.

Eye drops are not isotonic if colloidal medicinal substances are prescribed (Collargol, protargol), because isotonizing substances, being strong electrolytes, can cause coagulation.

Sodium chloride, sodium sulfate, sodium nitrate, boric acid, glucose are used to isotonize eye drops, taking into account their compatibility with medicinal substances. Boric acid for isotoning is advisable to use in the manufacture of solutions of drugs that are salts of strong acids and weak bases, because it not only suppresses their hydrolysis, but also provides a preservative effect. Sometimes it is

advisable to apply glucose for isotoning, because it is compatible with a large number of medicinal substances.

Isotonization of eye drops of sodium chloride, sodium sulfate and sodium nitrate is carried out by a pharmacist without a doctor's instructions, and boric acid and other substances only by agreement with a doctor.

The isotonic concentration of eye drops can be calculated by the same methods as in solutions for injection.

Lack of mechanical inclusions. Eye drops in the form of aqueous solutions of medicinal substances should be carefully filtered after production, as the presence of suspended particles, hair, etc. may damage the cornea and mucous membranes of the eyes.

Eye drops in pharmaceutical conditions are filtered through paper filters with ashless filter paper, does not change during sterilization. When making eye drops in large volumes (Intra drug preparations), they can be filtered through a No. 3 glass filter or membrane - with simultaneous sterilization (solution loss is 0.5%).

When mass production of eye drops in pharmacies, it is advisable to use devices for their filtration and subsequent packaging.

Technology eye drops. Taking into account the requirements for eye drops, their technology is similar to the technology of injection solutions.

All dosage forms for the treatment of eye diseases are prepared under aseptic conditions in compliance with the requirements of the current technical and technical documentation for sanitary treatment in pharmacies. But since aseptic manufacturing conditions do not ensure complete sterility of drugs, eye drops and lotions of heat-stable substances must be sterilized.

It should be noted that eye drops must not only be sterile, but also be kept sterile during their use.

Common in the manufacture of ophthalmic and injectable dosage forms isotonization, stabilization, sterilization and preservation.

Of great importance for eye drops is the observance of the accuracy of the concentration of solutes. These requirements arise due to the fact that eye drops are prescribed in small quantities.

In the manufacture of eye drops, and, mainly, during filtration, significant losses of substance occur due to its adsorption on filter materials (through a dry simple filter - up to 4.7%, and through a folded one - up to 3%), as well as due to dilution the original solutions when filtering them through paper filters, pre-washed with water.

In order to minimize the loss of drug substance in the manufacture of eye drops, use the following techniques.

1. The drug substance, soluble in water, is dissolved in a part (half amount) of the solvent and the solution is filtered into a vial for tempering through a folded filter and cotton wool rinsed with sterile water for injection, and then the filter is washed with the amount of solvent remaining. For example:

Rp .: Solutionis Pylocarpini hydrochloridi 1% 10 ml
Natrii chloride qs,

ut fiat solutio isotonica
Da. Signa. 2 drops in both eyes.

Eye drops with a highly soluble medicinal substance of the list A. First, do the calculations necessary for isotoning the solution specified in the recipe.

The table determines the isotonic equivalent of pilocarpine hydrochloride in sodium chloride, equal to 0, 22. Next, find the amount of sodium chloride, equivalent to 0.1 g of pilocarpine hydrochloride:

1,0 pilokarpinu gidrokhlorida- 0,22 NaCl
0.1 pilokarpinu hydrochloride - 0,022 NaCl

10 ml of the solution must be sodium chloride:

$$x = \frac{0,9 \times 10}{100} = 0,09 \text{ г}$$

Determine the amount of sodium chloride needed to isotone a 1% solution of pilocarpine hydrochloride:

0.09-0.022 = 0.068 = 0.07 g

The manufacture is carried out in an aseptic room or box. Measure 10 ml of water for injection. In a sterile dry stand in half the amount (5 ml) of water for injection dissolve 0.1 g of pilocarpine hydrochloride (prepared on demand) and 0.07 g of sodium chloride. The solution is filtered into a vial for dispensing through a sterile, pre-washed folded filter and cotton wool. Wash the filter with the remaining water for injection (5 ml). Check the qualitative and quantitative content of pilocarpine hydrochloride, as well as the purity of the solution. If necessary, filtered again through the same filter and cotton. The solution is hermetically sealed and sterilized. After sterilization, the eye drops are monitored for the absence of mechanical impurities and are issued for tempering with an additional label “handle with care”, the signature is written out, the bottle is sealed.

2. In cases when there is insufficient half the amount of solvent to dissolve the drug substance, the substance is dissolved in the entire prescribed amount of solvent and filtered into a measuring cylinder through a dry filter and cotton wool, and the amount of water that was not enough is added through the same filter and cotton wool to the required amount volume of solution.

As for the accuracy of concentration, the first method will be more accurate concentration, since more water is used to flush out the adsorbed substance.

3. If dry medicinal substances are prescribed in the amount of less than 0.05 g, then their concentrated solutions are used. In this case, the calculated amount of concentrated solutions and water is measured in a vial for tempering, observing the conditions of asepsis.

Rp .: Riboflavini	0.001
Acidi ascorbinici	0.02
Kali and iodide	0.3
Sol. Acidiborici	2% 10 ml

Misce. Da. Signa. 2 drops 3 times a day in both eyes.

The solution is hypertonic due to the prescribed quantities of potassium iodide and boric acid. All ingredients are used in the form of sterile concentrated solutions.

3.3 ml of sterile water for injection, 5 ml of a 0.02% solution of riboflavin in combination with boric acid 4%, 0.2 ml of a 10% solution of ascorbic acid, 1.5 ml of a 20% solution of potassium iodide. The solution is controlled for the absence of mechanical impurities and clog under running.

If it is necessary to manufacture an intra-pharmaceutical preparation of eye drops with medicinal substances discharged in the amount of less than 0.05 g, they can be prepared from dry substances, but the solution in this case will be prepared in 10 or 20-fold amount. For example:

Rp .: Riboflavini 0.002
Acidi ascorbinici 0,2
Solutionis Kalii iodide 2% 10 ml
Glucosi qs ut fiat solutio isotonica
Misce. Da. Signa. 2 drops 3 times a day in both eyes.

The required amount of anhydrous glucose for isotoning the prescribed solution is 0.11 g.

The solution is prepared in a 20-fold amount. It should be borne in mind that the joint sterilization of ascorbic acid with potassium iodide causes a change in the color of the solution as a result of the redox reaction.

Therefore, this method of making drops is recommended: 0.04 g of riboflavin is dissolved by heating in 200 ml of water for injection, the solution is cooled and 0.4 g of ascorbic acid and 2.2 g of glucose are dissolved in it, filtered and sterilized by flowing steam at 100 ° C 30 minutes. After cooling the solution under aseptic conditions, 4.0 g of potassium iodide is added, the solution is filtered into 10 ml vials, sealed and rolled in metal caps.

Rp .: Solutionis Riboflavini 0.01% 10 ml
Acidi ascorbinici 0.05
Misce. Da. Signa. 2 drops in both eyes.

Prescribed quantities of medicinal substances have practically no effect on the osmotic pressure of the solution; therefore, it is advisable to prepare it with a 0.9% solution of sodium chloride.

3.6 ml of sterile water for injection, 0.5 ml (10 drops) of a 10% solution of ascorbic acid, 5 ml of a 0.02% solution of riboflavin and 0.9 ml of a 10% solution of sodium chloride (or 0, 09 g of sodium chloride). The bottle is closed with a sterile rubber stopper, looking at the solution for the absence of mechanical impurities and clog under run-in.

Eye drops with ethacridine lactate should be isotonuvate 2% solution of boric acid, as it is incompatible with sodium chloride. Chlorides cause precipitation of ethacridine. The technology is ordinary.

Eye drops TIO-TEF. Thiophosphamide is prescribed in eye drops at a concentration of 1: 500, 1: 1000, 1: 2000. It is used in oncological practice. Drops are prepared using Ringer's solution as a solvent.

Eye drops containing sodium salts of norsulfazole and sulfapyridazin. For the treatment of eye infections, norsulfazole sodium 10% and sodium sulfapyridazine 10 and 20% are used.

Eye drops are prepared under aseptic conditions. When capping the vials with rubber stoppers of the I-52, I-51, IR-119 brands after sterilization at 120 ° C for 8 minutes, a change in the color of the norsulfazole sodium solution to yellow-brown color is observed, the cause of which is its interaction with the stoppers of these brands. To prevent direct contact of the solution with the plugs, one should place non-lacquered cellophane gaskets (GOST 7730-74), previously washed with purified water, under them. The shelf life of a 10% solution of norsulfazol sodium when stored in a dark place in the refrigerator for 30 days. and at room temperature - 10 days.

Ophthalmic solutions are used in the form of lotions, irrigation solutions (for irrigation in ophthalmology), solutions for cleaning, disinfecting and storing soft contact lenses. The requirements for eye solutions are basically the same as in eye drops: they must be sterile, stable, and free of mechanical impurities. The requirement that the lotions and irrigation solutions are isotonic is even more important than for droplets, because a larger amount of fluid collides with the eye.

The technology of eyewash and washes is similar to eye drops.

For processing and storage of contact lenses, solutions are used, which include antiseptic substances, non-ionic surfactants, polyvinyl, cellulose derivatives, polyethylene glycol. isotonic buffer solvents and other substances. For example, the Reno Multiplus universal isotonic solution from Bausch & Lomb (Italy) contains boric acid, sodium edetate, sodium tetraborate and sodium chloride. Active ingredients: polyaminopropyl-biguanide 0.0001%, hydroxyalkylphosphonate 0.03% and Poloxamine 1%. The drug cleans, removes impurities, protein and other deposits from soft contact lenses, destroys pathogenic microorganisms on their surface. Used for washing, moistening and storing contact lenses.

Suspensions and emulsions. Ocular suspensions are thin suspensions of medicinal substances in an aqueous or oily environment. Get their dispersion or condensation method. The main requirement for both water and oil emulsions is the required particle sizes. They should not exceed 30 microns.

Ophthalmic suspensions are manufactured in the factory. At production in drugstores - Ready suspensions dissolve with water.

Ocular emulsions are prepared by emulsifying aqueous solutions of drugs in sterile non-aqueous solvents. Mixed emulsifiers are used to stabilize ophthalmic emulsions.

Eye ointments (UNGUENTA OPHTALMICA SEU OCULENTA)

Eye ointments are designed for application to the conjunctiva of the eye tab for the lower eyelid with special spatulas. The composition of ointments varied. Often

there are ointments with antibiotics, sulfa drugs, mercury oxide, etc. Apply eye ointment for anesthesia, the expansion or contraction of the pupil, a decrease in inflammatory processes and a decrease in intraocular pressure.

The conjunctiva of the eye is a very delicate sheath, therefore eye ointments are divided into a separate group and additional requirements are imposed on them:

- Eye ointments should be prepared under aseptic conditions;
- The ointment base should not contain any impurities, should be neutral, sterile, evenly distributed over the mucous membrane
- Medicinal substances in eye ointments should be in the optimum degree of dispersion to avoid damage to the mucous membrane;
- Ophthalmic ointments should be easily and arbitrarily distributed over the moist mucous membrane. The range of bases used for eye ointments is small and expands very slowly. Most often used Vaseline varieties "for eye ointments." It is sufficiently resistant to the effects of the environment, indifferent to many medicinal substances, has no irritating properties. And yet, as an independent basis, it is not entirely convenient, as it does not mix well with the tear fluid.

If the recipe does not specify a base, then in the absence of an approved NTD for this recipe, in accordance with GF XI, a base consisting of 10 parts of anhydrous lanolin and 90 parts of Vaseline (“For eye ointments”) that do not contain reducing substances is used.

In this basis, lanolin helps to fix the ointment on the mucous membrane, as well as the complete absorption of medicinal substances. The components are fused in a porcelain (porcelain) cup when heated in a water bath. The molten base is filtered through several layers of gauze (in a drying cabinet at a temperature of 90-100 ° C) and 10.0 g are packed in dry sterilized jars, sealed and sterilized in an air sterilizer at 180 ° C for 30 minutes at 200 ° C for 15 minutes. The finished intramural basis is stored in a hiding place from light at a temperature not higher than 25 ° C for 2 days or at 3-5 ° C - 30 days.

In the absence of petrolatum “for eye ointments”, ordinary petrolatum is cleaned: 2% of activated carbon is added to the melted petroleum jelly in an enamel bowl, and the mixture is heated to 150 ° C with occasional stirring for 1-2 hours. Hot Vaseline is filtered through a filter paper and poured into sterile jars. Conduct chemical analysis for the absence of organic impurities. The petrolatum thus purified is odorless, slightly yellowish in color.

Use as a basis for eye ointments of freshly prepared glycerin ointment is not always advisable, because it has a strong water-absorbing effect and the irritant effect associated with it. Another disadvantage of the ointment is fast syneresis during storage.

Recently, gels of some high-molecular compounds (gums, sodium alginate, sodium carboxymethylcellulose, etc.) have been proposed as a basis for eye ointments. Basics are hydrophilic, so well distributed over the mucous membrane of the eye, easily give medicinal substances. But they have a significant drawback - they quickly undergo microbial spoilage and therefore require the addition of preservatives.

It should not be used as a base for eye ointments to quickly burn fats, as they are irritating; soap bases, which, due to the presence of surface-active properties, sharply reduce surface tension and exhibit an irritant effect; gelatinous bases, is a favorable nutrient medium for microorganisms.

The use of polyethylene oxide or glycolic media is not recommended due to the sharp difference in osmotic pressure. Emulsion bases of the type O / B are not very suitable due to a strong blurred vision. It is believed that in order to achieve an optimal effect on emulsion bases, it is better to give preference to the manufacture of suspension ointments, since the dissolution of medicinal substances in the aqueous phase of the emulsion bases may cause their subsequent recrystallization. In addition, aqueous bases in eye ointments are subject to stabilization.

The technology of eye ointments is similar to the technology of conventional ointments, but with observance of the conditions of asepsis. All auxiliary materials, ointment bases, medicinal substances that withstand high temperatures, cans for dispensing are sterilized by the methods specified in the Global Fund XI.

The need for aseptic manufacturing conditions is due to the fact that ointments may be suitable medium for the existence of microorganisms. Various bacteria, bacilli, mold and yeast fungi were found in non-sterile ointments with atropine sulfate, pilocarpine hydrochloride, xeroform, mercury oxide yellow. It should be noted that some sulfa drugs, which are part of the ointments, do not show a bacteriostatic effect on saprophytes and pathogenic microorganisms.

Microorganisms fall into the ointment of excipients, mainly from non-sterile bases. This is explained by the fact that carbohydrates, fats, oils, fat-like and especially hydrophilic substances are a good medium not only for the storage of microorganisms caught in them, but also for the growth of some. Therefore, when making eye ointments,as well as eye drops, it is advisable to add preservatives, as indicated in the SPh XI and in the pharmacopoeia of foreign countries. For this proposed benzalkonium chloride 1: 1000, a mixture of nipagin (0.12%) and nipazol (0.02%), 0.1-0.2% sorbic acid and other preservatives allowed for use.

An important factor in the manufacture of eye ointments (as well as dermatological) is to achieve the optimal degree of dispersion of medicinal substances administered (see Page 378). The required dispersion of substances is achieved by pre-dissolving or thoroughly rubbing them with a small amount of liquid, coming to the base.

Substances soluble in water (salts of alkaloids, Novocain, Protargol, Collargol, Resorcinol, Zinc Sulfate, etc.) are dissolved in a minimal amount of freshly made sterile water for injection, and then mixed with an ointment base. To speed up the dissolution of protargol, it is advisable to pre-moisten with a few drops of glycerin.

Substances that are insoluble or sparingly soluble in water and in the base (mercury oxide is yellow, kalomel, xeroform, zinc oxide, copper citrate, etc.), are introduced into the composition of eye ointments in the form of fine powders after thorough grinding with a small amount of liquid paraffin, glycerin , water or part of the molten base, if the drug substances more than 5%. The choice of fluid depends on the base used.

Substances soluble in the base are dissolved in a liquid suitable for the base or in a part of the molten base, if there are more than 5%.

Own technology of eye ointments. Prescription eye ointments varied. These are mainly two-phase and more complex dispersed systems.

Rp .: Hydrargyri oxydi fiavi 0.5
Olei Vaselini 0,5
Vaselini 20.0
Lanolini 4.0
Misce, fiat unguentum
Da. Signa. Mercury ointment yellow.

Suspension-type eye ointment with a solids content up to 5%, which contains a highly colored substance - mercury oxide yellow.

Ointment is prepared under aseptic conditions. In a sterile mortar, carefully rub 0.5 g of mercury yellow oxide in a dry form, then with liquid paraffin (0.5 g is added dropwise with a calibrated pipette). Then, parts are sterilized with petrolatum and anhydrous lanolin, pre-weighed into a sterile parchment capsule. All thoroughly mixed until uniform. Check the quality of the prepared ointment according to NTD. Released in a jar of dark glass.

PWC
Date Recipe No.
Hydrargyri oxydi flavi 0,5
Olei Vaselini gtts XV (0,1 = 3 krupl)
Vaselini pro oculi sterile 20.0
Lanolini anhydrici sterile 4.0
Addita aseptice m $_{zag.}$ = 25.0
Prepared: (signature)
Checked: (signed)

Sometimes the official ointment is discharged without specifying the base and constituent components, for example:

Rp.: Unguenti Hydrargyri oxydi flavi 10.0
Da. Signa. Mercury ointment yellow.

In this case, the ointment is prepared on the basis that specified in the documentation. The number of ingredients is determined in accordance with the pharmacopoeial prescription:

Mercury oxide yellow
Vaseline oil equally 2 parts
Vaseline (grade for eye ointments) 80 parts
Anhydrous lanolin 16 parts.

Calculations: Mercury oxide yellow	0.2 g
Vaseline oil	0.2 g
Vaseline	8.0 g
Anhydrous lanolin	1.6 g

Rp.: Pilocarpini hydrochloride	0.2
Vaselini	3.0
Lanolini	3.0

Misce, fiat unguentum
Da. Signa. Eye ointment.

Ointment emulsion with a toxic water-soluble drug substance. In a sterile mortar, 0.2 g of pilocarpine hydrochloride is triturated with 0.9 ml (18 drops) of sterile water for injection (30% by weight of prescribed aqueous lanolin) and mixed with pre-sterilized anhydrous lanolin and petrolatum to obtain a homogeneous mass. Let go in a glass jar with a lid, sho is screwed, in a sealed form.

Rp.: Unguenti Zinci sulfatis 0.5% 10.0
Da. Signa. Lay for the eyelid of the right eye 2 times a day.

Ointment-emulsion with a substance in the general list, soluble in water. In aseptic conditions, in a sterile mortar, dissolve 0.05 g zinc sulfate in a few drops of sterile distilled water, add 10.0 g of sterile base for ophthalmic eyes, mix thoroughly. The ointment is transferred to a sterilized glass jar, which is sealed with a plastic screw cap, with a sterilized gasket and made to release.

QUALITY CONTROL, STORAGE AND VACATION OF EYE MEDICINE FORMS

Rational packaging of eye drops is one of the most important conditions ensuring the extension of their shelf life.

Bottles and droppers designed for dispensing and storing eye drops, as well as cork should not change their quality. They must be clean, chemically resistant and meet the requirements of the relevant GOST or other technical documentation.

For dispensing and storage of eye drops, use bottles of neutral glass NS-1 (bottles for antibiotics), sealed with rubber stoppers (I-54 or I-51) under running in aluminum caps. Such packaging with repeated use can lead to microbial contamination, since the opening of the vials immediately leads to a violation of their sterility. Packaging for eye drops should provide sterility and be comfortable to use. These requirements are met by special bottles with pipettes made of polyethylene, mounted in a screw cap. The presence of a standard pipette allows you to accurately and easily dispense solution.

Eye drops, prepared in a pharmacy, are decorated with a basic pink label with the words “eye drops” and the additional “Store in a cool, dark place”, “Sterile” or “Prepared aseptically”.

Ophthalmic ointments are packed in 10.0 g of dry sterilized BVS cans and sealed with plastic caps that are screwed on and sterilized with parchment pads. Ophthalmic ointments are stored in accordance with the physicochemical properties of the substances in their composition at a temperature not exceeding 25 ° C or in a refrigerator (3-5 ° C) for 10 days. The shelf life of pilokarpin ointments 1%, 2% and thiamine 0.5%, 1% at a temperature of 3-5 ° C is 30 days.

When you leave the ointment, you must use a sterile container and always complete with a special stick for applying ointment. Convenient form of packaging tubes made of tin or aluminum with a screw cap. Fill tubes with special sterilized instruments, functioning with a syringe. Metal tubes should not be used for packaging ointments containing ingredients that can interact with metals. They are hygienic when used and allow longer to maintain sterility of the ointment. Tubes can be equipped with screw- on tips that allow injecting ointment for the eyelid. Recently, polymeric materials for disposable packaging of ointments are becoming more common.

Eye ointments are made with the labels “Full-time ointment”, additional “Keep in a cool, dark place”, “Prepared aseptically”.

Evaluation of the quality of eye drops, lotions and ointments is carried out in accordance with the regulatory documentation, that is, check the recipe, passport, packaging, design, color, absence of mechanical inclusions, deviation in volume (solutions) or mass (ointment). Eye ointments are checked for the same indicators as dermatological ointments (see. 22).

Quality control of eye drops is carried out in pharmacies with an analyst for all solutions, and in pharmacies without an analyst - for eye drops with atropine sulfate, silver nitrate, pilocarpine hydrochloride.

IMPROVEMENT OF THE TECHNOLOGY OF EYE MEDICINAL FORMS

In order to improve the quality and technology of ophthalmic dosage forms for filtering, dosage, packaging and sterilization of eye drops, compact high-performance instruments and devices should be developed for use in pharmacies and small industries. The quality and effectiveness of ophthalmic dosage forms will significantly improve with the introduction of new, more advanced excipients: a bio-adequate natural collagen polymer, aubazidan polysaccharide, carbopol (a copolymer of acrylic acid with polyalkyl polyol ether polyhydric alcohols), preservatives, stabilizers, buffer substances, prolongators, and t. P.

A radical improvement in the quality of eye drops, solutions, ointments and other forms is associated with the development of single-use packaging; the creation of disposable dosage forms: drug films (OLP), lamellae, aerosols, trituration tablets. Each of these dosage forms has its advantages. For example, aerosols provide rapid absorption of drugs; OLP, lamellae (gelatinous oval discs with a diameter of 3 mm) contribute to the continuous and long-term supply of the drug to the conjunctiva of the eye.

For prolongation of the therapeutic effect of the drug are also used semi-permeable contact lenses. Synthetic polymers are used for their production, in particular, polyglyceryl methacrylate.

More sophisticated and complex eye dosage forms include eye drops and solutions in a lyophilized form, highly dispersed emulsions, ophthalmic rods and other forms. Ophthalmic rods are proposed to be made from acrylic polymer. A medicinal substance is applied to one end of a 50 mm long rod. The rod is packaged in an air-tight polypropylene film and sterilized using ethylene oxide or a radiation method. The rod is applied to the conjunctiva of the eye for 2-3 seconds, while a thin layer of the drug substance dissolves in the tear fluid.

For use in ophthalmology again suggested patches. For example, a patch for the treatment of allergic conjunctivitis and other eye diseases is obtained by impregnating the corresponding substrate with a solution of ascorbic acid in a buffer mixture of sodium bicarbonate and boric acid.

The development of adequate rapid control methods will contribute to the improvement of the technology of eye dosage forms.

Antibiotics

Drugs containing antibiotics are usually presented by injectable dosage forms, oral, rectal and vaginal. In the extrusion formulations of pharmacies with antibiotics, dosage forms are prepared mainly for external use: eye drops, lotions, drops for the ears, nose, ointment, suppositories, powders (powders).

The constancy of the chemical composition, physical condition and pharmacological action of antibiotics should be stored both in the manufacture of medicines, and during their use by patients.

Requirements for antibiotic dosage forms:

- Manufacturing must be carried out under aseptic conditions. This is due to the fact that the antibacterial activity of antibiotics is reduced under the influence of microorganisms or their enzymes.
- The form of the dosage form must ensure the stability of the antibiotic during the process of technology and during storage;
- The dosage form should provide the necessary concentration of the antibiotic in the macroorganism at its minimum dosage.

Calculations of antibiotic activity of antibiotics. Antibacterial activity of antibiotics is expressed in units of action (AU), which correspond to specific weight parts of a chemically pure preparation, established by the method of biological standardization.

In some antibiotics (streptomycin, erythromycin, etc.), the unit of action corresponds to 1 μg of a chemically pure drug in the form of a base, acid, or salt.

If there is no such correspondence, then when recalculating the ED of antibiotics into weight ratios, you should use the data given in the corresponding private articles of the Global Fund, which indicate the relationship between the mass and units of action of some antibiotics.

Thus, 1 U of chemically pure crystalline benzylpenicillin corresponds to 0.0005988 mg of pure crystalline sodium benzylpenicillin salt.
In 1 mg of chemically pure sodium salt, theoretically 1670 ED. If 200,000 ED of benzylpenicillin is written out in the recipe, by the mass this amount will be:

200,000: 1670 = 120 mg = 0.12 g .

Or:

1 млн. ОД – 0,6 г бензилпенициллину

200000 ОД – x

$$x = \frac{200000 \times 0,6}{1000000} = 0,12 \text{ г}$$

Powder technology with antibiotics. Sophisticated antibiotic powders are used in surgical, dermatological and dental practice. they are prepared according to the general rules for the manufacture of complex powders, taking into account the properties of the incoming ingredients.
Antibiotics are added to sterilized and cooled powders under aseptic conditions.

Rp: Streptocidi
Sulfadimezini aa 2.0
Misce fiat pulvis subtilissimus
Da. Signa. For injection into the nasal cavity every 2 hours.

In a sterile mortar, rub down 2.0 g of streptocide with 20 drops of alcohol, then add 2.0 g of sulfadimesin. The mixture is poured onto the capsule, leaving approximately 0.2 g in a mortar. Then 0.2 g of ephedrine hydrochloride is introduced into the mortar, mixed thoroughly in several stages, and thoroughly rubbed, mixed with the mixture previously poured onto the capsule. The resulting mixture is sterilized at 150 ° C for 1:00, after which 0.12 g of sodium benzylpenicillin is added under aseptic conditions, following the rules of mixing.

Technology of liquid dosage forms. Liquid drugs with antibiotics are prescribed for internal (solutions, suspensions, less often - emulsions) and external use (nasal drops, lotions, eye drops). Of the drugs for external use 1/3 accounted for eye drops.

As solvents use purified water, alcohol, glycerin, vegetable oils. Solutions are prepared according to the general rules of manufacture. Feature - compliance with aseptic conditions. Filtration of solutions through normal filter paper should be avoided.

In most cases, pharmacies prepare only a sterile solvent, and dissolves are performed immediately before use.

Aqueous solutions. Sodium benzylpenicillin solutions. For their manufacture as solvents use isotonic sodium chloride solution: glucose solution; Novocain solution (0.25 and 0.5%). It should be borne in mind that solutions of novocaine with stabilizers have a pH of 3.8-4.5, glucose solutions 3.0-4.0. At the indicated pH values, the benzylpenicillin solutions are inactivated at normal temperature.

Therefore, benzylpenicillin must be dissolved immediately before administration. The solution is not consumed; it is not subject to further use, since benzylpenicillin is inactivated when it is withdrawn.

Rp .: Benzylpenicillini-natrii 200000 ED
Solutionis Natrii chloridi isotonicae 150 ml
Misce. Da. Signa. For industrial injuries.

First, prepare a sterile isotonic solution of sodium chloride, in which 0.12 g of benzylpenicillin sodium salt is dissolved.

Solutions of polymyxin sulfate. For production as an solvent, an isotonic solution of sodium chloride is used (immediately before use at the rate of 10,000-20000 IU per 1 ml of isotonic sodium chloride solution) or a 0.5-1% solution of novocaine.

Rp .: Polymixini M sulfatis 200000 ED
Solutionis Natrii chloridi isotonicae 200 ml
Misce. Da. Signa. Lotion for wetting tampons

Rp .: Laevoraycetini 0.02

By chemical structure, polymyxin is a complex compound comprising polypeptide residues. Different polymyxins have an additional letter. Polymyxinsulfate is applied topically (with weakly healing wounds, necrotic ulcers, bedsores, purulent otitis, inflammatory diseases of the eyes and ears) and inside. Parenteral administration is not allowed (renders nefro-and from effect).

Polymyxin Sulfate is stable in an acidic environment and decomposes into an alkaline one. The antibiotic activity is 8000 IU in 1 mg. According to this recipe, 0.25 g of antibiotic (2000000 IU) is dissolved in aseptic conditions in sterile isotonic solution of sodium chloride.

Eye drops. Eye drops with chloramphenicol. Solutions are prepared in fresh water for injection or isotonic sodium chloride solution under aseptic conditions. The dissolution of the antibiotic can be carried out by heating.

Levomycetin is used to treat typhoid and paratyphoid fever, pneumonia, dysentery, brucellosis, gonorrhea, trachoma, and other diseases caused by microorganisms that are susceptible to it. It is effective against rickettsia, spirochetes, pathogens of trachoma, lymphogranuloma venereum, etc. It affects bacteria strains resistant to penicillin, streptomycin, sulfonamides. An antibiotic is used in tablets and capsules, rectally in suppositories and locally in the form of aqueous solutions.

Levomycetin - a broad-spectrum antibiotic. However, it may not always be used simultaneously with other antibiotics. For example, it should not be used simultaneously with benzylpenicillin - the combination leads to a weakening of the therapeutic effect, and the treatment of pneumonia is antagonistic effect.

It should not be combined with drugs that inhibit blood formation (sulfonamides, pyrazoline derivatives, cytostatics). With simultaneous use of chloramphenicol and butamide, cases of hypoglycemic shock have been reported. The use of chloramphenicol in psoriasis, eczema, fungal and other skin diseases, pregnancy is contraindicated.

Rp.: Novocaini 0.1
Solutionis Acidi borici 2% 10 ml
Misce. Da. Signa. 2-3 to ap and 3 times a day in both eyes.

Recipe is compatible due to the presence of boric acid, which improves the solubility of chloramphenicol and increases the stability of novocaine. Boric acid and chloramphenicol (thermostable substance) is dissolved in warm water for injection, the solution is cooled and novocaine is dissolved in it. Sterilized by fluid steam at 100 ° C - 30 minutes. To increase the stability of the solution, you can add as a stabilizer 1 drop of a 0.1 M hydrochloric acid solution.

In ophthalmology, chloramphenicol is often combined with riboflavin, ascorbic acid and glucose. To improve the solubility of chloramphenicol and isotoning drops with chloramphenicol, you can use a sterile borobufer solution of the following composition: sodium tetraborate 0.02 g, sodium chloride 0.02 g, boric acid 0.11 g, water for injection to 10 ml. In the prepared borobufer solution dissolve chloramphenicol.

An aqueous solution of chloramphenicol for a long time retains stability (about 2 years), if stored at a temperature of + 5 ° C.

Eye drops with streptomycin are prepared under aseptic conditions on sterile isotonic solution of sodium chloride at a concentration of 10,000-100,000 IU of streptomycin per 1 ml of solution.

Streptomycin is often combined with penicillin and biomycin. Streptomycin stable at pH 7-8; when heated to 100 ° C, it is inactivated, so its solutions cannot be sterilized. Streptomycin can not be combined with acids, salts of alkaloids.
Drops with streptomycin do not lose activity for one month at room temperature.

Eye drops with biomycin (chlortetracycline hydrochloride) are prepared from a water-soluble preparation under aseptic conditions on a sterile buffer solution with this prescription:

Rp.: Biomycini 50000 ED
Natrii chloridi Natrii tetraboratis aa 0.05
Aquae pro injectionibus 10.0
Misce. Da. Signa. Eye drops.
Such drops persist for 2-3 days.

Ear and intranasal drops are prepared at a concentration of 10,000-100,000 U / ml. The solvent is water for injection, isotonic sodium chloride solution, as well as solutions of the respective medicinal substances.

Often, ephedrine hydrochloride is prescribed in nasal drops along with benzylpenicillin, and 0.1% solution of epinephrine hydrochloride. Such recipes can

not be considered rational, since these substances in 4:00 inactivate the antibiotic by 40%. Inactivation can be slowed down by storing the solutions in the refrigerator.

Rp .: Benzylpenicillini-natrii 100000 ED
Streptomycini sulfatis 200000 ED
Solutionis Natrii chloride 0,9% 20 ml
Misce . Da. Signa . Nasal drops.

In a glass containing 200,000 U of streptomycin sulfate, make 20 ml of sterile isotonic sodium chloride solution. The resulting solution is poured into a glass containing 100,000 IU of penicillin.

To increase the stability of some antibiotics (penicillin, chloramphenicol, bitsilina, etc.). Different buffer solutions are used as solvents.

Nose drops with neomycin sulfate. This is a fairly active antibiotic, but it has limited use, as it has high nephro and ototoxicity.

Although the ingestion of the antibiotic does not have a toxic effect, it should be taken in violation of renal excretory function, preservation of the intestinal mucosa, with cirrhosis of the liver, uremia due to increased absorption of the drug. Through these skin the drug is not absorbed. Neomycin sulfate is a chemically resistant substance, the drug solutions withstand sterilization. The drug is a white or yellowish-white powder, easily soluble in water, very little in alcohol, hygroscopic.

Rp .: Neomycini sulfatis 200000 ED
Solutionis Adrenalini hydrochloridi 0.1% qtts X
Sol. Natrii chloridi isotonicae 20 ml
Misce. Da. Signa. Nose drops.

Antibiotic solutions (0.5%) are prepared on water for injection or isotonic sodium chloride solution (at the rate of 5000 IU in 1 ml).

According to this recipe, 0.3 g of neomycin sulfate (100,000 U = 0.15) is dissolved in 20 ml of sterile isotonic sodium chloride solution, the liquid is filtered and 10 drops of adrenaline hydrochloride solution are added (standard cap meter).

Neomycin sulfate can be combined with gramicidin and erythromycin in the manufacture of topical medications. It should not be used with antibiotics such as streptomycin, monomitsin, kanamycin, gentamicin.

Injection solutions with antibiotics are prepared on pyrogen-free water for injection or isotonic sodium chloride solution.

Despite the instability of aqueous solutions of antibiotics, the search for water-soluble antibiotics continues intensively, because such antibiotics do not inactivate bilcabiomas of the blood, tissues, organs and do not form antigenic complexes with them.

Along with the search for water-soluble antibiotics, work is underway to create microcrystalline antibiotic suspensions using a variety of solvents. As non-aqueous solvents, propylene glycol, polyoxyethylene glycol, lactic acid

carboxamide and other solvents used to prepare tetracycline, chlortetra cyclin, oxytetracycline, chloramphenicol, etc. are used to make injection solutions of antibiotics.

Alcohol solutions. Levomycetin is also used in the form of alcoholic solutions, often in combination with sulfa drugs.

Rp .: Laevomycetini
Norsulfasoli-natrii aa 2.0
Spiritus aethylici 100 ml
Misce. Da. Signa. To rub skin.

In a sterile vial for dispensing are placed 2, 0 g of sterilized norsule sodium phasol and chloramphenicol and measure 100 ml of 90% ethyl alcohol, shaken until complete dissolution.

Rp .: Laevomycetini 3.0
Solutionis Acidi borici 2% 40.0
Spiritus aethylici 70% 50.0
Misce. Da. Signa. Protirats skin.

Levomycetin is dissolved in alcohol, then a solution of boric acid is added.
Suspensions. More stable than aqueous solutions of antibiotics is oil-based suspensions for injection. In the manufacture of suspensions, the degree of dispersion of the solid phase is important.

Rp .: Benzylpenicillini-natrii 1,000,000 ED
Olei Persicorum 100.0
Sterilisa!
Misce. Da. Signa. 1-2 ml intramuscularly 2 times a day.

100.0 g of peach oil is weighed into the vial for tempering, closed with a cotton swab and sterilized at 180 ° C for 30-40 minutes. Then, under aseptic conditions, the sodium salt of benzylpenicillin is triturated in a sterile mortar with a small amount of sterile oil, gradually adding all the oil. The prepared suspension is placed in a sterile vial for dispensing.

Rp .: Streptomycini sulfatis 100000 ED
Olei Jecoris Aselli seu
Olei Ricini 20.0
Misce. Da. Signa. For lubrication of wounds.

Suspension of the antibiotic streptomycin sulfate, is a yellow amorphous powder. Streptomycin forms a number of salts with acids, well soluble in organic solvents.

Due to the wide spread of resistant strains of gram-positive and gram-negative microorganisms and high toxicity, the role of streptomycin in the treatment of purulent infections has sharply decreased. The antibiotic is mainly used as an anti-

tuberculosis drug in combination with penicillin, polyxene, sulfanilamide preparations. Streptomycin contains an easily oxidized aldehyde group, turns into a carboxyl group, and with this conversion, the drug loses its antibacterial properties.

Therefore, streptomycin is incompatible with acids and alkalis, causing the decomposition of the drug and its inactivation. Thus, in 1 M solution of hydrochloric acid at 25 ° C, streptomycin loses 35% within 6:00, and 80% of its activity per day. In 0.1 M sodium hydroxide solution, streptomycin is inactivated within 3:00 by 50%.

Streptomycin is incompatible with neomycin, tetracycline, gentamic and kanamycinous, exhibiting ato and nephrotoxic effect. Streptomycin, both in dry form and in solution, is more resistant than the salts of benzylpenicillin.

Under aseptic conditions, 0.12 g of streptomycin sulfate is triturated with a small amount of pre-sterilized castor oil (a few drops to ensure a wedging effect), after which the remaining oils are added in several stages. The contents are transferred to the vial and drawn up to leave.

Technology of soft dosage forms. Ointment. In the manufacture of antibiotic ointments, special attention should be paid to the composition of the base and the method of administration of antibiotics.

Most are ointments made on anhydrous bases. It is believed that the most suitable basis for eye ointments - a mixture consisting of vaseline - 9.0 g ("for eye ointments") and anhydrous lanolin - 1.0 g.

The Institute of Antibiotics also offers other combinations: a mixture of 4 parts of anhydrous lanolin and 6 parts of vaseline (“for eye ointments”); the basis of the composition: paraffin 30.0 g, sunflower oil 70.0 g

Also proposed polyorganosiloxanes bases (silicones). Penicillin on such bases is maintained for a long time (up to 3 months or more). All bases for ointments with antibiotics are used only after their sterilization. Stored in jars of 10.0 g.

For the manufacture of ointments with antibiotics, it is recommended to use anhydrous hydrophobic or hydrophilic base or emulsion bases of the type M/B or B/O. For example, streptomycin ointment with sulfonamides can be prepared on an emulsion basis of this composition: self-emulsifying glycerol monostearate 12.0 g. Wax white 3.0 g, glycerin 5.0 g, liquid paraffin 10.0 g, propyl parahydroxybenzoate 0.035 g, water to 100 ml.

Ointments with antibiotics are prepared under aseptic conditions in compliance with the general rules of ointment manufacturing.

Ointments with salts of benzylpenicillin are prepared according to the type of trituration ointments, since the antibiotic is quickly inactivated in an aqueous solution.

Rp .: Unguenti Benzylpeniciliini-natrii 20.0
Da. Signa. Lay for ever 3–4 hours

The ointment must be prepared according to the approved recipe (FS 42-84-72): 0.65 g of sodium benzyl-penicillin, 20.0 g of anhydrous lanolin, vaseline to 100.0 g.

A bottle of penicillin, pre-rubbed with 10% alcohol, is opened with sterile forceps and 0.13 g of benzylpenicillin sodium salt is transferred to a sterile, slightly heated mortar. The drug is ground into a fine powder, then ground with a small amount of sterile base (4.0 g anhydrous lanolin and 16.0 g petrolatum), melted and cooled to 40 ° C, which is then added to penicillin in small portions with constant stirring until a homogeneous mass is formed. Place in a sterile jar with a screw cap and sterile gasket. Make out to leave. Shelf life ointment 10 days.

Penicillin ointment on petrolatum itself is not recommended, as they are ineffective for poor absorption of penicillin by the skin.

Rp .: Benzylpenicillini-natrii 500000 ED
Olei Persicorum 90.0
Cetacei 0,5
Lanolini 10.0
Misce, fiat unguentum
Da. Signa. To lubricate Bani affected areas

To the molten spermaceti add lanolin water, peach oil and mix. Penicillin is ground in a mortar, then the base is added in parts with stirring. Anhydrous ointments withstand longer storage (up to 4 months) than ointments prepared on the basis contain water (up to 1 month) at a temperature not higher than 10 ° C. It is not recommended to rub the antibiotic with oil due to the deterioration of its release from the ointment .

The introduction of fats in ointments with antibiotics is undesirable, since the peroxide compounds contained in them can cause the destruction of antibiotics. Irrational and prescription in their composition of tar and ichthyol. Ointment tetracycline ophthalmic (tetracycline 1%, Ditetracycline 10%, etc.) Prepare under aseptic conditions on a sterile basis. They are used in the treatment of trachoma, keratitis, corneal ulcers, acute conjunctivitis and other inflammatory eye diseases.

Rp .: Unguenti Tetracyclini hydrochloridi 1% 10.0
Da. Signa. Lubricate eyelids 2-3 times a day

0.1 g (100,000 U) of tetracycline hydrochloride are added to the pre-sterilized mortar, carefully ground, and then the parts are added to the molten base (to a temperature of 40 ° C). Ointment stored in a cool, dark place.

In the treatment of skin diseases, for example, acne, streptostaphilus, dermatitis, furunculosis, folliculitis, eczema, trophic ulcers, the use of 3% tetracycline ointment is recommended.

Tetracyclines are often prescribed to outpatients, but do not limit their use to pregnant women and children under 8 years of age. This is due to the possibility of tetracycline deposition in the tooth enamel, the development of early caries, as well as its negative effect on the formation of the bone skeleton. In these cases, it is

recommended to use semisynthetic tetracyclines with a prolonged action: metacycline and dioxycyline.

Erythromycin ointment (FS 42-1163-78):

Rp .: Erytromycini 1.111
Lanolini anhydrici 40.0
Natrii metabisulfitis 0.01
Vaselini pro oculi ad 100.0
Misce, fiat unguentum
Da. Signa. Ointment for lubrication of damaged skin areas

Ointment with erythromycin, which is a white powder, odorless, bitter taste, slightly soluble in water, easily - in alcohol, hygroscopic. The spectrum of antimicrobial action is close to penicillin, but compared to it, erythromycin is better tolerated and can be used for penicillin allergy.

Erythromycin is thoroughly ground with 10-12 drops of sterile vaseline oil. Sodium metabisulphite is dissolved in a few drops of sterile water, emulsified with cooled lanolin-petroleum jelly and the resulting emulsion is added to the suspension of erythromycin in several steps by careful rubbing. The ointment contains erythromycin 10,000 IU in 1.0 g ointment.

Amphotericin B ointment (VFS 42-545-76)

Rp .: Amphotericini 4.3
Olei Vaselini 20.0
Tweeni-80 1.0
Vaselini pro oculi ad 100.0
Misce, fiat unguentum
Da. Signa. Lubricate eyelid skin.

Ointment with amphotericinam, which is a yellow or orange powder, is practically insoluble in water and alcohol, is hygroscopic. Sensitive to light and heat. The antibiotic is effective against many pathogenic fungi. It is used intravenously, inhalation and topically (as an ointment). With the introduction of the gastrointestinal tract is practically not absorbed. When administered intravenously, it is very effective, but due to toxicity it should be used only as directed by a physician with precise dosage compliance. When amphotericin is dissolved in water or in a 5% glucose solution, a colloidal solution is formed.

Amphotericin is triturated with 2-2.5 g of petroleum jelly, after which the cooled alloy of petrolatum, twin-80 and petroleum jelly remaining oil is added in several stages with careful grinding, until a homogeneous mass is obtained. The ointment contains amphotericin B 30000 IU in 1.0 g. Levorinov ointment (FS 42-1144-78)

Rp .: Levorini 2.15
Lanolini anhydrici 10.0

Olei Vaselini 5.0
Vaselini pro oculi ad 100.0
Misce, fiat unguentum
Da. Signa. Causes on lesions of the skin

Ointment containing levorin, which is an odorless and tasteless dark yellow powder, is hygroscopic. Easily destroyed in acidic and alkaline environments. Virtually insoluble in water and alcohol. Levorin is used as an ointment for interdigital erosions and skin lesions caused by yeast-like fungi; they lubricate the affected areas 1–2 times a day for 10–15 days. The ointment contains levorin 500000 ED in 1.0 g.

According to this recipe, levorin is thoroughly ground with 20 drops of vaseline oil, and a cooled alloy of anhydrous lanolin with vaseline and vaseline oil is added to the mixture in several steps.

Suppositories. In practical medicine, the appointment of antibiotics in the form of suppositories is of great importance.

The absorption rate of antibiotics depends on the nature of the base for which cocoa butter, wax and various surfactants are used. Recently, it has been proposed to use hydrogenated oils as suppository bases. Suppositories are prepared by downloading or pressing, as the heat cannot be lured.

Suppositories with penicillin. Penicillin is ground with a small amount of milk sugar and in the form of a fine powder is injected into a suppository base. The content of penicillin in one rectal suppository is from 100,000 to 500,000 ED. When stored in a cool place, the activity of ready-made suppositories can be stored for 2 months. Sometimes, to accelerate the action of penicillin, it is dissolved in sodium citrate solution (1: 1000) and mixed with a suppository base. The stability of such suppositories is not more than 10 days.

Tetracycline Suppositories. Tetracycline hydrochloride is most often used for this purpose, which is caused by the less pronounced local irritant effect of this antibiotic. Suppositories containing 0.3 g (300,000 U) of tetracycline are usually prescribed.

Rp .: Tetracyclini hydrochloride 0.3
Olei Cacao qs
Misce, fiat suppositorium
Da tales doses № 6
Signa. 1 candle 3 times a day.

1.8 g of tetracycline hydrochloride are placed in a sterile mortar, triturated (without dissolving in water) and 16.2 g of crushed cocoa butter are added in portions with stirring. It is crushed to obtain a homogeneous plastic mass, from which six suppositories are pumped out, and drawn up for tempering.

QUALITY ASSESSMENT, STORAGE AND VACATION OF MEDICINAL FORMS with antibiotics

Dosage forms with antibiotics are assessed as well as other dosage forms - they check the correctness of documentation, packaging (capping), conduct organoleptic control (color, smell, sediment), check for the absence of mechanical impurities (liquid medicines), deviations in volume or mass. , homogeneity of mixing (powders, ointments), melting point, time of complete deformation (suppositories).

Storage of dosage forms with antibiotics is based primarily on the physicochemical properties of each individual antibiotic. For example, aqueous solutions of polymyxin M sulfate are stored for 7 days at a temperature of 4-10 ° C. Gramicidin is stored in an aqueous solution for not more than 3 days, while in alcoholic and fatty solutions it is not inactivated for a long time.

The general requirement for the storage of dosage forms with antibiotics is the temperature in a refrigerator, a place protected from light, the pH of the medium. In a buffer solution with a pH of 6.5, the stability of the salts of benzylpenicillin increases to 15–20 days at temperatures up to + 5 ° C.

Medicines with antibiotics are released in a sterile container, as much as possible eliminates microflora, make out the labels: "Cooked aseptically"

5. Materials activating students during the presentation of the lecture / questions, tasks, problem situations, etc. /.

Control questions:

1. Characteristics of eye dosage forms, classification and requirements for them.
2. Calculation of isotonic concentrations for the preparation of eye drops, lotions, washes.
3. Rules for the preparation of lotions, washes, suspensions, powders. Features of technology eye drops, depending on the solubility of drugs.
4. Using the IUD to prolong the action of eye drops. An assortment of concentrated solutions and preservatives in the preparation of eye drops.
5. Characteristics of the bases used for the preparation of eye ointments, their technology and sterilization.
6. Preparation of eye ointments. Features of zinc sulfate and resorcinol.
7. Quality assessment, registration for delivery and storage of medicines in accordance with the regulatory and technical documentation.
8. Requirements for antibiotic dosage forms.
9. Factors affecting the stability of drugs with antibiotics.
10. General rules for the preparation of liquid and solid drugs with antibiotics.
11. Characteristics of the bases for the preparation of ointments and suppositories and the rules for the introduction of antibiotics into them.
12. Assessment of quality, registration for delivery and storage of medicines in accordance with the regulatory and technical documentation.

Test items:

1. A pharmacy received a prescription for preparing eye ointment on a vaseline-lanolin basis. Specify in what ratio the pharmacist should prepare an ointment base.

* 9: 1
1:1
5: 1
6-4
7: 3

2 The pharmacy received a prescription for the preparation of eye drops containing protargol. Specify the substance that the pharmacist chose to dope-isolate eye drops.

Do not isotonic
sodium chloride
sodium nitrate
sodium sulfate
boric acid

3. A pharmacist prepared eye drops containing silver nitrate. Does he need to take the substance to ensure isotonicity?

* Sodium nitrate
sodium chloride
boric acid
glucose
sodium sulfate

4. For the manufacture of eye drops using a solution of riboflavin concentrate (1: 5000). Specify the amount of solution that needs to be measured, if 0.001 riboflavin is prescribed in the recipe:

* 5 ml
2 ml
3 ml
4 ml
1 ml

5. The prescription prescribed eye ointment with norsulfazol sodium. Specify the optimal ointment base:

* Alloy vaseline with lanolin (9: 1)
IV type emulsion base
Alloy vaseline with paraffin (6: 4)
Alloy vaseline with lanolin (6: 4)
Alloy vaseline with paraffin (8: 2)

6. A pharmacist must prepare eye drops with pilocarpine hydrochloride. Specify optimal isotonizing agent:

* Sodium chloride
sodium sulfate
glucose
boric acid
sodium nitrite

7. The patient needs to prepare eye drops with riboflavin. Does the substance need to be incorporated into the solution to ensure its isotonicity in the absence of instructions in the recipe?

* Sodium chloride.
Sodium sulfate.
Acid boron hydrochloric
Glucose.
Sodium nitrate.

8. The patient needs to prepare eye drops with prolonged sodium sulfacyl. What substance can I recommend to the doctor to prescribe in the composition of the drops in order to increase the duration of their action?

* Polyvinyl alcohol.
Gelatin.
glucose
Polyethylene oxide-400.
Sodium chloride.

9. Patient prepared eye ointment. How should a pharmacist introduce mercury oxide yellow into its composition to ensure an optimum degree of dispersion?

* Grind with sterile vaseline oil.
Grind with a sterile ointment base.
Pre-dissolve in purified water.
Pre-dissolve in ethyl alcohol.
Add to sterilized grounds.

10. The patient needs to prepare an eye ointment with pilocarpine hydrochloride. How should a pharmacist introduce pilocarpine hydrochloride?

* Dissolve in sterile purified water.
Grind with sterile vaseline oil.
Grind with a sterile base.
Grind with sterile vaseline.
Dissolve in melted base.

11. The prescription prescribed eye ointment with norsulfazole sodium . Specify the optimal ointment base:

* Alloy vaseline with lanolin (9: 1)
IV type emulsion base
Alloy vaseline with paraffin (6: 4)

Alloy vaseline with lanolin (6: 4)
Alloy vaseline with paraffin (8: 2)

12. A patient is prepared with 50 g of zinc ointment. What is the amount of zinc and vaseline and must pay a pharmacist at the same time?
A. 5.0 g and 45.0 g
B. 10.0 g and 40.0 g
C. 2.5 g and 47.5 g
D. 1.0 g and 49.0 g
E. 0.5 g and 49.5 g

13. The pharmacy received a prescription for the preparation of dermatological ointment with benzylpenicillin. Specify the type of prepared ointment:
A. Ointment-suspension I
B. Ointment solution
C. Ointment emulsion
D. Ointment alloy
E. combined

14. The pharmacy received a prescription for the manufacture of streptocidal ointment without indicating the concentration. What concentration of ointment will the pharmacist prepare?
A. 2%
B. 5%
C. 1%
D. 10%
E. 20%

6. General material and methodological support of the lecture:
- Training rooms;
- Overhead; slides;
- Illustrative materials.

7. Materials for self-preparation of students:
a). on the topic of the lecture / literature, questions, tasks, test tasks /;
b). on the topic of the next lecture / literature, a list of key questions, test items /.

8. The literature used by the lecturer to prepare the lecture.
Basis literature:

1. Drug technology. Study guide: Study guide for higher education institutions / A.I. Tikhonov, P.A. Logvin, S.A.Tikhonova, A.V. Mazulin, T.G. Yarnikh, A.S. Shpichak, A. M. Kotenko; Edited by A.I. Tikhonov - Kharkiv: NUPh; Original, 2009. - 432 p.

2. Medicine technology: study guide / A.S. Marchuk, N. B. Androshchuk - Kiev: Medicine, 2008. - 488 p.
3. Production of medicines. Quality control and regulation: prak.ruk. / Ed. Sh.K. Ged; per. from English V.V. Coastal. - SPb.: Profession, 2013. - 960 p.

Additional:

1. Soft dosage forms: thermal recipe: Methodical recommendations / A. I. Tikhonov, T. G. Yarnikh, A. V. Lukienko and others; Ed. A.I. Tikhonov. - M.: Publishing house NUPh; Golden Pages, 2003.-128 p.
2. Aseptic dosage forms: an extremporal formulation: Methodical recommendations / A. I. Tikhonov, L. V. Bondareva, T. G. Yarnikh, N. F. Orlovskaya and others; Ed. A.I. Tikhonov and T. G. Yarnikh. - M.: Publishing house NUPh; Original, 2005. - 184 p.
3. Solid dosage forms: extremporal formulation: Methodical recommendations / A. I. Tikhonov, T. G. Yarnikh, S. V. Gritsenko and others; Ed. A.I. Tikhonov - M.: Publishing House of the NUPh; Golden Pages, 2003. - 176 p.
4. Liquid dosage forms: an extremporal formulation: Methodical recommendations / A. I. Tikhonov, T. G. Yarnikh, N. F. Orlovskaya and others; Ed. A.I. Tikhonov and T. G. Yarnikh. - M.: Publishing house NUPh; Original, 2005. - 160 p.